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Timothy R. Deer
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Treatment of Chronic Pain by Interventional Approaches

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Textbook on Patient Management

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To my wonderful wife, Missy, and the blessings I have been given in my children Morgan, Taylor, Reed, and Bailie.
I also want to thank my team for their awesome, continued support: Chris Kim, Rick Bowman, Doug Stewart, Matt Ranson, Jeff Peterson, Michelle Miller, Wil Tolentino, and Brian Yee.

Timothy R. Deer, M.D.

To all of my mentors, colleagues, and patients who have taught me about pain medicine. I would also like to acknowledge the patience and love of my family, particularly my children, Isabelle and Adam, as well as Brad, PFP, and little Mia. I have discovered more about myself during my short career than I thought possible and hope to help many more people cope with pain in the exciting future.

Michael S. Leong, M.D.

To my very supportive wife, Gowthy, and my wonderful kids: Dhanya and Arjun Asokumar.

Asokumar Buvanendran, M.D.

To my very supportive wife, Claire, and my wonderful kids: Alex, Keira, and Grant.

Philip S. Kim, M.D.

To my children, Neha, Anjali, and Naresh, for their patience, support, and understanding.

Sunil J. Panchal, M.D.

Foreword to *Comprehensive Treatment of Chronic Pain by Medical, Interventional, and Integrative Approaches*

A brand new textbook is a testament to many things—an editor's vision, many authors' individual and collective expertise, the publisher's commitment, and all told, thousands of hours of hard work. This book encapsulates all of this, and with its compendium of up-to-date information covering the full spectrum of the field of pain medicine, it stands as an authoritative and highly practical reference for specialists and primary care clinicians alike. These attributes would be ample, in and of themselves, yet this important addition to the growing pain medicine library represents a rather novel attribute. It is a tangible embodiment of a professional medical society's fidelity to its avowed mission. With its commission of this text, under the editorial stewardship of highly dedicated and seasoned pain medicine specialists, the American Academy of Pain Medicine has made an important incremental step forward to realizing its ambitious mission, "to optimize the health of patients in pain and eliminate the major public health problem of pain by advancing the practice and specialty of pain medicine."

This last year, the Institute of Medicine (IOM) of the National Academies undertook the first comprehensive evaluation of the state of pain care in the United States. This seminal work culminated in a report and recommendations entitled "Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research." Clearly, as a nation, we have much work to do in order to meet the extraordinary public health needs revealed by the IOM committee. This comprehensive textbook is both timely and relevant as a resource for clinicians, educators, and researchers to ensure that the converging goals of the American Academy of Pain Medicine and the Institute of Medicine are realized. This book has been written; it is now all of ours to read and implement. Godspeed!

Salt Lake City, UT, USA — Perry G. Fine, M.D.

Foreword to *Comprehensive Treatment of Chronic Pain by Medical, Interventional, and Integrative Approaches*

The maturation of a medical specialty rests on both its ability to project its values, science, and mission into the medical academy and the salience of its mission to the public health. The arrival of the American Academy of Pain Medicine (AAPM)'s *Comprehensive Treatment of Chronic Pain by Medical*, *Interventional*, *and Integrative Approaches*: *the American Academy of Pain Medicine Textbook on Patient Management* is another accomplishment that signals AAPM's emergence as the premier medical organization solely dedicated to the development of pain medicine as a specialty in the service of patients in pain and the public health.

Allow me the privilege of brief comment on our progress leading to this accomplishment. The problem of pain as both a neurophysiological event and as human suffering has been a core dialectic of the physician-healer experience over the millennia, driving scientific and religious inquiry in all cultures and civilizations. The sentinel concepts and historical developments in pain medicine science and practice are well outlined in this and other volumes. Our history, like all of medicine's, is replete with examples of sociopolitical forces fostering environments in which individuals with vision and character initiated major advances in medical care. Thus the challenge of managing chronic pain and suffering born of injuries to troops in WWII galvanized John Bonica and other pioneers, representing several specialties, into action. They refused to consider that their duty to these soldiers, and by extension their brethren in chronic pain of all causes, was finished once pain was controlled after an acute injury or during a surgical procedure. They and other clinicians joined scientists in forming the IASP (International Association for the Study of Pain) in 1974, and the APS (American Pain Society) was ratified as its American chapter in 1978. Shortly thereafter, APS physicians with a primary interest in the development of pain management as a distinct medical practice began discussing the need for an organizational home for physicians dedicated to pain treatment; in 1984, they formally chartered AAPM. We soon obtained a seat in the AMA (American Medical Association). Since then, we have provided over two decades of leadership to the "House of Medicine," culminating in leadership of the AMA's Pain and Palliative Medicine Specialty Section Council that sponsored and conducted the first Pain Medicine Summit in 2009. The summit, whose participants represented all specialties caring for pain, made specific recommendations to improve pain education for all medical students and pain medicine training of residents in all specialties and to lengthen and strengthen the training of pain medicine specialists who would assume responsibility for the standards of pain education and care and help guide research.

Other organizational accomplishments have also marked our maturation as a specialty. AAPM developed a code of ethics for practice, delineated training and certification requirements, and formed a certifying body (American Board of Pain Medicine, ABPM) whose examination was based on the science and practice of our several parent specialties coalesced into one. We applied for specialty recognition in ABMS (American Board of Medical Specialties), and we continue to pursue this goal in coordination with other specialty organizations to assure the public and our medical colleagues of adequate training for pain medicine specialists. We have become a recognized and effective voice in medical policy. The AAPM, APS, and AHA (American Hospital Association) established the Pain Care Coalition (PCC), recently joined by

the ASA (American Society of Anesthesiologists). Once again, by garnering sociopolitical support galvanized by concern for the care of our wounded warriors, the PCC was able to partner with the American Pain Foundation (APF) and other organizations to pass three new laws requiring the Veterans Administration and the military to report yearly on advances in pain management, training, and research and requiring the NIH (National Institute of Health) to examine its pain research portfolio and undertake the recently completed IOM report on pain.

AAPM has developed a robust scientific presence in medicine. We publish our own journal, *Pain Medicine*, which has grown from a small quarterly journal to a respected monthly publication that represents the full scope of pain medicine science and practice. Annually, we conduct the only medical conference that is dedicated to coverage of the full scope of pain medicine science and practice and present a robust and scientific poster session that represents our latest progress. Yet, year to year, we lament that the incredible clinical wisdom displayed at this conference, born out of years of specialty practice in our field, is lost between meetings. Now comes a remedy, our textbook—*Comprehensive Treatment of Chronic Pain by Medical, Interventional, and Integrative Approaches*.

Several years ago, Editor Tim Deer, who co-chaired an Annual Meeting Program Committee with Todd Sitzman, recognized the special nature of our annual conference and proposed that the AAPM engages the considerable expertise of our membership in producing a textbook specifically focused on the concepts and practice of our specialty. Under the visionary and vigorous leadership of Tim as Editor-in-Chief and his editorial group, *Comprehensive Treatment of Chronic Pain by Medical*, *Interventional*, *and Integrative Approaches* has arrived. Kudos to Tim, his Associate Editor-in-Chief Michael Leong, Associate Editors Asokumar Buvanendran, Vitaly Gordin, Philip Kim, Sunil Panchal, and Albert Ray for guiding our busy authors to the finish line. The expertise herein represents the best of our specialty and its practice. And finally, a specialty organization of physician volunteers needs a steady and resourceful professional staff to successfully complete its projects in the service of its mission. Ms. Susie Flynn, AAPM's Director of Education, worked behind-the-scenes with our capable Springer publishers and Tim and his editors to assure our book's timely publication. Truly, this many-faceted effort signals that the academy has achieved yet another developmental milestone as a medical organization inexorably destined to achieve specialty status in the American medical pantheon.

Philadelphia, PA, USA Rollin M. Gallagher, M.D., M.P.H.

Preface to *Treatment of Chronic Pain by Interventional Approaches*

We are grateful for the positive reception of ***Comprehensive Treatment of Chronic Pain by Medical, Interventional, and Integrative Approaches: The American Academy of Pain Medicine Textbook on Patient Management*** following its publication last year. The book was conceived as an all-encompassing clinical reference covering the entire spectrum of approaches to pain management: medical, interventional, and integrative. Discussions with pain medicine physicians and health professionals since then have persuaded us that the book could serve even more readers if sections on each of the major approaches were made available as individual volumes – while some readers want a comprehensive resource, others may need only a certain slice. We are pleased that these "spin-off" volumes are now available. I would like to take this opportunity to acknowledge once more the outstanding efforts and hard work of the Associate Editors responsible for the sections:

Treatment of Chronic Pain by Medical Approaches:
The American Academy of Pain Medicine *Textbook on Patient Management*
Associate Editor: Vitaly Gordin, MD

Treatment of Chronic Pain by Interventional Approaches:
The American Academy of Pain Medicine *Textbook on Patient Management*
Associate Editors: Asokumar Buvanendran, MD, Sunil J. Panchal, MD, Philip S. Kim, MD

Treatment of Chronic Pain by Integrative Approaches:
The American Academy of Pain Medicine *Textbook on Patient Management*
Associate Editor: Albert L. Ray, MD

We greatly appreciate the feedback of our readers and strive to continue to improve our educational materials as we educate each other. Please send me your input and thoughts to improve future volumes.

Our main goal is to improve patient safety and outcomes. We are hopeful that the content of these materials accomplishes this mission for you and for the patients to whom you offer care and compassion.

Charleston, WV, USA — Timothy R. Deer, M.D.

Preface to *Comprehensive Treatment of Chronic Pain by Medical, Interventional, and Integrative Approaches*

In recent years, I have found that the need for guidance in treating those suffering from chronic pain has increased, as the burden for those patients has become a very difficult issue in daily life. Our task has been overwhelming at times, when we consider the lack of knowledge that many of us found when considering issues that are not part of our personal repertoire and training. We must be mentors of others and elevate our practice, while at the same time maintain our patient-centric target. Not only do we need to train and nurture the medical student, but also those in postgraduate training and those in private and academic practice who are long separated from their training. We are burdened with complex issues such as the cost of chronic pain, loss of functional individuals to society, abuse, addiction, and diversion of controlled substances, complicated and high-risk spinal procedures, the increase in successful but expensive technology, and the humanistic morose that are part of the heavy load that we must strive to summit.

In this maze of difficulties, we find ourselves branded as "interventionalist" and "non-interventionalist." In shaping this book, it was my goal to overcome these labels and give a diverse overview of the specialty. Separated into five sections, the contents of this book give balance to the disciplines that make up our field. There is a very complete overview of interventions, medication management, and the important areas of rehabilitation, psychological support, and the personal side of suffering. We have tried to give a thorough overview while striving to make this book practical for the physician who needs insight into the daily care of pain patients. This book was created as one of the many tools from the American Academy of Pain Medicine to shape the proper practice of those who strive to do the right things for the chronic pain patient focusing on ethics and medical necessity issues in each section. You will find that the authors, Associate Editor-in-chief, Associate Editors, and I have given rise to a project that will be all encompassing in its goals.

With this text, the American Academy of Pain Medicine has set down the gauntlet for the mission of educating our members, friends, and concerned parties regarding the intricacies of our specialty. I wish you the best as you read this material and offer you my grandest hope that it will change the lives of your patients for the better.

We must remember that chronic pain treatment, like that of diabetes and hypertension, needs ongoing effort and ongoing innovation to defeat the limits of our current abilities. These thoughts are critical when you consider the long standing words of Emily Dickinson…

"Pain has an element of blank; it cannot recollect when it began, or if there were a day when it was not. It has no future but itself, its infinite realms contain its past, enlightened to perceive new periods of pain."

Best of luck as we fight our battles together.

Charleston, WV, USA — Timothy R. Deer, M.D.

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Part I

Anatomy and Physiology of Pain

Neuroanatomy and Neurophysiology of Pain

1

Adam R. Burkey

Key Points

- All chronic pain, to a greater or lesser extent, alters nervous system physiology and is therefore neuropathic.
- Electrical neuromodulation may be employed against the peripheral and intraspinal nervous system in a variety of ways to "gate" the flow of pain information to consciousness.
- Modern functional imaging of the forebrain has confirmed and extended our understanding of pain neuroanatomy and may be an outcome measure for studies of pain in the future.
- In the future, research may be able to better match particular clinical characteristics to underlying pain physiology, understand how to act on autonomic and visceral pathways, and control glial and inflammatory activity to reduce neuropathic pain.

Introduction

The neuroanatomy and neurophysiology of pain can be discussed with regard to every level of the nervous system, from peripheral nerve to cerebral cortex. Rudimentary *nociception* is the physiologic perception of a potentially tissue-damaging stimulus and is the commonplace conception that holds when one claims that "something hurts." However, as we review here, "something hurting" for an extended period of time will induce changes in the nervous system that may be irreversible. For this reason, many experts believe that all chronic pain is, to some extent, *neuropathic*. This makes it often impossible to merely remove the thorn from the lion's paw (treat a defined bodily source) and eliminate chronic pain, as much as patients wish we could. Pain as a subjective, even abstract, experience involving a complex array of emotions may occur independent of *any* discernable bodily tissue damage, such as the case of fibromyalgia. For this reason, most chronic pain treatments – whether with medications, cognitive therapies or interventional procedures – attempt to alter physiological pain processing in the peripheral nerve, spinal cord, or forebrain.

In the modern era, there have been three watershed moments in the scientific understanding of pain. The first was the "gate theory" of Melzack and Wall [1]. This theory held that circuitry existed in the spinal cord whereby an innocuous stimulus could block transmission of a noxious stimulus to the brain. This theory is still discussed and referenced by researchers who study pain processing in the spinal dorsal horn. The second was the delineation of a descending pathway from the brain stem to the spinal dorsal horn that could block ascending pain-related information, the so-called descending inhibitory system [2]. This opened the door for the study of mechanisms of analgesia, as it became clear that many analgesics, including morphine, utilized this endogenous circuitry to produce their effects. Thirdly, the advent of functional imaging in the early 1990s has yielded a wealth of information on how chronic pain is processed in the forebrain, defining potential sites of action for novel analgesics and providing more objective data than previously available on chronic pain outcomes and the mechanisms of action of therapeutic interventions.

Pain Neuroanatomy and Physiology

Peripheral and Spinal Neuroanatomy

Primary afferent (or sensory) neurons provide ongoing information about the external environment and the internal bodily milieu. Primary afferent nociceptors (PANs) detect chiefly temperature, trauma, and acidosis of tissues [3].

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Their cell bodies reside in the "dorsal root ganglion" (DRG) which sits just outside the spinal cord. Their axons bifurcate within the ganglion, sending one branch out to innervate various tissues and the other to innervate the dorsal horn of the spinal cord. Most PANs have smaller cell bodies and thin lightly myelinated (Aδ) or unmyelinated (C) axons, the latter terminating as free nerve endings in various organs – skin, muscle, and visceral organs. The conduction velocities of PAN are slower than the large, heavily myelinated axons that act as motoneurons or mechanoreceptors that detect vibration or position sense.

Lightly myelinated Aδ nociceptors enter the spinal cord often in or near Lissauer's tract with terminations primarily in laminae I and IIo of the superficial dorsal horn [4]; some terminations can be found in deeper laminae III–V and X as well. A subset of Aδ nociceptors ramify rostrally and caudally through several spinal segments of Lissauer's tract before terminating. These neurons respond to different stimulus modalities (mechanical or thermal) and are thought to convey fast pricking or sharp pain.

Unmyelinated C fibers respond to a diversity of noxious mechanical, thermal, or chemical modalities. They are classified into two broad types: peptidergic and non-peptidergic [5]. Peptidergic C fibers carry TrkA, the high-affinity receptor for nerve growth factor, and contain peptides such as calcitonin gene-related peptide, substance P and/or galanin. The second type appears to lack peptide neurotransmitters, responds to glial cell line-derived neurotrophic factor, and can be identified using binding sites for the lectin IB4. Studies indicate that these two types of C fiber segregate differently in the dorsal horn. Non-peptidergic IB4-labeled C fibers gather in the central part of inner lamina II, while peptidergic fibers branch out through lamina I and outer lamina II, but with scattered terminals deeper (laminae III–V) [5].

Nearly all visceral afferents are small unmyelinated C fibers which express similar markers to somatic nociceptors, such as vanilloid receptor TRPV1 and tetrodotoxin-resistant sodium channels [6]. Visceral afferents terminate in laminae I, V–VII, and X of the spinal cord. Laminae I and V contribute fibers to the spinothalamic tract in the contralateral lateral-ventral portion of the cord; thus, visceral travels with somatic nociceptive information from both somatic C fibers (lamina I) and Aδ fibers (lamina V) rostrally [7, 8]. In addition, a second pathway for visceral pain information from medial lamina VII and lamina X propagates along the dorsal columns [9]. Viscerally innervated lamina X neurons are particularly numerous in the sacral spinal cord and important for pelvic and perineal pain transmission.

Peripheral and Spinal Physiology

Injury to peripheral nerves is believed to cause paroxysmal, spontaneous pain through changes in voltage-sensitive sodium channel expression that lead to ectopic action potentials in sensory neurons [10]. These Na(v) channels accumulate in neuromas and demyelinated areas of peripheral nerve in animal and human models. Four such channels are of particular interest given their restricted distribution in nociceptors and their experimental association with neuropathic pain: tetrodotoxin-sensitive Na(v) 1.3 and 1.7 and tetrodotoxin-resistant Na(v) 1.8 and 1.9 [11]. Demyelination and the more even distribution of sodium channels along axons after peripheral nerve injury can lead to difficulty with obtaining a peripheral block in response to local anesthetic agents.

A phenotypic switch has been observed after axotomy, whereby large Aβ fibers begin to express neuromediators that transmit nociceptive information, including substance P [12, 13]. Some investigators insist that a subset of Aβ fibers maintains extensive projections throughout the superficial dorsal horn which, after the phenotypic switch, could excite spinothalamic neurons [14]. There is a larger body of work to suggest ingrowth of large-diameter sensory afferents into the superficial dorsal horn when there has been loss of small-fiber inputs due to cell death [15]. Because large-diameter afferents transmit innocuous sensory information such as light touch, it is believed that a pathological change allowing them to excite the superficial dorsal horn – either through a phenotypic switch that provides them with pain-related neurotransmitters or pathological ingrowth into deafferented portions of superficial dorsal horn – underlies the phenomenon of mechanical allodynia.

Nociceptive afferents provided excitatory glutamatergic, and sometimes peptidergic (substance P), inputs to their respective spinal laminae that increase activity in spinothalamic projection neurons. Glutamate acts primarily on AMPA or NMDA receptors and substance P on the neurokinin-1 (NK1) receptor. Glutamatergic activity leads to increased intracellular calcium and changes in gene expression of these neurons, or, in some cases, neuronal cell death [16].

Two primary mechanisms reduce excitation in the dorsal horn. The first is presynaptic inhibition of neurotransmitter release from primary afferent terminals in the dorsal horn. Serotonergic, adrenergic, opioidergic, and dopaminergic receptors are present on nociceptive afferents whose activity will block calcium entry and vesicular release of glutamate or substance P. Secondly, dopaminergic D2, serotoninergic 5-HT1A, and GABAergic receptors on spinothalamic neurons will inhibit neuronal cell firing when those receptors are activated. The monoamines, serotonin, norepinephrine, and dopamine acting on pre- and postsynaptic receptors in the dorsal horn are released from the terminals of descending fibers from brain stem nuclei. As a sidenote, spinal presynaptic serotonergic 5-HT3, postsynaptic 5-HT2 and dopaminergic D1 receptors are all generally pro-nociceptive, in that activation of these receptors will either increase excitatory transmitter release and/or directly increase spinothalamic neuronal activity [17–19].

Intrinsic local inhibitory neurons containing GABA will reduce activity in spinothalamic neurons. About 30 % of neurons in superficial laminae I–III are inhibitory, all GABAergic of which some also contain glycine [4]. Most islet cells in the substantia gelatinosa contain GABA and receive excitatory input from C fibers; they provide monosynaptic, bicuculline-sensitive input to excitatory "central" neurons which also receive direct excitatory input from other C fibers. The "central" neurons, responding to convergent inputs from islet cells and C fibers, gate output from lamina I through the spinothalamic tract [20]. A recent study [21] detected large numbers of GABA-inhibitory interneurons postsynaptic to large, heavily myelinated dorsal root ganglia neurons (presumably Aβ fibers) in spinal laminae III–V, consistent with the gate theory of large-fiber inhibition of nociceptive transmission [1]. It has been shown that partial nerve injury will lead to loss of GABAergic inhibition in the superficial dorsal horn secondary to neuronal cell death [22, 23]; loss of this endogenous suppression of central sensitization is a key factor in the difficulty with treating neuropathic pain.

Inflammatory and immune mediators also maintain neuropathic pain. With peripheral nerve injury, mast cells, neutrophils, and macrophages will release immune mediators such as prostaglandin E2, histamine, and tumor necrosis factor-alpha [24]. Supportive glia and Schwann cells can also release nerve growth factor, interleukins, cytokines, chemokines, and ATP which excite axons under pathological conditions [25]. Central glial cells can modulate neuronal activity in other ways, i.e., by acting as ion buffers, and their role has lead to the term "gliopathic" pain [26].

Preganglionic sympathetic neurons, which reside in the intermediolateral cell column of the thoracic spinal cord to the upper second or third lumbar segments, are controlled by both spinal and supraspinal inputs. Particularly, they appear to be subject to tonic GABAergic inhibition which is lifted to quickly increase sympathetic outflow ("disinhibition") [27, 28]. Preganglionic sympathetic fibers exit through the ventral root of the spinal nerve and then connect to the paravertebral sympathetic chain via the "white ramus communicantes" to travel to the appropriate sympathetic ganglion to synapse with its postsynaptic neuron. Visceral afferents travel with the sympathetic nerves to that organ, and therefore, the clinician should consider the possibility of thoracic radiculopathy when confronted with poorly localized unilateral flank and abdominal or pelvic pain, especially if a separate thoracic dermatomal pain can be determined on careful interview.

Sympathetic nerve terminals have been observed to form basket structures around dorsal root ganglion cells after peripheral nerve lesions and can thereby activate these neurons [29, 30]. Nociceptive axons as well may exhibit adrenergic sensitivity in peripheral nerve. These anatomical observations may have relevance to mechanisms of sympathetically maintained pain and their responsiveness to blockade of sympathetic ganglia and dorsal column neuromodulation (see below).

Supraspinal Pain Neuroanatomy

Functional imaging methods have been a powerful complement to traditional anatomical methods in ascertaining the supraspinal networks involved in pain processing. The spinothalamic tract terminates in six distinct regions of the thalamus, mostly intralaminar and ventrolateral complex nuclei. Along the way, terminations from spinobulbar neurons, which travel with spinothalamic tract neurons, are found in the brain stem reticular formation, periaqueductal gray (PAG), parabrachial nucleus, and regions of catecholamine cell groups. It is also likely that the hypothalamus receives spinothalamic tract input either through a mono- or multisynaptic pathway.

The PAG and rostral ventromedial (RVM) nuclei of the brain stem are involved with descending pain inhibitory modulation already mentioned above [31]. The PAG controls spinal nociceptive activity through relays in the RVM and the dorsolateral pontine tegmentum. The RVM contains both serotonergic and non-serotonergic projection neurons that can increase or decrease nociceptive activity in the spinal dorsal horn. The dorsolateral pontine tegmentum sends noradrenergic fibers to the dorsal horn to reduce activity through alpha-2 receptor activation.

Ascending spinothalamic input from lamina I of the dorsal horn is relayed by the thalamus to four principal regions of the cerebral cortex: area 24c of the anterior cingulate gyrus, area 3a of the primary somatosensory cortex (SI), secondary somatosensory cortex on the parietal operculum (SII), and dorsal insular cortex. Not coincidentally, these four regions have shown activation in a consistent way across functional imaging studies, including PET and fMRI, using many different experimental paradigms [32, 33]. Ascending spinothalamic input from wide dynamic range neurons in lamina V is ultimately received in the SI and SII cortices. Of all the cerebral cortical areas activated by pain, the anterior cingulate cortex appears to be the most specific for pain itself. The insular cortex serves a more general role for visceral integration and monitoring bodily homeostasis [34]. Finally, nociceptive input to the parabrachial area may be relayed to the central nucleus of the amygdala, where a major lamina I pathway exists in rats [35]. This input could account in part for some of the emotional, "suffering," aspects of pain experience.

Clinical Applications

Neuromodulation

Virtually every level of the nervous system discussed above can be subjected to electrical neuromodulation with some benefit for chronic pain, particularly neuropathic pain. Here, we briefly list these targets with appropriate references for further review by the interventionalist.

Forebrain

Typically, the forebrain is modulated through superficial motor cortex stimulation or deep brain stimulation. To date, regions targeted for deep brain stimulation include the medial septal nuclei, sensory thalamus, and PAG. More commonly, superficial motor cortex stimulation is chosen for dense neuropathic pain conditions [36, 37]. Typical indications include central neuropathic pain, trigeminal neuralgia, phantom limb pain, and postherpetic neuralgia. Anatomic mapping is performed by identifying the central sulcus with electrophysiologic stimulation and monitoring. EMG and somatosensory-evoked potentials are used to match the motor cortex area with the pain pattern. The mechanism of action of motor cortex stimulation is unknown; it may have to do with the relationship of the motor cortex to suppression of activity in SI and SII somatosensory cortices.

Intraspinal Neuromodulation

The commonest location for placement of electrodes for pain relief is within the spinal canal. Dorsal column neuromodulation via epidural electrodes is an implantable, surgical treatment modality commonly used for chronic pain and vascular disorders [37, 38]. Several features of the neural target influence the efficacy of stimulation: a longitudinal rather than transverse orientation of the fibers relative to the electrode, the distance from the electrode to the fiber, and the fiber diameter itself [39]. Currently available devices activate heavily myelinated Aβ fibers, not the unmyelinated C fibers or lightly myelinated Aδ fibers. Every attempt should be made to align the electrode along the axis of the fibers being stimulated. Furthermore, neuromodulation will be more effective at levels of the spinal cord with less intervening CSF volume, such as at the lumbar and cervical enlargements, when leads are placed in the epidural space.

The ability of dorsal column neuromodulation to block neuropathic pain depends on endogenous mechanisms to reduce excitability in the dorsal horn. A substantive body of work implicates GABAergic mechanisms of analgesia for dorsal column neuromodulation [40]. Conversely, treatment failures for dorsal column neuromodulation may be attributable to loss of large-fiber function, transformation in the phenotype or connectivity of large fibers, or loss of GABAergic inhibitory networks in the dorsal horn.

For traditional neuromodulation, a Tuohy needle is placed into the epidural space after aseptic preparation of the skin several segments caudal to the final desired position. Using fluoroscopic guidance, the electrode is advanced into the midline position overlying the spinal segments to be stimulated. Trial stimulation is carried out using an external programmable pulse generator. The patient describes the location and type of paresthesia in relation to their pain. Sometimes, more than one electrode is required to cover all of the painful areas. A variety of paddle and alternately spaced quadric and octopolar leads are available to cover the necessary area of the dorsal columns; sometimes, staggered leads are placed one above the other in a linear fashion to cover a greater rostrocaudal number of segments.

With satisfactory stimulation obtained, the lead(s) are sutured into place for a trial period of up to 2 weeks. The needle is withdrawn without disturbing the electrode placement and anchored into place on skin with bandaging of a tension loop to decrease the likelihood of dislodgement. The externalized leads can be reprogrammed throughout the trial period to optimize capture of the painful territory. At any sign of superficial infection, they are removed. If successful, permanent leads can be placed in the dorsal epidural space and tunneled to a rechargeable, programmable battery pack.

Other intraspinal neural targets have been successfully utilized to provide relief from neuropathic pain. Electrodes may be placed laterally over the entering dorsal root entry zone, which includes the dorsal roots, Lissauer's tract, and the spinal dorsal horn; this technique has been referred to as "intraspinal nerve root stimulation" (INRS; Fig. 1.1). INRS benefits from a closer apposition of the electrode to the target fibers than in the dorsal columns. The electrodes are placed along the rostrocaudal axis of the spine and therefore are oriented in parallel to ramifying fibers in Lissauer's trace. Placement of an electrode along laterally over the entering dorsal roots uses the same approach as for midline dorsal column placement. Lateral fluoroscopic views should be used to ascertain that the electrode is not ventrally located in the epidural space but rather along the posterior border of the neural foraminae.

Selective nerve root stimulation (SNRS) involves targeting the dorsal root of the spinal nerve at the neural foramen through an intra- or extraspinal approach where the electrode lies in a parallel with the entering fibers. We include sacral nerve stimulation in this category. SNRS accomplishes the goal of capturing paresthesia in some difficult-to-treat lumbosacral segments where traditional methods fail. A cephalocaudal (retrograde) lateral epidural approach at L2/3 below the conus was developed to facilitate placement of the electrode "in line" with lumbosacral roots. Using this technique, a quadripolar electrode enters at midline and is rotated toward but not into the L4 foramen. The distal contact is commonly programmed as an anode and the three proximal contacts as cathodes. Appropriately positioned, one may capture the L4, 5 and S1 roots with a single lead. Retrograde cervicothoracic electrode placements have not been performed due to the risk of cord injury.

S2–4 roots can be captured by directing the quadrupole toward but not through the S2 foramen. For sacral neuromodulation, trial leads are commonly placed through the caudal sacral hiatus and advanced over the lumbosacral nerve roots of interest; if successful, a surgically implanted paddle lead may be placed via laminotomy. Conditions treated with this approach include interstitial cystitis and perineal and rectal pain syndromes.

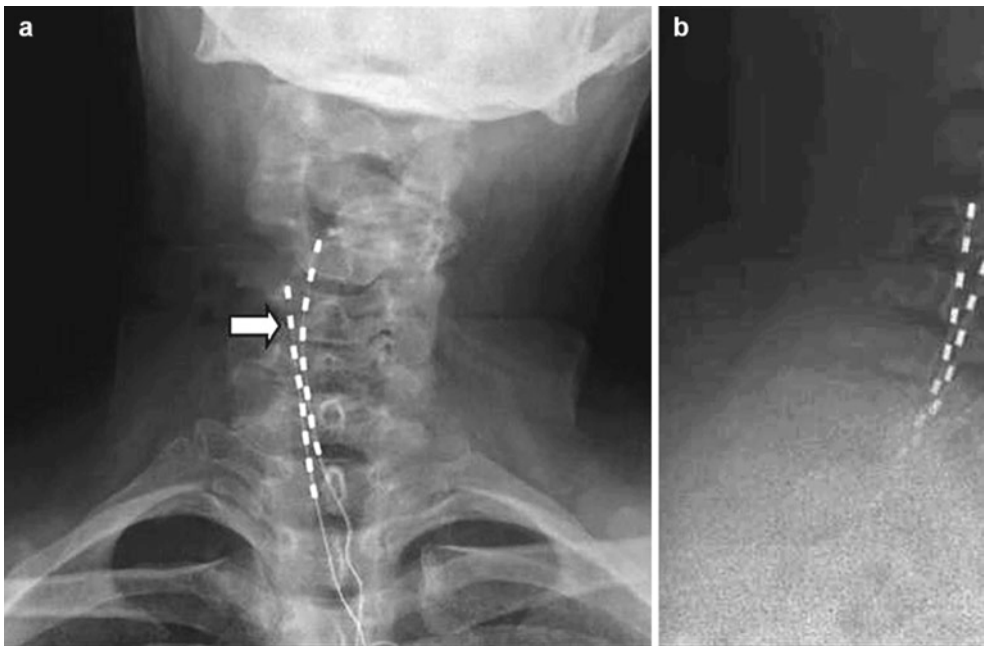

Fig. 1.1 Dual Octrode leads for INRS (a) The left, lateral lead (arrow) in this case overlies the entering fibers of C5, C6, and C7 for treatment of C6 dermatome central pain in an MS patient. The more medial lead guards the lateral lead to isolate stimulation over the dorsal root entry zone at C6. On the lateral view (**b**), the lateral lead is positioned immediately at the dorsal border of the neural foraminae. The more medial lead rises dorsally over the convexity of the spinal cord as it courses rostrally toward the dorsal columns [53]

The DRG is another potential target for neuromodulation (Fig. 1.2). The DRG is reliably located intraspinally between the pedicles of the neural foramen. This structure has been targeted with radiofrequency energy to treat radicular neuropathic pain. It may be that a reversible treatment like neuromodulation is preferable to a destructive technique like radiofrequency. In the lumbosacral region, a retrograde approach is generally used and the electrode into the neural foramen. The difference between this target and SNRS is that the electrode is advanced farther into the foramen with this procedure, isolating a single dermatome and acting on the sensory cell bodies of the DRG. Although it may be more effective for this dermatome, it has less breadth of coverage than SNRS which can capture several nerve roots.

Peripheral Nervous System

Peripheral nerves may be individually stimulated or an electrical field generated through an electrode array placed subcutaneously [41]. In peripheral nerve stimulation, an attempt should be made to direct the electrode along the trajectory of the target nerve. Common peripheral nerves treated with neuromodulation include ilioinguinal nerves for postherniorrhaphy pain, greater and lesser occipital nerves for occipital neuralgia, intercostal nerves for rib pain, and lower extremity nerves (saphenous, peroneal, tibial, sural) for foot pain. One may also use a combination of intraspinal and peripheral stimulation to treat, for instance, back and leg pain [42]. The lead is placed in proximity to the nerve rather than in contact to the nerve with most cases. In some cases, often because of lead migration or failure to capture with appropriate coverage, a paddle-type electrode is recommended for implantation.

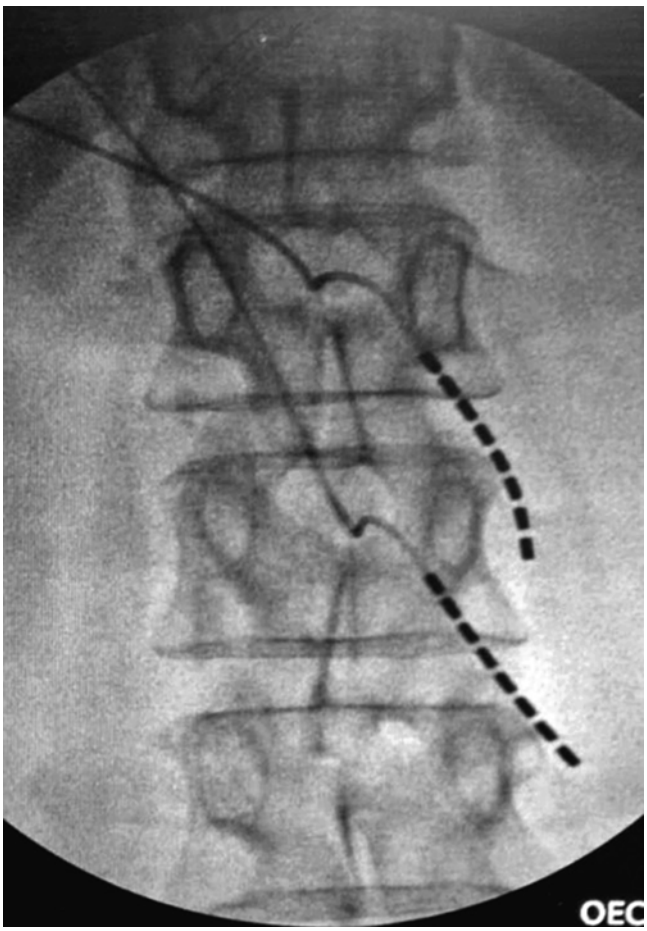

Fig. 1.2 DRG stimulation for postherpetic neuralgia. This patient had worsened symptoms with dorsal column neuromodulation. This arrangement of two leads stimulating the sensory neuronal perikarya at L1 and L2 provided 100 % relief with subthreshold stimulation (amplitude 0.5–0.8 mA with pulse width 120) (Photo courtesy of Dr. Christopher Vije, MD)

In some cases it is not possible to isolate a single nerve branch that is responsible for the pain problem. Implantation of dual electrodes with appropriate spacing will generate a peripheral field that captures the pain problem. There is evidence that the two leads can cross talk to complete an electrical circuit and are thus creating a true field and not functioning independently [43]. This has been performed for a variety of conditions including lower back pain and abdominal pain [44].

Intrathecal Drug Delivery

Carefully selected patients may benefit from the implantation of an intrathecal drug-delivery system, typically an opioid with or without an adjunctive medication. These patients have failed more conservative options and have poor benefit and/or unacceptable side effects from oral medications. It is considered a good option for some patients with cancer pain who require large doses of opioid and suffer from severe constipation or sedation.

Typically, the catheter enters the intrathecal space at the lumbar level and is tunneled to a programmable, refillable pump usually in the lower quadrant of the abdomen. The catheter tip should be advanced to the optimal spinal level for the worst pain. For instance, back pain should have the catheter delivering medication at T10 or to the upper cervical spine for head and neck pain. These pumps are not without risk; beyond the immediate surgical risks of hematoma, cord injury, and infection, granulomas may form over time and require surgical intervention.

Pumps are typically filled with morphine, but the interventionalist may use other opioids such as hydromorphone or fentanyl. Common adjuncts to the opioid are clonidine or a local anesthetic such as bupivacaine. Clonidine takes advantage of the endogenous alpha-2 receptor mechanisms of spinal analgesia but can be complicated by hypotension or sedation. Intrathecal bupivacaine can cause numbness, edema, incoordination, or urinary retention; in other cases, it is difficult to deliver a clinically significant amount of bupivacaine, given that bupivacaine cannot be concentrated beyond 0.75 % and the low volumes required for intrathecal infusion.

Intrathecal opioid pumps produce their analgesia through an action on the mu-opioid receptors which are equally distributed on presynaptic fibers and postsynaptic neuronal cell bodies in the dorsal horn. Over time, typically several years, significant tolerance can develop. The loss of GABAergic inhibitory interneurons in the dorsal horn secondary to direct morphine neurotoxicity is thought to be one mechanism of tolerance development [45]. This is one factor that has prompted the development of alternative agents, such as ziconotide [46]. Ziconotide acts as a N-type voltage-dependent calcium channel. It blocks the release of glutamate and pro-nociceptive peptides in the dorsal horn. It has a narrow therapeutic window, with significant side effects of sedation, hallucinations, and dizziness. It has the benefit of no apparent development of tolerance or dependence, however. It is currently used for severe neuropathic pain refractory to other therapies.

Future Directions

Functional Imaging of Pain

PET and fMRI have disclosed activations in certain brain areas with chronic pain, including the anterior cingulate and insular gyri and the somatosensory cortices and thalamus. In some studies, standard MRI has shown reductions in gray matter volumes as a consequence not cause of the chronic pain of such common conditions as irritable bowel syndrome and chronic back pain [47–49]. In the case of chronic low back pain, effective treatment in one study showed reversal of the gray matter changes [50]. Should reliable protocols for common conditions such as back pain be developed, imaging studies could become outcome measures for interventional therapies.

Neuropathic Pain

Technological improvements in neuromodulation will continue to enhance their efficacy and improve our ability to treat certain pain states. Chief among these improvements, already on the horizon, is the development of small, self-contained stimulator devices that may be placed directly next to the nerve root or peripheral nerve, obviating the need for tunneling electrode leads to a battery pack. This will improve accessibility of the DRG and peripheral nerve targets, in particular, to neurostimulation.

The field of neuromodulation, like most other in medicine, would benefit from cohort studies of these different approaches used in different neuropathic pain states. Although the utility of dorsal column neuromodulation for failed back surgery syndrome/lumbosacral nerve root injury syndrome is well-established [37, 51, 52], to date, only anecdotal reports exist for the utility of this and alternate neuromodulatory strategies for other chronic neuropathic conditions. For instance, one case of central pain from multiple sclerosis was successfully treated by INRS [53]. Positive results from SNRS have been reported for lumbosacral nerve injury syndrome, ilioinguinal neuralgia, vulvodynia, interstitial cystitis, neuropathic extremity pain, and pelvic and rectal pain [54–59]. Subcutaneous peripheral nerve or field stimulation has been tried for neuropathic head and neck pain, occipital neuralgia, inguinal neuralgia, and chronic pelvic or abdominal pain [60–65].

"Sensory profiles" for neuropathic pain could enhance the study of alternate strategies and indications for neuromodulation. The concept proposes that a particular pattern of sensory description corresponds to a specific physiological change, even among patients with the same disease process. Thus, allodynia may represent a greater GABAergic inhibitory deficit in the dorsal horn; numbness, a significantly greater degree of deafferentation; spontaneous pain, a greater degree of Aδ fiber activity; and so on. Physiology in turn determines the efficacy of neuromodulation. These "sensory profiles" could then be used to stratify patients within a population to address the issue of nonresponders.

A case in point is postherpetic neuralgia, where dorsal column neuromodulation and peripheral field stimulation have both been reported effective in several patients [66, 67], yet is a condition where neurostimulation is not generally regarded as a useful modality [68, 69]. A descriptive study of 2,100 patients with either PHN or DPN demonstrated differences in hyperalgesia and allodynia between the two populations [70]; five patterns of sensory symptom description were detected within these two populations although differing in frequency within each. Distinct neuropathic signs and symptoms in PHN (i.e., paroxysmal vs. continuous pain) are generated by different patterns of abnormality among primary afferent neurons (Aβ- vs. Aδ- and C fibers). This type of research where clinical description is matched to underlying physiology may point the way forward, in identifying subtypes of neuropathic pain responsive (or not responsive) to different approaches to neuromodulation. This could greatly reduce the number of unnecessary trials and failed implants (see Fig. 1.2).

Visceral and Autonomic Systems

There exists a great deal of information on the utility of dorsal column neuromodulation for chronic stable angina and nonreconstructable lower extremity ischemia (Fig. 1.3) [38, 71, 72]. These indications are more widely used in Europe; practitioners in the USA have not managed to partner with vascular surgery, cardiology, and primary care in such a way as to be able to provide this treatment modality to the appropriate patients effectively. There is also burgeoning interest in the use of cervical spinal cord stimulation to increase cerebral perfusion in low-flow states, including enhancing chemotherapy delivery to brain tumors and improving cerebral oxygenation in patients poststroke [73, 74].

For chronic visceral pain such as pancreatitis, a guarded tripolar lead array is frequently used to drive stimulation deeper into the dorsal columns. Presumably, this allows activation of fibers in the midline visceral pain pathway which engages inhibitory mechanisms in deeper laminae VII and X where visceroceptive neurons reside. This existence of this pathway has led some to promote the efficacy of T10 midline punctuate myelotomy for intractable cancer-related pelvic pain [75], which may be considered by the surgical interventionalist in their palliative care population.

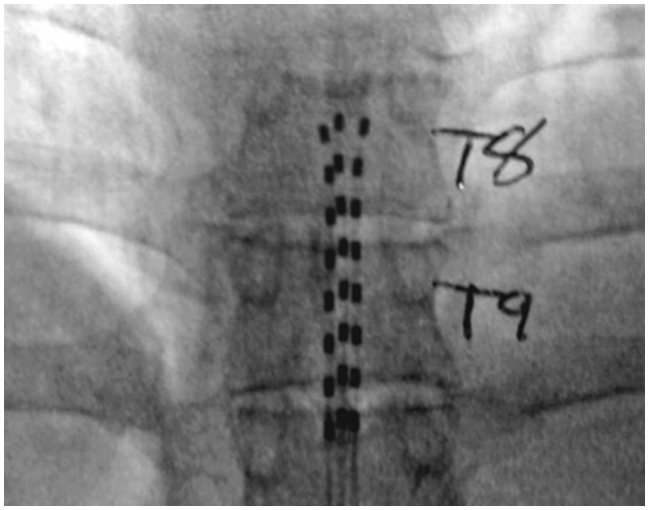

Fig. 1.3 Dorsal column tripole configuration. Using an Octrode lead on either side of a third Octrode allows one to "guard" the midline lead with positive charge. This drives the stimulation deeper into the dorsal columns and can prevent limb and thoracic dermatomal paresthesias. This arrangement has been used for chronic pancreatitis and axial low back pain

Intrathecal Drug Delivery

Currently available technology would benefit greatly from novel analgesics to deliver intraspinally. Gabapentin, a well-established drug for the treatment of neuropathic pain, is one such candidate for intrathecal administration [76, 77]. Alternatively, it may be that adjuncts to morphine, such as baclofen, enhance its efficacy and reduce tolerance development [78]. An intriguing possibility in this regard would be medications to inhibit proinflammatory mediators in the spinal cord. Cytokine and chemokine activation appears not only to drive neuropathic pain itself, but to specifically reduce analgesia and promote tolerance development associated with opioids [79, 80].

Summary

Pain is a neurological condition that affects every level of the nervous system. The most reasonable target for therapy remains the peripheral nerve and spinal dorsal horn, as first proposed by the gate theory; at more rostral levels, pain-related activity is distributed among a "pain matrix" whose complexity makes it difficult to act upon. Imaging of this pain matrix, however, may become an objective surrogate marker for studies of pain and its treatment. Studies of neuromodulation

for a variety of neuropathic pain states will benefit from correlation with clinical characteristics and physiology to reduce the number of failed implants. New medications, either alone or adjunctive to intrathecal opioids, will make infusion pumps a more attractive modality for pain control.

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Spinal Targets for Interventional Pain Management

2

Lawrence R. Poree and Linda L. Wolbers

Key Points

- Interventional techniques that target specific nociceptive transmission sites can reduce pain without having the systemic impact that oral medication have on other organ systems.
- Convergence of nociceptive afferent signals in the spinal cord may explain the clinical observation that injury of different organs may produce the same pain sensations.
- Destruction of specific spinal neural targets with either neurolytic solutions or thermal probes provides long-term relief for a limited number of pain conditions.
- The primary pharmacological receptors that are targeted for intrathecal medication management of pain include opioid receptors, alpha-2 adrenergic receptors, sodium channel receptors, and calcium channel receptors.
- Electrical stimulation can provide effective analgesia by targeting various spinal targets including the spinal cord, nerve roots, and dorsal root ganglia.
- New minimally invasive percutaneous techniques have recently been developed to address some of the structural pathologies including spinal stenosis caused by ligamentum flavum hypertrophy.

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Introduction

As noted in the previous chapter, the transmission of pain signals from the peripheral nervous system to the brain involves a variety of specialized neuronal and nonneuronal cells each with a host of specific receptors involved in the processing of these signals. The goal of this chapter is to briefly review the various image-guided interventional pain management techniques that target spinal structures aimed at reducing pain and improving patients' quality of life. Comprehensive medical management aims to accomplish these goals by utilizing systemic medications that target specific receptors throughout the peripheral and central nervous system. In many cases, this approach is successful with few untoward complications. However, in more severe pain conditions or higher doses of medications, patients may experience medication side effects and toxicities that limit the utility of a systemic approach. In contrast, interventional pain management techniques employ a variety of technologies to influence specific targets involved in nociceptive transmission while aiming to minimize the effects on systems not involved in the nociceptive process. For the purposes of this chapter, the interventional pain management techniques to be discussed will be limited to fluoroscopic procedures that target the structural and neural components in four distinctive spinal regions: the paraspinal region located immediately adjacent to the spine, the structural components of the spine including the bone and connective tissues, the intraforaminal region located within the spinal foramen, and the intraspinal region located within the spinal canal. Where appropriate, a distinction will be made between the epidural targets and intrathecal targets located within the intraspinal region. Knowledge of the spinal structures subject to interventional procedures is critical for all pain physicians, not just those who perform the interventions. For example, by understanding the spinal components involved in nociception and how they can be targeted, the clinician

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can explain not only how a patient with cholecystitis can present with clinical complaints of angina but also why targeting the spinal cord may be beneficial [1, 2]. While this clinical observation was a mystery when first described over 100 years ago, animal studies characterized the convergent spinal pathways and processing centers responsible for this clinical observation [3, 4]. Armed with this knowledge, the interventionalist is able to target these centers with interventional techniques to disrupt the nociceptive processing at the spinal level. The techniques discussed here include both established as well as emerging technologies.

Paraspinal Targets for Interventional Pain Management

Chapter 1 described the role that the sympathetic nervous system plays in both the transmission and maintenance of pain. With efferent sympathetic fibers traversing along the paravertebral sympathetic chain adjacent to the cervical through sacral vertebral bodies, it is no surprise that these nerve bundles are a common target for neural blockade and ablation in patients diagnosed with sympathetically maintained pain. In addition, these same nerve bundles are often conduits of visceral nociceptive afferent fibers. Neural blockade with local anesthetic of nerve fibers in the cervical and lumbar sympathetic chain is a common therapeutic technique used in the treatment of complex regional pain syndrome (CRPS) of the upper and lower extremities, respectively. In a recent multicenter review of randomized clinical trials, sympathetic blockade for the treatment of CRPS was given a score of 2B+. This score indicates that one or more RCTs demonstrate effectiveness and that the treatment is recommended by the group [5]. In the cervical spine, the cervicothoracic ganglion (aka stellate ganglion) sympathetic blockade is performed by advancing a needle to the anterior tubercle of the C7 vertebral body under fluoroscopic guidance. Injection of contrast confirms flow of the solution along the course of the cervical sympathetic chain in a craniocaudal direction and is followed by injecting 10 ml of local anesthetic (Fig. 2.1). Similarly, blockade of the lumbar sympathetic chain is performed by advancing a needle in the oblique fluoroscopic view to the anterior lateral surface of the L2 and/or L3 vertebral body under fluoroscopic guidance using a paramedian approach. Once proper needle placement is confirmed in the anterior-posterior and lateral views, 1 cc of contrast is injected and observed to spread in a craniocaudal direction and is followed by injecting 15 ml of local anesthetic (Fig. 2.2). In the thoracic spine, the sympathetic chain gives rise to the greater and lesser splanchnic nerves that provide sympathetic innervations of many visceral organs along with serving as a conduit for nociceptive afferents. As such, they are a favorite target for neural blockade and/or ablation in the treatment of visceral pain. For decades, the neural destruction of the celiac plexus with alcohol or phenol has been a mainstay in the treatment of pain associated with pancreatic cancer. While highly effective, this therapy is associated with significant risks, including inadvertent spread of neurolytic solution toward the nerve roots and lumbar plexus which may result in foot drop, paraplegia, sexual dysfunction, loss of anal and bladder sphincter tone, and dysesthesia [6]. To avoid these complications of chemical neurolysis, radiofrequency ablation is rapidly emerging as the preferred method for denervating the pancreas, especially in non-cancer patients [7]. The technique is accomplished by targeting the greater and lesser splanchnic nerves as they traverse along the lateral portion of the T11–T12 vertebral bodies (Fig. 2.3). Unlike the unpredictable

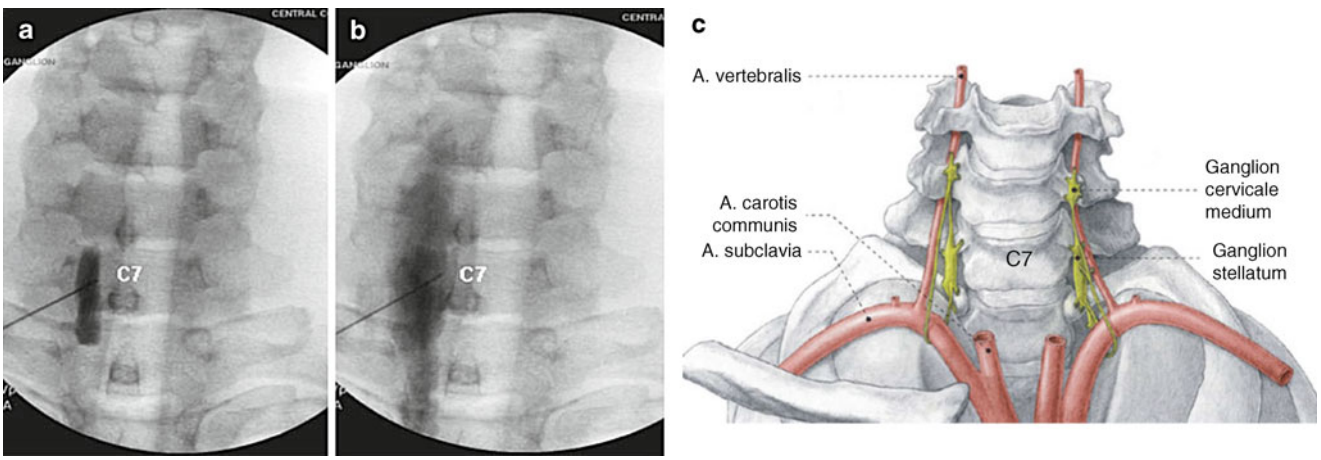

Fig. 2.1 (**a**) Right stellate ganglion block with needle at C7. (**b**) Contrast spreads from C5 to T2. (**c**) Anatomic illustration of the ganglion stellatum (aka cervicothoracic ganglion) (Fluoroscopic images courtesy of Lawrence Poree, MD Ph.D. Illustration courtesy of Rogier Trompert Medical Art. http://www.medical-art.nl; reprinted with permission from van Eijs et al. [5])

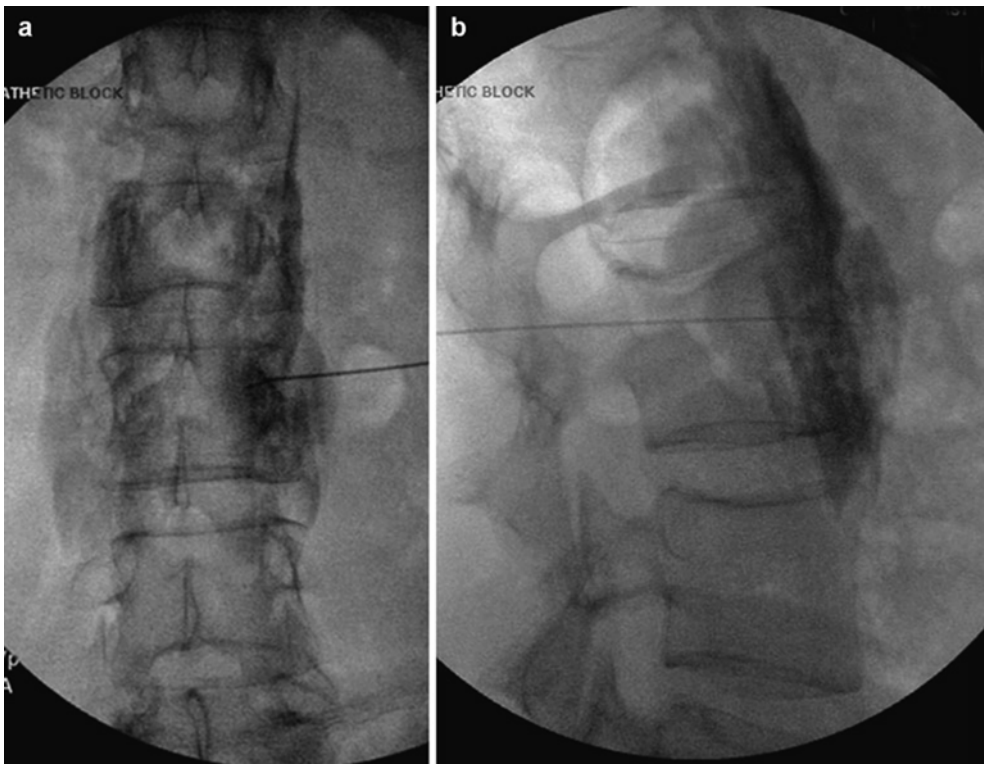

Fig. 2.2 Lumbar sympathetic block. (**a**) Needle placed on the anterolateral surface of the L3 vertebral body. (**b**) Contrast spreads from L2 to L4 (Fluoroscopic images courtesy of Lawrence Poree, M.D., Ph.D.)

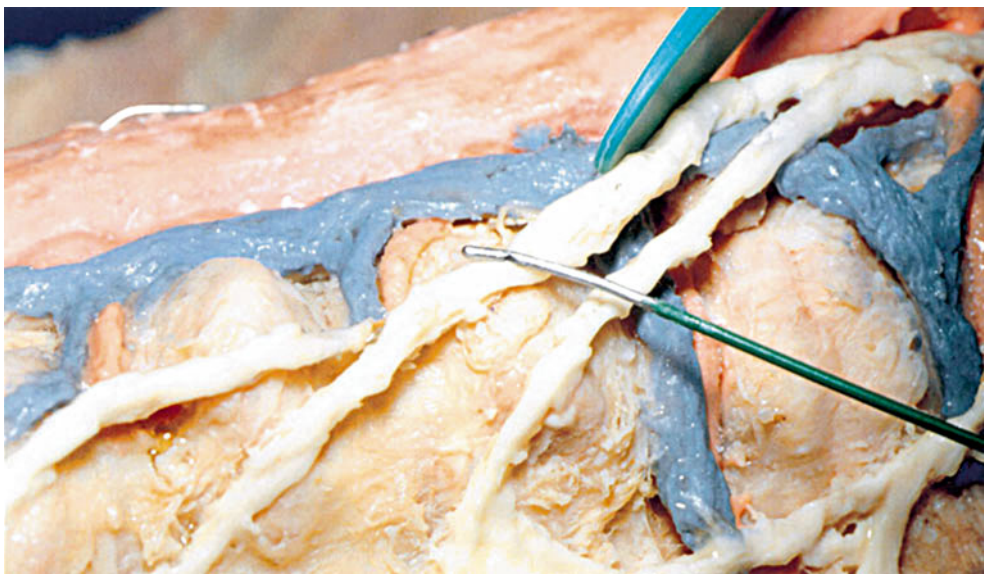

Fig. 2.3 15-mm active tip R-F (Racz-Finch) curved blunt needle for lesioning the splanchnics at T11–T12 placed over the splanchnic nerve dissected on a cadaver (With permission from Raj et al. [7])

flow of neurolytic solutions, RF lesions are limited to 1 mm lateral to the needle. Prior to lesioning, sensory stimulation at 50 Hz is performed up to 1 V to elicit stimulation in the epigastric region and motor stimulation at 2 Hz up to 3 V to rule out stimulation of the intercostal nerves as noted by lack of contraction of the intercostal muscles. Once the location is confirmed both fluoroscopically in the A/P and lateral projections and with sensory and motor stimulation, the area is anesthetized with local anesthetic and then lesioned at 80 °C for 90 s. A second lesion is performed by turning the curved needle 180° to widen the lesion size. The primary complication of splanchnic nerve blocks/RF lesions is pneumothorax if the needle punctures the diaphragm [8].

Similarly, local anesthetic blocks and radiofrequency lesions of the lower portion of the sympathetic chain is targeted to treat pelvic and perineal pain. For bladder and

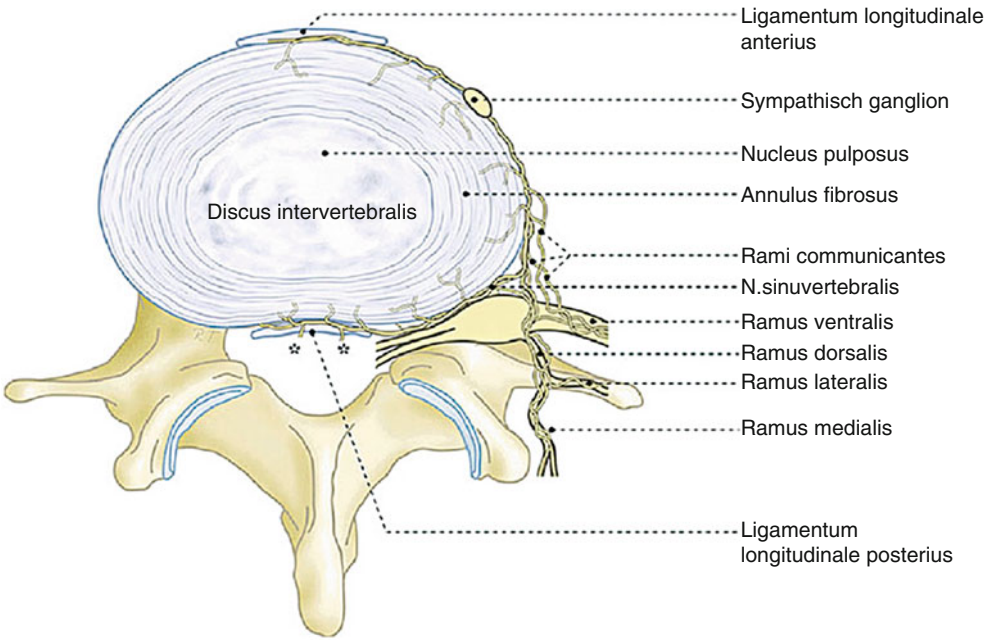

Fig. 2.4 Illustration of spinal innervation and targets for neural blockade/neurolysis including the sympathetic ganglia, ramus communicans, and ramus medialis (facet nerve) (Illustration courtesy of Rogier Trompert Medical Art. http://www.medical-art.nl. Reprinted with permission from Kallewaard et al. [20])

uterine pain, the superior hypogastric plexus block is employed, whereas for perineal, rectal, and vaginal pain, the ganglion of impar is the target. The superior hypogastric plexus is located on the anterior lateral border of the lower third of the L5 vertebral body and accessed via an oblique fluoroscopic view of the anterior lateral surface of the L5 vertebra or an L5–S1 transdiscal approach [9, 10]. The ganglion of impar is accessed by passing a needle through the sacrococcygeal ligament [11, 12]. Neurolysis of these structures with alcohol or phenol is typically reserved for those with cancer pain; however, botulinum toxin has emerged as a novel tool to aid in providing sympathetic neurolysis beyond the duration of local anesthetic but without the long-term sequel of alcohol or phenol [13, 14].

In addition to the sympathetic chain, another anterior column target for neurolysis is the ramus communicans (Fig. 2.4) [15, 16]. These nerves contribute to nociceptive innervation of the intervertebral disc. Radiofrequency ablation of these nerves at two adjacent levels was first reported to provide pain relief in patients with single level of discogenic pain over 20 years ago, but only one randomized clinical trial has been published on the procedure in that time period [17]. These nerves can be accessed via a 20° oblique fluoroscopic view with a 2-gauge spinal or RF needle advanced to the vertebral body just anterior to the posterior edge. The proper location is identified when sensory stimulation produces a sensation in the back at less than 1.5 V and motor stimulation at twice the sensory stimulation fails to cause contractions of the leg muscles. Once the proper location is identified, a radiofrequency lesion is made at 80 °C for 60 s. One randomized clinical trial compared radiofrequency lesioning of the ramus communicans with a sham treatment. The RF-treated group had significantly lower VAS scores and improved SF-36 scores as compared to the sham-treated group 4 months after treatment [18]. Although there are few studies and only one RCT, the quality of evidence supporting this procedure secured it a level 2B+ positive recommendation using a modified grading system [19, 20]. This procedure is also reportedly effective in the treatment of pain due to vertebral fractures as the ramus communicans also innervates the vertebral bodies. However, further studies are needed to make this a recommended procedure [21].

In the posterior column, the most common targets for paraspinal neurolysis are the medial branches of the spinal posterior rami (aka ramus medialis or facet nerves). These nerves branch off the spinal nerves as they exit the intervertebral foramen to innervate the facet joints (aka zygapophyseal joint). With aging and injury, the facet joint may become sclerotic and hypertrophied and contribute to chronic back pain. Denervating the joint by ablating the medial branch nerves relieves the pain and improves range of motion. The primary target for denervation is the medial branch nerve as it passes over the junction of the transverse process and pedicle in the lumbar spine and in the middle of the facet pillar in the cervical spine [22, 23]. Pain relief after a local anesthetic blockade of these nerves is the diagnostic criteria used to determine which spinal segments are contributing to a patient's back pain. Two of these nerves are lesioned for each painful facet joint as each joint is innervated by two separate medial branches. Radiofrequency neurolysis at 80° for 90 s

is the most common technique for neurolysis although cryoneurolysis is also effective. Two recent analyses of the available literature using the Cochrane Musculoskeletal Review Group criteria for interventional techniques for randomized trials and the Agency for Healthcare Research and Quality (AHRQ) criteria for observational studies evaluated the efficacy of radiofreqency neurotomies of the medial branch nerves to treat facet joint pain and found that the available evidence supported recommending this procedure for the treatment of lumbar and cervical facet joint pain. This recommendation is based on quality of evidence reaching a level II-1 or II-2 when utilizing the grading criteria developed by the US Preventive Services Task Force [24, 25].

Percutaneous facet fusion, a new interventional pain management procedure, has recently been introduced as another technique to address facet joint pain. This fluoroscopically guided technique identifies the facet joint in an oblique view, and using a percutaneous portal system, a drill is advanced to the facet joint. A hole is made large enough to insert an 8-mm bone dowel into the joint which is allowed to fuse over the course of 6 weeks. This technique presumes that fusing the facet joint will relieve facet joint pain, but more clinical trials are needed to fully evaluate the effectiveness of this procedure as a stand-alone procedure for facet pain [26].

Spinal Bone and Connective Tissue Targets for Interventional Pain Management

As patients age, the bone and connective tissue components of the spine are subject to a wide array of degenerative processes that contribute to chronic pain, including but not limited to, vertebral fractures, disc herniations and ruptures, and hypertrophy and sclerosis of facets joints and ligamentum flavum. In the past 10–20 years, various minimally invasive image-guided interventional procedures have been developed to address each of these conditions with varying degrees of success.

Vertebral fractures, a condition common to patients with osteoporosis, can cause both acute and chronic pain. Two fluoroscopically driven procedures have emerged to address this condition, vertebroplasty and kyphoplasty. These vertebral augmentation procedures involve fluoroscopic placement of a needle into the fractured vertebral body and introduction of bone cement in an effort to stabilize the vertebral fracture and regain vertebral height and reduce pain [27]. A systematic review of the available studies from 1980 to 2008 graded the level of evidence using the North American Spine Society guidelines and concluded that there was good evidence to recommend vertebral augmentation in the treatment of vertebral fractures, although only one of the 74 studies was a randomized clinical trial. Subsequently, four additional randomized clinical trials were published that offered conflicting recommendations, two supporting and two not supporting vertebral augmentation for vertebral fractures. The two in support were both open-label trials randomized to kyphoplasty versus medical management in one study [28] and vertebroplasty versus medical management in the other [29] with both having an inclusion criteria of edema noted on MRI. Each study reported significant decreases in VAS scores 1 month posttreatment in the augmented groups versus the medical management groups. Less of a difference was noted at the 1-year point, presumably due to fracture healing. In the kyphoplasty study, quality of life, mobility, and function also showed greater improvement in the surgical versus nonsurgical group. The two studies which did not support vertebral augmentation for vertebral fractures were sham versus vertebroplasty. All patients had radiographic evidence of vertebral fractures and back pain for less than a year, but not all had MRI evidence of edema [30, 31]. Each study reported trends of pain improvement in the vertebroplasty group at the 1-month time point that did not reach statistical significance. As each group continued to improve, there was no discernable difference between them in pain, physical functioning, or disability scores. The authors concluded that there was no significant difference between patients treated with vertebroplasty or a sham procedure. To help resolve these conflicting results, a more rigorous sham-controlled study was designed to include MRI evaluations by two independent radiologists, outcome measurements at 1 day, 1 week, 1,3,6, and12 months after treatment to include VAS, disability, and quality of life scores [32]. The results of this study are pending.

The intervertebral disc is another source of chronic spinal pain targeted by interventional procedures [33]. Derangements of the intervertebral disc can become a source of both acute and chronic back pain and is estimated to constitute up to 45 % of all cases of low back pain [19].

Herniated disc or extruded disc fragments can create pain as a result of a mass effect on neural structures including the spinal cord and exiting nerve roots. In addition, annular tears can allow leakage of the acidic nucleus pulposus leading to neural irritation of the sinuvertebral nerves that innervate the outer annulus as well as spinal nerves if the nucleus pulposus extends beyond the borders of the disc (Fig. 2.4). Diagnosis of this discogenic pain is most often determined by provocative discograms whereby 1–2 ml of contrast is injected into the disc and observed to reproduce concordant pain. The structural integrity of the disc is also evaluated by measuring intradiscal pressure to see if and at what pressure contrast may leak outside the normal boundaries of the nucleus pulposus up to a maximum of 100 psi, the normal pressure of a lumbar disc in the seated position (Fig. 2.5) [15, 19, 34]. Early interventional procedures attempted to treat discogenic pain with intradiscal injections of chymopapain, but anaphylaxis and clinical benefit less than that obtained with surgical discectomy lead

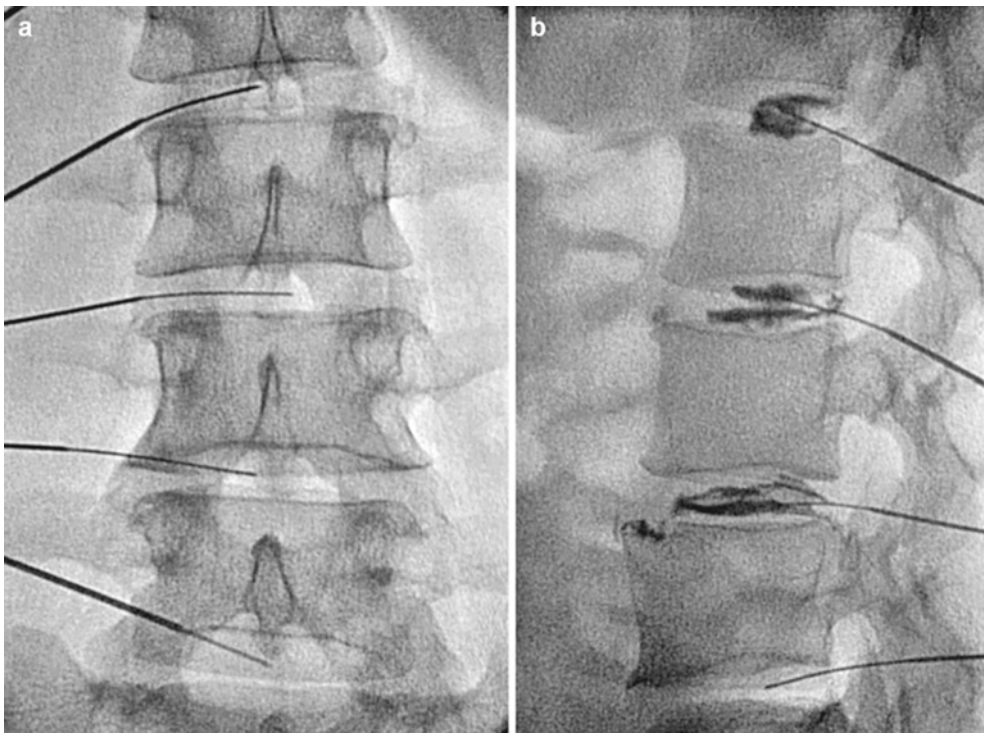

Fig. 2.5 (**a**) A/P fluoroscopic image of needles placed within lumbar disc. (**b**) Lateral view with injection of contrast, note posterior leakage of contrast at the L3–4 disc (Fluoroscopic images courtesy of Lawrence Poree, MD Ph.D)

to the abandonment of this chemonucleolysis technique [35]. In the intervening 20 years, a number of intradiscal procedures have been introduced utilizing a variety of lesioning, injection, and decompressive technologies, including intradiscal electrothermal therapy (IDET), annuloplasty and other radiofrequency lesioning techniques, injection of corticosteroids, ozone, hypertonic dextrose, and methylene blue, as well as nucleoplasty and other percutaneous disc decompression techniques [36–38]. A recent multicenter analytical review of the available studies of these procedures made the following recommendation [19]: "Intradiscal corticosteroid injections and RF treatment of the discus are not advised for patients with discogenic low back pain. The current body of evidence does not provide sufficient proof to recommend intradiscal treatments, such as IDET and biacuplasty for chronic, nonspecific low back complaints originating from the discus intervertebralis. We are also of the opinion that at this time, the only place for intradiscal treatments for chronic low back pain is in a research setting. RF treatment of the ramus communicans is recommended." (See section above on paraspinal targets for a review of RF lesioning of the ramus communicans.) The authors went on to conclude "…provocative discography remains the gold standard for the determination of the diagnosis of discogenic pain."

Minimally invasive lumbar decompression (MILD) is another new interventional pain management technique that targets the hypertrophic ligamentum flavum in patients with lumbar spinal stenosis and neurogenic claudication [39]. As patients age, the ligamentum flavum hypertrophies in part due to replacement of the normal elastin with collagen in the posterior fibers of the ligamentum flavum [40]. Mechanical stress of the ligament causes an inflammatory response with infiltration of macrophages and fibroblast that in turn leads to scar formation. In addition, loss of disc height leads to buckling of the ligament and further narrows the spinal canal [41]. In later stages, calcification and ossification of the ligament develops and contributes even further to thickening and inflexibility of the ligamentum flavum [42]. Until recently, this condition was treated initially with epidural steroid injections, and when this therapy no longer provided significant benefit, patients were treated with an open surgical decompression. The MILD procedure, performed with local anesthetic and minimal sedation, uses the placement of epidural contrast and fluoroscopy to outline the anterior border of the ligamentum flavum in a region where ligamentum flavum hypertrophy was identified on MRI images (Fig. 2.6). A small 5.1-mm trocar is advanced to the inferior lamina of interlaminar space to be treated. Removal of the trocar's stylet leaves a working portal through which instruments are passed and are used to remove osteophytes and the posterior fibers of the hypertrophied ligamentum flavum. Initial clinical trials revealed that this procedure showed statistically and clinically significant reduction of pain and improvement in the mobility as measured by VAS, ZCQ, SF-12v2, and ODI [43]. These improvements persisted at the 1-year follow-up [44]. A multicenter, randomized clinical trial is currently underway to compare the long-term benefits of the MILD procedure compared with epidural steroid treatments.

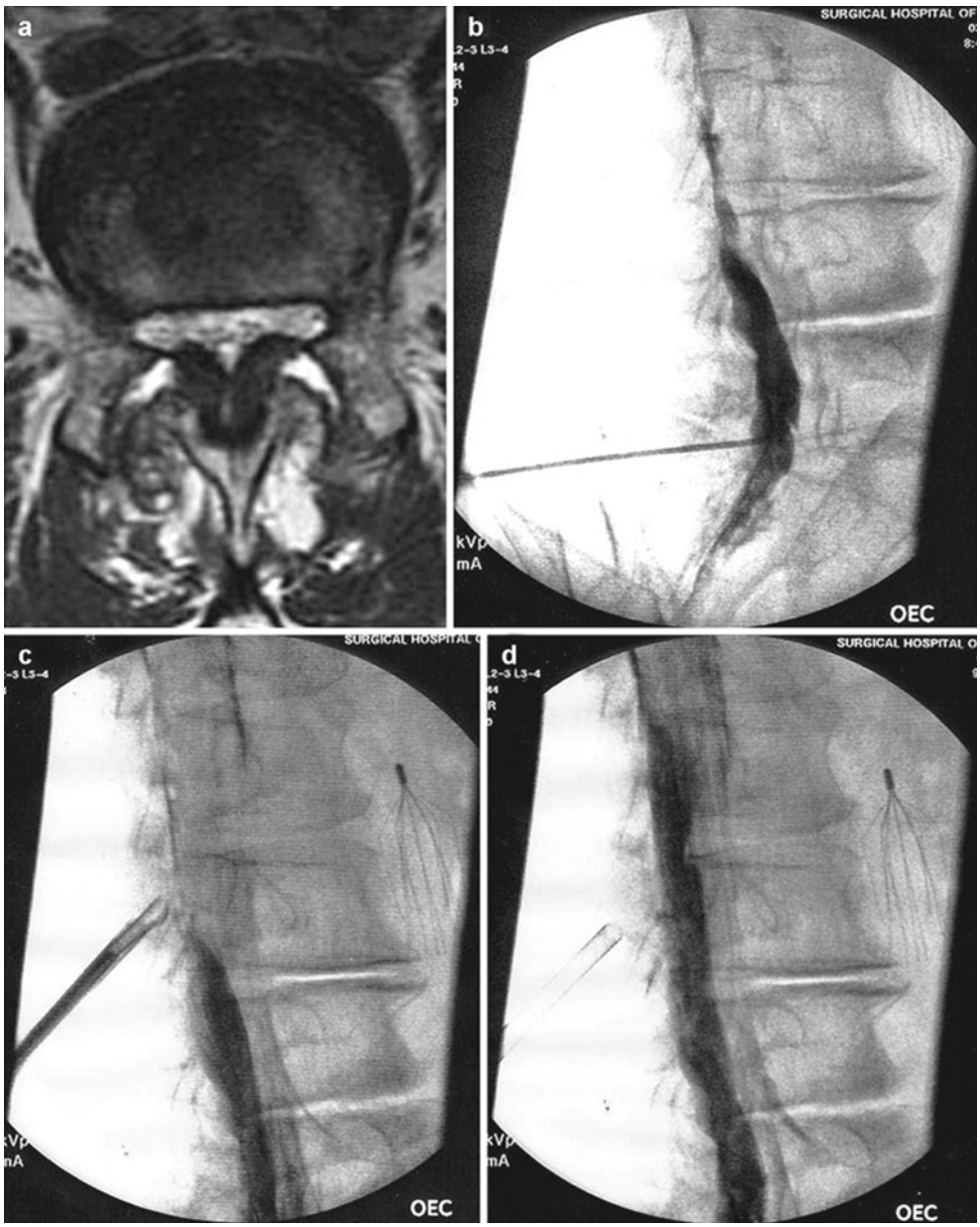

Fig. 2.6 (**a**) Axial MRI of lumbar spine showing spinal stenosis secondary to hypertrophy of the ligamentum flavum (LF). (**b**) Fluoroscopic image in contralateral oblique view showing epidurogram and failure of contrast to flow cephalad. (**c**) Tissue sculptor used to remove posterior portion of hypertrophic ligamentum flavum. (**d**) Epidurogram after decompression shows improvement in epidural flow (Images courtesy of Vertos Medical Aliso Viejo, CA)

Intraforaminal Targets for Interventional Pain Management

Of course, the most important interventional pain management target within the vertebral foramen is the dorsal root ganglion (DRG). The primary sensory afferent neurons in the ganglion are the principle link between peripheral nociceptors and the processing centers of the central nervous system. Injury of these nerves is common from mechanical trauma resulting from lateralized herniated disc or spondylolisthesis, chemical irritation from leakage of nucleus pulposus [45–48], and injury caused by infectious agents such as herpes zoster. All of these injuries can initiate a cascade of inflammatory mediators including cytokines that contribute to the development and maintenance of chronic pain [49]. Thus, it comes as no surprise that foraminal injection of glucocorticoids is a common target for interventional pain physicians [50, 51]. A recent analysis of the available literature using the Cochrane Musculoskeletal Review Group criteria for interventional techniques for randomized trials and the criteria developed by the Agency for Healthcare Research and Quality (AHRQ) criteria for observational studies evaluated the efficacy of transforaminal epidural steroid injections and found that the available evidence supported recommending this procedure for the treatment of lumbar radiculitis. The quality of this evidence was ranked utilizing the US Preventive Services Task Force and found to reach a level

II-1 for the short term and level II-2 for long-term management of lumbar nerve root and low back pain [52].

More recently, patients with acute lumbosacral radiculopathy due to intervertebral disc herniation have reportedly improved with transforaminal injections of clonidine [53]. The mechanism for this improvement remains uncertain; however, there may be multiple targets for intraforaminal clonidine. Chung and others observed that peripheral nerve injury leads to sympathetic nerve fiber spouting around the DRG, and this observation was hypothesized to contribute to the development of sympathetically mediated neuropathic pain [54]. Thus, clonidine, an alpha-2 agonist with sympatholytic actions on sympathetic nerve endings, may reduce the effects of increased sympathetic innervation of the DRG after nerve injury. Another possibility is via direct anti-inflammatory action. Liu and Eisenach demonstrated decreased hyperexcitability in rodent-injured nerves after clonidine was applied perinurally and attributed this to inhibition of pro-inflammatory cytokines and prostaglandins [55]. A peripheral site of action for the antinociception activity of an alpha-2 agonist was also suggested by Poree et al. in an animal model of neuropathic pain. In this model, the antinociceptive actions of dexmedetomidine, an alpha-2 agonist, was antagonized by prior treatment with a peripherally restricted alpha2AR antagonist that does not cross the blood-brain barrier. The authors suggested the DRG as a possible peripheral site of action for dexmedetomidine after nerve injury [56].

The DRG has also been targeted for electrical and pulsed radiofrequency stimulation. Although high temperature lesioning radiofrequency energy is successfully employed to denervate medial branch nerves, this technique is avoided in the larger mixed nerves as it may lead to deafferentation pain and painful neuromas. Pulsed and low temperature radiofrequency treatments do not cause neural destruction but instead expose the nerves to a high voltage low to moderate temperature environment. In a prospective randomized double-blind study, 67 °C RF was reported to provide long-term relief of cervical brachial pain [57]. A recent retrospective chart review of 50 patients who received pulsed (42 °C) and moderate temperature (56 °C) radiofrequency treatment of the DRG for lumbar radiculitis reported that all patients received at least a 50 % improvement in their pain [58]. Another group reported that when low temperature (42 °C) pulsed RF was used alone, 30 % of the patients received greater than 50 % pain relief [59]. The observation that even low temperature electric fields applied to the DRG could provide long-lasting pain relief has prompted the recent development of an implantable DRG stimulation system to provide a continuous electric field around the DRG [60]. Excellent results from multiple prospective clinical trials have resulted in approval of DRG stimulation for the treatment of chronic pain in Europe and Australia with clinical trials currently underway in the USA (Fig. 2.7).

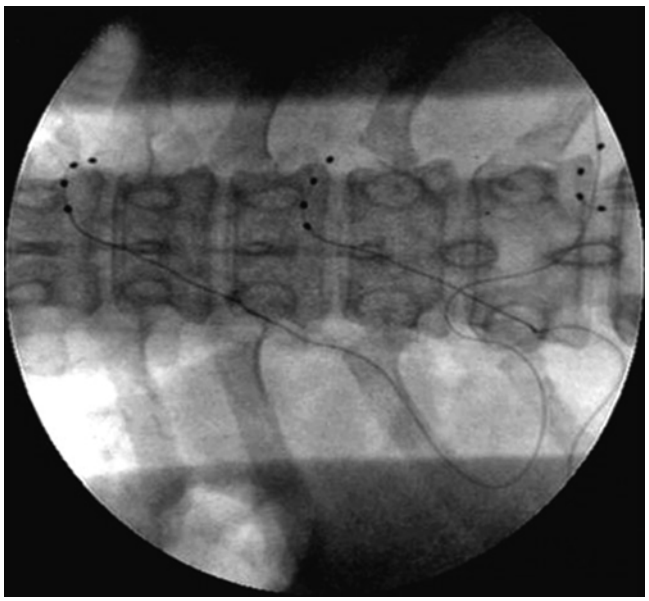

Fig. 2.7 Stimulating electrodes placed over dorsal root ganglia within the right T8–9, T10–11, and T12–L1 foramen. Stimulating electrodes placed over dorsal root ganglia within the right T8–9, T10–11, and T12–L1 foramen (Courtesy of Eric Grigsby MD, Napa Pain Institute, Napa, CA. and Jeff Kramer, Ph.D. Spinal Modulation, Menlo Park, CA [60]

Intraspinal Targets for Interventional Pain Management

Targeting the intrathecal space with opioids and local anesthetic has been available for cancer pain management since it was first reported in 1899 [61]. However, widespread utilization of intraspinal (epidural and intrathecal) analgesics outside of the operating room was not practical until the advent of long-term catheters and implantable pumps in the 1980s [62]. Dupen epidural catheters had an antimicrobial sleeve located at the skin exit site, thereby reducing the risk of infection and allowing for intraspinal delivery via an external pump for more than a year. While these catheters are no longer commercially available, they have been replaced by long-term epidural catheters attached to subcutaneous ports which provide even greater protection from infection [63]. For even longer-term intrathecal infusions and even greater protection against infection, implantable pumps have emerged as the preferred method for intrathecal delivery in the past 30 years. While these pumps are initially more expensive than externalized systems, they become cost neutral after 3 months and actually provide a cost savings thereafter as compared with externalized pumps [64, 65]. Most of the current systems are computer controlled, and some have the option for patient-controlled activation of programmed bolus doses [66]. The advantage of intrathecal management over systemic administration is one of

inhibition of nociceptive transmission at the spinal level and reduced systemic toxicity. In a randomized clinical trial comparing intrathecal drug delivery systems (IDDS) to comprehensive medical management (CMM), cancer patients treated with IDDS had less medication-induced toxicity, greater pain control, and longer survival than did CMM patients [67]. Nonetheless, it is estimated that only 10–20 % of patients with cancer-related pain fail comprehensive medical management using the World Health Organization guidelines and require more advanced pain management interventions such as IDDS [68]. Guidelines on appropriate selection of patients and intrathecal medication admixtures for patients with intractable cancer-related pain has recently been updated and includes the use of medications approved by the FDA for approved IDDS, medications that are by expert consensus, commonly used for IDDS therapy, and medications that are experimental and are recommended only as a means to provide greater analgesia in the final stages of life (Fig. 2.8) [70–72]. The common pharmacological targets for IDDS therapy include the mu-opioid receptors, calcium channels, sodium channels, and α-2 adrenergic receptors. Figure 2.9 shows the presynaptic and postsynaptic location of the receptors in the dorsal horn that forms the pharmacological basis of IDDS therapy, although, only morphine and ziconitide (aka SNX-111), a novel N-type voltage-sensitive calcium channel antagonist, are currently FDA-approved analgesics for IDDS therapy [70, 73–75]. As IDDS therapy gains greater acceptance for the treatment of intractable cancer pain, the appropriate position in a continuum of care for chronic non-cancer pain remains a source of debate. A recent review aimed at addressing this issue systematically evaluated the available literature using the Agency for Healthcare Research and Quality (AHRQ) criteria for observational studies and the Cochrane Musculoskeletal Review Group criteria for randomized trials. The level of evidence was determined using five levels of evidence, ranging from level I to III with three subcategories in level II, based on criteria developed by the US Preventive Services Task Force (USPSTF) [76]. The authors found 20 studies that met both the inclusions and exclusion criteria. Based on their analysis, they concluded that high-quality evidence supported a moderate recommendation for intrathecal infusion systems for cancer-related pain and that moderate quality of evidence supported a limited to moderate recommendation for non-cancer-related pain.

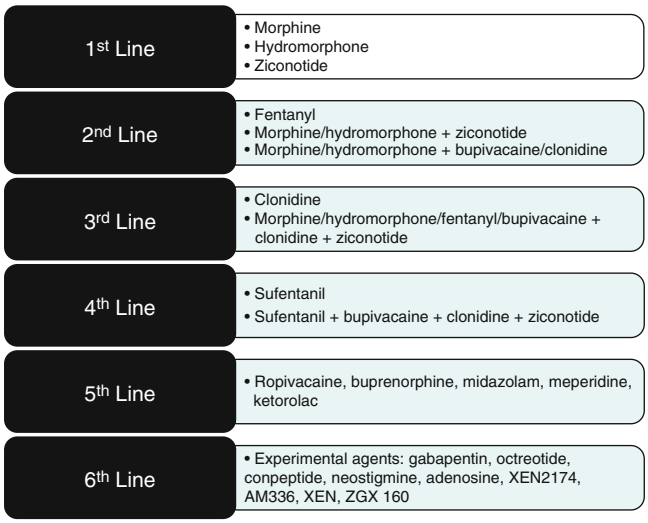

Fig. 2.8 Polyanalgesic algorithm for intrathecal therapy for cancer pain. With permission from Deer et al. [71])

In addition to pharmacological receptors, intraspinal neural structures are also targeted with electrical stimulation. Although the first spinal cord stimulator was implanted in 1967, the exact mechanism for electrical stimulation-induced analgesia remains elusive [77]. It is currently hypothesized that the analgesic effects of spinal cord stimulation are explained in part by the gate control theory proposed by Melzack and Wall whereby activation of large-diameter afferents activate segmental GABAergic interneurons [78, 79]. However, recent findings also suggest that supraspinal pathways are also involved in spinal cord stimulation analgesia [80]. Successful analgesia with spinal cord stimulation is dependent most upon proper placement of epidural electrodes over the spinal cord that are programmed to deliver the amplitude, frequency, and pulse width that successfully provides analgesia without untoward stimulation in areas that are not painful. The distance between electrodes being placed in an area that provides good analgesia ("sweet spot") and an area that does not can be as small as a few millimeters. Thus, successful stimulation can be lost if an electrode migrates even a few millimeters away from the ideal target. To circumvent this problem, most manufactures have devised more complex electrode arrays that allow for greater maneuverability of the electric field. While earlier systems employed as few as two or four electrode contacts per array, more recent spinal cord stimulation systems employ 16–20 contact arrays (Fig. 2.10b). In addition to spinal cord stimulation, intraspinal nerve roots can also be individually targeted (Fig. 2.10a). As with DRG stimulation discussed above, this technique is advantageous when the region of neuropathic pain has a small focal distribution and spinal cord stimulation activates areas outside the region of pain that is uncomfortable for the patient. This is especially true when the pain is due to injury to an isolated nerve [81, 82]. For example, Fig. 2.10c shows the electrode configuration in a patient receiving sacral nerve stimulation for persistent focal neuropathic pain in the pelvic floor after cystectomy and hysterectomy for chronic pelvic pain. Spinal cord stimulation failed to provide adequate analgesia whereas she continues to receive good analgesic benefit from sacral nerve stimulation 3 years after implantation.

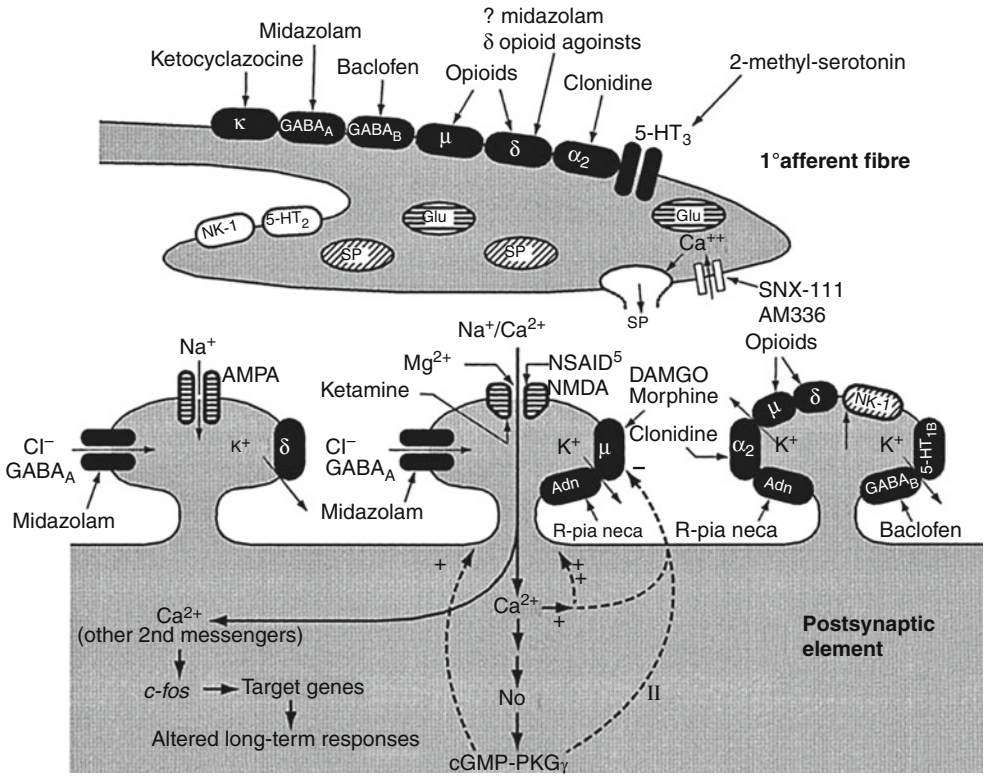

Fig. 2.9 Possible arrangement of pre- and postsynaptic receptors on structures in the dorsal horn of the spinal cord and potential sites of action of opioid and non-opioid spinal analgesics. Presynaptic release of the neurotransmitter glutamate (*Glu*) results in activation of the postsynaptic α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (*AMPA*) receptor, which controls a rapid-response sodium (Na^+) channel. Substance P (*SP*) interacts with the neurokinin (*NK-1*) receptor and results in activation of second messengers. With prolonged activation, the *N*-methyl-D-ASPARTATE (*NMDA*) receptor is primed, Glu activates the receptor, the magnesium (Mg^{2+}) plug is removed, and the ion channel allows entry of Na^+ and calcium (Ca^{2+}) ions. The increase in intracellular Ca^{2+} then triggers a number of second-messenger cascades. Production of nitric oxide (*NO*) increases via the Ca^{2+}/calmodulin-dependent enzyme NO synthase. NO may diffuse out of the neuron to have a retrograde action on primary afferents and also activates guanylyl cyclase, leading to increases in intracellular cyclic guanosine monophosphate (*cGMP*) and activation of cGMP-dependent protein kinases. Activation of the Ca^{2+}-dependent protein kinase C γ isoform (*PKCγ*) leads to phosphorylation of the NMDA receptor, which reduces the Mg^{2+} block (dotted line II) relating to the development of opioid tolerance. The increase in intracellular Ca^{2+} also results in the induction of proto-oncogenes such as c-*fos*, with a presumed action on target genes of altering long-term responses of the cell to further stimuli. *κ*, *μ*, and *δ* opioid receptors, *GABA* γ-aminobutyric acid, α_2 α_2 adrenoceptor, *5-HT* serotonin. Details of the potential analgesics are outlined in the text. *NSAID* nonsteroidal anti-inflammatory drug, *SNX-111* and *AM336* omega conopeptides that block neuronal Ca^{2+} channels. *DAMGO* [D-Ala^2,N-Me-Phe^4,Gly-ol^5]-enkephalin, *R-Pia* R-phenyl-isopropyl-adenosine, *Neca* N-ethylcarboxamide-adenosine (With permission from Walker et al. [69])

In spite of over 40 years of clinical experience and success, routine implementation of spinal cord stimulation in clinical practice has been stifled, in part due to limited well-controlled clinical studies, a trend that has reversed in recent years. In a randomized prospective crossover design study comparing spinal cord stimulation versus reoperation for persistent leg pain after spinal decompression, North et al. found that patients initially randomized to SCS were significantly less likely to cross over than were those randomized to reoperation. Patients randomized to reoperation required increased opiate analgesics significantly more often than those randomized to SCS [83]. Kumar et al. followed shortly thereafter with a multicenter randomized prospective clinical study comparing spinal cord stimulation with conventional medical management (CMM) [84, 85]. This study found that compared with the CMM group, the SCS group experienced improved leg and back pain relief, quality of life, and functional capacity, as well as greater treatment satisfaction for over 2 years. More recently, a multicenter randomized study of SCS versus sham treatment demonstrated that spinal cord stimulation but not sham treatment decreased the frequency of angina attacks [86]. These pivotal studies have opened the door to even more investigations of SCS for an even greater number of disease states including intractable angina, peripheral vascular disease, chronic pancreatitis, and chronic pelvic pain to name just a few [87–89]. As the clinical evidence grows in support of spinal cord stimulation for a wide range of chronic pain states, so does the resistance to approve this therapy by third-party payors due to concerns about initial cost. To address these concerns, Krames et al. proposed that

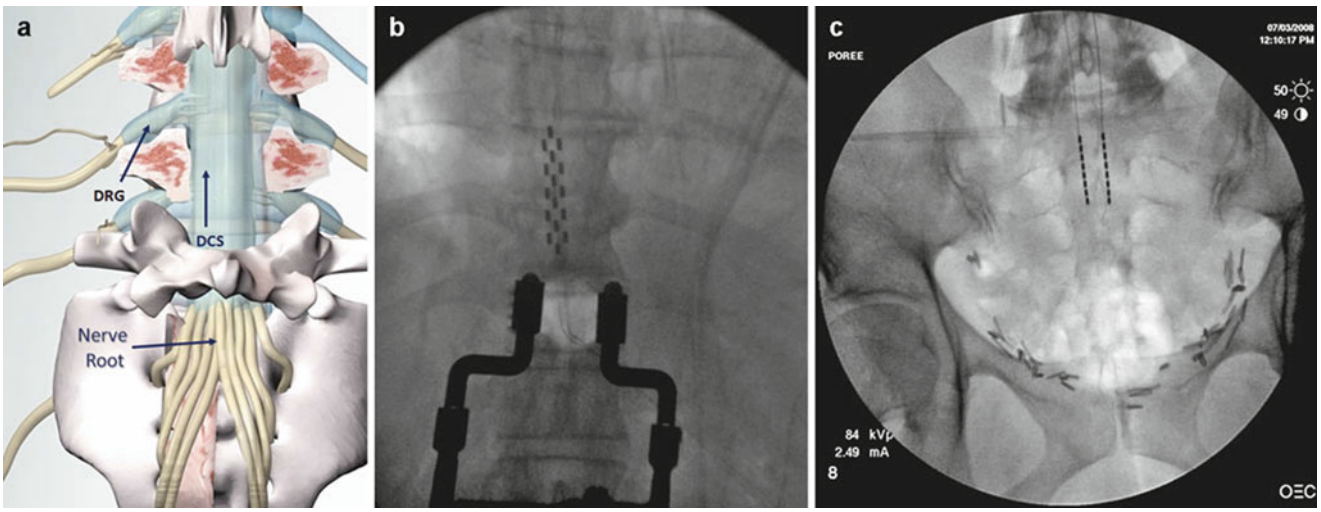

Fig. 2.10 (**a**) Illustration of intraspinal targets for electrical stimulation includes the dorsal columns (*DC*) of the spinal cord, the intraspinal nerve roots, and the dorsal root ganglia (*DRG*) (Courtesy of Jeff Kramer, Ph.D. Spinal Modulation, Menlo Park, CA) (**b**) Fluoroscopic image of intraoperative placement of 16 contact tripole paddle lead. Tripole configuration allows for greater maneuverability of the electric field. (**c**) Fluoroscopic image of retrograde placement of electrodes allows for stimulation of sacral nerve roots for patient with pelvic pain (Fluoroscopic images courtesy of Lawrence Poree MD PhD)

spinal cord stimulation, as with other advanced therapies, be subject to a more comprehensive evaluation process whereby the initial cost is balanced with long-term health-care cost, safety, efficacy, and appropriateness of other therapies. They termed this new algorithm the SAFE (safety, appropriateness, fiscal neutrality, and effectiveness) principle [65, 90]. The authors went on to use this algorithm to assess when SCS should be used in the treatment of failed back surgery syndrome (FBSS). They concluded that SCS should be considered before submitting a patient to either long-term systemic opioid therapy or repeat spinal surgery for chronic pain resulting from FBSS [91].

As health-care costs continue to rise and advanced technologies rapidly emerge, employing the SAFE principle may provide a more rational approach to making individual as well as intuitional decisions regarding appropriate selection of therapies and allocation of resources.

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Functional Anatomy and Imaging of the Spine

3

John C. Keel and Gary J. Brenner

Key Points

- Spine pain concepts and standardized terminology
- Spine anatomical structures and functional unit concept, a basic foundation to take to clinic and fluoroscopy suite
- Basic spine imaging modalities and examples
- Awareness of references such as NASS, IASP, and ACR publications, writings of great anatomists, for example, Bogduk

Introduction

Painful disorders of the spine are among our most common medical complaints. Over a lifetime, 60–80 % of adults experience at least one significant episode of back pain [1, 2]. In a single year, 15–20 % will have back pain, and 2–5 % of the entire population will seek medical attention for back pain [2]. Low back pain has been estimated as the fifth leading cause of all medical visits and the second leading cause of symptom-related medical visits [3]. In the United States, the estimated annual cost of back pain is $20 billion to $50 billion [4]. In particular, low back pain is one of the most important factors in medical costs and disability.

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Imaging of the spine is now nearly as ubiquitous as back pain itself. Imaging technology has become increasingly sensitive and detailed in its revelations, but improvements in images have outpaced our ability to interpret their significance, resulting in the conundrum of false-positive spine imaging [5]. Spine imaging is also expensive. A recent analysis of the Medical Expenditure Panel Survey (MEPS) from 1997 to 2005 showed that spine-related medical costs escalated significantly more than increases in general medical costs, and patients with spine problems accounted for a disproportionate share of expenditures. Spine imaging contributed to these costs without necessarily improving outcomes [6]. Several guidelines have been developed in hopes of ameliorating this trend, such as those of the American College of Radiology [7, 8].

This chapter introduces the essentials of spine anatomy and imaging. For the pain physician, mastery of spinal anatomy and imaging modalities is required to correlate clinical presentation with anatomic abnormalities and make a valid interpretation of the imaging.

Historical Background

The functional anatomy of the spine has been studied since antiquity. Imhotep, the founder of ancient Egyptian medicine, wrote about anatomy of the spine more than 4,500 years ago. The first description of spinal traction is in the Indian epic *Srimad Bhagwat Mahapuranam*, written between 3,500 and 1,800 B.C. Hippocrates (460–377 B.C.) described discs, ligaments, muscles, and curvatures of the spine and first described the effects of tuberculosis on the spine. He also devised the Hippocratic board and Hippocratic ladder to treat spinal deformities and performed spinal manipulation. Aristotle laid the philosophical foundation for kinesiology [9]. Galen (130–200 A.D.), the "father of sports medicine," wrote of the functional importance of spine anatomy and described spinal nerves in detail [10]. Vesalius (1514–1564),

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the "father of anatomy," made remarkably accurate observations about the spine [11] and described the spine as the "keel of the body [12]." The renowned medieval Persian physician, Ibn Sina (Avicenna), devoted eight chapters to the spine in *Al-Qanun fi al-Tibb (the Canons of Medicine)* [13]. Twentieth and twenty-first century spines experience great forces from automobiles and airplane ejection seats, and engineers collaborating with physicians have developed sophisticated models such as finite element analysis, in order to properly design equipment to protect the spine [14]. Technological advances and increased understanding of spine anatomy have led to more options for diagnosis and treatment of back pain, this major cause of human suffering.

Spine imaging is a most remarkable example of advancement in the diagnosis of painful spine disorders. In November 1895, Roentgen discovered X-rays, and within weeks, this powerful new tool was employed for medical use [15]. It is interesting for the pain physician to note that the first use of X-ray was really a form of fluoroscopy. In the 1930s, stratigraphy, planigraphy, and tomography techniques were developed, wherein the X-ray source and film are rotated in a precise way in order to obtain a picture of an internal structure, such as a vertebral fracture. Pneumoencephalography led to pneumomyelography in 1919, then Lipiodol myelography, using iodized poppy seed oil, in 1922. Pantopaque arrived in the 1940s, Conray in the 1960s, and the less toxic nonionic, water-soluble contrasts even later. Lindblom reported discography in 1948. Hounsfield invented computed tomography (CT) in 1973. MRI came into clinical use in 1984, after a long period of development [16].

Scientific Foundation and Relevance to Pain Care

The anatomic structures of the spine can be sources of somatic, inflammatory, neuropathic afferent, and peripheral deafferentation pain [17]. S*omatic pain* results from stimulation of nerve endings in bone, muscle, ligament, or joint. *Visceral pain* arises from stimulation of a body organ and can also be relevant to understanding back pain as visceral pain can both be referred to and radiate to the spine, for example, as in renal colic. *Inflammatory* pain results from pathology that, as the name suggests, involves inflammation; this can be either acute or chronic. Peripheral *neuropathic pain* results from stimulation of the axons or cell bodies of the peripheral nerve. *Central* or *deafferentation pain* can result from nerve root avulsion or injury to the spinal cord [18]. Furthermore, the spinal cord is a conduit for almost all pain, and so the spine is frequently the target of the pain physician's treatment modality, whether it is medication delivered orally, epidurally or intrathecally by catheter, or spinal cord stimulation [19].

In clinical practice, anatomic sources of pain have been referred to as *pain generators.* In order for an anatomic structure to be considered as a source of pain, several conditions should be present, as outlined in Table 3.1. Such criteria for the anatomic cause of back pain have come to be known as *Bogduk's postulates* and are analogous to Koch's postulates regarding bacterial cause of disease [17]. For example, several specific structures of the spine have long been known to have pain fibers. Table 3.2 summarizes pain fiber distribution in the vertebral column as described by Wyke in 1970 [20]. Understanding of the causes of spinal pain continues to develop.

The International Association for the Study of Pain (IASP) has published standardized definitions for spinal pain, based on perceived location of pain (Table 3.3) [11]. For example, lumbar spinal pain is pain felt to originate in an area of the low back below the T12 spinous process, above the S1

Table 3.1 Bogduk's postulates

1. The structure must have a nerve supply
2. The structure should be capable of causing pain similar to what is clinically observed (e.g., when provoked in normal volunteers)
3. The structure should be susceptible to painful disease or injury; such disorders should be detectable by clinical, imaging, biomechanical, or post-mortem tests
4. The structure should be shown to be a source of pain in actual patients, using reliable and valid diagnostic tests

Table 3.2 Vertebral column structures with pain-fiber innervation

Structure
Innervation characteristics
1. *Fibrous capsules of facet joints*
Plexus formations of unmyelinated nerve fibers, dense
2. *Ligaments: anterior longitudinal, posterior longitudinal, interspinous*
Free nerve endings
3. *Periosteum*
Plexus formations of unmyelinated nerve fibers, dense
4. *Fascia and tendons attached to periosteum*
Plexus formations of unmyelinated nerve fibers, dense
5. *Dura mater*
Plexus formations of unmyelinated nerve fibers, less dense
6. *Epidural adipose tissue*
Plexus formations of unmyelinated nerve fibers, variably dense
7. *Adventitial walls of arteries and arterioles to facet joints and cancellous bone*
Plexus formations of unmyelinated nerve fibers
8. *Walls of epidural and paravertebral veins*
Plexus formations of unmyelinated nerve fibers, dense
9. *Walls of blood vessels to paravertebral muscles*
Plexus formations of unmyelinated nerve fibers, dense
10. *Posterior anulus fibrosus of intervertebral disc*
Free nerve endings at the superficial posterior anulus

Innervation characteristics (Modified from Wyke [20])
See Wyke et al. for references cited

Table 3.3 Spinal pain defined by IASP

Cervical spinal or radicular pain syndromes
Thoracic spinal or radicular pain syndromes
Lumbar spinal or radicular pain syndromes
Sacral spinal or radicular pain syndromes
Coccygeal pain syndromes
Diffuse or generalized spinal pain
Low back pain of psychological origin with spinal referral

Table 3.4 Red flags of back pain that may prompt spine imaging

1. Recent significant trauma, or milder trauma, age >50
2. Unexplained weight loss
3. Unexplained fever
4. Immunosuppression
5. History of cancer
6. IV drug use
7. Prolonged use of corticosteroids, osteoporosis
8. Age >70
9. Focal neurologic deficit with progressive or disabling symptoms
10. Duration longer than 6 weeks

spinous process, and medial to the lateral borders of the erector spinae muscles. Sacral spine pain is felt to originate in the sacrum below the S1 spinous process, above the sacrococcygeal joints, and medial to a line between the posterior superior and inferior iliac spines [11]. Pain perceived as being localized around the spine is termed *axial pain.* In contrast, radiculitis or referred pain is perceived more peripherally.

Pain originating from an area of the body with relatively low sensory innervation may be perceived in, or referred to, a different part of the body with greater sensory innervation from the same spinal root level. This *somatic referred pain* is due to *convergence* of high and low sensory inputs at the central nervous system level, such as spinal segmental level or thalamus [17, 21]. For example, low back pain is often perceived as spreading to the buttock. The low back is innervated by the lumbosacral dorsal rami, while the buttock is innervated by the ventral rami of the same spinal segmental levels. The quality of somatic referred pain is deep, constant aching that is diffuse and hard to localize. While it is more often an origin of referred pain, sometimes pain is referred to the lumbar spine. Pain can be referred to the lumbar spine from the lower thoracic spine, abdominal organs, or sacroiliac joints. Muscles may also refer pain to the spine [22].

Distinct from somatic referred pain, *radicular pain* is perceived as arising from a limb or other structure due to ectopic activation of sensory afferent fibers, typically at a spinal root level [21]. The classic quality of radicular pain is intermittent shooting or lancinating and is perceived as traveling down a limb in a narrow band, congruent with the quality of pain that has been produced by experimental stimulation of injured nerve roots [17]. However, in clinical practice, there is variation in pain referral from radiculitis; such pain patterns can be described as dermatomal, myotomal, sclerotomal, or even dynatomal [23–25]. *Radicular pain* is not equivalent to *radiculopathy.* Radiculopathy involves motor or sensory conduction block and does not cause pain by itself, but can accompany radicular or referred pain [17].

Evaluation of pain disorders begins with a careful history and evaluation, and this may often suggest that the anatomical source is the spine. The next step for the pain physician often involves a decision to pursue spine imaging or analysis of imaging that has already been ordered by referring physicians. As noted earlier, the utility of spine imaging is controversial. Low back pain with or without radiculopathy may be self-limited and may not require imaging. However, if *red flags* are present (Table 3.4), imaging of the spine may be warranted [7]. ACR guidelines for chronic neck pain are less clear, especially regarding whiplash. For chronic neck pain, patients with neurologic features may need MRI or CT regardless of X-ray findings, and patients without neurologic features generally do not require imaging beyond X-rays. If X-rays reveal bony or disc destruction, MRI or CT with contrast may be indicated [8]. More details on specific imaging modalities will follow below, and figures will provide examples.

Spine Anatomy and Function

Viewed as a whole, the typical adult spine has primary curvatures that are kyphotic in the thoracic, sacral, and coccygeal spine and secondary lordotic curvatures that develop after birth in the cervical and lumbar spine (Fig. 3.1). In the frontal plane there are typically no curvatures. A frontal curvature of more than 10° is scoliosis; thoracic kyphosis is typically limited to 30–35° and lumbar lordosis 50–60°.

A functional segmental unit of the spine consists of three joints that join adjacent vertebrae: anteriorly, the intervertebral disc (Fig. 3.2) and posteriorly, the two facet joints at that level [27, 28]. This functional unit was first described by Junghanns as a "mobile segment [29, 30]." The functional unit model applies to all mobile segments of the spine except at the atlantooccipital (C0–C1) and atlantoaxial (C1–C2) junctions, where there are no intervertebral discs. The muscles and nerves of the spine are intimately related to the functional unit. The following sections describe the specific anatomical structures of the spine, with an emphasis on function and pain.

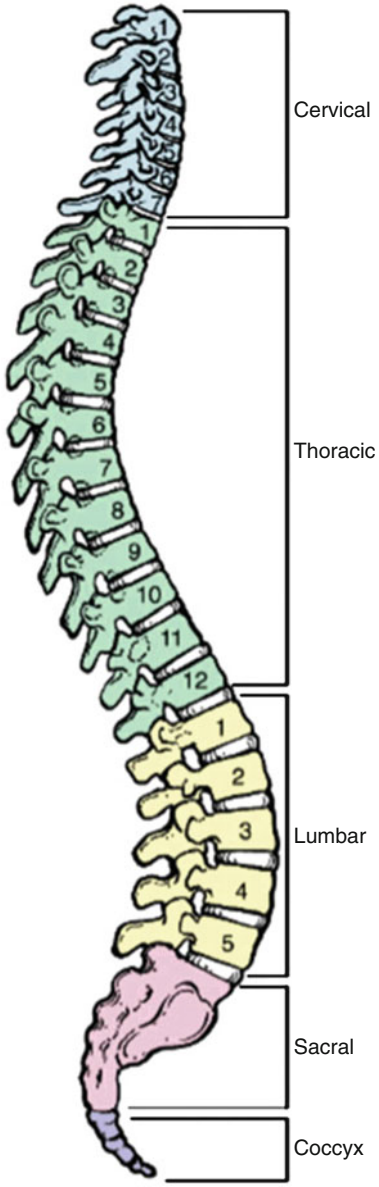

Fig. 3.1 Sagittal spine (Reprinted from Mathis [26])

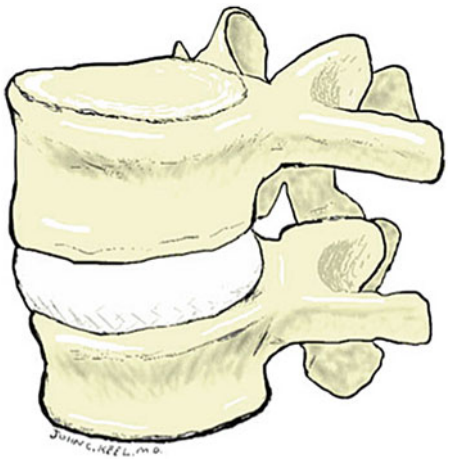

Fig. 3.2 Functional segmental unit

Osteology

The vertebral column as a whole consists of 33 vertebrae: 7 cervical, 12 thoracic, 5 lumbar, 5 fused sacral, and 4 fused coccygeal [31]. Vertebrae are irregular, composite bones, consisting of a ventral body and a dorsal neural arch. The exception is the atlas, which has no vertebral body. The load-bearing system of the vertebral bones can be understood as a tripod: one vertebral body interface and two (paired) facet joint interfaces [32]. For example, lumbar vertebral bodies bear 80–90 % of the weight load, and lumbar pedicles and laminae function as struts, supporting the tripod "legs." Pedicles connect the anterior and posterior weight-bearing elements, spanning from the transverse process to the body. Transverse processes originate at the junction of the pedicle and the lamina, while the spinous process originates at the junction of right and left laminae. The functional significance of the transverse and spinous processes is to increase the moment arm of muscles attaching to these sites [17, 32]. The vertebral bodies have thin cortical bone and cancellous trabecular bone in vertical, oblique, and horizontal patterns [31]. This overlapping trabecular medullary structure provides great strength, but the relative lack of overlap in the anterior portion may predispose to compression fractures.

Cervical vertebrae (Fig. 3.3) bear the least weight, and their vertebral bodies are relatively narrow in AP dimension and have distinct uncinate processes at their superolateral borders, which articulate with the vertebral body above (uncovertebral joint). Vertebrae C1–C6 have bilateral foramen transversarium containing the vertebral artery (C7 has this foramen without the vertebral artery). As shown in the figure, the vertebral artery is very susceptible to injury in the anterolateral approach for cervical transforaminal injections (Fig. 3.4). The transverse processes have anterior and posterior projections for attachment of muscles, and the projections form a groove which contains the exiting spinal nerve. The cervical articular pillars are oblique to the horizontal plane and appear stacked as a column. The atlas, C1, has no vertebral body and has unique articular processes for occipital condyle and axis. The axis, C2, is most recognized by the odontoid process or dens. The occipital-atlantoaxial complex allows nodding and rotational movements: about 50 % of flexion-extension is at C0–C1, and 50 % of rotation is at C1–C2. C6 transverse process anterior tubercle is known as Chassaignac's tubercle (also known as carotid tubercle, an important landmark for stellate ganglion blocks). Vertebra C7 has a larger inferior body, a large spinous process (*vertebra prominens)*, and steeply sloping articular pillars.

The defining features of the 12 thoracic vertebrae are the costotransverse and costovertebral articulations of the ribs (Fig. 3.5). Thoracic facets are arranged in the coronal plane in a way that allows rotation and side bending.

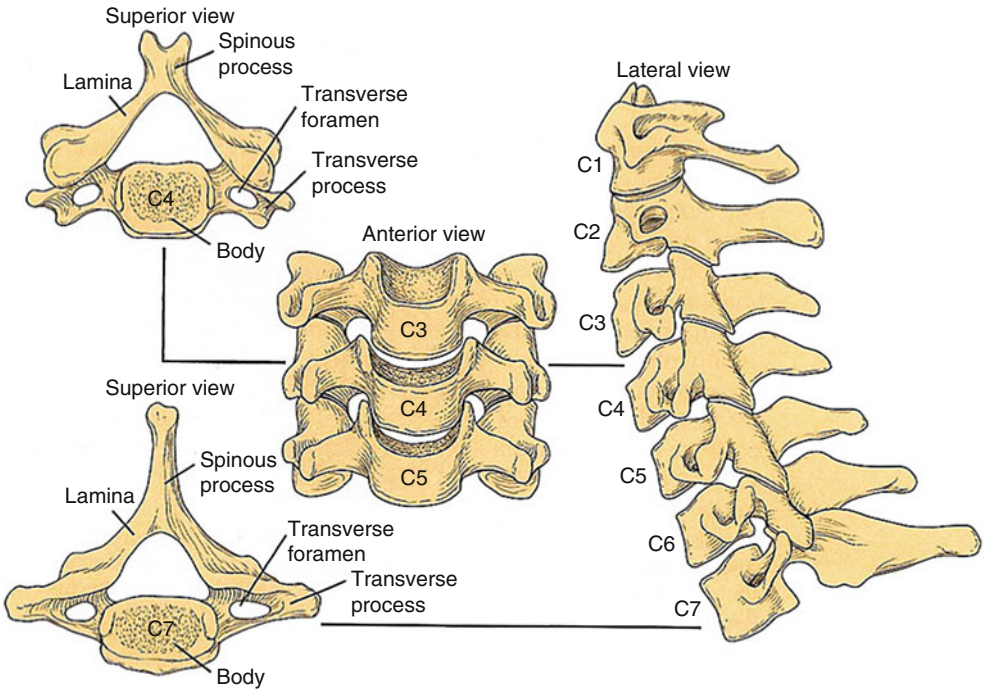

Fig. 3.3 Cervical vertebrae (Reprinted from Mathis et al. [33])

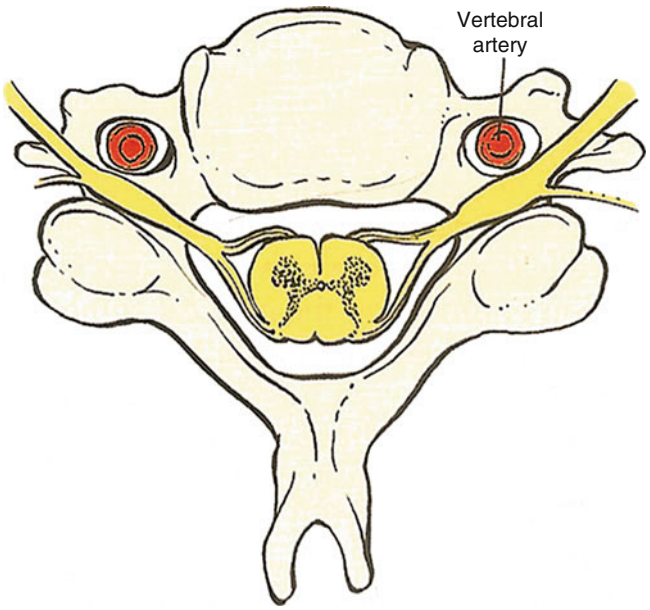

Fig. 3.4 Cervical vertebral artery (Reprinted from Mathis [26])

Typical features of lumbar vertebrae are shown (Fig. 3.6). L5 is usually largest and more wedge-shaped when viewed laterally, which allows the superior aspect of L5 to be closer to horizontal [34]. The L5 disc is also wedge-shaped, allowing 16° average angle between the respective superior and inferior surfaces of S1 and L5 [35]. L5 has thick transverse processes but has the smallest lumbar spinous process. L1 has the shortest and L3 the longest transverse processes [36]. L5–S1 facets tend to be more flat, while other levels are more curved [31]. Because L5 is angled, more of its axial load is transmitted by its posterior elements, including the transverse processes and iliolumbar ligaments [37]. The lumbar vertebral bodies have indentations in the posterior aspects of superior and inferior rims, vestigial uncinate processes that may contribute to posterolateral disc protrusions [17]. The mamillary process is an attachment site for longissimus and rotator muscles. The accessory process is thought to be a vestigial costal process and is an attachment site for longissimus muscles. The mamilloaccessory ligament joins these two processes; this structure may be an obstacle in medial branch blocks or radiofrequency ablation.

The sacrum (Fig. 3.7) is formed of five fused vertebrae and vestigial costal elements. The sacrum articulates with the ilium. The sacrum has a central canal which is the terminal portion of the spinal canal. The ventral primary rami of S1–S4 exit via anterior foramina, and the posterior rami exit the posterior foramina. The center of mass is anterior to the vertebral column in 75 % of adults, typically 2 cm anterior to S2 [31]. The sacrum is tilted forward so that the most superior sacral end plate is 50–53° from horizontal [31, 38]. The coccyx is usually four vertebrae, with the first being larger and having cornua.

Arthrology

Movements of the functional unit of the spine include flexion, extension, side bending, and rotation. The zygapophyseal joints limit motion depending on their orientation and function to protect the intervertebral discs from rotational

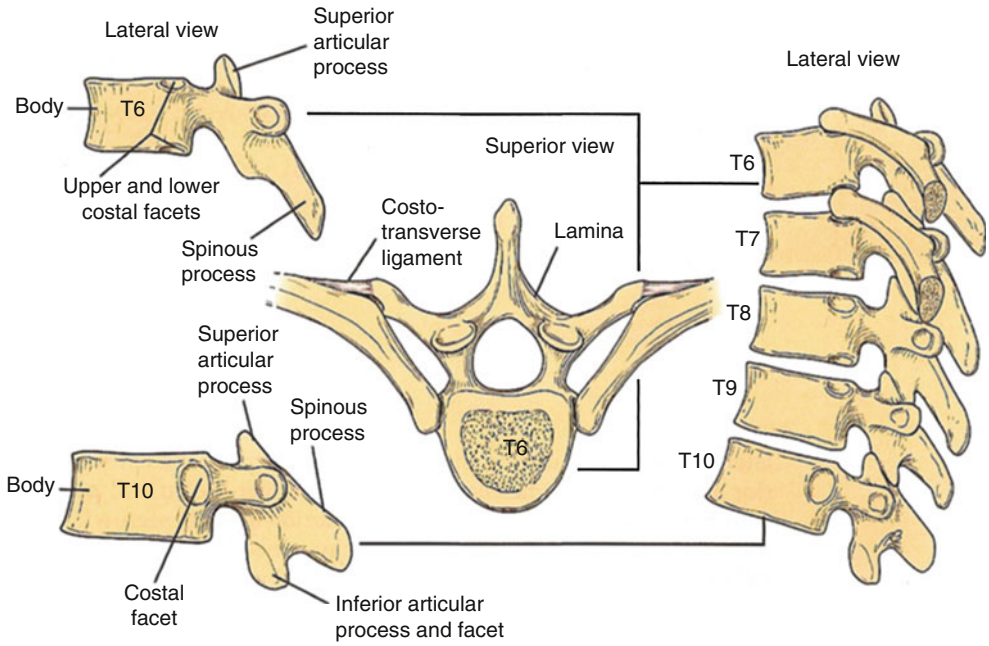

Fig. 3.5 Thoracic vertebrae (Reprinted from Mathis et al. [33])

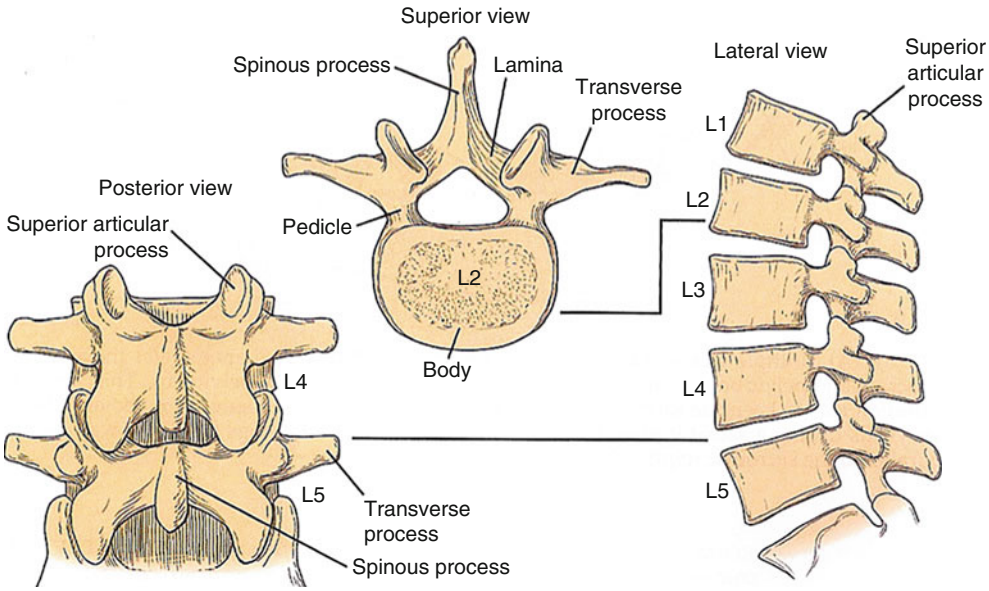

Fig. 3.6 Lumbar vertebrae (Reprinted from Mathis et al. [33])

and translational strains [36]. The cervical spine has the greatest mobility. The thoracic spine is limited by the rib cage, as well as long, overlapping spinous processes. The lumbar spine is a relatively mobile section between the less mobile thoracic and sacral sections of the spine.

A facet joint is a diarthrodial joint formed from the *superior* articular process of the more *caudal* vertebra and the *inferior* articular process of the more *cephalad* vertebra. The facet joint capsule exists at the dorsal, superior, and inferior margins and consists of the ligamentum flavum itself anteriorly [31]. The superior and inferior aspects of the joint capsule have loose pockets, subcapsular recesses that contain fat. Facet joints contain hyaline cartilage and *meniscoid* structures: fibroadipose meniscoids, adipose tissue pads, and connective tissue rims [17, 31, 39].

Facet joints have been known to cause pain since Goldwaithe's report in 1911 [40]. Ghormley coined the term "facet syndrome" to describe lumbosacral pain in 1933. Mooney and Robertson demonstrated referred pain from facet joints [41]. Lumbar facet joints bear about 20 % of the axial load and 40 % of the torsional and shear strength (as a pair). Recalling the tripod model, if the intervertebral disc is

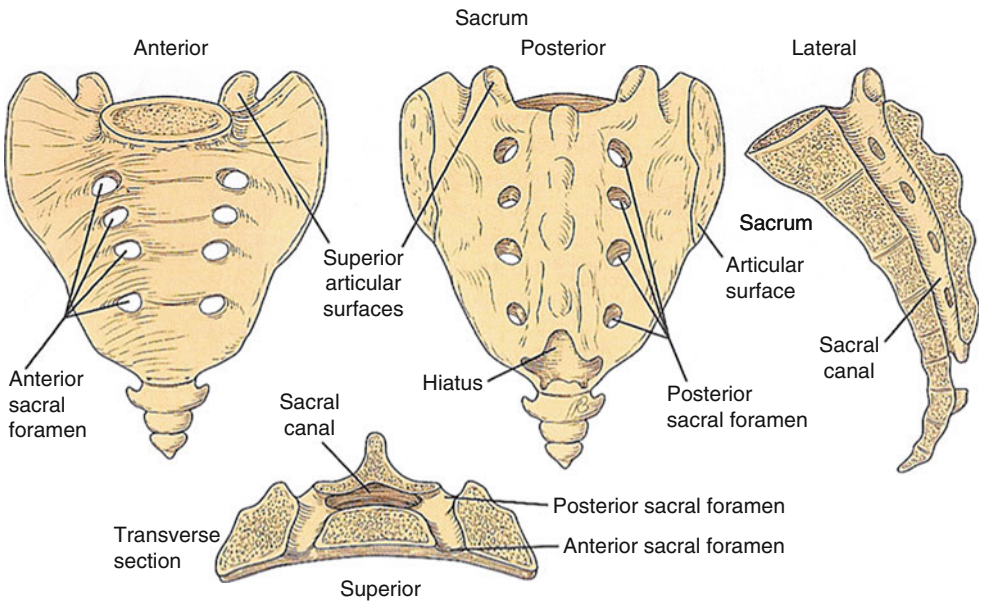

Fig. 3.7 Sacrum (Reprinted from Mathis et al. [33])

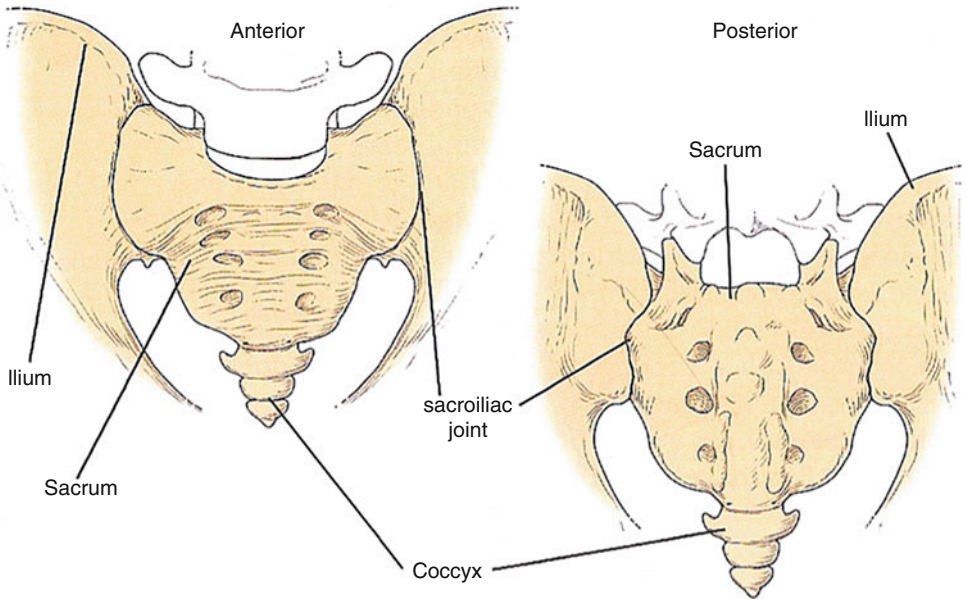

Fig. 3.8 Sacroiliac joint (Reprinted from Mathis et al. [33])

degenerated, the facets may bear up to 70 % of the axial load in that segment. They also bear more axial load with increased lumbar lordosis [27, 42]. Cervical and thoracic facet joints are also pain generators.

The sacroiliac joints consist of a C-shaped synovial portion and a syndesmosis portion (Fig. 3.8). The articular surface of the ilium is fibrocartilage, while the sacrum is hyaline cartilage that is much thicker [43]. Normal motion is slight, 2–3° in the transverse or longitudinal planes. *Nutation* (nodding) is the rotation of the sacrum that causes forward tilting in relation to the ilium. *Counternutation* is the opposite movement, where the sacrum tilts posteriorly in relation to the ilium [27]. The sacroiliac joints can also be a source of pain.

Brief mention is warranted that other spine joints are sometimes considered pain generators: atlantooccipital, atlantoaxial, uncovertebral, costotransverse, and costovertebral, have all been described as sources of pain. A transitional lumbosacral junction may have an *assimilation joint*, wherein a large L5 transverse process articulates with the sacrum. A pars defect may form a pseudoarthrosis that can be painful.

Intervertebral Disc: A Special Joint

Mixter and Barr, respectively, from the neurosurgery and orthopedic surgery services of Massachusetts General Hospital, are often cited as the first to recognize the importance of intervertebral disc herniations, although Mixter and Barr themselves cite several prior reports [44]. Although the intervertebral disc has been compared to a diarthrodial joint, it is correctly classified as a symphysis, a major cartilaginous synarthrosis [45]. Adjacent vertebral levels are separated by an intervertebral disc (except at C0–C1 and C1–C2). The functions of the disc are to distribute force and allow movement between adjacent vertebral bodies and to hold the vertebral bodies together. The discs also comprise 20–25 % of the total length of the spine, separating the vertebrae, allowing nerve roots and vessels to travel between vertebrae [27].

The intervertebral disc is the largest avascular structure in the body [46]. Each disc contains superior and inferior cartilaginous end plates, anulus fibrosus, and nucleus pulposus. Nucleus pulposus is 70–90 % water, variable with age, and proteoglycans are the majority of the remainder. Type II collagen fibers join with proteoglycans, forming the matrix of the nucleus. Embedded in the proteoglycans, toward the end plate regions, are chondrocytes that synthesize the substance of the nucleus.

The nucleus pulposus functions to bear weight and distribute forces across vertebral segments. The healthy nucleus distributes load very evenly, in a manner as a fluid, according to Pascal's law, a mechanism that dissipates force and prevents injury [32]. With age, the glycosaminoglycan and water content of the nucleus decrease, and the fibrocartilaginous content increases. This transfers load bearing to the anulus and other structures.

The anulus fibrosus is the external ring of the disc and is formed by 10–20 sheets of parallel collagen fibers (lamellae), each sheet having fibers oriented in alternating directions 30–70° from vertical. The anulus is mostly water (60 %). Collagen is half of the remaining portion. The anulus can be divided into three zones: the outer zone is made of fibrocartilaginous Sharpey's fibers that attach to the vertebral body. The intermediate and inner zones are also fibrocartilage, but do not attach to the vertebral body. The posterolateral fibers of the lumbar anulus are most prone to injury and degeneration. While the posterocentral disc may be protected by attachments of posterior longitudinal ligament, there are no extrinsic ligament attachments to support the posterolateral disc [47]. The lumbar posterior anulus is thinner radially due to the eccentric location of the nucleus. It is also longitudinally thinner, due to the lordotic curve of the lumbar spine, which means that a given amount of displacement causes relatively greater strain on these shorter fibers.

Vertebral end plates are cartilaginous structures at the superior and inferior aspect of each vertebral body, between the body and the disc. They are firmly attached to the disc by the collagenous fibers of the lamellae (intermediate and inner zones), which invest the fibrocartilaginous side of the end plate. Blood vessels on the surface of the vertebral bodies contact the hyaline side of the end plate, and nutrients diffuse through the end plate to the disc, a process of *imbibition [*48].

Table 3.5 Human studies on sensory innervation of intervertebral disc

Reference	Finding
Roofe [49]	Nerve fibers in disc and adjacent PLL
Malinsky [50]	Nerve endings in lateral outer 1/3 of annulus, encapsulated and non-encapsulated
Rabischong et al. [51]	Confirmed above
Yoshizawa et al. [52]	Confirmed above
	Also reported morphology similar to other known nociceptors
Bogduk [53]	Confirmed above
Palmgren et al. [54], Ashton et al. [55]	Immunohistochemical studies demonstrating sensory and autonomic fibers in the annulus

Several studies have confirmed nerve fibers in the outer portions of the anulus fibrosus, especially the posterolateral disc, likely rendering the disc capable of becoming a pain generator. Disc innervation may arise from sinuvertebral nerve, ventral rami direct branches, and rami communicans (Table 3.5) [17, 49–52, 54–57].

Pressure within the disc is affected by body position. The natural lordotic posture of the lumbar spine reduces vertical pressure on the disc. Direct vertical pressure increases fluid pressure within the disc. This can even lead to herniation of nucleus pulposus through defects in the end plate, known as Schmorl's nodes [first observed by Luschka [31]]. Fluid shifts in the disc also account for the 1–2 cm decrease in height that can be observed after a day of upright posture compared to the morning [58]. Disc pressure when standing is only 35 % of pressure when seated, while lifting greatly increases disc pressure and can be estimated at ten times the weight of the object lifted, as demonstrated in Nachemson's classic study [59].

Disc herniations can be classified as *protrusion, extrusion*, or *sequestration.* A protrusion has a base wider than the greatest extent of herniation (Fig. 3.9). Nucleus material extends into the epidural space in an extrusion, and the extent of herniation may exceed the width of the base (Fig. 3.10). In a sequestration, the nucleus material has been extruded as a fragment into the epidural space and has lost continuity with the disc. For further standardized terminology for description of location and type of disc herniations, the reader is referred to "Nomenclature and Classification of Lumbar Disc Pathology. Recommendations of the Combined Task Forces of the North American Spine Society, American Society of Spine Radiology, and American Society of Neuroradiology [47]."

Ligaments of the Spine

Ligaments of the spine are detailed in Tables 3.6, 3.7, and 3.8 [17, 32]. Of great practical interest to the pain physician is the ligamentum flavum, a paired structure, running from lumbar to cervical spine, composed of highly elastic fibers. There may be a narrow gap between the right and left halves [36]. It forms the posterior boundary of the epidural space as approached between vertebral lamina and may contribute to the boundary in the intervertebral foramen. On right and left, a ligamentum flavum attaches from the superior vertebral level to the adjacent level below. Laterally, fibers of ligamentum attach to the facet articular processes and form part of the joint capsule. Lateral fibers may attach to the pedicle. The lateral fibers of ligamentum contribute to the posterior boundary of the intervertebral foramen. In the lumbar spine, ligamentum flavum may be the strongest and most elastic of spinal ligaments and resists distraction and flexion. In the lumbar spine, ligamentum flavum can be 2–3 mm thick [36]. The elasticity is important to prevent buckling of the ligament, which can compress neural structures. Buckling can occur if there is loss of intervertebral disc height. However, the ligamentum flavum is less robust in the cervical and upper thoracic spine, and its paper thinness and midline absence may affect cervical or thoracic interlaminar injections [60]. The interspinous and supraspinous ligaments are relatively weak and are often the first to be sprained [31, 61]. The iliolumbar ligament is a complex structure that begins as a muscle and becomes a ligament in the third decade and is only present in adults [31, 62].

The "false ligaments" are variably present and function more like membranes and may be encountered during injection procedures. In particular, the aforementioned mamilloaccessory ligament forms a foramen containing the medial branch nerve and is ossified in 10 % of cases [31, 53].

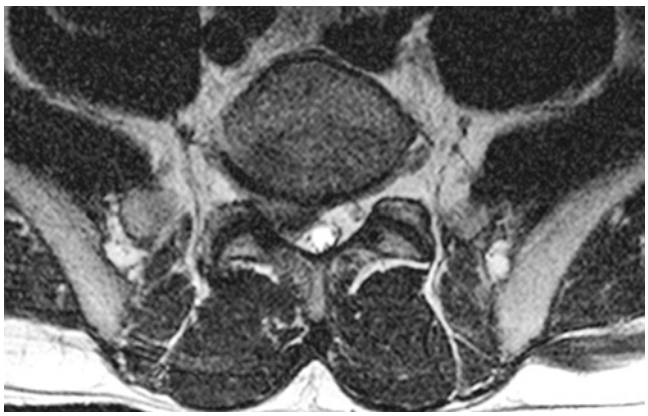

Fig. 3.9 Lumbar disc protrusion, rightward at L5–S1

Muscles of the Spine

True back muscles are comprised of four groups of extensors, innervated by posterior rami (Table 3.9). In contrast, *appendicular* or limb muscles are also located in the back, more superficially. True back muscles are dorsal, deep to thoracolumbar fascia, multilayered, and redundant, with numerous attachments, whereas ventral muscles that flex the spine may effectively cross many vertebral levels with few direct attachments [32, 46]. For example, abdominal muscles are primary forward flexors (rectus abdominis, internal and external obliques). Psoas and iliacus are weak flexors of the spine and primarily flex the hip. The quadratus lumborum is considered a posterior abdominal muscle [63]. It does act as a lateral lumbar flexor, attaching to the transverse processes [64]. Also of interest are the suboccipital muscles, including

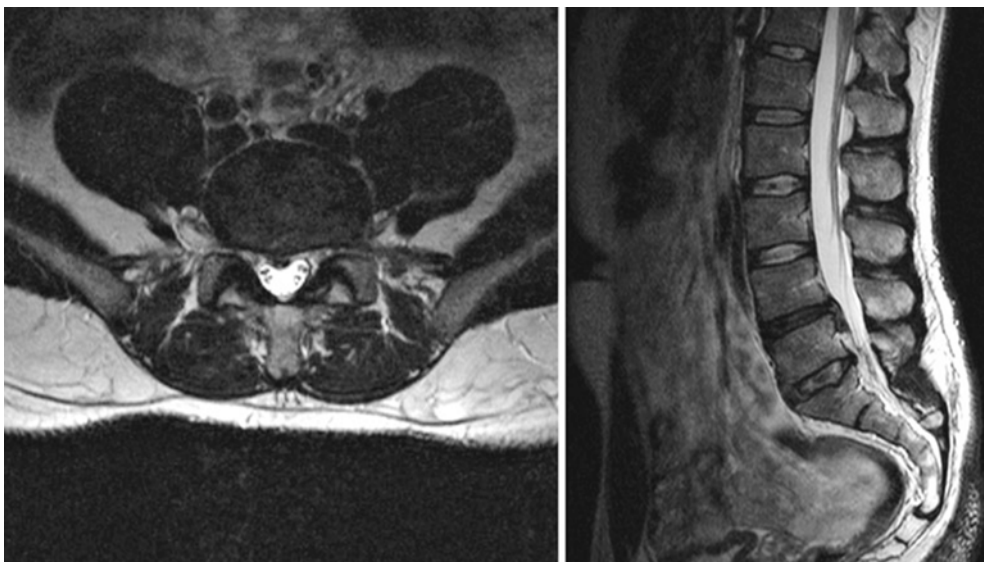

Fig. 3.10 Lumbar disc extrusion, central at L4–L5 with caudal subligamentous migration

Table 3.6 The ligaments of the spine

Ligament	Attachments	Function	Comments
Anterior longitudinal ligament	Cervical to sacral	Counters extension Stabilizes lordosis Restricts listhesis	Lumbar is most developed
Posterior longitudinal ligament	Cranium to sacrum	Resists flexion Reinforces posteromedial disc	Becomes tectorial ligament in cranium Can become ossified and cause stenosis
Ligamentum flavum	Cervical to lumbar Bifid	Resists distraction and flexion	See text
Interspinous	Adjacent spinous processes	Resists distraction and flexion	Lumbar is most developed Cervical may be absent
Supraspinous	Runs dorsally over spinous processes Terminates inferiorly at L4 in 73 %, L3 in 22 %, L5 in 5 %, is rarely at L5–S1	Resists distraction and flexion	
Iliolumbar	See separate table		
False ligaments	See separate table		

Table 3.7 The iliolumbar ligament

Portion	Origin	Insertion
Anterior	Anteroinferior border and tip of L5 transverse process	Ilium
Superior	Thickening of anterior and posterior quadratus lumborum fascia and anterosuperior L5 transverse process	Ilium
Posterior	Tip and posterior L5 transverse process	Ilium
Inferior	Lower L5 transverse process and L5 body	Superior and posterior iliac fossa
Vertical	Anteroinferior border of L5 transverse process	Iliopectineal line

Table 3.8 The false ligaments of the spine

Ligament	Attachments	Function	Comments
Intertransverse	Span adjacent pedicles	"Membranes"	Continue as middle layer of thoracodorsal fascia
Transforaminal	Variable	"Membranes"	May crowd spinal nerve
Mamilloaccessory	Mamillary and accessory processes	See text	See text

rectus capitis posterior minor and the suboccipital triangle formed by rectus capitis posterior major and obliquus capitis superior and inferior. For a complete description of specific pain referral patterns from individual muscles, the reader is referred to *Travell & Simons' Myofascial Pain and Dysfunction: The Trigger Point Manual* [22].

Table 3.9 True back muscles

Superficial to deep:	Individual muscles
Spinotransversales:	Splenius capitis
	Splenius cervicis
Erector spinae:	Iliocostalis
	Longissimus
	Spinalis
Transversospinal:	Semispinalis
	Multifidus
	Rotatores
Intersegmental:	Interspinalis
	Intertransversarius

Thoracolumbar Fascia

The anterior layer originates from anterior lumbar transverse processes and covers the quadratus lumborum. The middle layer originates from far lateral (tip) transverse processes, and the posterior layer arises from the midline. The posterior layer is an attachment site for latissimus dorsi and serratus posterior inferior. The thoracolumbar fascia layers join at the lateral border of erector spinae, where they become continuous with abdominal muscles (transversus abdominis and internal oblique). The posterior layer consists of deep fibers oriented caudo-laterally from the spinous processes and superficial fibers oriented rosto-laterally. This fiber arrangement, and continuity with abdominal muscles, allows abdominal muscle contraction to exert a force that resists spine flexion. The deep lamina of the posterior layer also functions as a series of accessory ligaments attaching the lumbar vertebrae to the ilium [65].

Spinal Canal and Foramina

The vertebral foramina are bounded by bone, including joints and ligaments. The superior boundary of the foramen is the inferior vertebral notch of the pedicle of the superior vertebra and part of the lateral-most ligamentum flavum. The inferior boundary is the superior vertebral notch of the pedicle of the inferior vertebral body. The anterior boundary includes the adjacent posterolateral vertebral bodies, that is, the inferior posterolateral part of the superior vertebral body and the superior posterolateral part of the inferior vertebral body, as well as the intervertebral disc. The anterior boundary also includes the lateral posterior longitudinal ligament and the anterior venous sinus. The posterior boundary is the pars interarticularis superiorly and facet joint inferiorly, as well as lateral ligamentum flavum. Therefore, two articulations form the boundaries of the foramen, the facet joint and the intervertebral body joint or disc; these allow the oval shape of the foramen to change with movement. The height of the disc also directly influences the size of the foramen. Proximally or medially, the foramen is bounded by dura. Especially in the lumbar spine, the foramen can be divided into three zones: the lateral recess, midzone, and exit zone [66]. The lateral recess contains the spinal nerve root that is descending to exit the next level.

In the lumbar spine, the intervertebral disc is located in the lower part of the anterior wall of the neural foramen. This is also true in the thoracic spine. However, in the cervical spine, the disc is in the middle of the anterior wall of the foramen. This relationship partly also determines which nerve is affected by disc herniations [32]. For example, a typical posterolateral disc herniation at L5–S1 will usually spare the L5 nerve root and is more likely to affect the most laterally placed nerve root in the spinal canal, which would be S1. In contrast, a C5–C6 herniation is likely to impact the exiting root, C6.

Nerve Supply to the Pain-Sensing Structures of the Spine

As the spinal nerve exits the neural foramen, it immediately divides into dorsal and ventral rami. Dorsal rami divide into medial, intermediate, and lateral branches. An exception is the L5 dorsal ramus which only divides into medial and intermediate branches. The typical medial branch nerve provides sensory innervation to two facet joints: (1) the inferior facet joint capsule that forms the posterior wall of its exiting foramen as well as (2) the superior facet joint at the next lower level. Thus, medial branch nerves are targets for treating pain from facet joints.

Table 3.10 Dorsal rami branches of lumbar spinal nerves

Lumbar dorsal rami of spinal nerve	Supplies motor innervation	Supplies sensory innervation
Medial branch	Multifidus muscle	Interspinous ligament
	Interspinalis muscle	Facet joints above and below
Intermediate branch L1–L4 only	Longissimus muscle	None
Lateral branch	Iliocostalis muscle	L1–L3: skin from iliac crest to greater trochanter

Medial branch nerve location is fairly consistent in relation to bony landmarks, which aids in targeting these nerves under fluoroscopic guidance. Medial branches of C3–C6 run across the center of the respective articular pillars, and C7 is high on the C7 superior articular process. The third occipital nerve alone innervates C2–C3 and runs directly across this joint, embedded in pericapsular fascia. Medial branches of T1–T3 and T9–T10 pass along the superolateral tip of the transverse process. Medial branches of T4–T8 pass posteriorly through the intertransverse space without contacting bone. Medial branch of T11 runs along the superior articular process of T12, and T12 medial branch follows the pattern of L1–L4. The lumbar medial branches of L1–L4 travel across the junction of the superior articular process and transverse process, then curve inferiorly and pass under the mamilloaccessory ligaments. The medial branch of L5 innervates the L5–S1 facet before it innervates the multifidus muscle. Lateral branches of dorsal rami supply longissimus, iliocostalis, and semispinalis muscles, as well as the skin over the medial two-thirds of the lumbosacral region (Table 3.10) [67].

The ventral ramus of the spinal nerve also gives rise to a somatic branch. The sympathetic trunk gives rise to the gray rami communicans. These join to form the sinuvertebral nerve, just outside the intervertebral foramen (recurrent meningeal nerve of Luschka). The sinuvertebral nerve courses medially into the foramen, dorsal to the posterior longitudinal ligament, where it sends ascending and descending branches to form a posterior plexus, providing innervation to structures adjacent to the spinal canal. These include the posterior longitudinal ligament, posterolateral disc (anulus fibrosus), ligamentum flavum, vertebral periosteum, dura, epidural fat, and local blood vessels.

An anterior nerve plexus also exists within the spinal canal, on the ventral aspect of the dura mater. It is formed by meningeal branches directly from the sinuvertebral nerve, branches from the posterior plexus, and perivascular branches. The ventral dura mater has nociceptive and autonomic innervation, whereas the posterolateral dura has little innervation. The dura has not been established as a typical

pain generator [56]. A plexus of nerves is also formed along the anterior longitudinal ligament, from gray rami communicantes. These innervate the anterolateral vertebral bodies and discs. However, most of this innervation consists of autonomic fibers, and these structures have not been established as typical pain generators [56].

Spinal Cord, Nerve Roots, Ganglia

The conus medullaris is the terminal portion of the spinal cord. In the adult, this terminal portion is typically at L1–L2. In the lumbar spine, the lumbar and sacral nerve roots form the cauda equina, an intrathecal structure. Dura and arachnoid form the epineurium of the spinal nerve as the nerve exits the foramen.

The spinal nerve proper exists only within the intervertebral foramen, where it is formed as dorsal and ventral roots from the spinal cord converge. The dorsal roots contain sensory afferent fibers. The dorsal root ganglion containing the cell bodies of these fibers lies within the upper medial intervertebral foramen. The ventral roots contain efferent motor and a few sensory fibers. The ventral roots of T1–L2 contain preganglionic sympathetic efferent fibers. The dorsal and ventral roots leave the thecal sac one level superior to their foraminal exit level, and they travel in the radicular canal, within an extension of dural sheath. This dural sheath is attached by fibrous bands near its origin to the periosteum of the pedicle under which the nerve will exit. The nerve roots pass through the lateral recess of the foramen, formed by an osseous groove in the base of the pedicle. Just distal to the dorsal root ganglion, within the neural foramen, the dorsal and ventral roots merge to form the spinal nerve. A fibrous band anchors the spinal nerve to the superior and inferior pedicle as it exits the foramen. As the spinal nerve exits the neural foramen, it immediately divides into dorsal and ventral rami.

Vascular Structures of the Spine

Of particular interest are the blood vessels that can be encountered during interventional spine procedures. The vertebral artery, deep cervical, and ascending cervical arteries can be injured with devastating result in the cervical transforaminal approach [68–70]. Other chapters describe atlantooccipital and atlantoaxial injections, which can also lead to vertebral artery injury. The spinal segmental arteries travel proximally along the path of the spinal nerve, into the foramen, to supply the spinal cord. The presence of spinal segmental arteries is variable. A large conjoined spinal segmental artery, the artery of Adamkiewicz, may enter any level from T7 to L4, but in 80 %, it enters on the left between T9 and L1 [71]. A more recent study of 120 radiculomedullary arteries revealed all between T2 and L3, with 98 % between T8 and L1, and 83 % on the left side, and often in the superior aspect of the foramen [72]. Spinal cord injury related to vascular insult is known to have occurred as low as S1 [73]. Vascular uptake has been reported in cervical interlaminar injections [74].

Spinal Cord Topology

The spinal cord is the conduit of pain of all types, so brief mention is made here of spinal cord topology. Other chapters will have more about receptor targets in the spinal cord. Targeting the spinal cord with treatment modalities can treat many types of pain, such as acute pain of labor, to the more chronic neuropathic and sympathetic pain syndromes. Melzack and Wall described the dorsal horn as the gate through which pain signals pass [75]. For example, spinal cord stimulation may work by stimulation of these dorsal columns, resulting in reduced activity of wide dynamic range neurons [76, 77]. Other chapters will describe spinal cord stimulation in more detail.

Spine Imaging

Choice of spine imaging involves consideration of several questions. How will information provided by imaging affect clinical decision making? What structure(s) needs to be visualized? Are there adverse effects or contraindications associated with obtaining the imaging? Are there "red flags" of a potential, more ominous condition, which might prompt more aggressive investigation? (Table 3.4) Described below are the most common imaging modalities encountered in the pain clinic, that is, X-rays, CT, MRI, and bone scans. The figures illustrate "fairly unremarkable" CT and MRI of the cervical and lumbar regions (Figs. 3.11, 3.12, and 3.13). Finally, several figures are used to illustrate important pain-related spine disorders (Figs. 3.14, 3.15, and 3.16). Other chapters will describe imaging modalities including fluoroscopy, provocative discography, and epiduroscopy. Relative sensitivities and specificities of patient history, X-ray, CT, and MRI are compared for spine conditions in Table 3.11 [79].

Radiographs, X-Rays

In patients with red flags suggestive of fracture, radiographs may be an acceptable, inexpensive initial choice. Fracture acuity typically cannot be judged by radiographs alone. Facet, sacroiliac, and intervertebral disc (disc space height and end plate changes) degenerative changes can be seen. Flexion-extension views may demonstrate instability at a

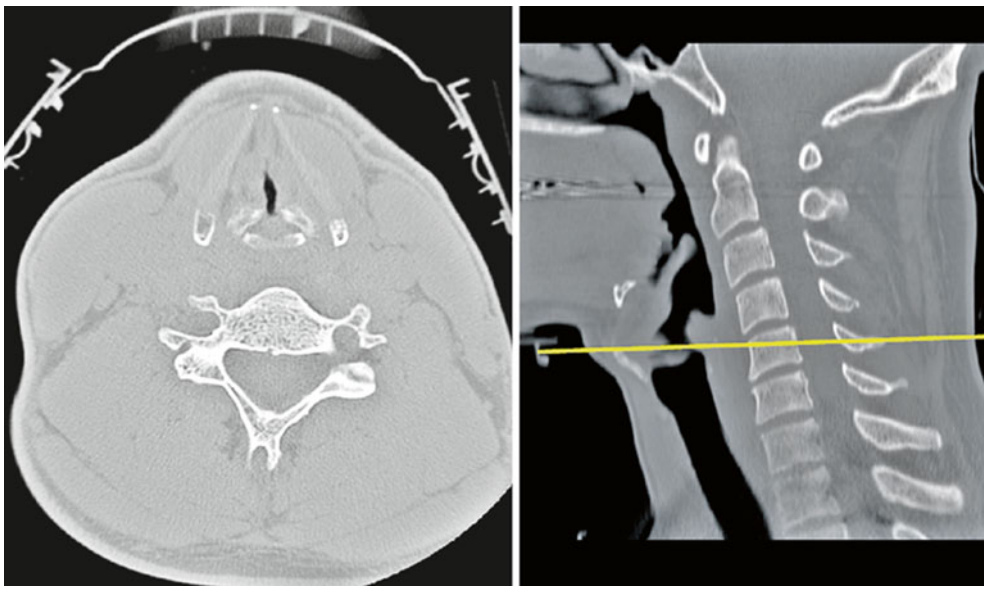

Fig. 3.11 Cervical CT and MRI. These images are relatively unremarkable studies from the same subject, comparing the appearance of the same structure on both CT and T2 MRI

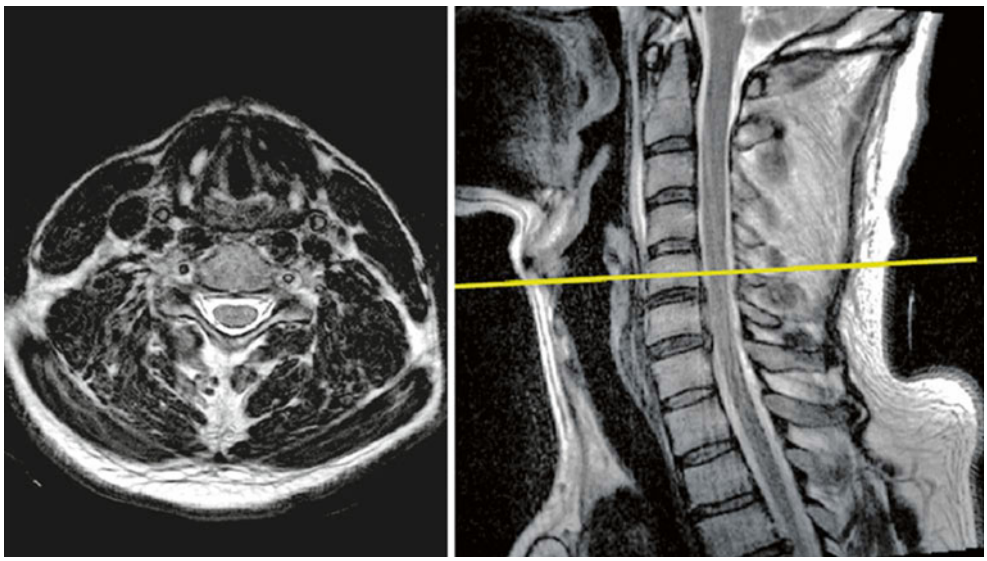

Fig. 3.12 Cervical CT and MRI. These images are relatively unremarkable studies from the same subject, comparing the appearance of the same structure on both CT and T2 MRI

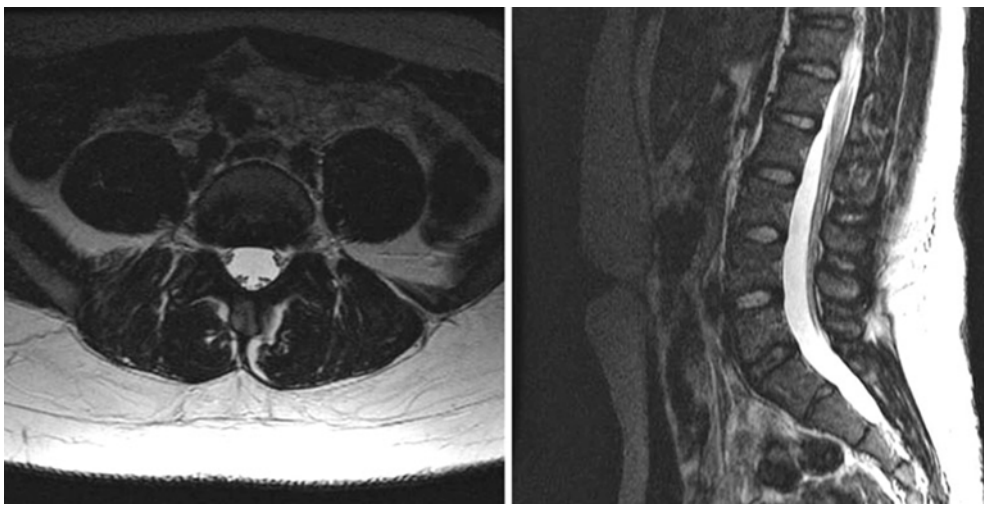

Fig. 3.13 Lumbar MRI. This unremarkable T2 MRI reveals normal disc hydration and height and no herniations or facet degeneration

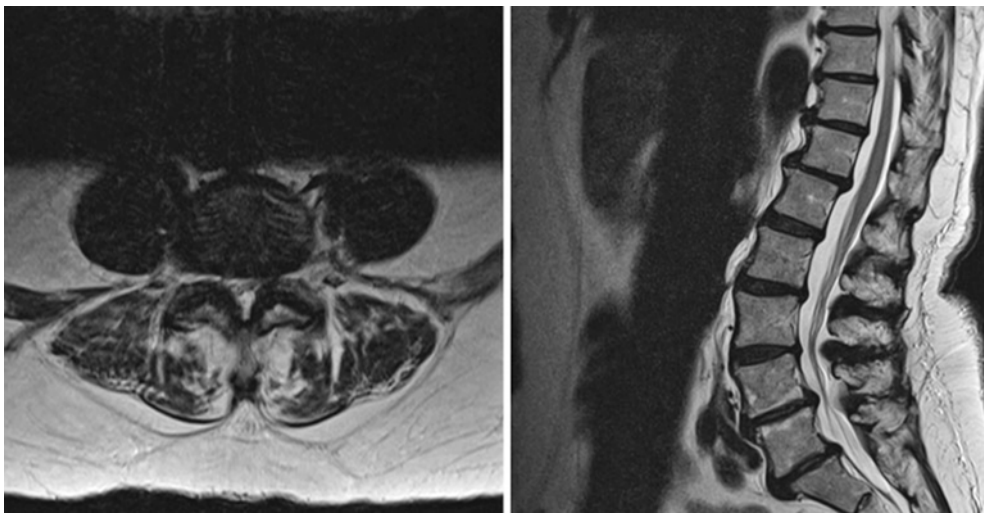

Fig. 3.14 Stenosis: L4–L5 disc degeneration, facet hypertrophy, ligamentum flavum hypertrophy, and central stenosis. There is also grade I anterolisthesis of L5 on S1

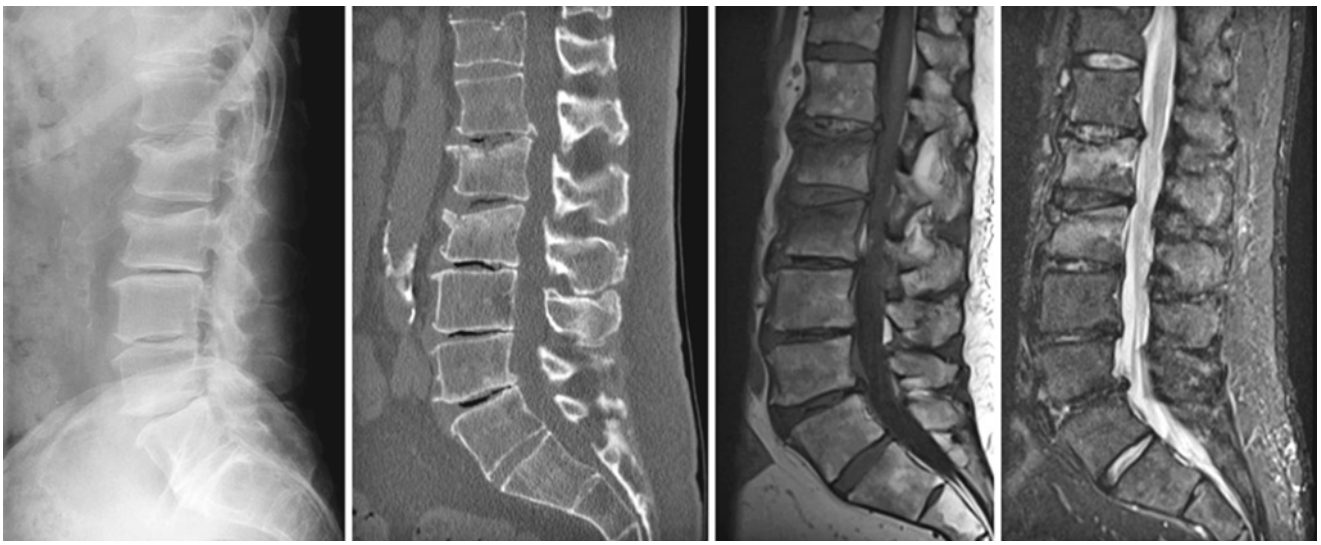

Fig. 3.15 Vertebral compression fractures. The same L1 and L2 compression fractures are seen on radiograph, CT, T1 MRI, and STIR MRI

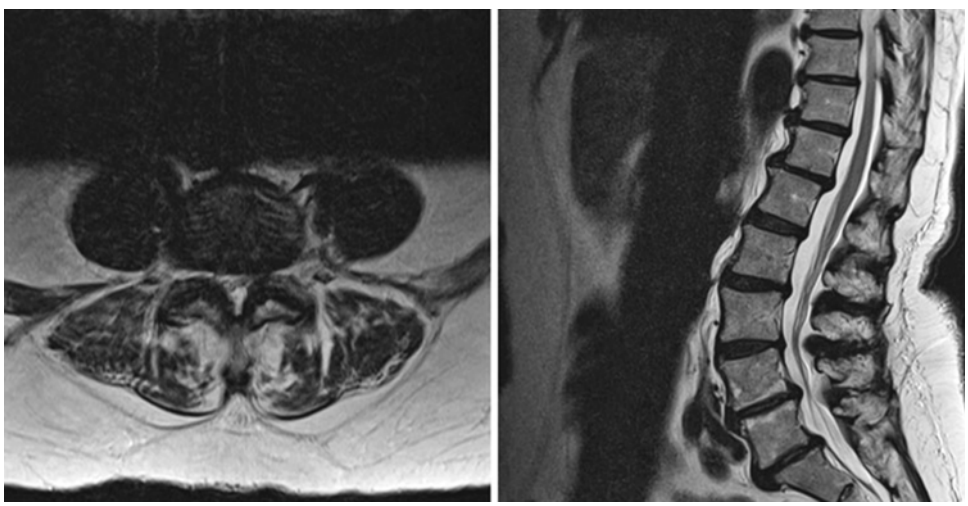

Fig. 3.16 Osteomyelitis. T1 MRI with gadolinium contrast shows bright enhancement in L1, L2 and disc, with destruction of end plates, in a patient with osteomyelitis (Reprinted from Yang et al. [78])

Table 3.11 Comparison of history, exam, radiography, CT, and MRI

Condition	History sensitivity/specificity	Radiograph sensitivity/specificity	CT sensitivity/specificity	MRI sensitivity/specificity
Cancer	No relief with bed rest >0.90, 0.46	0.60, 0.95–0.995		0.83–0.93, 0.90–0.97
Osteomyelitis	IVDA or infection 0.40, NA	0.82, 0.57		0.96, 0.92
Compression fracture	Age 50 or more 0.84, 0.61			
Herniated disc	Sciatica 0.95, 0.98		0.62–0.90, 0.70–0.87	0.6–1.0, 0.43–0.97
Stenosis	Age >65 0.77, 0.69		0.90, 0.80–0.96	0.9, 0.72–1.0

Modified from Jarvik and Deyo [79]

segment with listhesis. Pars defects may be seen readily on lateral and oblique views. Oblique views may also demonstrate encroachment of nerve pathways. Radiographs are often used to assess spinal curvatures. Radiographs demonstrate radiopaque implants such as fusion devices or spinal cord stimulators. Radiographs do carry risk of general and gonadal radiation exposure.

Computed Tomography

Computed tomography, or CT, uses X-rays to obtain images and is a superior modality when compared to MRI for observing bony cortex and trabeculae, but CT can also be used for soft tissue. For example, pre-procedure planning for kyphoplasty often includes CT to look for any fractures in the relatively anhydrous bony cortex, not visualized on MRI. CT can be a good imaging modality for patients with ferromagnetic implants that are not compatible with MRI. Modern helical multislice acquisition CT is very fast and thus does not require prolonged immobilization. Such CT acquisitions can be reconstructed to give images in multiple planes. Claustrophobia or morbid obesity is not typically problems preventing CT. Risks involve exposure to radiation (and may involve exposure to contrast, if used to detect abscess or tumor).

CT Myelography

Myelography carries risk as it is an invasive procedure involving lumbar puncture and injection of contrast, in addition to radiation exposure. Diagnosis is made by observing disruption of the contrast flow pattern. Therefore, the study does not give specific information about the cause of contrast flow alteration. Myelography may not visualize the lateral recesses. It may be useful in assessing the postoperative spine with metallic implants. CT myelogram outlines the cervical foramina with better resolution than MRI.

Magnetic Resonance Imaging

For most painful spine disorders, MRI is the best imaging modality to view soft tissue, discs, marrow, and nerves. MRI detects inflammation and edema and thus can detect acuity of spinal fractures. In MRI, the subject is placed in a very strong magnetic field, thereby aligning protons (hydrogen nuclei). The subject is then bombarded with various radio pulse sequences, and resonance of the hydrogen nuclei creates images. MRI "sees" proton density, which is essentially the amount of water in tissue. There are numerous types of sequence variations such as T1, T2, STIR (short tau inversion recovery), and various fat suppression techniques. Gadolinium contrast is bright on T1 images. The reader is directed to the ACR publication on contrast agents for more about the increasingly understood systemic risks of MRI contrast in the setting of renal disease (such as nephrogenic systemic fibrosis) [80]. There are no known risks from the MRI mechanism itself. MRI is contraindicated with certain metallic implants such as aneurysm clips or foreign bodies in the orbit. Claustrophobia is a common concern with MRI. Bony cortex does not show well on MRI.

Bone Scans, Scintigraphy, SPECT

This test involves injection of a radioactive substance such as Tc-methylene diphosphonate. Whole-body imaging is then performed via radiation detection. This method is useful in surveying the whole body for metabolically abnormal areas of skeleton. It has poor resolution and abnormal findings are nonspecific. The test takes many hours.

SPECT is a combined CT with single positron emission (SPE) tomography. The term "bone scan" is sometimes used to refer to SPECT. This modality increases the sensitivity and anatomic localization of spine and skeletal lesions. SPECT may have an increasing role in the imaging of spondylolysis [81].

Future Directions

Discogram

Discography, always controversial, is falling out of favor again, as it is well understood that confounds make this a flawed test, and risks, including now-established long-term risk of accelerated disc degeneration, are great compared with potential benefits [82]. Other chapters will provide more detail on discography.

Bone Mineral Density

Pain physicians are often medical spine experts and may be in the best position to initiate investigation and management of osteoporosis, the most common bone disease. In our facility, patients are screened, if not previously done, if a spine fracture is found or if they meet criteria established by the National Osteoporosis Foundation [83].

Ultrasound

Interest in ultrasound for intervention and diagnosis of musculoskeletal and pain conditions has exploded in the last few years [84, 85]. However, let us not forget so soon the widespread advocacy and abuse of diagnostic spine ultrasound in the 1990s [86, 87]. A prospective study found that paraspinal ultrasound is not accurate or reproducible in evaluating patients with cervical and lumbar back pain [87]. Several ultrasound-guided spine interventions have been described, including medial branch blocks, third occipital nerve blocks, and cervical epidural injections [88–92].

Conclusion

> Forasmuch as we have previously set down almost everything which concerns the lumbar vertebrae and have no wish to prolong the description of them unnecessarily, we shall offer a brief summary…. Vesalius [93]

The spine holds great significance in the human experience, as a foundation for movement and strength, as a leading cause of suffering, and as an eternal symbol of each. This chapter has introduced concepts of spine anatomy and imaging. To gain an even more advanced understanding of functional anatomy, the reader is urged to refer to the cited literature and to explore the embryological development of the spine, as well as gain awareness of *kinesiology*, the all-encompassing study of human movement*; kinetics*, the study of the forces involved in the movements of the body; and *kinematics*, the study of the positions and motions of body structures [94, 95]. Through this knowledge, pain physicians become the doctors of the spine, best suited to understand and apply information from advanced imaging. One day, there may be an imaging test for pain itself, and doctors then will look back at our RF with amusement, much as we recall the hot poker of Hippocrates. If they still be physicians, they will remember: *primum non nocere.*

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Part II

Neural Blockade and Neurolysis Blocks

Local Anesthetics

4

Michael S. Leong and B. Todd Sitzman

Key Points

- To describe local anesthetic pharmacology, types (amides, esters), and mechanism of action
- Typical dosages and local anesthetic used in clinical practice
- Common side effects from local anesthetics

Background

Local anesthetics in clinically appropriate concentrations will act on any part of the nervous system and on every type of nerve fiber to block conduction in a reversible manner without damage to nerve fibers or cells. This reversibility of action creates significant utility in diagnostic and therapeutic procedures. Local anesthetics (LAs) may abolish sensation in various parts of the body by topical application, injection in the vicinity of peripheral nerve endings and along major nerve trunks, or instillation within the epidural or subarachnoid space. The ensuing sensory block occurs locally and spreads to areas distal along the nerve pathway (Figs. 4.1 and 4.2).

Local anesthetics are composed of an acyl or aromatic group connected to an alkyl tertiary amine group by either an ester or amide bond. *Classification* into two groups is based on this bond which determines metabolic pathways. For the amino-ester LAs, there is relatively rapid breakdown by plasma cholinesterase to a common metabolite, para-aminobenzoic acid (PABA), with the exception of cocaine and articaine which have alternate metabolic pathways. Amino-amide LAs are metabolized by the cytochrome P450 system and conjugation as a route to elimination.

Thus, briefly, all local anesthetics have similar structures with an aromatic benzene ring and an amino group connected by a linkage. This linkage is either an amide or ester. All amide local anesthetics have an "I" in their generic name before "caine": lidocaine, bupivacaine, and ropivacaine. The other local anesthetics are esters: procaine and chloroprocaine. Local anesthetics block Na+ channels and stop nerve conduction of impulses.

Alkyl substitutions on LA increase the lipid solubility. The *potency* of LAs has been shown to be directly related to lipophilicity and is often expressed as the octanol-water partition coefficient.

All LAs are weak acids as quaternary amines and are positively charged. As tertiary amines, they are weak bases and uncharged. They must be in their lipophilic base form to access their site of action on the Na+ channel. The pKa of the LA and pH at the site of injection (usually physiologic pH of 7.4 but can be locally altered, e.g., in areas of infection) influence the amount of LA in base form and the *speed of onset* of block. The addition of bicarbonate to a solution to increase the pH and speed of onset can be done to epinephrine-containing LAs that are adjusted to an acidic pH for stability in commercial preparations. In general, the lower the pKa the LA has, the faster the onset. Other factors influencing the speed of onset include the concentration and amount of LA used and the anatomic location of injection or application.

LAs prevent generation and conduction of the nerve impulse by blocking voltage-gated Na+ channels within the cell membrane. This reduces or prevents the transient increase in Na+ permeability needed for depolarization and propagation of a nerve impulse. Not all nerve fibers are equally sensitive to block. A *differential sensitivity* to block is seen when

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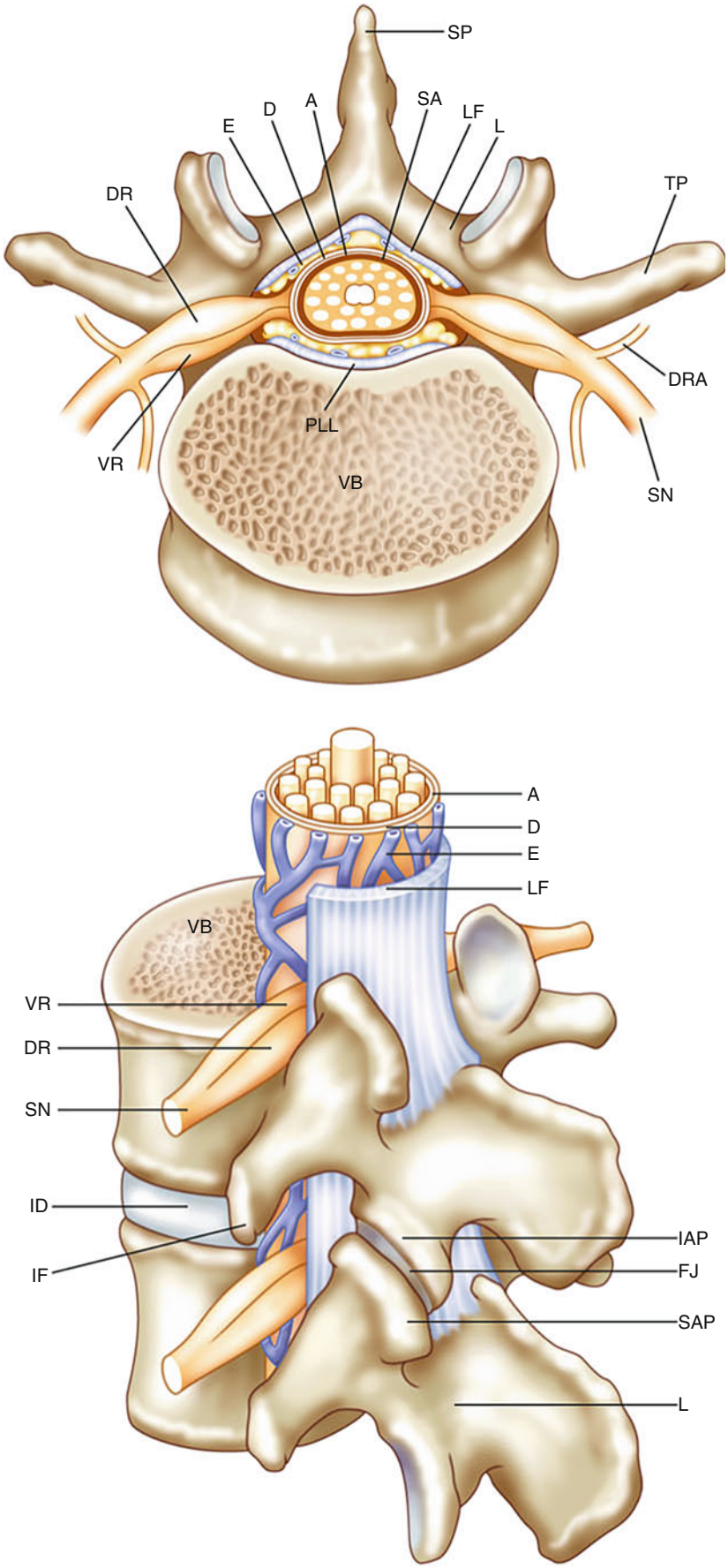

Fig. 4.1 Local anesthetics may abolish sensation in various parts of the body by topical application, injection in the vicinity of peripheral nerve endings and along major nerve trunks, or instillation within the epidural or subarachnoid space. The ensuing sensory block occurs locally and spreads to areas distal along the nerve pathway

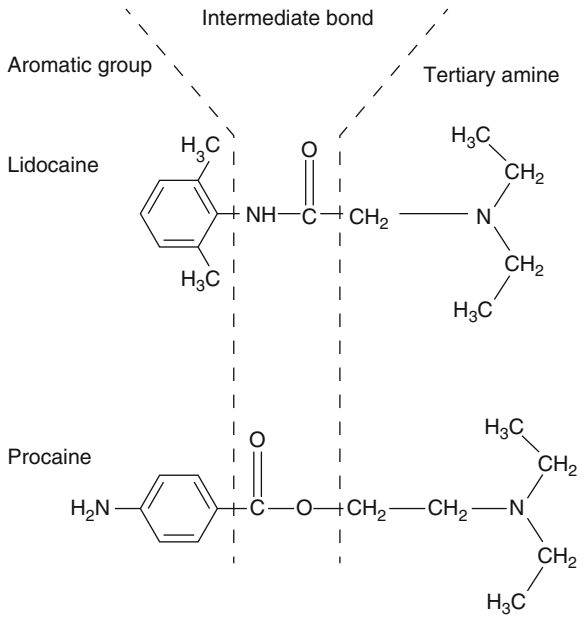

Fig. 4.2 Chemical composition and classification

the concentration of a LA is sufficient to block some nerve fiber types but not others. Clinically, small unmyelinated C fibers, autonomic fibers, and small myelinated A delta fibers (pain and temperature) are more sensitive than larger myelinated A gamma, A beta, and A alpha fibers (motor, proprioception, touch, and pressure). This differential sensitivity is of significant use in accomplishing pain or autonomic blockade without necessarily effecting motor block. LAs exhibit differences in their ability to provide differential sensitivity, and bupivacaine has been used for this capability since its introduction in 1963. More recently, ropivacaine is stated to be more motor sparing than bupivacaine with less cardiotoxicity at equipotent doses [1–3]. Interestingly, nearly the opposite differential sensitivity is seen with nerve in vitro studies. The reason for this is not known but thought to be due to phase block, which is the phenomenon that nerves that are frequently firing are more easily blocked, and anatomic considerations in nerve bundles.

A frequent consideration in the selection of a local anesthetic is *the duration of action*. There are multiple factors that determine duration of action. Increased lipid solubility of a particular agent generally increases its duration of action. As previously stated, the rate of metabolism can be a factor (e.g., amino-ester LAs). Generally, the speed of uptake and/or elimination from the site of deposition, which is also dependent on tissue perfusion, influences the duration of action. Perfusion of course is dependent on anatomic location (parauterine > intercostal > epidural > peripheral nerve > intrathecal) and sometimes is purposely manipulated by the addition of vasoconstrictors to decrease perfusion and uptake and thus prolong block.

Mixtures of LAs to produce quick onset and/or a prolonged duration have been intermittently advocated. The results of this practice are varied, controversial, and depend on the location of utilization and the particular LAs used. There is some evidence to suggest that peripheral nerve block with bupivacaine/lidocaine or ropivacaine/lidocaine versus bupivacaine or ropivacaine alone provides a quicker onset but shorter duration of action [4]. Studies on epidural use suggest no significant difference when used in combination in terms of speed of onset or change in duration of action [5, 6]. Benefits in terms of reduced toxicity have not been elucidated. Toxicity is presumed to be additive when considering the maximum doses of more than one agent, see Table 4.1.

The important properties of LAs including potency, speed of onset, duration of action, differential block, and toxicity are dependent on the physiochemical properties of a LA as well as the way that it is used. The practitioner must become familiar with the LAs available, their individual properties, and utility. At this time, the most frequently used include lidocaine, bupivacaine, and ropivacaine.

Lidocaine is typically administered in 0.5–2 % concentrations or 5 % as a topical gel. The onset of action is approximately 5 min, with a 1–2-h duration without epinephrine. The maximal safe dose is 3 mg/kg or about 250 mg without epinephrine. With epinephrine, the safe dosage increases to 7 mg/kg or about 500 mg. Bicarbonating 0.5 % lidocaine will decrease initial pain of injection site pain.

Bupivacaine has a slower onset of action of 5–10 min but longer duration of action 3–6 h. Typical concentrations used are 0.25–0.75 % without epinephrine. A maximal safe dose is 150 mg without epinephrine. Bupivacaine is highly cardiotoxic, so ropivacaine, a chiral version of bupivacaine, is sometimes used in its place particularly for higher volume injections. Ropivacaine has concentrations from 0.2 to 1 % and a maximal safe dose of 300 mg, which is less cardiotoxic than bupivacaine.

One of the authors has received many calls from other physicians about patients with "lidocaine" allergies. Other than skin testing, the best option is avoid amide local anesthetics and use an ester: chloroprocaine.

2-chloroprocaine is a rapid-onset local anesthetic similar to lidocaine. It works within 5 min and has a duration of 30–60 min. Moreover, it is the most rapidly metabolized local anesthetic in use. Prior concerns existed over reports of spinal toxicity when administered into the epidural space. New formulations have had the prior EDTA removed which may have caused paraspinal spasms in the past [7]. Chloroprocaine may not be used if the patient reports an allergy to suntan lotion that contains benzocaine, a topical ester local anesthetic.

Table 4.1 Infiltration anesthesia

	Plain solution			Epinephrine-containing solution	
Drug	Concentration (%)	Max dose (mg)	Duration (min)	Max dose (mg)	Duration (min)
Short duration					
Procaine	1–2	500	20–30	600	30–45
Chloroprocaine	1–2	800	15–30	1,000	30
Moderate duration					
Lidocaine	0.5–1	300	30–60	500	120
Mepivacaine	0.5–1	300	45–90	500	120
Prilocaine	0.5–1	350	30–90	550	120
Long duration					
Bupivacaine	0.25–0.5	175	120–240	200	180–240
Ropivacaine	0.2–0.5	200	120–240	250	180–240

Adverse Reactions

Probably, the most common reactions are *autonomic responses* or anticipatory reactions to medical procedures. These include tachycardia, sweating, hypotension, and syncope. They are characteristically short-lived with resolution in minutes requiring no treatment or can be treated with muscarinic blockers or ephedrine.

Another common reaction is the response to vasoconstrictor additives, usually *epinephrine* which is either inadvertently injected intravascular or rapidly absorbed. Symptomatically, this produces tachycardia, hypertension, and anxiety or feelings of doom. If injected peri- or intra-arterial, it can produce distal ischemia from arterial spasm. This can produce serious complications from organ ischemia.

Local anesthetics can cause *local and systemic toxicity*. LAs used in highly concentrated solutions may be neurotoxic. Local toxicity can also occur with intraneural injections even with normal concentrations.

Systemic toxicity is estimated to occur with an incidence of 7–20/10,000 for peripheral nerve blocks and 4/10,000 for epidural blocks [8, 9]. Toxic levels usually occur due to excessive dose, intravascular injection or other reasons for unanticipated rapid absorption, predisposing medical conditions (e.g., seizure disorder), or difficulties with metabolism or elimination. Usually, systemic toxicity results first in central nervous system then cardiovascular effects, but this obviously depends on the rate of increase in blood concentration as well as the individual patient's comorbidities. CNS symptoms consist of metallic taste, perioral numbness, dizziness, muscle twitching, and ultimately generalized seizures. Toxic cardiovascular effects include arrhythmias, cardiac depression, vasodilation, hypotension, and cardiac arrest/collapse. The potent lipophilic LAs are more cardiotoxic, and resuscitation is known to be difficult using usual resuscitation efforts and medications [2]. The use of 20 % intralipid has been shown to be effective for resuscitation from bupivacaine-induced cardiac toxicity [8–10]. The mechanism is uncertain but believed to be by extraction of the lipophilic LAs. There is evidence that it is more effective for bupivacaine and levobupivacaine than ropivacaine which is less lipophilic [10, 11], A published regimen consists of 20 % intralipid with a bolus of 1.2–2.0 ml/kg followed by infusion of 0.25–0.5 ml/kg. However, optimal dose has not been established [8].

Allergic reactions to LAs are relatively rare, constituting less than 1 % of adverse reactions [12, 13]. The majority of these allergic reactions are due to PABA from amino-ester LAs. PABA is a common metabolite of this class; there is near-complete cross-reactivity of allergy within this class of LA. Amino-amide LAs are exceedingly rarely responsible for allergic reactions, and because of their varying metabolic products, they do not have predictable allergic cross-reactivity. Paraben preservatives are structurally very similar to PABA and can show allergic cross-reactivity to amino-ester LAs. The commonest allergic reactions are delayed (24 h to a week) minor cutaneous rashes. These are generally self-limited and treated with antihistamines and topical corticosteroids. Of note is the possibility of allergic cross-reactivity to bisulfite preservatives in patients with known food allergies and to paraben preservatives in patients with sulfa antibiotic allergy.

Most local anesthetic allergies are to amide local anesthetic compounds, such as lidocaine or bupivacaine. Some patients also describe an allergy from a combination of the above agents mixed with epinephrine. Often, the epinephrine in the prior event was absorbed intravascularly causing an increase in heart rate.

An alternative to using amide local anesthetics are esters: chloroprocaine or procaine. The main question to ask is whether the patient had a "true" allergic reaction with skin rash, throat tightness, and difficulty breathing or swallowing. Moreover, if the patient has a rash to benzocaine, a common ester local anesthetic in suntan lotions, they may be allergic to esters. Typically, patients are allergic to one chemical

structure of local anesthetic: amides or esters, so the other class may be dosed during procedures.

Intrathecal administration of LAs or *spinal block* can cause dense and widespread block. Spinal anesthetic techniques have been used for more than a century. Inadvertent placement of LA intrathecal can produce partial to complete spinal block depending on the amount and location of injection. A high-level or complete spinal block will result in respiratory compromise by diaphragmatic and accessory muscle paralysis and, in addition, total sympathectomy. Immediate resuscitation can be required, including respiratory and cardiovascular support. Intrathecal administration of some LAs (lidocaine, chloroprocaine) and additives (metabisulfite) are suspected of causing toxic effects ranging from transient neurological symptoms (TNS) to ascending or adhesive arachnoiditis and permanent neurologic injury. There is significant controversy around the toxic effects of intrathecal local anesthetics and additives regarding etiology and incidence of the reported complications [14].

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Neurolytic Agents

5

Erin F. Lawson and Mark S. Wallace

Key Points

- Methods used to achieve neurolysis include surgical transection, cryoneurotomy, thermal radiofrequency, neuroselective toxins, and nonselective chemical ablation. None of these techniques completely destroy the nerve, and if the dorsal root ganglion is left intact, the nerve is capable of regeneration after which the pain will return.
- Nonselective neurolytic chemical agents including phenol, alcohol, and glycerol have potential for adverse outcomes. Classically, these agents are utilized in the setting of malignant pain when life expectancy is short. Imaging should be used when possible for these procedures. Heavy sedation of the patient should be avoided to allow patients to remain alert enough to report symptoms suggestive of any complication.
- Currently available neuroselective toxins include capsaicin and botulinum toxin.
- Capsaicin is a highly selective agonist for TRPV1 (vanilloid receptor 1 (VR1)). The prolonged exposure of small-diameter sensory neurons to small doses or short exposures to high doses of capsaicin result in a "desensitization" or "defunctionalization" of the nerve terminals.
- Exposure of nerve terminals to botulinum toxin has also been shown to result in rapid relief of pain. It is postulated that the botulinum toxin reduces peripheral and central release of neurotransmitters.
- Newer approaches such as pulsed radiofrequency ablation have widened the potential pool of patients for denervation due to decreased risk of permanent neurologic sequela.
- Sympathetic blocks are generally indicated for treatment of painful symptoms that are not confined to a dermatomal distribution, pain due to damage of peripheral nerve branches, pain caused or maintained by increased sympathetic tone, or pain due to circulatory disturbances.
- Intrathecal neurolysis provides a sensory block without a motor block. Positioning is of utmost importance. Thus, selection of neurolytic (hypobaric vs. hyperbaric) and patient cooperation is critical. Positioning is less critical with epidural neurolysis, which may be chosen to treat pain in the upper abdominal wall, thorax, or upper extremity.

Introduction

History

Neural blockade with neurolytic agents has been documented for the treatment of pain for over a century. In 1904, Schloesser was the first to report alcohol neurolysis for the treatment of trigeminal neuralgia [1, 2]. White, in 1935, applied alcohol neurolysis to the upper thoracic ganglia for the treatment of angina pain [3]. Doppler used phenol neurolysis to destroy presacral sympathetic nerves for treatment of pelvic pain in 1926 [3]. Mandl also studied phenol for cervical ganglion neurolysis in 1947 [3]. Today, the role of neurolytic agents is well established in the approach to cancer pain. Blocking neuronal transmission has the potential to relieve otherwise refractory cancer pain. However, all currently available neurolytic agents have potential for adverse outcomes making their use controversial in nonmalignant or nonterminal pain.

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Scientific Foundation

The specialty of pain medicine defines neurolysis as the selective, iatrogenic destruction of neural tissue to secure the relief of pain [4]. Methods used to achieve neurolysis include surgical transection, cryoneurotomy, thermal radiofrequency, neuroselective toxins, and nonselective chemical ablation. None of these techniques completely destroy the nerve, and if the dorsal root ganglion is left intact, the nerve is capable of regeneration after which the pain will return. This is an important point to convey to the patients as many will assume that if you destroy a nerve, the pain will cease forever. Of all the techniques, nonselective chemical ablation has the potential for the most side effects as the spread of the neurolytic agent is not controlled as with the other techniques where the control of the lesion is more precise. With the exception of neuroselective toxins, the ablative techniques are performed at the level of the axon after which a conduction block occurs. The chemical agents phenol, alcohol, and glycerol cause a dose-dependent, nonselective destruction of the nerve resulting in necrosis, death, Wallerian degeneration, and a complete conduction block in all fibers contained within the nerve [5]. When using neuroselective toxins, the agents are applied to the peripheral nerve terminals. For example, capsaicin is a highly selective agonist for TRPV1 (formerly known as vanilloid receptor 1 (VR1)), a ligand-gated, nonselective cation channel preferentially expressed on small-diameter sensory neurons, especially those nerve fibers that specialize in the detection of painful or noxious sensations [5, 6]. When capsaicin binds to the receptor, the TRPV1 calcium channel opens and calcium enters the intracellular space. The prolonged exposure of small-diameter sensory neurons to small doses or short exposures to high doses of capsaicin result in a "desensitization" or "defunctionalization" of the nerve terminals. The high concentration of intracellular calcium overwhelms the mitochondria, leading to dysfunction and nerve terminal death [7, 8]. Exposure of nerve terminals to botulinum toxin has also been shown to result in rapid relief of pain that cannot be explained by the muscle relaxation effect which takes days to take effect. It is postulated that the botulinum toxin is taken up by the free nerve endings where it cleaves the SNARE protein, SNAP-25. The peripheral release of neurotransmitters from the nerve terminal is dependent upon SNAP-25, and botulinum toxin reduces peripheral release of the neurotransmitter. Another mechanism is the transport of the toxin centrally where the SNARE proteins are cleaved resulting in the reduction of central release of neurotransmitters [9].

Patient Selection

Neurolytics are employed to produce long-lasting pain relief through disabling or destroying nerves. Due to potential for morbidity, neurolytics are selected after patients have failed noninvasive and less invasive therapy. Classically, these agents are utilized in the setting of malignant pain when life expectancy is short, which is the focus of this chapter. Pain is frequently inadequately controlled in cancer patients [10], leading to unnecessary suffering, physical debilitation, psychological deterioration, and avoidance of treatment. Cancer pain management has been identified as an international priority focus for improvement by the World Health Organization (WHO) [11]. While the WHO analgesic ladder usually establishes effective pain management for cancer patients with a less invasive approach, neurolytic procedures are required in 29 % of patients [12]. Although sometimes, more controversial, non-cancer patients with certain chronic pain conditions are also potential candidates for neurolysis. For example, some pain physicians do advocate for sympathetic neurolysis for patients with CRPS [13]. Newer approaches such as pulsed radiofrequency ablation have widened the potential pool of patients for denervation due to decreased risk of permanent neurologic sequela. For use of traditional nonselective neurolytic agents, however, a conservative approach continues to prevail. The use of chemical neurolytic blocks for chronic nonmalignant pain is controversial and not advocated by the authors of this chapter. Furthermore, it is critical that only experienced and skillful persons who are equipped to treat immediate effects perform these blocks [14]. Finally, radiographic guidance is recommended when appropriate.

Applications

Neurolysis is used to provide pain relief by interrupting pain transmission. It can therefore theoretically be applied anywhere along the sensory pathway. Peripheral nerves, sympathetic ganglia, and dorsal roots are all examples of potential targets for neurolysis. Peripheral nerve neurolysis is effective for painful symptoms limited to a single nerve distribution. Most peripheral nerves are mixed; therefore, peripheral neurolysis carries a high risk of motor block as well [13]. It is important to first perform a prognostic block with local anesthetic in order to assess efficacy. The local anesthetic block will determine appropriateness of location of block as well as provide the patient with an opportunity to evaluate the effect with a short-term block. If the patient is uncomfortable with the numb sensation or motor weakness, a neurolytic block is not indicated.

Sympathetic blocks are generally indicated for treatment of painful symptoms that are not confined to a dermatomal distribution, pain due to damage of peripheral nerve branches, pain caused or maintained by increased sympathetic tone, or pain due to circulatory disturbances. Stellate ganglion neurolysis is appropriate for upper extremity and possibly facial pain. Celiac plexus neurolysis is indicated for pain of the

upper abdominal viscera. Lumbar plexus neurolysis targets pain in the lower extremity. Superior hypogastric plexus neurolysis targets lower abdominal or pelvic visceral pain. Finally, ganglion impar neurolysis treats sympathetically maintained perineal pain.

Intrathecal neurolysis or rhizolysis of the dorsal root will provide a sensory block without a motor block. Positioning is of utmost importance. Thus, selection of neurolytic (hypobaric vs. hyperbaric) and patient cooperation are critical. Epidural neurolysis may also be chosen to treat pain in the upper abdominal wall, thorax, or upper extremity. Positioning is less critical; thus, this approach may be an option when positioning for subarachnoid neurolysis is difficult.

Limitations

Following neurolysis, the nerves typically regenerate over time with return of pain. Nerves may regrow unpredictably and may form neuromas. In such cases, not only does pain return, but it is often worse than the initial pain experience. However, with terminal cancer pain, onset of this complication often exceeds the life expectancy of the patient. Therefore, the life expectancy of the patient should be considered when performing neurolytic procedures for pain management. Furthermore, neurolysis does not necessarily provide complete neuronal blockade. The neurolytic block often clinically provides less analgesia than the local anesthetic block [15].

Complications

Complications arise from all aspects of the procedure. Complications from the needle entry site include infection, bleeding, perforation of a viscus or organ, pneumothorax, unintentional subarachnoid or epidural injection, vascular laceration or injection, and peripheral nerve trauma. Complications from sympathectomy especially with celiac plexus block include hypotension that may be severe and prolonged, diarrhea, and sexual dysfunction. These agents are nonselective; potentially catastrophic complications are possible. Complications from the neurolytic agent include motor block, paraplegia, neuropathic pain and dysesthesias, skin ulceration, soft tissue and muscle injury, phlebitis, thrombosis, and tissue ischemia [15]. Motor block is common and even expected with peripheral or neuraxial neurolysis due to the nonselective nature of most neurolytics. However, weakness and paraplegia may also occur during sympathetic blocks secondary to vascular injury. Bowel or urinary incontinence is possible following intrathecal neurolysis [16]. Although less devastating, neuralgias, hypesthesia, and anesthesia following neurolysis may be very distressing to patients expecting relief of suffering. These complications are more common following traditional neurolytic agents such as alcohol.

The Agents (Table 5.1)

Phenol

- Protein coagulation causes nonselective tissue destruction and initiates Wallerian degeneration in nerves [15].
- Intrathecal administration causes degeneration of large and small nerve fibers within the nerve roots but not the ganglia or spinal cord [17].
- It has affinity for vasculature and is toxic to vasculature [15]; therefore, use caution in vascular locations (celiac plexus).
- Neurolysis lasts for several months [18]; regeneration is more rapid than alcohol (14 weeks) [19]. Milder blockade (compared to alcohol).
- Concentrations <–2 % act as a local anesthetic and >5 % needed for neurolysis [18].
- Mixing possible with water or saline up to 6.67 %, mixing with glycerin for higher concentrations, and mixing with radiopaque dye possible.
- Not painful on injection.

Table 5.1 Agents, dose, and location: the good and the bad

Agent	Strength	Unique property	Negative properties	Systemic toxicity
Alcohol	50–100 %	Hypobaric, fast onset	Painful on injection, risk of neuritis (peripheral nerves)	Disulfiram-like reaction
Phenol	4–15 %	Hyperbaric, painless, slow onset	Shorter-lived, affinity for vasculature	Convulsions, cardiovascular collapse
Glycerol	50 %	Historically applied to Gasserian ganglion for treatment of trigeminal neuralgia	Inability to control the spread	Severe headache or local dysesthesia
Capsaicin	8 %	Nociceptor-selective, topical	Painful application, only for localized neuropathic pain	
Ammonium salts	10 %	Sensory fiber-selective, motor intact, lack of postblock neuritis	Nausea and vomiting, headache and paresthesia	Nausea and vomiting, headache and paresthesia

- Hyperbaric compared to CSF (especially when mixed with glycerol); position patients with the painful side down during intrathecal injection in order to coat the dorsal roots.
- Phenol diffuses out of glycerin slowly; there is time for patient positioning after injection.
- Glycerin's high viscosity requires at least a 20-gauge needle for injection.

Alcohol

- Induces Wallerian degeneration in peripheral nerves [20].
- Subarachnoid application causes Wallerian degeneration, demyelination, and degeneration in the dorsal roots, posterior columns, and dorsolateral tract of Lissauer [16].
- Neuronal regeneration in peripheral nerves and spinal cord begins after 1–3 months [16].
- Concentrations up to 33 % destroy sensory nerves but spare motor nerves when applied peripherally.
- Concentrations >33 % may cause paralysis.
- Concentrations 50–100 % are used intrathecally.
- 40 % alcohol is equipotent to 5 % phenol.
- Available in the United States in a 95 % concentration in 5-ml vials.
- Rapidly spreads from the injection site
- Requires larger volumes (than phenol due to rapid spread)
- Easily absorbed into the bloodstream [21], peak blood alcohol levels after injection are usually below the legal limit for driving unless accidental intravascular injection has occurred.
- Hypobaric compared to CSF.
- When performing intrathecal neurolysis, the patient must be positioned with the painful side up in order to coat the appropriate dorsal roots.
- Alcohol is painful on injection.
- Give local anesthetic prior to application to peripheral nerves.
- Intrathecal application less painful than peripheral, with only transient mild burning.
- Toxic to vasculature, causes vasospasm and possibly thrombosis [15].
- Toxic to connective tissue, causes necrosis.
- Inject small volumes and flush the needle with sterile saline prior to withdrawal [19].

Glycerol

- The mechanism of action is unclear, but it appears to cause Wallerian degeneration [19].
- Historically most commonly used to treat trigeminal neuralgia but newer options including radiofrequency lesioning are replacing the use of glycerol.
- Rarely used to treat cancer pain.
- Concentration of 50 %.

Ammonium Compounds

- Not often used clinically.
- High incidence of nausea and vomiting, headache, and paresthesia [22].
- Ammonium sulfate is 10 % effective for intercostal neuralgia without painful post procedure neuritis [23].
- Intrafascicular injection has been shown to be less neurotoxic than phenol 5 % and to spare motor function in animal models [24, 25].

Hypertonic Solutions

- Serious complications including death secondary to hypertonic saline make them clinically undesirable [26].
- Hypertonic saline 10 % NaCl has been used in percutaneous epidural neuroplasty for the treatment of radiculopathy and low back pain.
- Intrathecal hypertonic saline (10–15 %) has been shown to decrease pain by 50 % in cancer patients for up to 3 months [27].

Vanilloids

- Capsaicin (active ingredient in hot chili peppers) and resiniferatoxin (RTX) are available for use.
- Desensitize unmyelinated C pain fibers.
- Activate the transient receptor potential vanilloid receptor 1 (TRPV1) on unmyelinated C fiber nociceptors; influx of calcium and sodium ions depolarize the nociceptive afferent terminals; release of stored neuropeptides causes initial pain signaling followed by desensitization [28].
- Early desensitization of nociceptors by conduction block.
- Delayed desensitization by downregulating TRPV1 receptors [29].
- TRPV1 receptors have been identified in visceral organs, spinal cord, and DRG [29].
- Selective for nociceptors.
- Speed of onset and duration of analgesia depends on dose, duration, and frequency of exposure [30].
- Effect is temporary, lasting hours to days, and requires frequent reapplication to maintain effect.
- Topical application several times daily.

- The topical application of low-dose capsaicin (<1 %); an effective adjunct to the treatment of postherpetic neuralgia, postmastectomy pain, and diabetic neuropathy [31].
- NGX-4010 (8 % capsaicin patch) provides pain relief for up to 12 weeks after one 60-min application [32].
- NGX-4010 is proven effective in the treatment of HIV-associated distal sensory polyneuropathy [33, 34] and postherpetic neuralgia [32].
- Intrathecal resiniferatoxin has been shown to reduce pain in a canine bone cancer model [35]. Phase I clinical trials in cancer patients will start soon.

Clostridial Neurotoxin

- Botulinum toxin is neurotoxic to cholinergic nerves by blocking acetylcholine release.
- Analgesic effect also secondary to inhibition of calcitonin gene-related peptide (CGRP) release from afferent nerve terminals [36], substance P from dorsal root ganglia, and glutamate in the dorsal horn [37].
- Botulinum toxin (BTX) has seven serotypes (A–G) which consist of a heavy chain bound to a light chain by a disulfide bond [38]. The heavy chain binds the nerve terminal and facilitates internalization of the light chain. The light chain internally inhibits neurotransmitter vesicle docking on the plasma membrane [38].
- Neurotransmitter vesicular docking is mediated by the soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) complex which is the target for the BTX light chain.
- Normal nerve terminal function eventually recovers through restoration of the SNARE complex [37],
- Clinically, motor paresis develops within 5 days and lasts for several months.
- BTX is too large to penetrate the blood-brain barrier and is inactivated by retrograde axonal transport; therefore, there is no direct central nervous system effect [37]. Effective in treatment of painful muscle spasticity and myofacial pain, hyperhidrosis, hypersalivtion, and hyperlacrimation [38].
- In cancer patients, BTX has been shown to improve symptoms of radiation fibrosis syndrome [39] and neuropathic pain [40]. Currently approved for use in the United States are Onabotulinumtoxin A (Botox/Botox Cosmetic), Abobotulinumtoxin A (Dysport), and Rimabotulinumtoxin B (Myobloc).
- The dose equivalency is 20 U vs. 50 U vs. 2,000 U for Botox, Dysport, and Myobloc, respectively.
- BTX is injected into striated muscle in increments of units.
- Dosage units differ among the BTX products and are not comparable or convertible [41].
- BTX may be diluted in local anesthetic or sterile saline, and optimal dilutions have not been established for treatment of pain.
- Smaller effect or shorter duration of response seen over time due to development of antibodies against BTX [37].
- If antibodies are suspected, rotation to different serotype usually effective.
- Local complications include muscle atrophy, dysphagia, dysphonia, and ptosis.
- Systemic complications include dyspnea, respiratory compromise, weakness, and death. Systemic complications have mostly occurred in children treated for cerebral palsy-associated spasticity and have been reported between 1 day and several weeks following treatment [42].

Clinical Practice

The following clinical examples are the approaches the authors of this chapter have found most successful for neurolysis. These clinical descriptions are intended for example only and should be interpreted for use by experienced clinicians. We support the use of the following neurolytic agents for palliative pain control in patients with malignant pain. We urge caution when using these neurolytics in patients with non-cancer pain or those with normal life expectancy due to potential for permanent catastrophic complications. We endorse the use of imaging when possible for these procedures. We also recommend avoiding heavy sedation of the patient. Patients should remain alert enough to report symptoms suggestive of any complication.

While specific complication risks are mentioned below, complications may result from any aspect of neurolysis from technical procedural complications to agent-specific complications. Technical complications include infection, bleeding, perforation of a viscus or organ, pneumothorax, unintentional subarachnoid or epidural injection, vascular laceration or injection, and peripheral nerve trauma. Complications from the neurolytic agent include motor block, paraplegia, neuropathic pain and dysesthesias, skin ulceration, soft tissue and muscle injury, phlebitis, thrombosis, and tissue ischemia [15]. Although less devastating, neuralgias, hypesthesia, and anesthesia following neurolysis may be very distressing to patients expecting relief of suffering. These complications are more common following traditional neurolytic agents such as alcohol. Finally, neurolysis does not always provide complete neuronal blockade. The neurolytic block often clinically provides less analgesia than the local anesthetic block [15].

The strengths and volumes of neurolytic agents shown below are not supported by scientific literature but are based only on clinical experience. Absolute alcohol is available in the United States as ethanol 98 % and phenol 100 %. For

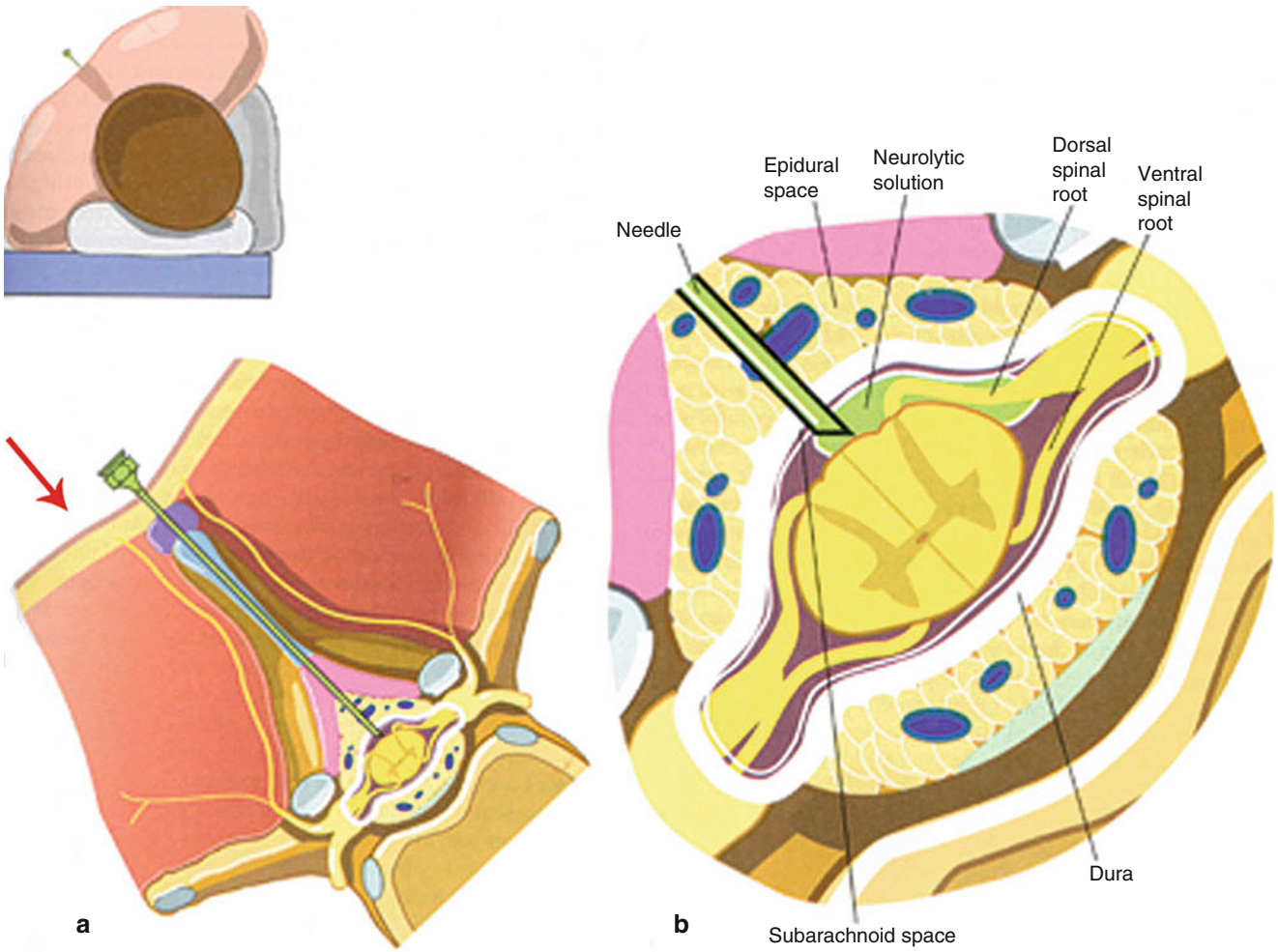

Fig. 5.1 Proper positioning of the patient with left-sided pain for intrathecal injection of alcohol (**a**) and close-up demonstration of proper needle entry into subarachnoid space (**b**). Note the 45° anterior tilt intended to bathe the posterior (sensory) nerve roots with hypobaric alcohol while sparing the anterior (motor) roots (With permissions from Waldman [44])

lower concentrations for clinical use, phenol must be diluted with saline by a compounding pharmacy.

Subarachnoid Neurolysis

- Appropriate for well-localized, unilateral pain limited to a few dermatomes.
- Cervical subarachnoid neurolysis should be performed at the spinal segment level to be blocked because cervical nerve roots pass horizontally from the cord through the intervertebral foramen [43].
- Upper thoracic subarachnoid neurolysis should be performed at the vertebral interspace of the dermatome to be blocked. Middle and lower thoracic subarachnoid neurolysis should be performed one or two segments above the vertebral interspace of the dermatome to be blocked due to the anatomic course of the thoracic nerve roots.
- Lumbar subarachnoid neurolysis should be performed at the T11–T12, and subarachnoid neurolysis for sacral dermatomes should be performed at the L1–L2 interspace.
- Intrathecal neurolysis or rhizolysis of the dorsal root will provide a sensory block without a motor block.
- Procedure
  - The patient should remain awake and alert throughout the procedure.
  - Sterile prep and drape.
  - Patient may be positioned sitting or lateral for initial needle positioning.
  - A 20- or 22-gauge 3.5-in. spinal needle is advanced to intrathecal space at level of desired dermatome.
  - After confirmation with (+) CSF, the patient is positioned for neurolytic injection.
  - Alcohol is hypobaric; position patient with painful side up; positioning is critical as alcohol diffuses quickly and sets up quickly. Patient should be positioned laterally

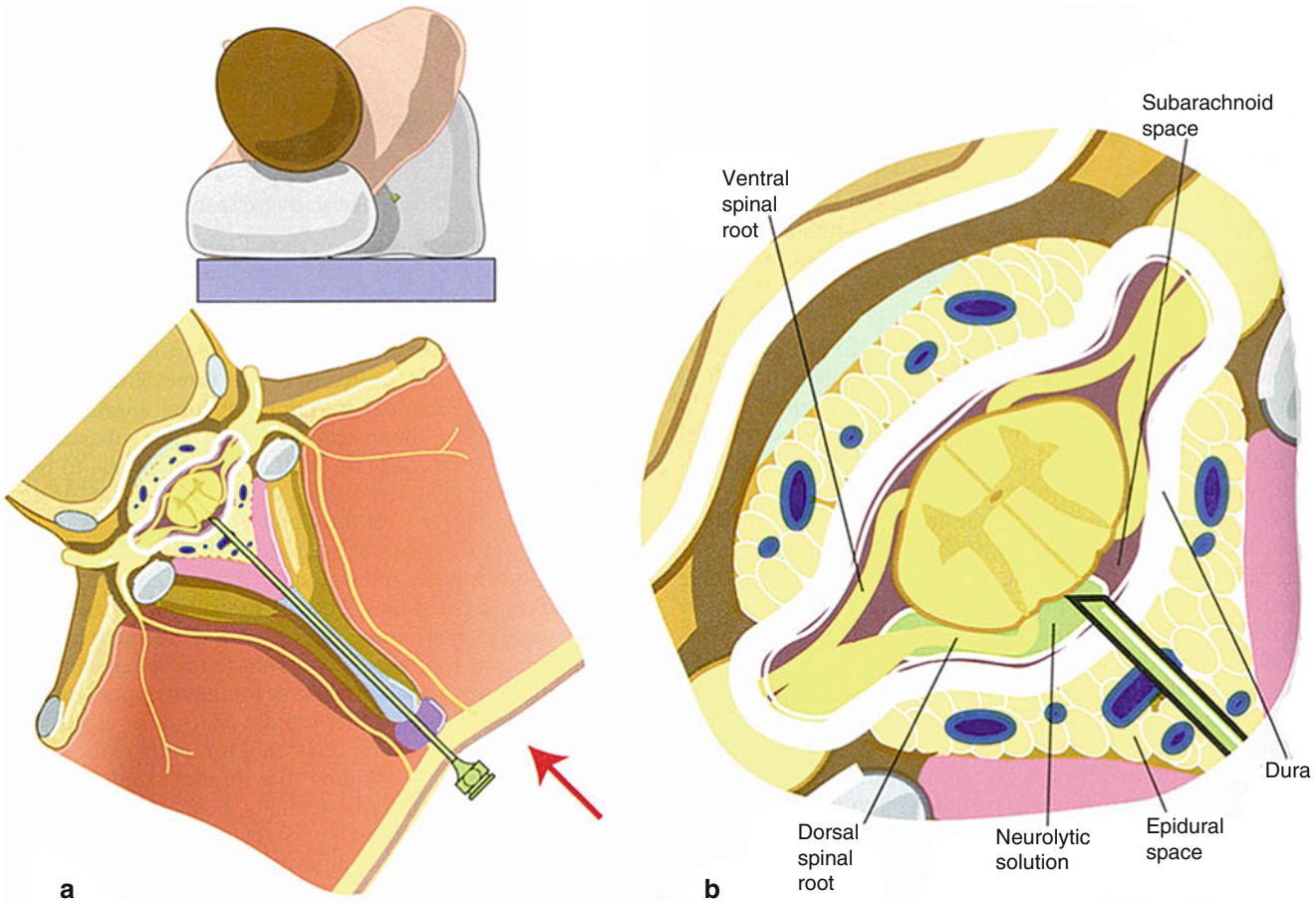

Fig. 5.2 Proper positioning of the patient with left-sided pain for intrathecal injection of phenol in glycerin (**a**) and close-up demonstration of proper need entry into the subarachnoid space (**b**). Note the 45° posterior tilt intended to bathe the posterior (sensory) nerve roots with hyperbaric phenol while sparing the anterior (motor) roots (From Waldman [45])

with 45 % forward tilt. Bilateral blocks with alcohol may be achieved with the patient in the prone position.
  - Phenol is hyperbaric but diffuses out of glycerol slowly; therefore, positioning is less critical and may occur after injection. Patient should be positioned with painful side down with a 45 % posterior tilt.
  - Absolute alcohol or phenol 6 % in glycerin, up to 1 ml is injected.
- Potential complications include painful setup (alcohol), coagulum with CSF (do not aspirate CSF prior to injection), bowel/bladder incontinence, lower extremity weakness, and motor block (Figs. 5.1 and 5.2).

Epidural Neurolysis

- Appropriate for well-localized bilateral pain limited to a few dermatomes including pain in the upper abdominal wall, thorax, or upper extremity. Positioning is less critical; thus, this approach may be an option when positioning for subarachnoid neurolysis is difficult. Epidural neurolysis has less predictable spread than with intrathecal neurolysis.
- Procedure
  - The patient should remain awake and alert throughout the procedure.
  - The patient is positioned with painful side down in 45 % posterior tilt.
  - The patient is prepped and draped in a sterile manner.
  - Lidocaine 1 % local skin and subcutaneous tissue infiltration.
  - 17–18-gauge Tuohy epidural needle inserted into epidural space with loss of resistance technique. Epidural catheter threaded under fluoroscopic guidance to level of painful dermatomes to be treated.
  - Injection of small volume of contrast is performed to confirm epidural spread and rule out intrathecal or intravascular spread.
  - Absolute alcohol 8–10 ml; phenol 15 % in glycerol/75 % of LA volume 8–10 ml is injected.
  - The patient should ideally remain in this position 40 min following injection.

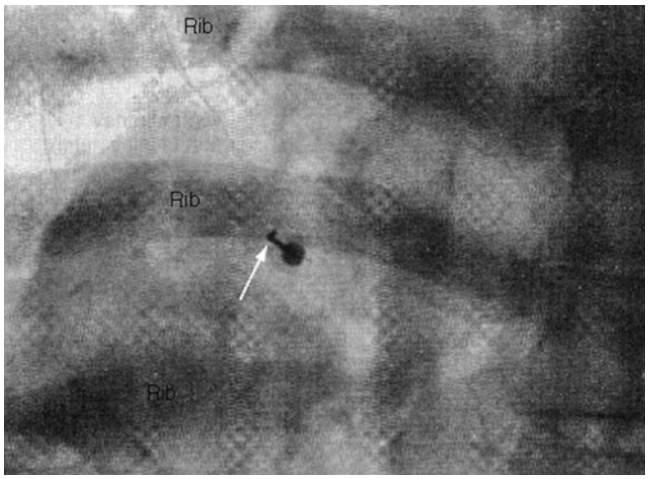

Fig. 5.3 Intercostal nerve block, anteroposterior view. The *arrow* indicates where the needle touches and stops below the rib (Raj Interventional Pain Management Image-Guided Procedures)

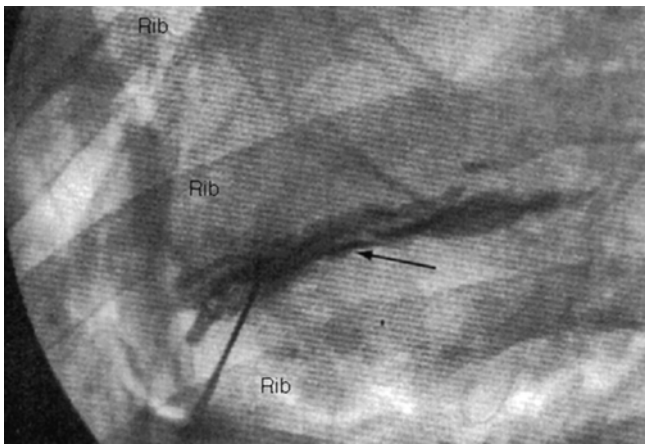

Fig. 5.4 Intercostal nerve block with contrast medium, anteroposterior view. The *arrow* indicates the spread of contrast in the intercostal groove (Raj Interventional Pain Management Image-Guided Procedures)

- Potential complications include motor block, numbness, neuritis, and deafferentation pain.

Peripheral Nerve Neurolysis

- Appropriate for pain localized to a single peripheral sensory nerve. Most peripheral nerves are mixed; therefore, peripheral neurolysis carries a high risk of motor block as well [13].
- Procedure: First, perform a prognostic block with local anesthetic in order to assess efficacy. The local anesthetic block will determine appropriateness of location of block as well as provide the patient with an opportunity to evaluate the effect with a short-term block. If the patient is uncomfortable with the numb sensation or motor weakness, a neurolytic block is not indicated.
- Ultrasound should be considered for nerve localization during the procedure.
- Procedure example: intercostal nerve neurolysis
  - The patient remained awake and alert throughout the procedure.
  - The patient is placed in the prone position.
  - The skin is prepped with chlorhexidine, and sterile drapes are applied.
  - The skin and soft tissues are anesthetized with lidocaine 1 %.
  - The injection is usually performed posteriorly at the angle of the rib just lateral to the paraspinous muscles [43].
  - A 20-gauge spinal needle is inserted percutaneously and advanced under fluoroscopic guidance using dorsal oblique, AP, and lateral projections.
  - The needle tip is advanced to contact bone at the dorsal caudal edge of the targeted rib. The needle is then advanced past the caudal and dorsal edge of the rib and stopped before reaching the ventral edge of the rib.
  - After negative aspiration for heme or air, contrast injection under live fluoroscopic guidance should spread longitudinally along the rib without evidence of intravascular spread.
  - 1–2 ml of 2 % lidocaine is injected to reduce the pain of the neurolytic agents. This is followed by absolute alcohol 1–2 ml, or phenol 6–12 % aqueous 1–2 ml is then injected.
- Potential complications include painful neuritis, motor weakness, and pneumothorax (Figs. 5.3 and 5.4).

Cranial Nerve Neurolysis

- Appropriate for pain localized to cranial nerves.
- Procedure example: Please see Sphenopalatine Ganglion Neurolysis described below
- CT guidance or use of digital subtraction fluoroscopy is recommended.
- 1 ml of 2 % lidocaine is injected followed by phenol 6–12 % aqueous 1 ml.
- Potential complications include painful neuritis and vascular injury with stroke.

Sphenopalatine Ganglion Neurolysis

- Appropriate for the treatment of intractable pain in the distribution of the maxillary nerve.

- Procedure
  - Position patient supine.
  - Sterile prep and drape of cheek on side where procedure is to be performed
  - The anterior view is taken with the C-arm, and the needle entry site is located under the zygoma in the coronoid notch. C-arm then rotated to a lateral view of the upper cervical spine and mandible. The patient's head is rotated until the rami of the mandible are superimposed one on the other. The C-arm is then rotated cephalad until the pterygopalatine fossa is visualized [46].
  - A 22-gauge 3.5-in. needle is advanced under fluoroscopic guidance until the needle tip is adjacent to the lateral nasal mucosa in the pterygopalatine fossa. The needle should never be advanced through resistance [46].
  - Aspirate should be negative for heme and CSF.
  - Inject 2 % lidocaine 1 ml followed by phenol 6–12 % 1 ml.
- Complications include hematoma if the maxillary artery or venous plexus is punctured; hypesthesia and numbness of the palate, maxilla, or posterior pharynx; meningitis; epistaxis; and trauma to the parotid gland or branches of the facial nerve (Figs. 5.5 and 5.6).

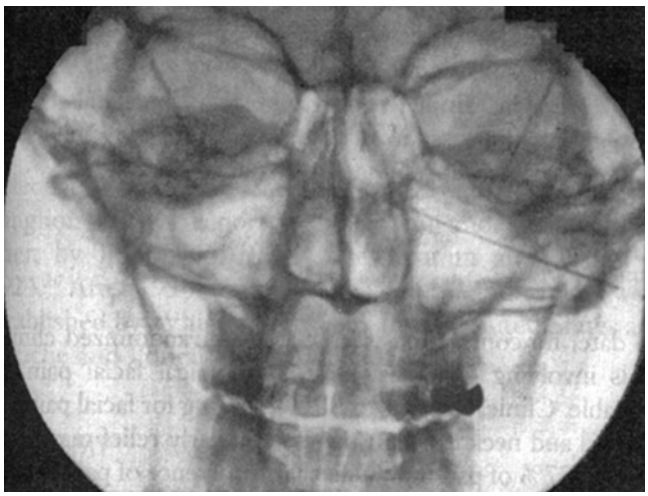

Fig. 5.5 The radiographic anteroposterior view of the face shows the needle tip at the lateral wall of the nose at the superomedial angle of the maxillary sinus (Raj Interventional Pain Management Image-Guided Procedures)

Thoracic Sympathetic Neurolysis

- Appropriate for the treatment of intractable pain of the upper two-thirds of the esophagus and pleuritic chest pain secondary to lung neoplasm [43]. The technical difficulty of multiple needle placements compared to effectiveness of epidural and subarachnoid neurolysis has limited the use of this procedure [43].
- Procedure
  - The patient should remain awake and alert throughout the procedure.

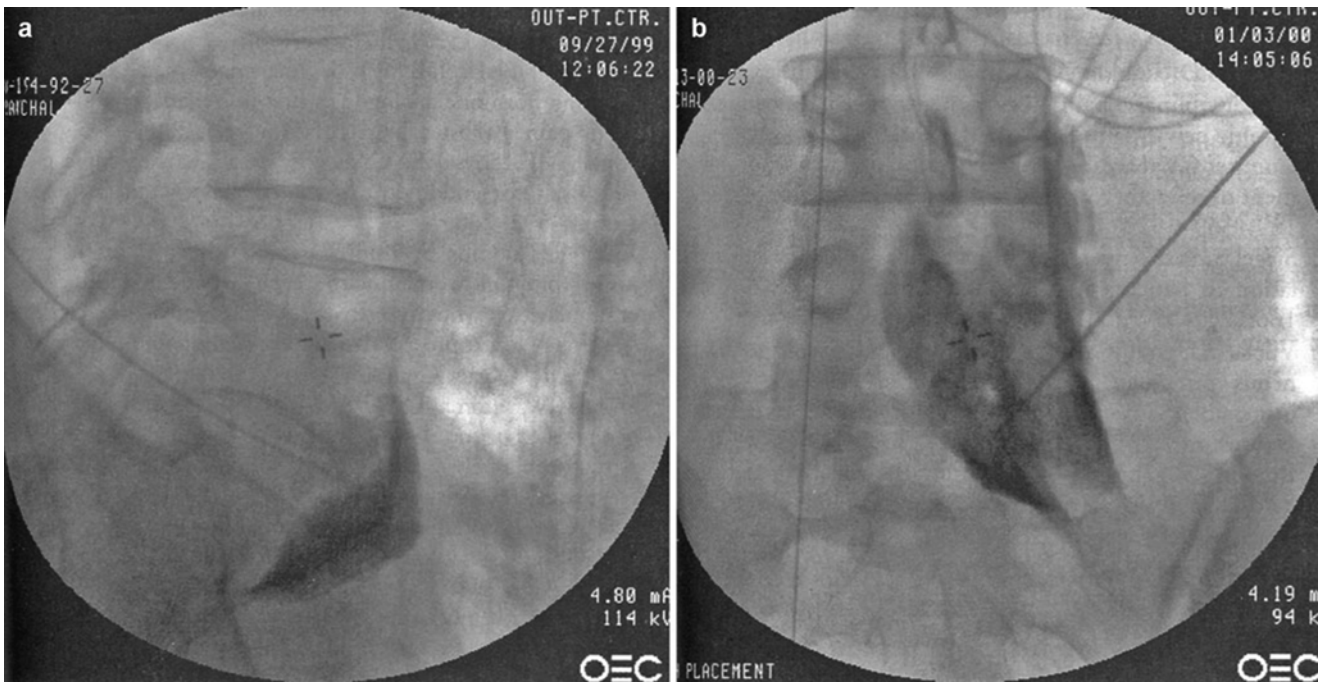

Fig. 5.6 (**a**) The radiographic lateral view shows the needle placed at the superior hypogastric plexus. (**b**) This image shows correct needle placement from the contralateral side. (Raj Interventional Pain Management Image-Guided Procedures)

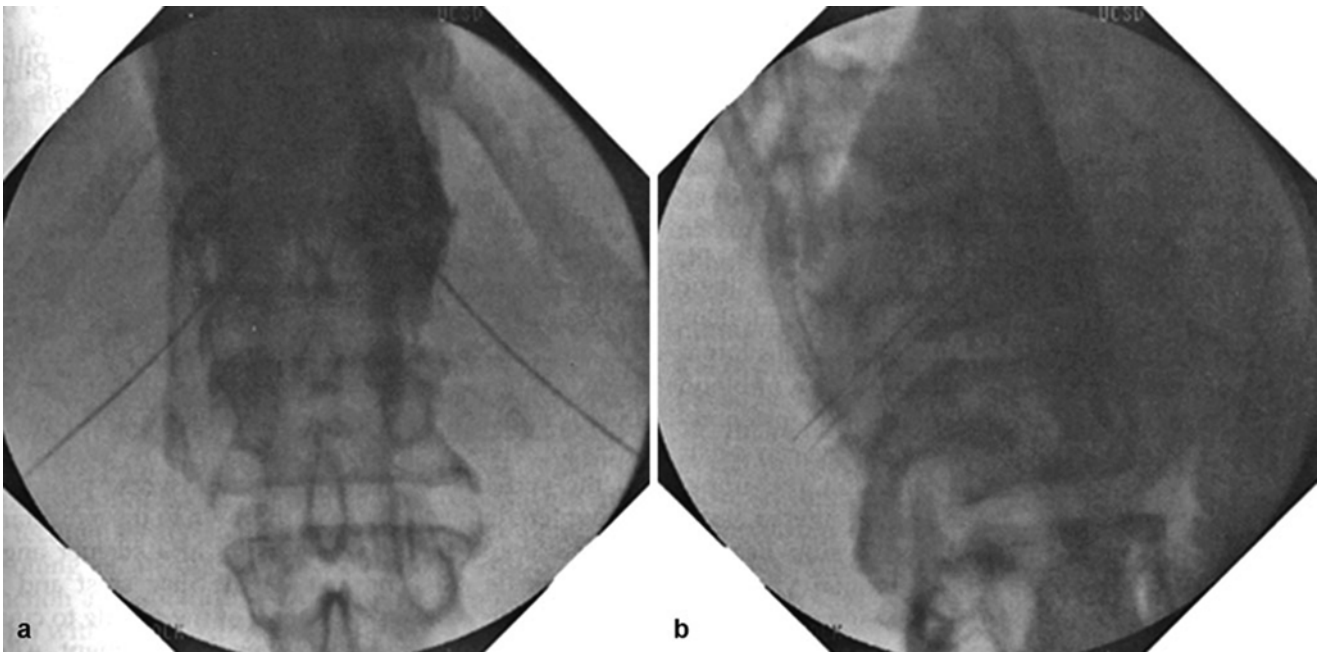

Fig. 5.7 Anteroposterior view (**a**) and lateral view (**b**) of correct needle locations for the retrocrural approach to the celiac plexus block. This technique requires bilateral needle placement, with the needle tip located at the anterolateral portion of L1 (Raj Textbook of Regional Anesthesia)

  - The patient is positioned prone with a pillow under the chest or optimal flexion of the thoracic spine.
  - Sterile prep and drape of the thorax.
  - The T2–T8 vertebral body levels may be approached based on location of pain. The selected vertebral body is "squared" under fluoroscopy. Rotate C-arm 20° oblique toward the ipsilateral side.
  - Local skin and soft tissue anesthesia with lidocaine 1 %.
  - A 20–22-gauge spinal needle is inserted percutaneously with tip directed to the lateral border of T2 above the third rib. Needle tip is advanced under fluoroscopic guidance to the lateral edge of the T2 vertebral body. The C-arm is then rotated laterally to view advancement of needle to the posterior third of the vertebral body while keeping needle tip in contact with the vertebral body edge.
  - After negative aspiration, contrast dye is injected under live fluoroscopy. Contrast should spread in a cephalocaudal direction along the thoracic vertebral column without any evidence of intravascular uptake.
  - Lidocaine 2 % 2.5 ml followed by phenol 10 % 2.5 ml is then injected.
- Complications include neuraxial injection, intravascular injection, nerve injury, pneumothorax, and intercostal neuralgia.

Celiac Plexus Neurolysis

- Appropriate for treatment of pain of upper abdominal viscera
- Procedure: posterior/retrocrural approaches
  - Fluoroscopic or CT guidance may be used.
  - The patient should remain awake and alert throughout the procedure.
  - The patient is positioned prone with a pillow under the abdomen.
  - Sterile prep and drape.
  - For fluoroscopically guided procedures, the L1 vertebral body is "squared" under fluoroscopic view, and then the C-arm is oblique to ipsilateral side to align the lateral tip of the transverse process with the edge of the L1 vertebral body. Needles are inserted bilaterally at the L1 vertebral body level.
  - The skin and soft tissues are anesthetized with lidocaine 1 %.
  - A 20–22-gauge 15-cm spinal needle of adequate length for body habitus is inserted percutaneously with tip directed over the inferior one-third of the lateral L1 vertebral body.
  - The needle is advanced under fluoroscopic guidance until contact is made with vertebral body. The C-arm is

then rotated laterally to visualize the needle tip advance to appropriate location. The left needle tip is advanced 1.5–2 cm past the edge of the vertebral body, and right needle tip is advanced 3–4 cm past the edge of the vertebral body. Neurolytic agent is injected posterior and cephalic to the diaphragmatic crura [43].
  - Aspiration should be negative for heme, CSF, urine, and thoracic duct fluid. Injection of contrast should demonstrate cephalocaudal spread without evidence of intravascular uptake. Injection of a test dose of injection solution is recommended.
  - Lidocaine 2 % 10 ml (transcrural) or 5 ml (retrocrural or splanchnic) followed by alcohol 95 % (10 ml for transcrural approach, 5 ml each side for retrocrural or splanchnic approach) is injected.
- Side effects include diarrhea, hypotension, and sexual dysfunction.
- Complications include severe and prolonged hypotension, paraplegia, PTX, bowel injury, major vascular injury, bleeding, weakness, and paraplegia secondary to vascular injury (Figs. 5.7a, b).

Superior Hypogastric Plexus Neurolysis

- Appropriate for the treatment of pelvic visceral pain
- Procedure
  - The patient should remain awake and alert throughout the procedure.
  - The patient is positioned prone with a pillow under the abdomen to reduce lumbar lordosis.
  - The lower back is sterilely prepped and draped.
  - The L5 vertebral body is identified under fluoroscopy.
  - Cranial tilt of the C-arm is utilized to align the top of the transverse process of L5 with the inferior border of the L5 vertebral body. The C-arm is then oblique ipsilaterally 20°. Needle entry site is 5–7 cm lateral to the midpoint of the L4–L5 interspinous space. Needles are advanced bilaterally.
  - Skin and soft tissues are infiltrated with lidocaine 1 %.

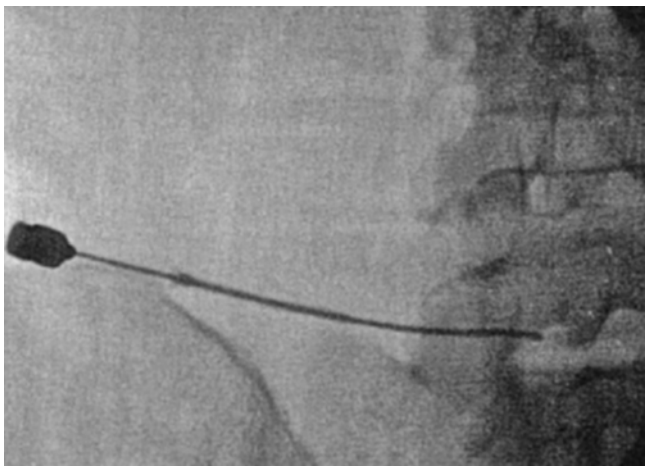

Fig. 5.8 Medial paraspinos approach: final position of the needle at L5 for hypogastric plexus block (posteroanterior view) (Raj Interventional Pain Management Image-Guided Procedures)

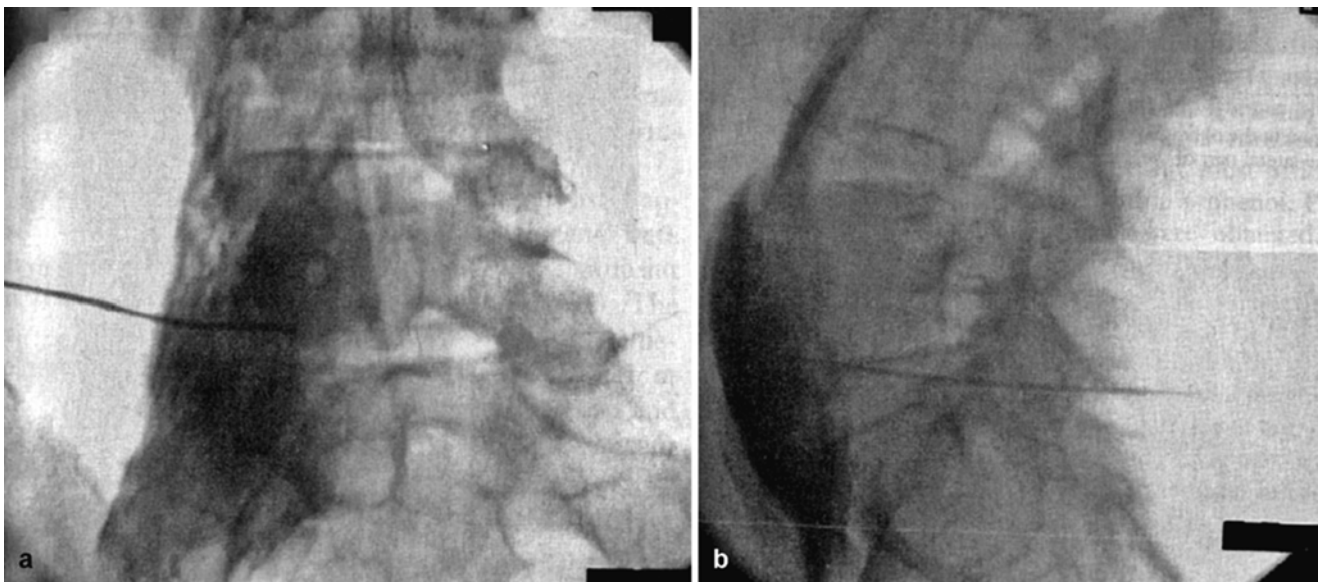

Fig. 5.9 (**a**) Posteroanterior view showing the dispersion of contrast Omnipaque (iohexol) solution to confirm the correct needle position. Note the solution spreading vertically hugging the spine. (**b**) Lateral view showing contrast solution spreading over the L5–S1 (Raj Interventional Pain Management Image-Guided Procedures)

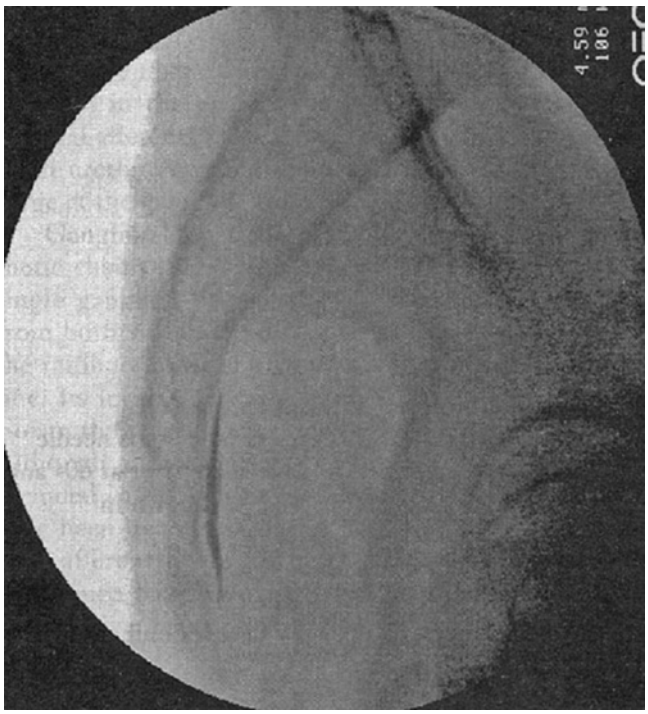

Fig. 5.10 Lateral fluoroscopic view that shows the needle tip in the perirectal space between rectum and the sacrum (Raj Interventional Pain Management Image-Guided Procedures)

  - A 20–22-gauge 15-cm spinal needle is advanced percutaneously to pass just over the top of the L5 transverse process and target the anterior edge of the lower portion of the L5 vertebral body bilaterally.
  - After negative aspiration, injection of contrast should reveal cranial–caudal spread along the vertebral column without evidence of intravascular spread.
  - Lidocaine 2 % 4 ml followed by phenol 10 % 4 ml is injected on each side.
  - Potential complications include intravascular injection, neuraxial injection, discitis, urinary injury, bladder/bowel incontinence, weakness, and paraplegia secondary to vascular injury (Figs. 5.8 and 5.9a, b).

Ganglion Impar Neurolysis

- Appropriate for treatment of perineal pain or pain of rectum or anus.
- Procedure
  - The patient should remain awake and alert throughout the procedure.
  - There are techniques described in the literature of patient positioning prone or in the lateral decubitus position. The prone positioning is discussed here.
  - Patient is positioned prone with a pillow under the pelvis.
  - Sterile prep and drape.
  - Lidocaine 1 % is infiltrated into skin.
  - Using AP and lateral fluoroscopic imaging, a 20-gauge 3.4-cm spinal needle is advanced through the sacrococcygeal ligament just anterior to the anterior border of the sacrum.
  - After negative aspiration, injection of contrast should reveal longitudinal spread along the anterior border of the sacrum without intravascular or rectal spread.
  - Lidocaine 2 % 2 ml followed by phenol 10 % 2 ml is injected.
- Potential complications include rectal trauma or perforation, periosteal injection, epidural injection, or sacral root injury (Fig. 5.10).

High Dose Capsaicin

- FDA approved for the treatment of postherpetic neuralgia.
- A single 1-h treatment can provide up to 3 months of pain relief.
- Each patch contains 8 % capsaicin in a localized dermal delivery system.
- The patch is 14 × 20 cm (280 cm^2) and contains a total of 179 mg of capsaicin or 640 μg/cm^2. The patch can be cut to the size of the affected area.
  - Identify the area to be treated which includes areas of hypersensitivity and allodynia.
  - Use the patch only on dry, intact skin.
  - If necessary, clip (do not shave) the patient's hair to improve adherence of the patch.
  - Use only nitrile gloves when handling the patch and cleansing capsaicin residue from the skin. After handling the capsaicin patch, avoid contact with eyes or mucous membranes.
  - The patch is cut to the size of the painful area. Up to four patches can be used at once.
  - Prior to patch application, the area is gently washed with mild soap and water and dried thoroughly. This is to remove skin oils which will absorb the capsaicin (which is fat soluble) and reduce drug delivery.
  - The FDA-approved procedure is to pretreat with topical lidocaine. However, the studies showed that pretreatment with topical lidocaine did not reduce the pain of application. In general, the procedure is well tolerated with mild discomfort. In the author's experience, pretreatment with topical lidocaine has no effect on the pain of application, and it is not necessary [47]. If desired, pretreatment with oral oxycodone and Valium works well.
  - The patch is applied and left in place for 1 h. To ensure that the patch maintains contact with the treatment area, a dressing, such as rolled gauze, may be used.

- Because aerosolization of capsaicin can occur upon rapid removal of the patches, remove the patches gently and slowly by rolling the adhesive side inward.
- After removal, generously apply cleansing gel to the treatment area and leave for at least 1 min to remove any residual capsaicin. Remove the cleansing gel with a dry wipe and gently wash the area with mild soap and water.
- Pain and erythema are the most common side effects of the treatment which rapidly resolves after removal. If pain is intolerable, application of local cooling or administration of appropriate analgesic medications are effective. In clinical trials, increases in blood pressure occurred during or shortly after exposure to the patch. Changes averaged less than 100 mmHg and appeared to be related to the amount of pain experienced with application.

Botulinum Toxin

- FDA approved for the treatment of migraine headaches.
- BTX is most effective for headaches and cervical and periscapular pain.
- Procedure
  - Myobloc comes premixed at 5,000 u/ml. Botox and Dysport should be diluted with either saline or local anesthetic at a concentration of 100 or 300 u/ml. Solutions are placed in a 1-ml tuberculin syringe.
  - Most common injections are into the following muscles:
    - Frontalis
    - Procerus
    - Orbicularis oculi
    - Temporalis
    - Masseter
    - Occipitalis
    - Cervical paraspinous
    - Trapezius
    - Levator scapulae
    - Supra- and infraspinatus
    - Rhomboids
    - Scalene muscles
    - Sternocleidomastoid
  - Injections are distributed through the different muscle groups depending on the painful area. Injections can be made on 0.025–0.05 ml increments. For migraines, the most common muscles injected are the frontalis, procerus, orbicularis, and temporalis. If the pain includes the cervico-occipital region, the upper cervical paraspinous and occipitalis muscles can be injected. Injections can also be inserted throughout the scalp. If scalp injections are performed, it is recommended that the patients wash their hair with chlorhexidine-based soap prior to treatment.
  - 100 U, 300 U, and 5,000 U of Botox, Dysport, and Myobloc are usually sufficient doses that can be spread throughout the muscle groups. However, some patients may require up to twice the dose.
  - Complications include ptosis if the injection is too close to the upper orbital rim. Even with properly placed injections in the frontal region, some patients may get a transient ptosis due to aberrancies in the muscles that provide upper eyelid tone. Injections in the cervical region can result in transient neck weakness.

Future Directions

Neurolysis for the treatment of refractory cancer pain continues to be an effective option. However, given the nonspecificity and complications associated with currently available agents, there is a need for further research in the area. Intrathecal resiniferatoxin holds the greatest promise due to the high specificity for the unmyelinated C fibers that transmit pain. However, a side effect of this therapy may be the inability to detect thermal pain which could lead to thermal injuries. Therefore, patients will require close observation and counseling on this risk. Topical 20 % capsaicin solution that is painted on the painful area is currently in clinical trials with postherpetic neuralgia. It was recently announced that the phase II trial met the primary end point and further trials are planned. This trial was performed without pretreatment with topical lidocaine, and the participants tolerated the procedure well confirming that pretreatment with lidocaine is not indicated. The application time is only 5 min which is considerably shorter than the 1-h application of the patch.

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Cryoanalgesia

6

Michael S. Leong, Philip S. Kim, and Lloyd Saberski

Key Points

Advantages

- Long history of analgesic treatment
- Treats nociceptive, neuropathic, and sympathetic maintained pain – coccydynia
- Produces Wallerian degeneration but leaves myelin sheath and endoneurium intact
- Anesthetic in treatment
- Low incidence of neuritis

Disadvantages

- Setup time for machine can be lengthy.
- Probe with introducer (up to 12 fr) can be large.
- Requires a separate nerve stimulator to test sensory and motor stimulation.
- Probe is not curved.

Future uses

- May be useful as office procedure for peripheral neuralgias
- Ultrasound guidance procedures with less sedation
- Randomization of cryoanalgesia with pulsed radio frequency

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Introduction

Cryoanalgesia is an interventional pain therapy that seems less popular than newer techniques, such as pulsed radiofrequency ablation. Many studies show efficacy in multiple acute and chronic pain conditions. From a patient's perspective, cryoanalgesia or "freezing" of the nerves makes sense since they routinely use ice as a passive treatment modality. In this era of practice, with increasing emphasis on durability of treatment during repeated blocks as well as concern for long-term side effects (steroid effects, neuritis from continuous radio frequency, cryoanalgesia), the authors will present an introduction to this valuable pain management technique and suggest its integration into current clinical practice.

History

Cryoanalgesia is truly a cross-cultural pain treatment option through two millennia. Cryoanalgesia is a technique in which cold is applied to produce pain relief. The analgesic effect of cold has been known to humans for more than two millennia [1]. Hippocrates (460–377 B.C.) provided the first written record of the use of ice and snow packs applied before surgery as a local pain-relieving technique [2]. Early physicians, such as Avicenna of Persia (980–1070 A.D.) and Severino of Naples (1580–1656), recorded using cold for preoperative analgesia [3, 4]. In 1812, Napoleon's surgeon general, Baron Dominique Jean Larrey [5], recognized that the limbs of soldiers frozen in the Prussian snow could be amputated relatively painlessly. In 1751, Arnott [6] described using an ice-salt mixture to produce tumor regression and to obtain an anesthetic and hemostatic effect. Richardson introduced ether spray in 1766 to produce local analgesia by refrigeration; this was superseded in 1790 by ethyl chloride spray.

Modern interest in cryoanalgesia was sparked in1961, after Cooper described a cryotherapy unit in which liquid

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nitrogen was circulated through a hollow metal probe that was vacuum insulated except at the tip. With this equipment, it was possible to control the temperature of the tip by interrupting the flow of liquid nitrogen at temperatures within the range of room temperature to −196 °C. Because the system was totally enclosed, cold could be applied to any part of the body accessible to the probe. The first clinical application of this technique was in neurosurgery for treatment of parkinsonism [7, 8]. In 1967, Amoils [9] developed a simpler handheld unit that used carbon dioxide or nitrous oxide. These devices were the prototypes for the current generation of cryoprobes used in cryoanalgesia. The coldest temperature applied today is approximately −70 °C.

Physics and Cellular Effects

Modern cryoneurolysis uses controlled cooling via the expansion of highly pressurized and compressed gas (nitrous oxide or carbon dioxide) through a narrow slit aperture. Cryoprobes are available in various sizes but with the same basic design: an inner and outer tube with outer insulation, except at the probe tip [9]. Gas under high pressure (650–800 psig) passes between the two tubes and is released through a small orifice into the chamber of the tip of the probe [10]. Compressed gas expands as it passes through the orifice, resulting in a rapid decrease in temperature at the probe tip (the Joule-Thomson effect). Absorption of heat from the surrounding tissues accompanies gas expansion and leads to the formation of an ice ball [10] by freezing of intracellular and extracellular water. Gas from the inner tube escapes and is scavenged through a ventilated outlet. The "closed-system" construction of the machine and probes allows for no gas to escape from the probe tip handle and the machine.

The rapid cooling at the tip results in temperatures of approximately −70 °C. Ice balls vary in size as a function of probe size, freeze time, tissue permeability to water, and presence of vascular "heat sinks." Modern cryoprobes develop ice balls approximately 3.5–5.5 mm in diameter.

Precise levels of gas flow are necessary for safe and effective cryoneurolysis. Inadequate gas flow will not result in tissue freezing, whereas excessive gas flow may result in freezing up to the stem of the probe with the potential for cold skin burns. Modern insulated cryoprobes and cryotherapy units have the ability for discriminative stimulation of sensory and motor nerves. Locating the precise "pain generator" with nerve stimulation is necessary because the size of the ice ball that can be generated may be large and can freeze other nontargeted tissues and nerves.

Histologically, the axons and myelin sheaths degenerate after cryolesioning (Wallerian degeneration), but the epineurium and perineurium remain intact, thus allowing subsequent nerve regeneration. The duration of the block is a function of the rate of axonal regeneration after cryolesioning, which is reported to be 1–3 mm/day [7]. Because axonal regrowth is constant, the return of sensory and motor activity is a function of the distance between the cryolesion and the end organ [1]. The absence of external damage to the nerve and the minimal inflammatory reaction to freezing ensure that regeneration is exact. The regenerating axons are unlikely to form painful neuromas. (Surgical and thermal lesions interrupt perineurium and epineurium.) Other neurolytic techniques (alcohol, phenol) potentially can produce painful residual neuromas because the epineurium and perineurium are disrupted, so regrowth is disordered.

A cryolesion provides a temporary anesthetic block. Clinically, a cryoblock lasts weeks to months. The result depends on numerous variables, including operator technique and clinical circumstances. The analgesia often lasts longer than the time required for axons to regenerate [11]. The reasons are still a matter of speculation, but it is obvious that cryoanalgesia is more than just a temporary disruption of axons. Possibly, sustained blockade of afferent input to the central nervous system (CNS) has an effect on CNS windup. One report suggested that cryolesions release sequestered tissue protein or facilitate changes in protein antigenic properties [7]. The result is an autoimmune response targeted at cryolesioned tissue. The first report of such a response was from Gander et al. [12] who showed tissue-specific autoantibodies after cryocoagulation of male rabbit accessory glands. This report was followed by a parallel clinical report of regression of metastatic deposits from prostatic adenocarcinoma after cryocoagulation of the primary tumor [13]. The significance for pain management is unclear; however, it does indicate that tumor growth and regression are affected by immune function. It is possible that immune mechanisms play a role in the analgesic response after cryoablation.

Indications and Contraindications

Cryoanalgesia can produce pain relief for weeks to months. Treatment does not permanently injure the nerves, and axonal regeneration is typical.

The median duration of pain relief is 2 weeks to 5 months [14, 15]. Cryoanalgesia is best suited for painful conditions that originate from small, well-localized lesions of peripheral nerves (e.g., neuromas, entrapment neuropathies, and postoperative pain) [11]. Longer than expected periods of analgesia has been reported and may result from the patient's ability to participate more fully in physical therapy or from an effect of prolonged analgesia on central processing of pain (preemptive analgesic effect). Sustained blockade of afferent impulses [16–19] with cryoanalgesia may reduce plasticity (windup) in the CNS and may decrease pain permanently [20].

Patient should be aware that the treatment entry site may be exposed to cryoanalgesia, especially if the probe or targeted region is superficial. Subsequently, numbness at the site of entry and possible skin depigmentation can occur if the ice ball frosts the skin.

Indications

- Focal peripheral nerves: neuromas, entrapment neuropathies
- Sympathetic maintained pain
- Postoperative pain

Contraindications

- Bleeding diathesis
- Local and systemic infection
- Patient consent

Pain Conditions

- Postoperative pain
- Post-herniorrhaphy (ilioinguinal nerve)
- Post-thoracotomy (intercostal nerves)
- Post-tonsillectomy (glossopharyngeal nerves)
- Chronic pain
- Facial pain syndromes
- Neuromas
- Intercostal neuralgia
- Facet arthropathy (cervical and lumbar)
- Interspinous ligaments
- Superior cluneal neuralgia
- Superior gluteal neuralgia
- Coccydynia
- Perineal pain
- Neuralgias of the groin (ilioinguinal, iliohypogastric, genitofemoral)
- Lower extremity neuralgias

Patient Preparation

The process of informed consent consists of discussing risk and benefits and specific contraindications to cryoneurolysis. Next, the cryoprobes are purged and machine checked. The patient is prepared under sterile conditions and is kept awake in order to determine location of pain generator by palpation and/or stimulation. Sensory and motor stimulations are then performed to identify the pain generator. Acceptable sensory stimulation thresholds are less than 0.4 mV. Motor stimulation should be 1.5 times greater than the sensory threshold. Cryoneurolysis is then performed using 3–4-min freeze cycles with 30-s thaw periods in between. During the thaw period, sensory stimulation should be performed to check the success of the initial freeze. Two or three additional freezes are then performed with 30-s thaw periods in between.

Postoperative Pain Control

Post-thoracotomy Pain

Intraoperative intercostal cryoneurolysis was first reported by Nelson in 1974 [21]. The treatment of intercostal nerves on each side of the thoracotomy incision makes sense to lesion. Initial retrospective studies showed significant efficacy, even up to 3 months after treatment. Unfortunately, a randomized study comparing epidural analgesia and intercostal nerve cryoanalgesia by Ju in 2008 [22] suggested a troubling side effect of allodynia-like pain for the cryoanalgesia group. Mustola in 2011 [23] confirmed these findings for a smaller group. Subsequently, the authors do not recommend intraoperative cryoanalgesia for postoperative pain management.

Post-herniorrhaphy Pain

Cryoneurolysis after herniorrhaphy was first described by Wood et al. in 1979 [24]. A cryolesion of the ilioinguinal nerve reduced analgesic requirements during the postoperative period. The follow-up study in 1981 compared recovery from herniorrhaphy among three study groups: patients treated with oral analgesics, patients undergoing cryoanalgesia, and patients receiving paravertebral blockade (the last two treatments supplemented with oral analgesics as needed). The study indicated that the cryoanalgesia group not only had less pain in the postoperative period but also used less opioid, resumed a regular diet earlier, were mobilized faster, and returned to work sooner [25]. Despite these successes, the technique is not widely used. Given its effectiveness and freedom from side effects, it is ideal for ambulatory surgery. After repair of the internal ring, posterior wall of the inguinal canal, and internal oblique muscle, the ilioinguinal nerve on the surface of the muscle is identified and mobilized. The surgeon elevates the nerve above the muscle, and an assistant performs the cryoablation.

Chronic Pain Management Technique: Tips for Best Placement

Cryoanalgesia utilizes an introducer technique to place the tip of the probe in the closest proximity to the targeted nerve. The introducers are large-bored intravenous catheters,

usually 14 or 16 ga but as large as 12 ga to accommodate the cryoprobe. The cryoprobe must be placed in a linear manner, and the tip cannot be curved due to the mechanism of the multiple treatment tubes carrying the nitrous oxide gas. The cryoprobe tip must be close enough to the targeted nerve to create a full ice ball and must extend far enough outside of the introducer catheter. Of course, regional anesthesia anatomy is imperative for the practitioner to place the cryoprobe appropriately and efficiently.

Several techniques are used to enhance precise placement of the cryoprobe, as follows:

1. Careful palpation with a small blunt instrument, such as a felt-tipped pen, can help to localize a soft tissue neuroma or another palpable pain generator.
2. An image intensifier (fluoroscopy) can identify bony landmarks.
3. Contrast medium improves definition of tissue planes, capsules, and spaces. (Nonionic contrast medium should be used in areas close to neural tissue.)
4. The nerve stimulator at the tip of the cryoprobe is used to produce a muscle twitch in a mixed nerve. The stimulator is set at 5 Hz for recruitment of motor fibers. The probe is closest to the nerve when the lowest output produces a twitch response. In general, twitches should occur at 0.5–1.5 V. Small sensory branches contain no motor component and do not twitch with electrical stimulation. These fibers are localized by using higher-frequency (100-Hz) stimulation, which produces overlapping dysesthesia in the distribution of the small sensory nerve. This procedure may reproduce the patient's pain. Use of low-output (<0.5–1.5 V) stimulation ensures closer placement of the cryoprobe to the nerve in question. The operator freezes the nerve for 2–3 min. Often, the patient has discomfort initially as cooling begins, but it should dissipate quickly. If significant pain persists beyond 30 s, the operator should investigate whether the ice ball is in the proper position. (If the ice ball is not sufficiently close to the nerve, and only partial freezing occurs, mostly of larger myelinated fibers, unchecked unmyelinated fiber input is left. This theoretically accounts for increased pain.) The brief cooling already may have altered nerve function, in which case, if positioning of the probe depends on feedback from the patient, it could be impeded. Before moving the probe, the operator must be sure to thaw the tip to prevent tissue damage from ice ball adherence to the tissues. In general, with closed procedures, two freeze cycles of 2 min each, followed by thaw cycles, are sufficient. In areas with a large vascular heat sink, longer periods of cryotherapy are necessary. Pain relief should be immediate and should be assessed subjectively and by physical examination while the patient is on the procedure table. All relevant clinical information should be recorded in the medical record. A hard-copy radiograph should be obtained for most procedures when a fluoroscope is used.

Facial Neuralgias

Craniofacial nerves can be cryolesioned with a percutaneous or open technique [26, 27]. Entrapment neuropathies and neuromas are more responsive to local anesthetic and cryodenervations than neuropathies of medical causes. Meticulous diagnostic injection ensures the best outcome with cryoablation [15]. If the patient has a good analgesic response to a series of local anesthetic injections, cryodenervation is an option. The technique of cryodenervations of cranial and facial nerves is the same as that for other peripheral nerves. A nerve stimulator is used to localize the nerve. Because these areas are densely vascular, injecting a few milliliters of saline solution containing 1:100,000 epinephrine is recommended before inserting the cryoprobe introducer cannula. A post-procedural ice pack applied for 30 min reduces pain and swelling.

Irritative neuropathy of the *supraorbital nerve* often occurs at the supraorbital notch [27]. Vulnerable to blunt trauma, this nerve often is injured by deceleration against an automobile windshield. Commonly confused with migraine and frontal sinusitis, the pain of supraorbital neuralgia often manifests as a throbbing frontal headache. At times, many of the hallmarks of vascular headache are present, including blurred vision, nausea, and photophobia. This neuralgia often worsens over time, perhaps owing to scar formation around the nerve.

Neuropathic pain in the distribution of the supraorbital nerve can be addressed with an open or closed cryoablative procedure as long as appropriate conservative therapy has failed and the pain responds to a series of test local anesthetic injections. For an open procedure, the incision is buried beneath the eyebrow, so the patient has no obvious scar. For the percutaneous technique, the introducer catheter should be inserted at the eyebrow line to avoid damage to hair follicles.

The *infraorbital nerve* is the termination of the second division of the trigeminal nerve. Irritative neuropathy can occur at the infraorbital foramen secondary to blunt trauma or fracture of the zygoma with entrapment of the nerve in the bony callus. Commonly confused with maxillary sinusitis, the pain of infraorbital neuralgia most often is exacerbated by smiling and laughing. Referred pain to the teeth is common, and a history of dental pain and dental procedures is typical. Cryoablation can be accomplished by an open or closed technique. The closed technique can be performed from inside the mouth through the superior buccolabial fold. In both operations, the probe is advanced until it lies over the infraorbital foramen. The intraoral approach has cosmetic advantages only.

The *mandibular nerve* can be irritated at many locations along its path. It is often injured as the result of hypertrophy of the pterygoids secondary to chronic bruxism, but it also can be irritated if the vertical dimension of the oral cavity is reduced owing to tooth loss or altered dentition. Pain is often referred to the lower teeth, and patients frequently undergo dental evaluations and procedures.

Injury to the *mental nerve*, the terminal portion of the mandibular nerve, frequently occurs in edentulous patients. Pain can be reproduced easily with palpation.

The *auriculotemporal nerve* can be irritated at many sites, including immediately proximal to the parietal ridge at the attachment of the temporalis muscle and, less commonly, at the ramus of the mandible. Patients often present with temporal pain associated with retro-orbital pain. Pain often is referred to the teeth. Patients frequently awaken at night with temporal headache. The pain, described as throbbing, aching, and pounding, can be bilateral, and it is commonly associated with bruxism and functional abnormalities of the temporomandibular joint, maxilla, and mandible. The clinician must rule out other medical causes for this form of headache, including temporal arteritis, before considering treatments for auriculotemporal neuralgia. Posterior auricular neuralgia often follows blunt injury to the mastoid area. It is common in abused women and usually involves the left side owing to the preponderance of right-handed abusers. The clinical presentation consists of pain in the ear associated with a feeling of "fullness" and tenderness. This syndrome often is misdiagnosed as a chronic ear infection. The posterior auricular nerve runs along the posterior border of the sternocleidomastoid muscle, superficially and immediately posterior to the mastoid.

The *glossopharyngeal nerve* lies immediately subjacent to the tonsillar fossa. This painful condition can be treated by applying the cryoprobe for two cycles of 2 min each after local anesthetic injections have produced the appropriate responses. This is essentially a simple procedure, but it has distinct advantages over injection of this cranial nerve at the tip of the mastoid, where injection could block the vagus nerve in addition to the spinal accessory nerves [26].

Many other common peripheral nerve injuries are amenable to cryodenervation, including most cutaneous branches and the occipital, suprascapular, superficial radial, and anterior penetrating branches of the intercostal nerves. Applied carefully, the techniques outlined in this chapter help to achieve the safest and the best possible outcomes.

Intercostal Neuralgia

Percutaneous cryolesions of the intercostal nerves can be offered for various pain syndromes, including postthoracotomy pain, traumatic intercostal neuralgia, rib fracture pain, and occasionally postherpetic neuropathy. For each of these conditions, a meticulous series of local anesthetic blocks are performed before consideration is given to cryoablation. The volume of local anesthetic should be kept to less than 3–4 ml to prevent tracking back into the epidural space. In addition, only two or three levels should be injected at any one time because systemic absorption could confound interpretation of the patient's response. Because the intercostal nerve runs with a large arterial and venous heat source, the use of two 4-min cryolesions at each level is suggested. The lesions should be made proximal to the pain at the inferior border of the rib. After the procedure, a chest film is obtained to check for pneumothorax. Effective blockade in some patients with postherpetic neuropathy suggests that this pain condition can have peripheral afferent input, as opposed to being strictly a central neuropathy.

A recent small retrospective study by Moore in 2010 [28] for CT-guided percutaneous cryoneurolysis for postthoracotomy syndrome showed efficacy, but no allodynic syndrome was seen in the open-cryotherapy studies.

Neuromas

Cryoanalgesia seems the most effective when prior diagnostic blocks have mapped out a discrete pain generator. Initial test local anesthetic injections should contain 1 ml or less per site for the optimal benefit of cryoanalgesia. Either lidocaine or bupivacaine is typically injected with the patient's response and duration of analgesia recorded, sometimes longer than the duration of the local anesthetic. If the neuroma is successfully targeted, cryoanalgesia at this site could be a successful option.

Facet Arthropathy

Cryoanalgesia utilizes the same approach as typical facet and medial branch blocks also detailed in this textbook. Lumbar facet cryodenervations are performed at three levels similar to radio-frequency techniques. A 12 ga introducer catheter is introduced to the junction of the transverse process and the pedicle, the Scottie dog's eye. After sensory and motor testing via a nerve stimulator, two cryolesions are made, each for 2 min duration. Cervical facet cryodenervations are performed in the same manner as the initial diagnostic blocks, either in a prone or lateral manner.

Interspinous Ligament Pain

Interspinous ligament pain is common after a spine operation (lumbar, thoracic, or cervical). Pain impulses from interspinous ligaments are carried by the medial branch of the posterior ramus. Patients report severe movement-related spine pain, identified to the midline, which is worsened with hyperextension and relieved by small volumes of local anesthetic injected into the interspinous ligament. When cervical interspinous ligaments are involved, the patient frequently complains of posterior cervical headache. This headache

often is mistaken for occipital neuralgia. Cryodenervation can be considered in local anesthetic responsive patients. The pain relief helps the patient to complete the necessary course of physical therapy.

Coccydynia

When coccygodynia has failed to respond to conservative therapy, including the patient's use of a donut pillow, NSAIDs, and local steroid injections, consideration can be given to coccygeal neural blockade as the coccygeal nerve exits from the sacral canal at the level of the cornu. Bilateral test injections should produce short-term analgesia before cryoablation is considered. For cryoablation of the coccygeal nerve, the probe must be inserted into the canal to make contact with the nerve. Accurate placement of the ice ball is facilitated by using the 100-Hz stimulator and gauging the patient's response. Care should be taken to prevent bending the relatively large cryoprobe while inserting it into the canal.

Perineal Pain

Pain over the dorsal surface of the scrotum, perineum, and anus that has not responded to conservative management at times can be managed effectively with cryodenervation from inside the sacral canal with bilateral S4 lesions. Test local anesthetic injections should produce a positive response before cryoablations are performed bilaterally at S4. Inserting the cryoprobe through the sacral hiatus up to the level of the fourth sacral foramen for placement of a series of cryolesions can provide good analgesia. Bladder dysfunction usually is not encountered, and analgesia lasts 6–8 weeks. Perineal pain is difficult to treat with intrathecal neurolytic agents without risking bladder and bowel dysfunction.

Ilioinguinal, iliohypogastric, and genitofemoral neuropathies often complicate herniorrhaphy, general abdominal surgery, and cesarean section. Patients present with sharp, lancinating to dull pain radiating into the lower abdomen or groin. The pain is exacerbated by lifting and defecating. If the patient is responsive to a series of low-volume test injections, consideration can be given to cryodenervation of the appropriate nerve. Significant care and time must be spent localizing the nerve with the sensory nerve stimulator. The patient may help to localize the pain generator by pointing with one finger to the point of maximum tenderness. These nerves are difficult to localize percutaneously, and that difficulty has led to frequent misdiagnosis of the pain generator. In an effort to improve the accuracy of diagnosis, Rosser et al. [29] developed the *conscious pain mapping* technique. In a lightly sedated patient, a general surgeon working with a pain management specialist performs laparoscopic evaluation of the abdomen in an operating suite. The genitofemoral nerve, lateral femoral cutaneous nerve, and other structures are easily visualized. Blunt probing and patient feedback help to direct the physician to the area of pain. At times, objects such as ligatures and staples are found wrapped around the nerve, in which case they should be removed. If direct mechanical or electrical stimulation to the nerve reproduces the pain, cryoablation can be performed under direct vision. (Cryoablation is chosen as the appropriate test because the effect of bupivacaine does not outlast the discomfort of the perioperative period. The cryoblockade provides weeks to months of reliable analgesia and helps physicians and patients to determine whether that structure under surveillance carried the pain information.) Pain usually returns. A repeat cryoablation is possible when analgesia is long or an open surgical procedure with sectioning and burying can be performed.

Lower Extremity Pain

Many cutaneous nerve branches are responsive to cryodenervation. The clinician always must perform a complete physical examination, with careful touching of the painful area. After the primary pain generator is localized, a series of low-volume local anesthetic injections can be given. If the patient has a consistent response, cryodenervations, as outlined earlier, can be employed. Some common lower extremity nerve pain syndromes that are often amenable to cryodenervation are described next.

Neuralgia resulting from irritation of the *infrapatellar branch of the saphenous nerve* develops weeks to years after blunt injury to the tibial plateau or after knee replacement. The nerve is vulnerable as it passes superficial to the tibial collateral ligament, pierces the sartorius tendon and fascia lata, and runs inferior and medial to the tibial condyle. The clinical presentation consists of dull pain in the knee joint and achiness below the knee. Patients tend to adopt an antalgic gait. Pain with digital pressure is diagnostic. Patients are considered candidates for cryodenervation when they respond consistently to local anesthetic blocks. A 12-gauge intravenous catheter is used as the introducer to prevent cold injury to the skin. Because prodding with a felt-tipped pen alone is sufficient to localize the pain generator, the sensory nerve stimulator does not have to be used.

Neuralgia secondary to irritation of the *deep and superficial peroneal and intermediate dorsal cutaneous nerves* can be seen weeks to years after injury to the foot and ankle. These superficial sensory nerves pass through strong ligamentous structures and are vulnerable to stretch injury with inversion of the ankle, compression injury owing to edema, and penetrating trauma from bone fragments. The intermediate dorsal cutaneous nerve runs superficial and medial to the lateral malleolus, continues superficial to the inferior extensor

retinaculum, and terminates in the fourth and fifth toes. This nerve is particularly vulnerable to injury after sprains of the lateral ankle. The clinical presentation consists of dull ankle pain that is worse with passive inversion of the ankle. Disproportionate swelling, vasomotor instability, and allodynia are remarkably common. Patients tend to adjust their gait to minimize weight bearing on the lateral aspect of the foot. Pain with digital pressure in the area between the lateral malleolus and extensor retinaculum is diagnostic.

Peroneal Nerve

Superficial and deep peroneal nerve injury often occurs in diabetic patients, who are vulnerable to compression injury from tight-fitting shoes, and is less common after blunt injury to the dorsum of the foot. The clinical presentation consists of dull pain in the great toe that is often worse after prolonged standing. Patients tend to adjust their gait to minimize weight bearing on the anterior portion of the foot. Pain with digital pressure in the area between the first and second metatarsal heads is often diagnostic.

Superior Gluteal Nerve

Neuralgia resulting from irritation of the superior gluteal branch of the sciatic nerve is common after injury to the lower back and hip sustained while lifting. After exiting the sciatic notch, the superior gluteal nerve passes caudal to the inferior border of the gluteus minimus and penetrates the gluteus medius. Vulnerable as it passes in the fascial plane between the gluteus medius and gluteus minimus musculature, the superior gluteal nerve is injured as a result of shearing between the gluteal muscles on forced external rotation of the leg and with extension of the hip under mechanical load. Rarely, it is injured by forced extension of the hip, an injury that may occur in a head-on automobile collision when the foot is pressed against the floorboards with the knee in extension as the patient braces for impact. The clinical presentation consists of sharp pain in the lower back, dull pain in the buttock, and vague pain to the popliteal fossa. Pain below the knee is unusual. Patients generally experience pain with prolonged sitting, leaning forward, or twisting to the contralateral side. Often, patients describe "giving way" of the leg. They usually sit with the weight on the contralateral buttock or cross their legs to minimize pressure on the involved side. With the patient in the prone position, the medial border of the ilium is palpated. The nerve is located 5 cm lateral and inferior to the attachment of the gluteus medius. The peripheral nerve stimulator is employed to ensure that motor units are not inadvertently blocked.

Future Directions

Cryotechnology offers potential analgesia for many different pain conditions both acute and chronic. Its effective and safe use on sensory and mixed nerves contrasts with radiofrequency technology, which has the potential to produce deafferentation pain syndromes particularly with continuous wave applied to peripheral nerves. The lack of controlled studies, the lack of uniform training, and the poor communication to referrers and patients have impeded widespread use of the technology. The application of ultrasound technology may expand the use of cryoanalgesia, with visualization helping the placement of the cryoprobe on larger nerves such as the intercostal nerves [30]. One area of interest could include a randomized study of cryotherapy compared to pulsed radio-frequency ablation for analgesia for peripheral neuropathies measuring efficacy and duration of effect. Given the long record for safety and the population's general acceptance of ice/cold-based therapies, cryoanalgesia could be revitalized for the future pain medicine providers.

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Radiofrequency: Conventional and Pulsed

7

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Key Points

- Radiofrequency uses an insulated needle with electrode and thermocouple to provide a precise controlled temperature lesion.
- The setup of a radiofrequency circuit [4–6] involves a generator to produce and drive the energy, a dispersive pad (grounding plate) to return energy to the generator, and an insulated introducer needle with an electrode and thermocouple to provide a precise, controlled temperature lesion.
- The exact mechanism of pulsed radiofrequency is unclear; however, pulsed radiofrequency is a *neuromodulatory* treatment option as opposed to the *ablative* conventional radiofrequency.
- Evidence exists for the routine use of CRF for treating pain due to trigeminal neuralgia and zygapophyseal joint pathology. Present data indicates that the benefit after pulsed radiofrequency may not be as long lasting when compared to conventional radiofrequency.
- Further investigations are warranted into the mechanism of PRF before disposing of this procedure as a viable technology.

Introduction

Radiofrequency technology, the manipulation of electrical energy to produce a desired clinical effect, has been utilized in various settings, including pain management, electrocardiology [1], and oncology [2]. In the pain management universe, radiofrequency energy has been utilized for many indications; however, the treatment of cervical facet syndrome, lumbar facet syndrome, and sacroiliac discomfort [3–5] is the most common application for this technology. Pulsed radiofrequency (PRF) is a relatively recent [4] entity designed to provide the benefit of conventional radiofrequency (CRF) with a decrease in side-effect profile.

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Physics of Radiofrequency

Before undertaking a discussion of radiofrequency, certain concepts of physics applicable to this technology must be reviewed to understand the technology. *Current* is the transfer of energy from an electrical source and is measured in hertz (Hz); *voltage* (volts) is the force that drives the current; *impedance* (ohms) is the resistance to the flow of current.

These concepts are represented by the following equation:

$$V = I \times R$$

where V is voltage, I is current, and R is impedance.

CRF involves controlled administration of alternating current electrical energy at 500 kHz (kilocycle/s) range. Current is utilized at the kilocycle Hz range, as alternating current (AC) at a lower frequency would be very painful in clinical use [6]. Direct current is not utilized in this radiofrequency technology as the frequency of this energy is zero and would lead to less precision during lesion formation.

The setup of a radiofrequency circuit [4–6] involves a generator to produce and drive the energy, a dispersive pad (grounding plate) to return energy to the generator, an insulated introducer needle to prevent dispersal of energy outside of the targeted area, and an electrode with a thermocouple to provide a precise area of therapy and temperature measurement.

The description of the electrical field that is responsible for the clinical effect of CRF is governed by Maxwell's equations on electromagnetism [4]. At the frequencies

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utilized in RF technology, electrical and magnetic fields are generated; however, the magnetic field's effect is negligible [7]. The current density that is responsible for clinical effect is a function of the electrical conductivity of tissue [8]. Structures that readily conduct electrical energy such as nervous tissue and water will have higher current density than those structures with a lower conductivity (bone). Also, the coagulated tissue that is produced during CRF may serve to affect impedance as the resultant tissue may decrease the flow of energy into tissues.

As energy flows from the generator via electrical current to the electrode, ions in tissue electrolytes are activated and oscillated [6–8]. As a result of the kinetic energy produced by this Brownian motion, heat is dispersed from the ions and is measured by the thermocouple. Increasing the flow of current will increase the resultant temperature, known as ohmic or resistive heating of tissue, as measured at the thermocouple. In summary, the tissue heats up the electrode, and the electrode does not heat up the tissue.

Temperatures utilized typically range from 80 to 90 °C, although the minimum temperature to produce irreversible neuronal interruption is 44 °C [9]. Higher temperatures may lead to side effects including hematoma, smoke, and gas formation, along with adherence to tissues to the probe [9]. Nociceptive input is theoretically reduced as the therapy is aimed for sensory nerve fibers.

Utilizing a temperature-time controlled process, a lesion is produced with treatment. Precision in lesions developed with the introduction of a 22-G RF cannula, smaller than previous devices [10]. The size of the lesion is affected by factors including the diameter of the electrode, the active tip length, tissue characteristics, and vascular supply near the lesion site. The lesion size and tissue injury can be evaluated through the relation between the current divided by the electrode surface area known as the current density. For a given constant current, with a decrease in electrode surface area, a greater current density, tissue heating and resultant lesioning will occur.

Power [11] provided by the generator, along with lesion time, also affects lesion size. Lesion time has been found to be significant in increasing the size of the heat effect up to 40 s. The temperature at the thermocouple along with the cannula size is an important factor in the size of the lesion, as heat generated in the process believed to be responsible for the clinical effects of radiofrequency.

Due to the shape of the needle and the electrode, an oblate spheroid lesion is produced [6, 8, 9, 11]. A temperature-controlled system is preferred over a voltage-controlled system as lesion size and temperature achieved can more reliably result, leading to a more predictable lesion. Voltage-controlled lesioning may produce temperatures below or above target range, leading to lesions of variable efficacy [9].

Physics of Pulsed Radiofrequency

Pulsed radiofrequency differs from CRF in that pulsed radiofrequency does not lead to a neurodestructive process [3, 4]. This theoretical benefit is important for sensitive nerves such as peripheral nerves in the head and neck, dorsal root ganglia, trigeminal ganglia, and peripheral nerves in the abdominal and inguinal regions [12, 13], and the lower extremity.

During the developmental phases of what is now known to be pulsed radiofrequency, interest was sought for the possible beneficial role of the magnetic field in treatment. Cosman et al. [14] determined that the magnetic component was an incidental vector that would have negligible effects toward clinical benefit [7]. It was then proposed to deliver energy in waves or pulses with a short rest period between generator activation. This rest period would allow the dispersal of the heat that was generated (as in CRF). This interrupted treatment would theoretically deliver electrical energy to elicit a clinical response, but not lead to the side effects of denervation and its resultant complications. In the initial description by Sluijter et al. [14], the pulses were for 20 ms separated by 0.5 s. This separation allowed for a rest period whereby heat that is generated by oscillatory motion would be allowed to dissipate via vascular runoff. Still, this treatment should not be thought of as a "nonthermal" lesion as there is increased temperature at the thermocouple. Consequently, as the pulse duration is a fraction of total pulse time (pulse duration + interpulse duration), voltage utilized during PRF is higher without risking increased temperature change with the higher energy.

PRF technology, however, may also lead to lesion injury. Heavner et al. [15] however showed that when PRF is utilized (10 ms duration at 2 Hz), coagulation begins to occur in egg-white media at a temperature of 60 °C. Therefore, regardless of technology, PRF vs. CRF, increased temperature at the tip can lead to coagulation and tissue injury. In essence, PRF as is currently used is a *neuromodulatory* treatment option as opposed to the *ablative* CRF.

The exact mechanism of PRF's clinical benefit is unclear; initially, PRF was believed to play a role in causing neuronal plasticity with upregulating of c-Fos [16] in rat DRG. c-Fos is a proto-oncogene that is expressed in response to neuronal activity and may have a role in nociceptive transmission. Animals were exposed to RF at the C6 dorsal root ganglion, via CRF at or PRF, at 38 °C for 120 s. Immunohistochemical assays for c-Fos were performed, and animals with PRF had an increased expression of the protein in laminae I and II of the spinal cord; this expression was not seen in animals exposed to CRF.

Additionally, c-Fos staining cells were found ipsilateral and contralateral to the side of PRF treatment. The implication of this finding is that PRF activates the dorsal horn laminae I and II neurons and could be a possible explanation for

the clinical benefit of PRF, as both CRF and PRF animals were subject to the same temperature. This choice to have the temperatures of both CRF and PRF by the authors in the experimental design of this study leads to the possibility of deducing that a factor *intrinsic* to PRF not seen in CRF would lead to c-Fos expression.

This c-Fos selectivity for PRF-treated animals was subsequently refuted in a study by Van Zundert et al. [17] where sham, PRF, and continuous RF were applied adjacent to the cervical DRG of rats. All three groups had induction of c-Fos with staining that was noted 7 days after treatment study. Additional research is warranted regarding the genetic changes that may result and be responsible for the clinical effect of PRF.

Cahana et al. [18] evaluated in vitro neuronal preparations to determine tissue effects of CRF at 42 ° C versus PRF at 38 and 42 °C. The electrical energy required in CRF was less than that in PRF, yet CRF was found to be a destructive lesion in which heat was generated, with PRF specimens showing less tissue injury [18].

Cosman and Cosman [6] have opined that the heat produced with the pulsed energy may be responsible for the clinical benefit of PRF. This heat is subsequently removed during the rest phase, however. Additionally, they suggest that electroporation may be a factor in leading to the clinical effect of PRF. This concept is the alteration in electrical conductance and membrane permeability of a cell membrane in response to an applied electrical field, theoretically leading to analgesic benefit after PRF.

Hagiwara et al. [19] have opined that the analgesic action of PRF involves the action of the accessory adrenergic pain pathways. Hamann et al. [20] have looked at the possible mechanism of PRF and suggest that PRF targets neurons with small diameter axons by evaluating the role of activating transcription factor 3 (ATF-3), a marker of cellular stress, in rats. DRG application of PRF led to an increased presence of ATF-3 in neurons. The authors suggest that PRF can lead to increased cell stress in the absence of direct thermal lesioning. The role of this factor and others in regards to PRF is yet to be fully elucidated.

A proteomic study [21] has also been performed in rats to look at protein expression in animals treated with PRF. L5 dorsal root ganglia were exposed to PRF and sham therapy. Western blotting of samples showed increased levels of gamma-aminobutyric acid (GABA) and decreased 4-aminobutyrate aminotransferase (enzyme involved in production of GABA) in animals treated with PRF. GABA is a neurotransmitter regulating neuronal excitability. Further studies are warranted in exploring the role of PRF on GABA [22, 23].

Histological Effects of Radiofrequency

Animal studies have been performed evaluating the histological effects of CRF therapy. In a study involving CRF of goat (DRG), de Louw et al. [24] found that a temperature of 67 °C at the DRG can lead to hemorrhagic loss of myelinated fibers. This neural destruction is absent if the CRF is performed *adjacent* to the DRG. Consequently, the heat lesion leads to neuronal injury after a radiofrequency procedure. Animal research has led to the theory that CRF was a selective lesioning modality, preferentially targeting C and A-δ fibers occurred before affecting the larger myelinated A-α and A-β fibers. Other studies have contradicted this result, and CRF is now widely thought of as leading to heat-induced equal destruction of all nerve fibers. Dreyfuss et al. [25] showed that RF neurotomy is a nonselective treatment that affects and coagulates all nerves as a result of EMG studies [26].

Vatansever et al. [27] compared the effects on the sciatic nerve of male Wistar rats. Five groups were studied: no procedure, sham procedure, 40 °C CRF for 90 s, CRF 80 °C for 90 s, and PRF for 240 s. CRF 40 °C showed the presence of endoneurial edema in the subperineurial and perivascular areas of the nerve. Light microscopy specimen evaluation demonstrated transverse myelin fibers damaged along with separation of the axoplasma. This separation would lead to impaired nerve transmission. Electron microscopy also confirmed alteration of myelin configuration. Additionally, lamellous separation with protrusion of myelin and accumulation of neurofilaments was found, pointing to a diagnosis of neurodegeneration.

CRF 80 °C showed significant endoneurial edema and evidence of Wallerian degeneration. Electron microscopy showed evidence of neurodegeneration, including epineurial thickening, lamellous separation, intra-axonal vacuolization, increased intracellular endoplasmic reticulum, and Schwann cell damage.

PRF demonstrated changes similar to CRF 40, but the severity of lesions was less.

Podhajsky et al. [28] observed effects of 80 °C CRF and 42 °C PRF lesions on rat DRG and sciatic nerves for 2, 7, and 21 days after initial treatment and found similar results. Massive edema in specimens was seen on day 2 with 80 °C treatment. Wallerian degeneration and tissue coagulation were observed on the 7th day after treatment. With 42 °C, edema was also seen on the 2nd day of treatment, but *regressed* and *resolved* by the 7th day.

Animal studies were also performed in rabbits [29] to evaluate PRF vs. CRF current on the DRG. Animals were in a PRF, CRF, control, or sham grouping. No changes noted at

2 weeks after treatment under light microscopy. By electron microscopic sections, CRF-DRG specimens showed degenerative changes including evidence of cytoplasmic vacuoles, a large endoplasmic reticulum, mitochondrial degeneration, and the loss of nuclear membrane material. PRF did not show the intensity of these changes, with just the presence of large vacuoles throughout the cytoplasm.

Studies on the Efficacy of Radiofrequency

Trigeminal Neuralgia

CRF has been utilized for patients with trigeminal neuralgia, a devastating neuropathic pain state, often very difficult to treat. Radiofrequency has been shown to be the best option for complete pain relief when compared to other approaches including surgical treatments [30]. Kanpolat et al. [31] performed radiofrequency trigeminal rhizotomy on patients with trigeminal neuralgia, looking at 1,600 patients over a 25-year period. Excellent relief of pain symptoms was noted initially with a decrease of 57.7 % at 5-year follow-up. The number of patients with complete relief after a single procedure decreased to 52.3 % by the time a 10-year follow-up was performed. The study also provided side effects that may be present in patients undergoing an ablative procedure on the gasserian ganglion, highlighting the risks of corneal reflex changes, keratitis, masseter muscle dysfunction, cranial nerve II and VI paralysis, and anesthesia dolorosa. PRF has been evaluated against CRF [32], with the former not as effective as the latter in treating the pain of trigeminal neuralgia.

Cervical Zygapophyseal Joints

The "facets" are in actuality the zygapophyseal joints (z-joints) that are made of adjacent articular processes. The term facet describes the curved cartilaginous lining of the z-joints. The joints are involved in the range of motion of the cervical spine. The zygapophyseal joints in the cervical spine may be implicated in 54–60 % of patients with chronic neck pain [33]. Neural innervation of the joint is provided by medial branches of the spinal nerves with each joint is innervated by the adjacent two medial branches.

After successful block of the joint or the medial branches that supply the joints, radiofrequency treatment can be performed for longer-term benefit of painful symptoms. Cohen et al. [34] have evaluated in a multicenter analysis the factors that predict success for cervical radiofrequency denervation and noted the presence of pre-procedure paraspinal tenderness as the best prognostic sign. Lord et al. [35] evaluated patients with chronic z-joint pain after motor vehicle accident in a double-blinded randomized controlled trial, treated with CRF for analgesic relief. A positive result of 100 % pain relief with three diagnostic/therapeutic blocks with local anesthetic and steroid was required prior to inclusion in the study. Patients had a median time from initial relief to 50 % of pain returning at 263 days.

Sapir et al. [36] evaluated patients with cervical whiplash symptoms undergoing cervical neurolysis. There was a statistical significance in improvement in patients VAS scores regardless of litigation status by patients. Long-term follow-up and benefit was noted of the radiofrequency procedure in a paper by McDonald et al. [37]. The median duration in their study of 28 patients diagnosed as having cervical zygapophyseal joint pain was 219 days. In a Cochrane analysis, Niemisto et al. [38] evaluated the efficacy of cervical radiofrequency and found limited evidence for short-term benefit.

Other Painful Conditions of the Cervical Spine

Slappendel et al. [39] published a report of the results of a randomized, double-blinded multicenter trial on the effect of CRF of the cervical DRG to treat cervicobrachial pain. This study evaluated the difference in temperature between two groups: one population was treated with CRF at 67 °C and the other group at 40 °C. Both patient groups developed a decrease in VAS scores; however, the 40 °C group maintained their decrease at 3-month follow-up. Van Zundert et al. [40] have evaluated PRF in the treatment of cervical radicular pain adjacent to the cervical DRG and found the technique be satisfactory at reducing discomfort for a mean duration of 9 months.

The concept of cervicogenic headache is a controversial topic in pain management circles. Difference of opinion exists between physicians as to whether this entity deserves a diagnosis or not [41].

Multiple papers [41–43] have provided a description of this unilateral headache that is present in the occipital or neck region, radiating to the temporal and/or frontal aspect of the cranium. Stovner et al. [44] have evaluated the use of radiofrequency denervation of facet joints for cervicogenic headache via a double-blinded, sham-controlled randomized double-blinded study. Twelve patients with unilateral cervicogenic headache were evaluated with half randomized to receive C2–C6 neurotomy and the others to receive sham therapy. Patients were followed for 2 years, with improvement noted at 3 months in the treated group. The authors followed patients for 2 years after the initial treatment and found no significant benefit for the use of this technology. Haspeslagh et al. [45] compared the use of radiofrequency of the medial branches supplying the z-joints, the dorsal root ganglion against an injection of local anesthetic at the greater occipital nerve with

subsequent application of transcutaneous electrical nerve stimulation. There was no evidence that cervical z-joint radiofrequency was superior to injection of the greater occipital nerve and TENS application. The results of this study may be questioned, however, because of the small sample size (15 patients) and a relatively large number of patient dropouts. Govind et al. [46] have evaluated radiofrequency denervation for headache pain by targeting the third occipital nerve a particularly tenacious nerve. Multiple lesions, larger electrode (greater than 22 G), were utilized for best clinical effect. Untoward side effects such as ataxia, paresthesia, numbness, and dysesthesia may result from this procedure.

Navani et al. [47] presented their report of the use of PRF in a patient with occipital neuralgia. The patient underwent PRF at the medial branches of C1 and C2 dorsal rami with three cycles of 42 °C for 120 s. The patient subsequently underwent another PRF treatment 4 months after initial therapy with improvement of symptoms. As with PRF in other cervical applications, the benefits of treatment as compared to CRF here are evident with less potential risk of neuritis pain induced by heat lesions. Further research is warranted for the use of PRF for this indication.

Thoracic

The thoracic zygapophyseal joints may be a source of discomfort in patients. These joints may be the source of thoracic spine and segmental discomfort in the thoracic region. Stolker et al. [48] evaluated thoracic facet joint CRF and reported benefit of neurolysis. Nearly half of patients were noted to be pain free after 2 months, 83 % of patients achieving greater than 50 % pain relief after 18–54-month follow-up. Cohen et al. [49] evaluated patients who were treated for post-thoractomy pain with PRF of thoracic DRG vs. those patients treated with analgesics or PRF of the intercostal nerves and found that PRF of the DRG was superior.

Lumbar Pain

The lumbar z-joints are also paired, diarthrodial joints that are involved in the range of motion of the lumbar spine. Goldthwait [50] first presented the lumbosacral articulation as a source of low back pain in 1911. After a series of medial branch or z-joint injections, radiofrequency therapy may theoretically improve patient pain for a longer period than the duration of the agents utilized during injection therapies. Cohen et al. [51] also studied the predictors of success for a radiofrequency procedure in the lumbar region and again found paraspinal tenderness to be the most significant predictor of success. Additionally, the degree of pre-radiofrequency analgesia (percent improvement after block) had *no effect* on post-radiofrequency effect in patients who had at least 50 % pain relief with blocks.

Dreyfuss et al. [25] found that patients with the longest time of relief were those patients who had resultant multifidus muscle denervation based on EMG study after CRF. Nath et al. [52] evaluated patients receiving a positive facet joint injection block who subsequently underwent sham or CRF. Patients who were actively treated had a statistically significant improvement in back and leg pain with improved range of motion, indicating that the beneficial effects noted by patients were not due to placebo effect.

Gallagher et al. [53] evaluated radiofrequency for the z-joints as a treatment for low back pain in a double-blinded prospective study. The visual analog scale (VAS) was utilized to evaluate pain scores and relief after therapy. Patients receiving radiofrequency were compared to sham therapy with VAS was improved at 1 month and 6 months versus sham therapy. Van Kleef et al. [54] also demonstrated the benefit of radiofrequency by studying a group of 31 patients in a prospective double-blind randomized trial. Patients with lumbar facet degeneration after chronic low back pain who had benefit (50 % pain relief) with medial branch blocks underwent CRF vs. sham-treated patients. Test subjects were evaluated 8 weeks after the trial, then at present at 3, 6, and 12 months after initial therapy. There was statistically significant difference between the groups with CRF patients exhibiting lower analgesic requirements and improved disability status vs. patients receiving the sham therapy. The goal of DRG CRF is to perform a selective blockade of afferent nerve conduction with avoidance of damage to the ganglion. Geurts et al. [55] published a multicenter randomized control trial for evaluating lumbar DRG CRF in patients with chronic lumbosacral pain. Patients were evaluated with VAS and also the SF-36 quality of life pain measure. The results of this randomized double-blinded placebo-controlled study were that there was that CRF of lumbar DRG *should not* be routinely performed as benefit was not seen.

Radiofrequency ablation in the lumbar z-joint region did not have benefit in one study [56]. This placebo-controlled clinical trial resulted in negative recommendation for lumbar radiofrequency ablation. The criticism of this study is that there was a high inclusion rate of patients in this study. Slipman et al. [57] showed that radiofrequency ablation while leading to clinical improvement of pain was rated as having level III evidence based on evidence-based medicine criteria based on review of the literature. Manichikanti et al. [58] performed their own review of the literature that resulted in *strong* evidence for short-term relief of pain symptoms, but *moderate* evidence for lumbar radiofrequency for longer-term relief. Kornick et al. reported on complications [59] of lumbar radiofrequency noting that in 116 denervation procedures in 92 patients that no motor or sensory deficits were present in patients. This of course assumes that motor and

sensory checks are performed by the operator before the lesioning procedure occurs.

Radiofrequency ablation has had effects for 6 months to a year [4]. In those patients who had repeat radiofrequency procedures, benefit may be achieved with the subsequent procedure. Schofferman and Kine [60] showed in a retrospective chart review of 20 patients who had an initial successful benefit with radiofrequency subsequently developed pain and then had a repeat radiofrequency procedure. Larger needle sizes (20-G electrode with a 10-mm active tip or a 16-G rhizotomy electrode) were utilized. Also, the CRF was 80 °C for 70 s. The mean duration of relief with the repeat RF was 11.6 months for a second RF procedure. Overall, improvement after repeat RF treatments was 10.6 months.

The first use of PRF was described by Sluijter in 1998 [14]. This prospective-controlled trial compared the results of utilizing the new technology with CRF at 42 °C. The authors concluded that PRF was superior to CRF at the parameters used due to a global perceived effect (GPE) that was higher in the former group.

Teixera has suggested the use of lumbar DRG PRF for surgical candidates with radicular pain. PRF DRG was recommended as an alternative to lumbar epidural injections as a treatment option, and 12/13 patients studied were able to avoid surgery for at least 1 year [61].

PRF has also been evaluated for use in patients having pain attributed to the z-joints in the lumbar region. Linder et al. performed a retrospective review [62] of patients undergoing PRF for low back pain. Patients in this study included those having back surgery and those with no history of prior surgical intervention. Prior to CRF, patients had analgesia with one diagnostic medial branch block. The authors found that PRF was beneficial in both patient populations, but more effective in patients who did not have prior back surgery. Mikeladzke et al. [63] evaluated the technology in patients with chronic z-joint pain and found that PRF was beneficial in providing pain relief lasting for almost 4 months.

Kroll et al. [64] performed a randomized double-blinded prospective study comparing CRF vs. PRF in the treatment of chronic z-joint pain. CRF was performed at 80 °C for 75 s and pulsed radiofrequency of 42 C with a pulse duration of 20 ms with a pulse rate of 2 Hz for 120 s. The VAS and the Oswestry Disability Questionnaire were utilized to gauge patient response to treatment at baseline and interval follow-up. There was no significant difference between CRF and PRF in long-term outcome. Additionally, there was greater improvement over time within CRF. A criticism of this study is the large dropout rate of 48 %.

Tekin et al. [65] evaluated the effects of CRF vs. PRF in 40 patients, with an additional 20 patients as control. The VAS and ODI were also utilized for evaluation at procedure, 6-month and 1-year follow-ups. While PRF and CRF patients had improvement in measured parameters, the maintenance of the decrease in VAS was greatest in patients who had CRF as opposed to patients with PRF. The result of therapy was longer lasting in the CRF group.

PRF has also been used in the lumbar region to treat discogenic pain [66]. High-voltage, long-duration PRF has been utilized to treat 8 patients. A 15-cm 20-G needle was placed in the nucleus pulposus for 20 min PRF at 2 × 20 ms at 60 V. The study achieved 100 % improvement of pain on a VAS query. Further controlled studies are mandated for applicability in this domain.

Sacroiliac

The sacroiliac joint may be a common cause of back pain. Goldthwait and Osgood [67] proposed the SI joint to be an independent source of back pain. Estimates of the source of discomfort attributed to the SIJ range from 18 to 30 % [68, 69].

RF ablation of the sacroiliac joint has also been attempted with mixed results. Ferrante et al. [70] published the first description of an RF technique of this pain generator by describing a "leap frog" technique of overlapping bipolar lesions, less than 1 cm apart, along the length of a sacroiliac joint. Lesions were created at 90 °C for 90 s. The distance between lesions was questioned for this bipolar approach [71]. Cohen and others [72, 73] then presented a description of a lateral branch block radiofrequency.

Burnham and Yasui [74] have also described the use of a lateral branch approach for CRF of pain attributed to the SI joint. Nine subjects underwent strip RF lesions at the lateral dorsal foramina at S1–S3 along with monopolar lesions at the L5 dorsal ramus. Patients were then evaluated every 3 months up to a year. The results of this small-numbered, prospective cohort study indicated a decrease in analgesic requirements and back and leg pain.

Cooled RF has also been described [75, 76]. This is a technology devised to decrease the heating occurring at the electrode tip during CRF. The result is decreased impedance at the electrode tip, with a theoretical delivery of higher energy, with a larger lesion size than CRF.

Cooled RF was associated with a greater number of positive RF outcomes, likely because of the larger diameter lesion size associated with this technology compared to CRF. Kapural et al. [75] published a retrospective review of 47 procedures on 27 patients in which cooled RF was utilized for dorsal rami of L5 and S1–S3 lateral branches. Patients exhibited improvement in function (as measured by the Pain Disability Index-PDI) and VAS.

Pulsed RF has also been described in one study, with patients receiving PRF of the medial branches of L4 and L5 and the lateral branches of S1 and S2. The duration of pain relief in this study was 20 weeks [77].

Inguinal

PRF would show a theoretical advantage over CRF with the less risk of post-denervation discomfort. Studies [78–80] performed, however, are case series, and results should be evaluated, noting the small numbers of patients, as no control is present to minimize the concern of placebo effect. Rozen et al. [78] performed PRF on five patients with persistent inguinal pain after inguinal hernia surgery. Patients were treated with PRF at T12, L1, and L2 ganglia with noted improvement of their symptoms.

Radiofrequency Techniques

Cervical Medial Branch Anatomy

In normal human anatomy, here are eight cervical nerves but seven cervical vertebrae. To account for this discrepancy, the first seven nerve roots exit above the vertebral body whose number they share. That is, C4 nerve root exits the intervertebral foramen between C3 and C4 vertebral bodies. The first two cervical levels do not have dorsal primary rami innervating structures. Ventral primary rami are responsible for injection the atlanto-occipital and atlanto-axial joints. Two medial branches arise separately from the C3 dorsal ramus.

The superior and larger division is known as the third occipital nerve (TON). The TON travels dorsally and medially around the superior articular process of the C3 vertebra, crossing the C2–C3 zygapophyseal joint either just below or across the joint margin. Innervation of the C2–C3 facet joints comes from the TON and an articular branch of the dorsal ramus. Practically speaking, blocking the TON on the C3 articular process will denervate the C2–C3 joint.

The C3–C4 to C7–T1 joints are supplied by the medial branches of the cervical posterior rami at the same level and from the level above. These medial branches curve dorsally and medially, wrapping around the midportion, "waist", of the articular pillars. On lateral view, medial branches are in the middle of the trapezoid of the articular pillar. Of note, the C7 medial branch lies higher on the lateral projection of the C7 articular pillar. The medial branch of C8 crosses the root of the T1 transverse process. This branch hooks medially onto the lamina of T1 and sends branches to C7–T1 joint. The medial branches provide sensory input from nociceptors at each joint level.

Technique of Cervical MBB RF [81]

Monitors are attached for heart rate, blood pressure, and oxygen saturation. The patient is placed in the prone position on the fluoroscopy table with arms at sides and padding for the knees, abdomen, and chest. The patient's cervical spine should be flexed 10–15° (chin to chest position). The dispersive pad should be placed on the patient away from but as close to the site of the procedure. Traction of the arms toward the feet may be required to visualize the cervical facet pillars, particularly those patients with short necks. After proper positioning is performed, the patient may receive an anxiolytic. It is imperative that the operator is able to communicate with the patient and that the patient not is overly sedated. Using anterior-posterior fluoroscopic visualization, the relevant anatomic level is identified. The articular pillar should be seen, and the waist of the pillar should be identified (Figs. 7.1 and 7.2). The skin and subcutaneous tissues of this region should then be anesthetized with 1 % lidocaine. Care should be taken not to anesthetize the medial branch being tested, stimulated, and treated with CRF. Curved or straight tip may be utilized for the procedure.

Thereafter, a 20–22-G needle (50-mm, 5-mm active tip, author's suggestion) is inserted to access the previously

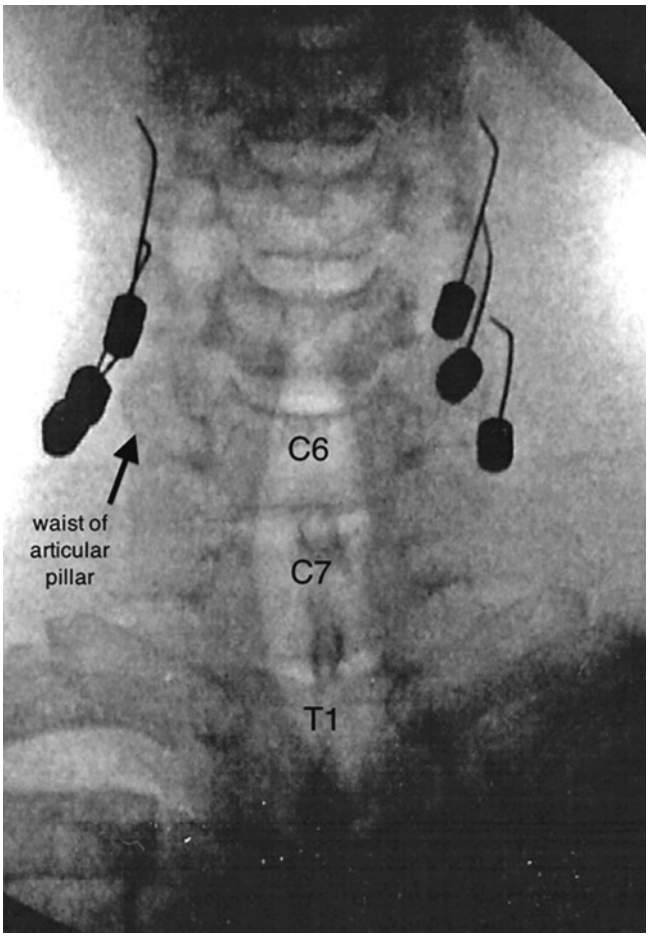

Fig. 7.1 Anterior-posterior view of needle placement for cervical z-joint medial branch radiofrequency procedure. Note the placement of the needles at the waist of the articular pillar. *C6* C6 vertebral body, *C7* C7 vertebral body, *T1* T1 vertebral body

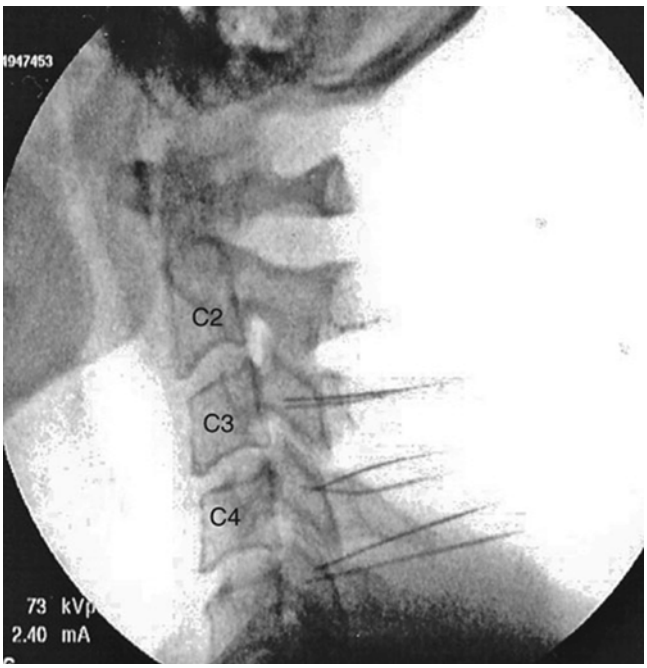

Fig. 7.2 Lateral view of needle placement for cervical z-joint medial branch radiofrequency procedure. Note the direction of the needles is parallel to the direction of the indicated nerves. *C2* C2 vertebral body, *C3* C3 vertebral body, *C4* C4 vertebral body

anesthetized areas to contact the medial branch at the waist of the articular pillar. The long axis of the needle should be parallel to the course of the nerve targeted to provide the best lesion, as the lesion shape is an oblate spheroid around the active tip. All needles to be placed should be done so before stimulation is tested to minimize patient discomfort. A thermocouple is then inserted into the needle, and sensory and motor nerve stimulation is performed.

Initially, sensory stimulation with 50-Hz current is performed to reproduce paresthesia localized to the site of discomfort at a delivered energy up to 1.0 V. If radicular stimulation is elicited, the needle should be repositioned as this may indicate dorsal root stimulation; a subsequent lesion at this location may then lead to motor or sensory dysfunction.

Next, 2-Hz motor stimulation should be performed to check that no motor recruitment other than localized neck muscle twitching is occurring. The upper threshold for motor stimulation should be 2.0 V. With a multilesioning system, stimulation would be checked at each site and then lesioning performed after successful testing occurs; in the situation of a generator that has single lesion capability, it is recommended that lesioning be performed immediately after checking stimulation at each level to decrease the likelihood of inaccurate lesioning.

Local anesthetic (0.5 ml) may be administered depending on operator preference: the discomfort of a heat lesion would be decreased by the local anesthetic. If the local anesthetic spreads beyond the needle at the lesion site, however, the risk of anesthetizing areas to be tested may occur, leading to motor/sensory stimulation that is inaccurate. Lesioning then progresses at a temperature setting of 80 °C for 90 s for CRF and 42 °C for 120 s at PRF (author's technique).

Patients should be advised that they may note a multiphase response to CRF therapy: an initial phase with relief of symptoms lasting for a few days, followed by a 2–3-week period of discomfort that may result from the heat lesion. Thereafter, prolonged relief may result. This phase of discomfort may not be seen in a patient undergoing PRF as the temperature is kept at a nonlesioning level.

Patients are seen back in the clinic 3 weeks after an initial CRF procedure. The operator may provide an oral analgesic or muscle relaxant for the patient's discomfort.

Complications

Assuming that the patient had successful sensory and motor stimulation with the initial procedure, complications are expected to me at a minimum with radiofrequency procedures. Sterile technique is of utmost importance during interventional procedures involving spinal and paraspinal needle placement. The patient should have anticoagulants discontinued [82] prior to therapy for the requisite period prior to treatment. Also, patients should be afebrile with no evidence of infection prior to interventional techniques.

Patients may notice discomfort at the needle sites, which may be relieved with oral and topical analgesics, muscle relaxants, and conservative measures such as heat or ice packs. Myofascial pain may occur after CRF, which is treated by local anesthetic/steroid trigger point injections.

Thoracic Medial Branch Anatomy

The thoracic medial branches [83] have a typical course that has been verified by anatomical dissection. The medial branches cross the superior and lateral aspect of the transverse process, then curving inferiorly and medially across the transverse process, travelling to the multifidus muscle. Unlike the medial branch of the lumbar region, where the medial branch is targeted in a superomedial location on the transverse process, the target point would be along a superolateral to inferomedial line on the transverse process. This arrangement typically occurs from T1 to T4 and also from T9 to T10 levels; variation to this occurs at the T5–T8 levels where the nerve may be displaced in a superior location and may not cross the lateral aspect of the transverse process.

Technique of Thoracic MBB RF [48, 83]

The technique of thoracic MBB RF is similar to the description provided above of cervical RF. The fluoroscope tube is obliqued 10–15° toward the ipsilateral side to show the articulation of the transverse process and adjacent rib. The operator should be cognizant of the location of the lungs in relation to the bony skeleton.

As described above, the target point of the medial branches is along the transverse process itself (Fig. 7.3). The skin and subcutaneous tissues of this region should then be anesthetized with 1 % lidocaine. Care should be taken not to anesthetize the medial branch being tested, stimulated, and treated with CRF. Curved or straight tip may be utilized for the procedure. Thereafter, a 20–22-G needle (100-mm, 10-mm active tip) is inserted to access the previously anesthetized areas to contact the medial branch at the transverse process.

Complications

In addition to the complications described in the cervical RF, the potential risk of pneumothorax exists due to accidental lung injury. Precision in evaluating perioperative fluoroscopy is required to note needle location vs. the lungs.

Myofascial pain may occur after CRF, which is treated by local anesthetic/steroid trigger point injections, being cautious of the risk of pneumothorax due to needle puncture of the pleura.

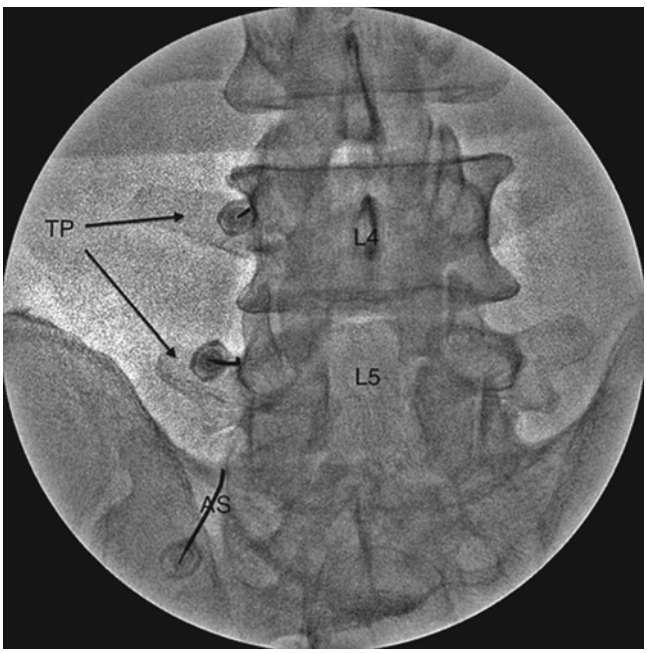

Fig. 7.3 Anterior-posterior radiograph of needle placement for lumbar medial branch RF procedure. *TP* transverse process of vertebral body, *AS* ala of sacrum, *L4* L4 vertebral body, *L5* L5 vertebral body

Lumbar Medial Branch Anatomy

In the lumbar region, the medial branch of the posterior ramus. The mamilo-accessory ligament is located in a groove on the base of the superior articular facet, adjacent to the base of the superior transverse process, the most reliable location for a medial branch block. Each joint has dual segmental innervation, and each segmental nerve supplies two facet joints plus the soft tissues overlying them. There is considerable innervation overlap in the lower lumbar region. The L5 medial branch contributes an inferior segment at the ala of the sacrum. The posterior opening of the S1 nerve root in the sacrum runs cephalad to supply the L5–S1 joint.

Technique of Lumbar MBB RF

The technique of RF is similar to the technique described above. An intravenous is started in the patient. The natural lordotic curve of the lumbar spine should be minimized by placing a pillow underneath the abdomen; using anterior-posterior fluoroscopic guidance, the relevant anatomic level is identified. The procedure may be performed by identifying the juncture of the transverse process of the lumbar spine along with the articular process at the relevant level (Fig. 7.4). The L5 medial branch sends a contribution inferiorly which is addressed by placing a cannula at the ala of the sacrum.

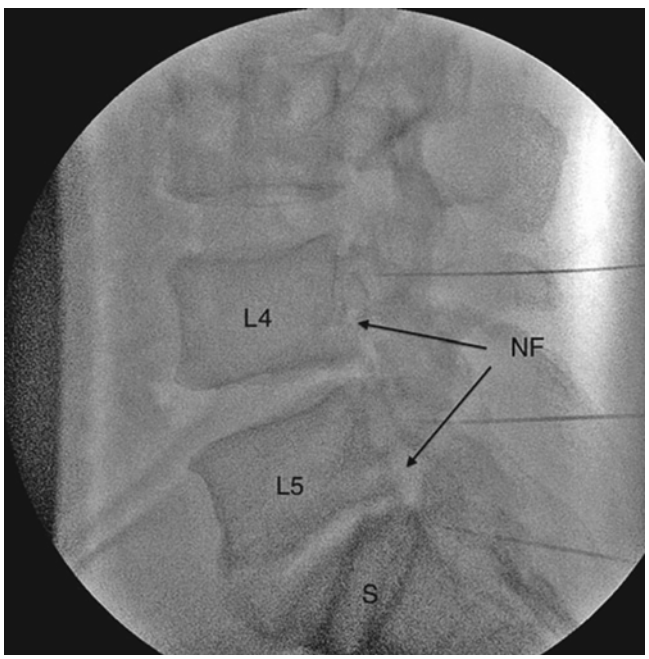

Fig. 7.4 Lateral view of needle placement for lumbar medial branch RF. Note location of needles in relation to relation to neural foramina. *L4* L4 vertebral body, *L5* L5 vertebral body, *S* sacrum *NF* neural foramina

Alternatively, the fluoroscope beam can be obliqued 15–20° to the ipsilateral side of the injection to visualize the "Scottie dog." The target point is the ear of the Scottie dog. Regardless of the technique being utilized, the long axis of the needle should be placed parallel to the direction of the target medial branch to maximize the resultant lesion with CRF. Curved or straight tip may be utilized for the procedure. Thereafter, a 20–22-G needle (100-mm, 10-mm active tip, author's suggestion) is inserted to access the previously anesthetized areas to contact the target point. All needles to be placed should be done so before stimulation is tested to minimize patient discomfort. A thermocouple is then inserted into the needle, and sensory and motor nerve stimulation is performed. Initially, sensory stimulation with 50-Hz current is performed to reproduce paresthesia localized to the site of discomfort at a delivered energy up to 1.0 V. If radicular stimulation is elicited, the needle should be repositioned as this may indicate dorsal root stimulation; a subsequent lesion at this location may then lead to motor or sensory dysfunction. Next, 2-Hz motor stimulation should be performed to check that no motor recruitment other than localized multifidus muscle twitching is occurring. The upper threshold for motor stimulation should be 2.0 V.

Complications

The complications are as previously described above.

Conclusion

Radiofrequency technology has widespread use [84] in interventional pain management. Evidence exists for the routine use of CRF for treating pain due to trigeminal neuralgia and z-joint pathology. Pain physicians have traditionally utilized PRF as a way to provide the benefits of CRF minus the complication of post-denervation pain. The literature indicates that benefit after PRF may not be as long lasting when compared to CRF. Before disposing of PRF as a viable technology [85], however, further investigation into the mechanism of both CRF and PRF would be warranted and refinement of technique should occur. Failure to do so would deny patients a powerful neuromodulatory technique in the treatment of chronic painful conditions.

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8 Atlanto-Axial and Atlanto-Occipital Joints Injection in the Treatment of Headaches and Neck Pain

Samer N. Narouze

Key Points

- Atlanto-axial joint (AAJ) injection with local anaesthetic is used to make a definitive diagnosis of pain stemming from the AAJ. AAJ injection with local anaesthetic and steroids may be indicated in the management of AAJ pain.
- AAJ with local anaesthetic is usually considered first to predict the response to AAJ radiofrequency lesioning or arthrodesis in intractable cases.
- Atlanto-occipital joint (AOJ) injection is rarely performed.
- Spinal cord injury and syringomyelia are potential serious complications of AAJ and AOJ injections. Vertebral artery injection/injury has been reported with serious morbidity. Inadvertent puncture of the C2 dural sleeve with CSF leak or high spinal spread of the local anaesthetic may occur with AOJ injection.

Introduction

Cervicogenic headache is referred pain from cervical structures innervated by the upper three cervical spinal nerves. The lateral atlanto-axial joint, which is innervated by the C2 ventral ramus, is a fairly common cause of cervicogenic headache. It may account for 16 % of patients with occipital headache [1]. In human volunteers, distending the lateral atlanto-axial joint (AAJ) with contrast agent produces occipital pain, and injection of local anaesthetic into the joint relieves the headache [1, 2].

Clinical presentations suggestive of pain originating from the lateral AAJ include occipital or suboccipital pain, focal tenderness over the suboccipital area or over the transverse process of C1, restricted painful rotation of C1 on C2, and pain provocation by passive rotation of C1.

These clinical presentations merely indicate that the lateral AAJ could be a possible source of occipital headache; however, they are not specific and therefore cannot be used alone to establish the diagnosis [3]. These clinical signs have a positive predictive value of only 60 % [1].

The pathology of lateral AAJ pain is usually osteoarthritis or post-traumatic in nature [4, 5]. However, the presence of osteoarthritic changes in imaging studies does not mean that the joint is necessarily painful; also the absence of abnormal findings does not preclude the joint from being painful, and the only means of establishing a definite diagnosis is a diagnostic block with intra-articular injection of local anaesthetic [1].

Indications

1. AAJ injection with local anaesthetic is used to make a definitive diagnosis of pain stemming from the AAJ.
2. AAJ injection with local anaesthetic and steroids may be indicated in the management of AAJ pain. Intra-articular steroids are effective in short-term pain relief originating from the lateral atlanto-axial joint [6, 7].
3. AAJ injection with local anaesthetic is usually considered first to predict the response to AAJ radiofrequency lesioning or arthrodesis in intractable cases. One report showed favourable long-term outcome after both pulsed and thermal radiofrequency lesioning of the AAJ [8]. In intractable cases, not responsive to more conservative management, arthrodesis of the lateral atlanto-axial joint may be indicated [9].

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Anatomy of the Atlanto-Axial Joint (AAJ) and Atlanto-Occipital Joint (AOJ)

It is very crucial to be familiar with the anatomy of the AAJ and atlanto-occipital joint (AOJ) in relation to the surrounding vascular and neural structures (Fig. 8.1) to avoid serious complications. The vertebral artery is lateral to the AAJ as it courses through the C2 and C1 foramina. The vertebral artery then curves medially crossing the medial posterior aspect of the AOJ to go through the foramen magnum.

The C2 nerve root, dorsal root ganglion, and its surrounding dural sleeve cross the posterior aspect of the middle of the joint. Therefore, during AAJ injection, the needle should be directed towards the junction of the middle and lateral thirds of the posterior aspect of the joint. This will avoid injury to the C2 nerve root medially or the vertebral artery laterally (Fig. 8.1) [1, 7]. Conversely, the AOJ should be accessed posteriorly from the most superior lateral aspect to avoid injuring the vertebral artery medially.

Technique of AAJ Injections

With the patient placed in the prone position and a pillow under the chest to allow for slight neck flexion, the fluoroscopy C-arm is brought to the head of the table in an anteroposterior direction. Under fluoroscopic guidance, the C-arm is rotated in a cephalad-caudad direction to better visualize the lateral AAJ. The needle insertion site is marked on the skin overlying the lateral thirds of the AAJ. The skin is prepped and draped in the usual sterile fashion, and a skin wheel is raised with local anaesthetic at the insertion site. Then a 22–25-G 3½ inches blunt needle is advanced towards the posterolateral aspect of the inferior margin of the inferior articular process of the atlas (C1). This will avoid contact with the C2 nerve root and dorsal ganglion, which crosses the posterior aspect of the middle of the joint. It is "better" to seek and touch the bone to safely establish the correct depth. At this point, a lateral view is obtained. The needle is withdrawn slightly, directed towards the posterolateral aspect of the lateral atlanto-axial joint, and advanced for couple of millimetres. Usually a distinctive pop is felt signalling entering the joint cavity. Careful attention should be paid to avoid the vertebral artery that lies laterally to the lateral AAJ as it courses through the C1 and C2 foramina. After careful negative aspiration for blood or cerebrospinal fluid, 0.1–0.2 ml of water-soluble nonionic contrast agent is injected to verify intra-articular placement of the tip of the needle.

Injection of the contrast agent is done under direct real-time fluoroscopy to check for inadvertent intra-arterial injection which is manifest by rapid clearance of the contrast agent. Anteroposterior and lateral views are obtained to insure that the contrast agent remained confined to the joint cavity without escape to the surrounding structures, especially the epidural space, or posteriorly to the C2

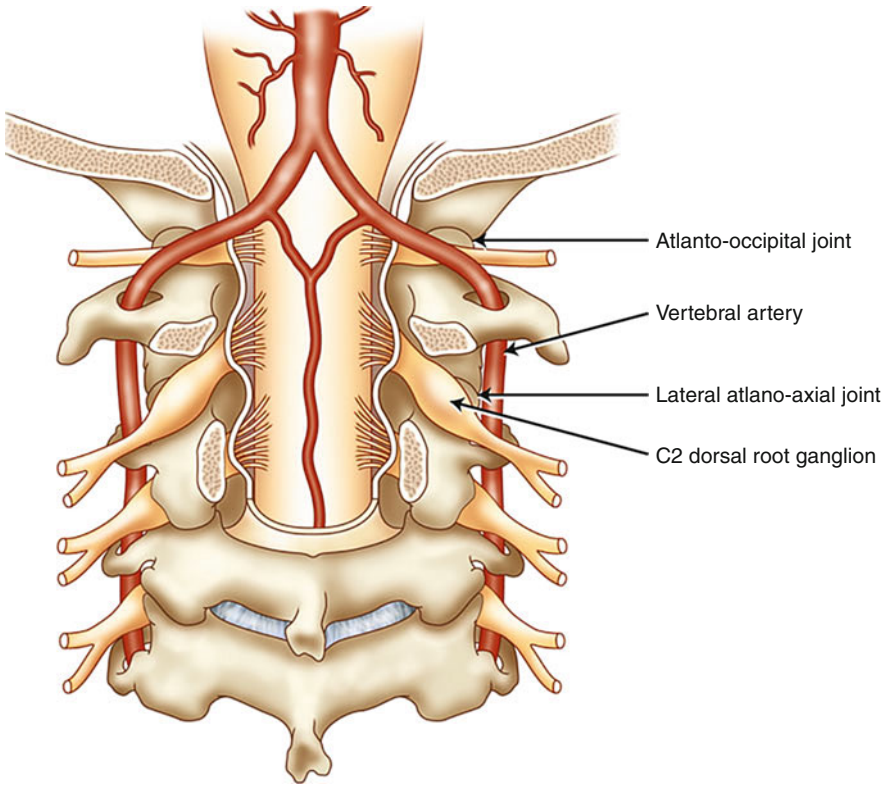

Fig. 8.1 Illustration showing the relevant anatomy of the atlanto-occipital and atlanto-axial joints

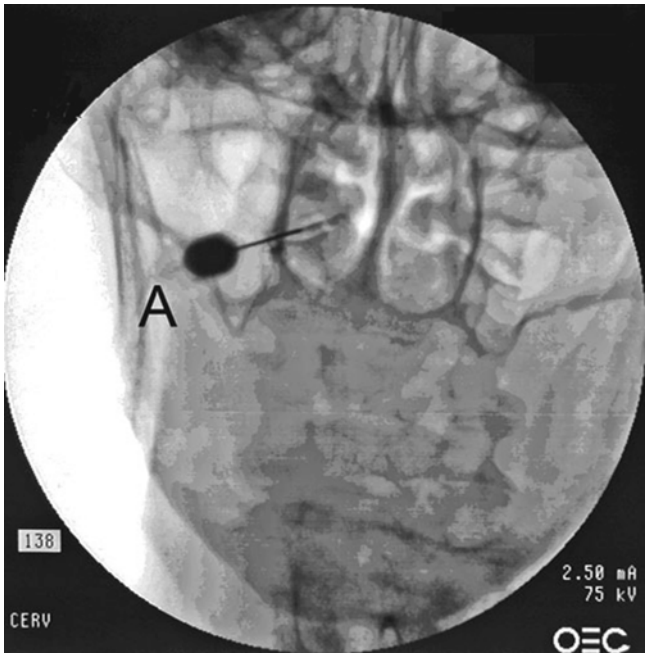

Fig. 8.2 Lateral atlanto-axial joint (AAJ) injection: AP view showing the needle (A) targeting the lateral third of the joint, and the contrast is contained within the joint space (Reproduced with permission from Ohio Pain and Headache Institute)

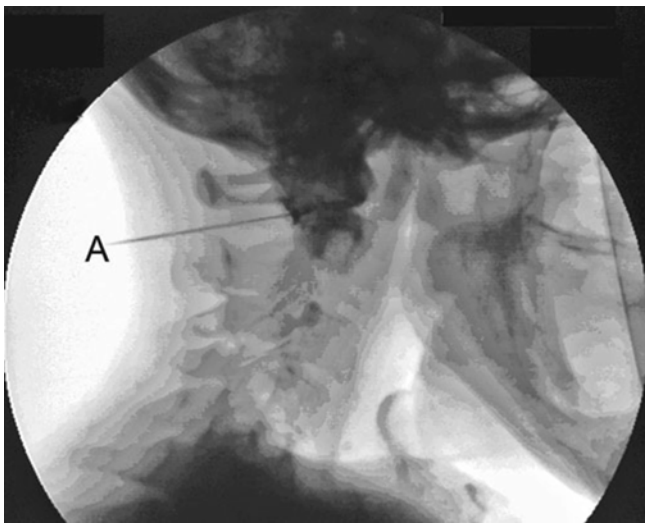

Fig. 8.3 Lateral atlanto-axial joint (AAJ) injection: lateral view showing the needle (A) and the contrast contained within the joint space (Reproduced with permission from Ohio Pain and Headache Institute)

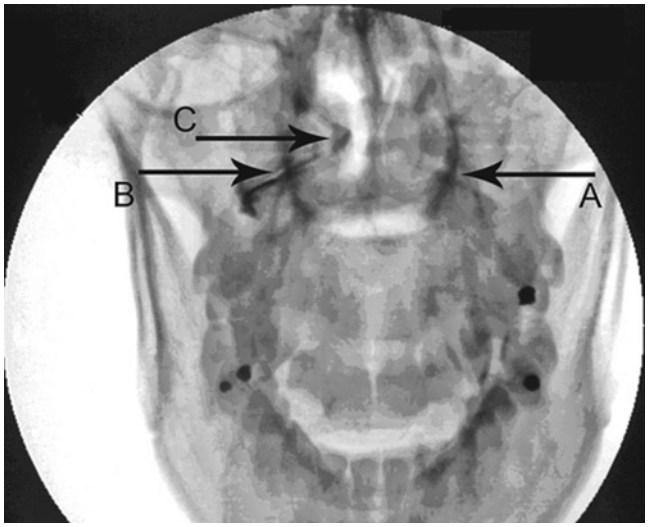

Fig. 8.4 Lateral atlanto-axial joint (AAJ) injection: *A* lateral atlanto-axial joint (AAJ). *B* contrast agent within the AAJ. *C* contrast spreading to the median atlanto-axial joint (Reproduced with permission from Ohio Pain and Headache Institute)

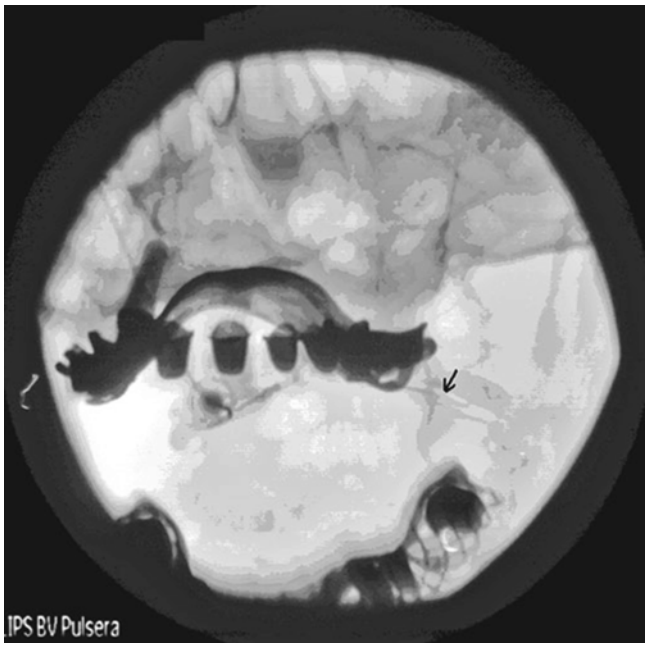

Fig. 8.5 Lateral atlanto-axial joint (AAJ) injection: Needle inside the left AAJ with the contrast spreading to the right AAJ (*arrow*) (Reproduced with permission from Ohio Pain and Headache Institute)

ganglion which will adversely affect the specificity of the block (Figs. 8.2 and 8.3). The anteroposterior view usually demonstrates the bilateral concavity of the joint with the contrast material inside the joint space (Fig. 8.2), and sometimes it shows that the lateral AAJ space communicates with that of the median atlanto-axial joint (Fig. 8.4) and the contralateral AAJ (Fig. 8.5). After careful negative aspiration, 1.0 ml of a mixture of bupivacaine 0.5 % and 10 mg of triamcinolone is injected.

Every effort should be made to make the injection true intra-articular and not periarticular injection. Those procedures are mainly utilized in the diagnosis of pain stemming

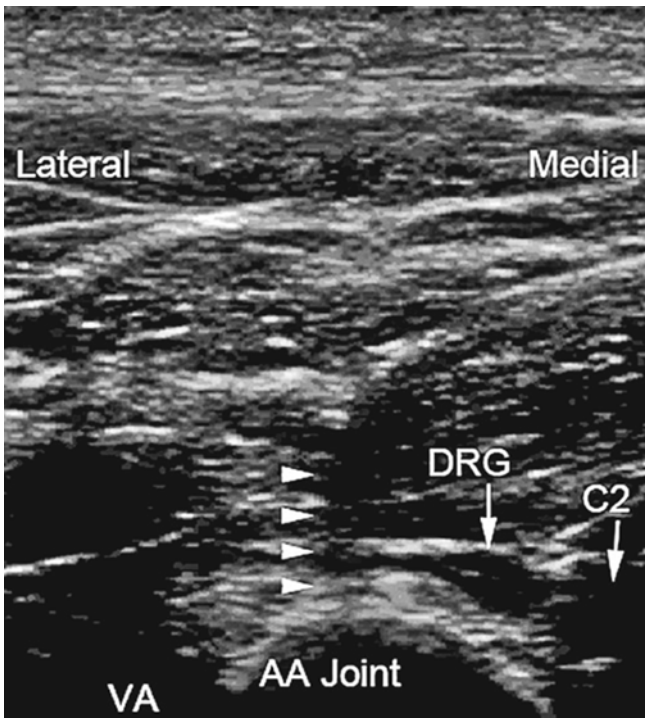

Fig. 8.6 Atlanto-axial joint (AAJ) injection. Short axis sonogram showing the needle targeting the AAJ (*arrowheads*). *C2* C2 nerve root, *DRG* dorsal root ganglion, *VA* vertebral artery (Reproduced with permission from Ohio Pain and Headache Institute)

from the joints, and periarticular injection is not target specific as the local anaesthetic may contaminate the C2 nerve root which crosses the posterior aspect of the AAJ. Intra-articular injection is more target specific as it selectively anesthetizes the joint [7].

Recently, ultrasound-assisted AAJ injection was reported. With real-time sonography, the vertebral artery can be identified laterally and the C2 dorsal root ganglion medially and accordingly; the needle can be advanced in-between (Fig. 8.6) [10].

Atlanto-Occipital Joint (AOJ) Injections

Indications

This procedure is rarely performed for few reasons. Isolated pain stemming from the atlanto-occipital joint (AOJ) is very rare, and usually the patient is presented with localized occipital pain that is aggravated mainly by head nodding. Activity modification and conservative management are usually all what is needed. Also the vertebral artery curves from lateral to medial crossing the posterior aspect of the C1 body which makes it vulnerable to injury while the needle is advanced towards the AOJ, especially with improper positioning of the patient.

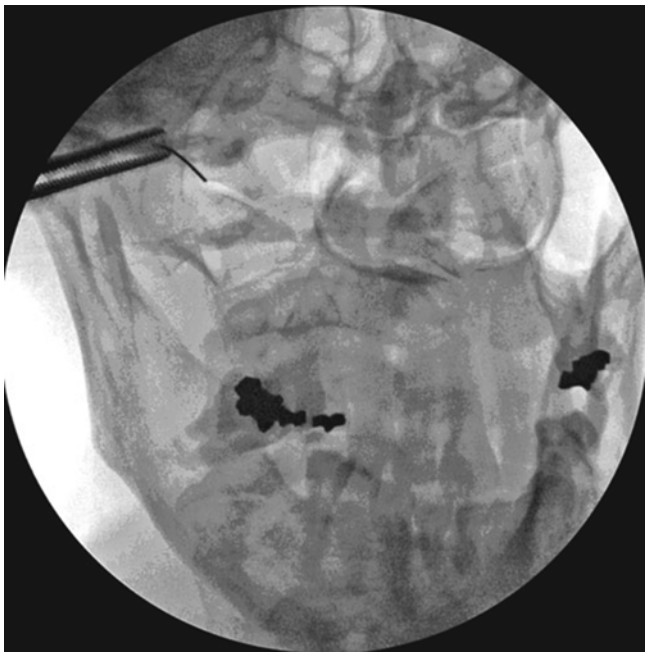

Fig. 8.7 Atlanto-occipital joint (AOJ) injection. AP view (Reproduced with permission from Ohio Pain and Headache Institute)

Technique of AOJ Injections

The positioning and approach is similar to that for AAJ injection. The patient needs to flex his head over the neck as much as possible (chin on chest) to open the suboccipital space posteriorly. The atlanto-occipital joint should be accessed posteriorly from the most superior lateral aspect to avoid the vertebral artery (Figs. 8.7 and 8.8).

More recently, ultrasound-assisted AOJ injection in conjunction with fluoroscopy was described. With real-time sonography, the vertebral artery is identified as it curves medially behind C1 body and accordingly can be avoided from the needle path, and then the procedure can be continued with fluoroscopy to confirm intra-articular placement of the needle (Fig. 8.9) [10].

Efficacy of AAJ and AOJ Injections

Narouze and colleagues [7] studied 115 patients with cervicogenic headache. Thirty-two patients had a clinical picture suggestive of atlanto-axial joint pain, and the diagnosis was confirmed in 15 patients with complete abolition of the headache (pain score of zero) after AAJ injection. The prevalence of AAJ pain among patients with cervicogenic headache was

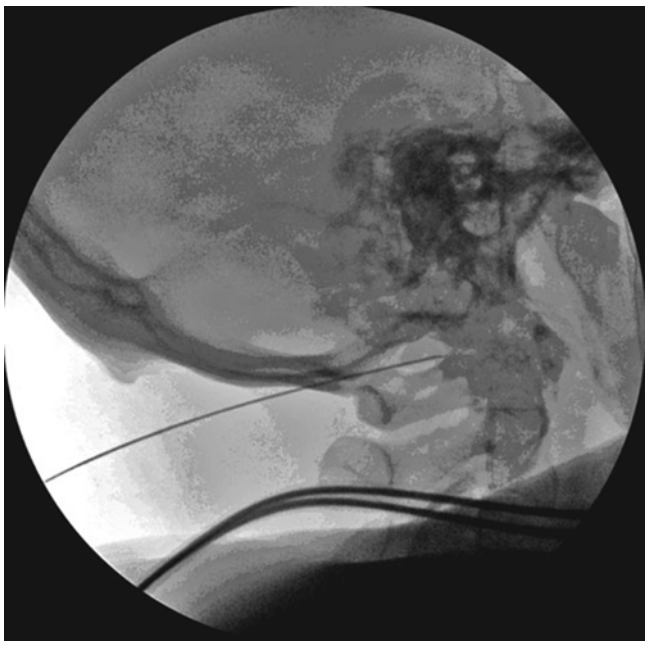

Fig. 8.8 Atlanto-occipital joint (AOJ) injection. Lateral view (Reproduced with permission from Ohio Pain and Headache Institute)

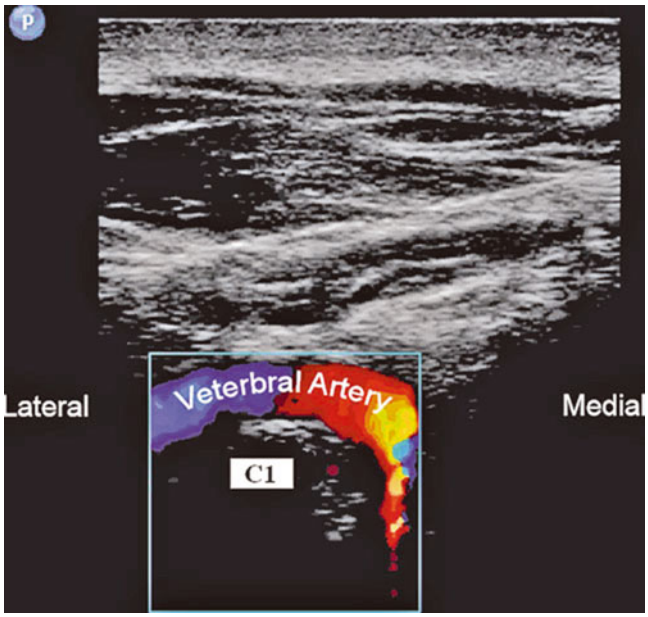

Fig. 8.9 Atlanto-occipital joint (AOJ) injection. Sonogram showing the vertebral artery as it curves medially posterior to C1 (Reproduced with permission from Ohio Pain and Headache Institute)

13 % (15/115 patients). At 1, 3, and 6 months after AAJ intra-articular steroid injection, the mean pain scores dropped from a baseline of 6.8 to 1.9, 3.6, and 3.7, respectively. The authors concluded that intra-articular steroid injection is effective in short-term relief of pain originating from the lateral AAJ. There is no data available to demonstrate the efficacy of AOJ intra-articular steroid injections.

Complications of AAJ and AOJ Injections

1. Spinal cord injury and syringomyelia are potential serious complications if the needle is directed further medially into the spinal canal [11].
2. Vertebral artery injection/injury was reported with serious morbidity. Injection of a contrast agent should be performed under real-time fluoroscopy, preferably with digital subtraction if available, prior to the injection of the local anaesthetic, as negative aspiration is unreliable [12]. Meticulous attention should be paid to avoid intravascular injection as vertebral artery anatomy may be variable. Recently, ultrasound-assisted AAJ and AOJ injections were reported in an effort to add more safety to the procedure as ultrasound can identify the relevant soft tissue structures nearby the joints (e.g. vertebral artery and C2 dorsal root ganglion) (Figs. 8.6 and 8.9) [10].
3. Inadvertent puncture of the C2 dural sleeve with CSF leak or high spinal spread of the local anaesthetic may occur with atlanto-axial joint injection if the needle is directed a few millimetres medially [11].

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Sphenopalatine Ganglion Block

9

Michael S. Leong, Mark P. Gjolaj, and Raymond R. Gaeta

Key Points

- The sphenopalatine ganglion is the most cephalad region of input for the superior cervical sympathetic ganglion.
- Sphenopalatine blockade is indicated to treat headache (cluster, migraine), atypical facial pain and neuralgias, and possibly other sympathetic maintained conditions.
- There are three main techniques for performing sphenopalatine ganglion blockade, the simplest using cotton pledgets to the middle turbinates of the nasal sinuses, the most advanced with fluoroscopic-guided technique.
- Further clinical studies are required to demonstrate efficacy in neuropathic pain conditions other than cluster headache and facial neuralgias.

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Introduction

A certain mystique surrounds the sphenopalatine ganglion as it seemingly rests in the middle of the head but is readily accessible for neural blockade. The sphenopalatine ganglion block is an older and relatively simple pain management block for treatment of headache (cluster and migraine) and facial neuralgias. This block was first described by Greenfield Sluder in 1908 for the treatment of nasal headaches [1]. Since it is localized to the back of the nasopharynx, it can be approached externally through the nares by using cotton pledgets soaked with local anesthetic to anesthetize this region. This simple approach has even been taught to headache sufferers to manage their own pain control at home [2]. Despite the ease of blockade, only recently has interest in the block been resurrected.

Anatomically, the sphenopalatine ganglion, also called pterygopalatine ganglion, is the superior most constellation of sensory (maxillary nerve), parasympathetic (greater petrosal nerve), and sympathetic (superior cervical ganglion) nervous system. The sensory branches of the palatine nerves pass through the ganglion from their origin as the sphenopalatine branches of the maxillary nerve. The parasympathetic portions arise from the nervus intermedius contribution of the greater petrosal nerve. These parasympathetic fibers are responsible for the secretory and vasodilatory functions of the various glands of the nasopharynx and lacrimal glands. The sympathetic fibers originate in the superior cervical plexus through the carotid plexus. The deep petrosal nerve then enters the ganglion to provide the sympathetic vasoconstriction function of the ganglion.

Alternative approaches to the sphenopalatine ganglion, intraoral and fluoroscopic radiofrequency ablation, have increased utilization of this procedure. Hence, a diagnostic and temporary sphenopalatine ganglion block via a nasopharynx approach in the pain management clinic can be used to predict whether further interventional fluoroscopic

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radiofrequency procedures should be attempted. In one study of the treatment of episodic cluster headache, 46 % of the 15 patients treated had a change in headache frequency for 18 months [3].

Literature Review

The main indications for the sphenopalatine ganglion block have traditionally been multiple headache conditions and facial neuralgias. Michael Sanders reported a 70-month follow-up study on 66 patients with cluster headaches, with 60.7 % of episodic patients having benefit and 30 % with chronic patients gaining benefit [4]. A more recent example of treatment of episodic cluster headache is Narouze's study above. Most recently, electrical stimulation of the sphenopalatine ganglion under fluoroscopic guidance seems effective for episodic cluster headaches [5]. Migraine, one of the most common headache syndromes, has been recognized as having cranial parasympathetic input to the trigeminovascular pain pathway, with intranasal lidocaine providing significant pain relief [6]. Similar to the cluster headache study above, electrical stimulation of acute migraine seems to be effective as well [7]. A case report by Shah and Racz demonstrated long-term relief of posttraumatic headache by sphenopalatine ganglion pulsed radiofrequency lesioning [8]. With regard to facial neuralgias, a case report of stereotactic radiosurgery has been used to treat sphenopalatine neuralgia [9]. Another case report reported treatment of trigeminal neuralgia [10]. A more extensive series for atypical facial and head pain using pulsed radiofrequency of the sphenopalatine ganglion in 30 patients showed 61 % having mild to moderate pain relief [11].

The sphenopalatine ganglion block has also been studied in other chronic pain conditions. Two case series have looked at its application to myofascial pain and fibromyalgia, with no differences between 4 % lidocaine and placebo [12–14]. Cancer pain due to carcinoma of the tongue and floor of the mouth has responded to sphenopalatine block [15]. Two cases of acute herpetic infection and even sinus arrest from postherpetic neuralgia have been treated with this block [16, 17]. One of the more intriguing case series involves two complex regional pain syndrome patients with lower extremity affected limbs [18]. Even after sympathetic blockade of the lower extremities had failed, sphenopalatine ganglion blocks with 4 % tetracaine provided 50 % pain reduction. Further clinical studies are required to demonstrate efficacy in neuropathic pain conditions other than cluster headache and facial neuralgias. Moreover, studies on block technique, full radiofrequency ablation versus pulsed and electrical stimulation, are also indicated.

Evidence-Based Assessment of Available Studies

Using the Guyatt grading strength of recommendations [19], most of the strongest studies were graded as 1C observational studies or case series: Sanders, Narouze, Ansarinia, Tepper, and Yarnitsky. These studies targeted episodic cluster headaches or migraine and had subject samples of five or more. In addition, Bayer's study of pulsed radiofrequency for treatment of atypical facial and head pain was also robust for an observational series – 30 subjects. Hence, the strongest recommendations for treatment so far include episodic cluster headaches, migraine headaches, atypical facial pain, and head pain.

The sphenopalatine ganglion block is a useful technique in the management of pain syndromes in the head region. Its application in the use of migraine is of particular interest in the future. More specific trials related to its treatment should be undertaken to clarify the exact indications and patient characteristics in which it would be useful. It is a safe technique with multiple approaches for both provocative testing and even therapeutic intervention with radiofrequency lesioning.

Intraoral Sphenopalatine Ganglion Block

This intraoral technique of blocking the sphenopalatine ganglion is also called the greater palatine foramen approach. It involves positioning the patient in a supine position, with the neck slightly extended using a pillow or foam wedge. The patient must have an appropriate oral aperture so that the practitioner can palpate the medial gum line of the third molar on the ipsilateral side. The foramen may be identified by a dimple on the medial aspect of the posterior hard palate [20]. A dental needle with a 120° angle is inserted into the foramen approximately 2.5 cm superiorly and slightly posterior [21]. The maxillary nerve is superior or cephalad to the sphenopalatine ganglion, so a facial paresthesia may be elicited if the placement is too deep. After negative aspiration for heme or cerebrospinal fluid, 2 mL of local anesthetic may be injected cautiously.

Sphenopalatine Ganglion Block via Anterior Approach

Access to the sphenopalatine ganglion is readily achieved through the nasal passages utilizing anesthetic-soaked pledgets and bayonet forceps or more easily with the use of

cotton tip swabs. In either case, patency of the nares should be ascertained by having patients breathe alternatively through each of their nares, with the opposite side pressed closed. In addition, patients with nasal polyposis or a history of friable nasal mucosa should be approached with caution.

Classically, a nasal speculum to distend the nares allows the larger pledgets with a large surface area to be placed straight back into the nasal passages in the area of the sphenopalatine ganglion. Direct application of local anesthetic through the mucosa to the ganglion is thus achieved. The string attached to the pledget allows for easy recovery. Unfortunately, many patients may not tolerate the insertion of the pledgets, and thus, more significant sedation may be required.

An alternative which is well tolerated by many patients with very light or no sedation is the use of cotton tip swabs dipped in local anesthetic. Patience is required for the utilization of this technique with liberal amount of local anesthetics on the cotton tip swabs. After assuring patency, a liberal amount of lidocaine jelly can be applied to the nares prior to insertion of the cotton-tipped swabs. After a few minutes for the anesthetic to take effect, the cotton tip swabs should be advanced into the nares slowly in a twirling fashion. Generally, at the level of the turbinates, there may be slight resistance which can be overcome with gentle pressure, patience, and twirling of the cotton tip swab. As the nasal passages and the level of sphenopalatine ganglion are directly back from the midface, the angle of the cotton tip swab should almost be perpendicular to the face and advanced until the end of the nasopharynx is appreciated. With patience, 3–4 cotton tip swabs can be advanced into each nares. Additional local anesthetic can be dribbled onto the cotton tip swabs to provide more local anesthetic. Generally speaking, the cotton tip swabs may be left in place for 20–30 min after which they are removed.

Sphenopalatine Ganglion Block via Fluoroscopic Approach

Contraindications

- Absolute: local infection (skin or paranasal sinus); coagulopathy
- Relative: anatomic abnormalities of sinuses secondary to genetics, trauma, or surgery

Key Anatomic Landmarks

- Pterygopalatine fossa
- Zygomatic arch
- Maxillary nerve

Potential Side Effects

- Numbness at the root of the nose and potentially palate
- Lacrimation of the eye on ipsilateral side
- Reflex bradycardia for radiofrequency lesions
- Bleeding, infection, and epistaxis

Perioperative Medication and Conscious Sedation

Please refer to the current American Society of Anesthesiologist's (ASA) guidelines for conscious sedation [22] and/or Leong and Richeimer's "Conscious Sedation for Interventional Pain Procedures" in Lennard's Pain Procedures in Clinical Practice, 3 ed., Elsevier [23]. Standard monitors should also be applied during and post-procedure, including blood pressure monitoring, EKG, and pulse oximetry.

Procedure

Positioning

Most descriptions of the procedure advise the patient to be in a supine position with anterior-posterior view used initially to visualize the orbit and maxillary sinuses.

Imaging

The image intensifier should be placed in a lateral view and tilted cephalad until the pterygopalatine fossa is visualized. When the two pterygopalatine plates are superimposed, one will visualize an inverted flower "vase" just posterior to the posterior aspect of the maxillary sinus [24].

Needle Placement

The needle (typical – 22 gauge, 3.5 in spinal needle) is placed under the zygoma in the coronoid notch after local anesthetic skin infiltration. Using an AP view of the orbit and maxillary sinuses, the needle is advanced medial, cephalad, and slightly posterior into the pterygopalatine fossa. The needle should be positioned lateral to the lateral wall of the nose but medial to the maxillary sinus. When the needle enters the fossa, patients may experience a paresthesia from contact with the maxillary nerve [25]. One to two milliliters of local anesthetic (1–2 % lidocaine) is injected at this region prior to advancing the needle into the anterior superior corner of the fossa. If any resistance is encountered, needle positioning should be stopped and redirected to prevent advancing through the lateral wall of the nose.

It is important to place the needle into the sphenopalatine foramen, particularly when using radiofrequency ablation to prevent damage to the maxillary nerve. When positioned correctly, the patient will have a paresthesia at the root of the nose

with nerve stimulation. If a paresthesia is felt in the upper teeth, the needle is placed too close to the maxillary nerve and needs to be redirected in a more caudal fashion [20].

Treatment

Local Anesthetic

One to two milliliters of lidocaine or bupivacaine with or without steroid may be placed at the sphenopalatine ganglion after negative aspiration for heme or CSF. A maximum of 5 mL of local anesthetic may be used for diagnostic block after negative aspiration. Numbness at the root of the nose as well as ipsilateral lacrimation may be a temporary result.

Radiofrequency

Lesioning can be performed using RFTC or pulsed EMF after a successful temporary block with local anesthetic. Typically a 20- or 20-ga, 10-cm, curved blunt-tipped RF needle is placed using a 5–10-mm active tip.

Confirmation of sensory paresthesia at the root of the nose should be elicited with approximately 0.5 V at 50 Hz. Again, if paresthesias are present in the upper teeth, the needle needs to be redirected caudally. Stimulation of the greater and less palatine nerves produces paresthesias of the hard palate. The needle is too lateral and anterior and needs to be redirected posteriorly and medially.

After best placement of the RF needle, RF lesioning is performed at 70–90 s at 80 °C. One to two lesions can be made after infiltration of 1–2 mL of local anesthetic. Pulsed RF does not require local anesthetic pretreatment since the lesioning is only at 42 °C for 120 s. Two to three lesions may be required for pulsed RF treatment.

As mentioned above, a reflex bradycardia may occur with RF and pulsed RF lesioning. A proposed mechanism suggests that a reflex similar to an oculocardiac reflex may be due to afferent transmission back to the dorsal vagal nucleus [26]. This reflex bradycardia stops with discontinuation of lesioning, but the patient may need atropine to complete the radiofrequency treatment.

Pharmacoeconomic Discussion of Sphenopalatine Blockade

Headache and facial pain produce both direct and indirect costs. Prescription drugs, physician office visits, emergency room visits, and inpatient hospitalizations represent the direct costs of an illness. For migraines alone, the national direct cost burden is estimated at $11 billion [Hawkins K. Value Health 2006;9:A85]. Indirect costs, due to missed workdays, short-term disability, and worker's compensation, make up over $13 billion annually, excluding presenteeism [27]. Presenteeism accounts for up to an additional $5 billion dollars annually of cost to employers in the United States [28].

In a large study of various pain disorders among the US workforce, headache was the most frequent cause of lost productive time over a 2-week period and caused the average affected individual to miss 3.5 h/week [29]. In the American Migraine Prevalence and Prevention (AMPP) study, the annual per person cost was $1,757 in episodic migraine and $7,750 in transformed migraine [30].

Approximately 15,000 new patients are diagnosed with trigeminal neuralgia each year in the United States alone [31]. An estimated 8,000 undergo surgery each year at an annual cost of greater than $100 million [32].

Sphenopalatine ganglion blockade represents a clinically and cost-effective intervention for facial pain and headaches. As shown in Table 9.1, the costs associated with sphenopalatine ganglion block match those of blocking one trigeminal nerve and are 20 % less than stellate ganglion block. When we consider the fact that patients can be instructed in performing the intranasal sphenopalatine ganglion block themselves, it becomes clear that it may be judged "the cheapest technique in the management of chronic pain" [33].

Summary

The sphenopalatine ganglion is located in the upper reaches of the nasopharynx and represents the most superior contribution of the superior sympathetic ganglion. Blockade of the

Table 9.1 Comparative costs of three nerve blocks

CPT code	Description	Medicare allowable – nonfacility	Medicare allowable – facility	Total
64505	Injection, anesthetic agent; sphenopalatine ganglion	$113.59	$92.39	$205.98
64510	Injection, anesthetic agent; stellate ganglion (cervical sympathetic)	$165.05	$75.59	$240.64
64400	Injection, anesthetic agent; trigeminal nerve, any division or branch	$129.45	$71.02	$200.47

sphenopalatine ganglion is easily achieved by a variety of techniques of increasing complexity, and it is deemed useful in the management of various pain syndromes of the head particularly migraine headache. Case series and observational studies have demonstrated its utility for treatment of painful syndromes, with the based designed study reaching 1C level of utility. While future studies should indeed be conducted to determine the exact indications and patient characteristics specific utility of the block, current practice provides a relatively safe and putatively effective treatment strategy for headache and facial pain. Local anesthetic blockade of the ganglion via the anterior nares approach is readily accomplished and serves as a therapeutic trial to determine whether more invasive and perhaps longer lasting treatment such as radiofrequency lesioning should be considered. The magnitude of patient suffering from migraine and facial pain and its societal implications with regard to economics and overall productivity should be a strong impetus to utilize sphenopalatine blockade via the multiple approaches until the definitive studies demonstrate the best algorithm for treatment.

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Occipital Nerve Block

10

Garret K. Morris and Michael S. Leong

Key Points

- Anatomically, the greater occipital nerve is associated with the C2 dorsal root and ganglion and receives a contribution from the medial branch of the posterior division of the third cervical nerve.
- Occipital nerve blocks are a common component of the pain physician's armamentarium.
- Despite the relative frequency with which these blocks are performed, there is no standardized protocol, and considerable variation in technique exists.
- Occipital neuralgia, by definition, responds favorably.
- Cervicogenic and cluster headaches also appear to be prime candidates for the intervention.
- Migraineurs may obtain benefit, although the evidence is less substantial.
- Peripheral neuromodulation may be a viable option.
- Occipital nerve blocks are not predictive of the success of occipital peripheral nerve stimulation.

Introduction

Occipital nerve blocks have been performed for more than 50 years and are commonly employed in modern practice to treat pain not only in the distribution of the greater occipital nerve but also with increasing frequency in the treatment of myriad other painful conditions of the head and neck. Despite this prevalence, however, no formal, "standardized" protocol exists. Rather multiple, differing techniques for deposition of local anesthetic around the nerve have been described in the literature, making comparative analysis challenging. Regardless, evidence to date supports substantial analgesic benefit of the procedure, and future investigation may very well elucidate an even greater scope of implementation.

Anatomy

The origin of the greater occipital nerve can be traced back to the second cervical level, where an extradural convergence of root filaments forms the C2 dorsal root and ganglion, lateral to the atlantoaxial ligament and inferior to the obliquus capitis inferior. Here, the ganglion is confined to the intervertebral foramen: atlantoaxial joint ventrally, posteromedial arch of the atlas and lamina of the axis dorsally, posterior arch of the atlas rostrally, and lamina of the axis caudally. Following a horizontal course within the foramen, the second cervical nerve emerges and almost immediately divides, yielding the largest of all cervical posterior divisions and coursing below the obliquus capitis inferior and between the posterior arch of the atlas and the lamina of the axis. Here, the dorsal ramus splits into four braches, including a large medial branch known as the greater occipital nerve (GON) due to its size and anatomical course.

The subsequent path of the GON is critical to understanding the pathological states to which it is related. Following its emergence from the dorsal ramus, the GON quickly turns medially, coursing transversely and dorsally over the belly of the obliquus capitis inferior muscle and deep to the semispinalis capitis, splenius capitis, splenius cervicis, and trapezius. The nerve continues cephalad, penetrating the semispinalis capitis and trapezius and joining the occipital artery. In this area, the GON receives a contribution from the medial branch of the posterior division of the third cervical nerve, ascending parasagittally and obliquely to innervate

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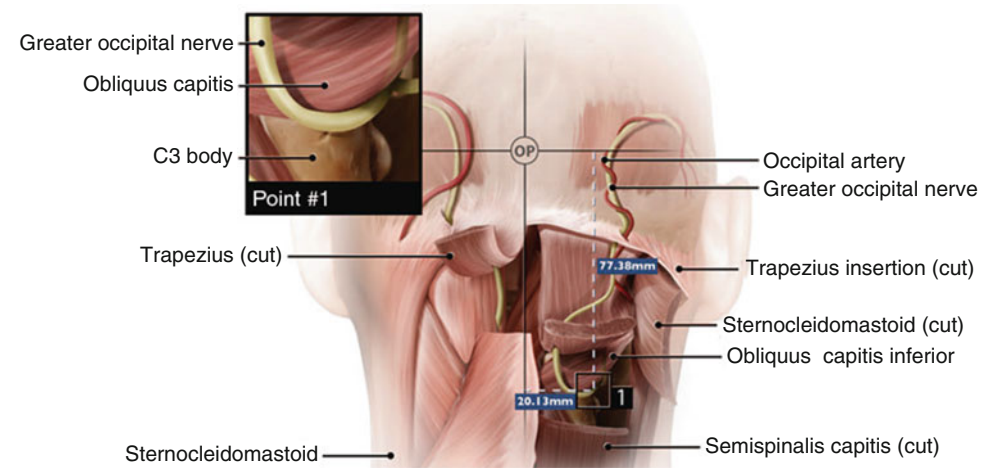

Fig. 10.1 Schematic illustration depicting compression point 1, where the nerve exits from deep to the obliquus capitis, wrapping around as it moves cranially and superficially (With permission from Janis et al. [4])

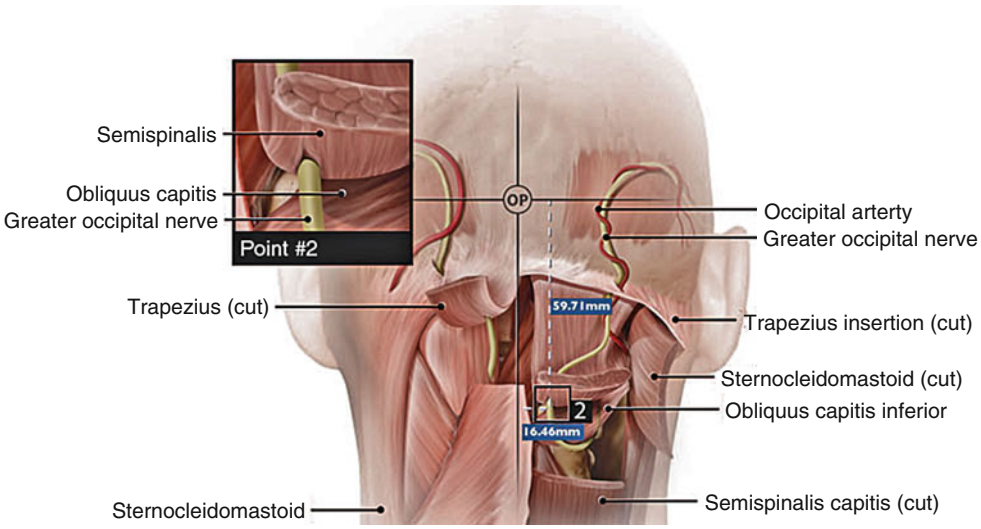

Fig. 10.2 Schematic illustration depicting compression point 2, the entrance of the nerve into the semispinalis muscle (With permission from Janis et al. [4])

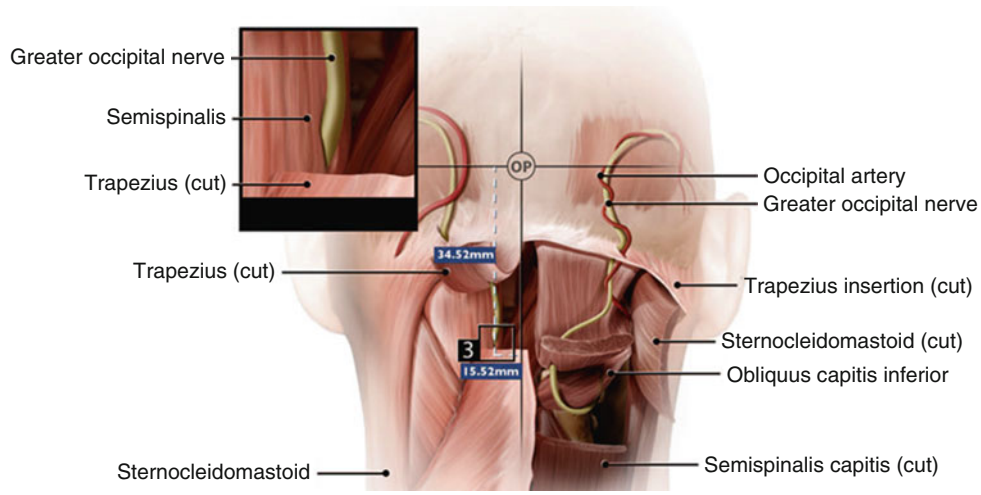

Fig. 10.3 Schematic illustration depicting compression point 3, where the greater occipital nerve exits from the semispinalis muscle (With permission from Janis et al. [4])

the posterior occiput, vertex as far as the coronal suture, and as far laterally as the mastoid [1–5].

Over this complex anatomical path exist numerous locations with the potential to create entrapment neuropathies or compression injuries. From proximal to distal, these include (Figs. 10.1, 10.2, 10.3, 10.4, 10.5, and 10.6):

1. The space between the vertebral bones of C1 and C2
2. The atlantoaxial ligament as the dorsal ramus emerges

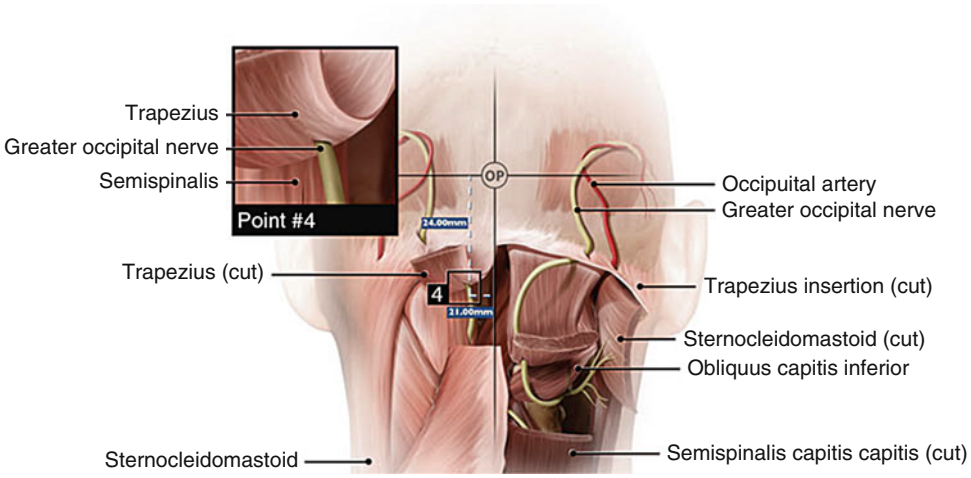

Fig. 10.4 Schematic illustration depicting compression point 4, where the nerve enters the trapezius (With permission from Janis et al. [4])

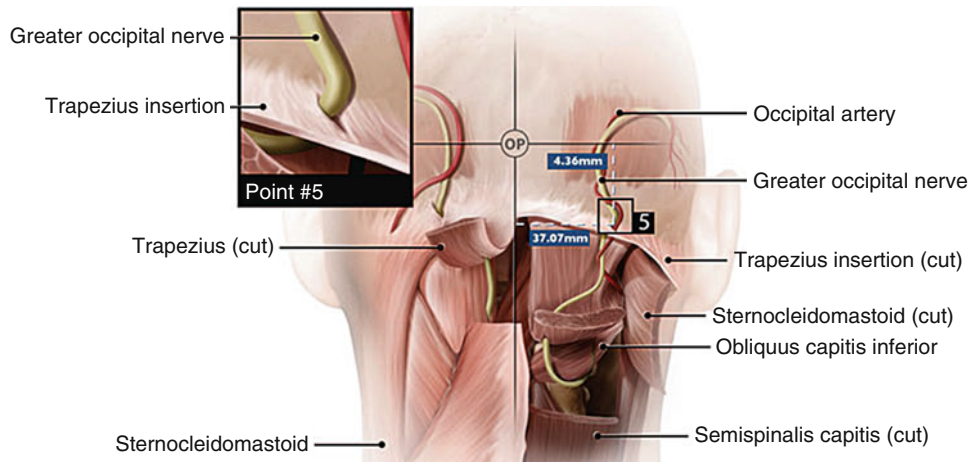

Fig. 10.5 Schematic illustration depicting compression point 5, where the nerve enters the trapezius insertion (With permission from Janis et al. [4])

3. The deep to superficial turn around the inferiolateral border of the obliquus capitis inferior muscle and its tight investing fascia
4. The deep side of semispinalis capitis, where initial piercing can involve entrapment in either the muscle itself or surrounding fascia
5. The superficial side of semispinalis capitis, where completion of nerve piercing muscle and its fascia again poses risk
6. The deep side of the trapezius as the nerve enters the muscle
7. The tendinous insertion of the trapezius at the superior nuchal line
8. The neurovascular intertwining of the GON and the occipital artery

Traumatic extension injuries (i.e., whiplash) have also been proposed as potential causes, although a definitive mechanism by which such injury could occur has yet to be fully elucidated (Fig. 10.7) [7–9].

Technique

As with all interventional procedures, a thorough and in-depth understanding of the relevant anatomy is an absolute a priori requirement to both successful neural blockade and minimization of potentially deleterious consequences. Unfortunately, despite the common frequency with which this block is internationally performed, there exists no standardized protocol for performing the procedure in either daily clinical practices or peer-reviewed medical literature.

Anatomical landmark identification [3, 10], point of maximal tenderness isolation [11], typical headache pain reproduction [11], ultrasonic Doppler flowmetry-assisted occipital artery localization [12], nerve stimulator guidance [13], and ultrasound image assistance [9] have all been employed in an effort to reproducibly identify the appropriate injection site. Nevertheless, the exact location for deposition of injectate varies widely in published studies in terms of both mediolateral and rostrocaudal orientation. All too often, no formal

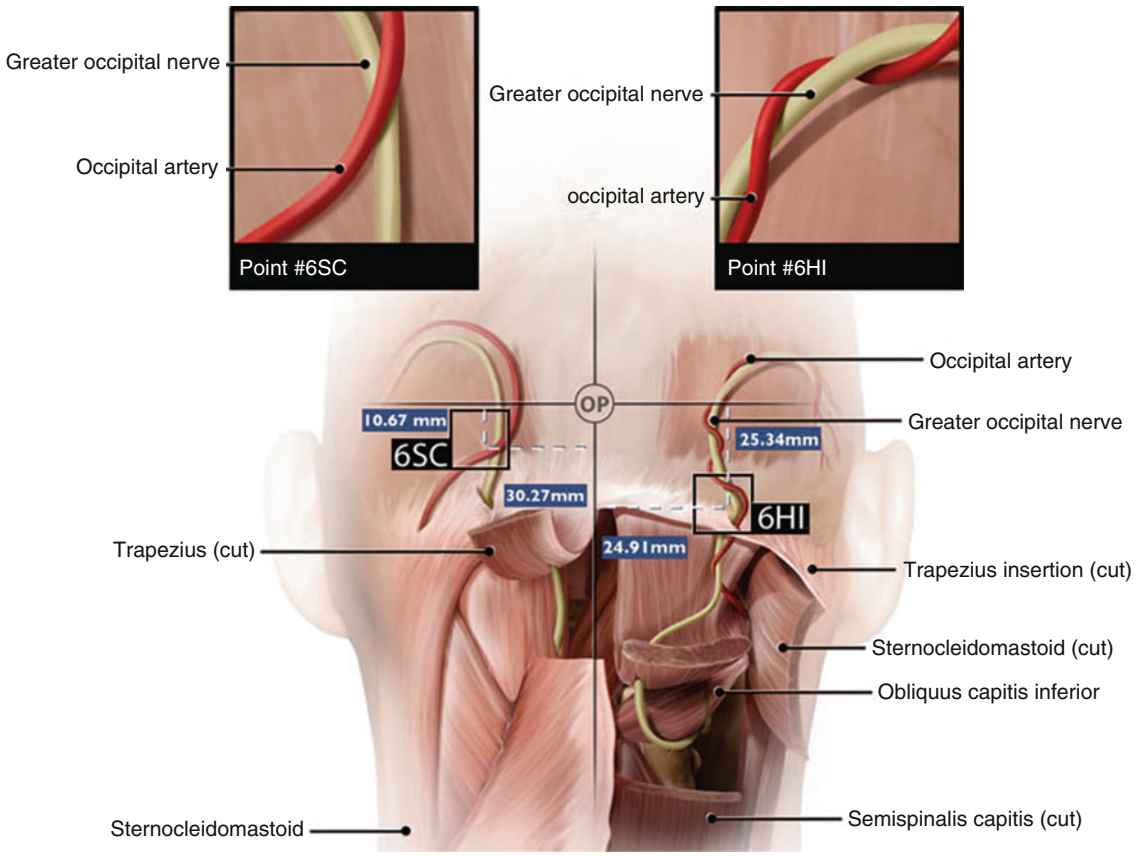

Fig. 10.6 Schematic illustration depicting compression point 6. Different types of greater occipital nerve–occipital artery relationships are shown. *SC* single cross, *HI* helical intertwining (With permission from Janis et al. [4])

protocol is described at all, with authors simply stating that medications are injected in the "region of the greater occipital nerve" [14]. Clinically these discrepancies in localization may be serendipitously alleviated somewhat by the not inconsequential injectate volumes employed, frequently five or even as many as 10 ml [15]. As such, any notion of specificity is rendered suspect at the very least and quite implausible at most, as in so doing yields procedures more akin to general field blocks than selective peripheral neural blockade.

Many authors employing landmark identification suggest palpation of the occipital artery, which frequently courses just lateral to the nerve. However, several pertinent issues may conspire to obscure such identification. One, anatomical variations to conventionally accepted neurovascular association are common. Two, the zone of palpation lies cephalad to typical hairlines, which may make palpation infeasible in the overly hirsute. Three, the occipital artery quite often lacks the vasodynamic bounding of more sizable vessels and thus may not be easily discernable, especially in patients of excess habitus. For these reasons, ultrasonic Doppler flowmetry may be employed to increase the likelihood of arterial localization, with purported increases in success rate and density of blockade, along with decreases in symptoms of vascular uptake as compared to more traditional approaches.

Although multiple techniques have been described, the clinical or statistical superiority of one method over competing approaches has never been validated. The practitioner, therefore, is left with myriad options from which to choose, depending on their personal experience, comfort level, and skill set. At the very least, it would appear that identification of the inion is a prerequisite to block performance, as is a topographical appreciation for the underlying subcutaneous and intermuscular course of the nerve.

Isolating a suitable location for injection is only one aspect of the procedure, however, which leads to the choice of injectate. Published study protocols have varied widely, including the use of both short- and long-acting local anesthetics, sometimes but not always including epinephrine, with or without a number of different steroids, plus or minus additives including but not limited to opioids and alpha-2 agonists. Botulinum toxin has also been employed with some success. Additionally, the chosen injectate volumes are far from uniform, with a single milliliter employed in some trials and as much as 10 ml in others.

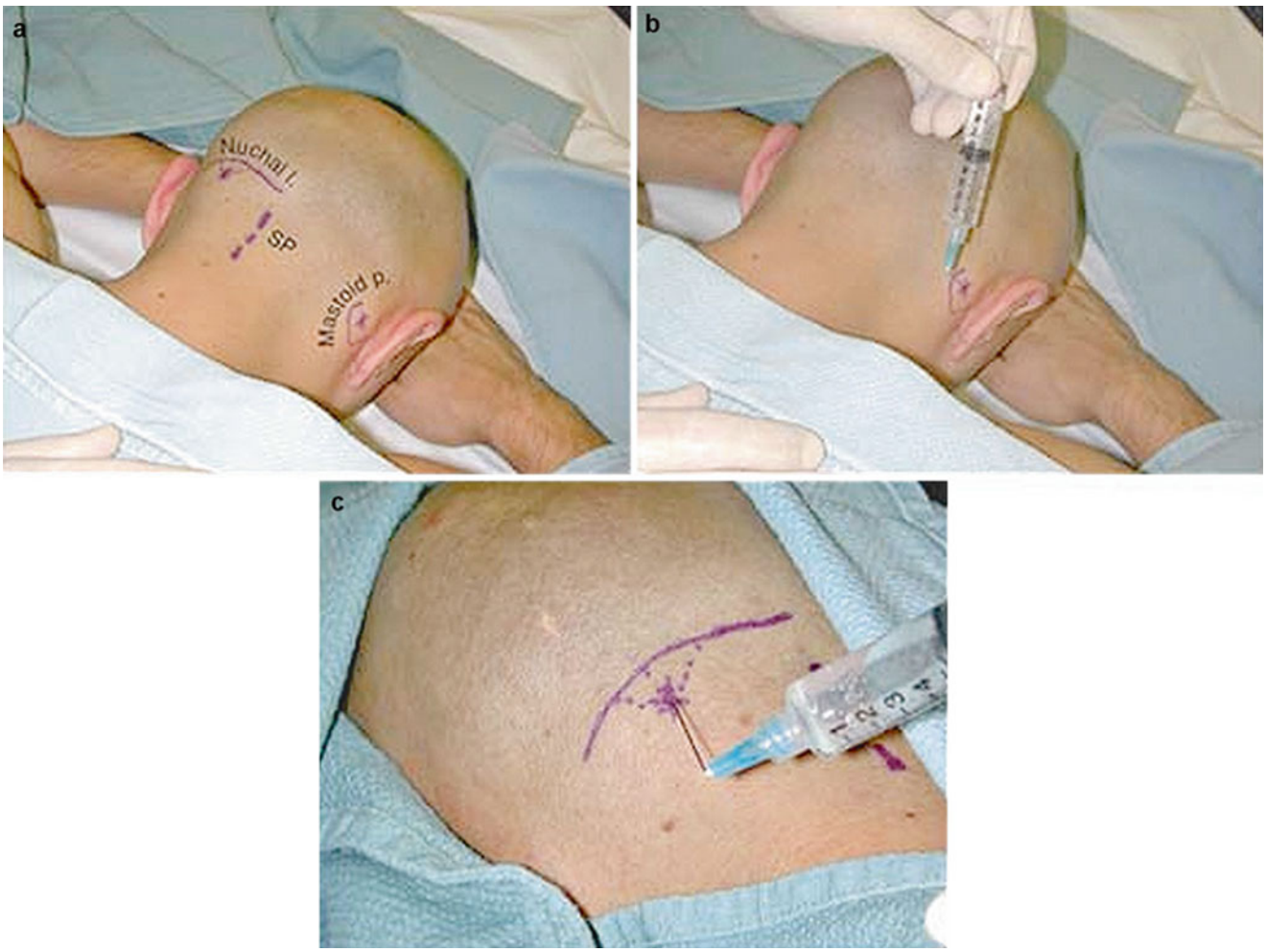

Fig. 10.7 (a) Surface anatomy of the occipital area. (SP spinous processe). (b) Lesser occipital nerve injection at the mastoid process. (c) Greater occipital nerve blockade at the superior nuchal ridge. Anatomic landmarks for greater and lesser occipital nerve block (From Chelly [6]. Copyright ©2009 Lippincott Williams & Wilkins)

What this implies, of course, is that there is either insufficient evidence at this stage to ascribe superiority of one medication regimen over another or, perhaps equally likely, there is simply no appreciable advantage to be elucidated. For instance, Naja et al. [16] injected 3 ml of a 10-ml mixture that included 3 ml of lidocaine 2 %, 3 ml of lidocaine 2 % with epinephrine 1:200,000, 2.5 ml of bupivacaine 0.5 %, 0.5 ml of fentanyl 50 mcg/ml, and 1 ml of clonidine 150 mcg/ml. The authors suggest that this mixture demonstrates superior longevity that exceeds the expected duration of action of the local anesthetic alone. However, Arner et al. [17], using 0.5 % bupivacaine alone, obtained analgesia that exceeded the expected duration of effect in 18/38 consecutive patients treated for peripheral neuralgia. Thus, the incremental improvements in dose response attributable to additives remain uncertain.

Lastly, there exists some evidence to substantiate the efficacy of frequently repeated injections over single interventions to achieve prolonged analgesia. Naja et al. [18] performed occipital nerve blocks repeatedly in 47 patients with cervicogenic headache and were able to achieve a 6-month period of pain relief in 96 %. Interestingly, the authors found that the number of blocks required to reach this end point could be predicted by adding one injection for every 3 years of headache history. Similarly, Caputi and Firetto [19] succeeded in obtaining a 50 % or greater reduction in the total pain index in 23/27 patients using repetitive local anesthetic-only blocks in the treatment of chronic migraineurs.

Indications

1. Occipital neuralgia
2. Cluster headache
3. Cervicogenic headache
4. Migraine

5. Cancer pain in the region [10]
6. Headache associated with muscular spasm or tension [10]
7. Anesthesia of posterior scalp [10]
8. Postconcussive headaches
9. Atypical orofacial pain [20]
10. Abnormal head movements, tinnitus, and dizziness associated with history of trauma [21]
11. Postdural puncture headache [13]
12. Rescue treatment for headaches proving recalcitrant to other measures
13. As an adjuvant to medication-overuse headache

Likely Ineffective

1. Tension headache
2. Hemicrania continua
3. Chronic paroxysmal hemicrania

Contraindications

1. Patient refusal
2. Bleeding diathesis
3. Local or systemic infection
4. Local neoplastic disease

Evidence-Based Review

In recent years, numerous studies have been published demonstrating the efficacy of GONB in multiple chronic pain and other conditions. Quite surprisingly, however, there are few randomized, double-blind, placebo-controlled trials, and the preponderance of evidence available is confounded by methodological discrepancies in diagnosis, technique, treatment, and outcome. Regardless, the available evidence does suggest that several conditions are likely to respond favorably to GONB. Perhaps this ambiguity in diagnostic response is more attributable to insufficient understanding of underlying pathophysiology and resultant overlap in ascribed diagnoses. Alternatively, the functional anatomical convergence of the occipital afferents and the trigeminal nerve complex in the proximal cervical spinal cord may render multiple distinct disease states susceptible to the same intervention. Evidence for this theory is supported by multiple findings. Goadsby et al. [22] showed that the cervical dorsal horn and trigeminal nucleus caudalis show increased metabolic activity during stimulation of the occipital nerve, suggesting that the second-order neurons overlap in their nociceptive processing. This finding was supported by the work of Piovesan et al. [23], who elicited pain in the distribution of the trigeminal nerve, including parasympathetic activation suggestive of trigeminal autonomic activation, during sterile water injection over the greater occipital nerve. More recently, Busch et al. [24, 25] have shown decreases in the nociceptive blink reflex area and increase in the reflex latency following occipital nerve blockade. The functional connectivity between cervicooccipital afferents and the trigeminal nerve complex would, as it appears, be central to the evidentiary link between GONB and its efficacy in the conditions described below. However, the response of primary headache disorders, in addition to occipital neuralgia, to GONB is felt by some to subvert the block's value as a diagnostic tool [26].

Cervicogenic Headache

Multiple studies have repeatedly shown positive responses to GONB in patients with cervicogenic headaches. Naja et al. [16] in a randomized, double-blind, placebo-controlled clinic trial investigated the efficacy of GONB and lesser occipital nerve block in patients with a diagnosis of cervicogenic headache. The facial nerve was also blocked in this study in patients with pain that extended into the orbital area. Using nerve stimulator guidance for localization, the authors injected 10 ml of a mixture containing 2 % lidocaine, 0.5 % bupivacaine, epinephrine, fentanyl, and clonidine to prolong duration of effect. The procedure reduced VAS and TPI scores by 50 % ($P = 0.0001$), as well as reducing associated symptoms including duration and frequency of headache and analgesic consumption ($P < 0.05$). In a prospective, open-label, case-series follow-up study that involved repeat injections as needed, the authors were able to achieve a 6-month period of pain relief in 96 % of the study participants in the setting of medication tapering. The study patients received an average of 5.3 injections, and the authors concluded that following the initial injection, patients would require one additional injection for each 3 years of headache history to achieve 6 months of relief. Multiple other unblinded studies have corroborated the findings of Naja et al. [27–29].

Cluster Headache

Cluster headache, like cervicogenic headache, has shown statistically significant improvement when treated by GONB in a number of studies. In a double-blind, randomized, placebo-controlled trial, Ambrosini et al. [30] randomized patients with cluster headache to receive 2 % lidocaine with either short- or long-acting betamethasone or normal saline. Headaches resolved in 85 % of patients, lasted for more than 4 weeks in 61 % and more than 4 months in 38 %. Retrospective analyses have also concluded that cluster headaches may respond to GONB. Afridi et al. [31] injected

3 ml of 2 % lidocaine plus 80 mg of methylprednisolone into a subgroup of patients with refractory cluster headache and found complete resolution in 53 % and partial resolution in an additional 16 %. The mean duration of benefit in this population from a single injection was 17 days. Likewise, Peres et al. [32] injected 14 cluster headache patients with 3 ml of 1 % lidocaine and 40 mg of triamcinolone, with 64 % of the study population rendered headache-free following injection and a mean duration of benefit of 13 days.

Occipital Neuralgia

According to the second edition of the International Headache Classification (ICHD-2), efficacy of GONB is, by definition, assumed. That is, in addition to the appropriate symptom complex and physical examination findings, pain must be, at least temporarily, alleviated by blockade of the occipital nerve. As such, prospective investigations determining response in patients presumed to have the diagnosis are rendered redundant. Retrospective analyses have been carried out, however. Anthony [14], using diagnostic criteria that included "unilateral occipital headache … with or without referral to the ipsilateral orbital or supraorbital areas, circumscribed tenderness over the GON … and hypoalgesia, hyperalgesia or dysaesthesiae in the area of distribution of the GON," found complete headache relief in 75 of 86 patients treated with GONB. The mean duration of relief in this study was 31 days when 160 mg of methylprednisolone was incorporated into the injectate. In another retrospective analysis performed by Tobin and Flitman [11], patients received GONBs if they had "significant headache pain … and if pressure on an ON reproduced their headache pain." In this group of patients, the authors achievewd a 78 % success rate with local anesthetic and steroid and quite interestingly noted that systemic medication overuse increased the rate of failure threefold, more so in migraneurs than in patients diagnosed with occipital neuralgia.

Migraine Headaches

The evidence supporting GONB in migraneurs is not as compelling as it has been in other conditions (see above), but the procedure has been shown beneficial in some patients nonetheless. In a prospective, open-label, single-treatment-arm study, Weibelt et al. [33] decreased the number of headache days per month by at least 50 % in 78/150 patients, and 90/150 reported their symptoms to have subjectively improved. In a double-blind, controlled, crossover study, Piovesan et al. [34] found that GONB did not reduce the number or duration of migraine attacks, but did conclude that the intensity of headache symptoms was reduced 60 days following the injection. In a prospective, open-label, uncontrolled study, Caputi and Firetto [19] used GONB and supraorbital nerve blocks in on migraine patients whose physical examination was notable for tenderness to palpation over the respective nerves. The authors injected these areas until the tenderness had diminished to less than half its baseline value and noted that 5–10 injections would produce lasting and increasing benefit for as much as 6 months in 85 % of the patients studied. Afridi et al. [31] found benefit with GONB in patients with intractable migraine, obtaining complete or partial (>30 % improvement) response in 46 % of the injections, with a median duration of response of 30 days. Notably, the authors found no correlation between local anesthesia over the distribution of the GON and migrainous response. Gawel and Rothbart [35] retrospectively reviewed GONB with local anesthetic and steroid in their own migraine population and found that 54 % of patients with non-posttraumatic migraineurs felt "significantly better" for up to 6 months following the injection. The authors also noted that in patients with a diagnosis of posttraumatic migraine, the benefit was greater, with 72 % of patients reporting such benefit. The improved response rate in posttraumatic migraineurs has been substantiated by other studies, including Tobin and Flitman [11] who obtained 100 % efficacy (12/12) in post-concussive migraineurs.

Other Uses

The implications of convergence between the trigeminal nerve complex and occipital afferents suggest that the infiltration of medications around the GON may have applications well beyond typical occipital neuralgia. For instance, a recent prospective, randomized, single-blind, clinical study investigated the efficacy of nerve stimulator-guided GONB for the treatment of postdural puncture headache, with 68.4 % of the patients achieving complete relief after one to two blocks, with the remaining 31.6 % experiencing relief after three or four injections [13]. Given the side effect profile of epidural blood patches, this study raises the possibility of an equally effective treatment with far less risk, especially in the immunocompromised and/or anticoagulated postsurgical population.

Another potential avenue of pursuit in GONB involves the mitigation of withdrawal symptoms in patients being treated for chronic medication-overuse headaches. Afridi et al. [31] noted that in patients treated for migraine, there was no statistically significant association between block response and medication overuse. Data from Tobin and Flitman [11] is less supportive, but these authors still demonstrated a 56 % success rate even in those patients overusing abortive agents. In fact, the response rate in medication overusers

was quite similar between the two studies, 20/31 (65 %) in Afridi et al. vs. 14/25 (56 %) in Tobin and Flitman's. Considering the difficulty with which many patients with medication-overuse headache wean from their pharmaceuticals, a procedure with the potential to moderate their course would certainly be advantageous.

Occipital Nerve Stimulation

Occipital nerve stimulation has become an increasingly popular modality for treating intractable headaches. In 1999, Weiner et al. [36] reported on a small group of patients with occipital neuralgia who had beneficial effects from subcutaneous neural stimulation. Since that initial report, use of occipital nerve stimulation has extended to more global headache diagnoses, such as migraine [1, 37, 38]. In the past, practitioners have used occipital nerve blocks to predict success with occipital nerve stimulation. However, recent studies show that occipital blocks are not useful for predicting success with occipital stimulation [39, 40]. Indeed, the most recent publication of the ONSTIM trial by Saper and others shows that response to occipital nerve block was not part of inclusion criteria [41].

Cautions

Despite the volume of scientific literature available supporting the use of GONB and the evidence for benefit in a number of clinical conditions, the results must be taken with caution. There are no uniform methods for GONB application, nor were the patient populations studied homogenous. Additionally, with rare exceptions, the bulk of data currently available was derived from uncontrolled investigations, confounding any conclusions that may be drawn. Determining whether the study findings are the result of the explicitly stated pathophysiological associations or more serendipitous interactions will require more focused investigation.

Another issue that clearly needs to be further delineated relates to the location of injection and the tissues through which the needle passes. Although advocated as primary block of the GON, it seems rather obvious that injections performed more medially and caudally, where the GON exits the semispinalis capitis, are in fact also infiltrating local anesthetic into the paraspinal muscles. In effect, this represents a trigger-point injection in addition to any neural blockade that may be taking place and may be responsible, at least in part, for the finding by Afridi et al. [31] that anesthesia in the distribution of the greater occipital nerve did not correspond to degree of pain relief. This situation is made all the more ambiguous by the propensity of many practitioners to inject not according to any distinct anatomical location but rather in the area of greatest tenderness to palpation or reproduction of typical headache symptoms. Specifically, what is being "blocked" during such procedures is unclear, and as such, the mechanism of underlying pathophysiologic modification and subsequent clinical improvement remains uncertain.

Conclusions

Occipital nerve block has been, and will almost certainly remain, a frequently implemented tool in the pain physician's armamentarium. The procedure has proven effective for several conditions, including, by definition, occipital neuralgia, but also cervicogenic and cluster headaches. There also appears to be a role for treatment in migraineurs, although further investigation is needed. Despite the prevalence of the block, numerous technical variances obscure definitive conclusions.

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Neural Blockade for Trigeminal Neuralgia

11

Ali Mchaourab and Abdallah I. Kabbara

Key Points

- Review the history and epidemiology of trigeminal neuralgia.
- Highlight the clinical manifestations of trigeminal neuralgia.
- Review relevant anatomy of the trigeminal nerve and ganglion.
- Summarize the current treatment modalities and their effectiveness.
- Discuss neural blockade of the trigeminal nerve and ganglion and its application.
- Review potential complications of different invasive modalities.

Historical Background

The first case report of trigeminal neuralgia (TN) dates back to 1671, where it proved fatal to the unfortunate Johannes Laurentius Bausch, a physician. Later works by Nicolaus Andre, John Fothergill, and Charles Bell established "tic douloureux" as a disorder of the trigeminal nerve [1, 2]. In ancient times, facial pain was described by the Arabic physician Ibn Sina (980–1073). The description of interventional therapy dates back to 1677 when Locke applied sulfuric acid to the face of the Duchess of Northumberland to treat her facial pain [3].

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The incidence of trigeminal neuralgia is estimated at 4–5 in 100,000 [4] with more prevalence in women (ratio of 1:1.5) [5]. It is the most common form of facial pain in people older than 50 years of age, and its highest incidence occurs in the ages between 50 and 70 years [3]. Described by Peter Jannetta as "the worst pain in the world," its presentation and management continues to present a challenge to modern-day medicine. In this chapter, the authors will review the current nonsurgical invasive modalities used to treat trigeminal neuralgia, placing an emphasis on proper diagnosis which is key for success.

The Clinical Syndrome

Clinical Manifestations

Trigeminal neuralgia pain is a neuropathic pain located in the distribution of the trigeminal nerve or cranial nerve V. It is classically described as sharp, stabbing, lancinating, electric shock-like, short lasting, intermittent and variable, and almost always unilateral. It is often so intense as to interfere with daily routines, speaking, or even eating. Pain can occur spontaneously, or can be triggered by movement or touching of the face or mouth. Therefore, patients typically avoid touching that area of their face, shaving, and chewing. Eating habits are affected, and often patients report weight loss. The fore mentioned avoidance is a valuable clue to diagnosis. In other facial pain syndromes, the opposite occurs: Patients tend to rub or massage the painful area of their face [6].

A typical attack lasts for seconds and is followed by a refractory period, a period of relief that lasts for seconds, minutes, or even hours. Any of the three branches of the trigeminal nerve may be affected. Typically, the neurologic examination is either normal or demonstrates a subtle decrease in sensation in the affected distribution, perhaps including suppression of the ipsilateral corneal reflex.

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Table 11.1 Differential diagnosis of trigeminal neuralgia

Differential diagnosis of trigeminal neuralgia		
	Primary clinical characteristics	Mimicking characteristics
Glossopharyngeal neuralgia	Severe transient, stabbing or burning pain in the ear, base of the tongue, jaw, and tonsillar fossa	Pain in facial area; triggers can be chewing, swallowing, talking, or coughing
Geniculate neuralgia	Impairment of CN-VII sensory part; related to herpes zoster; pain is usually in the different ear structures	Pain may radiate from the ear to the face; has a burning dysesthetic quality
Herpetic and postherpetic neuralgia of the trigeminal nerve	Pain is steady and sustained, burning and aching. Often regresses in 2–3 weeks, months in patients older than 70 years of age	The steady pain is accompanied by shooting and sharp pain that radiates and is provoked by mechanical stimuli
Herpetic and postherpetic neuralgia of the cervical dorsal root ganglia	Steady pain in face, ear, and occiput	Facial pain, unilateral
Occipital neuralgia	Pain radiates following the greater occipital nerve distribution to the frontal region	Burning, unilateral pain that can radiate to the forehead, mimicking ophthalmic distribution of the trigeminal nerve
Atypical facial pain	Continuous aching or burning pain; unilateral or bilateral	Burning facial pain; may follow the nerve branches distribution; infrequently exacerbated by eating/talking
Rare disorders, that is, Raeder syndrome, trigeminal nerve neuritis from tumors, and other diseases	Usually Horner syndrome without anhidrosis	Sudden onset severe frontotemporal burning; often in periorbital or trigeminal distribution
Others: dental pathology, ear, nose, and throat; cluster or migraine headaches; temporomandibular joint syndrome	Variable presentations and patterns	Can mimic trigeminal neuralgia

Differential Diagnosis

The etiology of trigeminal neuralgia is not fully understood. Abnormality of the trigeminal nerve myelin sheet has been described but not agreed upon [7]. Trigeminal neuralgia is divided into primary or idiopathic and secondary where a compressive etiology is identified such as a vascular structure or tumors, or a disease etiology such as multiple sclerosis. Establishing a diagnosis of trigeminal neuralgia is instrumental to a successful management strategy especially if surgical or invasive interventions are being considered. Pathognomonic criteria for diagnosis include paroxysmal pain that lasts from a fraction of a second to 2 min and pain characterized as intense, sharp, stabbing, and precipitated by trigger factors. Table 11.1 lists facial pain syndromes that could share some of the clinical manifestations of trigeminal neuralgia. The authors cannot stress enough the importance of establishing a firm diagnosis prior to proceeding to management, especially invasive modalities. A false-positive diagnosis will not only lead to failure of treatment but to possible non-indicated invasive treatments that carries potential morbidity and mortality (Table 11.1).

The Gasserian Ganglion

Anatomy

Studying the gross and neuroanatomy of the trigeminal nerve is an essential task prior to neural blockade. The trigeminal nerve has both sensory and motor fibers. Visceral efferent fibers contribute to innervate some muscles of mastication and facial expression. Through its somatic afferent fibers, the trigeminal nerve transmits nociception, light touch, and temperature sensation from the skin of the face, teeth, anterior two thirds of the tongue, the nose, and oral cavity mucosa. Figure 11.1 shows the three branches of the trigeminal nerve (ophthalmic, maxillary, and mandibular).

The gasserian ganglion, also known as the trigeminal ganglion or the semilunar ganglion, sits in an invagination of the dura mater of the posterior cranial fossa, known as Meckel's cave (Fig. 11.1). Injection of local anesthetic in Meckel's cave, which contains cerebrospinal fluid, can potentially lead to total spinal anesthesia or spread to other cranial nerves. Its three sensory divisions, the ophthalmic (V1), maxillary (V2), and mandibular (V3), divide and exit anteriorly as shown in

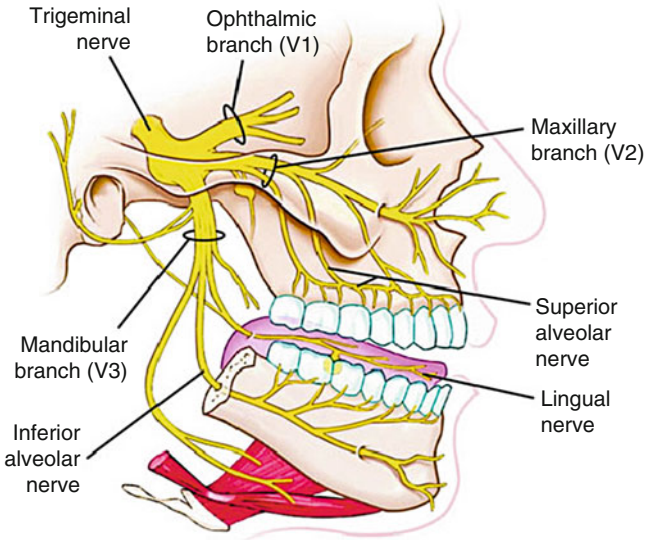

Fig. 11.1 The division of the three branches of the trigeminal nerve after exiting the middle cranial fossa (Copyright Elsevier)

Fig. 11.1. The mandibular branch exiting through the foramen ovale has clinical applications as the reader will see in this chapter.

Blockade of the gasserian ganglion has been applied as surgical anesthetic for procedures of the head and neck in very limited instances. More commonly, it is used as a treatment for trigeminal neuralgia after failure of conservative therapy and also for cancer pain involving the face. Trigeminal ganglion neurolysis has been effective when oral therapy fails. The palliation of cancer-related pain arising from direct nerve involvement or surgical trauma has successfully been accomplished through blockade of the trigeminal ganglion or its divisions. Neurolysis of the trigeminal ganglion relieves cluster headaches refractory to oral therapy [8–12] and intractable atypical facial pain [13, 14].

Techniques for Gasserian Ganglion Blockade

To decrease the chances of adverse events, the use of radiological guidance such as computed tomography [15], fluoroscopy [16], or ultrasonography [17] along with a blunt-tipped curved needle is highly recommended. The blockade of the trigeminal ganglion has been performed without radiological guidance in the past but is not advisable. Those measures not only increase patient's safety but also improve the access to the main anatomical landmark, the foramen ovale.

The patient is placed in a supine position with the head slightly extended. Facial skin is sterilely prepped. It is recommended that conscious sedation be administered for patient comfort with blood pressure, pulse oximetry, and electrocardiogram monitoring. Fluoroscopic x-ray guidance is used. The skin entry site is usually located approximately 2–3 cm lateral to the commissural labialis (the corner of the mouth) in a mid-pupillary line. Localization of the foramen ovale is critical to the success of this block. The anteroposterior fluoroscopic view usually shows the petrous ridge through the orbit, and 1 cm medially, it also shows a dip in the petrous ridge. Rotation of the C-arm head obliquely away from the nose approximately 20–30° and approximately 30–35° in the caudo-cranial direction will bring the foramen into view just medial to the mandible and at the top of the petrous "pyramid." Lidocaine 1 % is applied to the skin and subcutaneous tissue over the shadow of the foramen ovale. For a diagnostic local anesthetic block, a 22-g B-bevel needle, 8–10 long, is used (for radiofrequency lesioning, an RFA 10-cm needle with a 2–5-mm active RFA tip is used). The needle is advanced through the entry point toward the foramen ovale, rotating the needle tip as needed to keep it on course initially downward and laterally, then medially aiming for the foramen ovale. To prevent intraoral entry, placement of one finger in the mouth could be done. When bone is encountered, the needle could be walked posteriorly along the skull into the foramen. A lateral view should be obtained, revealing the needle through the foramen ovale in a trajectory superior and toward the medial aspect of the external auditory meatus. A mandibular nerve paresthesia is commonly elicited. It is mandatory to test negative aspiration of cerebrospinal fluid (CSF) confirming that the needle did not penetrate the dura matter. The needle position is confirmed with injection of nonionic water-soluble contrast and negative aspiration of blood and CSF. For diagnostic local anesthetic blockade, small increments of local anesthetic (lidocaine 2 %, bupivacaine 0.5 %, or ropivacaine 0.5 %) are injected for a total of 1 ml. Monitoring the patient is essential to confirm that local anesthetic did not reach the CSF, putting the patient at risk of inadvertent spinal anesthetic and potential respiratory arrest. Figure 11.2 illustrates the trajectory of the needle in correct placement for the gasserian block.

Chemical Neurolysis

Currently, the most common agent used for neurolysis of the trigeminal ganglion is glycerol [18–24], knowing that phenol [25] and alcohol [26–28] have also been used in the past. A neurolytic solution up to 0.5 ml should be injected in small increments preferably of 0.1 ml to avoid inadvertent spread to structures of the brain stem. For the technique using glycerol, the needle is advanced into the trigeminal cistern and free CSF flow is confirmed. When using a hyperbaric neurolytic agent, the patient should sit with the head tipped forward for 2 h [29]. This maneuver ensures spread of the injectate to the maxillary and mandibular branches, sparing the ophthalmic branch. Acute unilateral total visual loss after gasserian phenol injection has been reported [30].

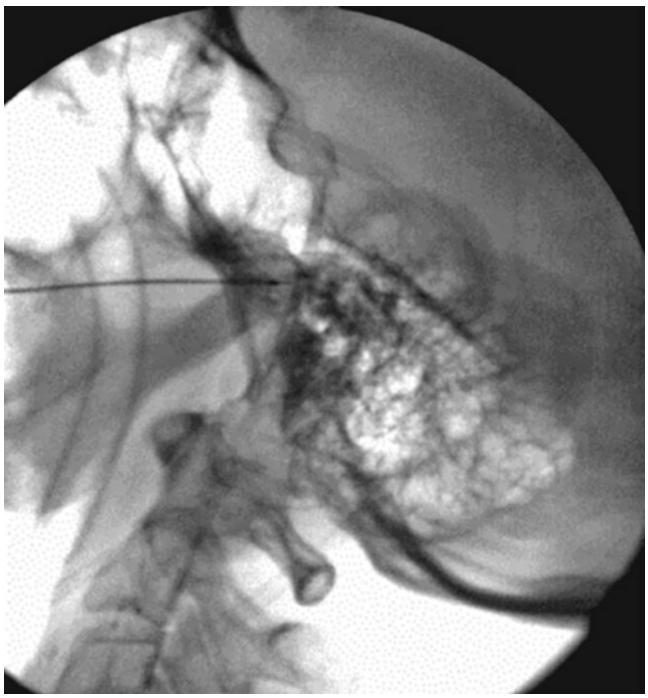

Fig. 11.2 Lateral fluoroscopic view showing trans-foramen ovale gasserian ganglion block: needle is in position and radio-opaque dye classic spread is shown

Radiofrequency Ablation

Conventional radiofrequency (RF) neurolysis is performed at temperatures ranging from 60° to 90° centigrade, for duration of 60–90 s. Knowing that the mandibular branch is the only branch carrying motor fibers, motor stimulation at 2 Hz within a range of 0.1–1.5 V will reproduce muscle contraction of the lower mandible. While performing lesioning for V1 or V2, motor stimulation at 2 Hz is not expected to show any muscular contraction. For confirmation of needle position, sensory stimulation at 50 Hz preferably below 0.6 V should precede any treatment. A correct needle position should reproduce a tingling-like sensation or paresthesia in the distribution of the targeted nerve branch. Adjustment of the needle position is performed to optimize desirable sensory patterns prior to any lesioning. Patient alertness and cooperation is of paramount importance: Patient feedback on where the sensation is elicited will help the physician complete the desired block successfully (Fig. 11.2). Understanding the anatomy and how the rootlets of the trigeminal ganglion lay in a superomedial to inferolateral plane is very important: In case of a non-desirable motor response, the practitioner will adjust the needle from a lateral position to a more medial one. Confirmation of negative blood flow should be documented. Up to 0.5 ml of 0.5 % bupivacaine or 0.2 % ropivacaine should be injected prior to RF lesioning to alleviate procedure-related discomfort. If RF lesioning is performed on the 1st branch of the trigeminal nerve (V1), temperature should be limited to 60° to preserve the corneal reflex.

Pulsed radiofrequency [31–34] is another option for neurolysis usually done at 42 °C for 120 s. Even though Erdine et al. [35] could not confirm its effectiveness in this study, it is still being performed with variable results.

The Trigeminal Nerve Branches: Opthalmic, Maxillary, and Mandibular

Anatomy

The ophthalmic branch (V1) of the trigeminal branch is a purely sensory branch [36]. It enters the orbit via the superior orbital fissure. In turn, it divides into three branches, the frontal, nasociliary, and lacrimal nerves. The latter two provide innervations to nasal structures and the lacrimal gland, respectively. The supraorbital and the supratrochlear are terminal branches of the frontal nerve: They exit the orbit anteriorly and provide innervations to upper eyelid, forehead, and anterior scalp. As illustrated in the next paragraph, they are clinically most significant of the V1 branches.

The maxillary branch (V2) is also a pure sensory branch [37]. It exits the middle cranial fossa into the pterygopalatine fossa in a horizontal fashion through the foramen rotundum. Then, it passes through the inferior orbital fissure to the orbit before exiting to the face via the infraorbital foramen. That passage through the four facial compartments lead to the division of the many branches of V2 to four regional groups of branches. Understanding the exit of V2 from the middle cranial fossa to the face simplifies the understanding of its innervations of facial structures (Fig. 11.1). Table 11.2 summarizes the four groups and the facial areas they innervate.

The mandibular nerve is formed by the joining of the large sensory mandibular division of the trigeminal nerve and a small motor nerve root. They both cross the foramen ovale leaving the middle cranial fossa and forming the mandibular nerve [37]. This combined trunk then divides into a small anterior and larger posterior trunk (Fig. 11.1). Prior to this division, it gives off the nervus spinosus, innervating the dura matter and mucosal lining of the mastoid sinus, and the internal pterygoid, innervating the internal pterygoid and sending branches to the otic ganglion.

From the anterior trunk comes the buccinator nerve to innervate the skin and mucous membrane overlying the buccinator muscle. The anterior trunk also gives off three motor branches: the masseteric, deep temporal nerves, and the external pterygoid nerve. They provide motor innervations to the masseter muscle, temporalis muscle, and external pterygoid muscle, respectively.

Table 11.2 The four regional groups of V2

The four regional groups of V2	V2 nerve branches	Facial areas innervated
1. Intracranial group	Middle meningeal nerve	The dura matter of the middle cranial fossa
2. Pterygopalatine group	Zygomatic nerve	The temporal and zygomatic region
	The sphenopalatine branches	The mucosa of the maxillary sinus, upper molars, upper gums, and the mucous membrane of the cheek
3. Infraorbital canal group	Anterosuperior alveolar branch	Incisors, canines, anterior wall of the maxillary antrum, floor of nasal cavity
	Middle superior branch	Premolars
4. Infraorbital facial group	Inferior palpebral branch	Conjunctiva and skin of lower eyelid
	External nasal branch	Side of the nose
	Superior labial branch	Skin of the upper lip and part of the oral mucosa

The posterior trunk contains mostly sensory fibers. The following branches come off the posterior trunk: The auriculotemporal nerve provides sensory innervations to the following structures – the tympanic membrane, the lining of the acoustic meatus, the posterior temporomandibular joint, the parotid gland, the skin overlying the temporal region, and the skin anterior to the tragus and helix. The lingual nerve innervates the dorsum and lateral aspects of the anterior 2/3 of the tongue, the lateral mucous membrane, and the sublingual gland. The inferior alveolar nerve innervates the lower teeth and the mandible. Its terminal branch, the mental nerve, innervates the chin and the skin and mucous membrane of the lower lip.

Blockade of the Ophthalmic Branch

The most commonly blocked branches of V1 are the supraorbital and supratrochlear branches. To block the supraorbital nerve, the patient is placed in a supine position. The landmark for this block, the supraorbital foramen, is palpated along the upper border of the orbit. After skin prepping, with precautions not to spill any disinfecting solution in the eye, a 25-gauge, 1.5-in.-long needle is introduced into the skin through the identified supraorbital foramen in a perpendicular plane to the skin. Some paresthesia is usually elicited; then, 3–4 ml of local anesthetic solution (lidocaine 1–2 %, bupivacaine 0.5 %, or ropivacaine 0.2 %) is injected in a fanlike fashion. Radiofrequency lesioning for the supraorbital nerve as a treatment for postherpetic neuralgia has been described. The technique for radiofrequency lesioning is similar to the local anesthetic block with the exception of using a RFA needle and confirmation of positive sensory response at 2-Hz stimulation in the somatic nerve distribution. To achieve a blockade of the supratrochlear branch of the ophthalmic division, simply direct the needle medially at the level of the supraorbital foramen and repeat similar steps as described above.

Blockade of the Maxillary and Mandibular Branches

The preferred approach for blockade of the maxillary (V2) and the mandibular (V3) branches of the trigeminal nerve is through the mandibular notch, also known as the coronoid notch. These blocks could be done without radiologic guidance. However, fluoroscopic guidance is highly recommended. Patient is placed in supine position, and the x-ray C arm is placed in a lateral view. The patient is asked to open and close his/her mouth few times if possible to facilitate palpation of the mandibular notch which could be marked. After skin sterilization, the skin is anesthetized with lidocaine 1 %. A 22-g B-bevel needle, 8–10 cm long is used (for radiofrequency lesioning, an RFA needle, 10 cm long, with a 2–5-mm active RFA tip is used). The needle is introduced under fluoroscopic guidance at the site already marked and advanced in a horizontal plane. Fluoroscopic guidance is used to direct the needle tip through the infratemporal fossa (Fig. 11.3). A small-angulation cephalad and slightly posterior will allow the needle to be in proximity to the lateral nasal mucosa taking extreme care not to pierce through it. The end point of the advancement of the needle is the lateral pterygoid plate. If the maxillary nerve is the final target, a slight superior and posterior angulation will elicit paresthesia into this nerve distribution (nose ridge, upper lip, gum, and face). If the mandibular nerve is targeted, a slight caudad and anterior angulation usually elicits paresthesia in its somatic distribution (lower mandible, lower lip, lower jaw, and tongue). If radiofrequency lesioning is planned, sensory testing at 50 Hz should be achieved preferably below 0.6 V in the nerve distribution prior to any treatment. Negative aspiration of blood and CSF should be demonstrated prior to any treatment. Figure 11.4 shows the advancement and final position of the needle. Figure 11.5 shows RF needle in position.

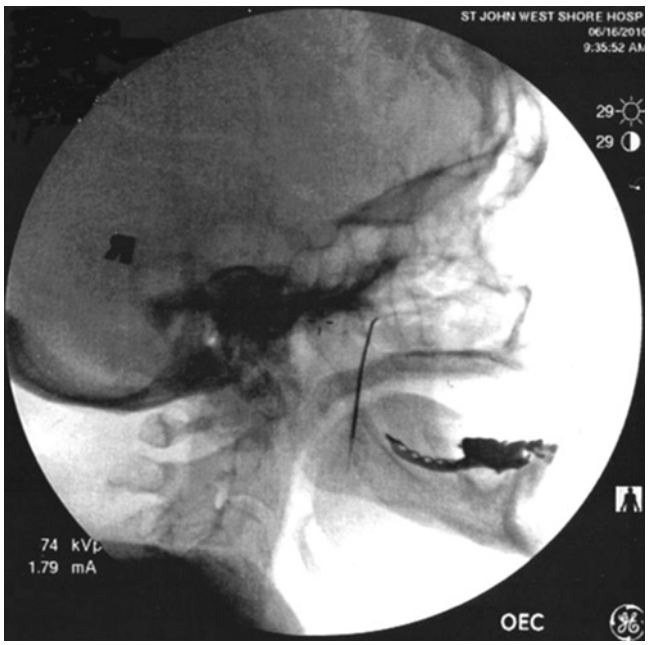

Fig. 11.3 Lateral fluoroscopic view showing needle though the coronoid notch in position for advancement

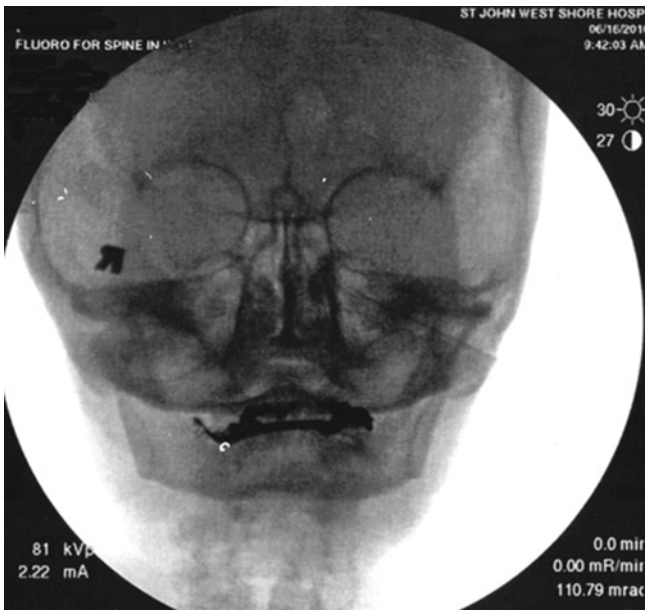

Fig. 11.4 Anteroposterior fluoroscopic view showing needle advancement for maxillary nerve block

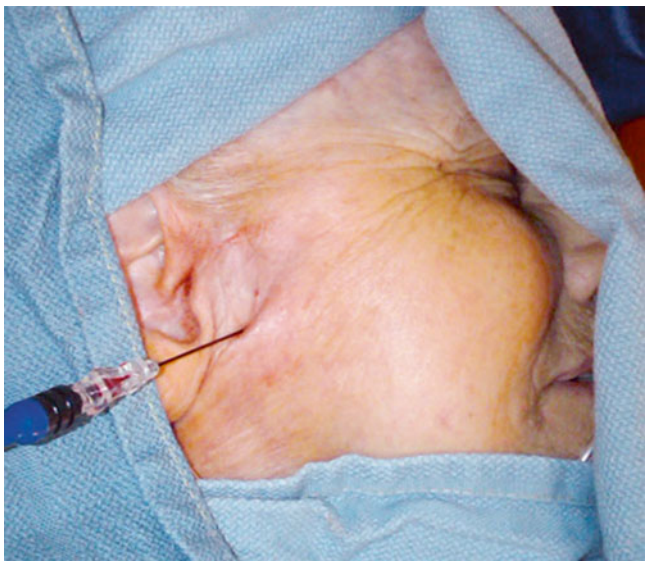

Fig. 11.5 Final needle placement for radiofrequency lesioning of the maxillary nerve

Efficacy and Safety

The efficacy and safety of radiofrequency (RF) lesioning for trigeminal neuralgia have been described in the literature. Review of current literature reveals one retrospective uncontrolled chart review [38] and four prospective uncontrolled clinical trials [39–42]. No randomized sham-controlled trials on the value of RF treatment of the trigeminal ganglion have been published. An initial complete pain relief was reported in 83–99 % of patients treated with RF ablation in some studies [39, 40, 43–49]. Repeating the procedure has increased the long-term efficacy in three studies [38, 40, 42]. Kanpolat et al. [38] reviewed the records of 1,600 patients that received percutaneous radiofrequency rhizotomy as a treatment for trigeminal neuralgia. Even though initially up to 97.6 % reported acute pain relief at 5-year follow-up, only 57.7 % reported complete pain relief with a single procedure. This figure reaches 94.2 % for patients receiving multiple procedures. At 10- and 20-year follow-up, the percentage for single procedure was 52.3 % and 41 %, respectively, and for multiple procedures was 94.2 % and 100 %, respectively. The authors concluded that this technique is safe and effective.

Long-term safety from prospective uncontrolled and retrospective clinical studies up to 20 years was demonstrated. Taha and Tew [50] conducted a 15-year prospective study following 154 patients with trigeminal neuralgia treated with percutaneous stereotactic radiofrequency rhizotomy. Initial success was reported at 99 % after a single treatment. Similar results were confirmed in a prospective study by Scrivani et al. following 215 patients with trigeminal neuralgia for 15 years following rhizotomy. They found that patients had pain relief in 92 %. Table 11.3 summarizes the efficacy of RF lesioning for facial pain, trigeminal neuralgia, and headache.

Other retrospective comparative studies examined the safety and efficacy of RF lesioning compared with other established treatment modalities, such as microvascular decompression (MVD), balloon microcompression, glycerol

Table 11.3 Results of radiofrequency lesioning studies

Study	Technique	Results (%)	Number of patients	Comments
Kanpolat et al. [38]	RF	41–100	1,600	TN, 20-year follow-up
Taha et al. [39]	RF	99	154	TN, 15-year follow-up
Zakrzewska et al. [41]	RF	36–40 months pain-free	48	Chronic facial pain
Onofrio [43]	RF	86	140	Mainly TN
Tew et al. [44]	RF	93	>100	TN elderly
Sengupta and Stunden [45]	RF	92	39	TN
Piquer et al. [46]	RF	69	98	TN, 4.5-year follow-up
Maxwell [54]	RF	100	8	Migrainous neuralgia
Spincemaille et al. [47]	RF	85	53	TN, 2-year follow-up
Grunert et al. [55]	RF	92	250	TN
Choudhury et al. [56]	RF	78	40	TN
Moraci et al. [48]	RF	97	605	TN
Taha and Tew [11]	RF	100	7	Cluster HA
Yoon et al. [49]	RF	87	81	TN
Scrivani et al. [40]	RF	83–92	215	TN, 5-year follow-up

Table 11.4 Results of studies on gasserian neurolysis with glycerol

Study	Results (%)	Patient number	Comments
Dieckman et al. [57]	92	55	TN
Spaziante et al. [58]	94	50	TN
Saini [52]	59–8	552	Follow-up 2–6 years
Young [59]	86	162	TN
Burchiel [60]	80	60	TN
Waltz et al. [61]	80	200	TN
Van de Velde et al. [62]	76	20	TN
Ischia et al. [19]	92	112	TN
Borda et al. [63]	64	120	TN
Cappabianca et al. [53]	93	191	TN
Kondziolka et al. [64]	59	53	With MS 11-year follow-up
Linderoth and Hakanson [65]	90	23	Facial pain
Ekbom et al. [8]	57	7	Cluster HA
Pieper et al. [12]	83	18	Cluster HA

rhizotomy, partial trigeminal rhizotomy, neurectomy, and alcohol block [50, 51]. Taha and Tew [50], in an extensive review, concluded that the highest rate of recurrence of pain is associated with glycerol rhizotomy. Trigeminal motor dysfunction is highest with balloon compression, while initial pain relief is best achieved with radiofrequency rhizotomy and MVD. Oturai et al. [51] sent questionnaires to 316 patients previously treated over 16 years for trigeminal neuralgia. They reported a success rate of 83 %, 51 %, and 42 %, respectively, after radiofrequency lesioning, neurectomy, and alcohol block. They concluded that radiofrequency lesioning has the highest success when compared to neurectomy and alcohol block. Table 11.4 summarizes studies conducted on the efficacy of glycerol neurolysis. The largest group of patients studied with glycerol neurolysis was reported by Saini [52]. After a single injection, 59 % and 8 % reported pain relief at 2 and 6 years, respectively. The best reported results with glycerol neurolysis were reported by Cappabianca, 93 % success within days of procedures [53].

There are fewer studies that address pulsed radiofrequency lesioning. One randomized controlled study indicates the superiority of conventional RF lesioning over pulsed RF lesioning for the management of idiopathic trigeminal neuralgia [35]. In a trial of 40 patients with trigeminal neuralgia randomized to receive pulsed versus conventional RF lesioning of the trigeminal ganglia, Erdine et al. [35] confirmed the effectiveness of the conventional lesioning. Only 10 % of the pulsed RF group reported

improvement. The authors concluded that pulsed RF lesioning was not an effective treatment for trigeminal neuralgia (Tables 11.3 and 11.4).

Complications and Side Effects

Complications are expected after neural blockade of the trigeminal nerve and the gasserian ganglion. Prior to any injection involving the trigeminal nerve, patient should be warned about potential common side effects including severe headache, dysesthesia, and significant facial or subscleral hematoma regardless of the technique used. Intravascular injection, more dangerously in the carotid artery, is a devastating complication. In an extensive review comparing results and complications of percutaneous techniques performed as a treatment for trigeminal neuralgia, Taha and Tew reviewed 6,205 cases of RF ablation, 1,217 cases of glycerol injection, and 759 cases of balloon compression [50]. Facial numbness was the most common side effect reported varying between 60 % with glycerol and 98 % with RF. Anesthesia dolorosa was reported in less than 4 % [50, 66, 67]. The incidence of loss of the corneal reflex, ulceration, keratitis, and hypesthesia has all been reported [20, 43, 47, 60–63]. Dysesthesia occurs at the same rate independent of the technique and procedure. Acute unilateral total visual loss after Gasserian ganglion phenol injection has been reported [30]. Rhinorrhea after percutaneous radiofrequency lesioning is reported [68]. Masticatory muscle weakness was reported in many studies and was found to be reversible over time [50, 69–71]. Infection is always a potential complication with any of the techniques used. Due to the proximity to brain stem structures, a potential risk of meningitis is possible and had been reported in 24 out of 7,000 cases reviewed by Sweet [72]. Reactivation of a dormant herpetic infection is reported with the use of different techniques especially after trigeminal balloon compression [73]. Total spinal anesthesia, respiratory arrest, and fracture of the pterygomaxillary fissure are possible. Having mentioned how frequent and intractable some of these complications can be, it is recommended that only providers with adequate training and expertise perform these facial invasive procedures.

Neuro-Modulation for Trigeminal Neuralgia

With the emergence of neuro-modulation, we have witnessed a shift from neuro-destructive techniques to more neuro-modulatory ones. While deep brain and motor cortex stimulation have been used for treatment of trigeminal neuropathic pain and trigeminal neuralgia, the results are variable and the procedures are very invasive and complex. Attempts to place percutaneous neuro-modulatory electrodes at the gasserian ganglion using the trans-foramen ovale technique are being performed by trained neurosurgeons. However, technical limitations related to migration of electrodes have limited the success of such trials. While it is worthwhile mentioning because of its relatively less-invasive nature, the data on gasserian ganglion stimulation for trigeminal neuralgia is insufficient to recommend it use.

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Glossopharyngeal Nerve Block

12

Kenneth D. Candido and George C. Chang Chien

Key Points

- Glossopharyngeal neuralgia is characterized by unilateral paroxysmal pain in the oropharynx, nasopharynx, larynx, base of the tongue, tonsillar region, and lower jaw.
- Techniques for extraoral, intraoral, fluoroscopic, or ultrasound-assisted procedures have been described in the literature. Injections of local anesthetic and/or steroids or alcohol neurolysis and radiofrequency ablation are all options in management.
- Extraoral (peristyloid) technique is ideally performed under live fluoroscopy.
- The styloid process can be found equidistant between the mastoid process and the ipsilateral angle of the jaw.
- The advantages of the intraoral anterior tonsillar pillar method are that the ATP is easily identified and exposed and the tongue movement does not trigger the gag reflex.
- The posterior tonsillar pillar method becomes more difficult in patients with large tongues or small oral opening and may cause greater gag reflex.
- To test success of the glossopharyngeal nerve block (GNB), the operator can test for an obtunded gag reflex as a clinical indicator for analgesia.
- Patients need to be monitored for a minimum of 30 min following the block to verify that there has been no systemic response to the injected local anesthetic solution.

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Introduction

The glossopharyngeal nerve (cranial nerve IX) is an important consideration as a pain generator or modulator in cases of recalcitrant pain of the face and neck. Although uncommon as an etiology of head and neck pain (0.57–1.3 % of cases of facial pain) [1–3], impingement or injury to the glossopharyngeal nerve can lead to glossopharyngeal neuralgia, a potentially life-threatening disease [4, 5]. Therefore, it is vital that the interventional pain management specialist learns to recognize disease of CN IX as well as to become facile with techniques of providing analgesia to this important structure.

Glossopharyngeal neuralgia, or Weisenburg-Sicard-Robineau syndrome, was first described by the American neurologist T.H. Weisenburg in 1910 in a case of facial pain misdiagnosed as tic douloureux (trigeminal neuralgia) secondary to a cerebellopontine tumor [6]. Although the French neurologists Jean-Athanase Sicard and Maurice Robineu also published cases in 1920 where they treated cases of atypical facial pain by dissection of the ninth cranial nerve [7], it was the British neurologist Wilfred Harris who coined the term "glossopharyngeal neuralgia" in 1921 [3, 4].

Glossopharyngeal neuralgia is characterized by unilateral paroxysmal pain in the oropharynx, nasopharynx, larynx, base of the tongue, tonsillar region, and lower jaw and can also radiate to the ipsilateral ear. These attacks are excruciatingly painful and typically described as sharp, stabbing, "shocks of electricity" that can last from seconds to minutes [2, 3, 8]. These painful attacks are triggered by stimulation to the oropharynx such as mechanical swallowing, yawning, coughing, laughing, chewing, and sensory stimulation such as cold, salty, acidic, or bitter foods [2, 3].

In 217 cases of glossopharyngeal neuralgia seen at the Mayo Clinic [9], 57 % of the cases were in patients greater than 50 years old, while 43 % were between the ages of 18 and 50. Twelve percent of these patients had bilateral

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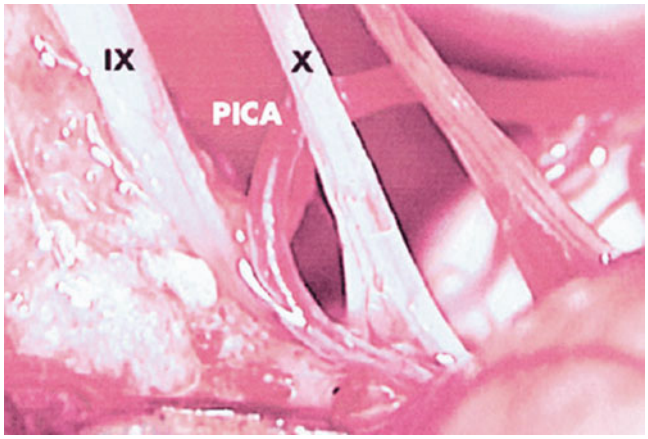

Fig. 12.1 Relationship of the glossopharyngeal nerve (*IX*) to the posterior inferior cerebellar artery (*PICA*) (Adapted from: Takaya [13])

involvement, but a bilateral frequency as high as 25 % has been reported [10]. Additionally, 12 % of the patients exhibited both glossopharyngeal and trigeminal neuralgia [9]. A greater prevalence in males has also been reported by some authors [2], while others have reported no difference in prevalence by gender.

Cardiovascular symptoms such as bradycardia, hypotension, and even cardiac arrest may accompany the attacks in 1–2 % of people with glossopharyngeal neuralgia [4, 5, 11]. It is believed that the close association between the glossopharyngeal nerve and the vagus nerve (CN X) underlies, in part, the etiology between glossopharyngeal neuralgia and these cardiac symptoms [12]. Seizures have also been associated with episodes of GPN [5, 13, 14].

Although most cases of glossopharyngeal neuralgia are categorized as "idiopathic," it is thought that the majority cases of glossopharyngeal neuralgia are caused by vascular compression of the glossopharyngeal nerve [11, 15].

Kawashima studied 14 cases of idiopathic GPN. In all of the cases, vascular compression on the glossopharyngeal nerve was found [16]. Most commonly, it is the posterior inferior cerebellar artery (PICA) (Fig. 12.1) followed by the anterior-inferior cerebral artery (AICA) that compresses the glossopharyngeal nerve [11, 16–18].

Other causes for GPN include tumors with local invasion [19], parapharyngeal abscess [20], trauma [21], multiple sclerosis [22], and carotid puncture [4].

Reported Causes of Glossopharyngeal Neuralgia (GPN)

- Trauma [21]
- Eagle's syndrome [23]
- Cerebellopontine angle tumors [4]
- Infection/parapharyngeal space lesions [20]
- Multiple sclerosis [24, 25]
- Posterior fossa arteriovenous malformation
- Arachnoiditis [26]
- Ossified styloid ligament
- Elongated styloid process
- Direct carotid puncture [4]
- Metastatic head and neck tumors [19]
- Chiari malformation [26]

Glossopharyngeal neuralgia may mimic trigeminal neuralgia. Both may present with facial/jaw pain worse elicited by the same mechanical and sensory mechanisms. Cases may be difficult to differentiate in patients with pain in the region of the tragus or deep to the angle of the jaw [2]. However, compared to trigeminal neuralgia, glossopharyngeal neuralgia is relatively rare [1–3]. A diagnostic interventional block may be useful in differentiating the two etiologies and indeed may be the only mechanism available to the interventional pain management physician to definitively establish CN IX as being responsible for the pain.

Anatomy

The glossopharyngeal nerve (cranial nerve IX) is a mixed function nerve with motor, sensory, and special sensory fibers. The rootlets originate in the upperpart of the postolivary sulcus, between the olive and the inferior peduncle of the medulla oblongata, and exit the cranium with parasympathetic nerve fibers from the salivatory nucleus, the vagus and spinal accessory nerves (CN X and XI) via the jugular foramen. All three cranial nerves lie between the internal jugular vein and the internal carotid artery (Fig. 12.2).

The glossopharyngeal nerve has many distributive branches including the tympanic, carotid, pharyngeal, muscular, tonsillar, and lingual. The tympanic branch innervates the tympanic membrane. The carotid branch innervates the carotid sinus and carotid body. The pharyngeal branch carries sensory nerve from the walls of the pharynx. The tonsillar branch transmits sensory nerves from the tonsils. The lingual branch innervates the anterior surface of the epiglottis, the posterior third of the tongue, and the vallecula.

The motor component innervates the stylopharyngeus muscle, which elevates the pharynx during talking and swallowing. The sensory portion innervates the palatine tonsils, the posterior third of the tongue, and the mucous membranes of the oropharynx. Special sensory afferent fibers transmit information for taste from the posterior third of the tongue.

The carotid branch of CN IX, the carotid sinus nerve, innervates carotid body and carotid sinus. Therefore, damage to this branch has important implications for regulation of blood pressure, pulse, and respiration.

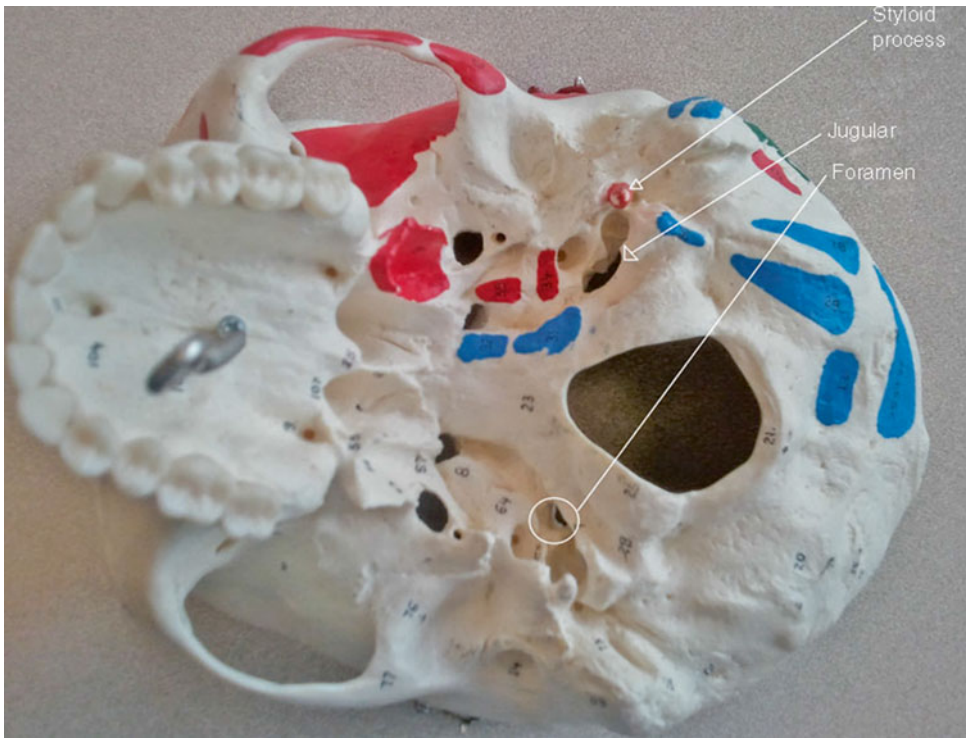

Fig. 12.2 Base of the skull: the jugular foramen is where the glossopharyngeal, vagus, and accessory nerves exit the cranium (Photo courtesy of Kenneth D. Candido, M.D.)

Indications for GPN Block or Neurolysis

- Glossopharyngeal neuralgia (GPN)
- Post-tonsillectomy pain control [27]
- Cancer pain [28–30]
- To reduce gag reflex for awake endotracheal intubation [31]
- Singultus (hiccups) [32]
- Carotid sinus syndrome [33]
- Patients that are poor candidates for microvascular decompression

Diagnosis

Imaging

High-resolution MRI [34, 35] or CT scan of the head may reveal tumor, bony erosion, multiple sclerosis plaques, abscess, or infection. Three-dimensional visualizations of the brain stem may identify, or MRA may show neurovascular compression or arteriovenous malformation. Visualization of the offending vessel was better in cases of compression from the PICA compared to the AICA [34].

Balloon Test Occlusion

Hasegawa et al. reported a case where magnetic resonance imaging suggested that the right vertebral artery (VA) was pressing on the glossopharyngeal nerve [36]. Balloon test occlusion of the VA was used to confirm the cause of the neuralgia. The neuralgia disappeared and reappeared with balloon inflation and deflation. Balloon test occlusion may be useful in the diagnosis of GPN and the selection of the most appropriate surgical treatment [36, 37].

Medical Treatment

Medical control treatment of GPN is similar to treatment for other forms of neuropathic pain, including trigeminal neuralgia. Antiepileptic drugs and tricyclic antidepressants alone or in combination have been studied with variable efficacy [38]. There is also a case report of GPN refractory to AEDs that responded well to opioids [39].

Antiepileptic drugs which have been used include carbamazepine, lamotrigine, diazepam, and gabapentin; tricyclic antidepressants used have included amitriptyline and nortriptyline [40–44].

Interventional Techniques

Techniques for extraoral, intraoral, fluoroscopic, or ultrasound-assisted procedures have been described in the literature. Injections of local anesthetic and/or steroids, or alcohol neurolysis [45] and radiofrequency ablation [46, 47] are all options in management of glossopharyngeal nerve dysfunction.

Although ultrasound-assisted intervention has been reported [48], the use of fluoroscopy also allows the advantage of real-time imaging of the contrast media, so that in cases in which the needle tip has penetrated either the carotid or jugular systems, this activity should be observable and intravascular injection subsequently preventable or at least minimized.

Patients need to be monitored for a minimum of 30 min following the block to verify that there has been no systemic response to the injected local anesthetic solution. Even taking these precautions and using fluoroscopic or ultrasound guidance does not completely eliminate the possibility of local anesthetic spillover onto the vagus nerve (with resultant ipsilateral vocal cord paralysis) or onto the spinal accessory nerve (weakness of the trapezius muscle).

To test success of the glossopharyngeal nerve block (GNB), the operator can test for an obtunded gag reflex as a clinical indicator for analgesia [27]. There is a strong relationship between extent of the obtunded gag reflex and the extent of post-tonsillectomy pain relief [27].

Extraoral (Peristyloid) Technique with Fluoroscopy

The patient is placed supine with the head rotated slightly opposite from the affected side. The styloid process is used to identify the course of the GPN. Once identification of the mastoid process and the ipsilateral angle of the mandible is performed, the styloid process can be found equidistant between these structures (Figs. 12.3a–d and 12.4a, b).

The skin overlying the styloid process should be prepped and draped in sterile fashion. A small skin wheal is made over the styloid process using a 25-gauge, 1.5-in. needle and 3–4 mL of 1 % plain lidocaine. Next, a 22-gauge, 1.5–2 in. blunt-tipped needle may be advanced perpendicular to the skin toward the process, aiming for its posterior aspect. The styloid process should be met at a depth approximating 1.5–4 cm. Once the styloid process is encountered, the needle is slightly withdrawn and "walked off" posteriorly. Aspiration should be performed to ensure that there is no blood or cerebrospinal fluid. Next, 1 mL of water-soluble, iodinated contrast media should be incrementally injected under live continuous fluoroscopy. Then, barring any intravascular spread, a short-acting, preservative-free (lidocaine, mepivacaine) and dilute (1 % concentration) anesthetic with epinephrine 1:200,000 (5 μg/mL) in a volume of 3–5 mL should be incrementally injected in divided doses. Nonparticulate corticosteroid (dexamethasone, betamethasone) may be added to the injectate, although there is no literature support to a salubrious effect of adding an anti-inflammatory glucocorticoid medication.

Intraoral Technique (Figs. 12.5 and 12.6)

Anterior Tonsillar Pillar Method [31, 49, 50]

The patient is asked to open the mouth widely (Fig. 12.5). The operator may choose to anesthetize the tongue to facilitate the procedure. The tongue is swept to the opposite side with a tongue depressor, laryngoscope blade, or with gloved fingers. A 25-gauge, 3.5-in. spinal needle is inserted 0.5 cm deep, just lateral to the base of the anterior tonsillar pillar (ATP). Use of a spinal needle is advantageous for visualization of the tonsillar pillars by keeping the syringe out of the patient's mouth [51]. After careful aspiration for blood or cerebrospinal fluid, 2 mL of local anesthetic (LA) or LA plus nonparticulate steroid is injected. The advantages of this method are that the ATP is easily identified and exposed, and the tongue movement does not trigger the gag reflex (Fig. 12.6).

Posterior Tonsillar Pillar Method

The patient is asked to open the mouth widely. The tongue is depressed down with a laryngoscope blade (if done in the OR) or else with a tongue blade as described above. A 22-gauge, 3.5-in. spinal needle bent 1 cm from the distal end is directed laterally into the submucosa along the caudal aspect of the PTP (palatopharyngeal fold). After careful aspiration for blood and cerebrospinal fluid, 2 mL of local anesthetic and/or steroid is injected. The PTP method becomes more difficult in patients with large tongues or small oral opening and may cause greater gag reflex [52].

Potential Complications/Side Effects

Potential undesirable side effects of glossopharyngeal nerve block may include the following:

- Dysphagia secondary to weakness of the stylopharyngeus muscle [9]
- Upper airway obstruction/loss of protective reflexes secondary to bilateral nerve block [53]
- Ecchymoses/hematoma – trauma to internal carotid artery and/or internal carotid vein

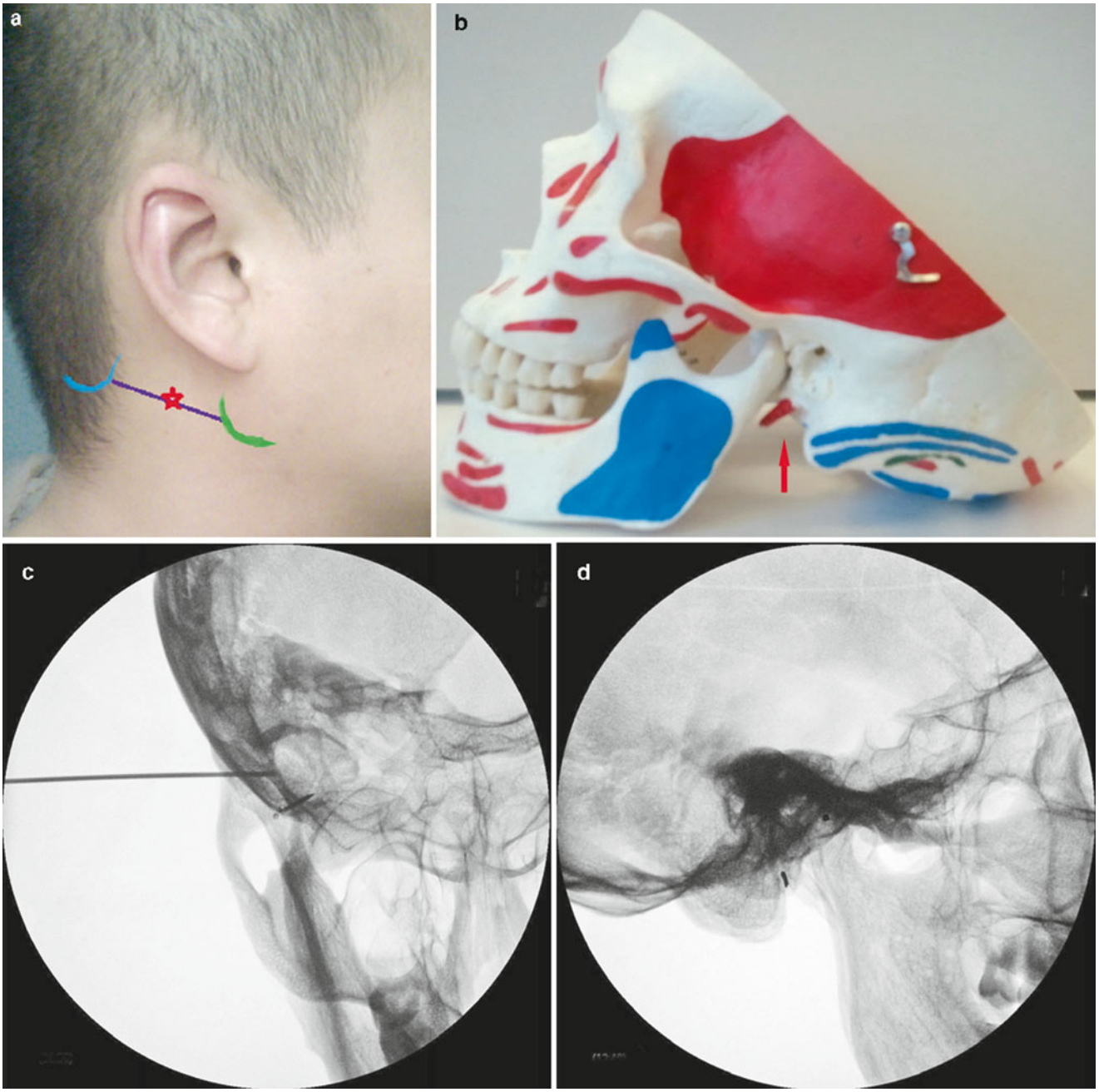

Fig. 12.3 (**a**, **b**) Surface anatomy: glossopharyngeal nerve block (Photo courtesy of George C. Chang Chien, D.O.). (**c**) AP fluoroscopic image of right GPN block (Photo courtesy of Steven D. Waldman, M.D., JD). (**d**) Lateral fluoroscopic image of right-sided GPN block (Photo courtesy of Steven D. Waldman, M.D., JD)

- Infection
- Trauma to the nerve
- Toxicity due intravascular injection of local anesthetic
- Tachycardia from vagus nerve block
- Hoarseness/dysphonia secondary to vagus nerve block and paralysis of the ipsilateral vocal cord
- Post-procedure dysesthesias or anesthesia dolorosa
- Cardiovascular complications resulting in acute onset hypotension with right bundle branch block secondary to dissection of the uppermost rootlets of the vagus nerve [54]
- Block of the hypoglossal nerve with resultant tongue weakness (CN XII)
- Trapezius muscle weakness secondary to inadvertent block of the spinal accessory nerve (CN XI)

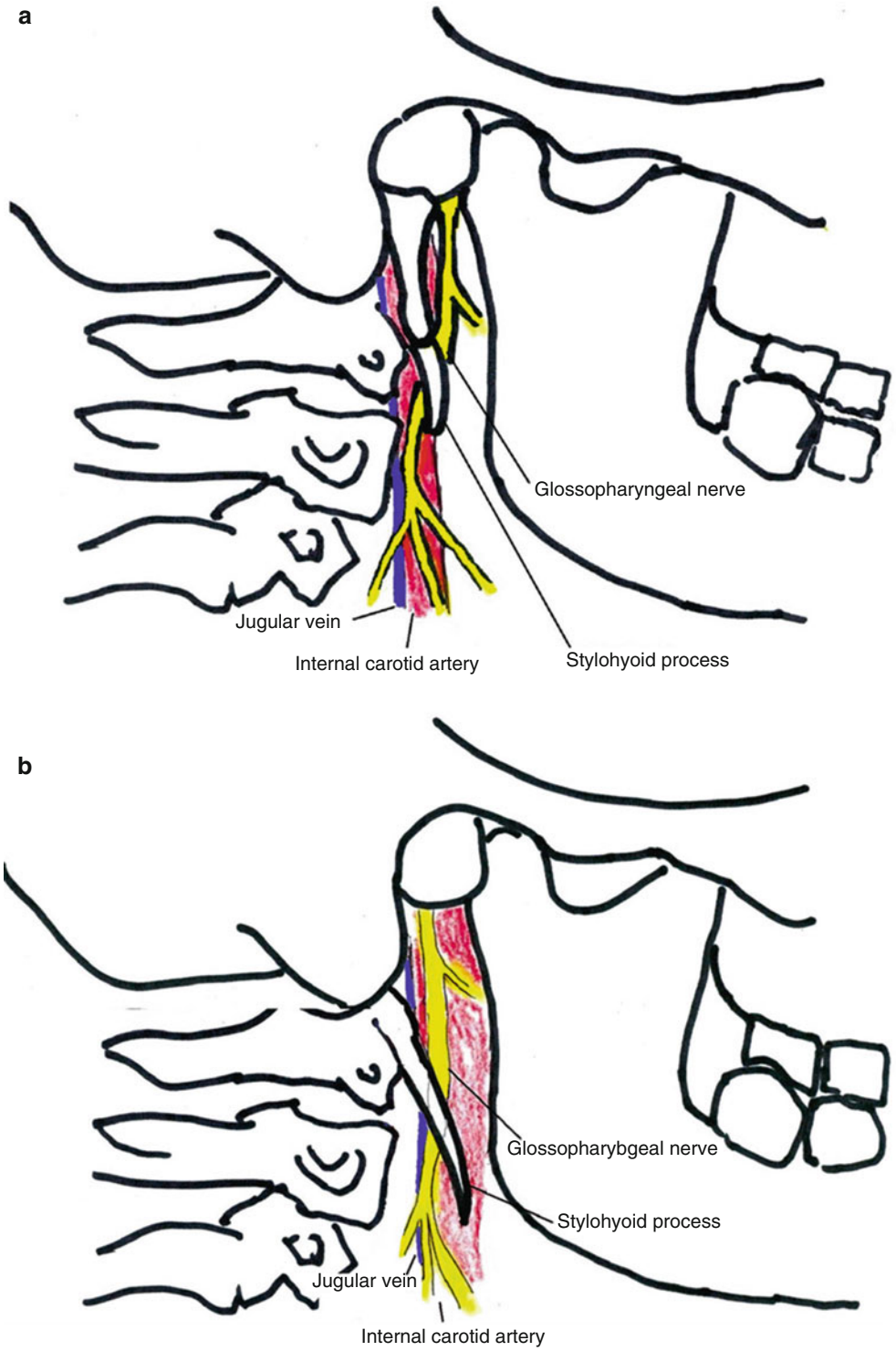

Fig. 12.4 (**a**, **b**) Demonstrated is the relationship between the glossopharyngeal nerve and the styloid process. Ossification of the stylohyoid ligament (**a**) and elongation of the styloid process (**b**) can both cause compression of the glossopharyngeal nerve (Images courtesy of George C. Chang Chien, D.O.)

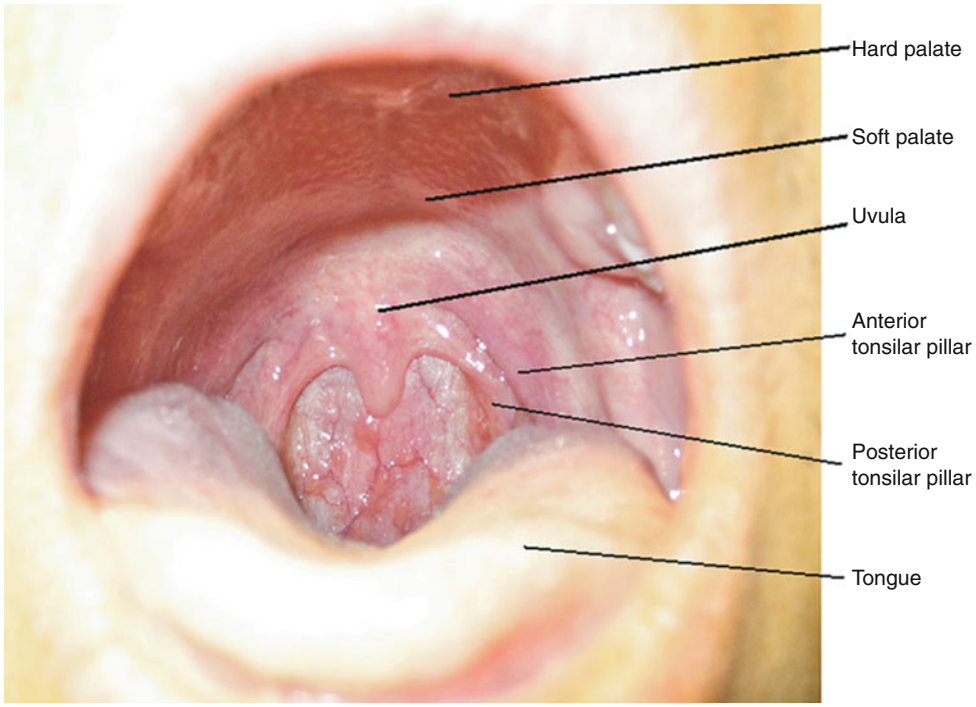

Fig. 12.5 Anatomy for intraoral GPN block (Photo courtesy of George C. Chang Chien, D.O.)

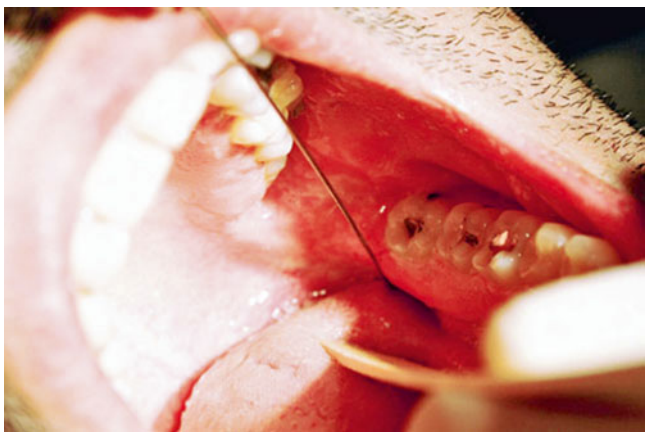

Fig. 12.6 Lateral tongue sweep prior to LA injection, needle in place (Photo courtesy of Kenneth D. Candido, M.D.)

Surgical Treatment

Surgical resection of the glossopharyngeal nerve performed for pain control was first described by Dandy in 1927 [8]. This remains an option in severe cases refractory to interventional pain management or microvascular decompression [55–58]. Two cases have been reported of successful pain treatment of GPN with use of the gamma knife [59].

Summary

In summary, facial pain continues to be a problem that is difficult to diagnose and even more difficult to treat [60]. The complicated neuroanatomical relationships between the glossopharyngeal nerve and other cranial structures, neural as well as osseous and ligamentous and vascular, create an imposing challenge for even seasoned interventional pain management physicians. The use of glossopharyngeal nerve block as part of a multidisciplinary and multimodal approach to pain control should be part of every pain physician's armamentarium.

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Cervical Plexus Block

13

Gerald A. Matchett and Sean Mackey

Abbreviations

CPB	Cervical plexus block
SCM	Sternocleidomastoid muscle
CEA	Carotid endarterectomy

Key Points

- Cervical plexus block is safe and reliable for surgical anesthesia and analgesia.
- Superficial cervical plexus block has a lower complication rate than deep cervical plexus block.
- The most common complication of a cervical plexus block is phrenic nerve dysfunction.
- Superficial cervical plexus bock is sufficient for most surgical indications because of ready spread of local anesthetic within the fascial planes in the neck.
- Cervical plexus block may be useful in select patients with chronic pain disorders such as cervicogenic headache and cervicalgia arising from the cervical plexus.

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Introduction

The purpose of this chapter is to provide an overview of the historical and current clinical use of the cervical plexus block (CPB). Historical interest in CPB dates to the 1840s, when reports described various topical therapies for cervical neuralgia arising from the cervical plexus [1]. Needle-based techniques were introduced in the early 1900s, and large case series describing CPB for open neck surgery soon followed [2, 3]. Numerous indications for CPB have been described for both acute and chronic pain (Table 13.1).

Anatomy of the Cervical Plexus

The cervical plexus is comprised of three loops that arise from the anterior rami of the cervical roots of C2–C4 (Fig. 13.1). The loops of the plexus lie anterior to the levator scapulae and scalenus medius muscles and posterior to the sternocleidomastoid (SCM) [4, 5]. Deep terminal branches of the plexus innervate deep muscular structures such as the scalenus medius, trapezius, levator scapulae, and SCM and communicate with the spinal accessory nerve. The superficial branches innervate the skin over the lateral head and neck via the occipital, anterior cutaneous, great auricular, and supraclavicular nerves (Fig. 13.2) [4, 5].

Techniques for Blocking the Cervical Plexus

Cervical plexus blocks are usually classified as "superficial" or "deep." Historically, a "superficial" block implied injection of local anesthetic into subcutaneous tissue without violating the fascial planes investing the SCM [6]. However, in current practice, a "superficial" block usually indicates administration of local anesthetic subcutaneously, around the SCM, and deep to fascial planes around the SCM [7, 8]. A "deep" block implies a plexus block at the level of the

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transverse processes of the cervical vertebrae [9]. Some have suggested the concept of an "intermediate" plexus block, defined by administration of local anesthetic subcutaneously and just deep to the investing fascial layers of the SCM [10]. However, as a practical matter, this definition overlaps considerably with what is currently known as a "superficial" block. In this chapter, we will use the term "superficial" to indicate an injection both in the skin and into layers just deep to the SCM as is commonly done today.

Table 13.1 Indications for cervical plexus block

Atypical cervicogenic headache
Cervicalgia
Carotid surgery
Thyroid surgery
Parathyroid surgery
Lymph node biopsy in the neck
Surgery on the mastoid process
Central line placement (awake)
Other head and neck surgery

A "deep" block refers to an injection at the level of the transverse processes of the cervical spine. A "combined" cervical plexus block usually refers to the combination of a deep and superficial block.

Although the cervical plexus may be approached anteriorly, laterally, or posteriorly, the most common practice today is an anterolateral approach for both superficial and deep plexus blocks (Fig. 13.3a–f) [4, 9]. The superficial block is usually performed at the midpoint between the mastoid process and the sternal notch at the posterior edge of the sternocleidomastoid muscle (Fig. 13.3a–c). Local anesthetic is injected along the SCM, just deep to the SCM, and in the general direction of the terminal branches of the plexus [4].

Deep CPB is traditionally performed with three separate injections at the transverse process of C2–4 [4]. Historically, this block is performed using surface and bony landmarks, although our preference is to use fluoroscopic guidance with injection of iodinated contrast to help confirm needle placement. The bony landmark for this block is traditionally the C6 transverse process. This can be palpated, and C4–2 can be identified on a line drawn between C6 transverse process

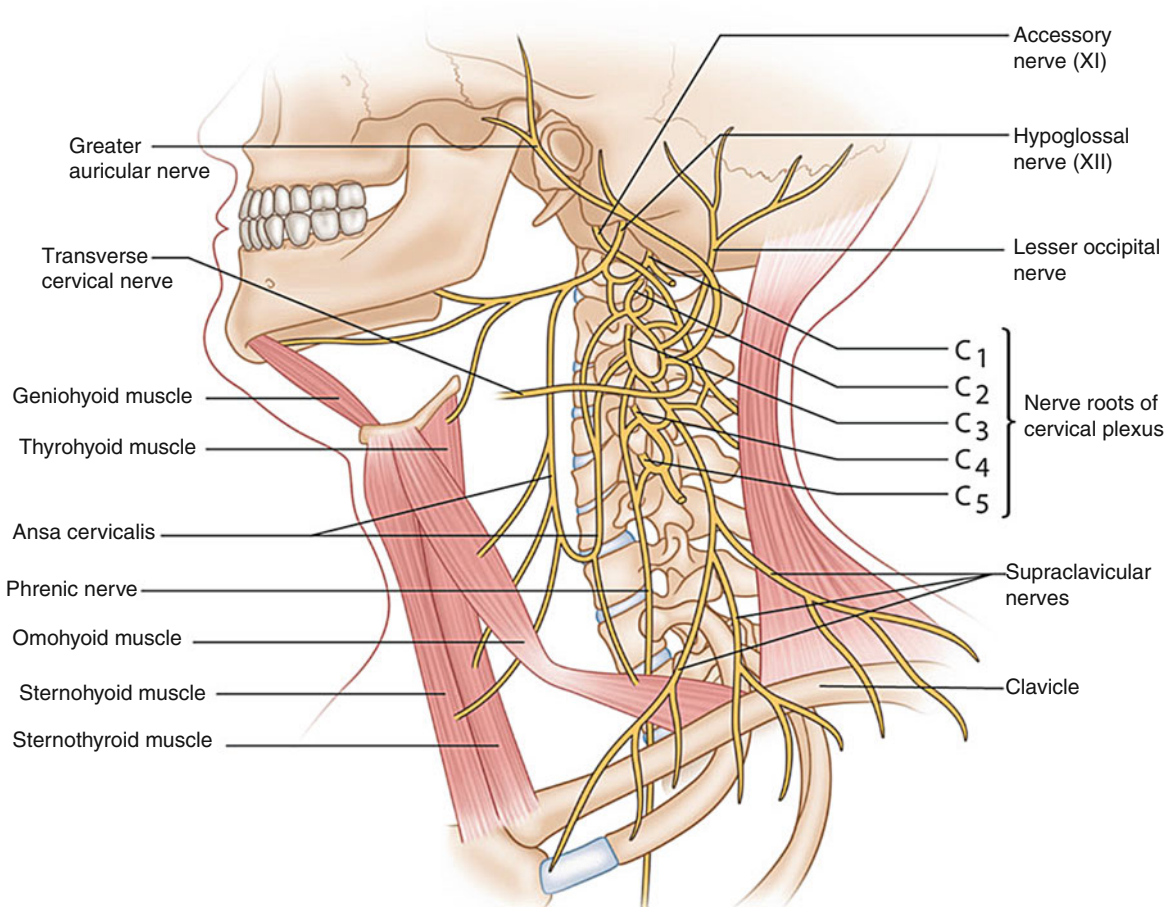

Fig. 13.1 Anatomy of the cervical plexus. Diagram of the cervical plexus as it emerges from the cervical roots of C2–4. Note the close relationship between the cervical plexus and the phrenic nerve, which is usually affected by a deep cervical plexus block

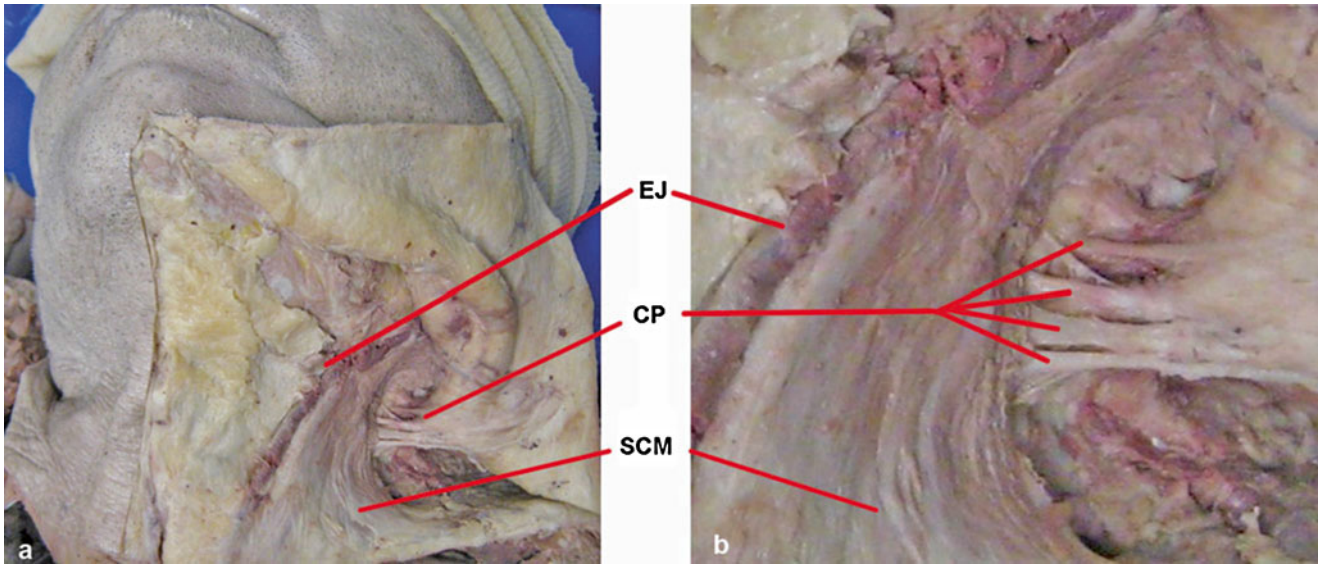

Fig. 13.2 Branches of the cervical plexus in situ. (**a**, **b**) Superficial cutaneous dissection of the left neck demonstrates the sternocleidomastoid (*SCM*), the external jugular vein (*EJ*), and the four branches of the cervical plexus (*CP*) emerging just posterior to the SCM. These branches are the great occipital, great auricular, transverse cervical, and supraclavicular nerves. In this dissection, the skin has been reflected posteriorly to the left (Courtesy of G. Matchett, made at the Gross Anatomy Lab at Stanford University School of Medicine)

and the mastoid process (Fig. 13.3d–f). Alternately, a single injection at the transverse process of C3 or C4 may be used [9]. Needle placement for the deep block may be facilitated by surface landmarks, elicitation of paresthesias, elicitation of muscle twitches from levator scapulae [13], ultrasound [14, 15], or fluoroscopy [16]. Studies comparing single versus multiple injection techniques have reported similar outcomes [13, 17].

Local anesthetic spreads easily in the compartments of the neck after a superficial CPB. This has been demonstrated by cadaver study (Fig. 13.4) and clinical experience [7]. Likewise, after deep CPB, local anesthetic spreads easily, especially when large volumes are given (>20 mL) [18].

Indications: Surgical Anesthesia

The most common indication for CPB is surgical anesthesia. For example, the block may be used in addition to, or in place of, general anesthesia for carotid endarterectomy (CEA). Table 13.1 provides a list of common surgical indications.

Indications: Cervicalgia and Cervicogenic Headache

Historical interest in CPB arose out of a desire to treat cervicalgia arising from the cervical plexus [1]. A case series in 1955 reported the use of the block in 63 patients with atypical cervicogenic headache, 57 of who appeared to benefit from CPB [19]. Recent case series report similar findings. Goldberg et al. [16] described a 39-patient case series of deep cervical plexus block for atypical headaches that appeared to coincide predominately with a cervical or brachial plexus distraction-type injury. A majority of patients experienced a significant decrease in average pain scores immediately after the blocks, and a return to pre-block pain level took an average of 6.6 weeks [16]. Selective cervical plexus blocks may also be useful as an aid in diagnosis of atypical orofacial pain [20].

Choice of Local Anesthetic for Cervical Plexus Block

Bupivacaine and ropivacaine are commonly used for CPB, although nearly any local anesthetic can be used (Table 13.2). Pharmacokinetic studies have confirmed the safety of adding epinephrine to local anesthetic solutions for cervical plexus block [28–30]. This may help prolong the blockade and reduce serum concentration of local anesthetic [30]. Epinephrine may be associated with mild sympathomimetic effects on heart rate and blood pressure [29, 31].

Long-acting local anesthetics are usually used for CPB in order to ensure adequate duration of block (Table 13.2). Most comparative studies of one long-acting local anesthetic to another have reported similar clinical outcomes at equipotent doses [23, 32, 33]. Ropivacaine (0.75 or 1 %) was reported to be superior to mepivacaine (2 %) in the setting of deep

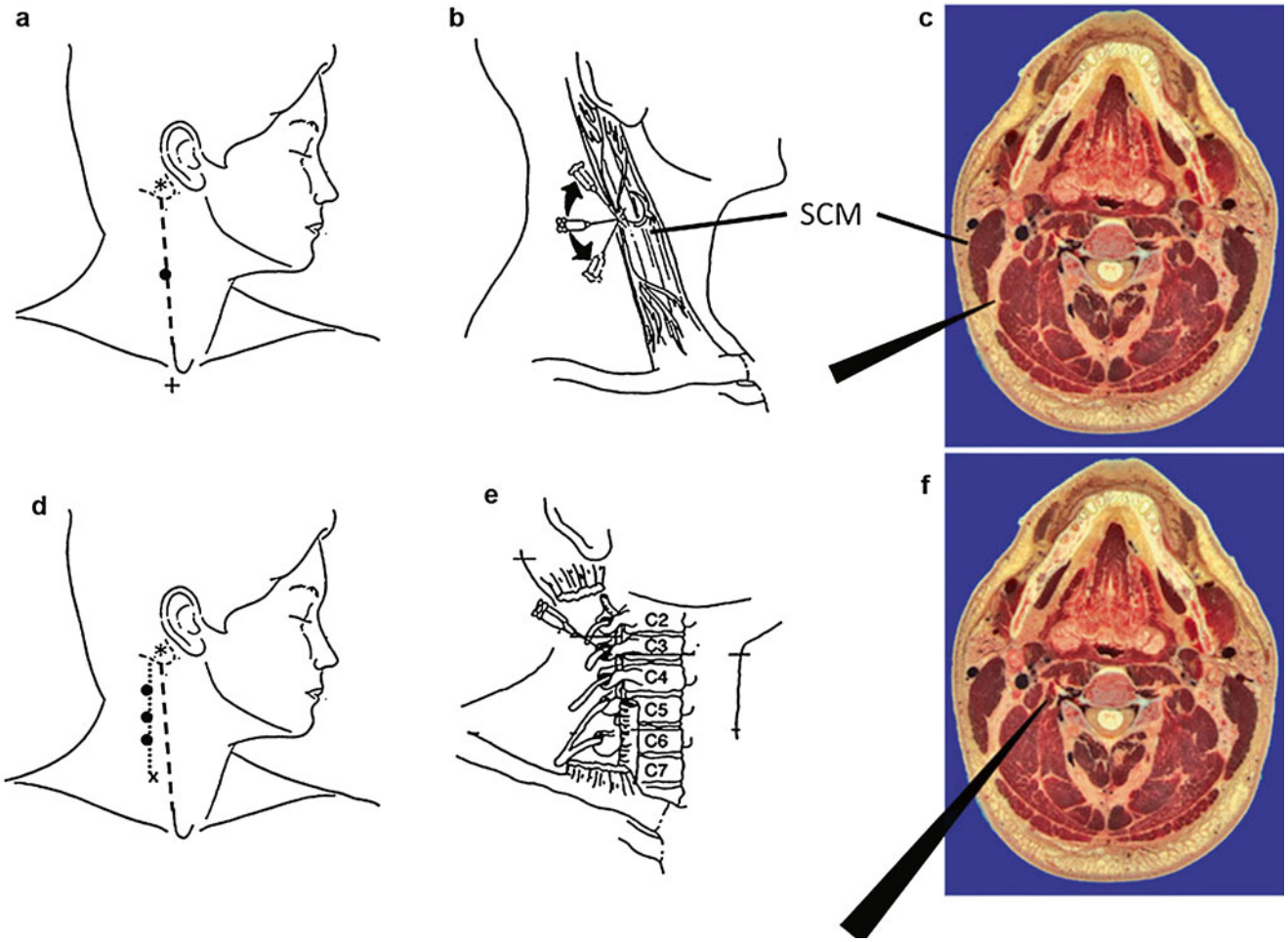

Fig. 13.3 Techniques for blocking the cervical plexus. (**a**) The superficial cervical plexus can be approached at the midline of the posterior border of the sternocleidomastoid (*SCM*) (*dashed line*). The SCM can be identified superiorly by the mastoid process (*) and inferiorly by the sternal notch (+). (**b**) Needle passage for a superficial block should be superior, inferior, and just deep to the sternocleidomastoid (*SCM*). (**c**) In transverse view at C4, the needle should pass just deep to the SCM. (**d**) The deep cervical plexus block can be performed by three individual injections at C2–4 or alternately can be performed by a single injection at C3 or C4. Typically, the location for the injections is noted by palpation of the C6 transverse process (*point x*). The transverse process of C2–4 can be identified superiorly to C6 on a line drawn between the mastoid process and the C6 transverse process (dotted line). In an average adult, the transverse processes of C4–2 are approximately 2, 4, and 6 cm superiorly on the line connecting the mastoid process and C6. Once the transverse (superior tubercle) is contacted by the needle, the needle should be withdrawn 1–2 mm and local anesthetic injected following negative aspiration for blood. (**e**) Schematic diagram showing correct needle placement at C3. (**f**) Transverse section showing the transverse process of C4 (**a**, **d –** Reprinted with permission and adapted from Paul et al. [11]. © License from Wolters Kluwer Health License, 2009; **b**, **e** – Reprinted with permission and adapted from Stoneham and Knighton [12]. © License from Oxford University Press License, 2009; **c**, **f** – Reprinted with permission and adapted from the Visible Human Project of the National Library of Medicine – USA)

cervical plexus block for CEA in one study [34]. Studies suggest that higher concentration local anesthetic solution (e.g., 0.75 % ropivacaine instead of 0.375 % ropivacaine) may be preferable for duration and density of block [27].

Reports have described other drugs such as clonidine [25] or corticosteroids [16] as part of CPB. The addition of clonidine (50 μg) to ropivacaine (150 mg) for superficial cervical plexus block was found to shorten the onset time and improve the quality of surgical anesthesia [25]. Steroids may be included for CPB in the setting of cervicalgia or cervicogenic headache [16].

Contraindications

Contraindications include patient refusal, marginal pulmonary status, severe coagulopathy, local infection, and severe anatomic distortion. Baseline pulmonary status is important to consider before a deep cervical plexus block. Deep blockade usually results in phrenic nerve paralysis with hemidiaphragmatic dysfunction, and this can potentially lead to respiratory distress in a patient with marginal baseline pulmonary function [4].

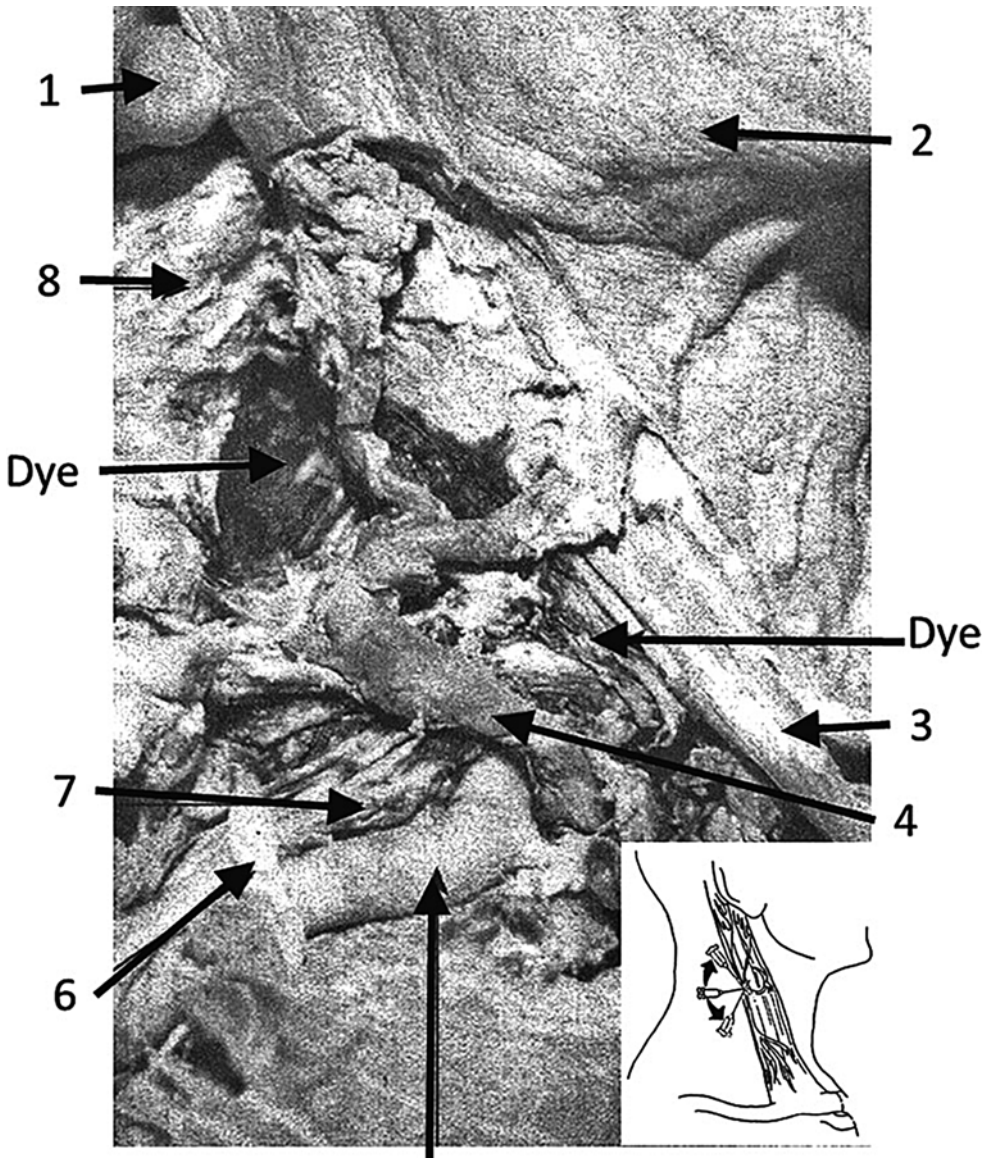

Fig. 13.4 Spread of local anesthetic with cervical plexus blocks. Superficial plexus block with methylene blue dye administered just deep to the sternocleidomastoid in a cadaver study. Following injection, methylene blue dye is widely distributed in the neck. 1-Ear, 2-mandible, 3-sternocleidomastoid muscle, 4-internal jugular vein, 5-subclavian artery, 6-omohyoid muscle (cut), 7-brachial nerve plexus, 8-trapezius muscle (cut). The inset picture denotes the orientation of the cadaver (Adapted and used with permission from Pandit et al. [7]. © License from Oxford University Press License, 2009)

Complications

Blockade of the *superficial* cervical plexus is extremely safe and complications are very rare [35]. Most complications, serious or otherwise, occur with *deep* CPB [35]. A quantitative meta-analysis of 69 published reports covering more than 10,000 individual blocks found that deep CPB is significantly more likely to be associated with serious block-related complications and the need to convert to general anesthesia than superficial CPB (Fig. 13.5) [35].

The most common complication of deep CPB is phrenic nerve block which leads to hemidiaphragmatic dysfunction. This may occur in 55–100 % of patients who have a deep block [4, 36]. In patients with marginal pulmonary status, this may interfere with respiration and ventilation [36, 37]. Other common complications include the need for supplemental infiltration of local anesthetic (53 % of the time with carotid endarterectomy surgery) [38], and the need to convert from regional to general anesthesia (4.2 % of the time with carotid endarterectomy surgery) [39]. Table 13.3 provides a list of complications, most of which occur with deep blockade.

Table 13.2 Sample protocols for cervical plexus block

Local anesthetic	Dose	References
Superficial		
Bupivacaine	0.375 %, 1.4 mg/kg (average = 30 mL)	[21]
Bupivacaine	0.375 %, 20 mL	[22]
Levobupivacaine	0.5 %, 1 mg/kg	[23]
Levobupivacaine	0.5 %, 0.35 mL/kg	[24]
Ropivacaine	0.75 %, 20 mL + clonidine 50 mcg	[25]
Ropivacaine	1 %, 10 mL	[26]
Ropivacaine	0.75 %, 1.5 mg/kg	[23]
Ropivacaine	0.375–0.75 %, 20 mL	[27]
Deep		
Bupivacaine	0.25 %, 3–5 cc per level (C2–4)	[4]
Bupivacaine	0.375 %, 20 mL at C4	[9, 22]
Bupivacaine	0.25 %, 10 mL + 80 mg methylprednisolone (C2–4)	[16]
Lidocaine	2 % ± bicarbonate and epinephrine, (3–5 cc per level)	[4]
Mepivacaine	1.5 % ± bicarbonate and epinephrine, (3–5 cc per level)	[4]
Ropivacaine	0.5 %, 3–5 cc per level	[4]
Combined		
Bupivacaine	0.375 %, 1/3 of dose placed at C4 (deep), 2/3 of dose placed superficially, total dose = 1.4 mg/kg	[21]
Levobupivacaine	0.5 %, 0.2 mL/kg placed at C3, then 0.15 mL/kg placed superficially	[24]
Ropivacaine	0.375–0.75 %, 10 mL at C4 followed by 20 mL placed superficially	[27]

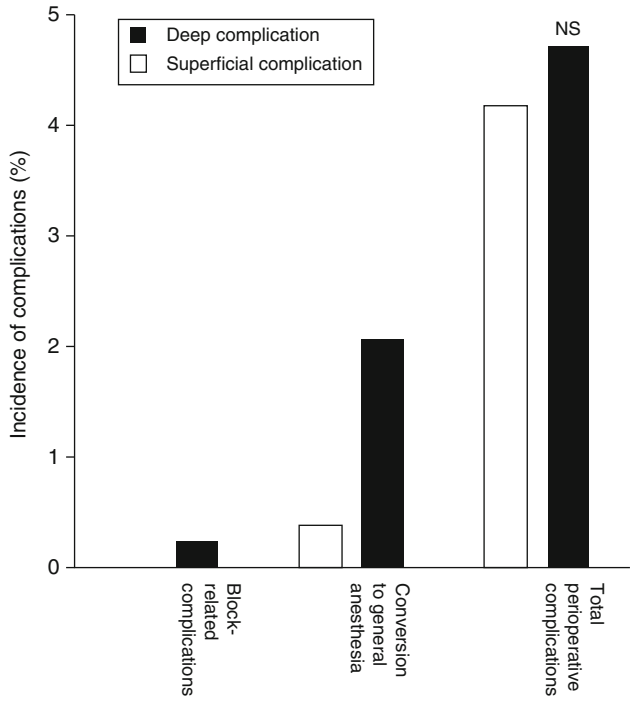

Fig. 13.5 Complications. In a large quantitative review of more than 10,000 patients who received cervical plexus block for carotid endarterectomy (CEA) surgery, the rate of serious, block-related complications for deep cervical plexus block was significantly greater than the rate of serious, block-related complications. Likewise, the rate of conversion to GA was significantly higher in the deep plexus block. The overall rate of serious complications associated with CEA surgery was the same in both groups. * indicates statistical significance, $p < 0.05$ for deep versus superficial comparison. *NS* not statistically significant (Reprinted and adapted with permission from Pandit et al. [35]. © License from Oxford University Press, 2009)

Bilateral Cervical Plexus Block

Bilateral regional anesthetic procedures in the neck should be approached with caution. Bilateral *superficial* CPB has been described for surgical anesthesia for thyroidectomy in several small randomized studies [42, 43, 44]. However, given the relatively small amount of randomized data available, the absolute safety of this technique cannot be assured.

The safety of bilateral *deep* CPB is very uncertain. A small number of studies have reported the successful use of bilateral deep blocks for thyroid surgery, although this was done in the context of immediate induction of general anesthesia with definitive airway control [45, 46]. Given the likelihood of phrenic nerve paralysis with deep blockade, bilateral deep blocks should probably be avoided. In one small case series of bilateral combined (superficial and deep) cervical plexus block, 1/18 patients required conversion to general anesthesia because of respiratory distress (coughing) [47].

Superficial Versus Deep Cervical Plexus Block for Surgical Anesthesia

Several studies have compared superficial versus deep CPB in the context of surgical anesthesia. A prospective, randomized trial of superficial CPB versus combined CPB (both superficial and deep block) for parathyroidectomy reported equivalent outcomes between the two groups [24]. Notably, there was no discernable benefit from adding the deep block

Table 13.3 Complications of cervical plexus block

Complication	Frequency	References
Common		
Phrenic nerve block or hemidiaphragmatic dysfunction	55–100 %	Occurs with deep CPB, occurs rarely with superficial CPB [4, 36]
Local anesthetic supplementation required during carotid endarterectomy	53 %	[38]
Blood aspirated during block placement	30 %	[38]
Block failure or conversion to general anesthesia for carotid endarterectomy	.039, 3, 4.2 %	[35, 39, 40]
Blockade of extraneous nerves such as cranial nerves	4.2 %	[40]
Uncommon		
Hematoma	0.6 %	[40]
Intravascular injection	0.6 %	[38]
Respiratory distress	0.1–0.3 %	[38, 41]
Seizure	0.3 %	[38]
Local anesthetic toxicity	0.2 %	[38]
Rare		
Infection	<<1%	
Intrathecal injection	<<1%	
Permanent nerve injury	<<1%	
Paralysis	<<1%	
Death	<<1%	

to the superficial block. This finding is consistent with earlier case series of parathyroidectomy under superficial cervical plexus block [48]. Similarly, at least two studies have compared superficial versus deep blocks for awake CEA and found no clear benefit from the deep block [21, 22]. Given the higher complication rate of deep CPB compared to superficial CPB, there is a growing consensus that superficial cervical plexus block is preferable for most surgical indications, especially CEA. A recent quantitative meta-analysis of cervical plexus block supports the relative safety of superficial block over deep block (Fig. 13.5) [27].

The most plausible explanation for why superficial CPB is apparently as effective as deep CPB for surgical anesthesia relates to the ease of spread of local anesthetics. Local anesthetic solutions can spread easily through compartments in the neck after superficial (Fig. 13.4) [7] or deep [18] CPB. Superficial CPB is sufficient for most surgical indications, including carotid or thyroid surgery.

Outcome Data: Cervical Plexus Block Combined with General Anesthesia

Many surgical procedures may be performed with the combination of general anesthesia and CPB (Table 13.1). At least six recent prospective, randomized studies have examined the effect of combining a CPB with general anesthesia for thyroidectomy. Of these six studies, four reported a benefit of superficial cervical plexus block [42, 45, 46, 49]. These benefits included reduced intraoperative and/or postoperative analgesic use [45, 46, 49] and improved visual analog pain scores [42, 45, 46]. The other two studies reported essentially equivalent outcomes between patients with and without cervical plexus block for thyroidectomy done under general anesthesia [43, 44]. The combination of CPB with general anesthesia in CEA is associated with improved postoperative pain control and patient satisfaction [26].

Outcome Data: Cervical Plexus Block in Place of General Anesthesia

Many surgical procedures of the head and neck may be performed under regional anesthesia by CPB alone (Table 13.1). A case series published in 1934 reported a strong benefit of regional anesthesia with CPB over general anesthesia for thyroid surgery (n = 125) [3]. It seems likely that the benefit of regional anesthesia in this case series may have related to the relative danger of general anesthesia in the 1930s.

Recent studies have largely reported equivalent patient outcomes between surgeries performed with regional anesthesia alone via CPB versus surgeries under general anesthesia. The largest study to examine this question is the General Anesthesia versus Local Anesthesia for Carotid Endarterectomy (GALA) study [39]. In the GALA study, 3,526 patients scheduled for CEA were randomized to either general anesthesia (GA) or local anesthesia (LA) via CPB. The outcomes of this study included stroke, myocardial infarction,

or death within 30 days after surgery. No difference in outcome between GA and LA was found, and the authors concluded that both techniques are appropriate. The 2009 Cochrane Database Review on the subject covering 4,335 patients echoes this conclusion [50].

Small studies have suggested improved hemodynamic stability during CEA with CPB than without [51, 52], and the GALA study reported similar findings in subgroup analyzes [39]. In the GALA study, more patients in the GA group required intermittent treatment for hypotension compared to the CPB group (43 % in the GA group vs. 17 % in the CPB group). Conversely, more patients in the CPB group required intermittent treatment for hypertension compared to the GA group (28 vs. 13 %). Of the two groups, hemodynamic manipulations were far more likely to be required in the GA group compared to the CPB group (72 vs. 54 %).

Conclusion

CPB is a safe and reliable plexus block that is widely used to provide surgical anesthesia and analgesia. CPB may also be useful in chronic pain disorders that arise from the cervical plexus. Both deep and superficial blocks are supported by current literature. Superficial block is safer than deep block, and superficial blockade is sufficient for most surgical indications because of ready spread of local anesthetic within the fascial planes in the neck.

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Stellate Ganglion Blockade

14

Mehul Sekhadia, Kiran K. Chekka, and Honorio T. Benzon

Key Points

- Stellate ganglion blocks can be useful in the diagnosis and treatment of a variety of conditions; evidence is needed through randomized and controlled studies but is difficult to obtain.
- There are a variety of techniques available for both diagnostic blockade and neurolysis, but they should only be performed by those trained adequately to perform and monitor the outcomes of the blocks along with potential complications.
- The safety of stellate ganglion blocks and neurolysis is enhanced by the use of image guidance.
- The use of ultrasound is increasing and may increase efficacy, decrease complications, and reduce exposure to radiation.
- Regardless of technique, stellate ganglion block is a safe procedure when performed by properly trained physicians.

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Introduction

Physicians first began performing blocks of the sympathetic nervous system almost 100 years ago. In 1920, Jonnesco described the cervicothoracic block which Lawen [1] performed for the differential diagnosis of abdominal pain [1]. Kappis then used sympathetic blocks, including stellate blocks, for the treatment of several pain syndromes [2]. After World War I, a fair amount of research was done to elucidate the anatomy and function of the stellate ganglion, and soon after, the early techniques and indications for sympathetic blockade were developed. After World War II, these blocks became popular for the management of causalgia and reflex sympathetic dystrophies [2].

Sympathetic blocks can be used for diagnostic, prognostic, and therapeutic purposes. Diagnostic blocks are done to determine if acute or chronic pain is sympathetically mediated or independent. If a diagnostic block provides excellent relief of symptoms, then it is more likely that neurolysis or surgical sympathectomy would be beneficial [3]. Therapeutic blocks in series have been studied in the treatment of such syndromes such as complex regional pain syndromes [3, 4], phantom limb pain [1], postherpetic neuralgia [5, 6], ischemic pain [7], and cancer pain [8]. These blocks are usually an integral part of a comprehensive functional restoration program [4].

Once a block is performed, it is essential to verify that [1] the sympathetic chain was actually blocked and [2] that no other neural structures were blocked. The best practical model for monitoring blockade is by watching for a change in limb temperature without significant somatic sensory or motor blockade. While sympathetic blocks are performed for a plethora of reasons, there are only a few randomized, placebo-controlled, outcome studies to demonstrate their effectiveness [9]. Anecdotally, when the blocks provide pain relief, they can be profoundly effective in managing a

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patient's pain and facilitating participation in essential rehabilitation regimens. In this chapter, we intend to describe sympathetic anatomy and blockade technique, proper post-block monitoring, and the evidence which is there for sympathetic blockade.

Anatomy

There are three interconnected ganglia which make up the cervical sympathetic chain: the superior, middle, and inferior cervical ganglia. In 80 % of people, the lowest cervical ganglion fuses with the first thoracic ganglion and is commonly referred to as the stellate ganglion, so named because of the characteristic appearance [8, 10]. In the remaining 20 % of people, the first thoracic ganglion is named the stellate ganglion.

The cervical ganglia receive nerve fibers from two major contributors: (1) preganglionic fibers from the lateral gray column of the spinal cord and (2) myelinated preganglionic cell axons from the anterolateral horn of the spinal cord. These fibers originate in the upper thoracic segments, traverse the ventral rami, and then form the white rami communicantes, which enter into the thoracic ganglia and then traverse cephalad. The head and neck sympathetic innervations arise predominantly from T1 to T3, while the innervation of the upper extremity originates predominantly from T2 toT6. From these segments, the fibers climb cephalad through the sympathetic trunk into the cervicothoracic ganglion where they synapse. Then, the postganglionic fibers travel directly to the head and neck or to the brachial plexus to innervate the arm.

These postganglionic fibers control vasoconstrictor and sudomotor functions of the face and neck, secretory fibers to the salivary glands, dilator pupillae, and nonstriated muscle in the eyelid and orbitalis. As a consequence, blockade of these fibers results in ptosis, miosis, enophthalmos, and abolition of face and neck sweat response. Further, the stellate ganglion sends a gray ramus communicans to the seventh cervical, eighth cervical, and first thoracic nerves. There is also a cardiac branch and occasionally a vagal branch.

Most of the sympathetic innervation to the head and neck as well as the ipsilateral upper extremity can be blocked at the stellate ganglion. At this structure, preganglionic fibers synapse or traverse to a more cephalad ganglion and then send postganglionic fibers to the appropriate structures. Most preganglionic fibers which synapsed at a more caudad level still send their postganglionic fibers through the stellate ganglion. The first three intercostal nerves may also carry sympathetic innervation directly to the brachial plexus entirely bypassing the stellate ganglion. This anomalous pathway ("Kuntz's nerves") would not be blocked by a stellate ganglion blockade and maybe by an explanation for inadequate sympathetic blockade after an appropriately performed stellate block.

The cervical sympathetic chain lies just medial to the carotid space and is enclosed by the lateral aspect of the alar fascia which separates it from the retropharynx. Just posterior is the prevertebral musculature. This fascial plane is not entirely closed off from other tissue planes. Any medication deposited in this fascial plane may spread to the brachial plexus, spinal nerve roots, the prevertebral portion of the vertebral artery, and between the endothoracic fascia and the thoracic wall muscle at the T1–T2 level causing blockade of these structures and resultant side effects of stellate blockade. The stellate ganglion is consistently located anterior or just lateral to the longus colli muscle between the inferior margin of the seventh cervical transverse process and the first rib. At this level, the vertebral artery and vein are anterior (in the direct path of an anterior needle placement), and the C7 and T1 nerve roots are posterior to the ganglion.

By the C6 level, in over 90 % of patients, the vertebral artery is posterior to the sympathetic chain and shielded by bone. The variability in the size of the longus colli muscle can affect block success and complication rates and may explain ineffective neurolysis in a block responder [11].

Indications

Table 14.1 is a list of indications and contraindications for stellate ganglion block [1, 8]. This list includes diagnoses with variable amounts of research supporting their usage. Some indications are based on case reports or case series while others have legitimate outcome studies which are discussed later in this chapter.

Contradictions

See Table 14.1.

Techniques

There is huge range in stellate block success rates described in the literature (16–100 %) [12].

Seemingly, using some sort of guidance improves block success, but in practice, there continues to be debate on whether to use guidance and what sort of guidance should be used.

While CT guidance provides a very high success rate [13], there is the associated higher dose radiation and the typical inefficiencies and cost associated with CT which makes it less popular.

Ultrasound can be used to easily visualize superficial soft tissue structures including the stellate ganglion [14].

Table 14.1 Indications and contraindications

CRPS I and II
Vascular insufficiency—Raynaud's, vasospasm, vascular disease
Accidental intra-arterial injection of drug
Postherpetic neuralgia and acute herpes zoster
Phantom pain
Frostbite
CRPS breast and postmastectomy pain
Quinine poisoning
Hyperhidrosis of upper extremity
Cardiac arrhythmias
Angina
Vascular headaches
Neuropathic pain syndromes including central pain
Cancer pain
Atypical facial pain and trigeminal neuralgia
Hot flashes
Contraindications
Coagulopathy (patients on warfarin or low-molecular-weight heparin, patients on aspirin or nonsteroidal anti-inflammatory agents are possible contraindications)
Contralateral pneumothorax (or contralateral phrenic palsy)
Systemic or local infection
Glaucoma
Bradycardia

Also, the longus capitis muscle has been described as a possible landmark for cervical sympathetic block [15]. In this chapter, we describe the most commonly used surface landmark, ultrasound- and fluoroscopic-guided techniques. The techniques for CT-guided blocks are virtually identical to the fluoroscopic techniques.

Minimum requirements for stellate ganglion blocks:

- Informed consent
- IV access
- Standard resuscitative equipment
- ASA standard monitors
- Monitoring sympathetic blockade
- Fluoroscope (C-arm), ultrasound, or computed tomography
- 22- or 25-gauge needle, 2.5–3.5 in. long
- Local anesthetic—lidocaine versus bupivacaine
- Contrast—Omnipaque® or Isovue® (if using fluoroscopy)

Surface Landmark (Nonimage-Guided) Technique

The "blind" or non-guided techniques rely on the use of palpable surface landmarks to determine the site of injection. Typically, the patient is placed supine with slight neck extension using towels +/− a shoulder roll with the mouth open (an open mouth results in more relaxed neck musculature). The cricoid cartilage in the adult is a fairly accurate landmark to identify the C6 spinal level. Others have advocated using the skin crease caudad to the thyroid as a landmark to identify C6. Chassaignac's tubercle is identified with palpation at the C6 level. In most individuals, the tubercle is located approximately 3 cm cephalad to the sternoclavicular joint at the medial border of the sternocleidomastoid muscle. The carotid artery and trachea are gently retracted laterally. After intradermal local anesthetic injection with a 27-G needle, either 22- or 25-gauge Quincke or pencil-point needle is placed perpendicularly in an anterior-to-posterior fashion until the needle contacts bone at which point it is withdrawn 2 mm. After negative aspiration, 0.5–1 ml of 1 % lidocaine is injected slowly while the patient is awake and responsive to detect aberrant spread of the local anesthetic to surrounding structures. If negative, 5–8 ml of either 1 % lidocaine or 0.25 % bupivacaine is injected incrementally and frequent aspiration. The patient is then monitored for a minimum of 30 min to assess response to the blockade.

Fluoroscopic Technique

Positioning is unchanged from the blind procedure. The "C-arm" is then moved to achieve a posterior-anterior (PA) image. Then, using cephalad or caudad tilt, the end plates or C6 (or C7) are lined up. Either level can be utilized so long as the operator has thorough knowledge of the anatomy described in the previous section. The C7 level is preferred because of its closer proximity to the stellate ganglion, but the vertebral artery is uncovered at this level unlike at the C6 level where the vertebral artery travels posterior to Chassaignac's tubercle. To avoid the vertebral artery at C7, the needle should be placed more medial on the transverse process (see Fig. 14.1).

Local anesthetic is infiltrated with a 27-gauge needle intradermally at the site of injection as guided by the fluoroscope. Then, a 25-gauge by 1.5- or 2-in. needle is advanced coaxially to the anterior transverse process of the chosen level. Once contact is made, the needle is withdrawn 2 mm so that it is not in contact with periosteum and the stylet is removed. A lateral image can be taken to confirm that the needle is anterior to the vertebral body. A precontrast-flushed extension set is then connected to the needle, and after negative aspiration for blood, under live, real-time fluoroscopy or digital subtraction angiography, 1–5 ml of contrast is injected. The optimal spread of contrast should cover the C6–T2 levels to ensure blockade of the stellate ganglion (see Fig. 14.2). A test dose is then injected with 0.5–1 ml of 1 % lidocaine through the extension tubing (to minimize needle movement) assuring that the local anesthetic passes through the tubing. The patient is continuously assessed for possible intravascular or neuraxial spread which can result in seizure or high spinal.

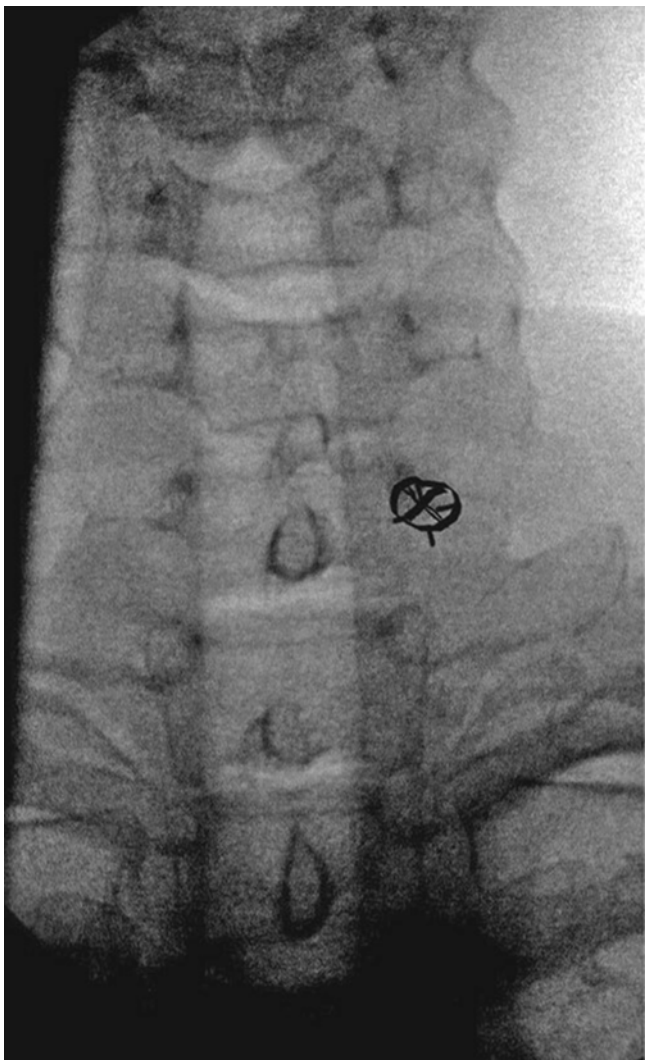

Fig. 14.1 Initial landmark (*x*) for the anterior approach to the stellate ganglion block

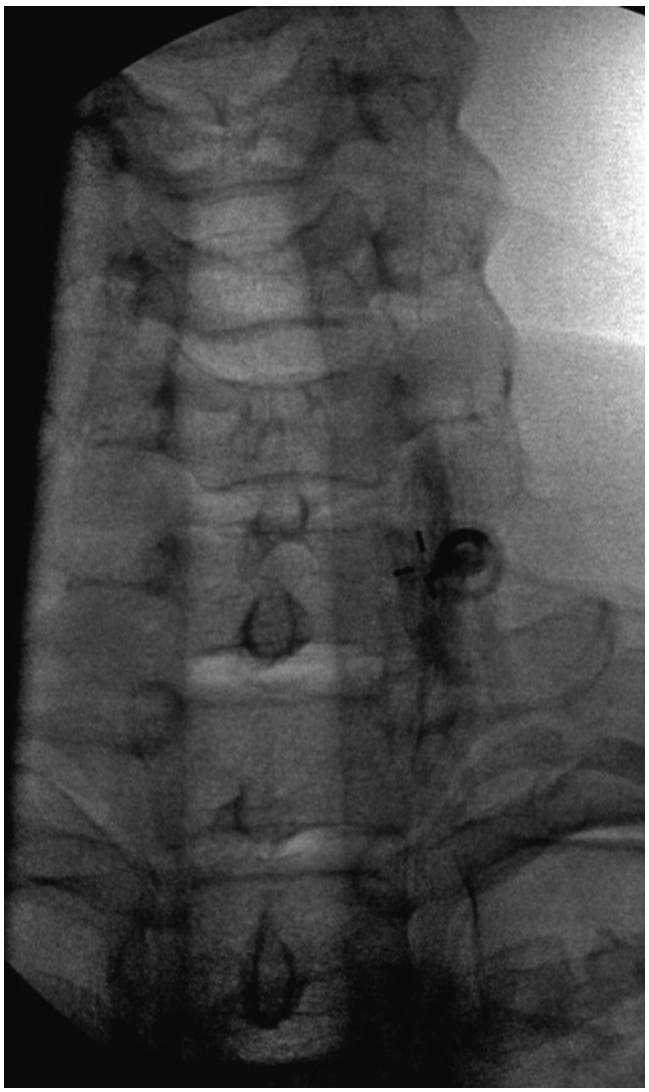

Fig. 14.2 Injection of contrast after needle placement demonstrating correct spread along the anterolateral borders of C5–T1

If the test dose is negative, then approximately 5–10 ml of local anesthetic is injected incrementally. The greater the volume injected, the greater is the likelihood of spread to the recurrent laryngeal nerve, phrenic nerve, or brachial plexus. It is important to frequently aspirate during the injection and pause between boluses of injectate.

Other Fluoroscopic Approaches [16]

Patient preparation is unchanged with the patient placed in the supine position with established IV access. The head is then turned contralateral to the side to be blocked. The fluoroscope is used to identify the C5–C6 disk on AP view, and ipsilateral oblique rotation is added until the neural foramina are clearly demarcated. On this image, the target of the injection is the junction of the uncinate process and the vertebral body of C7. A 25-gauge needle is then passed coaxially with the fluoroscope beam until it reaches the target. As with all image-guided procedures, it is important to keep the needle coaxial and, in this case, avoid the needle going posterior into the foramina (direct entry into the thecal sac). Once contact with bone occurs, the stylet is removed and contrast is injected as described above in the previous section. The major reported advantage of this technique is that only 3–5 ml of local anesthetic is needed to block the stellate ganglion as opposed to the other techniques described which use as much as 15–20 ml. Another advantage of the technique is that the needle is placed obliquely to allow for placement at C7 while avoiding the vertebral artery (which is anterior to the stellate ganglion) and the pleural dome in nonemphysematous patients (based on cadaver studies).

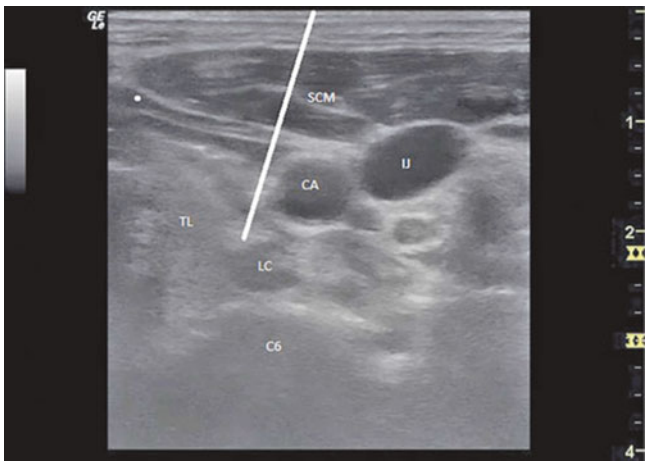

Fig. 14.3 Ultrasound-guided approach to stellate ganglion block done at C6 level. *TL* thyroid lobule, *LC* longus colli muscle, *CA* carotid artery, *IJ* internal jugular vein, *SCM* sternocleidomastoid muscle

The authors outlined the following benefits [16]:

- Eliminating or pushing away vasculature and pressing on the potentially painful Chassaignac's tubercle
- Minimize the chance of intravascular injection
- Minimize esophageal perforation
- Minimize the chance of recurrent laryngeal nerve paralysis
- Reduce the volume of local anesthetic
- Easy to teach trainees

There is currently no prospective outcome data on this technique.

Ultrasound-Guided Approach

A newer ultrasound-guided technique for stellate ganglion blockade was first described by Kapral et al. (Fig. 14.3) [17]. Kapral et al. hypothesize a decrease in the incidence of retropharyngeal hematoma and increase the safety and efficacy of the block. Ultrasound allows direct visualization of the thyroid gland, vertebral artery, esophagus, pleura, nerve roots, longus colli muscle, and the correct fascial planes for nerve blockade along with real-time, direct visualization of local anesthetic spread [14, 18].

Positioning for the procedure is unchanged from the landmark-based technique. This block is considered an "expert" block by most ultrasonographers and should not be done by ultrasound beginners. A linear array, 3–12 MHz frequency probe (ideally with a small footprint) is placed transversely at the level of C6, just lateral to the trachea on the ipsilateral side. The carotid artery is easily visible with the use of ultrasound and can be a very good landmark. While some practitioners are performing exclusively ultrasound-guided blocks, many still use fluoroscopy to identify the C6 level, to verify what structures the needle is traversing, and to perform a live dye study. Sometimes, the ganglion itself can be visualized, but typically the goal is to use an in-plane approach and deposit medication in the fascial plane anterior to the longus colli muscle (which is almost always easily identified). Typically, small aliquots of 1–3 ml are injected under real-time visualization to verify a fill pattern in the appropriate fascial plane.

One validation study using the ultrasound approach showed that at the C6 level, the cervical sympathetic trunk lays entirely subfascially, and as a result, a subfascial injection via the lateral approach ensures reliable spread of solution to the stellate ganglion [14]. There are no randomized, prospective, outcome studies on using the ultrasound approach. One safety concern with ultrasound-guided injection is that there are no well-studied and validated contrast materials which can be used to insure that the injection is not intravascular. Still, one can use epinephrine to increase sensitivity, and others have reported a "wisping" in a visualized vessel when the injectate is intravascular.

Posterior Approach

Currently, the posterior approach is used principally when [1] a sympathectomy was not achieved using another technique or [2] when the block is being done as a diagnostic measure prior to percutaneous neurolysis (or rhizotomy) or surgical sympathectomy. Some advocate that this approach should be utilized for all upper extremity sympathectomies [19].

For this approach, the patient is in the prone position, and image guidance is an absolute necessity (usually fluoroscopy, but CT can be utilized). After IV placement and proper positioning, an AP image of T2 and T3 vertebrae is obtained. The C-arm is then rotated obliquely until the lateral margin of the transverse process is just overlapping the lateral margin of the vertebral body. Next, cephalocaudad tilt is used to square off the first rib. The target structure is the midpoint of the T2 or T3 vertebra. Pneumothorax is a significant concern which can be minimized by decreasing the degree of oblique angle. Practitioners often balance the concern for pneumothorax against the likelihood of a challenging or suboptimal needle placement as a result of decreased obliquity. As with anterior techniques, coaxial needle placement greatly reduces complications. Final needle position should be verified with a lateral image showing the needle at the midpoint of the vertebral body.

Next, 0.5–3 ml of contrast is injected under real-time imaging or digital subtraction angiography to observe for vascular uptake or extraneous spread. Local anesthetic of 5 ml is then injected in divided doses, and the patient is monitored for sympathetic blockade.

Comments

Variable injection volumes have been suggested from 5 to 20 ml [20]. Feigl et al. [20] cadaver study using the blind paratracheal approach at the C6 level showed that 5 ml of injectate almost always demonstrated spread over the C6–T2 levels without ventral or lateral spread. Injectate of 10–20 ml almost always spread to these spaces which in live humans can result in recurrent laryngeal nerve and phrenic nerve blockade. In another study, Hardy et al. [21] demonstrated that with 10 ml of local anesthetic injection, there is only a 10 % incidence of recurrent laryngeal nerve block, whereas with a 20 ml injection, the rate increases to 80 %. However, larger volumes may be needed to obtain complete blockade of T1 and T2 ganglia if injection is done at C6 compared to C7 [22].

Neurolysis

Percutaneous neurolysis can be simply performed using chemical (phenol or alcohol) neurolysis or radio-frequency (both pulsed and thermal) techniques. Radio-frequency techniques create small discrete lesions; chemical lesions are typically larger and less discrete. Both techniques have been utilized at the stellate ganglion. Usually if a diagnostic block consistently provides good but transient relief, neurolysis is a next potential therapeutic step. There are no randomized, placebo-controlled, prospective trials on the use of neurolytic agents for nonmalignant pain.

Chemical Neurolysis

Two to 3 ml of aqueous phenol (3–6 %) or alcohol (50–100 %) should be enough volume to neurolyse the ganglion without spread to adjacent structures [23]. Phenol is usually the agent of choice because of a decrease in incidence of neuritis post-procedure. Neurolysis can be performed using an anterior approach at C6 or C7 or using a posterior approach at T2 or T3 for upper extremity problems. Always inject a local anesthetic test before injecting the neurolytic to insure that no somatic sensory or motor nerves are destroyed.

Radio-Frequency Lesioning

Thermal radio-frequency (RF) lesioning produces discrete lesions whose size can be modulated with needle tip selection. Further, RF generators allow practitioners to perform nondestructive pulsed lesioning. Test dosing is not always necessary as stimulation can be used to verify that other neural structures are not at risk for neurolysis. Still local anesthetic is typically injected for patient comfort during lesioning.

RF lesioning is done at the C7 level because the probe must be in very close proximity to the structure being lesioned. Stimulation can be done while the patient is saying "EE" to see if there is any stimulation of the recurrent laryngeal nerve or phrenic nerve. A 22-gauge 50-mm cannula with a 5-mm active tip can be placed using an anterior approach with fluoroscopic guidance. Stimulation is performed at 2 Hz and up to 2.5 V (usual for motor stimulation) to assess prior to injection of local anesthetic and lesioning. The posterior approach at T2 and/or T3 will most likely avoid these two nerves [8, 24].

After placing the probes, the stylets are removed and sensory and motor testing is performed. Next, dense local anesthetic (i.e., 2 ml of 2 % lidocaine) is injected for thermal lesions. For pulsed lesions, the needle tip is withdrawn because the target should be in front of the needle, as opposed to parallel to the needle for thermal lesions. Sensory stimulation should be done (50 Hz) to determine the lowest threshold of stimulation, and motor stimulation should be done if doing a thermal lesion (2–5 Hz up to 3 V). Pulsed lesions are carried out at 42°, pulsed mode, 2 × 20 ms/s, 40–45 V (to titrate the temperature to 43°) for 120 s. With thermal lesioning, tip temperature is brought to 80 °C for 60–90 s [1, 8].

Complications

As with all interventional pain procedures, only those with proper training and experience should be performing these blocks. The potential complications for sympathetic blocks are real but if done properly, are rare. The risks with neurolysis are more severe (and potentially more permanent).

Stellate Ganglion Blockade and Neurolysis [8]

- Bleeding/hematoma
- Pneumothorax, hemothorax
- Vertebral artery injury or inadvertent injection
- Inadvertent injection into neuraxis
- Esophageal trauma
- Tracheal trauma
- Phrenic nerve injury
- Brachial plexus injury
- Recurrent laryngeal nerve injury
  - Neuritis—any nerve or plexus listed above
  - Postsympathectomy syndrome

Monitoring the Adequacy of Sympathetic Blockade

Stellate Block:

- Horner's syndrome (ptosis, miosis, enophthalmos, and anhidrosis)
- Guttman's sign (nasal stuffiness)

- Hyperemia of the tympanic membrane
- Warmth of face
- Increased temperature of the upper extremity by at least 1 °C

Successful stellate ganglion blockade results in Horner's syndrome (ptosis, miosis, and anhidrosis). Other signs include unilateral nasal stuffiness (Guttman's sign), hyperemia of the tympanic membrane, and warmth of the face. The presence of Horner's syndrome signifies cephalic sympathetic blockade but does not verify upper extremity sympathetic blockade [25, 26]. If the block is used to treat the shoulder or upper limb, additional signs are needed to determine sympathetic blockade in the area. Complete block is reliably detected when a test of adrenergic fiber activity (thermography, plethysmography, laser Doppler flowmetry) is combined with a test of sympathetic cholinergic (sudomotor) fiber activity (sweat test, sympathogalvanic response).

Increase in skin temperature is the most practical and simple clinical sign of sympathetic blockade. Commonly, skin temperature is measured by using adhesive thermocouple probes that are placed distally on the extremity being monitored. For continuous skin temperature measurements, thermocouple devices are placed bilaterally. Infrared thermography can provide average sensitivity to skin temperature changes as minute as 0.1 °C. Another qualitative thermography technique is liquid crystal thermography, with reported sensitivity of about 0.8 °C. Different investigators considered different increases in skin temperature as signifying effective sympathetic blockade. After a stellate ganglion block, skin temperature increases of 1.5 °C [26], 3.8 °C [27], and 7.5 °C [13] have been considered as signifying successful sympathetic blockade. Hogan et al. [26] state that ipsilateral limb temperature should increase to a value greater than the contralateral temperature in the presence of successful sympathetic blockade. Stevens et al. found that a temperature increase that was 2 °C higher than the contralateral was attained with complete sympathectomy in most patients [28]. The magnitude of temperature increases after complete sympathetic blockade is largely dependent on the starting temperature [29]. With sympathectomy, skin temperature will nearly approximate core body temperature in the absence of peripheral vascular disease. Therefore, the upper limit of skin temperature in the fingers and toes is about 35–36 °C [30] in patients without significant organic peripheral vascular disease [29]. Patients whose baseline skin temperatures are low because of vasoconstriction (i.e., later stage CRPS patients) will attain a large temperature increase with complete sympathetic blockade. In a vasodilated patient (i.e., early stage CRPS), one cannot expect a large temperature increase.

Most other measures of sympathectomy are technically complex and usually infeasible in the typical clinical setting, but they are oftentimes used in research and academia. Laser Doppler flowmetry measures skin blood flow. A 50 % or greater increase in the skin blood flow is used to signify successful sympathetic block. Blood flow can also be accurately measured using plethysmographic methods such as venous-occlusion plethysmography. In this technique, a transducer is placed on the finger to measure the change of the finger volume over time. A tourniquet is inflated around the finger to a pressure which is greater than venous pressure but still allows arterial blood to enter the finger. The finger's rate of volume increase is measured using the volume transducer, and a plethysmographic trace is generated and then analyzed. First, a rapid increase is seen followed by a plateau phase which signifies that a sufficient amount of blood has entered the finger to equalize the venous pressure with tourniquet pressure. In the presence of sympathectomy, the upward slope is drastically increased due to a significant increase in the pulse wave. Kapural et al. found volume plethysmography better measured blood flow than skin surface temperature gradients than blood flow measurements by laser Doppler flowmetry [31].

Usually in a laboratory setting, the presence of complete sympathectomy can be verified by checking for abolition of sweat response and abolition of the sympathogalvanic response (SGR) [26, 28–35]. Today, ninhydrin and cobalt blue tests are most commonly used to verify abolition of sweating response. Benzon et al. have modified the preparation of the two sweat tests [34]. For the cobalt blue filter paper, 0.5 M $CoCl_2$ in 70 % ethanol is used, while 2 % ninhydrin in 70 % ethanol with 1 ml of 4 M acetate buffer (pH 5.5) per 100-ml solution is utilized for the ninhydrin filter paper. The solutions (cobalt blue or ninhydrin) are applied evenly on a Whatman no. 1 filter paper at 2 ml/100 cm^2. The papers are dried at room temperature and stored in a desiccator. Once setup is complete, cobalt blue paper or ninhydrin filter paper is clear taped to dry skin. If the patient still has the ability to sweat, cobalt blue paper will turn pink, and ninhydrin filter paper will have purple dots appear. The ability to sweat suggests that sympathectomy to the area tests was not complete.

Sympathogalvanic responses can be measured using the electrocardiogram, and the setup is simple. The right arm (RA) and left arm (LA) leads are placed on the limb being tested on the dorsum and palm (or sole). The other leads are placed contralaterally. Then, the patient is exposed to a stimulus such as deep breath, startling noise, or a pinprick. In healthy controls, either a monophasic up or down deflection or a biphasic response is seen. With partial sympathectomy, amplitude is diminished. With complete sympathectomy, a flat line trace is seen.

Benzon showed that sweat testing is more reliable than the SGR in predicting complete sympathetic blockade [34], but both had a sensitivity of 90 %. The specificity of the SGR was 56 % compared to 100 % for the sweat tests, resulting in stated accuracies of 74 and 95 %, respectively [34]. Whether or not a complete sympathectomy is achieved is really only

clinically relevant when optimal (or complete) analgesia is not attained [35]. For example, patients can have full resolution of symptoms even with a partial sympathetic blockade. But if the patient has partial relief of symptoms, then the residual pain may be due to a somatic or central in etiology, or the remaining symptoms could be sympathetically mediated if only a partial sympathectomy was achieved [35]. Partial relief of symptoms occurs after the block due to a partial sympathectomy may be due to technique issues or to aberrant pathways (i.e., Kuntz's nerves) which were not blocked.

Studies

In this section, we present the data that is available for the efficacy of stellate ganglion blocks and rhizotomy.

In 2007, Day [36] reviewed 11 articles consisting of 4 case reports, 5 case series, 1 retrospective review [37], and 1 double-blind, placebo-controlled study. Using Guyatt's criteria, Day concluded that most evidence for stellate blocks was either 1B or 1C grade, including the randomized and blinded trial which had a very small sample size. There is one prospective comparison of RF ablation at T2 and T3 versus phenol/RF at T2 for severe Raynaud's phenomenon [38]. Fifty patients were randomized into the two groups and ablated, but no diagnostic blocks were done. Patients were followed for 3 months, and statistically significant improvement in visual analog pain scores, quality of life, and limb temperature were found in both arms. While the study was not placebo-controlled, it was concluded that both techniques showed efficacy in the treatment of Raynaud's disease [38].

Conclusions

Stellate ganglion block is an important tool in the arsenal of treating sympathetically mediated pain syndromes. The careful attention to patient selection, anatomical landmarks, and potential complications can lead to the successful use of this procedure.

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Epidural (Cervical, Thoracic, Lumbar, Caudal) Block/Injections

15

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Key Points
- Epidural steroid injections are relatively safe.
- Strict aseptic technique needs to be used.
- Fluoroscopic guidance is recommended.

Introduction

One of the first descriptions of access to the lumbar epidural space was described by Pages in 1921 [1]. Anesthesia through a caudal route had been reported much earlier, but his was the first to describe a method for accessing the lumbar epidural space. Since then, various epidural injection techniques have been developed, and there have been dramatic increases in their use, not only for acute and labor pain, but for chronic pain as well. The loss of resistance technique was described [2] as the "hanging drop" technique [3]. Soon after corticosteroids were introduced in the mid-twentieth century, physicians started using them in the epidural space.

The cervical, thoracic, and lumbar epidural spaces can be accessed using multiple approaches including interlaminar, transforaminal, and caudal approaches. All have the same purpose, which is to deliver higher concentrations of corticosteroid directly in the area of an inflamed nerve root. This is an alternative to the less targeted oral route, which leads to increased systemic side effects. All areas of the epidural space can be accessed including the cervical, thoracic, and lumbar regions.

Scientific Foundation

Epidural injections are believed to be effective due to targeted delivery of local anesthetic and/or corticosteroids to the space where spinal nerve roots travel on their way from the spinal cord to the body.

Corticosteroid molecules are highly protein-bound in plasma and enter the cell membrane by active transport after binding to surface proteins. Once inside the cell, they combine with glucocorticoid receptors, and the combined complex is taken into the nucleus by active transport. They upregulate production of anti-inflammatory proteins and repress the expression of pro-inflammatory proteins. Specifically, the enzyme phospholipase A2 which is involved in the formation of arachidonic acid is inhibited. Arachidonic acid is essential for the formation of inflammatory mediators. Glucocorticoids also suppress the expression of cyclooxygenase (COX-1 and COX-2), which adds to the anti-inflammatory effect. Overuse of corticosteroids may lead to many adverse effects including Cushing's syndrome, avascular necrosis, peptic ulcers, cataracts, immunosuppression, hyperglycemic syndromes and osteoporosis.

Anatomy of the Epidural Space

The epidural space starts at the point where the periosteal layer of the foramen magnum comes together with the dura. The inferior boundary is at the sacrococcygeal membrane, the anterior boundary is the posterior longitudinal ligament, the posterior boundary is the ligamentum flavum, and the lateral boundaries are the pedicles and the intervertebral foramina. The space contains fat, lymphatics, and venous plexus. The ligamentum flavum is thin in the cervical region and

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thickens as you move caudal [4]. In the cervical region, the distance between the ligamentum flavum and the dura is 1.5–2 mm at C7 (due to cervical enlargement) as opposed to the lumbar region where at L2, it is 5–6 mm.

Cervical Epidural Injections

There are two approaches to access the cervical epidural space: translaminar and transforaminal. There are no studies that have shown that one is better than the other; however, complications associated with each are significantly different [5]. A systematic review published in Pain Physician in 2009 looked at the efficacy of translaminar cervical epidural injections and concluded that they provide a significant effect on cervical radicular pain [6]. There are no major studies looking at the efficacy of transforaminal cervical epidural steroid injections.

Indications

This procedure has multiple indications for head, neck, shoulder, and upper extremity pain. Table 15.1 shows these indications.

Contraindications

Absolute: unwilling patient, localized infection over procedure area, current anticoagulant use (see current america society of regional anesthesia (ASRA) and pain medicine guidelines on anticoagulants), increased intracranial pressure (ICP), bleeding diathesis, and patient that cannot remain still during the procedure.

Relative: allergy to medications that will be injected (contrast, local anesthetic, steroid) pregnancy, immunosuppression, systemic infection, and anatomic changes that would prevent a safe procedure (congenital or surgical).

Table 15.1 Common indications for cervical epidural injections

Cervical radiculopathy
Cervical degenerative disk disease
Cervical disk herniation
Cervical spinal stenosis
Cervical postlaminectomy (failed neck) surgery syndrome
Cervical vertebral compression fractures
Postherpetic neuralgia/herpes zoster
Complex regional pain syndrome (I and II)
Peripheral neuropathy (diabetic, chemotherapy induced, etc.)
Phantom limb pain
Cancer-related pain

Cervical Epidural Transforaminal Epidural Injection Technique

Because of the risks associated with this procedure, only physicians who have training and experience in using fluoroscopy as well as precise injection techniques should perform this procedure. All patients should be fully monitored, and equipment to handle airway, local anesthetic toxicity, and cardiovascular emergencies should be readily available.

Although physicians may have different techniques, the primary aspects of all must include proper positioning of the patient in order to optimize visualization of the anatomy of the cervical spine at the target level(s). After discussing risks and benefits, answering questions, and obtaining written informed consent, an intravenous line is placed (for sedation or for emergency access). The patient is taken into the procedure suite and can be placed in the supine, oblique, or lateral position depending on physician preference. The area of the neck is prepped and draped in a sterile manner. The fluoroscopy beam is then adjusted to visualize the intervertebral foramen at its maximum diameter, usually an anterior oblique view. The anterior surface of the superior articular process of the inferior vertebrae (posterior aspect of foramen) is identified, and the entry point is marked. The skin and subcutaneous tissues are anesthetized with 1 % lidocaine. A 25-gauge needle is then directed toward the anterior portion of the superior articular process. It should always be directed toward this bony landmark, as going directly toward the foramen could result in a needle being placed too deep and into the spinal cord. Once the superior articular process is contacted, the depth of the needle should be noted. Repositioning of the needle should never exceed this noted depth by more than a few millimeters. The needle is then carefully adjusted so that it passes into the intervertebral foramen. The needle should always remain slightly anterior to the superior articular process. It should never be in the anterior portion of the intervertebral foramen as this may risk injection into the vertebral artery.

Once the needle is in the correct position, the fluoroscope is repositioned for a true anteroposterior (AP) view. This will allow the physician to see the depth of the needle. The correct depth is when the tip of the needle lies opposite the sagittal midline of the silhouettes of the articular pillars. If the needle contacts the existing nerve root, the patient will feel radicular pain. At this point, the needle should be slightly withdrawn and the procedure halted until the sensation disappears. If the sensation does disappear, the needle can be redirected back to its intended position, but avoiding the exact spot that caused the radicular pain. Fluoroscopy should be used to check in an oblique direction as well as an AP view to confirm needle position and depth. Only after this is done should anything be injected.

After negative aspiration is confirmed, less than 1 ml of contrast solution is injected under live fluoroscopy. It should enter the intervertebral foramen and outline the spinal nerve. It is of utmost importance to be sure there is no intra-arterial injection of contrast. Although this location of needle placement usually will not contain a radicular or a vertebral artery, these arteries can be atypically located. In case of an intra-arterial injection, the contrast will move and disappear during live fluoroscopy. If this is the case, one can redirect the needle until contrast is not seen entering an artery. However, it may be more prudent, given the severity of possible intra-articular injection through the punctured site, to abort the procedure. If contrast injection leads to rapid dilution of the contrast material, it may imply that there has been subarachnoid needle placement. In this case, abort the procedure and give enough time for the puncture to heal as injection even into another location may lead to entrance of medication into the subarachnoid space through the puncture hole created.

Once it has been confirmed by AP and oblique views that there has been correct needle placement, contrast injection has been negative for intra-arterial and subarachnoid injection, the contrast appropriately outlines the spinal nerve, and injection of contrast is negative for pain or paresthesia, the local anesthetic and steroid can be given. How much steroid depends on whether the pain is monoradicular or multiradicular. If monoradicular, betamethasone (3–6 mg), triamcinolone (20–40 mg), or dexamethasone (7.5–10 mg) can be used. If multiradicular, betamethasone (12 mg), triamcinolone (80 mg), or dexamethasone (15 mg) can be used.

Once the medication has been injected, the needle is removed with a saline or local anesthetic flush to clear the needle and track of steroid. The area that was prepped should be cleansed and a bandage placed over site of needle insertion. The patient should then be taken to a recovery area where they should be monitored for complications resulting from conscious sedation as well as complications from the procedure itself.

Cervical Translaminar Epidural Injection Technique

This procedure can be performed by either a loss of resistance technique or a hanging drop technique. One technique has not been shown to be better than the other; thus, the choice of technique is based on physician preference.

Loss of Resistance Technique

After discussing risks and benefits, answering questions, and obtaining written informed consent, an intravenous line is placed (for sedation or for emergency access).The cervical interlaminar technique can be performed in either a sitting, lateral, or prone position. Each position has its own advantages and disadvantages. Since most pain practitioners use fluoroscopy to perform cervical epidural injections, the prone or lateral position is utilized. The cervical spine should be flexed to maximize the opening of the intervertebral spaces.

Once the patient is appropriately positioned, the neck is prepped and draped in a sterile manner, and AP fluoroscopy is used to identify the interspace that will be entered. A 17- or 18-gauge Tuohy needle (3.5 in.) is suitable for most patients. The lamina of the inferior vertebra (i.e., the lamina of T1 if performing a C7–T1 injection) is noted on AP fluoroscopy. The skin and subcutaneous tissues overlying the area are then anesthetized with 1 % lidocaine. The epidural needle is then slowly advanced under intermittent fluoroscopy until contact is made with the lamina. The depth of the needle should be noted. Once the lamina has been contacted, the stylet is removed and a lubricated 5-ml glass syringe is connected to the needle. The syringe can be filled with air, sterile saline, or both. The needle is then walked off the lamina and into the epidural space. This should be performed using a two-handed technique with the hand holding the needle stabilized against the patient's neck to protect against needle movement if the patient moves. The syringe is slowly advanced while always maintaining continuous pressure against the plunger. Once the bevel passes into the epidural space, there is a sudden loss of resistance. The syringe is then removed from the needle, and 1 ml of contrast is injected. Epidural spread of the contrast should be noted. If subarachnoid spread (dilution) is noted, the procedure should be aborted as the puncture site may act as a gateway for local anesthetic and steroid to enter the subarachnoid space even if the injection is attempted in another intervertebral space.

Once needle location in the epidural space is confirmed, negative aspiration for blood and cerebrospinal fluid (CSF) must be confirmed; then, the medication can be injected. The needle is then withdrawn with a local anesthetic or saline flush to remove steroid from the needle and injection track.

The spread of medication in the epidural space is dependent on volume of injectate, dilation of the veins, anatomic differences in the epidural space, and age and height [7]. A number of local anesthetics can be used including lidocaine and bupivacaine. Generally, about 7 ml is enough volume to adequately cover the nerve roots with local anesthetic and steroid [8].

Hanging Drop Technique

The hanging drop technique is an alternative to the loss of resistance technique to signify entrance into the epidural space. The technique is similar to the loss of resistance technique initially as the Tuohy needle is advanced until lamina is contacted. At this point, instead of attaching a glass/plastic

loss of resistance syringe, the needle is filled with saline until a bubble of fluid is visible at the hub. The needle is slowly advanced, and once the needle enters and passes through the ligamentum flavum, the drop of fluid is drawn in. This is thought to be due to the pressure in the epidural space being lower than atmospheric pressure. A lateral fluoroscopic view can be used to confirm proper positioning of the needle tip in the epidural space. The remainder of the procedure is similar to that described for a loss of resistance technique.

As an alternative to cervical transforaminal injections, a catheter can be used through the translaminar approach and directed to the nerve root as it comes off of the spinal cord. A smaller amount of medication can then be used. There is a much lower risk of injection into a vertebral artery or into a radicular artery while still accomplishing a selective nerve root block. No studies have been published comparing the efficacy of this approach versus a transforaminal approach.

Complications

Drug Related

Corticosteroids: mostly due to systemic absorption and are short-lived. It includes rash, nausea, pruritis, and hyperglycemia. More severe reactions include a Cushingoid response and adrenocortical failure.

Local anesthetics: rash, nausea, and accidental intrathecal injection with resultant spinal anesthesia. Systemic absorption can lead to seizures and refractory cardiac arrhythmias.

Procedure Related

Complications can be associated with both routes of access. These include postdural puncture headaches, infection, development of epidural hematoma (which could lead to quadriplegia), subarachnoid injection leading to a complete spinal block, and direct cervical spinal cord trauma. However, the incidences of these complications are lower in interlaminar injections if the procedure is carried out in a cooperative patient using fluoroscopy and contrast medium [9]. Multiple case reports of serious complications have been reported after cervical transforaminal injections, ranging from paraplegia to death. This is thought to be due to accidental injection of particulate steroid into a cervical radicular artery. This may lead to spinal cord infarction followed by impairment. As stated previously, no head-to-head comparisons have been done between interlaminar and transforaminal cervical epidural steroid injections. Given the positive results seen with the interlaminar approach and the serious complications associated with the transforaminal approach, it may be prudent to consider the former rather than the latter.

Thoracic Epidural Injections

This procedure is becoming more common in the chronic pain management arena. Similar to the cervical epidural procedure, the spinal cord can be injured during this procedure. It must also be remembered that the artery of Adamkiewicz can be located anywhere in the lower thoracic levels.

Indications

There are multiple uses for thoracic epidurals. One of the most common chronic pain uses is for treatment of postherpetic neuralgia. The thoracic dermatomes are the most common location for occurrence of postherpetic neuralgia. It has been shown that performing an epidural with local anesthetic during an acute herpes zoster outbreak may actually prevent PHN from developing [10].

Pain from metastatic disease to the thoracic spine can be treated with epidural analgesia. It is rare for there to be a disk herniation in the thoracic spinal cord, but this too will benefit from injection of local anesthetic and steroid into the epidural space. Other less common indications include pain from angina, pancreatic disease, or incisional neuralgia after thoracotomy or breast surgery.

Contraindications

Absolute: unwilling patient, localized infection over procedure area, current anticoagulant use, bleeding diathesis, increased ICP, and patient that cannot remain still during the procedure.

Relative: allergy to medications that will be injected (contrast, local anesthetic, steroid), pregnancy, immunosuppression, systemic infection, and anatomic changes that would prevent a safe procedure (congenital or surgical).

Thoracic Translaminar Epidural Injection Technique

After discussing the risks and benefits, answering questions, and obtaining written informed consent, the patient is brought into the procedure room and placed in a prone position. The skin overlying the thoracic region is then prepped and draped in a sterile manner.

The angulation of the thoracic spinous process differs at the cephalad and caudal portions of the thoracic levels. They are long and triangular when seen in a transverse section. They are directed obliquely downward and overlap each other between T5 and T8 [11]. This would make a midline approach to the

epidural space very difficult if not unfeasible. The epidural space measures between 3 and 5 mm in width.

AP fluoroscopy can be used to identify the entry level. If the space is above T5 or below T8, a midline or paramedian approach can be used. Between T5 and T8, a paramedian approach must be used due to caudal angulation of the spinous process. The midline approach is performed in the same manner as lumbar level injections (see lumbar procedure in detail). It must be kept in mind that direct injury to the spinal cord is a risk at the thoracic and upper lumbar levels, unlike the lower lumbar levels.

For a paramedian approach, first, anesthetize the skin and subcutaneous tissues with 1 % lidocaine. Starting at 2 cm lateral to the spinous process, advance a 17- or 18-gauge Tuohy needle until contact is made with the lamina. Then, advance the needle 45° to the skin in a cephalad direction and a 30° angle to the midline. This is done with intermittent fluoroscopy to be sure the needle is in a correct path. A loss of resistance syringe is then attached. The needle is then angled cephalad, and for a right-handed practitioner, the left index finger and thumb is placed on the hub and rested on the patient's back. This will help stabilize the needle against inadvertent patient movement.

The loss of resistance technique can be done with continuous pressure on the syringe until there is loss of resistance. Another technique is to make small millimeter advances followed by tapping of the syringe plunger to confirm loss of resistance and entry into the epidural space. Once there is loss of resistance, lateral fluoroscopy can be utilized to confirm location of the needle tip in the epidural space. A false loss of resistance can occur in the subcutaneous tissue, though not commonly in the thoracic levels. It is also possible that a loss of resistance may not occur until the needle is in the subdural or subarachnoid space. Injection of contrast in the subdural space will give a "shifting lake" appearance, and injection in the subarachnoid space will lead to a myelographic pattern of contrast spread. Careful needle control as well as fluoroscopic images in the lateral view will minimize inaccurate needle placement.

Complications

Drug Related

Corticosteroids: mostly due to systemic absorption and are short-lived. It includes rash, nausea, pruritis, and hyperglycemia. More severe reactions include a Cushingoid response and adrenocortical failure.

Local anesthetics: rash, nausea, and accidental intrathecal injection with resultant spinal anesthesia. Systemic absorption can lead to seizures and refractory cardiac arrhythmias.

Procedure Related

Procedural complications include postdural puncture headache (from accidental dural puncture and CSF leak), vasovagal reaction, subdural infiltration, neural injury, and permanent injury to the spinal cord (if in the upper lumbar levels). Permanent spinal cord injury can be secondary to either direct needle trauma or disruption of blood supply to the spinal cord. The artery of Adamkiewicz is a major artery that supplies the lumbar region of the spinal cord. It enters the spinal canal in 80 % of people between T8 and L3 on the left [12]. Injury can be avoided by making sure the needle is not too lateral in the neural foramen on AP fluoroscopy [12].

Lumbar Epidural Injections

Given the high prevalence of back pain and radiculopathy, placing corticosteroid and local anesthetic into the lumbar epidural space is one of the most common procedures performed for chronic pain management. There are many structures in the lumbar region that can lead to pain, including the skin, muscle, fascia, facet joints, intervertebral disk, and the dura of the nerve root. Radicular pain may not always be secondary to nerve root compression by an intervertebral disk (i.e., many patients will have disk herniation by MRI, but not all will have radicular symptoms). Radicular pain can be due to partial axon damage, formation of a neuroma, intraneural edema, and impaired microcirculation [13].

A systematic review by Parr et al. [14] found positive correlations (Level II-2) between short-term pain relief of disk herniation or radiculitis with epidural corticosteroids. Evidence is lacking for long-term relief as well as short- and long-term relief of pain due to spinal stenosis and discogenic pain without radiculitis. This review was performed using studies that employed a blind injection technique (without fluoroscopy), and thus, may have limitations (i.e., incorrect subcutaneous placement of medication leading to false negatives).

Indications

There are many indications for lumbar epidural nerve block, with the most common being lumbar radiculopathy. Table 15.2 shows the more common indications.

Contraindications

Absolute: unwilling patient, localized infection over procedure area, current anticoagulant use, bleeding diathesis, increased ICP and patient that cannot remain still during the procedure.

Table 15.2 Common indications for lumbar epidural injections

Lumbar radiculopathy
Lumbar degenerative disk disease
Lumbar disk herniation
Lumbar spinal stenosis
Lumbar postlaminectomy (failed back) surgery syndrome
Lumbar vertebral compression fractures
Postherpetic neuralgia/herpes zoster
Complex regional pain syndrome (I and II)
Peripheral neuropathy (diabetic, chemotherapy induced, etc.)
Phantom limb pain
Cancer-related pain

Relative: allergy to medications that will be injected (contrast, local anesthetic, steroid), pregnancy, immunosuppression, systemic infection, and anatomical changes that would prevent a safe procedure (congenital or surgical).

Lumbar Transforaminal Epidural Injection Technique

After discussing the risks and benefits and obtaining written informed consent, the patient is taken to the fluoroscopy suite and placed in a prone position. The area of the lumbar spine is then prepped and draped in a sterile manner. AP fluoroscopy is used to identify the level to be injected. An oblique view is then obtained toward the side that will be injected. This is done until the superior articular process of the inferior level is in line with the 6 o'clock position of the pedicle of the superior level. Once the correct view has been obtained, the entry point is marked and the skin and subcutaneous tissues overlying the area are anesthetized with 1 % lidocaine. Using intermittent fluoroscopy, the needle is guided to the target point in small increments. The area in which it is appropriate to place the needle has the following boundaries on AP view: the upper border is a line that runs under the pedicle at the 6 o'clock position, the lateral boundary is a sagittal line that runs caudad from the lateral aspect of the pedicle to the segmental nerve, and the hypotenuse of this triangle connects the two lines and runs parallel to the lateral border of the nerve [15]. It is in this area where there is the least chance of hitting a segmental nerve or a vascular structure. Once the caudal aspect of the pedicle at the 6 o'clock position is encountered, the needle tip is turned caudad until it slips off the pedicle and into the neural foramen. Using a needle with the tip bent away from the bevel can make this step of the procedure easier to accomplish. Lateral fluoroscopy is then used to confirm that the needle is in the neural foramen. Occasionally, if the needle is placed too deep, the patient may experience a paresthesia due to accidental touching of the segmental nerve. The needle should be withdrawn and the paresthesia allowed to resolve. If the paresthesia does not resolve, the patient may be unable to tolerate the remainder of the procedure.

Once the needle is in the correct location, both AP and lateral fluoroscopy should be used to verify its position prior to injection. The AP view should show the needle just inferior to the 6 o'clock position of the superior level's pedicle. Lateral fluoroscopy should show the needle tip in the foramen below the pedicle and in the middle portion of the foramen. Once the needle position is confirmed and negative aspiration for blood or CSF has been observed, 1 ml of contrast is injected during live fluoroscopy in an AP view. The contrast should be seen outlining the nerve root and flowing into the epidural space. The medication can now be injected. The needle is removed with a local anesthetic or saline flush to clear the needle and injection track of steroid. The area that was prepped should be cleansed and a bandage placed over site of needle insertion. The patient should then be taken to a recovery area where they should be monitored for complications resulting from conscious sedation as well as complications from the procedure itself.

Lumbar Translaminar Epidural Injection Technique

After discussing the risks and benefits and obtaining written informed consent, the patient is taken to the fluoroscopy suite and placed in a prone position. A pillow or cushion can be placed under the abdomen to decrease lumbar lordosis and open up the intervertebral space. The area of the lumbar spine is then prepped and draped in a sterile manner. AP fluoroscopy is used to locate the target entry level. Cranial/caudal tilting can be done until the interspace is optimally visualized.

Once the site is chosen and the area is anesthetized, the needle is placed toward the side that the patient has pain (i.e., a patient with left lower extremity radiculopathy over the L4 dermatome should have the needle placed at the left-hand portion of the L4–L5 interspace). A 17- or 18-gauge Tuohy needle is directed under fluoroscopic guidance until the inferior lamina of the entry level is contacted. A loss of resistance syringe is then attached. The needle is then angled cephalad, and a two-handed technique is used to stabilize the needle and advance it slowly toward the epidural space.

The loss of resistance technique can be done with continuous pressure on the syringe until there is loss of resistance. Another technique is to make small millimeter advances followed by tapping of the syringe plunger to confirm loss of resistance and entry into the epidural space. Once there is loss of resistance, lateral fluoroscopy can be utilized to confirm location of the needle tip in the epidural space. A false loss of resistance can occur in the subcutaneous tissue. It is also possible that a loss of resistance may not occur until the needle is in the subdural or

subarachnoid space. Injection of contrast in the subdural space will give a "shifting lake" appearance, and injection in the subarachnoid space will lead to a myelographic pattern of contrast spread. Careful needle control as well as fluoroscopic images in the lateral view will minimize inaccurate needle placement.

After confirming accurate needle placement, negative aspiration should be confirmed for blood and CSF, and 1–2 ml of contrast is then injected to visualize epidural spread. The contrast should have a smooth flow during injection. Once appropriate spread of contrast is confirmed, the medication can be injected. If the target level cannot be entered successfully, lower level can be chosen followed by placement of a catheter through the needle and advanced to intended level.

Injection of the medication may lead to transient paresthesia. It may or may not correspond to the same distribution where the patient has chronic pain. Caution must be exercised to avoid intraneural injection which would cause immediate and severe pain. If severe pain occurs on injection, the needle should be repositioned.

Complications

Drug Related

Corticosteroids: mostly due to systemic absorption and are short-lived. It includes rash, nausea, pruritis, and hyperglycemia. More severe reactions include a Cushingoid response and adrenocortical failure.

Local anesthetics: rash, nausea, accidental intrathecal injection with resultant spinal anesthesia. Systemic absorption can lead to seizures and refractory cardiac arrhythmias.

Procedure Related

Procedural complications include postdural puncture headache (from accidental dural puncture and CSF leak), vasovagal reaction, subdural infiltration, neural injury, and permanent injury to the spinal cord (if in the upper lumbar levels). Permanent spinal cord injury can be secondary to either direct needle trauma or disruption of blood supply to the spinal cord. The artery of Adamkiewicz is a major artery that supplies the lumbar region of the spinal cord. It enters the spinal canal in 80 % of people between T8 and L3 on the left [12]. Injury can be avoided by making sure the needle is not too lateral in the neural foramen on AP fluoroscopy [12].

Other complications associated with procedure are rare, but many case reports have been written. These include infectious processes like meningitis, abscess, and an epidural hematoma (a surgical emergency).

Table 15.3 Common indications for caudal epidural injections

Lumbar radiculopathy
Lumbar degenerative disk disease
Lumbar spinal stenosis
Lumbar postlaminectomy (failed back) surgery syndrome
Postherpetic neuralgia/herpes zoster
Complex regional pain syndrome (I and II)
Peripheral neuropathy (diabetic, chemotherapy induced, etc.)
Phantom limb pain
Cancer-related pain
Sacral/coccygeal neuralgia
Interstitial neuritis
Pelvic pain
Penile/testicular pain

Caudal Epidural Injection

The caudal approach to the epidural space was performed years prior to the lumbar approaches. The first published report was done in 1901 [16]. It has been used for many purposes including obstetric and pediatric anesthesia. Table 15.3 describes some of the indications for a caudal block with emphasis on what is seen in a chronic pain clinic.

One of the primary uses for the caudal approach to the epidural space is in patients who have had lumbar surgery which could make lumbar approaches more difficult or even impossible. Severe degenerative changes may also warrant a caudal approach.

Indications

See Table 15.3.

Contraindications

Absolute: unwilling patient, localized infection over procedure area, current anticoagulant use, bleeding diathesis, increased ICP and patient that cannot remain still during the procedure.

Relative: allergy to medications that will be injected (contrast, local anesthetic, steroid), pregnancy, immunosuppression, systemic infection, and anatomic changes that would prevent a safe procedure (congenital or surgical).

Caudal Epidural Injection Technique

After discussing risks and benefits, answering questions, and obtaining written informed consent, the patient is brought into the procedure room and placed in a prone position.

A cushion can be placed under the lower abdomen which will decrease lumbar lordosis and help decrease the angle of the sacral hiatus. The skin overlying the lower lumbar and gluteal region is prepped and draped in a sterile manner. This procedure can be performed with or without fluoroscopy. Lateral fluoroscopy can be used to identify the sacral hiatus. Manual palpation can also be used to identify the sacral cornu at the entrance to the sacral hiatus. Once the sacral hiatus has been identified, the skin and subcutaneous tissues can be anesthetized. A 22- or 25-gauge needle can be used to enter the sacral canal. It does not need to be longer than 1.5 in. A 17- or 18-gauge Tuohy needle can be used if the plan is to thread a catheter to the lumbar region for more targeted block.

The needle is then inserted at a 45° angle until a "pop" is felt which signifies passage through the sacrococcygeal ligament and then angled caudal to avoid contact with the bone inside the sacral canal. The needle is then advanced about 1 cm, negative aspiration for blood is confirmed, and if using fluoroscopy, contrast can be injected to confirm placement of the needle in the canal. If fluoroscopy is not being used, air can be injected and palpation for crepitus can be performed. If there is resistance to injection of air or contrast, the needle can be rotated as the bevel may be against the bony wall of the sacral canal.

Once the needle is correctly placed, either a medication can be directly injected or a catheter can be placed and advanced to a higher level for a more targeted injection. The medication can then be injected slowly. The spread of medication depends on many factors including the volume and rate of injection. If a catheter is used, less volume can be used as the medication is deposited near the nerve roots, causing pain.

Once the medication has been injected, the needle is removed with a saline or local anesthetic flush to clear the needle and track of steroid. The area that was prepped should be cleansed and a bandage placed over site of needle insertion. The patient should then be taken to a recovery area where they should be monitored for complications resulting from conscious sedation as well as complications from the procedure itself.

Complications

Drug Related

Corticosteroids: mostly due to systemic absorption and are short-lived. It includes rash, nausea, pruritis, and hyperglycemia.

Local anesthetics: rash, nausea, and accidental intrathecal injection with resultant spinal anesthesia. Systemic absorption can lead to seizures and refractory cardiac arrhythmias.

Procedure Related

Procedural complications include postdural puncture headache (from accidental dural puncture and CSF leak), vasovagal reaction, subdural infiltration, and neural injury. Infection, although rare, can be a higher risk with this approach given the needles entry site closer to the anus when compared to lumbar approaches. This is very important consideration especially in immunocompromised patients.

Future Direction for Epidural Injections

Although studies have been performed on the effectiveness (both cost and therapeutic), many studies have been of low grade quality or of insufficient power to make meaningful determinations. There need to be more randomized controlled trials performed on each form of access to the epidural space. Comparison studies should also be performed to determine if access through one route is better than another (i.e., cervical translaminar vs cervical transforaminal).

Conclusion

There are multiple indications for performing epidural steroid injections in the cervical, thoracic, and lumbar regions. There are also many ways to access the epidural space. Each has its benefits and risks, and these must be considered when choosing which route to use in a given patient.

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Transforaminal Epidural Steroid Injections

16

Todd B. Sitzman

Key Points

- Epidural steroid injections are a clinical and cost-effective method for treating acute and chronic spinal pain.
- Transforaminal epidural injections are a more specific treatment than interlaminal epidural injections for radicular but not axial back pain.
- Many pain medicine specialists believe that cervical transforaminal epidural injections are contraindicated given the relatively high-risk benefit ratio; extra training is necessary to complete these procedures safely.

Introduction

Epidural steroid injections (ESIs) play a fundamental role in the treatment of acute and chronic spinal pain and have shown clinical and cost-effectiveness. This is especially true when used in well-selected patients as part of a conservative, non-surgical rehabilitative program. While the epidural space can be targeted by interlaminar, transforaminal, or caudal approaches, this chapter will focus on transforaminal epidural steroid injections (TFESI) including anatomic considerations, patient selection, technique, and outcome. Complications and risk mitigation will be covered elsewhere.

Anatomic Considerations

Knowledge of spinal anatomy, specifically the epidural space, is of significant importance when deciding upon which approach to utilize for an ESI. The epidural space lies between the osseoligamentous structures of the vertebral canal and the dural membrane shielding the contents of the thecal sac: cerebrospinal fluid, nerve roots, and spinal cord. While the thecal sac extends from the foramen magnum to approximately the S2 level, the epidural space extends to the level of the sacral hiatus at S4 or S5.

The epidural space contains adipose tissue, loose areolar tissue, arteries, lymphatics, and a rich venous plexus network. Contiguous with the thecal sac along its entire spinal course, the epidural space is anatomically divided into posterior and anterior compartments. The pain medicine specialist must fully appreciate the anatomy of the epidural space and how it relates to the ESI technique being considered. The posterior epidural space, typically accessed using an *interlaminar* approach, is bordered anteriorly by the thecal sac and posteriorly by the ligamentum flavum and the laminae. The anterior epidural space, most often accessed by a *transforaminal* approach, is bordered anteriorly by the vertebral body, intervertebral disc, and posterior longitudinal ligament and posteriorly by the thecal sac. The sacral epidural space may be accessed inferiorly by a *caudal* approach via the sacral hiatus. There are relative advantages of using one ESI approach over another depending upon the targeted pain generator, anatomic considerations (e.g., previous spinal surgery, decreased interlaminar space), and medical conditions (e.g., anticoagulation status). Interlaminar and caudal ESI approaches are discussed in other chapters. This chapter will focus on the transforaminal ESI techniques, benefits, cautions, and a review of the literature regarding efficacy over non-transforaminal ESI techniques.

A misperception is that transforaminal ESIs have greater diagnostic and therapeutic specificity than interlaminar ESIs. The relative diagnostic "specificity" of a transforaminal ESI corresponds to radicular pain only – not for axial back pain. A smaller volume of injectate, local anesthetic and corticosteroid, used in the transforaminal ESI approach may be more selective for one spinal nerve level. However,

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the injectate also affects several additional neural structures including the sinuvertebral nerve and dorsal primary ramus and its branches.

Patient Selection

Transforaminal ESIs can have a therapeutic role in the treatment of:

- Disc herniation
- Spinal nerve root compression
- Spinal nerve root irritation – traumatic
- Spinal nerve root inflammation – infectious, e.g., herpes zoster
- Spinal stenosis – foraminal or central canal

There may also be a diagnostic role for TFESIs in patients with radicular pain resulting from nerve root compression or in the planning for decompressive surgery [1, 2]. TFESIs may also benefit patients with radicular symptoms at the level of prior decompressive surgery. TFESIs avoid the potential for false-negative results and complications associated with an interlaminar approach at the site of previous surgery. In such cases, epidural fibrosis and adhesions may hinder the spread of epidural injectate from reaching the intended neural target, and scar tissue may increase the risk of dural puncture associated with interlaminar ESIs [1, 2].

Lumbar Transforaminal Approach

The patient is positioned in the prone position on the fluoroscopic table. An oblique view is obtained, aligning the pedicle of the superior vertebra with the superior articular process of the inferior vertebra. The target site is the 6 o'clock position of the pedicle. The skin over this target site is marked and prepped with an appropriate skin antiseptic. Using sterile technique throughout, the skin and subcutaneous tissues are anesthetized with 1 % lidocaine. A spinal needle is slowly advanced toward the target 6 o'clock position of the pedicle using intermittent fluoroscopic imaging. It is not necessary to advance the needle until bony contact, but imaging in multiple fluoroscopic planes (anterior-posterior, oblique, and lateral) is recommended to ensure proper needle tip position. The "safe triangle" for needle tip location, as visualized on an anterior-posterior fluoroscopic plane, corresponds to the following locations: *base* of the triangle is the inferior border of the pedicle, medial *side* of the triangle is the exiting spinal nerve, and lateral *side* of the triangle is lateral border of the vertebral body. The protection offered by the "safe triangle" relates to neural structures, not to vascular structures including the artery of Adamkiewicz.

Following negative aspiration for blood and cerebrospinal fluid, injection of 1 ml of radiocontrast agent under continuous fluoroscopic visualization should reveal contrast spread medially into the neural foramen and the epidural space. Once proper contrast flow has been determined, injection of local anesthetic and steroid admixture may be injected.

Thoracic Transforaminal Approach

In theory, the transforaminal approach to the thoracic epidural space is similar to the lumbar approach. However, there are anatomic differences that must be appreciated. The pedicles of the thoracic vertebrae are directed posterosuperiorly from the transverse process, and there are two costal articulations that are not present in the lumbar spine. In addition to zygapophysial joints, the head of each rib articulates with a superior costal facet at the posterolateral aspect of the vertebral body – located lateral to the base of the pedicle. A transverse costal facet is located at the lateral border of the transverse process. Visualized in the lateral fluoroscopic view, the relatively large neural foramina are bounded superiorly by the inferior undersurface of the pedicle and inferiorly by the superior articular process of the more caudal vertebra.

The patient is positioned in the prone position on the fluoroscopic table. An ipsilateral oblique view of approximately 20° is needed to visualize the pedicle. The target site is the 6 o'clock position of the pedicle. The skin over this target site is marked and prepped, and local anesthetic is infiltrated. A spinal needle is slowly advanced toward the target 6 o'clock position of the pedicle using intermittent fluoroscopic imaging. Fluoroscopic imaging in the oblique, anterior-posterior, and lateral planes is mandatory to ensure that the needle tip is in the superior aspect of the neural foramen, at the 6 o'clock position of the pedicle. Following negative aspiration for blood and cerebrospinal fluid, injection of 1 ml of radiocontrast agent under continuous fluoroscopic visualization should reveal contrast spread medially into the neural foramen and the epidural space. Once proper contrast flow has been determined, injection of local anesthetic and steroid admixture may be injected.

It is mandatory that radiocontrast injection occur under live fluoroscopy to visualize the possibility of vascular uptake. The *artery of Adamkiewicz* supplies the anterior spinal artery of the spinal cord and usually enters the superior aspect of a single neural foramen on the left from T9 through L4. Therefore, when performing left-sided TFESIs, it is recommended to advance the needle toward a more inferolateral position within the neural foramen than in the lumbar spine. Nevertheless, the location of the artery of Adamkiewicz is variable and can traverse the neural foramen bilaterally from T7 through S1. If fluoroscopic imaging reveals contrast flow anteriorly and at the midline, this usually represents trespass of the artery of Adamkiewicz. The needle should be withdrawn and the TFESI postponed while

observing the patient for signs of anterior spinal artery ischemia. Additionally, only non-particulate corticosteroid should be administered with TFESIs to minimize the risk of embolic vascular occlusion of the anterior spinal artery should an intra-arterial injection occur.

Cervical Transforaminal Approach

The cervical epidural space is extremely vascular and is associated with an increased risk of unrecognized vascular injection. The potential for an intravascular injection, specifically arterial, with a subsequent catastrophic event, demands extreme vigilance when performing cervical TFESIs. In fact, many pain medicine specialists feel that there is no indication for a cervical TFESI given the relatively high-risk benefit ratio. Some practitioners would rather use an upper thoracic interlaminar epidural approach and place a radiopaque catheter up to the cervical treatment region for an inside out transforaminal injection.

Following informed consent, the patient is positioned in either a lateral decubitus position or a supine oblique position with a pillow or wedge placed under the ipsilateral shoulder to maintain this position. An oblique fluoroscopic view is obtained to reveal the target neural foramen. The actual needle target is the posteromedial aspect of the mid-superior articular process in the oblique view. This skin over this site is marked, prepped with antiseptic, and anesthetized with 1 % lidocaine. Using sterile technique throughout, the tip of a spinal needle (usually 22-guage) is slowly advanced until it contacts the superior articular process (SAP). Maintaining needle tip over the bony SAP minimizes the risk of inadvertent advancement through the neural foramen into the subarachnoid space – and the potential for cervical cord contact. Once the needle touches the SAP, it is gently walked ventromedially into the posterior aspect of the foramen. Care should be taken to maintain needle tip location in the mid-portion of the posterior neural foramen as the vertebral artery is usually located anteriorly and other vasculature is located superiorly.

After negative aspiration for blood and cerebrospinal fluid, injection of 0.5 ml of radiocontrast agent under continuous fluoroscopic visualization should reveal contrast spread and an outline of the proximal cervical nerve root. In the anterior-posterior view, the contrast agent should spread medially through the neural foramen into the lateral epidural space. Once proper contrast spread location is confirmed in multiple fluoroscopic planes, the local anesthetic and steroid admixture may be injected.

Complications

Transforaminal ESIs possess the potential for catastrophic complications. In general, these complications result from improper needle placement, infection, local anesthetic effect, or corticosteroid effect.

Needle placement complications include pain at the injection site, nerve root injury, puncture of the dural sac, spinal cord injury, epidural hematoma, and postdural puncture headache [3]. Infection risks may include skin or epidural abscess, meningitis, and osteomyelitis. Local anesthetic complications may include motor block or weakness, hypotension, cardiac arrhythmia, seizure, and allergic reaction. Lastly, corticosteroid effects may be more sensitive in some individuals than others. These adverse effects may include fluid retention, elevated blood pressure, hyperglycemia, suppression of the hypothalamic-pituitary-adrenal axis, Cushing syndrome, steroid myopathy, facial flushing, and allergic reaction.

While the complication rate of TFESIs is reported to relatively low, there is the potential for catastrophic events such as paraplegia, quadriplegia, stroke, and death. The mechanism of action is secondary to intra-arterial injection of particulate steroids into a radicular artery supplying the spinal cord, or with cervical TFESIs, direct trauma, or injection into a cervical radicular artery directly feeding into the anterior spinal artery. Intermittent fluoroscopic imaging may frequently miss intra-arterial uptake of contrast. As a result, not only is continuous fluoroscopic imaging of contrast spread mandatory when performing TFESIs at any spinal level, the use of digital subtraction fluoroscopy is highly advised for all cervical TFESIs.

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Facet Injections and Radiofrequency Denervation

17

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Key Points

- The facet joint (zygapophyseal) is a common cause of pain in both the cervical and lumbar spine and less frequently in the thoracic region.
- The innervation of these joints is well defined and varies based on the spinal region being evaluated.
- Lumbar facet arthropathy is characterized by low back pain, unilateral or bilateral, with or without radiation. The pain is described usually as a deep, dull ache; is difficult to localize; and frequently is referred into the buttock, groin, hip, or posterior thigh to the knee.
- Denervation of the medial branch can be accomplished by using either radiofrequency ablation or cryoneurolysis.
- The radiofrequency lesion generator has the following critical functions: (1) continuous online impedance measurement; (2) nerve stimulation; (3) monitoring of voltage, current, and wattage during radiofrequency lesioning; and (4) temperature monitoring. Electric impedance is measured to confirm the continuity of the electric circuit and to detect short circuits.
- Impedance is usually 300–500 in extradural tissue. The nerve stimulator is used to detect proximity to sensory or motor fibers of the segmental root. Stimulation at 50 Hz is used to detect sensory fibers; 2 Hz is used to detect motor fiber stimulation.

Introduction

Each spinal segment from C2 caudal possesses three joints: anteriorly, the disc and associated uncovertebral joint and posteriorly, the paired facet joints. For almost a century, the lumbar facet (zygapophyseal) joint has been considered a significant source of low back pain. Ghormley was the first to describe the facet syndrome, which he defined as a lumbosacral pain with or without radiculopathy, occurring most often after a sudden twisting or rotary strain of the lumbosacral region [1]. Hirsch et al. injected hypertonic saline in the region of the lumbar facet joints, which resulted in pain in the sacroiliac and gluteal regions with radiation to the greater trochanter [2]. Mooney and Robertson performed saline intra-articular facet injections that resulted in a similar pain referral pattern; however, they noted that the pain was relieved by intra-articular local anesthetic injection [3]. Similar findings were produced in the cervical spine, with cervical facet injection of hypertonic saline by Pawl, resulting in neck pain and headache [4].

While low back pain has typically been attributed to degenerative discs, surgical removal of the disc usually does not result in relief from axial back pain. A spinal fusion, which stops the motion of the facet joint, often is required for adequate control of back pain. The pathophysiology of low back pain is a complex issue, with various soft tissues and bony structures of the spine that should be considered as a possible pain generator, and commonly, there is contribution from more than one structure. Among these, the facet joint is involved more frequently.

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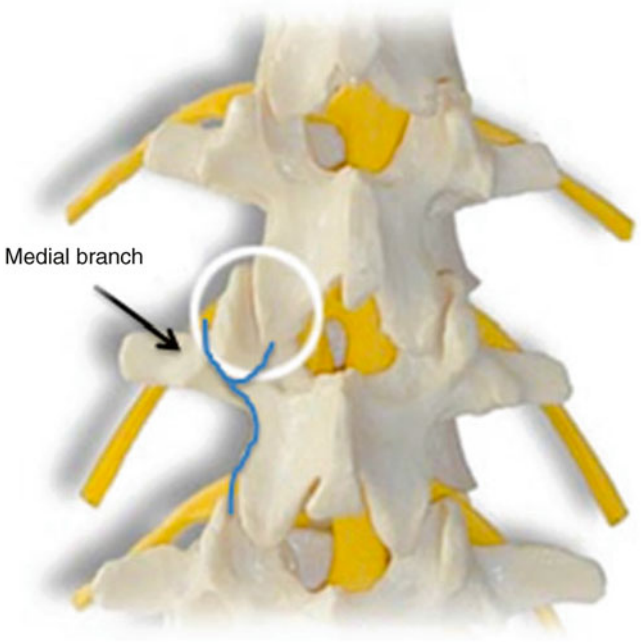

Fig. 17.1 Spine model where a lumbar facet joint is located within a white circle, and the course of a medial branch bifurcating after crossing the transverse process is shown to contribute to a dual innervation pattern

Anatomy

Facet Joints

The facet joints are paired diarthrodial synovial joints formed by the inferior articular process of one vertebra and the superior articular process of the vertebra below [5]. They are present from the C1–C2 junction to the L5–S1 junction. A tough fibrous capsule is present on the posterolateral aspect of the joint. There is no fibrous capsule on the ventral aspect of the facet joint. Instead, the ligamentum flavum is located ventrally, in direct contact with the synovial membrane. Adipose tissue surrounding the spinal nerve is in direct contact with adipose tissue located in the superior recess of the facet joint, allowing direct spread of injectate from the joint to the epidural space and potentially to the spinal nerve [6, 7]. The capacity of the joint space averages only 1.0–2.0 mL in total volume. Communications between ipsilateral or contralateral facet joints do occur, often via defects in the pars interarticularis. These account for some of the spread of anesthetic that can occur during facet intra-articular injections.

Facet Innervation

Each spinal nerve root divides into a posterior and anterior ramus. The posterior ramus, also known as the sinuvertebral nerve of von Luschka, divides approximately 5 mm from its origin into medial, lateral, and intermediate branches. In turn, the medial branch divides into two branches that supply both the facet joint at the same level and the joint at the level below [8]. Therefore, each joint has a dual innervation supply (Fig. 17.1). The location of the medial branch and its divisions vary from the lumbar, cervical, and thoracic regions in relation to the bony structures. In the lumbar region, the medial branch is located in a groove at the base of the superior articular facet, where it crosses the transverse process posteriorly and inferiorly. It then divides, sending a branch medially and cephalad to the joint at the same level and a branch inferiorly to the joint below. The medial branch also supplies the multifidus and interspinalis muscles as well as the ligaments and periosteum of the neural arch [2]. Therefore, neural blockade of the medial branch is not specific for facet joint pain. There is some evidence of joint innervation from a third ascending branch, which originates directly from the mixed spinal nerve (Fig. 17.1) [5, 9, 10]. Innervation of the cervical facet region differs in that the medial branch predominantly supplies the facet joints, with minimal innervation of the posterior neck muscles [11]. The C3–C4 to C7–T1 facet joints are supplied by the medial branches from the same level and the level above [12, 13]. These branches wrap around the waist of each articular pillar bound to periosteum by investing fascia and the tendons of the semispinalis capitis [4]. The medial branch of C8 crosses facet innervation. The C3 medial branch divides earlier in its course into a deep, superficial (3rd occipital nerve) branch (Fig. 17.2). The deep C3 medial branch descends to innervate the C3–C4 facet joint; the superficial medial branch (3rd occipital nerve) traverses the lateral and dorsal surface of the C2–C3 facet joint before entering the joint capsule [11, 13, 14]. The atlantooccipital and lateral atlantoaxial joints receive innervation from the C1 and C2 ventral rami.

The thoracic facet joint innervation has a pattern similar to that of the lumbar region, except for findings from a study of four cadavers that demonstrated consistency of the medial branch course at the superolateral aspect of the transverse processes. The medial branches at these levels travel lateral from the foramen, cross the superior lateral border of the transverse process, and course medial to innervate the corresponding facet joint and level below. However at the T5–T8 levels, the inflection point of the nerve occurs at a point just superior to the superolateral corner of the transverse processes [15].

Pathophysiology

Intervertebral disc space narrowing occurs as the disc degenerates and loses hydration. The change in segment height can cause subluxation of the facet joints, resulting in abnormal stresses on the joint and nerve root impingement. Other sequelae, such as capsular irritation and local inflammation,

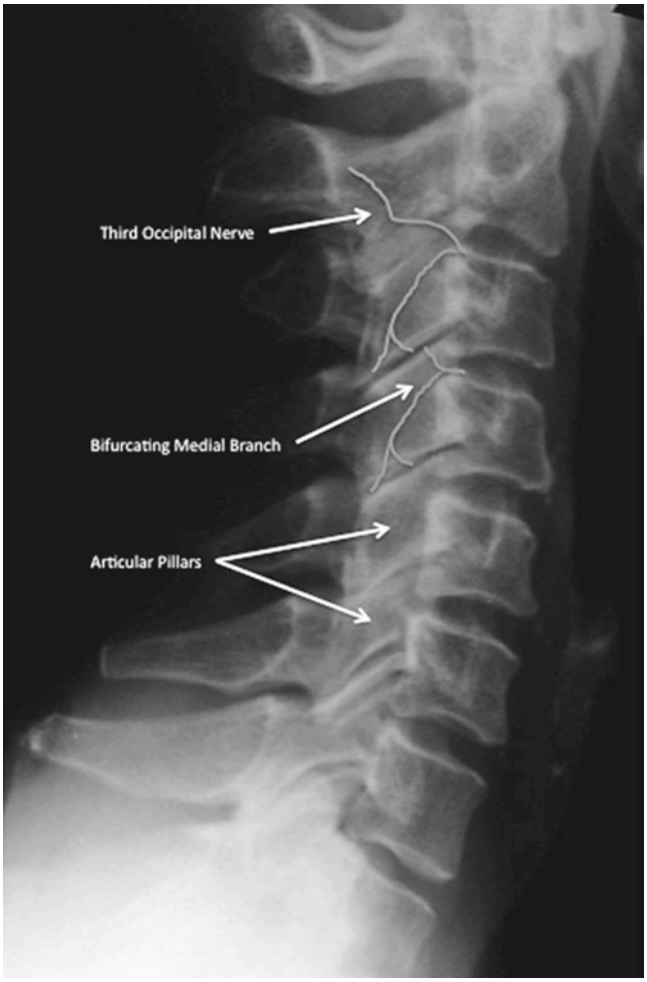

Fig. 17.2 Lateral radiograph of cervical spine identifying the articular pillars, demonstrating the bifurcation of the medial branch at C4 for a dual innervation pattern and the course of the third occipital nerve

may result in reflex spasm of the erector spinae muscles. As degeneration proceeds, abnormal motion leads to osteophyte production, further exacerbating the symptoms [16]. That the facet joint is a source of nociception has yet to be universally accepted. Opponents submit that local anesthetic blockade of the facet joint with subsequent pain relief lacks validity. This position is supported by observations of contrast injection spilling over into the epidural space or intervertebral foramen [7]. Pain elicited with hypertonic saline or relief with local anesthetic administration may be due to action on neural structures or on other pain-sensitive tissues. Proponents for the facet joint as a site of nociception point to the presence of substance P in facet capsule neurons [17]. In addition, most of the mechanosensitive somatosensory units in the facet joint are group-III high-threshold, slow-conduction units, which are thought to mediate nociception [18–20]. Chronic inflammation may lead to fluid accumulation and distension, stimulating the richly innervated synovial villi inside the capsule, resulting in pain.

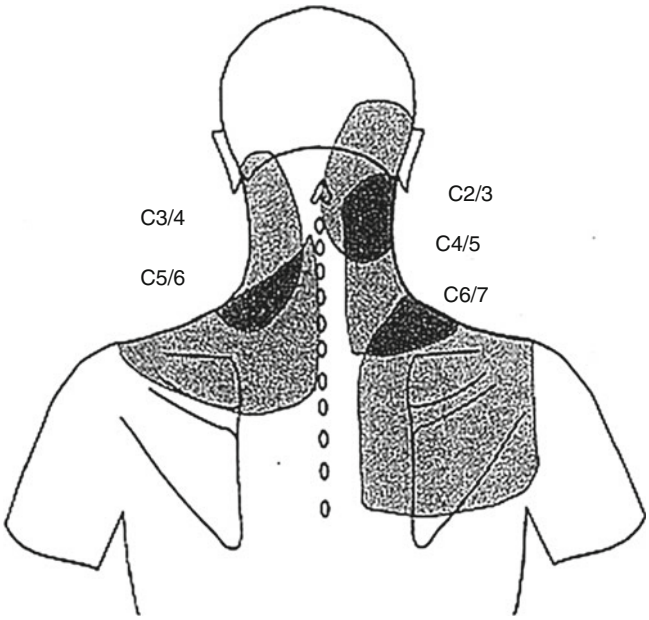

Fig. 17.3 The C3–C4 facet joint refers pain over the posterolateral cervical region, following the course of the levator scapulae. The lower cervical facet joints refer pain to the base of the neck and down to the scapulae

Facet Block: Diagnostic or Therapeutic Tool?

Lumbar facet arthropathy is characterized by low back pain, unilateral or bilateral, with or without radiation. The pain is described usually as a deep, dull ache; is difficult to localize; and frequently is referred into the buttock, groin, hip, or posterior thigh to the knee. Fukui et al. described referral patterns for thoracic facet joints [21].

Some patients describe a sudden onset of pain, usually associated with twisting or bending. There is no exacerbation of the pain with Valsalva maneuver. In contrast to discogenic pain, sitting does not severely aggravate pain secondary to facet arthropathy. The cervical facet joints also cause pain described as deep and aching. Referral patterns vary, depending on which level is of concern. The C1–C2 facet joint may refer pain to the occipital and postauricular region [22]. The C2–C3 facet joint may cause pain referred to the occiput, ear, vertex, forehead, or eye [23, 24]. The C3–C4 facet joint refers pain over the posterolateral cervical region, following the course of the levator scapulae. The lower cervical facet joints refer pain to the base of the neck and down to the scapulae (Fig. 17.3) [23]. Physical examination often reveals tenderness over the facet joints and involves associated muscle spasm. The pain is exacerbated by extension or lateral bending as opposed to flexion as well as prolonged sitting. A few patients may exhibit mechanical hyperalgesia over the associated innervated skin. Whereas range of motion in all directions may be reduced, extension and rotation are most uncomfortable. Straight leg raise is usually negative. To make

the diagnosis of a painful facet joint requires the typical history and physical findings already described in combination with diagnostic blocks. The use of facet block for diagnosis is hampered by certain pitfalls. There is a lack of a corresponding cutaneous innervation to the facet joint and thus an inability to determine when complete blockade has occurred. Injection into the joint often results in joint capsule rupture and spillage of local anesthetic into the epidural space or intervertebral foramen, which can interrupt nociceptive impulses from alternative sites [20, 25–27]. The medial branch nerve innervates muscles, ligaments, and periosteum in addition to the facet joints, again limiting specificity of the test. Facet blocks should be avoided in patients with systemic infection, infection at the site, or coagulopathies or in patients who refuse the procedure. Needle placement for facet injection as well as local anesthetic delivery can result in pain provocation. A provocative response that is concordant with the patient's ongoing complaints lends further support to the notion that the facet joint is the pain generator. Facet injections are commonly used for both therapeutic and diagnostic interventions. Intra-articular steroid injection often produces significant pain relief that outlasts the action of a local anesthetic [26, 28–30]. Although therapeutic benefit from steroid has been demonstrated, duration of outcomes is limited, similar to intra-articular steroids delivered to other joints [3l–33]. Intra-articular block also does not correlate well with the success of radiofrequency denervation (only 64 %); therefore, medial branch block is the preferred procedure as a trial prior to facet denervation [34].

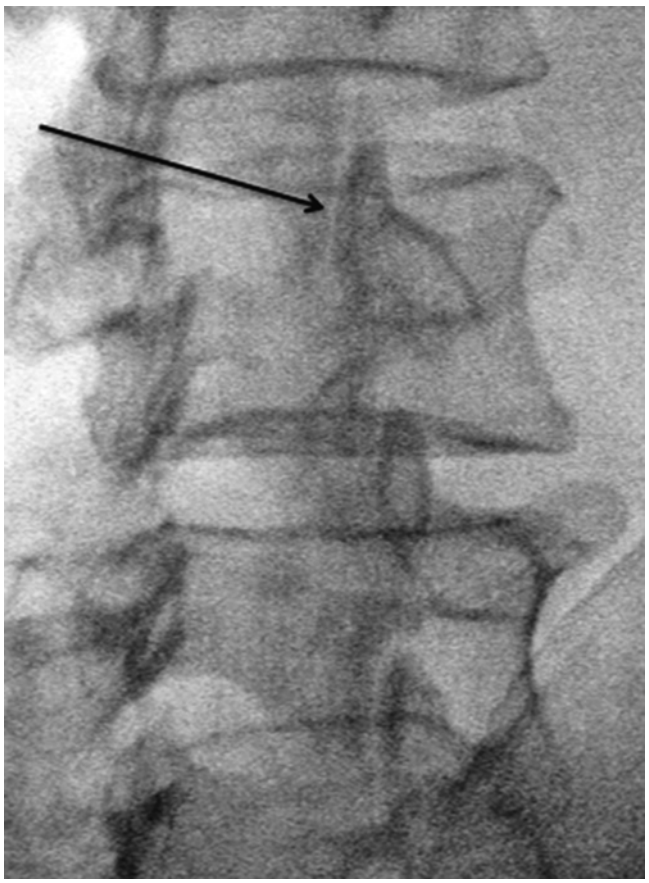

Fig. 17.4 "Scotty dog" view of facet joint at a 30° angle for intra-articular injection

Technique

Lumbar and Thoracic Facet Blocks

For facet joint injection, the patient is positioned prone, with an abdominal cushion to reduce lumbar lordosis. Sterile preparation and draping of the back are performed. Intra-articular injection requires oblique fluoroscopic views. Best results are achieved at a 30–45° plane to "open" the joint. Either the table or the C-arm can be rotated for optimal viewing. The entry point through the skin then is identified and marked with the aid of a radiopaque instrument. The skin is infiltrated with 1 % lidocaine using a 25-gauge needle. A 22-gauge, 3.5-in. spinal needle then is introduced via the skin wheal and advanced into the joint using a trajectory parallel to the fluoroscopy beam. Local anesthetic alone or with steroid (0.25 % bupivacaine and 20 mg Depo-Medrol (methylprednisolone acetate)) is delivered in a volume of 1.0–1.5 mL. Volumes in excess of 2 mL will rupture the capsule and spill over into the epidural space (Fig. 17.4). For medial branch block, the patient is positioned prone, and the transverse process for each branch to be blocked is identified using fluoroscopy. Approximately 5 cm from the midline, a skin wheal is raised, and a 22-gauge, 3.5-in. spinal needle is advanced to the medial end of the transverse process, contacting the dorsal surface of the process near the superior edge. The L-5 medial branch is blocked at the groove between the ala of the sacrum and the superior articular process of the sacrum (Fig. 17.1). A total volume of 1.0 mL of 0.5 % bupivacaine is delivered at each site, and the patient is questioned for concordance compared with the original pattern of referred pain (Fig. 17.5). The technique is slightly altered for the thoracic levels, where the superolateral aspect of the transverse processes is the ideal site for placement.

Cervical Facet Block

The patient is ideally positioned prone to reduce potential injury to the vertebral arteries, but a lateral position has also been described. Sterile technique and needles are used as previously outlined. Needles are introduced 1–2 cm lateral to the waist of the articular pillar, guided by a posteroanterior view on fluoroscopy. The needle then is advanced to the centroid of the articular pillar as seen on a lateral view (Figs. 17.6 and 17.7). Again, 1.0 mL of local anesthetic is deliv-

ered. Intra-articular injection at the cervical level is not favored for several reasons. Cervical joint spaces are small and narrow. Further, the epidural space is immediately medial to the joint, and the vertebral artery is just lateral to the joint. Therefore, direct injection into cerebral circulation or blockade of cervical nerve roots is of great concern.

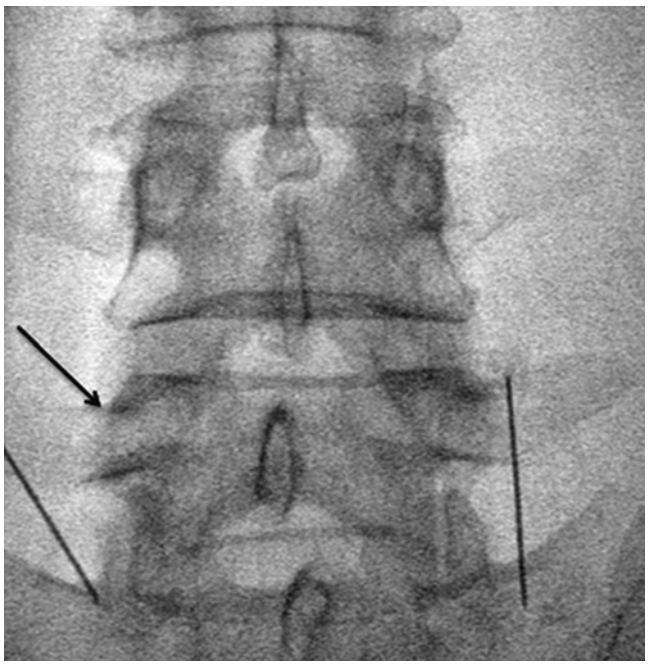

Fig. 17.5 AP view of lumbar facet medial branch block with needle at groove of sacral ala and arrow pointing to desired placement at superomedial aspect of the L5 transverse process

Facet Joint Denervation

Denervation of the medial branch can be accomplished by using either radiofrequency ablation or cryoneurolysis. This chapter will focus on the radiofrequency method in terms of its mechanism of action, followed by the results of long-term outcome studies.

Conventional Radiofrequency Ablation

The radiofrequency lesion generator has the following critical functions: (1) continuous online impedance measurement; (2) nerve stimulation; (3) monitoring of voltage, current, and wattage during radiofrequency lesioning; and (4) temperature monitoring. Electric impedance is measured to confirm the continuity of the electric circuit and to detect short circuits. Impedance is usually 300–500 Ω in extradural tissue. The nerve stimulator is used to detect proximity to sensory or motor fibers of the segmental root. Stimulation at 50 Hz is used to detect sensory fibers; 2 Hz is used to detect motor fiber stimulation. Ford et al. demonstrated that if the electrode is resting on the nerve, 0.25 V will be required to produce discharge, whereas 2 V will be required to produce discharge at a distance of 1 cm [35]. Therefore, monitoring voltage is important in determining proximity. Temperature monitoring occurs at the tip of the electrode only, with a thermocouple technique, producing a thermodionic voltage that is proportional to temperature. Bogduk et al. performed lesions in egg whites and meat and found that radiofrequency lesions do not extend distal to the electrode tip. Instead, lesions extended radially around the electrode tip in the shape of an oblate spheroid with a maximal effective

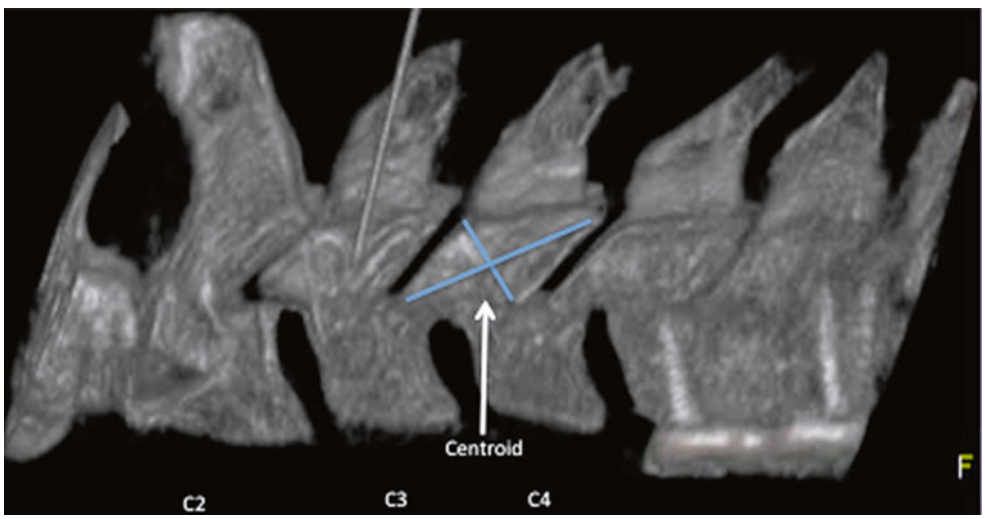

Fig. 17.6 With a lateral view of the cervical articular pillar, the intersection of lines connecting the opposite corners locates the centroid of the articular pillar where the medial branch typically will be found

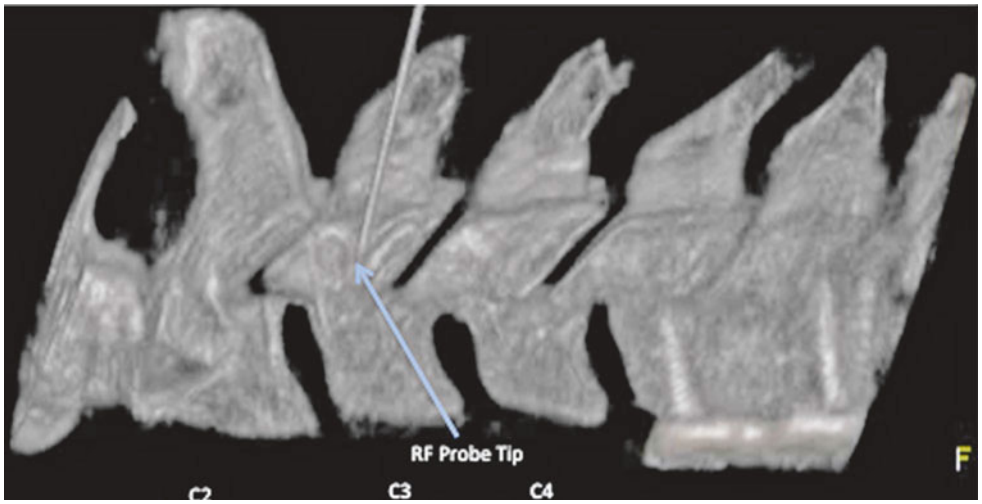

Fig. 17.7 Lateral view of 3-D reconstructed image demonstrating needle placement at the centroid of the C3 articular pillar

Table 17.1 Relationship of lesion size with tip sizes and temperatures

Authors	Electrode diameter (mm)	Exposed electrode tip length (mm)	Tip temperature (C)	Transverse lesion size (mm)	Test medium
Bogduk et al. [38]	186	5	80	2.2 ± 0.4	Egg
	226	4	80	1.1 ± 0.2	Egg
	226	4	90	1.6 ± 0.2	Egg
Cosman et al. [36]	216	3	65	2–4	Egg
Guy, et al. [37]	216	2	60	3.7	Rabbit cortex
	216	2	70	5.5	Rabbit cortex
	216	2	80	7.2	Rabbit cortex
Vinas et al. [39]	206	4	80	4.9	Rabbit cortex

radius of 2 mm using a 21-gauge electrode with a 3-mm exposed tip [38]. Table 17.1 demonstrates a survey of varying tip sizes and temperatures with the corresponding lesion size. The first signs of coagulation occur at 62 °C, but it is important to note that neural destruction begins at 45 °C. The maximal lesion size is attained once the "working" temperature is maintained for 20–40 s. Maintaining the temperature for longer periods did not result in any discernible increase in lesion size [39]. Although initial reports indicated selectivity for small fibers, Uematsu conclusively showed that radiofrequency at higher temperatures indiscriminately damages both small and large fibers [40]. Placement of the probes requires positioning of the active tip along the course of the medial branch as previously described (see Figs. 17.8 and 17.9).

Retrospective studies of lumbar facet RF denervation have demonstrated similar rates of success. Goupille et al. showed a 38.4 % success rate at 2-year follow-up, and North showed a 45 % success rate with a mean follow-up of 3.2 years [41–43]. North et al. went further, concluding that there was no difference in success for bilateral denervation for bilateral pain compared with unilateral denervation for unilateral pain [43]. Goupille et al. reported that patients who did not have prior spine surgery had better success with denervation, whereas North's group did not show any statistical difference between these groups (Table 17.2). Van Kleef et al. performed a lumbar facet RF denervation double-blinded RCT in 31 patients with 80 C lesions at L3–L4, L4–L5, and L5–S1 with a sham control. At 8 weeks, mean VAS score was 4.8 for controls and 2.8 for the treated group. This was statistically significant for both differences in VAS but for Oswestry scores as well. In the treated group, 10/15 patients were successfully treated (at least 2-point reduction on VAS and greater than 50 % pain relief) at 8 weeks, and of these patients, seven were still a success at 12 months [44]. Nath et al. performed a sham-controlled RCT of lumbar facet RF denervation in 40 patients after at least 80 % pain relief was documented from controlled medial branch blocks. The RF group had multiple lesions performed at each level. At 6 months, the RF group had statistically significant improvement in VAS scores and with the patients' global assessment in comparison to the sham group. There was also

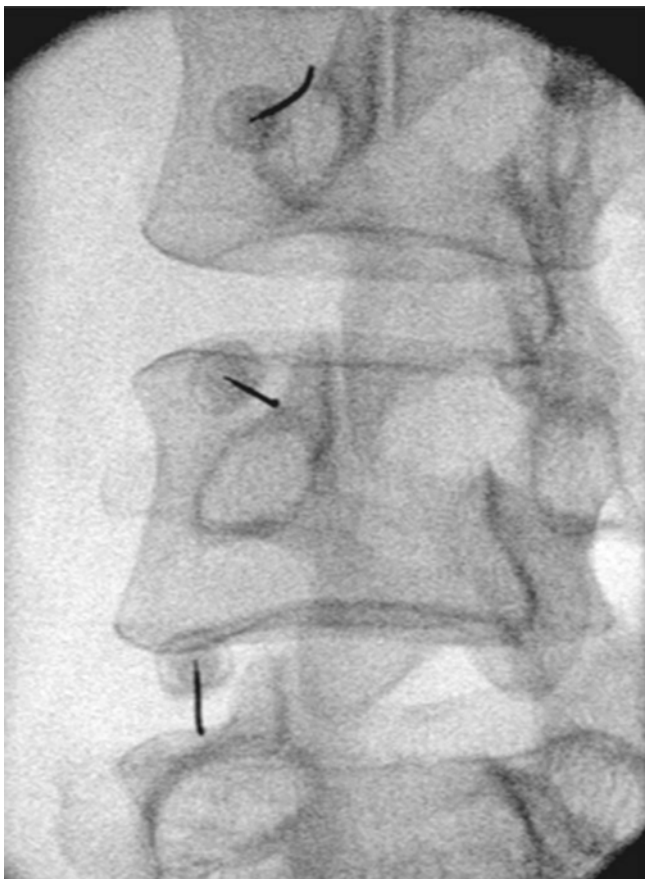

Fig. 17.8 Oblique view demonstrating placement of RF cannulae after contact with the "eye" of Scotty dog and slipped off the superior margin of the transverse processes

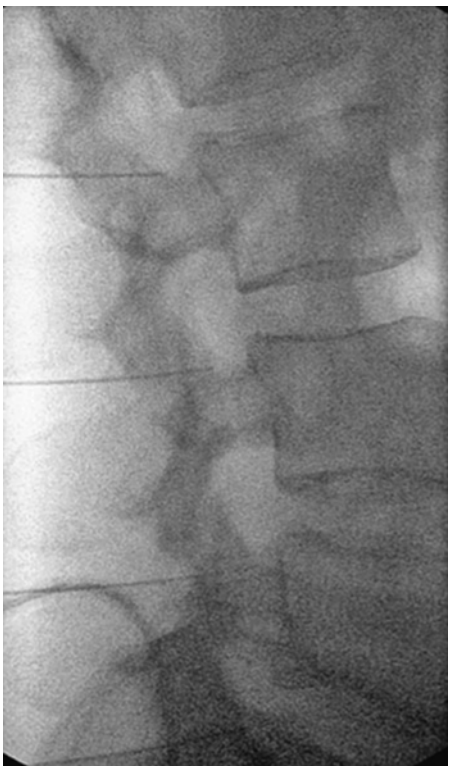

Fig. 17.9 Lateral view of placement of RF cannulae along the lumbar superior articular processes

significant improvement in secondary measures such as spine range of motion, quality of life measures, and physical exam findings posttreatment [45]. A 10-year prospective clinical audit of lumbar facet RF denervation in 209 patients was able to have 2-year follow-up data on 174 of the patients. Of these individuals, 119 (68.4 %) had good (>50 %) to excellent (>80 %) relief at 6 months. At 12 months, 81 patients still had good to excellent relief, and this was maintained in 36 patients at 24 months (Table 17.2).

Stolker et al. reported on 40 patients who underwent thoracic facet denervation with a mean follow-up of 31 months [47]. They found that 44 % were pain-free and 39 % had greater than 50 % relief. Stolker and coworkers also performed a cadaver study, with fluoroscopic guidance, in which radiofrequency denervations were performed bilaterally at T1–T12. They found that 61 % of the lesions hit neural tissue, but none hit the medial branch stem (the "target") [48]. The nerve stimulator should be used in an attempt to reproduce the patient's usual pain complaints and achieve better localization of the thoracic medial branch.

A randomized, double-blind trial of 24 patients with cervical facet pain after a motor-vehicle accident was performed to compare percutaneous radiofrequency denervation of multiple lesions at 80 °C with controls. Patients were selected for study after confirmation of cervical facet syndrome by use of double-blinded, placebo-controlled diagnostic local anesthetic blocks. Follow-up assessment was performed to determine the time until pain returned to 50 % of the preprocedural level. Radiofrequency patients had a median duration of relief of 263 days compared with 8 days in the control group [49]. In a separate study, psychological distress was measured by the McGill Pain Questionnaire and the SCL-9O-R psychological questionnaire in patients with whiplash injury. A significant resolution of psychological distress was associated with pain relief from cervical facet radiofrequency denervation [50]. A prospective study was performed to assess for differences in outcomes of cervical facet RF denervation for treatment of whiplash symptoms based on litigation status. Patients with pain that persisted after 20 weeks were referred for RF treatment and followed for 1 year (N = 46). There was significant improvement in pain immediately after treatment and at 1 year follow-up, but no statistical difference between litigants and nonlitigants. Pain scores for nonlitigants were reduced by 2.0 immediately and by 2.9 at 1 year and by 2.5 and 4.0, respectively, for litigants [51].

Table 17.2 Series showing lumbar facet RF denervation

Author, year	Technique	Study design	*N*	Length of follow-up	Outcomes	Key details
Goupille et al. 1993 [43]	Conventional RF	Retrospective	103 enrolled, 86 completed questionnaire	24 months	38.4 % had >50 % pain relief	Success rate was higher with no prior discectomy
North et al. 1994 [43]	Conventional RF	Retrospective	42	Mean follow-up of 3.2 years	45 % had >50 % pain relief	Assessment by disinterested 3rd party, no difference in success regardless of prior history of back surgery
Van Kleef et al. 1999 [44]	Conventional RF	Prospective, randomized double-blind, sham-controlled	31	12 months	Success = >50 % pain relief and ≥2-point decrease in VAS score Treated: 46.7 % at 6 months and at 12 months Sham: 18.8 % at 6 months and 12.5 % at 12 months	Excluded patients with prior history of back surgery
Nath et al. 2008 [45]	Conventional RF	Prospective, randomized double-blind, sham-controlled	40	6 months	Treated patients had mean decrease of VAS score by 1.9, only 0.4 decrease in the sham group	Treated patients had improved physical exam findings and statistically significant decrease in analgesic use
Gofeld et al. 2007 [46]	Conventional RF	Prospective, observational	209 treated, 174 completed 2-year assessment	24 months	Success = >50 % pain relief At 6 months, 68.4 % had success, 46.5 % at 12 months, 20.7 % at 24 months	83.2 % of patients with success reduced analgesic consumption

In regard to recurrence of pain and repeat treatment, two reports of small (20 and 24 patients) retrospective studies of repeat procedures after successful RF were identified for cervical and lumbar facet denervation. In both series, more than 80 % of patients had >50 % relief from repeat RF treatment, and mean duration of relief from subsequent RF treatments was comparable to the initial treatment [52, 53].

Pulsed Radiofrequency Ablation

Pulsed radiofrequency (PRF) treatments involve the application of short pulses of RF energy to neural tissue ranging from 5 to 50 ms with a frequency ranging from 1 to 10 Hz. The most common setting described is 2 Hz and 20 ms, with the goal of keeping the tissue temperature below the denaturation threshold of 45 °C. This method has been theorized to be non-ablative and provide relief by inducing intracellular changes, but has not been determined to have either of these benefits in a definitive manner [54–56]. In vitro studies suggest that PRF may change morphology of mitochondria, alter axonal structures, and has been demonstrated to reduce neuropathic pain behavior in the rat Chung model as well as sciatic nerve ligation study in rabbits [56, 57]. The clinical experience for utilization of PRF for lumbar facet pain has been positive, but does not appear to enjoy the same duration of effect as conventional RF. Tekin et al. performed a randomized trial of PRF vs. conventional RF, with similar rates of improvement at 6 months, but only the RF group had maintained benefit at 1 year [58]. Van Zundert et al. randomized 23 patients to PRF vs. sham treatment, and had better results immediately, but not significantly different at 6 months [59].

Complications

Complications from facet block are infrequent and transient. A brief exacerbation of pain may occur and last a few days to a few weeks. Intrathecal injection has been reported, as well as one case of chemical meningitis [60]. Epidural blockade has occurred, and vertebral artery puncture and strokes have been described at the cervical level. Radiofrequency dener-

vation resulted in postprocedure pain in 13 % of patients in one study; the pain resolved spontaneously over 2–6 weeks. No persistent motor or sensory deficits were reported.

Systematic Literature Reviews

A 2007 systematic review of facet joint interventions utilizing AHRQ criteria found that the evidence for pain relief with RF denervation is moderate for short- and long-term pain relief at the cervical and lumbar levels but was indeterminate for thoracic facets [61]. A 2009 systematic review of diagnostic utility and therapeutic effectiveness of cervical facet joint interventions by Falco et al. found level II-1 or II-2 evidence (controlled trials without randomization, and cohort or case control studies from more than one center) for RF neurotomy in the cervical spine using the US Preventive Services Task Force (USPSTF) quality ratings [62]. Using the same rating system, Datta and colleagues found level II-2 and level II-3 (cohort or case control studies from more than one center, and multiple time series with or without the intervention) evidence for lumbar radiofrequency neurotomy [63]. Van Boxem and colleagues in a review of evidence for continuous and pulsed RF note that RF at the cervical and lumbar level has produced the most solid evidence, and differences in outcome among RCTs can be attributed to differences in patient selection and/or inappropriate technique [64].

Conclusion

The facet joints are a common source of axial spine pain with well-described referral patterns, but methods for diagnosis remain underutilized. Specificity of local anesthetic injection is limited, but medial branch block is clearly preferred compared with intra-articular injection when attempting to prognosticate relief from denervation.

Local anesthetic injections as well as RF denervation are performed easily, are well tolerated by patients, and are extremely safe. Meaningful pain relief can be achieved in about 50 % of patients for a significant duration. Directions for future study include investigation of outcomes of thoracic facet RF denervation with a randomized controlled trial, and for patients with multiple areas of degenerative changes, outcomes of combined denervation treatments across targets are desirable.

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Intercostal Nerve Blocks

18

Eduardo M. Fraifeld

Key Points

- Intercostal nerve blocks are relatively simple procedures that can prove effective in the properly selected patient.
- The anatomical knowledge required to do this procedure is straightforward.
- Despite the perceived simplicity of the procedure, the risks are serious and should be carefully considered prior to doing the block.
- The use of fluoroscopy is helpful in determining landmarks for needle placement.

> And the Lord God caused a deep sleep to fall upon the man, and he slept; and He took one of his ribs, and closed up the place with flesh instead thereof. (Genesis 1:21)

Introduction

Intercostal nerve blocks (INBs) are relatively simple to perform and can provide excellent analgesia or anesthesia to the human torso. They provide relatively well-defined anatomical coverage, making them both an excellent diagnostic tool and a reliable therapeutic procedure. In addition, they are among the simplest of peripheral nerve blocks performed with a relatively low incidence of complications.

Many consider epidural anesthesia (see Chap. 34) the best method of providing analgesia to the torso; however, it requires greater technical skills and has potential side effects including undesired hypotension, urinary retention, and risks of nerve root or spinal cord injury. Furthermore, the widespread use of anticoagulants often results in epidural techniques being contraindicated due to coagulopathy. Interpleural block (see Chap. 38) has similarly been suggested as a reliable method with the added advantage of a localized sympathetic block. However, its shorter lasting effect and resulting significantly higher plasma concentrations of local anesthetic [1] make it less optimal choice.

Increasingly, the literature is looking at paravertebral nerve blocks (PVNBs) as a better alternative to epidurals. One recent systematic review and meta-analysis of randomized trials comparing PVNB with epidural analgesia showed equivalent analgesia with better outcomes in PVNB [2] corroborating findings in previous studies [3–7].

Anatomy

The intercostal nerves originate from 12 paired thoracic nerve roots that are intimately associated with the thoracic ribs (see Figs. 18.1, 18.2 and 18.3). Knowledge of their anatomy and relation to surrounding structures is vital to successfully performing these procedures.

Ribs

- True ribs – first to seventh, connect directly to the sternum through costosternal cartilages.
- False ribs – eight to tenth, so-called because their cartilages do not reach the sternum directly but instead attach to the rib immediately above.
- Floating ribs – 11th and 12th, only reach to cover the back and do not have attachment to the sternum.
- Costochondral joints – the articulation between the rib and the cartilage connecting them to the sternum. They start at the first rib, just lateral to the sternum. As they go inferior, they become more lateral till the tenth rib; it is almost at the anterior axillary line.

Nerves

As the thoracic nerve roots emerge from the intervertebral foramen, they immediately split into the ventral rami that form

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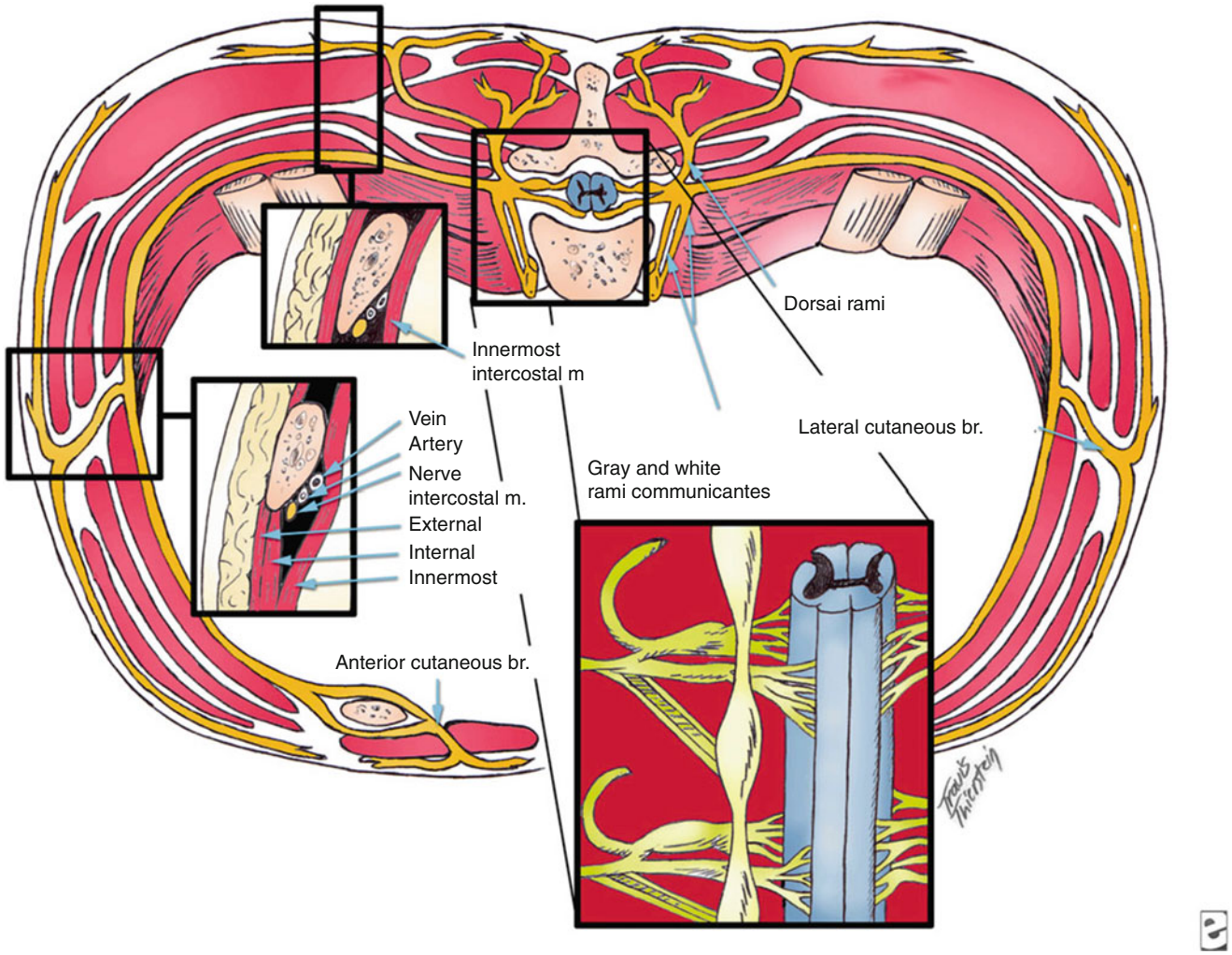


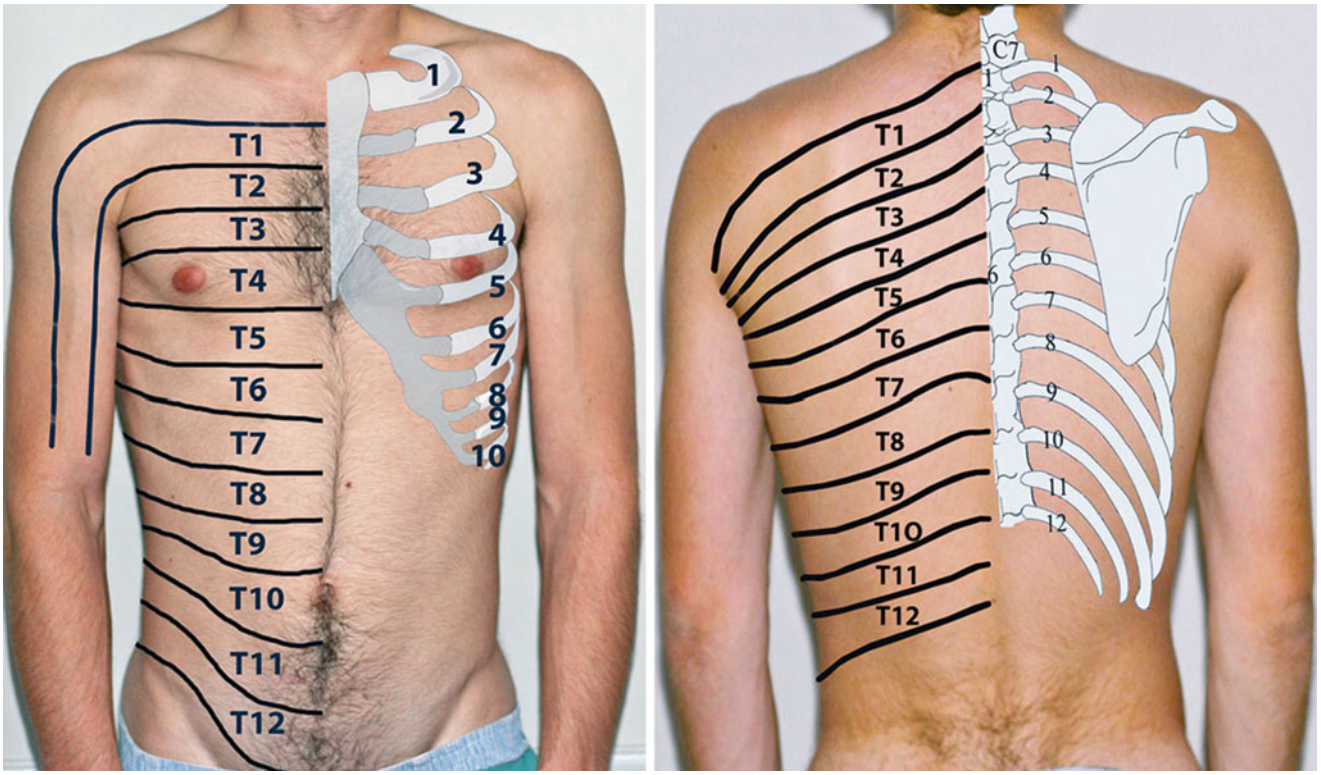
Fig. 18.1 Branches of thoracic spinal nerve roots (Reprinted with permission from eMedicine.com, 2010. Available at: http://emedicine.medscape.com/article/1143675-overview)

the intercostal nerves and the posterior rami (see Fig. 18.1). Anterior branches form the gray and white rami communicantes of the thoracic sympathetic chain. The posterior rami innervate the zygapophyseal (facet) joints, muscles and skin of the thoracic midline, and paraspinous area of the back.

The intercostal veins, arteries, and nerves (VAN) travel for the most part in the costal grove, protected from direct trauma with the nerve being most inferior on the edge of the rib. After exiting the foramen, the intercostal nerves are near the middle of the intercostal space between the parietal pleura and the inner side of the intercostal muscles. As the nerve approaches the angle of the rib, the nerve then emerges between the internal intercostal muscle layer and the outer portion of the innermost intercostal muscle to its location on the costal groove.

Small collateral nerve branches develop as the intercostal nerve progresses anteriorly, innervating the intercostal muscles and the ribs. At about the midaxillary line (MAL), the lateral cutaneous nerve arises. The lateral cutaneous nerve splits into posterior and anterior branches that innervate the skin of the chest wall from the scapular line to midclavicular line. The intercostal nerve continues anteriorly within the costal groove between the internal intercostal muscle layer and the outer portion of the innermost intercostal muscle, but as it progresses anteriorly, it once again emerges internal to the innermost intercostal muscle. As intercostal nerves approach the sternum, they emerge as the anterior cutaneous branches, innervating the anterior chest.

- Thoracic nerve roots – branch into the dorsal primary rami and the anterior rami which become the intercostal nerves.
- Dorsal primary rami – innervate the posterior midline and paraspinous muscles and skin.
- Intercostal nerves – innervate distinct band-like segments of muscles (myotomes) and skin (dermatomes).
- Collateral branches – arise from the intercostal nerves to innervate the intercostal muscles and ribs.



Figs. 18.2 and 18.3 Dermatomes of thoracic nerve roots and relation to ribs

- Lateral cutaneous nerve branches – arise in the MAL and divide into anterior and posterior branches to innervate the skin of the majority of the torso.
- Anterior cutaneous nerves – divide into medial and lateral branches to innervate the skin of the anterior torso
- Cross innervation – as the nerves travel distally, they overlap so that even total loss of a single nerve root is unlikely to produce a noticeable sensory loss. To develop a complete sensory loss, usually you have to block two to three intercostal nerves.
- The optimal site for injection of the intercostal nerve is at the angle of the ribs where they are the thickest as noted in various studies [8–10]. This is about 15 cm from the spinous process [3, 4].

Special Considerations

1. First, intercostal nerve arises from the ventral ramus, but a portion of the ventral ramus goes on to join the brachial plexus.
2. Second, intercostal nerve also supplies a small branch of the ventral ramus to the brachial plexus.

Dermatomal Distribution

Dermatome distribution maps of intercostal nerves have long been published from a variety of sources and should always be viewed as approximations [11, 12]. In particular as noted above, a single intercostal nerve block seldom results in a total anesthesia of single dermatome due to cross innervation; however, dermatome charts can be used as a guide in selecting level of placement of intercostal nerve blocks (see Figs. 18.2 and 18.3).

Local Anesthetic

Local anesthetic choices are similar as in other nerve block procedures, the most common being lidocaine or bupivacaine. For single-shot INB, a volume of 3–5 mL is usually more than adequate per level injected. Total dose however should be monitored to reduce the risk of systemic toxicity. Alkalinization of the local anesthetic for intercostal nerve blocks has been found to be of little clinical benefit [13].

The use of epinephrine has been proposed as a possible increased safety factor by constricting local vessels and reducing uptake or by producing a tachycardia as a warning sign of accidental intravascular injection. However, other studies have called this into question and shown increased hemodynamic changes compared to other types of nerve blocks [14].

For continuous INB, an infusion of 0.25 % bupivacaine at 2 mL/h is usually adequate.

Clinical Applications

INB has been shown to be useful for a variety of anesthetic and analgesic uses in the distribution of the torso. Among these are:

1. Post-thoracotomy pain
2. Post-rib fracture pain
3. Cancer pain
4. Mastectomy and breast surgery pain
5. Shingles pain
6. Intercostal neuralgia
7. Costochondritis
8. Abdominal wall pain

Studies have shown that INB for post-thoracotomy pain offers advantages in preserving effort-dependent pulmonary function compared to opioid analgesia [15, 16].

The first three intercostals also innervate sensation portions of the upper arm and axilla, while the lower intercostals from T6 to T12 innervate the muscles of the upper abdomen and overlying skin [17]. Therefore, intercostal nerve blocks at the appropriate level can easily control symptoms in the affected region, allowing for decreased dependence on opioid analgesics. This can be useful in cases where one needs to avoid respiratory depressant or mental status changes.

Effective perioperative analgesia with continuous INB also has been demonstrated to reduce the incidence of chronic post-thoracotomy neuralgia [18]. While bupivacaine single-shot INB is reported to last longer than lidocaine, no significant difference has been reported in the outcome between infusions of lidocaine or bupivacaine for continuous infusions [19].

Trauma to an intercostal nerve by thoracotomy can lead to either pain or a sensory loss over the skin of the affected nerve or pain assisting in identifying the level injured. Similarly, trocar placement during laparoscopic procedures such a cholecystectomy can lead to similar problems. Numerous studies also have looked at use for a variety of conditions as noted above. Most studies are anecdotal, as noted in a recent case report on treatments for costochondritis [20].

Technical Tips

- Some studies have suggested that a short-beveled needle is likely to be safer and more accurate for INB [21].
- Continuous intercostal catheter analgesia is a more efficient way of performing INB, allowing a longer therapeutic effect. For most applications, an epidural catheter kit is the most convenient to use.
- Use of elastomeric infusion pumps has been shown to be a safe and effective adjunct in postoperative pain management after thoracotomy [22].

Paravertebral Nerve Block

The thoracic paravertebral space is a somewhat triangular space that is laterally continuous with the intercostal space [23, 24]. Anatomical borders are:

- Medial border – vertebral body, intervertebral disk, and spinal foramina
- Posterior border – transverse process, superior costotransverse ligaments, and ribs
- Anterior border – parietal pleura

Intercostal nerves, their collateral branches and posterior primary rami, and the thoracic sympathetic chain all pass through the paravertebral space, making it an ideal site for blockade of the various afferent nociceptive nerve impulses [25].

The mechanism of action of the PVNB is intercostal nerve block via the paravertebral spread of local anesthetic [26]. Spread of a mean of six dermatomes (range, five to seven) has been demonstrated by injection of methylene blue at thoracotomy and infusion of contrast medium in postoperative patients [26]. Techniques described have included blind placement [27, 28], by neurostimulator [29], by loss of resistance, by and ultrasound.

Clinically, PVNB is comparable with epidural block in respect to pain relief but without the well-known side effects of the epidural analgesia [30]. PVNB is therefore seen as a useful technique for pain control of breast, thorax, and abdomen, and many have considered it the technique of choice [31–33]. While one prospective study failed to that show a single-shot PVNB was superior to continuous wound infiltration [34], the technique of continuous catheter PVNB is gaining popularity. The ability to perform this effectively at bedside with ultrasound guidance [35] also simplifies the ability to perform this procedure in a greater variety of settings.

The effectiveness of PVNB injections with local anesthetic and steroids in acute herpes to prevent postherpetic neuralgia has been studied and been shown to be useful [36].

Complications

Complication rates for INB are low. They are reported to include:

1. Intravascular systemic injection with subsequent local anesthetic toxicity
2. Pleural puncture and pneumothorax
3. Hematoma
4. Neural injury
5. Infection
6. Total spinal anesthesia

Many studies have documented the higher plasma levels of local anesthetic concentrations after intercostal nerve block [37] relative to other nerve block locations. However, the incidence of local anesthetic toxicity is low.

Pneumothorax, one of the most commonly thought of complications, is actually also rare. One study in surgical patients looked at over 100,000 individual nerve blocks and found no severe systemic toxic reactions, and the incidence of pneumothorax was 0.073 % [38]. Another study in patients who received INB for rib fractures due to trauma showed a higher rate of 1.4 % [39], still a low rate considering the higher risk of pneumothorax in rib fractures.

Rare complications can include total spinal anesthesia. This may occur by inadvertent injection into a dural cuff extending outside the intervertebral foramen [40, 41]. This has been reported with paravertebral block injections and catheter placement [42], and similarly, neurolytic injections have led to total spinal cord injuries.

Procedure Description

Intercostal Nerve Block

- Standard monitors are applied.
- Patient is place in a comfortable prone position.
- Sedation with a combination of midazolam (0–3 mg) and fentanyl (0–150 μg).
- Identify the posterior spinous process by palpation and mark on skin.
- Draw a paramedian line at the lateral edge of the paraspinous muscles.
- Palpate for the inferior edge of each rib at this line and mark the skin at this site at the previously marked line.
- Inject local anesthetic into the skin at each one of the planned injection sites.
- Connect a 4-cm 25-gauge needle to a control syringe with the local anesthetic of choice.
- Use the nondominant hand and index and middle fingers to again palpate the inferior edge of the rib at the planned injection site (Fig. 18.4).

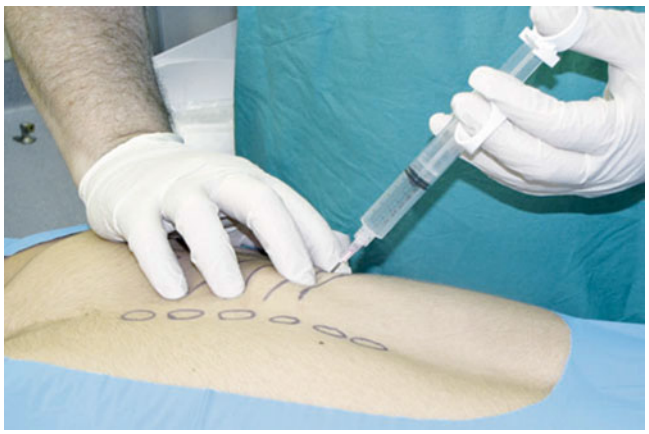


Fig. 18.4 Note the cephalic angle, initially aimed to the inferior rib edge

- Retract the skin over the rib.
- Holding the control syringe in the dominant hand, insert the needle in a slight cephalic direction towards the lower edge of the rib being palpated (Fig. 18.5).
- Carefully advance the needle until it contacts the rib.
- The nondominant hand will now release the skin and be used to steady the needle. This is of most importance to protect any movement by the patient resulting in unintentional lung puncture.
- Carefully walk the needle tip of the inferior edge of the rib and advance into the intercostal groove (about 2–4 mm) (Figs. 18.6 and 18.7).
- After negative aspiration for blood and air, 3–5 mL of local anesthetic solution is injected.

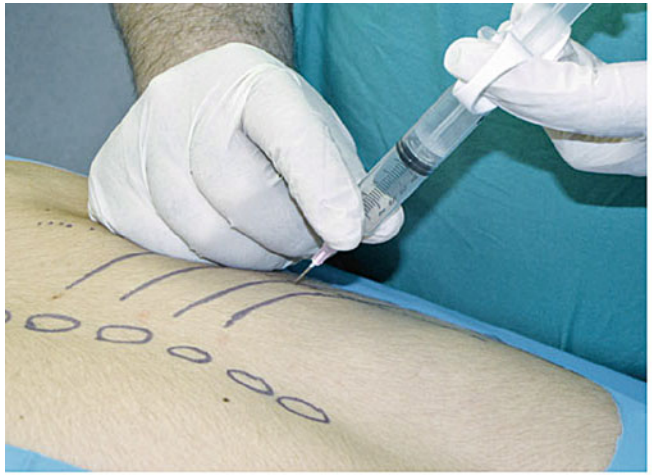
The procedure is repeated as outlined above at each planned level of injection. Intercostal nerves may also be injected along the midaxillary line if only an anterior block is desired such as a breast block.

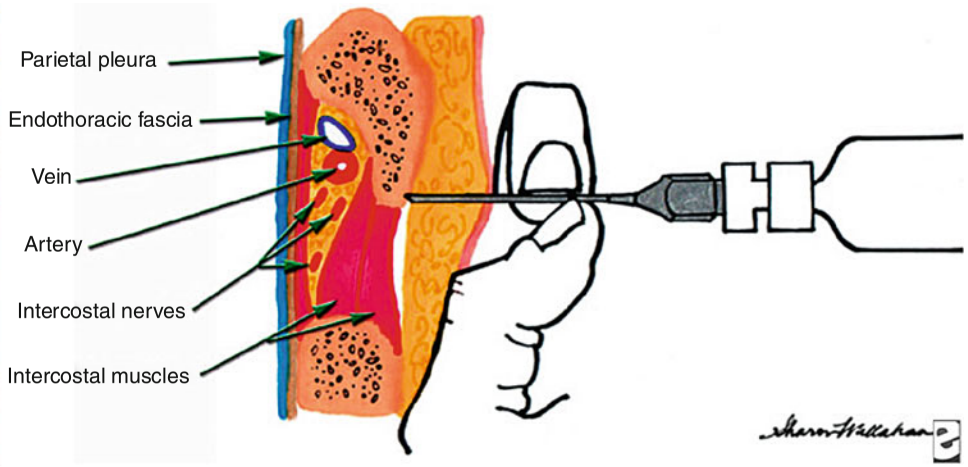
Tips

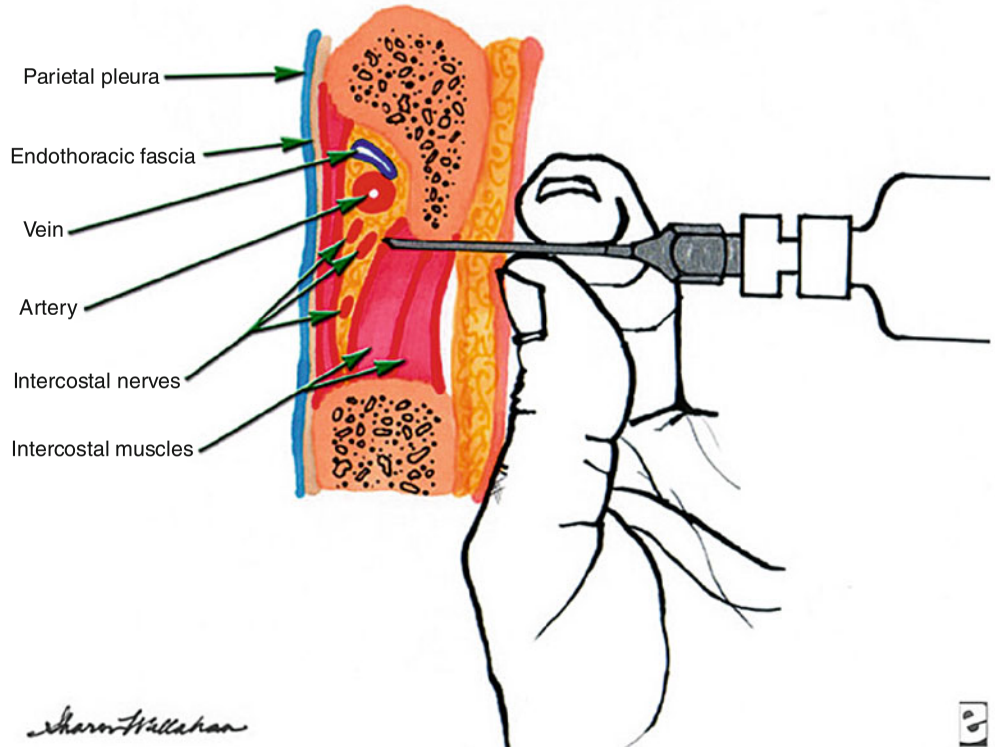
- Palpation is best done by feeling for the intercostal spaces and sling fingers up to palpate lower edge of rib.
- Wetting fingertips and skin with the prepping solution allows fingers to slide over skin, making it easier to count ribs by palpation.
- In the obese patient, identification by palpation may be impossible and ultrasound guidance and fluoroscopy are both useful. At this time, there is inadequate data demonstrating the superiority of one method over the other.

Fluoroscopy Tips

- Read Chap. 4 regarding imaging for procedures and safety.
- For fluoroscopic guidance, follow directions as above. Tilt the fluoroscope in an ipsilateral direction slightly to get better visualization of the ribs and to move the hands and syringe from blocking the view (Fig. 18.8).







Figs. 18.5, 18.6, and 18.7 Bracing needle with hand firmly resting on patient will allow control of the needle and prevent accidental lung puncture if patient moves suddenly (Reprinted with permission from eMedicine.com, 2010. Available at: http://emedicine.medscape.com/article/1143675-overview)

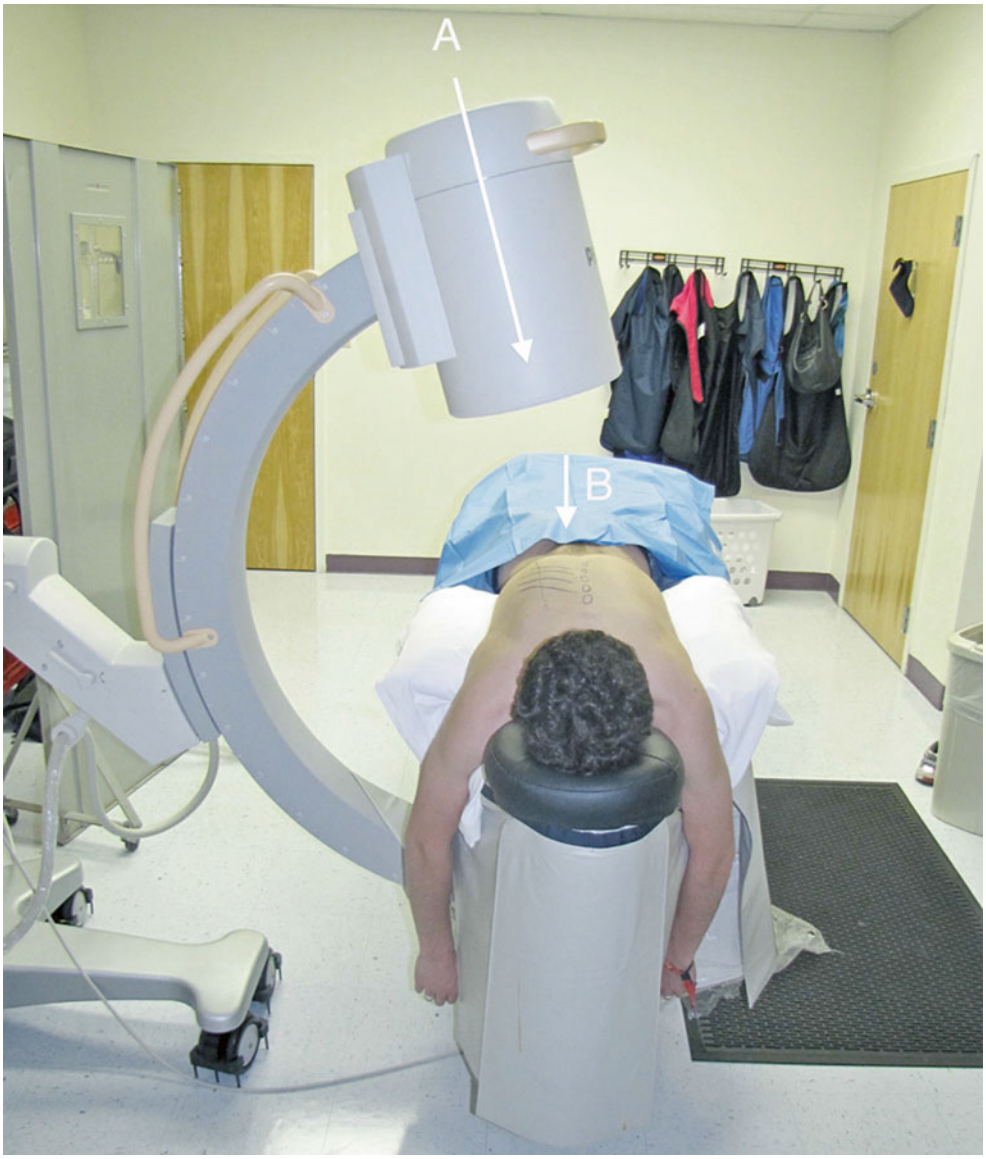


Fig. 18.8 (*A*) Direction of fluoroscopy beam. (*B*) Direction of needle insertion

- Usage of microbore extension tubing can allow for more precise control of needle and remove obstruction of view caused by hand holding syringe.
- Contrast injection is helpful to rule out intravascular uptake and show filling into the costal grove and between the intercostal muscles (Fig. 18.9).
- With severely painful ribs, procedure can be more comfortably done in lateral position (Fig. 18.10) or alternately in sitting position with patient braced to prevent inadvertent movement.

Paravertebral Nerve Block

- One to four steps as above.
- Mark skin entry point about 3 cm lateral to marks.
- Using a technique as above, insert the needle perpendicular to the skin.
- Advance the needle 2–4 cm, depending on body habitus, until the transverse process is contacted.
- The needle is then pulled back slightly and walked of the caudal edge of the transverse process.
- The needle is then advanced another 1.5–2 cm.
- After negative aspiration, 3–5 mL of local anesthetic is injected per level.
- Neurostimulator technique is performed with a 5-cm insulated needle in a similar fashion.
- Initially, stimulation of the paraspinous muscles is seen.
- On entering the paravertebral space, the needle is manipulated in an angular direction and by rotation of needle, not by in/out manipulation.

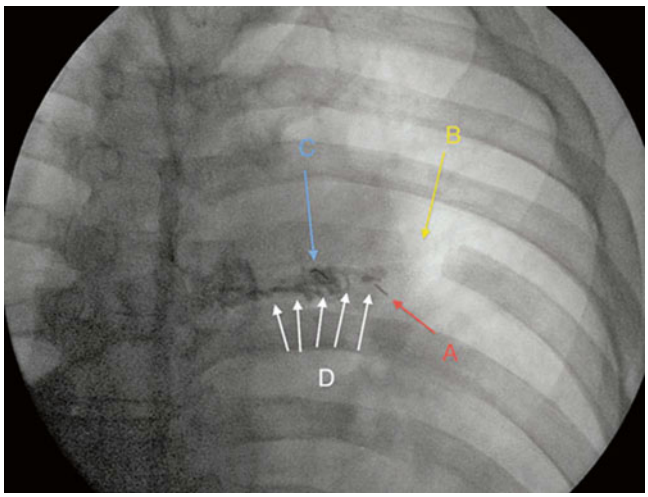


Fig. 18.9 (*A*) Surgical clip on intercostal artery. (*B*) Resected sixth rib from thoracotomy. (*C*) Needle placed for intercostal injection. (*D*) Contrast spread along intercostal groove and between intercostal inner muscles. Note that on medial side, contrast begins spread into paravertebral space

- Correct needle placement will result on stimulation at 0.4–0.6 mA of intercostal, low abdominal, inguinal, or cremaster contraction depending on the level being stimulated.
- Local anesthetic injection is then performed as above.

Paravertebral Nerve Block: Ultrasound Guided

Numerous reports have shown the value and possible increased safety of using ultrasound guidance [43].

- Standard monitors are applied.
- Patient is placed in a comfortable prone position.
- Sedation with a combination of midazolam (0–3 mg) and fentanyl (0–150 μg).
- Identify the posterior spinous process by palpation.
- Ultrasound scanning is done on the short axis lateral to the midline (Fig. 18.11).
  - Identify the ribs (Fig. 18.12).

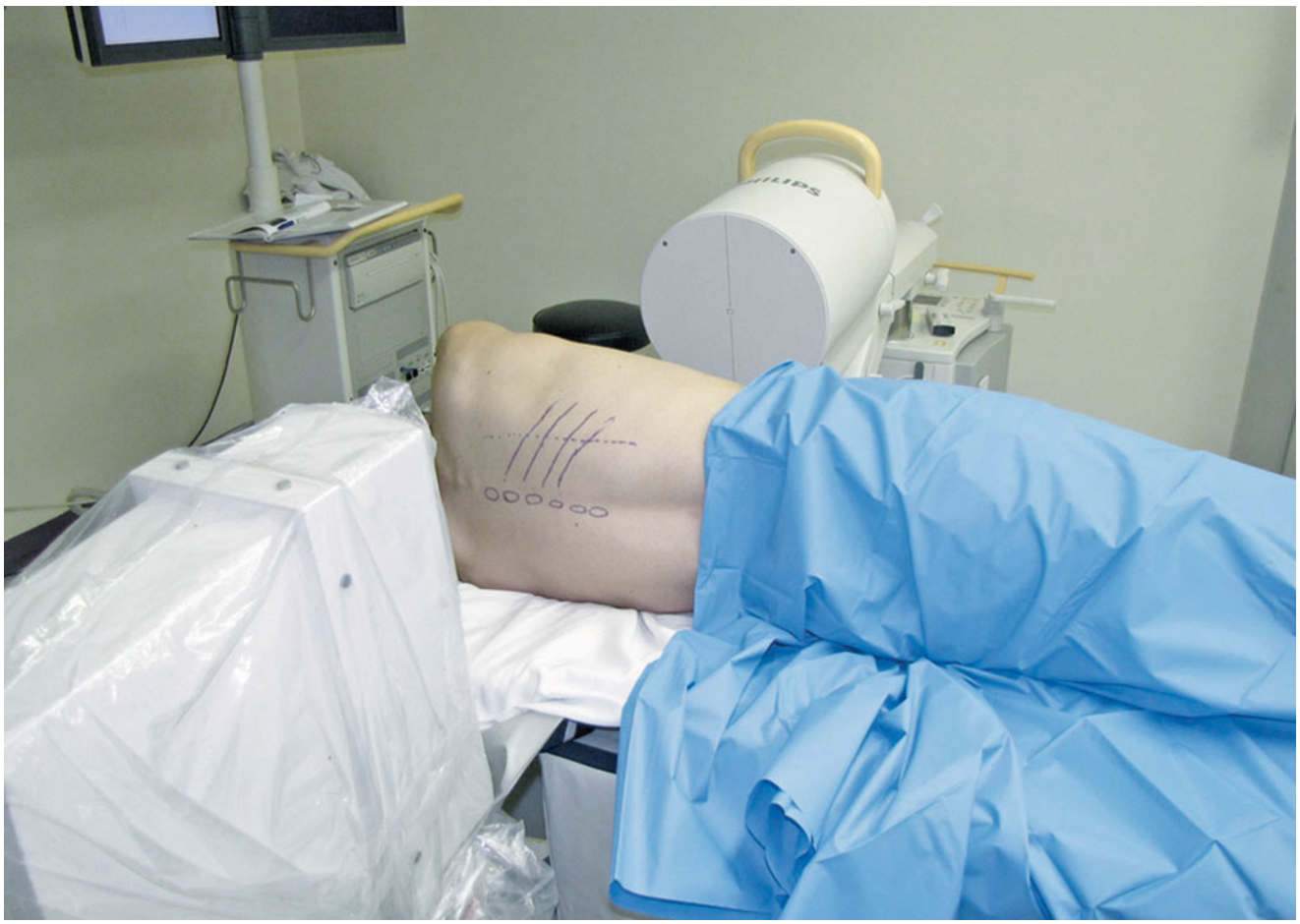


Fig. 18.10 Lateral placement for fluoroscopic intercostal nerve block. Can also be used with ultrasound

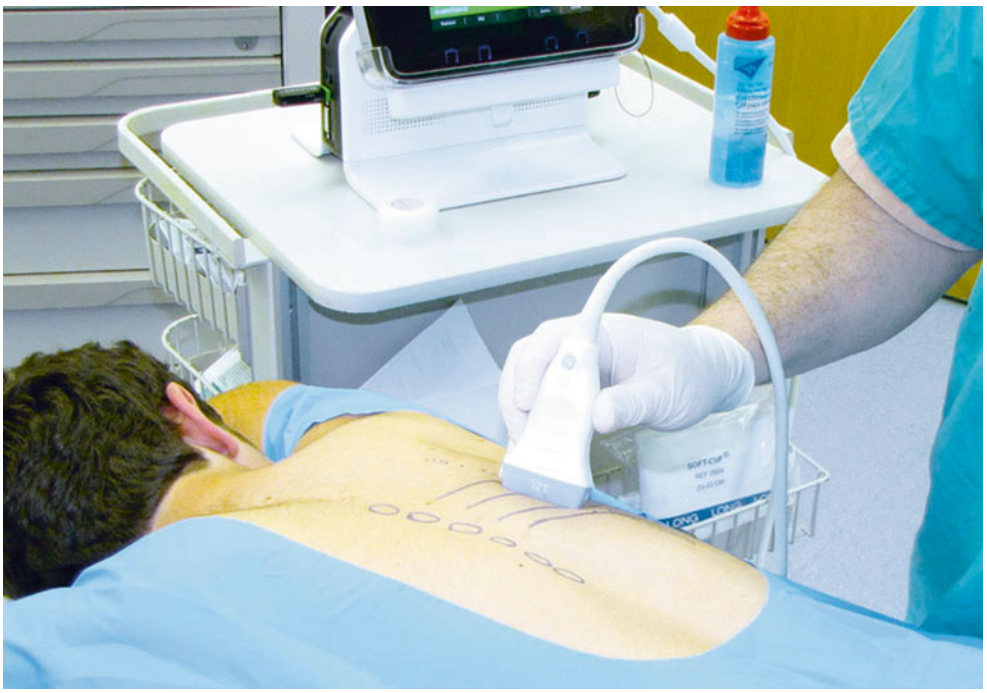


Fig. 18.11 Short axis view placement of linear ultrasound probe

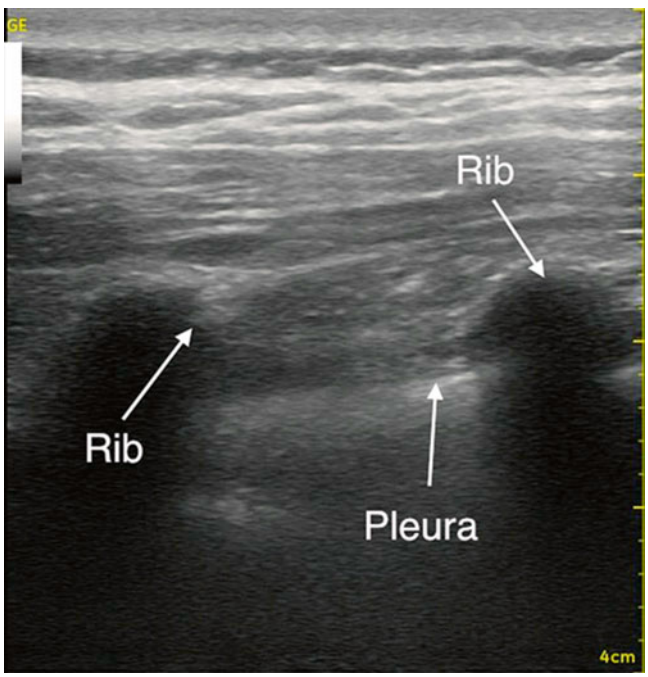


Fig. 18.12 Short axis view of ribs

  - Identify visceral and parietal pleura by having patient take deep breath.
  - Look for movement with respiration over each other.
- Rotate ultrasound so that it is on long axis to the rib midline (Fig. 18.13).

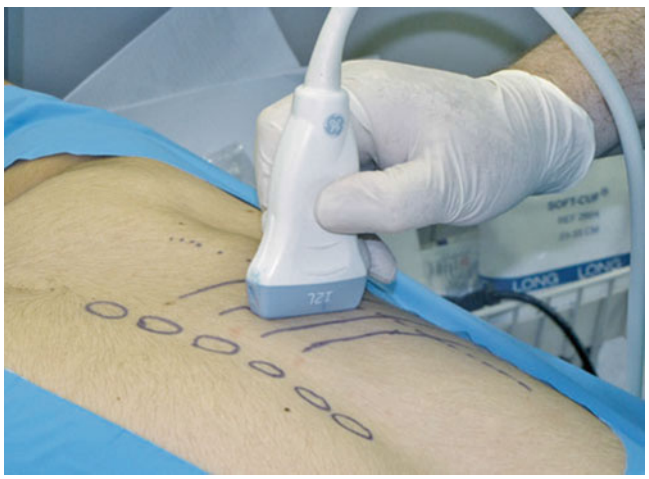


Fig. 18.13 Longitudinal placement of ultrasound for view of rib

- Tilting probe side to side to get a sweeping view will help identify the muscles (Figs. 18.14 and 18.15).
- After identifying the location of entry, the skin is marked.
- Local anesthetic is infiltrated in the skin and subcutaneous tissue with Lidocaine 1 % using a 25-gauge needle.
- A 17-gauge Touhy needle is then inserted at the end of the ultrasound probe, in plane with the probe.
- The needle is advanced incrementally, aiming for the space between the internal intercostal muscle layer and

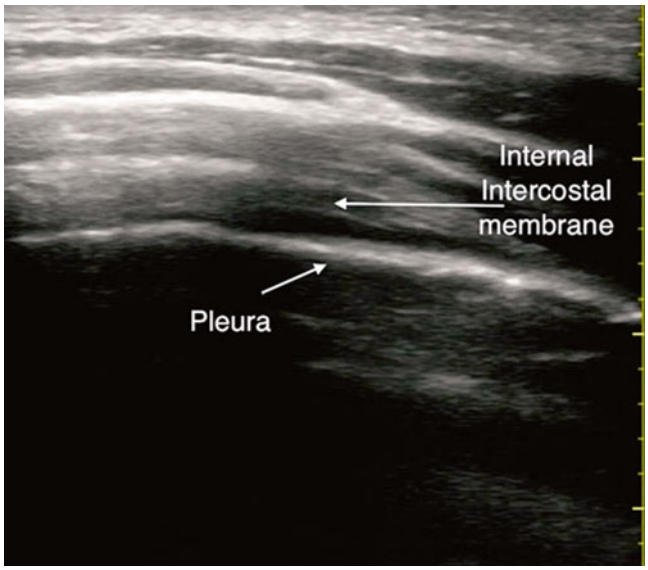


Fig. 18.14 Tilting ultrasound probe will allow a view of intercostal muscles and pleura

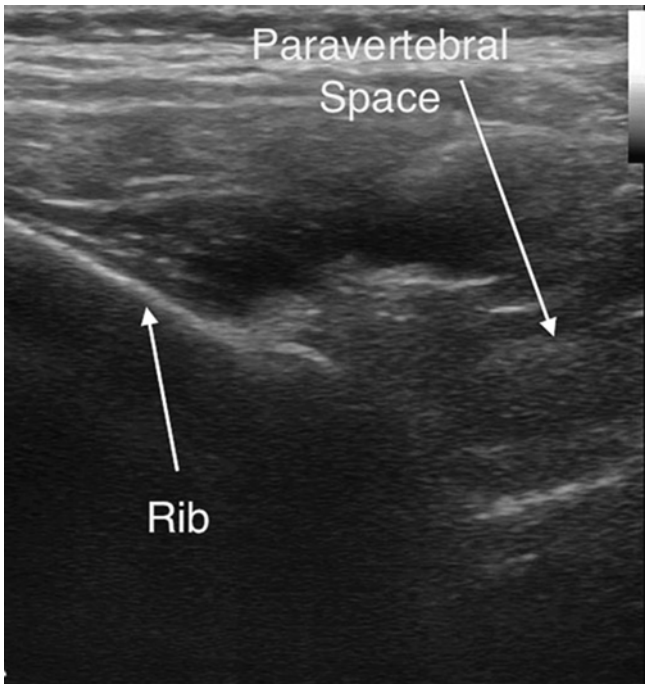


Fig. 18.15 More medical placement allows a view of edge of rib and paravertebral space

the outer portion of the innermost intercostal muscle where the intercostal nerves reside.

- Small boluses of normal saline (1–2 mL) are injected as the needle is advanced between the muscle layers in order to dilate the space.
- Once the correct space is identified and slightly dilated, the syringe is disconnected from the needle hub.
- The patient is asked to breathe deeply looking for any airflow to rule out inadvertent pleural puncture.
- The syringe is reconnected. And aspiration is made for air or blood.
- After negative aspiration, 10 mL of local anesthetic is injected. A 19-gauge epidural catheter is advanced about 3–6 cm beyond the tip of the needle.
- The Touhy needle is removed over the catheter and taped to the skin.
- Reexamine the patient 15–30 min later and determine if the dermatome coverage of the block is adequate.

Tip: In obese patients, the movement of skin in relation to the intercostal nerve groove can be quite significant. Feeding some additional catheter into the adipose tissues as the needle is removed can reduce the incidence of catheter movement out of the proper space.

Infusion can then be started with the local anesthetic of choice.

Tips

- Have all equipments ready prior to starting procedure.
- Gently sweep side to side (during step 7a above) while on long axis view to not only identity muscle layers but to also identify tip of needle.
- Contrast injection and fluoroscopy can be used to confirm paravertebral spread of local anesthetic.

Future Directions

Future methods to prolong the effect of intercostal nerve blocks without increasing risks such as higher plasma concentrations of drugs will no doubt increase the usefulness of procedures such as intercostal nerve blocks in clinical practice. Studies on the injection of microcapsules of dexamethasone and bupivacaine are encouraging [44]. As the technology of 3-D echo continues to improve, it is likely to simplify this procedure and make bedside application even easier and safer.

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Intrapleural Catheters

19

Kevin E. Vorenkamp and Lynn R. Kohan

Key Points

- Reistad and Stromskag first described intrapleural analgesia in 1986.
- Intrapleural analgesia involves placing a catheter into the tissue plane within the chest wall (the intrapleural space) so that infusion of local anesthetic spreads to several nerves.
- The anatomy of the intrapleural space allows different types of nerve fibers to be anesthetized such as somatic, sympathetic, intercostal, and paravertebral nerves thereby increasing its overall utility in a variety of painful conditions.
- The main complication is the incidence of pneumothorax, which can range from 1 to 5 %.
- Intrapleural analgesia can be used in the management of pain for the upper extremity, chest wall, thoracic viscera, and upper abdominal viscera.
- Intrapleural catheter infusions offer an alternative technique that remains a viable option for a variety of pain states, especially if contraindications exist to other techniques.

Introduction

Reistad and Stromskag first described intrapleural analgesia in 1986 [1]. The "intrapleural" space refers to the space *inside* or *within* the pleural cavity, although the terms "interpleural" (referring to the same space *between* the visceral and parietal pleurae) and "subpleural" (referring to *below* the parietal pleura) have also been used to describe the same space. Providing analgesia by infusing medications into the intrapleural space has been used in a variety of cases including but not limited to upper abdominal surgery, thoracic wall trauma, breast surgery, nephrostomy, esophagectomy, and thoracic surgery, in addition to chronic pain conditions such as chronic pancreatitis, complex regional pain syndrome (CRPS), and postherpetic neuralgia It is a relatively simple technique to learn with a low incidence of complications and few contraindications. It involves placing a catheter into the tissue plane within the chest wall (the intrapleural space) so that infusion of local anesthetic spreads to several intercostal or paravertebral nerves. The main complication is the incidence of pneumothorax, which can range from 1 to 5 % depending on the technique that is used to find the intrapleural space [2]. This complication combined with the risk for local anesthetic toxicity has limited its use; however, it can be used safely when performed with the proper technique.

History/Background

Mandl first described intrapleural injection in 1947 when he injected 6 % phenol into the intrapleural space of experimental animals without any evidence of pleural irritation or necrosis [3]. In 1978, interest in utilizing the intrapleural space for therapy resurfaced. At this time, Wallach injected tetracycline and lidocaine for malignant pleural effusions [4, 5]. The concept of intrapleural analgesia was first published in 1986 by Reistad and Stromskag as a way of treating pain after open cholecystectomy, kidney surgery, and breast surgery. Prior to that time, interest had focused on injecting multiple intercostal nerves. A cadaver study by Nunn and Slavin showed that local anesthetic of a single intercostal nerve gained access to other intercostal nerves in adjacent spaces above and below the injection site by means of both the intercostal and intrapleural spaces [6].

Kvalheim and Reistad demonstrated fluid spread by injecting local anesthetic and radiological contrast through a catheter that had been placed in the intercostal space. They found that, in addition to providing excellent

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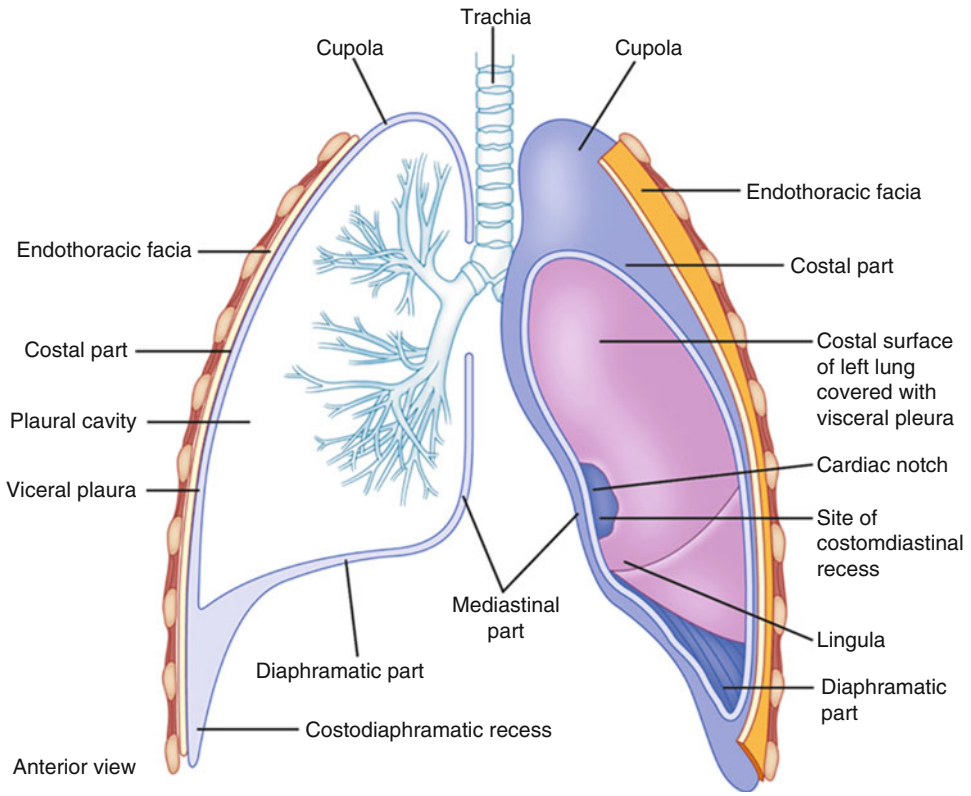

Fig. 19.1 Anterior view demonstrating the four parts of the parietal pleura

analgesia, the contrast spread over the lung surface, leading them to conclude that the catheter was actually placed in the intrapleural space. They therefore decided to reproduce this type of analgesia by deliberately placing the catheter in the intrapleural space.

Anatomy

The visceral pleura surrounds the lungs. At the chest wall, diaphragm, and mediastinal borders of the lung, the pleura reflects back on itself to form the parietal pleura, which adheres to the chest wall. There are four parts of the parietal pleura: the mediastinal, which lines the mediastinum; diaphragmatic, which lines the diaphragm; costal, which lines the thoracic wall; and superiorly, the cupola (cervical), which extends superior to the first rib (Fig. 19.1).

The line where the costal pleura becomes diaphragmatic pleura is called the costodiaphragmatic reflection. The line where costal pleura becomes mediastinal pleura is called the costomediastinal reflection. The right pleural reflection passes across the sternoclavicular joint and proceeds near the midline of the sternum, inferiorly from the level of the second rib to the 6th costal cartilage, swings laterally to cross the 8th rib in the midclavicular line, the 10th rib in the midaxillary line, and the 12th rib posteriorly, near the midline. The left pleural reflection is similar except at the 4th costal cartilage; the line swings laterally to the left border of the sternum. At the left and right costodiaphragmatic reflection, the pleura extends caudally without intervening lung tissue. This caudal extension forms a potential space (in the pleural cavity), the costodiaphragmatic recess. At the costomediastinal reflection, on the left side, lung tissue does not extend up to the costomediastinal reflection because of the cardiac notch in the left lung, and another potential space, the costomediastinal recess, is formed.

As these lines of reflection are fixed, intrapleural analgesia can technically be instituted anywhere with those boundaries.

Anteriorly, laterally, and posteriorly, the parietal pleura is in close approximation to the intercostal nerves. The parietal pleura has abundant sensory innervation from the phrenic and intercostal nerves (Fig. 19.2). Superiorly, the lower roots of the brachial plexus pass a short distance over the cupola before reaching the first rib. Medially, the sympathetic chain, splanchnic, phrenic, and vagus nerves are also adjacent. Because the epidural and subarachnoid spaces are further away, they are generally not thought to be involved during an intrapleural injection. However, since these spaces are only separated from the parietal pleura by fat and loose connective

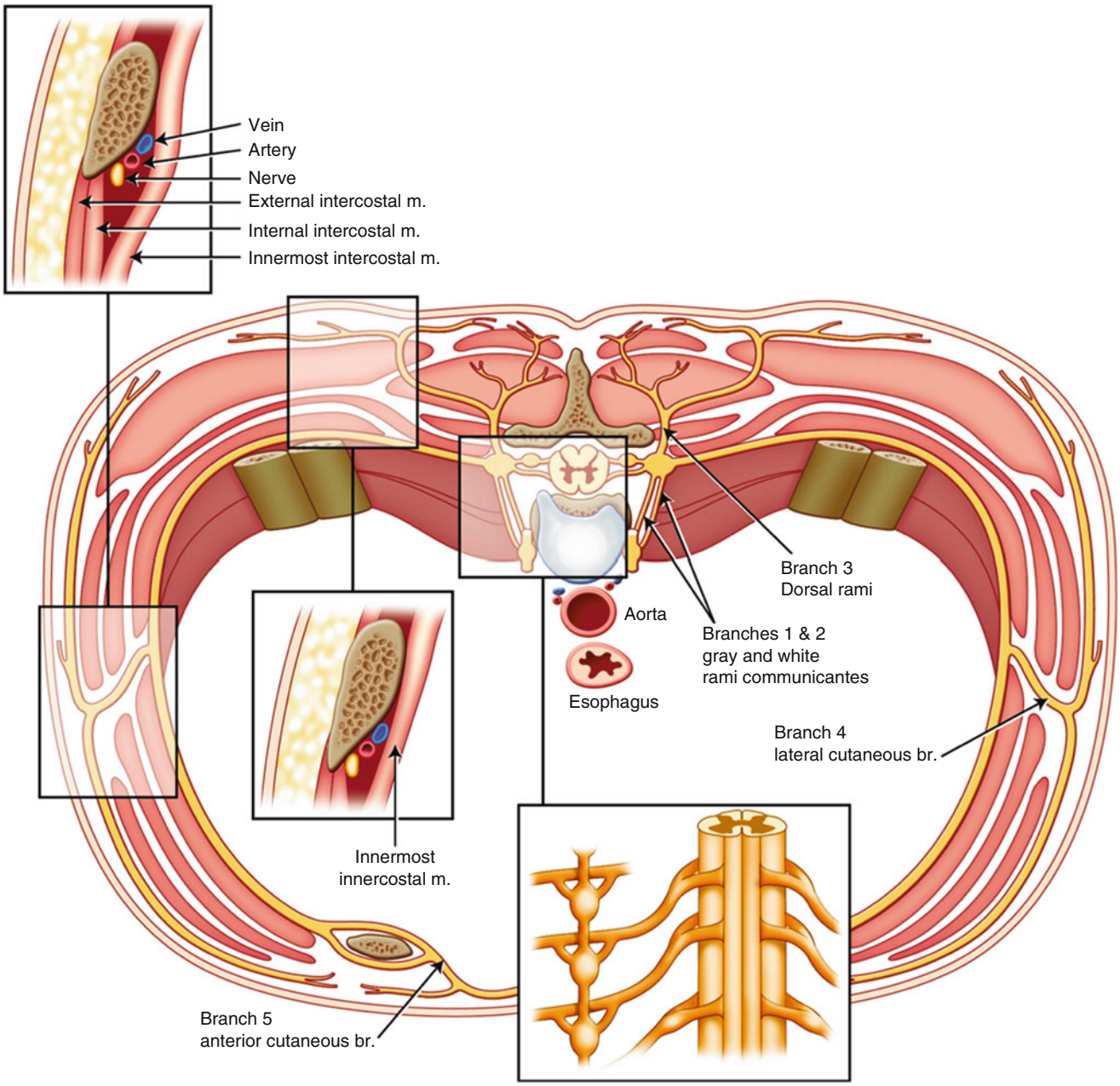

Fig. 19.2 Nerve supply of the thorax and intrapleural space

tissue of the epidural and paravertebral spaces, there may be tracking of anesthetic solution if there is a breach of the parietal pleura.

The visceral pleura is the innermost layer that is adherent to the substance of the lungs. It is continuous with the parietal pleura at the hilus of the lung. The intrapleural cavity is the potential space between the visceral and the parietal pleura. The space is 10–20 μm in width and has a static volume of 0.1–0.2 ml/kg. The micron-covered mesothelial surface of the parietal pleura facilitates the absorption of the local anesthetic and its diffusion into the intrapleural space. The pleura receives innervation from the phrenic and sympathetic nerves, and therefore, intrapleural administration of anesthetics may affect neural conduction on both types of nerves. Intrapleural analgesia can be accomplished by placing the anesthetic solution between the parietal and visceral pleurae, in this potential space (Fig. 19.3). Intrapleural analgesia can also be accomplished by placing a catheter deep to the internal intercostal muscle but superficial to the parietal pleura.

The intercostal space of the posterior chest wall has three layers: the external intercostal muscle; the posterior intercostal membrane, which is the aponeurosis of the internal intercostal

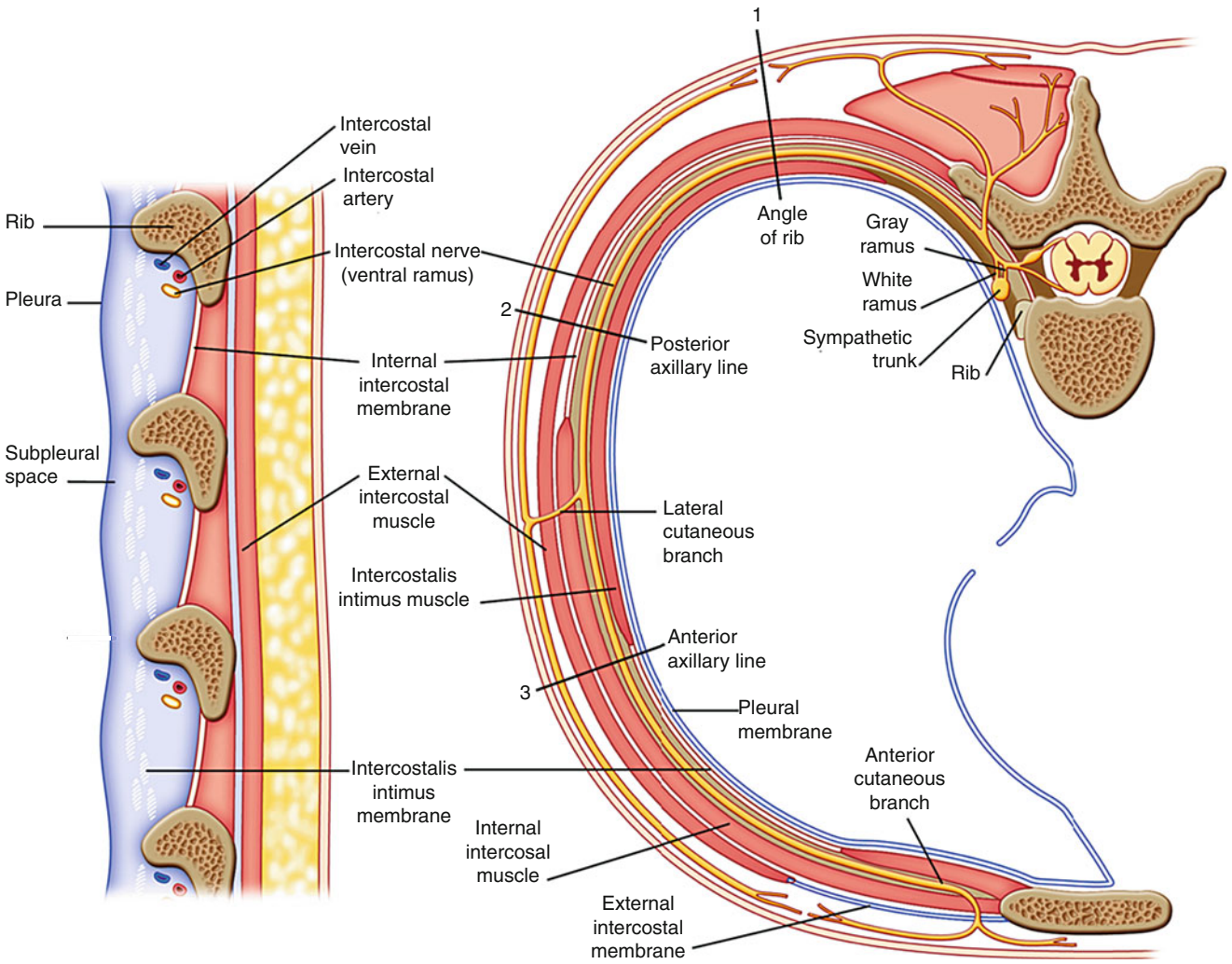

Fig. 19.3 Anatomy of the pleural cavity after (*left*) and before (*right*) injection of solution into the intrapleural space

muscle; and the intercostalis intimus muscle, which is a continuation of the transversus abdominis. The intercostal nerves lie in between the posterior intercostal membrane and the intercostalis intimus. The intercostal intimus is incomplete and allows fluid to pass freely into the intrapleural space, whereas the posterior intercostal membrane forms a complete barrier beneath the external intercostal muscle.

Therefore, as previously stated, intrapleural analgesia can be accomplished in one of two ways. A catheter can be placed either deep to the internal intercostal muscle but superficial to the parietal and the visceral layers of the pleura or the catheter can be placed between the parietal and the visceral layers of the pleura. The local anesthetic can thus spread to adjacent intercostal nerves and paravertebral nerves, but spread to the epidural or subarachnoid space does not usually occur. Local anesthetic that is placed in the intrapleural space will diffuse out to anesthetize the thoracic somatic and lower cervical and thoracic sympathetic nerves that lie close to the parietal pleura.

Indications

Intrapleural analgesia can be used in the management of pain for the upper extremity, chest wall, thoracic viscera, and upper abdominal viscera. It can also be used in more emergent pain states such as rib fractures, acute herpes zoster, and cancer pain. In addition, intrapleural analgesia has been found to be effective for percutaneous thoracostomy tubes, nephrostomy tubes, and biliary drainage tubes. It is also used in surgeries of the breast, chest wall, and flank. Additional pain states in which intrapleural analgesia can be used include postherpetic neuralgia, metastasis to the lung and liver, and post-thoracotomy pain (Table 19.1).

Table 19.1 Indications for intrapleural analgesia

Type of surgery	Investigator	Evidence
Gall bladder	Tyagi et al. [7]	Supportive
	Shrestha et al. [8]	
	Dravid et al. [10]	
Gall bladder	Yaseen et al. [9]	Nonsupportive
Liver	Therasse et al. [11]	Supportive
Renal	Trivedi and Robalino [12]	Supportive
	Baude et al. [15]	
	Greif et al. [16]	
Breast	Colpaert et al. [17]	Supportive
	O'Donoghue et al. [18]	
CABG	Ogus and Selimoglu [19]	Supportive
Thoracotomy	Yildirim et al. [20]	Nonsupportive
	De Cosmo et al. [21]	
	Joshi et al. [22]	
Thoracotomy	Demmy et al. [23]	Supportive
Rib fractures	Wulf et al. [24]	Supportive
	Graziotti and Smith [25]	
	Knottenbelt et al. [26]	
Chronic pain	Reiestad et al. [27]	Supportive
	Reiestad et al. [28]	
	Perkins [29]	
	Dionne [30]	
	Fineman [31]	
	Lema et al. [32]	
	Main [33]	
	Myers and Lema [34]	
	Ahlburg et al. [35]	

Gall Bladder and Liver Surgeries

There have been numerous studies examining the effectiveness of intrapleural analgesia in patients undergoing cholecystectomies. Tyagi et al. studied the effects of intrapleural block in patients undergoing open cholecystectomy. He found that patients undergoing general anesthesia, with a preemptive intrapleural block, had lower mean systolic and diastolic blood pressures, improved hemodynamic stability, and utilized less isoflurane compared to a group who just received general anesthesia without an intrapleural block [7]. Another study on a patient undergoing open cholecystectomy found effective postoperative pain control for 24 h after receiving an intrapleural injection preop of 20 ml of 0.5 % bupivacaine in divided doses and postop an infusion of 0.125 % bupivacaine at a rate of 10 ml/h through a catheter [8]. In contrast, a study by Yaseen comparing the number of dermatomes blocked and time to regression of block between a group receiving an intrapleural block and a group receiving intercostal blocks found that the intercostal block group had more dermatomes blocked and had a more gradual regression of their block than did the group receiving an intrapleural block [9]. In contrast to open cholecystectomy, there has been less research investigating the use of intrapleural block following laparoscopic cholecystectomy. One such study found that intrapleural analgesia can be a very effective and safe method of pain control in patients undergoing laparoscopic cholecystectomy [10].

Liver

Intrapleural analgesia has also been found to be effective in cases involving percutaneous hepatobiliary drainage. A case study showed improved hemodynamic stability and lack of respiratory adverse effects in patients receiving intrapleural analgesia for percutaneous hepatobiliary drainage [11]. The same study also demonstrated lower pain intensity scores and less opioid requirement in patients receiving intrapleural analgesia during biliary drainage.

Renal

Intrapleural analgesia has also been found to be effective in patients undergoing percutaneous nephrostomy and nephrolithotomy. Studies in patients who received intrapleural analgesia have demonstrated adequate postop pain relief after percutaneous nephrostomy [12] and during extracorporeal shock wave lithotripsy [13, 14]. Two studies have found adequate pain relief without significant side effects in patients having undergone nephrectomies [15, 16].

Breast Surgeries

Intrapleural analgesia has been found to be effective in breast reconstructive surgeries. Colpaert found that in women undergoing latissimus dorsi flap reconstruction, patients who received intrapleural analgesia had lower morphine PCA requirements than patients who did not receive intrapleural analgesia. In addition, there were significantly lower levels of nausea and vomiting in the group having received the intrapleural analgesia [17]. Similar findings were reported by O'Donoghue who also found lower morphine requirements postop in patients who had received intrapleural analgesia both in the form of boluses and as a continuous infusion through the intrapleural catheter [18].

Coronary Artery Bypass Graft (CABG) Surgery

The role of intrapleural analgesia has also been investigated in regard to CABG. Ogus found that a group of patients, who had received boluses of 0.5 % bupivacaine every 6 h for 4 days after

undergoing CABG, had shorter times to extubation, increased PaO_2 and decreased $PaCO_2$, and increased FEV1, FCV, VC, MVV, and FEF 25–75 %. In addition, they were found to have decreased postoperative opioid requirements and shorter ICU stays, although total hospital stay was unchanged [19].

Thoracotomy

The effectiveness of intrapleural analgesia in post-thoracotomy pain has shown mixed results. Overall, it appears that thoracic epidural analgesia or paravertebral blocks are more effective than intrapleural analgesia in relieving pain following thoracotomy. Yildirim compared intrapleural analgesia to thoracic epidural analgesia and found that those receiving thoracic epidural analgesia had better postop respiratory function, lower VAS pain scores, and better ABGs than those who received intrapleural analgesia [20]. Supporting this evidence, DeCosmo found that intrapleural analgesia was not as good as paravertebral blocks or thoracic epidural analgesia for patients with post-thoracotomy pain [21]. Similarly, Joshi found thoracic epidural analgesia or paravertebral blocks to be more effective than intercostal or intrapleural blocks in the management of thoracotomy patients. He concluded that intercostal blocks may be an alternative to thoracic epidural or paravertebral blocks in certain circumstances in which epidurals or paravertebral blocks were contraindicated but could not advocate intrapleural analgesia in such circumstances due to lack of effectiveness [22].

There has been a recent study which showed a possible role for intrapleural analgesia delivered via thoracostomy (chest) tube in patients undergoing non-rib-spreading thoracoscopy. Thirty patients with non-rib-spreading thoracoscopy were divided into three groups: those who did not receive any local anesthetic in the intrapleural block, those that received intermittent boluses of 30 ml of 0.25 % bupivacaine every 6 h, and those that received a continuous infusion of 0.25 % bupivacaine at 5 ml/h. He found that total VAS pain scores and fentanyl consumption were lower in the groups receiving intermittent boluses and continuous infusions than in the control group [23].

Rib Fractures

There have been many studies confirming the effectiveness of intrapleural analgesia in the treatment of multiple rib fractures [24–26]. Intrapleural analgesia may be particularly appealing in these cases as it may be difficult for the patient to assume a position enabling the placement of a thoracic epidural catheter. Additionally, if the patients already have a chest tube in place, a technique such that employed by Demmy could be utilized to avoid needle placement altogether [23].

Chronic Pain

Reistad et al. observed significant pain relief in upper extremity CRPS patients who had received five daily injections of 0.5 % bupivacaine through a catheter in the intrapleural space. Three of the seven patients were pain free for 4–10 months, while three of the other patients had minimal pain requiring no medications [27]. The same group later proved the effectiveness of intrapleural analgesia in the treatment of severe postherpetic neuralgia [28]. It has also been effective in the treatment of chronic ischemic pain of the upper limb [29] as well as various other pain states including tumors involving the brachial plexus [30], pain in the chest wall from metastatic bronchiogenic carcinoma [31], esophageal cancer [32], esophageal rupture [33], and chronic pain in terminally ill patients with pancreatic, renal cell, breast cancer, and lymphomas [34]. In addition, it has been found to be effective in patients with upper abdominal cancers and benign and neoplastic pancreatic pain [35, 36].

Contraindications and Complications

Overall, intrapleural catheter placement and infusion of local anesthetic into the intrapleural space is safe and well tolerated. One of the primary complications of the block may be pneumothorax, although other potential complications exist (Table 19.2). One of the potential advantages of intrapleural analgesia over other techniques (thoracic epidural analgesia, paravertebral) is that there are fewer contraindications, especially if the plan is to deliver intrapleural analgesia via a catheter through an existing thoracostomy tube (Table 19.3)

Table 19.2 Complications of intrapleural catheter placement and analgesia

Complications
Pneumothorax
Systemic local anesthetic toxicity
Catheter misplacement
Horner's syndrome
Phrenic nerve paralysis
Infection
Pleural effusion-serous or blood-stained
Intrabronchial injection
Ipsilateral bronchospasm
Cholestasis
Administrative error
Bronchopleural fistula
Direct myocardial depression

Table 19.3 Contraindications to intrapleural analgesia

Absolute contraindications
Patient refusal
Allergy to local anesthetic
Extensive infection at block or catheter site
Relative contraindications
Emphysema
Bullous lung disease
Recent pulmonary infection or empyema
Pleural adhesions or pleurodesis
Hemothorax
Coagulopathy
Contralateral phrenic nerve paralysis

Technique

Spread of local anesthetic within the intrapleural space is determined by gravity and to a lesser extent the volume of anesthetic and location of the catheter. Intrapleural catheters are most commonly placed posteriorly with the patient in the lateral or semi-prone position. They have also been placed near the midaxillary line or anteriorly with the patient supine. The most important aspect of this technique is detection of negative intrapleural pressure. Therefore, the technique should be performed in awake patients either pre- or postoperatively or in patients under general anesthesia who are breathing spontaneously. Placement should be avoided during positive pressure ventilation, because the intrapleural pressure is no longer negative, thereby making this risk of pneumothorax or tension pneumothorax greater.

The technique used and thus the patient position should be based on the selection of nerves that are to be blocked. To treat sympathetically mediated pain of the upper extremity, the patient should be placed with the affected side up in order to block the lower cervical and upper thoracic sympathetic chains. After injecting the anesthetic solution, the patient should be placed in the head-down position in order to avoid block of the thoracic somatic nerves. In order to obtain a block of the thoracic somatic nerves including the thoracic spinal nerves and corresponding intercostal nerves, as well as the thoracic sympathetic chain, the patient is placed in the oblique position with the affected side down and the patient's back propped up against a pillow to encourage pooling of the anesthetic into the intrapleural gutter next to the thoracic spine. This will allow the anesthetic to maximally cover both the somatic and sympathetic nerves. If the patient cannot lie on the affected side secondary to rib fractures or other issues, the catheter can be placed with the patient in the sitting position or with the affected side up. After the injection, the patient can be placed supine and tilted away from the affected side to allow the flow of the anesthetic toward the intrapleural gutter next to the thoracic spine.

As described by Waldman [37], once the patient is in the appropriate position, the 8th rib is identified on the affected side. Next, the skin is marked at a site 10 cm from the origin of the rib. This area is prepped and draped in a sterile manner. The index and middle finger are then placed on the rib bracketing the side of needle insertion. This area is then anesthetized with local anesthetic, such as 1 % lidocaine. An 18-gauge, 9-cm-styletted Hustead or Touhy needle is then inserted through the previously anesthetized area. The needle is advanced perpendicular to the skin, aiming for the middle of the rib that is being bracketed by the ring and middle fingers. The needle usually hits bone at approximately ½ inch. Additional anesthetic is usually required at this point secondary to the sensitivity of the periosteum. After hitting bone, the needle is withdrawn slightly and walked off the superior margin of the rib, avoiding trauma to the neurovascular bundle that lies beneath the rib. In contrast to individual intercostal nerve blocks, where the entry point is at the inferior border of the rib, the entry point for intrapleural analgesia should be at the *superior* border of the rib to avoid trauma to the intercostal nerve and blood vessels by the large Touhy needle. As soon as bony contact is lost, the stylet is removed and the needle is attached to either a well-lubricated 5-ml syringe with a plunger containing air or 0.9 % preservative-free saline with the plunger removed. The needle and syringe are slowly advanced toward the intrapleural space. The needle is then "walked off" the superior edge of the rib. It should be advanced either just past the posterior intercostal membrane or between the parietal and the visceral pleural space. When the needle is positioned just past the posterior intercostal membrane, a "pop" is often felt. In contrast, when the needle is positioned between the parietal and visceral pleurae, a loss of resistance is encountered that is similar to that of epidural anesthesia. The pleural pressure remains negative throughout the respiratory cycle, whereas the pressure in the intercostal space oscillates from negative to positive at the end of inspiration and expiration, respectively. Spontaneous ventilation should be maintained during the procedure. Controlled ventilation increases the risk of tension pneumothorax during positive pressure ventilation. At this point, the plunger of the syringe, if utilizing the air method, will usually advance under its own response to the negative pressure of the intrapleural space. The syringe is then removed, and a catheter is advanced 6–8 cm into the intrapleural space. If utilizing the saline method, the column of saline in the syringe will fall once the intrapleural space has been identified. A catheter is then passed through the open-ended syringe barrel, through the saline and needle, and into the intrapleural space. The advantage of the saline technique is that no air is introduced or allowed to be entrained into the intrapleural space.

After careful aspiration for heme or air, the catheter is taped in place with sterile tape and the patient is placed in the appropriate position to allow block of the appropriate nerves. Twenty to 30 ml of local anesthetic can be injected in divided doses with negative aspiration between doses and with careful observation for signs of local anesthetic toxicity. If a higher concentration of local anesthetic is used, such as 0.5 % bupivacaine, then smaller volumes, such as 10–12 ml, can be used. Alternatively, a continuous infusion can be given via a pump. If long-term use is anticipated, the catheter should be tunneled to reduce the risk of infection. Plasma concentration of the local anesthetic peaks at 15–20 min after injection. Adding epinephrine to the solution slightly delays and reduces peak plasma concentration. For continuous infusion, a rate of 0.125 ml/kg/h is usually employed (10 ml/h for an 80-k patient).

The technique for tunneling the catheter can be performed as follows [37]. After the Touhy or Hustead needle has contacted bone at approximately ½ in., and with the needle still in place, a #15 blade scalpel is used to dissect all the subcutaneous connective tissue away from the needle. A small curved clamp can then be placed into the incision, and a small pocket is created overlying the superior part of the interspace that is made by blunt dissection. This technique will allow the catheter to lie in the subcutaneous space without kinking. After the pocket is made, the needle is removed, and a malleable tool is bent in the contour of the patient's chest wall. The tunneling device is then inserted in the subcutaneous pocket and guided laterally around the chest wall. The tunneling device is guided to the anterior chest wall. When it reaches its exit point, it is turned away from the patient so that the sharp tip is against the patient's skin. A scalpel is then used to cut down onto the tip. The tip of the tunneling device is then advanced through this exit incision and covered with a sterile dressing.

The styletted Touhy or Hustead needle is then reintroduced into the subcutaneous pocket and advanced until contact with the rib is made again. The needle is then slightly withdrawn and walked superiorly off the rib, again to avoid trauma to the neurovascular bundle. Once bony contact is made, the stylet is removed and the syringe attached. The needle is advanced until the tip penetrates the parietal pleura at which point a "pop" is usually felt. At this point, the plunger of the syringe will usually advance secondary to negative pressure of the intrapleural space. The syringe is removed, and a catheter is advanced 6–8 cm into the intrapleural space. The needle is then removed and withdrawn over the catheter. The catheter is aspirated. If no air or heme is identified, the distal end of the catheter is attached to the proximal end of the tunneling device. The tunneling device is then withdrawn from the exit incision, bringing the catheter with it into the subcutaneous tunnel. After the distal end of the catheter is drawn through the tunnel, the tunneling device is removed and the remaining catheter is withdrawn until the excess catheter falls into the subcutaneous pocket. An injection port is then attached to the distal end of the catheter. The port can then be injected with saline to ensure the integrity to the catheter. If the catheter injects easily without leakage, the midline incision can be closed. It can be closed with two layers of 4-0 nylon sutures. One must be careful to avoid damage to the catheter during closure of the incision. The catheter is then taped in place, and the patient should be turned to the appropriate position in order to block the desired nerves.

Another technique was described for use during breast reconstructions [17]. In this study, the intrapleural space was identified using a variation of a technique described by Scott [38]. In this technique, the analgesia is given after the patient has been anesthetized under general anesthesia. The patient is positioned supine. The midaxillary line at the 4th or 5th intercostal space is identified. A 16G Touhy epidural needle is connected to a three-way tap, a fluid-giving set, and a bag of saline, which is suspended at least 60 cm above the patient. Under sterile conditions, the needle is inserted perpendicularly to the skin until the negative pressure of the intrapleural space is reached and saline starts running into the cavity. This is visible through the drip chamber in the infusion line. In this study, they used the three-way stop cock in order to facilitate consecutive bolus injection of local anesthetic and passage of a flexible epidural catheter for continuous infusion. While the catheter is being inserted, the proximal part of the needle is held downward to act as a water tap and avoid air entrapment. The procedure takes about 10 min.

An alternative approach in patient who has a chest tube in place is to infuse the local anesthetic through a catheter placed in the chest tube. For this technique, a 20-gauge epidural catheter with a flexible tip can be utilized. This catheter is inserted through the previously placed chest tube. The stiffness of this catheter allows for better advancement within the intrapleural space. The catheter can be inserted approximately 4–5 cm. After insertion, local anesthetic can be infused. It is important to clamp the chest tube temporarily (approximately 20 min) after infusion of the local anesthetic to prevent the local anesthetic from being removed to the suction of the chest tube.

Bupivacaine and lidocaine are two of the more commonly used agents for intrapleural analgesia. The most common agent appears to be 0.25 % or 0.5 % bupivacaine. These concentrations can either be delivered as a single injection or as a repeated bolus. Typical quantities include10–40 ml/injection. A single injection of 20 ml of 0.5 % bupivacaine with 5 mcg/ml of epinephrine has been found to reliably produce a cutaneous sensory block from T4 to T10 but has even been reported to produce cutaneous sensory block from T1–T12 [38]. The onset using this quantity and concentration of bupivacaine is usually within about 1–3 min. Complete pain relief has been achieved in about 30 min, and the analgesic duration is about 7 h. If a continuous infusion is to be used, lower concentrations from 0.125 to 0.375 % bupivacaine are

typically chosen. The infusion is usually started after a bolus of 20 ml of 0.5 % bupivacaine [17].

Lidocaine 2 % with 1:200,000 epinephrine has not been found to produce consistent dermatomal analgesic levels.

Opioids can be added to the local anesthetic to improve pain control and to decrease the need to systemic narcotics. Intrapleural opioids may act on opioid receptors in peripheral nerves.

Clonidine has also been used safely in the intrapleural space to increase the effectiveness with intrapleural analgesia.

Future Direction

More studies are needed to determine the overall clinical effectiveness of intrapleural catheters in various chronic pain conditions. Research should focus on alternatives to bupivacaine including NMDA receptor antagonists, steroids, or alpha-2 agonists as potential therapeutic options. In addition, ultrasound-guided intrapleural blocks may be a safer approach to lessen the risk on pneumothorax.

Summary/Conclusions

In summary, intrapleural analgesia is a relatively simple technique that can be used in a variety of situations for many diverse pain states. It has been proven to provide excellent analgesia over the chest wall and upper abdomen. It is generally a safe and easy procedure to perform, especially in cases where epidural analgesia may be difficult or contraindicated. The anatomy of the intrapleural space allows different types of nerve fibers to be anesthetized such as somatic, sympathetic, intercostal, and paravertebral nerves thereby increasing its overall utility in a variety of painful conditions. A variety of substances can be employed to achieve analgesia such as bupivacaine, ropivacaine, clonidine, or opioids. The technique rarely leads to systemic toxicity and has been shown to improve a variety of respiratory parameters in certain conditions [39]. At the current time, it appears that thoracic epidural analgesia and paravertebral blocks offer superior analgesia to intrapleural catheter infusion of local anesthetic for thoracotomy. However, intrapleural catheter infusions offer an alternative technique that remains a viable option for a variety of pain states, especially if contraindications exist to other techniques.

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Epidural Lysis of Adhesions: Percutaneous and Endoscopic Techniques

20

Timothy Y. Ko and Salim M. Hayek

Key Points

- The purpose of using the lysis of adhesion technique is to bypass scar tissue and improve delivery of high concentrations of injected medications to the targeted area.
- The ideal patient would be one who may be suffering with more radicular symptoms from epidural fibrosis in close proximity to a nerve root.
- Identifying filling deficits that correlate well with patient's symptoms improves the likelihood of success.
- Minimizing the amount of adjustments to the catheter in the needle reduces the risk of equipment malfunction and risk to the patient.
- Resistance to the advancing catheter or epiduroscope should be respected as force may result in a complication.

Introduction

Epidural lysis of adhesions is an interventional technique that was initially described in 1989 [1]. It was designed to address refractory low back and leg pain due to epidural scarring by delivering high concentrations of injectable medication to targeted areas. These areas of scar tissue develop due to many reasons including postsurgical resection and chemical irritation from leaking nucleus pulposus. The contribution of epidural fibrosis to intractable low back pain and lumbosacral neuritis has been debated [2]. Kuslich and colleagues [3] performed an extensive evaluation on the origins of lumbar back pain throughout 193 operations under progressive local anesthesia delivered sequentially to different surgical planes. Back pain could be mostly reproduced by stimulation of the outer layer of the annulus fibrosis and the posterior longitudinal ligament. Sciatica could only be reproduced by stimulation of swollen, restricted, or compressed nerve roots. While epidural fibrosis itself was not painful, patients that had prior laminectomies were found to have perineural fibrosis that lead to painful and sensitive nerve roots [3]. The lysis of these adhesions has been reported to reduce pain in several prospective studies and systematic reviews [4–7].

The rate of lumbar spine surgery has grown exponentially in Western culture [8–10]. Studies like Weinstein and colleagues' Spine Patient Outcomes Research Trial (SPORT) have suggested a central role for spinal surgeries [11]. In their 4-year combined as-treated analysis, patients who underwent spine surgery for a herniated disk achieved greater improvement than the nonoperative cohort in all primary and secondary outcomes except work status. With this growth in surgical intervention, the number of failed back surgery syndrome has become an increasingly common diagnosis [12] for the interventional pain physician to treat. There is quite a range of treatment modalities for intractable back pain in patients who have had previous spine surgery. Conservative treatments include physical therapy, biofeedback, medication management, and epidural steroids. The use of epidural steroid injections for managing this syndrome is very common; unfortunately, only a moderate proportion of these patients have shown long-term and functional improvement in the failed back surgery population [13, 14]. Two recent studies do show some promise with the use of caudal epidural steroid injections in the failed back surgery and spinal stenosis populations [15, 16]. The purpose of using a lysis of adhesion technique is to bypass scar tissue and improve delivery of high concentrations of medications of injected drugs to the targeted area. The evidence for percutaneous

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lysis of epidural adhesions has been found to be moderate to strong in managing the pain for post-lumbar spine surgery syndrome [4, 13].

Indications for Epidural Lysis of Adhesions

Lysis of adhesions is a more advanced technique to provide relief of pain. Typically, it is preceded by more conservative treatments including physical therapy, transcutaneous electrical nerve stimulation, anti-inflammatories, muscle relaxants, membrane stabilizers, and traditional epidural corticosteroid injections. Once these have demonstrated failure, then consideration of this technique should be discussed with the patient. Ideally, this procedure was designed to aid in the management of pain related to failed back surgery syndrome, chemically sensitive disks, and other scenarios where epidural fibrosis and inflammation occur [17]. The ideal patient would be one who may be suffering with more radicular symptoms from epidural fibrosis in close proximity to a nerve root. The placement of the catheter or endoscope into this area allows for appropriate adhesiolysis and relief of pain. Indications for epidural lysis of adhesions according to the originator of this technique include post-laminectomy syndrome, disk disruption, metastatic carcinoma of the spine, multilevel degenerative arthritis, facet pain, spinal stenosis, and pain unresponsive to spinal cord stimulation and spinal opioids [18]. Caution should be used when selecting patients in order to improve overall outcome and reduction of complications.

Contraindications for Epidural Lysis of Adhesions

The usual absolute contraindications for interventional pain techniques exist and are as follows: sepsis, chronic infection, coagulopathy, local infection at site of the procedure, and patient refusal. Relative contraindications to consider include arachnoiditis or any other situation where there is significant disruption in the tissue planes in close proximity to the dura. There is an increased risk of inadvertent subdural administration of these medications that can lead to complications. One may consider referring appropriate candidates to practitioners with more experience in this technique.

Patient Preparation

The risks, benefits, and alternatives to the procedure should be explained in great detail to the prospective patient. An informed consent should be signed with the patient. The obvious benefits are pain relief and improved physical function. There is a possibility for reversal of some neurological symptoms. The usual risks include bleeding, infection, and reaction to any of the injected medications. Other risks include worsening of pain, no pain relief at all, damage to blood vessels, and dural puncture which may lead to a spinal headache.

A complete history and physical with well-documented neurological and/or urological findings should be documented before endeavoring with this technique. Appropriate imaging such as MRI, CT scans, and even CT myelograms are helpful, but epidural fibrosis is best diagnosed when performing an epidurogram with contrast and live fluoroscopy [19, 20]. Visualizing filling deficits that correlate well with patient's symptoms improves the likelihood of success.

Medications for Neuroplasty

There are many combinations of local anesthetic and corticosteroid preparations for this procedure. None have been found to be superior over the other; therefore, the final combination can be left to the individual practitioner to decide upon.

Hypertonic Saline

Hypertonic saline induces a shift of fluid from an intracellular to extracellular space across an osmotic gradient it generates. Traditionally, the applications for its use have been using the intravenous route in trauma, hyponatremia, and shock.

In the epidural space, this promotes an increase in fluid and possible improvement in flow of fluid around nerve roots and fibrosis. Other mechanisms of action include selective C fiber blockade of dorsal rootlets that may be related to elevated chloride ion concentrations [21]. Other work, on frog spinal neurons, showed some activity on GABA receptors that depresses the lateral column evoked ventral root response with the overall reduction in spinal cord water volumes [22]. Efficacy of the use of hypertonic saline alone in the epidural space has been determined in several studies [23, 24].

Complications with the use of epidural hypertonic saline are found mostly with inadvertent intrathecal injection. These complications include hypertension, tachycardia, and tachypnea with pulmonary edema [25]. Management of these sequelae is supportive in nature and would require intensive monitoring as they may be severe and life threatening. It is imperative for careful determination of epidural injection of contrast to avoid this potential complication. A dural puncture should postpone continuation of this procedure.

Hyaluronidase

Hyaluronidase is used for its ability to purportedly disrupt epidural adhesions. It catalyzes the hydrolysis of hyaluronic acid which is a major constituent in human tissue. This increases permeability in tissue planes and aids in the dispersement and delivery of medication. Hyaluronidase disrupts the proteoglycan ground substance in the adhesions of the epidural space and facilitates subsequent injections of local anesthetic and corticosteroids through the matrix. It does not affect collagen fibers [26]. Currently, there are animal-derived hyaluronidase available (Hydase TM – PrimaPharm Inc, Vitrase – ISTA Pharmaceuticals, and Amphadase – Amphastar Pharmaceuticals) as well as an FDA-approved (for subcutaneous administration) recombinant "human" hyaluronidase (Hylenex – Halozyme Therapeutics). Some potential risk arises as some patients may be allergic to these preparations, particularly the purified animal preparation which may have limited their use especially in the pediatric population [27, 28]. The use of human recombinant hyaluronidase is less likely to cause allergic reaction as it has up to 100 times greater purity than the reference standard, animal-derived formulation based on enzymatic activity [29, 30]. Reported allergic reactions include erythema at the site to urticaria and angioedema in those patients receiving human recombinant hyaluronidase (less than 0.1 %) [31].

The addition of hyaluronidase as part of the injected medications into the epidural space is controversial. Early studies comparing its use in adhesiolysis revealed a trend in the data toward reducing the need for additional treatments, but no evidence to support its exclusive use was found [7]. In fact, many subsequent studies and techniques were performed with only hypertonic saline [23, 24]. Subsequent systematic reviews also have not shown analgesic efficacy evidence from the addition of hyaluronidase [5, 32]. Emerging studies are showing some benefit of the addition of hyaluronidase to hypertonic saline, local anesthetics, and corticosteroids. Of note, all available studies have looked at hyaluronidase isolated from animal sources (bovine testes).

Yousef and colleagues [26] reported a prospective double-blinded, randomized study evaluating the addition of hyaluronidase to a typical caudal epidural steroid injection with hypertonic saline for patients with failed back surgery syndrome. They found that addition of hyaluronidase significantly reduced pain in long-term follow-up at 6 and 12 months compared to the hypertonic saline, local anesthetic, and corticosteroid group. Outcome measures included significant reduction of opioid and increased mobility in the lumbar spine [26]. Further study is needed in demonstrating a clear effect of hyaluronidase in lysis of epidural adhesions.

Technique

Two percutaneous methods will be described in the following sections. The first will be the Racz technique [33, 34] performed over the course of 3 days, and the second will be a modified version proposed and studied by Manchikanti performed over the course of a single day. Numerous variations to these techniques have been proposed as well, including transforaminal approaches [34, 35].

The Racz Classical Technique

In the operating room:

1. The patient is placed into a prone position, and the general location of the sacral hiatus is prepared and draped in a sterile fashion. The appropriate amount of sedation can be administered based on physician and patient preference. The careful administration of midazolam and fentanyl is common practice, and the use of any stronger intravenous agents is usually unnecessary.
2. A local lidocaine anesthetic skin wheal is raised 1–2 cm inferior to the sacral hiatus. A small skin nick can be made with an 18-gauge needle to facilitate entrance of the larger epidural needle. A 15- or 16-gauge RK or Coudé epidural needle is placed into the sacral hiatus either using a midline approach or with an angle starting from the contralateral side of the suspected pathology. This initial angle allows for the final tip position to be biased toward the ipsilateral location of suspected fibrosis.
3. Fluoroscopy should be used first in a lateral approach to visualize the needle entry into the caudal space (Fig. 20.1). The needle can then be advanced in the anteroposterior view just below the S3 level to prevent accidental puncture of a low lying dura. Injection of a small amount of nonionic contrast can be used to ensure epidural location.
4. After negative aspiration for cerebrospinal fluid and blood, 5–10 ml of nonionic water soluble contrast (either Omnipaque 240 or Isovue 300) is injected smoothly under live fluoroscopy. An unremarkable epidurogram may have a "Christmas tree" pattern, the central canal making up the "trunk" of the tree and the nerve roots the "branches." An abnormal epidurogram will reveal filling deficits in areas of the presumed fibrosis (Fig. 20.2). This filling deficit should clinically correlate with the patient's symptoms before proceeding with the next step. There are some clinicians that perform the epidurogram after the catheter is in place by the suspected site of fibrosis (Fig. 20.3).

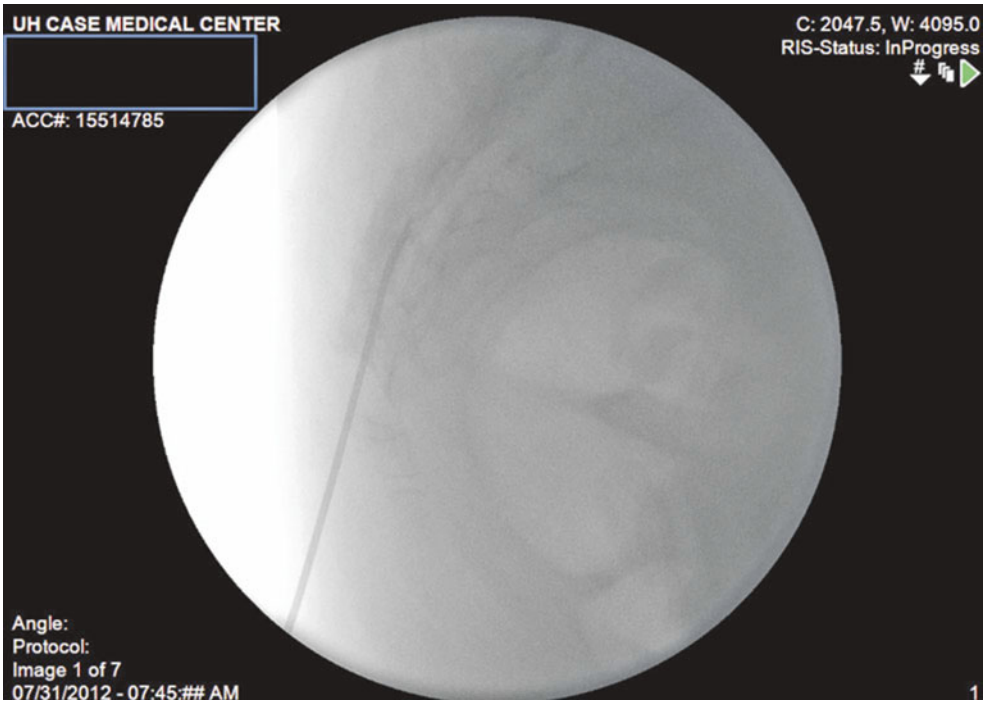

Fig. 20.1 Lateral View: A 16 g Coude needle enters the caudal canal

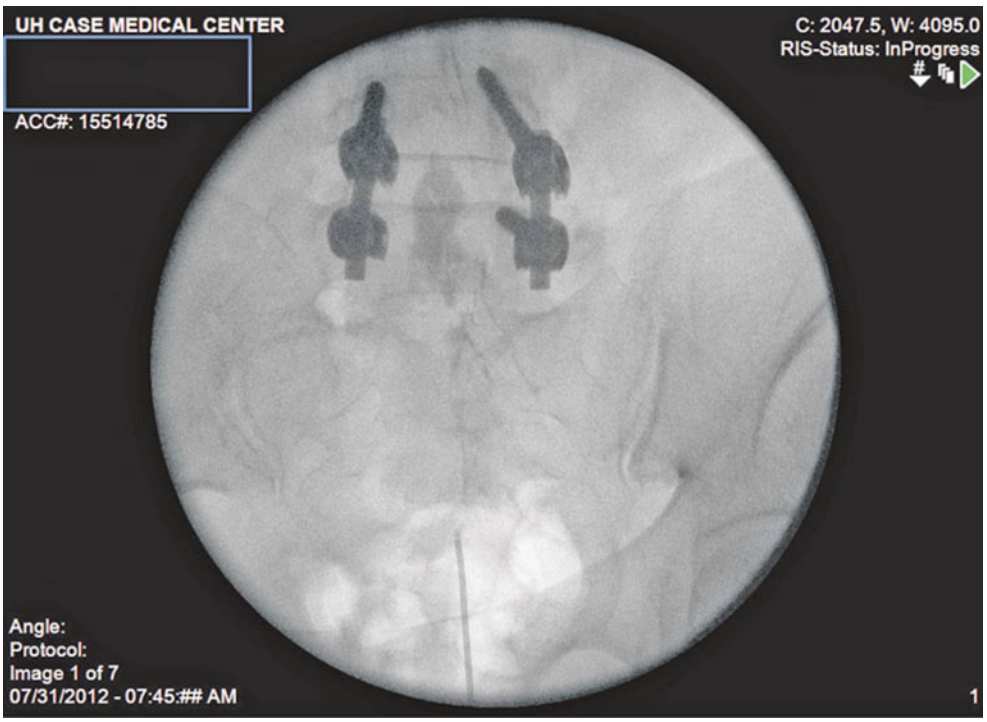

Fig. 20.2 Epidurogram: Injection of 2 ml of iohexol 240 with spread of contrast to L4/L5 junction with filling defect along right L5 nerve root

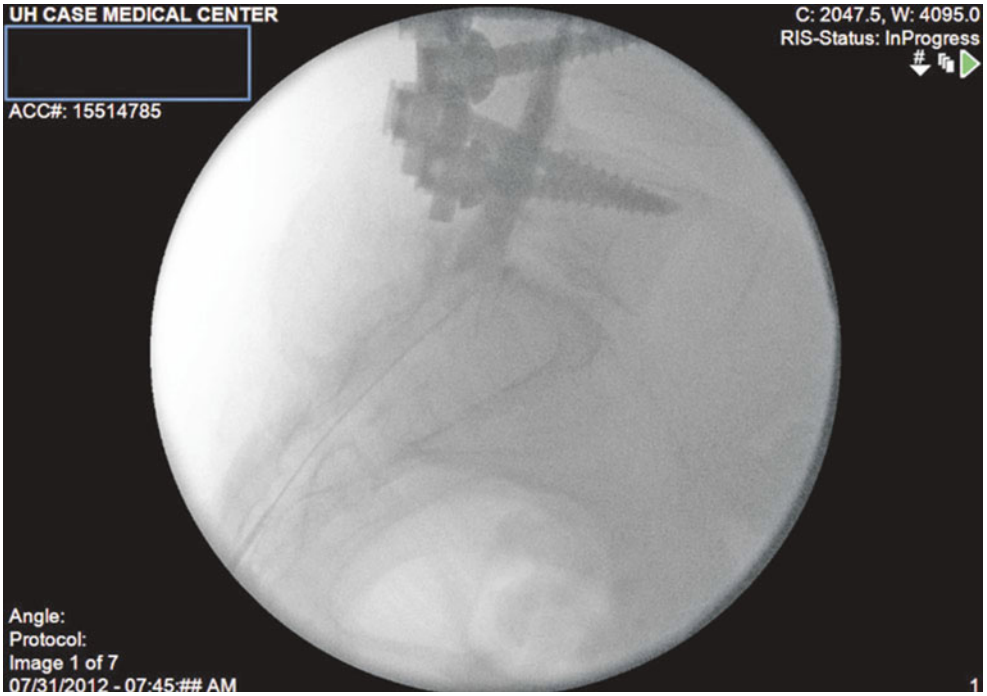

Fig. 20.3 Lateral View: The Racz catheter is advanced into the anterior epidural space until resistance is met

5. If the filling deficit correlates with symptoms, then a Racz Tun-L-Kath® or similar flexible catheter should be directed toward the area of filling deficits (Fig. 20.4). Placing a small bend to the tip of the catheter may improve the ability to steer toward these areas of filling deficits. A 30° bend in the first 1–2 cm of the catheter should be sufficient. Ventral placement of the catheter should be confirmed under lateral fluoroscopy.
6. After correct placement, inject 10 ml of preservative-free normal saline with or without 1,500 units of hyaluronidase into the area surrounding the filling defect. Follow this with 2–3 ml more of contrast to visualize opening of the scarred area and spread of the injectate in the epidural space (Fig. 20.5).
7. Prepare a 10-ml syringe of 9 ml of 0.5 % lidocaine and 40 mg/ml of triamcinolone diacetate. Other common corticosteroid preparations include 40–80 mg methylprednisolone (Depo-Medrol®), 25–50 mg triamcinolone diacetate (Aristocort®), 40–80 mg triamcinolone acetonide (Kenalog®), and 6–12 mg betamethasone (Celestone Soluspan®) [36]. Administer a 3-ml test dose and wait for several minutes to confirm no signs of intrathecal injection. Resume the smooth injection of the rest of the syringe if the test dose reveals no untoward signs.
8. Remove the needle under live pulsed fluoroscopy and secure the catheter to the skin with tape. Place triple antibiotic ointment over the puncture site and place sterile dressings. Attach a bacteriostatic filter to the catheter.

In the postanesthesia care unit 20 min later:

1. Infuse 10 ml of 10 % hypertonic saline over the course of 30 min. If the patient complains of pain, add several ml of 0.5 % lidocaine, wait for 5 min, and then resume.
2. At the end of the infusion, flush the catheter with preservative-free normal saline.

On days 2 and 3:

1. Inject 10 ml of 0.5 % lidocaine, wait for 25–30 min, and then infuse 10 ml of 10 % hypertonic saline over 30 min.
2. Flush catheter with 2 ml of preservative-free NS.
3. Repeat above on day 3, remove catheter, and place sterile dressings.

Modified Techniques [23] (Day 1)

The entrance into the caudal space is performed as described above. Adhesiolysis is carried out utilizing a Racz® catheter (EpiMed International, Inc.), with final positioning of the catheter on the side of the defect and the source of pain and an additional injection of contrast to identify successful adhesiolysis.

1. Following the completion of the adhesiolysis and repositioning of the catheter, an injection of 5 ml of lidocaine 1 % preservative-free with 6 mg of betamethasone phosphate acetate mixture should be injected.
2. After waiting 10–15 min, provided that there is no evidence of subarachnoid blockade, 6 ml 10 % sodium

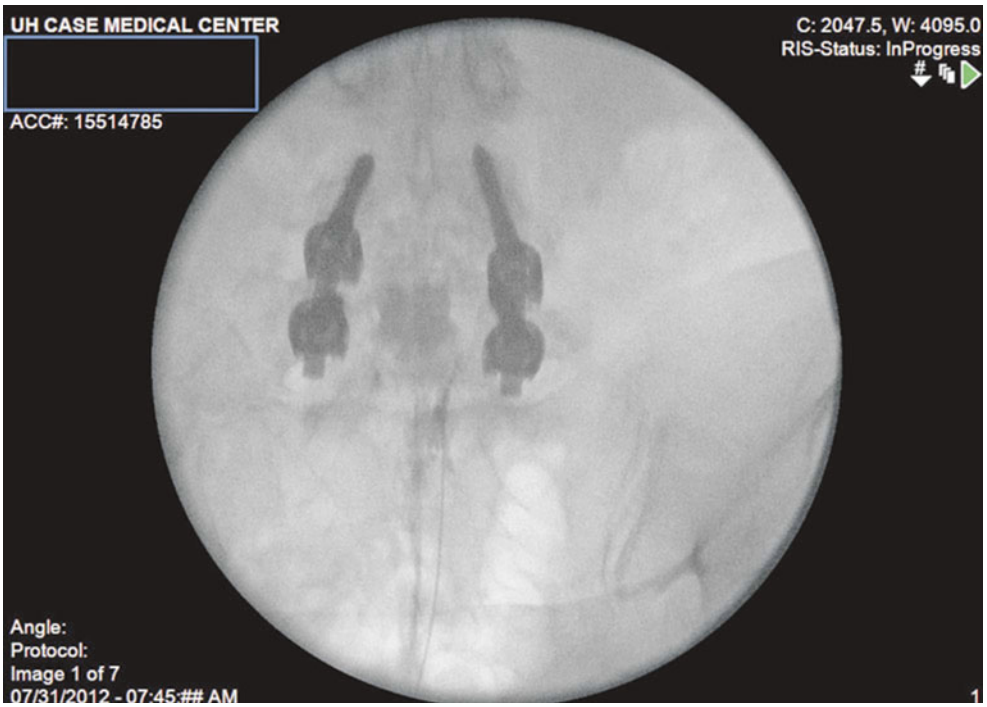

Fig. 20.4 AP View: The Racz catheter is seated more towards the filling defect on the right. The bevel is biased to the right side

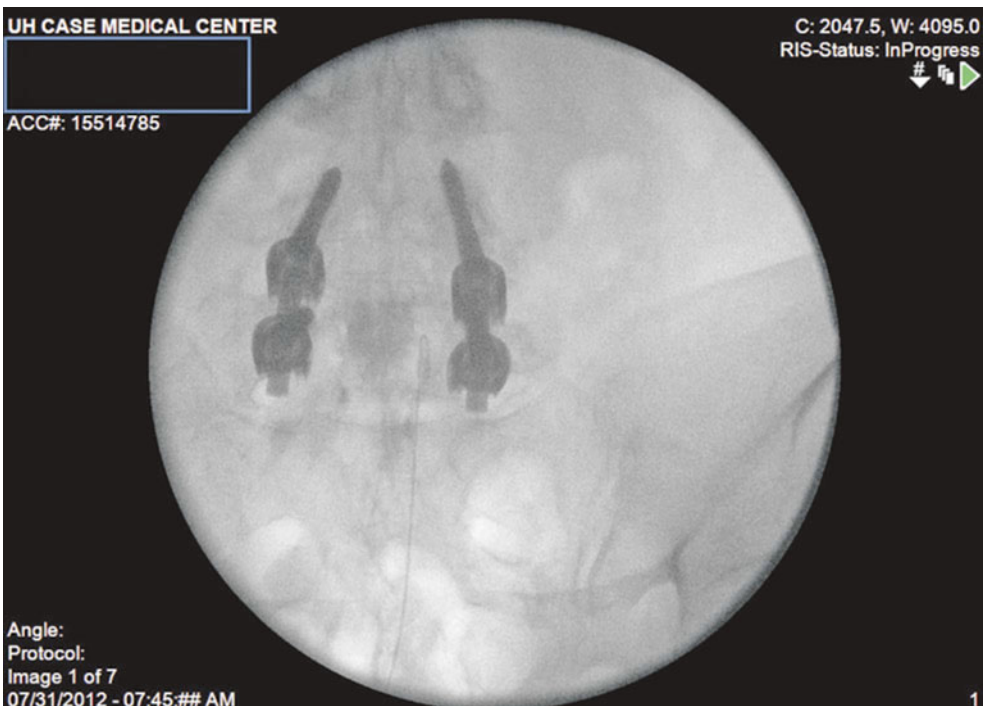

Fig. 20.5 Repeat injection of local anesthetic with mechanical manipulation of catheter results in advancement of the catheter to top of L5 vertebral level

chloride solution in two divided doses of 3 ml over 10–15 min is administered. The catheter is then removed, and the patient may be discharged home when stable.

Endoscopic Lysis of Adhesions

The first in vivo exam of the spinal canal was performed by J. L. Pool in 1937 and was complicated by hemorrhage. Through persistence and refinement of his technique, he was able to document over 400 cases by 1942 with successful observation and identification of neuritis, herniated nucleus pulposus, hypertrophied ligamentum flavum, neoplasms, and arachnoid adhesions [37, 38].

Further improvements in endoscopy and fiber-optic light sources improved percutaneous placement. Ooi and Morisaki from Japan were credited for these advancements throughout the 1960s and 1970s [37]. Shimoji and associates were the first to report the concomitant use of fiber-optic light sources and flexible fiber-optic catheters instead of rigid metal endoscopes. Fluoroscopy was used in conjunction with their technique which aided in identifying the spinal level in view. Significant anatomical findings including aseptic adhesive arachnoiditis and clumped nerve roots were also visualized with the use of this new technology [39]. Epiduroscopy may be useful in confirming a physiological basis for radiculitis when other diagnostic studies such as MRI are negative [37]. Direct visualization can be used to confirm clinical observations that may not otherwise be discovered by traditional tests. This would be a strong indication to use this technique over a percutaneous route if the practitioner has had appropriate training and experience.

Endoscopic Technique

The patient is placed into a prone position. Standard American Society of Anesthesiology recommendations for moderate sedation should be used. Prophylactic antibiotics should be administered prior to the start of the procedure.

1. After proper sterile preparation and draping, a skin wheal is raised over the sacral hiatus using 1–2 ml of 1 % lidocaine with a 25-gauge needle. A 16-gauge RK needle is then advanced into the hiatus under lateral and AP fluoroscopy.
2. An epidurogram is then performed with the injection of 10 ml of nonionic contrast dye.
3. A 0.9-mm guide wire is inserted through the needle, which is then advanced under fluoroscopic guidance to the level of suspected pathology and contrast filling defect. This is followed by a small incision with a #11 blade and advancement of a 9-French dilator with catheter (sheath) over the guide wire.
4. Once the catheter is advanced to the tip of the guide wire, the wire is removed. Following this, a 0.8-mm fiber-optic spinal endoscopic video-guided system is introduced into the catheter through the valve and is advanced until the tip is positioned at the distal end of the catheter, as determined by video and fluoroscopic images. The endoscope should be placed ventrolaterally toward the suspected side of the lesion.
5. In conjunction with gentle irrigation using normal saline, the catheter and fiber-optic endoscope are manipulated and rotated in multiple directions, with visualization of the nerve roots at various levels. Gentle irrigation is carried out by slow, controlled infusion. It is recommended that the infusion rate of saline irrigation should not exceed 30 ml/min and that the total infused volume should be less than 100 ml. (There will be retrograde flow that should not be counted toward the total volume) [37]. For prolonged cases with larger irrigation volumes, a continuous subarachnoid needle may be placed for continuous CSF pressure monitoring. Adhesiolysis and decompression are carried out by distension of the epidural space with normal saline and by mechanical means utilizing the fiber-optic endoscope. Visualization will be achieved only if the epidural space is kept distended by repeated injections of saline. Some structures that may be easily visualized include the dura mater.
6. Confirmation is accomplished with the injection of nonionic contrast material, and an epidurogram is performed on at least two occasions. Following completion of the procedure, generally, lidocaine 1 %, preservative-free, mixed with 6–12 mg of betamethasone acetate or 40–80 mg of methylprednisolone is injected after assuring that there is no evidence of subarachnoid leakage of contrast.
7. If pathology is determined to be at multiple levels, the procedure can be carried out at multiple levels, and the injectate should be injected in divided doses.

Complications

The usual risks of an invasive epidural procedure exist. The most commonly reported complications in percutaneous and endoscopic adhesiolysis include dural puncture, bleeding, infection, damage to blood vessels and nerves, unintentional dural puncture, inadvertent injection of medications, and catheter shearing [40].

Catheter shearing can occur as a result of frequent adjustment of the catheter against the needle. A Tuohy needle should not be used for this procedure as the back edge of the needle is a cutting surface and would shear the catheter [33]. Methods to minimize this include placement of the initial needle tip in the direction of the suspected lesion.

This will minimize the amount of times the catheter will need to be adjusted and steered. Catheter shearing can present a problem of retained hardware. Removal of the catheter can require surgical intervention or the use of epidural endoscopy. Manchikanti described a case where this occurred, and the use of endoscopy alone was not sufficient, ultimately arthroscopy forceps where utilized to remove the catheter [41].

Other cases have been reported where fragments of the Racz catheter were sheared off and trapped in an L5-S1 foramen. Karaman and colleagues report on an incident where the catheter fragment was left in position in the epidural space. Careful monthly follow-up for a year revealed the patient to respond well to the neurolysis, and a decision was made to forgo an aggressive surgical resection to recover the very small fragment [42].

Until recently, there had been no published reports of serious side effects like arachnoiditis, paralysis, or bowel or bladder dysfunction. Justiz and colleagues describe the case of a 73-year-old woman who opted for endoscopic lysis of adhesions for severe scarring of the epidural space. Subsequently, the patient developed a neurogenic bladder with urinary retention. Three years later, she experienced resolution of the neurogenic bladder symptoms that coincided with the use of the antibiotic nitrofurantoin. Upon discontinuation of the antibiotic, the patient noted that she was unable to void spontaneously. With reinstitution of nitrofurantoin, the patient was once again able to void effectively and has been maintained on nitrofurantoin for >3 years [2].

Infection is a frequent concern when performing any neuraxial technique. Strict aseptic technique should be standard practice; however, infections still occur. Meningitis is a rare but reported complication of this particular procedure as well. Wagner and colleagues reported an incidence of severe meningitis with significant neurological sequelae after an epidural lysis of adhesions for unspecific low back pain. They cautioned that this procedure should be done under strict aseptic technique [43]. It is recommended to proceed with careful patient selection before embarking on this intervention to reduce overall complications.

The risk of damage to blood vessels is usually determined during administration of contrast. Venous uptake can be seen during live fluoroscopy and should prompt the interventionalist to adjust placement of the catheter accordingly especially if very little contrast remains in the epidural space after the injection. Arterial uptake should definitely prompt redirection of the catheter for fear of a thrombotic event if particulate steroid is injected. This seems to be a rare phenomenon either due to the elasticity of arterial walls in relation to the catheter or due to the overall prominence of venous vasculature in the caudal space.

Unintentional dural puncture can also be prevented using few precautions. The most important would be to avoid advancing the needle above the level of the S3 foramen as there is a chance of puncturing a low lying dura. The second manner would be to avoid advancing the catheter against resistance. Due to epidural fibrosis, the dural plane may become more distorted in relation to the epidural space. While the tips of the catheters are flexible, they are still able to puncture the dura given enough applied force. The injection of contrast will also be indicative of proper placement. If an inadvertent dural puncture occurs while performing a percutaneous adhesiolysis, the practitioner should consider canceling the procedure and reschedule for a future date.

During epiduroscopy, a dural puncture does not necessitate a mandatory cancelation of the case in the hands of expert practitioners. Shah and Heavner [44] reported two successful completions of endoscopic adhesiolysis and decompressive neuroplasty after inadvertent subarachnoid and subdural punctures with the endoscope. They were able to retract the endoscope and visualize the dural tears in each situation. The epidural catheter was then advanced into the epidural space and was confirmed under direct visualization and appropriate contrast flow identified epidural placement.

Complications may arise when direct visualization during epiduroscopy is compromised. The epidural space needs to be distended by repeated injection or infusion of saline to maximize the field of view. Careful monitoring of total volumes will prevent increased epidural pressures from developing. At times, the anatomical structures will be difficult to discern, and retraction of the endoscope may bring structures into view better. Easily recognized structures include dura mater, ligamentum flavum, epidural fat, fibrous connective tissue, and blood vessels. Spinal nerve roots may be difficult to identify. The concurrent use of fluoroscopic guidance can help identify the level being viewed on the screen and aid in orienting the interventionalist [37].

Complications may also arise when the cerebrospinal fluid pressure becomes elevated during epiduroscopy. The increase in epidural pressures is transmitted into the subarachnoid space to the optic nerve sheath, compressing the optic nerve and its vasculature. The vasculature compression ruptures retinal blood vessels, leading to retinal hemorrhage. In a review by Gill and colleagues, there have been only a dozen reported cases. The common finding was retinal hemorrhage with recovery occurring in 79.2 % of cases [45]. Bolus injections with or without epiduroscopy were considered the precipitating event. The volume varied between 20 and 120 ml of solution. To prevent this complication, it is recommended that the infusion rate of saline irrigation should not exceed 30 ml/min and that the total infused volume should be less than 100 ml [37]. For prolonged cases with larger irrigation volumes, a continuous subarachnoid needle may be placed for continuous CSF pressure monitoring.

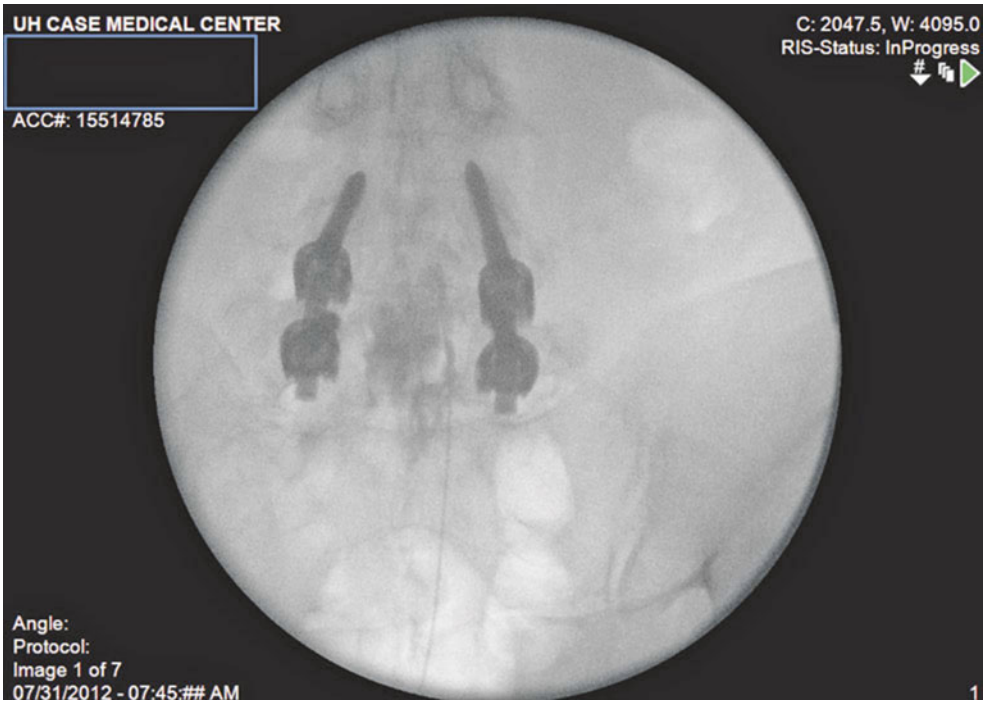

Fig. 20.6 Further catheter manipulation and contrast injection results in expansion of contrast spread to mid L4 vertebral level

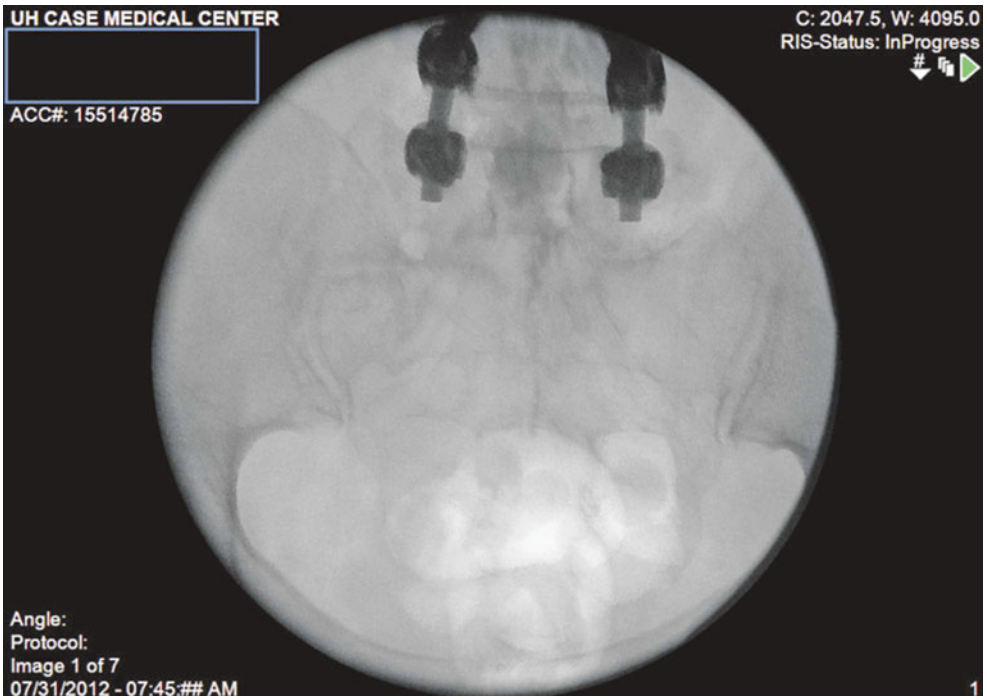

Fig. 20.7 Final medication spread after depositing local anesthetic and steroids. Contrast has spread well into L4 and along the contour of the right L5 nerve root

Outcomes

There is some good evidence for short- and long-term relief with the use of percutaneous adhesiolysis. Unfortunately, there is still a paucity of literature in regard to the overall efficacy for this technique to solidify the role of adhesiolysis in the treatment algorithm of patients with intractable pain. Several randomized studies of this technique support its use in an interventionalist's armamentarium. Veihelmann et al. [46] evaluated 99 patients with chronic low back pain and sciatica (13 with prior back surgery). Nerve root compromise was confirmed by MRI and CT. A control group of 52 patients were treated with physical therapy. Forty-seven other patients underwent epidural neuroplasty with percutaneous adhesiolysis. The group undergoing neuroplasty had a catheter placed through the sacral hiatus to the level of the pathology after epidurogram. Postprocedure follow-up occurred at 3, 6, and 12 months. The outcome measures included the visual analog scale for the back and leg, Oswestry disability score, Gerbershagen score (explain briefly what it is), and analgesic score. An intent-to-treat analysis was performed. Among the adhesiolysis patients, there was a significant decrease in the VAS and Oswestry scores at 1, 3, 6, and 12 months. Twenty-eight patients undergoing adhesiolysis were able to decrease I Gerbershagen grade compared to 2 PT patients. The Gerbershagen score is commonly used in German pain clinic. It is a 4-axis operationally defined staging system for the chronicity of pain [47]. Epidural neuroplasty significantly reduced pain and functional disability in patients with chronic low back pain and sciatica caused by disk protrusion or failed back surgery syndrome in short-term (<6 months) and long-term (at 12 months) follow-up [46].

Another study by Manchikanti et al. [24] randomized 75 patients into three different treatment groups. Group I (25 patients) was a control group that received epidural catheterization but no adhesiolysis and injection of local anesthetic and steroid. Group II (25 patients) was treated with epidural adhesiolysis, followed by injection of normal saline, local anesthetic, and steroid. Group III (25 patients) consisted of adhesiolysis followed by injection of local anesthetic, hypertonic saline, and corticosteroid. Follow-up occurred at 3, 6, and 12 months. Outcome measures used included the VAS pain scale, Oswestry Disability Index 2.0, work status, opioid intake, range of motion measurements, and psychological evaluation by P-3. Significant improvement in these outcomes was found at 12-month follow-up. Seventy-two percent of patients in Group III (adhesiolysis and hypertonic saline neurolysis) and 60 % of patients in Group II (adhesiolysis only) compared to 0 % of Group I (control) demonstrated improvement. There was positive short-term (<6 months) and long-term relief (>6 months). In this study, adhesiolysis patients received good relief with or without hypertonic saline in neurolysis.

Heavner et al. [7] studied the efficacy and use of hypertonic saline and hyaluronidase in the percutaneous adhesiolysis. Eighty-three subjects with radiculopathy and low back pain were assigned to one of four epidural neuroplasty treatment groups: (a) hypertonic saline plus hyaluronidase, (b) hypertonic saline, (c) isotonic saline (0.9 % NaCl), or (d) isotonic saline plus hyaluronidase. Subjects in all treatment groups received epidural corticosteroids and local anesthetics. The results revealed 24 subjects did not complete the study. Most of the other 59 subjects receiving any of the four treatments as part of their pain management obtained significant relief immediately after treatment. Visual analog scale (VAS) scores for the area of maximal pain (VASmax; back or leg) were reduced in 25 % or more of subjects in all treatment groups at all posttreatment follow-up times (1, 3, 6, 9, and 12 months). A smaller fraction of subjects treated with hypertonic saline or hyaluronidase and hypertonic saline required more additional treatments than did subjects receiving the other treatments. The investigators were able to conclude that percutaneous epidural neuroplasty, as part of an overall pain management strategy, reduces pain (sometimes for over 1 year) in 25 % or more of subjects with radiculopathy and low back pain refractory to conventional therapies. The use of hypertonic saline may reduce the number of patients that require additional treatments.

There have been very few randomized double-blinded studies evaluating the efficacy of endoscopic neurolysis. Manchikanti and colleagues [48] did one such study in a prospective, randomized, double-blind trial to determine the outcome of spinal endoscopic adhesiolysis to reduce pain and improve function and psychological status in patients with chronic refractory low back and lower extremity pain. A total of 83 patients were evaluated, with 33 patients in Group I and 50 patients in Group II. Group I served as the control, with endoscopy into the sacral level without adhesiolysis, followed by injection of local anesthetic and steroid. Group II received spinal endoscopic adhesiolysis, followed by injection of local anesthetic and steroid. Among the 50 patients in the treatment group receiving spinal endoscopic adhesiolysis, significant improvement without adverse effects was shown in 80 % at 3 months, 56 % at 6 months, and 48 % at 12 months. The control group showed improvement in 33 % of the patients at 1 month and none thereafter. A significant number of patients obtained long-term (>12 months) relief with improvement in pain, functional status, and psychological status. This technique of spinal endoscopic adhesiolysis with targeted delivery of local anesthetic and steroid was found to be an effective treatment in a significant number of patients with chronic low back and lower extremity pain without major adverse effects.

Summary

There has been an evolution of epidural neuroplasty over the last several decades [34]. Epidural adhesiolysis is a valuable technique in placing medications into areas of the epidural space that would otherwise be inaccessible by basic injections. There are many ways to perform adhesiolysis, and it is important for the practitioner to understand their limits before proceeding. Referral to a practitioner with more experience should be considered with more difficult cases. Careful selection of patients is important to avoid any untoward complications which are rare but serious. There is some evidence to support the use of this technique in an interventionalist's armamentarium to reduce suffering and pain particularly in patient with lumbar post-laminectomy syndrome, but more prospective randomized controlled studies are needed to solidify the role and value of epidural adhesiolysis.

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Thoracic and Lumbar Sympathetic Nerve Block and Neurolysis

21

Tim J. Lamer and Jason S. Eldrige

Key Points

- Preganglionic sympathetic neurons originate in the IML of T1–L2/3 and travel sequentially via the ventral root and then white rami communicantes to the paravertebral sympathetic chain or prevertebral ganglia. Postganglionic neurons originate in the sympathetic chain or prevertebral ganglia and then travel to (1) innervate end-organ structures or (2) follow a spinal nerve to the periphery via the postganglionic gray rami communicantes.
- Alcohol and phenol, in a variety of concentrations with various additives, are the two most commonly used neurolytic chemicals. Each has unique properties and side effects that warrant particular attention. Continuous radiofrequency involves the application of heat, generated by RF waves and typically held at 80 °C, to thermocoagulate nerve fibers.
- *Kuntz fibers*, arising from the upper thoracic sympathetic ganglia, may provide unrecognized sympathetic innervation to the upper extremity and be a contributory factor in stellate ganglion blocks which result in partial/incomplete sympathectomy.

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Background and Historical Perspective

Sympathetic blockade of the thoracic and lumbar regions has been long described in the medical literature; initial techniques for a percutaneous thoracic block (paravertebral approach) were documented by Kappis in 1919 [1]. Earlier descriptions which postulated the role of the sympathetic system in the development and maintenance of neuropathic pain are detailed in the medical literature of the early 1900s. The sympathetic contribution to so-called causalgia was theorized in 1916 by Leriche, who argued that periarterial excision of sympathetic fibers may be of therapeutic benefit in relieving pain [2].

Over the next 20–30 years, various chemical and surgical techniques to denude, disrupt, ligate, or otherwise destroy the thoracic sympathetic innervation were devised. Most of these aforementioned methods were of limited therapeutic utility due to the inherent risks of open surgical techniques and the incomplete understanding of the complexities in relevant anatomy and physiology of the sympathetic system. One of the first percutaneous approaches to thoracic sympathetic blockade was accomplished by Leriche and Fontaine in 1925, who utilized a paravertebral technique [3]. Another noteworthy discovery, germane to the therapeutic success of stellate ganglionectomy for relieving upper extremity pain, was described by Albert Kuntz [2] in 1927. Kuntz noted that approximately 20 % of the population have sympathetic innervation to the upper extremity which does not pass through the stellate ganglion [4]. These so-called *nerves of Kuntz* (or *Kuntz fibers*) are composed of branches from the T2 and T3 thoracic sympathetic ganglia that route directly to the brachial plexus without passing through the sympathetic trunk proper. Contemporary clinical and cadaveric studies demonstrate that significant Kuntz Fibers occur more frequently than previously thought, with some studies claiming a 20–60 % incidence. As such, this *anatomic loophole* continues to be a scapegoat for failure to fully alleviate sympathetic-mediated symptoms after endothoracic surgical

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sympathectomy [4]. Additionally, the aforementioned discoveries have led to significant interest in procedures designed to ablate the T2 and T3 thoracic sympathetic ganglia [3–6].

Regardless, thorascopic sympathectomy (particularly endoscopic or video-assisted techniques) has enjoyed continued development and refinement over the last few decades. In addition, Wilkinson in 1979 was one of the first to illustrate a percutaneous approach to thoracic sympathetic structures for the purpose of chemical or radiofrequency neurolysis [6]. Fluoroscopic- and CT-guided percutaneous procedures are well described, but more recently, ultrasound technology has led to a revitalization of the procedure due to its presumed increased margin of safety while allowing similar diagnostic and therapeutic endpoints [7, 8].

The concept of lumbar sympathetic blockade was similar to the historical evolution of thoracic level sympathetics; the apparent first report in the literature was documented by Brunn and Mandl in 1924 using a paravertebral approach [9]. Similar to thoracic level interventions, lumbar sympathetic block was initially proposed as a therapy for vascular malperfusion (*Raynaud's disease*) and neuropathic "causalgia." The Second World War, primarily due to the frequency of lower extremity neuropathic injury, helped popularize interest in the lumbar sympathetic block [10]. Although several techniques of merit have been described, it is the original paravertebral approach of Kappis and Mandl described in the early 1920s that remains most popular [9]. Unlike the thoracic level, however, lumbar sympathetic blockade remains a commonly used interventional technique by pain practitioners worldwide.

Anatomic Considerations of the Sympathetic Nervous System

The sympathetic nervous system, a subset of the autonomic nervous system, subserves the body's need for rapid mobilization due to stress. As such, its chief role is one of initiation and maintenance of the familiar *fight-or-flight response*: characterized by peripheral extremity vasoconstriction, catecholamine surge, hastening of cardiopulmonary function, antagonism of intestinal activity, shunting of blood volume to large muscle groups, and many other functions. By clarifying the end function of this system in one's mind, the reader is better able to understand and even anticipate the anatomic connections required for sympathetic functionality to be established.

Alternatively known as the thoracolumbar nervous system, sympathetic nerves originate with cell bodies located in the intermediolateral horn (IML) of the T1 through L2–3 level of the spinal cord. These thoracolumbar cell bodies in the IML then give rise to preganglionic nerve fibers, which travel via the ventral root of the segmental spinal nerve and form white rami communicantes on their way to the paravertebral ganglia (i.e., sympathetic chain) or prevertebral ganglia (Fig. 21.1). When the preganglionic sympathetic nerve travels to the sympathetic chain (i.e., paravertebral ganglion), it has one of three choices for further course: synapse at the segmental paravertebral ganglion with a postsynaptic neuron, traveling up/down the sympathetic chain to synapse with a postsynaptic neuron at a remote level, or continue to pass through until synapsing with a postganglionic nerve in a prevertebral ganglion (Fig. 21.2) [11]. The postganglionic neuron then travels onward via the *gray rami communicantes* or prevertebral plexus to various final end-organ sites; typical postganglionic targets include the pupils, heart, blood vessels, sweat glands, and various visceral structures [2, 10–13]. It should be noted that *gray rami communicantes* (unmyelinated) allow for efferent connection between postganglionic sympathetic nerves to the segmental spinal nerve for vasomotor/sudomotor/pilomotor function, while *white rami communicantes* (myelinated) provide for efferent/afferent connections between preganglionic sympathetics (along with visceral afferents) and the central neuraxis (Fig. 21.2) [2, 10]. Consequently, the white rami communicantes form the sole pathway for neural traffic between the central nervous system and peripheral sympathetic system [10].

The sympathetic chain (paravertebral ganglia) extends from the top of the cervical spine down to the coccyx, traveling as two sympathetic trunks located along the anterolateral portion of the vertebral column. It is further subdivided into 23 sets of paired ganglia in the cervical [3], thoracic [12], lumbar [4], and sacral [4] regions, plus one single unpaired ganglion impar [2, 10–13]. Prevertebral ganglia, which provide neural intercession between the sympathetic chain and the postganglionic end-organ target, consist of specific ganglia and/or plexi located in the head, chest, abdomen, and pelvis. The major prevertebral sympathetic structures include the ciliary/otic/sphenopalatine/submaxillary ganglia, cardiac plexus, pulmonary plexus, celiac ganglia, superior and inferior mesenteric ganglia, and superior and inferior hypogastric plexuses [2, 10, 11].

The two anatomic areas most relevant to the discussion of this chapter are the cervicothoracic and lumbar ganglia regions. The cervicothoracic sympathetic region is principally composed of superior, middle, inferior, and stellate ganglia in the cervical region, along with 12 paired paravertebral ganglia in the thoracic region. The stellate ganglion, which is chiefly formed by the convalescence of inferior cervical and first thoracic ganglia elements, is of particular interest and lies ventrolaterally to the body of C7 with extension to the lateral portion of the T1 vertebral body [2, 11]. As mentioned previously, anatomic variants may include *Kuntz Fibers* which are postganglionic sympathetic branches from upper thoracic sympathetic ganglia (primarily T2 and T3) that may have direct neural connections to the brachial plexus external to the normal paravertebral (sympathetic chain) pathway.

Caudal to the stellate ganglion lies the *thoracic sympathetic chain*, which continues in a linear course along the

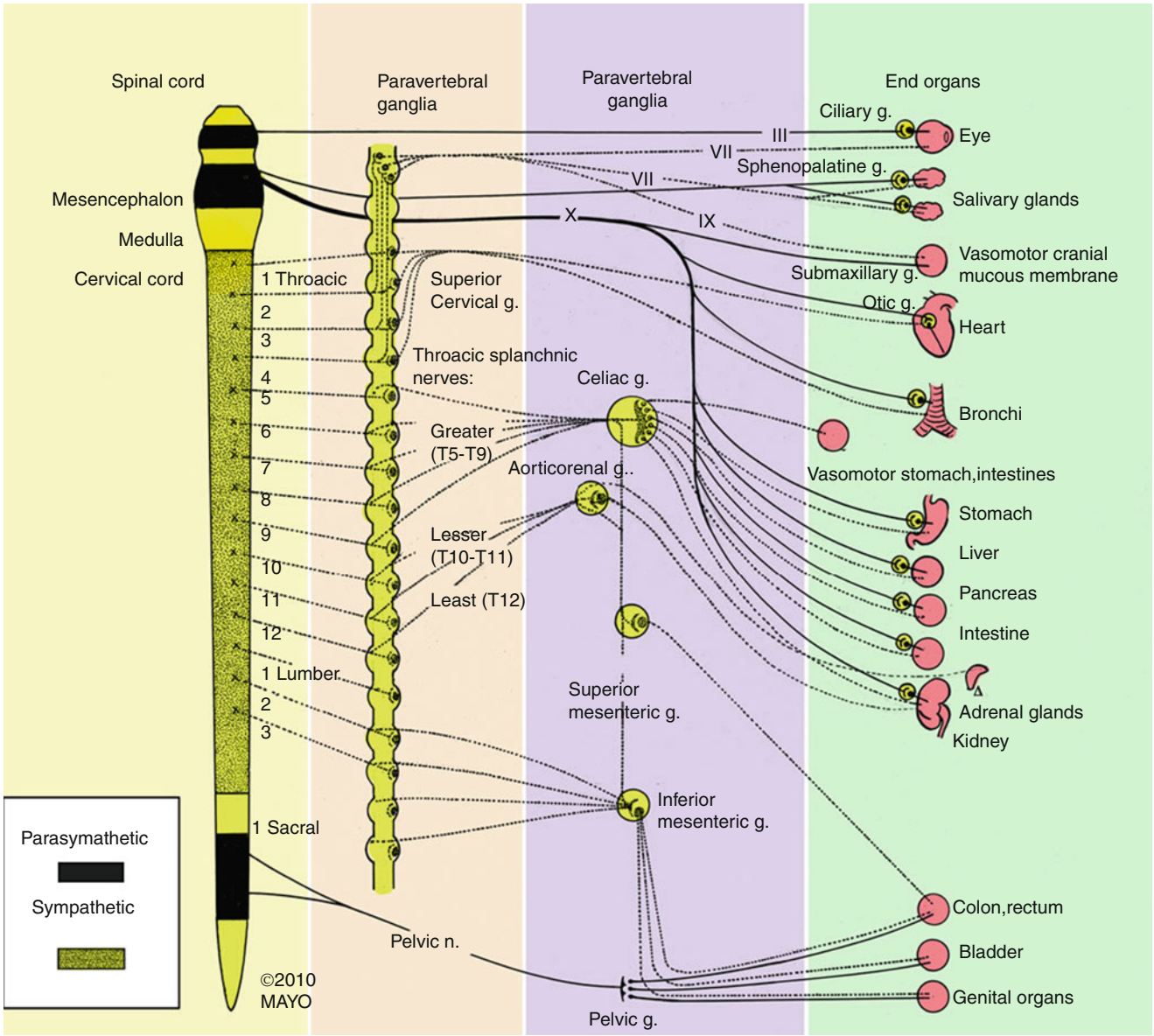

Fig. 21.1 Autonomic nervous system schematic, with special emphasis on common anatomic pathways of the sympathetic nervous system (With permission © Mayo Clinic, 2010)

dorsolateral aspect of the thoracic vertebral bodies; it is punctuated by paired segmental thoracic ganglia that lie just slightly caudad of the vertebral body midline (Fig. 21.3) [2, 9, 11]. The thoracic chain lies anterior to the head/neck of each rib in close approximation to the costovertebral interface and is bounded anterolaterally by the pleura of the lung [2, 11]. In the mid to lower thoracic regions, the sympathetic chain migrates to a more anterolateral position, relative to the vertebral bodies and lies at the anteromedial interface of the iliopsoas fascia as it further extends to the lumbar level. Typically, the lumbar sympathetic chain is found to have four discrete paired ganglia, but significant anatomic variation exists. Anatomic dissections have demonstrated a propensity for clustering of most significant lumbar sympathetic ganglia at L3, which tends to be the classical target of percutaneous-based pain interventions [2]. More specific discussions regarding thoracic and lumbar sympathetic anatomy will follow in the interventional technique sections.

Methods of Neurolysis

Specific mention should be made of chemical neurolytic agents, since they are less commonly used and have unique properties that warrant particular attention. The most commonly used neurolytic chemicals are alcohol (33–100 %) and phenol (2–12 %, with or without glycerol additive). Alcohol is hypobaric relative to CSF, causes significant

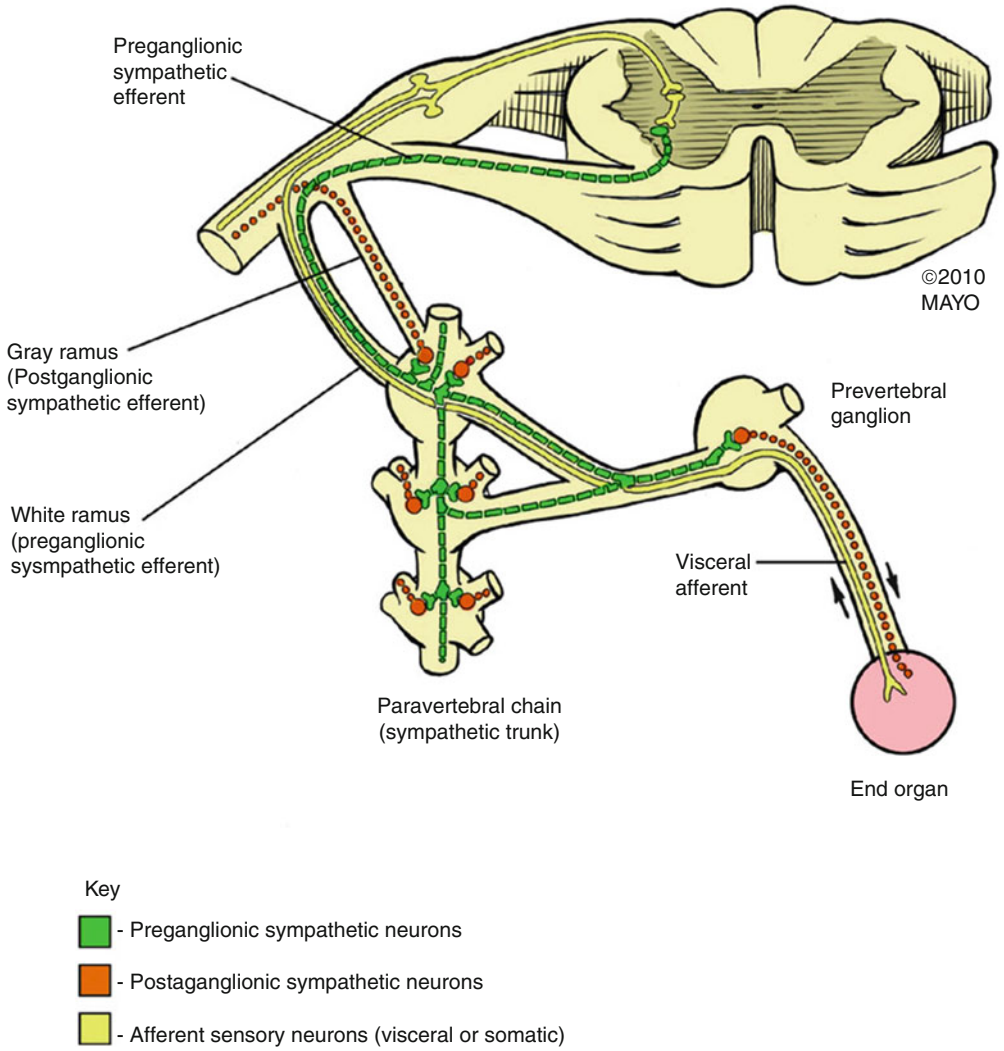

Fig. 21.2 Schematic of the central cord, exiting spinal nerve, and traditional anatomic path of the sympathetic nervous system that originates in the central lateral horn. Note that typical procedural targets include the lateral paravertebral chain (sympathetic trunk and ganglia) and/or the prevertebral ganglion/plexus (With permission © Mayo Clinic, 2010)

pain/burning upon injection, and induces Wallerian degeneration from the direct neurodestructive effects of ethanol. Notably, alcohol may allow for selective neurolysis of small sensory fibers (sparing motor) when used in low concentrations less than 33 % [14]. Phenol is hyperbaric relative to CSF when glycerol 4–10 % is added, has local anesthetic properties that minimize discomfort when injected, and may enable selective neurolysis of sensory nerves when used in small concentrations (typically 2–3 %). Phenol imparts neurolysis due to denaturing of protein, which may explain its predilection to cause vascular injury (risk of spinal infarction with subarachnoid use, erodes Dacron graft material, etc.). While less likely than phenol to cause direct vascular injury, alcohol has been associated with increased risk of vascular spasm and subsequent ischemic blood flow [14]. Lastly, phenol has been linked with arrhythmia and cardiovascular collapse; the mechanism is not fully elucidated, but likely relates to phenol's sodium channel antagonist properties.

Continuous radiofrequency ablation (RFA) relies upon the application of heat, generated by continuous radiofrequency (RF) waves, to cause thermocoagulation of nerve fibers. This technology heats adjacent tissue to 80 °C, typically for 90 s. Recognize that sensory testing at 50 Hz and 1 V and motor testing at 2 Hz and 3 V may help establish whether intercostal/somatic nerves are being stimulated. If one is unable to elicit somatic nerve (intercostal) stimulation at 2 Hz and up to 1.5 V, it is much less likely that thoracic sympathetic ganglion RFA will cause injury to the segmental somatic nerve [8]. Additionally, post-RF neuritis sometimes develops after lesioning; this is usually self-limited, spontaneously resolves, and may be treated with steroid administration (prophylactically or after neuritis develops).

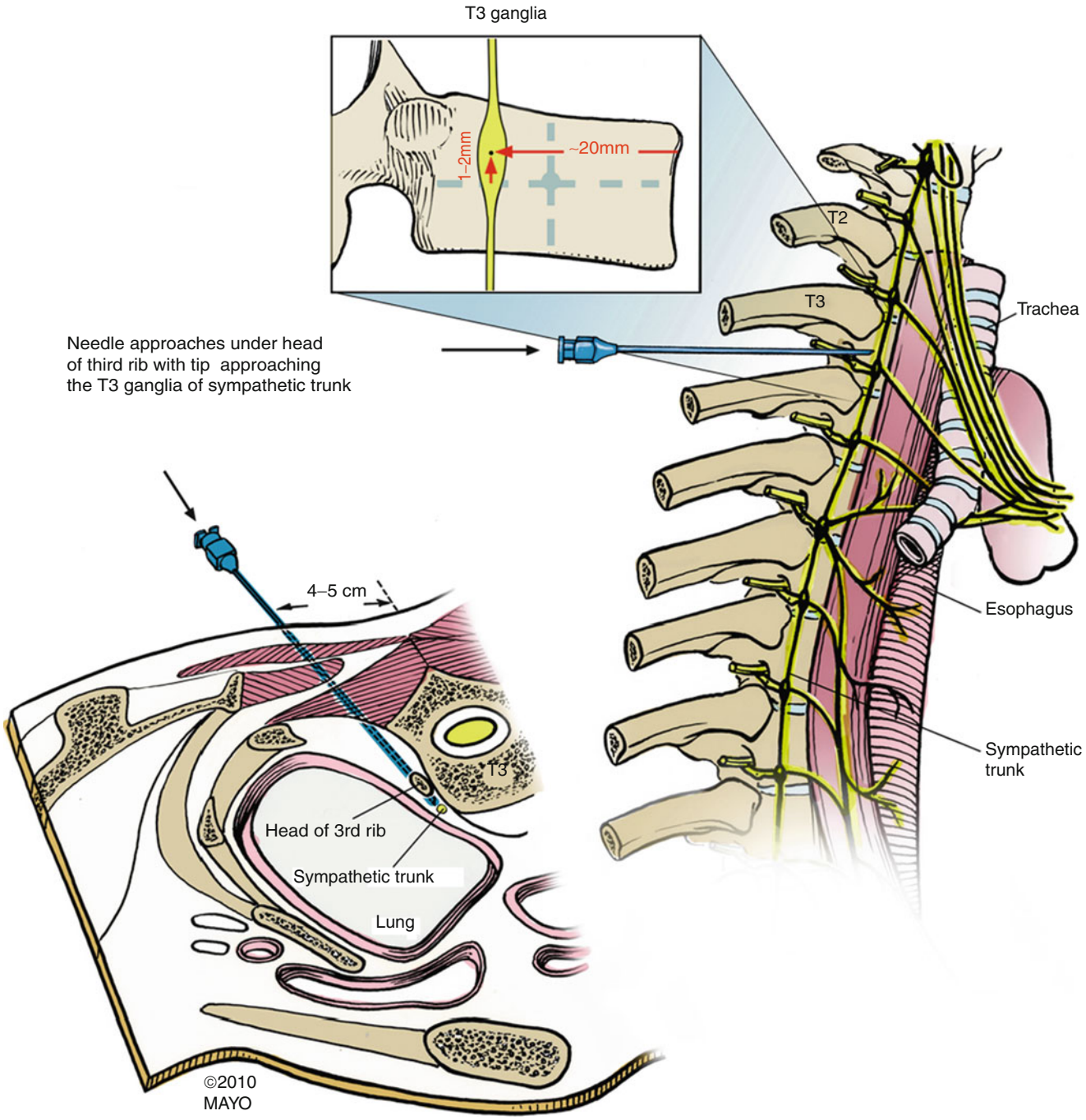

Fig. 21.3 Thoracic sympathetic ganglion block, using classic fluoroscopic technique, denoting the sagittal and axial views of the final position of the procedural needle tip (With permission © Mayo Clinic, 2010)

Thoracic Sympathetic Block

Specific Anatomy and Physiology

The thoracic sympathetic nerves typically consist of 12 paired paravertebral ganglia that punctuate the sympathetic chain at each thoracic vertebral level. These thoracic level paravertebral trunks travel dorsolaterally relative to the vertebral body, just anterior to the transverse process and posterior to the pleura of the lung [2, 11–13]. The superior most thoracic ganglion (T1) typically fuses with the inferior cervical ganglion (C8) to form the stellate ganglion in the majority of patients [2, 11–13]. The upper thoracic sympathetic chain runs anterior and just lateral to the head of the rib, with the ganglia located slightly caudad to the inferior edge of the head of the rib (Fig. 21.3).

As one progresses down the thoracic spine, the sympathetic chain gradually moves closer to the anterolateral position on the vertebral body assumed in the lumbar region. The thoracic sympathetic ganglia lie just inferior of the true vertical midpoint of the vertebral body, though the anteroposterior position moves more ventrally as one descends down the thoracic spine [8, 9]. To be sure, once at the T11 level, the low thoracic sympathetic chain has assumed a much more anterolateral position with individual ganglia located against the lateral surface of the vertebral body.

As mentioned previously, anatomic variants may include *Kuntz Fibers*, which are postganglionic sympathetic branches from the T2 and T3 (possibly T4) sympathetic ganglia that may have direct neural connections to the brachial plexus external to the normal paravertebral (sympathetic chain) pathway. The clinical relevance of this common anatomic pathway (10–20 % prevalence) is that a perfectly performed stellate ganglion block may not result in a complete sympathectomy for the entire upper extremity. *Kuntz fibers*, arising from the upper thoracic sympathetic ganglia, may provide unrecognized sympathetic innervation to the upper extremity [3, 6]. Consequently, it is possible to perform a successful stellate ganglion block that causes only a partial sympathectomy to the upper extremity due to unblocked *nerves of Kuntz*; this may appear clinically indistinguishable, in terms of asymmetric extremity temperature change, from a successful stellate blockade in patients without significant Kuntz Fibers. Thus, one must consider that sparing of Kuntz Fibers *may* be responsible for a stellate ganglion blocks that fail to relieve pain (regardless of evidence for successful sympathectomy). The primary clinical impetus for development of thoracic sympathetic blocks was an attempt to target these *Kuntz Fibers* at T2 and T3, though the techniques described can readily be applied throughout the thoracic spine.

Indications and Contraindications

Indications for thoracic level sympathetic block include hyperhidrosis, upper extremity vascular malperfusion (Raynaud's), and upper extremity or thoracic level sympathetically maintained neuropathic pain, along with visceral pain syndromes from the heart, lung, and/or esophagus. In general, because of the overlap in anatomic territory and existence of Kuntz fibers, one should consider upper thoracic level (T2 or T3) sympathetic blockade for any of the commonly accepted indications described for the stellate ganglion. Along with thoracic and upper abdominal visceral pain, consideration should be given for post-thoracotomy pain (particularly if sympathetic features are evident), postherpetic neuralgia, frostbite injuries to the upper extremity, and phantom breast pain [13].

Contraindications include the typical neuraxial *absolutes* of localized infection (skin or adjacent structures), systemic infection, and bleeding diathesis or coagulopathy. *Relative* contraindications relate primarily to the underlying function of adjacent anatomic structures, namely, pulmonary impairment and/or aneurysm of the great vessels (aorta or vena cava).

Complications and Expected Side Effects

Expected side effects from thoracic sympathectomy include ipsilateral Horner's syndrome, adjacent somatic nerve block, and cardiac accelerator fiber block. Unexpected, though entirely possible, complications include intrathecal, subdural, epidural, intravascular (intercostal, azygous, aorta) injections. Also possible, though very unlikely, is the danger of esophageal perforation if the needle is placed too anteriorly. The most feared of the complication is unintended puncture of the lung pleura and consequent development of pneumothorax. Pneumothorax may present with a delayed clinical presentation, which necessitates informing the patient of probable warning signs and when to seek medical attention. If using neurolytic techniques, damage to somatic nerves may occur from spread through the epidural, paravertebral, intervertebral foramen, or even intrathecal space (less likely); this may result in significant sensory and/or motor deficits that are not reversible.

Procedural Technique for Block Neurolysis

There are various descriptions of blocks and/or neurolysis to the thoracic sympathetic chain, but our discussion will focus on percutaneous approaches and intentionally omit reviews on surgically open and endoscopic techniques. One should also assume that real-time imaging, typically with ultrasound and/or fluoroscopy, should be utilized in order to optimize the safety, accuracy, and precision of these techniques. In particular, without the ability to visualize the lung, the risk of pneumothorax cannot be entirely eliminated. The technical procedure is similar throughout the thoracic spine, but the details described below are *most specific to the T2–3 levels* [7, 8, 11, 13]:

1. Plan to use a posterior approach, placing the patient prone.
2. If using fluoroscopy, orient the image intensifier in the true AP position, slightly oblique (15–20°, ipsilateral), with enough cephalad angulation to be in-plane with the neck of the rib at T2 or T3. This will allow coaxial placement of the procedural needle to a target point just anteroinferior to the head of the T2 or T3 rib (where the thoracic ganglion lies, see Fig. 21.3).

3. Initially, enter the skin approximately 2.5–5 cm lateral from true midline (depending upon degree of obliquity used) and coaxially advanced to the inferior edge of the rib or transverse process as applicable, depending upon degree of cephalad angulation used.
4. After touching bone, minimally redirect inferiorly until passing through the costotransverse ligament. The costotransverse ligament can be "felt" by a distinctive pop, or a loss or resistance technique can be utilized with a fluid or air-filled syringe. In either case, passage through this ligament heralds arrival at the retropleural space.
5. The needle should be closely approximated to the lateral edge of the adjacent vertebral body. The final needle tip position will be approximately just cephalad and posterior to the true midpoint along the dorsolateral aspect of the T2 or T3 vertebral body (Fig. 21.3).
6. Injection of contrast will demonstrate spread along the dorsolateral aspect of the thoracic vertebral column. If one breaches the parietal pleural, the lung dome will be outlined and the needle is too lateral (monitor patient for pneumothorax).
7. Proper sterile technique should be observed at all times, with appropriate monitoring established beforehand and local anesthetic infiltration taking place prior to the placement of the procedural needle. Aspiration should be negative for CSF, blood, and air before injecting local anesthetic, chemical neurolytic agents, or applying radiofrequency ablation. Care should be taken to verify no foraminal spread of contrast prior to neurolysis. Lastly, the use of local anesthetic test doses and/or digital subtraction angiography will help elucidate unintended vascular uptake prior to neurolytic procedures.
8. *Ultrasound procedural pearls*: With the recent renewed interest in perioperative paravertebral blocks, there are several techniques described utilizing real-time ultrasound. It has long been recognized anatomically that the sympathetic chain runs in the ventral region of the paravertebral compartment, such that intended somatic blockade of the segmental innervation often leads to ipsilateral sympathectomy. Ultrasound has the distinct advantage of allowing in-plane visualization of needle placement, while also allowing direct visualization of costotransverse ligament, transverse processes, and the underlying lung pleura (Fig. 21.4). This likely translates into improved safety, in regard to pneumothorax risk specifically [7].

Efficacy (Measurable Endpoints for Success and Literature Review)

The single most effective measure for determining the successful sympathetic blockade is measurement of ipsilateral asymmetric temperature rise in the affected region [14]. This occurs because of the reflexive regional vasodilation that occurs once the concomitant sympathetic tone to that area is attenuated. Notably, with thoracic level blocks, it

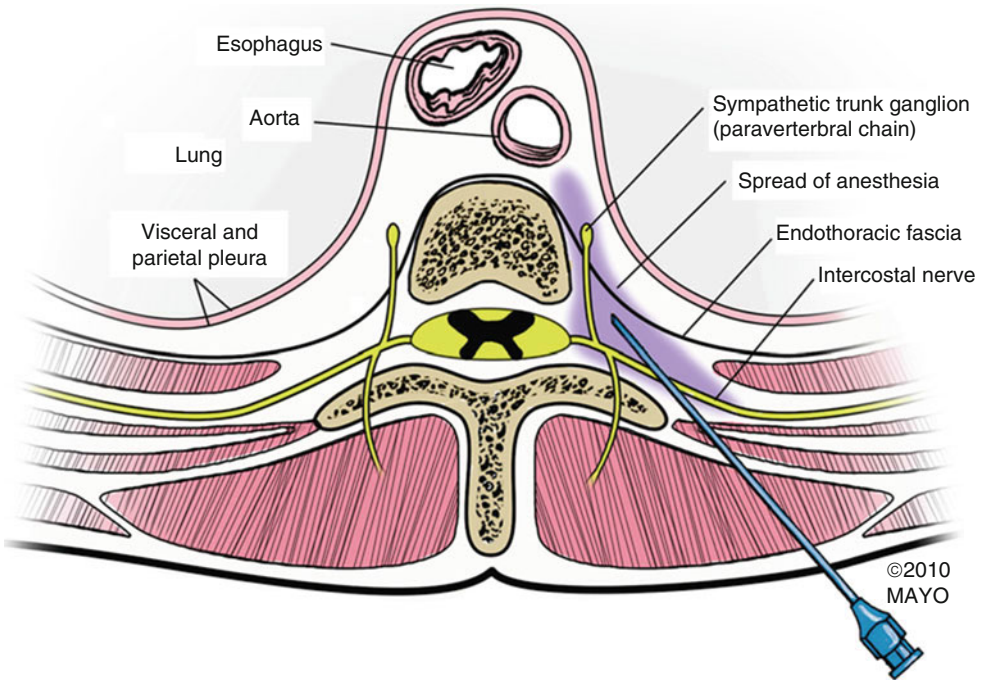

Fig. 21.4 Paravertebral space schematic, denoting the position of thoracic somatic and sympathetic nerves/ganglia relative to the lung retroparietal space (With permission © Mayo Clinic, 2010)

may be challenging to accurately record the cutaneous skin temperature; use of an infrared measuring device is often helpful. One should also observe asymmetric, ipsilateral sudomotor paralysis and anhidrosis (i.e., decreased sweat production). It is possible to observe an ipsilateral Horner's syndrome if the ascending cervical sympathetic chain is disrupted, though this is much less commonly observed, compared to stellate ganglion level blocks.

Unfortunately, there is a general paucity of robust medical evidence for efficacy in blocking thoracic sympathetic nerves (regarding pain indications). A recent review of the sympathetic block literature performed by Miles Day in 2008 demonstrated only two significant articles (one case report, one case review) related to percutaneous technique [13]. There are several other medical reports and case series available for review in abstract form, but double-blind, randomized prospective trials continue to be lacking. The aforementioned review article by Day summarizes the evidence for percutaneous thoracic sympathetic block as being grade 1C–2C, defined as having low-medium quality evidence, where benefits may not clearly outweigh risks in all circumstances and the best clinical action may differ depending upon patient circumstance and societal values [13]. Consequently, there remains a significant need for larger studies, randomized trials, and long-term data.

Lumbar Sympathetic Block

Specific Anatomy and Physiology

The paired lumbar sympathetic trunks lie along the anterior lumbar vertebral bodies at the inferomedial margin of the psoas muscles (Figs. 21.1 and 21.5). The lumbar sympathetics send sympathetic efferent fibers to the lower extremities and lower abdominal and pelvic visceral organs. Some visceral afferent fibers from the lower abdominal and pelvic organs travel along the course of the sympathetic fibers and ultimately to the spinal cord via the lumbar splanchnic nerves. Some anatomists have mentioned the existence of sympathetic fibers crossing the midline to the contralateral trunk, while others have failed to demonstrate this [15, 16]. These crossing fibers have been mentioned as a possible explanation

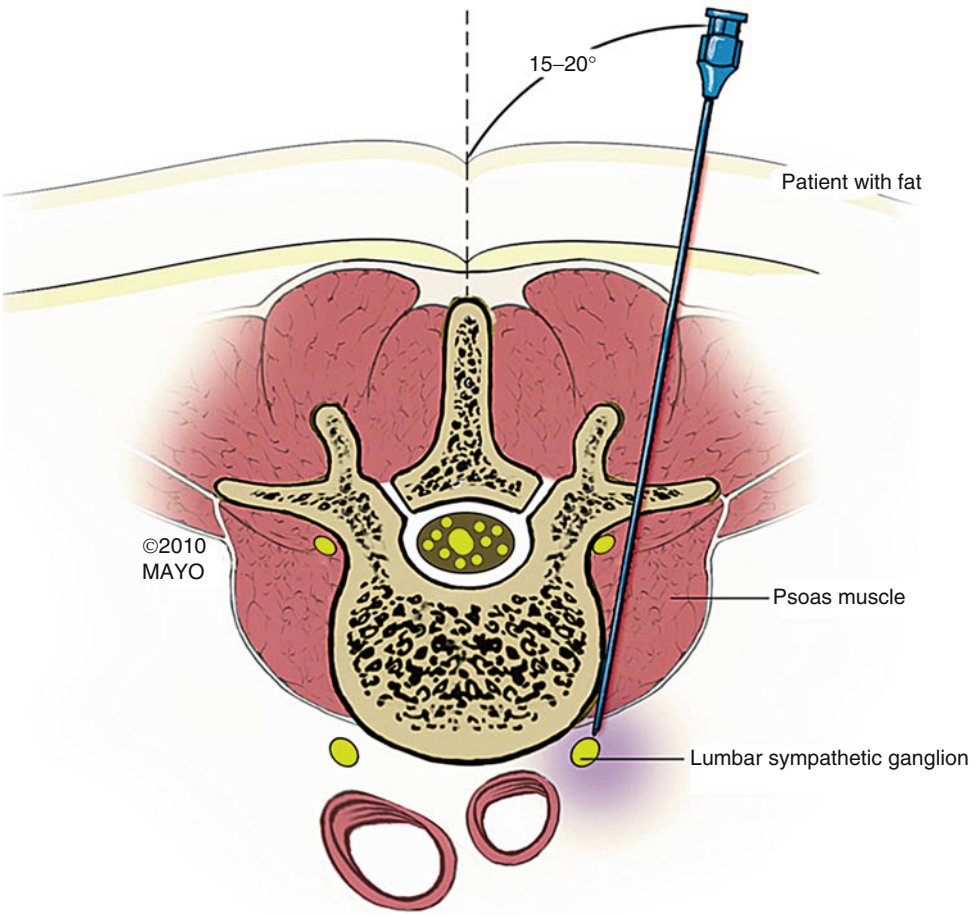

Fig. 21.5 Axial schematic of the typical needle trajectory for blocking the lumbar sympathetic ganglia at the L2 or L3 vertebral level (With permission © Mayo Clinic, 2010)

for a seemingly technically successful sympathetic block failing to produce evidence of a sympathectomy.

Indications

Historically, lumbar sympathetic blocks (LSB) have been reported to treat a vast array of unrelated conditions including hyperhidrosis, postherpetic neuralgia, frostbite, phantom limb pain, and renal colic, to name a few [11]. Current indications for lumbar sympathetic block include complex regional pain syndrome (CRPS), peripheral vascular disease, with painful ischemic neuropathy, and some vascular pain syndromes. Despite the widespread use of LBS for the above indications, most of the literature support comes from anecdotal series and case reports rather than controlled trials.

The use of sympathectomy and sympathetic blocks for the treatment of CRPS was first described by Leriche and Fontaine in the 1930s [17]. The continuing use of sympathetic blocks for the diagnosis and treatment of CRPS and "sympathetically mediated" pain syndromes is based upon a large body of anecdotal reports, case series, and long-standing historical use. There are no high-quality RCTs in adults and only one RCT in a pediatric population [13, 18].

For lower extremity peripheral vascular disease (PVD), definitive management consists of surgical or minimally invasive bypass or angioplasty of the obstructed segments. Sympathetic blocks have a treatment role in those patients with symptomatic occlusive disease that is not amenable to surgery or in patients who are medically unsuitable for surgery.

A reasonable approach is to consider sympathetic neurolysis for patients who have failed medical therapy, who are not candidates for reconstruction or angioplasty, and who have ischemic pain and/or evidence of poor tissue perfusion. In most cases, it is advisable to first perform a diagnostic local anesthetic block to assess the degree of pain relief and demonstrate objective evidence of improved tissue perfusion.

Complication and Side Effects

Intravascular uptake or injection into the aorta, the vena cava, or the segmental radicular vessels can result in local anesthetic toxicity. These risks can be minimized by the usual block precautions of careful aspiration, use of a local anesthetic test does, and real-time fluoroscopic contrast injection. Needle trauma to the lumbar plexus nerves within the psoas muscle, the exiting nerve roots at the intervertebral foramen, or the radicular arteries can also occur and may result in temporary or permanent nerve injury.

Complications after neurolytic block are related to injection of the neurolytic agent near a somatic nerve or spread of the injected neurolytic agent from the area of the sympathetic trunks to a somatic nerve or nerve root. The use of fluoroscopy and small controlled volumes of injectant can help to minimize this complication. The genitofemoral nerve or L2 nerve roots are most commonly affected. This so-called post-neurolysis genitofemoral neuralgia has been reported in up to 5–10 % of cases and usually presents with neuropathic pain symptoms (burning, dysesthesia, allodynia) in the groin or anteromedial thigh [19].

Rare complications include organ puncture (kidney, ureter), intervertebral disk puncture, and retroperitoneal hematoma.

Procedural Technique

Over the years, numerous variations and techniques have been described to perform LSBs. Historically, most of the procedures involved needle entry at L2 or L3, approximately 6–7 cm from the midline, advancing the needle until it contacts the vertebral body and then "walking" the needle anteriorly off of the vertebral body until it slips off the body and through the anterior psoas muscle fascia, at which point the injectant is deposited [20].

Currently, image-guided LSB is the preferred technique. CT-guided techniques have been described, but there are few if any real advantages of this method over fluoroscopic guidance, and the increased expense and radiation exposure cannot be justified for most cases [21]. Ultrasound-guided techniques have been recently described, and, as techniques and equipment improve, this technique may become the preferred method in the future.

Currently, a fluoroscopic-guided approach is the preferred technique for most patients. The description that follows is suitable for the majority of patients encountered in clinical practice, though modifications may be needed for some patients depending on factors such as body habitus, spine surgery or spine deformity, etc.:

1. The patient is place prone, with a pillow under the pelvis and lower abdomen to straighten the lumbar lordosis.
2. Appropriate monitors are placed and sterile preparation and draping is performed.
3. Fluoroscopic guidance is then performed to identify and mark the surface landmarks and needle entry point(s). A single-needle technique should be performed at L2 or L3. Iliac vessels become more closely opposed to the vertebral bodies at the lower lumbar levels, increasing the likelihood of an intravascular injection.
4. The skin and deeper tissues are appropriately infiltrated with local anesthetic.
5. A 22-gauge needle with a curved tip works very well for this block. A 5–6-in. (12–15 cm) needle will suffice for the majority of patients.
6. Start with the fluoroscope at the midline posterior anterior position to identify the L2 or L3 vertebral bodies.

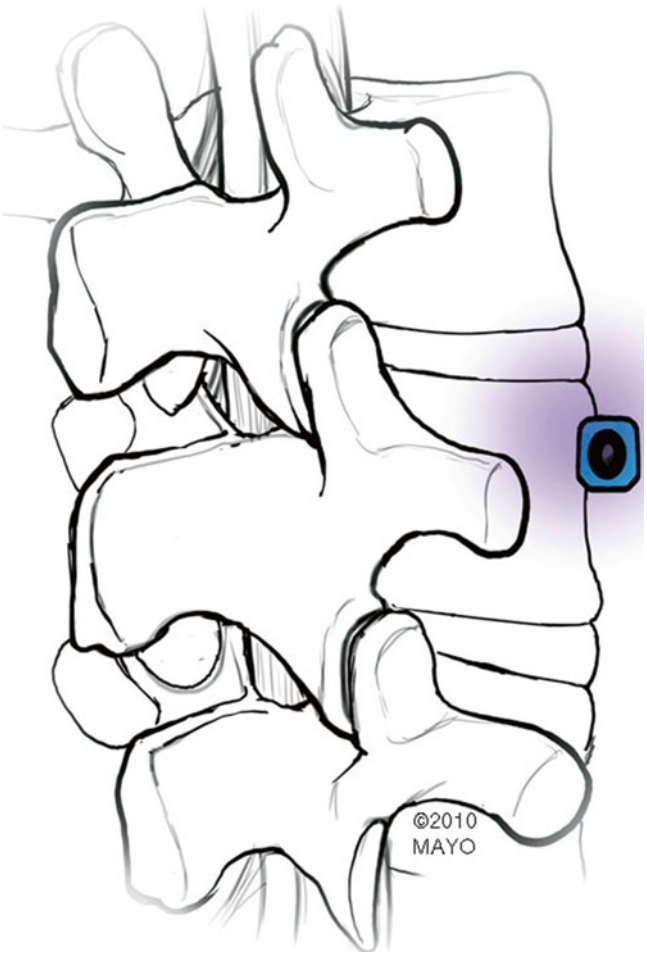

Fig. 21.6 Schematic representation of the needle trajectory during LSB in a coaxial or "in-line" plane relative to the fluoroscopy image intensifier (oblique view) (With permission © Mayo Clinic, 2010)

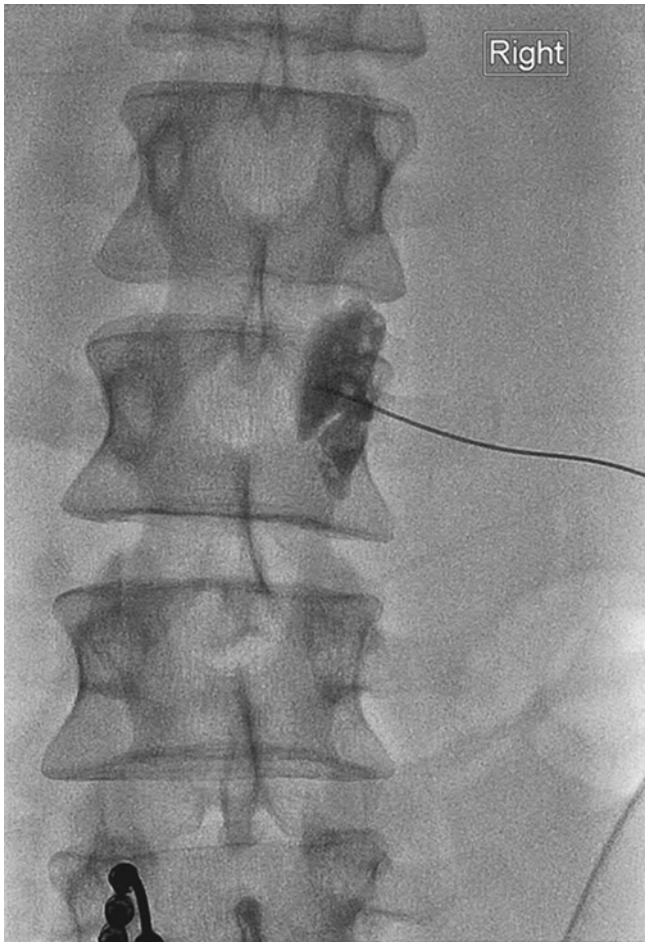

Fig. 21.7 Fluoroscopic image of right-sided lumbar sympathetic block, AP view

Then, rotate the fluoroscopic beam approximately 15–20° from the sagittal plane (5–6 in. from midline in most patients) using this view. In this oblique view, the needle entry point should align with the anterior margin of the vertebral body approximately one-third of the distance caudal from the superior end plate of the vertebral body using a coaxial or "in-line" plane trajectory relative to the fluoroscope beam (Fig. 21.6). It is then advanced in 1-cm increments, using the curved needle tip to make adjustments in the trajectory to keep the needle tip coursing to the anterior margin of the vertebral body. Contact should be made at the anterior edge with the need curved medially. Then, the needle is curved 180° to point lateral and advanced to just slide past the vertebral body. Then, the fluoroscopic beam is turned to a lateral position and the tip advanced until it is even with the anterior margin of the vertebral body (Figs. 21.7, 21.8, 21.9, and 21.10). With experience, you should sense the needle tip pass or "pop" through the anterior psoas fascia.

7. Then, 1.0 ml of contrast is injected to be sure the needle tip is not in the psoas muscle and to verify that the solution layers are out in the anticipated location of the lumbar trunk (Figs. 21.7 and 21.8). Then, the fluoroscopic beam is turned to the posterior anterior orientation to again verify that the needle tip is in the correct location and that the contrast is not within the psoas muscle. If there is any question, another 1.0–2.0 ml of contrast can be injected. If there is a concern or question about vascular uptake, 1.0–2.0 ml of contrast should be injected using real-time injection, preferably with digital subtraction fluoroscopy.
8. Once the needle tip position is satisfactory, then inject 3–5 ml of local anesthetic.
9. For neurolytic injections, a smaller volume (1–2 ml) is recommended to decrease the possibility of posterior spread into the psoas muscle. This may reduce the likelihood of neuralgia.
10. In order to demonstrate a successful block pre- and post-procedure, measurements of distal extremity skin temperature or laser Doppler flowmetry should be

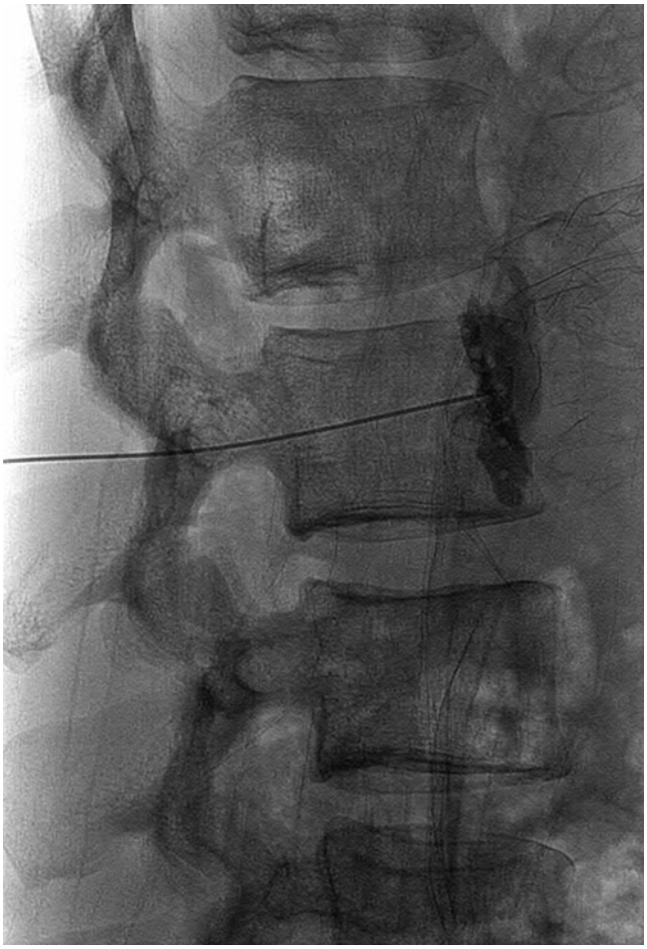

Fig. 21.8 Fluoroscopic image of right-sided lumbar sympathetic block, lateral view

preformed. Unless the patient has rather severe peripheral vascular disease (PVD), you should expect the skin temperature of the distal foot to rise to within approximately 3 °C of the core body temperature [22].

Efficacy

There is a paucity of well-designed randomized controlled trials (RCT) regarding the use of LSB for CRPS. In adults, a recent Cochrane review identified only one trial involving a very small number of patients, and the conclusion was that no consensus could be drawn concerning effectiveness [13, 23].

A recent double-blind, placebo-controlled trial of LSB in children with CRPS demonstrated significant pain reduction and improvement in sensory dysfunction compared to placebo and intravenous lidocaine [18]. Based upon the current literature, it is reasonable to continue to use local anesthetic lumbar sympathetic blocks as part of a comprehensive treatment program in patients with early-stage CRPS that have not improved with less invasive conservative therapies.

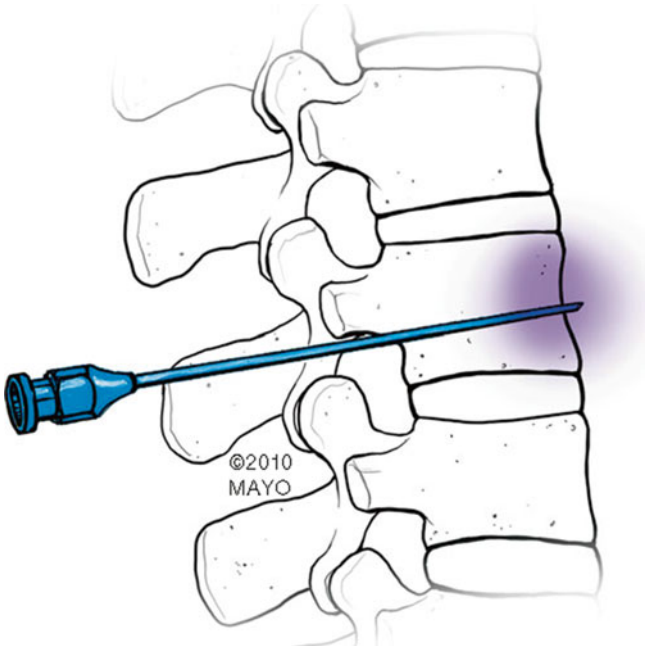

Fig. 21.9 Schematic representation of the final needle position for LSB, in the posterior anterior plane (With permission © Mayo Clinic, 2010)

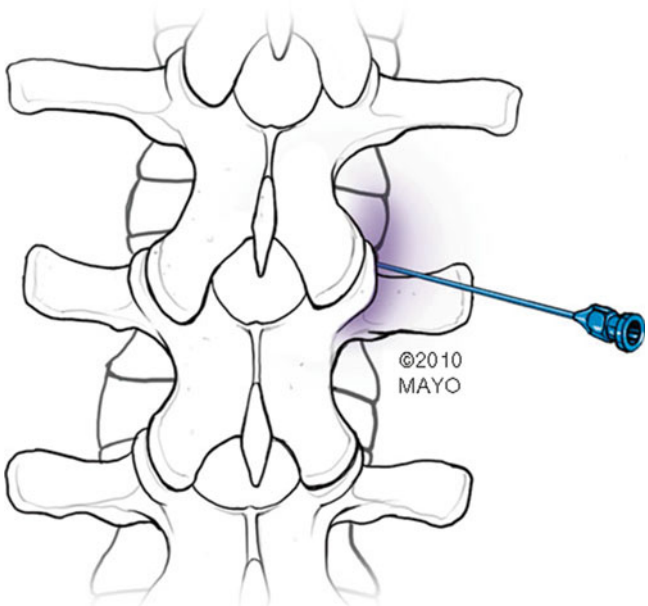

Fig. 21.10 Schematic representation of the final needle position for LSB in the lateral trajectory (With permission © Mayo Clinic, 2010)

There are several single center case series and two small RCTs that have examined the effectiveness of neurolytic LSB for patients with PVD [24–32]. In the RCTs, there was subjective symptomatic improvement (pain relief) but no significant improvement in objective testing such as ankle brachial pressure index (ABPI) and treadmill walking distance. Table 21.1 lists the clinical trials that have examined

Table 21.1 Summary review of research trials, which have studied the results of chemical sympathectomy in patients with peripheral vascular disease (PVD)

Sympathetic blocks for PVD				
Investigation	Patient number	Procedure[a]	Satisfactory response (%)	No response (%)
Hughes-David and Redman [28]	97	1	69	31
Strand [32]	167	3	56	44
Cousins et al. [24]	368	1,2	80	20
Haimovici et al. [27]	171	3	55	45
Froysaker [25]	32	3	5.5	94.5
Myers and Irvine [30]	26	3	69	31
Rosen et al. [31]	37	1	38	62
Fyfe et al. [26]	25	1	25	75
Mashiah et al. [29]	373	1	58.7	41.3

[a]1, Phenol sympathetic block; 2, Alcohol sympathetic block; 3, Local anesthetic sympathetic block

the results of chemical sympathectomy in patients with PVD. Based on the literature, it is reasonable to continue to consider lumbar sympathetic neurolysis to treat patients with painful lower extremity who have not responded to medical or surgical treatment or who are not candidates for surgery or angioplasty.

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Celiac Plexus, Splanchnic Nerve Block, and Neurolysis

22

Melinda M. Lawrence, Salim M. Hayek, and Joshua D. Goldner

Key Points

- Visceral abdominal pain secondary to upper gastrointestinal malignancies and pancreatic disease can be very challenging to control.
- Optimization of pain may often require a multimodal approach to obtain adequate analgesia.
- Numerous studies have shown that patients who suffer from viscerally mediated upper abdominal pain may experience great benefit from celiac plexus neurolysis. Regardless of the technique used, studies have shown that celiac plexus neurolysis has a long-lasting benefit in up to 70–90% of patients with pancreatic cancer.
- Neurolysis of the celiac plexus is a relatively safe procedure with commonly occurring mild side effects and uncommonly occurring serious adverse events.
- Celiac plexus neurolysis can be used as an alternative to or in conjunction with opioid analgesics for improvement in pain management and quality of life.
- It is important to keep in mind that celiac plexus blockade will only eliminate visceral-mediated pain but would not otherwise alter musculoskeletal or neuropathic components of pain; that should be clearly explained to the patient prior to entertaining the block.
- Intrathecal drug delivery is a valuable option in those who fail to have adequate relief from celiac plexus neurolysis or diagnostic block.

Introduction

In 1914, Max Kappis [1] performed the first celiac plexus block. Since the first reported celiac plexus block (CPB), there has been abundance of literature describing many indications, techniques, and complications associated with this procedure [1–9]. The celiac plexus innervates the gastrointestinal tract between the distal third of the esophagus and the transverse colon, including the liver, biliary tract, kidneys, spleen, adrenals, and mesentery. Due to the widespread visceral innervation of the gastrointestinal tract by the celiac plexus, blockade of these nerves is often used to treat viscerally mediated abdominal pain in patients with pancreatic cancer, upper abdominal malignancies, and chronic pancreatitis [2, 3]. Patients who undergo celiac plexus blockade have often failed to respond to conservative medical management, which may include nonsteroidal anti-inflammatories and opioids. Neurolytic celiac plexus blocks have been found to decrease post-procedural opioid consumption [4], improve pain control, improve mood, reduce pain interference with activity, and possibly increase life expectancy [5]. Typically, a diagnostic celiac plexus block is first performed, and if successful, it is then followed by a therapeutic neurolytic block with either ethanol or phenol for the purpose providing long-lasting relief. Physicians have reported performing this procedure with a wide variety of modalities including anatomical landmarks, radiography, computed tomography, fluoroscopy, bedside ultrasound, and endoscopic ultrasound [2, 6, 7].

Anatomy

Sympathetic innervation of the abdominal viscera originates in the anterolateral horn of the spinal cord. Preganglionic axons from T5 to T12 leave the spinal cord with the ventral spinal routes to join the white communicating rami en route to the sympathetic chain. These preganglionic sympathetic nerves are unique in that their axons do not synapse in the sympathetic

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chain; they pass through the chain and synapse at distal sites. Distal sites of synapse include the celiac, aorticorenal, and superior mesenteric ganglia [8]. The greater, lesser, and least splanchnic nerves provide the major preganglionic contribution to the celiac plexus and transmit the majority of nociceptive information from the viscera. The splanchnic nerves are contained in a narrow compartment made up by the vertebral body and the pleural laterally, the posterior mediastinum ventrally, and the pleural attachment to the vertebra dorsally. This compartment is bounded caudally by the crura of the diaphragm. The volume of this compartment is approximately 10 ml on each side.

The greater splanchnic nerve has its origin from the T5–10 spinal roots. The nerve travels along the thoracic paravertebral border through the crus of the diaphragm into the abdominal cavity, ending on the celiac ganglion of its respective side. The lesser splanchnic nerve arises from the T10–11 roots and passes with the greater nerve to end at the celiac ganglion. The least splanchnic nerve arises from the T11–12 spinal roots and passes through the diaphragm to the celiac ganglion [9].

Intrapatient anatomic variability of the celiac ganglia is significant, but the following generalizations can be drawn from anatomic studies of the celiac ganglia. The number of ganglia varies from 1 to 5 and range in diameter from 0.5 to 4.5 cm. The ganglia lie anterior and anterolateral to the aorta. The ganglia located on the left are uniformly more inferior than their right-sided counterparts by as much as a vertebral level, but both groups of ganglia lie below the level of the celiac artery. The ganglia usually lie approximately at the level of the first lumbar vertebra [9].

The celiac plexus is the largest prevertebral plexus and is composed of the right and left celiac ganglia, a dense network of parasympathetic and sympathetic efferent and afferent nerve fibers. The plexus is located in the epigastrium anterior to the crura of the diaphragm and the body of the first lumbar vertebra; it surrounds the celiac artery and the top of the superior mesenteric artery. The whole plexus is found posterior to the stomach and omental bursa. The right half of the plexus lies behind the upper part of the head of the pancreas, the small part of the duodenum, the lower end of the portal vein, and the inferior vena cava. The left half is covered by the pancreas and splenic vessels. The plexus is found to be anterior to the abdominal aorta. The phrenic arteries are superior and the renal vessels inferior to the plexus, while suprarenal vessels often pass through the plexus.

The celiac plexus occupies an area about 3 cm in length by 4 cm in width. In the transverse plane, it occupies the region between the two adrenal glands and extends beyond the lateral borders of the aorta on both sides. In the longitudinal plane, it occupies the area delineated by the celiac artery above and the renal arteries below. It is in front of the entire L1 vertebra and often the upper part of the L2 vertebra.

Techniques

Retrocrural

The retrocrural or posterior approach involves needle placement posterior and cephalad to the diaphragm. The patient is positioned prone, with the pillows placed under the abdomen to decrease lumbar lordosis. A 20- or 22-gauge needle that is 12–18 cm long is used for the procedure. Needle entry should be immediately caudal to the 12th rib and 7–8 cm lateral to the midline. Positioning of the needle toward the midline will depend on which nerves are to be blocked (splanchnic nerves vs. celiac plexus). To block the celiac plexus, one would direct the needle to the L1 spinous process, whereas the splanchnic nerves are blocked more cephalad toward the 11th or 12th thoracic spinous processes. The needle is inserted on left side at an angle of 45° and advanced following the direction of 12th rib medially until contact is made with the vertebral body of L1. The needle is then withdrawn a bit and redirected to pass by the vertebral body to a point 1–2 cm beyond anterior margin of the vertebral body or until aortic pulsation is felt. The procedure is repeated on the right side, and contrast medium is injected after negative aspiration under fluoroscopic guidance; at this time, a diagnostic block or neurolysis may be performed. The crus is the anatomical determinant of whether a block is a true celiac or splanchnic nerve block. If the needle tip is posterior to the crus, then the nerves blocked will be splanchnic. The crus attaches posteriorly at the T12 and L1 vertebral bodies; at these levels, the needle tip may be anterior or posterior to the crus. At T11, the needle tip will always be posterior to the crus and result in a splanchnic block [9].

Transcrural Approach

In the transcrural or anterocrural technique, the needle passes through the crus of diaphragm with the tip located anterior and caudad to the diaphragm just anterior to the aorta. The technique is similar to the retrocrural approach except that the needle is advanced 1–2 cm deeper. A loss of resistance should be felt once the crus of the diaphragm is pierced. The needle tips should be just anterolateral to the wall of the aorta bilaterally. With the one-needle method, the needle is

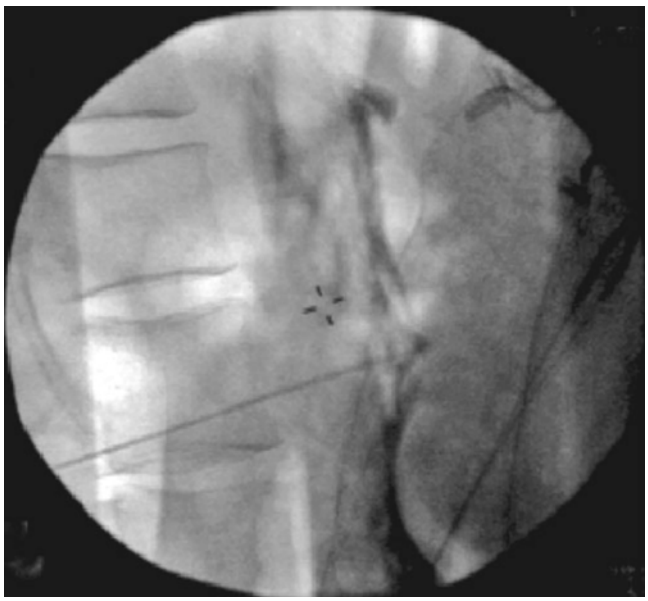

Fig. 22.1 Transaortic celiac plexus block. Lateral view

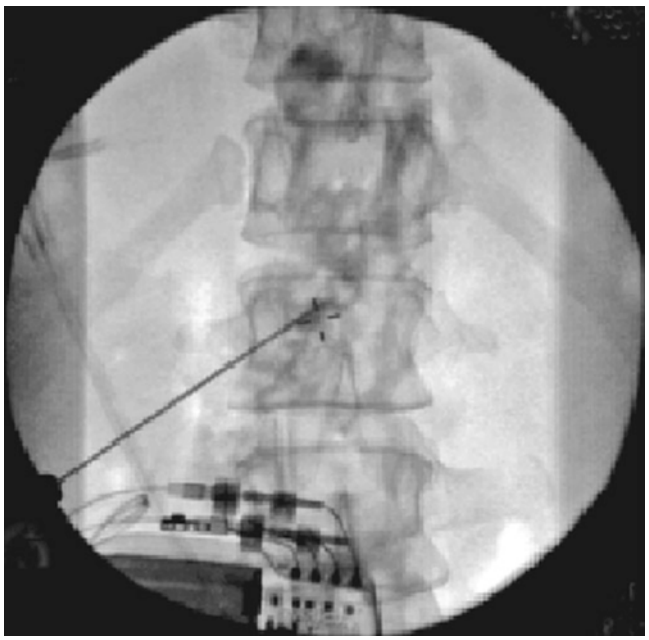

Fig. 22.2 Transaortic celiac plexus block. AP view

inserted 5–6 cm off the midline on the right at the level of lower edge of L1 vertebral body and after passing it, advanced adjacent to the anterolateral wall of the aorta [9].

Transaortic Approach

The needle is placed immediately anterior to the aorta and is advanced slowly with frequent aspiration until the blood appears and the aorta is entered. The needle is then advanced until blood aspiration has stopped, and contrast is injected. Fluoroscopy confirms correct needle position in lateral projection; the needle tip projects just anterior to the edge of the lower third of the body of L1 and in posteroanterior projection; the needle lies in a plane between the left lateral edge of the body of L1 and spinous process (Fig. 22.1) [10].

Fluoroscopic imaging is one of the most commonly used methods of imaging for celiac plexus block [11]; however, there are many other imaging techniques that can be used, including computerized tomography-guided [12], injection by direct visualization [12], magnetic resonance imaging, and ultrasound-guided [13–15]. Ultrasound imaging can be used with a variety of techniques, including endoscopic [16, 17] and percutaneous [18].

In the literature, many approaches to celiac plexus blockade have been documented and include retrocrural, antecrural, transaortic, transcrural, transdiscal, and transabdominal. There are few studies on the different techniques used for celiac plexus neurolysis, and those that do exist demonstrate varying results. One study found no difference in pain scores with neurolysis between the retrocrural, transaortic, and bilateral chemical splanchnicectomy groups [10]. In a nonrandomized, prospective, case-controlled study of 59 patients [19], celiac plexus neurolysis was compared to videothoracoscopic splanchnicectomy. Stefaniak et al. [19] found that both techniques had similar efficacy in pain reduction and decreased daily opioid consumption. Celiac plexus neurolysis, however, was found to be associated with significantly improved physical, emotional, and social well-being with the added benefit of being less invasive [19]. As mentioned previously, in the meta-analysis by Eisenberg et al. [2], positive short-term outcomes from celiac plexus neurolysis, regardless of imaging modality used, were reported (Fig. 22.2).

Splanchnic

The patient is placed in the prone position with a pillow placed under the abdomen to decrease lumbar lordosis. The inferior margins of the 12th rib are identified and marked back to the T12 vertebral body. The spinous process of the L1 vertebral body is then identified and marked. A point approximately 2 in. slightly inferior and lateral to the spinous process of L1 is marked. Typically, 20-gauge, 12-cm needles are inserted bilaterally. The needles are initially oriented 45° toward the midline and about 35° cephalad. Once bony contact with the T12 vertebra is made and the depth noted, the needles are withdrawn to the subcutaneous tissue and redirected so that the needles may walk off the lateral surface of the T12 vertebral body. The needle tips should be

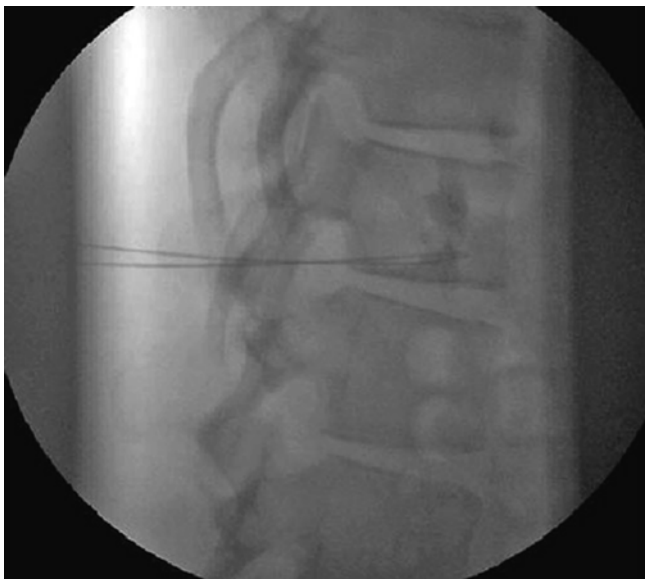

Fig. 22.3 Splanchnic nerve block. Lateral view

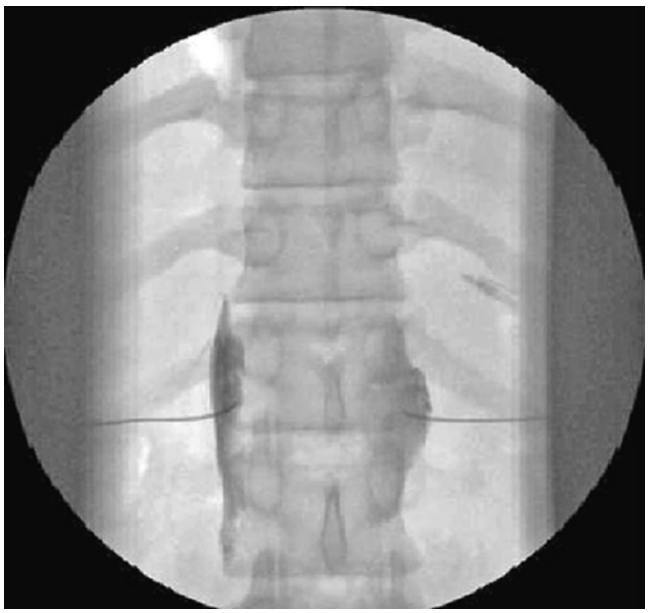

Fig. 22.4 Splanchnic nerve block. AP view

at the junction of the anterior and lower third of the vertebral body in a lateral view. Contrast should be confined to the midline and concentrated near the T12 vertebral body in the fluoroscopic anteroposterior view. A smooth posterior contour can be observed that corresponds to the psoas fascia on the lateral view. The contrast should be observed to be entirely retrocrural. If there is precrural spread, the needles are withdrawn slightly back through the crura of the diaphragm (Fig. 22.3) [9].

The use of pulsed radio-frequency ablation of the splanchnic nerves has been described as an alternative to splanchnic neurolysis for the treatment of pancreatic and upper abdominal pain [20–22]. Raj et al. [21] reported that up to 40% of patients had excellent pain relief after a thoracic splanchnic nerve block, with only 15% of patients reporting poor results in a series of 107 patients with abdominal pain [21]. One study consisting of eight patients with chronic pancreatitis and two patients with chronic abdominal pain of an unknown etiology found that splanchnic radio-frequency ablation resulted in decreased pain scores, opiate usage, and hospital admissions for pain control [20]. Garcea et al. [20] also found patients to have improvement in their level of anxiety, daily activity, mood, and overall perception of health. One advantage of radio-frequency lesioning of splanchnic nerves is that the tissue that is damaged can be more precisely controlled, allowing the technique to be safer and perhaps more reliable than with the use of a neurolytic agent [21]. Radio-frequency lesioning also has the advantage of an immediate effect unlike neurolytic agents which could take anywhere from 7 to 10 days to achieve neurolysis (Fig. 22.4) [21].

Neurolytic Agents

Neurolytic celiac plexus blocks are commonly performed with 50–100% alcohol and 6–12% phenol. The mechanisms of action of alcohol include dehydration; extraction of phospholipids, cholesterol, and cerebrosides; and precipitation of mucoproteins and lipoproteins. These actions result in sclerosis and separation of the myelin sheath, edematous Schwann cells, and axons. The basal lamina of the Schwann cell tube is often spared, and the axon can regenerate along the previous course; if the ganglion is injected, it may produce cell destruction with no subsequent regeneration [23]. The mechanism of action of phenol depends on its concentration, protein denaturation occurs at concentrations less than 5%, and concentrations higher than 5% produce protein coagulation, nonspecific segmental demyelination, and orthograde degeneration [24, 25]. Axons of all sizes are affected and appear edematous, except posterior root ganglia which are unaffected by phenol. Some have suggested that phenol has a greater affinity for vascular than neuronal tissue [23, 26].

There are advantages and disadvantages to both alcohol and phenol as neurolytic agents. Alcohol is an irritant for soft tissue and is associated with a burning dysesthesia that warrants prior or simultaneous injection of local anesthetic. Alcohol spreads quickly from the injection site due to high solubility in the body. The higher solubility of alcohol can make it challenging to reach the targeted nerve; this also makes a larger volume of injectate necessary to increase the chance of neurolysis of the targeted tissue while also

increasing the likelihood of damage to surrounding nerves. An advantage of not using a local anesthetic is that pain along the target nerve will confirm correct needle placement [23]. Phenol used in a concentration of 5–10% causes neurolysis by causing protein coagulation and necrosis when applied to nerves [24, 25]. Phenol is suspended in glycerol, and its high viscosity limits its spread. Phenol also has an advantage of being painless on injection. Just like alcohol, phenol has also been associated with the development of neuritis. However, there are many more case reports of persistent paraplegia following neurolysis with alcohol than with phenol. A study published by Abdalla and Schell [13] reviewed all of the previously reported cases (1974–1998) of temporary or permanent paralysis following neurolysis with alcohol or phenol. In that study, 10/11 cases involved alcohol as the neurolytic agent versus 1/11 in which phenol was used.

Complications may be related to spread of neurolytics to nearby structures, resulting in deafferentation pain of somatic nerves and neuritis. The intravascular spread of the neurolytic solution to the spinal cord may occur with any paraspinal block using neurolytics [13, 27–33]. Even with direct intraoperative visualization, administration of a neurolytic has been reported to lead to permanent paraplegia [13]. Alcohol results in pain upon injection and has been associated with neuritis following neurolysis. With a retrocrural approach, the spread of the neurolytic agent is limited by the diaphragm. Higher quantities of neurolytic agents are often used for the retrocrural approach, and the spread of the agent may cause increased risk of neurolysis to the somatic nerve roots with resulting paraplegia and/or neuritis [13].

Efficacy

The first double-blinded, randomized, controlled trial that studied the benefits of chemical splanchnicectomy in pancreatic cancer patients was done by Lillemoe et al. [5]. Chemical splanchnicectomy was performed with alcohol versus saline placebo at time of exploratory laparotomy for biopsy, staging, and possible palliative gastrointestinal bypass. In follow-up, mean pain scores were found to be lower in the alcohol group at 2, 4, and 6 months ($p < 0.05$). In this study, patients who underwent splanchnicectomy had a longer duration of pain relief (7.2 vs. 3 months of placebo, $p < 0.0001$) and needed lesser amounts of opioids compared to patients who received the placebo (46 and 68%, respectively, $p < 0.05$). Patients in both groups received rescue neurolytic celiac blocks, but time to rescue was significantly longer in those who underwent chemical intervention. In patients who did not have preoperative pain, chemical splanchnicectomy significantly reduced later pain scores and delayed or prevented onset of pain ($p < 0.05$).

Another double-blinded, randomized, control trial more recently conducted by Wong et al. [34] randomized 100 patients into two groups that received either a neurolytic celiac plexus block or analgesic therapy alone with a sham injection. This resulted in a greater reduction in pain intensity ($p = 0.01$) and showed improvement in quality of life ($p = 0.001$) in the first week after randomization in the neurolytic block group. In the first 6 weeks, fewer patients reported moderate to severe pain (rated as ≥5/10 on pain scale) in the neurolytic block group versus those in the systemic analgesic group (14 and 40%, respectively, $p = 0.005$). Although fewer patients in the neurolysis group required rescue blocks versus systemic analgesic group (6 and 20%, respectively), this finding was not statistically significant ($p = 0.07$). Overall, there was no significant difference between the groups for opioid consumption, frequency of adverse opioid effects, quality of life, and survival. However, pain relief was improved in the neurolysis group. In a randomized, double-blind study by Polati et al. [35], the efficacy of neurolytic CPB was compared with pharmacological therapy in the treatment of pain from pancreatic cancer. Twenty-four patients were divided into two groups: 12 patients underwent neurolytic CPB (group 1), and 12 were treated with pharmacological therapy (group 2). Immediate and long-term efficacy, mean analgesic consumption, mortality, and morbidity were evaluated at follow-up. Patients in group 1 reported significant pain relief compared with those in group 2 immediately after the block ($p < 0.05$), but long-term results did not differ between the groups. Overall, the mean analgesic consumption was lower in group 1. They also found a decrease in drug-related adverse effects including constipation (5/12 in group 1 vs. 12/12 in group 2), nausea, and/or vomiting (4/12 in group 1 vs. 12/12 in group 2) ($p < 0.05$).

A prospective study of 50 consecutive pancreatic cancer patients [35] assessed the efficacy of neurolytic celiac plexus blocks depending on primary tumor location. Patients with pancreatic head cancer experienced more pain relief (92% relief) from neurolysis when compared to those with pancreatic body/tail cancer (29% relief). Study results are likely secondary to more advanced tumors in those with body and tail tumors; in which case, neurolysis was ineffective for pain control [36].

Eisenberg et al. [2] performed a meta-analysis of the efficacy and safety of neurolytic celiac plexus blocks from 24 papers including two or more patients with abdominal cancers (total of 1,145 patients included). Good to excellent pain relief was reported in 878/989 patients at 2 weeks. Ninety percent of patients had partial to complete pain relief at 3-month postneurolysis and 70–90% percent had relief until death, even if beyond 3 months after neurolysis.

Although literature has clearly shown that there is a significant reduction in pain scores for most patients following neurolytic celiac plexus blocks, there have also been studies to support that celiac plexus neurolysis may also alter opioid consumption, quality of life, and overall patient survival. Survival in patients with pre-procedure pain was significantly increased by up to 15 months in the celiac plexus neurolysis group versus the placebo group in one study ($p = 0.0001$) [5]. Data also suggested that there may be improved mood and lower levels of disability; however, this was not statistically significant [5].

A more recent study also supports a significant positive effect on duration of life and mood scores following neurolytic celiac block [37]. This study found a correlation between a reduction in pain and increase in longevity. Overall, neurolytic block, when compared to medical management alone, improved pain, elevated mood, reduced pain interference with activity, and was associated with an increase in life expectancy [37].

Despite the commonality of decreased pain scores throughout the literature, not all studies were able to reproduce the results found by Lillemoe et al. [5] and Staats et al. [37]. Multiple studies were unable to find statistically significant differences between medically managed patients and patients who underwent neurolysis, when evaluating quality of life [6, 34, 38]. However, the results from Kawamata et al. [38] indicate celiac plexus blockade does not directly improve quality of life in patients with pancreatic cancer pain, but it may prevent deterioration in quality of life by the long-lasting analgesic effect, limitation of side effects, and reduction of morphine consumption, compared to treatment only with NSAIDs and morphine.

Conflicting results regarding reduction in opioid consumption have been found throughout the literature. Kawamata et al. [38] found a delayed but significant reduction in opioid requirement 4–7 weeks after neurolysis and that consumption continued to decrease over time. Another study found that celiac plexus neurolysis caused a significant but not complete decrease in opioid consumption; patients experienced a mean reduction of 40–80 mg/day of oral morphine [4]. A multicenter, randomized, control trial of 65 patients [39] with pancreatic and upper abdominal cancer found no difference in pain relief or opioid consumption between patients who underwent medical management versus celiac plexus neurolysis or thoracic splanchnicectomy.

Mercadante et al. [40] published a randomized trial of 20 patients, two groups of 10 patients each who were followed until death; pain scores and side effects of their treatment were recorded. Both groups received 1 week of pharmacotherapy, after which group A continued with NSAID-opioid management that followed the World Health Organization stepwise approach and group B who received neurolytic plexus blocks. Although there was a reduction in visual analogue scale pain scores in both groups, there was no statistical significant difference between the two. However, there was a significant decrease in opioid consumption in the celiac plexus neurolysis group; some effects were seen up to 7 weeks after neurolysis or until death.

A recent meta-analysis published in 2011 by Arcidiacono et al. [41] identified six randomized control trials, published between 1993 and 2008, which compared the percutaneous posterior bilateral block (five studies) or the intraoperative block (one study) with standard analgesic therapy for pancreatic and upper abdominal cancer pain. The mean difference for the visual analogue scale pain score at 4 weeks was significant ($p = 0.004$) for the experimental group celiac plexus block. The improvement in pain control coincided with a reduction in opioid consumption; the mean difference in the use of analgesic therapy in the two groups was much greater in the celiac plexus block group ($p < 0.00001$) versus those managed with standard pharmacologic therapy. Decreased opioid usage persisted until the death of the patient, with significantly lower opioid requirements in the CPB group ($p < 0.00001$). Although opioids were never completely stopped, their reduction translated into fewer side effects such as constipation, which was significantly higher in the control group ($p < 0.0001$) [41].

Complications

In general, celiac plexus blockade and neurolysis are considered relatively safe procedures. Adverse events are usually mild and transient, but serious complications including nerve damage, paraplegia, and aortic dissection may occur rarely. The most commonly reported adverse events are transient and include local pain (96%), hypotension (38%), and diarrhea (44%) [2]. A meta-analysis by Eisenberg [2] reports serious adverse events in only 13/628 or 2% of patients undergoing celiac plexus blockade. Serious events reported by Eisenberg et al. [2] included lower extremity weakness and paresthesia, epidural anesthesia and lumbar puncture, hematuria, pneumothorax, and shoulder, chest, and pleuritic pain. Davies [42] reported that paraplegia occurred in 1 of 683 patients undergoing celiac plexus blockade. This would be the most concerning risk for patients undergoing a neurolytic CPB. Hardy and Wells [43] found that during injection of the celiac plexus, the injected fluid typically spreads as high as midthoracic and cervical levels. A proposed etiology for development of paraplegia following neurolysis is the superior spread of injected alcohol or phenol causing spasm or thrombosis of the artery of Adamkiewicz [30, 31, 44]. The neurolytic-induced vasospasm of the artery of Adamkiewicz may occur secondary to compromised perfusion due to surrounding tissue edema or by direct contraction of the arterial muscle wall [45–47]. Paraplegia may also result from direct

injection of neurolytic agents into the artery of Adamkiewicz or radicular artery [27, 29, 44, 48]. Even when CPB neurolysis has been performed under direct visualization by an open anterior approach, paraplegia has been a complication likely because of the close anatomical proximity of the celiac plexus to the artery of Adamkiewicz [49].

O'Toole and Schmulewitz [50] reported a complication rate of 1.8% after performing 220 endoscopic ultrasound-guided blocks on 158 patients. This study reported four complications, including asymptomatic hypotension after neurolysis, retroperitoneal abscess after celiac plexus block, and severe self-limited post-procedural pain in two patients after celiac plexus block [50]. Reports of retroperitoneal bleed and abscess [51], urinary retention [36], hiccoughing [52], bowel perforation, gastroparesis [53], hemorrhagic gastritis [54], loss of anal and bladder sphincter function [42], ejaculatory failure [55], anterior spinal artery syndrome and paraplegia [27, 30, 44], aortic dissection [56], and aortic pseudoaneurysm [57] have also been described.

Aortic dissection is one of the most concerning complications and has been reported to arise from the use of a transaortic approach to celiac plexus block [56, 58]. Loss of resistance technique may not prevent complications as one case report by Naviera et al. [58] described; they reported an atheromatous aortic plaque presenting as a loss of resistance and resulted in an aortic dissection. Reports have also documented needle aspiration of blood, cerebral spinal fluid, and urine prior to injection [59].

Celiac plexus block technique may be associated with increased incidence of complications depending on approach. In a prospective, randomized study of 61 patients with pancreatic cancer, Ischia et al. [10] compared the efficacy and incidence of complications associated with three approaches to celiac plexus neurolysis, including retrocrural, transaortic, and transcrural. Orthostatic hypotension occurred more often when the retrocrural (50%) or splanchnic (52%) technique was used than when the anterocrural approach (10%) was used. In contrast, transient diarrhea was more frequent with the anterocrural approach (65%) than with the splanchnic nerve block technique (5%) but not the retrocrural approach (25%). The incidence of dysesthesia, interscapular back pain, reactive pleurisy, hiccups, or hematuria was not statistically different among the three groups. Complications may be decreased with the use of blunt needles and appropriate imaging techniques [60].

Conclusions

Management of visceral abdominal pain that is often secondary to pancreatic and upper gastrointestinal malignancies can be very challenging. Optimization of pain may often require a multimodal approach to obtain adequate analgesia. Numerous studies have shown that patients who suffer from viscerally mediated upper abdominal pain may experience great benefit from celiac plexus neurolysis. Regardless of the technique used, studies have shown that celiac plexus neurolysis has a long-lasting benefit in up to 70–90% of patients with pancreatic cancer [2]. Neurolysis of the celiac plexus is a relatively safe procedure with commonly occurring mild side effects and uncommonly occurring serious adverse events. Celiac plexus neurolysis can be used as an alternative to or in conjunction with opioid analgesics for improvement in pain management and quality of life. However, it is important to keep in mind that celiac plexus blockade will only eliminate visceral-mediated pain but would not otherwise alter musculoskeletal or neuropathic components of pain; that should be clearly explained to the patient prior to entertaining the block.

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Superior Hypogastric Plexus, Ganglion Impar Blocks, and Neurolysis

23

Bryan S. Williams

Key Points

- Nearly 4% of women have ongoing chronic pelvic pain, and approximately 15–20% have had chronic pelvic pain of at least 1-year duration at some point in their lives (18–50).
- Many pelvic pain conditions can be attenuated by enteral or parenteral medications, along with psychosocial, physical therapy strategies. When conservative measures fail to provide adequate pain relief, interventional strategies can be employed.
- Patients with a history of vague, dull, burning, poorly localized pain of visceral origins (visceral pain) have been the patients thought to benefit from blockade of the superior hypogastric plexus or ganglion impar.
- Neuropathic pain usually manifests as allodynia and hyperalgesia and generates burning, lancinating pain, and paresthesias. The interruption of visceral pain transmission from the pelvis to the spinal cord can be accomplished by blocking the sympathetic pathway.
- The efficacy of local anesthetic blockade of the superior hypogastric and ganglion impar is based on the selective interruption of the sympathetic ganglia in those patients with sympathetically mediated pain. Patients without sympathetically mediated pain may not show attenuation in pain when a local anesthetic block is performed.

Introduction

Chronic pelvic pain (CPP) of malignant or nonmalignant origins can be attenuated by blockade of the superior hypogastric plexus (SHP) [1, 2] or the ganglion impar (GI) (ganglion of Walther) [3]. Attempts to interrupt sympathetic pathways from the pelvis have been made since the late nineteenth century [4]. In 1921, Leriche performed a periarterial sympathectomy of the internal iliac arteries on a patient with "pelvic neuralgia," and later in the twentieth century. Plancarte et al. [2] showed excellent results from hypogastric plexus block in patients with chronic pelvic pain of malignant origins. The pelvis is innervated by an array of networking neural structures including sympathetic, parasympathetic, and somatic pathways. The SHP is the caudal, retroperitoneal, presacral confluence of the lumbar sympathetic chain. It is located anterior to the abdominal aorta at the L5–S1 intervertebral disk, with the common and internal iliac arteries and veins on either side. The SHP provides innervation to the descending and sigmoid colon, rectum, bladder, prostate, prostatic urethra, testes, seminal vesicles, vaginal fundus, uterus, and ovaries. The GI is the solitary, retroperitoneal termination of the left and right sympathetic chains located anterior to the sacrococcygeal junction. The ganglion of Walther provides innervation to the distal vagina, distal rectum, distal urethra, vulva, and perineum. Analgesia to the organs in the pelvis is possible because the afferent fibers innervating the pelvic structures travel with the sympathetic nerves, trunks ganglia, and rami. Patients with a history of vague, dull, burning, poorly localized pain of visceral origins (visceral pain) have been the patients thought to benefit from blockade of the SHP or GI. These patients include those with pelvic malignancies and nonmalignant origins (e.g., endometriosis).

Background

Malignant- and nonmalignant-associated chronic pelvic pain is a significant cause of pain. Chronic pelvic pain may be defined as noncyclic pain with duration of 6 or more months that localizes to the anatomic pelvis, the abdominal wall at or below the umbilicus, the lumbosacral back, or the buttocks and is of sufficient severity to cause functional disability or lead to medical care effects approximately 1 in 7 women [5].

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CPP has been shown to be far more common in women as compared with men. Nearly 4% of women have ongoing CPP, and approximately 15–20% have had CPP of at least 1-year duration at some point in their lives (18–50) [5–7]. In one study of reproductive-aged women in primary care practices, the reported prevalence rate of pelvic pain was 39% [8]. Office visits to gynecologists have been estimated at 10% [9] resulting in 18% of all hysterectomies and up to 40% of all gynecologic laparoscopies performed by gynecologists [10]. This yields 881.5 billion dollars in health-care costs in the United States per year [5]. Malignant-related pain is equally significant with the overall prevalence of pain at 53% in patients of all stages combined and 58–69% in those with advanced cancer [11].

In males, an analogous condition chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) causes significant pain. Approximately 8.2% of men have prostatitis at some point in their lives. Estimates range from 2.2 to 16% in population-based studies [12–18]. Although prostatitis has been linked to pelvic pain, CP/CPPS has not been scientifically demonstrated to be primarily either a disease of the prostate or the result of an inflammatory process [15, 19]. The disease is named to recognize the limited understanding of the etiologies of this syndrome for most patients and the possibility that organs other than the prostate gland may be important in the cause of this syndrome [15, 20]. The new consensus definition recognizes genitourinary pain complaints as a primary component of this syndrome and includes several exclusion criteria, such as presence of active urethritis, urogenital cancer, urinary tract disease, urethral stricture, or neurological disease affecting the bladder [15]. Whether CPPS is a recognizable disease or not, blockade of the superior hypogastric plexus or ganglion impar may attenuate the pain complaint.

Scientific Foundation

Plancarte et al. [2] first described a percutaneous approach to blocking the superior hypogastric plexus and ganglion impar [3], and since many alternative descriptions have been published [21–26], pain may be nociceptive or neuropathic or mixed. The distention of visceral structures may present as vague, poorly localized, deep, crampy, and dull in nature, while somatic pain may present as well localized and often sharp. Neuropathic pain usually manifests as allodynia and hyperalgesia and generates burning, lancinating pain, and paresthesias. In particular with cancer-related pain, a neuropathic component may be present as pelvic masses invade neural structures. The interruption of visceral pain transmission from the pelvis to the spinal cord can be accomplished by blocking the sympathetic pathway. The blockade interrupts transmission of the pain signal from sympathetic pathways to the brain. In addition to local anesthetic blockade, neurolysis of the sympathetic axis has been employed to attenuate pain primarily in those suffering from malignant-related pain.

The efficacy of local anesthetic blockade of the SHP and GI is based on the selective interruption of the sympathetic ganglia in those patients with sympathetically mediated pain. Patients without sympathetically mediated pain may not show attenuation in pain when a local anesthetic block is performed. Since the ganglia may not purely be sympathetic, a ganglion/plexus block may not fully provide analgesia from pelvic-derived pain. The efficacy of superior hypogastric and ganglion impar local anesthetic blocks has been examined; although no randomized, placebo-controlled trials have been published, several publications report the efficacy of local anesthetic blocks and neurolytic procedures [27, 28]. High-quality studies are lacking and should be performed, but the use of local anesthetic sympathetic blockade serves a role in the treatment algorithm of visceral pain.

Neurolysis has traditionally been performed in malignant-related visceral pain. Local anesthetic blocks are performed prior to neurolysis as a prognostic measure, although successful temporary blockades do not guarantee the success of neurolysis [29]. The strongest evidence for neurolytic procedures is in those patients with pancreatic cancer [30, 31]. Plancarte et al. [2] present data that neurolysis of the superior hypogastric plexus produces a 70% VAS reduction. Chemical neurolysis with phenol (5–10%) or alcohol (50–100%) disrupts the transmission of pain signals by denaturing proteins and extracting fatty substance, causing Wallerian denaturation and necrosis of neural tissue. Alcohol may cause local pain on injection and neuritis. Phenol has some local anesthetic properties and, unlike alcohol, is not painful on injection. The effects of chemical neurolysis may persist between 3 and 6 months, although the response can vary depending on the extent of malignancy. Neurolysis is less commonly used for nonmalignant pain due to the risk of neuritis. The properties of the agents are presented in Table 23.1.

Patient Selection

These blocks may be associated with morbidity, and it is prudent to understand the indications, the relevant anatomy, and the appropriate patient selection. Patients with moderate to severe pain not controlled with oral analgesics and/or medication-related side effects are ideal candidates for interventional therapy.

Indications

- Acute intervention for acute pain
- Temporary treatment for chronic pain conditions until medication shows efficacy

Table 23.1 Neurolytic agents

	Alcohol	Phenol
Mechanism of action	Dehydration, phospholipid extraction leading to Wallerian denaturation	Protein coagulation, segmental demyelination, and necrosis of all neural elements
Concentration (%)	50–100	5–10
Clinical onset	Fast	Slow
Clinical duration	Long	Short
Pain on injection	Yes	No

- Pain affecting the pelvic visceral structures
  - *SHP*: descending and sigmoid colon, rectum, bladder, prostate, prostatic urethra, testes, seminal vesicles, vaginal fundus, uterus, and ovaries
  - *GI*: distal vagina, distal rectum, distal urethra, vulva, and perineum
- Malignant-related pain unresponsive to oral or parenteral medications (neurolysis)
- Excessive sedation or unacceptable side effects from oral or parenteral medications

Contraindications

- Patient refusal
- Coagulopathy
- Local/intra-abdominal infection and sepsis

Equipment

Superior Hypogastric Plexus Block

- Preparation kit, sterile gloves, surgical cap and mask, 18-gauge introducer needle, 22-gauge 5- or 7-in. spinal needle, extension tubing
- Fluoroscope
- Medications
  - Lidocaine 1%
  - Contrast media (e.g., iohexol)
  - Bupivacaine 0.5% or ropivacaine 0.5% and lidocaine 2%
  - Cefazolin 1 g (for intravenous infusion)

Ganglion Impar Block

- Preparation kit, sterile gloves, surgical cap and mask, 22-gauge 3.5-in. spinal needle, extension tubing
- Fluoroscope
- Medications
  - Lidocaine 1%
  - Contrast media (e.g., iohexol)
  - Bupivacaine 0.5% or ropivacaine 0.5% and lidocaine 2%

Neurolysis (Superior Hypogastric and Ganglion Impar)

- Preparation kit, sterile gloves, surgical cap and mask, 22-gauge 5- or 7-in. spinal needle (SHP) or 3.5-in. spinal needle (GI), extension tubing
- Fluoroscope
- Bupivacaine 0.5% or ropivacaine 0.5%
- 50–100% alcohol or 5–10% phenol

Technique

Superior Hypogastric Plexus Block (Transdiscal Approach)

Fluoroscopy guidance is recommended and is described. The patient is placed on the fluoroscopy table in the prone position. After sterile preparation and drape have been accomplished, an anterior-posterior (AP) fluoroscopic image of the lower lumbar spine is obtained, centered on the L5–S1 junction. The end plate of the sacrum is aligned, reducing parallax. The fluoroscope is angled obliquely 25–30° until the superior articular process of the sacrum is approximately one-third of the lateral portion of the disk and 25–30° cephalad, placing the L5–S1 intervertebral disk space into plane view. A site just lateral to the superior articular process "the window" is marked and anesthetized using 1% lidocaine (Fig. 23.1). An 18-gauge spinal introducer needle is inserted and advanced under coaxial technique and intermittent fluoroscopic guidance towards the L5–S1 intervertebral disk. Following this, a 5-in. or 7-in. 22-gauge spinal needle is inserted through the 18-gauge introducer needle. The spinal needle is then advanced to enter the intervertebral disk (Fig. 23.2). The fluoroscope is rotated to lateral position, and the needle is advanced under intermittent fluoroscope until the needle is observed to be anterior to the L5–S1 disk. Then, 1–3 ml of contrast medium (Omnipaque 300 M) is injected anterior to the disk confirming correct needle placement (Fig. 23.3). An AP view is obtained confirming midline placement of the needle (Fig. 23.4). Following this, 8 ml of lidocaine 2%, 8 ml of bupivacaine 0.5% (16 ml total) is then injected with negative aspiration every 3 ml, utilizing intermittent fluoroscopy tracking the

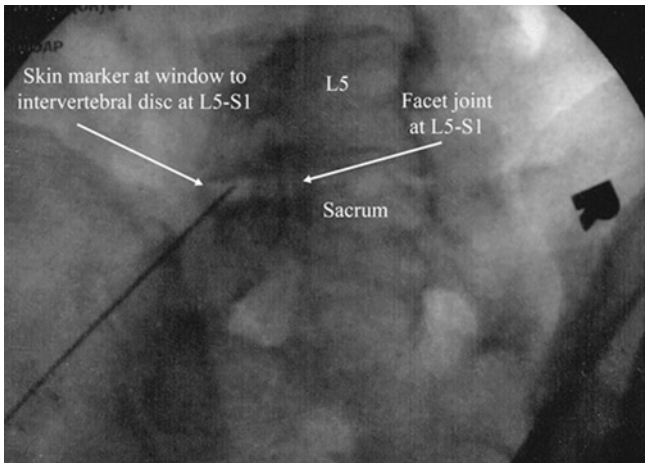

Fig. 23.1 Oblique radiographic view of entrance site

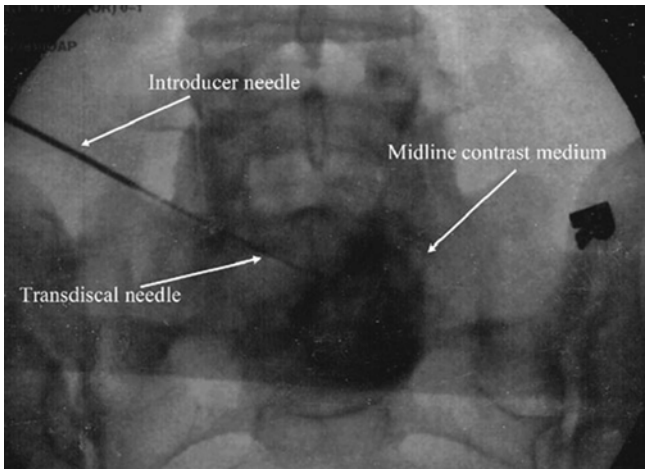

Fig. 23.4 AP radiographic view of transdiscal contrast medium

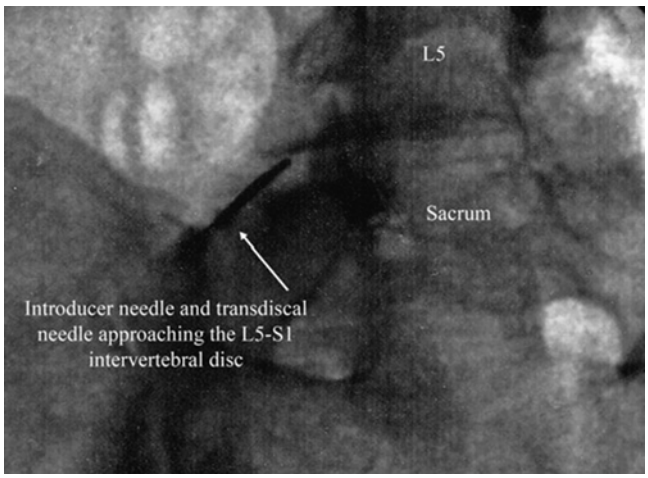

Fig. 23.2 Oblique radiographic view of transdiscal needle

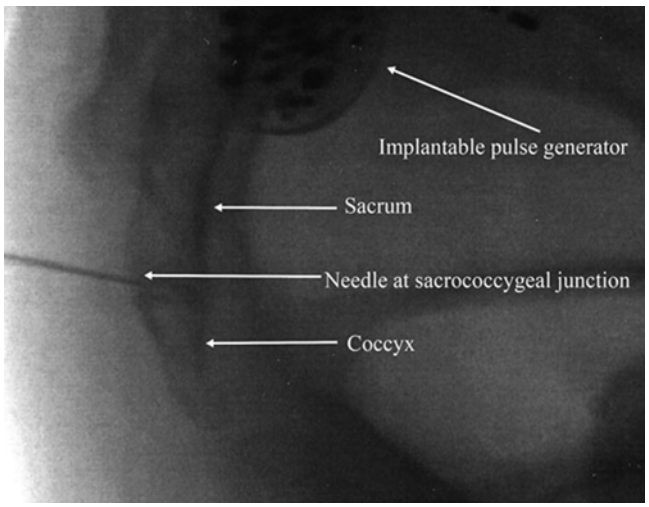

Fig. 23.5 Lateral radiographic view of transacrococcygeal approach

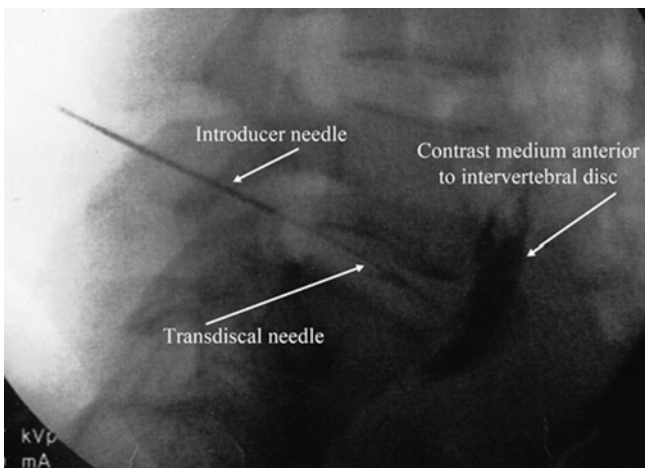

Fig. 23.3 Lateral radiographic view of transdiscal needle

spread of the residual contrast anterior to the L5–S1 disk. Neurolysis is performed with phenol 5–10 ml of 5–10% or 5–10 ml of 50–100% alcohol. The needle is flushed with 2 ml of lidocaine 1% to prevent tracking of neurolytic agent and retracted from the subcutaneous tissue and skin.

Ganglion Impar Block (Transsacrococcygeal Approach)

Fluoroscopy guidance is recommended and is described. The patient is placed on the fluoroscopy table in the prone position. After sterile preparation and drape have been accomplished, an anterior-posterior fluoroscopic image of the sacrum is obtained. The ganglion impar block is approached by rotating the fluoroscope to the lateral position and anesthetizing the area overlying the sacrococcygeal junction. A 3.5-in. 22-gauge spinal needle is inserted and advanced under intermittent fluoroscopy towards and into the sacrococcygeal disk (Fig. 23.5). The needle is advanced until the

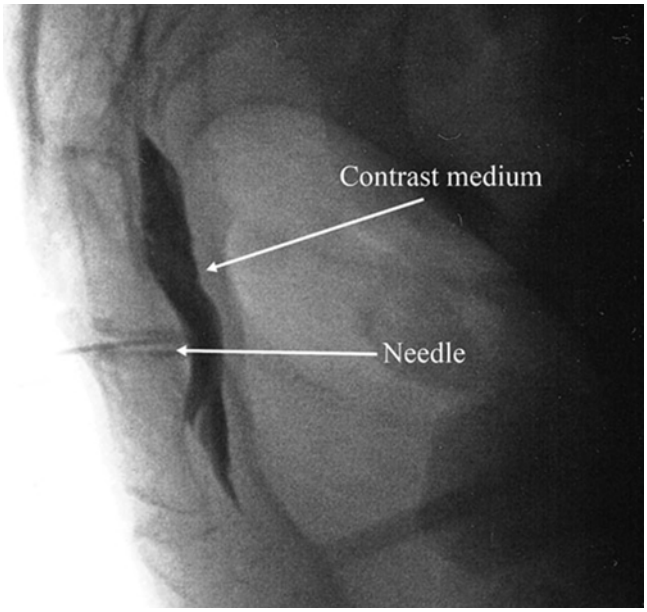

Fig. 23.6 Lateral radiographic view of contrast medium anterior to sacrum

needle is witnessed anterior to the sacrococcygeal disk. One to 3 ml of contrast medium (Omnipaque 300 M) is injected anterior to the disk, confirming correct needle placement. This may produce a "comma sign" in the lateral view (Fig. 23.6). An AP view is obtained confirming midline placement of the needle. Following this, 2 ml of lidocaine 2%, 2 ml of bupivacaine 0.5% (4 ml total) is then injected. Neurolysis is performed with phenol 1–3 ml of 5–10% or 1–3 ml of 50–100% alcohol. The needle is flushed with 2 ml of lidocaine 1% to prevent tracking of neurolytic agent and retracted from the subcutaneous tissue and skin.

Future Directions

Effective treatment of chronic pelvic pain remains limited. Many pelvic pain conditions can be attenuated by enteral and parenteral medications, along with psychosocial, physical therapy strategies. When conservative measures fail to provide adequate pain relief, interventional strategies should be employed. These strategies include hypogastric and ganglion impar block or neurolysis. Although a very limited number of studies have been published relating the efficacy of these interventional techniques, the prevalence and health-care costs associated with chronic pelvic pain warrant use of superior hypogastric plexus blocks, ganglion impar blocks, and neurolytic procedures in selective cases (e.g., malignant-related pain). Future work is required to confirm the findings of existing studies for nonmalignant pain and assist in developing a treatment strategy for pelvic pain patients.

Summary/Conclusions

Chronic pelvic pain causes significant disability and distress in men and women resulting in significant health-care causes. Specific causes and pathogenesis of CPP are poorly understood and difficult to identify, and treatment is often limited. When conservative therapy fails, sympathetic blocks and neurolysis can be efficacy and should be considered. These blocks can help reduce the requirement for oral analgesics while decreasing tolerance and side effects which develop with increasing doses and prolonged use of opioid medications. Whatever treatment is used, the approach and treatment of men and women with chronic pelvic pain should be multidisciplinary and targeted at different levels of the problem including symptomatic treatment of pain.

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Peripheral Neurolysis

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Beth Mintzer and Jagan Devarajan

Key Points

- Similar to central neuraxial neurolysis, neurolytic techniques can be utilized in peripheral nerves, sympathetic ganglia, and specific ganglia in order to alleviate pain arising from these structures.
- They are predominantly used for cancer pain management though they prove to be efficacious with minimal side effects for some benign conditions as well.
- Neurolysis can be performed by three means: physical (e.g., cryoprobe), chemical (e.g., phenol), and electrical (using high-frequency electrical current). All are aimed at interrupting the generation or propagation of action potentials along the corresponding neural structures.
- Alcohol (50–100 %) and phenol (6–10 %) are commonly used chemical neurolytic agents; glycerol (50–100 %) is exclusively used in Gasserian ganglion neurolysis.
- Cryoprobe works on Joule–Thomson effect, and pulsed radiofrequency acts by producing rapidly changing electrical field in a temperature-independent mechanism. It modulates the inflammatory response caused by the injury. It also initiates cascade of genetic events resulting in cellular proliferation which leads to decrease in pain and edema. It is presumed to cause less damage to nervous tissue.
- Trigeminal ganglion is located in apex part of petrous part of temporal bone in the middle cranial fossa, and one of the modalities of treatment of trigeminal neuralgia includes neurolysis with glycerol.
- The Gasserian ganglion can be targeted by many approaches: glycerol rhizolysis, application of radiofrequency thermocoagulation, balloon compression, and stereotactic radiosurgery using gamma knife.
- Radiofrequency thermocoagulation is associated with higher success rates, nevertheless, associated with greater incidence of complications.
- Sphenopalatine neurolysis is utilized in the treatment of sphenopalatine neuralgia and is performed by neurolysis infrazygomatic fluoroscopic-guided approach.
- Intercostal neurolysis serves in palliation of pain in the chest due to tumors involving breast, lung, and chest wall.
- Brachial plexus neurolysis is very seldom used due to fear of weakness and sensory disturbances.
- Celiac plexus neurolysis is indicated in refractory pain due to pancreatic adenocarcinoma and other intra-abdominal visceral malignancies.
- There are controversies surrounding the efficacy of block in improving quality of life and increase in life expectancy; nevertheless, it is consistently proven to provide superior analgesia compared to conservative management.
- Superior hypogastric plexus is commonly used to treat pain due to pelvic malignancies, though it has occasionally used in severe pain due to endometriosis.
- Neurolysis is one of the mainstays of treatment for Morton's neuroma due to compression of interdigital nerve and stump neuroma.
- Neurolysis of ganglion impar is occasionally used in pelvic pain.

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Introduction

The argument can be made that pain management is practiced best as a multidisciplinary specialty, and that interventional therapy is often required after conservative management and medication management have failed to provide adequate pain relief. Occasionally conventional therapeutic options fail because of the rapid progression of the disease such as in malignancy or in cases of uncontrolled proliferation of nerve fibers and unregulated transmission of nerve impulses. Very often, nontraditional methods of treatment need to be deployed to control a patient's pain. These methods include neurodestructive procedures. In general, neuroablative procedures are undertaken predominantly in malignant patients where pain control cannot be achieved with medications or in cases in which medications cause intolerable side effects.

Prevalence of pain among cancer patients is generally greater than 50 %, and as disease progresses, the incidence increases to 58–69 %, and its severity increases as well [1]. More often, these patients have a limited lifespan, and the provision of analgesia and improved quality of life will outweigh potential adverse effects arising from these interventional procedures. Various issues need to be considered before contemplating performance of these kinds of procedures, as the potential complications can be quite disabling. Often, in fact, they are permanent. Etiology of the pain, progression of the disease, expectations of the patients and their families, and availability of expertise should be analyzed thoroughly before the procedures. Despite their risks, neurolytic blocks nevertheless remain in the armamentarium of cancer pain management [2].

In the previous chapter, we discussed intrathecal and epidural neurolysis for intractable pain. In this chapter, we will discuss features of neurolysis at the level of ganglion, nerve roots, and peripheral nerves.

Substances Used for Neurolysis

There are three types of peripheral neurolysis reported in the literature. Chemical neurolysis is achieved by application of phenol, alcohol, or glycerol, or ammonium nitrate at the level of the peripheral nervous system. Physical neurolysis is by application of a cryoprobe to individual nerves. Electrical neuroablation is application of high-frequency electrical current resulting in disruption of transmission of nerve impulses.

The properties and side effects of different chemical agents used for neurolysis are discussed in the previous chapter. In brief, phenol is used in concentrations of 6–10 % and alcohol 50–100 %. Application of alcohol is painful; however, it is associated with longer duration of block (8–24 weeks). Phenol, on the other hand, is painless due to its local anesthetic properties but results in somewhat shorter duration of action (8–12 weeks). Glycerol is commonly used for trigeminal ganglion neurolysis. Glycerol is used only in trigeminal neurolysis, and the commonly administered concentration is 50–100 % [3].

Cryoanalgesia is based on the physical principle of Joule–Thomson effect [4]. Joule–Thomson effect results in rapid change in temperature when a gas is allowed to expand from a high pressure to low pressure in an adiabatic manner. The cooling is due to the fact that energy in the form of work is required to overcome the long-range attraction between gas molecules as they expand. A cryoprobe is a hollow tube with a smaller inner tube. Either N_2O or CO_2 is passed through the smaller tube at a pressure of 600–800 psi and is released into the larger tube where the pressure drops to 10–15 psi. The expansion decreases the temperature, resulting in the formation of an ice ball at the tip of the probe at a temperature of −70 °C. The probe may have nerve stimulator capability in order to localize the nerve better before freezing. Application of an ice ball on the surface of the nerve disrupts conduction of nerve impulses. Low temperature also causes severe vascular damage of vaso nervorum which causes severe endoneural edema. The long-term effect may also be explained by an autoimmune phenomenon with antibodies directed against the proteins released as a result of cryoablation. The degree of successful cryoablation depends on the temperature (how low) and duration of exposure to the cold. It also depends on the proximity of the probe to the nerve, the size of the probe and resultant ice ball formed, and the temperature of surrounding tissues. The use of a larger probe and accurate localization of the nerve with both ultrasound and nerve stimulator will improve the success rate.

The other approach is to apply high-frequency electrical current which would cause coagulation necrosis of the surrounding nerves [5]. This procedure is commonly referred to as radiofrequency ablation. The electrical energy is delivered in a circumferential manner around the needle tip. Pulsed radiofrequency has been used to treat pain arising from peripheral nerves and axial skeleton [6, 7]. In addition to heat production, exposure of nerve to radiofrequency electrical field causes changes in genetic expression of the nerves resulting in pain relief. Application of electrical current to the target in bursts of 20 ms followed by a quiescent period of 480 ms facilitates heat to be carried away.

Neurolysis

Peripheral Neurolysis Involving Ganglia

Trigeminal Neurolysis

Anatomy

The trigeminal ganglion is located within a fold of dura mater which is called Meckel's cave [8]. This fold of dura covers the posterior two thirds of the ganglion. It is situ-

ated in the apex of the petrous portion of the temporal bone in the middle cranial fossa. It is bound medially by the cavernous sinus with the trochlear and optic nerves situated within it and superiorly by the inferior surface of temporal lobe and posteriorly by the brain stem. These boundaries reinforce the importance of placing the needle accurately in order to avoid serious side effects. Preganglionic fibers exit the brain stem and travel to synapse with second-order neurons in the Gasserian ganglion (GG) [9]. The GG is formed by three series of rootlets which originate from the ventral surface of brain stem at the midpontine level. The first rootlet is V1, the ophthalmic division, which passes through the superior orbital fissure and receives sensory afferents from the forehead and nose. The second is the maxillary division (V2), which consists of sensory afferents from the upper jaw and exits skull through the foramen rotundum, then entering the orbit through the inferior orbital fissure. The mandibular division (V3) passes through the foramen ovale and provides sensory supply to the lower jaw.

Indications

Though neurolysis of the trigeminal ganglion is predominantly used to treat persistent trigeminal neuralgia [10], this intervention has been used successfully to treat both cluster headache [11, 12] and atypical facial pain [13, 14]. It is also commonly utilized to treat refractory cancer pain [15] in the distribution of the V2 and V3 divisions of the trigeminal nerve.

Refractory trigeminal neuralgia can be treated by minimally invasive procedures percutaneously. These procedures can be neuroablative with destruction of the nerve or nonablative in which the nerve is decompressed without affecting nerve function.

Neuroablative procedures can be done at three levels [16]. They are done at the peripheral nerve, at the Gasserian ganglion, or at posterior fossa. The peripheral neurolysis is intended to destroy the sensory nerves innervating triggering zone for headache. The Gasserian ganglion can be targeted by many approaches: glycerol rhizolysis, application of radiofrequency thermocoagulation, balloon compression, and stereotactic radiosurgery using gamma knife. The posterior approach is intended to do partial rhizotomy surgery through gamma knife and microvascular decompression posterior fossa surgery. All techniques except surgical sensory rhizotomy are minimally invasive and require short hospital stay. Next trigeminal neurolysis at the level of the Gasserian ganglion is discussed in detail.

Approach to Gasserian Ganglion Through Foramen Ovale

It should be done under fluoroscopic guidance which aids in correct placement of the needle and decreases the incidence of adverse reactions. The use of a curved blunt-tipped needle is strongly recommended to facilitate access to the foramen and to decrease the incidence of complications.

Patient should be supine with the head slightly extended. The entry point is 2.5 cm lateral to the angle of mouth at midpupillary line. Sterile preparation and drape cannot be overemphasized. C-arm intensifier should be obliquely rotated contralaterally away from the nose 20–30°. C-arm is then rotated 30–35° in the cephalocaudal direction to bring foramen ovale into view. Fine adjustments are made to get the best possible view of the foramen ovale. The needle is advanced slowly after raising local anesthetic wheal at the skin entry site. The direction of the needle should be superior and towards the medial aspect of the external auditory meatus. After the needle contacts the bone, a lateral view should be utilized fluoroscopically to confirm the position of the needle, which is then advanced slowly through foramen ovale. If the tip of the needle does not enter the foramen ovale, the needle is usually redirected slightly posteriorly to negotiate through the foramen. Occasionally paresthesias in the distribution of the mandibular nerve may be elicited. After negative aspiration of blood and CSF, nonionic water-soluble contrast should be injected to confirm the needle position. Occasionally CSF can be seen at the needle tip, though this has not been shown to affect the outcome of the results. Absolute alcohol or phenol can be used to lyse the ganglion, but most commonly glycerol is used for neurolysis. The amount of glycerol required for neurolysis of the ganglia is usually 0.3–0.5 ml [17]. Local anesthetic test dose may be injected before neurolysis. Glycerol is usually injected in 0.1 ml increments in order to avoid spillage into surrounding intracranial structures. The patient is usually seated with his/her head tipped forward [18].

Currently, radiofrequency neuroablation is more frequently performed and is associated with higher success rates [19]. In conventional radiofrequency, the probe is heated to 60–90 °C and usually applied for 60–90 s. Local anesthetic must be injected in order to decrease the pain due to the high temperature. Electromagnetic field pulsed radiofrequency is another way to cause ablation of the trigeminal ganglion. The principle behind pulsed radiofrequency is that the nerve is considered to act as a capacitor and the high electric field created by EMF produces holes in the capacitor-like-acting nerve, thereby interrupting the transmission of signals. This lesioning is presumed to block sensory transmission selectively through A delta and C fibers. EMF lesioning is done at lower temperatures than conventional radiofrequency, and the working range of temperature is 42 °C and is applied for 120 s [20, 21].

Percutaneous microcompression of the trigeminal ganglion is performed by inserting a No. 4 Fogarty balloon catheter percutaneously through the foramen ovale and inflating it for a minute [22, 23]. Gamma knife surgery is the latest technique for trigeminal neurolysis and works by delivering cobalt-60 radiation to the root of the trigeminal nerve through stereotactic MRI approach [16, 24]. Selective neurolysis of the V2 and V3 divisions of the trigeminal nerve

is possible for specific situations in patients with cancer-related pain [25].

These branches can be accessed below the zygomatic arch in the center of the coronoid notch by directing the needle in a perpendicular plane. The needle is advanced until the lateral pterygoid plate is encountered. If the needle is withdrawn and redirected superiorly and anteriorly, the maxillary nerve is encountered; if directed posteriorly and inferiorly, the mandibular nerve can be blocked. One to 2 ml of 6 % aqueous phenol is required to block the individual nerves.

The success rates of percutaneous glycerol rhizolysis (GR) and radiofrequency thermocoagulation (RFTC) are variable, and the studies in the literature are not uniform. Udipi et al. had shown 58.9 % success rate for GR and 84.6 % for RFTC which were not statistically significantly different from each other [26]. The recurrence rates were also not different between the two groups. Tew et al. [27] had reported a success rate of 93 % in a group of elderly patients who had undergone RFTC of the trigeminal ganglion. In the remaining 7 %, 5 % required repeat RFTC to which they responded well to treatment. In a study by Onofrio et al., all patients with classic trigeminal neuralgia responded well to RFTC, and those who were diagnosed with other types of neuralgia did not respond well [28]. Hundred percent pain relief was obtained in patients who suffered from chronic migrainous headaches [29]. The recurrence rate of headache has been reported to be 7 % in a follow-up period of 7 years. Recurrence rates in other studies were reported at 15 % [30] and 16 % [31], respectively. Glycerol rhizolysis has been shown to be successful in 92 % of patients by Dieckman et al. in 1–4 years of follow-up [32]. Spaziente has also obtained similar success rates in his patients [33].

However, Saini et al. in a large study involving 552 patients have shown a success rate of 68 % [34]. A cumulative 27.7 and 40.9 % relapsed in 1 and 2 years, respectively, after GR. Meta-analysis by Lopez had shown RFTC to have higher success rates compared to glycerol rhizolysis and stereotactic radiosurgery; nevertheless, it is associated with greatest number of complications [35]. The success rates in the literature in general are reported as 80–90 % in 1–2 years, and the relapse rate is 20–30 %. The success rates for GGGR are 80–90 % in patients who are diagnosed with cluster headaches [12, 36, 37].

Percutaneous microcompression (MC) of trigeminal neuralgia has been shown to be 93.2 % effective compared to improvement in 81.8 % of patients who underwent RFTC. However, the recurrence rates were 56 and 452.4 % following MDC and RFTC, respectively, and the recurrence occurred in a shorter period of time (6.5 months) compared to 18.5 months following RFTC [38].

Side Effects

Trigeminal neuralgia is associated with side effects which can be explained by the innervation of the trigeminal nerve. The trigeminal nerve serves as afferent pathway for corneal reflex; trigeminal ganglion blockade may result in loss of corneal reflex which can lead to hypesthesia, exposure keratitis, and corneal ulceration. Due to loss of innervation of masticatory muscles by the mandibular nerve, masticatory weakness can be observed. The incidence of numbness and paresthesia in the distribution of the trigeminal nerve is variable and ranges from 29 to 63 % [28, 39–41]. Anesthesia dolorosa can occur but the incidence is very low (0–1 %) [41–43]. Herpes simplex virus reactivation (incidence up to 10 %) has also been reported following GR [42].

Sphenopalatine Ganglion Neurolysis

Sphenopalatine ganglion (pterygopalatine ganglion or Meckel's, SPG) [44] is a major parasympathetic ganglion which is associated with branches of the maxillary nerve. It is located in the pterygopalatine fossa and consists of sensory, sympathetic, and parasympathetic roots. The boundaries of the pterygopalatine fossa are the posterior wall of maxillary sinus anteriorly, medial plate of pterygoid process posteriorly, the sphenoid sinus superiorly, and infratemporal fossa laterally. The ganglion is located on the posterior aspect of middle turbinate of the nose and lies very close to the lateral wall of the nose. Both maxillary artery and nerve are located within this region. Sensory branches arise from the maxillary nerve and are distributed along the nasal membranes, soft palate, and pharynx. The postganglionic sympathetic fibers which relay through the sphenopalatine ganglion are distributed to the lacrimal gland and nasal and palatine mucosa.

Indications for Neurolysis

The main indication for neurolysis is sphenopalatine neuralgia [45, 46], a painful condition of the head and neck where the patient experiences unilateral facial pain across the root of nose. This pain occasionally spreads retro-orbitally to the occiput and mastoid process. This painful syndrome related to irritation of the SPG can occur due to the existence of deformities such as a deviated nasal septum or nasal spur or a vasomotor phenomenon. Blockade of the sphenopalatine ganglia is occasionally used in the treatment of trigeminal neuralgia [47, 48] due to retrograde effect. It can also be used in the treatment of cluster headache, migraine, herpes zoster ophthalmicus, and atypical facial pain [49, 50] disorders.

Techniques

Neurolysis is performed by infrazygomatic fluoroscopic-guided approach [18]. A diagnostic block with local anesthetic is essential before proceeding with neurolysis.

Patient is positioned supine for the procedure.

The head is placed inside the C-arm and is passively rotated until rami of the mandible are superimposed. C-arm

is tilted cephalad until pterygopalatine fossa is visualized. When the two pterygopalatine plates are superimposed, it will resemble a "vase." The needle insertion point is under the zygoma and anterior to the ramus of the mandible. The direction of the needle should be in a medial, cephalad, and slightly posterior direction towards the pterygopalatine fossa. The tip of the needle is advanced until it is adjacent to the lateral nasal mucosa. The needle tip is confirmed by an anteroposterior view. Extra care should be taken when advancing along the lateral nasal mucosa so as not to perforate it. If paresthesia in hard palate is felt, it indicates stimulation of the greater and lesser palatine nerves and requires redirection of needle posteriorly and medially. If paresthesia is felt on upper teeth due to stimulation of the maxillary nerve, the needle should be directed in a more caudal and medial direction. Contrast is injected to confirm the position of needle and to help predict the spread of neurolytic agent. It also is used to indicate vascular (or CSF) uptake so that the needle tip intravascular injection is avoided.

If spread is correct and there is no evidence of vascular uptake of contrast, then after negative aspiration neurolytic agent is injected in 0.1 ml increments. If radiofrequency lesioning is the preferred method of neuroablation, then it is performed twice at 67–80° for 70–90 s. Pulsed radiofrequency lesioning [46] is an alternative and is performed at 42 °C for 120 s and requires 2–3 lesions. A case report involving stereotactic radiosurgery has been reported to be successful for the treatment of sphenopalatine neuralgia [51].

Efficacy

RFTC of SPG has been found to be effective in relieving pain in patients with sphenopalatine neuralgia [46]. Duration of pain relief varied from 6 to 34 months. It has been shown to relieve intractable ear pain following herpes zoster ophthalmicus [52].

In cluster headache, the efficacy of sphenopalatine ganglion neurolysis was reported to be 60–70 % efficacious and 30 % in atypical headache [53]. Topical application of local anesthetic through the intranasal approach has been used to block the sphenopalatine ganglion. Local anesthetic soaked cotton-tipped applicator is inserted through the ipsilateral nose parallel to the zygomatic arch and advanced towards the back of the nasopharynx. To provide complete blockade, a second applicator can also be inserted superior and posterior to the first one. Sphenopalatine ganglion is located a few millimeters beneath lateral wall of nasal mucosa [54]. In a similar way, 88 % phenol has been applied to eight patients in an attempt to relieve sphenopalatine neuralgia [55]. This approach, however, is not generally recommended, as it has the potential of causing a perforation of the lateral nasal mucosa.

Side Effects

Hematoma formation is a potential complication due to the presence of a venous plexus in front of the pterygopalatine fossa. SPG blockade can cause sensory disturbances like numbness, hypesthesia, or dysesthesia in the region of the palate, maxilla, and posterior pharynx [46, 53]. The side effects are usually transient. The Konen reflex can occur [56], described as a bradycardia following blockade of SPG. It has a mechanism similar to that of the oculocardiac reflex. With recent introduction of pulsed radiofrequency, most side effects can be minimized.

Glossopharyngeal Nerve

Neurolysis of the glossopharyngeal nerve may be indicated in patients with refractory pain in the posterior third of the tongue and the oropharynx [25]. The nerve can be infiltrated by tumors of tonsils, tongue, and hypopharynx and can cause severe pain. This block may be diagnostic in Eagle's syndrome or glossopharyngeal neuralgia in which pain is distributed unilaterally across oropharynx, earlobe, and face. This pain syndrome is caused by compression of glossopharyngeal nerve due to presence of elongated styloid process or ossification of the stylohyoid ligament [57, 58].

The patient is kept in the supine or lateral decubitus position. The needle is inserted halfway between the angle of the mandible and the mastoid process. The styloid process is encountered at a depth of 3 cm, and the needle is withdrawn and redirected slightly posteriorly, just past the styloid process. Paresthesia can be elicited in the oropharynx, and 1 ml of 6 % phenol or absolute alcohol can be injected after negative aspiration. Pulsed radiofrequency can also be used for glossopharyngeal neuralgia which has been shown to be 50–75 % efficacious [59, 60]. Complications include deafferentation pain, neuritis, intravascular injection of neurolytic agent, and infection.

Blocks in Thorax

Intercostal nerve block can be utilized for palliation of pain in the chest due to tumors involving breast, lung, and chest wall. The pain can arise from the tumor itself or tumor-infiltrating nerves causing neuralgia [8]. Usually multiple intercostal nerve blocks are required to cover the region of pain.

It is very important to identify the dermatomes involved and the respective intercostal nerve which needs to be blocked. A diagnostic block with local anesthetic is absolutely necessary to predict the response.

Patients are positioned in the prone position for this procedure. The relevant intercostal nerve and the corresponding rib are identified with the aid of fluoroscopy or ultrasound. The intercostal nerve, along with its artery and nerve, runs along the inferior border of the rib. The puncture site is approximately 6 cm lateral to the midline. Usually a 22-gauge 50-mm needle is long enough to perform the block. The needle is advanced until it contacts the inferior border of the rib and then walked off the margin slightly. Radiocontrast dye is injected which can be seen to spread along the inferior border of the rib. Two to 3 ml of 6 % phenol is required to perform the block. Complications include hematoma, pneumothorax, neuritis, and intravascular injection. The most dangerous complication ever reported was occurrence of paraplegia which had happened to a patient with scoliosis who had undergone intercostal neurolysis with 7.5 % phenol [61]. It was postulated to be caused by diffusion of phenol through intervertebral foramen into spinal cord, damaging sensory and motor nerve roots. Usually somatic pain responds well to intercostal block.

For intractable visceral pain, interpleural phenol has been used in a case report. It was used to alleviate the suffering of a patient with pain due to esophageal cancer [62]. Ten milliliters of 6 % phenol mixed with bupivacaine produced 2 days of pain relief. This was followed by interpleural administration of 18 ml of 10 % phenol which produced substantial pain relief for 4 weeks until the patient's death. No postmortem histopathological changes were found which could be attributed to the effects of phenol.

Upper Extremity Neurolysis

Cancer pain in upper extremities is commonly due to Pancoast tumors and metastases or tumors involving the bone and soft tissues. Tumor invasion of the brachial plexus due to axillary metastases can cause intractable pain in the upper extremity. The brachial plexus originates from anterior primary rami of C5–T1 and provides innervation to the upper extremity. Brachial plexus neurolysis is performed very rarely as the incidence of side effects like numbness and paralysis is very high, and hence this procedure is usually restricted to terminally ill patients. Moreover, peripheral nerve stimulation and the availability of radiofrequency ablation make neurolysis fairly obsolete.

Neurolysis should be performed proximal to the nerves which act as pain generator. Most patients with involvement of neural structures may have preexisting sensory and motor weakness which should be carefully documented. This can also make identifying the nerve by nerve stimulator difficult; in these situations, identification with ultrasound can be very helpful.

To treat the pain secondary to Pancoast tumors, the interscalene approach to blockade of the brachial plexus is required. The brachial plexus can be identified by ultrasound, after which diagnostic local anesthetic injection is helpful to determine the degree of pain relief which can be achieved. To perform neurolysis, 15–20 ml 6 % phenol can be injected slowly in increments. Side effects are intravascular injection, subarachnoid or epidural spread causing unwanted side effects, hematoma, pneumothorax, and involvement of phrenic nerve.

Involvement of the lumbosacral plexus by tumor causes pain in the lower extremities. This pain can be managed with central neuraxial neurolysis by selective blockade of sensory innervation. Transforaminal epidural phenol administration [63] to cause selective blockade of nerve root has been reported to alleviate pain successfully in the lower extremities due to leiomyosarcoma. Phenol was administered in two stages at three levels without any untoward side effects. Reportedly obturator nerve neurolysis successfully reduced adductor spasticity resulting from different pathological processes [64, 65].

The lytic effect lasted for a maximum of 3 months. It allowed for a decrease in VAS scores and improvement in range of motion and personal hygiene. Cryoanalgesia has been used to provide successful long lasting relief of adductor spasm and pain [66].

Details of the procedures for obturator nerve and transforaminal block are discussed elsewhere in the textbook.

Phenol neurolysis has also been used for certain conditions causing nonmalignant pain [67].

The pain was persisting even after opioids, NSAIDs, and adjuvants. The conditions where the neurolysis was effective were Tietze's syndrome, ilioinguinal nerve, medial branch neurolysis, lumbar sympathetic nerves, intercostal nerve, genitofemoral neuralgia, and meralgia paresthetica [67]. Neurolytic paravertebral block with phenol appears to have limited use [68]. There were no serious complications such as tissue necrosis or flaccid paralysis. Minor complications like local hematoma and pain occasionally occurs which usually resolve in 2 weeks. In 25 % of patients, a single injection is usually effective but in rest multiple setting was required. Concentration of phenol used was 4 %. Cryoablation has been reported to provide good pain relief in a patient with neuropathy of femoral component of genitofemoral nerve [69].

Neurolysis of Stump Neuroma

Phantom pain is quite common after limb amputation and the incidence could be as high as 72 % [70]. The incidence of stump pain is 50 % [71]. Development of stump neuroma is

frequently associated with complex pathophysiology of development of both stump and phantom pain. Neuromas lead to reorganization of central neuronal circuits which cause structural and functional changes in somatosen-sory cortical areas corresponding to amputated limb. Neurosclerosis of neuromas with phenol has been suggested as one of the treatment modalities for stump pain. Both blind- and ultrasound-guided administration of phenol have been shown to be effective. Complete pain relief was achieved in 26 % of patients, and rest of patients had more than 70 % decrease in VAS score [72, 73].

The success rate was much higher than even injecting under direct vision during surgery. An alternative is to apply cryoprobe to cause neurolysis in patients who had undergone amputation. The cryoprobes were applied under electrophysiological guidance. Sixty second freeze thaw cycles were applied using 2-mm cryoprobe [74]. The cycles were repeated until tenderness over the region of neuroma disappears to a maximum of five cycles. Nine out of ten patients experienced significant pain relief of more than 3 months.

Interdigital Nerve Compression of the Foot

The major cause of foot pain is interdigital nerve compression, commonly known as Morton's neuroma [75]. It causes numbness and burning in the toes, sensory disturbances, and a feeling of ball in the foot. This syndrome is due to entrapment of digital nerve between the metatarsal heads and beneath the intermetatarsal ligament. An intermetatarsal bursa can also compress the nerves causing symptoms. It can be managed by orthotic, pharmacological, or surgical methods. Application of alcohol or phenol is also a method to manage the condition in order to cause remission of symptoms.

Intermetatarsal space was accessed through dorsal approach, and 2.5 ml of 5 % phenol was injected after eliciting paresthesia, and the success rate was 80.3 %. Alcohol injection was also utilized; however, it required multiple injections, and 74 % of feet were improved after five settings of neurolysis treatment [76]. Complications included pain and erythema which usually resolve by 24 h.

Neurolysis in Abdomen

The ganglia which innervate abdominal and pelvic viscera include the celiac plexus, superior and inferior mesenteric plexuses, superior hypogastric plexus, and ganglion impar. Usually treatment with neurolysis of these ganglia is restricted to patients who have pain arising from malignancy. The celiac plexus provides sympathetic innervation to the liver, stomach, pancreas, gallbladder, spleen, kidneys, adrenal glands, small intestine, and a portion of the large intestine. Nociceptive afferents from bladder, prostate, rectum, uterus, ovaries, and vagina relay through the superior hypogastric plexus. The sympathetic chains terminate in the unpaired ganglion impar (ganglion of Walther) which carries visceral afferents from the distal rectum, anus, perineum, distal urethra, and vulva.

Celiac Plexus

It is a collection of 1–5 ganglia and contains fibers from the thoracic and lumbar sympathetic chains (sympathetic), vagus (parasympathetic), and the phrenic nerves (motor). The thoracic splanchnic nerves (greater, lesser, and least) arise from roots of T5–T12 paravertebral sympathetic ganglia and terminate in the celiac plexus.

Indications

Neurolytic block of the celiac plexus is used for both malignant [77] and nonmalignant pain. The most common and popular indication is pain arising from pancreatic adenocarcinoma [78, 79], although it has been used occasionally in chronic pancreatitis. It is reserved for patients whose pain cannot be controlled with opioids and/or who have developed intolerable side effects from opioids [80]. The optimal therapeutic effect is obtained if the procedure is performed early in the illness, and it has been postulated to prolong life expectancy [81] as well. However, later in the disease process, the incidence of complications arising from the block increases [82]. It can also be considered for treatment of visceral pain originating from malignancy involving stomach, liver, and pancreas.

Celiac plexus is located in the retroperitoneal region anterior to the crus of the diaphragm around the origin of celiac artery from the aorta. It is situated at the level of T12 and L1 vertebral bodies.

Procedure

Celiac plexus block can be performed percutaneously by fluoroscopic method (most common), directly during surgery, via CT guidance, and by endoscopic ultrasound. This block is most commonly performed by posterior percutaneous approach [83, 84]. Depending on the position of the needle tip, the procedure could be termed retrocrural [85] or precural [86].

Injection into the retrocrural space actually achieves blockade of the splanchnic nerves only (splanchnic nerve block), whereas precrural spread of the drug causes actual blockade of the entire celiac plexus. Retrocrural injection, however, also achieves spread of drug into the precrural space as well. According to the route of needle insertion, one can use a paravertebral (classic) approach or the transdiscal [85] or transaortic [87] route.

Although technique of celiac plexus block is described elsewhere in the textbook, we will describe the classic approach in which needle is inserted via paravertebral location with a posterolateral approach. In this technique, the needle is advanced until it contacts the lateral surface of the vertebral body. This approach requires bilateral injection of medication to achieve complete blockade of the plexus. In transaortic or transdiscal approach, a single injection is used. The efficacy of administration of drug via different approaches remains the same [87]. Transdiscal retrocrural approach is simpler and less invasive, though there exists the risk of infection of the intervertebral disk (diskitis).

The needle for CPB is inserted either under fluoroscopic or CT guidance [88, 89].

Loss of resistance to saline-containing antibiotics technique is used in transdiscal approach. Though CT-guided approach helps to place the needle more precisely, the efficacy is not different from that of fluoroscopy guidance. Contrast is often injected to confirm the needle tip position and rule out intravascular injection. A "butterfly-wing" shadow is seen in anteroposterior view in the transcrural approach, whereas a wedge-shaped appearance is seen in the retrocrural technique; 20–25 ml of 50–75 % alcohol is used for neurolysis (10 ml on each side if bilateral injections were planned). For splanchnic nerve block, needle is inserted at a higher level T10–T12 level. The anterior approach via CT guidance helps one avoid puncture of aorta (and lungs) and allows better visualization of structures. It can also be performed via an endoscopic ultrasound approach which allows simultaneous tissue sampling as well.

Expected and relatively common side effects include hypotension (38 %) and diarrhea (44 %) [90]. Rare complications also include infection, neuritis, pneumothorax (2 %), and renal, aortic, and intestinal injuries. Serious neurological complications like paraplegia is very rare but can occur, thought to be due to injury of the artery of Adamkiewicz. Spinal and epidural spread is possible though a rare complication [91–94]. Contrast injection before neurolytic administration helps reduce the incidence of many of these complications. When a semilateral diffusion of contrast medium is found, an additional inferior mesenteric plexus block can be performed using a transdiscal approach at the L2–L3 level. Though transdiscal approach is potentially associated with inflammation, degeneration, infection, and dislocation complications, no such complications have been reported [85, 86]. Acute alcoholic intoxication-like symptoms have been reported due to rapid absorption of alcohol from the surrounding venous plexus. Abdominal aortic dissection has been reported following celiac plexus block.

Efficacy

Meta-analysis of the studies involving celiac plexus neurolysis with 1,145 patients concluded that 89 % of patients had excellent pain relief for 2 weeks and 90 % had partial to complete pain relief for the duration of 3 months [95]. Patients with malignancy involving all upper abdominal structures manifest benefit in the same way as that of patients with pancreatic adenocarcinoma. However, in a study by Wong et al. [96], celiac plexus neurolysis was associated with larger decrease pain scores in the first week compared to systemic opioids group; however, the consumption of opioids, side effects, and quality of life were not different between them. After 1 week, though percentage of patients who had severe pain was lower in neurolytic group, the quality of life was not improved by neurolysis.

Rykowski et al. in his study found better control of pain when the tumor is confined to pancreas. Neurolysis was more effective in patients with tumor involving head of pancreas [97]. Stefeniak et al. compared two methods of invasive celiac plexus neurolysis to control patient [98]. Percutaneous neurolytic group was associated with decreased pain and improved quality of life compared to control group. The follow-up period was up to 8 weeks. Staats et al. in a similar study had shown not only improvement of pain with neurolytic block but also was associated with elevated mood and improved life expectancy [81]. Elevated mood with neurolytic therapy will counter the depression causing decrease in immune function and antitumor activity. Vranken et al. in his small study involving 12 patients had also shown improved pain and quality of life with neurolytic celiac plexus block, but the effect was short lived [99]. Mercadante et al. [100] in a prospective controlled multicenter trial also had shown similar positive results with decreased opioid consumption and improved gastrointestinal adverse effects with neurolytic blocks. In the meta-analysis, Yan et al. found reduction in pain scores and opioid usage up to 8 weeks though there was no difference in the survival [95].

The predictors of poor pain relief are advanced age and prior surgery. There is no improvement in quality of life or survival in patients who had undergone EU-guided celiac plexus neurolysis. It did reduce the amount of morphine consumption and improved quality of pain relief.

The literature is not clear whether celiac plexus block improves quality of life and life expectancy; however, there is definite improvement in pain scores associated with reduction in opioid consumption for a variable duration of 2 weeks to 3 months.

Superior Hypogastric Plexus Block

Pain secondary to pelvic metastatic disease or de novo malignant tumors involving pelvic structures may be treated with superior hypogastric plexus blockade [101].

Superior hypogastric plexus is located in the retroperitoneal region bilaterally extending from the lower third of fifth lumbar body to the upper third of first sacral body. Nociceptive sympathetic fibers from pelvic viscera like

prostate, bladder, uterus, ovaries, vagina, and rectum are carried through this superior hypogastric plexus. This plexus divides and forms into the inferior hypogastric plexus in front of S3 and after receives more parasympathetic innervations from S1–S3 [102].

Blockade of the superior hypogastric plexus is performed under fluoroscopy guidance with the patient in the prone position. The needle is inserted 5–7 cm lateral to the midline in the classic posterior approach. The tip of the needle is placed just anterolateral to the lower third of L5 and placement is confirmed in both anteroposterior and lateral views [103]. Ten milliliters of neurolytic agent is required to achieve complete blockade.

Superior hypogastric plexus neurolysis has been reported to provide excellent pain relief without major side effects in a patient with endometriosis which is unresponsive to medical treatment [104]. Superior hypogastric plexus blockade can also be performed from the anterior aspect of the patient via CT scan or ultrasound guidance [105]. CT-guided bilateral transdiscal approach [106] has been demonstrated to overcome anatomic obstacles to the block. It is an excellent choice in patients with intractable pain with genitourinary, rectal, and pelvic malignancies. This approach is particularly useful when challenges are encountered in doing classic posterior approach or when the sacral promontory [107] makes it impossible to place the needle at the correct location. The other obstacles occasionally encountered were osteophytes, surgically fused spines, orthopedic hardware, transverse process of L5, and an enlarged iliac crest. The risk of diskitis is possible but very rare, and disk rupture is a potential complication but never has been reported. Inferior hypogastric plexus can also be blocked by accessing it through the sacral foramen [102]. Superior hypogastric plexus block can also be done from anterior approach as well [108]. Complications include intravascular injection, neuraxial injection, diskitis, neuritis, and bladder and bowel dysfunction.

The success rate of the block was reported as 70 % in patients with pelvic pain associated with cancer [103]. In another study, the success rate was 72 % after repeated chemical neurolysis of the superior hypogastric plexus [109].

Ganglion Impar Block

The ganglion impar is located in the retroperitoneal region at the level of sacrococcygeal junction. It is an unpaired structure and marks the termination of the two sympathetic ganglia (chains). Neurolysis of this ganglion is useful in pelvic pain, but the published experience of neurolysis of this ganglion is limited.

For this procedure, the patient can be in either the prone or lateral decubitus position. A 20-gauge 1.5″ needle is inserted through the sacrococcygeal in the midline and advanced until the tip of the needle is positioned posterior to rectum [110]. Care should be taken to avoid puncture of the rectum. Contrast medium is injected to confirm the position and bilateral spread, and then, after negative aspiration, 4–6 ml of neurolytic agent may be injected in slow increments. Ultrasound can also be used to perform this block.

A modified technique has been described for thermocoagulation of ganglion impar where a two-needle technique is utilized. The first needle was placed through the sacrococcygeal ligament, the transsacrococcygeal needle, and the second one through a coccygeal disk, the transdiscal needle. A lateral view is shown in fluoroscopy which should include sacrum and coccyx. The tip of the needle should be placed 1–2 mm anterior to the sacrococcygeal ligament [111]. Complications include rectal puncture, caudal injection, and inadvertent intravascular administration.

Anesthesia Dolorosa (Deafferentation Pain)

Anesthesia dolorosa is described as pain in the distribution of an anesthetized area due to injury to the nerve. It has been reported more often after trigeminal rhizolysis though it could occur in other conditions associated with neurolysis and stereotactic surgery or any trauma causing nerve injury. The incidence is variable and reported to be between 0 and 5 % of patients who had Gasserian neurolysis.

Patients usually complain of altered sensation and pain in the injured area. The pain is often described as stabbing or burning or shooting and exacerbated with exposure to cold or rapid temperature changes [112].

There is no effective management of this condition. Shooting or lancinating pain can be managed with anticonvulsants, and burning pain can be treated with tricyclic antidepressants or serotonin reuptake inhibitors. If patient does not respond to above options, intravenous lidocaine or ketamine can be tried. Motor cortex stimulation is also used with intention of nonnociceptive sensory input replacing nociceptive pain [113].

Conclusion

Chemical neurolysis of peripheral nerves and sympathetic ganglia seems to be a relatively safe and cost-effective part of management of pain due to malignancy. Though there can be potentially dangerous complications, generally these are rare. Careful patient selection and counseling before blockade are important. The most commonly performed procedures are celiac plexus and superior hypogastric plexus neurolysis. The success rate (ability to achieve pain relief) of these procedures is >80 % for the first 3 months. These blocks are associated with good pain relief, reduction in the

amount of opioid consumption, and hence reduction in side effects. Though they have also been shown to improve quality of life and survival, these benefits have not been conclusively established.

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Central Neuraxial Neurolysis

25

Beth Mintzer and Jagan Devarajan

Key Points

- Central neuraxial neurolysis is selective destruction of the sensory rootlets at the spinal cord to prevent transmission of nociception.
- Every effort is made to preserve motor, bladder, and bowel function.
- With the advent of continuous opioid delivery systems and the internalized intrathecal pump, this technique is needed less often and has fallen out of favor and use.
- This is a therapy offered to patients with pain due to malignancy who have limited life expectancy.
- The intrathecal (subarachnoid) route is preferred more often than the epidural route.
- Phenol (5 %) and absolute alcohol (33–100 %) are the commonly used therapeutic agents.
- Phenol is hyperbaric in relation to CSF and is required to be administered in patients positioned with the painful dermatome and sclerotome on the dependent side.
- Absolute alcohol is hypobaric relative to CSF and is injected with the painful segment on the nondependent side.
- Phenol injection is less painful and usually results in a shorter duration of effect compared to injection of alcohol, the latter of which causes burning pain and may provide up to 6 months pain relief in approximately 50 % of patients.
- Spread of phenol is better controlled than the spread of alcohol. After injection of alcohol, the patient needs to remain in the same position for a longer period of time (at least 30 min) than after phenol injection to diminish spread to other unintended regions of the spinal cord.
- Increased intracranial pressure and coagulopathy are contraindications to the performance of the procedure.
- The epidural route for neurolysis is occasionally chosen for patients with midline, bilateral, and extensive distribution of pain.
- Patient selection, informed consent, and follow-up care cannot be overemphasized.
- Complications of central neuraxial neurolysis include muscle weakness and bladder and bowel disturbances, which generally are transient and gradually improve over a period of 4–6 months. Permanent bladder dysfunction, however, occurs in 0.8 % of patients.
- Deafferentation pain and loss of sensory modalities in the involved dermatomes can be disturbing to a subgroup of patients.

Introduction

Central neuraxial neurolytic blockade is intended to destroy, selectively, sensory dorsal nerve roots and rootlets between the spinal cord and dorsal root ganglion (DRG) to prevent transmission of nociceptive impulses through the spinal cord [1]. Preservation of motor, bladder, and bowel function is the goal with optimal analgesia.

In the past two decades, this technique has fallen out of favor for several reasons. The development of intrathecal opioid delivery systems for the management of nonmalignant and malignant pain syndromes substantially decreased, to a large extent, the need for subarachnoid neurolysis. Moreover, fear of potential and disastrous complications of the procedure, accompanied by decreased experience with

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the technique, has rendered pain practitioners less than enthusiastic about the use of this intervention. Nevertheless, it is still an effective method of analgesia in cancer patients with terminal disease states. It remains more commonly performed in developing countries where access to opioids and dedicated follow-up care is limited [1].

It is a very effective method in those patients who have already undergone diversion procedures for bladder and bowel invasion. The greater susceptibility of the dorsal nerve rootlets compared to dorsal root ganglia and the separation of sensory and motor components in the spinal cord allow this technique to be used for selective disruption of nociceptive sensory pathways with preservation of motor function.

Patient selection plays a major role in the success of the procedure [2]. Application of selective neurolytic agent with the patient in the appropriate position cannot be overemphasized. It is important to understand that only a small subset of patients with pain due to malignancy is suitable for this procedure. It should also be emphasized that subarachnoid neurolysis is more effective in ameliorating somatic pain than visceral pain [3]. It is not found to be useful for neuropathic cancer pain. Despite these limitations, adverse effects can be minimized in experienced hands, and this is still a useful method of analgesia in selective patients.

History

Chemical neurolysis was developed to circumvent the adverse effects associated with surgical neurectomy performed for providing pain relief in earlier days. Neurolysis has been described as early as 1863 when Luton used the technique of subcutaneous injection of irritants to provide relief for sacral neuralgia. However, subarachnoid neurolysis was not performed until 1931 when Dogliotti performed subarachnoid neurolysis with alcohol to provide analgesia for intractable sciatica. Following this procedure, Suvansa used intrathecal carbolic acid for the treatment of tetanus [4]. Nevertheless, phenol was used for analgesic purposes only after 25 years. Maher from Liverpool reported the use of phenol for intractable pain in the trunk, pelvis, and legs, and he used phenol in combination with silver nitrate. Miller described usage of 10 % ammonium sulfate for intercostal neuralgia [5], and Korsten applied *n*-butyl p-aminobenzoate via the epidural route [6].

Pharmacology

Absolute alcohol and phenol are agents typically used for subarachnoid neurolysis and glycerol for blockade of the gasserian ganglion.

Phenol

Phenol is also known as carbolic acid. Chemically, it has a structure of C_6H_5OH where a hydroxyl group is substituted for a hydrogen atom in the benzene ring. It is available as a white crystalline solid. Therefore, it has to be prepared by the pharmacy as an injectate. Phenol is clear and less soluble in water than in alcohol or other organic compounds. It is mixed with distilled water, glycerin, or radiographic contrast dye for clinical use. Glycerin is required to dissolve the crystals when phenol is used at a concentration higher than 6.7 %. The phenol-glycerin mixture is made by dissolving 0.6–1 g of phenol crystals in 10 ml of dehydrated, sterilized glycerin to yield an effective concentration of 6–10 % [7]. Solution in glycerin is more viscous, requiring the use of large bore needles for administration. It is unstable at room temperature and needs refrigeration. If refrigerated, it can be stored up to a year as phenol itself is bactericidal and fungicidal [8]. When exposed to air, it undergoes oxidation and turns reddish in color. The major advantage of phenol is its very slow spread which limits its site of action to a very localized area.

Phenol is available in 4–12 % solution and is hyperbaric in relation to cerebrospinal fluid (CSF). The action of phenol is concentration-dependent, with concentrations of 1 % producing local anesthetic effect without any destruction of axons and 12 % producing maximal axonotomic effect which may cause spinal cord infarct, arachnoiditis, or meningitis [9]. An injection of 5 % solution produces more sensory blockade; a concentration greater than 5 % can affect motor function [10]. It is the preferred agent for use in the epidural space due to a differential blockade [10, 11]. Concentrations greater than 5 % cause protein denaturation, resulting in segmental and nonspecific demyelination [12] and Wallerian degeneration [13]. Phenol has a biphasic action: initially, it causes warmth and numbness due to its local anesthetic effect, followed by nonspecific degeneration of axons [14]. It thus allows one to assess the analgesic effect over 24 h which then helps to make decisions about repeated injection. Phenol produces a less intense block for shorter duration of effect compared to alcohol. It takes about 14 days for the degeneration of nerves and another 14 weeks for regeneration.

Lifschitz et al. have shown results of 1–2 months of pain relief in 52 % of patients and more than 2 months relief in 14 % of patients [15]. Phenol is metabolized rapidly through conjugation and oxidation in the liver. Its inactive metabolite is excreted in the urine. It is very unlikely to produce any systemic effects at doses clinically used for subarachnoid neurolysis (10 ml of 10 % solution). Doses exceeding 600–2,000 mg are neurotoxic to the central nervous system and can result in convulsions and stupor, followed by cardiovascular collapse [16]. Due to the systemic side effects, it is not advisable to use in vascular areas where systemic absorption can be very high [17].

Absolute Alcohol

Alcohol is used as an alternative to phenol for producing neurolysis. It is available in 1 or 5 ml ampules at a concentration of 100 %. Unlike phenol, it is associated with burning dysesthesia at the time of administration. The severity and duration of discomfort depend on the concentration of alcohol used. Local anesthetic may be used first to minimize the painful side effect. However, this burning sensation may be helpful to localize the dermatomal level of injection and action of the drug. It has a specific gravity of 0.789–0.807 and is hypobaric in relation to cerebrospinal fluid. Thus, the effect of alcohol is influenced by the position of the patient opposite to that of phenol. It is more soluble and hence spreads faster than phenol from the site of injection. It is also rapidly removed from the CSF by uptake and diffusion. Hence, a relatively large amount of solution is required to produce a given effect at a localized site of injection. Caution is necessary, however, as large volumes may result in surrounding tissue damage. Alcohol can produce arterial vasospasm in clinically effective concentrations and volumes, and hence, paraplegia is a risk during its administration by causing vasospasm of the artery of Adamkiewicz. This is similar to the risk of paraplegia during its use in celiac plexus block.

The mechanism of action of alcohol is by dehydration and extraction of cholesterol, phospholipids, cerebrosides and precipitation of mucoproteins. The nerve fibers and myelin sheath are sclerosed [18], resulting in demyelination and subsequent Wallerian degeneration [19]. Histopathology demonstrates patchy areas of demyelination in the posterior columns, Lissauer's tract, and dorsal roots [20]. These changes have also been observed in peripheral nerve injections and spinal nerve root injections. Alcohol has also been shown to be direct neurotoxic to posterior column of spinal cord. Alcohol produces inconsistent effects on sensory and motor discrimination; the lowest concentration of 33 % has been shown to produce satisfactory analgesia without motor compromise. The duration of effect of alcohol exceeds that of phenol and has been shown to last for more than 6 months in 50 % of patients who have undergone this procedure. CSF uptake with subsequent decrease in concentration takes up to 30 min to occur [21]; patients are required to remain in the same position used for administration of the alcohol for at least 30 min after injection.

The consensus is that the spread of hyperbaric phenol is better controlled compared to that of alcohol at the expense of decreased duration and potency of effect. If the patient cannot lie on the painful side, alcohol may be used preferentially.

Patient Selection

This may be the most important part of the entire procedure as it so strongly influences the success of the procedure. Great care should be exercised, as the adverse effects of the procedure can be severely disabling. This procedure is reserved for patients who have a short life expectancy of no more than 12 months and who have pain at a localized site not exceeding two to three dermatomes. Patients with diffuse and bilateral pain may not be suitable for this technique. Patients with bilateral pain may undergo the procedure two times, with the more painful side treated first, followed by ablation of pain on the other side at a later date. All other more conservative measures should be tried before resorting to this more destructive process. Patients should have undergone a thorough diagnostic workup including a detailed history and physical examination, laboratory tests, and imaging modalities, as appropriate. Evaluation for preexisting neurological deficits should be systematically performed and documented for medicolegal purposes. The diagnosis of the condition should be certain. One can consider performing a diagnostic injection with local anesthetic either before or at the time of the procedure. This may be especially helpful before phenol, as hyperbaric local anesthetic mimics the neurolytic agent fairly well. In contrast, it is difficult to get local anesthetic to have the same specific gravity as absolute alcohol, making it more difficult to perform a valid diagnostic block. Nevertheless, some practitioners routinely perform subarachnoid block with local anesthetic so that the patient may experience sensory blockade to decide that he/she can tolerate the "numbness." Strict selection criteria can be relaxed in those patients who have already developed bladder and bowel dysfunction and have undergone some kind of surgical drainage procedure such as an ostomy or conduit [10]. It should be remembered that the procedure is generally reserved for patients with pain from either somatic or visceral origin, and diagnosis of origin and type of pain should have been determined beyond doubt.

Contraindications

Anything which precludes performance of subarachnoid block contraindicates this procedure. Coagulopathy and presence of infection at the intended site of needle puncture prevent performance of this technique. Patients who are unable to understand and accept the potential adverse effects of the procedure and, generally, patients with neuropathic pain are not suitable candidates for this treatment modality. The presence of either primary or secondary tumor at the site of administration and elevated intracranial pressure are contraindications to the procedure. Subarachnoid neurolysis should generally not be utilized if six or more spinal segments are involved in the painful syndrome.

Preparation for Procedure

Informed Consent

It is paramount that patients understand the risks and adverse effects associated with the procedure. The possibilities of motor paresis, paralysis, and bladder and bowel dysfunction

should be emphasized. They should have realistic expectations of analgesia from this procedure, i.e., improved comfort, decreased opioid requirements, and hence fewer side effects from opioids. They should be aware that this procedure probably will not completely eliminate the pain and will not control the primary source of pain. Numbness may result from the procedure, and the duration of effect varies between 1 and 6 months and may require that this procedure be repeated. Tumor may continue to grow and expand and produce pain in other sites.

Preparation

Neurolytic block should be performed at the level where the spinal cord receives the sensory rootlets from the affected dermatome(s). If there are any bony secondary metastases causing pain, the relevant sclerotome should be sought to target the block accurately at the site of pain.

It is essential to have a complete understanding of the affected dermatomes and the site of entrance of the specific dorsal nerve root in the vertebral column. Cervical nerve roots exit a level higher than their corresponding vertebrae and the remaining roots below their respective vertebral bodies. In the thoracic, lumbar, and sacral regions, nerve roots emerge from the spinal cord several segments above the level at which they exit through corresponding intervertebral foramina in the vertebral column due to differential growth of bony vertebral column and the spinal cord. Since the effects of alcohol are most pronounced at the level of the fine rootlets (i.e., fila radicularia), it is advisable to perform alcohol neurolysis at the level of origin of the nerve rootlets from the spinal cord.

A decision should be made whether hyperbaric phenol or hypobaric alcohol will be used during the procedure. If the patient cannot lie on the affected side, alcohol is a reasonable choice. The amount and concentration of the neurolytic agents administered determine the therapeutic and toxic effects of the drugs. Greater than recommended, therapeutic volumes can be used in the thoracic region, which is more distant from the brachial and lumbosacral plexuses. Similarly, upper limits of volume utilized can be liberal in terminally ill bedridden patients in whom mobility and continence are of less concern. It is also preferable to use smaller volumes and multiple needle approaches than one large volume and a single needle approach. Great care should be taken to minimize turbulence and barbotage during injection to prevent untoward aberrant spread of the agent and subsequent neurological injury.

Patients should be given instructions regarding the requirement to remain immobile during the procedure and for 30 min after the procedure, as movement from the original position can result in blockade and destruction of unintended nerve roots without any therapeutic benefit. The patient may be expected to have some discomfort during needle placement and should expect to assume a potentially uncomfortable position immediately following the procedure. He/she should be prepared in advance to provide real-time feedback responses concerning the development of burning, warmth, numbness, or any unpleasant sensation, as well as pain relief experienced during and after the procedure. Assistance from one or more additional people is required to help the patient maintain his/her position and to assess and monitor vital signs during the procedure. Sedation needs to be kept to a minimum in order to obtain accurate feedback information and optimal cooperation from the patient. Observance of sterile precautions is mandatory and can be per usual protocol.

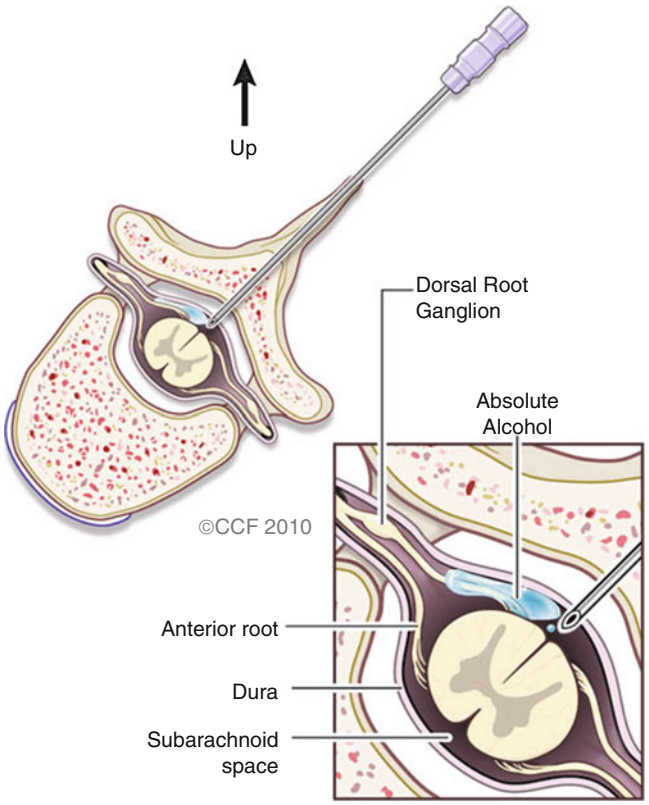

Fig. 25.1 Quieting dorsal nerve roots – alcohol and phenol

Alcohol Neurolysis

The patient should be positioned in lateral decubitus position with the painful side in a nondependent position. The patient is generally rolled 45° anteriorly (forward) to bring the dorsal nerve roots into a superior position, facing up (Fig. 25.1). The patient should be stabilized in this position with straps and bolsters and folded sheets to maximize comfort while maintaining support. Fluoroscopy should be used to confirm the position of needle in the appropriate intervertebral space. A relatively large bore needle (22 G) should be used to ensure free flow of CSF and to minimize jet effects of injection.

The bevel is oriented to the nondependent side to maximize the delivery of the alcohol toward targeted nerve roots which are positioned uppermost. Either a pencil point (e.g., Whitacre™) tip or cutting bevel (e.g., Quincke™) can be used for the procedure.

There are arguments for and against administration of a test dose. It is difficult to make local anesthetic as hypobaric as alcohol to determine accurately the behavior of the proposed alcohol injection. A small dose of lidocaine can be used to minimize the burning and unpleasant sensation associated with alcohol injection, but this will prevent the use of the symptoms of burning after alcohol injection as a valuable indicator of the particular segments which are going to be involved. Alcohol should be injected in 0.1-ml increments from a tuberculin syringe to ensure accuracy of volume administered. The patient should be asked to report the development of any burning sensation after each aliquot of injection and the location of such burning. The presence of a burning sensation at the painful area gives a strong indication that the injected drug has reached the corresponding site. The maximum injected volume required to produce the beneficial effect is usually 1 ml. If the patient indicates a burning sensation just cephalad or caudal to the original area of pain, the table can be tilted head up or down to modify the spread of neurolytic agent. However, if the unpleasant sensation is perceived distant from the painful areas, the spinal needle should be withdrawn and reinserted at a level below or above the initial site of injection as directed by the patient's perception of dysesthesia relative to the site of pain.

The needle should be flushed free of the alcohol or phenol with 0.2–0.3 ml of preservative-free normal saline or CSF before its withdrawal in order to avoid spilling of the drug in the subcutaneous tissue. Injection of 0.1–0.2 ml of neurolytic drug at a discordant site is associated with minimal demonstrable neurological damage. Constant communication and feedback from the patient is crucial to the success of the procedure and can greatly prevent unintentional neurologic deficits from occurring. If pain is present covering three or four segments, separate injections should be made at each level, observing the above precautions with each injection.

Phenol Neurolysis

As phenol is hyperbaric, the patient should be positioned with his/her painful side in a dependent position with slight posterior tilt to the torso so as to direct the solution to the posterior rootlets (Fig. 25.1). In patients with sacral pain, this procedure can be done in sitting position. Phenol is a viscous solution necessitating a larger bore needle to perform this procedure. Warming the phenol by immersing the ampoule in hot water prior to aspiration into the syringe reduces the viscosity and makes it easier to inject. The bevel of the needle should be directed inferiorly. Extreme care should be taken to minimize the likelihood of splashing phenol by creating a firm seal between the syringe and hub of the needle. Otherwise, due to the extreme viscous nature of the solution and subsequent increased pressure to inject the solution, the seal can break and the phenol solution can splash onto intact skin of the patient or even into the eyes of the clinician. Unlike alcohol, phenol does not produce any burning sensation during injection. It actually produces relatively mild warmth and tingling due to its local anesthetic properties. After the injection, the stylet should be replaced into the needle and the needle tip washed by the CSF to minimize the potential for sinus formation and backache due to the escape of residual drug as the needle is withdrawn.

Neurolysis is less common in the cervical region due to several factors. Compactness of the spinal cord and nerve roots make it difficult to perform a selective block. The compactness of neural elements in the cervical region makes selective neurolysis of sensory nerve roots more challenging to accomplish without causing unwanted adverse effects. Moreover, since the brachial plexus is in the cervical region, these adverse effects can be quite troublesome. In cases where the brachial plexus itself is involved in the pain syndrome, it may be a neuropathic rather than a somatic type of pain and therefore often resistant to successful treatment with subarachnoid neurolysis. Subarachnoid neurolysis for pain in the thoracic region is very effective but technically challenging compared to performance in the lumbosacral region due to the presence of the spinal cord. However, the consequences of motor dysfunction are less pronounced in the thoracic area, and paralyses of intercostal muscles usually are well tolerated. Intrathecal neurolysis in the lumbosacral region can be very effective for pain in the pelvic, perineal, rectal, and genital area, especially when it has been refractory to traditional therapeutic options.

A subarachnoid catheter technique has also been reported for use in neurolysis of selective thoracic posterior nerve roots for provision of analgesia in patients with lung cancer and pain [22]. The advantage of the catheter technique is simplicity and avoidance of multiple injections. A 19-G radiopaque catheter was inserted into the subarachnoid space through a 17-G Tuohy needle and was guided fluoroscopically cephalad to the spinal segment where analgesia was desired. After confirming the placement of the subarachnoid catheter, 0.4 ml of alcohol was injected at each level as the catheter was withdrawn slowly. Alcohol was injected at each level to produce the desired effect until a predetermined inferior level to be blocked was achieved.

Epidural Neurolytic Block

Despite the fact that epidural injection and catheter placement is a commonly performed technique, epidural neurolysis has been very disappointing in its results, probably because of

reduced contact of neurolytic agent with the nerve roots due to the dural barrier. The potential for alcohol neuritis and disastrous complications of inadvertent intrathecal injection have made this technique less popular. This technique has been reported as early as 1940 for the treatment of pain due to general carcinomatosis. Nevertheless, there is less risk of bladder and bowel dysfunction with this approach. Solutions can be injected in an incremental fashion daily until the desired effect is obtained. CT scan or MRI should be performed prior to initiation of the procedure to rule out the presence of epidural tumor which could bleed during epidural needle placement. Uncontrolled bleeding, especially with tumor invasion and neovascularization, can lead to epidural or spinal hematoma.

Epidural neurolysis is more useful for midline and bilateral pain, as gravity plays little role in the spread of alcohol and phenol in the epidural space. Epidural administration is more preferable over the subarachnoid technique in patients with extensive topographic distribution of pain. Intracranial spread and meningeal irritation are uncommon. Overnight stay in the hospital may be required to titrate the injection to desired therapeutic effect given the need for multiple injections and titration to desired effect [23]. Use of at least a 20-G epidural catheter is required to allow for the injection of highly viscous phenol solutions in the epidural space. The suggested dosages are 0.5–5.0 ml, starting with the lower dosage. Confirmation of the site of injection and spread of medications with fluoroscopy and radiopaque contrast dye is highly desirable [24]. Fluoroscopy confirmation of the tip should be performed for every additional injection. Butamben has been successfully used via the epidural route for the treatment of both malignant and nonmalignant pain [25].

Although subdural neurolysis has been described in the older literature, particularly in the cervical region, due to technical difficulties and unpredictable distribution of drugs in the space, it is not used.

Efficacy

Patient selection and meticulous procedural technique are essential for the success of neuraxial neurolysis. Often, incomplete analgesia results, and therefore, patients should be informed realistically about reasonable expectations from the procedure. It is difficult to compare results of various studies, as the site of injection, choice of drug, presence and growth of tumor, and definition of pain relief vary between different investigations. The success rate of subarachnoid neurolysis is slightly better with alcohol than of that with phenol, and complications are slightly higher with phenol than with alcohol [11, 15, 26, 27]. Table 25.1 illustrates the complications from two different types of neurolytic agents although there are no randomized studies. Phenol has been reported to give moderate to excellent pain relief in at least 50 % of the patients for at least a month.

Follow-up Care

Follow-up care is essential and obligatory following neuraxial neurolytic blockade. The aim of the post-procedural examination is to assess the efficacy of the block, taper systematically the dosage of systemic analgesic medications, and to address any adverse effects which may have occurred.

Functional pain scores and activity levels should be monitored. It can take up to a week for the patient to sense and appreciate the complete efficacy of the block. Hence, a 1-week follow-up is necessary to determine if there are any unblocked segments and to discuss the requirement of an additional procedure. Systemic opioid dose should be reduced gradually to avoid precipitation of any withdrawal symptoms. A suggested plan would be to reduce the dosage by a quarter to a third every week [28]. This reduction in opioid dosage may help minimize systemic opioid side effects and avoid sedation. This follow-up opportunity may also be utilized to identify adverse effects and institute appropriate rehabilitation as necessary.

Activities of daily living should be measured periodically as well. Frequent evaluation in follow-up also will assist the clinician to determine early the recurrence of pain and allow him/her to intervene in a timely fashion.

Complications

Complications depend upon the site of injection and the neurolytic agent used. Subarachnoid neurolysis is associated with potential major complications such as disability and

Table 25.1 Comparison of reported complications due to intrathecal phenol or intrathecal alcohol

Neurolytic agent	Phenol (n = 704) (%)	Alcohol (n = 704) (%)
Bladder dysfunction	9.0	3.5
Rectal sphincter dysfunction	2.0	0.0
Headache	3.0	0.0
Paresis	12.9	3.9
Dysesthesia	8.0	3.8

Modified from Charlton and Macrae [29]

loss of urinary and fecal continence. However, the majority of the complications are transient. The incidence and duration of complications vary. In a review of complications following subarachnoid neurolysis, Gerbershegan found that 51 % of complications resolved in a week, 21 % in a month, and 9 % in 4 months. However, 18 % of complications persisted even after 4 months [26].

The incidence of permanent paresis/paralysis and bladder dysfunction is 0.8 % each [26, 29]. One large case series reported a complication incidence of 14.3 % with 2.2 % [1] of those complications resulting in irreversible injury [1]. Neurolytic substances injected in the intrathecal space can cause aseptic meningitis. The most concerning event is the spread of the neurolytic agent to structures other than those intended as targets of the neurolytic agent. Neurolysis of sacral parasympathetic roots may cause bowel and bladder dysfunction.

Muscle weakness is more common with lumbosacral neurolysis, as the anterior and posterior nerve roots are in close proximity to each other below the level of L1. The motor dysfunction following neurolysis can be due to three different mechanisms: direct toxicity, arterial thrombosis causing spinal cord infarction, or arterial vasospasm. Direct toxicity can be caused by aberrant spread of neurolytic agent or via direct injection of the agent into the spinal cord [30, 31]. In a case series involving spinal cord injury following use of neurolytic agents, only one patient of 12 developed an injury due to direct toxicity [31]. Thrombosis of posterior spinal arteries causing infarction of the posterior spinal cord has been reported following phenol neurolysis [32]. Permanent paraplegia due to vasospasm of thoracic spinal arteries following alcohol injection has been reported in one case in which the symptoms were delayed by 1 day following the procedure [33]. The above mechanism was similar to that of paraplegia following celiac plexus neurolysis [34–36]. The mechanism of bladder and bowel disturbances is due to interruption of parasympathetic supply from anterior nerve roots of S2, S3, and S4 [29]. However, bladder disturbance has been shown to occur during blockade of thoracic segments as well.

Postdural puncture headache can occur following puncture of the dura by a large bore needle, though the incidence of persistent headache was lower than expected. Patt et al. reported a 6.1 % incidence of PDPHA (5 out of 82) when using ≥22-G needles. Two of these five headaches resolved spontaneously [28]. Epidural abscess, spinal hematoma, and aseptic meningitis are very rare potential complications. Systemic side effects can occur; these include malaise, nausea, headache, and dysesthesia, all of which may persist for as long as 2–3 weeks after the procedure. They occur more commonly with the injection of phenol at multiple levels due to the systemic effects of phenol. The other possible side effect can be loss of touch and position sensation due to involvement of the posterior columns; this sensory hypesthesia can be very disturbing for some patients.

Summary

1. Central neuraxial neurolytic block is a technique of providing analgesia for cancer patients that dates back to the 1930s. It is not frequently utilized for analgesia in the twenty-first century; nonetheless, it is a very effective mode of pain relief in a carefully selected patient population.
2. This procedure would be beneficial and worth considering in patients with a shortened life span, in patients with intractable pain not responding to conventional modes of analgesia, and in patients who have already lost bladder and bowel function or have undergone diversion procedures.
3. Patient selection and informed consent process play major roles in determining the overall success of the procedure.
4. Patients and/or families should be made aware of the limitations of efficacy of the technique and the potential for adverse effects.
5. Selection of appropriate neurolytic agent and proper positioning of the patient during the procedure cannot be emphasized enough.
6. Most of the adverse effects are transient, and the incidence of major adverse events, especially with respect to paralysis, is probably less than 1 %.

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Provocative Discography

26

Irina Melnik, Richard Derby, and Ray M. Baker

Key Points

- Discography is an invasive diagnostic procedure not intended to be an initial screening examination due to associated potential risk to a patient.
- It is a confirmatory test, which can reveal the true source of pain and thus leads to precise and effective treatment as well as might help patients to avoid unnecessary surgical interventions.
- The value of the test is not only in providing morphologic characteristics of the disc structure and degrees of internal annular disc disrupture but also in providing unique clinical information by potentially evoking patients typical/concordant pain and confirming a specific level of the painful disc.
- As a provocative test, discography is liable to false-positive results, which can be potentially avoided by adherence to strict operational standards and interpretation criteria, including pain ≥7/10, pressure <50 psi a.o., concordant pain, ≥ grade 3 annular tear, volume ≤3.5 mL, and the presence of a negative control disc.
- Technical challenges, potential complications, and interpretation mistakes can be avoided with proper selection of patients, including favorable psychological profiling, use of sterile technique, intravenous and intradiscal antibiotics, judicious use of sedation, and good technical training of a practitioner.
- Emerging alternative approaches including anesthetic discography and functional discography are gaining attention, as well as noninvasive MRI spectroscopy and other imaging tests, as an attempt to provide similar clinical information without putting patients at a potential short- or long-term risk.

Introduction

Discography was introduced in the 1940s to diagnose herniation and internal annular disruption of the lumbar and subsequently cervical and thoracic intervertebral discs [1, 2]. While the development of CT and MRI scans unquestionably provide the physician with invaluable information, discography combined with a post-discography CT scan remains the most accurate method of detailing internal annular disruption and disc morphology [3]. Unlike noninvasive imaging tests, pressurizing the disc adds critical information if significant concordant pain is reproduced; and more importantly, a negative response to provocation discography assists in identifying negative discs for which surgery is not recommended. Theoretically, speed- and pressure-controlled injection of contrast media into the disc nucleus stimulates nerve endings via two mechanisms: a chemical stimulus from contact between contrast dye and sensitized nociceptors and a mechanical stimulus resulting from the fluid-distending stress simulating loading [4]. In the outer one-third of the normal disc, dissections and histochemical analysis reveal innervation by branches of the sinuvertebral nerves, the gray rami communicantes, and the ventral rami [5–8] which contain well-characterized nociceptive nerve fiber peptides such as substance P, VIP (vasoactive intestinal peptide), and CGRP (calcitonin-gene-related peptide) [9–11]. Distinct from normally aging discs, "pathologically painful"

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discs show a process of neo-innervation extending along annular fissures as well as to the inner annulus and nucleus pulposus which likely explains the pain of provocation discography [12–14].

Conceptually, provocation discography is an extension of the clinical examination, tantamount to palpating for tenderness [15]. In addition, post-discography CT findings suggest a firm correlation between a degree of a demonstrable annular disruption and reproduction of pain by disc stimulation [16, 17]. In a study by Vanharanta et al. greater than 75 % of painful discs on provocative discography (PD) had a grade 3 or greater annular tear. Provocation discography is particularly useful in challenging or inconclusive cases unresolved by MRI or myelography, such as in post-discectomy discs or recurrent disc herniations [18].

Provocative discography is an invasive diagnostic test, not intended to be an initial screening examination. Over the past decade, there have been debates challenging the validity and accuracy of discography, its long-term safety, and a need for alternative approaches such as functional anesthetic discography or innovative noninvasive biochemical imaging tests [19]. In this chapter, we discuss indications for provocative discography, technical considerations, and procedural descriptions as well as potential complications and future directions.

Indications and Contraindications

According to the position statement on discography by the North American Spine Society [3]:

> Discography is indicated in the evaluation of patients with unremitting spinal pain, with or without extremity pain, of greater than 4 months' duration, when the pain has been unresponsive to all appropriate methods of conservative therapy. Before discography, the patients should have undergone investigation with other modalities which have failed to explain the source of pain; such modalities should include, but not be limited to, either computed tomography (CT) scanning, magnetic resonance imaging (MRI) scanning and/or myelography.

The single purpose of discography is to obtain useful clinical information. The test endeavors to confirm or refute the hypothesis that a particular disc is a source of patient's familiar or accustomed pain. Since it is a provocation test, disc stimulation is liable to false-positive results; however, a recent meta-analysis of asymptomatic subjects demonstrated that a false-positive rate of less than 10 % can be obtained [20] if the discographer adheres to ISIS/IASP operational standards and interpretation criteria: pain ≥7/10, pressure <50 psi a.o., concordant pain, ≥ grade 3 annular tear, volume ≤3.5 mL, and the presence of a negative control disc [21, 22].

Since abnormal disc morphology alone is not diagnostic, as shown on CT and MRI scans of subjects asymptomatic of low back pain [23], the prime indication for discography is to help to distinguish which disc is symptomatic. A parallel application is to identify asymptomatic discs. When a single disc is found to be symptomatic in the presence of adjacent asymptomatic discs, focused surgical therapy can be entertained. Patients with symptomatic or abnormal discs at multiple levels constitute a greater surgical challenge. Identification of asymptomatic discs which do not require intervention is also clinically invaluable.

Indications and Inclusion Criteria

- Failed conservative treatment for low back pain of probable spinal origin.
- Ongoing pain for greater than 4 months.
- Other common pain generators have been ruled out (e.g., facets, sacroiliac joints).
- Symptoms are clinically consistent with disc pain.
- Symptoms are severe enough to consider surgery or percutaneous interventions.
- Surgery is planned and the surgeon desires an assessment of the adjacent disc levels.
- The patient is capable of understanding the nature of the technique and can participate in the subjective interpretation.
- Both the patient and physician need to know the source of pain to guide further treatments.

Contraindications

- Unable or unwilling to consent to the procedure or to cooperate
- Inability to assess patient response during the procedure
- Coagulopathy (INR > 1.5 or platelets < 50,000/mm)
- Known localized or systemic infection
- Pregnancy (to prevent fetal radiation exposure)

Relative Contraindications to Discography

- Allergy to contrast medium, antibiotics, or local anesthetics
- Congenital, postsurgical, and anatomical derangements or psychological problems that can compromise safety and success of the procedure (including spinal cord compression and myelopathy in case of cervical and thoracic procedures)

Preprocedural Evaluation and Patient Preparation

Preprocedural Evaluation

A thorough patient evaluation as well as patient education about the nature of the procedure is critical to ensure optimal performance and the utility of the test. The evaluation should include history, physical examination, previous medical conditions, prior surgeries, medications, and allergies. Information about pain is recorded, including onset of symptoms, nature, frequency, and distribution of pain as well as its intensity in 0–10 pain scale. In most cases of lumbar discography and all cases of thoracic and cervical discography, an MRI or CT scan should be reviewed prior to discography. Furthermore, since false-positive rates may increase with severe somatization disorder, psychometric testing should be included such as DRAM (Distress and Risk Assessment Method) [24]. Prior to the procedure, patients have to understand the importance of reporting and recognizing whether the test reproduces their usual or so-called concordant pain and be able to distinguish this pain from other pain. Concordant pain is necessary to determine a positive response. For this reason, it is advisable to have a trained observer independently monitor patient pain responses while the operator concentrates on the technical aspects of the procedure.

Patient Preparation

Since the disc is a relatively avascular structure, there is an increased risk of discitis – a rare but serious potential complication of the discography procedure. The most common pathogens are *Escherichia coli*, *Staphylococcus aureus*, or *Staphylococcus epidermidis*. Intravenous (IV) antibiotic prophylaxis should be administered within 15–60 min before the procedure using cephazolin 1 g, gentamicin 80 mg, or ciprofloxacin 400 mg. For patients allergic to penicillin, clindamycin 900 mg is a possible alternative [25–27]. In addition, many discographers add 2–6 mg/mL of a cephalosporin antibiotic to the nonionic contrast solution [28]. The procedure should be performed under sterile conditions with double gloves. It is recommended to handle and touch any needle only with sterile gauze or instruments, not a gloved hand. Many injectionists scrub, gown, and glove as for an open surgical procedure. The C-arm image intensifier should also be draped.

As a provocative test, discography is at best uncomfortable and at worst very painful. For this reason, it is recommended that patients be judiciously sedated to manage anxiety, opiate withdrawal, and possible extraneous pain related to disc access. Patient response should be monitored with dosages titrated to establish a level of sedation permitting the patient to be conversant and responsive after needle placement. Short acting sedatives or analgesics are recommended, such as midazolam and fentanyl.

Technique of Lumbar Discography

Patient Position

Most lumbar discs can be safely and readily accessed using a postero-oblique, extrapedicular approach when patient lies in a prone oblique position on a fluoroscopy table. This technique, which has been described by Trosier [29] and modified by Aprill [30], prevents the potential complications associated with thecal puncture from a transdural approach [31]. Elevating the target side approximately 15° allows the fluoroscopy tube to remain in a more AP projection and reduces radiation scatter. If needed, a folded towel or soft wedge can be placed under the patient's flank to prevent side bending of the lumbar spine. A pillow or bolster can be placed under the patient's abdomen to slightly flex the spine and decrease the lumbar lordosis. Monitoring and light sedation are initiated. On the side selected for puncture, a wide area of the skin of the back is prepped and draped from the costal margin to the mid-buttock and from the midline to the flank. The puncture side should be opposite the patient's dominant pain to eliminate confusion between pain reproduced during contrast injection and the pain of penetrating the outer annulus fibrosus.

Disc Puncture

Prior to injection, a fluoroscopic examination of the spine is performed to confirm segmentation and to determine the appropriate level for needle placement. Using AP view, the beam should be parallel to the inferior vertebral endplate. After selecting the target disc using AP view, the fluoroscopic beam is axially rotated until the facet joint space is located midway between the anterior and posterior vertebral margins. In this view, the insertion point is 1 mm lateral to the lateral aspect of the superior articular process (SAP) and allows needles to be advanced parallel to the beam (Fig. 26.1).

Prior to needle placement, a skin wheal is made with lidocaine 1 % (~1 cc) using a 25-gauge 1.5-in. needle. To anesthetize the needle track, one can use a 25-gauge 3.5-in. needle advanced under to the level of the SAP. Excessive use of local anesthetic may obscure nerve root impairment and could potentially anesthetize the sinuvertebral and ramus

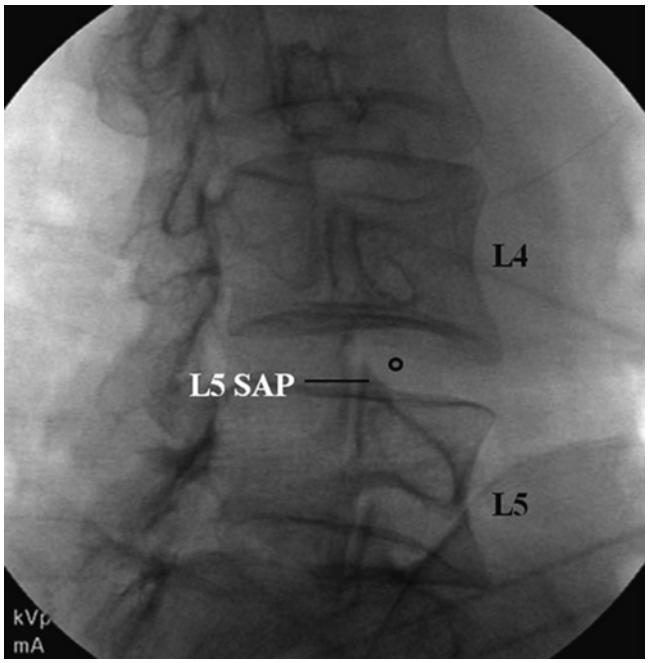

Fig. 26.1 In this view, the insertion point is 1 mm lateral to the lateral aspect of the superior articular process (*SAP*) and allows needles to be advanced parallel to the beam

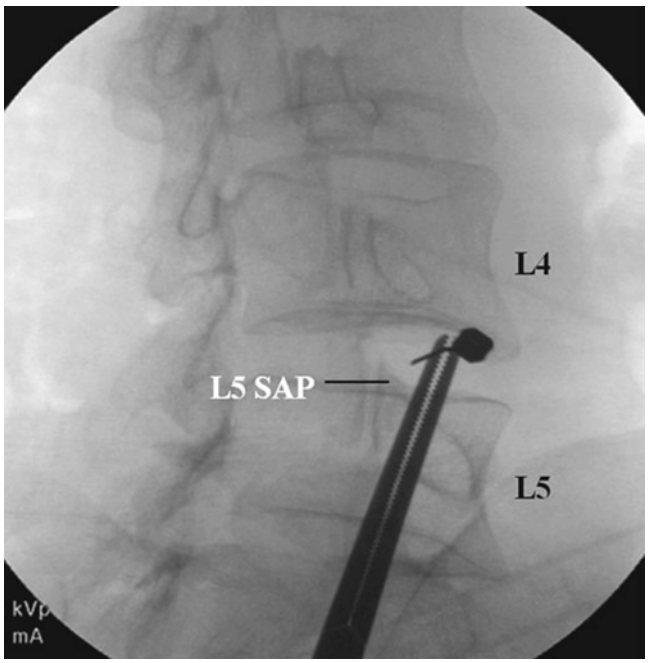

Fig. 26.2 The introducer needle is advanced parallel to the fluoroscopic beam using an oblique fluoroscope view

communicans nerves, thus altering the evoked pain response during disc stimulation and creating a false-negative response. A single- or double-needle technique may be used; however, both the North American Spine Society and the International Spinal Injection Society recommend a double-needle approach due to lower risk of disc infection (although single-needle techniques have proved adequate and safe since the use of prophylactic antibiotics) [3, 25, 32].

Puncture of L1–L5 Intervertebral Discs

In the double-needle technique, a styletted 25-gauge, 6-in. needle is placed into each disc through a 20-gauge 3.5-in. introducer needle under fluoroscopic guidance. To protect the discographer's hand from radiation exposure, forceps may be used to grasp the introducing needle. The introducer needle is advanced parallel to the fluoroscopic beam using an oblique fluoroscope view (Fig. 26.2). If bony obstruction is encountered, the physician must confirm whether the needle has contacted the SAP or the vertebral body. If necessary, the needle may be slightly withdrawn and its trajectory modified. The introducer needle can be either advanced just over the lateral edge of the SAP or advanced to the margin of the disc. After confirming introducer needle position with a lateral view, a 25-gauge, 6-in. discogram needle is slowly advanced into the center of the disc through the introducer needle while monitoring the lateral view. A slight bend placed on the end of the discogram needle facilitates navigation. When the needle contacts the disc, position should be checked using AP and lateral views, with the ideal positioning of the needle on the line between midpoint of pedicles on AP view and posterior vertebral margin on lateral view (Fig. 26.3a, b).

Contact with the annulus fibrosus is characterized by the perception of firm resistance and frequently the patient experiencing a momentary sharp or sudden aching sensation in the back or the buttock. The needle is then advanced to the center of the disc. This requires confirmation both in AP and lateral views (Fig. 26.4a, b). If the needle tip is in the midline of the disc on the AP view but anterior on the lateral view, the needle entered the disc too far laterally. If the needle tip is centered on the AP view but posterior on the lateral image, the needle entered the disc too far medially.

Puncture of L5-S1 Intervertebral Disc

Disc access at the L5-S1 interspace can be more challenging because of an overlying iliac crest and broader interfacetal distance at that level. In this case, a curved, double-needle technique is recommended. The fluoroscopy tube is rotated only far enough to bring the facet joint space approximately 25 % of the distance between the anterior and posterior vertebral margins. The introducer needle is inserted between the S1 SAP and the iliac crest (Fig. 26.5). The discography needle is advanced under direct fluoroscopic vision, while the introducer needle is simultaneously retracted slightly.

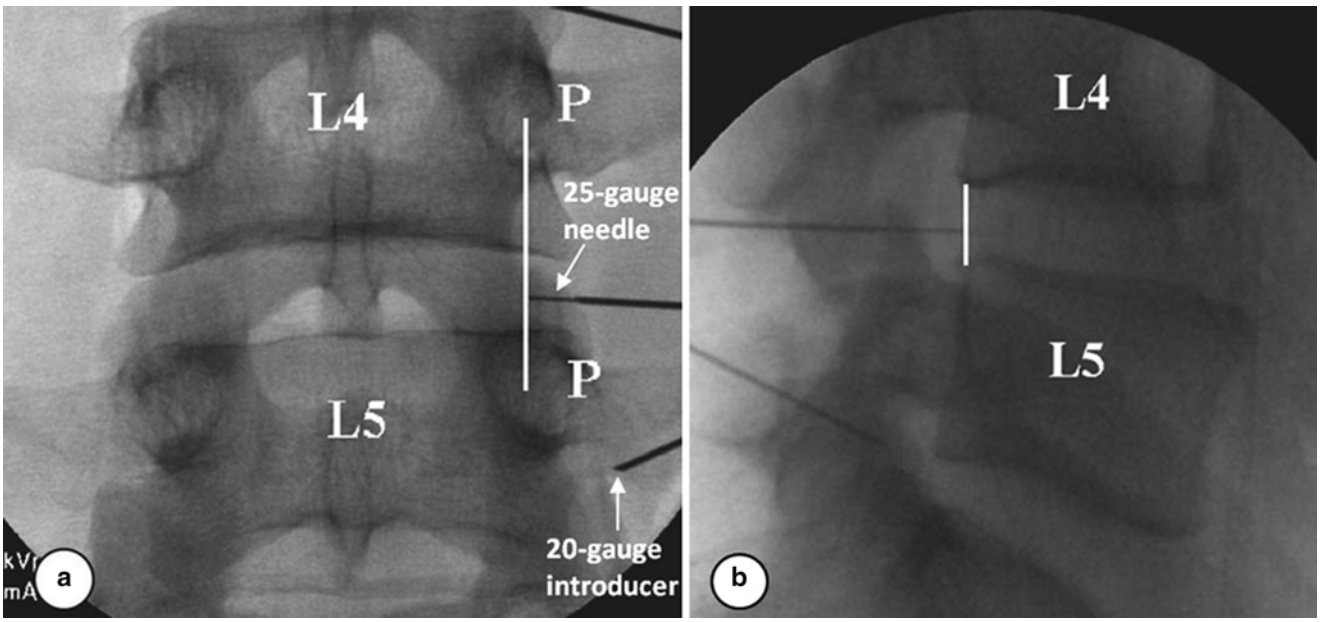

Fig. 26.3 (**a**, **b**) When the needle contacts the disc, position should be checked using AP and lateral views, with the ideal positioning of the needle on the line between midpoint of pedicles on AP view and posterior vertebral margin on lateral view

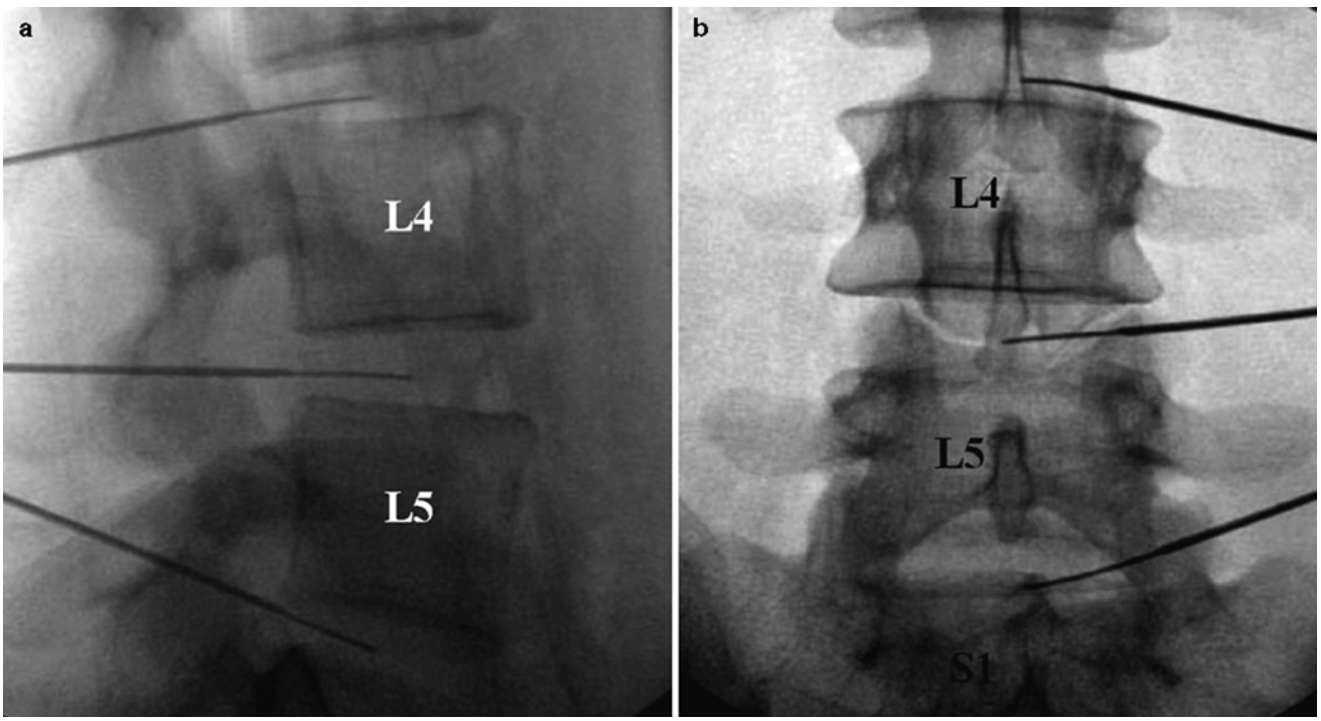

Fig. 26.4 (**a**, **b**) Contact with the annulus fibrosus is characterized by the perception of firm resistance and frequently the patient experiencing a momentary sharp or sudden aching sensation in the back or the buttock. The needle is then advanced to the center of the disc. This requires confirmation both in AP and lateral views

This unsheathes the discography needle, which should be turned so that the curve or bend bows the introducer needle in a medial and posterior direction through the "safe triangle." If the needle fails to track medially and posteriorly, it will not pass toward the center of the disc and may strike the ventral ramus, in which case the needle should be removed and its curvature accentuated. If the needle is blocked by the SAP, the inner needle is retracted into the introducer needle, and the pair is advanced to the lateral edge of the S1 SAP. The inner discography needle may then be directed toward

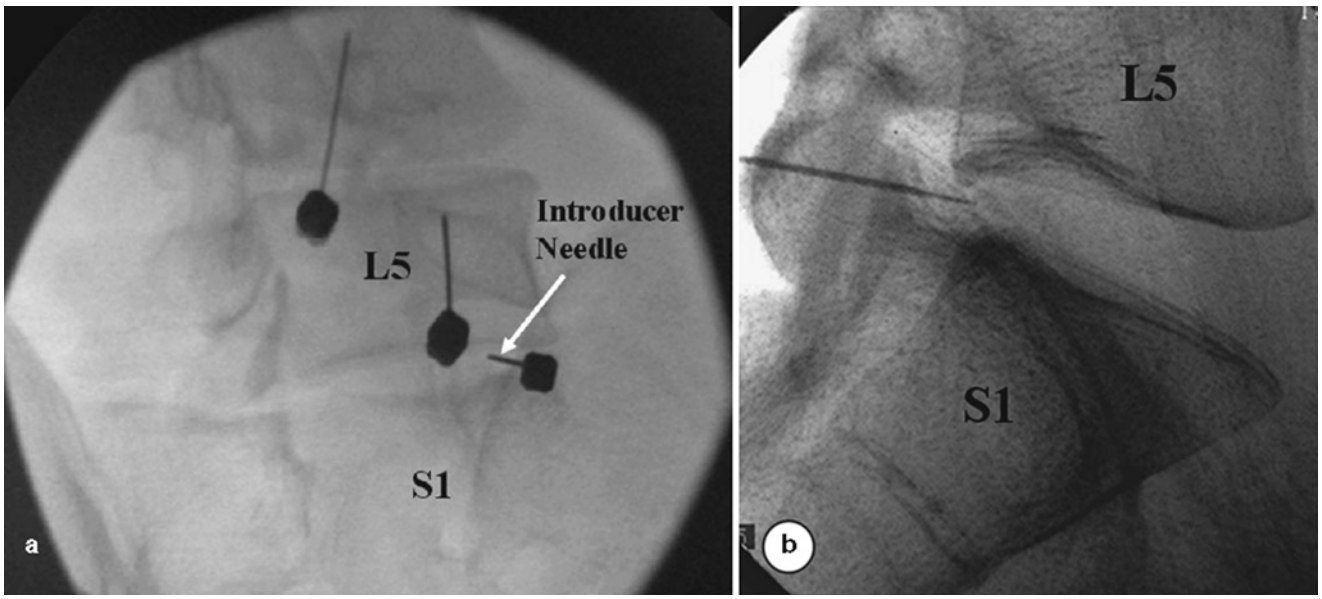

Fig. 26.5 (**a**, **b**) The fluoroscopy tube is rotated only far enough to bring the facet joint space approximately 25 % of the distance between the anterior and posterior vertebral margins. The introducer needle is inserted between the S1 SAP and the iliac crest

the center of the disc. Ideally, the needle should be within 4–5 mm of the center on AP and lateral fluoroscopy (Fig. 26.6a, b).

Provocation Using Pressure Manometry

Provocation

Once the needle tip is in the center of nucleus pulposus, nonionic contrast medium mixed with antibiotic is injected into each disc at slow velocity, using preferably a controlled injection syringe with digital pressure readout. The disc is slowly pressurized by injecting 0.5 mL increments through a syringe attached to a pressure measuring device, while recording the opening pressure, the injection pressure, the location of contrast medium, and any pain response evoked. Injection continues until one of the following end points is reached: pain response ≥7/10, intradiscal pressure >50 psi a.o. above opening in a disc with a grade 3 annular tear or 80–100 psi a.o. with a normal-appearing nucleogram, or a total of 3.5 mL of contrast has been injected. Typical opening pressures are 5–25 psi a.o., depending on the degree of nuclear degeneration; if it exceeds 30 psi a.o., this usually indicates that the needle tip is lodged within the inner annulus and needs to be repositioned.

Imaging

AP and lateral images of all injected discs are saved as part of the permanent record. A variety of fluoroscopic patterns may occur in abnormal discs: cotton ball, lobular, irregular, fissured, and ruptured (Fig. 26.7a) [33]. The appearance of the normal nucleus following the injection of contrast medium is classic: the contrast medium assumes either a lobular pattern or a bilobed "hamburger" pattern (Fig. 26.7b). Contrast medium may extend into radial fissures of various lengths but remain contained within the disc (Figs. 26.7 and 26.8). Contrast may escape into the epidural spaces through a torn annulus or through a defect in the vertebral end plate [34]. In other cases, the disc can look completely fissured and disrupted. However, none of these patterns alone are indicative of whether the disc is painful; that can be ascertained only by the patient's subjective response to disc injection.

Post-discography axial CT scanning provides the most accurate depiction of internal disc architecture. The location of degeneration is described by dividing the disc into four quadrants [17]. If the contrast is confined to the nucleus, then no quadrant disruption is present; if the contrast is dispersed, then its location is described (e.g., single quadrant disruption, right posterior; two-quadrant disruption, left anterolateral and right posterior, etc.). The degree of radial and annular

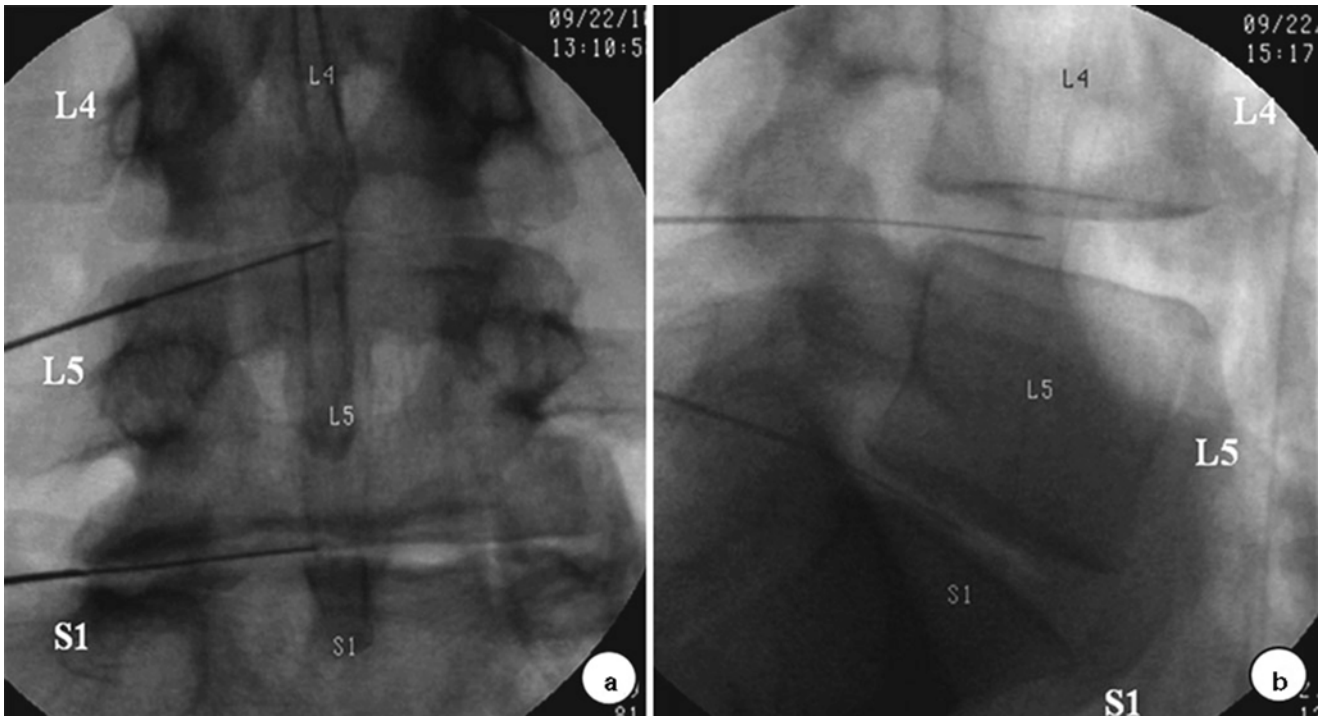

Fig. 26.6 (**a**, **b**) The inner needle may then be directed toward the center of the disc. Ideally, the needle should be within 4–5 mm of the center on AP and lateral fluoroscopy

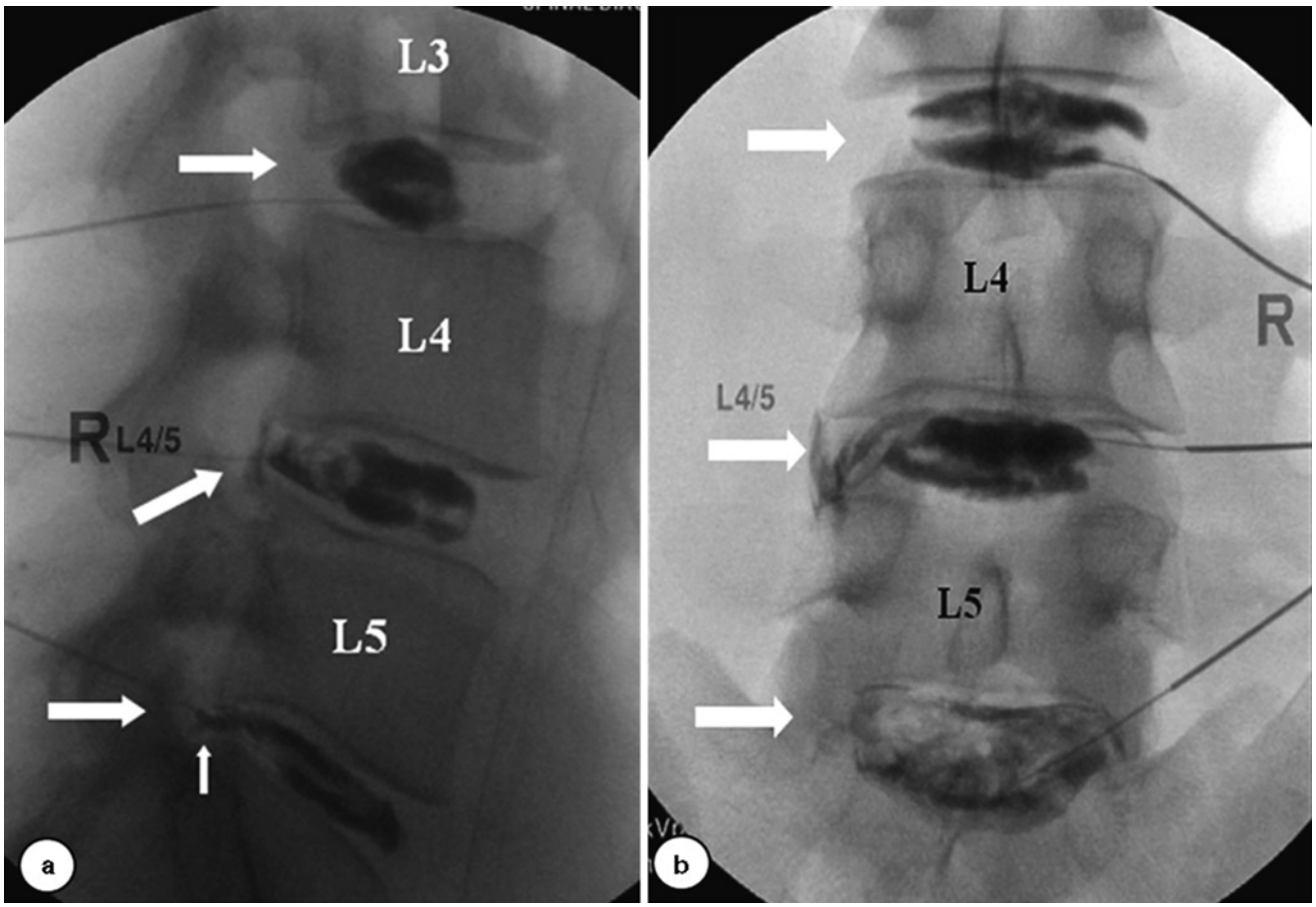

Fig. 26.7 (**a**) A variety of fluoroscopic patterns may occur in abnormal discs: cotton ball, lobular, irregular, fissured, and ruptured. (**b**) The appearance of the normal nucleus following the injection of contrast medium is classic: the contrast medium assumes a either a lobular pattern or a bilobed "hamburger" pattern

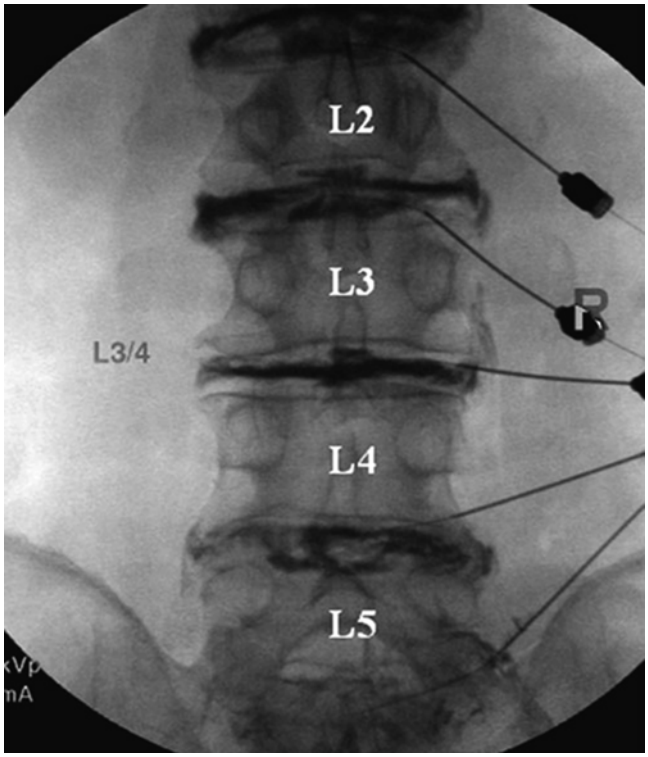

Fig. 26.8 Contrast medium may extend into radial fissures of various degrees

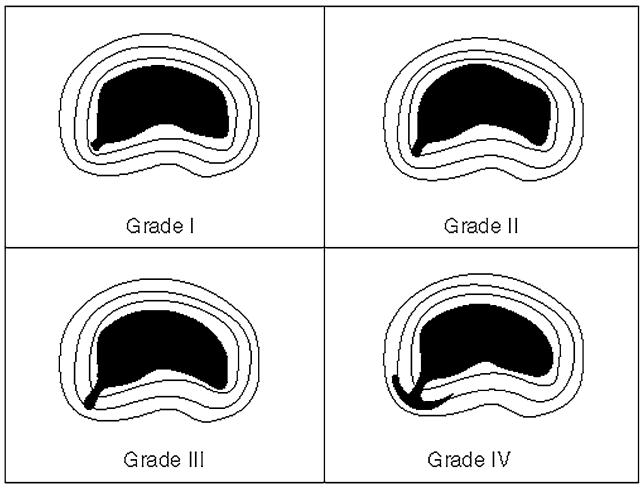

Fig. 26.9 The degree of radial and annular disruption is most commonly described [17, 35] using the modified Dallas discogram scale

disruption is most commonly described [17, 35] using the modified Dallas discogram scale (Fig. 26.9) [32, 35–37]. Grade 0 describes contrast contained within the nucleus; grades 1–3 describe degree of fissuring extending to the inner, middle, and outer annulus, respectively; grade 4 describes a grade 3 annular fissure with a greater than 30° circumferential arc of contrast. A grade 5 annular tear indicates rupture or spread of contrast beyond the outer annulus (Fig. 26.8).

Interpretation

Discography is a provocational test which attempts to mimic physiologic disc loads and evoke the patient's pain by increasing intradiscal pressure with an injection of contrast medium. Increased intradiscal pressure is thought to stimulate annular nerve endings, sensitized nociceptors, and/or pathologically innervated annular fissures. The intensity of the provocation stimulus must be carefully controlled through the skilled operation of a manometer syringe or an automated manometer, permitting more precise comparisons between patient discs and between discographers. Most abnormal discs will be painful between 15 and 50 psi a.o. [38] and are termed "mechanically sensitive" based on a four-type classification introduced in the 1990s by Derby et al. in respect to annular sensitivity [39]. Discs which are painful at pressures <15 psi a.o. are termed low-pressure positive or "chemically sensitive" discs [39]; if discs are painful between 15 and 50 psi a.o., they are termed "mechanically sensitive" discs. Indeterminate discs are painful between 51 and 90 psi a.o., and normal discs are not painful on provocation. An operator using manual "thumb" disc pressurization to 100 psi a.o. reported to have higher false-positive rate in asymptomatic subjects than other operators [24, 40]. If a disc is painful at >50 psi a.o., the response must be reported as indeterminate, because it is difficult to distinguish between a pathologically painful disc and the pain evoked from simply mechanically stimulating a normal or subclinically symptomatic disc. To limit false-positive responses, the most up-to-date discography standards are set at a pressure criteria of <50 psi a.o. to define a positive response [32, 41].

Injection speed is also a confounding factor and may account for inter-operator variability in results and increased false-positive responses. At high injection speeds, the true intradiscal pressure (dynamic pressure) is higher than the recorded static pressure [42]. The dynamic pressure, measured only in research settings, is the actual pressure which would be recorded with an intradiscal pressure sensor. Currently, the pressure is measured indirectly via a manometric syringe which records plateau static pressures, post-injection. The pain during activities of daily living is more closely correlated to dynamic peak pressure [39]. Static pressure is reflective of dynamic pressure when recorded by needle sensor and manometer only at slower injection speeds (<0.08 mL/s) [42].

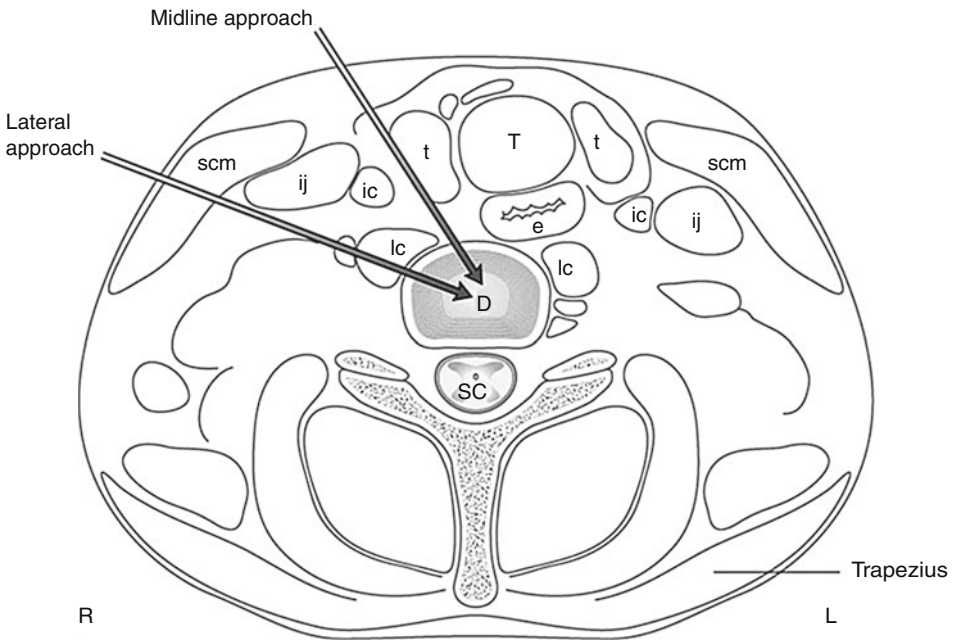

Fig. 26.10 Pressure is applied with the index finger to the space between the trachea and the medial boarder of the sternocleidomastoid

Pain assessment during the disc provocation is the most important information obtained from discography. If the patient's pain intensity, location, and character are similar to or the same as the patient's clinical symptoms, the criteria for concordant pain are satisfied. A true positive pain response is ≥7/10, sustained for greater than 30–60 s; true discogenic pain is less likely to decrease rapidly. Pain which resolves within 10 s should be discounted. It is recommended to confirm all positive responses with manual repressurization with a small volume. If repressurization does not provoke concordant ≥7/10 pain at <50 psi a.o., then the response is considered indeterminate. Clinically, patients with discogenic pain tend to have increased pain postoperatively and an exacerbation of symptoms lasting 2–7 days.

Technique of Cervical Discography

Patient Position

The patient is placed supine on the fluoroscopy table with a cushion placed under his or her shoulders to slightly hyperextend the neck, which may help to improve a disc access. While the side to be punctured in lumbar discography is that opposite the patient's dominant pain, a right-sided approach is used for cervical discography because the esophagus lies to the left in the lower neck. The patient's neck is prepared and draped in a sterile fashion.

Disc Puncture

Midline Approach

The disc level to be studied is identified on the AP view of fluoroscopy. The tube is rotated in a cephalad-caudal direction to bring the end plates parallel to the beam. Pressure is applied with the index finger to the space between the trachea and the medial boarder of the sternocleidomastoid muscle (Fig. 26.10). Firm but gentle pressure will displace the great vessels laterally and the laryngeal structures and trachea medially. Below C4, the right common carotid artery and the internal carotid artery above C4 are palpated. The fingers are insinuated until they encounter the anterior surface of the vertebral column. Since the carotid artery is manually displaced to allow safe needle passage into the disc, and the carotid body may be compressed, administration of IV atropine is therefore suggested to minimize the possibility of vasovagal response [43, 44]. The needle entry point should be medial to the medial border of the sternocleidomastoid muscle, thus avoiding the pharynx superiorly and the apex of the lungs inferiorly. A shorter 25-gauge 2.5-in. needle is recommended for easier and safer handling. With the point of the needle just medial to or under the index finger, both the needle and the index finger can be moved in unison. The trachea is pushed medially by the fingernail of the index finger, and when the needle overlies the disc at 20–40° angle, the needle is introduced through the skin directed toward the anterior lateral aspect of the disc (Fig. 26.11).

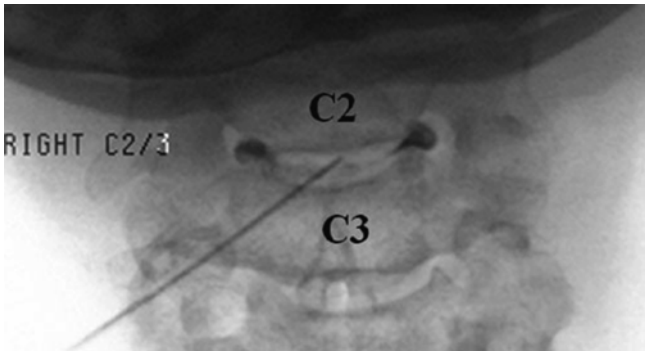

Fig. 26.11 The trachea is pushed medially by the fingernail of the index finger, and when the needle overlies the disc at 20–40° angle, the needle is introduced through the skin directed toward the anterior lateral aspect of the disc

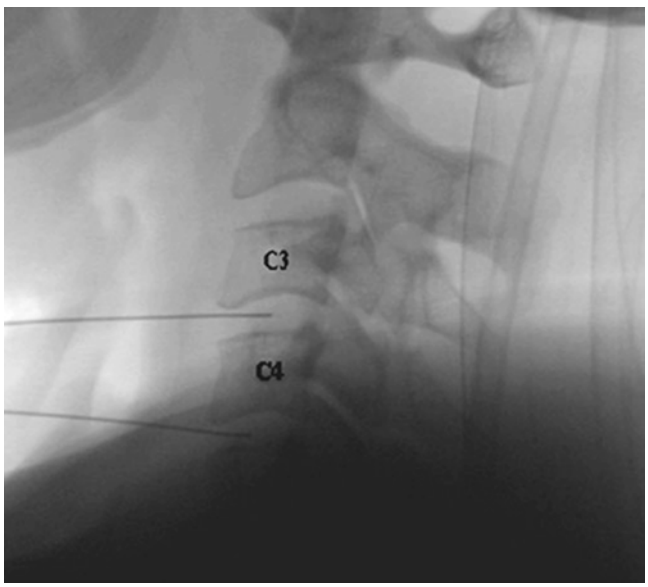

Fig. 26.12 Once the needle is passed several millimeters into the disc, the lateral view is used to guide further advancement, taking precaution to not pass the needle through the disc and into the epidural space or spinal cord

Once the needle is passed several millimeters into the disc, the lateral view is recommended to guide further advancement, taking precaution to not pass the needle through the disc and into the epidural space or spinal cord (Fig. 26.12). In order to gauge the depth of penetration, the needle may be directed to and touch the anterior disc body just above or below the disc margin before the insertion into the center of the disc.

Lateral Approach

In this approach, after aligning the vertebral end plates of the target level, the fluoroscopic beam is axially rotated until the anterior margin of the uncinate process is moved approximately one-quarter of the distance between the anterior and posterior lateral vertebral margins. In this view, the target insertion point is 1–2 mm medial to the anterior margin of the uncinate process (Fig. 26.13). The skin entry point will be over the lateral neck muscles and posterior to the great vessels or trachea. Pressure displacement of the great vessels is difficult and usually not done. This region is highly vascular, and patients have to be observed for signs of hematoma. Before and during the injection of contrast, the needle position within the center of a disc and a spread of contrast material inside the disc have to be confirmed with both AP and lateral fluoroscopic images (Fig. 26.14a, b). At C7-T1, the medial approach is preferred to avoid puncturing the apex of the lung.

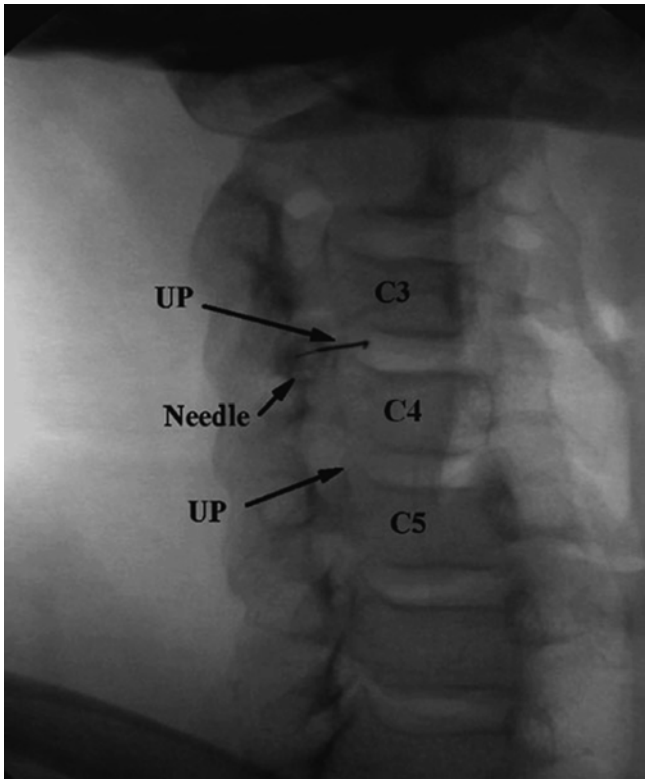

Fig. 26.13 In this approach, after aligning the vertebral end plates of the target level, the fluoroscopic beam is axially rotated until the anterior margin of the uncinate process (*UP*) is moved approximately one quarter of the distance between the anterior and posterior lateral vertebral margins. In this view, the target insertion point is 1–2 mm medial to the anterior margin of the uncinate process (*UP*)

Provocation and Interpretation

The clinical utility of provocative discography for solving puzzling presentations of atypical pain resulting from cervical discogenic lesions has been demonstrated. In a systematic review of the literature, Manchikanti showed a significant role for cervical discography in selecting surgical candidates and improving surgical outcomes, when strict criteria requiring a concordantly painful disc and two negative controlled discs, one above and one below the affected level, are utilized [45].

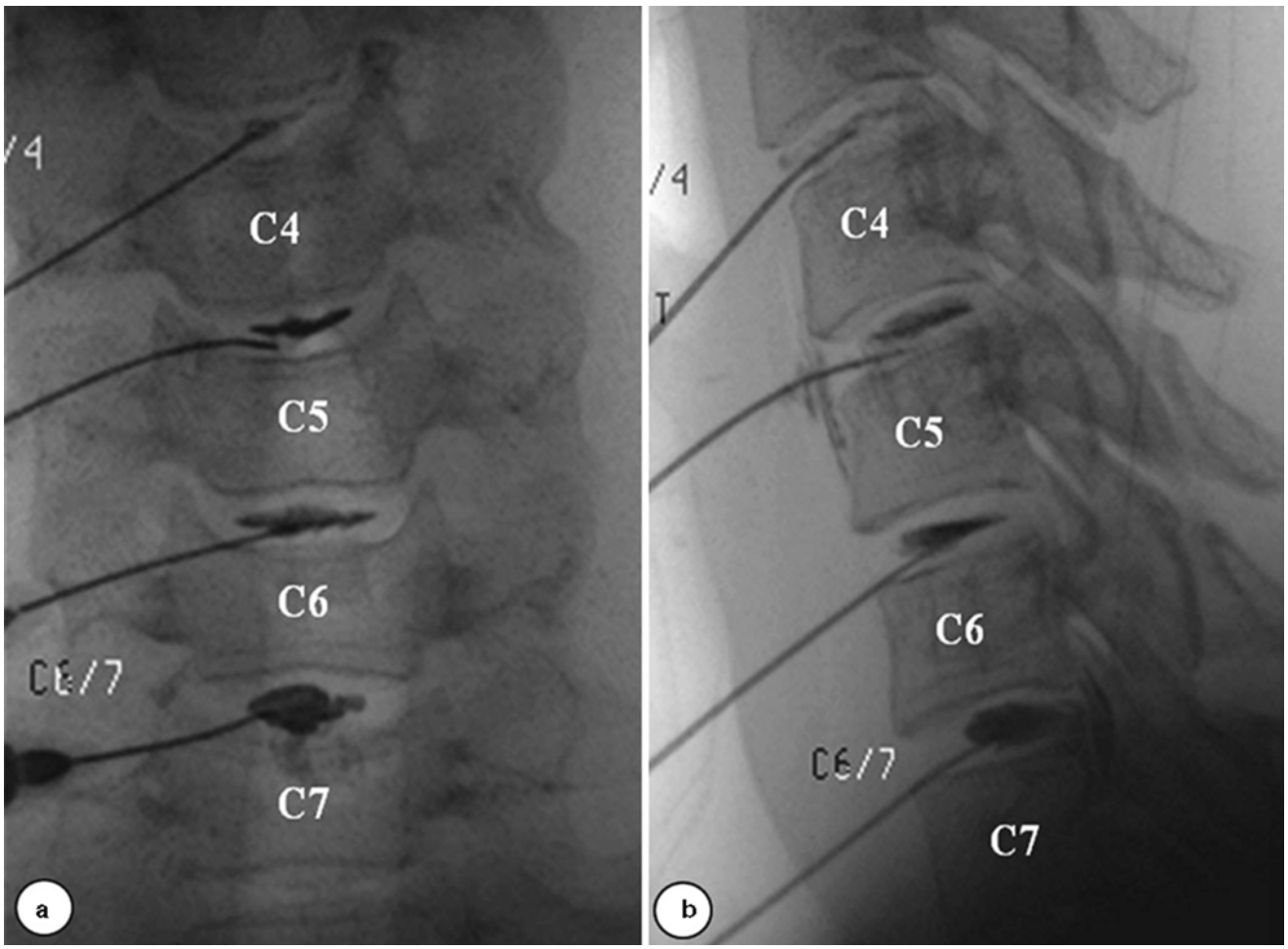

Fig. 26.14 (**a**, **b**) Before and during the injection of contrast, the needle position within the center of a disc and a spread of contrast material inside the disc have to be confirmed with both AP and lateral fluoroscopic images

Normal cervical discs hold only 0.25–0.5 mL of fluid, and intradiscal injection of normal discs should not be painful. Schell et al. demonstrated an average pain response during disc stimulation in asymptomatic subjects as 2.2/10, whereas it was 5.2/10 in patients with neck pain. He showed that MRI cannot reliably identify the sources of neck pain and provocative discography results had better correlation between cervical discogenic pain and annular disc disruption compared to MRI [46, 47]. A 1–3-mL syringe with contrast media is attached to the needle. Manual syringe pressure is increased slowly until the intrinsic disc pressure is exceeded. Concordancy and pain intensity are recorded at 0.2 mL increments. A positive response requires provocation of significant (>6–7/10) concordant pain during a confirmatory repeat injection of another 0.1–0.2 mL of contrast. Without an asymptomatic "control" disc, there is no evidence that the patient can discriminate between symptomatic and asymptomatic discs, especially in case of multiple concordant pain levels. It is observed that pressurization of the cervical discs will often cause separation of the end plates, and this movement may cause pain secondary to a symptomatic z-joint. It is recommended to rule out z-joint pain following an analgesic block protocol before performing cervical discography [48].

Technique of Thoracic Discography

Patient Positioning

The patient lies prone on the fluoroscopy table. Skin is prepared and draped in a sterile fashion. As a rule, the side to be punctured is that opposite the patient's dominant pain.

Disc Puncture

The current standard technique of thoracic discography was described by Schellhas et al. in 1994 [49]. After the selection of the target disc on AP view and the alignment of vertebral endplates, the fluoroscopic beam is then rotated ipsilaterally

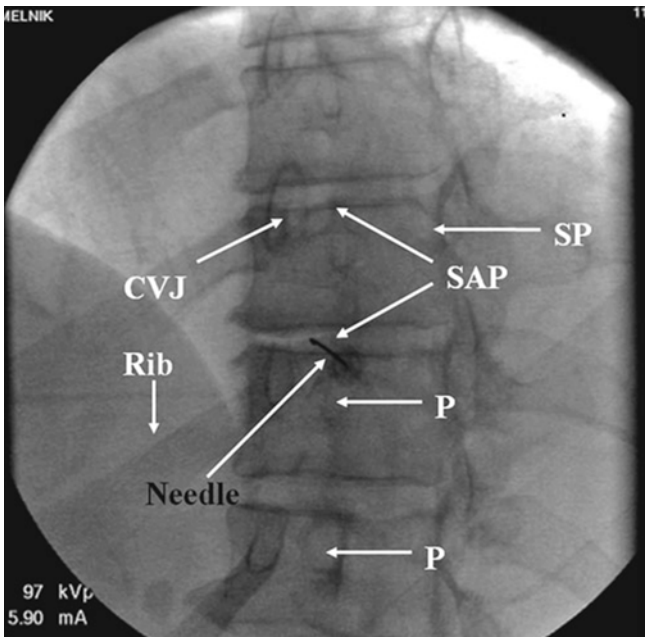

Fig. 26.15 Typically, this degree of ipsilateral rotation will superimpose the tip of the spinous process on the edge of the contralateral vertebral body. In this view, the insertion point is just lateral to the interpedicular line (P-pedicle) and approximately 3 cm lateral to the spinous process at the opening between the superior articular process (SAP) and the costovertebral joints (CVJ)

until the corner of the intervertebral disc space is visualized between the superior articular process (SAP) and the costovertebral joint (CVJ). Typically, this degree of ipsilateral rotation will superimpose the tip of the spinous process (SP) on the edge of the contralateral vertebral body. In this view, the insertion point is just lateral to the interpedicular line (Fig. 26.15) and approximately 3 cm lateral to the spinous process. Most discographers prefer a single-needle technique using 23–25-gauge, 3.5-in. needle. A slight bend placed on the end of the needle will facilitate changing directions by needle rotation. The trajectory of the needle is roughly parallel and behind the rib as it passes anterior to attach to the spine at the costovertebral joints. Aiming point is a round to square section of the posterior lateral disc that can be seen through a 1–3-mm opening between the SAP and the rib (Fig. 26.15). The needle should be advanced in short increments and the direction changed as necessary by needle rotation. If one stays medial to the costovertebral junction and just lateral to the SAP, there is no chance of penetrating the lung. It may be hard to visualize thoracic SAP; however, it always projects above the pedicle, which is easily visualized. Although passage of the needle behind the rib is usually uneventful, passage of the needle between the rib and SAP might be difficult due to the small aperture, requiring correctional rotations of the bent needle. Once the needle has passed anterior to the SAP using lateral fluoroscopic view, the needle bend is turned posteriorly to facilitate advancing the needle in a more posterior direction (Fig. 26.16a, b).

Provocation and Interpretation

Nonionic contrast medium is slowly injected into each disc in 0.2–0.3 mL increments under direct fluoroscopic observation, while recording pain response, including behavior, pain intensity, and concordance as well as morphologic abnormalities such as grade 1–3 annular tears or end plate defects. The normal thoracic nucleus usually looks like either a diffuse, elongated homogenous or lobulated pattern (Fig. 26.17). The end point is reached if the pain is >6/10, intradiscal pressure reaches a firm end point, or a total of 2.5 mL of contrast has been injected. CT-discography is often performed to define the exact location and size of annular fissures and protrusions. The most important information obtained is if there is a presence of concordant pain with evoked pain intensity >6/10 in the presence of at least one negative control disc.

Postprocedural Care

After the procedure, patients are taken to the recovery room for vital signs and clinical status monitoring by nurses trained in spine injection management. The patient is checked immediately and 30 min postprocedure for any subcutaneous bleeding. Analgesic medications (oral, IV, or IM) are provided as needed. The patient is advised that he or she may experience an exacerbation of typical symptoms for 2–7 days and may experience postprocedure discomfort, including difficulty swallowing after cervical discography and lingering back pain after lumbar discography. The patient is instructed to contact the office if he or she develops fever, chills, or severe (or delayed) onset of pain. Patients are observed and discharged according to institutional protocol. Typically, the patient is discharged to the care of a responsible adult and instructed not to drive for the remainder of the day. Patients are contacted by phone 2–4 days postprocedure to screen for possible complications or adverse side effects.

Potential Risk and Complications

Lumbar Discography

Complications can result from the disc puncture itself, misadventures during needle placement, or medications used during the procedure. Complications vary from minor (e.g., increased low back pain, nausea, headache) to major

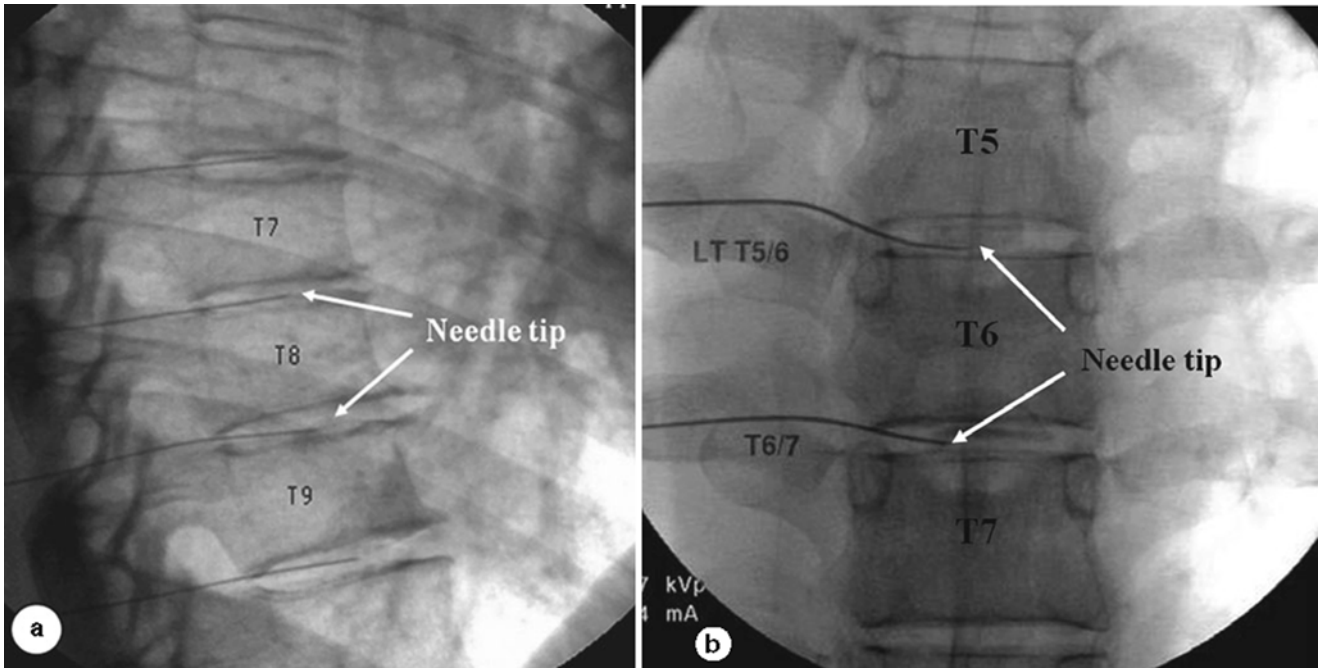

Fig. 26.16 (**a**, **b**) Once the needle has passed anterior to the SAP using lateral fluoroscopic view, the needle bend is turned posteriorly to facilitate advancing the needle in a more posterior direction

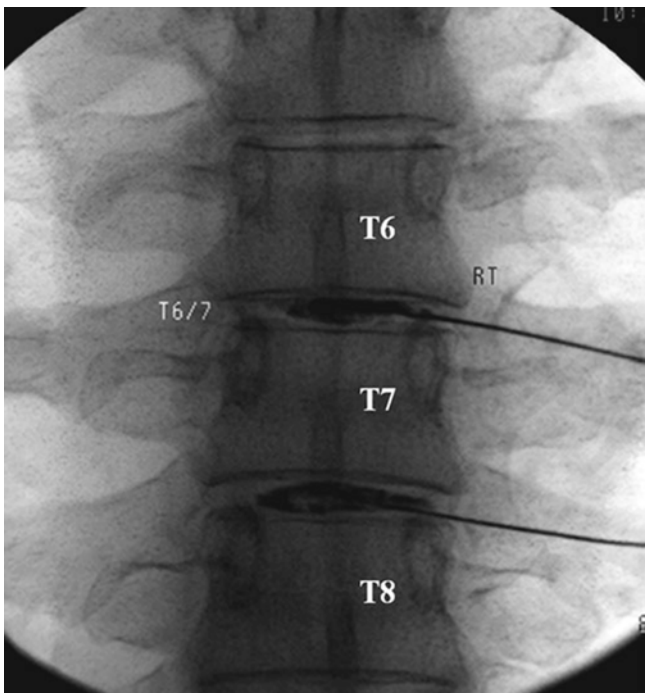

Fig. 26.17 The normal thoracic nucleus usually looks like either a diffuse, elongated homogenous or lobulated pattern

(discitis, seizures, permanent neurologic injury, and death) [26, 50, 51]. Discitis is the most common serious complication of discography, reported to be less than 0.15 % per patient and 0.08 % per disc [3]. The incidence of discitis has been clearly diminished with the double- vs. single-needle technique [25]. Also, with careful preprocedure screening for infection (e.g., UTI or skin), aseptic skin preparation, styletted needles, and intravenous and intradiscal antibiotics, discitis is now very rare. However, even with prophylactic antibiotics, an epidural abscess after discography has been reported [52, 53].

Clinically, the patient with discitis presents with severe, unremitting, disabling axial pain beginning 5–21 days following the procedure, sometimes accompanied by fever and chills. Investigative tests may require blood work, including CBC, c-reactive protein (CRP), sedimentation rate (ESR), and blood cultures as well as a contrast-enhanced MRI and a disc biopsy. Empyema or abscess formation requires CT-guided drainage or surgical intervention [54–56]. Striking a ventral ramus is a potential hazard, but may be avoided by careful attention to correct technique. Other complications include spinal cord or nerve root injury, cord compression or myelopathy, urticaria, retroperitoneal hemorrhage, nausea, convulsions, headache, and, most commonly, increased pain [3]. An increase in the rate of disc degeneration over time following discography was also recently reported in a single small cohort study and requires further investigation [19]. Meanwhile, it is suggested to use smaller discography needles, gauges 25 or less.

Cervical Discography

Inadvertent passage of the needle through the cervical disc in the AP plane can cause spinal cord injury or post-thecal puncture cephalgia, which can be avoided by using a shorter

needle, using a lateral view during needle advancement and conformation of needle depth penetration by touching the anterior vertebral margin prior to passage into the disc [46]. Penetration of viscera such as the pharynx and esophagus is not a problem per se, but increases the risk of infection such as epidural and retropharyngeal abscess and discitis [56–59]. The reported incidence of discitis is 0.1–0.5 % [58, 60]. Needle passage through the carotid artery may result in a hematoma which could potentially cause an airway obstruction, especially in patients with coagulation problems [46].

Thoracic Discography

The main complications include pneumothorax, discitis, and neural injury. Pneumothorax can complicate cervical, thoracic, or lumbar discography, but more frequent in the thoracic spine. A small traumatic pneumothorax after percutaneous needle procedures can be treated conservatively and usually does not require chest tube insertion [61].

Discussion

The single purpose and objective of disc stimulation is to identify a painful intervertebral disc. As in the case of palpation for tenderness, provocation does not reveal pathology or the cause of pain; it only indicates the structure that when stressed, reproduces the patient's pain. If an explicit, pathoanatomical diagnosis is to be made, such as internal disc disruption, the discography must be supplemented by post-discography CT in order to reveal the fissures characteristic of this condition. Another, not least important value of discography is in identification of "negative discs" in response to a disc stimulation, thus limiting the number of levels requiring surgical intervention or a need for interventional disc procedures altogether. However, the diagnostic power of discography remains controversial [62]. As a provocative test, it has been criticized to have a potentially high false-positive rate [24]. The reasons for that can occur due to technical errors, due to neurophysiological phenomena, or due to psychosocial factors [32].

Correct technical performance is paramount to the accuracy of the discography results and has been underestimated over the past decades, leading to questionable medical outcomes and important legal implications. Discography without strict standards for pressure, volume, speed of injection controls, and limits is unsupportable. Dynamic and static pressures, volumes, and pain responses must be gathered and documented using a consistent and reproducible technique, preferably using a controlled injection syringe with digital pressure readout rather than manual pressurization [63]. It was shown that speed-sensitive dynamic pressure is more liable to provoke a positive pan response, thus requiring a slow injection rate (0.05–0.1 mL/s), which most accurately reflects the pressures transferred to the outer annulus [63]. Many of the reported false-positive responses occurred at pressures of 50 psi a.o. or greater. In addition, provocation response should not be accepted as a positive unless it can be confirmed by a repeat pressurization, and pain does not decrease more than 50 % over 30 s. Transient pain provocation may occur when an asymptomatic fissure opens or a thin membrane sealing the outer annulus ruptures during disc pressurization.

Central hyperalgesia also has to be taken into account as a physiological phenomenon when the perception of stimuli from a receptive field is facilitated by ongoing nociceptive activity arising from adjacent or nearby but separate receptive fields. In this regard, formal studies have shown that in patients with no history and no symptoms of back pain, but with a painful donor site on the iliac crest, disc stimulation can evoke back pain [40], producing false-positive response.

Concerns have been raised regarding psychological comorbidity and psychosocial factors as significant confounding factors in patients undergoing discography, questioning the results of discography in patients with chronic pain or somatization disorders other than back pain [40]. Evidence indicates that patients with chronic or chronic intermittent low back pain respond similarly to disc stimulation as do asymptomatic volunteers undergoing discography, as was shown by Derby in a prospective controlled study of patients with grade 3 disc tears [64]. Shin also confirmed that a majority of patients with grade 4 tears could distinguish between "positive" and "negative discs" by magnitude of pain response, causing doubt on the argument that a majority of patients with chronic pain undergoing discography would overreport pain [65].

In addition, a randomized controlled trial comparing discography results of 25 patients with and without somatization disorder found no significant difference in positive responses between groups [66]. There was also no difference in positive responses in patients with depression and/or general anxiety disorder. That calls into question the results of a limited Carragee study of six somatization patients, where only four of six were able to complete their discography test because of pain [24]. Derby et al. [67] reported DRAM scores of 81 patients undergoing discography: 15 % (12/81) were normal, 52 % (42/81) were at risk, and 33 % (27/81) were abnormal (distressed, depressive or somatic). The positive rates of discography were not statistically significant by subgroup ($p > 0.05$). In patients with chronic low back pain, no correlation was found between presenting DRAM score and discography result.

A recent meta-analysis of studies of asymptomatic subjects undergoing discography showed a high specificity of 0.94(95% CI 0.89–0.98) and a relatively low false-positive rate of 6 % [20]. This critical examination of most studies in the literature since the 1960s showed that an acceptably low

false-positive rate can be achieved when strict ISIS/IASP standards for a positive discography are utilized: pain ≥7/10, concordant pain, pressure <50 psi a.o., ≥grade 3 annular tear, volume limit ≤3.5 mL, and presence of a negative control disc.

In regard to post-discectomy subjects, it appeared that they have a slightly higher false-positive rate of 15 % per patient and 9.1 % per disc, as a group. Given our limited knowledge of discography in post-discectomy patients and the possibility that provocation may open previously healed granulation tissue along surgical planes, discographers have to consider pressure- and speed-controlled manometry and to use lower limits for pressure and volume when defining a positive value. Another recent concern raised by Carragee et al. [19] is a long-term risk that discography, as an invasive test, can potentially cause damage to punctured discs over time and result in accelerated disc degeneration. The authors showed a 21 % increase in the degree of disc degeneration using small gauge needles and an increase in the number of new disc herniations of all types in the discography vs. control group over 10 years. These results require attention and further investigation. It would be important to determine what proportion of those degenerative discs can be attributed to rather expected natural history of accelerated degeneration in this small cohort of patients with known cervical disc disease. Those patients might be already genetically predisposed to accelerated disc degeneration and multilevel spondylosis, compared to the normal population, as was shown in a well-designed twin study, when 74 % of degenerative findings at the lower lumbar levels were accounted for the heritability [68].

Even though the diagnostic power of discography remains controversial, it is a relatively safe and sensitive test for identifying painful discs, which may predict surgical outcomes. In a multicenter surgical and nonsurgical outcome study after pressure-controlled discography, Derby et al. [39] stated that precise prospective categorization of positive discographic diagnoses may predict treatment outcomes, surgical or otherwise, thereby greatly facilitating therapeutic decision-making.

Summary

Discography, when indicated and correctly performed, is a safe and sometimes powerful complement to the overall clinical context and is not intended to be a stand-alone test. Despite the controversy, this test can provide valuable information regarding the possible discogenic origin of pain and provide intricate details of inner disc morphology and annular disc disruption, when combined with a post-discography CT scan. It is not a screening procedure but rather a confirmatory one. Recent advances in discography technique, including use of pressure-controlled manometry and strict diagnostic criteria, helped to improved validity of this test significantly. In patients with chronic intractable neck or back pain but negative or indeterminate imaging findings who are being considered for surgical intervention, discography can help to localize the symptomatic level and potentially benefit the patients by surgical intervention or by avoiding it in case of "asymptomatic discs." Newer noninvasive imaging technologies like magnetic resonance spectroscopy, measuring biochemical markers of inflammation that could potentially correlate with "painful disc" on discography, are gradually emerging. They have the potential to replace more invasive disc stimulation tests in the near future, but to this day, discography remains the criterion of standard for the diagnosis of discogenic pain.

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Brachial Plexus Block

27

Chester Buckenmaier III

Key Points

- Brachial plexus block is an ideal anesthetic for upper extremity surgery since plexus anatomy allows easy access by a variety of approaches.
- A detailed understanding of brachial plexus anatomy is essential for the safe and efficient application of all the approaches to brachial plexus block.
- As with all regional anesthetics, brachial plexus block should be performed in areas with standard monitors and emergency life support equipment.
- The existence of the brachial plexus "sheath" is supported by a preponderance of evidence as demonstrated in cadavers and with radiopaque injections.
- All approaches to the brachial plexus are suitable for continuous peripheral nerve block catheters.
- Brachial plexus block is particularly well suited for ultrasound technology though this technology does not preclude the need for the clinician to maintain a detailed understanding of anatomy.

History of the Brachial Plexus Block

The first brachial plexus block was performed less than a year following Carl Koller's discovery of the anesthetic properties of cocaine in 1884. William S. Halsted injected each of the roots of the brachial plexus with cocaine under direct visualization after surgical exposure. In some respects, the anesthetic method was as extensive as the surgical procedure [1]. In 1911, G. Hirschel described a percutaneous technique for brachial plexus blockade by injecting local anesthetic around the axillary artery [2]. A century later, the science of brachial plexus block has become one of the most important anesthetic and analgesic techniques for the upper extremity.

The advantages of regional anesthesia include superior pain control, reductions in the surgical stress response, and preservation of immune function, among many others [3]. The numerous benefits of perioperative surgical stress attenuation using regional anesthesia were recently highlighted when breast cancer surgery patients were noted to have a reduced incidence of cancer recurrence or metastasis compared to patients who underwent breast cancer surgery under general anesthesia [4]. Brachial plexus block for upper extremity surgery has been suggested as an ideal anesthetic approach for most upper extremity surgery patients due to the profound analgesia provided, the anatomical realities of the plexus that allow relatively easy access by the anesthesiologist through a variety of approaches, and the excellent operating conditions afforded the surgeon [5]. As with all regional anesthetic techniques, a detailed understanding of brachial plexus anatomy, to include surrounding structures, is essential for the safe and efficient application of all the approaches to brachial plexus block.

Pearls of Brachial Plexus Block

As with any medical procedure, proper patient consent for the block procedure, conformation of side to be blocked, and documentation of the block is essential. Providers should counsel patients regarding the risks of regional anesthesia that include, but are not limited to, block failure, local anesthetic toxicity, and potential nerve injury. Additionally, patients should be informed that normal protective reflexes and proprioception for the blocked upper extremity will be diminished or absent for 24 h and they should therefore take special care of the blocked limb. All regional anesthetics should be performed in areas with standard monitors, oxygen, suction, airway, and emergency advanced cardiac life support equipment and medications. During local anesthetic

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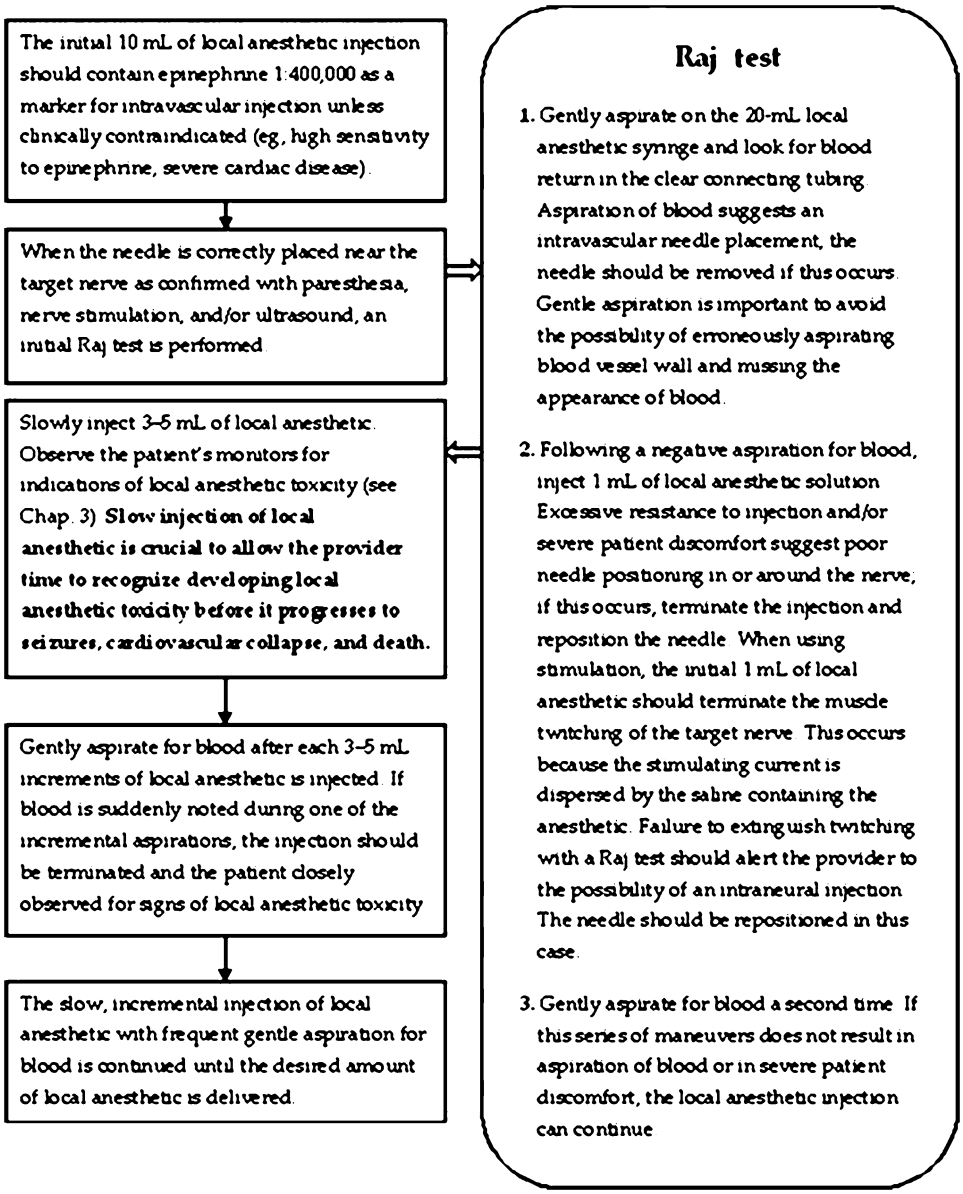

Fig. 27.1 The preferred local anesthetic injection procedure used at Walter Reed Army Medical Center (With permission from Buckenmaier and Bleckner [71])

injections, constant vigilance is required for signs and symptoms of developing local anesthetic toxicity. Slow injections with frequent aspirations for blood are one of the best defenses against this complication. The preferred local anesthetic injection procedure used at Walter Reed Army Medical Center is provided in Fig. 27.1. Recommended techniques and conditions to minimize local anesthetic toxicity from intravascular injection for all blocks are provided in Table 27.1.

Anatomy of the Brachial Plexus

The brachial plexus is commonly formed from the five roots (anterior rami) of vertebrae C5 through T1 (Fig. 27.2). Considerable morphological variations in brachial plexus formation have been described, even on contralateral sides of the same individual, though sex, race, or side of the body does not appear to influence this variation [6]. The brachial plexus can be

Table 27.1 Recommended techniques and conditions to minimize the risk of local anesthetic intravascular injection

Standard monitoring with audible oxygen saturation tone
Oxygen supplementation
Slow, incremental injection (5 mL, every 10–15 s)
Gentle aspiration for blood before injection and every 5 mL thereafter
Initial injection of local anesthetic test dose containing at least 5–15 μg epinephrine with observation for heart rate change >10 beats/min, blood pressure changes >15 mmHg, or lead II – wave amplitude decrease by 25 %
Pretreatment with benzodiazepines to increase the seizure threshold to local anesthetic toxicity
Patient either aware or sedated but still able to maintain meaningful communication with the physician
Resuscitation equipment and medications readily available at all times
If seizures occur, patient care includes airway maintenance, supplemental oxygen, and termination of the seizure with propofol (25–50 mg) or thiopental (50 mg)
Local anesthetic toxicity that leads to cardiovascular collapse should immediately be managed with prompt institution of advanced cardiac life support (ACLS) protocols
With permission from Buckenmaier and Bleckner [71] Intralipid (KabiVitrum, Inc., Alameda, California) 20 % 1 mL/kg every 3–5 min, up to 3 mL/kg, administered during ACLS for local anesthetic toxicity can be lifesaving. Follow this bolus with an Intralipid 20 % infusion of 0.25 mL/kg/min for 2.5 h

described as "prefixed" when C4 brachial plexus contributions occur or "postfixed" when T2 contributions are noted. Uysal et al. [7] surveyed 200 fetuses noting the common C5 through T1 contribution that occurred 71.5 %, prefixed plexuses were observed 25.5 %, and the postfixed plexus was noted in 2.5 %.

The brachial plexus is typically further categorized into four major components or sections as it passes into the upper extremity (Fig. 27.2). Each of these components is bounded by distinct anatomical structures [8]:

- Three trunks. The anterior rami of the plexus roots commonly coalesce into three major trunks with roots: C5 and C6 forming the superior trunk, C7 contributing to the middle trunk, and C8 and T1 making up the inferior trunk. The trunks are most easily identified as they pass between the anterior and middle scalene muscles. Anatomical variation exists in the relationship between the scalene muscles and the trunks with the most common variation being penetration of the anterior scalene muscle by the C5 and/or C6 roots [9]. These anatomical variants can have clinical significant when performing regional anesthetic blocks of the brachial plexus trunks.
- Six divisions. Each trunk divides into an anterior division (anterior flexor nerves of the arm) and a posterior division (posterior extensor nerves of the arm) for a total of six divisions (three anterior, three posterior). The separation of the trunks into divisions occurs at the level of the first rib. The divisions then pass posterior to the midpoint of the clavicle through the cervicoaxillary canal.
- Three cords. The six divisions emerge posterior to the clavicle to coalesce once again to form three cords. The cords are named based on their position in relation to the axillary artery as this neurovascular bundle passes into the axilla. The *lateral cord* (lateral to the axillary artery) is composed of the anterior divisions of the superior and middle trunk. The *medial cord* consists of only a continuation of the anterior division of the inferior trunk. The lateral and medial cords therefore give rise to nerves that ultimately service the flexor surface of the arm. The *posterior cord* is formed from the posterior divisions of all three cords. The posterior cord contains all of the nerves that will supply the extensor surface of the arm.
- Five terminal branches. The five major nerves of the upper extremity are derived from the three cords. The *musculocutaneous nerve* (C5–C7) arises from the lateral cord and supplies the coracobrachialis, biceps brachii and brachialis muscles, and the skin to the lateral forearm. The lateral cord (C6–C7) and medial cord (C8–T1) both contribute to the formation of the *median nerve* which innervates anterior forearm muscles and the thenar half of the skin and muscles of the palm. The *ulnar nerve* is a branch of the medial cord (C7–T1) and supplies the forearm and hand medial to the midpoint of digit four. The shoulder joint and lateral skin over the deltoid muscle are innervated by the *axillary nerve* that branches from the posterior cord. Finally, the largest branch of the posterior cord gives rise to the *radial nerve* (C5–T1) which supplies all of the posterior compartment muscles and most of the posterior skin of the arm. Numerous other named nerves branch off of the brachial plexus though knowledge of the five major nerves is adequate for most clinical blocks of the brachial plexus.

A discussion of brachial plexus anatomy would be incomplete without addressing the considerable controversy that surrounds the existence of a "sheath" surrounding the brachial plexus and includes the artery, vein, and investing connective tissue. Multiple authors have described the anatomical

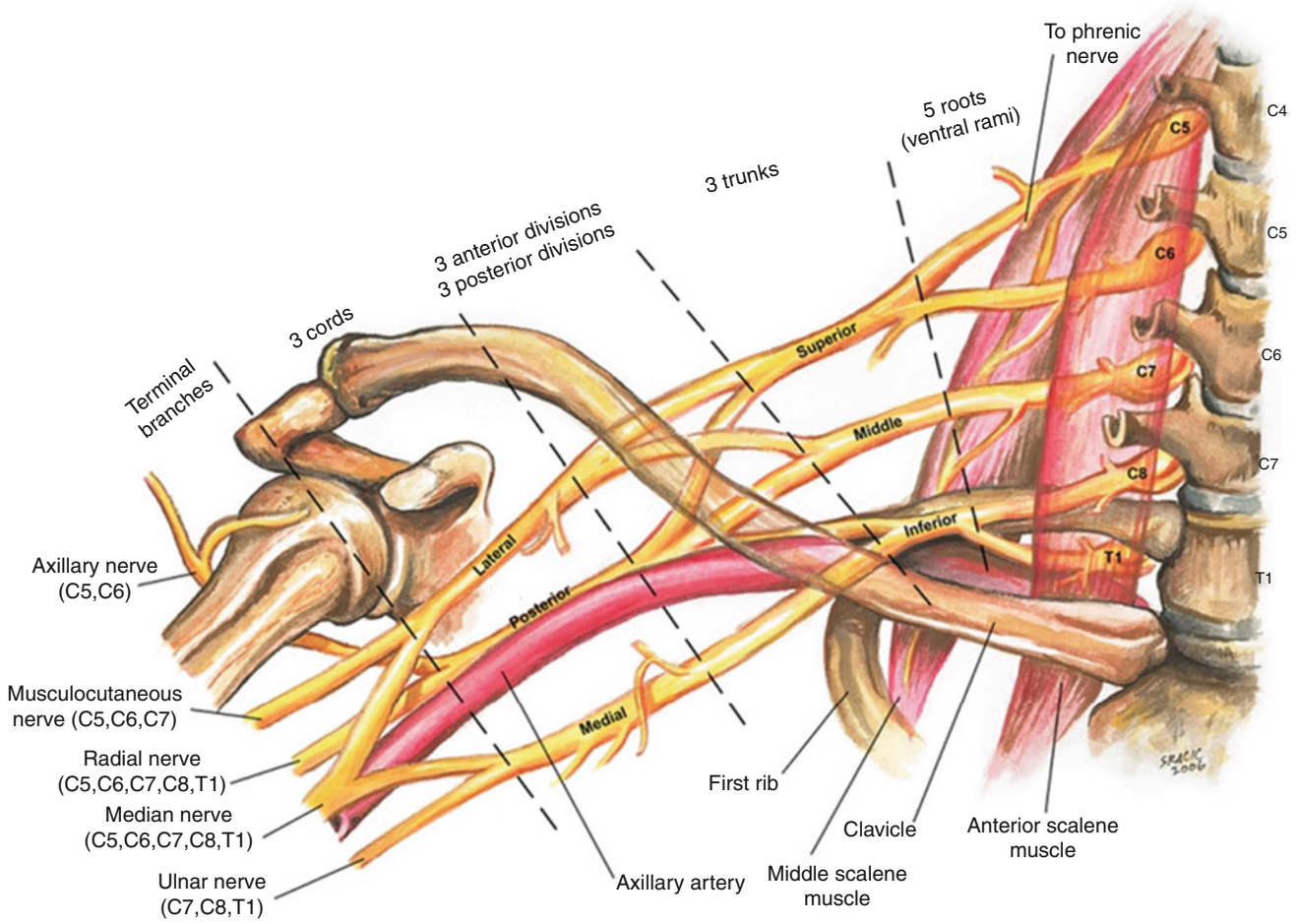

Fig. 27.2 Brachial plexus anatomy (With permission from Buckenmaier and Bleckner [71])

structure referred to as a sheath, perhaps most famously by Winnie [1] who noted the muscles surrounding the brachial plexus contribute fascia that we "conceive of as the 'sheath of the brachial plexus.'" Other authors have debated whether the sheath is a single tube or compartmented structure [10, 11]. Still others have rejected the existence of the sheath outright [12]. Recently, Franco et al. [13] performed systematic dissections on 11 embalmed cadavers and determined that a sheath-like structure surrounding the brachial plexus filled with loose connective tissue could be demonstrated in every specimen (Fig. 27.3a, b). The clinical significance and existence of a structure enveloping the brachial plexus has been suggested by both radiopaque local anesthetic injections [14] and observations during injections under direct ultrasound guidance [15]. Regardless of the term used to describe the investment of fascia that surrounds neurovascular structures, the preponderance of evidence suggests the brachial plexus sheath is a reality. The clinical significance of this structure continues to be debated and is worthy of additional study.

Subsequent sections of this chapter will describe common regional anesthesia blocks for the brachial plexus to include interscalene, supraclavicular, infraclavicular, and axillary block. Each block will be presented with a discussion of pertinent anatomy, followed by approaches using both nerve stimulation and ultrasound guided. The approaches described in detail are preferred by the author and used in daily clinical practice. This should not deter the reader from exploring other methodologies that are referenced with no further explanation.

Interscalene Block of the Brachial Plexus

The interscalene block described by Winnie in 1970 [16] is performed at the level of the C6 vertebral body (Chassaignac's tubercle). At this level, the roots of the brachial plexus pass the transverse processes of the vertebral bodies where they are invested between the fascia of the anterior and middle

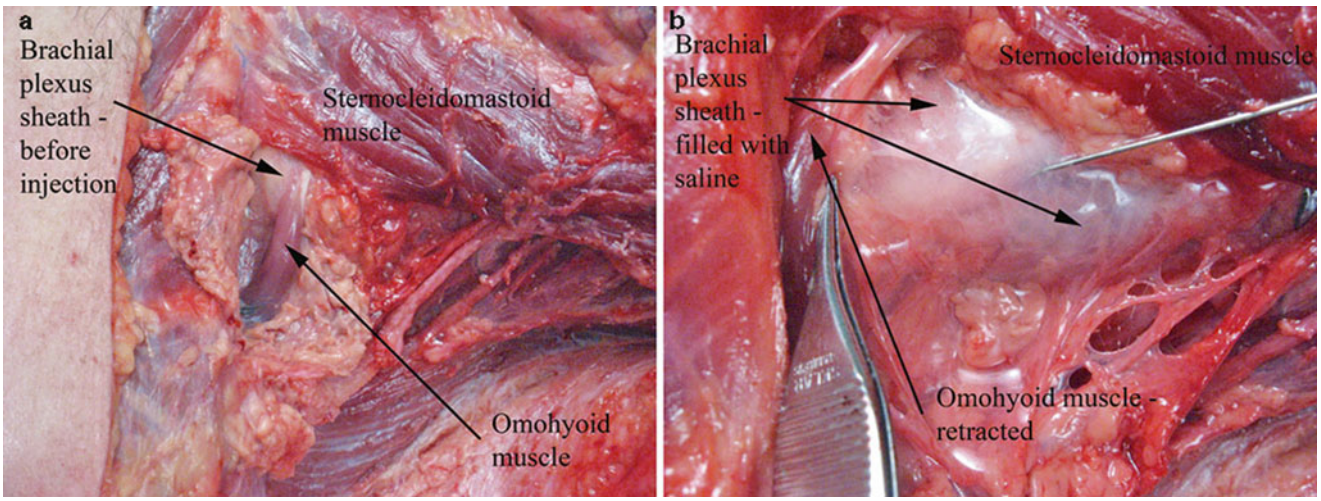

Fig. 27.3 (**a**) Brachial plexus sheath before and after injection with saline in a fresh cadaver specimen. Before: Prior to injection with saline. (**b**) Brachial plexus sheath before and after injection with saline in a fresh cadaver specimen. Before: prior to injection with saline (With permission from Buckenmaier and Bleckner [71])

scalene muscles as the plexus passes between these muscles (Fig. 27.4). This provides a convenient compartment that local anesthetic can be deposited, to bathe the C5–C7 roots, resulting in consistent block of the shoulder muscles to include the deltoid, supraspinatus infraspinatus, and teres major muscles. Therefore, interscalene block of the brachial plexus is most commonly selected for operations on the shoulder, clavicle, or upper arm. This block is typically not selected for operations of the hand or forearm due to unpredictable spread of local anesthetic to the C8–T1 nerve roots (ulnar nerve). Inconsistent spread of local anesthetic to C3–C4 can result in posterior shoulder (cape area) sparing that should be considered for large operations on the shoulder (Fig. 27.5). Supplemental blocks such as an intercostobrachial nerve block (subcutaneous injection of local anesthetic from the axilla to the midpoint of the clavicle) are used to supplement the interscalene block for major shoulder surgery. Paravertebral blocks at T1–T2 can be added for procedures that include significant posterior shoulder dissections.

The close proximity of the phrenic nerve lying anterior on the anterior scalene muscle usually results in paresis of the hemidiaphragm on the side blocked. Though most patients tolerate the loss of one hemidiaphragm with ease, the use of this block should be reconsidered in a patient that cannot tolerate a reduction in pulmonary function. Proximal spread of local anesthetic to the cervical plexus (C3, C4) and cervical sympathetic chain can result in a transient Horner's syndrome and vocal hoarseness in some patients [17]. While this condition is self-limited, patients can become unnecessarily concerned if the possible occurrence of this side effect is not part of pre-block counseling. Perhaps the most devastating complication associated with this block is the unintended injection of local anesthetic into the vertebral artery located posterior and medial to the brachial plexus at this level. This error can lead to rapid cardiovascular collapse with few, if any, clinical signs warning of systemic local anesthetic toxicity [18]. Proper slow injection technique, with frequent gentle aspiration for blood every 3–5 mL of local anesthetic injected, is critical to guard against intravascular needle placement.

Procedure

The patient is placed supine with the head turned to the non-operative side. Major external landmarks include the lateral border of the sternocleidomastoid muscle (SCM – best defined by having the patient lift their head off the bed 1 in.), the external jugular vein, the cricoid cartilage which corresponds to the C6 level, and the clavicle (Fig. 27.6). Regardless of the technology used to perform any block of the brachial plexus, it is worthwhile to examine and mark the patient's pertinent anatomy prior to attempting needle placement. It is important not to confuse the more medial sternal head of the SCM with the clavicular head when palpating the lateral edge of this muscle, especially in obese patients. The jugular vein often crosses the lateral boarder of the SCM at the level of C6 (not the case in Fig. 27.6). At the level of C6, the lateral border of the SCM is gently palpated, and then fingers are moved just lateral to palpate the interscalene grove (between the anterior and middle scalene muscles). Initial needle placement is within the groove at the level of C6.

Stimulation blocks are typically performed with 22-gauge, 5-cm, insulated needles with the stimulator initially set at 1.0–1.2 mA (Fig. 27.7). References are available for the technique and clinical applications of peripheral nerve stimulation [19].

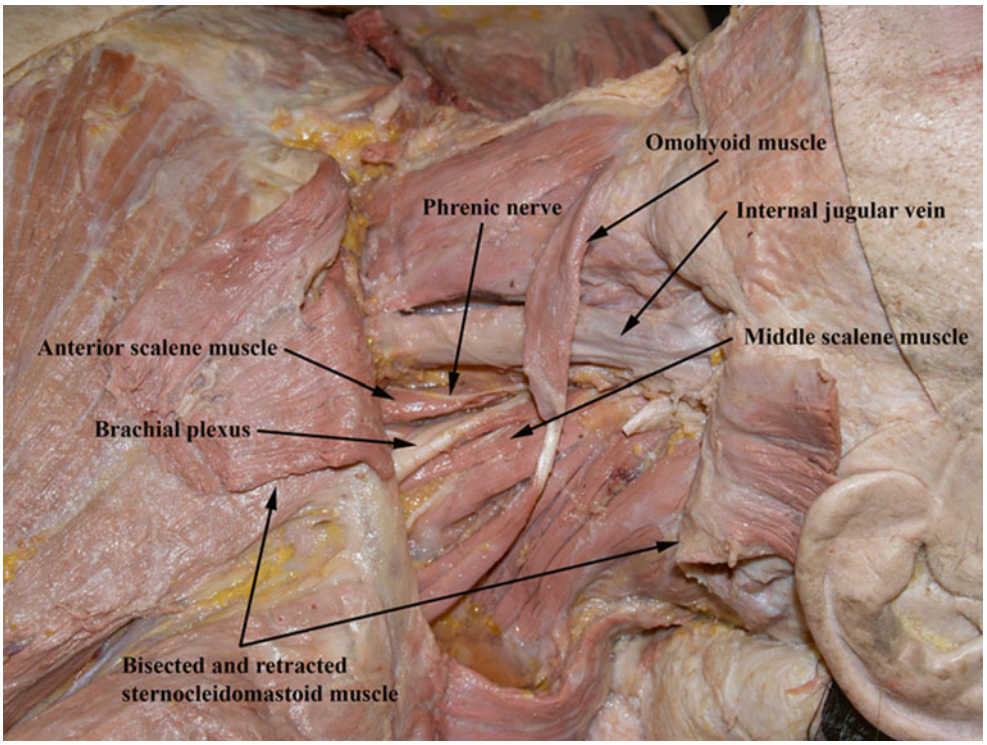

Fig. 27.4 Brachial plexus dissection above the clavicle (With permission from Buckenmaier and Bleckner [71])

A muscle twitch of the deltoid, biceps, or triceps at 0.5 mA or less indicates adequate proximity of the needle tip to the plexus for local anesthetic injection [20]. In most adults, the brachial plexus is rarely deeper than 1–2 cm below the skin. Trapezoid muscle stimulation suggests that the needle tip is posterior to the plexus while diaphragm stimulation indicates a needle tip that is too anterior. Local anesthetic volumes of 30–40 mL are sufficient to block the plexus in most adults. Modifications of the described interscalene method have been proposed to facilitate indwelling catheters [21], and posterior approaches have also been described [22]. Dagli et al. [23] compared the variations of the interscalene block and determined there was no reduction in complications and less satisfactory anesthesia compared to Winnie's classic approach.

Beginning with the last decade of the twentieth century, ultrasound technology has become a powerful tool to identify nerves and accurately place needles and local anesthetics. Preliminary data suggests that the addition of ultrasound to block procedures can improve success rates and decrease complications [15, 24, 25]. In some cases, ultrasound technology may be the only option available to place a regional anesthetic block when it is indicated [26]. A discussion on the physics and use of ultrasound is beyond the scope of this chapter though excellent references are available [27, 28]. The interscalene block is particularly well suited for ultrasound guidance due to the presence of good ultrasound landmarks and the superficial location of the brachial plexus at this level.

Preparation for an ultrasound-guided block is similar to a stimulation block. The use of external landmarks, when preparing for an ultrasound block, is no less important than when preparing for stimulation blocks. The external marks facilitate optimal ultrasound probe position and can reduce anatomy identification errors. The concurrent use of nerve stimulation with ultrasound can enhance block accuracy by providing objective evidence (motor nerve stimulation) that ultrasound-imaged targets are indeed nerves [29]. A high-frequency (5–12 MHz) linear probe is usually selected. Anatomical identification of the plexus at the C6 level is made easier if the probe is initially placed at the level of a supraclavicular block to identify the brachial plexus just lateral to the readily detectable subclavian artery. Once the plexus is located, it can be slowly traced cephalad to observe the three nerve trunks of the plexus as they pass between the middle and anterior scalene muscles (Fig. 27.8). The plexus is usually approached with the needle placed lateral within the plane of the ultrasound probe beam (Fig. 27.9). In-plane ultrasound-guided interscalene block allows real-time imaging of the needle in relation to target nerves and surrounding structures (Fig. 27.10). It also supports visualization of the local anesthetic injection allowing more accurate placement of medication around target nerves [30].

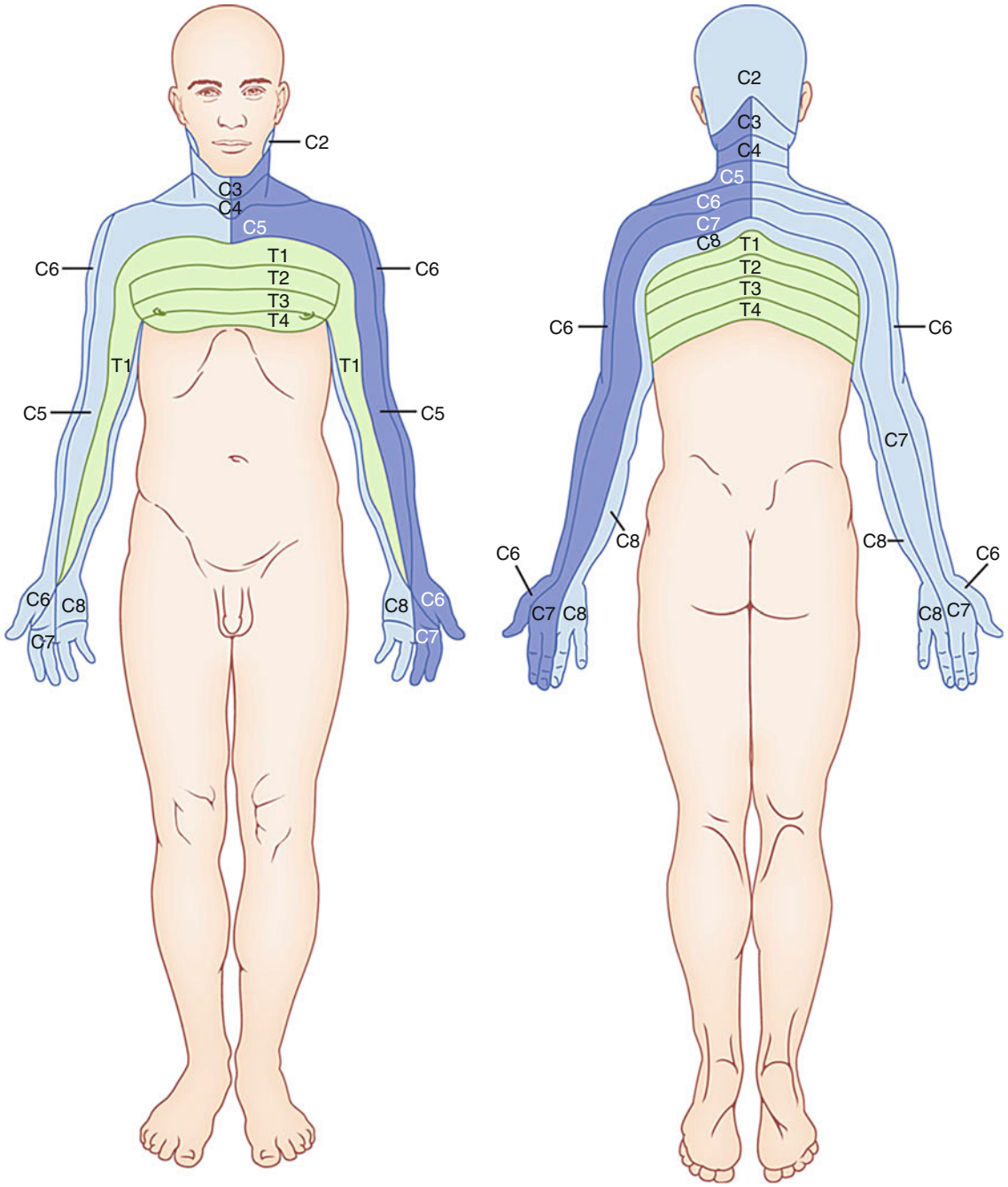

Fig. 27.5 Dermatomes anesthetized with the interscalene block (*dark blue*)

Many providers prefer out of plane needle placement when using ultrasound, though needle tip localization can be more difficult with this approach [31]. Practitioners often distribute local anesthetic to create the "donut sign" which is produced when hypoechoic local anesthetic surrounds the more echogenic nervous tissue. The most efficient block of the brachial plexus is produced when local anesthetic encircles the nerve structures. Authors have suggested that ultrasound guidance my also result in lower local anesthetic dosage requirements [32].

Supraclavicular Block of the Brachial Plexus

The supraclavicular approach, or subclavian perivascular technique [33], for blocking the brachial plexus is ideal for anesthesia and analgesia of the upper arm from the mid-humeral level down to the hand (Fig. 27.11). If a tourniquet of the brachium is planned for surgery, an intercostobrachial nerve block should be considered as a supplemental block. Anatomically, blockade of the brachial plexus just cephalad

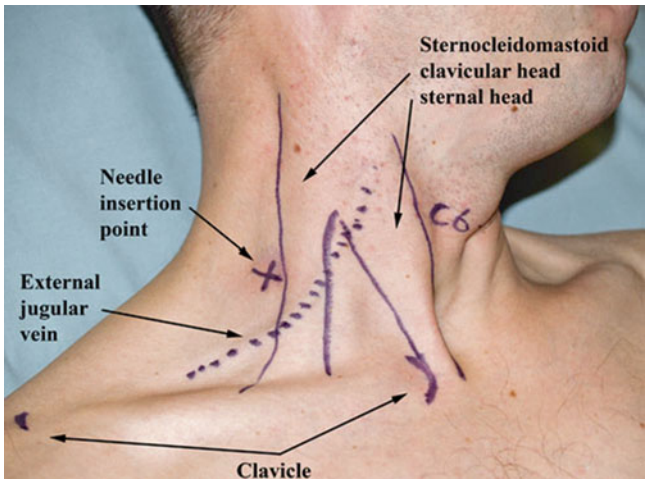

Fig. 27.6 External anatomy for interscalene block labeled (With permission from Buckenmaier and Bleckner [71])

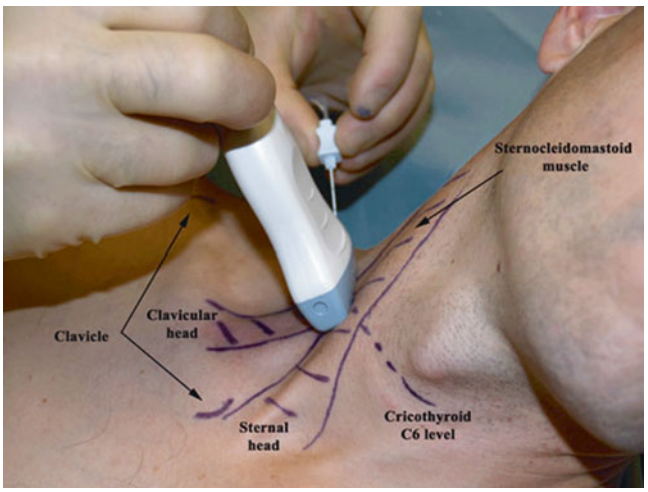

Fig. 27.9 Ultrasound-guided interscalene brachial plexus block (With permission from Buckenmaier and Bleckner [71])

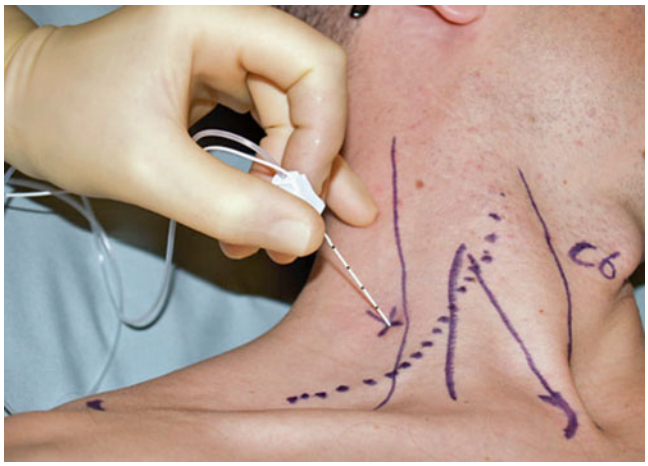

Fig. 27.7 Stimulating needle position for interscalene block (With permission from Buckenmaier and Bleckner [71])

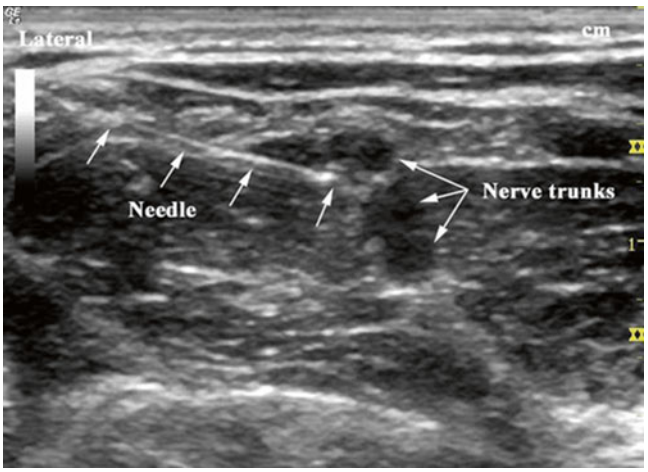

Fig. 27.10 In-plane needle placement during ultrasound-guided interscalene block (With permission from Buckenmaier and Bleckner [71])

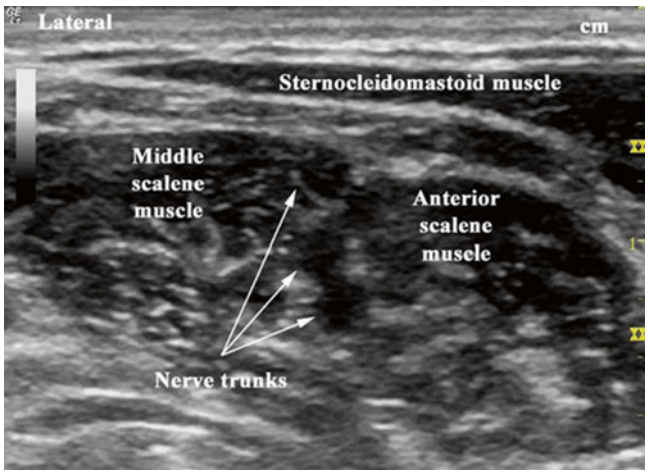

Fig. 27.8 Brachial plexus trunks at the level of C6 with ultrasound (With permission from Buckenmaier and Bleckner [71])

to the clavicle is facilitated by the compactness of the plexus trunks and divisions as these nerves pass under the midpoint of the clavicle. Packed together at this point, the brachial plexus is more easily surrounded by local anesthetic resulting in rapid block onset and high success rates. Franco et al. [34] determined that the unique supraclavicular anatomy of the brachial plexus allowed injection of local anesthetic during stimulation-assisted block at currents as high as 0.9 mA rather than the typical 0.5 mA recommended for most stimulating blocks with no reduction in block success.

Unlike the interscalene approach which results in a 100 % incidence of hemidiaphragmatic paresis that can result in subjective symptoms of respiratory difficulty, the supraclavicular approach results in hemidiaphragmatic paresis only about 50 % of the time and is rarely associated with respiratory complaints [35]. At the level of the clavicle, the apex of

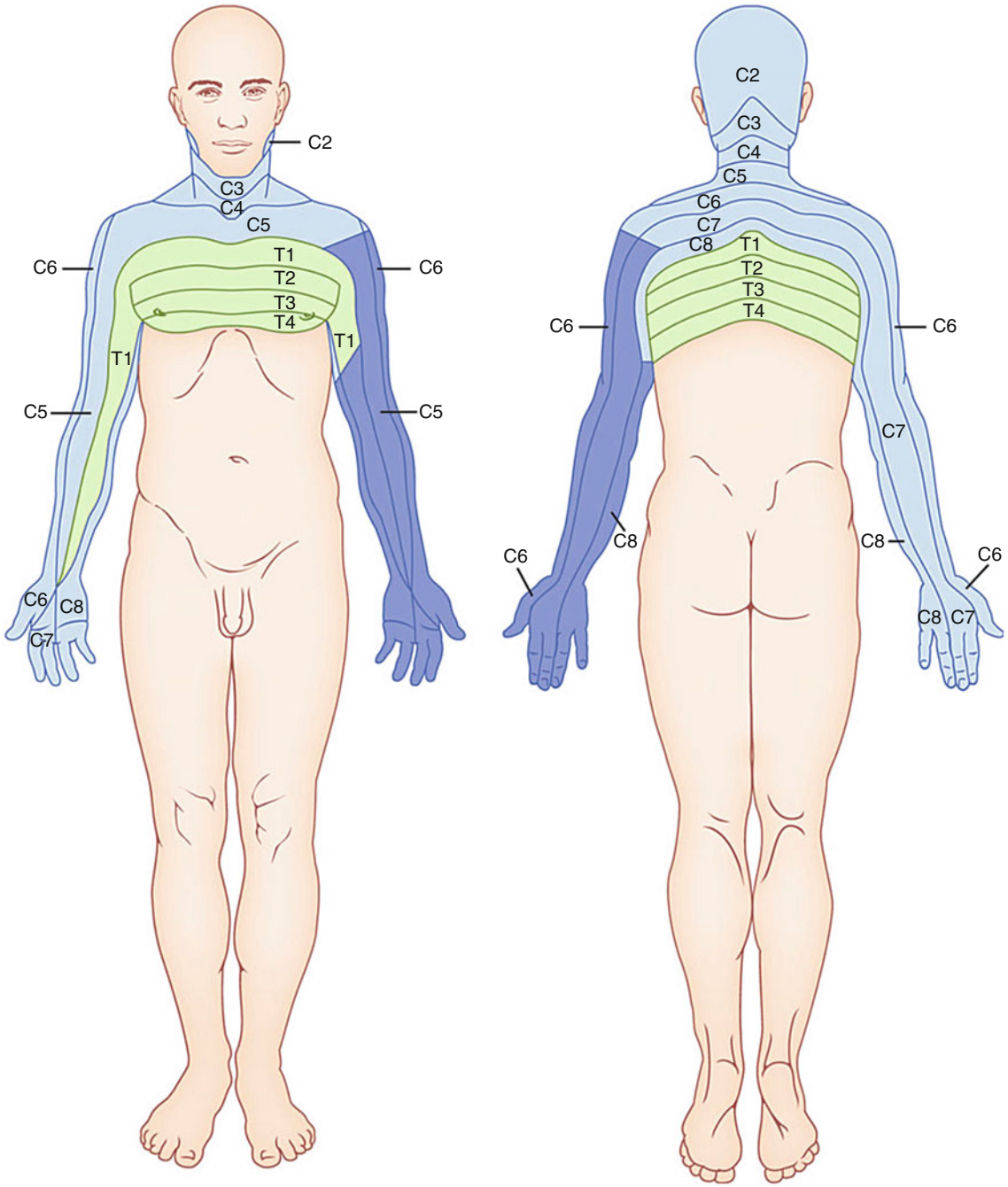

Fig. 27.11 Dermatomes anesthetized with the supraclavicular block (*dark blue*)

the lung is just medial and posterior to the brachial plexus (deep to the first rib), so the complication most often associated with the supraclavicular block approach is pneumothorax. Using paresthesia techniques, authors in the 1960s described incidences of pneumothorax greater than 6 % [36]. For this reason, the technique fell out of favor until modern block technology and refinements in the approach reduced the incidence of this complication to less than 1 % [37–39]. Signs and symptoms of a large pneumothorax include sudden cough and shortness of breath. Should these symptoms manifest during the block procedure, the patient should undergo a chest X-ray prior to going to the operating room.

Procedure

The head of the supine patient is turned to the nonoperative side. External landmarks for the supraclavicular approach are similar to those used for the interscalene block (Fig. 27.12).

The interscalene groove is palpated at the level of C6, and the fingers are then moved caudad within the groove to a point approximately 1 cm cephalad from the clavicle. This is the needle insertion point for stimulating blocks. The groove below C6 can sometimes be difficult to palpate due to the overlying omohyoid muscle. The subclavian arterial pulse is often palpable just medial to the needle insertion point by rolling the index finger over the top of the clavicle. This can be used as an additional confirmatory landmark.

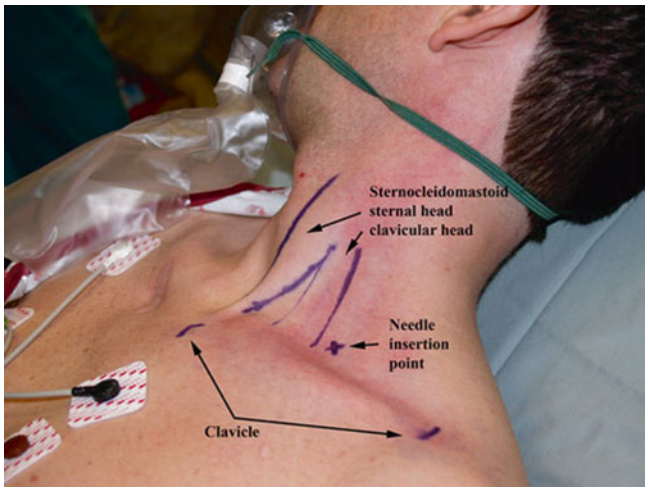

Fig. 27.12 External anatomy for the supraclavicular block labeled (With permission from Buckenmaier and Bleckner [71])

Supraclavicular stimulation blocks are typically performed with 22-gauge, 5-cm, insulated needles with the stimulator initially set at 1.0–1.2 mA. The provider stands at the patients head and directs the needle toward the axilla (Fig. 27.13). Proper needle placement in proximity to the brachial plexus is indicated by flexion or extension of the digits at 0.9–0.5 mA or less [34, 37]. Aspiration of blood or blood observed in the clear tubing suggests the needle tip is too medial and may have penetrated the subclavian artery. Persistent musculocutaneous nerve stimulation (biceps contractions) with needle advancement suggests too lateral a needle placement. Pectoralis muscle stimulation indicates anterior needle placement, and scapular stimulation suggests the needle is posterior to the brachial plexus. Local anesthetic volumes of 30–40 mL are usually injected to block the brachial plexus using this approach. Other stimulating supraclavicular block techniques have been described that purportedly reduce the risk of pneumothorax [40, 41].

Authors have suggested that the addition of ultrasound technology to the supraclavicular block has enhanced speed of block placement, improved block success, and provided superior anatomy identification compared to use of stimulation for the block [42, 43]. A high-frequency (5–12 MHz) linear probe is used for this block. The ultrasound probe is positioned directly above the clavicle in the supraclavicular fossa (Fig. 27.14). This plane gives the best transverse view of the brachial plexus, typically located lateral and slightly superior to the subclavian artery at a depth of 2–4 cm. The nerves appear as hypoechoic circles with hyperechoic rings

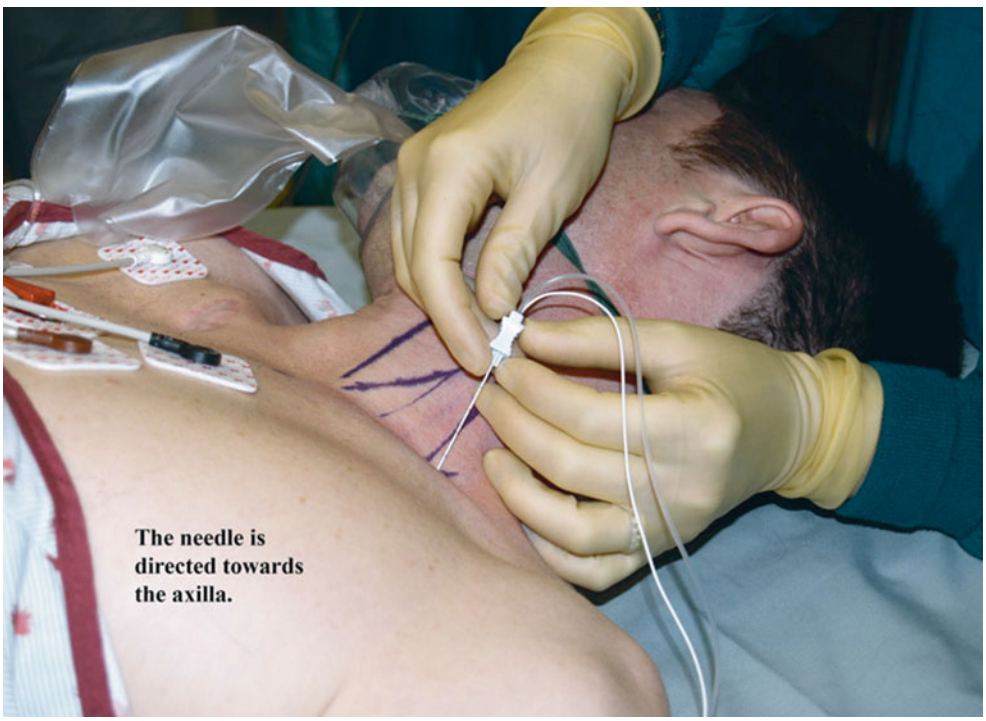

Fig. 27.13 Stimulating needle position for supraclavicular block (With permission from Buckenmaier and Bleckner [71])

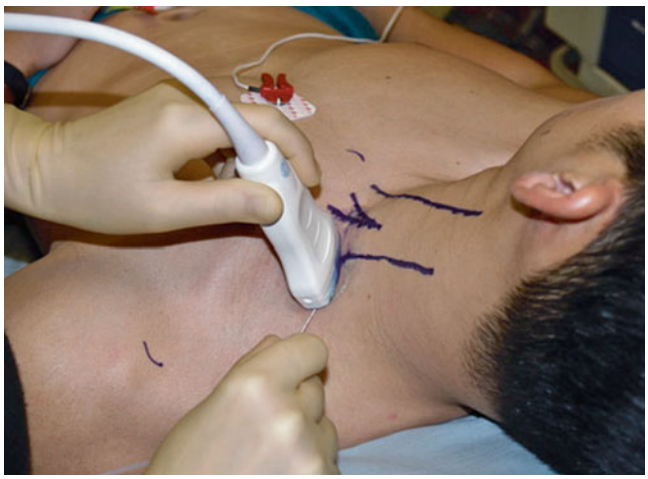

Fig. 27.14 Ultrasound-guided supraclavicular brachial plexus block (With permission from Buckenmaier and Bleckner [71])

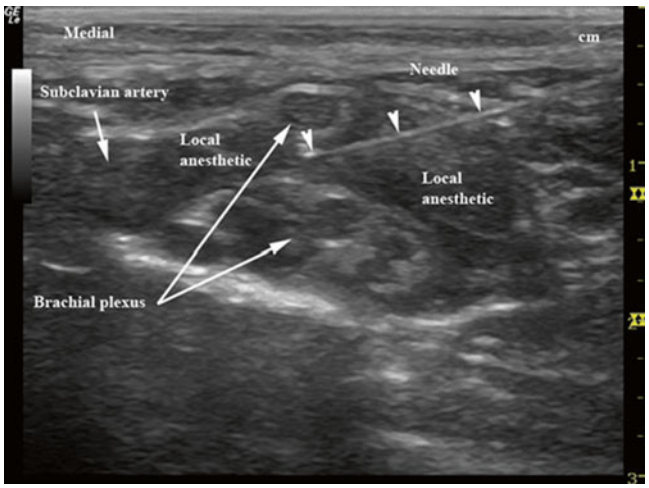

Fig. 27.16 In-plane needle placement for the supraclavicular block with ultrasound. Local anesthetic has been dynamically placed to surround the brachial plexus (With permission from Buckenmaier and Bleckner [71])

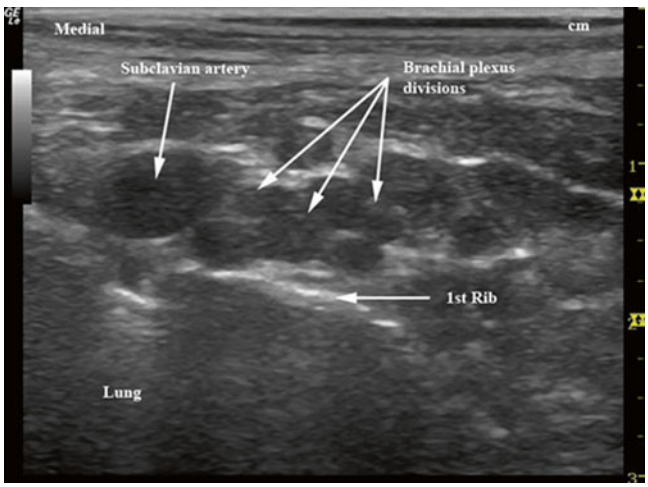

Fig. 27.15 Brachial plexus divisions in the supraclavicular fossa with ultrasound (With permission from Buckenmaier and Bleckner [71])

that are sometimes described as a "bundle of grapes" (Fig. 27.15). The needle is inserted at the lateral end of the ultrasound probe and advanced under direct visualization of the entire needle shaft down to the brachial plexus. It is very important to always keep the tip and shaft of the needle in clear view to ensure the needle is not being placed in areas that can result in pneumothorax or vascular puncture. The local anesthetic can be spread precisely by injecting small aliquots, observing spread, and adjusting the needle as necessary for complete envelopment of the brachial plexus (Fig. 27.16). Supraclavicular blocks can also be performed using out-of-plane approaches though there is no clinical data to support any particular out-of-plane technique [31].

Infraclavicular Block of the Brachial Plexus

The infraclavicular block of the brachial plexus is ideal for operations distal to the elbow (Fig. 27.17). In marked contrast to the quick onset of supraclavicular blocks placed with stimulation, infraclavicular blocks with stimulation take considerably longer to achieve the same level of block in most cases. This is explained by the less compact nature of the brachial plexus as it begins to spread around the axillary artery. The introduction of ultrasound-guided techniques that allow manipulation of anesthetic spread appears to have eliminated this difference between the two approaches [44, 45].

The infraclavicular block is performed at the level of the brachial plexus cords. The three cords – lateral, medial, and posterior – are named by their relation to the axillary artery at this level. When compared to the supraclavicular approach, local anesthetic injected for the infraclavicular block tends to remain below the clavicle, so clinical problems related to unintended block of the phrenic, recurrent laryngeal, or cervical sympathetic nerves do not tend to be issues [46]. The infraclavicular block is also associated with a lower incidence of pneumothorax [47]. Excessive angulation of the block needle toward the axilla may result in inadequate blockade of the musculocutaneous and axillary nerves which can be a problem when stimulation is used.

Procedure

Multiple approaches to the brachial plexus from the infraclavicular approach have been described [2, 47–49]. With the patient's arm externally rotated and abducted, the coracoid

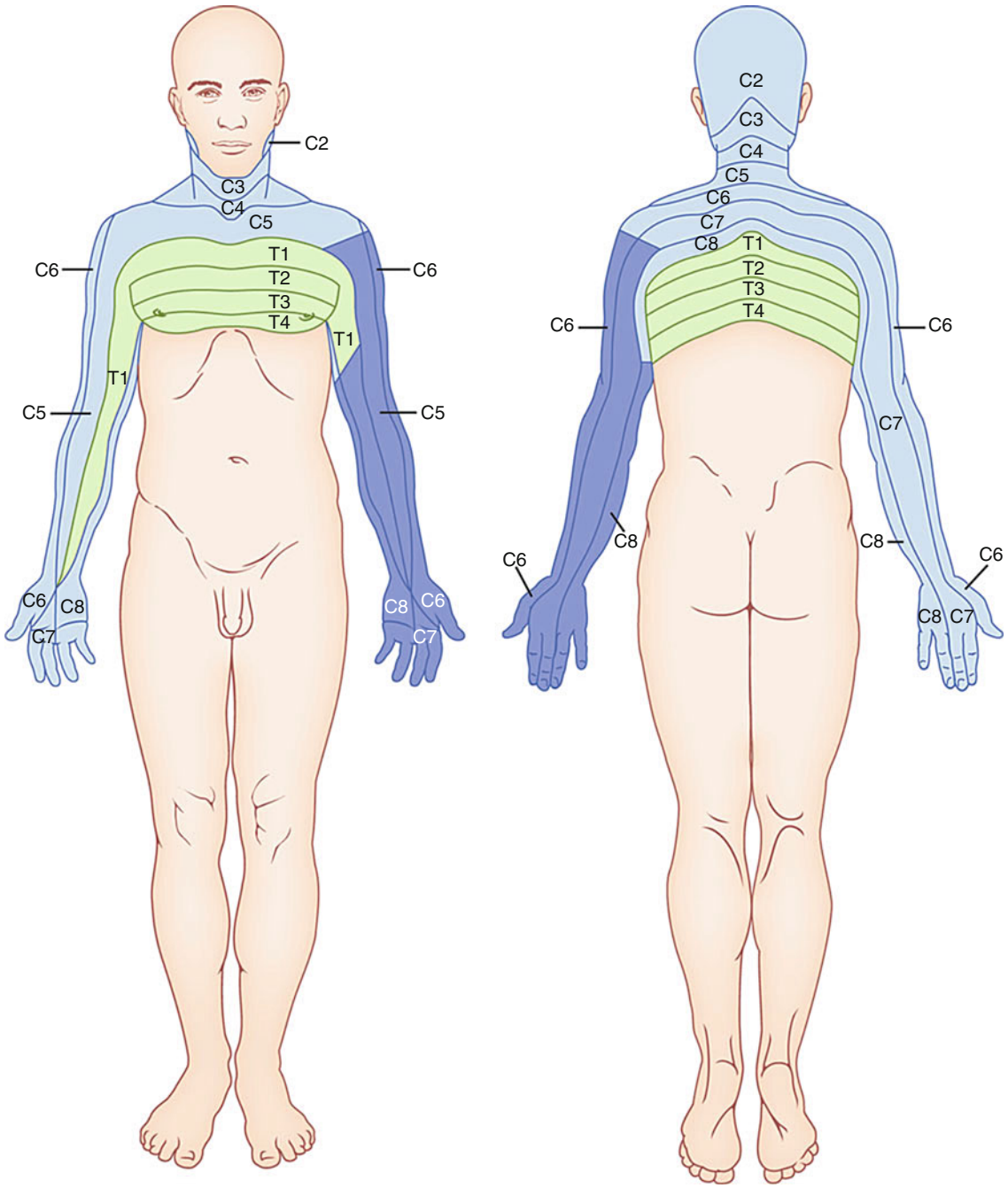

Fig. 27.17 Dermatomes anesthetized with the infraclavicular block (*dark blue*)

process can be palpated and a mark 2 cm medial and 2 cm caudal to the process is made for the initial needle position (Fig. 27.18). The axillary arterial pulse can be palpated in the axilla and is a useful landmark for aligning the needle with the brachial plexus as it passes into the brachium. A simple alternative to the coracoid landmark is the deltopectoral groove (Fig. 27.19). This approach does not necessitate manipulation of the patient's arm. The groove between the deltoid and pectoralis muscles is easily palpable in most patients. The needle is inserted approximately 1 cm caudal to the clavicle within the groove and directed deep toward the axilla.

Infraclavicular stimulation blocks are performed with 22-gauge, 10 cm, insulated needles with the stimulator initially set at 1.0–1.2 mA. Stimulation of the posterior cord (extension of the wrist/fingers) or stimulation of multiple cords simultaneously has been associated with high success rates for brachial plexus block at this level using 30–40 mL

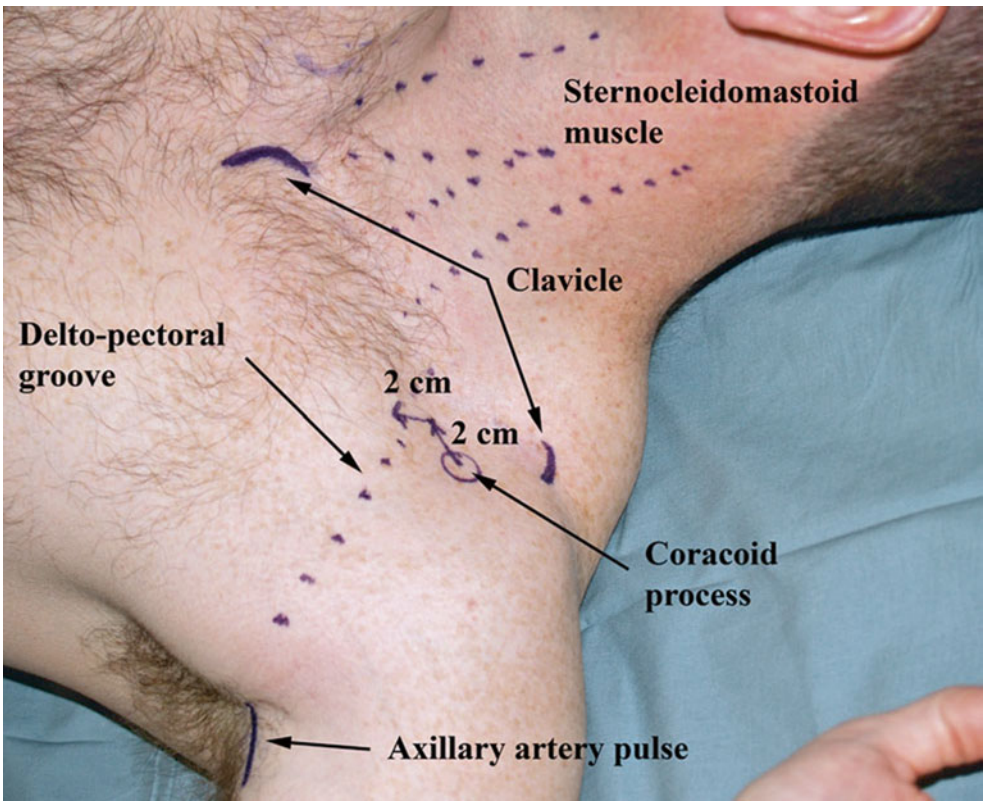

Fig. 27.18 External anatomy for the infraclavicular nerve block (With permission from Buckenmaier and Bleckner [71])

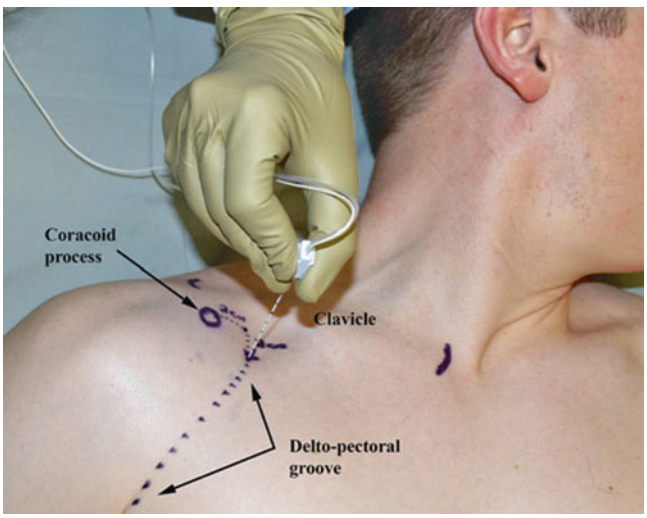

Fig. 27.19 Deltopectoral groove for the infraclavicular block (With permission from Buckenmaier and Bleckner [71])

of local anesthetic [50]. Identification of which cord is being stimulated was elegantly described by Borene et al. [51] with their recognition that the fifth digit (pinkie) moves "toward" the cord that is being stimulated. With the arm positioned anatomically, lateral cord stimulation will move the pinkie laterally (pronation of the forearm), posterior cord posteriorly (extension), and medical cord medially (flexion). In most adults, 30–40 mL of local anesthetic will block the plexus. As noted above, the latency of this block can be long when stimulation alone is used.

As with other brachial plexus blocks, the introduction of ultrasound technology has been suggested to improve the accuracy of local anesthetic injection, improve block success, and decrease complication rates [52]. Though the preponderance of evidence continues to support this hypothesis, large, controlled trials remain lacking, and the issue is controversial.

The linear, high-frequency (5–12 MHz) probe is again selected for this approach. The needle is inserted in-plane at the cephalad (lateral) aspect of the probe (Fig. 27.20). The primary landmark for this block is the axillary artery. With the axillary artery viewed in cross section, the cords of the plexus appear as hyperechoic densities located lateral, medial, and posterior to the artery (Fig. 27.21). The needle is inserted, under constant visualization, to the posterior aspect of the axillary artery, and local anesthetic is injected with the goal of surrounding the artery with local. After the posterior portion of the artery is surrounded, it is often necessary to reposition the needle to the anterior aspect of the artery to complete the injection. Care should be taken to ensure

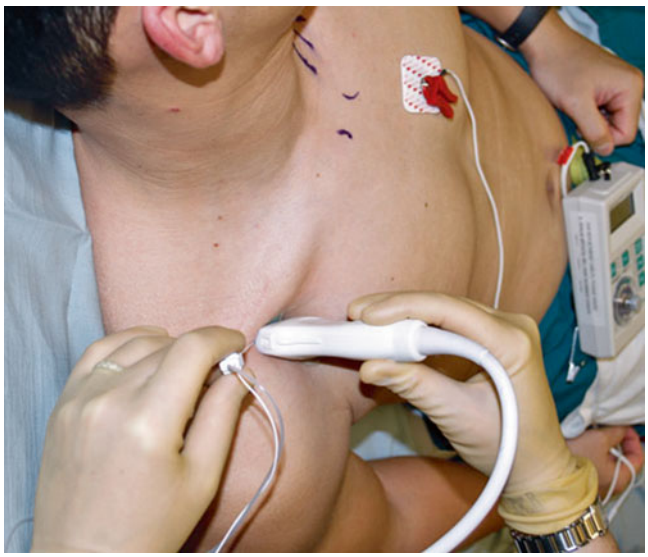

Fig. 27.20 Ultrasound-guided infraclavicular brachial plexus block (With permission from Buckenmaier and Bleckner [71])

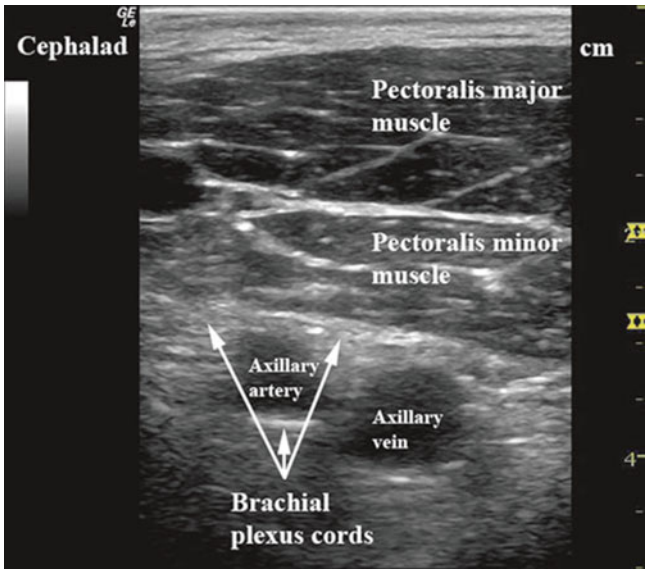

Fig. 27.21 Cords surrounding the axillary artery in the infraclavicular region (With permission from Buckenmaier and Bleckner [71])

injected local anesthetic remains below the pectoralis muscle fascia, local injected above this plane will likely not contribute to the block. Furthermore, assiduous needle technique to maintain the needle under direct ultrasound view throughout the block to avoid vascular puncture is important to avert intravascular injection of local anesthetic or cause bleeding in this difficult to compress region of the body.

Axillary Block of the Brachial Plexus

The axillary block is the most distal block of the brachial plexus (Fig. 27.22). For a number of decades prior to widespread use of stimulation or ultrasound, the axillary block was considered the best block of the brachial plexus because it avoided the most feared complication of pneumothorax [53]. Considerable debate centered on the need to elicit needle paresthesias when performing the axillary block. Selander et al. [54] compared active paresthesia seeking blocks with blocks using only the arterial pulse as a landmark and noted a significant increase in postanesthetic nerve lesions in the paresthesia group prompting them to recommend avoidance of this paresthesia-seeking technique for nerve blocks. As nerve stimulation became more widely accepted, it was determined that paresthesia was related to motor responses using stimulation with currents less than 0.5 mA, which is the threshold current most often used today [55]. Paresthesia quickly fell out of general favor though providers continue to use the technique. Before the widespread availability of ultrasound, considerable debate surrounding the axillary brachial plexus block was common in the medical literature. Authors discussed virtues of single or multiple injection techniques [56, 57] and transarterial [58, 59] and perivascular approaches [60]. Arguably, this debate was fueled by the negligible risks of respiratory compromise secondary to pneumothorax or phrenic nerve blockade that plagued other approaches. Notwithstanding this fact, the axillary brachial plexus block has the highest failure rate of the approaches discussed and was only appropriate for operations of the hand and forearm. As with other blocks of the brachial plexus, the advent of ultrasound technology has taken the "bite" out of much of this controversy with higher success levels and faster block onset being noted with ultrasound-guided axillary block [61, 62].

The anatomy of the brachial plexus at the level of the axilla explains why the block tends to enjoy less success compared to more proximal blocks. The plexus at this point has divided into the five individual nerves of the forearm that quickly diverge as they pass into the arm. The musculocutaneous nerve has already left the plexus at this level as it dives into the belly of the coracobrachialis muscle and must be blocked separately. Successful application of this block for surgery requires a clear understanding of surgical goals. Additionally, sufficient time must be incorporated into the analgesic plan to ensure all involved nerves are blocked or if some key nerves are spared, time is available for supplemental blocks.

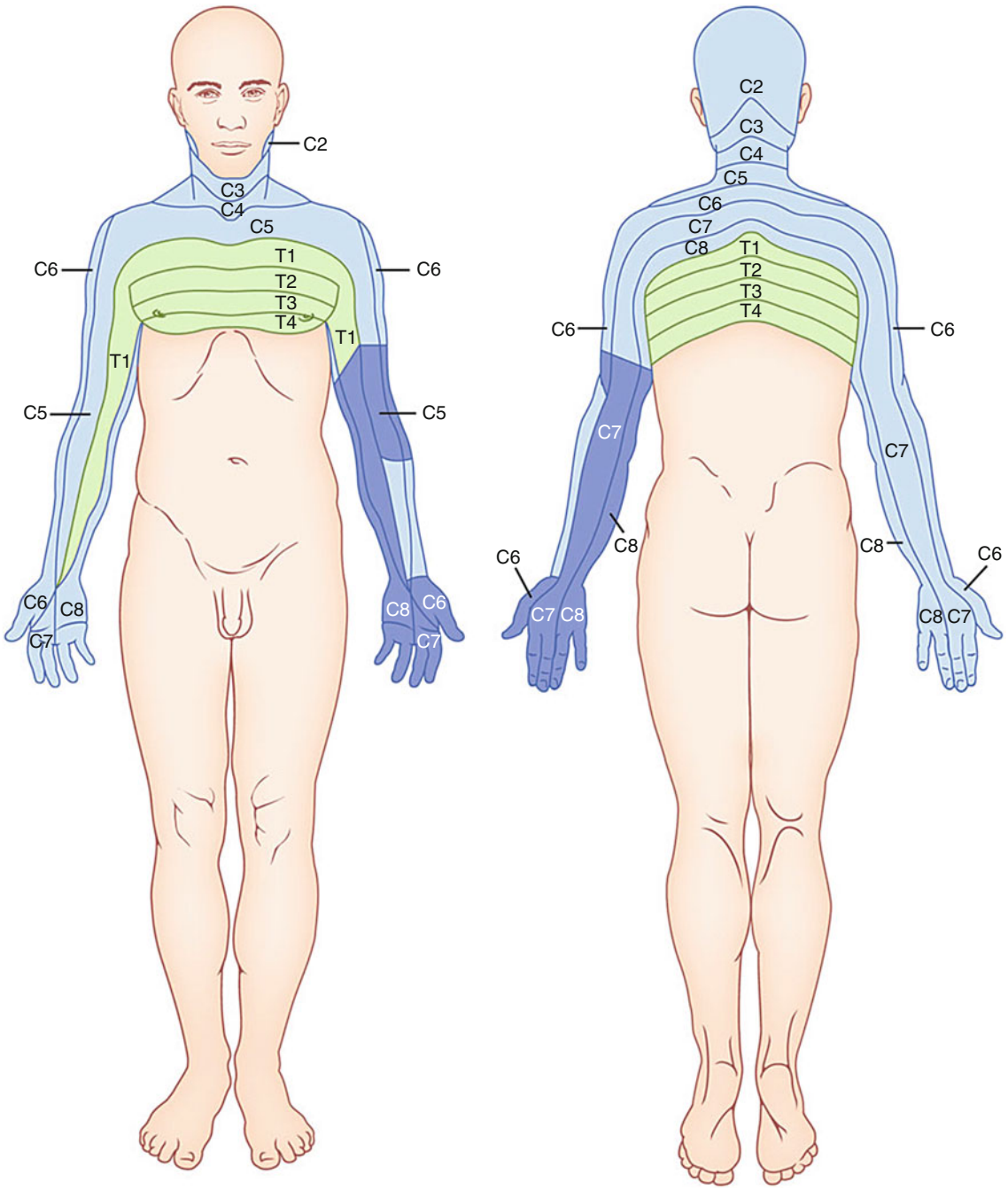

Fig. 27.22 The axillary block is the most distal block of the brachial plexus

Procedure

As noted, there are multiple approaches to the axillary block. The majority depend on the axillary arterial pulse as a landmark. The median, ulnar, and radial nerves can be anesthetized, as a group, with 30–40 mL of local anesthetic, with stimulation resulting in finger flexion and/or thumb opposition at 0.5 mA or less. These nerves can also be individually stimulated and anesthetized, with both methods appearing equally successful. When using stimulation, it has been shown that actual stimulation of the musculocutaneous nerve, in addition to the nerves surrounding the axillary

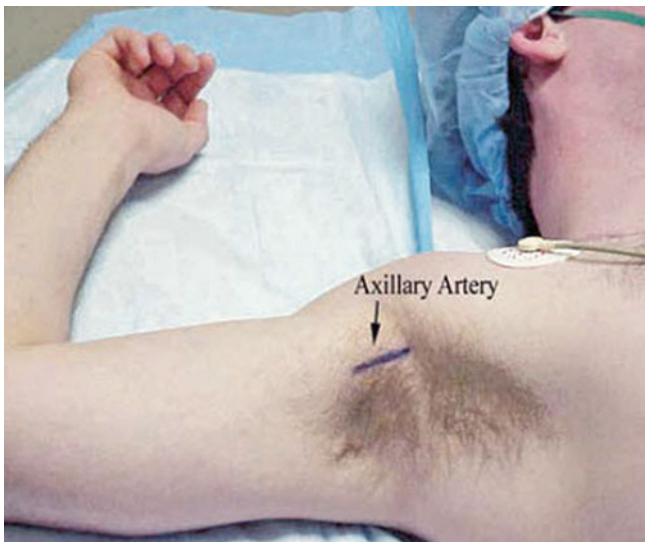

Fig. 27.23 External anatomy for axillary brachial plexus block (With permission from Buckenmaier and Bleckner [71])

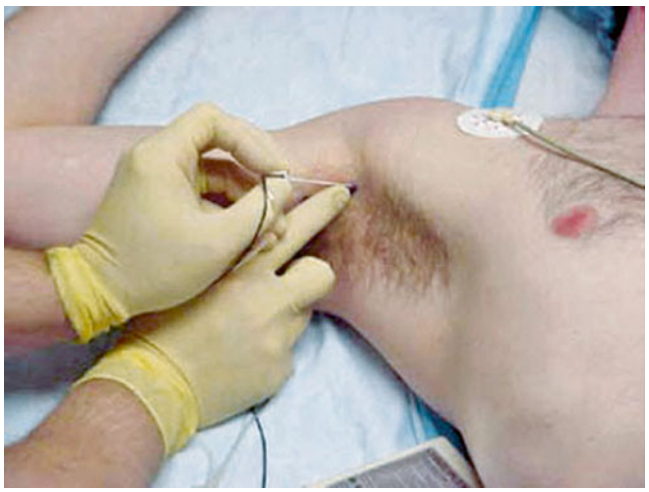

Fig. 27.24 Stimulating needle for axillary brachial plexus block (With permission from Buckenmaier and Bleckner [71])

artery, is more successful than a simple injection into the coracobrachialis muscle [63]. It is important to note that local anesthetic spread within the axillary sheath may not consistently surround all the nerves within the compartment due to connective tissue barriers, positioning effects, or other factors [64]. Allowance for appropriate block setup time and physical examination to determine block success is essential to avoid failed blocks in the operating room. Evidence suggests the application of ultrasound visualization can mitigate the majority of these anatomical issues that can complicate axillary stimulation blocks [65].

The patient is positioned supine with the operative arm abducted and externally rotated (Fig. 27.23). The axillary arterial pulse is palpated proximal in the axilla, and the needle is inserted superior to the axillary artery at a 45° angle (Fig. 27.24). The coracobrachialis muscle for the musculocutaneous block is identified by displacing the biceps muscle laterally while the coracobrachialis muscle is palpable just medical to the biceps. A 22-gauge, 5 cm, insulated needle is used with the stimulator initially set at 1.0–1.2 mA.

For the ultrasound-guided axillary block, the patient is positioned the same as for stimulation. The high-frequency (5–12 MHz) linear probe and a 5-cm, 22-gauge needle are also used. The probe is placed high in the axilla, and the needle is directed from the cephalad end of the probe, in-plane (Fig. 27.25). Typical anatomical relations of the nerve to the axillary artery are as follows: the median nerve is located superficial and slightly cephalad to the artery, the radial nerve is located deep to the artery, and the ulnar nerve is located caudad to the artery (Fig. 27.26). Ultrasound allows dynamic injection of local anesthetic around the axillary artery to ensure adequate nerve exposure to the medication (Fig. 27.27). The musculocutaneous nerve can also be visualized within the substance of the coracobrachialis muscle and blocked separately under direct ultrasound visualization (Fig. 27.28). Once identified, 10 mL of local anesthetic is usually sufficient to block the musculocutaneous nerve.

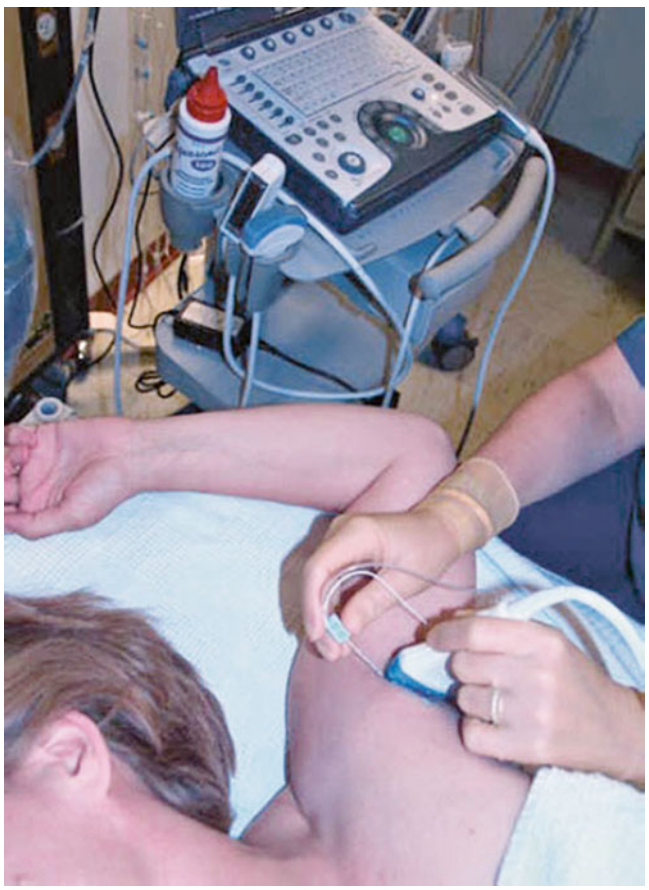

Fig. 27.25 Ultrasound-guided axillary brachial plexus block (With permission from Buckenmaier and Bleckner [71])

Continuous Peripheral Nerve Block

All of the approaches to the brachial plexus are suitable for placement of continuous peripheral nerve block (CPNB) catheters. CPNB techniques provide superior analgesia compared to opioids [66, 67], have relatively few serious complications [68], maintain analgesia long after the trauma or surgical event [69], and can be used safely in the ambulatory patient population [70]. Approaches for placing needles for CPNB are the same as single injection blocks described above. A complete discussion on the placement of CPNB catheters is beyond the scope of this chapter, but technical aspects pertaining to CPNB catheters are available for download at Defense and Veterans Pain Management Initiative website (www.dvpmi.org/maraa-book-project.html) [71].

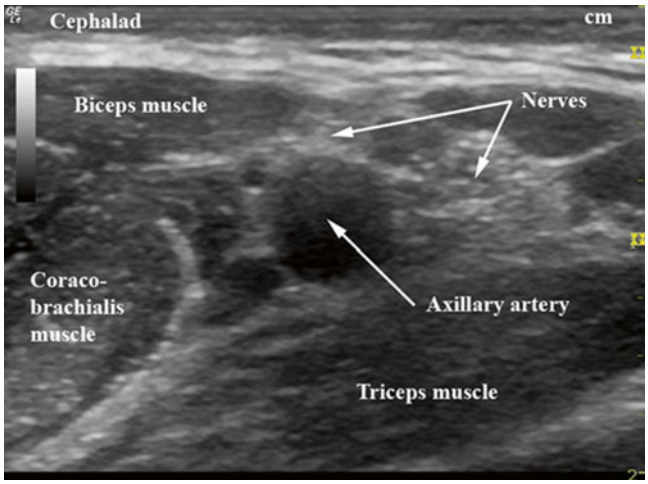

Fig. 27.26 Ultrasound view of the brachial plexus in the axilla (With permission from Buckenmaier and Bleckner [71])

Conclusion

Modern advances in needle, stimulator, and ultrasound technology have greatly enhanced the efficiency and safety of placing needles in proximity to the brachial plexus for anesthesia and analgesia. The ability to provide consistent and complete blockade of the brachial plexus has revolutionized many operations of the upper extremity and enhanced recovery and rehabilitation from countless surgical procedures and traumatic events. Perhaps, one of the best examples of the advantages of regional anesthesia exists currently on the modern battlefield where the pain of traumatic extremity wounds is eased daily through the application of the techniques described here [72]. The clinical study of the anatomy and techniques for brachial plexus block is truly worth the clinician's effort and attention.

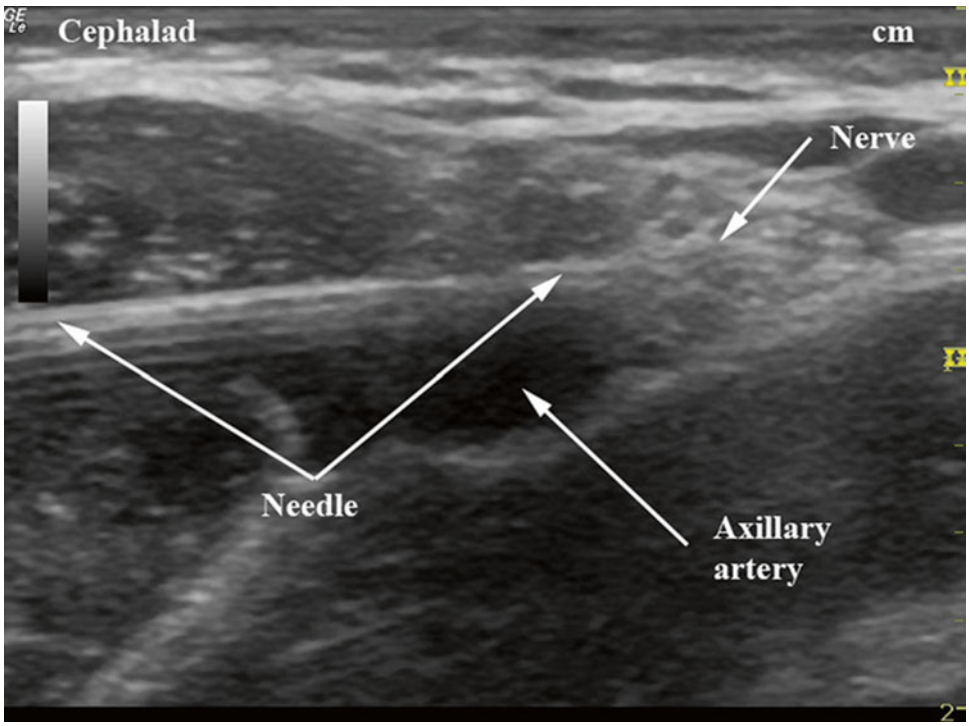

Fig. 27.27 Ultrasound needle placement for axillary brachial plexus block (With permission from Buckenmaier and Bleckner [71])

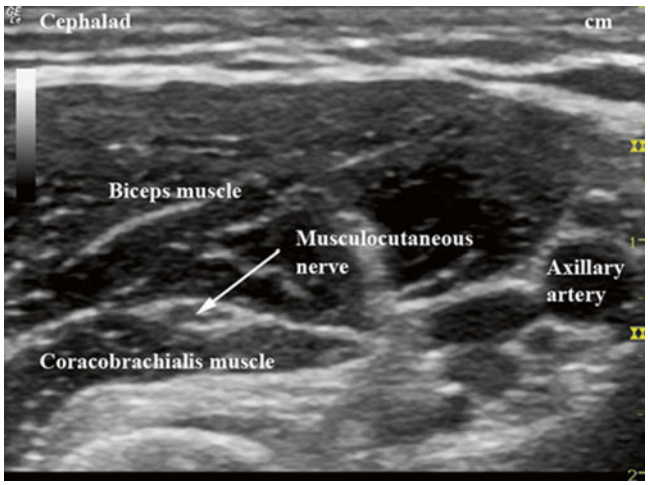

Fig. 27.28 Ultrasound anatomy of the musculocutaneous nerve (With permission from Buckenmaier and Bleckner [71])

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Suprascapular Nerve Block

28

Brian Belnap and Gagan Mahajan

Key Points

- The suprascapular nerve, due to its superficial location in the supraspinous fossa, is a readily accessible nerve that is easy and safe to block.
- The suprascapular nerve block (SSNB) can be a useful tool in the management of a variety of acute and chronic shoulder pain conditions.
- There is evidence that a SSNB may be effective in certain chronic shoulder conditions, e.g., glenohumeral degenerative joint disease, adhesive capsulitis, and rotator cuff degenerative tears.
- While the SSNB has been traditionally performed based on anatomic landmarks, imaging guidance utilizing fluoroscopy, CT, and ultrasound has been described.
- The suprascapular nerve block is a safe and effective procedure and should be considered in the management of postoperative pain following shoulder arthroscopy, scapular fractures, adhesive capsulitis, rotator cuff degenerative tears, and glenohumeral arthritis.

Introduction and Historical Background

The suprascapular nerve, due to its superficial location in the supraspinous fossa, is a readily accessible nerve that is easy and safe to block [1–12]. The suprascapular nerve block (SSNB) has been utilized for well over 60 years to address various causes of shoulder pain. Early advocates of the SSNB reported its usefulness in treating shoulder pain secondary to rotator cuff degenerative tears [13]. Subsequent studies expanded its indications to include conditions such as glenohumeral degenerative joint disease, adhesive capsulitis, and postoperative shoulder pain following arthroscopic surgery [2, 4–11, 14–20]. The technique of the SSNB has evolved over the years. Early reports favored blocking the suprascapular nerve at the suprascapular notch; however, more recent advocates suggest blocking the nerve at the supraspinous fossa to minimize the risk of major complications.

Clinical Applications

The SSNB can be a useful tool in the management of a variety of acute and chronic shoulder pain conditions. For acute shoulder pain, reports have primarily described its use in postoperative pain management following arthroscopic shoulder surgery and shoulder dislocations [2, 6–8, 16, 18]. Ritchie and colleagues performed a prospective, double-blind, randomized controlled trial on 50 patients, half of whom received the SSNB and the other half a placebo injection of saline just prior to shoulder arthroscopy [2]. Both groups were given patient-controlled analgesic systems postoperatively. Compared to the placebo group, in the immediate postoperative period, the SSNB group demonstrated a 51 % reduction in demand and 31 % reduction in morphine use, a reduction in visual analog and verbal pain scores, and a more than fivefold reduction in the incidence of nausea. At 24-h follow-up, the SSNB group had a 40 % reduction in analgesic consumption and a reduction in verbal pain scores at rest and with abduction. Singelyn and colleagues performed a prospective, randomized placebo-controlled trial with 120 patients scheduled for elective arthroscopic shoulder acromioplasty and divided the patients into four groups: placebo, SSNB, interscalene brachial plexus block,

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and intra-articular shoulder injection with local anesthetic. Patients in the SSNB and interscalene brachial plexus block groups were found to have equally and significantly lower pain scores immediately after surgery when compared to placebo and intra-articular shoulder injection, but at 4-h follow-up, patients in the interscalene brachial plexus block group were found to have better pain relief and higher satisfaction scores when compared to all groups. The authors concluded that while the interscalene brachial plexus block was superior, the SSNB was an acceptable alternative in patients considered to be at higher risk for complications from the interscalene brachial plexus block, such as those with chronic obstructive pulmonary disease [18]. One retrospective review of 20 patients who received a SSNB combined with an axillary nerve block prior to arthroscopic shoulder surgery reported excellent results [8]. None of the patients required general anesthesia, opioids, or analgesics during the surgery. Fifteen of the 20 patients required NSAIDs for mild to moderate postoperative pain, but none required opioids. All were discharged the same day and were able to start physical therapy the following day. Randomized controlled trials are needed to confirm the effectiveness of the combined blocks.

One case report suggested that a SSNB may be helpful in addressing pain control for fractures of the scapula, but there were mixed results from case reports as to the effectiveness of the SSNB during reduction from an anterior shoulder joint dislocation [21–23]. A SSNB was not found to be helpful in treating shoulder tip pain following laparoscopic surgery or shoulder pain following thoracotomy, as both are considered to be referred pain to the shoulder [24, 25].

There is evidence that a SSNB may be effective in certain chronic shoulder conditions, e.g., glenohumeral degenerative joint disease, adhesive capsulitis, and rotator cuff degenerative tears [4, 5, 9–11, 14, 15, 17, 19, 23]. Shanahan et al. performed a randomized, double-blind, placebo-controlled trial evaluating 108 shoulders with chronic shoulder pain of at least 3-month duration due to osteoarthritis or rheumatoid arthritis. The SSNB group received 10 ml of 0.5 % bupivacaine and 40 mg of methylprednisolone, while the control group received 5 ml of saline infiltrated subcutaneously, well away from the suprascapular nerve [5]. Using the Shoulder Pain and Disability Index (SPADI), the authors evaluated the patients at 1, 4, and 12 weeks following the procedure. At week one, 67 % of the shoulders in the SSNB group showed at least a ten-point improvement on the overall SPADI score compared with 23 % in the control group. At week four, SPADI scores improved by 66 and 11 % in the SSNB and control groups, respectively. At week 12, SPADI scores improved by 55 and 18 % in the SSNB and control groups, respectively.

Gado and Emery conducted a double-blind study in 26 patients (52 shoulders) with bilateral rheumatoid arthritis, comparing the outcomes of a SSNB with 2 ml of bupivacaine 0.5 % on one side with 2 ml of bupivacaine 0.5 % plus 1 ml (40 mg) of methylprednisolone on the other side [19]. Significant improvements were made with both treatments in regards to pain, stiffness, and range of motion, but overall results favored the bupivacaine-only treatment. Thus, the inclusion of steroid offered no additional benefit.

The SSNB may have some usefulness in treating adhesive capsulitis [3, 4, 14]. Dahan et al. conducted a double-blind, placebo-controlled study on 34 patients with adhesive capsulitis for at least 4 weeks [4]. Patients received a series of three SSNBs at 7-day intervals with either 10 ml of 0.5 % bupivacaine or 10 ml of saline. Two weeks after the final injection, there was a 64 and 13 % reduction in pain (as measured by the McGill-Melzack Pain Questionnaire) for the treatment and control group, respectively. However, there was no statistically significant difference in shoulder range of motion. Jones et al. performed a randomized trial of 30 patients with chronic adhesive capsulitis and compared SSNB using 9.5 ml of 0.5 % bupivacaine and 20 mg triamcinolone with glenohumeral intra-articular joint injection using 20 mg triamcinolone and 4.5 ml of 2 % lidocaine [3]. Doing a SSNB one time was found to produce a faster and more complete resolution of pain and restoration of range of motion than a series of glenohumeral intra-articular injections.

Di Lorenzo et al. performed a prospective, randomized, crossover study on 40 patients who had chronic shoulder pain secondary to rotator cuff tear. Patients were randomized to receive physical therapy alone followed by physical therapy plus SSNB with 10 ml of 1 % lidocaine [17]. Patients who received a SSNB plus physical therapy had decreased severity and frequency of perceived pain, improved compliance with physical therapy, more normal sleep patterns, and increased compliance with their rehabilitation program in comparison to those who received physical therapy alone. Other studies that included chronic shoulder pain from multiple etiologies in their treatment groups also showed benefit from utilizing a SSNB [9, 11, 15, 26].

A few case series reported efficacy using pulsed mode radiofrequency of the suprascapular nerve in the treatment of chronic shoulder pain [27–29]. In their study of 13 shoulders with chronic pain of 3-month duration or longer, Liliang et al. showed that pulsed radiofrequency (38–42 °C and 45 V for 180 s) of the suprascapular nerve effectively treated chronic shoulder pain [28]. At 1- and 6-month follow-up, 76 and 69 % still had >50 % pain relief, respectively. Furthermore, mean SPADI scores at a 6-month follow-up showed a significant decrease along with 82 % of patients decreasing their pain medication requirements. Randomized controlled trials are needed to confirm these and other preliminary findings.

Suprascapular Nerve Anatomy

The suprascapular nerve originates from the upper trunk of the brachial plexus with major contributing fibers from the C5 and C6 nerve roots [11, 17, 30]. It travels posteriorly and laterally toward the supraspinous fossa and enters via the suprascapular notch (Fig. 28.1). Once it reaches the notch, it travels inferior to the superior transverse scapular ligament and laterally toward the base of the coracoid process where it splits into sensory and motor fibers. The motor fibers supply the supraspinatus muscle and then curve around the spinoglenoid notch to terminate in the infraspinatus muscle. The sensory fibers supply the acromioclavicular and glenohumeral joint capsules and the conoid, trapezoid, and coracoacromial ligaments. It is generally well accepted that the supraspinatus nerve provides approximately 70 % sensory innervation to the shoulder joint [11, 30].

Suprascapular Nerve Block Technique

The technique of the SSNB can be performed utilizing either a direct or indirect technique. The direct technique involves blocking the suprascapular nerve at the suprascapular notch, just as the nerve enters the supraspinous fossa [1, 21, 32–34]. The patient is placed in a seated position with the hands resting on the thighs. A line is drawn along the scapular spine from the tip of the acromion to the medial border of the scapula. After identifying the inferior angle of the scapula, a second line bisecting this angle is drawn and extended upward as far as the superior border of the scapula, intersecting the line drawn along the scapular spine and forming four quadrants (Fig. 28.2). The angle of the upper outer quadrant is bisected, and a point is marked on the line 1.5 cm from the apex of the angle. After the area is prepped and draped, the needle is advanced perpendicularly until the scapula is contacted and then redirected until it slides into the suprascapular notch.

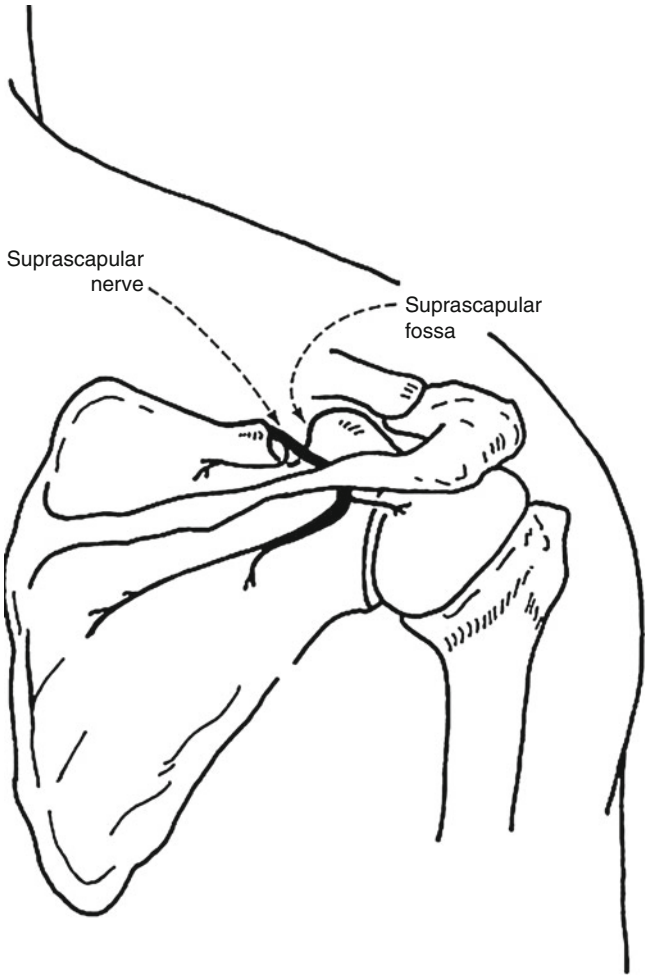

Fig. 28.1 Anatomy of the suprascapular nerve (From Waldman [31], with permission)

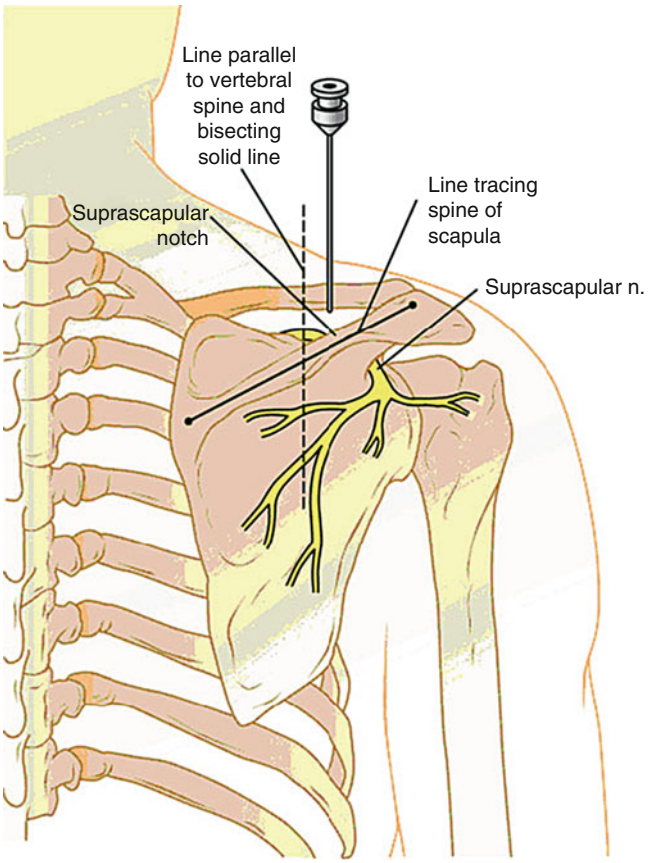

Fig. 28.2 Suprascapular nerve block. A *line* is drawn along the scapular spine and then bisected by a *second line* parallel to the vertebral spine. The entry point is 2–3 cm into the upper outer quadrant. The needle is directed from the top to avoid deep entry into the suprascapular notch, which could risk pneumothorax (From Rathmell et al. [35], with permission)

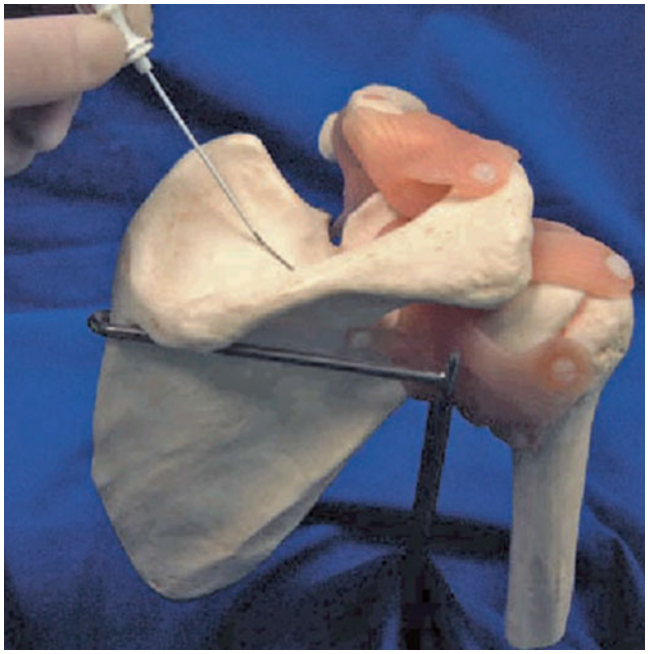

Fig. 28.3 The Meier technique (From Meier et al. [9], with permission)

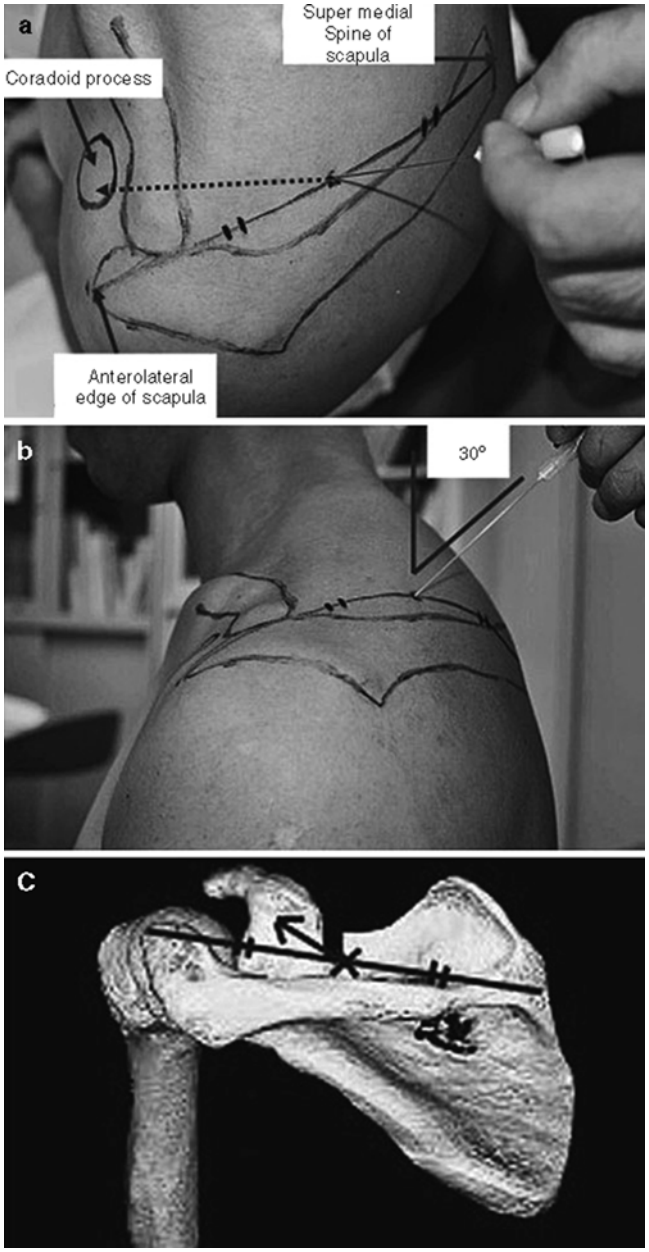

Fig. 28.4 (**a**) The needle is inserted to contact the bone toward the coracoid process from the midpoint of the anterolateral edge of the acromion and super medial angle of the scapular spine. (**b**) The needle is inclined at a 30° angle toward the dorsal direction from the axis of the body and inserted until it reaches the base of the coracoid process. (**c**) The needle can be inserted toward the sensory branch of the suprascapular nerve passing the base of the coracoid by the method shown in panels (**a**, **b**) (From Matsumoto et al. [6], with permission)

At this point, the needle is slightly withdrawn, aspiration is performed to rule out intravascular location, and local anesthetic is injected [1, 14]. Some authors describe utilizing a nerve stimulator to visually confirm contraction of the supraspinatus and infraspinatus muscles to verify proximity to the suprascapular nerve prior to placing the injectate. Keratas and Meray utilized EMG guidance with the direct technique to confirm proximity to the suprascapular nerve and reported superior results to traditional methods [14]. While the theoretical advantage of the direct technique includes placing the injectate immediately next to the suprascapular nerve as it emerges from the suprascapular notch, there is a slight increased risk of pneumothorax.

In more recent years, some investigators have advocated various versions of an indirect technique that involves placing the needle away from the suprascapular notch to avoid the risk of pneumothorax [36]. Dangiosse et al. described blocking the suprascapular nerve by injecting the local anesthetic into the floor of the suprascapular fossa [11]. The needle is introduced into the fossa 1 cm cephalad to the middle of the spine of the scapula, parallel to the blade, and until the bony floor of the supraspinous fossa is reached. Meier et al. described another variance to the indirect technique by drawing a line from the medial end of the spine of the scapula to the lateral posterior border of the acromion. After halving this line, the injection site is established 2 cm medial and 2 cm cranial from this point (Fig. 28.3). Using a 22-gauge, 6-cm needle, and nerve stimulator, the needle is advanced in a lateral direction on the floor of the fossa at an angle of 75° to the skin surface and toward the head of the humerus. Based on cadaveric studies showing the sensory branches of the suprascapular nerve course along the base of the coracoid process, Matsumoto et al. proposed blocking the nerve fibers at this location. The insertion point is the midpoint of the anterolateral angle of the acromion and the medial edge of the scapular spine. The needle is inclined at a 30° angle toward the dorsal direction from the axis of the body and inserted until it reaches the base of the coracoid process (Fig. 28.4).

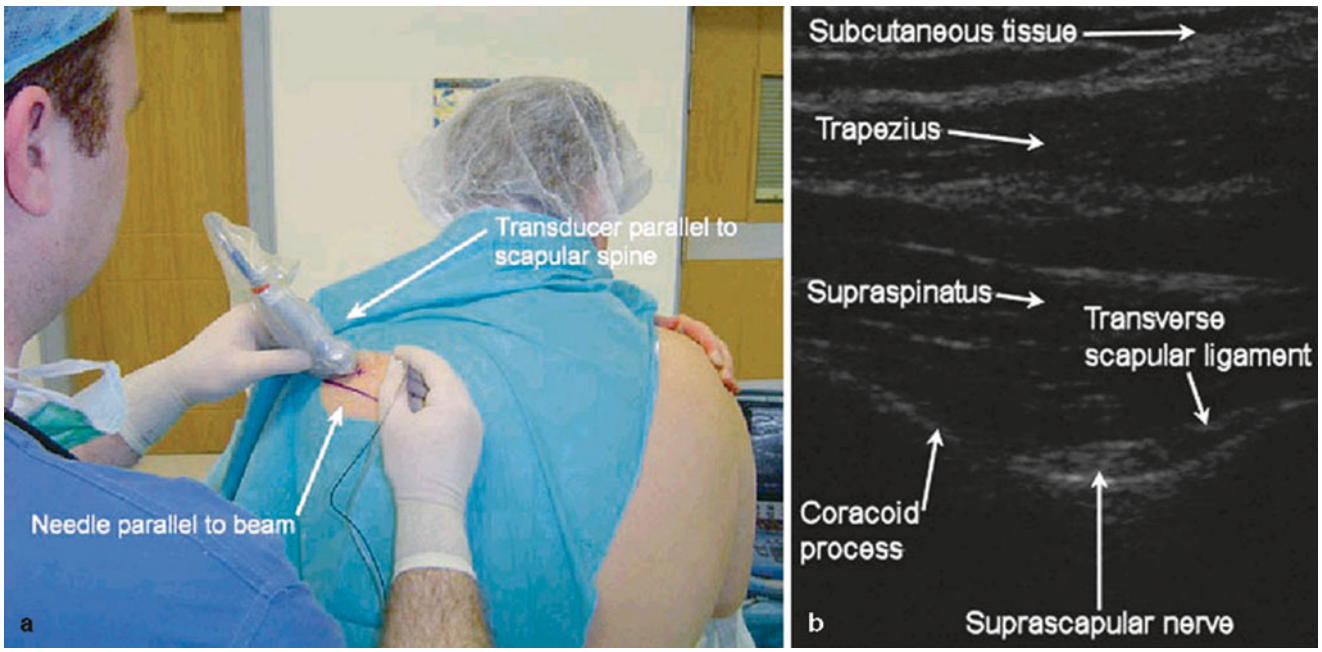

Fig. 28.5 (**a**) Ultrasound transducer and needle orientation for the ultrasound-guided suprascapular nerve block. (**b**) Transverse view of suprascapular fossa and scapular notch with a SonoSite ultrasound system and a 6–13-MHz linear transducer (From Harmon and Hearty [38], with permission)

Preliminary results in eight patients experiencing severe pain after rotator cuff repair surgery resulted in effective pain relief. The average postoperative VAS scores of the eight patients were 5.4 ± 2.7. Notably, the volume of injectate varies in most reports from 5 to 15 ml while performing either the direct or indirect technique although most reported using a volume of 10 ml of local anesthetic.

While the SSNB has been traditionally performed based on anatomic landmarks, imaging guidance utilizing fluoroscopy, CT, and ultrasound has been described [26, 31, 37, 38]. One author recommended using fluoroscopy to identify the suprascapular notch when performing the direct technique, especially when it is difficult to locate the suprascapular notch via the anatomic approach. The patient should be placed in the prone position with the fluoroscope slightly lateral to midline at the T2–3 level with a slight cephalocaudad tilt [31]. In a non-randomized controlled trial of 40 patients with chronic shoulder pain, Schneider-Kolsky et al. performed a CT-guided SSNB with a direct approach and reported improvement in SPADI scores at 30 min, 3 days, weeks, and 6 weeks post injection [26]. While these results were encouraging, Shanahan et al.'s randomized controlled trial failed to show any difference in pain, disability, or patient satisfaction between CT-guided and traditional nonimage-guided SSNBs [37]. Two case reports reported favorable results using ultrasound guidance. Harmon et al. described first placing the ultrasound transducer in a transverse orientation over the scapular spine (see Fig. 28.5) [38]. The transducer is then gradually moved in a cephalad and slightly lateral direction until the suprascapular notch and transverse scapular ligament are identified. The suprascapular nerve lies just inferior to the ligament. However, a subsequent cadaveric study revealed that the structure previously identified under ultrasound guidance as the transverse ligament was the fascia layer of the supraspinatus muscle [39]. Therefore, an ultrasound-guided SSNB appears to be an indirect technique with the injectate placed near the nerve in the suprascapular fossa, rather than a direct technique in the suprascapular notch as previously believed.

The SSNB is considered a safe technique and is associated with few side effects and complications [1–12]. While pneumothorax is a possible serious complication, the incidence is less than 1 %. Furthermore, this complication has only been described with the direct technique in which the end of the needle is placed directly in the suprascapular notch and approximates the superior aspect of the lung [36]. In order to minimize this complication, Parris and colleagues suggest internally rotating the ipsilateral arm and placing the hand on the opposite shoulder in order to elevate the scapula away from the chest wall [12]. Most other complications described in the literature have been transient in nature and similar to minor complications associated with most other kinds of interventional procedures [1, 3–6, 9, 11, 12]. Goldner reported performing over 1,000 direct SSNBs, with the only occasional minor complication being temporary postinjection tenderness [34]. Dahan et al. reported performing over 2,000 indirect SSNBs and reported no significant complications other than a few vasovagal reactions and postinjection tenderness [4].

Conclusion

The suprascapular nerve block is a safe and effective procedure and should be considered in the management of postoperative pain following shoulder arthroscopy, scapular fractures, adhesive capsulitis, rotator cuff degenerative tears, and glenohumeral arthritis [1–12, 14–19]. Its low rate of complications and ease of use in the office setting make it a very useful procedure. It remains unclear whether the direct or indirect approach to blocking the suprascapular nerve is superior and whether the use of a nerve stimulator, EMG, or imaging guidance is essential to maximizing the effectiveness of the block. Clearly, recent trends have favored utilizing the indirect technique to minimize the risk of pneumothorax. Further randomized controlled trials are needed to compare the efficacy of the various SSNB techniques. The use of ultrasound guidance for SSNB is an area of particular interest for further studies. Ultrasound involves no radiation exposure to the patient or clinician and may facilitate an equally or more effective block as compared to other techniques. Furthermore, lower volumes of local anesthetic can be used due to the ability to visualize and inject immediately near the suprascapular nerve.

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Intradiscal Annuloplasty for the Treatment of Discogenic Pain

29

Leonardo Kapural

Key Points

- Establishing diagnosis of discogenic pain remains difficult secondary to lack of studies explaining clear mechanisms of pain generation and its nonspecific clinical features.
- Provocation discography remains the only available test linking the morphologic abnormalities seen on MRI with clinically observed pain, and its predictive value can be improved using a strict guideline.
- Several new minimally invasive intradiscal techniques for discogenic LBP control have been introduced, but sufficient clinical evidence is lacking.
- DiscTRODE annuloplasty and conventional nuclear RF seem to be ineffective in reducing pain and improving functional capacity in patients with discogenic LBP.
- IDET and intradiscal biacuplasty can provide positive therapeutic effect in well-selected patient groups.
- Strict clinical selection criteria significantly improve results of annuloplasty for lower back discogenic pain.
- Patients with presence of one or two levels of disc degeneration on magnetic resonance imaging (MRI) and one or two disc levels positive on provocation discography are appropriate candidates for annuloplasty.
- Serious complications following percutaneous interventional procedures for back or leg pain are infrequent.

Introduction

The term discogenic pain refers to pain arising from the disc itself. Discogenic pain is cited as the most common cause of chronic low back pain, accounting for approximately 26–39 % of patients with such pain etiology [1]. Internal disc disruption (IDD) is the most common diagnosis leading to chronic low back pain and one of the major causes of chronic neck pain [1, 2]. Discogenic pain is a significant medical challenge, in terms of its clinical, social, economic, and public health implications. An extensive body of literature suggests that discogenic pain is likely to be multifactorial. The most significant risk factors are genetic inheritance, environmental influences, and lifestyle choices. Although available literature supports hypothesis that the intervertebral disc is an independent chronic pain generator, research related to the epidemiology of discogenic pain is still in its formative stage [1–3].

Establishing Diagnosis of Discogenic Pain

Establishing diagnosis of discogenic pain remains difficult secondary to its nonspecific clinical features. Patient frequently describes more typical features of such pain as being persistent low back, groin, and/or leg pain that worsens with axial loading and improves with recumbency. These features alone, however, are frequently insufficient to establish an accurate diagnosis as many factors contribute to the complexity of this condition. These include other potential sources of pain in the spine causing symptoms of similar distribution area and character, present psychosocial factors and clear limitations of available diagnostic tools. In addition, different specialties dealing with the lower back pain employ various diagnostic approaches without clear consensus in diagnosing discogenic pain.

In the absence of signs or symptoms related to neurologic deficit, imaging should be utilized when the pain remains persistent despite continuous conservative management. MRI (magnetic resonance imaging) is frequently employed imaging test to evaluate intervertebral discs. Three changes detected on MRI could be of interest: low signal intensity of the disc on T2 weighting, high-intensity zone (HIZ), and vertebral and/or end-plate changes. Disc degeneration with

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reduced water content within the disc produces a low signal intensity, or "black disc," on T2-weighted images. Such change is associated with disc degeneration and correlates poorly with the presence of discogenic pain versus any other pain in the lower back. The high-intensity zones (HIZ) are associated with presence of annular fissures within the disc, but it is not clear if they correlate with the presence of discogenic pain. Positive predictive value of HIZ to suggest that the pain origin is within the disc could be as high as 87–90 % [4–6]. HIZ are, however, present in a large number of asymptomatic discs as well (25–39 %) [7]. In addition, degenerative disc disease is often associated with nearby bone sclerosis, so-called modic type I–III changes [8, 9]. Those could be more prevalent in patients with low back pain and positive discography. Modic changes appear to have a high sensitivity, but low specificity for discogenic pain [10].

To date, provocation discography is the only available method linking the morphologic abnormalities seen on MRI with clinically observed pain, and its predictive value has been repeatedly questioned mainly as a result of reported higher false-positive rates [11–13]. Based on currently published data, it is difficult to draw any conclusion on predictive value of MRI findings and the presence of concordant pain on provocation discography. There are several reasons for that: defining disc degeneration on MRI may vary significantly, and the criteria used to establish presence of discogenic pain during provocative discography are still evolving [14].

Once the diagnosis of discogenic pain has been suggested, the next challenge involves instituting an effective therapy. Traditionally, surgical approaches of lumbar fusion with instrumentation and various disc arthroplasties were utilized. Common characteristic of those surgical approaches is an extensive surgery in the lower back with prolonged recovery interval and questioned efficacy in treating pain of discogenic origin. In an effort to provide percutaneous, minimally invasive treatment for discogenic pain in patients with relatively well-maintained disc height, several therapies were developed utilizing heat in the annulus fibrosus (annuloplasty procedures). Such therapeutic modalities have been used despite a somewhat poorly understood relationship between the therapeutic effects and, if any, histologic changes observed [15–18]. Most clinicians believe that the likely mechanism of pain relief by annuloplasty is denervation of the tissue or destruction of the nociceptors and less likely any alteration of the collagen fiber structure in the annulus, like collagen denaturation and coalescence [15–18]. Three annuloplasty technologies still available in clinical practice are intradiscal electrothermal therapy (IDET; Smith & Nephew, London, UK), discTRODE (Radionics Inc., Burlington, MA), and intradiscal biacuplasty (Baylis Medical, Montreal, Canada).

Mechanisms of the Pain Relief by Annuloplasty

Disc degeneration is associated with significant changes within the disc nucleus and annulus (Fig. 29.1a, b), like delamination or tearing of the lamellar layer of the annulus and dehydration and loss of nuclear material. Those physical changes are frequently associated with biochemical and cellular changes. Production of inflammatory cytokines, including

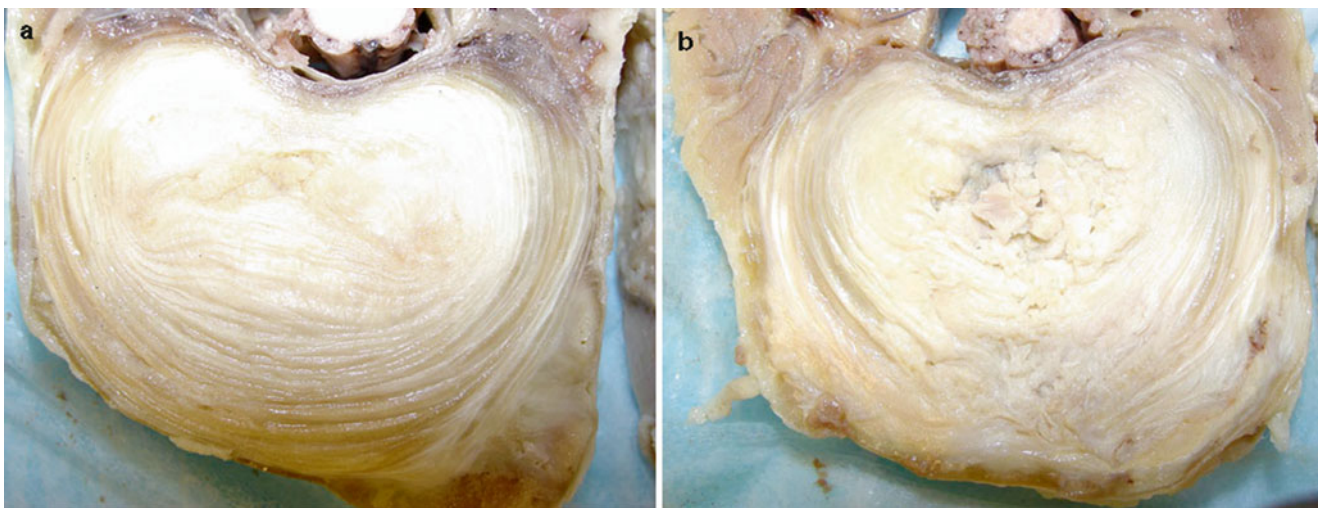

Fig. 29.1 Degenerative changes in the lumbar intervertebral discs. Human lumbar spine fixed in 10 % neutral buffered formalin for 1 week is shown. Individual lumbar segments were prepared, taking care to preserve the posterior elements. (**a**) Mostly intact annulus with minor lamellar disorganization in a minimally degenerated disc with the absence of fissuring. (**b**) Lamellar disorganization in a degenerated lumbar disc with presence of radiating tear extending to the outer 1/3 of the annulus. There may be some loss of the nucleus on this gross dissection of the human spine (With permission from Baylis Medical Company © Copyright)

tumor necrosis factor-α (TNF-α), nitric oxide, and matrix metalloprotineases (MMPs), is increased [19, 20]. Extensive vascularization in degenerated disc, mostly along annular fissures, may facilitate introduction of these inflammatory cytokines [19]. Nociceptors that are normally limited to the outer third of the annulus penetrate further into the degenerated disc along neovascularization of the areas around the newly formed fissures [21–24]. Immunohistochemical studies confirmed nociceptive origin (C- and Aδ-fibers) of newly formed neural tissue, thought to be responsible for the presence of discogenic pain [20, 23]. In addition, it is possible that inflammatory cytokines provide further sensitization of these ingrown nerves. Therefore, destroying these nociceptive fibers may eliminate, at least partially, possible source of the lower back pain.

Temperatures reached during biacuplasty or IDET may be sufficient to cause nerve destruction which occurs at 42–45 °C or higher [25–27]. However, evidence from the basic science studies to demonstrate neuroablation by delivered heat as the mechanisms of action for discogenic pain relief remains unavailable until this date.

The temperature profiles of the latest intradiscal heating procedure and one with most promising clinical data, intradiscal biacuplasty, were investigated in both porcine and human cadaveric lumbar discs. Histological examination could not detect signs of tissue degradation due to heating or changes in the collagen structure in both degenerated and nondegenerated intervertebral discs [28, 29].

Intradiscal Electrothermal Therapy (IDET)

The first effective minimally invasive therapeutic alternative to fusion surgery or arthroplasty came in the form of intradiscal electrothermal therapy (IDET) [30, 31]. IDET is performed using a thermal catheter, resistive coil (SpineCATH, Smith & Nephew Endoscopy, Andover, MA), that is percutaneously introduced to the interface between the posterior annulus and nucleus under multiplanar fluoroscopic control (Figs. 29.2a–d and 29.3a, b).

There are dozens of prospective case series and reports and a single, randomized, controlled trial that provided data on the IDET efficacy ([30–41]; Table 29.1). However, one, randomized, controlled trial and several published case series failed to demonstrate any clinical benefit of the IDET procedure [37, 41]. The first randomized, sham-controlled trial provided class I evidence that IDET is an efficacious annuloplasty procedure in properly selected patients [36]. It seems that IDET could provide rather long-term pain relief as evidenced at 1-year and 2-year follow-ups ([30–41]; Table 29.1). When used in general population of the patient with lower back pain, it seems that those with overlapping inflammatory arthritides or nonspinal conditions that may mimic lumbar discogenic pain and those patients with multilevel degenerative disc disease do not benefit from the IDET annuloplasty [39, 42, 43]. It seems that the variation in patient selection and provided heating techniques are thought to account for most of the differences seen in clinical results [30, 31, 36, 37, 39, 41–50]. Pauza and colleagues' use of provocation discography, rather than MRI/discography combined criteria for the patients enrollment, may have contributed to high number of patients needed to treat – five to achieve >75 % improvement in one patient [36]. Overweight patients [42] and patients receiving workers' compensation benefits [43, 50] represent additional patient subsets that are unlikely to benefit from the IDET.

Technique

The IDET procedure is performed under local anesthesia and mild intravenous sedation in sterile conditions. IV antibiotics, most frequently 1 g of cefazolin or 1 g of vancomycin, should be given 30–60 min before the procedure. Patients are positioned prone using midabdomen support to correct for the lumbar lordosis. Using local anesthesia, a 17-gauge needle is inserted under fluoroscopic guidance into the targeted disc. Through that same needle, a catheter with thermal resistive coil is navigated until positioned appropriately within the disc. The key is to position such catheter across all of the semicircumference delineated by the interphase of the posterior annulus and nucleus (Fig. 29.3a, b). The thermal resistive coil generates gradual rising temperature inside the disc up to 90 °C in 0.5 °C increments. The temperature is then maintained at 90 °C for 4 min according to manufacturer protocol (Smith & Nephew, London, UK). Patient is then brought to the recovery area and discharged home with instructions regarding functional rehabilitation program. The goals of such rehabilitation after the annuloplasty are pain control and reduction of inflammation, providing early supervised stretching and mobilization of tissue. In order to achieve functional restoration, addressed are extensor muscles, which may be deconditioned, as well as abdominals, trunk rotator, and trunk/hip flexors. During that time interval of 4–6 weeks, manual manipulative therapy is avoided.

Intradiscal Biacuplasty

Intradiscal biacuplasty employs bipolar RF electrodes to heat posterior annulus of the intervertebral disc. Although recently described, it could be the most promising of all annuloplasty methods [33, 34, 51]. This method works specifically by concentrating RF current between the active electrodes placed on the tip of two straight probes (Fig. 29.4a, b). The larger area of the posterior annulus is ablated by internally cooling

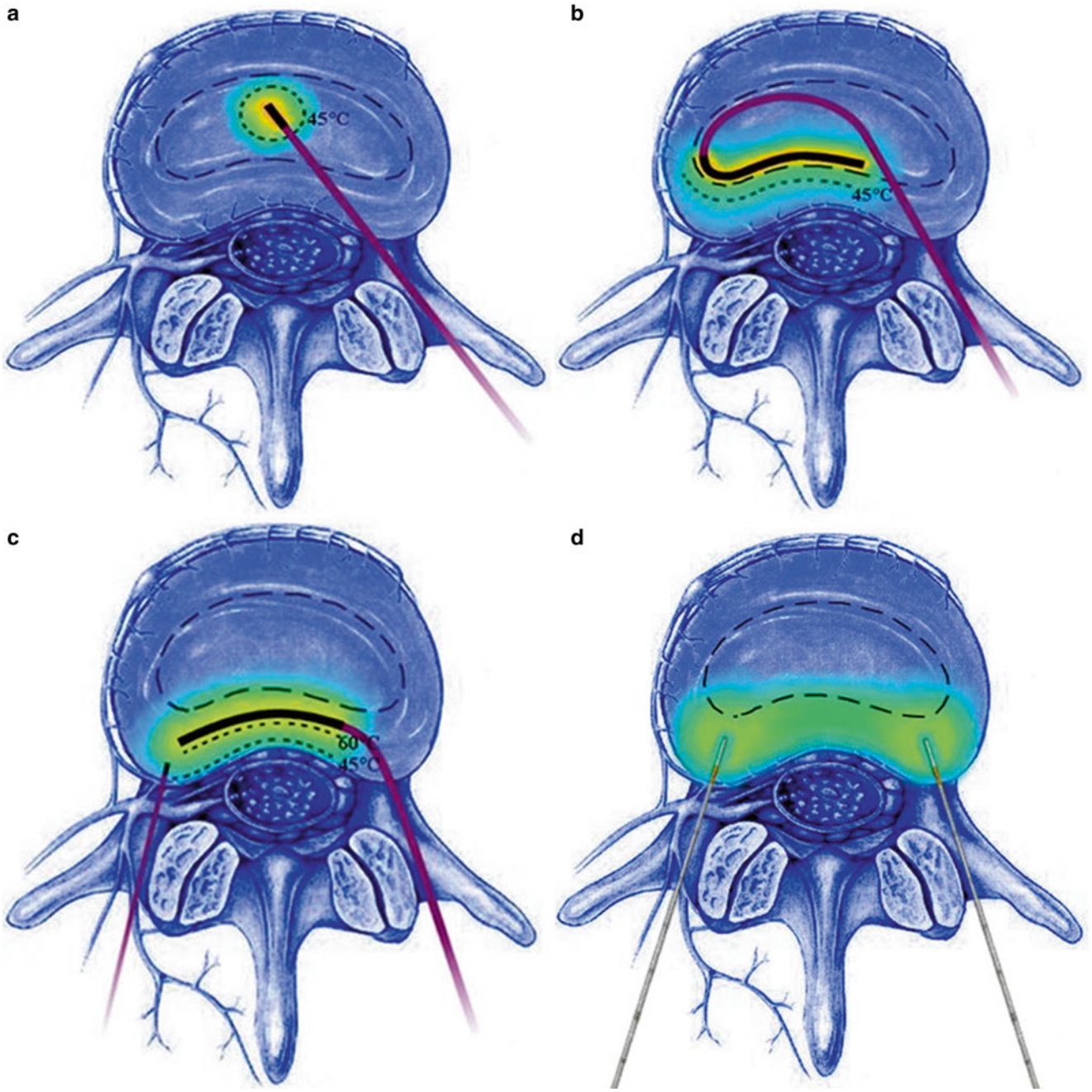

Fig. 29.2 Diagram of the heat-delivering electrodes within the intervertebral disc and approximate temperature that can be produced during four different minimally invasive procedures aimed to treat discogenic pain. (**a**) Intranuclear radio frequency. The RF electrode is positioned in the middle of the nucleus. Temperature achieved may not be sufficient to denervate posterior annulus when the heat source is inside the nucleus. (**b**) Intradiscal electrothermal therapy (IDET). Resistive coil is placed between the annulus and nucleus and along the posterior annulus. Optimal temperature dissipates several millimeters and may affect a very limited area of the annulus. (**c**) DiscTRODE™ (radio-frequency electrode) is positioned within the posterior annulus. (**d**) Intradiscal biacuplasty. Radio-frequency electrodes are positioned inside the posterior annulus to achieve optimal bipolar heating and possible nociceptor denervation (With permission from Baylis Medical Company © Copyright)

the electrodes [29, 52] (Figs. 29.2a, b and 29.4a, b). Two intradiscal electrodes are first placed bilaterally in the posterior annulus of the intervertebral disc, and then generator temperature is increased gradually over a period of 10 min to 50 °C with final heating for another 5 min. Additional two monopolar lesions over 2.5 min are then produced bilaterally at 60 °C in order to extend lesion laterally and to achieve appropriate temperature increase to extended area of posterior annulus. During this time, the patient should be awake and communicating to the physician.

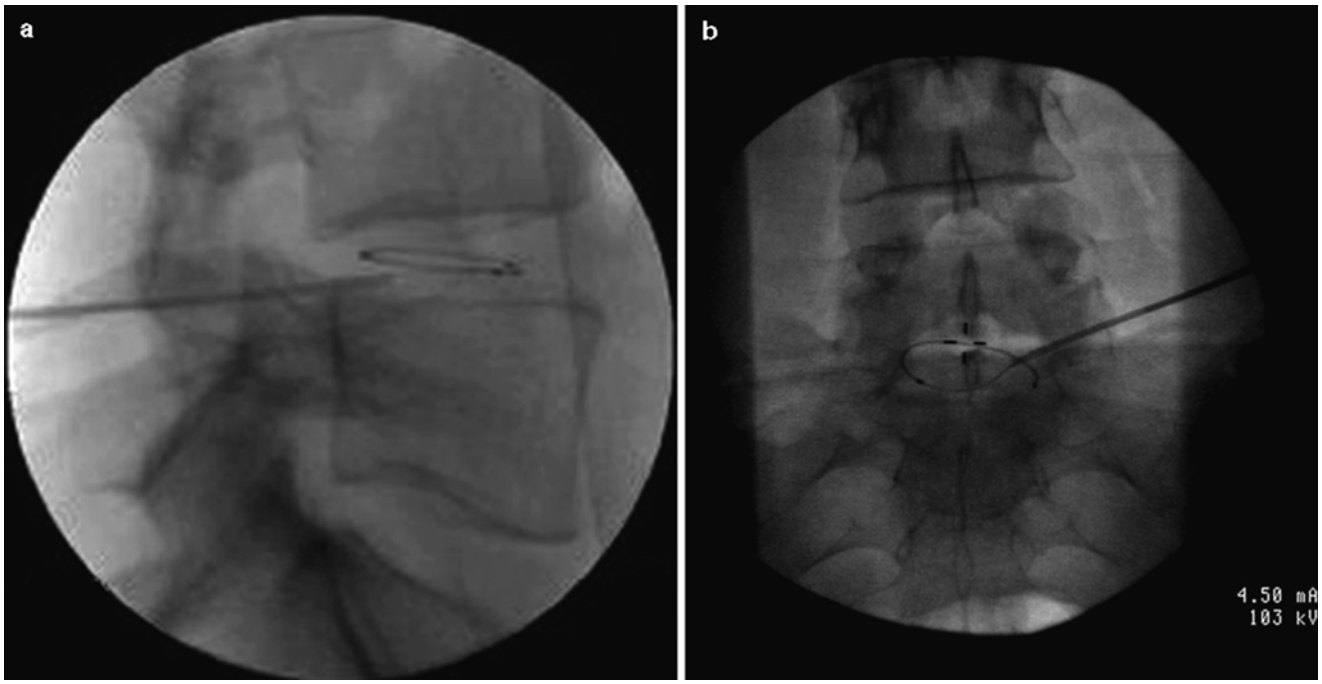

Fig. 29.3 The fluoroscopic views of the final electrode position during IDET procedure used for the treatment of discogenic pain. IDET resistive coil properly positioned just between annulus and nucleus of the lumbar intervertebral disc. (**a**) Lateral view of the final coil position within L4–5 lumbar disc. (**b**) Anterior view of the IDET coil when cranial tilt of the fluoroscope is used to clearly show a full circle of the coil placed inside the disc at the interphase between the annulus and nucleus (With permission from Baylis Medical Company © Copyright)

Table 29.1 Pertinent studies on various types of annuloplasties when used for the treatment of discogenic lower back pain

Author name	Year	Type of intervention	Indications of procedure	Patients (#)	Type of study	Outcomes	Complications	Conclusions
Assietti et al. [32]	2010	IDET	Single-level DDD and discogenic pain, >60 % disc height	50	Prospective	VAS 68 % decrease, ODI from 59.0 ± 7.6 % to 20.1 ± 11 % at 24 m	None	Safe and effective
Kapural et al. [33, 34]	2008	Biacuplasty	Single- or two-level DDD and discogenic pain, >50 % disc height	15	Prospective pilot	7 of 13 >50 % VAS, ODI to 17.5, and SF-36-PF from 51 to 67 at 12 m	None	Safe and effective
Kvarstein et al. [35]	2009	DiscTRODE™	Chronic LBP, discogenic pain	23	Prospective randomized, double-blind	No improvement study or sham at 12 m	None	Do not recommend use of discTRODE
Pauza et al. [36]	2004	IDET	DDD and discogenic pain, >80 % disc height	64	Randomized sham-controlled prospective	56 % >2 VAS change, 50 % patients >50 % relief at 6 m	None	Safe and effective
Freeman et al. [37]	2005	IDET	Multilevel DDD, workers' comp included		Randomized sham-control prospective	Oswestry unchanged	None	Ineffective
Jawahar et al. [38]	2008	IDET	DDD and discogenic pain, >80 % disc height, WC patients	53	Prospective	VAS reduction 63 %, ODI 70 %	None	Useful in carefully selecting WC patients
Kapural et al. [39]	2004	IDET	Single- or two-level DDD and discogenic pain, >50 % disc height vs. multilevel DDD	34	Prospective matched study	1,2-DDD >50 % improvement in VAS and PDI	None	IDET procedure effective only in one- or two-level DDD
Karaman et al. [40]	2011	Biacuplasty	Single- or two-level DDD and discogenic pain., >50 % disc height	15	Prospective observational	78.6 % >10 points Oswestry; >2 points VAS	None	Safe and effective

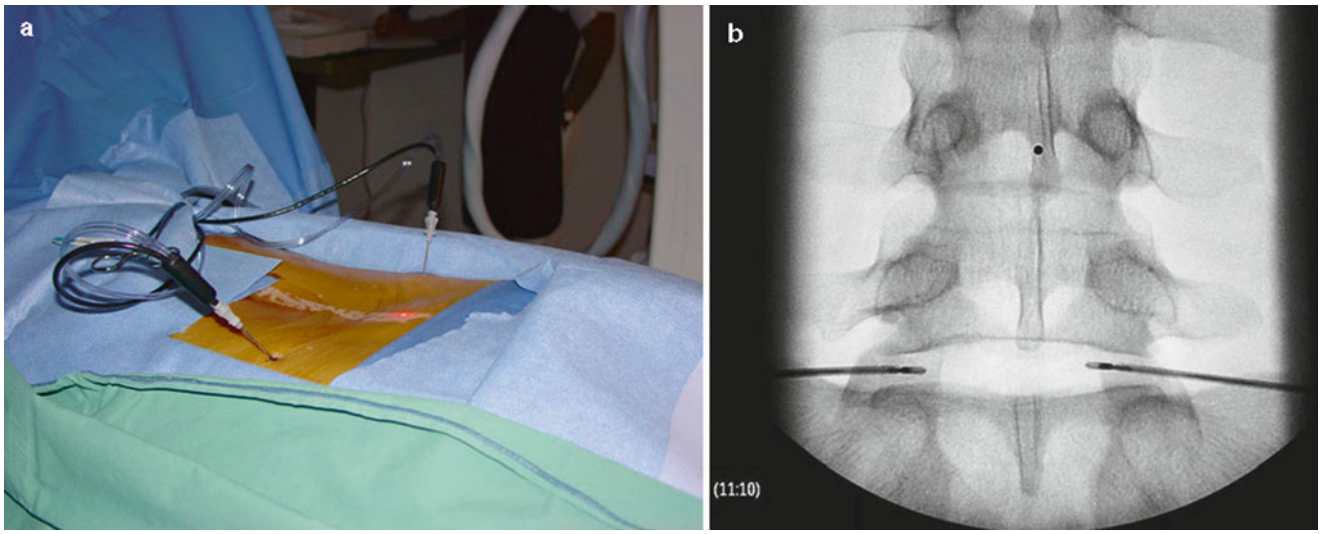

Fig. 29.4 Intradiscal biacuplasty electrodes properly positioned in bipolar fashion via introducers inside the patient's back (**a**) and shown in anterior-posterior view inside L5–S1 lumbar intervertebral disc (**b**). Note that the electrodes are positioned in the middle of the disc and away from the end plates and bony structures (With permission from Baylis Medical Company © Copyright)

The first case report on biacuplasty documented significant improvements in functional capacity and VAS pain score at 6 months following the procedure with no perioperative complications. Later, three prospective case series involving 8, 15, and 15 patients, respectively, were completed, during which significant pain relief and improvement in the function were achieved at 3, 6, and 12 months after biacuplasty [33, 34, 40, 53]. In the European case series [53] involving eight patients, there was an average of 50 % pain reduction at 3 months with an overall good patient satisfaction. No patients reported any post-procedural pain, often associated with other therapies, and there were no reported complications. During the prospective pilot study involving 15 patients, reported were improvements in several functional capacity measures after the procedure with no complications [33, 34]. Improvements in Oswestry index were sustained from 23.3 at baseline to 16.5 points at 1 month and stayed same at 12 months. The prospective, randomized sham study is being currently completed in order to accept or refute results achieved during pilot study.

The latest prospective, observational study showed that 78.6 % of the patients had Oswestry score improvement of 10 points or more with 57 % of the patients having 50 % or more pain relief at 6 months after the procedure [40]. Authors concluded that their data are in agreement with other two studies data published earlier [33, 40, 53].

Intradiscal biacuplasty seems to provide several improvements over the IDET. There is minimal disruption to the native tissue architecture, and thus the biomechanics of the spine is less affected. The relative ease of electrode placement eliminates the need to thread a long resistive coil like in IDET procedure. Lower peak heating temperatures within the disc annulus compared to IDET do allow better patient tolerance. In addition, internal cooling of the probes limits excessively high temperatures in the disc that may cause tissue adherence [29, 52].

Technique

The procedure is completed under fluoroscopy with the patient lying in the prone position. Light sedation and analgesia can be provided for relaxation and pain control before and during the procedure, but the patient should be able to communicate with physician throughout the procedure. Two 17-G TransDiscal introducers are introduced to annulus bilaterally (Fig. 29.4a, b). Oblique view similar to optimal lumbar discography view is achieved. The introducer should be directed along the SAP (superior articular process) and enters the disc in the lower half. This will ensure the electrodes are sufficiently far away from the end plates and exiting nerve root. The introducers are advanced into the disc until the tips appear to be aligned with the medial edge of the pedicles in an anterior-posterior (AP) image and in the lateral fluoroscopic view just piercing the disc. Two 18-G TransDiscal probes are then placed inside the disc through provided introducers. Probe placement should be checked in the AP and lateral views to ensure appropriate disc entry points and depth of the probe. The generator controls delivery of RF energy by monitoring the temperature at the tip of the probe. The temperature increases gradually over the period of 10 min to 50 °C with final heating at 50 °C for another 5 min.

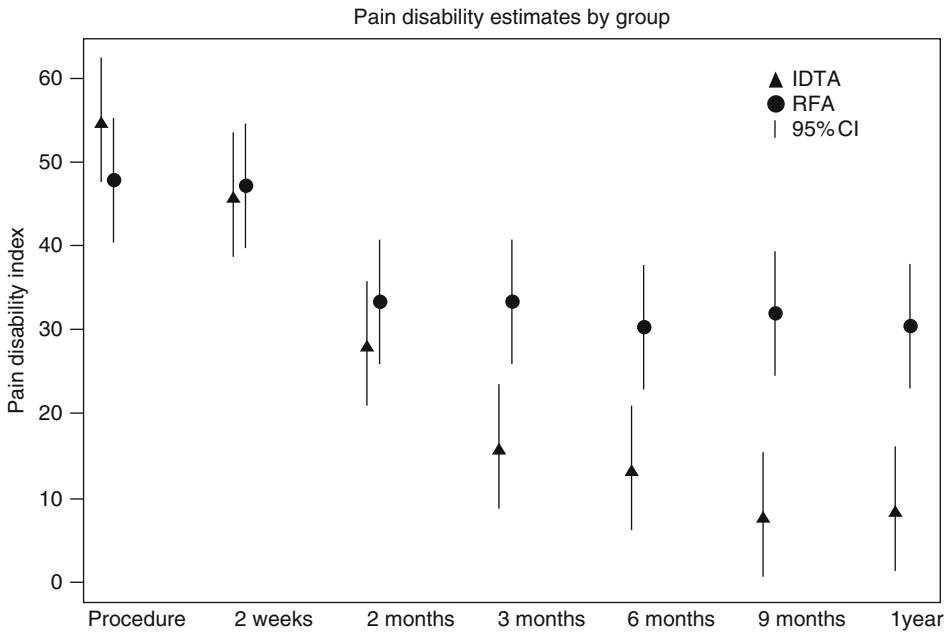

Fig. 29.5 The mean pain disability index (*PDI*) scores and 95 % confidence intervals by group at each time point following either intradiscal thermal annuloplasty (*IDET*) or radio-frequency posterior annuloplasty (*RFA*) using mixed-effects model analysis. The IDTA and RFA treatment groups did not differ significantly in their baseline PDI scores. By 3 months and at all subsequent time points, the IDTA group had significantly lower mean PDI scores than the RFA group (With permission from Kapural et al. [55])

Following completion of the procedure, patient is required to wear a brace and follow physical therapy instructions over a rehabilitation period with same rehabilitation goals as listed above for the IDET procedure.

Other Annuloplasty and Nucleoplasty Procedures for Treatment of Discogenic Back Pain

Several other intradiscal radio-frequency methods to treat discogenic pain are approved for use in the United States. The original Sluijter radio-frequency (RF) technique in which the nucleus (and not the annulus) is heated to 70 °C for 90s was proven ineffective in a randomized trial [54]. The novel annular probe termed "discTRODE" has been also shown ineffective in improving pain or function in patients with lumbar discogenic pain and during comparison study shown inferior to the IDET procedure (Fig. 29.5) [35, 55].

Complications

Rare complications of the lumbar annuloplasty procedures can be divided into infectious, hemorrhagic, neurological, allergic, and other less specific complications [56, 57]. Most frequent are minor procedure-related side effects like temporary pain exacerbation and vasovagal reactions. More serious complications include discitis, spinal abscesses, and vertebral osteomyelitis. Other serious neurological complications such as cauda equina and nerve root damage are exclusively caused by misplacement of trocars, probes, or heating elements [58–61].

Conclusions

Several new minimally invasive intradiscal techniques for pain control have been introduced recently, but sufficient clinical evidence of their efficacy and extent of application is still lacking. While discTRODE™ annuloplasty and conventional nuclear radiofrequency are ineffective in reducing the pain and improving functional capacity in patients with discogenic back pain, IDET and intradiscal biacuplasty may produce positive therapeutic effect in appropriately selected patients.

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Percutaneous Disc Decompression

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Stanley Golovac, Salim M. Hayek, and Fnu Kailash

Key Points

- At any time during the procedure, if a patient reports any lower extremity sensation (radicular pain or burning foot), the procedure should be stopped and the position of the trocar or probe assessed with anteroposterior and lateral fluoroscopic views and repositioned as necessary.
- Like all intradiscal procedures, multiplanar fluoroscopy should be used for confirmation of needle and probe placement. Sedation should be optimized to maintain meaningful communication between the operator and patient.
- If back pain occurs during PLDD, it may be due to the heating of adjacent vertebral end plates or increased pressure within the disc from trapped gas. In such cases, the position of the optical fiber should be checked to ensure it is away from the end plates, and the interval between the pulses should be increased. Aspiration could also be applied through the sidearm fitting to avoid the trapping of gas.
- If no aspirated material is present in the Dekompressor probe after 3 min of activation, the procedure should be discontinued.

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Introduction

Approximately two-thirds of individuals living in western countries suffer from an episode of low back pain during their lifetimes [1]. Low back pain is one of the leading reasons for multiple visits to physicians, and its rising prevalence is a significant factor in lost productivity, disability, and increased healthcare use [2–4]. Further, low back pain has had a substantial impact on the US economy, with healthcare expenditures swelling by 65 % from 1995 to 2005 [5].

"Nonspecific" low back pain with an unexplained etiology is currently the most prevalent low back pain group [6]. According to the best available evidence and proven diagnostic techniques, structural disorders of intervertebral discs, facet joints, and the sacroiliac joint are the three most important etiologies of the types of low back pain collectively known as "specific" low back pain [7]. Based on studies that employed controlled diagnostic injections, the relative prevalence of intervertebral discs, facet joints, and the sacroiliac joint as a source of low back pain has been estimated at 39 % [8], 15 % [9], and 19 % [10], respectively.

Lumbar disc prolapse accounts for less than 5 % of all low back problems, yet is the most common cause of radicular symptoms [11]. Given the incomplete understanding of the exact natural course of disc herniation and inconsistent findings in trials that compared surgery and conservative care, clinicians are often faced with the challenging choice of surgery versus nonsurgical care for the treatment of patients.

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Historical Background

Historically, there have been paradigm shifts between operative and nonoperative treatment, and no single modality has been proven superior in long-term studies. In 1934, William Jason Mixter, a neurosurgeon, and Joseph Barr, an orthopedic surgeon, published a landmark article in the *New England Journal of Medicine* that established an association between the intervertebral disc and sciatica [12]. Their work led to a paradigm shift from conservative to surgical management for sciatica. This shift spurred innovations in diagnostic and surgical techniques designed to minimize the trauma of therapeutic interventions.

Conversely, the famous retrospective study of Saal and Saal supported conservative management and showed the resolution of pain in more than 90 % of the subjects treated nonoperatively [13]. This result is comparable to the 4-year outcomes in the nonoperative arm of a landmark study by Henrik Weber [14]. However, in a combined (randomized and observational cohort) as-treated 4-year analysis of large multicenter trial (Spine Patient Outcomes Research Trial: SPORT), patients who underwent surgery for lumbar disc herniation fared better than patients treated nonoperatively in all primary and secondary outcomes except work status [15]. Unfortunately, methodological weaknesses in both trials, including significant crossover between the operative and nonoperative arms and the use of as-treated analysis (vs. intention to treat analysis), undermine the validity of any conclusions drawn from this analysis.

Hence, in light of the generally favorable natural course of lumbar radiculopathy associated with lumbar disc herniation, conservative care and minimally invasive treatment modalities should be considered as the first-line treatment options, while an immediate referral to surgery should be made if the patient exhibits a progressive neurologic deficit or the signs and symptoms of cauda equina syndrome. The relative advantages for surgical decompression include rapid pain relief and functional improvement in those who have failed conservative management.

Evolution of Minimally Invasive Percutaneous Disc Decompression

Traditionally, conventional discectomy has been the gold standard treatment for sciatica refractory to conservative management. With the introduction of surgical microscopes in the 1970s, comparable results could be achieved with "microdiscectomy," which has the advantages of a smaller surgical incision and enhanced operative field view [11].

In the 1960s, three decades after Mixter and Barr's publication, there was once again a paradigm shift, as the field returned to a minimally invasive approach in the treatment of lumbar disc disease. Lyman Smith was the first to perform percutaneous injection of chymopapain (a proteolytic enzyme) for the treatment of unrelenting sciatica, a technique he called chemonucleolysis (CNL) [16]. In 1975, Japanese orthopedic surgeon Hijikata introduced "percutaneous manual nucleotomy," a technique that decompressed a herniated disc by the fenestration of the annulus and the partial resection of the nuclear material [17].

Over time, CNL and percutaneous manual nucleotomy fell out of favor due to fatal enzymatic complications and technical limitations, respectively. However, the desire of clinicians for minimally invasive therapies in the field of spine surgery has continued to lead to breakthroughs in percutaneous intradiscal therapies.

Minimally Invasive Percutaneous Disc Procedures

As one would expect, minimally invasive procedures are associated with smaller surgical scars, rapid convalescence, less postoperative analgesic consumption, lower costs, and less spinal instability. In an updated Cochrane review, Gibson and Waddell concluded that, in general, surgical discectomy procedures are superior to chemonucleolysis and other forms of percutaneous discectomy [11]. However, in several trials, most nonrandomized and uncontrolled, the success rate of percutaneous disc decompression ranged from 50 to 90 % [18–20].

Percutaneous Disc Decompression

The postulated mechanism of indirect decompression techniques entails that the excision or degradation of a portion of the central nucleus results in the reduction of intradiscal pressure and prolapsed disc retraction, thus allowing for indirect nerve decompression and the potential resolution of radicular pain [21].

Understandably, the selection of the appropriate patients with specific disc pathoanatomy would be crucial in a study to obtain successful outcomes with the chosen percutaneous disc decompression technique. Carragee and others have demonstrated that clinical (symptom duration, litigation status), demographic (age), morphometric (disc size and shape evident on MRI/CT scans), and intraoperative (type of disc herniation) variables have prognostic significance in terms of treatment outcomes [22, 23]. Small (<6 mm) and contained disc protrusions (intact outer annulus and posterior longitudinal ligament) are less likely to resorb spontaneously and are associated with fair or worse surgical outcomes after discectomy [22–24]. Individuals with contained disc

protrusions may potentially benefit from percutaneous disc decompression. Percutaneous decompression can be accomplished through several techniques, including chemical (chemonucleolysis and ozone), thermal (Radiofrequency Coblation®, Acutherm®, and light amplification by stimulated emission of radiation (laser)), and mechanical (automated percutaneous lumbar discectomy and Dekompressor®) means. However, each technique has its limitations, and the full efficacy of each is unknown due to a paucity of high-quality evidence.

Procedural Anatomy

For any percutaneous disc procedure, access to the intervertebral disc is achieved with an extrapedicular posterolateral approach performed under fluoroscopic guidance (an oblique view) through a triangular working zone known as Kambin's triangle [25]. The exiting nerve root, superior articular process of the facet joint, and superior end plate of the distal vertebra make the three dimensions: more specifically, the hypotenuse, perpendicular, and base, respectively, of Kambin's triangle. Further fluoroscopic maneuvers are performed to access the disc as follows:

1. The target disc is identified via fluoroscopy with an anteroposterior view in which the vertebral end plates are aligned perfectly ("squared off view").
2. An oblique view of the target disc is obtained in which the superior articular process (SAP) of the facet joint of the target segment lies against the midpoint of the intervertebral disc.
3. A puncture point is identified over the target point at the mid-height of the target disc and ventral to the SAP projection. The introducer (trocar) entered in a coaxial fashion at this insertion point should avoid the spinal nerve as the nerve passes superolaterally.

Patient Selection

The radiologic identification of a disc herniation congruent with a patient's history and physical examination is mandatory before the contemplation of a percutaneous disc procedure. Magnetic resonance imaging (MRI) is both sensitive and specific and has been reasonably reliable in the diagnosis of lumbar disc herniation [26]. Additionally, as mentioned above, MRI findings (the size of disc herniation and the containment status of the herniation) have been found to have significant impact on surgical outcomes. In a prospective study by Weiner et al., MRI was found to be 70 % accurate in identifying the containment status of a lumbar disc herniation [27].

The other important prerequisite is the demonstration that a patient's symptoms emanate from the level of the disc proposed to be targeted for decompression. In the case where morphological changes are evident on MRI at multiple disc levels, the culprit level can be determined by the performing of selective nerve root blocks and the identification of the nerve root block that leads to the resolution of pain symptoms. In cases where there are equivocal findings on MRI or a lack of pain relief after selective nerve root block, provocative discography is warranted to find the symptomatic disc and assess its containment [28].

Indications [28]

1. Predominately radicular pain lasting more than 6 months.
2. The failure of conservative treatment.
3. A small contained disc herniation evident on MRI or computed tomography (CT)/discography.
4. The residual disc height of the involved disc is more than 50 % of the original disc height.

Contraindications [28]

In addition to the usual contraindications for any neuraxial intervention (such as systemic infection, local infection, coagulopathy, and patient refusal), contraindications particular to percutaneous disc decompression are as follows:

1. Severe disc degeneration, as evidenced by residual disc height <50 % of the original disc height on imaging
2. Large disc herniation that occupies more than one-third of the spinal canal
3. Extruded or sequestered nucleus pulposus at the proposed level of intervention
4. Previous lumbar back surgery (laminectomy, discectomy, or fusion) at the proposed level of intervention
5. Progressive neurologic deficit
6. Structural deformities such as spondylolisthesis, spinal canal stenosis, scoliosis, tumor, or fracture

Automated percutaneous lumbar discectomy, laser discectomy, Radiofrequency Coblation®, and Disc Dekompressor are the most common percutaneous disc decompression techniques used and are discussed below.

Automated Percutaneous Lumbar Discectomy (APLD)

After "percutaneous manual nucleotomy" fell out of favor and the use of CNL diminished due to adverse effects, refinements in surgical techniques led to the emergence of APLD in 1984. To overcome the inherent limitations of manual nucleotomy with a large cannula (5–8 mm diameter) and the cumbersome manual removal of nucleus pulposus, Onik et al. developed a smaller 2-mm probe with a single side port that potentially reduces the risk of nerve root injury and facilitates the easier removal of tissue with an all-in-one suction cutting device [29].

Procedure

After adequate preparation, the aspiration probe is placed through a 2.5-mm-sized cannula that had been positioned against the annulus over the affected side of the protrusion as outlined above (posterolateral approach under fluoroscopic guidance). The aspiration probe is a sharpened cannula that is pneumatically driven and fitted through an outer needle. Disc fragments are aspirated by the combination of irrigation and suction through an inner cannula connected to a collection bottle. The procedure is discontinued when aspiration ceases to be productive. The patient is then allowed to recover and discharged home on the day of the procedure.

Evidence of Efficacy

Clinical studies have yielded conflicting results about this procedure, and thus its effectiveness is yet to be determined. The initial prospective evaluations and case series reported promising outcomes and had success rates of 75–85 % [18, 30]. However, later randomized trials reported lower success rates of 29–37 % and the inferiority of APLD to techniques such as surgical discectomy and CNL [31, 32], although it should be noted that Revel's study [32] was subsequently criticized for inappropriate patient selection. In their systematic review, Hirsh and coworkers identified four randomized controlled trials and reported there was modest evidence that supported the use of APLD in properly selected patient populations with contained disc herniation [33].

Percutaneous Laser Disc Decompression (PLDD)

The declining popularity of chemonucleolysis and APLD led to the emergence of alternative techniques that employed thermal energy techniques such as laser and radiofrequency nucleotomy. Arguably, the advantage of thermal techniques is that they provide a combination of mechanical decompression and modification of intradiscal biochemical milieu, which can lead to the reduction of neuropathic (radiculopathic) and nociceptive pain, respectively [21, 34].

Procedure

The first clinical application of PLDD occurred in 1986 [35]. Various types of lasers have since been described in the literature, including those with wavelengths close to the infrared region (Nd:YAG, Ho:YAG, and diode lasers) and those with visible green radiation (potassium-titanyl-phosphate (KTP) laser) [36].

The working principle of PLDD is similar to other decompression techniques; access to intervertebral disc is achieved as outlined above except with a smaller diameter needle (18-gauge needle), followed by the introduction of 400-μm optical fiber for transmission of laser energy. The fiber optic channel is often used for visualization (LASE® endoscopic discectomy). If the endoscope is used for visualization, dilators are advanced over the guide needle for the introduction of the endoscope. Different protocols have been reported in the literature in terms of the type of laser, duration of the treatment, and impulsion energy used to achieve decompression. Gangi and coworkers [37] reported that the application of a 1,064-nm Nd:YAG laser in short pulses of 0.5–1 s with pauses of 4–10 s was effective, while Choy and coworkers [38] reported the use of a 1,064-nm Nd:YAG laser in short pulses of 1 s and pauses of 1 s led to a favorable outcome. As with APLD, the patient is then allowed to recover and discharged home on the day of the procedure.

Evidence of Efficacy

To date, most observational studies on PLDD have reported favorable outcomes. Tassi, Choy, and coworkers reported a success rate of 70–89 % based on the results from multiple centers and approximately 20,000 procedures. The complication rate (complications were mainly discitis) ranged from 0.3 to 1.0 %, and there was a recurrence rate of 4–5 % over a 23-year follow-up period [19]. In a systematic review that encompassed 14 observational studies, Singh and coworkers reported that there was only modest evidence that the use of PLDD led to short- and long-term pain relief and that the procedure had a success rate of 56–87 % [39]. However, the lack of well-designed randomized clinical trials and the methodological weakness of the above studies question the validity of these conclusions.

Radiofrequency Coblation® [Plasma Disc Decompression (PDD)/Nucleoplasty]

PDD is a technique that uses bipolar radiofrequency energy and is based on the principle of the Coblation® (controlled ablation) technology patented by ArthroCare Corp. (Sunnyvale, CA, USA). This technology leads to the formation of a precisely focused plasma field of high-energy ionized particles close to the tip of an RF electrode (SpineWand™) that causes the dissolution and vaporization of nearby nucleus tissue [40]. Compared to laser discectomy (which has a high thermal output), plasma-based disc ablation works at a lower range of temperatures (40–70 °C), which could potentially result in minimal tissue charring and less collateral tissue damage [41].

Procedure

After adequate preparation, the appropriate intervertebral disc is accessed with a 17-gauge obturator stylet through the extrapedicular posterolateral approach mentioned above. A SpineWand™ device is advanced through the introducer needle, and a pathway is established between the anterior

and posterior annular margins that establishes the proximal and distal limits of the excursion. Thereafter, Coblation® is commenced and typically consists of six alternative cycles of ablation and coagulation that cause the excavation of the cavity and a volumetric reduction of approximately 1 ml nuclear tissue. During ablation mode, the SpineWand® is advanced. This creates a plasma field and causes a molecular dissociation process that converts the tissue into a gas that exits through the introducer needle. During coagulation mode, the SpineWand® is retracted along the same pathway. This induces collagen shrinkage, which consolidates the ablation process. The patient is then allowed to recover and discharged home on the day of the procedure.

Evidence of Efficacy

Despite the favorable results from preclinical and observational studies in terms of the safety profile and clinical outcomes, the paucity of well-designed methodologically sound clinical trials makes the true efficacy of this modality questionable. Gerges and coworkers reported modest evidence of its efficacy in a pooled analysis of 14 publications (one randomized trial and 13 observational studies) in terms of various outcome measures of pain and function and showed a median percentage of improvement of 62.1 % (range: 6.25–84 %) [42]. It should be noted that the trial that reported the 6.25 % improvement was criticized for inappropriate patient selection, including the inclusion of patients with moderately degenerated discs and noncontained disc herniation [43]. Further, a prospective nonrandomized uncontrolled comparative study reported favorable outcomes in terms of analgesic consumption and degree of disability [44].

Mechanical Disc Decompression

Advancements in automated discectomy led to Dekompressor® (Stryker Corporation, Kalamazoo, MI, USA) being added to the armamentarium of mechanical decompression in 2002. This device is a disposable, battery-operated, handheld rotational motor that is attached to a helical probe. The outer cannula measures 1.5 mm and contains an inner rotating probe. The benefits of Dekompressor include its smaller profile than other devices, the ability to obtain a disc sample for biopsy, and the avoidance of thermal damage to neural structures.

Procedure

The system is deployed into the affected side of the disc of interest through a 17-gauge introducer needle previously positioned under fluoroscopic guidance as mentioned above. When fully advanced, the base of the probe locks onto the hub of the introducer needle in a manner in which at least one full thread length of the probe tip extends beyond the end of the cannula. The probe is activated and advanced slowly (≈1 cm/10 s) under fluoroscopic guidance and draws out tissue based on Archimedes' screw pump principle. Approximately 0.5–2 cc nucleus pulposus is removed. The patient is then allowed to recover and discharged home on the day of the procedure.

Evidence of Efficacy

Scientific evidence supporting the use of Dekompressor is very limited. Two observational studies and one prospective nonrandomized uncontrolled comparative study have reported favorable outcomes in regard to short- and long-term pain relief [44–46]. A systematic review of percutaneous lumbar mechanical disc decompression with the Dekompressor published in 2009 indicated level III (weak) evidence for Dekompressor having a positive effect on both short- and long-term pain relief due to a lack of high-quality studies [47].

Post-procedural Care [28]

Post-procedural rehabilitation protocols vary according to the type of procedure as follows:

1. Generally, sitting, bending, twisting, and lifting more than 10 lb is limited for the first week or so.
2. Patients may experience flare-ups of back pain, especially after thermal ablation, for several days after the procedure. Analgesics can be prescribed according to patient needs. Patients who experience discomfort at the site of insertion after the local anesthetic wears off may use an ice pack at the insertion site the day of the procedure and warm moist heat the following day.
3. Activity restriction is generally prophylactic in nature to prevent reherniation. The return to activity varies on a case-by-case basis. Many patients resume work and daily activities by 1 week after mechanical disc decompression. The average times to resume activities after a thermal ablation procedure such as laser are as follows:
   (a) Sedentary activity: 1–2 weeks after the procedure
   (b) Light duty: 2–4 weeks, depending upon activity
   (c) Resumption of full duty: 6–10 weeks

Complications

In general, complication rates of the percutaneous disc decompression procedures themselves appear low. The most common complications that follow are due to improper needle placement, a complication that could occur in any intradiscal therapy:

1. Transient paresthesias and the exacerbation of back pain during the first several days post-procedure are the most

common complications that require supplemental analgesics.
2. Superficial skin infection.
3. Paraspinal abscess.
4. Discitis.

Potential complications due to intradiscal procedures are:

1. Reflex sympathetic dystrophy or causalgia
2. Vascular injury
3. Abdominal perforation [48]
4. Aseptic spondylodiscitis (presumably from heat damage to a disc or the adjacent vertebral end plate)
5. Cauda equina syndrome [48]
6. Epidural fibrosis after Coblation® [49]
7. Breakage of the probe needle

Conclusion

With innovative refinements in intradiscal techniques and a better understanding of the disease process, minimally invasive techniques for the treatment of lumbar disc herniation associated with lumbar radiculopathy will continue to evolve as a viable alternative to more invasive surgical options in the appropriate clinical setting. As in all of pain medicine, improved patient selection and robust blinded clinical trials are needed to properly evaluate the efficacy of these techniques and establish their place in the paradigm of lower back pain treatment.

In the era of technology-driven surgical techniques in which the field is driven by the notion of "less is more," I believe that endoscopic techniques will be the predominant technique used in future spine procedures. Refinements in endoscopic techniques, in conjunction with further developments in gene therapy and application of biomaterials, may further revolutionize spine procedures and lead to better outcomes.

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The Racz Procedure: Lysis of Epidural Adhesions (Percutaneous Neuroplasty)

31

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Key Points

- Back pain and radiculopathy are identifiable by epidurogram and provocative tests (i.e., neural mapping and saline distention).
- Neural mapping is stimulating the nerve roots one by one to the point of paresthesia. Patients inevitably recognize the pain when the appropriate pain-generating nerve root is stimulated.
- Injection target sites for epidural lysis of adhesion procedures is the ventral-lateral epidural space, whereas the injection target site for back pain is the ventral midcanal that is achieved through percutaneous neuroplasty and can be provocated with saline distention.
- The "dural tug" is a provocative clinical test which is performed while the patient is sitting with straight legs on the examination table. The thoracolumbar spine is actively flexed by the patient with the neck in neutral position. At the end of thoracolumbar active range, the cervical spine is passively flexed by the examiner in a rapid manner. This maneuver pulls on the dura and reproduces pain at the site of pathology.
- Physicians who possess three-dimensional procedural skills typically have a shorter duration learning curve for lysis of adhesions and percutaneous neuroplasty which result in improved patient outcomes.

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Introduction

Back pain is an exceedingly common condition and is often treated with surgery when patients have failed traditional conservative treatment. Despite the best efforts of treating surgeons, these patients are often left with significant postoperative pain, and reoperation or chronic opiate therapy is frequently felt to be the only alternative. A large portion of pain in this patient population is directly attributable to epidural adhesions that prevent normal nerve root movement along with adhesions affecting the ventral epidural structures. Lysis of adhesions is a minimally invasive procedure that was initially developed to spare patients from an additional surgery. Since its inception, the procedure has proved effective for a variety of additional etiologies beyond postsurgical back pain. Through site-specific targeting, lysis of adhesions involves the placement of a catheter in the neuroforamen of the affected nerve root. A fluid foraminotomy is performed when hyaluronidase, local anesthetic, corticosteroid, and hypertonic sodium chloride are injected through the catheter. This releases the nerve root from epidural adhesions and increases neuroforaminal cross-sectional area. Additionally, adhesiolysis opens venous runoff and decompresses high-pressure epidural veins.

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Percutaneous neuroplasty via a transforaminal approach evolved from the caudal approach. Lysis of adhesions via the caudal approach involves introducing a catheter through the sacral hiatus and advancing it to the affected nerve root in the ventral-lateral epidural space. On the other hand, transforaminal percutaneous neuroplasty achieves a midline catheter placement in the epidural space that is able to target the two most heavily innervated structures in the spine—the posterior annulus fibrosus and the posterior longitudinal ligament [1]. Apart from a surgical approach, the ventral epidural structures have been otherwise inaccessible.

The benefits of lysis of adhesions and percutaneous neuroplasty have been demonstrated in numerous studies including case series, observational studies, and randomized-controlled trials leading to an evidence rating of "strong" (SORT 1B or 1C) for post–lumbar surgery syndrome in the most recent American Society of Interventional Pain Physicians evidence-based guidelines. In addition to an evidence rating of strong, recommendation was also made that this procedure could be used without reservation in most circumstances.

Adhesiolysis will be used interchangeably with lysis of adhesions and percutaneous neuroplasty throughout the remainder of the chapter.

CPT Codes

There are two current procedural terminology (CPT) codes assigned to adhesiolysis depending on the number of infusions. CPT 62263 is used for a staged three-series infusion over 2–3 days; CPT 62264 denotes a one-time infusion in an outpatient surgery center model.

Low Back Pain and Radiculopathy Secondary to Epidural Adhesions

Kuslich et al. demonstrated that sciatica could only be produced by stimulation of a swollen, stretched, restricted (i.e., scarred), or compressed nerve root [1]. Contrary to all sciatica relating to the nerve root, back pain was found to be the result of multiple tissues—most commonly the posterior longitudinal ligament and the outer layer of the annulus fibrosus. Additionally, Kuslich demonstrated that the facet joint capsule and synovium were rarely indicated as an etiology of back pain [2].

Epidural fibrosis is caused by surgical trauma, annular tears, infection, hematoma, or intrathecal contrast [3]. Its indisputable presence has been demonstrated in many studies [4–7]. While epidural fibrosis itself is not a pain generator, it serves to entrap nerve roots making them more susceptible to compressive forces and tension [8]. For example, Ross et al. [9] correlated extensive peridural scarring with a 3.2-fold increase in recurrent radicular pain.

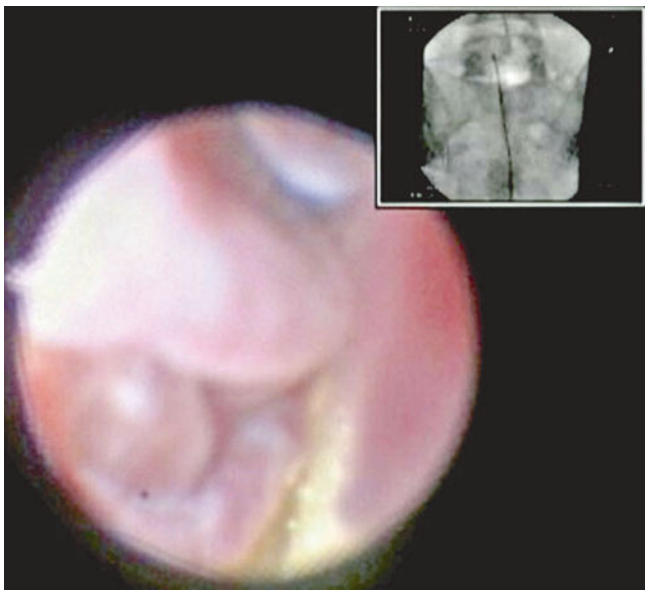

Fig. 31.1 Engorged blood vessels in the epidural cavity as observed during epiduroscopy. Inserted in upper right corner is fluoroscopy showing location for epiduroscopy tip (left anterior border of L5)

Fluid Foraminotomy

Foraminal stenosis secondary to epidural fibrosis with corresponding nerve root entrapment is frequently evident after an epidurogram and signified by lack of epidural contrast flow at those levels. The lysis procedure effectively serves as a fluid foraminotomy reducing foraminal stenosis caused by epidural fibrosis. In addition to increasing foraminal cross-sectional area, adhesiolysis serves to decompress distended epidural venous structures that may exert compression at nearby spinal levels (Fig. 31.1) and inevitably cause needlestick-related epidural hematomas. Adhesiolysis has led to the development of flexible epiduroscopy that was primarily initiated, pursued, and to this day supported by Dr. James Heavner [10–12].

The Diagnosis of Epidural Fibrosis (Adhesions)

As with any patient, a thorough musculoskeletal and neurologic examination should be performed. In addition to standard dural tension provocative tests, we recommend a provocative test called "dural tug." To perform the test, the patient should be made to sit up with a straight leg, bend forward until their back pain starts to become evident, and rapidly flex the head and neck forward. During this maneuver, the dura is stretched cephalad and if adhered to structures such as the posterior longitudinal ligament, the most heavily innervated spinal canal structure, the movement of the dura will elicit back pain that is localized to the pain generator.

The dural tug maneuver is no longer provocative after percutaneous neuroplasty (Fig. 31.2a–e).

Imaging modalities with utility in the diagnosis of epidural fibrosis include MRI, computed tomography (CT), and epiduroscopy; however, the best way to diagnosis epidural fibrosis is through an epidurogram [13–16]. In contrast to MRI or CT, an epidurogram is able to demonstrate filling defects which can be correlated with a patient's symptoms in real time. The sensitivity and specificity of MRI and CT for detecting epidural fibrosis are 50 and 70 %, respectively [17].

Patient Selection

There are many conditions for which the lysis of adhesions procedure may be appropriate for. The most common indication is for neck or back pain and radiculopathy secondary to postsurgical epidural fibrosis. Other indications include disk disruption, metastatic carcinoma of the spine leading to compression fracture, multilevel degenerative spondylosis, spinal stenosis, and pain unresponsive to spinal cord stimulation and spinal opioids [18].

Contraindications

Absolute contraindications to adhesiolysis include sepsis, chronic infection, coagulopathy, local infection at procedure site, syrinx formation, and patient refusal. Although not an absolute contraindication, arachnoiditis poses significant risk when performed by interventional pain physicians with limited experience with adhesiolysis. In arachnoiditis, the risk of loculation and subdural or subarachnoid spread is significantly increased; it is for this reason that we suggest the referral of these patients to a more experienced physician if doubt should arise.

Benefits and Risks

In order to obtain informed consent, risks and benefits should be discussed with the patient prior to performing adhesiolysis. Potential benefits of the procedure include pain relief, increased function, and the possible reversal of neurologic symptoms. Risks include, but are not limited to, bruising, bleeding, infection, reaction to medications used (i.e., hyaluronidase, contrast, local anesthetic, corticosteroids, hypertonic saline), damage to nerves or blood vessels, no or little pain relief, bowel/bladder incontinence, worsening of pain, and paralysis. In our practice, we have never seen an allergic reaction to hyaluronidase and neither was any reported on a survey of large groups of ophthalmic anesthesiologists in its use with retrobulbar blocks [28]. Additionally, patients with a history of urinary incontinence should have urodynamic evaluation by a urolo-gist before the procedure to document the preexisting urodynamic etiology and pathology.

Anticoagulant Medication

Any medication that prolongs bleeding and/or clotting should be held prior to performing adhesiolysis. We suggest contacting the physician prescribing the anticoagulant prior to holding it for adhesiolysis—typically the patient's primary care physician or cardiologist. We suggest the following times to withhold anticoagulant or antiplatelet medications prior to adhesiolysis: nonsteroidal anti-inflammatory 4 days, aspirin 7–10 days, clopidogrel (Plavix) 7 days, ticlopidine (Ticlid) 10–14 days [19], warfarin (Coumadin) 5 days [18], subcutaneous heparin a minimum of 12 h, and low-molecular-weight heparin 24 h [19]. Nonprescription homeopathic medications that prolong bleeding should also be withheld for approximately 2 weeks. These include fish oil, vitamin E, Gingko biloba, garlic, ginseng, and St. John's wort. We also routinely perform laboratory analysis as close to the day of the procedure as possible. Laboratory studies to ensure adequate coagulation status that we use include a complete blood count, prothrombin time, partial thromboplastin time, and a platelet function assay, or bleeding time.

Preoperative Laboratory Evaluation

In addition to the aforementioned coagulation parameters discussed, each patient should undergo a complete blood count and clean-catch urinalysis to rule out any underlying infection. As with all elective procedures, any abnormal laboratory value should warrant cancellation of adhesiolysis and further workup by the patient's primary care physician.

Technique

Adhesiolysis is most routinely performed in the lumbar and caudal regions of the spine, but can also be performed in the cervical and thoracic regions. This chapter will provide detailed explanation of the caudal and lumbar transforaminal placement of catheters.

Adhesiolysis is performed under strict sterile conditions in the operating room with prophylactic broad-spectrum antibiotics given prior to the procedure and on postoperative day 1. We currently prefer cefazolin 1 g intravenously or clindamycin 600 mg intravenously for those allergic to penicillin. All procedures are performed with an anesthesiologist or nurse anesthetist providing monitored anesthesia care and/or appropriate sedation.

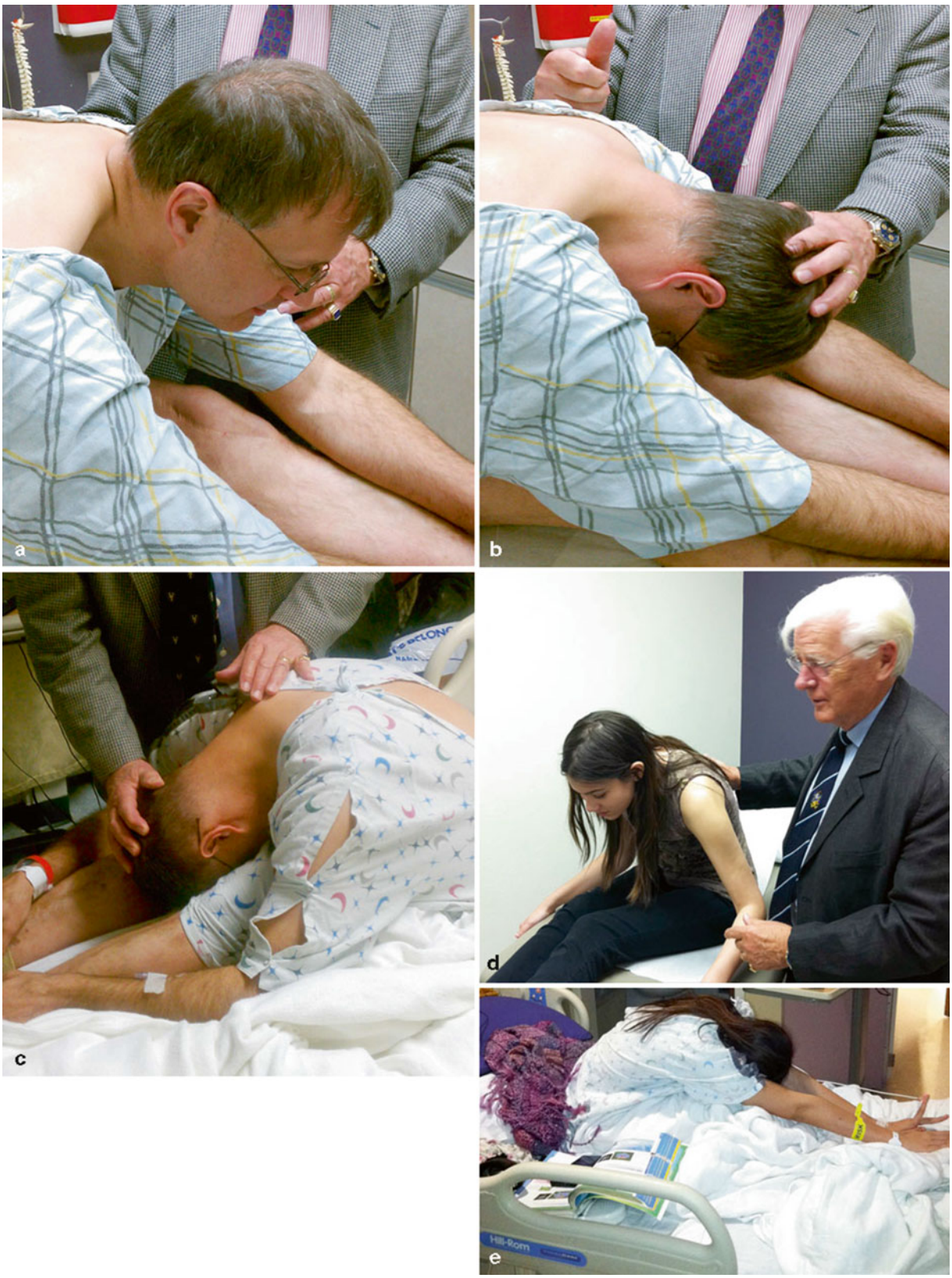

Fig. 31.2 (**a**) The "dural tug" maneuver being performed prior to percutaneous neuroplasty. (**b**) Note pain reproduction prior to full neck flexion secondary to dural adhesions. (**c**) Patient after percutaneous neuroplasty with pain-free neck and back flexion due to treatment of dural adhesions. (**d**) There is decreased spine flexion prior to treatment secondary to dural adhesions. (**e**) After treatment, the same patient demonstrates increased painless flexion of the spine

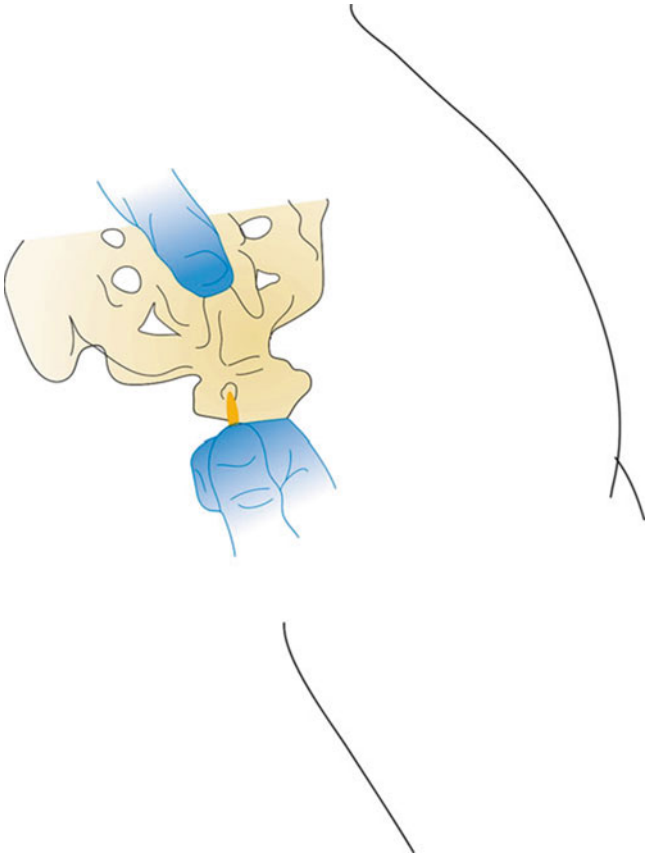

Fig. 31.3 Caudal lysis sequence—first find sacral hiatus and tip of coccyx

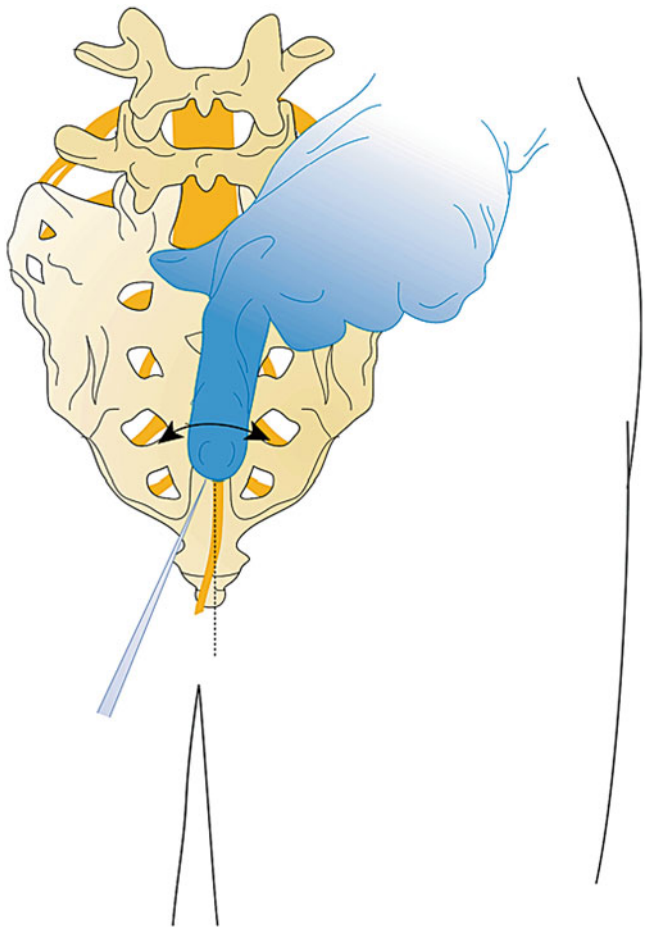

Fig. 31.4 Roll palpating index finger to identify the sacral cornua and thus the target sacral hiatus

Lysis of Adhesions via a Caudal Catheter

The patient is placed in the prone position on the operating room table. Lumbar lordosis is minimized through the use of pillows placed under the abdomen. The patient's low back and buttocks are sterilely prepped and draped. To begin the procedure, the sacral hiatus is identified through palpation or with AP fluoroscopic guidance. If using palpation, the sacral hiatus can be identified slightly caudal to the sacral cornu and mimics the feel of the area between two knuckles on the dorsum of the hand. A skin wheal should be made approximately 5 cm caudal and 2.5 cm lateral to the sacral hiatus over the contralateral buttock to the targeted nerve root. The distal approach is advocated to reduce the frequency of meningitis by effectively tunneling the catheter. The skin wheal is then superficially punctured with an 18-gauge needle; through the same puncture site, a 15- or 16-gauge RX Coudé 2 needle is inserted and directed toward the sacral hiatus. The RX Coudé 2 is initially advanced at a 45° angle via fluoroscopic guidance or by palpation of sacral hiatus with the left index finger (Figs. 31.3 and 31.4). Once through the sacral hiatus, the needle angle is then dropped to 30° and advanced under lateral fluoroscopic guidance into the caudal epidural space. AP fluoroscopic views should also be obtained to assure midline needle placement which will assist in directing the catheter. The needle should be advanced no further cephalad than the S3 level to prevent inadvertent dural puncture in patients with low-lying dura.

The RX Coudé 2 needle is used as opposed to other needles for several reasons including an angled tip, slightly blunted distal tip, and a non-cutting back edge of the needle opening. The non-cutting back edge of the needle opening allows for catheter manipulation with minimal risk of shearing. Tuohy needles have a cutting back edge of the needle opening which increases the risk of catheter shear.

Once midline in the caudal epidural space, an epidurogram is performed using 10 mL of nonionic, water-soluble contrast. Omnipaque and Isovue are typically the contrast agents of choice and are suitable for myelography. Ionic water-insoluble contrast agents (Hypaque or Renografin) or ionic water-soluble contrast agents (Conray) must never be used. Injection of ionic contrast can result in seizures and death—inspect your contrast agent carefully prior to use. Additionally, aspiration prior to contrast injection should be performed to rule out intravascular or intrathecal injection.

Slowly inject the contrast agent and observe for filling defects. A normal epidurogram will have a "Christmas tree" pattern with the central canal being the trunk and the outline of the nerve roots making up the branches. An abnormal epidurogram will have areas where the contrast does not fill (Fig. 31.5). These are the areas of presumed epidural fibrosis and typically correspond to the patient's radicular complaints. If vascular uptake is observed, the needle needs to be redirected.

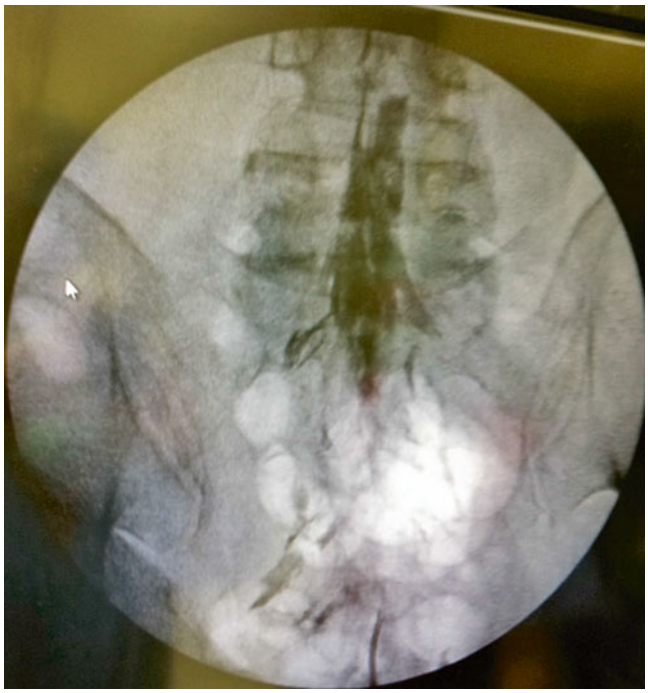

Fig. 31.5 Initial dye injection Omnipaque 240 (10 mL) in a patient with multilevel spinal stenosis showing filling defects bilaterally; pain worse on right side

After turning the distal opening of the needle ventral-lateral, insert a TunL Kath or TunL-XL-24 (stiffer) catheter with a bend on the distal tip through the needle (Fig. 31.6). The bend should be 1 in. from the tip of the catheter and at a 30° angle (Fig. 31.7). The bend will enable the catheter to be steered to the target level. Under continuous AP fluoroscopic guidance, advance the tip of the catheter toward the ventral-lateral epidural space of the desired level (Fig. 31.8). The catheter can be steered by gently twisting the catheter in a clockwise or counterclockwise direction. Avoid "propelling" the tip (i.e., twisting the tip in circles) because this makes it more difficult to direct the catheter. Do not advance the catheter up the middle of the sacrum because this makes guiding the catheter to the ventral-lateral epidural space more difficult. Ideal location of the tip of the catheter in the AP projection is in the foramen just below the midportion of the pedicle shadow (Figs. 31.9 and 31.10). Check a lateral projection to confirm that the catheter tip is in the ventral epidural space.

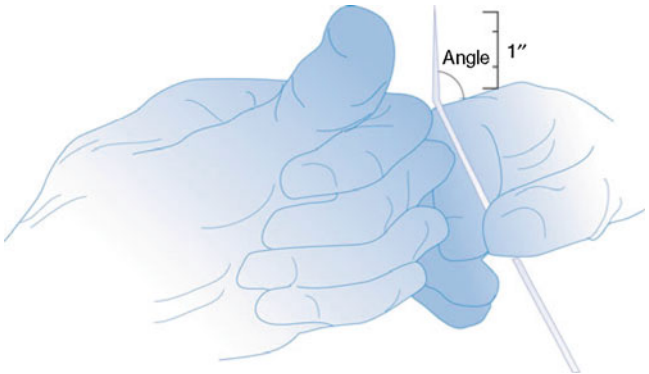

Fig. 31.7 The Epimed Racz catheter is marked for the location of the bend, or use the thumb as reference for the 15° angle bend

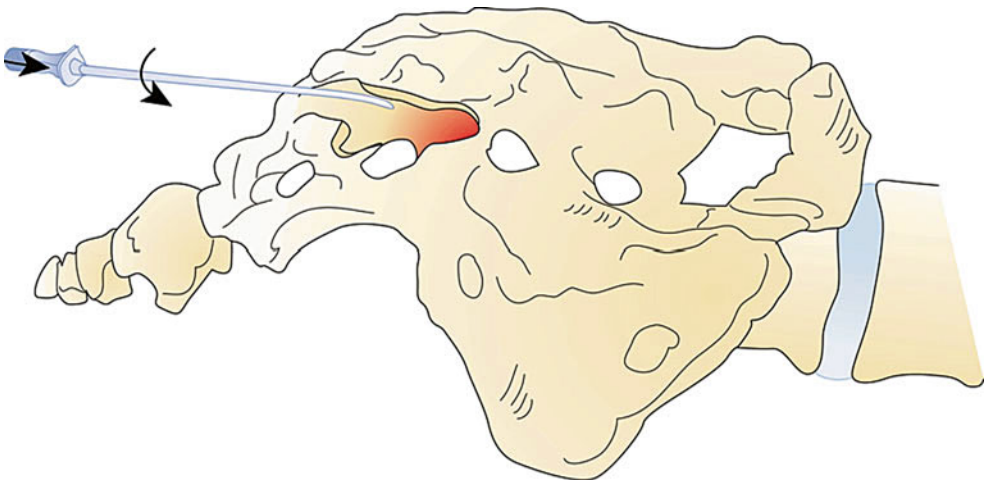

Fig. 31.6 The needle is placed through the sacral hiatus into the sacral canal and rotated in the direction of the target. Do not advance beyond the S3 foramen

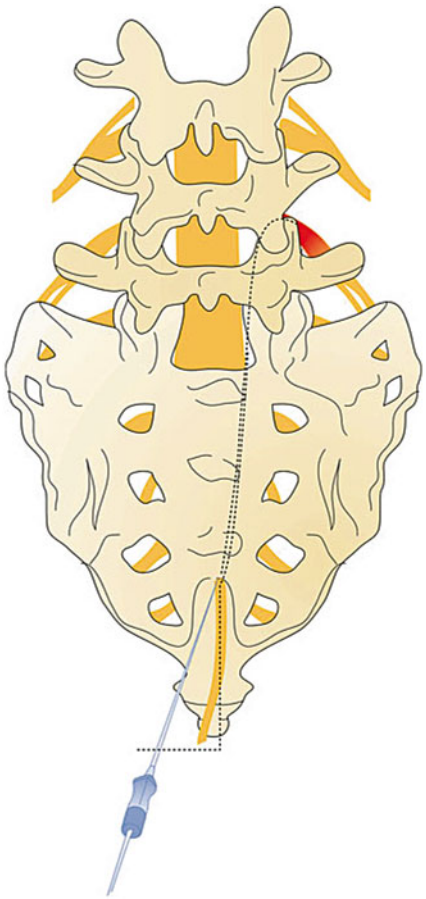

Fig. 31.8 The direction of the catheter is just near the midline, direct the curve under continuous fluoroscopic guidance to the ventral-lateral target site. The needle rotation, as well as the catheter navigation, may need to be used to reach the target

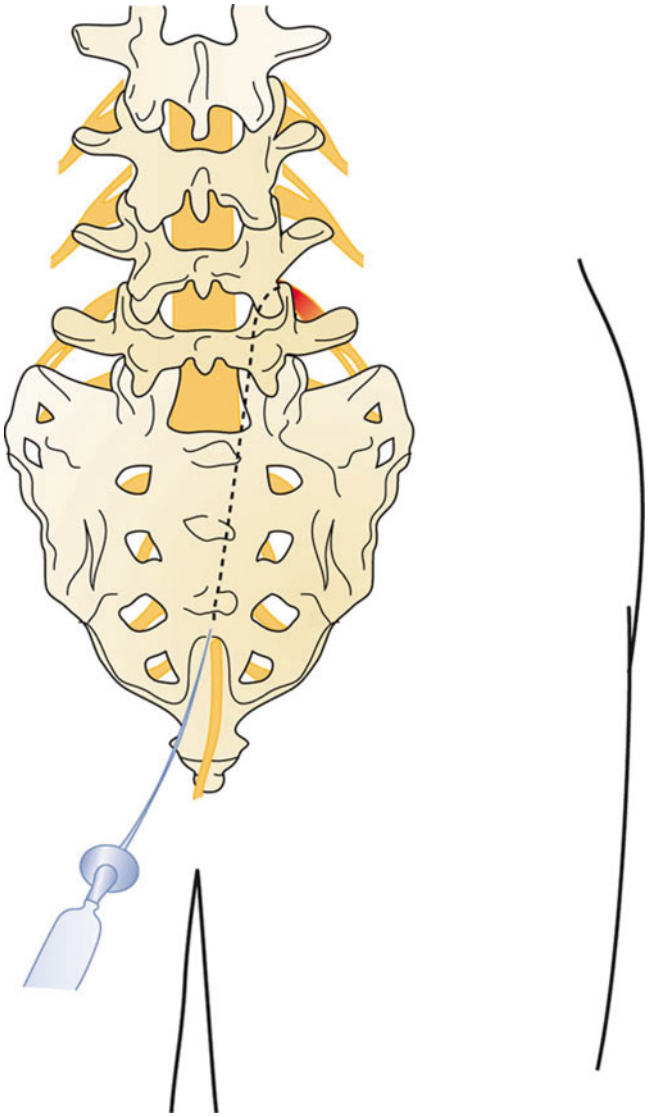

Fig. 31.9 The needle is removed, and the catheter is placed in the ventral-lateral epidural space ventral to the nerve root

Once at the target, inject 2–3 mL of additional contrast through the catheter under real-time fluoroscopy in an attempt to outline the "scarred in" nerve root. If vascular uptake is noted, reposition the catheter and reinject contrast. Preferably, there should not be vascular runoff, but infrequently secondary to venous congestion, an epidural pattern is seen with a small amount of vascular spread. This is acceptable as long as the vascular uptake is venous in nature and not arterial. Extra caution should be taken when injecting the local anesthetic to prevent local anesthetic toxicity. Any arterial spread of contrast always warrants repositioning of the catheter. We have never observed intra-arterial placement in over 25 years of placing soft spring-tipped catheters.

Inject 1,500 U of hyaluronidase dissolved in 10 mL of preservative-free normal saline. A newer development is the use of Hylenex or human-recombinant hyaluronidase, which carries the advantage of a reportedly increased effectiveness at the body's normal pH compared to bovine-recombinant hyaluronidase [20]. This injection may cause some discomfort, so slow injection is preferable. Observe for "opening up" (i.e., visualization) of the "scarred in" nerve root. A 3-mL test dose of a 10-mL local anesthetic/steroid (LA/S) solution is then given. Our institution used 4 mg of dexamethasone mixed with 9 mL of 0.2 % ropivacaine. Ropivacaine is used instead of bupivacaine for two reasons: the former produces a preferential sensory versus a motor block, and it is less cardiotoxic than a racemic bupivacaine. Doses for other corticosteroids commonly used are 40–80 mg of methylprednisolone (Depo-Medrol), 25–50 mg of triamcinolone diacetate (Aristocort), 40–80 mg of triamcinolone acetonide (Kenalog), and 6–12 mg of betamethasone (Celestone Soluspan). If, after 5 min, there is no evidence of intrathecal or intravascular injection of medication, inject

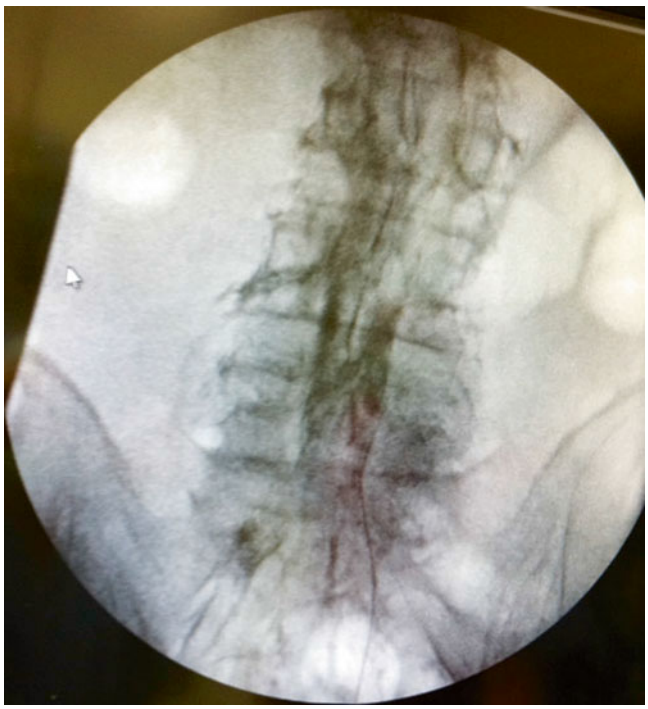

Fig. 31.10 Catheter (24 × L) is threaded to right lateral L4 neural foramen

the remaining 7 mL of the LA/S solution. Remove the needle under continuous fluoroscopic guidance to ensure the catheter remains at the target level (Fig. 31.11). Secure the catheter to the skin using nonabsorbable suture and coat the skin puncture site with antimicrobial ointment. Apply a sterile dressing and attach a 0.2-μm filter to the end of the catheter. Affix the exposed portion of the catheter to the patient with tape and transport the patient to the recovery area.

A 20- to 30-min period should elapse between the last injection of the LA/S solution and the start of the hypertonic saline (10 %) infusion. This is necessary to ensure that a subdural injection of the LA/S solution has not occurred. A subdural block mimics a subarachnoid block, but it takes longer to establish, usually 16–18 min. Evidence for subdural or subarachnoid spread is the development of motor block. If the patient develops a subarachnoid or subdural block at any point during the procedure, the catheter should be removed and the remainder of the adhesiolysis canceled. The patient needs to be observed to document the resolution of the motor and sensory block. If no difficulty with the catheter is noted, 10 mL of the hypertonic saline (assuming single catheter placement) is then infused through the catheter over 30 min. If the patient complains of increased pain at any point during the hypertonic saline infusion, the infusion is stopped and

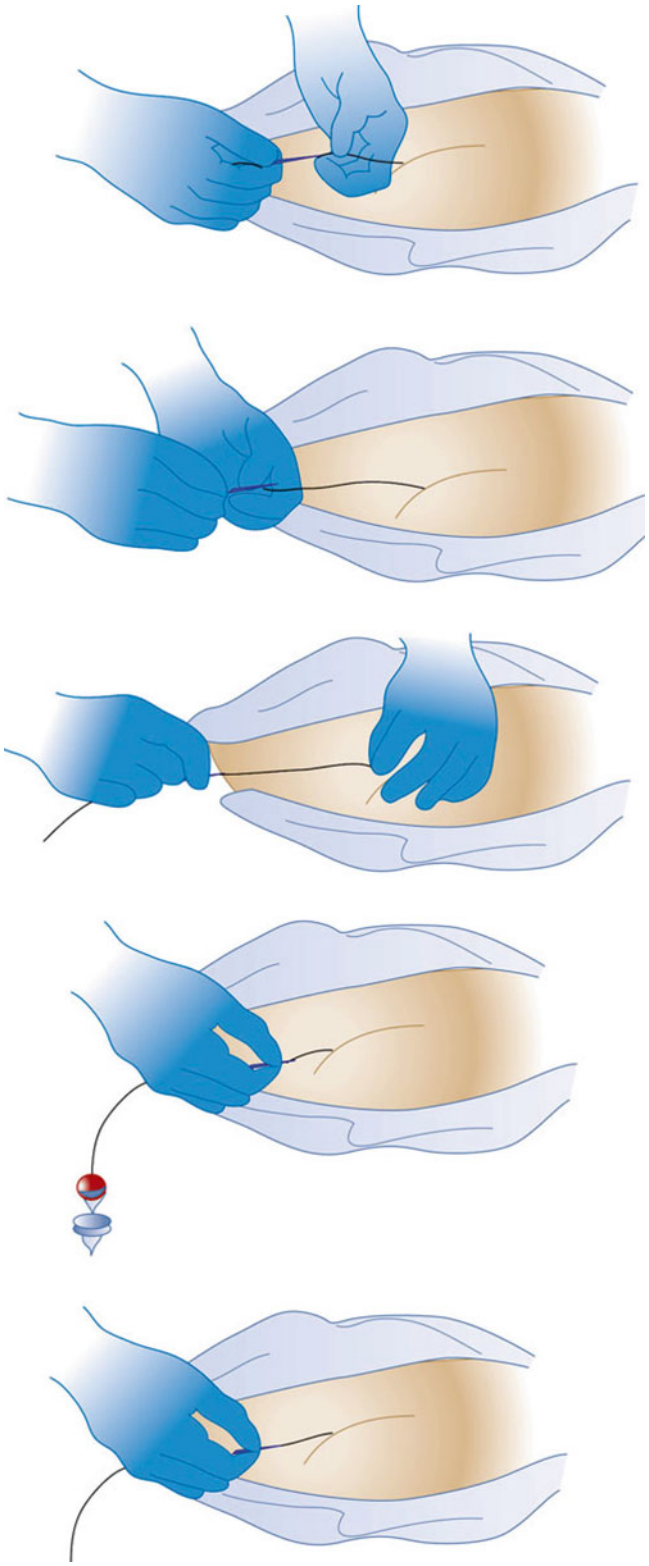

Fig. 31.11 Five picture sequence of removal of the needle to prevent dislodging the catheter from target site before suturing and application of dressing

an additional 2–3 mL of 0.2 % ropivacaine is injected and the infusion is restarted. Alternatively, 50–75 μg of fentanyl can be injected epidurally in lieu of the local anesthetic. After completion of the hypertonic saline infusion, the catheter is slowly flushed with 2 mL of preservative-free normal saline and the catheter is capped.

Our policy is to admit the patient for 23-h observation status and do a second and a third hypertonic saline infusion the following day. On the day after the procedure, the catheter is twice infused (separated by 4- to 6-h increments) with 10 mL of 0.2 % ropivacaine without steroid and 10 mL of hypertonic saline (10 %). Using the same technique as the first infusion, a 3-mL test dose of ropivacaine 0.2 % is injected. If after 5 min, no signs or symptoms of catheter migration are evident (i.e., motor block), the remaining 7 mL of ropivacaine 0.2 % is injected. An additional 20 min is allowed prior to infusion of 10 mL of hypertonic saline (10 %) over 30 min. At the end of the third infusion, the catheter is removed, tip inspected for intactness, and a sterile dressing applied. The patient is discharged home with 5 days of oral cephalexin at 500 mg twice a day or oral levofloxacin (Levaquin) at 500 mg once a day for penicillin-allergic patients. Clinic follow-up is in 30 days.

Caudal Lysis of Adhesions Technique Tips

Occasionally, interventional pain physicians with limited experience performing caudal lysis of adhesions may experience difficulty with catheter advancement and placement. It is recognized that there is a learning curve encountered and the following tips are offered. First, the placement of the needle should be such that easy access is gained for the procedure. While this tip seems self-evident, the initial skin wheal placed for caudal access is extremely important to ensure appropriate needle placement. As previously mentioned, the skin entry site should be approximately 5 cm caudal and 2.5 cm lateral to the sacral hiatus on the opposite buttock of the target. Failure to start at this location results in an angle that makes initial midline catheter advancement difficult. Second, the tip of the needle should be precisely in the midline of the caudal epidural space as viewed on AP fluoroscopic images. Again, off-center needle tip location predisposes the catheter to premature deviation and difficulty with proper advancement. Lastly, take your time when advancing the needle into the caudal epidural space and advancing the catheter. Remember, immediately ventral to the sacrum is the lower abdominal cavity and caution should be taken to prevent inadvertent bowel puncture. Advancing and steering the catheter should be performed slowly and with finesse to ensure an appropriate path to the target.

The initial catheter advancement is near the midline and the steering starts at the S3 level. The most difficulty comes from a catheter going to the lateral sacral wall and bouncing off.

Lysis of Adhesions and Percutaneous Neuroplasty via Transforaminal Catheters

Transforaminal catheters can be used to perform lysis of adhesions for levels difficult to access from the caudal approach or to perform percutaneous neuroplasty. Lysis of adhesions is performed when the catheter is placed in the ventral-lateral epidural space and is used to target epidural fibrosis associated with nerve roots. Percutaneous neuroplasty, on the other hand, is performed when the catheter is advanced from the foramen cephalad into the ventral epidural space. The percutaneous neuroplasty catheter position allows interventions to be directed at pain associated with the posterior annulus fibrosus and/or the posterior longitudinal ligament.

The following steps detail lumbar transforaminal catheter introduction for both lysis of adhesions and percutaneous neuroplasty. After the target level is identified with an AP fluoroscopic image, the superior vertebral end plates are superimposed (“squared off”), which is usually achieved with 15–20° of caudocephalad tilt of the fluoroscope. The fluoroscope is then obliqued approximately 15° to the side of the target and adjusted until the spinous process is rotated to the opposite side. This fluoroscope positioning allows the best visualization of the superior articular process (SAP) that forms the inferoposterior portion of the targeted foramen. The image of the SAP should be superimposed on the shadow of the disk space on the oblique view. The tip of the SAP is the target for the needle placement (Fig. 31.12). Raise a skin wheal slightly lateral to the shadow of the tip of the SAP. Pierce the skin with an 18-gauge needle and then insert a 15- or 16-gauge RX Coudé 2 needle and advance using gun-barrel technique toward the tip of the SAP. Continue to advance the needle medially toward the SAP until the tip contacts bone. Rotate the tip of the needle 180° laterally and advance about 5 mm (Fig. 31.13). Rotate the needle back medially 180° (Fig. 31.14) and place the second protruding stylet. This stylet is designed to prevent nerve root damage as the needle is advanced into the neuroforamen. As the needle is advanced slowly under lateral fluoroscopic guidance, a clear “pop” is felt as the needle penetrates the intertransverse ligament. The tip of the needle should be just past the SAP in the posterior foramen. In the AP plane, insert the catheter slowly into the foramen. Advance catheter to the midcanal position; the catheter tip is between the dura and the posterior longitudinal ligament. Injection of 2 mL of preservative-free saline produces pain on the same side as the catheter tip, indicating this to be the back pain generator (Figs. 31.15, 31.16, and 31.17). The injection of preservative-free normal saline during percutaneous neuroplasty allows reproduction and provocation of the patient’s low back pain creating better understanding of its elusive mechanism and helps to point to appropriate therapy.

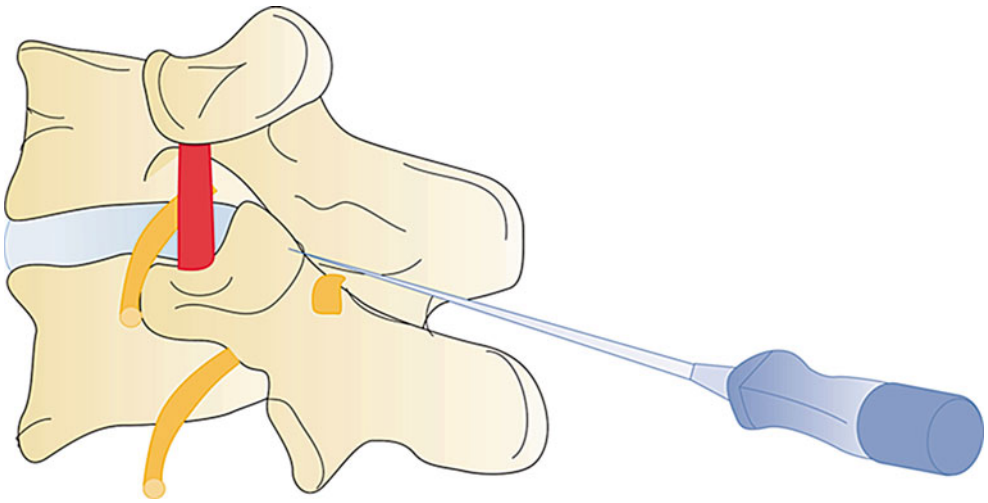

Fig. 31.12 Transforaminal lateral-oblique view. Target the SAP with the advancing RX Coude needle

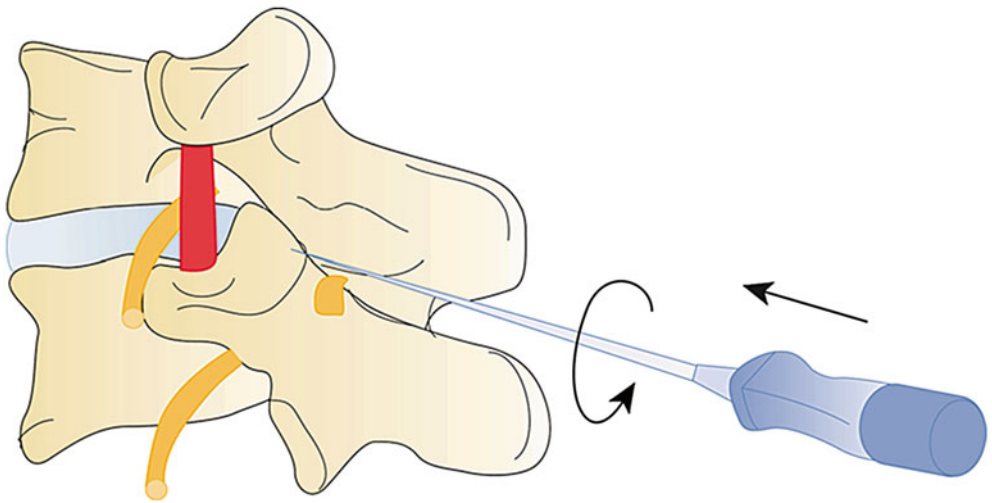

Fig. 31.13 Following bony contact with SAP. Lateral rotation of 180° to allow passage toward the target

The target position of the transforaminal catheter for lysis of adhesions should be the ventral-lateral epidural space along the path of the exiting nerve root. The target position of the percutaneous neuroplasty catheter will be slightly cephalad to the level of the foramen of entry and in the midline of the spinal canal as demonstrated on AP fluoroscopic views. Confirm that the catheter is in the anterior epidural space with a lateral image. Anatomically, the catheter is in the foramen above or below the exiting nerve root. If the catheter cannot be advanced, it usually means the needle is either too posterior or too lateral to the foramen. It can also indicate that the foramen is too stenotic to allow passage of the catheter. The needle can be advanced a few millimeters anteriorly in relation to the foramen, and that will also move it slightly medial into the foramen. If the catheter still will not pass, the initial insertion of the needle will need to be more lateral. Therefore, the fluoroscope angle will be about 20° instead of 15°. The curve of the needle usually facilitates easy catheter placement.

Inject 1–2 mL of contrast to confirm epidural spread (Fig. 31.18). When a caudal and a transforaminal catheter are placed, the 1,500 U of hyaluronidase is divided evenly between the two catheters (5 mL of the hyaluronidase/saline solution into each). The LA/S solution is also divided evenly, but a volume of 15 mL (1 mL steroid and 14 mL 0.2 % ropivacaine; of the total volume, 5 mL is transforaminal and 10 mL is caudal) is used instead of 10 mL. Remove the needle under fluoroscopic guidance to make sure the catheter does not move from the original position in the epidural space. Secure and cover the catheter as described previously.

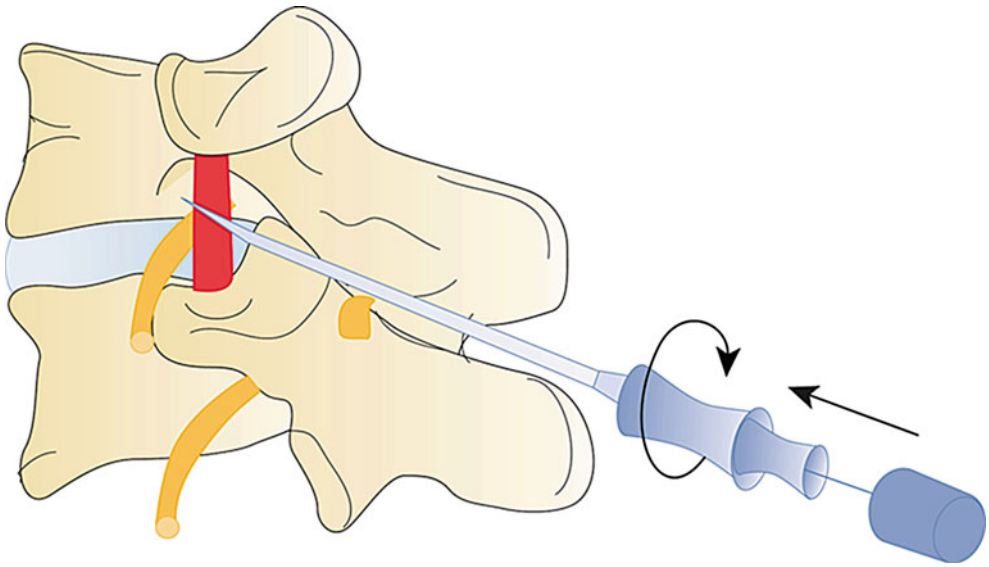

Fig. 31.14 Note the intertransverse ligament. The needle tip with the RX Coude 2 that has 1-mm protruding blunt stylet will pass through the ligament and will be less likely to damage the nerve

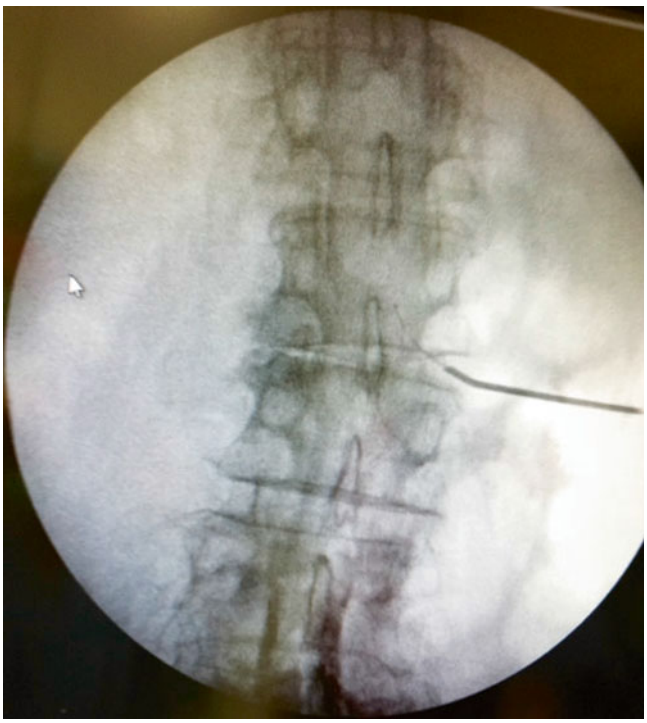

Fig. 31.15 RX Coude 2 needle is navigated around superior pars of L3 in the posterior neuroforamen, and a 24 × L catheter is threaded into the ventral midcanal epidural space

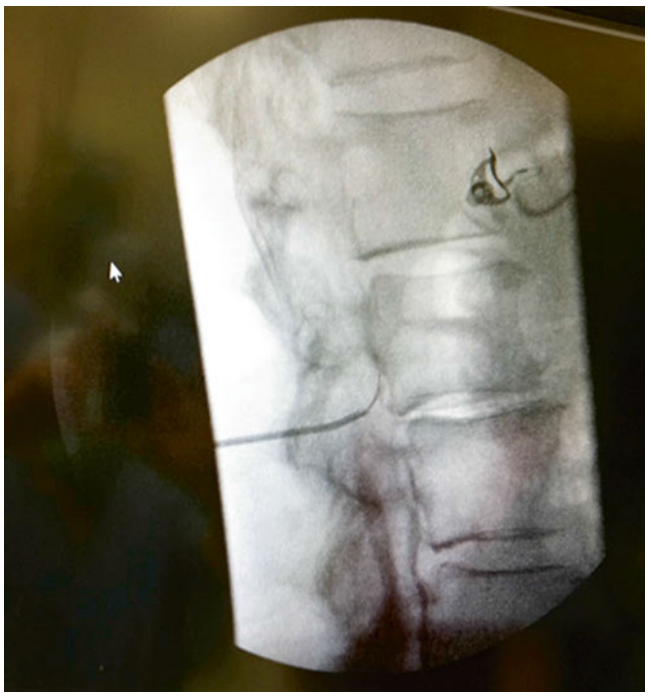

Fig. 31.16 Injection of 2 mL of preservative-free normal saline produces right-sided back pain

The hypertonic saline solution is infused at a volume of 4–5 mL per transforaminal level and 8–10 mL per caudal catheter over 30 min. The hypertonic saline injection volume should always be less than or equal to the local anesthetic volume injected to avoid pain from injection. The second and third infusions should be performed as detailed above in the section "Lysis of Adhesions via a Caudal Catheter" with the adjusted volume of injectate for multiple catheters. It behooves the practitioner to check the position of the transforaminal catheter under fluoroscopy before performing the second and third infusions. The catheter may advance across the epidural space into the contralateral foramen or paraspinous muscles

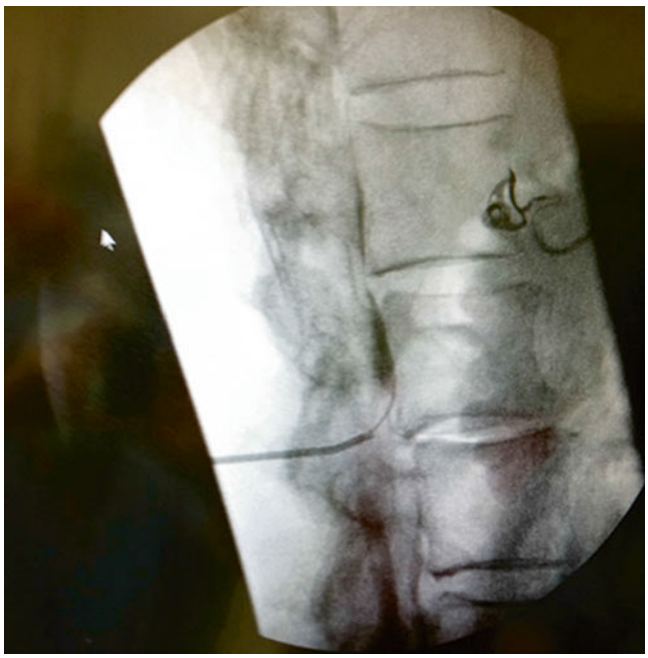

Fig. 31.17 Injection of 5 mL of Omnipaque 240 followed by 5 mL of 750 U of hyaluronidase (bovine compounded) and 5 mL 0.2 % ropivicaine with 20 mg of triamcinolone

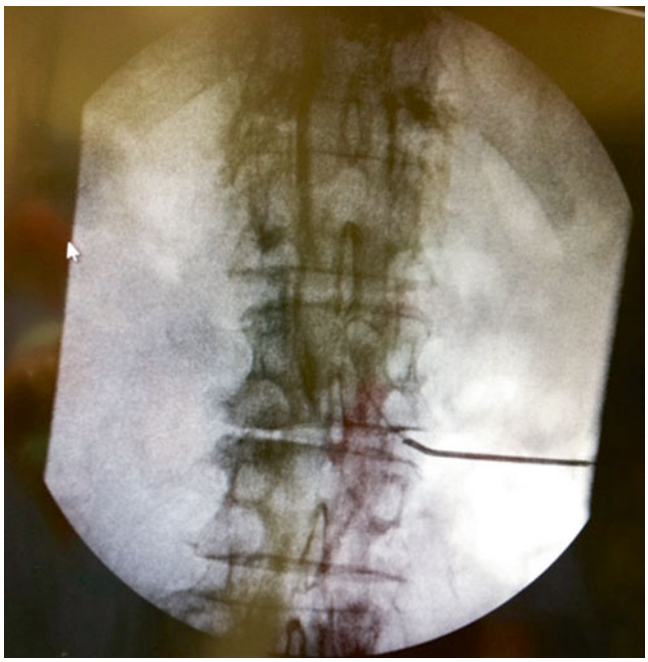

Fig. 31.18 AP view following contrast injection

or more commonly back out of the epidural space into the ipsilateral paraspinous muscles. This results in deposition of the medication in the paravertebral tissue rather than in the epidural space. As with the caudal approach, remove the transforaminal catheter after the third infusion.

Cervical and Thoracic Approaches: Epidural Mapping

Cervical and thoracic approaches to the aforementioned procedures, in addition to epidural mapping, are beyond the scope of this chapter due to chapter length limitations. Recommended reading Intech Article Open Access [21, 22].

Neural Flossing

The protocol for epidural adhesiolysis has been aided by neural flossing exercises that were designed to mobilize nerve roots by "sliding" them in and out of the foramen (Fig. 31.19). This breaks up weakened scar tissue from the procedure and prevents further scar tissue deposition. If these exercises are done effectively three to four times per day for a few months after the procedure, the formation of scar tissue will be severely restricted.

Complications

As with any invasive procedure, complications are possible. These include bleeding, infection, headache, damage to nerves or blood vessels, catheter shearing, bowel/bladder dysfunction, paralysis, spinal cord compression from loculation of the injected fluids or hematoma, subdural or subarachnoid injection of local anesthetic or hypertonic saline, and reactions to the medications used. We also include on the consent form that the patient may experience an increase in pain or no pain relief at all. Although the potential list of complications is long, the frequency of complications is very rare and the risk decreases significantly with experience performing the procedure.

Subdural spread is a complication that should always be watched for when injecting local anesthetic. During the caudal adhesiolysis, particularly if the catheter is advanced along the midline, subdural catheter placement is a risk (Figs. 31.20 and 31.21). Identification of the subdural motor block should occur within 16–18 min. Catheters used for adhesiolysis should never be directed midline in the epidural space.

Conclusion

Epidural adhesiolysis has evolved over the years as an important treatment option for patients with intractable cervical, thoracic, and low back and leg pain. Studies show that patients are able to enjoy significant pain relief and restoration of function. Manchikanti's studies show that the amount and duration of relief can be achieved by repeat procedures [23].

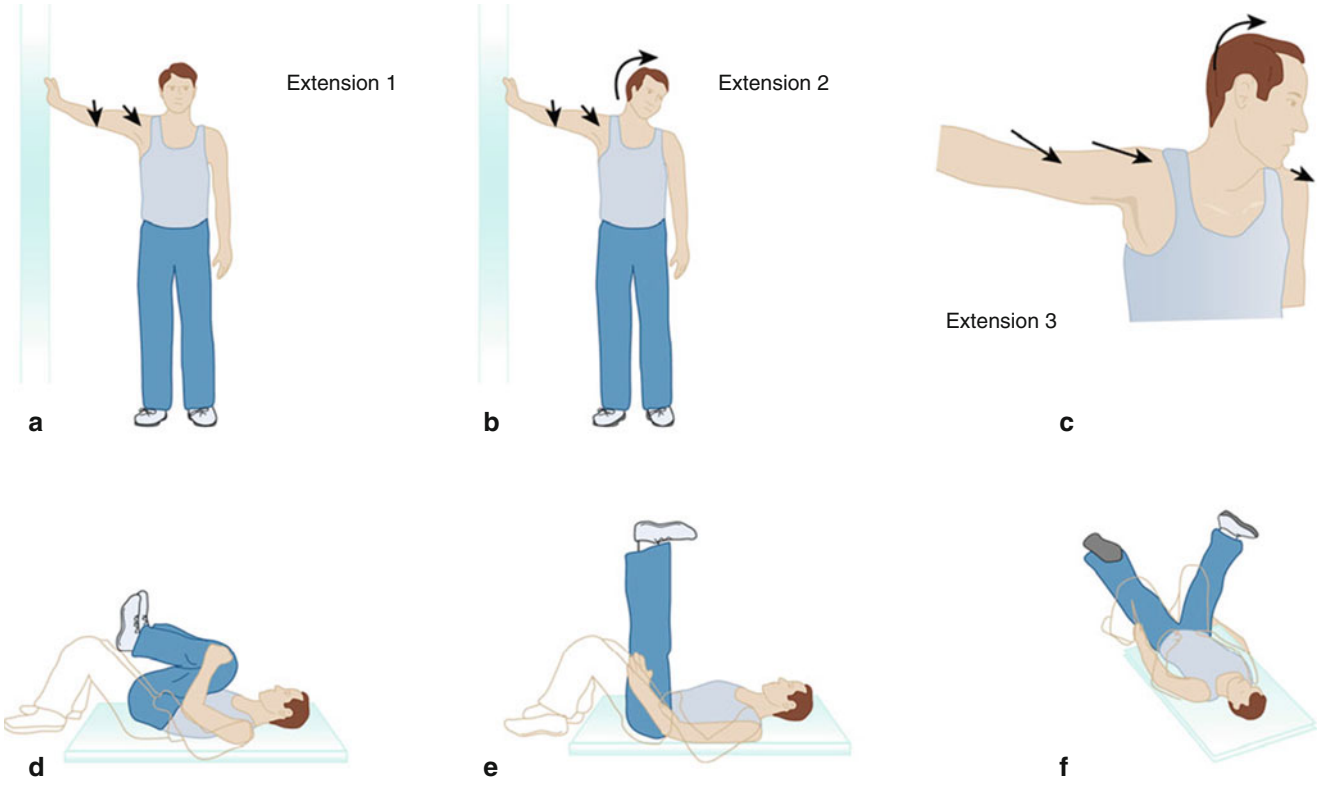

Fig. 31.19 Neural flossing exercises. (**a**) Standing erect, firmly grasp a stable surface (e.g., a door frame) with outstretched arm. Press elbow and shoulder forward. (**b**) Next, slowly tilt head in opposite direction from outstretched arm to achieve gentle tension. (**c**) Finally, rotate chin toward opposite shoulder as is comfortable. Hold this final position for approximately 20–30 s. (**d**) Lay down supine on an exercise mat without a pillow. Slowly bring both knees close to the chest with bent legs, and hold this position for 20 s. Release and assume a neutral position. (**e**) Again in supine position, raise both legs to 90°, with knees straight while lying flat on a firm surface. Hold for 20 s. Assume a neutral position and rest briefly. (**f**) Bring both legs to a 90° angle while lying supine. Slowly spread legs in a V shape, as much as is comfortable, and hold for 20 s

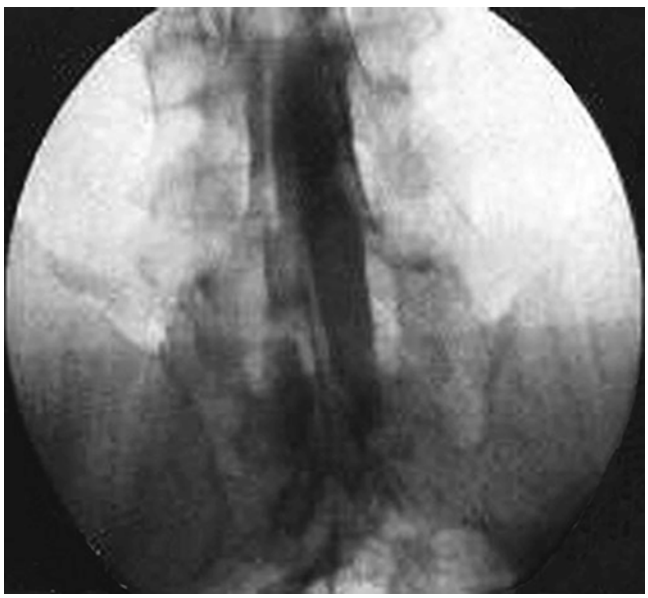

Fig. 31.20 Midline catheter placement enters subdural space. There is also some epidural dye spread. But the patient starts to complain of bilateral leg pain

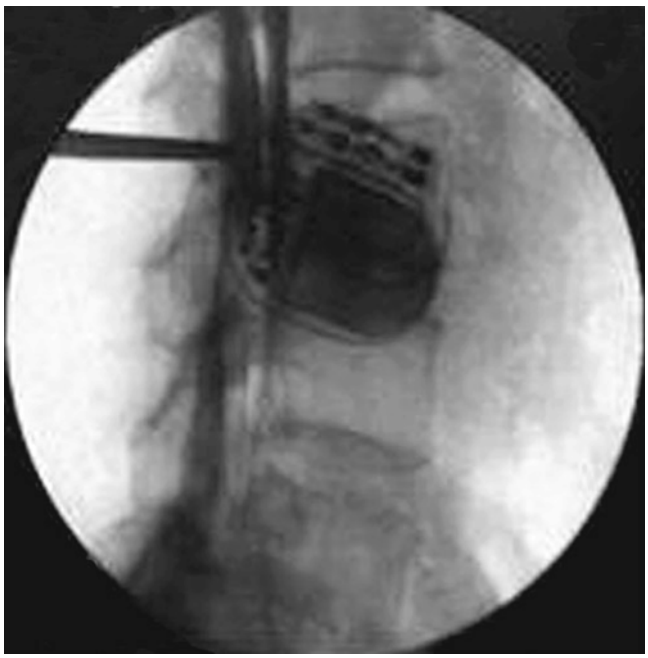

Fig. 31.21 A marker on the skin surface indicates subdural accumulation of contrast. A 22-gauge spinal needle and extension set with syringe was placed in the subdural space, and 12 mL fluid was aspirated (not seen on image). The patient reported immediate reversal of bilateral leg pain

Recent prospective randomized double-blind studies on failed back surgery and spinal stenosis show 75 and 80 % improvement in visual analog scale scores and functional improvements at 12 months' follow-up [24, 25]. The evolution in the recognition of the site-specific importance of the catheter and medication delivery together with the fact that physicians need to acquire the skills to be able to carry out the procedure led to the improved outcomes seen in recent prospective randomized studies. Contradictory opinion usually originates from physicians who have never done the procedure or have never learned how to navigate the epidural space and quote earlier information that was published along the evolutionary trail.

This is evidenced by the fact that results seen at the Texas Tech International Pain Center surpass even the strongest randomized-controlled trials and may be related to both how the procedure is performed and patient involvement including doing "neural flossing" exercises. This is due to both familiarity with the procedure itself and combining the procedure with aggressive neural flossing exercises. Large numbers of patients have been spared unnecessary surgery or repeat surgery by the use of adhesiolysis and at tremendous cost savings, which is based on the cost-effectiveness studies [26, 27].

Facet pain is commonly encountered approximately 1 month post-adhesiolysis and can be confirmed with provocative testing and diagnostic facet blocks. Radiofrequency facet denervation gives us the best long-term outcome. Recognition of the above has led to the algorithmic thought process where disc- and facet-related therapeutic considerations always follow adhesiolysis.

Patients who have undergone both lysis of adhesions and percutaneous neuroplasty experience reduction of pain-related radiculopathy and back pain. Lumbar disc-related procedures are extremely rare in the post-adhesiolysis period as some of the pathology causing back pain and radiculopathy is reversed. Spinal cord stimulation does not preclude the effectiveness of adhesiolysis. Spinal cord stimulation is either more effective following adhesiolysis or, if adhesiolysis is performed post-spinal cord stimulation, is equally effective in achieving enhanced pain relief.

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Sacroiliac Joint Injection and Radiofrequency Denervation

32

Sunil J. Panchal

Key Points

- Sacroiliac joint pain is often a problem that is mimicking of other conditions which may delay the diagnosis.
- The SI joint as a pain generator is confirmed by appropriate response to fluoroscopically guided local anesthetic injection.
- Treatment of the joint is most commonly performed with injection of steroid by fluoroscopic guidance accompanied by physical medicine.
- Radiofrequency ablation should be considered in recurrent joint pain that is not resolved with steroid injection, physical medicine, and other conservative measures.
- New methods of radiofrequency ablation are evolving, and the physician should be well versed in options to treat this common malady.

Introduction

Sacroiliac (SI) joint pain is an often under-recognized condition affecting a significant number of patients with axial low back pain. Mapping studies have demonstrated that the SI joint can cause radiation of pain to the hip, groin, and posterior leg to the knee. This pattern of pain overlaps that of lumbar facet referral maps and also has been confused by clinicians with sciatica. Studies have demonstrated that historical and physical examination findings and radiological imaging are insufficient to diagnose SI joint pain. Most commonly, the method used to diagnose the SI joint as a pain generator is with fluoroscopic-guided local anesthetic blocks. Treatment initially consisted of intra-articular steroid injections but has evolved to include radiofrequency denervation, with a variety of techniques that will be discussed in further detail in this chapter.

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Anatomy

The sacroiliac (SI) joint is the largest axial joint in the body, with an average surface area of 17.5 cm^2 [1].

There is significant variability in the size, shape, and contour of the SI joint, even from one side versus the other within the same individual [2, 3]. The SI joint is commonly described as a large, auricular-shaped, diarthrodial synovial joint, but only the anterior third of the interface between the sacrum and ilium is a true synovial joint. The rest of the junction is created from a complex set of ligamentous connections. Due to an absent or rudimentary posterior capsule, the SI ligamentous structure is more extensive dorsally and functions as a connecting band between the sacrum and ilia [4]. The primary function of this ligamentous system is to limit motion in all planes of movement. During pregnancy, the ligaments are looser due to elevated levels of relaxin and thus allow the mobility necessary for vaginal delivery [5]. The SI joint is also supported by a network of muscles that create stabilizing forces to the pelvic bones. Some of these muscles, such as the gluteus maximus, piriformis, and biceps femoris, are functionally connected to SI joint ligaments, so their actions can affect joint mobility. The potential for vertical shearing is present in approximately 30 % of SI joints, owing to the more acute angulation of the short, horizontal articular component [6].

Age-related changes in the SI joint begin in puberty and continue throughout life. During adolescence, the iliac surface becomes rougher, duller, and coated in some areas with fibrous plaques. Surface irregularities, crevice formation, fibrillation, and the clumping of chondrocytes manifest in individuals in their 30s and 40s. By the time individuals reach their 60s, motion at the joint may become markedly restricted as the capsule becomes increasingly collagenous and fibrous ankylosis occurs [4].

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SI Joint Innervation

The innervation of the SI joint is complex and variable in several reports in the literature. The lateral branches of the L4–S3 dorsal rami are described as composing the major innervation to the posterior SI joint [1]. Some investigators claim that L3 and S4 also contribute to the posterior nerve supply [7, 8]. The anterior joint is innervated by L4–S2 ventral rami [9–12], but some reports include ventral rami from as high as L2. It is important to note that there is significant variability of the posterior lateral branch nerves in regard to location and number in each patient, as well as side to side in the same individual. These nerves vary in regard to the tissue plane, with some directly on bone and others in the soft tissue. This variability will have strong implications in assessing results from denervation techniques. It is also important to understand that nociception in this area may originate from more than the synovial joint. Animal and human cadaver studies have identified nociceptors in the joint capsule and also in the surrounding ligaments [13].

Functional Role of the SI Joint

The SI joints provide stability and are involved in the transmission and dissipation of truncal loads to the lower extremities, limiting *x*-axis rotation and facilitating parturition. The SI joint rotates about all three axes, approximately 1–2° in each direction [14–16]. Sturesson et al. [17] measured multiple SI joint movements in 25 patients diagnosed with SI joint pain. No differences were found between symptomatic and asymptomatic joints, with the conclusion that three-dimensional motion analysis was not useful for identifying painful SI joints in most patients. However, hypermobility has been associated as a cause of SI joint pain in patients with traumatic instability, multiparity, muscular atrophy, and lower motor neuron disease [18].

Prevalence

The prevalence of LBP emanating from the SI joints has been reported to be as high as 30 %. The methodology of prevalence studies has included either physical examination findings and/or radiological imaging techniques to arrive at a diagnosis of SI joint pain. A retrospective study by Bernard and Kirkaldy-Willis [19] found a 22.5 % prevalence rate in 1,293 adult patients presenting with LBP based predominantly on physical examination. Schwarzer et al. [20] conducted a prevalence study involving 43 consecutive patients with chronic LBP principally below L5–S1 using fluoroscopically guided SI joint injections. With significant pain relief after LA injection as the sole criterion for diagnosis, the prevalence of SI joint pain was determined to be 30 %. The presence of groin pain was the only referral pattern found to distinguish patients with SI joint pain from those with LBP of non-SI joint origin. Maigne et al. [21] conducted a prevalence study in 54 patients with unilateral LBP using a series of blocks done with different LA based on International Spinal Injection Society guidelines [22]. Nineteen patients had a positive response (≥75 % pain relief) to the lidocaine screening block. Among these patients, 10 (18.5 %) responded with ≥2-h pain relief after the confirmatory block with bupivacaine and were considered to have true SI joint pain (95 % CI, 9–29 %). SI joint injury has previously been described as a combination of axial loading and abrupt rotation. This may result in capsular or synovial disruption, capsular and ligamentous tension, hypomobility or hypermobility, extraneous compression or shearing forces, abnormal joint mechanics, microfractures or macrofractures, chondromalacia, soft tissue injury, and inflammation. The experience of pain in this region from a variety of associated structures is confirmed from studies that demonstrated significant pain relief after both intra-articular and periarticular SI joint injections [23–26]. Risk factors for SI joint pain include leg length discrepancy [27], gait abnormalities [28], prolonged vigorous exercise [29], scoliosis [30], and spinal fusion to the sacrum [31]. Lumbar spine surgery has been associated as well due to SI ligament weakening and/or surgical violation of the joint cavity during iliac graft bone harvest [32] and postsurgical hypermobility [33]. Pregnancy increases risk in women for SI joint pain due to increased weight gain, exaggerated lordotic posture, mechanical trauma of parturition, and hormone-induced ligamental laxity [5, 34]. Inflammation of the SI joints occurs early in all seronegative and HLA-B27-associated spondylarthropathies [35]. In a subset of patients with Reiter's syndrome/reactive arthritis, the disease is due to infection [36]. A retrospective study by Chou et al. [37] assessed the inciting events in 54 patients with injection-confirmed SI joint pain and found that trauma was the cause in 44 % of patients, 35 % were idiopathic, and 21 % were attributed to the cumulative effects of repeated stress. Of the 24 patients who reported trauma as the cause of their pain, the most common events were motor vehicle accidents (n = 13), falls onto the buttock (n = 6), and childbirth (n = 3).

Diagnosis

Many physical examination tests have been promoted as diagnostic tools in patients with presumed SI joint pain [38]. Several involve distraction of the SI joints, such as Patrick's test and Gaenslen's test. However, clinical studies have demonstrated that medical history or physical examination findings

are not consistently reliable in identifying dysfunctional SI joints as pain generators [20, 39, 40]. Also, Dreyfuss et al. [41] found 20 % of asymptomatic adults had positive findings on three commonly performed SI joint provocation tests. Provocative SI joint maneuvers and alignment/mobility tests are also unreliable [42–49], but reproducibility has been found to be greater for provocative tests than for mobility and alignment assessments. In the Dreyfuss et al. study [40] conducted in 85 patients with injection-confirmed SI joint pain, there was moderate agreement among clinicians with regard to provocative maneuvers of painful joints but were still found to lack diagnostic utility.

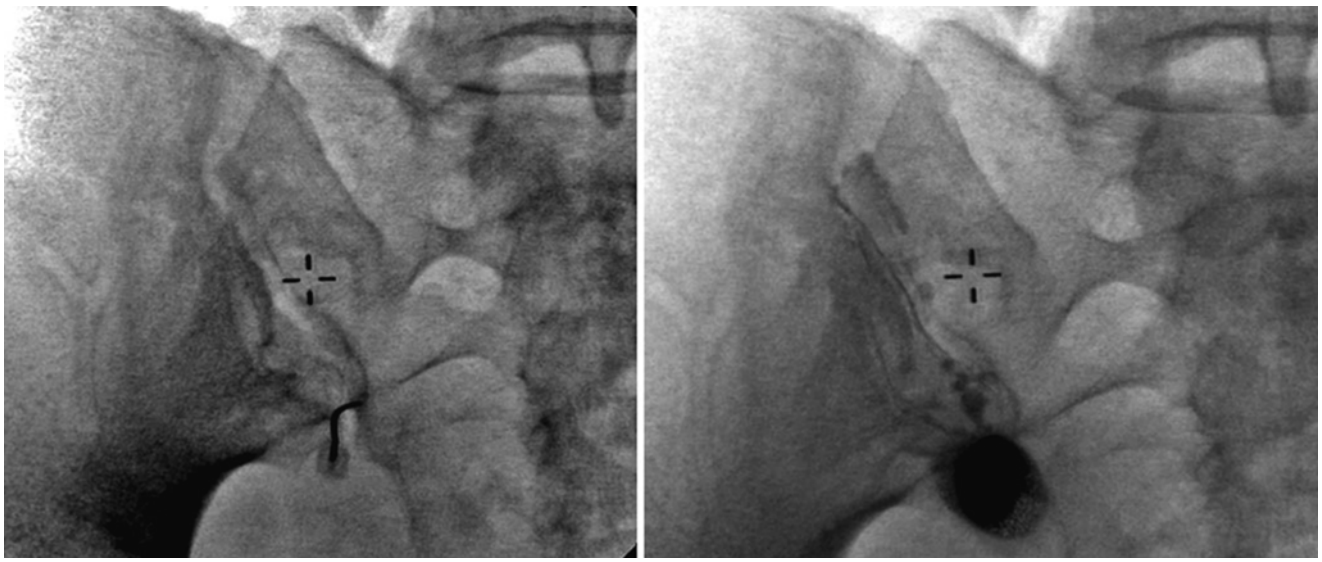
Radiologic studies of patients with SI joint pain have limited benefits as well. Maigne et al. [50] and Slipman et al. [51] found sensitivities of 46 and 13 %, respectively, for the use of radionuclide bone scanning in the identification of SI joint pain. Even though these studies had high specificites (89.5 % for Maigne et al. [50] and 100 % for Slipman et al. [51]), the low sensitivities lead to the conclusion that bone scans are a poor screening test for SI joint pain. Diagnostic injections and symptoms have correlated poorly with CT and radiographic stereophotogrammetry [17, 52]. A retrospective analysis by Elgafy et al. [52] found CT imaging to be 57.5 % sensitive and 69 % specific in diagnosing SI joint pain.

Mapping studies of pain referral patterns from SI joints provide some useful information. Fortin et al. [53] performed provocative SI joint injections using contrast and lidocaine in ten asymptomatic volunteers. Sensory changes were localized to the ipsilateral medial buttock inferior to the posterior superior iliac spine in six of the ten subjects. In two subjects, the area of hyperesthesia extended to the superior aspect of the greater trochanter. The last two subjects experienced sensory changes radiating into the upper thigh. Then in a follow-up study, independent examiners selected 16 individuals among 54 with chronic LBP whose pain diagrams most closely resembled the pain referral patterns obtained in the first study [54]. These 16 patients proceeded to undergo provocative SI joint injections with contrast and LA. All 16 experienced concordant pain during the injection, with 14 obtaining pain relief after deposition of LA. Ten patients reported ≥50 % pain reduction. Six of the 16 patients had ventral capsular tears revealed during arthrography. After the SI joint injections, provocative discography and lumbar facet joint injections were performed in nine patients each. No one had a positive response to either. Slipman et al. [55] conducted a retrospective study to determine the pain referral patterns in 50 patients with injection-confirmed SI joint pain. In contrast to the findings by Fortin et al. [53] and Schwarzer et al. [20], the authors found the most common referral patterns for SI joint pain to be radiation into the buttock (94 %), lower lumbar region (72 %), lower extremity (50 %), groin area (14 %), upper lumbar region (6 %), and abdomen (2 %). Twenty-eight percent of patients experienced pain radiating below their knee, with 12 % reporting foot pain. Based on the existing data, the most consistent factor for identifying patients with SI joint pain is unilateral pain (unless both joints are affected) localized predominantly below the L5 spinous process [20, 40, 53–55].

Diagnostic Blocks

An analgesic response to a properly performed diagnostic block is the most reliable method currently available to confirm SI joint pain. However, there are several factors to take into consideration when interpreting the results of a diagnostic intra-articular local anesthetic block. These factors include a possible placebo response, extravasation of local anesthetic to surrounding pain-generating structures such as muscles, ligaments, and lumbosacral nerve roots. Other factors that may lead to unimpressive responses include inadequate spread of local anesthetic to the anterior and cephalad portions of the SI joint as well as pain from coexisting lumbar facet arthropathy. A pilot study by Fortin et al. [53] attempted to map SI joint referral patterns in asymptomatic volunteers, in which extravasation of contrast (mean volume of 1.6 mL) occurred in 9 of 10 subjects during SI joint injection, with half having at least moderate spread outside the joint. Following injection of local anesthetic, lower extremity numbness occurred in 40 % of the subjects, indicating unintended neural blockade of the lumbosacral nerve roots. In the Maigne et al. [21] study, 3 of the initial 67 patients were excluded because of "sciatic palsy" after the screening block, and another 7 were excluded because penetration of the SI joint was unable to be performed. Others have reported less frequent (≤5 %) failure rates with fluoroscopically guided SI joint injections [20, 40, 56]. More pronounced degenerative changes in the elderly and those with spondylarthropathies may lead to greater technical challenges. CT imaging may be another option for difficult cases [24, 57]. Blind SI joint injections are unreliable as demonstrated by Rosenberg et al. [58] who performed a double-blind study in 37 patients (39 joints) to determine the accuracy of clinically guided SI joint injections using CT imaging for confirmation. The authors found that intra-articular injection was accomplished in only 22 % of patients, whereas sacral foraminal spread occurred 44 % of the time. In three patients, no contrast was seen on CT scanning, indicating likely vascular uptake. In 24 % of injections, contrast extended into the epidural space (Figs. 32.1 and 32.2).

In order to reduce the incidence of false-positives, it is appropriate to consider a series of SI joint blocks. In a prospective study of 67 patients with unilateral LBP, SI joint-compatible referral patterns, and joint tenderness, Maigne et al. [21] investigated the prevalence of SI joint pain using a series of blocks with two different local anesthetics.



Figs. 32.1 and 32.2 SI Joint intra-articular injection before and after 1-ml nonionic contrast injection

Of the 54 patients who completed the study, 19 obtained ≥75 % pain relief with the lidocaine screening block. After the confirmatory block with bupivacaine, only 10 of the 19 patients achieved ≥75 % pain relief lasting 2 or more hours, resulting in a prevalence rate of 18.5 %. The false-positive rate of 17 % in this study is less than that previously reported for lumbar facet blocks [59]. Since there is not another methodology to serve as a diagnostic "gold standard," we cannot determine the true sensitivity or specificity of intra-articular blocks. However, from a practical standpoint, with a low-risk profile of SI joint blocks, it is appropriate to proceed with this methodology and base treatment plans from the information gleaned. It is important to point out that while a series of blocks to demonstrate a consistent response may represent an ideal, it also incurs increased costs and an increased length of time until the patient is adequately treated.

Treatment

Non-interventional management of SI joint pain may include the use of shoe inserts to address leg length discrepancies as well as physical therapy and osteopathic or chiropractic manipulation to address altered gait mechanics and spine malalignment [60, 61]. However, there are no prospective, controlled studies supporting these modalities. Nonsurgical stabilization programs have been advocated including the application of pelvic belts that reduce the sagittal rotation of presumed incompetent SI joints in pregnant women [62, 63] to exercise-induced pelvic stabilization programs [64]. Ankylosing spondylitis (AS), an inflammatory rheumatic disease with spine and SI joint involvement that manifests as spondylitis and sacroiliitis, has been treated with pharmacologic approaches, but the results are muddled due to systemic involvement and cannot give specific conclusions as to the SI joints.

Intra-articular injections with steroid and LA can serve the dual function of being therapeutic and aiding in diagnosis. It is beneficial to blind the patient to the local anesthetic chosen, use a pain diary to assess the first phase response to local anesthetic, and then assess the second phase response to the anti-inflammatory effect of the steroid. Controlled studies demonstrate good relief for a majority of patients from a single dose of fluoro-guided intra-articular or periarticular steroid 1–2 months after injection, with a limited number of individuals still showing benefit at 3 or 6 months. Prospective observational studies of image-guided SI joint injections to demonstrate good to excellent pain relief lasting from 6 months to 1 year. As with any pharmacologic treatment, the length of duration of response to a single-dose steroid is less of a function of the effectiveness of the drug but rather an issue of how long other factors cause symptomatic inflammation to recur. Therefore, the decision to utilize steroid injections as a long-term treatment plan depends on the interval needed to maintain improvement, quality of relief, and potential adverse effects related to the cumulative dose of corticosteroids.

Radiofrequency Denervation Procedures

Radiofrequency (RF) denervation procedures are utilized to provide prolonged pain relief to patients with injection-confirmed SI joint pain. The techniques used have ranged from denervating the joint by performing intra-articular

lesions, lesioning the lateral branches that provide a portion of the SI joint innervation [65–68], to the combination of ligamentous as well as neural RF ablation [69]. All of the techniques described cannot completely denervate the SI joint, and an analysis of the methodology of the techniques is important to place the published success rates in proper perspective as well as provide insight as how to possibly improve results. It is important to remember that percutaneous RF denervation procedures should not be expected to alleviate pain emanating from the ventral SI joint. In one study [20], ventral capsular pathology was shown to account for 69 % of all CT pathology in the 13 patients with a positive response to diagnostic SI joint blocks. Also, nociceptors have been confirmed to exist on the ligamentous tissue and likely need to be addressed as well (Table 32.1).

Intra-articular Approach

The first study of RF denervation of the SI joint utilized the intra-articular approach. In this study, 33 patients were treated, some on both sides, for a total of 50 joints. The patients underwent diagnostic SI joint injections to determine eligibility. RF lesions were performed with a bipolar technique with probes placed approximately 1 cm apart and leapfrogged for each lesion. Patients were assessed for VAS scores, pain diagrams, physical exam changes, and change in opioid consumption. A successful result was defined as a ≥50 % decrease in VAS for at least 6 months. With this definition, 36.4 % were considered responders, and in this group, the average duration of response was 12 months and also demonstrated a normalization of SI joint pain provocation tests as well as a reduction in opioid consumption. An in vitro study suggests that success rates could be improved upon by reducing the distance between the cannulae when performing bipolar RF lesions, as spacing the cannulae 4–6 mm apart maximized the surface area of the lesion [70]. Another factor to take into consideration is that when bipolar lesioning is performed, the power output is regulated to maintain the desired temperature at one of the cannulae, and there is often a difference in the temperature achieved at the other cannula, often being 5–10° lower, which also affects the size of the area lesioned. Therefore, monopolar lesions placed closely together may provide a more consistent result.

Lateral Branch Approach

This technique involves lesioning of the L4 and L5 dorsal rami as well as the lateral branches from S1 to S3 (or S4). Studies utilizing this approach have some variability as to the methods and results. Retrospective studies had a range of results including one with 8 of 9 patients with ≥50 % relief after 9 months and another with 64 % of 14 patients achieving >50 % relief at 6 months. A larger retrospective study had 52 % of 77 patients achieve at least 50 % relief at 6 months, but had variability in technique, as conventional as well as cooled RF treatments were included. The prospective studies performed are all very small in size (n = 9, 28) and had success rates at 6 months at 67 and 57 %, respectively. Another prospective study reported success rates as high as 70 % in 38 patients, but only reported results at 3 months post-procedure (Fig. 32.3).

Emerging Concepts

Other techniques which have been reported on a limited basis in the literature include a prospective trial in 22 patients of pulsed RF lesions from 39 to 42 °C of the L4 and L5 medial branches and the S1 and S2 lateral branches. A >50 % reduction in pain was achieved in 73 % of patients for a short time. Only seven patients had relief that lasted from 17 to 32 weeks. A retrospective case series of 26 patients was reported using cooled RF probes with the theoretical benefit of achieving larger sized lesions. In this study, lesions were performed at L5 and 2–3 lesions at the S1–S3 neuroforamina. This technique had 50 % of the patients achieve ≥50 % relief at 3–4 months posttreatment. There are no other reports to date that have investigated outcome at 6 months or greater. Gervagez et al. [69] utilized CT-guided RF treatment with denervation of the L5 dorsal ramus and the interosseous SI ligaments at three locations in 38 patients. After 3 months, 34.2 % of patients were pain-free, and 31.6 % had a substantial decrease in pain.

Conclusions

The SI joint is a common cause of axial low back pain which may also radiate to the hips, groin, and posteriorly to the knee in up to 30 % of patients. Historical and physical examination findings have limited reliability as tools in the diagnosis of SI joint pain, thus diagnostic blocks remain the most commonly used method for diagnosing this disorder. While there may be debate as to validity of utilizing injections as a diagnostic tool, they are useful as a prognostic tool prior to performing denervation treatments. Intraarticular and periarticular corticosteroid injections have been shown to provide benefit lasting from 1 month to 1 year in patients with and without spondylarthropathy [71–78]. Like any pharmacologic treatment, this is less a function of the duration of action of the corticosteroid but rather a reflection of the variability of recurrence of inflammation. Over the last decade, the emergence of RF denervation techniques has provided a useful option in providing longer lasting relief in patients

Table 32.1 Published clinical studies of radiofrequency treatment of sacroiliac joint pain

Author, year	Technique	Study design	*N*	Treatment	Outcomes	Key details
Ferrante et al. (2001) [68]	Intra-articular	Retrospective	33 (50 joints)	Multiple, 90 °C, 90-s lesions at approx. 1-cm intervals	At 6 months, 36.4 % had >50 % pain relief, average duration of responders was 12 months	Only the postero-inferior joint was lesioned
Cohen and Abdi (2003) [65]	Lateral branch	Retrospective	18 (9 underwent RF)	80 °C, 90-s lesions of L4 and L5 dorsal rami and S1–S3 lateral branches	13/18 had 50 % pain relief from prognostic blocks, 8/9 of RF-treated patients had >50 % pain relief at 9 months	Criteria for RF treatment were >50 % pain relief from prognostic blocks
Yin et al. (2003) [67]	Lateral branch	Retrospective	14	80 °C, 60-s lesions of L5 dorsal ramus and variably the S1–S3 lateral branches	At 6 months, 64 % had >50 % pain relief, 36 % had complete relief	Criteria for RF treatment were >70 % pain relief after 2 separate SI joint deep interosseous ligament injections
Cohen et al. (2009) [79]	Lateral branch	Retrospective	77	80 °C, 90-s lesions of L4 and L5 dorsal rami and S1–S3 lateral branches	At 6 months, 52 % had ≥50 % pain relief	Criteria for RF treatment were >50 % pain relief from intra-articular SI joint block. Limitations include variable technique (conventional and cooled RF treatments)
Burnham and Yasui (2007) [80]	Lateral branch	Prospective	9	3 conventional lesions at L5 and 3 bipolar strip lesions for S1–S3 dorsal rami	67 % success rate at both 6 months and at 12 months	Criteria for RF treatment were >50 % pain relief for both an SI joint block and a prognostic lateral branch block
Cohen et al. (2008) [81]	Lateral branch	Randomized, placebo controlled	28	Conventional lesions at L4 and L5 and cooled probable lesions at S1 and S2, and some at S3 or S4	At 6 months, 57 % had >50 % pain relief, 14 % success at 12 months	Criteria for RF treatment were >75 % pain relief from SI joint block Only 14 % of control patients had relief at 1 month, none beyond that
Buijs et al. (2004)	Lateral branch	Prospective observational	38 (43 joints)	80 °C, 60-s lesions of S1–S3 lateral branches in all subjects, and L4–L5 dorsal rami in half of subjects	At 12 weeks, complete pain relief at 34.9 % sites and >50 % pain relief at 32.6 % sites	Criteria for RF treatment were >50 % pain relief from SI joint blocks. No difference in outcomes with or without L4 and L5 lesions
Vallejo et al. (2006) [82]	Pulsed RF of lateral branches	Prospective	22	39–42 °C, pulsed RF lesions of L4 and L5 medial branches and S1–S2 lateral branches	16 patients (73 %) had >50 % pain relief for a short time: 6–9 weeks (4 patients), 10–16 weeks (5 patients), 17–32 weeks (7 patients)	Criteria for RF treatment were >75 % pain relief after >2 SI joint injections
Kapural et al. (2008) [83]	Cooled RF	Retrospective case series	26	Lesion at L5 and 2–3 lesions at S1–S3	At 3–4 months, 50 % had >50 % pain relief	Criteria for RF treatment were 2 SI joint blocks with >50 % pain relief
Gevargez et al. (2002) [69]	CT-guided RF lesion of L5 dorsal ramus and posterior interosseous SI ligaments	Prospective observational	38	90 °C, 90-s lesions	At 3 months, 34.2 % were pain-free, 31.6 % reported substantial decrease in pain	Criteria for RF treatment were response to CT-guided SI joint injections

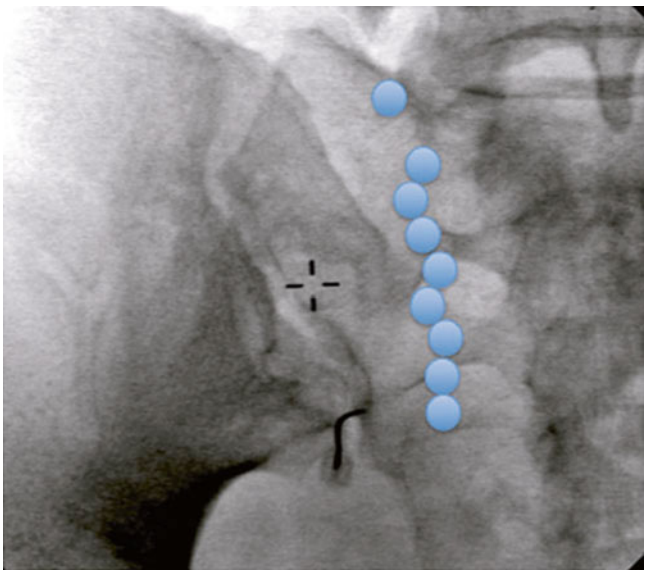


Fig. 32.3 Lesion sites on the sacrum for the lateral branch approach (sites for L5 dorsal rami and lateral branches from S1 to S3 are marked in *blue*)

with SI joint pain. All of the techniques described only partly denervate the SI joint and the surrounding tissue with nociceptors and can be improved upon. The concept of bipolar strip lesioning has been found to require close proximity of probe placement, which at that distance will provide equivalent lesions with monopolar lesioning at the same interval. Future research will need to be done to determine if success rates may be improved upon by utilizing this methodology to more completely denervate both the articular joint as well as the ligamentous nociceptors. This could be promising as responders to this approach have been documented to maintain benefits for at least 1 year. RF lesioning of the lateral branches results in a successful outcome in slightly greater than 50 % of patients, but follow-up has been limited, and longer term studies are needed. Pulsed radiofrequency lesioning has been unimpressive for this indication. The utilization of emerging tools to create larger lesions may simplify the denervation of a large target region but needs to be more fully investigated in regard to safety.

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Vertebral Augmentation: Vertebroplasty and Kyphoplasty

33

Philip S. Kim

Key Points

- Vertebral compression fractures are a common painful condition of osteoporosis.
- Metastatic disease can also lead to painful compression fractures.
- Although most fractures heal over time, some patients experience pain even with conservative therapy.
- The consequence of vertebral fractures can lead to increased mortality and morbidity.
- The psychosocial consequences of multiple fractures lead to poor self-esteem, depression, social isolation, and, ultimately, a poor quality of life.
- A detailed history and physical imaging evaluation are standard in confirming the diagnosis of acute compression fractures.
- Open surgical fixation is rarely utilized, given the poor quality of bone and anchoring for surgical hardware.
- Advanced age makes most patients poor surgical and anesthesia candidates.
- Percutaneous vertebral augmentation or vertebroplasty can be performed by the injection of cement into fractured trabecular bone to stabilize and relieve pain.
- Kyphoplasty is an alternative approach.

Summary

Vertebral compression fractures are a common painful condition of osteoporosis. Metastatic disease can also lead to painful compression fractures. Although most fractures heal over time, some patients experience pain even with conservative therapy. The consequence of vertebral fractures can lead to increased mortality and morbidity [1]. The psychosocial consequences of multiple fractures lead to poor self-esteem, depression, social isolation, and, ultimately, a poor quality of life [1–3]. A detailed history and physical imaging evaluation are standard in confirming the diagnosis of acute compression fractures. Open surgical fixation is rarely utilized, given the poor quality of bone and anchoring for surgical hardware. Advanced age makes most patients poor surgical and anesthesia candidates. Percutaneous vertebral augmentation or vertebroplasty can be performed by the injection of cement into fractured trabecular bone to stabilize and relieve pain. Kyphoplasty is an alternative approach. A balloon is placed in the compressed fracture to create a cavity where cement is placed to stabilize the fracture and restore vertebral height. Recent randomized studies have suggested limited effectiveness of vertebroplasty over controls [4, 5]. Thus, academic controversy has ensued over these negative results [6–9]. Modifications in the vertebral augmentation has been developed in sacroplasty and technical components of lumbo-thoracic augmentation.

Introduction

Osteoporosis is manifested by low mineral density or by the presence of fragility fractures. The occurrence of an atraumatic vertebral fracture is sufficient enough to establish a diagnosis of osteoporosis. In 1996, the incidence of osteoporotic vertebral compression fractures was 700,000 which surpasses the combined fractures of the ankle and the hip [10]. For several decades, vertebral compression fractures were thought to be benign and self-limited. This view evolved from at least two-thirds of fractures never being reported by patients to their physicians [11]. If diagnosed, most patients underwent conservative treatment.

Over 90% of patients with metastatic or advanced stage cancer will experience significant pain [12]. Approximately, half of these patients experience bone pain [46]. That is roughly 400,000 US citizens annually. Majority of the

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metastasis comes from breast, lung, and prostate cancers. Bone metastasis of the spine may lead to significant pain, poor quality of life, and morbidity. Treatments for painful osseous metastases include analgesics, glucocorticoids, radiation, ablative techniques, surgical approaches, and vertebral augmentation.

PMMA (polymethylmethacrylate) has been used in orthopedic treatment and dentistry to fill voids and grout. Specific uses include fixation in total joint arthroplasty. In spine surgery, PMMA has been used to reconstruct defects from open corpectomy and transpedicular application of PMMA to improved screw purchase in osteoporotic bone. The first reported use of percutaneous application of PMMA was performed in 1984 by Galibert and Deramond for C2 hemangioma [13]. The use of modified angioplasty balloon to reduce a vertebral fracture and create a cavity for placement of PMMA was described by Mark Reiley, MD [14]. Over decades, the technique of percutaneous vertebral augmentation has evolved with large-bore needles and modified PMMA.

Other fillers and cement have been proposed beyond PMMA. The concerns of PMMA are the high temperature that rises during the polymerization which can cause tissue damage and the lack of bioactivity [13, 15]. Bioactive composite materials such as calcium phosphate cement and Cortoss have been developed. These cements have varying elastic modulus and compressive strengths. It is thought stiffer cements can lead to increase stress on endplates of adjacent vertebrae, leading to higher fracture rate [16]. An interesting blood-mixed polymethylmethacrylate (PMMA) mechanical study was done to modify properties of PMMA (ahn). This mix was found to have a lower elastic modulus due to the higher porosity, less heating, and ease of placement through the trocar [17].

Pathophysiology and Patient Evaluation

Vertebral compression fractures occur due to weakened bone, causing severe pain and morbidity. These compression fractures are typically induced by osteoporosis, tumors, or traumatic injury. Typically, these fractures occur where load bearing is the greatest. Certain factors and habits which may frequently result in a loss of bone mass frequently may lead to osteoporosis. These factors include women of increased age, lack of calcium and vitamin D in the diet, and the high intake of cigarettes and coffee [18].

Vertebral compression fractures typically occur spontaneously or as a consequence of minimal trauma, resulting from spinal loading during daily activities such as bending, lifting, and climbing stairs [19]. The most common locations are the midthoracic region (T7–T8) and the thoracolumbar junction

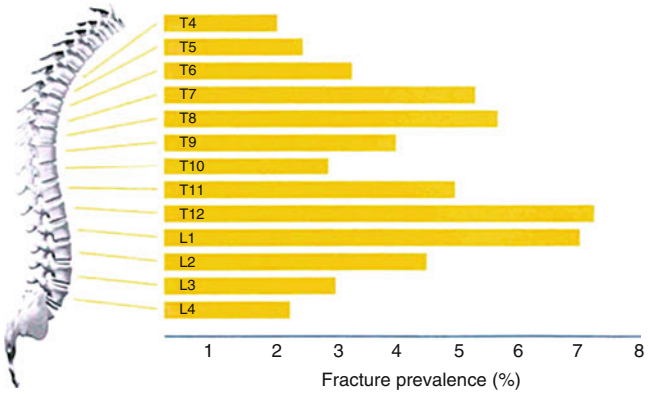


Fig. 33.1 Vertebral compression fractures typically occur spontaneously or as a consequence of minimal trauma, resulting from spinal loading during daily activities such as bending, lifting, and climbing stairs [19]. The most common locations are the midthoracic region (T7–T8) and the thoracolumbar junction

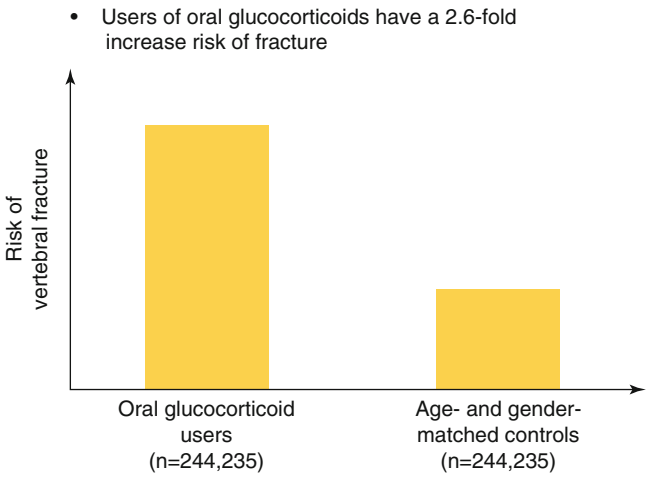
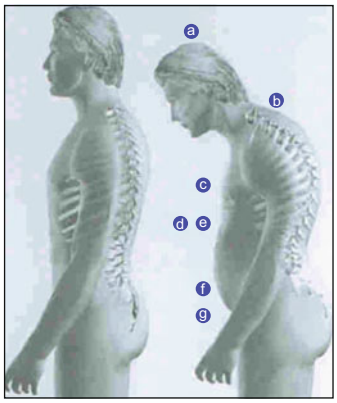


Fig. 33.2 When thoracic kyphosis develops, the midthoracic region receives tremendous load during flexion of the spine leading to potential compression fractures. Secondary contributors to osteoporosis include hypercalcemia, abnormal thyroid, and renal functions [18]. Users of oral glucocorticoids have a 2.6-fold increase risk of fracture

(see Fig. 33.1) [19]. These correspond to areas of the spine where there is the greatest burden during these common daily activities. When thoracic kyphosis develops, the midthoracic region receives tremendous load during flexion of the spine leading to potential compression fractures. Secondary contributors to osteoporosis include hypercalcemia, abnormal thyroid, and renal functions [18]. Users of oral glucocorticoids have a 2.6-fold increase risk of fracture (see Fig. 33.2) [20].

Osteolytic metastases and myeloma can cause the destruction of vertebral bodies and fractures, leading to pain and disability. Patients with advanced cancer can present with bone metastases to the vertebral bodies. The incidence of metastatic



a. Height loss
b. Upright posture becomes impossible
c. Pulmonary volume loss due to anterior wedging of the spine
d. 12 rib rests on the iliac crest
e. Narrowed gab between ribs and ilium
f. Protruding abdomen
g. Distension, constipation, early satiety, eructation

Fig. 33.3 As the spine changes with significant kyphosis, the downward angulation of the ribs leads to the 12th rib resting on the iliac crest. This results in the abdomen protruding and can lead to symptoms of distension, constipation, early satiety, and eructation

lesion to the spine depends on the primary cancer: 80% of patients with prostate cancer, 50% with breast cancer, 30% with lung, thyroid, or renal cell cancer [21]. Rarely, benign tumors such as spinal osteoid osteoma and aneurismal bone cysts can lead to instability and painful compression fractures. Vertebral augmentation can be used to reinforce and stabilize fractures related to tumors.

The multiple consequences of vertebral fractures can lead to increased morbidity and mortality. Pain and disability increases with kyphosis and vertebral compression fracture [1]. The physical consequences include pulmonary compromise. Studies suggest that there is decreased lung capacity and reduced pulmonary function with vertebral height loss and decreased lung volume [2]. As the spine changes with significant kyphosis, the downward angulation of the ribs leads to the 12th rib resting on the iliac crest. This results in the abdomen protruding and can lead to symptoms of distension, constipation, early satiety, and eructation (see Fig. 33.3). Above all, the forward position of the thoracic spine leads to strain of the posterior elements of the thoracic spine as the patient attempts to straighten his or her spine.

As seen by the author, the forward expansion of the abdomen leads to forward loading of the lumbar sacral spine, thereby exacerbating discogenic pain. The limited ability of the sacrum to flex and extend may load the sacroiliac joint and cause pain. Weakened physical function can lead to restricted daily activities, resulting in required assistance from family or hired help. The psychosocial consequences of the limitation of activities are seen with their reduced ability to fulfill their accustomed social roles and dependency upon others. This leads to poor self-esteem, depression, and social isolation [1, 3, 22]. There is also increased incidence of sleep disturbances. The number of depressive symptoms rises with the increased number of fractures. Studies reveal high mortality and reduced quality of life years (QALY) with vertebral compression fractures [1].

In addition to a detailed history and examination, imaging evaluations are standard in confirming the diagnosis of acute compression fractures. The radiologic findings on plain films may show subtle height loss changes. Comparison films are helpful to determine acute versus chronic fractures. Unfortunately, occult vertebral fractures are common with false-negative rates of 27–45% by radiologists [23].

MRI is the study of choice with T1 and STIR sagittal sequences. Acute vertebral compression fractures are revealed with marrow edema within the vertebral body. Assessment of spinal canal compromise and fractures of the pedicles is important. CT scan may be a useful alternative combined with a nuclear bone scan when the patient is not a good candidate for MRI. Bone scan may be helpful in fractures greater than 3–4 months in age where there is no marrow edema on MRI.

Treatment Goals

The treatment goals of vertebral compression fractures include pain management, rest, rehabilitation, and restoration of mechanical stability. Pain management usually involves use of opioids and nonsteroidal anti-inflammatories (NSAIDS). Medical management may also include treatments for osteoporosis: calcium, vitamin D, bisphosphonates, or nasal Miacalcin.

Prolong bedrest may allow the compression fracture to stabilize but can lead to fatigue and loss of muscle strength and bone density in elderly patients [24]. Other concerns of patients in prolonged bed rest are pressure sores and deep vein thrombosis in older patients. Back braces may offer support and stabilize the vertebral compression fractures. Limited contact orthoses such as the tri-pad Jewett extension brace are commonly used. Many patients do not tolerate the braces, citing discomfort and difficulty when putting on and removing them. Rehabilitation should be planned to strengthen bone density and increase core strength.

Mechanical instability of vertebral fractures with neurologic compromise is possible. Open surgery such as anterior decompression and stabilization may be needed. Stable, painful compression fractures may be treated by vertebral augmentation either vertebroplasty or kyphoplasty.

The mechanism of pain relief associated with vertebroplasty and kyphoplasty is unknown. Fractured vertebral bodies lose both strength and stiffness. Strength is related to the ability of the vertebral body to bear load, and stiffness limits micromotion within the compromised vertebral body. Restoration of stiffness and strength is augmented by placement of PMMA, reducing painful micromotion [25]. Large amounts of cement are needed to restore stiffness and less for

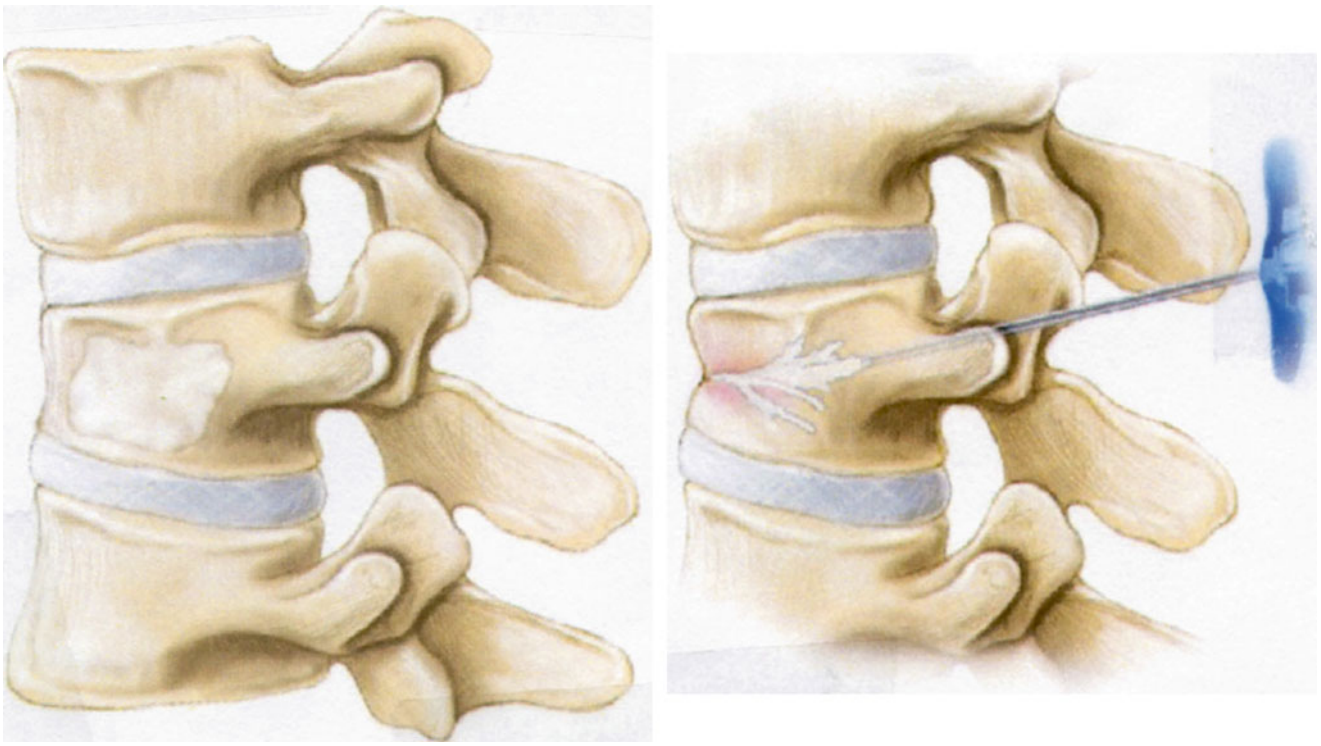


Fig. 33.4 Vertebroplasty is the percutaneous placement of cement in fractured trabecular bone, leading to an "internal cast"

strength [25]. Other mechanisms of pain relief may involve the thermal and cytotoxic reaction of PMMA. It has been hypothesized that the heat of polymerization causes thermal necrosis of neural tissue, explaining pain relief in patients. In vivo studies mapping temperatures from polymerization may rise greater than 50 °C leading to potential damage to interosseous nerves, periosteal nerves [26]. Temperature may also play a role in slowing tumor growth and apoptosis in osteoblasts exposed to 48 °C for 10 min or more. The cytotoxicity of PMMA may also have an antitumoral effect and could be potentially neurotoxic [27].

Vertebroplasty is the percutaneous placement of cement in fractured trabecular bone, leading to an "internal cast" [27] (see Fig. 33.4). The standard indication is for painful compression fractures refractory to medical therapy. The typical causes include osteoporosis, metastatic disease, multiple myeloma, and osteonecrosis. The contraindications are systemic and local infection, uncorrectable coagulopathy, retropulsion of vertebral body or tumor, posterior wall destruction, and radicular symptoms. Benefits for the patients are increased range of motion with pain relief. The procedure is typically done under monitored anesthesia care and as an outpatient procedure.

The alternatives are poor. These are conservative medical management, i.e., opioid therapy, physical therapy, bracing, and potential open surgery fixation. The cement is placed through fluoroscopically or CT-guided trocars.

The most common access is the transpedicular approach. Other approaches can be parapedicular, anterolateral (cervical), and posterior (sacral). The complications may include the following: infection, bleeding, pulmonary embolus, local trauma, paralysis, and even death. Fortunately, these complications are rare.

Kyphoplasty has been introduced as an alternative approach [28] (see Fig. 33.5). It is considered a "balloon-assisted vertebroplasty." This procedure involves percutaneous placement of a balloon in the vertebral body. Through the same large-bore needle, bone cement is placed into the cavity created by the balloon. The balloon is intended to restore vertebral body height in addition to creating the cavity.

Three new modifications on lumbo-thoracic augmentations have been reported. Vertebral body stenting is a new method for vertebral augmentation [29]. Once a compression fracture is reduced with a balloon, a vertebral body stent (VBS) is left in place to maintain the reduction and then stabilized with PMMA. This concept comes from peripheral artery stenting seen in interventional cardiac procedures. So far, it is only reported in human cadaveric specimens [29].

Another similar modification is vesselplasty [30]. The purpose is to obtain control of the volume of void created in the vertebral body, prevent the leakage of bone filler material, and restore vertebral body height. Vesselplasty was designed by Jerry Lin, chairman of A-Spine Holding Group Corporation (Taipei, Taiwan), and was first performed

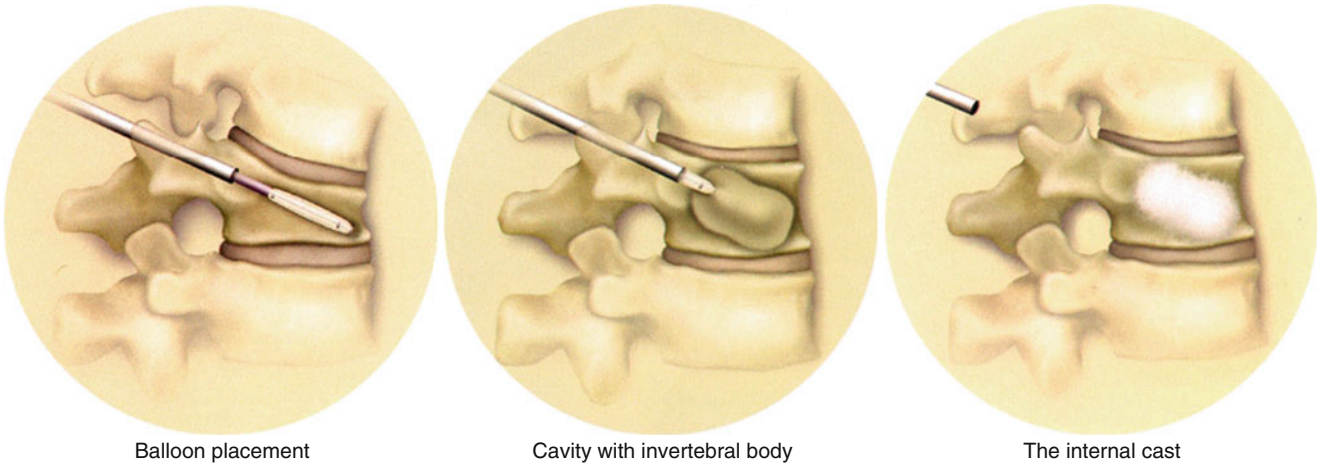


Fig. 33.5 Kyphoplasty has been introduced as an alternative approach [28]

in 2004 by Darwono [30]. A case series of 29 patients who underwent vesselplasty was performed with significant benefits of pain relief, improved mobility, and no complications [30].

Lordoplasty is a modification of vertebroplasty which has been developed as an alternative technique for the treatment of osteoporotic compression fractures [31]. It is known that percutaneous vertebroplasty is successful in producing pain relief but may not reduce the overloading of the anterior column of the spine and the height of the vertebral body. Kyphoplasty can restore the height and lordosis, but kyphotic angle is limited up to 6–9° due to collapse of height after deflating bone temps [31]. In lordoplasty, the vertebral body above and below the compression fracture is accessed with cannulae (see Fig. 33.6) [31]. Through the cannulae, cement is placed and allowed to harden. The compression fracture is also accessed. The fracture is reduced by ligamentotaxis with a lordosing force applied via the cannula in place and using the facet joints as a fulcrum (Fig. 33.7) [31]. The anterior height is reduced and maintained by a cross bolt. The vertebral fracture is augmented with PMMA. Once the cement hardens, the cannulae are removed (Fig. 33.8) [31]. To date, lordoplasty has been reported with successful case reports [31].

Sacral insufficiency fractures (SIFs) are being identified as a cause of back pain and disability in the elderly population [32]. The mainstay of treatment has been analgesics and physical therapy. Sacroplasty for SIFs evolved from the success of vertebroplasty and kyphoplasty in the treatment of compression fractures of lumbar and thoracic spine. Sacroplasty is the injection of PMMA cement into the fracture zone of the sacral ala with the purpose of pain relief with restoration of mechanical integrity. Using either fluoroscopic and CT guidance, various reported results have been published [32]. A review of the literature reports a multitude of case reports and one prospective observational cohort study [32].

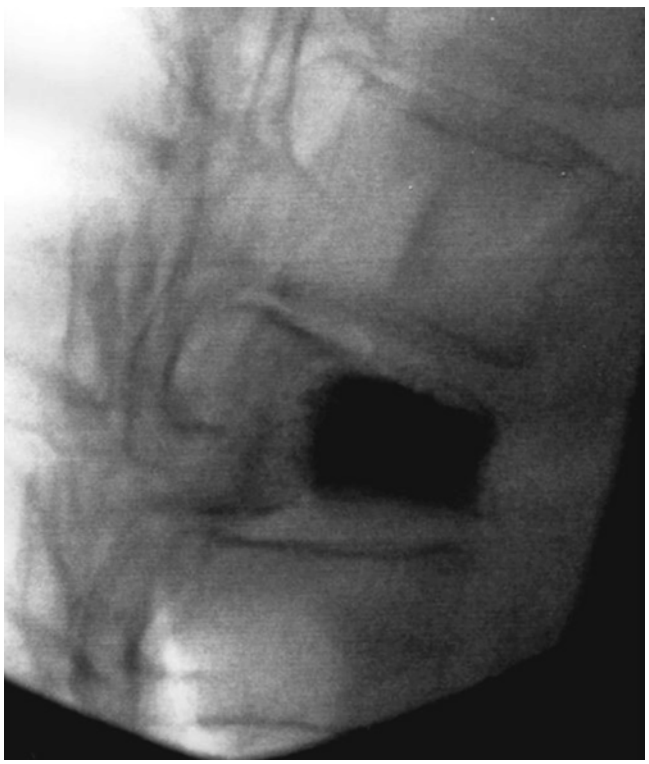


Fig. 33.6 In lordoplasty, the vertebral body above and below the compression fracture is accessed with cannulae

After reviewing published literature, a position statement on percutaneous vertebral augmentation by American Society of Interventional and Therapeutic Neuroradiology, American Association of Neurological Surgeons/Congress of Neurological Surgeons, and American Society of Spine Radiology has determined that the clinical response rate comparing kyphoplasty and vertebroplasty is similar [28]. There is no proven advantage of kyphoplasty compared to vertebroplasty in regard to pain relief, height restoration, and complication rate [28].

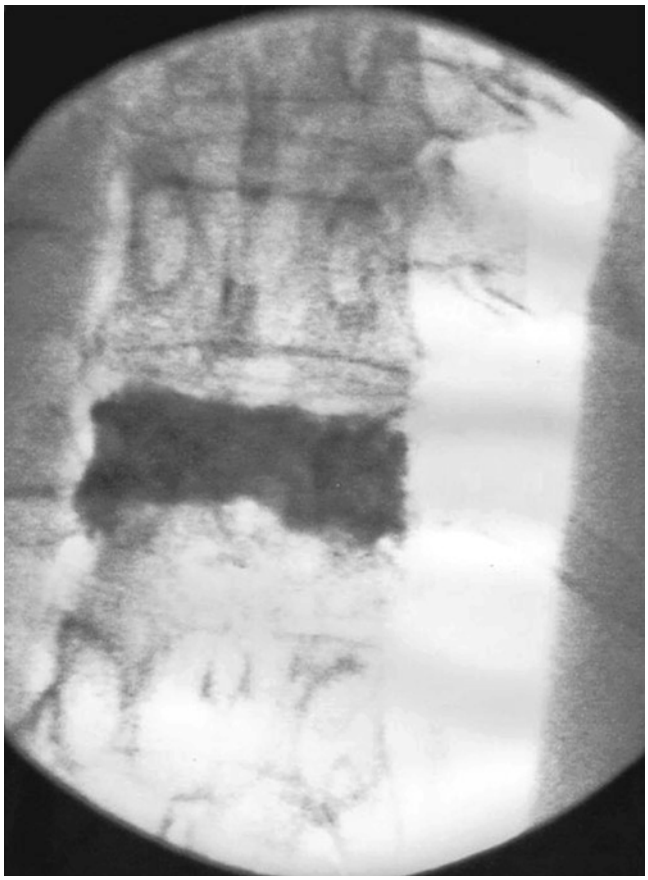


Fig. 33.7 Through the cannulae, cement is placed and allowed to harden. The compression fracture is also accessed. The fracture is reduced by ligamentotaxis with a lordosing force applied via the cannula in place and using the facet joints as a fulcrum

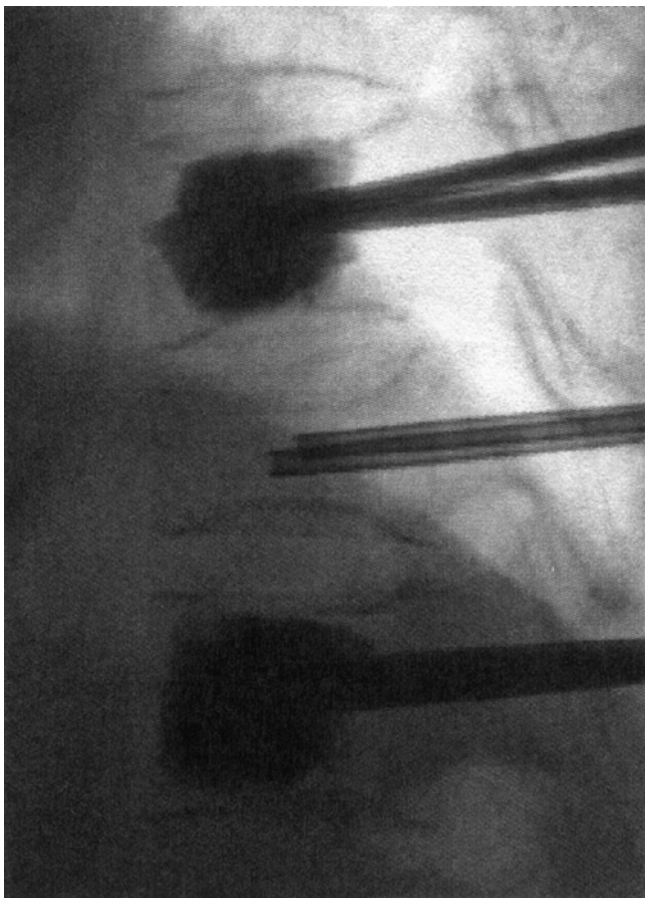


Fig. 33.8 The anterior height is reduced and maintained by a cross bolt. The vertebral fracture is augmented with PMMA. Once the cement hardens, the cannulae are removed

Technique

Vertebroplasty and kyphoplasty rely on small incisions to place large-bore needles with radiographic guidance with fluoroscopy or CT guidance. These procedures are either done under general anesthesia or monitored anesthesia care. The procedure itself is not painful especially if local anesthesia is placed, but the duration of the procedure and position of the patient may necessitate at least intravenous sedation. Comorbidities such as poor cardiac dysfunction may need to be monitored. In patients with poor medical condition, medical clearance is advised. Anticoagulations are stopped prior to the procedure. Preoperative antibiotics are usually given as with many surgical implants. Sterile surgical preparation and draping are done.

The critical step is to have an understanding and visualization of the fractured vertebra. Poorly osteoporotic bone, especially in large patients, may offer a challenge. Spinal deformities such as scoliosis may hamper proper visualization of the bone landmarks to perform the procedure successfully. If the bone is not visualized with confidence under fluoroscopy, the case should be aborted. CT guidance is then suggested. The landmarks necessary to perform the procedure under fluoroscopy are the pedicles, vertebral bodies, and disc space in the anterior-posterior, lateral, and oblique views. Real-time three-dimensional fluoroscopic guidance using cone beam CT has been proposed to provide better accuracy and results [33]. A stereotactic guidance system using computer tomography is also proposed to improve accuracy and safety of procedure [34].

There are multiple approaches to access the thoracic and lumbar fractures' vertebral body [28]. The most common is posterior transpedicular approach. Bipedicular needles are usually placed at each level. Another approach is the parapedicular. For cervical, the anterolateral view is needed, a similar approach to cervical discography. For sacral fracture, a posterior approach is taken.

This author's approach to lumbar and thoracic fractures is to square the endplates of the fractured vertebral bone on an anterior-posterior view. On the oblique view, the pedicle is identified with clear definition of the medial border. The skin and tissue for the planned entry site are anesthetized with a

local anesthetic. The needle will be placed at "eye of the scotty dog" and placed "straight down the barrel." The needle is gently tapped with a hammer staying lateral to the medial edge of the pedicle. Constant visualization of the needle is needed with fluoroscopy to stay away and lateral to the spinal canal. Needle position is usually anterior to the third of vertebral body on lateral view. PMMA is prepared to allow polymerization in a viscous consistency that still allows passage through the needle. This reduces risk of extravasation. Once confirmed in position on the anterior-posterior and lateral views, the prepared PMMA is injected slowly watching its spread within the vertebral body, under constant fluoroscopy. Once the spread is seen heading to the posterior third, the injection is completed (see Figs. 33.9 and 33.10).

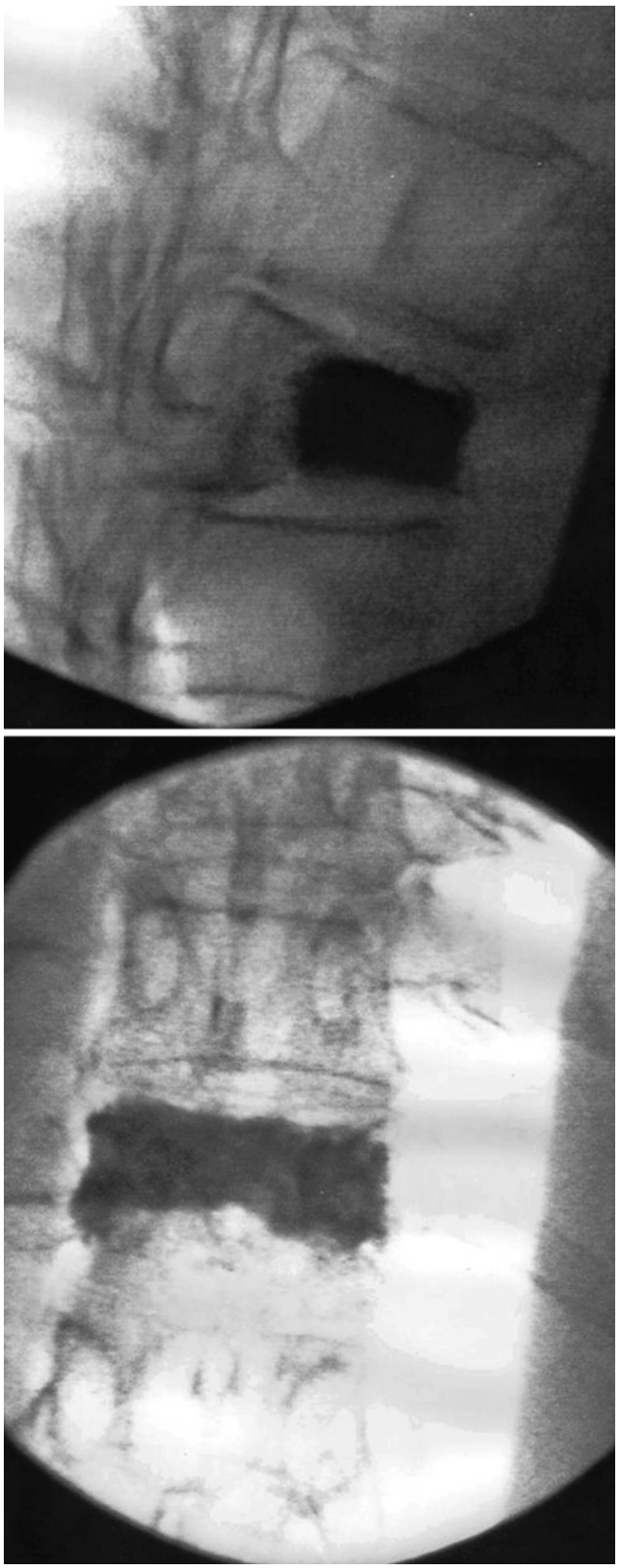
Like vertebroplasty, the same approach is taken with kyphoplasty. Once access to the vertebral body is complete, a guide pin is placed where a large-bore (8 gauge) cannula is placed. Through this cannulae, an inflatable bone tamp or balloon is advanced. A bipedicular approach is recommended. Once both balloons are inflated and the fracture is realigned, a cavity is created. This is where PMMA is placed.

Standards and guidelines in the vertebroplasty can be found in the American College of Radiology's "Standards for the Performance of Percutaneous Vertebroplasty" and the Society of Interventional Radiology's "Quality Improvement Guidelines for Percutaneous Vertebroplasty" [35].

Clinical Research

More than 100 studies have addressed the clinical outcomes of vertebroplasty [28]. The type of studies range from small, retrospective, uncontrolled case series to prospective randomized studies. Literary reviews about the efficacy of vertebroplasty conclude that when used for patients with osteoporotic compression fractures, substantial and immediate pain relief, improved functional status takes place. Minimal short-term complications have been noted. In 2007, there was a position statement on percutaneous vertebral augmentation. This consensus statement, developed by the American Society of Interventional and Therapeutic Neuroradiology, the Society of Interventional Radiology, the American Association of Neurologic Surgeons/Congress of Neurological Surgeons, and the American Society of Spine Radiology, concluded that the evidence supports vertebroplasty as being beneficial for the relief of pain and improved quality of life [28].

An example of a study supporting this statement was published in 2002 by Zoarski et al. In this study, a Musculoskeletal Outcomes Data Evaluation and Management Scale (MODEMS) spinal interventional questionnaire was done [36]. In the study, 30 patients with 54 symptomatic osteoporotic vertebral compression fractures had less than satisfactory response to conventional therapies. On the other hand, significant post-procedure benefits of



Figs. 33.9 and 33.10 PMMA is prepared to allow polymerization in a viscous consistency that still allows passage through the needle. This reduces risk of extravasation. Once confirmed in position on the ante rior-posterior and lateral views, the prepared PMMA is injected slowly watching its spread within the vertebral body, under constant fluoroscopy. Once the spread is seen heading to the posterior third, the injection is completed

vertebroplasty were demonstrated in four MODEMS modules: treatment score ($p < .0001$), pain and disability ($p < .0001$), physical function ($p = .0004$), and mental function ($p = .0009$). Long-term follow-up continued for 18 months. At the end of the study, 22 of 23 patients remained satisfied with their outcomes.

A recent prospective of randomized studies, published in the 2009 New England Journal of Medicine, showed that compared to control groups, vertebroplasty offered no proven advantage [4, 5]. The Buchbinder and Kallmes studies showed negative results which directly contradicts 100 of published studies showing positive outcomes. A common initial response to these findings was one of disbelief and surprise. A commentary by North American Spine Society serves to understand and explain the findings. In both studies, there are questions regarding patient selection, enrollment, control group, and outcomes.

Both studies accepted patients with fractures of less than 1 year, and it is known that pain from osteoporotic fractures diminishes over time. It is reasonable to conclude that in 3–6 months, fracture pain reduces naturally and would then be comparable to relief from vertebroplasty. The enrollment of patients was difficult in the Kallmes et al. study. Eighteen hundred and twelve were initially screened, and only 131 entered the study. The pain severity and functional compromise of those patients who refused participation were not reported. Thus, there exists an unquantifiable selection bias in the final patient group.

Both control groups in these studies were not really sham groups. Injection of anesthetic into the facet capsule and/or periosteum may have a beneficial effect in patients with facet mediated pain. Thus, another criticism takes us back to patient selection and outcomes. It is unclear if there was an effort to determine if the back pain originated from the osteoporotic fracture site. With experienced spine care providers, percussion and palpation of the spinous processes are critical to determine the level of maximum tenderness, i.e., painful compression fractures. History, physical examination, and imaging are critical to determine if pain is coming from a compression fracture, stenosis, facet, or degenerative disc.

The controversy of Kallmes and Buckbinder studies still remains. A meta-analysis of the combined individual patient-level data was performed on Kallmes and Buckbinder studies [9]. Powered by subgroup analysis, the two blinded trials of vertobroplasty failed to show advantage of vertebroplasty over placebo. Recent commentary is raised the concern that the reason why the sham-treatment group improved over time is that vertebral compression fractures heal naturally [6, 7]. Additionally, injections with local anesthetics can have long-lasting effect beyond the expected duration of local anesthetic as seen with selective nerve root blocks for lumbar radiculopathy [37]. Other practitioners have consternation and questions on the selection bias and statistical power of the studies [7].

The clinical outcome data for kyphoplasty are not as extensive as vertebroplasty [28]. Lieberman et al. reported in a phase I efficacy study of kyphoplasty in the treatment of painful compression fractures [38]. Thirty patients demonstrated significant improvements in Short Form (SF)-36 bodily pain scales from 11.6 to 58.7 ($p = .0001$). In 2009, a randomized controlled trial comparing nonsurgical treatment of vertebral compressions to balloon kyphoplasty showed the efficacy and safety of the procedure [39]. Three hundred patients were randomly selected to receive kyphoplasty versus nonsurgical treatment. Quality of life measures, SF-36, and safety measurements were taken over 12 months. Mean improvements in SF-36 physical components were seen. The frequency of adverse effects did not differ between groups. There were two serious complications noted (hematoma and urinary tract infection).

Currently, there is no published investigation which has compared vertebroplasty to kyphoplasty. Thus, the 2007 consensus statement on percutaneous vertebral augmentation developed by the American Society of Interventional and Therapeutic Neuroradiology, the Society of Interventional Radiology, the American Association of Neurologic Surgeons/Congress of Neurological Surgeons and the American Society of Spine Radiology concludes that the clinical response to kyphoplasty and vertebroplasty is equivalent [28]. There is no proven advantage in regard to pain relief, vertebral height restoration, or complication rate.

Complications

Vertebroplasty and kyphoplasty have identical complications [40]. With kyphoplasty, there is the reported spinal canal intrusion with the balloon tamp and cortical wall disruption from balloon misplacement. Complications can be divided into medical- and anesthesia-related complications, instrumentation, extravasation of PMMA, and adjacent segment spinal fractures.

Medical and anesthesia complications are uncommon as these minimal invasive procedures have minimal physiologic impact. In patients with severe cardiovascular compromise, laying in the prone position is difficult. Conversely, performing general anesthesia on these patients becomes a greater challenge. Cases of ileus, myocardial infarction, and congestive heart failure have been reported [13]. Careful attention to patient position is paramount as osteoporotic bones have fractured from sternum to ribs. Hemodynamic compromise has been associated with packing of the PMMA during hip replacement surgery. Transient systemic hypotension has been reported with packing cement in vertebroplasty [41].

Instrumentation complications exist from placing needles outside of the pedicles and into the spinal canal [40]. Operator inexperience, poor imaging equipment, and severe spinal

deformity are the usual explanations. Uncontrolled bleeding and infection are extremely rare.

The most frequently reported complication is PMMA cement extravasation [40]. PMMA can exit out of any fracture line or cleft and vertebral venous plexus. Using viscous PMMA impregnated with barium, and under high-quality imaging, can reduce the incidence of these problems. The PMMA is injected slowly under live fluoroscopy. Extravasation of cement has flowed into the spinal canal with severe neurologic compromise. The rate of clinically significant leakage has been reported at up to 6% [42]. Higher rates of leakage have been identified when trying to treat fractures related to angiomas and metastatic disease, 2.5–10% [13]. It is likely that cortical destruction and occult fracture lines are to blame. PMMA leakage into the disc space may occur due to undetected fracture cleavage lines. Rates of 0–65% have been reported but most are considered clinically insignificant [13]. Epidural leakage is more of a concern leading to potential cytotoxic and exothermic damage to nerve roots. Liquid PMMA may leak out into the venous system, resulting in a rare case of pulmonary embolus. There is no published report of pulmonary embolus with kyphoplasty. The creation of a void in the vertebral body may compact the cancellous bone, causing it to act as a dam and prevent extravasation of the cement.

An issue of increased risk of fracture at an adjacent level has been raised. Grados et al. found a slight but statistically significant increase in adjacent segment fracture risk in a long-term vertebroplasty follow-up study [42]. It is not known if this is due to placing a hard material, PMMA, in close juxtaposition to the soft, osteoporotic bone of the adjacent vertebral levels. It is also possible that these adjacent fractures represent the natural progression of osteoporosis. Recent study has reviewed risk factors of compression fractures in adjacent vertebrae [43]. It appears lower bone mineral density, a preexisting fracture, a greater restoration rate of vertebral height after vertebroplasty, and intradiscal cement leakage during vertebroplasty are factors for future fracture of adjacent vertebral bodies [43]. On the other hand, another study suggests that percutaneous vertebroplasty is not a risk factor for new osteoporotic compression fractures [44]. VERTOS II is a prospective, multicenter randomized controlled trial comparing percutaneous vertebroplasty with conservative therapy. A total of 202 patients were studied looking at incidence, distribution, and timing of new vertebral compression fractures using spine radiographs [44].

Overall, the complication rates of vertebroplasty and kyphoplasty are reported similar [28]. Six major complications were reported in 531 patients (1.1%) treated with kyphoplasty in a multicenter study [45]. Four of these had neurologic complications. This is similar to the complication of vertebroplasty (1.3%) when used for osteoporotic fractures.

Recommendations and evaluations of complications can be found in the American College of Radiology's "Standards for the Performance of Percutaneous Vertebroplasty" and the Society of Interventional Radiology's "Quality Improvement Guidelines for Percutaneous Vertebroplasty" [35].

Conclusion

Vertebral augmentation with vertebroplasty or kyphoplasty is a medically appropriate treatment for painful vertebral compression fractures refractory to medical therapy [35]. Vertebral compression fractures are common and are often debilitating. Although most fractures heal within a few weeks to months, a minority of patients continue to suffer pain that does not respond to conservative therapy.

Vertebral compression fractures are often a leading cause of admission to nursing and intermediate care facilities. These patients are rarely provided with open surgical fixation due to the poor quality of bone for surgical fixation and the patient's tolerance of the surgery and anesthesia. Percutaneous vertebral augmentation is now an established therapy and should be reimbursed by payors as a safe and effective treatment of compression fractures.

Newer augmentation techniques are now available to treat sacral fractures and sacroplasty. Robotic assistance and alternative imaging may allow even safer placement of needles with reduced radiation exposure [40]. Currently, a number of alternative cements to PMMA are being tested. A number of companies have looked at alternatives to PMMA. A bioresorbable injectable cement called Cordis has been approved by the FDA. This bioactive material closely mimics the mechanical characteristic of bone.

Further clinical studies and econometric analysis are being done to determine the financial impact on society. Further prospective and randomized studies are needed to establish the benefits of vertebroplasty and kyphoplasty over standard conservative treatment.

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Piriformis Injection

34

Nathan J. Harrison and Gagan Mahajan

Key Points

- Piriformis syndrome is characterized by pain located in the buttock, with or without "sciatica," or radiation into the posterior thigh. It remains a controversial diagnosis of exclusion and debate continues due to a lack of consensus on its definition and pathophysiology.
- Before the diagnosis of piriformis syndrome is made, a broad differential should be considered in a patient presenting with "sciatica": lumbar disc herniation, facet arthropathy, sacroiliitis, myofascial pain and trochanteric bursitis.
- When the hip and knee are extended, as in standing, the piriformis muscle externally rotates the hip. When the hip is flexed to 90°, as in sitting, the piriformis muscle abducts the thigh.
- The sciatic nerve usually exits below the piriformis. However, variability exists in the exiting sciatic nerve in relation to the piriformis.
- There are no definitive laboratory tests and imaging tests that can unequivocally diagnose piriformis syndrome.
- Commonly used physical exam maneuvers include: Freiberg's sign, Pace's maneuver, Lasègue's sign, and Beatty's maneuver.
- Treatment of piriformis syndrome can include one or more of the following: activity modification and physical therapy, medicinal therapies, piriformis muscle injection, and surgery.

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Introduction

In 1928, Yeoman described a condition of "sciatica" that he theorized occurred secondary to the close anatomic relationship of the piriformis muscle, anterior sacroiliac ligament, and adjacent branches of the sciatic nerve [1]. Frieberg and Vinke also believed that sacroiliac joint pathology could spread an inflammatory reaction to involve the piriformis muscle and sciatic nerve [2, 3]. In their 1934 study, they aimed to identify the physiologic mechanism of Lasègue's sign (buttock pain and tenderness with palpation in the greater sciatic notch while the hip is passively flexed to 90° and the knee is passively extended to 180°) and later introduced Freiberg's sign (buttock pain with passive, forced internal rotation of the hip), physical examination findings which they believed could identify the piriformis muscle as the source of sciatica [2, 3]. In 1934, Mixter and Barr described lumbar disc herniation as a cause of sciatica, calling into question the theories proposed by Yeoman and Frieberg [4]. In 1937 and 1938, Beaton and Anson described six possible variations of the exiting sciatic nerve in relation to the piriformis muscle and suggested that this relation could cause sciatic pain and coccydynia if the piriformis muscle was inflamed or in spasm [5, 6]. However, it was not until 1947 that Robinson first introduced the term "piriformis syndrome," which he found was associated with six signs and symptoms: (1) a history of trauma to the gluteal and sacroiliac regions; (2) pain in the region of the sacroiliac joint, greater sciatic notch, and piriformis muscle that may travel down the limb causing gait difficulties; (3) acute exacerbation of the pain with stooping or lifting with some relief of pain by applying traction to the affected extremity; (4) a palpable, tender, sausage-shaped mass over the affected piriformis muscle; (5) a positive Lasègue's sign; and (6) depending on the duration of symptoms, gluteal atrophy [7].

Despite the advances in imaging and electrophysiological testing since piriformis syndrome was first described, it

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remains a diagnosis of exclusion with ill-defined clinical signs, diagnostic tests, and treatments.

Scientific Foundation

Anatomy

Branches of the ventral rami of the S1 and S2 nerve roots innervate the piriformis muscle. It is a pyramid or pear-shaped muscle that is superiorly co-localized with five short, external rotator muscles (superior and inferior gemmelli, obturator internus and externus, and quadratus femoris) [8, 9]. The piriformis muscle originates medially from the ventrolateral surface of the second, third, and fourth sacral foramina and exits posterolaterally, filling most of the greater sciatic foramen as it passes to insert on the superior border of the greater trochanter [10]. When the hip and knee are extended, as in standing, the piriformis muscle functions synergistically with the five other external rotators to externally rotate the hip. When the hip is flexed to 90°, as in sitting, the piriformis muscle abducts the thigh. Along with several other external rotators, the piriformis muscle works to stabilize and steady the femoral head in the acetabulum. When the piriformis muscle contracts, its diameter may significantly increase and potentially lead to compression of the accompanying sciatic nerve, depending on its course through the greater sciatic foramen [11]. The sciatic nerve, which is a continuation of the sacral plexus and contains fibers from the L4–S3 nerve roots [10], usually exits below the piriformis and superior to the gemmelli [6]. However, Beaton and Anson proposed that variability exists in the exiting sciatic nerve in relation to the piriformis muscle and described six possible arrangements [5, 6]. Of the six theoretical arrangements described, only four of these variations were actually found in their cadaveric studies: the sciatic nerve exited below the piriformis muscle in 84.2 %, the sciatic nerve divisions passed both through and below the piriformis muscle in 11.7 %, the sciatic nerve divisions passed above and below the piriformis muscle in 3.3 %, and the sciatic nerve passed through the piriformis muscle in 0.8 % (Fig. 34.1) [6].

Epidemiology and Pathophysiology

While an evolution of the definition of piriformis syndrome and its many etiologies has occurred, there has yet to be a clear, consensus definition. The lack of a consensus definition makes determining prevalence of piriformis syndrome difficult. Incidence rates range from 5 to 36 % of patients with buttock pain and sciatica symptoms [12]. Pace and Nagle described a 6:1 female to male ratio while others suggested a 1:1.4 female to male ratio [13, 14].

Attempts at classifying the various causes of piriformis syndrome include determining whether the symptoms are due to a primary or secondary piriformis syndrome. Primary piriformis syndrome refers to pathology intrinsic to the piriformis muscle, such as myofascial pain, pyomyositis, and myositis ossificans secondary to an inciting event such as direct trauma to the sciatic notch and gluteal region [7, 15]. This trauma may occur with prolonged sitting; prolonged and combined hip flexion, adduction and internal rotation; and certain sports activities [11, 16–18]. The latter include cyclists who ride for prolonged periods of time, tennis players who constantly internally rotate their hip with an overhead serve, and ballet dancers who constantly "turn out" or externally rotate their hip while dancing [11]. Pain may occur due to inflammatory and edematous changes in the muscle and surrounding fascia, which in turn cause a compressive neuropathy [18].

Secondary piriformis syndrome refers to all other cases in which the symptoms of posterior buttock pain and sciatica depend on the location of the pathology in relation to the structures adjacent to the sciatic notch, and includes the anatomic variations of the exiting sciatic nerve and piriformis muscle leading to sciatic nerve compression [5, 6, 15]. Such compression may occur with piriformis muscle hypertrophy, chronic inflammation, or muscle spasm which can then affect the sciatic nerve directly, especially with the nerve variations that pass through the muscle instead of beneath. Finally, secondary piriformis syndrome causes may include any lesions or structures causing a "pelvic outlet syndrome" such as pelvic tumors, endometriosis, and aneurysms or arterial malformations [15].

Clinical Examples

Diagnosis

Before the diagnosis of piriformis syndrome can be made, a broad differential should be considered in a patient presenting with sciatica. More common disorders, such as lumbar disc herniation, facet arthropathy, sacroiliitis, myofascial pain and trochanteric bursitis, can present with symptomatology similar to piriformis syndrome. There are no pathognomonic signs or symptoms, nor are there definitive laboratory tests and imaging tests that can unequivocally diagnose piriformis syndrome. However, numerous attempts have been made to describe the most common features and to provide diagnostic tools.

Symptoms and Physical Exam Findings

When he first introduced the term piriformis syndrome [7], Robinson assigned six signs and symptoms that are still widely regarded as useful today: (1) a history of

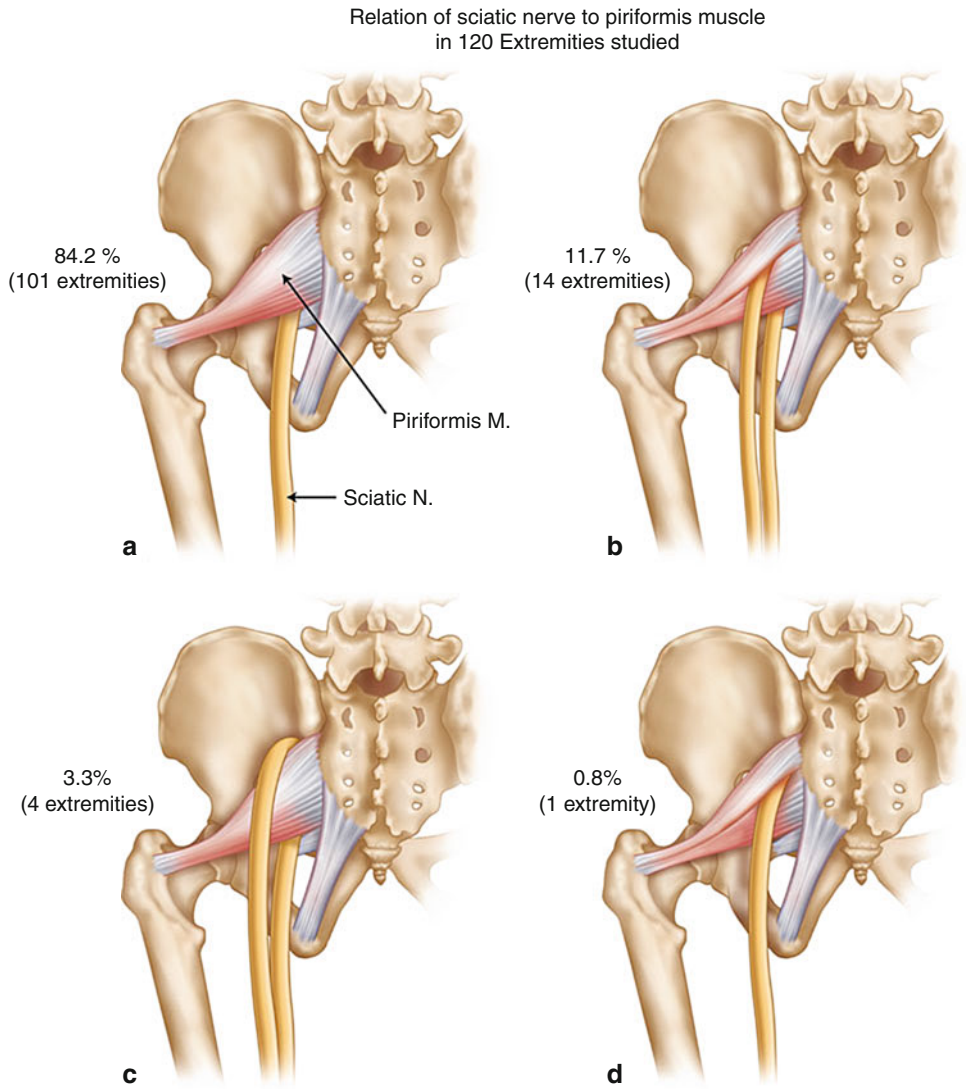

Fig. 34.1 Relation of the sciatic nerve and its subdivisions to the piriformis muscle [6]. (**a**) The sciatic nerve exits below the piriformis muscle. (**b**) The sciatic nerve division passes both through and below the piriformis muscle. (**c**) The sciatic nerve division passes above and below the piriformis muscle. (**d**) The sciatic nerve passes through the piriformis muscle

trauma to the gluteal and sacroiliac regions; (2) tenderness in the region of the sacroiliac joint, greater sciatic notch, and piriformis muscle which often radiates to the hip; (3) acute exacerbations of pain with stooping or lifting and relief upon traction to the affected extremity; (4) a palpable, sausage-shaped mass over the piriformis muscle during an acute exacerbation; (5) a positive Lasègue's sign; and (6) depending on the duration of symptoms, gluteal atrophy.

Piriformis syndrome most commonly presents with a deep, aching buttock pain on the affected side. The pain may radiate to the hip, lower back and posterior thigh but rarely below the level of the knee. Squatting, prolonged sitting, and climbing stairs often exacerbate the pain. There may also be pain with bowel movements and dyspareunia in females. In physical exam, the ipsilateral foot may be noted to lie in an externally rotated position due to a contracted piriformis muscle [12, 19–22]. A contracted piriformis muscle may be elicited as a palpable mass on rectal exam [16].

The commonly used physical exam maneuvers are described here:

- *Freiberg's sign*: Buttock pain with passive, forced internal rotation of the hip [2].
- *Pace's maneuver*: Buttock pain with resisted abduction of the affected leg while in the seated position [13].
- *Lasègue's sign*: Buttock pain and tenderness to palpation in the greater sciatic notch with the hip passively flexed to 90º and the knee passively extended to 180° [3].

Table 34.1 Rehabilitation exercises for piriformis syndrome

1. *Piriformis stretch*: Supine position with knees flexed and feet flat on the floor. Rest the ankle of the injured leg over the knee of the uninjured leg. Grasp the thigh of the uninjured leg and pull that knee towards the chest. The patient will feel stretching along the buttocks and possibly along the outside of the hip on the injured side. Hold for 30 s. Repeat three times
2. *Standing hamstring stretch*: Place the heel of the patient's injured leg on a stool about 15 in. high. Lean forward, bending at the hips until a mild stretch in the back of the thigh is felt. Hold the stretch for 30–60 s. Repeat three times
3. *Pelvic tilt*: Supine position with the knees bent and feet flat on the floor. Tighten the abdominal muscles and flatten the spine on the floor. Hold for 5 s, then relax. Repeat ten times. Do three sets
4. *Partial curls*: Supine position with the knees bent and feet flat on the floor. Clasp hands behind the head to support it. Keep the elbows out to the side and do not pull with the hands. Slowly raise the shoulders and head off the floor by tightening the abdominal muscles. Hold for 3 s. Return to the starting position. Repeat ten times. Build up to three sets
5. *Prone hip extension*: Prone position. Tighten the buttock muscles and lift the right leg off the floor about 8 in. Keep the knee straight. Hold for 5 s and return to the starting position. Repeat ten times. Do three sets on each side
White [33]

- *Beatty's maneuver*: While lying in a lateral decubitus position on the unaffected side, buttock pain is elicited in the affected extremity when the patient actively abducts the affected hip and holds the knee several inches off the table [23].
- *FA(d)IR*: An acronym for flexion, adduction, and internal rotation of the affected hip. The maneuver prolongs the H (Hoffman)-reflex on nerve conduction studies [47].

Diagnostic Tests

In addition to clinical findings, numerous diagnostic tests have been proposed to identify piriformis syndrome. However, controversy remains regarding the true utility of these studies. Imaging studies of the lumbar and pelvic region are routinely obtained and best serve to exclude other well-defined causes of buttock and radicular leg pain such as lumbar disc herniations. MRI or CT of the pelvis may reveal inflammatory changes or edema of the affected muscle. While anatomic variations of the muscle and exiting sciatic nerve may be noted, the significance of these findings is unclear. Several case reports using MRI and CT have revealed unilateral hypertrophy of the piriformis muscle on the affected side in patients with piriformis syndrome [24, 25]. A study by Filler et al. examined MR neurography showing sciatic nerve hyperintensity at the sciatic notch in patients with hypertrophy (and occasionally atrophy) noted on MRI of the affected piriformis muscle [26]. The authors concluded that this additional imaging improved the sensitivity and specificity of identifying piriformis syndrome to 64 and 93 %, respectively [26]. However, others contend numerous theoretical and methodological flaws in this study. For instance, Beatty notes that the clinical diagnostic maneuver used by Filler et al. stretches the piriformis muscle, the sciatic nerve, and stresses the sacroiliac joint and thus constitutes a nonspecific sciatic nerve test [27]. Tiel et al. challenge that although pain relief may be obtained with injection of the piriformis muscle, this does not definitively diagnose piriformis syndrome [27, 28]. Furthermore, Tiel et al. state that the Filler study did not use a gold standard against which to compare the MR neurography and, therefore, true sensitivity and specificity measurements cannot be made [28].

Electrophysiologic testing in piriformis syndrome may represent a promising diagnostic tool. Fishman et al. have described prolongation (>3SD) of the posterior tibial or peroneal H-reflexes on FA(d)IR test and purport greater than 83 % sensitivity and specificity in diagnosing piriformis syndrome [29, 30]. While this would provide an effective objective diagnostic tool, critics disagree with the diagnostic criteria and methodology used in the study [31].

Treatment

After excluding other causes of low back, sciatica, and hip pain, piriformis syndrome can be diagnosed and therapy may begin. The mainstay treatment of piriformis syndrome consists of activity modification and physical therapy, with the goals of reducing pain and spasm of the piriformis muscle and correcting the pathology of compression of the sciatic nerve (Table 34.1) [32, 33]. The patient should be provided a home therapy program that may be combined with other modalities, such as heat, ultrasound, and manual techniques. Pharmacological treatments such as nonsteroidal anti-inflammatories (NSAIDs) and muscle relaxants may compliment physical therapy programs. Fishman et al. found 79 % of patients had symptom reduction with NSAIDs, muscle relaxants, ice, and rest [30].

If conservative therapy fails to provide adequate resolution of symptoms, intramuscular piriformis muscle injections may be warranted. Numerous injection techniques have been described utilizing CT guidance, fluoroscopic guidance, ultrasound, and combined fluoroscopic and EMG guidance (Table 34.2) [17, 34, 35]. Injected medications typically consist of local anesthetic and corticosteroid. Fishman et al. described injection of 2 % lidocaine 1.5 ml and triamcinolone 0.5 ml (20 mg) in patients with clinical

Table 34.2 Piriformis injection techniques

Approach #1: *Fluoroscopic guidance without EMG localization* [17, 46]
1. The patient is placed in a prone position
2. The skin is prepared and draped in a sterile manner
3. The expected position of the piriformis muscle is identified under fluoroscopic guidance with the beam directed in an anteroposterior direction. The landmarks utilized include the greater trochanter relative to the lateral border of the sacrum and sacroiliac joint on the affected side
4. Visualize an imaginary line connecting the greater trochanter and the lower border of the sacrum
5. A superficial skin wheal is placed overlying the ischial, bone medial to the acetabulum and parallel to the target site of injection
6. A 22- or 25-gauge 3½-in. (6 in. if the patient is morbidly obese) spinal needle is advanced to a point along the imaginary line near the pelvic brim until the posterior ischium is contacted
7. Contrast media is injected to visually confirm a classic sausage-shaped piriformis myogram (Fig. 34.2)
Approach #2: *Fluoroscopic and EMG guidance* [17]
1. Repeat steps 1–3 as described in approach #1
2. A superficial skin wheal is placed overlying the 2 o'clock position (left side) or 10 o'clock position (right side) of the acetabulum of the affected leg
3. An EMG needle is advanced until the 2 or 10 o'clock position of the acetabulum is contacted (Fig. 34.3)
4. The patient is asked to contract the piriformis muscle by externally rotating and slightly abducting the affected hip
5. Placement of the EMG needle is adjusted until maximum motor unit action potentials (MUAPs) are demonstrated while the patient is externally rotating and abducting the hip. Once the MUAPs are localized, the patient is asked to stop contracting the piriformis muscle, and contrast media is injected to visually confirm a classic sausage-shaped piriformis myogram (Fig. 34.2)

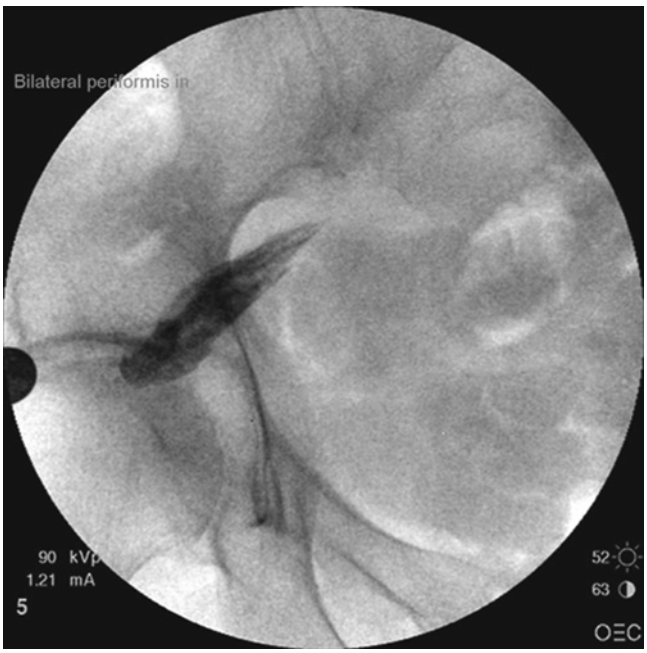

Fig. 34.2 Piriformis myogram

criteria for piriformis syndrome and prolonged H-reflex on nerve conduction studies [30]. With an average follow-up of 10.2 months, 79 % of these patients reported at least 50 % improvement in symptoms [30].

Botulinum toxin represents an additional treatment alternative. Botulinum toxin is a potent neurotoxin with seven serotypes (A–G), all of which (except type G) are produced by the gram-negative anaerobic bacterium, *Clostridium botulinum* [36, 37]. The four clinically available forms of botulinum toxin – onabotulinumtoxinA (Botox), abobotulinumtoxinA (Dysport), incobotulinumtoxinA (Xeomin), and rimabotulinumtoxinB (Myobloc), all inhibit presynaptic release of acetylcholine, thereby leading to muscle relaxation [36]. Studies in embryonic rat cells show that onabotulinumtoxinA may have a direct analgesic effect by inhibiting substance P from nerve terminals [38]. Food and Drug Administration (FDA) approval for onabotulinumtoxinA includes the treatment of strabismus, blepharospasm, upper limb spasticity, cervical dystonia, hyperhidrosis, chronic migraine headache, and frown lines [39]. FDA approval for abobotulinumtoxinA includes cervical dystonia and frown lines, while FDA approval for rimabotulinumtoxinB includes cervical dystonia only [40]. FDA approval for incobotulinumtoxinA includes cervical dystonia and blepharospasm [41]. Off-label uses include treatment of cervicogenic headaches, focal dystonias and spastic conditions due to cerebral palsy, stroke, and acquired brain injury [37]. Early investigations of intramuscular onabotulinumtoxinA for piriformis syndrome demonstrated improvement in symptoms. In their randomized, placebo-controlled crossover study involving nine patients, Childers et al. in 2002 demonstrated significant improvement in symptoms of pain intensity, distress, spasm, and interference of activities in all subjects of the onabotulinumtoxinA group [29]. Although the effects diminished, they persisted for all but one measure (spasm) at the end of 10 weeks [29]. In that same year, Fishman et al. reported a double-blind, placebo-controlled study comparing onabotulinumtoxinA (200 units mixed with preservative-free normal saline, 2 ml total volume) versus a combination of 2 % lidocaine 1.5 ml plus triamcinolone 0.5 ml (20 mg) versus preservative-free normal saline 2 ml [42]. Clinical improvement

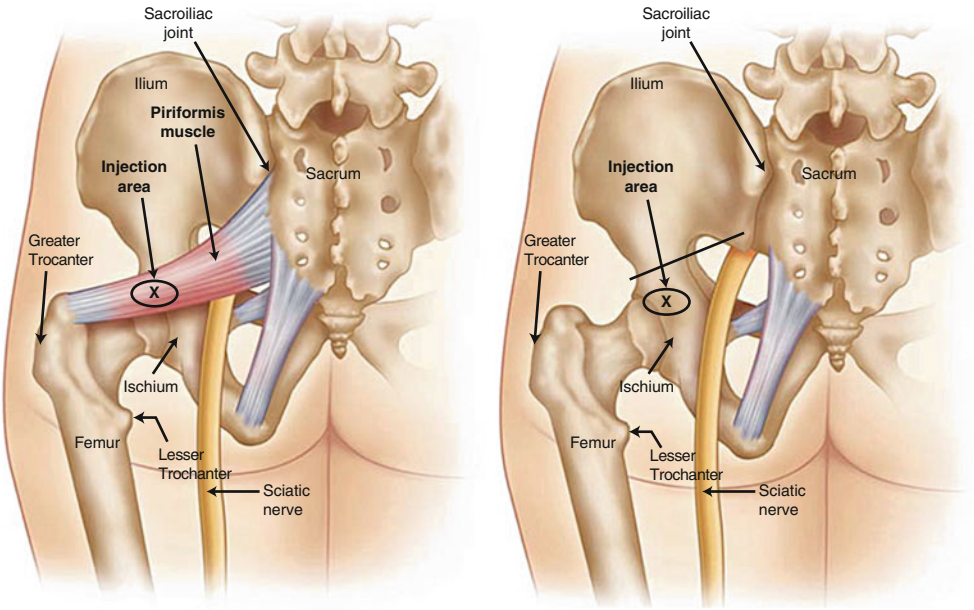

Fig. 34.3 Diagram of needle placement for piriformis injection (see Table 34.2) [17]

of at least 50 % on the VAS was reported in 65, 32, and 6 % of patients who received onabotulinumtoxinA, lidocaine plus triamcinolone, and placebo, respectively [42]. Most recently, Yoon et al. compared abobotulinumtoxinA (150 units in a 3 ml total volume) versus 1 % lidocaine and dexamethasone 5 mg in 20 patients [43]. Pain intensity scores were significantly lower in the onabotulinumtoxinA group at all follow-up time points. Because treatment in the experimental group was so much more effective, the control group was withdrawn at 4 weeks [43].

Finally, if all other conservative measures have proven inadequate, surgical management might be an option [7, 18, 44]. The procedure involves resecting the piriformis muscle itself or the muscle tendon near its insertion at the greater trochanter, and may include dissection of the sciatic nerve from the piriformis muscle if compression exists. While there is no definitive indication for proceeding to surgical management, outcome may be related to whether the etiology is secondary to trauma and/or the presence of electrodiagnostic abnormalities. Benson and Schutzer demonstrated excellent results in 11 of 14 patients with posttraumatic piriformis syndrome who underwent release of the piriformis tendon and sciatic neurolysis [18]. Of the 14 patients, preoperative electrodiagnostic studies were performed in only eight subjects who had obtained relief with surgical release [18]. Interestingly, however, six of these eight patients had definite findings of sciatic nerve compression at the level of the piriformis [18]. Conversely, Barton study showed relief in only one of four patients with nontraumatic piriformis syndrome who underwent piriformis tendon release [45].

Conclusion/Future Directions

Piriformis syndrome largely remains a diagnosis of exclusion. While its prevalence is not clear, there exist a certain number of patients whose "sciatica-type" symptoms are due anatomical variations causing compression or irritation of the sciatic nerve. Electrophysiologic tests and MR neurography may serve as accurate diagnostic tools in identifying piriformis syndrome, but more conclusive studies need to be performed. Conservative treatments including NSAIDs and physical therapy remain the first-line therapies for addressing piriformis syndrome. If these efforts are minimally successful or unsuccessful, patients may obtain relief with inclusion of piriformis muscle injections utilizing a combination of corticosteroid and local anesthetic. Recent studies with intramuscular botulinum toxin injections show promise for more long-term benefit, but larger studies with longer term follow-up need to be done. Surgical resection of the piriformis muscle has been performed successfully in cases of intractable pain, but comprehensive studies do not yet exist to support this intervention.

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Botulinum Toxin in the Management of Painful Conditions

35

Robert Gerwin

Key Points

- Botulinum toxin inhibits the release of neurotransmitters involved in the activation of sensory neurons.
- The release of substance P, glutamate, and calcitonin gene-related peptide is thought to be inhibited by botulinum toxin.
- Botulinum toxin is effective in reducing the frequency and intensity of migraine headaches. High-quality studies, class 1 data, A-level recommendation as effective.
- Botulinum toxin is effective in relieving nonspecific low back pain. High-quality, class 1 studies, A-level recommendation as effective.
- Botulinum toxin is possibly effective in treatment of neck and upper back pain, but results of studies are mixed. Class III studies, C-level recommendation as possibly effective.
- The studies of the use of botulinum toxin in myofascial trigger point pain are inconclusive due to the small number and poor quality of the studies. Class I studies but U-level recommendation of inadequate or conflicting studies.
- Studies of the treatment of pelvic pain are encouraging, but more and better studies need to be done (class III data and U-level recommendation of inadequate data).
- A variety of other painful conditions are now being investigated, including neuropathic pain. Results are mixed but this seems to be a promising area in need of more and better studies. Data is class III–IV and recommendation for use is level U (inadequate or conflicting data).

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Introduction

Botulinum neurotoxin (BoNT) has been used clinically to impair muscle contraction and thereby has become useful in treating conditions characterized by persistent muscle spasticity, muscle spasm, or contraction. It has more recently been found to reduce pain in clinical pain syndromes. This chapter will present the current state of knowledge about the clinical use of BoNT in the treatment of painful conditions. It will also review the mechanism of action of BoNT with regard to inhibition of nociceptive activity.

Mechanism of Action of Botulinum Toxin

The activation of peripheral nociceptors and the subsequent activation of secondary neuronal pathways lead to pain perception. In a nutshell, nociceptive impulses from peripheral neurons are transmitted through the spinal cord to the brain where they activate a number of distinct centers including the somatosensory cortex where pain is perceived. The transmission of nociceptive impulses through the spinal cord are facilitated and inhibited by descending modulating impulses that pass through the spinal cord and have the potential to alter the quantity of ascending nociceptive impulses reaching the brain. BoNT can alter this process and dampen the cascade of events involved in pain perception, leading to a reduction in pain intensity. The mechanism of action of BoNT in this respect is partially understood and continues to be investigated. Botulinum toxin enzymatically cleaves the SNARE proteins that anchor synaptic vesicles to the cell membrane in the motor nerve terminal, allowing acetylcholine and other neurotransmitters to flow through the motor nerve terminal membrane fusion pore into the synaptic space. Botulinum toxin has an effect on sensory neurons and sensory perception as well, by inhibiting the release of neurotransmitters involved in activation of sensory neurons.

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This chapter will review what is known about the action of BoNT on pain perception. The work to be reviewed will focus on studies with botulinum neurotoxin type A (BoNT-A) unless otherwise specified, as most studies have been done with this subtype of BoNT.

Botulinum toxin is approved by the Food and Drug Administration (FDA) in the United States for the treatment of strabismus, blepharospasm associated with dystonia, cervical dystonia, upper limb spasticity, and axillary hyperhidrosis. All other uses of botulinum toxin in the United States are off-label uses. This chapter will report on the studies of BoNT in pain management and will discuss the results of studies of BoNT in certain pain states. The information in this article should not be construed to advocate the general off-label non-FDA-approved usage of BoNT.

Mechanism of Action of BoNT in Alleviation of Pain

The mechanism of action of BoNT on muscle contraction is the inhibition of the release of the neurotransmitter acetylcholine at the neuromuscular junction. The action of BoNT on nociception is mediated by a similar inhibition of neurotransmitter release from peripheral nociceptors [1]. The release of Substance P (sub P), glutamate, and calcitonin gene-related peptide (CGRP) are all thought to be inhibited by BoNT.

Patients suffering from dystonia and dystonia-related pain experienced pain relief when treated with BoNT [2, 3]. Moreover, pain relief generally occurred before onset of its effect on the dystonia itself [4, 5]. In addition, pain relief outlasts the effect of BoNT on muscle in a masticatory muscle model [6], indicating that botulinum toxin has an analgesic effect that is quite separate from its effect on acetylcholine at the neuromuscular junction.

In vitro studies have demonstrated that the release of sub P [7, 8] is inhibited by BoNT. The inhibition of sub P was directly related to the degree of SNAP-25 cleavage. These studies established the inhibition of neuropeptide release by BoNT in inflammatory pain models, an effect that is in addition to the inhibition of acetylcholine release in the motor nerve terminal.

BoNT was shown to inhibit phase 2 of formalin-induced nociceptive behavior in the rat model. There was no effect on acute thermal nociception, considered to be consistent with the lack of effect on phase 1 of the response. This is also true in humans. The effect was associated with a reduction in formalin-induced release of the excitatory amino acid glutamate [9].

Migraine headache involves activation of the trigeminovascular system. The interest in botulinum toxin as a treatment of migraine headache has led to its study in trigeminal sensitization. The action of BoNT has been studied in the skin, particularly with relation to the activation of peripheral nociceptors by capsaicin. Botulinum toxin administered subcutaneously inhibits the extent of capsaicin-induced perceived pain area, pain intensity, secondary hyperalgesia, flare area, blood flow, and skin temperature in male subjects [10, 11]. Neurogenic vasodilation is reduced as well as capsaicin-evoked pain in human skin [12]. An effect was observed on cutaneous heat thresholds but not on electrical or pressure pain thresholds. The effect of BoNT appears to be mediated through an action on C-fibers and on TRPV1-receptors. In contrast, in one study injection of BoNT-A subdermally in the forearm did not alter the pain response to capsaicin [13]. In summary, BoNT works in nociception much in the same way that it does at the neuromuscular junction, by preventing the release of neurotransmitters by sensory nerve endings.

Clinical Studies of Botulinum Toxin in Pain Syndromes

BoNT has been studied in a number of pain syndromes. There has been great interest in the possible benefit of BoNT in headache syndromes, and recent studies have supported that usage. Its role in musculoskeletal pain syndromes has been less thoroughly studied. The benefit of treatment with BoNT in low back pain and neck pain is better established than in myofascial pain syndromes, where the results of studies have been contradictory. There is clearly a role for BoNT in the treatment of pelvic pain syndromes. There are either too few studies or inadequate or negative studies in some other conditions. Randomized controlled studies (RCT) are presented where available. Open label and uncontrolled studies are generally not cited in this chapter.

BoNT in Musculoskeletal Pain Conditions

Low Back and Joint Pain (Table 35.1)

There have been several studies that have shown a beneficial effect of botulinum toxin on low back pain. The studies were done on individuals with chronic low back pain that was predominantly unilateral and who did not have an identifiable acute source of pain like a herniated disc. Back pain in this sense can be called nonspecific low back pain. Foster et al. [14] evaluated the effect of botulinum toxin A over 8 weeks on nonspecific low back pain in a randomized, double-blind study. Botulinum toxin type A 40 units or saline was injected unilaterally at five different lumbar levels. Relief was greater than 50 % (VAS score) in 73 % of the botulinum toxin type A-treated subjects compared to 25 % of the saline control group ($p = 0.012$). A follow-up open-label study by the same group was conducted over 14 months. The outcomes in the open-label extension of the study included the change in the VAS, the number of pain days, and the Oswestry

Table 35.1 Low back treatment protocol

Muscles	Units of onabotulinumtoxinA (Botox)
Lumbar paraspinal muscles	5–50 units bilaterally at each vertebral level (includes the multifidi and the lumbar iliocostalis muscles)
Psoas muscle	50–100 units
Quadratus lumborum	25 units

Note: The dosages given here are specific for Botox® brand of onabotulinum toxin type A. The number of units to be used is specific for each type and brand of BoNT (onabotulinum toxin Botox®, Dysport® brand of botulinum toxin type A, and Myobloc® brand of botulinum toxin type B), and are not interchangeable. Clinicians should be familiar with reconstituting the freeze-dried onabotulinum toxin type A without denaturing it and should be familiar with the dosing schedules of any particular form of BoNT that is to be used in a given situation

Table 35.2 Injection dosing schedule recommended for chronic, intractable neck pain

Muscle	Units of BoNT-A
Upper trapezius	15–40 units distributed through the muscle
Splenius capitis	5–10 units
Splenius cervicis	5 units
Semispinalis	5–10 units as 5 units in each of 1–2 units sites
Oblique capitis inferior	5 units
Levator scapulae	25 units
Medial scalene	5 units

The doses recommended are for unilateral injection. The same doses are used on the contralateral side for bilateral treatment. The adverse side effect that is potentially of concern is neck weakness manifested by inability to maintain the neck in an erect, upright posture

functional status scale. Botulinum toxin type A was found to significantly reduce pain over a 14-month period of time during which repeated injections were given. Ninety-one percent of initial responders maintained responsiveness over the duration of the open-label trial [15].

Neck and Upper Back Pain (Table 35.2)

There are few randomized, controlled studies of the use of BoNT in neck and upper back pain. Göbel et al. [16] found that BoNT-A (Dysport®) significantly reduced or eliminated upper back myofascial pain compared to saline (51 vs. 26 %, $p = 0.002$) 5 weeks after injection. However, another study of BoNT-A treatment of pain emanating from cervicothoracic myofascial TrPs showed that low dose (50 units total), higher dose (100 units total), and saline all resulted in a decline in pain and disability scores, with no benefit of BoNT over placebo, but those in the subgroup of subjects who received a second injection of BoNT-A experienced such a high incidence of becoming asymptomatic that the authors concluded that further studies were warranted. In contrast, a RCT, double-blinded study of the effect of BoNT-A in the treatment of refractory neck pain, in which 33 of 47 subjects had neck injury (72 %), resulted in a significant number of subjects classified as excellent responders who had a ≥50 % decrease in VAS for pain, ≥30 % reduction in pain days, and 2 grades or more improvement in the Modified Oswestry Pain Questionnaire (6/23 in the BoNT-A group vs.1/21 in the control group). Pain intensity was greater in the BoNT-A group at baseline, but was significantly decreased at 2 months compared to the saline control group ($p < 0.0018$). Injections were made in the trapezius, splenius, and rhomboid muscles as clinically indicated, using 20 units per injection site and ranged in total from 150 to 300 units. No information was given about the criteria for selection of specific injection sites, but it appears that the injection sites were selected to give a general distribution of BoNT-A in the muscles treated, as opposed to injecting in myofascial trigger points. This well-designed and executed study clearly shows efficacy of BoNT-A treatment for chronic neck pain.

Myofascial Pain Syndromes

Pain in myofascial pain syndrome (MPS) is generated by a tender, taut band that is the fundamental feature of the myofascial trigger point (MTrP). It is thought that relaxation of the taut band through inhibition of acetylcholine release from the motor nerve terminal at the neuromuscular generation and inhibition of the release of neurotransmitters at the sensory nerve will result in decreased pain from MTrPs. However, the few studies that have looked at this have not supported this concept. Often-quoted studies include those of Ferrante et al. [17], Graboski et al. [18], Kamanli et al. [19], and Ojala et al. [20]. Ferrante et al. [17] stopped all pain medication prior to the trial injections, then gave all subjects amitriptyline, ibuprofen 800 mg qid, and prn propoxyphene/apap. In this RCT, subjects were given either BoNT-A (10, 25, or 50 units/trigger point) or saline in up to 5 trigger points. Patients were excluded if they had more than 5 trigger points or more than 2 trigger points in on trapezius muscle, or more than one trigger point in any other single surface muscle. There was no difference in rescue medication, or in pressure pain threshold between saline injected groups and those injected with BoNT-A. Both the lowest dose and highest dose BoNT-A outperformed saline, but not to a significant degree. Some of the possibilities include the fact that all subjects were treated with adjuvant pain medication and that

saline is not an inactive control. Finally, the standard deviation of the sum of pain intensity differences, a reflection of the primary outcome measure, was so great that differences between the saline group and the BoNT-A were not significant. For these reasons, the results of this study cannot be seen as conclusive. Graboski et al. [18] compared BoNT-A to bupivicaine. A maximum of 8 trigger points were injected with either 25 units of BoNT-A or saline in this RCT. The end point was a return to 75 % of pre-injection pain. At that time, subjects were injected with the other substance (a crossover study). There was no statistically significant difference between the two treatments. Bupivicaine was considered cheaper. Outcome measures were changed in pain scores and duration of relief. Although there was no significant difference between groups, there was a definite trend toward greater decrease in pain and greater duration of effect with BoNT-A. Possible issues were the low number of subjects completing the trial (17 subjects in all) and the limited number of trigger points injected. Kamanli et al. [19] compared BoNT-A, lidocaine, and dry needling. Pain scores were lower in the subjects treated with BoNT-A and dry needling, and visual analogue scale significantly decreased in the lidocaine and BoNT-A groups at the single follow-up visit of 4 weeks. A single trigger point was treated. BoNT-A was not inferior to lidocaine or dry needling. However, in this study, as well as in the other two studies, no attempt was made to provide a comprehensive treatment to clear all relevant trigger points. In clinical practice, one would treat all of the trigger points deemed to be relevant in producing a pain syndrome. In this regard, inactive trigger points that are known to cause dysfunction [21] also need to be treated. In partial treatments, trigger points tend to recur more quickly. Studies that use pressure pain thresholds as a measure have not shown that this measurement reliably reflects inactivation of trigger points.

Ojala et al. [20] did a single-blind, RCT, crossover design, injecting either saline or BoNT-A in up to six neck and shoulder muscles bilaterally and then injecting the trigger points with the other substance 1 month later. There was no difference between groups 1 month after the second injection when subjects had received both saline and BoNT-A 1 month apart. However, after the first month, before the saline group received BoNT-A, subjects treated with BoNT-A had a significantly greater decrease in pain than those treated with saline. BoNT-A has a peak motor effect at about 6 weeks, and effectiveness is maintained from 10 to 14 weeks in most subjects. Hence, one would expect a difference 1 month after the first injection and no difference 1 month after the crossover injection.

There are a number of other studies that address this issue. Pain in patients with temporomandibular joint disorders was treated with BoNT-A injected into the masseter and temporalis muscles in a randomized, controlled study [22]. The result was a decrease in pain and an improvement in psychological status. Both the studies of Göbel et al. [16] and Wheeler et al. [23] were suggestive of a benefit for BoNT at a certain time and under certain circumstances.

It helps to be very clear in defining the desired outcome using BoNT. All studies show that BoNT treatment of myofascial trigger points can respond well to BoNT, but the placebo effect has also been striking. It is essentially like giving a lidocaine trigger point injection that lasts between 10 and 14 weeks in duration. The local twitch response that marks a successful trigger point injection with lidocaine is generally lost after BoNT injection. The number of lidocaine trigger point injections needed to treat an MPS is usually reduced and sometimes eliminated altogether for the duration of action of the toxin. The effectiveness of the toxin in MPS seems to depend on the care with which the trigger point zone is injected and the comprehensive clearing of TrPs in a functional muscle unit. Treatment of trigger points in only one muscle instead of a functional muscle unit may be a reason why spontaneous pain was not reduced 28 days after BoNT-A was injected in an infraspinatus muscle trigger point [24].

BoNT in Headache Management

Migraine Headache (Tables 35.3, 35.4, and 35.5)

The headache literature is very mixed on the issue of the effectiveness of BoNT in the treatment of headache in general, and migraine in particular. This literature was reviewed through 2007/2008 in Gerwin [25]. The literature prior to 2010 can be summarized by saying that the results of the many studies done in patients with migraine and other headaches varied in their outcome. One of the reasons for variability this is the lack of uniformity in subject selection, sites, and dosing schedules used. Silberstein et al. [26], in a RCT of chronic migraine showed that patients treated at predetermined fixed sites with low-dose onabotulinumtoxinA (25 units total) had a significantly reduced migraine frequency and a reduction in the use of medications compared to the carrier alone, but the higher dose of 75 units showed no benefit. A RCT using lower doses of BoNT in the temporalis mus-

Table 35.3 Treatment of migraine headache by Botox: migraine protocol

Muscle	Units of onabotulinumtoxinA (Botox)
Temporalis	25 in a linear or diamond grid
Procerus	5
Corrugator	5 each
Frontalis	10–20

Table 35.4 Follow-the-pain protocol for use in chronic tension-type headache and migraine

Muscle with trigger points referring pain to headache regions	Units of onabotulinumtoxinA (Botox)
Temporalis	25 in a linear or diamond grid
Masseter	2–4
Zygomaticus	2–3
Pterygoid	2–3
Sternocleidomastoid (inject only one side)	10–15
Splenius capitis	5
Splenius cervicis	5
Oblique capitis inferior	5
Semispinalis	5–10
Levator scapulae	10–25
Upper trapezius	25–40

Table 35.5 Combined migraine and follow the pain for most migraine headaches

Muscle	Units of onabotulinumtoxinA (Botox)
Upper trapezius	25–40
Sternocleidomastoid (inject only one side)	10–15
Temporalis	25 in a linear or diamond grid
Procerus	5
Corrugator	5
Splenius capitis and cervicis	5
Semispinalis	5
Oblique capitis inferior	5

cles and omitting injection of glabellar muscles showed a 50 % reduction in headache days in 30 % of the active treatment group, but the 25 % of the placebo group showed the same response, so the results were not significant [27]. A study using three different dosing schedules of BoNT-A and using a low dose (7.5 units) of BoNT as an active control showed equal reduction in headache frequency in all groups [28]. A small study failed to show benefit of BoNT-A in reduction of headache frequency or severity compared to placebo, but headache index worsened in the placebo group, but not in the active treatment group, suggesting that BoNT had a protective effect in headache severity. Studies of episodic migraine fared no better [29, 30]. However, there two studies that indicated that BoNT-A to be of benefit in the treatment of migraine [31, 32]. The largest and most comprehensive RCT, to date, of 1,384 subjects was done by the PREEMPT Chronic Migraine Study Group [33] and found that onabotulinumtoxinA (BoNT-A) was superior to placebo in the primary outcome measure of reduction in frequency of headache days at all time points in the 24-week double-blinded portion of the trial. In addition, onabotulinumtoxinA was superior to placebo in six secondary outcome measures: mean change from baseline in frequencies of headache days, moderate or severe headache days, cumulative hours of headache on headache days, headache episodes, migraine episodes, and the proportion of patients with severe Headache Impact Test-6 score. Acute medication use in the treatment group was not statistically better than placebo. The size of the study and the thoroughness of evaluation make this a landmark study. The authors point out that the study was not made against a comparator. The authors themselves refer to a pilot study comparing onabotulinumtoxinA to topiramate [34], an FDA-approved drug for the prevention of migraine. In this study, subjects were randomly assigned to either onabotulinumtoxinA or to topiramate. The study was placebo controlled.

Technique

There are two approaches to treatment of migraine headache with BoNT. One is the so-called migraine protocol and the other has been called the "follow-the-pain" protocol. In practice, a third approach is often utilized, which is a combination of the two protocols. No uniform approach has been determined for either protocol, and the studies done to establish doses have been few and preliminary at best. Therefore, there is no established best practice based on acceptable medical evidence in terms of dosing or sites to be injected. What is recommended here is based on a combination what has been published and on the author's experience as to what has generally worked best. However, the recommendations in this chapter include the protocol in the largest trial to date that showed efficacy of onabotulinumtoxinA in the management of chronic migraine headache [33].

The "migraine protocol" involves injecting BoNT into the corrugator muscles, the procerus muscles, and the temporalis muscles (Fig. 35.1). Many physicians who treat migraine with BoNT include the frontalis muscle as well. I do not do that, but I combine the migraine protocol with the "follow-the-pain" protocol, instead.

The "follow-the-pain" protocol is best characterized as injecting sites in the neck and shoulders that refer to the places where headache pain is felt in the head. This is essentially treating regions in head, neck, and shoulder muscles that refer pain to various places in the head that are characteristic of that person's migraine headache. An early test of the concept of "follow the pain" is in the 1981 paper by Tfelt-Hansen et al. [35] in Denmark, in which the authors showed that headache could be decreased or eliminated in large percentage of subjects with migraine by injecting muscles outside of head, that is, muscles in the neck and shoulder, that cause pain. An elegant study that specifically looked at sites in muscle that cause pain to be referred specifically to places of headache complaint showed that injection of these referral sites in head, neck, and shoulder, done on a repeated basis, result in a significant reduction in migraine headache frequency and intensity [36].

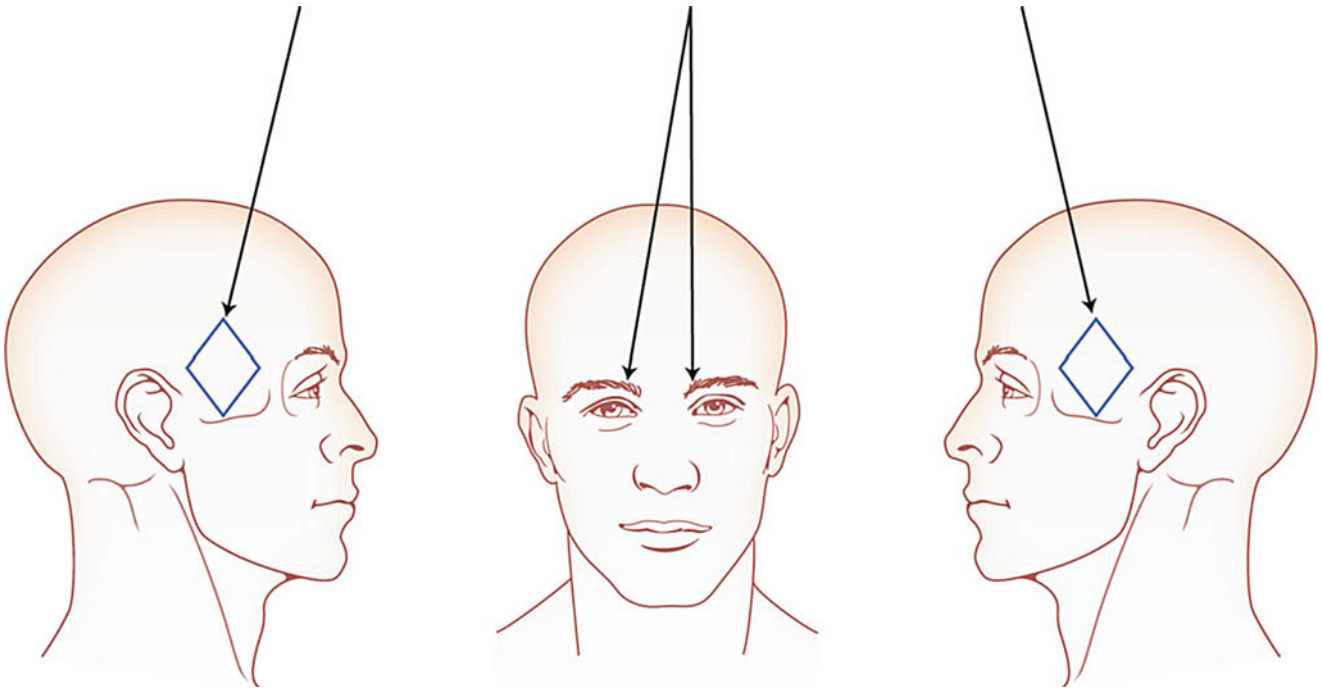

Fig. 35.1 Procerus: between and inferior to the corrugator muscle

The muscles and sites to be injected are those that harbor tight and tender taut bands. The taut bands are hardened regions of muscle that are tender to palpation. They are relevant to the patient's pain when they result in pain referred to the region of headache. This applies not only to migraine but also to tension-type headache and to cervicogenic headache. It also applies to involvement of masticatory muscles that not only directly cause headache pain but that indirectly affect headache by activating trigger points in the cervical musculature.

Chronic Tension-Type and Cervicogenic Headache (CTTH) (Table 35.4)

The headaches of interest in this headache subgroup are those of ≥15 headache days per month, the generally accepted headache frequency for chronic daily headache. There have been few studies of the effect of BoNT on headache that target this group specifically. Many of the studies of chronic daily headache did not distinguish between migraine headache and tension-type headache. Of the few studies that specifically targeted CTTH, three used fixed-dose and fixed-site injection of BoNT-A. They showed no significant reduction in headache frequency [37–39], although in one study, the BoNT-A-treated subjects showed a significantly greater percentage with ≥50 % reduction in headache days compared to the placebo group [39]. One pilot study [40] of great interest looked at the myofascial trigger points (MTrP) that referred pain to typical headache sites, a strategy that builds on many recent studies of the relationship of myofascial trigger points to headache symptomatology, a subject recently summarized in the text by Fernandez-de-las-Peñas et al. [41]. Harden et al. [40] identified trigger points in the neck and upper shoulder, including the sternocleidomastoid and the upper trapezius muscles, and the splenius capitis muscle. They injected 25 units of BoNT-A into each of up to 4 MTrP per subject, using up to 100 units. This was a randomized, double-blinded, placebo-controlled study, but it was quite small, with only 12 subjects in the treated group and 11 subjects in the placebo group. There was a significant decrease in headache days in the BoNT-A-treated group through week 10, but the effect was gone by week 12. This is consistent with the expected duration of effect of BoNT-A on muscle. An open-label extension of the study included 12 subjects from both the BoNT-A and placebo groups. It again showed a significant reduction in headache frequency compared to the original placebo group, for the first 2 months. This study was limited by the small number of subjects and by the small selection of the muscles considered (there were no facial muscles like the masseter and temporalis muscles, and neither the splenius cervicis, oblique capitis inferior, nor semispinalis muscles were injected, although the authors implied that injection of the splenius capitis might have treated multiple underlying muscles). A randomized, single-blinded, placebo-controlled study utilizing a combination of a fixed injection site and "follow-the-pain" approaches also showed significant improvement in the subjects treated with BoNT-A at 1 month, in headache days per month, headache severity,

and the in the Henry Ford Headache Disability Inventory [42]. In both the Harden et al. study [40] and the Hamdy et al. study [42], side effects were minor and transient. Another small study of headache associated with myofascial trigger points randomized 45 subjects to treatment with dry needling, lidocaine injections, and botulinum toxin [43]. All three groups showed fewer headaches, shorter headache duration, and decreased pain intensity. Those treated by botulinum toxin also showed a decreased use of rescue medication and less post-injection soreness. The authors concluded that botulinum toxin is no better or worse than the other two treatment modalities, but that it is more expensive and should be reserved for refractory cases of headache.

The conclusion that one can draw from the studies is that treatment of chronic daily headache, particularly of the migraine headache type, with botulinum toxin type A is effective, but BoNT has not been shown to be necessarily more effective than treatment with lidocaine or intramuscular therapy (IMT) with solid, monofilament needles (dry needling). The role of botulinum toxin is uncertain if derived solely from these studies. It would seem sensible to use botulinum toxin only in those cases of chronic daily headache where conventional drug therapy is unsatisfactory either because of ineffectiveness of prophylactic drugs or because of unacceptable side effects, and when lidocaine injections or IMT are effective but too short lasting. Several unanswered questions remain. Is BoNT effective when lidocaine injections of trigger points fail to relieve headache? Should subjects first be treated with lidocaine injections or IMT before being treated with BoNT?

The protocol for treatment of headache generally follows a migraine protocol in those patients with migraine features (Tables 35.3 and 35.5). In both those patients with migraine and in those with tension-type and cervicogenic headache, BoNT is injected in the trigger points themselves. Injection of BoNT into trigger points is not as exacting as injection of lidocaine or IMT into trigger points, because BoNT spreads through tissues and will alter transmitter release over about a 2.5-cm diameter around the injection site. The area of spread is directly related to the concentration of BoNT, so that there is greater spread with greater dilution. A concentration of 5–2.5 units of BoNT-A is commonly used. This is achieved with 2–4 per 0.1 cc respectively of preservative-free saline/100 units in reconstituting the freeze-dried product. See Tables 35.3, 35.4, and 35.5 for recommendations of the number of units to be injected in trigger points in various muscles.

BoNT in Pelvic Pain Conditions (Table 35.6)

Botulinum toxin has been used to treat conditions of the pelvic/hip region, including piriformis syndrome, other gluteal muscle pain syndromes, and levator ani muscle pain syndromes. In addition, it has been used in viscerosomatic pain syndromes including the abdominal wall muscle pain component of endometriosis, interstitial cystitis, and irritable bowel syndrome. Botulinum toxin has been injected directly into the bladder in the treatment of interstitial cystitis and irritable bladder.

Table 35.6 Pelvic/hip pain protocol

Muscle	Units of onabotulinum toxinA (Botox)
Quadratus lumborum	25
Lumbar paraspinals	
Multifidi	5–10 per vertebral level
Lumbar iliocostalis	5–40 per vertebral level
Tensor fascia lata	15–25
Gluteus medius	25–50
Gluteus minimus	25–50
Piriformis	25 units proximally and 25 units distally
Obturator Internus	25 units medial to the ischial tuberosity
	25 units lateral posterior to the greater trochanter (the muscle is usually indistinguishable from the gemelli laterally)
Levator ani	25 units distributed in 5–10 unit aliquots, given with the needle inserted through the gluteus maximus with digital guidance (rectal or vaginal)
Gluteus maximus	25–50
Adductor magnus iliococcygeal head	25
Hamstrings (upper medial)	25
Pectineus	10–15
Adductor brevis/longus	25

Treatment of the levator ani syndrome with botulinum toxin is reported to decrease coital pain (dyspareunia) and menstrual pain (dysmenorrheal), to increase sexual activity, and to produce relaxation of the pelvic floor muscles [44, 45]. In the Jarvis et al. [44] study, women were treated in the lithotomy position and given conscious sedation. The puborectalis and pubococcygeus muscles were identified by digital examination through the vagina. The needle is guided along the examining finger, the injection made through the vaginal mucosa. No woman experienced fecal incontinence from treatment with botulinum toxin. The amount of botulinum toxin type A that was injected was 10 units per side.

Botulinum toxin type A injected into the bladder wall in patients with painful bladder syndrome reduced mean VAS scores, and daytime and nighttime urinary frequency [46]. Daytime frequency and nocturia, and pain, decreased significantly after BoNT-A (Dysport and Botox) was injected into 20–30 sites in the trigone and floor of the bladder submucosally through a cystoscope in women with interstitial cystitis [47]. Studies done by a Urology Department failed to show such benefits to intravesical injection of BoNT-A [48], but when hydrodistension was added to intravesical BoNT-A treatment, there was a significant improvement in pain and urinary frequency [49].

Vestibulodynia is another distressing pain syndrome that is being approached by injection of BoNT. In one open-label study, the injection of BoNT-A 35 or 50 units into the pelvic floor muscles resulted in a significant decrease in pain [50]. An anecdotal report of two patients treated with BoNT-A injected into the levator ani muscle to reduce coital pain, reduce pelvic floor tension, and reduce vestibular hyperalgesia resulted in improvement in coital pain in one patient but no reduction in vestibular hyperalgesia [51].

Ureteral stent placement for the treatment of ureteral obstruction can result in postoperative pain, increased urinary frequency, and urgency. One postulated cause is detrusor muscle spasm at the site of the intramural ureter. A randomized, single-blind study of the periureteral injection of BoNT-A showed a significant decrease in postoperative pain with a corresponding decrease in the use of opiate medications in this condition [52]. Urinary function was no different among those treated with BoNT-A and those not so treated.

Pelvic/Hip Pain Injection Technique (Table 35.6)

Injection of the pelvis/hip muscles for mechanical and viscerosomatic pain syndromes requires the examination of the low back muscles, the gluteal region muscles, the adductor muscles, the pelvic floor muscles, and the adductor magnus muscle. The quadratus lumborum muscle can refer pain widely in the low back and the pelvic region. The lumbar multifidi and the lumbar iliocostalis muscles refer pain to the sacroiliac joint and widely in the gluteal region. The pelvic floor muscles can give rise to local pain as well as pain referred to the hip and to both the groin and to the gluteal fold. The piriformis muscle gives rise to local pain, pain at the sacroiliac joint, and pain at the trochanter region, and can compress the sciatic nerve giving rise to sacroiliac joint pain. Most of the muscles, including the piriformis, obturator internus, and levator ani, can be injected from the outside the pelvis, rather than intrapelvically. So that there is almost never a need to inject through the rectum, even if a flute is used to guide the needle. Digital guidance through the vagina or through the rectum can be used to direct the needle. A 1.5-in., 25-gauge needle can be used for the more superficial muscles, and a 3.5-in., 25-gauge needle is adequate for almost all of the deeper muscles, including the piriformis and gluteus minimus muscles. The obturator internus can be injected medial to the ischial tuberosity at a point where the ischial tuberosity is concave to the anus, about 5 cm rostral to the inferior tip of the tuberosity. To inject the portion of the obturator internus that covers the obturator foramen requires a transvaginal approach.

BoNT in Other Painful Conditions

There is one RCT, double-blinded study that shows BoNT-A to be effective in reducing pain in chronic neuropathic pain [53]. BoNT-A was injected intradermally (20–190 units) into the painful area. Pain and allodynia were significantly reduced from 2 to 14 weeks after injection, whereas thermal perception thresholds were not altered. The only notable adverse effect was pain during the injections.

Painful Knee Osteoarthritis

A pilot double-blinded, RCT of BoNT-A injected intra-articularly showed that BoNT-A was better than intra-articular corticosteroid at 8 weeks [54]. The author of this chapter has found that BoNT injected into myofascial TrPS of the vastus medialis and lateralis muscles reduces knee pain as well. Injection of BoNT-A into the vastus lateralis muscle significantly reduced refractory anterior knee pain [55], showing the benefit of treating referred pain from muscle to knee. Injection of BoNT-A 25 units is often enough to provide 10–14 weeks of knee pain relief, enough to allow adequate rehabilitation to take effect. In general, if a vastus medialis or lateralis muscle trigger point responds to lidocaine injection or IMT, but the relief is not maintained, the BoNT can be an effective alternative. However, part of the rehabilitation process is to strengthen the quadriceps muscle, and weakening the muscle with BoNT is theoretically counterproductive. There are no published studies that have examined this question.

Sacroiliac joint pain was relieved by injection of BoNT-A intra-articularly [56]. Other studies of the effectiveness of BoNT may be confounded by pain originating in structures that are not treated by intra-articular injections of BoNT-A but that neverthele cause knee pain, like tendons, ligaments, and referred pain from muscle.

Shoulder pain in spastic post-stroke hemiplegia (Table 35.7 and Fig. 35.2) was successfully treated with BoNT-A (Dysport)

Table 35.7 Injection of BoNT-A (Botox) in post-stroke spastic shoulder hemiparesis

Muscle	Units of onabotulinum toxin (Botox)
Subscapularis	25–50
Latissimus dorsi	25–50
Teres major	10–25
Infraspinatus	25–40
Supraspinatus	25–35
Levator scapulae	25
Pectoralis major	25–50
Pectoralis minor	25

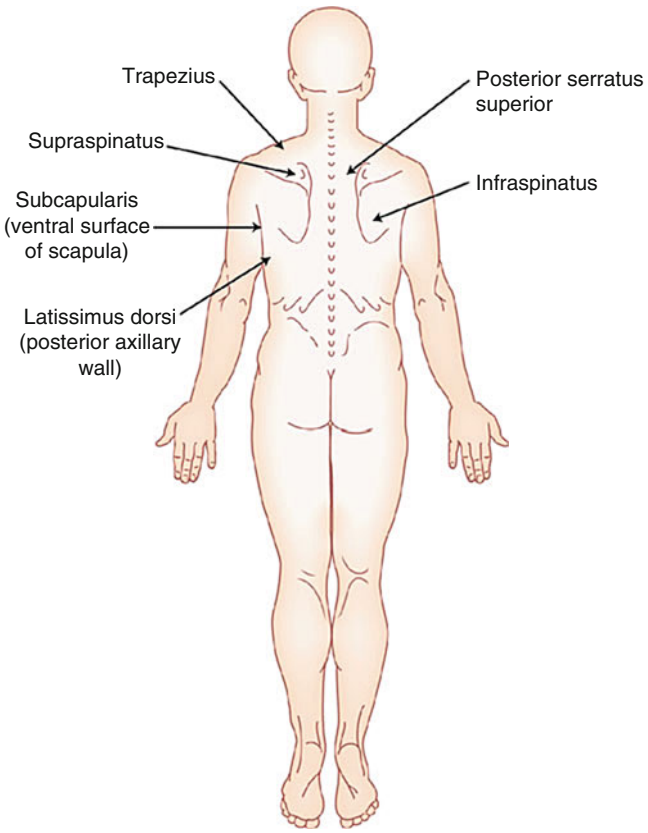

Fig. 35.2 Shoulder pain in spastic post-stroke hemiplegia

using 500 Speywood units injected into the subscapularis muscle [57]. Lateral rotation was also improved. However, another study using BoNT-A (Botox), 50 units injected into each of two sites in the subscapularis muscle, failed to show any greater improvement than placebo over 12 weeks [58]. Even though the placebo injection was not an inactive control (injection of saline and IMT are both active treatments), improvement with saline is not expected to last for 12 weeks. A third study showed a strong trend toward significant improvement in hemiplegic shoulder pain treated with intramuscular BoNT-A into three muscles and intra-articular saline compared to intra-articular injection of triamcinolone acetonide and saline injections into muscle ($p = 0.051$) [59]. Overall, it seems reasonable to treat pain associated with post-stroke spastic hemiplegia with BoNT if there is no response to conventional therapy. The key to successful treatment is the inclusion of all affected spastic muscles that includes the subscapularis, the pectoralis major and minor, the latissimus dorsi and teres major, and the supraspinatus muscle. None of the published studies included this wide a range of muscles.

Postwhiplash neck pain is a controversial area of treatment. Treatment of four sites in RCT trial, both acute and chronic, were treated with either BoNT-A or placebo and monitored to 24 weeks. Significantly greater reduction in pain was noted at 24 weeks in number of patients with greater than 50 % reduction of pain. This is not a clinically realistic treatment schedule. Treatment would be tailored to inject all muscles that have symptomatic trigger points, and to reinject trigger points that persist after the first injection. Physical therapy would be provided for subjects as well. Thus, this study does not give adequate guidance for clinical practice. Chronic facial pain associated with masticatory muscle overactivity responded well to BoNT-A injections into the masticatory muscles in a RCT [60].

Plantar fasciitis responded significantly to BoNT-A given as 40 units given close to the calcaneal tuberosity and 30 units given in the middle of the foot, in a RCT, double-blind, placebo-controlled trial [61].

Conclusion

Botulinum toxin has now been shown in many studies to be effective in reducing the intensity and frequency of pain in a variety of clinical pain syndromes. Much work still remains to define more specifically the conditions which are appropriately treated with BoNT and what treatment protocols are most effective.

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Emerging Imaging Tools for Interventional Pain

36

Marc A. Huntoon

Key Points

- The earliest approaches to procedures in pain medicine were often hampered by the limitations of the sightless, surface landmark-driven "art of medicine." Imaging levels the playing field, as it were, by allowing all physicians to see exactly what was done.
- Image-guided options for the pain clinician included fluoroscopy, C-arm flat detector CT, ultrasound, and MRI.
- It is critical that image-guided procedures are used for proper medically indicated indications.
- New uses of imaging such as ultrasound may change the way we do current procedures. The placement of peripheral stimulation leads and the refill of difficult to access pumps are two examples of use of these emerging tools.

Introduction

The introduction of image guidance for precise targeting of anatomical structures, accurate reproduction of successful procedures, and storage of a procedural record was an important step forward for modern pain medicine. The earliest approaches to procedures in pain medicine were often hampered by the limitations of the sightless, surface landmark-driven "art of medicine." Imaging levels the playing field, as it were, by allowing all physicians to see exactly what was done. Obviously, the ability to review critical images as part of a quality management process might improve medical outcomes. However, as for many advances, there are concerns that imaging could be used by government payers, insurers, or others to restrict one's ability to participate in procedural care or receive remuneration for the procedure if the stored image does not meet specific standards [1]. Additionally, at the start of the new decade, clinicians find that technologies of the future must prove to be cost-effective. It is possible that certain technologies might improve care outcomes, but not be widely adopted by the medical community due to the fact that they do not meet a certain value threshold. Simply put if a particular image-guidance technique produces only minimal improvements by some measure (clinical outcome, decreased complication rate, etc.) but at a greater cost, the best value alternative will survive [2]. Finally, many of the procedures in interventional pain have not yet been justified by medical evidence [3]. Thus, the question of which image-guidance technique is superior (fluoroscopy, computed tomography (CT), or ultrasound (US)) for a given procedure [4] may be mute if the guided procedure is medically futile.

There are currently many barriers to adoption of image-guidance technologies. These include not only up-front equipment acquisition costs but also a significant investment in time for the requisite imaging workshops and mentored skill acquisition ("on-the-job practice time") [2].

The risks of any image-guidance technique considered for routine use are also of significance. Recent scrutiny of the risk/benefit ratio of CT scanning relative to alternative techniques has been increasingly discussed in the literature. Several publications have suggested that the rate of increase in the number of annual CT scans (now over 72 million per year) has led to detrimental effects in human health, with hard to quantitate tangible benefits [5, 6]. Cancer risk relative to dose radiation from CT has been modeled after longitudinal population-based studies of cancer occurrences in atomic bomb survivors [6]. One study suggested that, based on year 2007 CT scans, one could anticipate about 14,000 or more future cancer deaths [5]. This chapter aims to describe some of the current work going on in image guidance and imaging in general as these topics relate to pain procedures. Specific

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areas where one technique may be superior to another or emerging techniques are also discussed.

C-Arm Flat Detector CT

A number of complex interventional pain procedures have emerged over the last decade, with new imaging modalities following suit. Simple target blocks such as interlaminar or transforaminal epidurals, facet procedures, and sacroiliac injections are quite easily accomplished with fluoroscopy. However, some procedures such as vertebral augmentation (vertebroplasty, kyphoplasty), celiac and hypogastric plexus neurolysis, diskography and other disk access procedures, and minimally invasive surgical procedures may be more easily accomplished with 3-dimensional fluoroscopy systems. In addition, some believe that neuromodulation procedures might be more readily accomplished with the capability to visualize in three dimensions. For example, peripheral neuromodulation procedures might be more facile with an imaging technique that showed soft tissue structures in three-dimensional or to similarly be able to detect if a spinal cord stimulation lead had migrated anteriorly. It would be an obvious advantage to avoid the hassle of bringing the conventional fluoroscopy unit back into the field and redraping it for sterility just to obtain a lateral image to verify a spinal stimulation leads location in the dorsal epidural space.

All of these modern three-dimensional systems have multifunctionality. C-arm flat detector CT (FDCT) or C-arm cone-beam CT (CBCT) may utilize different gantries but are essentially similar descriptions of these devices [7]. These systems offer what may be viewed as a "Star Wars" operating arena, where advanced optical tracking, integration of several imaging modalities (US, digital subtraction angiography, fluoroscopy, and CT) all occur in a single suite. Fluoroscopy works well to view bone structures, but in essence, there are very few procedures intended to target boney structures. Exceptions include vertebral and sacral augmentation, transpedicular fusion, etc. Yet, even in these cases where a bone target is sought, knowledge about the location and alignment of other structures such as the spinal canal, nerve roots, blood vessels, etc., is desirable to avoid complications. The limited CT scan capability of many of these systems is another plus. Instead of an image intensifier, most units have a flat detector computed tomography (FDCT) capability, which is not real time but delayed by only a few seconds. Flat panel detection enhances the accuracy and safety of the procedure as compared to plain fluoroscopy [7]. In general, interventional radiologists have been the main users of these systems, but at least two academic pain medicine practices in the United States are using equipment with these FDCT capabilities. FDCT utilizes a single rotation of the fluoroscope gantry, as opposed to conventional CT wherein there are multiple detectors and a requirement for several rotations of the gantry as the patient is moved in and out of the scanner [7]. The resulting volumetric data set from a FDCT is not as high quality as a modern 64 slice CT, but patient access is easier and more similar to conventional fluoroscopy. With FDCT, the patient stays in the same position through the imaging cycle. CT images are delayed by approximately 5–20 s. Although the images from FDCT scanning are of lower resolution, the images are most often quite adequate for the intended procedure. For example, at the author's institution, we are investigating the necessity for the traditional post-diskography CT, when compared to intraoperative FDCT images (Fig. 36.1).

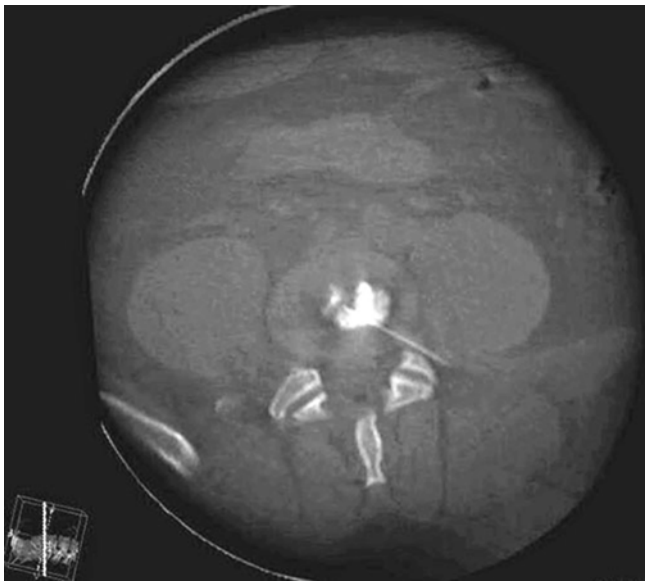

Fig. 36.1 Pictured is an axial CT acquisition with FDCT demonstrating a diskogram of a structurally normal disk. Provocative testing did not yield any pain at this level

FDCT systems produce increased scatter radiation, which can result in artifacts and inaccuracies in CT calculations. Anti-scatter grids that may increase patient radiation dose are commonly used to overcome this problem. However, radiation doses are less than that for a single helical CT [7].

Cone-beam CT/FDCT units are increasingly popular for intraoperative minimally invasive surgery [8]. Transpedicular fusions are one area where this technology is being used with success. Some of the touted advantages of modern imaging system use intraoperatively are (1) reduced time for image acquisition compared to repeatedly bringing a conventional fluoroscope into the field, (2) decreased incidence of transgression of the pedicle, (3) reduced overall operating time, and (4) reduced dose of radiation to both the surgeon and the patient. For example, a recent study compared intraoperative computer-assisted spinal navigation to serial radiography for posterior fusions at the L5/S1 level. The navigation system shortened the operative time by about 40 min compared to serial radiographs [9]. More recently, a Japanese group compared isocentric three-dimensional

fluoroscopy with navigation to conventional fluoroscopy for percutaneous screw placements. This large study included 300 percutaneous screw placements of which half were inserted with the advanced imaging and half with conventional fluoroscopy. They then evaluated post-procedural accuracy with 2-mm axial slice CT imaging. The authors found that there were 7.3 % exposed screws and zero perforated pedicles in the three-dimensional image group compared to 12 % exposed screws and 3.3 % perforated pedicles in the conventional fluoroscopy group. This was a statistically significant difference for pedicle screw misplacement ($P < 0.05$) [10]. In a previous study of conventional two-dimensional fluoroscopy, Weinstein et al. noted a 21 % rate of misplaced pedicle screws, with the vast majority being on the medial side (towards the spinal canal) [11]. The performance of celiac or superior hypogastric plexus neurolytic blocks is potentially impeded by the size of the local tumor burden or lymphadenopathy which may limit spread of the alcohol or phenol neurolytic solution. Other soft tissue structures such as the renal cortex, thoracic duct, abdominal aorta, or inferior vena cava for celiac plexus blocks or the iliac veins, L5/S1 disk, and L5 nerve root for superior hypogastric plexus blocks may be injured by two-dimensional guidance alone. Thus, a three-dimensional imaging system may improve block accuracy and decrease potential complications. Goldschneider et al. [12] used a 3D-RA system to perform celiac plexus blocks in children with good outcomes.

When performing vertebral augmentation procedures, it is normally considered a contraindication to proceed if a retropulsed fragment is pushing posteriorly into the spinal canal, due to the risk of neurological injury as polymethyl methacrylate (PMMA) cement is injected into the vertebral body. Knight et al. demonstrated the utility of CBCT imaging for this exact scenario, however, with a successful vertebroplasty in a patient with a retropulsed bone fragment [13]. The utilization of three-dimensional technology to better treat patients seems likely to grow as the creativity of proceduralists catches up to the capability of the imaging.

Magnetic Resonance Guidance

The use of magnetic resonance imaging (MRI) has lagged behind some of the other imaging modalities but may have significant future uses. Most physicians who treat patients with complex spine disease appreciate the superiority of the imaging of soft tissue structures with MRI. However, the lack of real-time injection, the limited access to the patient, and the need for MRI-safe equipment were significant problems to overcome. Some of the advantages of MRI imaging are the lack of radiation risks (making it potentially superior for the care of pregnant women and children as well as decreasing risks to the operator), the familiarity of spinal injectionists with MRI images, and the ability to avoid contrast dyes for patients with allergies. Disadvantages of MRI-image guidance with optical tracking include distortion of imaging with needle bending, which may malposition the graphic overlay. This may increase the number of images necessary to accurately reach the target [14]. Sequeiros and colleagues evaluated the feasibility of MR guidance with an optical tracking system for diskography. The authors found that the results were similar to those with conventional fluoroscopy or CT. A 0.23 T open configuration MRI unit was utilized. Only one complication, a collapsed disk, occurred during their study of 35 patients, with 34 procedures completed [14]. In another study, Streitparth et al. studied the outcomes of spinal injection procedures such as nerve root injection, facet joint, and sacroiliac joint injections performed in an open-field MRI of 1.0 T with vertical field orientation [15]. The authors found that proton-density-weighted turbo spin-echo (PDw TSE) technique was optimal for the image guidance. They studied 183 total injections in 53 patients. Target delivery of injectate was achieved in 100 % of the nerve root blocks, but only 87 % of the facet and sacroiliac joint injections. Posterior osteophytes limited appropriate spread in some patients. There were no major complications. MRI-image guidance has not yet come of age but may continue to grow for particular procedures. Certainly, the advantages of soft tissue imaging and lack of radiation risks warrant ongoing research.

Ultrasound

Ultrasound is another technique that has become more popular with anesthesiologists for regional block procedures and with physiatrists for musculoskeletal diagnosis and joint injections over the last decade. Some chronic pain practitioners are advocating use of ultrasound for additional procedures [2]. The ability to visualize soft tissue targets (such as nerves, blood vessels, muscles, and ligaments), evaluate for anatomic variants, and the lack of risk from radiation are attractive reasons to use US. Multiple feasibility studies have been published examining the merits of various blocks of small sensory or mixed nerves, including the ilioinguinal/iliohypogastric, saphenous, lateral femoral cutaneous, suprascapular, pudendal, intercostal, and greater occipital nerves to name a few, have turned up in the last few years [16–21]. The advantage of many of these blocks is that they had previously been targeted mostly utilizing surface landmarks. Thus, the accuracy of blockade should be increased by any of the soft tissue image-guidance techniques. Some papers have examined the use of US for axial targets, but the deeper location of these blocks, the dropout (dark hypo-acoustic window causing poor visualization) caused by bone and lack of real-time contrast injection capability, renders procedures such as epidurals, selective spinal nerve blocks, facet joint

blocks, lumbar, celiac and pelvic sympathetic blocks, and a few others extremely difficult and requiring of significant experience and skill.

Sympathetic Blocks

Stellate ganglion block is an example of one sympathetic block which may be advantageous for US blockade. Kapral et al. was the first to describe this technique and noted a decrease in the number of accidental vascular punctures in an ultrasound group compared to a surface landmark group [22]. Recently summarized risks of vertebral artery or deep/ascending cervical artery uptake or neck hematoma punctuate the seriousness of complications. A review from Japan reported 27 cases of retropharyngeal hematoma after stellate ganglion block (SGB) [23]. Narouze and colleagues have described the possibility of esophageal puncture as an additional risk [24]. Celiac plexus block has been studied using an anterior approach. Injury to bowel or organs is the main risks of anterior approaches. One study that is best characterized as US-assisted celiac plexus block had good success, but by today's standards, the imaging is poor [25]. As current CT and fluoroscopy techniques are good, it is unlikely that ultrasound will make great inroads in this area.

Trigger Point and Muscular Injections

There is little glamour in the performance of deep muscular and trigger point injections, which are usually office-based procedures. Only in the thoracic area or the abdomen is there any real risk of a major complication. Fluoroscopy is basically unnecessary for these soft targets. However, ultrasound may have real advantages, as the different muscle and fascial layers can be visualized well. A deep muscle like the piriformis muscle could be targeted more accurately using US. US offers the opportunity to perform a diagnostic exam (hip rotation) to aid needle localization in the correct muscle, whereby fluoroscopy could show a contrast-striated pattern, for example, but the needle could mistakenly be in a gluteal muscle. Studies suggest excellent accuracy [26]. Trigger points in other areas have been improved by US targeting [27]. Previous closed claim data shows the danger of pneumothorax from a misplaced trigger point in the thoracic area [28].

Zygapophyseal (Facet) Joint Injections and Medial Branch Blocks

Lumbar approaches to the facet joints and the medial branch nerves have been conducted. One trial compared ultrasound-guided facet joint injections to computed tomography (CT)-guided injections [29]. Ultrasound compared favorably to the outcomes from CT in this trial. The patients with larger body mass could not be performed with US, however. Ionizing radiation doses were reduced during the study, with the US group demonstrating a mean of 14.2 ± 11.7 versus 364.4 ± 213.7 mGy.cm for the group blocked utilizing CT. The US group was also blocked in a shorter time span, which may be advantageous in a busy practice [29]. Lumbar medial branch blocks have been investigated too. One study compared blocks of the medial branches performed with US or fluoroscopy. US consistently produced blocks at the correct level suggesting precise placement, with 95 % of the needles in correct anatomical position to effectively interrupt nerve conduction [30].

A study of US utilized for third occipital nerve block procedures in the cervical spine also demonstrated good results [3] as 23 of 28 needles were placed correctly [31]. Given the fact that fluoroscopically guided procedures targeting the third occipital nerve require a three-needle approach on or around the C2/3 zygapophyseal joint, the results are intriguing.

Epidural Blocks

Epidural injections are possible with US, but due to the high reliability of fluoroscopy, it is unlikely that significant change is imminent for the performance of these techniques. Likewise, CT is unlikely to induce a significant change in physician performance for these procedures with the possible exception of cervical transforaminal procedures. All the major approaches including interlaminar, caudal, transforaminal, and selective spinal root blocks have been studied using ultrasound guidance. The one area where change may occur in the short term is for caudal injections. The sacral hiatus is identified readily with US. Caudal needles placed with US in one study of 70 patients yielded 100 % accuracy as verified by caudal epidurogram [32]. Another study examined color flow Doppler as a surrogate for contrast injection with excellent reliability of the technique in most cases [33].

Neuromodulation

Ultrasound can also be utilized to target peripheral nerves at multiple sites including the upper and lower extremities, as well as epicranial sites such as the occipital and supraorbital nerves. Two anatomical feasibility studies of peripheral nerve stimulation electrode placement next to upper and lower extremity neural targets have been conducted [34, 35]. These were followed by an initial case series of nine patients showing that the majority of patients had good long-term stimulation [36]. In one study, simulated movement of the limbs after ultrasound-guided placements demonstrated resiliency of the placement despite continuous passive motion (CPM) [35]. Occipital nerve stimulation placement is

also possible with US, either directly next to the artery and nerve or in a specific fascial layer [37]. Another target for peripheral nerve stimulation is the groin, for example, the ilioinguinal nerve [38].

Combination Imaging

Very limited study has been performed to date, but there may be some scenarios where two imaging modalities at once are used for additive or synergistic effects. For cancer therapy of bone tumors, percutaneous cryoablation is often utilized. Imaging with CT to visualize the external margins of the tumor and correlation with ice-ball formation are often used. CT-fluoroscopy technique is used to pass the cryoprobe, which may also be visualized with US [39]. Other combinations of imaging modalities may be used depending on the complexity of the procedure.

Conclusion

Pain medicine procedures are challenging, and most require some form of image guidance. Increasing attention to radiation risks, physician skill levels, and procedural outcomes and safety are important future considerations. As healthcare costs rise, the relative value of imaging for individual procedural performance will be paramount. Ultrasound will have some utility, particularly for nerve, joint, and superficial targets. As the move to minimally invasive surgery takes hold, advanced FDCT systems may also be utilized with increasing frequency. But in the final analysis, best practice may continue to favor fluoroscopy for some procedures. It will likely fall to comparative outcomes researchers to answer the questions of which imaging is appropriate for a select procedure in the future.

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Part III

Neuromodulation

A History of Neurostimulation

37

Jeffrey T.B. Peterson and Timothy R. Deer

Key Points

- The earliest documented use of electricity to treat pain occurred around 63 AD.
- The Leyden jar made the storage of electrical current possible.
- Many early attempts at using electricity to treat pain were unsuccessful.
- Norman Shealy is credited with the development of modern neuromodulation.
- There are many new therapies on the horizon.

Discovery and Early Applications

The word "electricity" comes from the word "*ēlektron*," the Greek word for amber. Greek scientists found that when Amber, the fossilized resin of trees, was rubbed with another material, it created sparks of electricity. The capture or harnessing of these sparks led to the ability to utilize electricity in many applications, including the treatment of human disease conditions.

The earliest documented use of electricity to treat pain occurred around 63 AD. Scribonius Largus discovered that pain from gout could be relieved by contact with a torpedo fish (Fig. 37.1) and suggested that this treatment would be effective for generalized pain relief and treatment:

> For any type of gout, a live black torpedo should, when the pain begins, be placed under the feet. The patient must stand on a moist shore, washed by the sea, and he should stay like this until the whole foot and leg up to the knee is numb. This takes away present pain, and prevents pain from coming on if it has not already arisen [1].

In the seventeenth century, Gilbert, a famous scientist of the time, described the use of lodestone, a piece of magnetic iron ore, to treat pain. He wrote that the electromagnetic qualities of the lodestone could be used to manage pain symptoms of headaches, mental disorders, and marital infidelities with varying degrees of success [2].

Dutch physicist Pieter van Musschenbroek, University of Leyden, is credited with a breakthrough in the storage of electrical charges. This device he developed, the Leyden jar (Fig. 37.2), stored an electrical charge that was constructed by placing water in a metal container suspended by insulating silk cords and placing a brass wire through a cork into the water. In 1746, Jean Jallabert employed a Leyden jar and discovered that electricity could be used to stimulate muscle fibers [3]. Jallabert treated a paralyzed limb in a locksmith causing involuntary contractions, regeneration of muscle, and increased blood flow. Jallabert's report inspired many scientists, and over the following two decades, there were several reports of successful treatment of neuromuscular disorders and disease. In1756, Leopaldo Caldani noted that a Leyden jar could be discharged in the vicinity of a mounted and dissected frog's leg, which subsequently caused the leg to twitch. This discovery led many to proclaim electricity as a miracle cure for many diseases and that its use in stimulating areas of the body had far-reaching applications [4]. Benjamin Franklin, the first American credited with using neurostimulation, was intrigued by these experiments and conducted his own research on the treatment of painful conditions. After many failed experiments, Franklin concluded that successful claims of pain treatment were without merit

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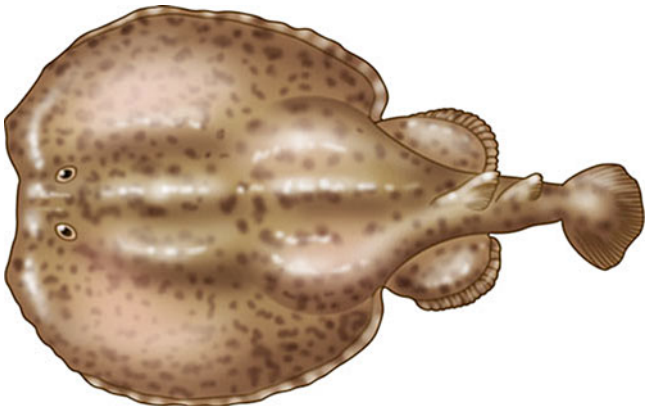

Fig. 37.1 The torpedo fish. An early treatment option

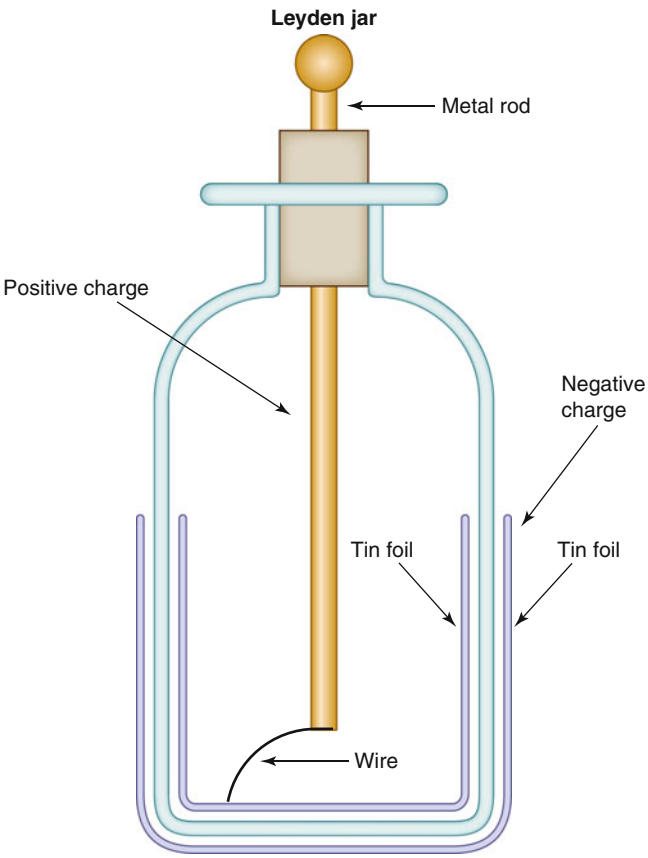

Fig. 37.2 The Leyden jar

and reported that his tests produced nothing more than discomfort for his subjects. It should be noted, however, that Franklin used high-voltage stimulation in his experiments, which caused true adverse effects of burning and injury to his test subjects.

In 1840, Guillaume Duchenne used a process of "electro puncture" to map muscle function, using electrically charge

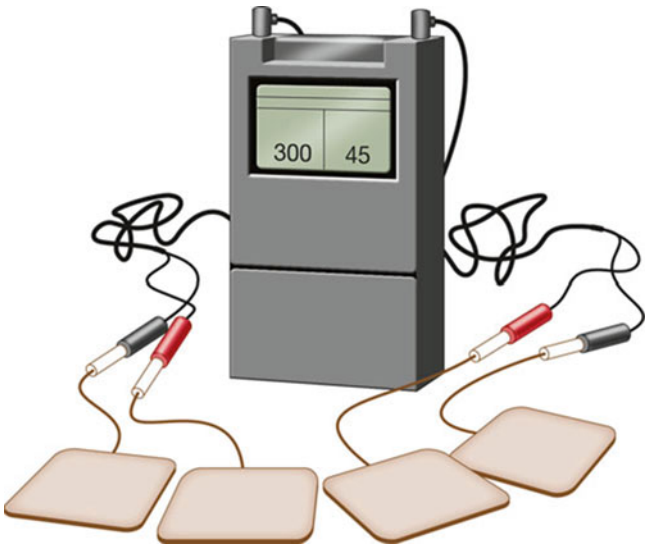

Fig. 37.3 A modern TENS unit

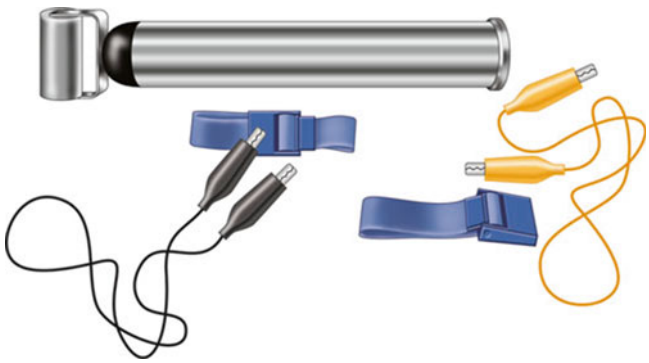

Fig. 37.4 The Electreat device

needles that were inserted into the skin. Duchenne's book "De L'electrisation Localise" described direct muscle stimulation and indirect nerve stimulation and contributed to greater understanding of the effects of electrical current on these systems.

Between 1884 and 1886, Sir Victor Horsley introduced the first practical application of intraoperative neurostimulation when electrical stimulation was used to identify a specific cortical in a patient with epileptic foci [5].

Modern Treatment Protocols

By the beginning of 1900s, many devices were commercially available to treat painful conditions. Transcutaneous electrical nerve stimulation devices, comparable to today's TENS (Fig. 37.3) units, as well as devices like the Electreat (Fig. 37.4), which sold as many as 250,000 units over 25 years, were present in many physician's offices. These electrical

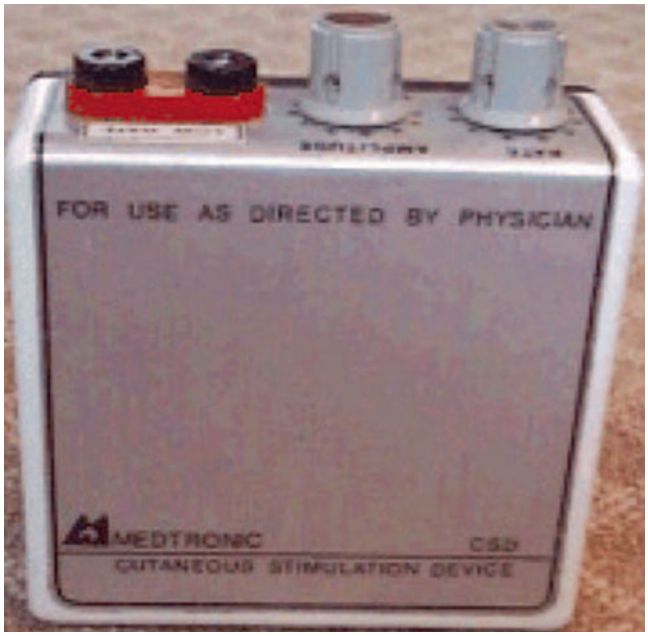

Fig. 37.5 Early Medtronic stimulation device

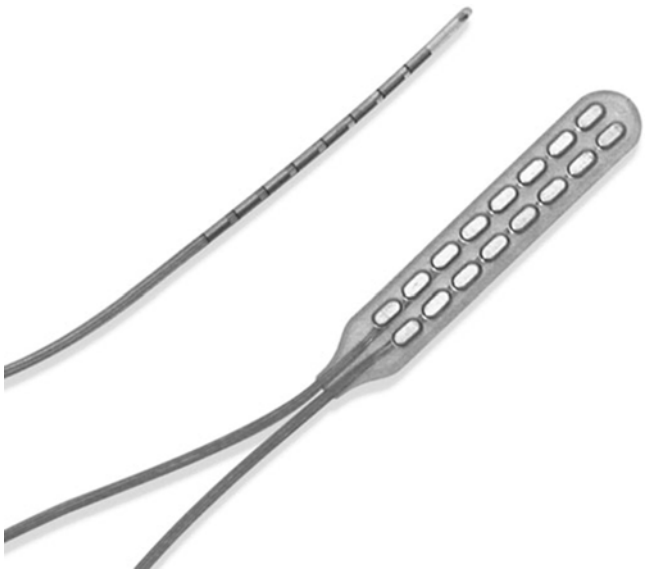

Fig. 37.6 Modern lead design

devices were used to treat medical problems such as gout, baldness, arthritis, and marital "issues." Although these crude devices may have produced few positive results, they did foreshadow the development of today's common treatment options.

The breakthrough in the use of neurostimulation in modern medicine came about in the 1960s.

Norman Shealy and colleagues described the use of electrical current to modulate the nervous system and change the perception of pain and suffering [6]. Shealy codeveloped a stimulating "lead" that would work on the dorsal columns of the spinal cord. The device used a platinum electrode design with a positive and negative electrode to treat end of life cancer pain. Shealy referred to these devices as "dorsal column stimulators." The leads were attached to an external cardiac generator device. In 1968, Medtronic (Minneapolis, Minnesota) obtained FDA approval to market these devices for the treatment of pain (Fig. 37.5). This early development was not without difficulty, as many serious complications were associated with these early devices including spinal fluid leakage and compression of the spinal cord. These safety issues led many to believe that this type of treatment was not safe, and until the development of extradural placement, many were concerned about employing these treatment methods.

During the last three decades, there have been significant improvements in technology. Early systems employed two contact leads composed of platinum; newer leads use eight contact leads made from titanium, significantly reducing complications associated with lead migration or lead fracture (Fig. 37.6). Surgical laminotomy leads have been improved with the development of new configurations capable of giving more direct stimulation. Complex programming devices and models, rechargeable batteries, and lower profile wire connectors and wiring are all now widely available. Other advanced technologies including the Epiducer (Fig. 37.7) (St. Jude Neurological, Minneapolis, MN), a percutaneous sheath that may simplify placement of paddle leads and complex percutaneous arrays, and Spinal Modulation's (Menlo Park, CA) DRG stimulation device (Fig. 37.8) are also rapidly expanding the neurostimulation options that are available to patients, while improving safety and patient outcomes.

Fig. 37.7 The Epiducer lead delivery system

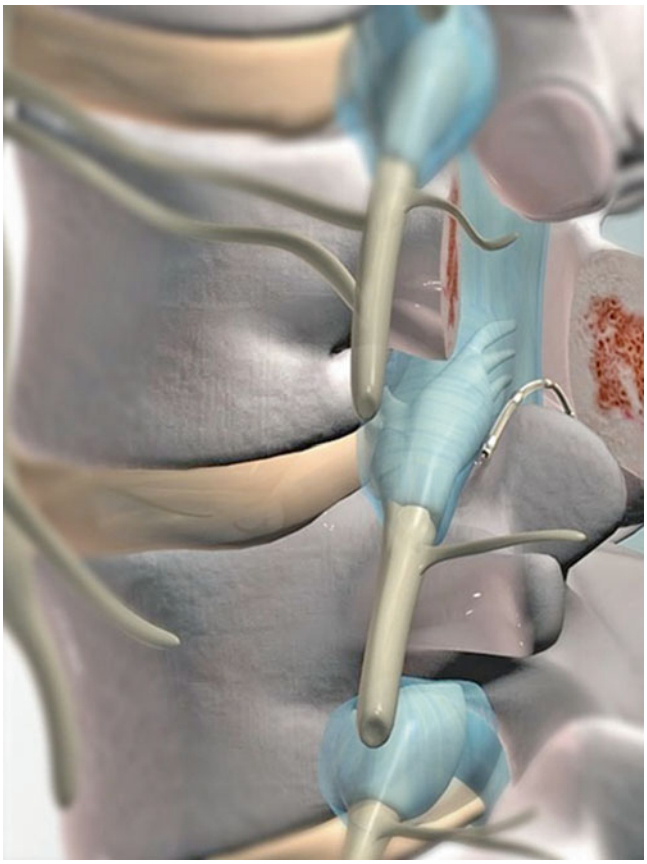

Fig. 37.8 Spinal modulation – DRG stimulation

In the future, physicians will be able to combine advanced imaging with these technologies and track the individual patients' response to neurostimulation. This pain response feedback may open a door to fully customizable treatment options and allow individualized medical therapies.

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Stimulation of the Peripheral Nerve and Peripheral Nerve Field

38

Jason E. Pope, Timothy R. Deer, Eric J. Grigsby, and Philip S. Kim

Key Points

- Stimulation of the peripheral nerve is a critical part of the pain treatment algorithm for neuropathic pain.
- Stimulation of the peripheral nerve field is helpful in conditions where the conventional SCS is not possible or contraindicated.
- These techniques may be used to supplement other implants such as spinal cord stimulation systems or intrathecal drug delivery.
- Complications of PNS and PNFS are limited and are generally much less of a risk than implants in the epidural space.
- The therapies continue to evolve, and further product development is needed to achieve optimal outcomes in a cost effective manner.

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Introduction

Neuromodulation by stimulation is most likely active by changing the balance in excitatory and inhibitory fibers based on the theory of Melzak and Wall [1]. Since its introduction, neuromodulation strategies have progressively been advancing into the periphery. Peripheral nerve stimulation (PNS) is the direct electrical stimulation of named nerves outside of the neuroaxis. Peripheral nerve field stimulation (PNFS) is the stimulation of unnamed small nerves in the vicinity of pain by superficial, subcutaneous lead placement. Historically, PNS can be performed via an open surgical or percutaneous technique, well described by Stanton-Hicks [2, 3]. The percutaneous technique for both PNS and PNFS has now become more common and presents less risk and invasiveness to the patient. Because of this evolution to less invasive therapies, and the applicability to modern pain practice, this chapter will focus on these more practical approaches to targeting the nervous system.

Similar to spinal cord stimulation, patient selection is crucial to treatment success. PNS and PNFS are indicted for chronic neuropathic pain of peripheral nerve origin. Unlike the evidence supportive of spinal cord stimulation (SCS), peripheral nerve stimulation, and even less so for peripheral field stimulation, lacks strong leveled evidence from prospective, randomized, blinded studies. Further, many percutaneous neuromodulatory stimulation devices are not approved for PNS or PNFS by the FDA and are classified as "off label." Commonly accepted clinical indications for PNS include complex regional pain syndrome type II where there has been injury to the peripheral nervous system, neuropathic pain from mononeuropathy or plexopathy from a variety of causes, and headache (trigeminal neuralgia, occipital neuralgia, supraorbital neuralgia, cervicogenic headache, hemicrania continua, migraine) [4]. PNFS indications are less defined, as the mechanism is still being determined. Further, although spinal cord stimulation (SCS) for radicular pain secondary to

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failed back surgery syndrome (FBSS) is well accepted and validated, PNFS alone or in combination with epidural leads have anecdotal success for axial back pain for FBSS [5]. Sometimes conventional SCS may be contraindicated prior to PNFS. PNFS may be placed to supplement regions such as axial low back and neck that are not covered with SCS.

Comorbid psychiatric illness significantly reduces interventional treatment success rates [6], mindfully appreciating that approximately 20–45 % of chronic pain patients have accompanying psychopathology [7]. Subsequently, it is paramount to identify candidates suitable for concurrent treatment or exclude patients that require additional psychiatric treatment. Poor treatment outcome was identified in patients with presurgical somatization, depression, anxiety, and poor coping; however, some patients experience improvement in these factors once the pain is under better control, so these issues are not contraindicated [8].

Ideal candidacy for PNS and PNFS has yet to be determined. While some advocate a successful nerve block prior to the trial, others argue that a previous successful nerve block is unnecessary and is not predictive of outcome. Notwithstanding, a trial prior to implantation is mandatory. With the open technique (not described here), some advocate a direct to implant approach in an effort to reduce repetitive procedural morbidity [7]. This can be accomplished by a staged technique when indicated, with the initial implant of the lead prior to finalizing the system by generator placement at a later date. Failure of conservative and traditional management of neuropathic or mixed nociceptive/neuropathic pain is usually recommended.

Contraindications

Patients with local infection near the injection site, coagulopathy, allergy to injectate, or comorbidities/conditions that prevent fluoroscopic needle guidance or consent should be avoided. In regard to bleeding risk, the use of needles outside the neuroaxis makes the use of guides by the American Society of Regional Anesthesia less appropriate for guidance in these cases, despite their most recent argument [9]. Clinical judgment is required, as permanent neurologic sequela is less likely in the periphery.

Scientific Foundation

Peripheral neuromodulatory success requires an anatomic appreciation for the architecture of the peripheral nerve. Peripheral nerves are composed of axons encased by Schwann cells, with or without a myelin sheath. The cell body of the sensory nerve is unipolar and is located in the dorsal root ganglion. Sensory afferent nerve cell bodies extend an axon and dendrites that permit synaptic communication with neighboring cells. In addition to creating a transmembrane potential essential for nerve conduction, they also provide a means for nutritional flow, an important rate-limiting step for nerve repair [10]. Axons enclosed in myelin have gaps, termed nodes of Ranvier, and are utilized to increase conduction velocity. The axons are encased within the endoneurium and bundled into fascicles and surrounded by perineurium. These fascicles divide and fuse to form multiple plexi along the nerve trunk, with discrete topographic architecture. The vasculature of the peripheral nerve resides in the perineurium [11]. The perineural bundles are then finally encased by epineurium (Fig. 38.1).

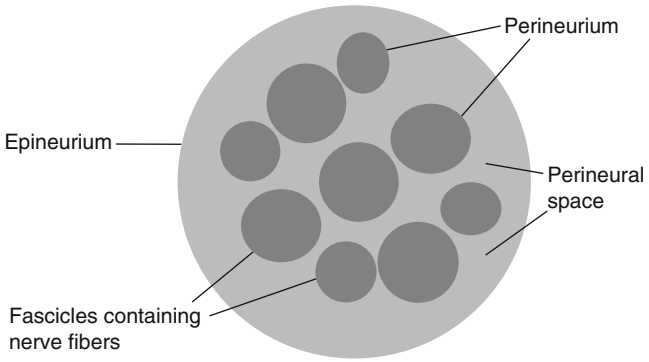

Fig. 38.1 Peripheral nerve architecture [12]

Table 38.1 Nerve fiber classification, diameter, and conduction velocity [13]

Description of nerve fibers	Group		Diameter (μm)	Conduction velocity (m/s)
Myelinated somatic		Alpha α	20	120
		Beta β		
	A	Gamma γ		S-40 (pain fibers)
		Delta ∂	3–4	S-40 (pain fibers)
		Epsilone	2	5
Myelinated visceral (preganglionic autonomic)	B		<3	3–15
Unmyelinated somatic	C		<2	0.5–2 (pain fibers)

Peripheral nerves can be categorized based on their conduction velocity and diameter (Table 38.1).

The aforementioned nerve layers and inconsistent fascicular topographic arrangement provide an anatomic explanation not only for the impendence to overcome but also the cumulative effect of cathodal stimulation employed in peripheral neuromodulation [14]. PNS and PNFS directly inhibit primary nociceptive afferents and suggest central sensitization can be subverted by peripheral nociceptive suppression. Moreover, percutaneous PNS and PNFS approaches

utilize devices that were designed for use in the epidural space, and therefore peripheral use is accompanied by frequent, although minor, complications.

Image guidance is recommended to perform percutaneous PNS. Unlike the spine, the use of imaging in the periphery is complex and is impacted by patient positioning, variation in bony landmarks, and obesity. Consequently, neuropathic pain peripheral nerve targets are only limited by the ability to visualize them, either directly or indirectly (by anatomic correlation to well-defined osteal landmarks or using US guidance and/or fluoroscopy). Common sites include the supraorbital, the infraorbital, and the greater occipital nerves in the head and neck; the ulnar, median, and suprascapular nerves in the upper extremity; the intercostal, ilioinguinal, iliohypogastric, and genitofemoral nerves in the trunk; and the lateral femoral cutaneous, saphenous, sciatic, and posterior tibial nerves in the lower extremity.

Clinical Examples

PNS and PNFS trialing and permanent implantation require a meticulous sterile preparation and wide enough operative fields to visualize the necessary surgical targets. Further, peripheral nerve stimulation is only limited by the ability to visualize the target nerve and IPG implantation location. Peripheral nerve stimulation targets will be discussed separately.

Trigeminal Peripheral Nerve Stimulation

Terminal branch trigeminal targets include the supraorbital and infraorbital nerves, as illustrated in Fig. 38.2.

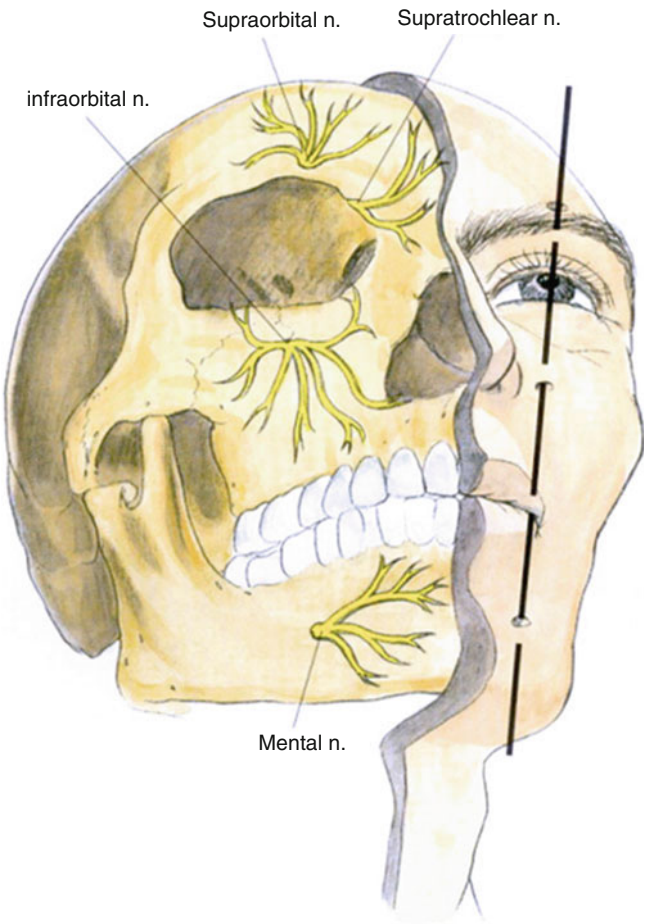

Fig. 38.2 Terminal branches of the trigeminal nerve [15]

Infraorbital Nerve Stimulation Trial

The infraorbital nerve is one of the terminal branches of the maxillary division of the trigeminal nerve and exits via the infraorbital canal (please refer to Fig. 38.3).

The patient is positioned supine, prepped, and draped in sterile fashion (alcohol should be avoided in the face to avoid corneal irritation). Fluoroscopy is used in the anterior-posterior view to approximate the target. The target site is the infraorbital foramen on fluoroscopy. If it cannot be appreciated, the lead is placed approximately 1 cm below the orbit and just lateral to the ipsilateral nose, as described by Slavin et al. [16]. The entry point is lateral and inferior to the eye over the zygoma. Again, after judicious local anesthetic use at the entry point, a bent introducer needle to accommodate the contour of the face is inserted and directed to the target zone under fluoroscopy. Once the needle is in the correct position, the percutaneous cylindrical lead is introduced with care not to direct the distal tip of the needle too superficial to avoid lead tip erosion. The introducer needle is withdrawn slightly to allow intraoperative testing (Fig. 38.3).

Once therapeutic stimulation is achieved, the needle and stylet are removed, leaving the lead in place. After serial imaging to confirm placement, the lead is sutured in place, and a sterile dressing is applied and taken to the recovery area.

Supraorbital Nerve Stimulation Trial

Slavin et al. described the most commonly employed technique for terminal branch trigeminal nerve stimulation [16, 17]. The patient is positioned and prepared as discussed for the infraorbital nerve stimulation. Fluoroscopy is used in the anterior-posterior view to approximate the target. A skin wheel is raised using 1 % lidocaine and is raised approximately 3–4 cm lateral to the lateral corner of the eye. An incision is then made, where a standard 14 G Tuohy needle (bent to allow and follow the contour of the face), is directed toward the midline

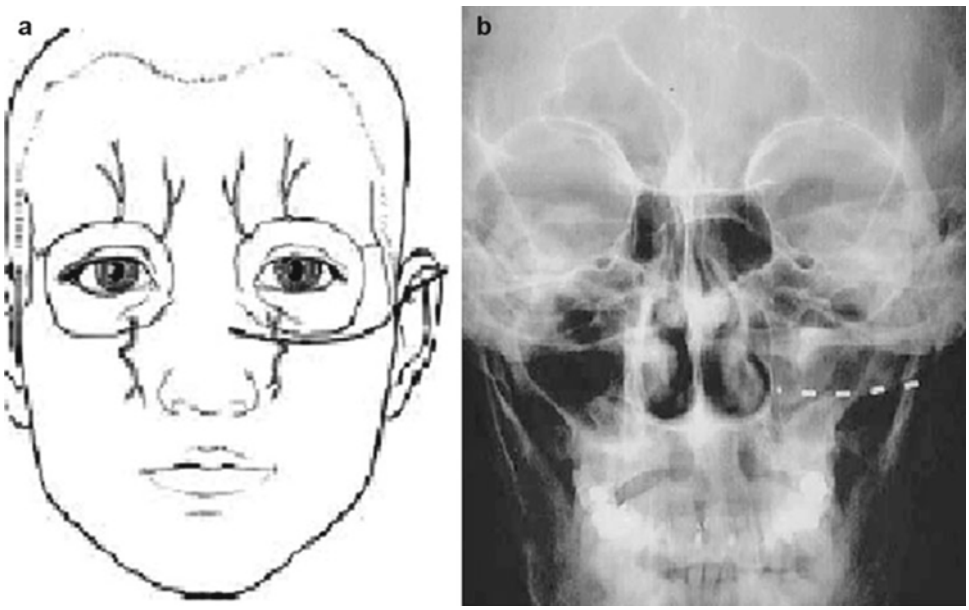

Fig. 38.3 Diagram of infraorbital lead placement (**a**) and fluoroscopic image (**b**) [12]

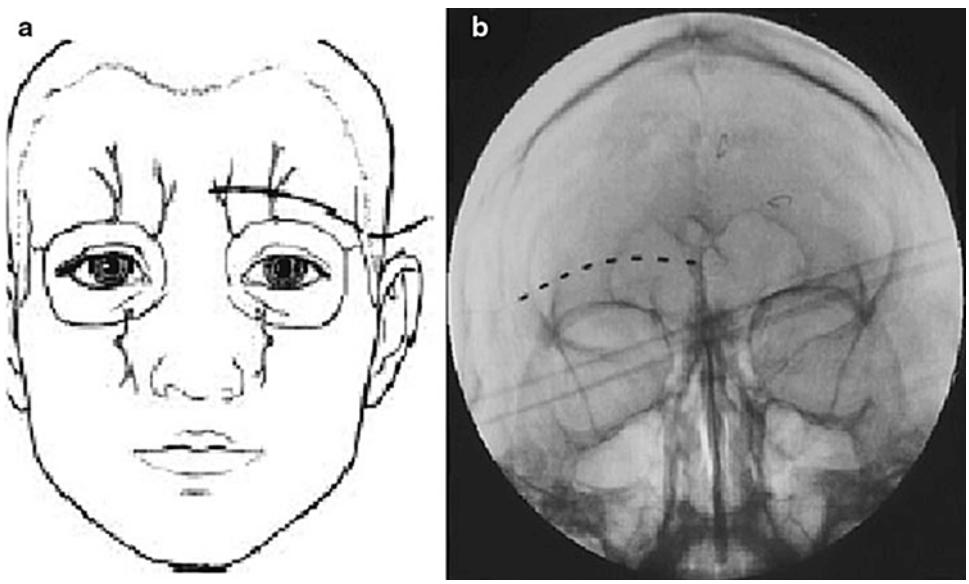

Fig. 38.4 Diagram of supraorbital lead placement [16] (**a**) and AP radiograph of electrode under fluoroscopy (**b**) [18]

approximately 1 cm above the supraorbital ridge until it is approximately 1 cm from the midline (Fig. 38.4). Avoiding too superficial trajectory will avoid lead tip erosion.

The stylet is removed, the percutaneous electrode is placed, and the needle is withdrawn to allow for intraoperative stimulation testing. Judicious use of local anesthetic at the puncture site will allow for intraoperative testing.

Once the desired therapeutic paresthesia overlying the patient's pain is achieved, the needle is withdrawn and removed while performing serial fluoroscopic guidance to ensure no inadvertent lead migration. The externalized lead is then secured with the supplied plastic anchor of the surgeon's choosing and nonabsorbable sutures. A sterile dressing is applied and the patient is taken to the recovery area.

Supra- and Infraorbital Nerve Permanent Implant

For the permanent implantation of both the infra- and supraorbital leads and IPG, general anesthesia is recommended (with laryngeal mask airway if feasible). The patient is again positioned supine with a slight contralateral head turn to provide access to the retroauricular location. A meticulous sterile prep and drape is required to accommodate tunneling and IPG site location. Commonly, the infraclavicular sight is chosen.

The permanent percutaneous lead is inserted as described for the trial. An additional incision is made in the ipsilateral retroauricular location after appropriate topicalization. Two techniques have been described for tunneling the lead's IPG connection portion. One is simply using the introducer needle with stylet in place (bent to accommodate the contour of the tunneling from the retroauricular incision to the anterior incision). The stylet is then removed, the lead introduced, and the needle withdrawn, leaving the tunneled lead.

From the retroauricular location, the lead is secured with the supplied plastic anchor using nonabsorbable suture. A stress loop is recommended (approximately 2–3 cm in diameter), and the lead is attached to the extension cable. It is recommended to place the extension cable connection in close approximation to the retroauricular incision to allow for easy access if reoperation is required.

IPG site location is largely the surgeon's preference [19]. In tunneling to infraclavicular and periscapular, one must remain in the posterior triangle of the neck and avoid the suprascapular nerve. Tremendous care is needed to avoid the external jugular which is adjacent to and superficial to the sternocleidomastoid muscle. Specifically, one must recognize the mobility of neck and shoulder especially if placing IPG in infraclavicular and periscapular. Measurement of length of extensions and electrodes is necessary to accommodate the flexion and extension of the neck. Avoidance of placement around osteal structures may reduce pain overlying the IPG device.

Regardless of IPG location, careful dissection (avoiding excessive blunt dissection), meticulous hemostasis, and anchoring to the perimuscular fascia are crucial to avoid IPG dislodgement. Anchoring to the perimuscular fascia is crucial and requires the use of tiny and soft or suture anchors given the limited subcutaneous tissue present.

Copious non-pressurized irrigation is performed at all incision sites, and layered closure is performed with absorbable suture. It is recommended to avoid placing sutures overlying the IPG, as this may impair wound healing and increase the chance of wound dehiscence. Sterile dressing is applied and the patient is recovered in the postoperative area.

Greater Occipital Nerve Stimulation Trial

The greater occipital nerve is also known as the second occipital nerve and is the medial branch of dorsal primary rami of C2. After discovery of the trigeminocervical complex, the greater occipital nerve has become a popular target for the treatment of headache [20–22]. Anatomic dissection characterizes the location from osteal landmarks, including the mastoid process and the occipital protuberance [23–25]. (It is generally found 1.4–1.6 cm lateral from the external occipital protuberance and 2.91–3.7 cm inferior). The nerve is consistently medial to the occipital artery (see Fig. 38.5).

There are multiple techniques described to stimulate the greater occipital nerve, with major differences centering on target location (C1–2 vs. nuchal ridge/retromastoid), lead trajectory orientation (medial to lateral or lateral to medial), and type (percutaneous cylindrical vs. paddle) (Fig. 38.6) [17, 26, 27].

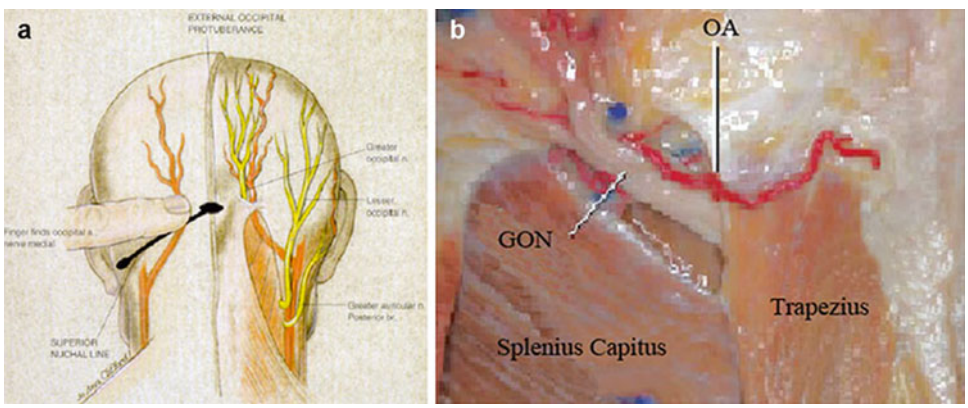

Fig. 38.5 Greater occipital nerve diagram (**a**) and anatomic dissection (**b**) [15, 26]

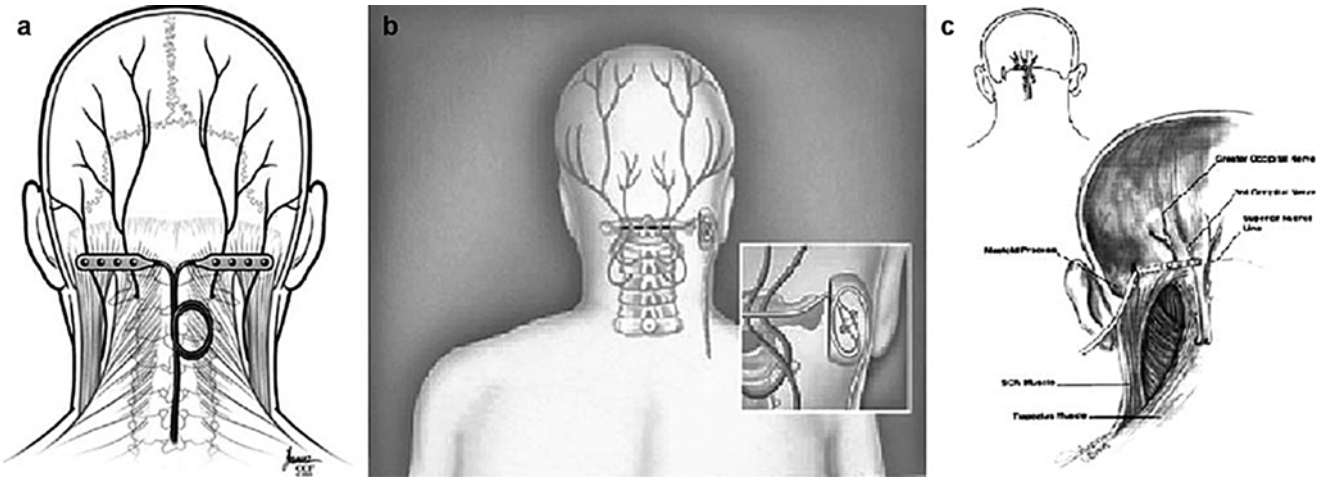

Fig. 38.6 Diagrams of percutaneous and paddle ONS lead placements (**a**) paddle placement (**b**) percutaneous placement (**c**) paddle placement [5, 17, 27]

Variation in location and lead type implantation for occipital nerve stimulation qualifies the initial high migration rates and aberrant muscular stimulation with percutaneous leads [17, 22, 26]. Proponents of paddle leads argue that less migration may occur because of the larger surface area of the lead and unidirectional current [27]. Muscle spasms of splenius capitis may be subverted by placement of the electrodes at or above the nuchal line, as opposed to the C1–2 level, where too superficial of a lead placement may increase the chance of erosion and burning sensations, while too deep a placement may cause aberrant muscular stimulation.

The trial is performed with the patient in the prone position. The surgical site is prepared by hair and meticulous sterile prep and drape in the normal fashion, leaving the entry site exposed. Image guidance is a prerequisite; fluoroscopy is commonly employed. After the target location is chosen, the incision site is identified. Care must be taken not to anesthetize the greater occipital nerve, and therefore judicious local anesthetic should be used at the incision site using 1 % lidocaine. The medial, nuchal line approach will be described here in further detail (Fig. 38.7).

An incision is made in the midline just caudal to the occipital protuberance. The needle is bent to accommodate the contour of the head. Under fluoroscopic guidance, lead is placed along the nuchal ridge ipsilateral to the target greater occipital nerve. Once appropriate lead position is achieved, the needle is withdrawn slightly to allow for intraoperative stimulation testing. Once therapeutic stimulation is achieved, the needle is removed and the lead is secured using the plastic anchor provided and nonabsorbable suture. A sterile dressing is applied, and the patient is further recovered and programmed in the recovery room.

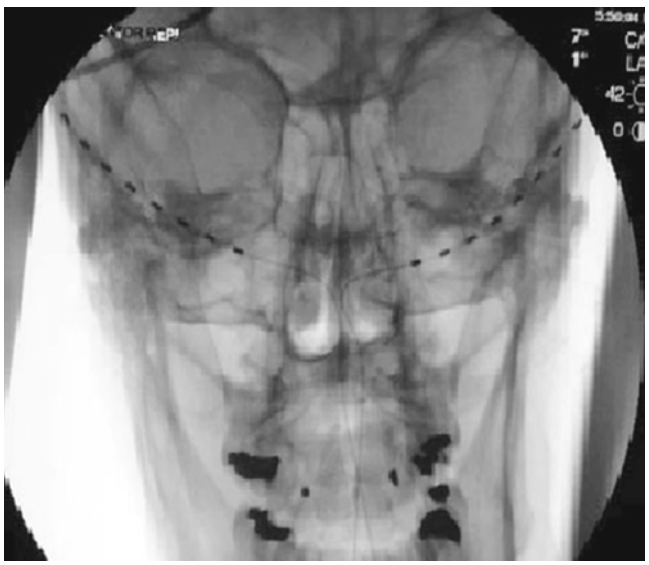

Fig. 38.7 Percutaneous cylindrical lead placement in AP fluoroscopic projection

Greater Occipital Nerve Permanent Implant

Preparation and anesthesia and the lead placement procedure are largely the same for the occipital nerve trial and implant. The surgical prep site is extended to a larger area, however, to accommodate the IPG location. As discussed previously, IPG location and migration rates have been compared with superior outcomes suggested by infraclavicular and abdominal locations versus periscapular and gluteal sites, respectively. Like SCS, strain loops are created at the incision site by careful lateral dissection. Plastic anchors and nonabsorbable

sutures are used to suture the lead to the dorsal fascia. A third incision is made and carefully dissected to accommodate the IPG. If extensions are needed and tunneling is required over a great distance, additional incisions with sequential tunneling may be required. Irrigation is performed at all incision sites, and layered closure is recommended, again, with care not to create a suture line overlying the implanted device. Sterile dressings are applied and further programming is performed in the recovery area.

Ulnar Nerve Stimulation Trial

The ulnar nerve is the most caudal portion of the brachial plexus, arising from the medial cord with nerve roots originating at C8–T1. The nerve descends medially to the brachial artery in the proximal arm, anterior to the medial triceps of the triceps, and at the elbow, it resides in the grove of the medial epicondyle.

Patient is positioned supine and patient preparation, including sterile prep and preoperative antibiotics, is performed in the usual manner. As described by Huntoon et al. [28] from the reliable and easily identified ulnar nerve location at the medial epicondyle, the nerve is traced in the axial sonographic view to approximately 9–13 cm proximal. Once the nerve is located, a skin wheel is raised with lidocaine 1 % and a skin nick is created. Under a live axial view of the ulnar nerve, the needle is then introduced via the long axis of the probe, placing the lead deep, adjacent, and perpendicular to the ulnar nerve. The needle is retracted and stimulation testing commenced. Anchoring of the lead to the skin was performed using the plastic anchors and nonabsorbable suture (Fig. 38.8).

Median Nerve Stimulation Trial

The median nerve arises from C5–8 and T1 roots and is more distal from the lateral and medial cords. It descends anterolateral to the axillary and brachial artery, where it lies medial to it and the biceps muscle tendon in the cubital fossa. Tracking distally in the forearm, the median nerve descends between the heads of the pronator teres muscle, and in the wrist, it resides between the tendons of the flexor carpi radialis and the flexor digitorum superficialis (Fig. 38.9).

The patient is positioned supine and preparation is performed in the usual manner. As described by Huntoon et al. [28] the ultrasound probe is placed in the transverse position and scanned distally until approximately 4–6 cm distal to the antecubital fossa between the pronator teres heads.

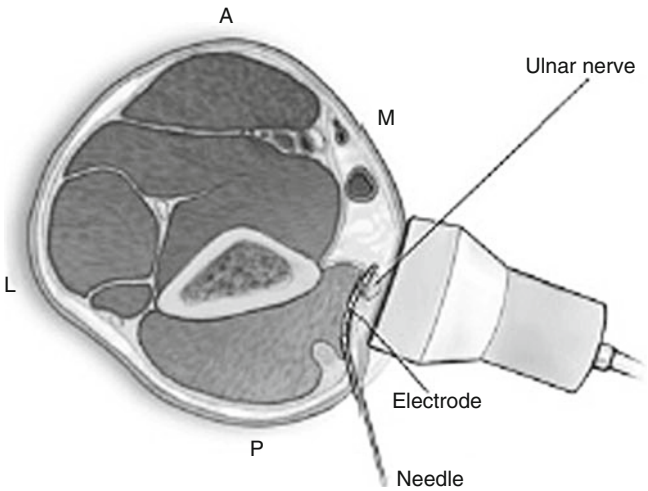

Fig. 38.8 The lead placement is aided by ultrasound guidance

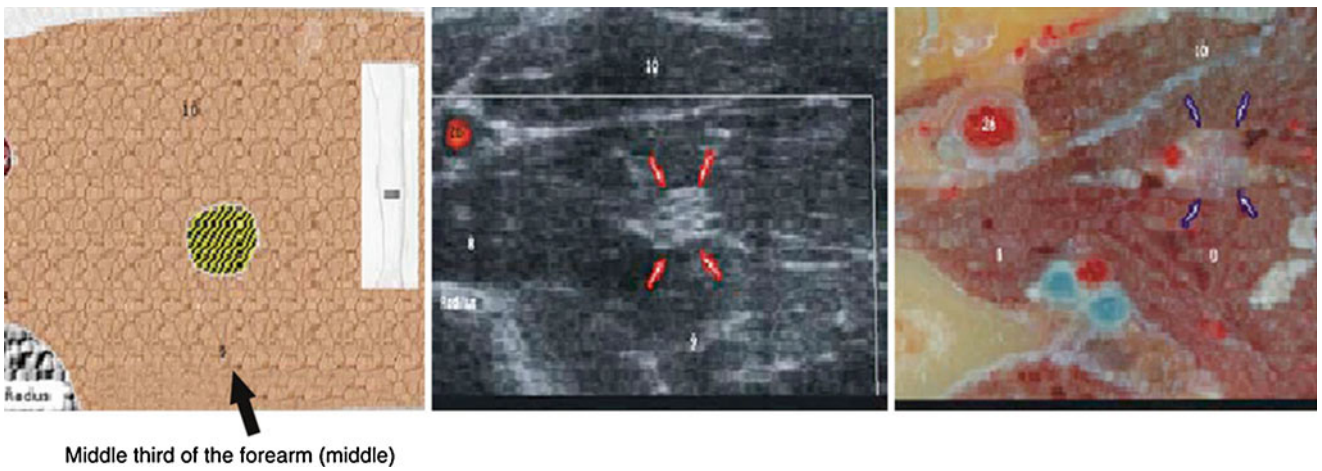

Fig. 38.9 Tracking distally in the forearm, the median nerve descends between the heads of the pronator teres muscle, and in the wrist, it resides between the tendons of the flexor carpi radialis and the flexor digitorum superficialis

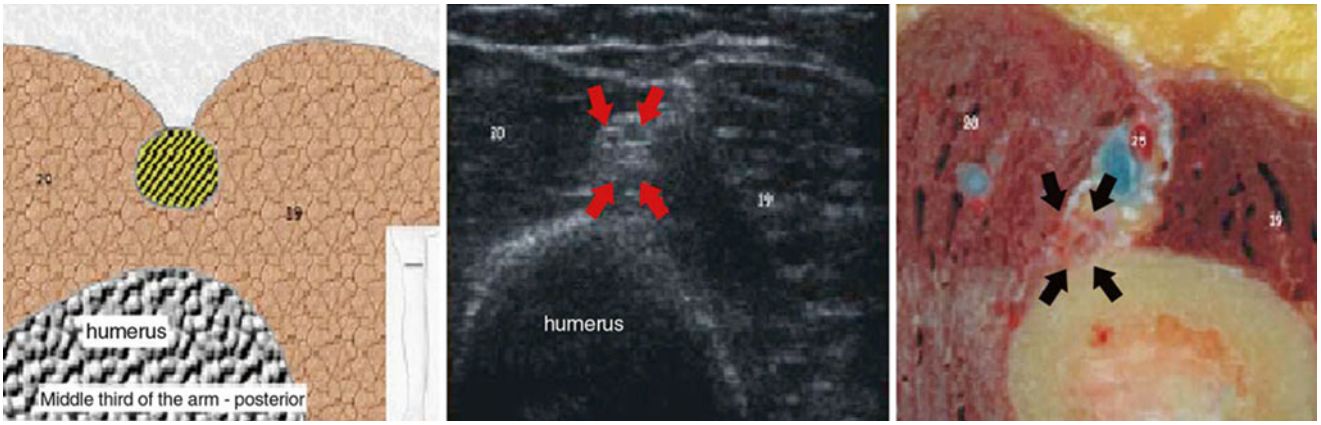

Fig. 38.10 The radial nerve is reliably located lateral to the humerus at approximately 10–14 cm proximal to the lateral epicondyle deep to the lateral head of the triceps. The radial nerve is outlined by the red *arrows* in the ultrasound image and the black arrows in the anatomic dissection. (Basic Human Anatomy. O'Rahilly, Muller, Carpenter and Swensen. Copyright © O'Rahilly 2009)

After careful topicalization with 1 % lidocaine at the incision site only, a skin incision is made and under ultrasound guidance and 14-G needle is introduced in the longitudinal plane with the target nerve maintained in the axial plane with care to place it adjacent to the nerve. Once the needle is in the optimal position, the needle is retracted and stimulation testing is performed. Once therapeutic stimulation is achieved, anchoring of the lead to the skin is performed using the plastic anchors and nonabsorbable suture. A sterile dressing is applied. The patient is then transported to the recovery room for further programming.

Radial Nerve Stimulation Trial

The radial nerve has origins from the posterior cord from roots C5–8. Again, as described by Huntoon [28], the nerve travels obliquely to the humerus at the proximal arm, along with the deep brachii artery. The nerve is reliably located lateral to the humerus at approximately 10–14 cm proximal to the lateral epicondyle deep to the lateral head of the triceps (Fig. 38.10).

The patient is positioned supine and preparation is performed as described previously. As described by Huntoon et al. [28] the ultrasound probe is placed in the transverse position and scanned distally until approximately 10–14 cm proximal to the lateral epicondyle. After careful topicalization with 1 % lidocaine at the incision site only, a skin incision is made and under ultrasound guidance and 14-G needle is introduced in the longitudinal plane with the target nerve maintained in the axial plane with care to place it adjacent to the nerve. Once the needle is in the optimal position, the needle is retracted and stimulation testing is performed. Only after therapeutic stimulation is achieved, anchoring of the lead to the skin is performed using the plastic anchors and nonabsorbable suture to the skin. A sterile dressing is applied and the patient is transported to the recovery room for further programming.

Median, Ulnar, and Radial Permanent Implant

The patient preparation, anesthesia, and placement of the lead are the same as the trial procedure. The surgical prep site is extended to a larger area to accommodate the IPG location. Instead of anchoring to the skin for the permanent percutaneous placement, Huntoon recommends placement of the device in the upper chest (infraclavicular site) or abdomen for the upper extremity [28, 37].

Lead extensions and serial incisions are required to connect and tunnel the leads to the IPG. Sterile dressings are applied and programming is performed in the recovery room.

Peroneal Nerve Stimulation Trial

The sciatic nerve is formed from the L4 to S3 nerve roots and can be subdivided into medial and lateral compartments. The medial portion of the sciatic nerve is functionally the tibial nerve, formed by the ventral branches of the L4–5 and S1–3, while the posterior branches of the ventral rami make up the peroneal nerve. The sciatic nerve descends and the rostral portion of the popliteal fossa, splitting formally into the tibial nerve medially and the common peroneal nerve laterally. The popliteal fossa's lateral boarders are the semimembranosus and semitendinosus medially, the biceps femoris laterally, and the gastrocnemius muscle caudally. The popliteal artery is medial to the neural targets (Fig. 38.11).

The patient is positioned to access the popliteal fossa of the afflicted leg after patient preparation, monitoring, and meticulous sterile prep and drape, as previously described. Axial ultrasound scanning is performed from the popliteal crease cephalad [37]. The tibial and peroneal nerves coalesce to from the sciatic nerve just cephalad to the aforementioned popliteal fossa. Identification of the popliteal artery is essential to avoid vascular entry. Once the desired nerve location is

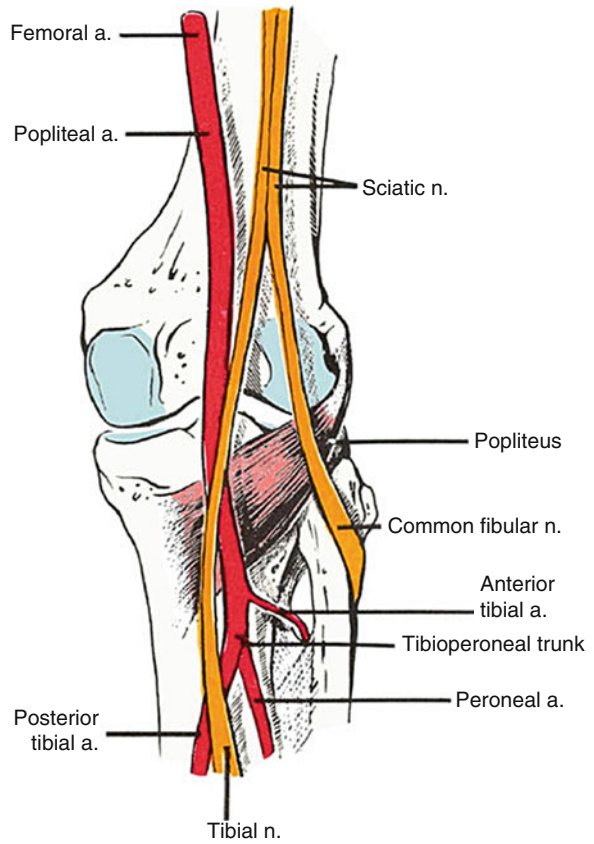

Fig. 38.11 The popliteal fossa's lateral boarders are the semimembranosus and semitendinosus medially, the biceps femoris laterally, and the gastrocnemius muscle caudally. The popliteal artery is medial to the neural targets

visualized, judicious topicalization of the skin entry site with 1 % lidocaine is performed. The introducer needle is then placed deep to the bifurcation of the sciatic nerve in a posterolateral to anteromedial direction [28]. Care to avoid muscular entry is essential. The electrode is introduced and the needle is retracted to allow for testing. Once therapeutic testing is achieved, the needle is withdrawn, the lead sutured to the fascia of the biceps femoris muscle using the plastic anchor and nonabsorbable suture, a sterile dressing applied, and the patient transported to the recovery room for further stimulation testing.

Saphenous Nerve Stimulation Trial

The saphenous nerve is a purely sensory nerve that is a distal cutaneous branch of the femoral nerve and therefore has contributions from the L2 to 4 nerve roots. It descends along the medial aspect of the thigh and posterior to the sartorius muscle. In the caudal thigh, the nerve lies between the tendons of the sartorius and gracilis muscles (or vastus medialis muscle more distally), where it can be reliably located just proximal to the medial aspect of the knee and approximates the geniculate artery (Fig. 38.12).

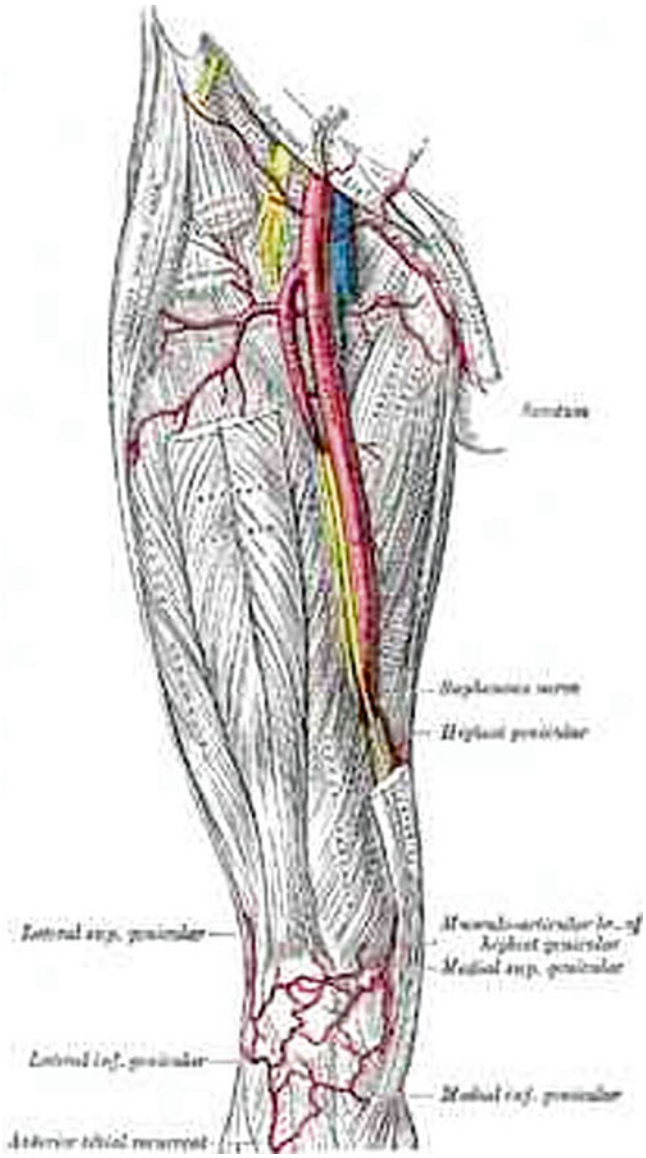

Fig. 38.12 Depiction of saphenous nerve [29]

The patient is positioned supine with slight ipsilateral extremity hip external rotation. After appropriate patient preparation, monitoring, and field prep and drape, axial scanning of the afflicted extremity is performed for an anatomic survey. The saphenous nerve is predominately hyperechoic, and Doppler survey to identify the geniculate artery may help identify the target. After needle entry topicalization with 1 % lidocaine, a small skin incision is made and the 14-G introducer needle is introduced and directed to the facial plane between the sartorius muscle and vastus medialis using an in-plane approach, avoiding muscle penetration. Once the needle approximates the nerve, the stimulation lead is placed and the needle retracted to allow for stimulation testing. Once therapeutic stimulation is achieved, the needle is removed and the lead is sutured to the vastus medialis fascia using a plastic anchor and nonabsorbable suture.

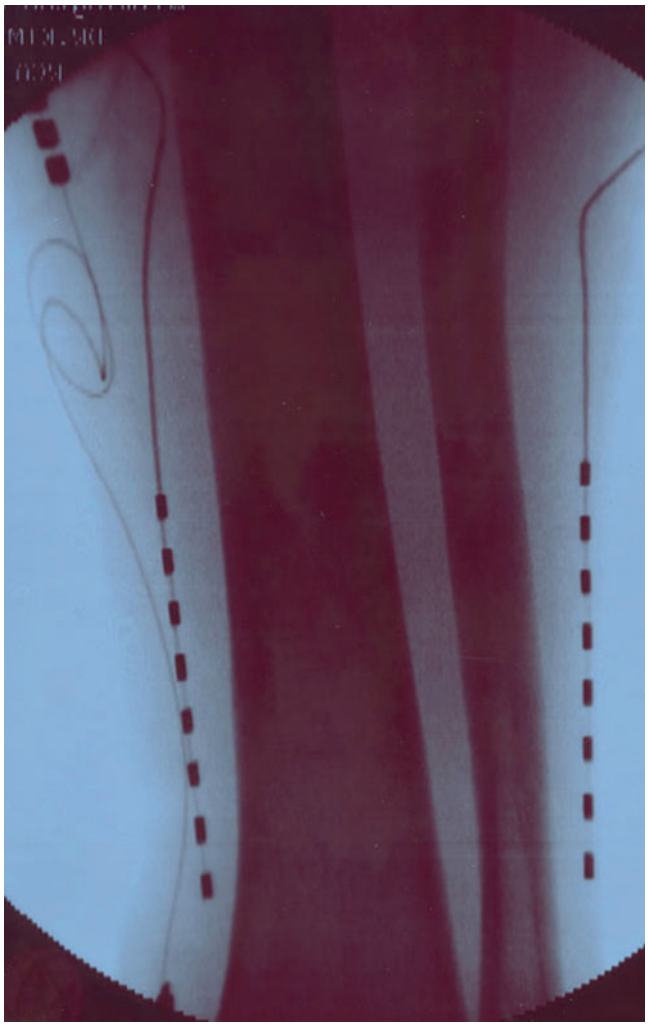

Fig. 38.13 Peripheral leads placed along the saphenous and superficial peroneal nerves

A sterile dressing is applied and the patient is transported to the recovery area for further programming.

One author has placed electrodes to cover the saphenous and superficial peroneal nerves at the midpoint of the tibia. By placing medial and lateral to the tibia, stimulation is identified following the sensory coverage of the saphenous and superficial peroneal nerves (see Fig. 38.13). Successful trial with paresthesia coverage with pain relief have led to implantation of peripheral lead and generator placed in the medial calf.

Lateral Femoral Cutaneous Nerve (LFCN) Stimulation Trial

The lateral femoral cutaneous nerve is a branch of the posterior divisions of the L2–3 nerve roots and is also an exclusively sensory nerve. It travels lateral to the border of the psoas muscle and courses toward the anterior inferior iliac spine (ASIS), where it passes under the inguinal ligament, lying between the fascia lata (deep) and iliaca (superficial), providing sensory information from the lateral thigh. LFCN neuropathy is called meralgia paresthetica.

The patient is positioned supine with slight ipsilateral extremity in neutral position. After appropriate patient preparation, monitoring, and field prep and drape, axial scanning of the afflicted extremity is performed for an anatomic survey from the ASIS along the inguinal ligament. After appropriate needle entry site topicalization, a stab incision is made and the 14-G needle is introduced superficially along the longitudinal axis of the probe to lay in close proximity to the lateral femoral cutaneous nerve just caudal to the inguinal ligament. Once needle placement is optimized, the lead is introduced, placing the lead perpendicular to the course of the nerve. The needle is retracted and once therapeutic stimulation is achieved, the needle is retracted and the lead is anchored to the fascia lata with the supplied plastic anchor and nonabsorbable suture.

Intercostal Nerve Stimulation Trial

Intercostal nerves originate as the anterior rami of the paired exiting nerve roots and travel under the adjacent rib with close approximation to the intercostal vein and artery. Care must be taken not to violate the pleura. After aseptic preparation and monitoring as described previously, the patient is positioned either prone or in the lateral decubitus position. Under fluoroscopic guidance and after topicalization with 1 % lidocaine, a skin incision is made to accommodate the introducer needle. The needle should be bent to follow the curve of the rib. Once the needle is verified to be in the correct location, the lead is inserted and the needle retracted for stimulation testing. Once therapeutic stimulation is achieved, the needle is retracted and the lead is anchored with the supplied plastic anchor and nonabsorbable suture (Fig. 38.14).

Iliohypogastric, Ilioinguinal, Genitofemoral Nerves

The iliohypogastric and ilioinguinal nerves both arise from the L1 nerve root and emerge lateral to the psoas muscle. The nerves course in the anatomic plane of the internal oblique and transversus abdominal muscles. The genitofemoral nerve arises from the L1 and L2 nerve roots and emerges on the anterior surface of the psoas muscle. Its genital branch travels through the inguinal canal and, in males, supplies sensory information from the scrotal skin. In contrast, the ilioinguinal nerve supplies the groin. These nerves are amenable to peripheral stimulation, and care must be taken to ensure appropriate needle placement without violating the peritoneal

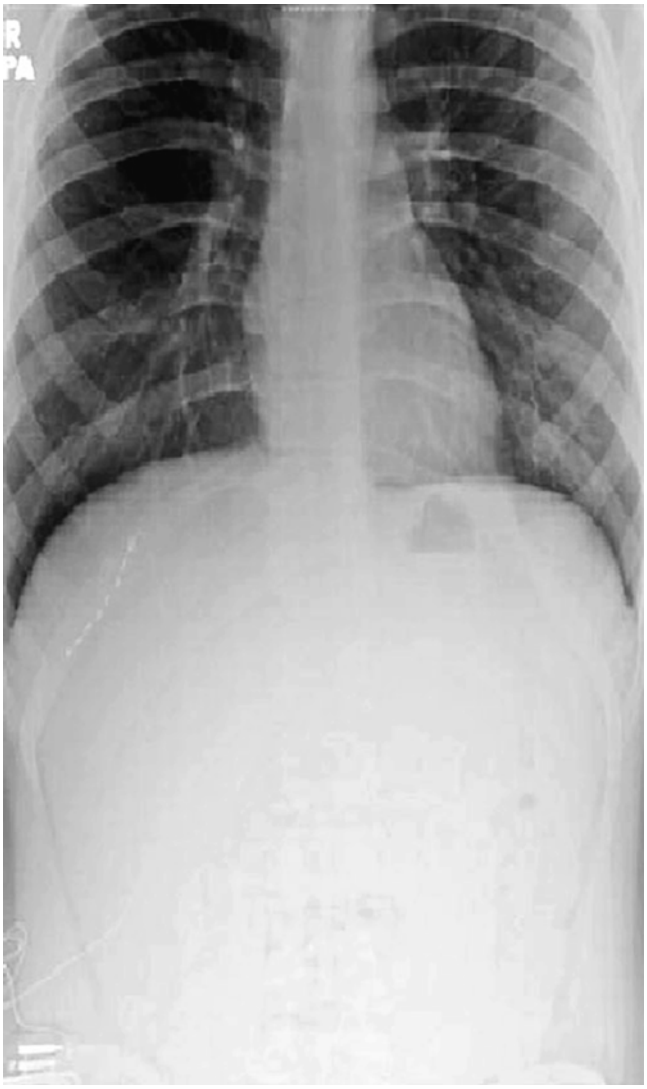

Fig. 38.14 Radiograph of T11 intercostal nerve percutaneous PNS [30]

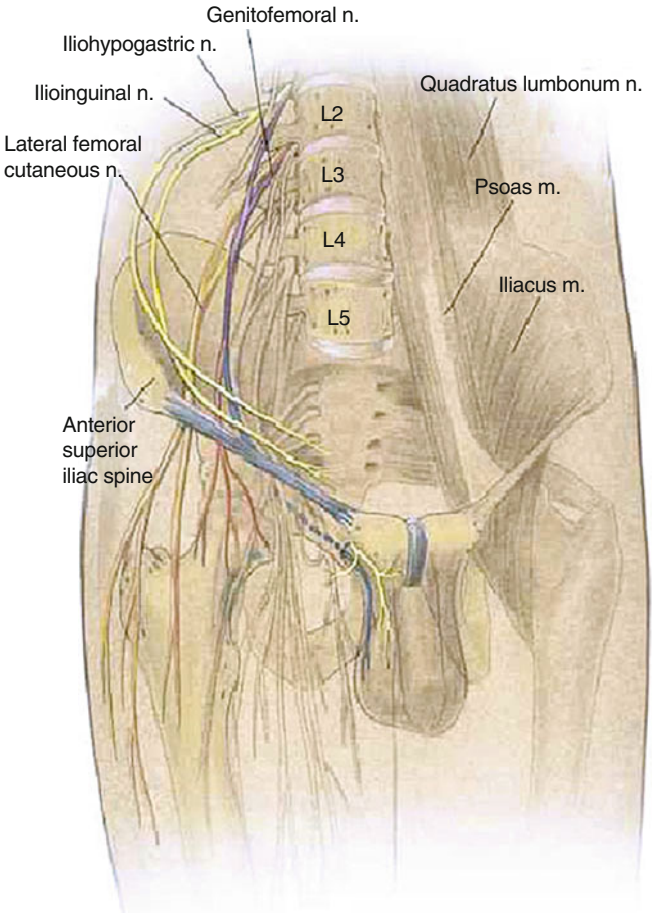

Fig. 38.15 Diagram of ilioinguinal, hypogastric and genitofemoral courses [15]

cavity; image guidance via ultrasound is recommended. As these nerves are difficult to locate [31, 32], the line between PNS and PNFS begins to blur (Fig. 38.15).

Peripheral Field Stimulation

As described previously, there is poor prospective data justifying PNFS. Nevertheless, the available evidence does suggest some efficacy in treating chronic neuropathic pain syndromes [33]. PNFS has also been used in conjunction with SCS to treat both back and leg pain, with inter- and intra-lead programming [34]. Common areas where PNFS has been employed include axial thoracic and lumbar back pain, failed back surgery syndrome (FBSS), greater trochanteric pain after total hip arthroplasty, post-herniorrhaphy pain, chronic abdominal pain, knee pain, and post-thoracotomy pain [5, 33, 35].

Peripheral Field Stimulation Trial

The patient preparation and anesthesia are the same for the aforementioned named peripheral nerve neuromodulatory targets. Surgical site preparation is obviously dependent on the area of the painful area, and therefore the patient position needs to accommodate any easy operative field access. The leads are generally introduced to "bracket" the area of neuropathic pain, with the area of coverage approximately 180 × 90 mm, [36] while others advocate placing the lead centrally in the painful area [33].

Judicious anesthetizing is achieved at the desired entry site with 1 % lidocaine. A stab incision is created and the 14-G introducer needle is inserted near the target area subcutaneously under image guidance. After needle position finalized, the percutaneous lead is introduced, the needle is withdrawn, and stimulation testing commences. As described previously, if unpleasant and burning sensations are reported, the lead is likely too deep and needs to be redirected more superficially. The lead is then secured to the skin using a plastic anchor and nonabsorbable suture and a sterile dress-

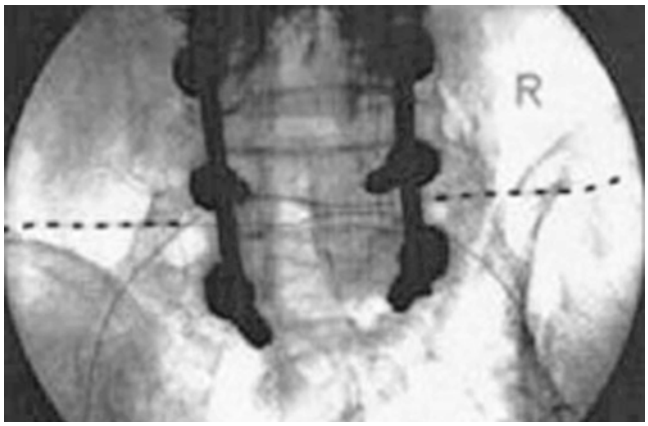

Fig. 38.16 PNFS for FBSS [33]

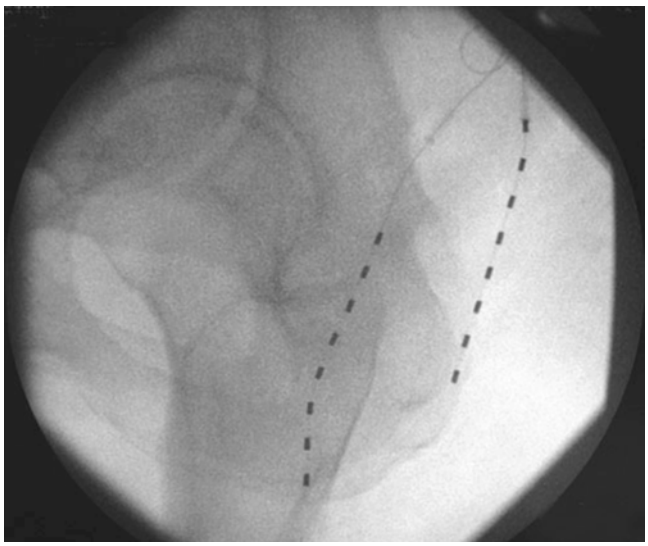

Fig. 38.17 PNFS for thigh pain following greater trochanteric bursectomy [5]

ing is applied. The externalized lead is then connected to the externalized battery, and the patient is transported to the recovery room for more complex programming (Figs. 38.16, 38.17, and 38.18).

Peripheral Field Stimulation Permanent Implant

The peripheral nerve implant following a successful trial proceeds in the same manner as the trial with the additional prep and draping to include the battery site. The strategies and techniques that have been described previously can be translated to PNFS permanent placement.

Successful trial stimulation is defined as at least 50 % pain reduction and/or 50 % improvement in function. Trial periods commonly last for 5–7 days. Unlike spinal cord stimulator trials, PNS trials may be better tolerated for longer periods, as there is very low morbidity or mortality innate to the superficial nature of the device placement. Once a trial is terminated and deemed successful, 3–4 weeks is usually allowed before permanent device placement.

Future Directions

Technical and surgical modifications of the leads and IPG originally designed for SCS are necessary. Further clinical and basic research is needed for the field to grow.

Stimulation in the periphery and centrally has been described working in parallel and concert. The StimRouter, designed to be a small self-contained lead with an external battery supply, is one example of the many advancements on the horizon (Fig. 38.18) [34].

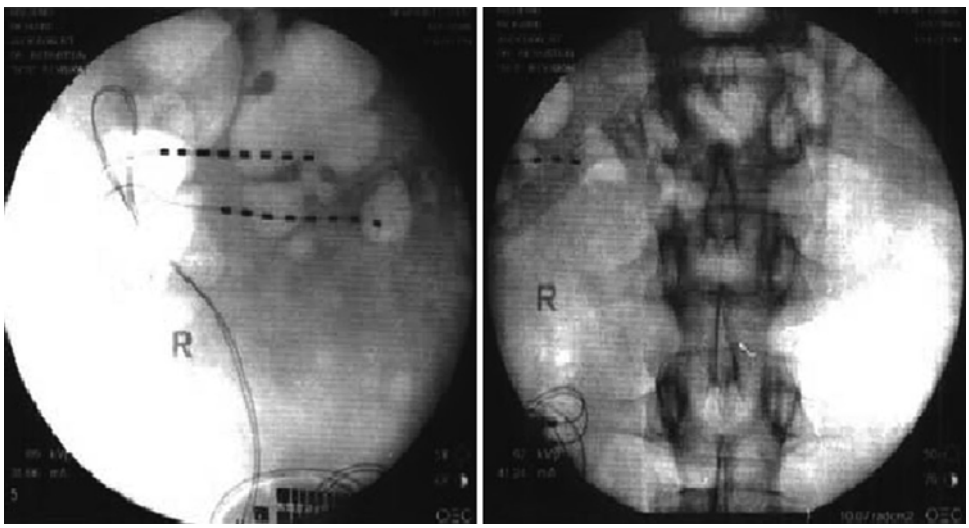

Fig. 38.18 Stimulator router

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Spinal Cord Stimulation

39

W. Porter McRoberts, Daniel M. Doleys, and Kevin D. Cairns

Key Points

- While important, success in neuromodulation is dependent upon much more than technical aptitude. Of inestimable importance is awareness on the part of the implanter of the often surreptitious risks and elusive pitfalls in the process of patient selection, trialing, and implantation. This text seeks to expose, and then prepare the implanter for, those potential perils.
- Pain, being both multidimensional and multifactorial, has a significant psychological component. Therefore, a full understanding of the meaning of pain to the individual patient will provide the implanter with insights that may either doom or support the use of neuromodulation as a treatment.
- A multidisciplinary approach utilizing systematic behavioral and psychological treatment may sculpt patients with maladaptive coping skills or inappropriate expectations into better candidates with higher chances of treatment success.
- The mechanism of action of spinal cord stimulation (SCS) is not completely understood but likely involves several pathways including blocking nociceptive neurons at the level of the dorsal horn of the spinal cord, changes in neurotransmitters affecting supraspinal inhibitory pathways, and possible stimulation of spinothalamic tracts affecting blood flow, among other mechanisms.
- SCS has been shown to be a cost-effective and safe treatment, with several studies demonstrating superior efficacy as well as reduced cost compared to reoperation in patients who have already undergone spinal surgery.
- While the traditional approach of antegrade thoracic SCS may treat many patients, specific neural targets in the cervical cord, entering first-order sensory nerve roots or rootlets, or specific lumbar or sacral nerve root fibers require specialized techniques detailed here.

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Introduction

Since 1967, when Dr. Norman Shealy first demonstrated the temporary but complete abolition of pain implanting a dorsal column stimulator in a terminally ill cancer patient, great technological revolution and refinement has made spinal cord stimulation (SCS) widely available as a stable, long-term treatment option for chronic pain [1]. Compared to destructive techniques or other surgical approaches, SCS is unique in that it is both testable as a screening trial, using temporary percutaneous electrodes, and ultimately when implanted it is a reversible, augmentative treatment without damaging and thus permanent consequences.

SCS may represent the most stable and effective long-term treatment for pain yet devised, as increases in technology and miniaturization in the past 40 years led to implantable methods and technology, yielding a treatment that is cost effective, ubiquitous, and effectual.

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At least 116 million, or one in four, American adults suffer from chronic pain every year, costing as much as $635 billion annually [2]. The National Academy of Sciences in their recent publication, Relieving Pain in America: A Blueprint for Transforming, Prevention, Care, Education and Research, lists the first underlying principle as "effective pain management is a moral imperative, a professional responsibility, and the duty of people in the healing professions" [2]. In addition, as our population ages, so too does the prevalence of chronic pain and associated functional limitation and difficulty in performing activities of daily living. In a water-shed study investigating the incidence of chronic pain, von Korff et al. reported population data of 1,016 patient sample health maintenance organization enrollees, finding 45 % with persistent pain, 8 % with severe and persistent pain, and 2.7 % with severe, persistent pain-limiting activity for 7 days or greater [3]. Chronic neuropathic pain has a reported prevalence of 1.5–8 % in the general or primary care population [4]. The specialty of interventional pain medicine finds itself at a confluence of increasing societal awareness of chronic pain, rapidly evolving improvements in neuromodulation techniques and technology, and increasing demand for safe, effective, and cost-appropriate pain treatments.

The use of electrical measures to treat pain entered the treatment continuum early in medical history. Around 15 A.D., Scribonius Largus, a Roman physician, reported that a torpedo fish could be used to apply an electrical charge to patients to relieve pain [5]. The living fish was applied to the painful area to relieve pain treating such conditions as gout and headache [6]. Largus reported that Anteros, a freedman of Nero, was "cured" of the pains of gout using this technique, and Dioscorides, his contemporary, recommended "electroichthiotherapy" for headache [6]. Throughout the middle ages, the use of the torpedo fish persisted, treating chronic headache, unilateral headache as, well as vertigo [7]. Benjamin Franklin later experimented with electricity for pain relief and other afflictions [8]. Multiple other treatises were published on the use of electricity for pain relief as well as other medical and surgical applications, the most comprehensive authored by Beard and Rockwell [9].

In 1965, Ronald Melzack and Patrick Wall published their gate control theory, which adroitly departed from the popular theories of pain of Descartes, von Frey, and Goldscheider [10]. Their new paradigm not only set the stage for the development of SCS but also posited that pain was perceptual and modifiable through pathways of inhibition, both centrally and in the periphery. They surmised that the substantia gelatinosa acted as a form of central control summating the competing nociceptive and antinoceptive inputs and then sent the modified afferent signal rostrally (see Fig. 39.1).

Building on the gate control theory, Shealy et al. [1] implanted a 70-year-old man dying of bronchogenic carcinoma via laminotomy, sewing the 3 × 4-mm electrodes to the dura. That evening in the postoperative setting, they began stimulation with 10–50-Hz and 400-ms pulse width at 0.8–1.2 V and 0.36–0.52 mA. Both his incisional pain and original chest pain were immediately abolished. Small changes were made throughout the remaining day and the next in response to discomforts. Eventually, the patient died on postoperative day 2 from a left hemispheric embolization from subacute bacterial endocarditis. Despite the abbreviated nature of this nascent trial, Shealy et al. [1] confirmed the suspicion that pain was not only modifiable at the spinal cord level, but that the clinical effect of electrical current in the spinal canal was of great importance to the human condition. Since that moment, SCS has undergone rapid evolution towards efficacy and safety.

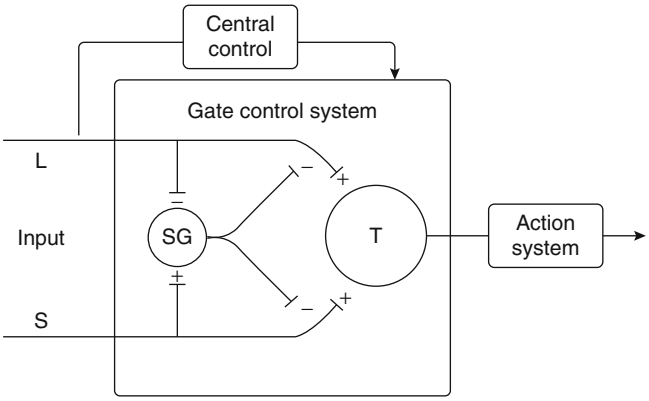


Fig. 39.1 Gate control theory

This chapter will detail in short the scientific foundation of implantable SCS, the clinical use of SCS including patient selection and psychological screening, and trialing and implant techniques, with special attention to concepts that may diminish risk and complications and improve likelihood of success. Throughout the chapter, resources for further reader education will be included. Lastly, future directions for research surrounding spinal cord stimulation are summarized.

Patient Selection and Diagnostic Work-Up

Mechanism of Action

Chronic pain from injury to the central or peripheral nervous system can be managed by stimulating nerve fibers in the dorsal column via percutaneous or surgical electrode array placement, first described by Dr. Shealy in 1967 [1]. The exact mechanism of action of SCS is incompletely understood, however, likely involves both physiologic, orthodromic stimulation, and nonphysiologic, antidromic stimulation, respec-

tively [11]. While several mechanisms of action have been described for SCS, the most accepted theory of pain relief can be explained by the gate theory first described by Melzack and Wall in 1965 [10]. This groundbreaking yet simplistic model describes the interaction of large sensory fibers and nociceptors and how they influence the transmission of neural impulses by second-order projection neurons in the dorsal horn. Placement of electrode arrays in the epidural space depolarizes A-beta nerves orthodromically in the posterior columns and antidromically via dorsal column collateral fibers, thereby inhibiting pain transmission to the brain [11]. Large, A-beta nerve activation causes depolarization of neurons in the dorsal horn and "closes the gate" for the transmission of A-delta and C-fibers to the projection neuron. In addition, large A-beta neuron activation inhibits GABAnergic pathways that influence wide dynamic range neurons that can become hyperexcitable in chronic pain states. Evoked paresthesia is targeted towards the specific region of pain, although the inhibition of pain is most likely related to activation of interneurons that suppress pain and not the antidromic depolarization resulting in the evoked paresthesia noted by the patient. Since the publication of the gate theory of pain transmission, it is clear that there are additional components to the transmission and processing of pain that include descending inhibitory pathways, alterations of neurotransmitters in the brain, as well as other tracts in the spinal cord that may be involved [12, 13]. The supraspinal descending inhibitory effects likely involve serotonin and norepinephrine and clinically may be related to patients noting pain relief several hours after the SCS system is turned off.

Inhibition of the sympathetic system by SCS is another potential mechanism to alleviate pain. Kemler et al. showed that in a group of patients with CRPS, pain relief did not depend on vasodilation, arguing against the inhibition of the sympathetic system by SCS to be vital for neuropathic pain relief [14]. It is possible, however, that stimulation-induced inhibition of the sympathetic system by SCS may be beneficial in patients with peripheral vascular disease where vasodilation may help with nociceptive pain related to ischemia, and it is likely that the underlying disease plays a large factor into the mechanism that ultimately results in pain relief [15].

The type of nerve population depolarized is determined by the placement of the electrode arrays and the stimulation parameters utilized. Different neural structures have different stimulation thresholds. The lowest threshold neural structures are located in the dorsal root entry zone, followed by the lateral fibers in the posterior columns, and the highest threshold fibers are the most medial. The somatotopic organization of the central nervous system persists in the dorsal columns and lead placement, and programming strategies are determined by the target neural element [16]. While importance has been historically placed on the cephalocaudal placement of SCS leads, more attention has been placed on the medial to lateral placement as well with multicolumn arrays, showing promise in more targeted stimulation given the medial to lateral somatotopic organization of nerves in the dorsal spinal cord and their ability to create guarded arrays. For that reason, placement of percutaneous SCS leads is generally preferred to be in the physiologic midline to maximize stimulation of the dorsal columns and minimize stimulation of the dorsal root entry zone. In addition, the frequency of SCS stimulation also effects which nerve population is depolarized [17]. Higher frequencies tend to stimulate a greater proportion of A-beta fibers, while lower frequencies stimulate more A delta and C fibers.

Functional MRI has demonstrated important changes in the way pain is processed in the brain in patients with chronic pain and how SCS may influence the central nervous system. The challenges with functional magnetic resonance imaging (fMRI) evaluating SCS and peripheral nerve field stimulation (PNfS) include minimizing heating of the contacts with pulsed radio frequency (RF) as well as fMRI, revealing widespread areas of activation and inhibition in the brain and the difficulty in interpretation [18]. In a healthy patient with an occipital nerve stimulator system, areas of activation were predominantly seen in the hypothalami, the thalami, the orbitofrontal and prefrontal cortex, the periaqueductal gray (PAG), the inferior parietal lobe, and the cerebellum. Deactivation was seen in primary areas (M1, V1, A1, and S1), the amygdala, the paracentral lobule, the hippocampus, S2, and SMA [19]. Kovaks et al. noted that the effects of stimulation were more pronounced with tonic stimulation rather than burst stimulation [19].

Patient Selection

Selecting the right patient is essential for a positive response to neuromodulation therapies. Among the diagnoses that have noted consistent benefit from SCS are lumbar post-laminectomy syndrome (PLS), radiculopathy, polyneuropathy, and complex regional pain syndrome (CRPS) [20, 21]. In general, patients with a history of spinal surgery with primarily leg pain have been shown to benefit significantly from SCS. North et al. [22, 23] in their seminal study randomized patients who had a history of lumbar surgery into repeat surgery and SCS groups and showed superiority of SCS to reoperation. In addition, in the same cohort of patients, North et al. demonstrated significant cost savings of SCS to repeat back surgery in intention to treat, treat as intended, and final treatment analysis [24]. The cause of post-laminectomy syndrome likely involves changes in peripheral sensitization as well as central windup phenomena in the spinal cord. Anatomically, these patients may present with epidural fibrosis, arachnoiditis, junctional stenosis above or below surgical site, or a completely normal MRI

Table 39.1 SCS outcome data

References	Number of patients	Follow-up	Results
Kumar et al. [20]	410	8 years	74 % had >50 % relief
Cameron [32]	747	Up to 59 months	62 % had >50 % relief
Van Buyten et al. [31]	123	3 years	68 % had good to excellent relief
Aló et al. [93]	80	30 months	Mean pain scores declined from 8.2 at baseline to 4.8

with normal postsurgical changes. In cases of instability with movement on flexion/extension x-rays, surgical referral is warranted. In addition, significant central canal stenosis in the thoracic or cervical spine impinging the spinal cord would be a contraindication for SCS implantation.

While in the USA the primary indications for SCS are radiculopathy, PLS, and polyneuropathy, emerging applications are being shown in Europe. The benefit of SCS in widespread small vessel coronary artery disease with chronic angina has been described [25]. In addition, there has been some evidence that the ability of SCS to cause vasodilation can potentially treat the underlying cause of peripheral vascular disease as well as mask its symptoms [26].

Case reports of more challenging diagnosis to treat with SCS have been reported including postherpetic neuralgia [27], post-thoracotomy syndrome [28], phantom limb pain, stroke central pain syndrome [29], spinal cord injury, and multiple sclerosis [30]. Case reports and small case series have been published describing benefit from SCS therapies in these patient populations, and it is unclear why these diagnoses have such variable response to treatment.

Outcomes/Cost-Effectiveness

Multiple studies have demonstrated clinical efficacy of SCS, with reduction in pain, improvement of function, and reduction in pain medicines well documented (see Table 39.1). In addition, SCS has been shown to be cost effective in several studies. North et al. [24] demonstrated significant cost savings in a cohort of patients who had spinal surgery when comparing SCS to repeat spine surgery. The cost for success for SCS was $48,357 compared to the cost for success with repeat spine surgery being $105,928 (treated as intended). Mekhail et al. compared patients with SCS systems to those without and noted a yearly cost savings of $30,221 per year attributed to less ER visits, less diagnostic tests, and lower utilization of health-care resources [31]. Of note, the timing of SCS implantation may be of great importance as Van Buyten et al. has shown a significant reduction in efficacy when neuromodulation therapies are delayed with 85 % of patients realizing significant pain relief within 2 years of their pain beginning compared to 9 % of patients who have had pain for more than 15 years [32].

Psychological Evaluation for SCS

Background

Pain is well recognized as being multidimensional and multifactorial. Therefore, any therapy designed to affect pain, particularly in the chronic pain setting, should logically include a comprehensive or multidisciplinary evaluation. The psychological assessment should be considered as an integral and significant aspect of this evaluation process given the well-documented impact of psychosocial variables on the experience of pain.

Scores of studies involving thousands of chronic pain patients utilizing SCS therapy have been published. Although the results are touted as generally positive (the majority of patients report a 50 % or greater reduction is pain), reviews of the literature [33–35] have revealed a loss of pain relief in up to 50 % of patients at 1–2 years post-implant despite their having successfully "passed" a period of trial stimulation and the presence of a functional SCS unit. Indeed, one study [36] reported that 100 % of patients reported success at 16 months but only 59 % at 58 months. Psychological factors may play an important role in understanding this apparent loss of efficacy. An overemphasis on the SCS technology, while potentially economically rewarding (new power supplies, electrodes with more contacts, increased programming options, multiple electrode arrays), may come up short of a solution. In part, it may be equally advantageous to take the position of trying to discover "how to make what works, work better" rather than merely "tinkering with the technology." It is important to remember that the SCS trial is essentially an "acute" procedure being used to "predict" a "long-term" outcome with a "chronic disease." While computer modeling provides invaluable information about electrode disbursement patterns at the level of the spinal cord, it should not be mistaken to represent anything other than a guideline to achieving more specific patterns of stimu-

lation, which may or may not be associated with greater and more prolonged pain relief.

Inclusion/Exclusion Criteria

Previous guidelines for "patient selection" have focused on exclusion criteria. For example, Daniel et al. [37] cited personality disorders [38], drug dependence, unstable family and personal relationships, poor vocational adjustment, and involvement in litigation/compensation as "red flags." Nelson et al. [39] suggested the presence of suicidality or homicidal, severe depression or other mood disorders, somatization/somatoform disorder, alcohol or drug dependency, unresolved compensation/litigation issues, lack of social support, and/or neurobehavioral cognitive deficits to be considered as contraindications of SCS therapy. In a conversation with Dr. Kumar (April 2004), he developed the "Kumar warning signs" which include *K* – "kannot" possibly live without this device; *U* – unlimited utilization, overuse of health-care resources; *M* – misunderstood, "nobody understands me, only you can help me doctor"; *A* – affective disorder, major psychopathology; and *R* – "REALLY…its only my pain I have no other problems," symptoms inconsistent with physical findings. The European Federation of IASP Chapters [51] declared major psychiatric disorders (active psychosis, severe depression or hypochondria, and somatization disorder), poor compliance and/or insufficient understanding of the therapy, lack of appropriate social support, and drug and alcohol abuse or drug-seeking behavior as contraindications.

Doleys [40] adopted a different approach when outlining 16 "hypothesized" positive indicators including a history of compliance with previous treatments, behavior and complaints consistent with pathology, behavioral/psychological evaluation consistent with patient complaints and reported psychosocial status, realistic concerns regarding "illness," mildly depressed, generally optimistic regarding outcome, and ability to cope with setbacks without responding in an emergent fashion. He went on described patient and physician beliefs "potentially" associated with positive and negative outcomes. In each of the cases above, the features outlined emerged from consensus, "common sense," clinical experience, and/or generalization of other literatures. None at this point has been experimentally validated and replicated.

The frequency with which a formal psychological assessment is carried out betrays what appears to be an almost universal acceptance of the role of psychological factors in chronic pain and pain therapies, including SCS. A Canadian survey [41] found that only 25 % of 13 participating centers reported routine psychological screening prior to SCS implantation, compared to 61 % of centers in a UK survey [42]. Although a "psychological screening" is required by Centers for Medicare & Medicaid Services (CMS) (Medicare health-care insurance) in the USA, the incidence of it in non-Medicare populations approximated 25 % [43]. The most common reasons given for the discrepancy between the support for psychological screening and its actual utilization were (a) lack of or inadequate insurance coverage, (b) lack of physician insistence, (c) patient refusal, and (d) lack of an appropriate evaluator. The cost of most psychological evaluations approximates 1–3 % or less of the total cost of the SCS trial and implantation in the USA. If screening/pretreatment prevented only 2–3/100 patients from failing treatment and the removal of the device, a cost savings would be realized [43].

Brief Literature Review

Celestin et al. [44] performed a systematic review of outcomes relating to lumbar surgery and SCS. They were able to identify only four SCS studies that met their criteria for the review. A successful outcome was defined as 6 months or more duration, decreased pain, increased function, and reduced health-care utilization. Depression, anxiety, somatization, poor coping, and hypochondriasis tended to be associated with poorer outcomes, but none was found to be statistically significant. Sparkes et al. [45] examined the literature on psychological variables affecting SCS outcomes spanning 1982–2008. In summarizing their review, they noted that the Minnesota Multiphasic Personality Profile (MMPI) [46] was the single most common test administered. The psychological variables studies included depression, hysteria, anxiety, mania, hypochondriasis, paranoia, defensiveness, joy, belief pain out control, catastrophizing, and psychopathic deviate. It was concluded that (a) depression probably correlates negatively, (b) mania possibly has a positive correlation, (c) hysteria was possibly negative, and (d) hypochondriasis was mixed [45].

One of the coauthors (DMD) recently participated as a member of group of clinicians and researchers organized by the American Pain Foundation to develop a consensus guideline for SCS therapy (in preparation). Nineteen studies from among several hundreds covering the period from 1990 to 2010 were selected on the basis of the information in their respective abstracts to be reviewed regarding their reported use of a psychological/psychiatric evaluation prior to SCS trialing or internalization. Twelve of the 19 studies noted using one or more psychometrically validated instruments or questionnaires. The content or makeup of the psychological screening was often based on theoretical bias. For example, Heckler et al. [47] and Molloy et al. [48] tended to favor behavioral/functionally oriented tests/questionnaires, Dumoulin et al. [49] a more psychoanalytic approach, and Lamé et al. [50] focused on the hypothesized impact of catastrophizing.

Only seven studies listed any psychological inclusion or acceptance criteria. Most often, the criteria was stated in the form of a very general statement, for example, "no contraindications," or "psychologically uncomplicated." Eight studies outlined psychological exclusion criteria. The often cited exclusion criteria were high levels of psychological distress, psychosis, somatization, alcohol/drug issues, and/or unresolved secondary gain issues, for example, pending litigation. Fourteen studies performed some type of pre post-internalization analysis on one or more of the tests results from the pre-implant screening. In nearly every case, this analysis was carried out for the purpose of determining the effect of SCS therapy. A few studies addressed psychological "predictors." In one, depression, especially when combined with age and the McGill score, predicted 88 % of 34 patients. Lamé et al. [50] found that catastrophizing did not predict outcomes in a group of CRPS patients. North et al. [51] reported that none of their psychological tests predicted the outcome, and Kupers et al. [52] and May et al. [36] noted that the patients with a "positive screen" did better than patients where caution or reservations were entered. In some cases, the emphasis was on predicting those who would proceed from trial to implant versus "outcome" predictors. A variety of tests/questionnaires were used. The MMPI, Beck Depression Inventory (BDI) [53], and the Oswestry Disability Questionnaire (ODQ) [54] were among the most common. It may be difficult to establish a commonly agreed upon interview format and battery of tests/questionnaires. Perhaps, the best approach at this point is to follow Deyo et al. [55] recommendation to obtain information regarding the qualitative/quantitative aspect of "pain," along with an assessment of mood, function, and personality features.

Elements of Psychological Evaluation

Unfortunately, the psychological evaluation is often construed as part of patient "selection." As such, the goal is seen as one of "clearing" the patient, a concept that has never been defined, clarified, or objectified [56]. This approach encourages a dichotomous decision of "go" or "no-go," with little regard to interventions that might improve the probability of a good long-term outcome [57]. It is herein suggested that the patient selection/evaluation aspect of SCS therapy should be considered as a *process* and not an event. The process begins with the review of records and the initial consultation and extends through the trial and up to the point that a decision is made to internalize or not. A systematic behavior/psychological assessment is part of the process. Patient selection is best conceptualized as longitudinal and focused on the identification of patient characteristics that implicates the patient as a good candidate for SCS or is potentially modifiable by psychological/behavioral interventions (CBT) designed to enhance the short- and long-term outcomes.

For the psychological evaluation to provide the most useful information and therefore to be of minimum benefit to the patient and clinician, the following components are recommended. First, the assessment should be conducted by an appropriately trained, knowledgeable, and experienced mental health clinician. Second, it should include a face-to-face interview with the patient and when possible the participation of a significant other. Data from the clinical interview should be supplemented by the use of well-known and validated test (s)/questionnaires. At least one of the clinical instruments employed should contain a mechanism for detecting dissimulation (i.e., a "fake-bad" or "fake-good" scale). The use of generic (overall quality of life) and disease-specific (pain rating) measures should be considered. It would be important for the evaluator to have post-trial and/or post-internalization contact with the patients, or least the outcome data, to determine the accuracy of the recommendations generated by the evaluation.

Unfortunately, the psychological evaluation all too often is treated necessary nuisances. Patients are sent to "outside" consultants with little or no interest or experience in chronic pain or SCS therapy merely as a means of satisfying insurance or regulatory guidelines. Worse, computer-scored and interpreted tests are administered by the physician as a mechanism to satisfy the requirement. Even when such tests are administered by a psychologist, the American Psychological Association Ethical Guidelines [58] requires patient contact prior to rendering an interpretation of the test results. Finally, periodic updated brief assessments may well assist in adjustments of the therapeutic algorithm and improving long-term outcomes [59].

Despite the potential limited prognostic value, the evaluation process can and should serve several other functions [60]. First, it can be used to facilitate the development of an individualized treatment plan. Second, it provides an opportunity to properly prepare and educate the patient and significant other for the trial, possible internalization, and long-term treatment. Third, psychological interventions designed to mitigate the impact of maladaptive psychological issues (i.e., poor coping, limited acceptance, etc.) can be implemented and create a patient with a more favorable prognosis. And finally, the psychological evaluation process can be used as a means of addressing potentially modifiable problems and therefore may enhance the overall efficacy of therapy and prevent an overemphasis on the development of absolute exclusionary criteria. It can also help to fulfill the requirements of "informed consent"[61].

Our own approach to the evaluation process includes a clinical interview along with the administration of the BDI,

Table 39.2 Complications associated with spinal cord stimulation and their diagnosis and treatment

Complication	Diagnosis	Treatment
Complications involving the neuraxis		
Nerve injury	CT or MRI, EMG/NCS/physical exam	Steroid protocol, anticonvulsants, neurosurgery consult
Epidural fibrosis	Increased stimulation amplitude	Lead reprogramming, lead revision
Epidural hematoma	Physical exam, CT, or MRI	Surgical evacuation, steroid protocol
Epidural abscess	Physical exam, CT or MRI, CBC, blood work	Surgical evacuation, IV antibiotics, ID consult
Postdural puncture headache	Positional headache, blurred vision, nausea	IV fluids, rest, blood patch
Complications outside the neuraxis		
Seroma	Serosanguinous fluid in the pocket	Aspiration, if no response surgical drainage
Hematoma	Blood in pocket	Pressure and aspiration, surgical revision
Pain at generator	Pain on palpation	Lidoderm patches, injection, revision
Wound infection	Fever, rubor, drainage	Antibiotics, incision and drainage, removal
Device-related complications		
Unacceptable programming	Lack of stimulation in area of pain	Reprogramming of device, revision of leads
Lead migration	Inability to program, x-rays	Reprogramming, surgical revision
Current leak	High impedance, pain at leak site	Revision of connectors, generator or leads
Generator failure	Inability to read device	Replacement of generator

From Deer and Stewart [61]. With permission
CT computed tomography, *MRI* magnetic resonance imaging, *IV* intravenous, *CBC* complete blood count, *EMG* electromyography, *NCS* nerve conduction studies, *ID* infectious disease specialist

McGill Pain Questionnaire, ODI, and MMPI. The assessment period is also used as an opportunity to educate the patients and significant other as to the various aspects of SCS therapy as well as allowing them to become familiar with the hardware by manipulating it. Addressing expectations that can be supported by the existing outcome literature and identifying functionally related goal which can be measured during the trial are fundamental. We also obtain a "functional level of pain" (FLOP). That is, the patient is asked at what level of pain do they feel they can be more accepting of their condition, existing residual pain, and more functional. Patients needing a pain level of less than 3/10 may be very unrealistic and require further education.

Summary

To the extent that "pain" remains a primary or significant outcome, and given the generally accepted multidimensional and biopsychosocial nature of pain, it seems logical and consistent to recommend a pre-SCS trial/implant psychological screening. In addition to pursuing the identification of "predictors," emphasis should also be given to the development of treatment algorithms based on the psychological evaluation. This algorithm may well call for pre- and/or post-implant psychological intervention(s).

Clinical Approaches to Spinal Cord Stimulation

Complications

Once the decision to trial SCS has been made, great attention to planning is required. Every effort, increasing awareness of risk, mitigates that risk and compounds the probability of success for the patient and surgeon. Despite a familiarity with the operating room, many implanting physicians' native medical training falls outside the surgical realm and thus attention to detail becomes paramount. Familiarity with the most common complications sharpens the implanter's level of surveillance for missteps and pitfalls. Deer and Stewart [61] familiarizes some of the more common complications of SCS in Table 39.2.

Reported complication rates are variable and difficult to interpret across populations and studies; however, Turner et al. [63] identified an overall complication rate of 34 %, a rate of surgical revision at 23 %, and deep infection at 0.1 %. Kumar et al. [64] found infection rate of 2.7 %, epidural fibrosis to affect 19 %, and a lead complication rate of 5.3 %. Cameron [33] summated that lead migration complicated 13.2 % of cases, infection affected 3.4 %, and lead fracture 9.1 %. Complication severity is highly variable varying from unwanted paresthesia to epidural abscess, hematoma, and paralysis. Nevertheless, careful preoperative risk assessment moderates

risk and should begin not when entering the operating theater but with the patient and as soon as the treatment is considered.

Preoperative Risk Assessment

Risk reduction begins long before consideration of trial. Risk of neural injury is diminished by a thorough survey focusing on the anatomy of the spine and contents. The implanter needs awareness of anatomical or surgical changes, scarring or fibrosis, and canal stenosis or listhesis that could challenge the deployment of a percutaneous or possibly a paddle lead. Imaging, not only the spinal canal at the neural target, but also the approach will greatly aid in safety and avoidance of difficulty [65]. Anatomy may degrade or change and impair the safety of the implant in the years following implant and narrow cervical canals. For example, it may portend further degradation and stenosis with resultant cord compromise in time.

Concomitant disease states beg recognition and exploitation of treatment, and there should be a low threshold for involvement of primary care clinicians or specialists to assist in rejuvenation prior to surgery. Diseases of immunity such as diabetes as well as recent or ongoing infections such as human immunodeficiency virus increase the probability of infection. The bleeding profile should be assessed and any medications or interactions that influence bleeding appreciated and removed from the clinical setting in adequate time to allow normal hematologic function. New-generation anticoagulants without clear data regarding surgical bleeding risk, for example, should encourage partnership with cardiology or hematology. Education regarding preoperative prophylaxis against methicillin-resistant *Staphylococcus aureus* with antiseptic soaps and use of intranasal mupirocin may reduce operative infection [66, 67]. Hair clipping around the operative area may additionally be of benefit [68, 69]. Compliance issues need attention, and lastly, the patient needs adequate education regarding, and durable documentation reflecting, not only potential harms but also their role and responsibility in the endeavor in the short- and long-term.

The Percutaneous Trial of Spinal Cord Stimulation

The trial not only introduces the patient to the experience of paresthesia and tests the ability to meaningfully ameliorate pain but functions also as a provisional assessment of the technique as well: the appropriateness of neural targets and the approach to them. It is the primacy of pain location and thus neural targets that backwardly determine every part of the testing and implant process. Lastly, the trial serves as a team gathering, not only of the physician and patient, but also of the stimulator representative, nurses, and family members who will be assisting in the trial and in educating the patient about their new, potential treatment.

On the trial day, a concise but thorough pre-procedure review is prudent; the addition of a checklist will ensure thoroughness. Evaluate the patient's skin, not only at the planned operative site area, but also globally for infection. Begin preoperative IV antibiotics with efficacy against common skin pathogens in light of the local and hospital antibiogram. Within the cerebral spinal fluid (CSF) shunt literature, perioperative antibiotics administration is a significantly effective prophylactic measure [70]. Consultation with infectious disease colleagues is prudent regarding surgical standard of care especially in patients with suspect immunology or history of infection. Check coagulation status with a review of medicines taken and consider platelet count or bleeding profile if necessary. In addition, plan for positioning on the table in regards to the patient's habitus and the optimum amount of kyphosis at the level of entry [71]. Particularly, obese persons may require significant bolstering under the abdomen in thoracic lead placement. Whatever time is lost in positioning is likely gained by facility of entry and lead positioning.

The skin is the major source of surgical pathogens, and optimization of preoperative skin antisepsis diminishes infection. Several choices of surgical preparatory agents with differing bacteriocidal specificity exist. Alcohols denature proteins and are highly effective against both gram-negative and gram-positive bacteria, even those multidrug resistant, as well as fungi, mycobacteria, and some viruses [72]. Iodine, most commonly Betadine, is effective against gram-positive, gram-negative, mycobacteria, and viruses and fungi [72]. Chlorhexadine gluconate is very effective against gram-positive bacteria, somewhat so against gram-negative bacteria, but minimally so against spores and tubercle bacilli. Chlorhexadine provides residual antiseptic activity and when combined with alcohol may be superior to iodine-based preparations [73]. Cleaning with multiple preparations may further diminish bacterial counts, due not only to the expanded action of the differing agents but also to the increased time of exposure to the agents. Prepping first with iodine-based preps followed by others may confer added benefit as blood, serum, and other protein-rich biomaterials diminish the antimicrobial effect of povidone-iodine [74]. The surgical skin preparation should extend at least 6 cm from the proposed surgical site [62], but there is no reason to limit the size of the prep. Draping with plastic adhesive border prior to the prep delineates the area to be prepped and prevents inadvertent contamination. After the skin preparation and then draping with sterile towels, taking great care not to contaminate the surgeon's gown, a laparotomy drape or other large surgical drape covers the remaining patient.

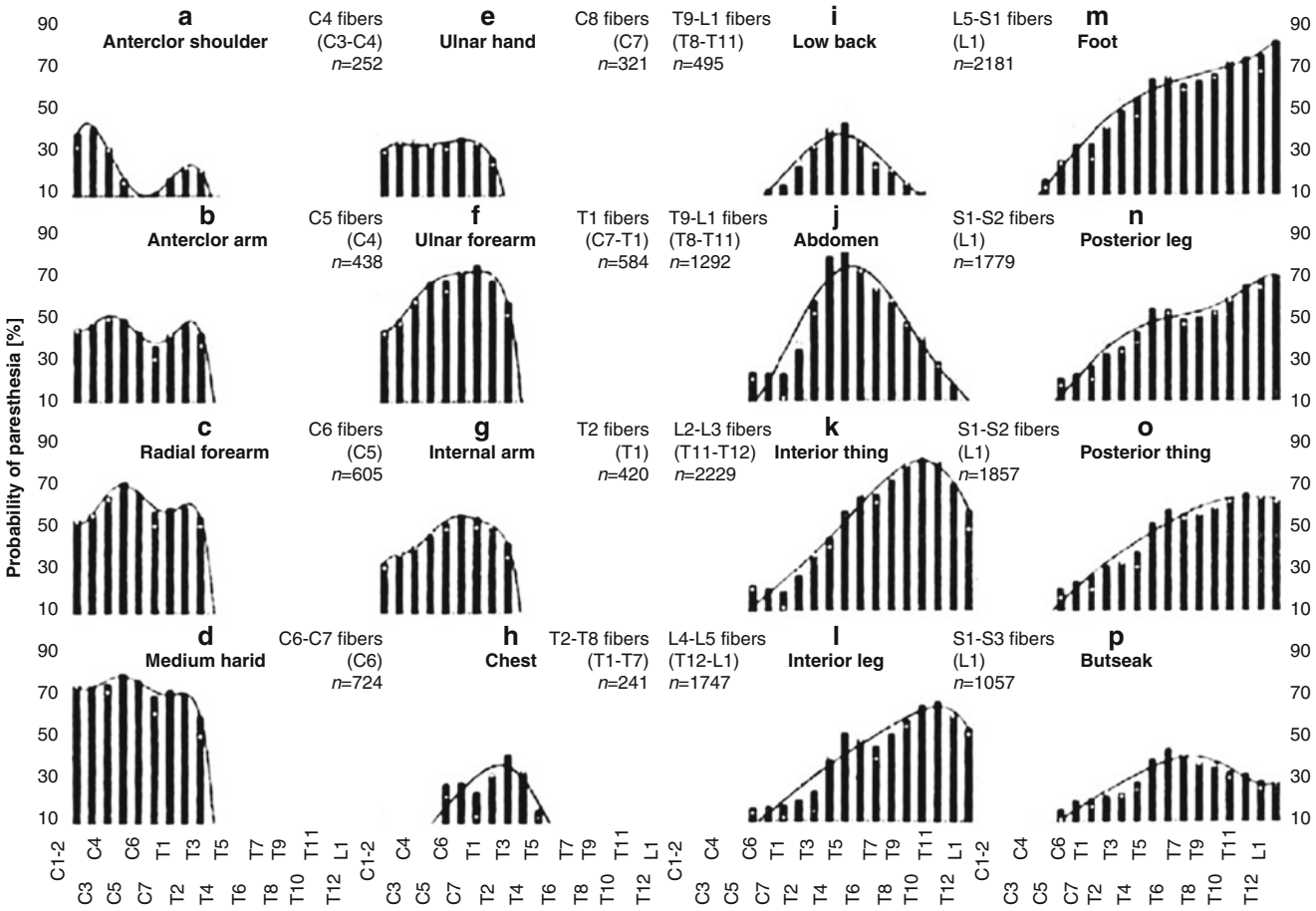


Fig. 39.2 Probability of paresthesia plots for 16 body areas as a function of the vertebral level of stimulation: *white squares* (original data), *bars* (averaged data), and curves fitting the averaged data (From Holsheimer and Barolat [75]. With permission)

Drying of the skin permits excellent adhesion for occlusive and impregnated plastic drapes like Ioban™ (3M Health Care, Inc). There is no consensus as to the degree of surgical operative preparation for the trial and permanent implant, but arguably, the greater the prophylaxis, the lower the risk for infection.

The aim of anesthesia, patient comfort and tranquility, must be balanced with the danger of oversedation, as the most sensitive neural monitoring equipment in the awake patient. The appropriate use of local anesthetic and limitation of sedation during periods of electrode placement renders the awake and conversant patient sensitive to minute changes in neurologic status, thus alerting the physician to avoid injury.

Regarding electrode placement, the aim should be to safely depolarize the nerves, which will present paresthesia to overlap the patient's pain. Holsheimer and Barolat have carried out significant work on neural mapping of the dorsal columns and likelihood ratios of paresthetic coverage in particular [75, 76, 77] (see Figs. 39.2 and 39.3). Alo and Holsheimer additionally summarize certain requirements for clinical efficacy:

1. The evoked paresthesia must consistently cover the entire painful area.
2. The cathode and resultant electrical field must focus on the corresponding dorsal column fibers to allow maximum paresthetic coverage of the painful area.
3. For coverage of bilateral pain, the cathode field should be focused on the "physiological" midline of the cord. In single-electrode SCS, by implication, this electrode should be centered on the spinal cord midline which may differ by up to 2 mm from the radiological midline.
4. If the pain is unilateral, the electrode may be displaced by up to 1 mm on the corresponding side of the physiological midline.
5. When the patient's pain is both unilateral and segmental, the electrode may be placed more laterally, thereby stimulating primarily the corresponding dorsal root fibers.
6. Even if requirements 1–5 are satisfied, anatomically precise paresthesia alone does not relieve pain as paresthesia is a

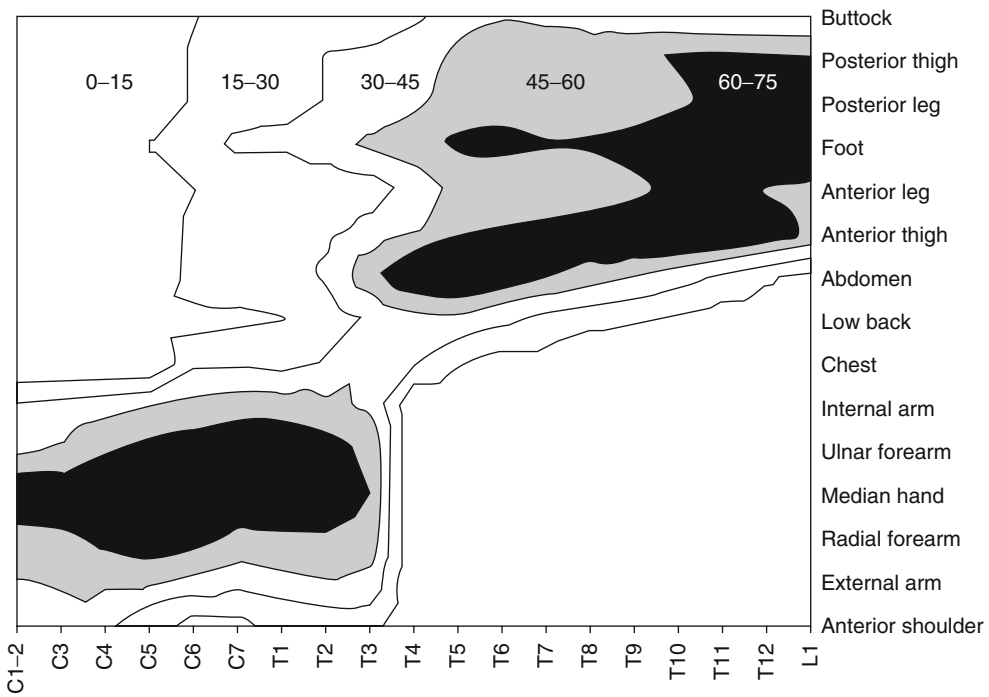


Fig. 39.3 Three-dimensional plot showing probability of paresthesia contours as a function of the vertebral level of stimulation (*x-axis*) and the body area (*y-axis*) (From Holsheimer [76]. With permission)

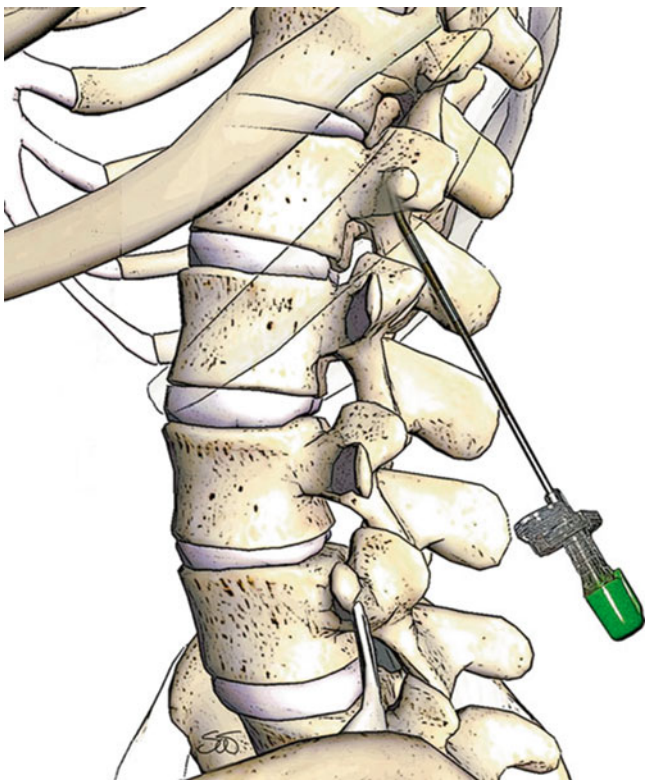


Fig. 39.4 Correct sagittal angle of incidence for thoracic spinal cord stimulator lead placement

necessary but often insufficient criterion for achieving relief.

Once the best location has been selected, then attention is turned to the site of ligamentum flavum entry. Enough lead length must lie in the epidural space proximal to the electrode array to provide stability of the lead in the space, and so entry through the flavum must occur at least one to two vertebral levels caudal to the anticipated array placement. Additionally, so as to allow for appropriate sagittal angle of incidence (less than 45°), appropriate skin entry should occur about one to one-half vertebral bodies inferior to the interlaminar entry point (see Fig. 39.4) [76]. As the depth of the spine increases, as in obese persons, the skin entry site must move inferiorly to maintain the appropriately shallow angle of needle entry. The sagittal angle is important: the flatter angle greatly increases the ease of lead manipulation especially in the first few centimeters of travel from the needle. Additionally, as the angle of incidence, needle to dura, decreases, so too does the risk of neural injury. Too flat of a needle approach, however, blocks the needle's ability to pass under the inferior edge of the superior lamina and thus through the ligamentum flavum. Additionally, the coronal angle of the needle can be largely estimated by the angle of the chevron made by the spinous process of the inferior lamina usually 10–20° off of midline (see Fig. 39.5). If a lead persists in tracking to the contralateral side of entry, the implanter may halt attempts to pilot the lead and, if planned,

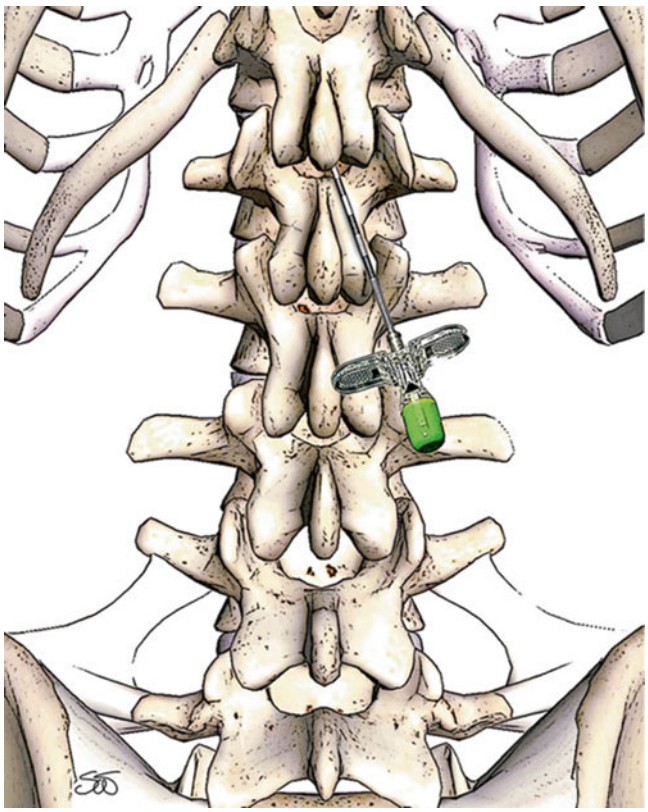


Fig. 39.5 Correct coronal angle of attack to allow midline lead deployment, and to allow for the anatomy of the spinous process

introduce the second lead on the other side, providing a firm vector to recurve the lead back cephalad. If the interlaminar space permits, dual needle with unilateral approach may be also performed. While losing the benefit of "banking," the single-sided approach allows the implanter to easily visualize the depth of the first needle, thus allowing possibly more expeditious placement of the second needle.

After skin entry has been selected and cutaneous anesthesia provided, a small portal is suggested with a scalpel such as an 11 blade, so both the spinal needle used for deeper anesthesia and the introducer needle passes easily between the skin edges and avoid potential contamination with superficial and intradermal flora. Loss of resistance can be performed either with a medium such as saline or air, or conversely with the lead itself, carefully advancing the needle in either contralateral oblique or lateral view with constant exiting pressure placed on the lead tip with careful advancement of the needle [78]. Entry through the ligamentum flavum should be in the medial third of the interlaminar space, thus allowing the lead entry to be close to midline. This approach when combined with the rule that cephalad lead navigation remains within the confines of the lateral borders of the spinous process projection on anterior-posterior fluoro virtually guarantees posterior epidural lead placement. However, a low threshold for lateral and confirmative views is warranted.

Clearly, the entry through the ligamentum flavum and the initial lead entry into the spine is the most dangerous aspect of the entire procedure as injury to either the dura, nerve roots, or cord can result. To fail to recognize errant placement of either needle or lead and then to subsequently proceed greatly increases the consequences of the error. As noted above, safety and subsequently expediency are served by minimal use of sedation and excellent intra-trial communication between surgeon and patient regarding new paresthesias or pain in the extremities. Gentle loss of resistance, early use of transverse fluoro angles, negative aspiration of cerebral spinal fluid, as well as lead testing for perception amplitudes consistent with epidural placement further reduce risk.

Failure to recognize error compounds the consequences. If it becomes apparent that the dura has been compromised, the surgeon must stop, survey the degree of injury, and then make the decision to either proceed with a different approach or cease and allow the dura to heal before returning. There is no clear consensus on methodology of management. Eldrige et al. detail two cases of SCS lead placement complicated by CSF lead and postdural puncture headache [80]. Generally, in the setting of positive CSF return in the needle, the entry site is forfeited and another selected for entry. If the rent is large, this may also complicate the nearby attempt. Generally, if an epidural lead can be placed and an absence of CSF is seen at the skin despite different patient positions, and sufficient post-procedural time has elapsed, it is likely safe to send the patient home with education on surveillance and instruction on quick notification and return to the clinic for management if CSF is seen. Prophylactic blood patch is initially discouraged as may increase risk of infection.

Ease of lead manipulation increases with experience, but several tips aid the neophyte. Lead advancement generally occurs with the nondominant hand, and steering, either by manipulation of the steering stylette, or the lead body itself with the other hand. As the degree of tip curvature increases, the lead turns more adroitly; however, once linear travel is desired, the curvaceous lead may become more fickle. Advancement in a less than satisfactory direction (even in settings where a return to midline is anticipated) should also be avoided as the wrong path in epidural fat can become established and new vectors more difficult to establish. Exiting the needle with the lead is the most difficult point at which to establish good lead control, and fortunately, when the lead tip is still close to the needle tip rotating, the bevel of the needle can provide additional control. If good lead control remains elusive early in the course, consider reestablishing the entrance in the epidural space more centrally.

Partial withdrawal of the stylette may allow a straighter tip for periods of linear advancement and may also allow

easier entry from the needle into the epidural space in cases of steep needle angle, tender dura or nerve, or in cases where the lead prefers to steer laterally as opposed to midline. Occasionally, use of the straight stylette is suggested when axial lead integrity is required with a straight lead tip.

Once the desired location is reached, intraoperative testing ensues. Success is most likely when the target neural tissue is depolarized, generating paresthesia in the area of the patient's pain. The target should lie near the middle of the electrode array as if axial lead migration occurs reprogramming success is likely. Extensive work has been done not only with computer modeling but also with retrospective investigation regarding lead placement and neural recruitment [62, 80–91]. Ideally, the cathode should capture the target with low pulse width and amplitude, placing the paresthesia in the center of the pain. This will allow for wider paresthesia with increasing amplitude and pulse width. This concept is crucial, and testing is easily performed rapidly by the implanter and assistants using newer rapid programming algorithms, essentially trolling the lead for the best target and rapidly testing hundreds of permutations. If testing reveals paresthesia in the dermatome corresponding to the dorsal root entry zone fibers near the electrode, then the array may be too lateral, but this may be desirable as depolarization of first-order neurons may provide quite meaningful paresthesia. If very low amplitudes produce paresthesia, this signifies close and possibly undesirable proximity to either cord (in the intrathecal space) or nerve root itself.

Once the electrode array position is maximized, the needle and stylette are removed with attention to lead stability comparing pre- and post-removal fluoroscopic images. Prophylactic advancement of the lead by one to two electrodes prior to removal allows the implanter to pull down and reposition the lead back to the desired location with ease prior to anchoring. The methods for lead security or anchoring are multiple. Paramount in selection of technique is limitation of lead movement for the trial and especially limitation of cephalad movement as externalized; thus, contaminated lead can migrate into the patient. Because of this risk, often direct ligature of the lead to the skin is performed with direct tie to lead analogous to the technique used in securing a drain tube. Sacrifice of lead integrity for lead security may be warranted as trial leads are used for short duration. Significant work has been done on anchoring with several published approaches [92, 93]. Newer, titanium-sleeved, anchors from all companies may reduce likelihood of migration greatly.

After the completion of lead placement, there remain several important steps. Numerous and differing protocols for wound dressing exist; however, there are several universal maxims: patient comfort is paramount, strain relief coils protect inadvertent lead tension from influencing epidural movement, the location of lead taping should permit activities such as sleeping with minimal compromise, and most importantly, the dressing serves as a barrier to contamination of the operative site. Additionally, constant surveillance for infection, and education of the patient regarding such, is appropriate as epidural abscess demands early recognition and intervention [94]. The benefit of post-procedural oral antibiotics is unproven and debatable and, despite lack of evidence for use with most any surgery, remains a fairly common practice among American implanters. The main risk of indiscriminate use of postoperative antibiotics remains development of resistant strains of bacteria. The patient must additionally be educated regarding the sentinel signs of neural compromise as seen in evolving epidural hematoma as again early recognition and decompression radically improves outcomes [62, 95]. Lastly, the external pulse generator is programmed. Reprogramming soon after initial placement will be necessary, so prior to discharge tentative follow-up arrangement is made.

Dual and Triple Lead Techniques

While depolarization of target neural fibers is the aim, occasionally collateral and undesirable neural recruitment occurs. The clinical result is paresthesia outside the painful target, and while often tolerable, occasionally disagreeable stimulation limits the intensity and usefulness of the target paresthesia. Dual and triple lead approaches were developed not only to increase the redundancy and thus safety of the system but also to guard or hyperpolarize lateral fibers against the generated electrical field, or conversely to selectively activate those fibers [86, 96–101]. Percutaneous, three-lead arrays are thus a perfectly reasonable effort in spinal cord stimulation.

Single lead systems with expert placement satisfied many, but eventually gave way to transverse dual lead systems, allowing increased lateral control and with the introduction of lead splitters to transverse tripolar arrays and thus the ability to guard or hyperpolarize laterally entering dorsal roots and rootlets.

Technically, the introduction process into the epidural space of multiple leads is similar to a single lead. To pass all leads at the same interspace, however, requires either three separate needle placements or use of the Epiducer™ percutaneous lead delivery system (St. Jude Medical, Plano, TX) (see Fig. 39.6). Occasionally, the interlaminar space may be insufficiently accommodating for three leads, and multiple spaces must be used to complete access. Although using multiple spaces is acceptable practice, the efficacy of electrical field guarding is dependent upon the interelectrode proximity in separate leads acting in concert. Electrodes which are freely mobile *in relation to others in the same montage* present a dynamic and often ultimately confounding programming challenge. While trialing, the instability of the system may be

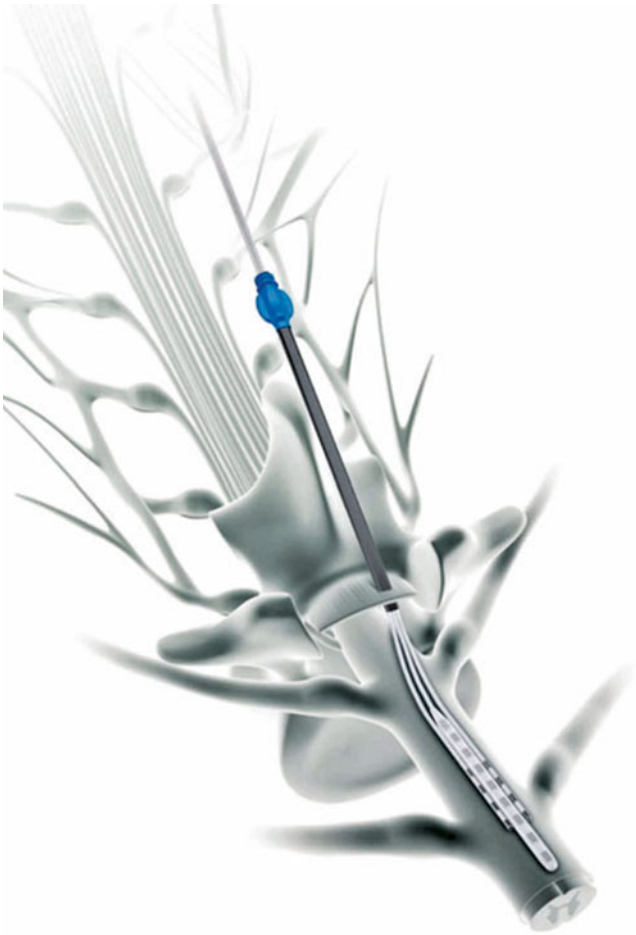


Fig. 39.6 Epiducer (St. Jude Neuromodulation) lead introducer

overcome by frequent reprogramming; however, once permanently implanted, every effort should be made to ensure a rooted and immutable electrode array. Leads entering at the same interlaminar space permit anchoring to contiguous tissues and perhaps even to each other. As the superiority of tripolar arrays over dual column arrays has yet to be established, the Achilles heel of the percutaneous tripolar technique may lie in the inherent difficulty in producing montage stability. The Epiducer™ may greatly benefit this effort as it allows percutaneous, three-lead implantation all from the same site. Additionally, Epiducer™ allows placement of dual paddle lead or tripolar arrays, utilizing both paddle and percutaneous leads deployed through the same entry.

Electrode Placement in the Cervical Region

Electrical modulation of neuropathic pain in the upper extremities generally requires cervical lead placement. However, possibly, also treated by cervical neuromodulation may be intractable neck and upper extremity pain [102, 103], neuropathic facial pain [104], unstable angina [105], four-limb neuropathic pain [106], headache, craniocervical pain [107], as well as low-brain perfusion syndromes [108, 109]. In addition, some literature argues that cervical and lumbar devices for the treatment of chronic regional pain are similar in efficacy and safety [110]. With cervical stimulation, similarity exists in lead introduction and steering, but the architecture differs significantly from the more capacious canal of the thoracolumbar junction, where most implanters are comfortable. Entering the space at a level with posterior displacement of the cord, for example, places the patient at increased risk. Of additional concern is the increased mobility of the cervical canal, which may also increase the likelihood of lead migration, but also yield an unwanted higher variability in paresthesia intensity based on neck movement. Bracing in the postoperative weeks may limit movement and permit the leads to scar into place. Pre-procedural awareness and review of imaging of the canal and approach is required as well as attention to the dynamic nature of the anterior and posterior column, which may in time degrade further diminishing the available space for the cord. Entering the dorsal epidural space several levels caudal to the cervical spine allows the lead plenty of distance for stability. Many implanters enter the canal at the typical thoracolumbar junction and then tunnel cephalad all the way to the cervical cord. This approach minimizes the need for extensive extra-canal tunneling, but the increased distance from the lead array to the anchor may amplify the risk of lead migration. In addition, the implanter must have survey a completely patent canal from a low entry to high placement, and this may not always be present, especially in postoperative spines.

Similar to thoracic placement, cervical lead placement allows multiple locations for implantable pulse generator (IPG) implantation with the same aims: to minimize discomfort and likelihood for migration and complication. Many implanters continue to tunnel to the buttock, while others place the IPG in the precordial area, posterior axillary line, or even in the soft tissue of the high back. Success is largely dependent upon selecting a location which does not interfere with underwear, clothing, or sleep and allows the patient to manipulate programs and charge the IPG if appropriate. Lastly, it is advisable to confirm and document preoperative discussion with the patient with skin marking confirming the patient's choice of location.

Programming

It is beyond the scope of this chapter to attempt to fully present the depth of knowledge regarding stimulation of the dorsal columns. However, familiarization with several tenets of programming will serve the implanter well. Norman Shealy [1] nearly 45 years ago was restricted to the same

parameters of stimulation as today: pulse amplitude (I) measured in either milliamperes (mA) or volts (V), pulse width (PW) measured in microseconds (ms), and frequency of pulse (F) measured in cycles per second or hertz (Hz). With conventional SCS systems available today, analgesia can only be provided when evoked paresthesia overlaps at least the majority of painful body areas and this should be the first aim [111–113]. Once the electrodes are placed, refinement of stimulation must occur via programming. Depolarization occurs secondary to electrical field generation near neural tissue.

Despite a long-held belief that the dorsal columnar fibers are activated in SCS enabling the gate control system and thus suppression of ascending afferent pain signals, most predictive models, however, suggest that secondary to their large size and the law of fiber recruitment, it is the dorsal root fibers that are first activated [10, 114, 115]. Stimulation of both cord and nerve root causes paresthesia and either may be useful, but generating useful paresthesia from depolarization of dorsal column fibers requires either medial electrode placement, guarding of lateral fibers, or lower energies.

Pulse energy and thus the threshold of neural depolarization is a product of the stimulus strength (amplitude) and stimulus duration (pulse width). A curvilinear strength-duration curve relationship exists between the two so that with increases in either amplitude or pulse width so too does the likelihood of neural recruitment [79, 116]. Holsheimer et al. show that increases in pulse energy translate into sequentially larger recruitment fields of neural fibers relative to the cathode resulting in increases in the perceived area of paresthesia [81]. Specific widening of pulse width translates into caudal extension of paresthesia area as the larger and smaller dorsal column fibers have a mediolateral distribution [79]. The limit to increasing energy and thus density of paresthesia is often painfully intense stimulation of lateral dorsal root fibers. To this end, bipolar, tripolar, and ultimately five-column arrays were developed in order to apply dense electrical fields to the cord with increasing specificity in medial to lateral arrangement while guarding the lateral entering dorsal root nerve fibers.

The majority of neuronal excitation occurs in the vicinity of the cathodal electrode, and with monopolar stimulation, the threshold stimulus of the anode is about five times that of the cathode [90]. Also determined by the same study was that the influence of the anode on recruitment area was negligible at any distance beyond 30 mm. The anode does, however, have significant impact on the shape of the cathodal field within that distance and can be used to "steer" or "block" the field. With bipolar stimulation, Holsheimer et al. [88] showed an ability to block the propagation of action potentials near the anode, thus guarding the lateral neural tissue from stimulation (see Fig. 39.7).

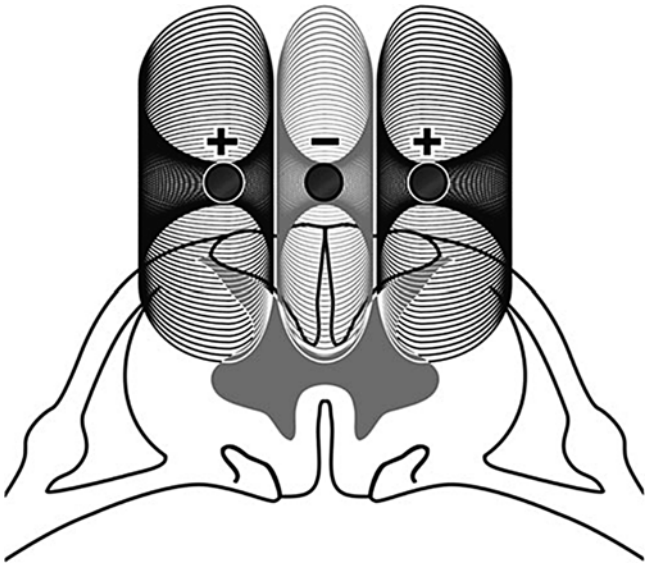


Fig. 39.7 A tripolar array demonstrating the effect of anodal blocking

The Tunneled Trial

Performing a tunneled trial adds additional complexity and secondary to the use of an incision, possible infection risk, and therefore must be performed in a controlled operating environment. Prior to tunneled trialing, considerations usually saved for the permanent implant should be made preoperatively: IPG pocket placement and tunneling requirements should be anticipated; adequate lead lengths and extension lengths should be considered.

Lead placement is carried out in similar fashion to percutaneous trialing, but once the leads are placed, the incision is dissected down to thoracodorsal fascia and to the point of lead penetration. The leads are then anchored to the fascia using permanent anchoring techniques. Enough lead should remain to allow tunneling to the pocket with sufficient strain relief, or shorter leads are selected with anticipation of permanent extensions. Undermining, pocket creation and tunneling is then performed contralateral to the ultimate IPG pocket location. This pocket will house any redundant lead and lead extension. Often, the cutdown is performed with the needles in place if this is the case, either bipolar cautery is suggested or the epidural needles should be pulled sufficiently back to prevent electrical conduction to intraspinal contents. From this pocket, a tunnel is formed laterally away from the midline incision and ultimately out through the skin. Lead extensions, once connected, are passed out, and the midline incision is irrigated and closed.

If, upon completion of trialing, permanent implantation is desired, then the surgeon reopens the midline incision, disconnects the trialing extensions and removes them clean to

dirty, irrigates clean to dirty, and then closes the proximal portal to the tunneling track. Pocket creation can be made from the midline incision using blunt dissection away from the tunneled side, or an additional incision for pocket creation may be made opposite to the side of trial tunneling and then the leads either tunneled to the pocket or extensions used. Argument against use of extensions includes the possible increase in system complexity and points of failure as well as scar formation about the extension headers and thus increased lead strain [117]. If the trial fails the patient, then removal of the system is the aim. Reentry into the midline incision is required to dissect the anchors and remove the lead array.

Permanent stimulator implantation requires the same attention to detail, hemostasis, and sterility that any open spine procedure demands. If the trial is successful, it has not only shown the patient the possible impact neuromodulation can have in their life but it has also informed the surgeon regarding neural targets, ease of approach, and need for specific patient positioning.

Lead Selection

Neuromodulation's early history was forged with a bipolar array with often-excellent coverage and paresthesia. Simple elegance had limitations; however, lead migration led to surgical revision, and complex pain patterns were more difficult to treat. Today, there exists an ever-expanding compendium of options to help and possibly bewilder the implanter. Despite these options, the goal is unchanged: well-placed, stable, and useful paresthesia delivered safely. As the complexity of the pain pattern increases likely, too will the need for complex electrode arrays. Trialing will commonly take place with cylindrical leads as they confer the advantage of easy removal, lower cost, and the general ability to allow good testing of the eventual array. Lead selection for the ultimate array is commonly dependent on the training of the implanter. Percutaneous access has until recently only allowed cylindrical lead deployment; however, the Epiducer™ (St. Jude Neuromodulation™, Plano, TX) does allow slim, single-column paddle, and multiple-lead deployment through a single needle stick. The individual leads' properties influence the decision.

Cylindrical leads offer ease of deployment and steering, can be used in trialing and permanent implant settings, do not require laminotomy for placement of removal, are generally thinner than paddle leads, and take up less epidural space. They may be placed in single, dual-columnar, and "tripolar" arrays [118]. However, they require greater energies than paddles for similar paresthesia, are generally more likely to migrate (but the incidence may fall with new anchors), and in the setting of thick dorsal cerebral spinal fluid as seen in the lower thoracic levels may require energies which recruit lateral entering fibers at painful levels, and lastly, if placed proximal to sensitive ligamentum flavum, flaval stimulation may preclude tolerable dorsal column stimulation. Additionally, if "current steering" or anodal blocking is required, the stability of an array with three independent columnar leads placed in tripole is tenuous. Occasionally, however, multiple neural targets may beg stimulation, distant to each other, and demand the plasticity of an array spread over longer distances, for example, the high-thoracic cord, lumbar nerve root, and cervical cord. Lastly, percutaneous electrode arrays can be placed "cross midline" with excellent coverage of lower extremities as well as buttock pain [119].

Paddle leads when compared to cylindrical ones use less energy as a whole, resist migration, are stable across the midline, and easily placed by most surgeons, but require special surgical skill for laminotomy. They are thicker, with dorsal shielding protecting the possibly sensitive flavum. The electrodes lie more ventrally and closer to the cord, further increasing electrical economy and fidelity with less likelihood of undesired dorsal root or rootlet stimulation. Removal is dependent upon a surgeon, often at the expense of additional laminar bone.

Multicolumn paddle arrays allow for single lead placement and complex and accurate electrical fields that may allow coverage of more complex pain patterns with single lead deployment.

Percutaneous paddle leads, while single column in design, allow for significantly lower energies and thus the reconsideration of primary cell batteries as long-term power solutions.

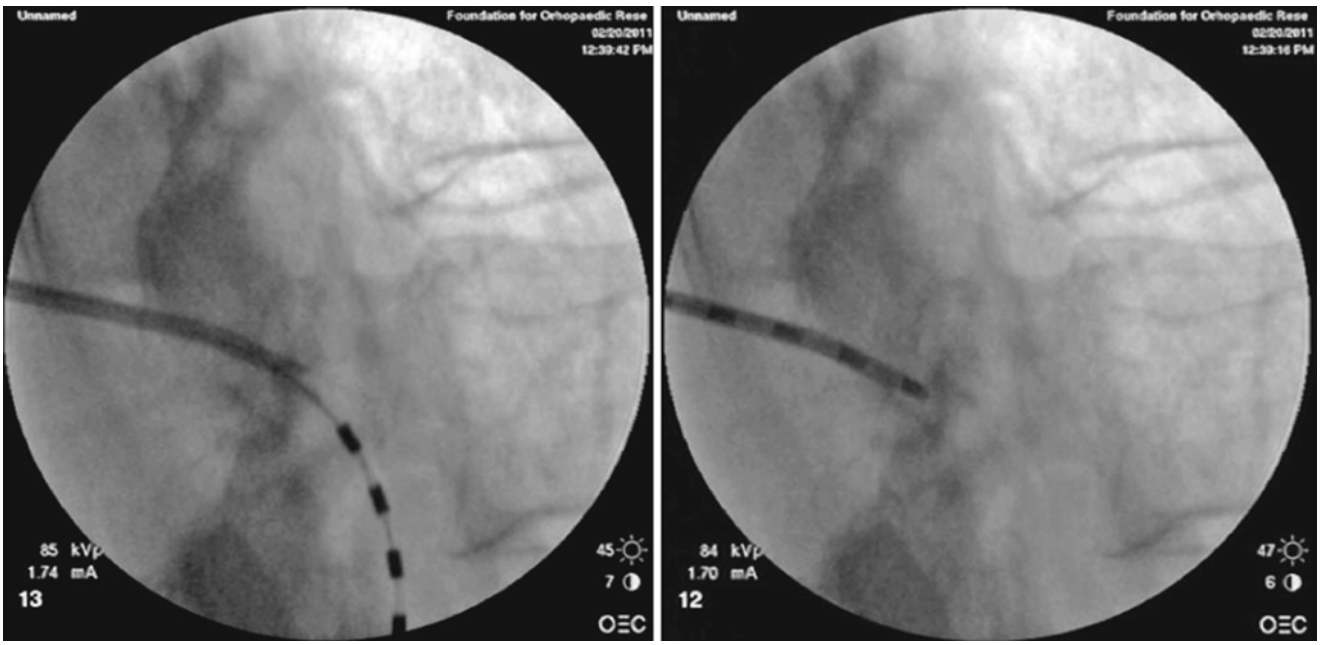
The combination of percutaneous paddle leads with guarding cylindrical leads through a single needle stick may provide increased stability of a tripolar system.

Implantable Pulse Generator Selection (IPG)

As with leads design, innovation in IPGs has been rapid, with improvements in rechargeability, size, and contact number. Presently, each company makes a rechargeable IPG; however, only Medtronic™ and St. Jude Neuromodulation™ make primary cell IPGs, and St. Jude alone continues to make a radiofrequency-powered IPG.

Each has distinct advantages and disadvantages.

Smaller than conventional IPGs, radiofrequency-powered units such as the Renew™ radiofrequency system from St. Jude Medical™ offer high power in 8 and 16 contact designs and relatively high-frequency ceilings compared to conventional IPGs. They require for use, however, an external power source, which may be cumbersome. They usually cost less than battery-powered or rechargeable IPGs. Once implanted, they last decades as cell depletion or failure is of minimal concern.



Figs. 39.8 and 39.9 A lateral fluoroscopic film demonstrating adequate angle for retrograde lead deployment

Non-rechargeable battery-powered IPGs, produced by both Medtronic™ and St. Jude Medical™, generally confer most of the benefits of rechargeable IPGs, but lack the ability for charging. Useful in situations requiring low-power consumption as in efficient arrays, they may also be beneficial in persons who do not want to or may not have the cognitive discipline to tend the rechargeable battery. Additionally, they cost less than rechargeable IPGs.

Rechargeable programmable IPGs confer the benefit of high-power output with the ability to recharge and thus greatly lengthen the time between IPG failure and thus system revision. The majority of implanted systems utilize rechargeable IPGs, as with innovation, their size too has diminished making them quite comfortable housed in a variety of locations with minimal vexation.

Lumbosacral Nerve Root Stimulation and Retrograde Approaches and Technique

Stimulation of the sacral nerve roots can be performed with retrograde stimulation of the cauda equina and as well as in usual antegrade fashion overlying the conus at the terminal cord around T12–L1. The approach can be somewhat more challenging, however, secondary to the normal lumbar lordosis. Additionally, placing percutaneous leads sagittally over the conus at such a mobile segment makes stability difficult. Placing the lead across the midline, however, crossing over the conus and passing through the plica mediana dorsalis durae matris may stabilize the lead [120]. In order to selectively stimulate a nerve root, the lead and thus stimulating electrode must be close to either the exiting nerve at its corresponding foramen or along the descending course in the fan of cauda equina caudal to the conus medullaris. For lower lumbar and for sacral nerve roots, this is best accomplished utilizing a retrograde needle approach and lead placement.

Sacral nerve root stimulation may be beneficial in the treatment of interstitial cystitis [121], painful bladder syndrome and chronic pelvic pain [122], fecal incontinence [123], and chronic anal fissures [124]. Similar to antegrade approaches, selection of interlaminar entry permits enough lead proximal to the electrode array for stability. As with every approach, planning begins with selection of neural target. The neural roots of L3 and roots caudad are most amenable to this technique. In the lumbar spine, the natural angle (in the cephalo-caudad dimension) of the laminar shingling steepens which each subsequent cephalad interlaminar space, limiting the easiest and functional entry points to just a few. This is clearly illustrated by the following technical description of technique.

Skin entry is determined by fluoroscopic angle. In terms of orbital travel angle, align the fluoroscope in sufficient caudo-cephalad angulation striving for maximum retrograde angulation, while allowing enough visual patency of the interlaminar space so as to permit passage of the usual 14-gauge introducer needle. Use of a coude-tipped introducer needle such as the 14-gauge epidural needle – RX Coudé®(Epimed, Irving, TX) allows a maximally diminished angle of incidence to the dura when entering into epidural space (see Figs. 39.8 and 39.9). Differing from antegrade

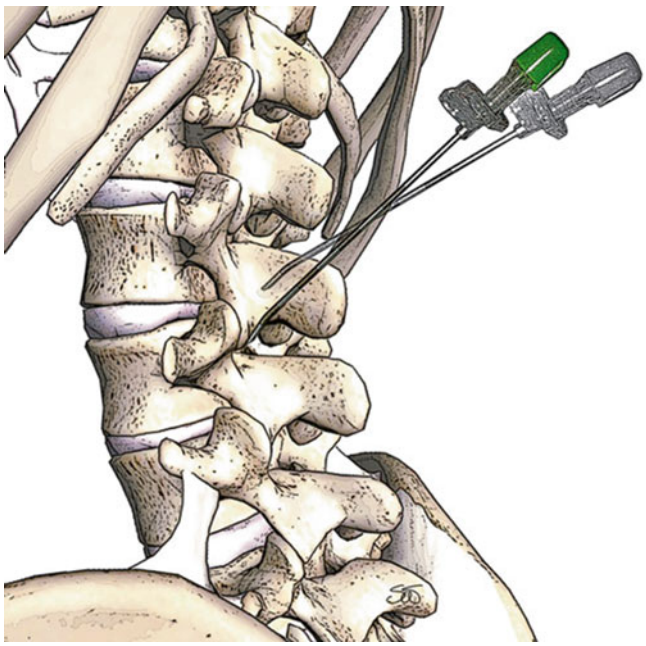


Fig. 39.10 Lateral view of "walking" the needle caudally off the inferior lamina before advancing through ligamentum flavum as used in retrograde lead deployment technique

needle introduction, the angle of fluoro greatly approximates the angle of needle introduction. Select for skin entry a site overlying the inferior edge of the superior lamina just paramedian to midline. From this point, guide the needle deeper to the superior laminar edge just selected. The needle will be very close, if not exactly in plane and on point with the x-ray beam. Once contact is made, increase the retrograde angle and walk inferiorly the needle tip off the inferior lamina into the interlaminar space (see Fig. 39.10). Advance as experience allows, confirming the depth on lateral projections if necessary. Once contact with ligamentum flavum is made, remove stylette and advance with loss of resistance technique. The steeper the angle, the less compliant the lead will be to direction towards the midline. It will want to fall off to either side, generating either advantage or frustration based on the selected target. Guidance to more caudal neural targets, such as sacral nerve fibers, will be best served by an initially midline approach with later ultimate vectoring to the targeted fibers.

As lead pliability is increased with temperature as well as de-styletting, when passing the lead through the rather acute angle encountered at the needle tip, wait a moment to warm the lead in the needle, and partially withdraw the stylette before advancing lead out the needle tip. Attentive advancement is warranted not only because of the aggressive angle to the dura mater but also as the initial course of the lead greatly predicts the ultimate course.

Lead stability and durability at this highly mobile segment is critical. Using an anchor with a nose, such as the Cinch™ and Swift-Lock™ anchor (St. Jude Neuromodulation, Plano, TX), when placing a permanent lead may protect the lead through the extreme angle encountered as the lead curves and dives deeply to the epidural space. Additionally, undermining the wound superiorly for a strain relief pocket allows for the lead to continue cephalad reducing the lead deviation and thus stress before recurving to the IPG pocket.

Long-term tenability of both the lead and electrode arrays in retrograde placement is more challenging, and every effort to diminish movement in the postoperative, healing phase will benefit stability. Lumbosacral bracing or use of a postoperative abdominal binder may limit movement to allow scarring to occur.

Percutaneous antegrade lumbar and sacral nerve root stimulation may be tempting via a caudal approach through the sacral hiatus; however, caution is advised as with any perirectal surgery or procedure, there is increased incidence of surgical infection, and with indwelling spinal hardware, the consequences can be disastrous. If lead migration plagues the retrograde approach, surgical consultation for sacral laminotomy or laminoplasty with paddle lead placement may be the most stable and sterile option.

The Permanent Implantation

The decision to permanently implant the electrode array is one made jointly with discussion between the patient and physician. Information obtained by the trial such as the appropriateness of neural targets, whether different lead locations would be more clinically useful, and the utility of the therapy for particular complaints influences planning for the permanent implantation. Additionally, configuration of the system and IPG placement must be discussed with the patient taking into account handedness, adiposity and body mass, and clothing preferences, especially important being constricting belt lines, dexterity, sleeping preferences, power requirements, and IPG selection. The implanter may want to consider referral for surgical paddle lead implantation for a variety of reasons: while trialing, painful ligamentous stimulation was unavoidable, power requirements were very high, complex pain patterns demanded specifically focal paresthesia, or due to complex canal anatomy or cord rotation, consistent paresthesia was difficult to elicit. Variable intensity as a function of position is often secondary to thick dorsal cerebral spinal fluid at the thoracic levels; paddle leads may ventrally displace the dura diminishing the effect of position on paresthesia intensity. Lastly, if the physician is uncomfortable with, or inexperienced with permanent implantation, the surgery should be referred to a more seasoned implanter, or surgeon familiar with the process.

As previously mentioned, identification and then diminution of surgical risk is paramount especially in terms of infection, cardiac status, bleeding, and identification of postoperative compliance issues. Permanent implant begs a full preoperative clearance from the patient's primary physician. However, development and implementation of a preoperative information and risk-screening packet reviewed with the patient ensures consistency and lowers the likelihood of unforeseen circumstances affecting the implant.

In the preoperative holding area, the physician should mark the operative site, but more explicitly focusing on IPG location and lead pathways. Once preoperative antibiotics are infused, the patient is moved to the operative suite with attention to previously mentioned details.

Several variations in percutaneous implantation exist.

Leads placed first: With this approach, the introduction needles are deployed through the skin, much like a trial, and then after appropriate lead placement, the initial incisions are created. The midline incision either passes through both needle incisures, or is created along the sagittal midline between the needles down to the thoracodorsal fascia then undermining to access the needles as they pass through the fascia. Needles are then removed and leads anchored to fascia, ultimately tunneled to the pocket. Attractive with this approach is the ability to ensure lead placement prior to the committal that occurs with making an incision. However, the undermining process, which essentially must be made with the needles in place to protect the lead from the scalpel, is somewhat awkward and may increase risk of needle movement and possible dural injury. Also, the use of monopolar cautery is discouraged with needles passing to epidural space for risk of intraspinal conduction. This risk is minimized if nonconductive introduction devices are employed.

Incisions made first: Forming the pocket early in the surgery and then packing the pocket with gauze increases intrapocket pressure, limits bleeding, and may help prevent seroma formation later. Additionally, in making the incisions first, the use of cautery is limited only by the preoperative status of the patient, as no needles are yet intraspinal. The main drawback of the technique is the obvious: if spinal access is thwarted, then the patient has risked incision for nothing. However, experientially, if one level is particularly difficult, adjacent levels and patient perseverance often rewards with success.

Prior to incision, cutaneous and then deeper soft tissue anesthesia and hemostasis can be achieved with infiltration of local anesthetics with epinephrine. While there may be a dearth of literature supporting cutaneous anesthesia for control of postsurgical pain [125], preemptive analgesia has been shown to improve postoperative pain control [126]. More importantly, adequate local anesthesia promotes patient comfort thus diminishing patient movement and allows very light to no sedation during lead placement. Additionally, useful is infiltration with local anesthetic, appropriate for use in spinal blockade, all the way down to the lamina along the anticipated lead introducer track. With good local anesthesia, the patient can be surprisingly comfortable intraoperatively, allowing intimate and cogent feedback regarding the appropriateness of paresthesia coverage, as well as possible neural compromise.

Attention to hemostasis and development of a skill set with facility using electrocautery, intra-wound pressure, hemostatic agents, and vessel ligature is vital not only for patient safety during the operation, but also the elimination of dead space and loculated fluid or blood collection during wound closure diminishes infection and seroma risk postoperatively.

The parasagittal incision should be carried down all the way to the posterior thoracodorsal fascia and associated spinous processes. Some undermining may be needed to allow good angle for the lead and anchor, but it is important to expose fascia as anchoring must be to a stable substrate to minimize lead migration. Once the lead is deployed and testing confirms optimal placement, it is important to fluoroscopically confirm the lead has maintained location through the processes of de-styletting, needle removal, and anchoring. Saved fluoroscopic images document the placement.

Anchoring is a minimally studied component of the process, but it appears the inclusion of an internal, metal sleeve such as titanium improves stability compared to Silastic material alone [127]. All current companies now produce a metal-sleeved anchor. Nonabsorbable suture such as Nurolon™ or Ethibond Excel™ (Ethicon, New Jersey) provides excellent long-term strength with minimal tissue reaction, especially compared to silk [128].

Creation of the IPG pocket, despite being deceptively easy, merits attention. As noted previously, anatomic location and documented communication with the patient are essential. The pocket should be of sufficient depth to allow good protection from the skin and the external environment, clothing, and bumps against hard objects, but still superficial enough to allow communication and charging. Too large a pocket encourages seroma formation and allows movement. Too small a pocket may predispose to wound dehiscence and poor wound edge approximation, so the pocket should be just large enough to house the IPG and associated redundant lead and connectors if used. Implanting particularly thin patients may present challenges regarding pocket pain in time. If during pocket creation there appears to be insufficient adipose to protect the IPG, incising and then undermining the thoracodorsal fascia, gluteal aponeurosis or local fascia, and placing the IPG sub-fascially may protect against painful trauma to the subdermis. Additionally, closing the fascia over the IPG improves wound and skin approximation and reduces tension upon the closure. While seromas are

very rare with this technique, IPG migration may be a bit more common, so a stitch ligating the header to the fascia may be advantageous. Tunneling to the pocket can be quite painful requiring either deeper sedation or local anesthetic infiltration of the anticipated needle track.

While culminating the procedure, wound closure and wound dressing are critical last steps; done adeptly, they secure and protect the system from infection and migration. Seeing the approaching finish line, it may be tempting to rush the closure; but time and attention spent here will mature into dividends later. Wound irrigation diminishes bacterial counts [129] and reduces incidence of early and late postoperative infections [130]. Multilayer closure is used for gentle approximation without dead space until tissues restore their intrinsic strength and wound healing is complete. While the tissues undergo repair, the strength of the wound remains dependent upon the suture and thus the surgeon's attention to detail and discipline [131]. Running suture, while expedient, risks wound dehiscence as any compromise of part of the suture results in unraveling and large areas of wound compromise. Skin closure aims for excellent wound edge approximation and cosmesis.

Despite great variation in postsurgical wound dressing, the intention of the dressing is uniform: to protect the wound from soilage and bacterial contamination, to add integrity to the underlying wound closure if possible, to provide thermal regulation and an optimum environment for wound healing, and ultimately, to provide comfort to the patient.

Conclusion

The evolution of neuromodulation of the spinal cord has, if anything, been marked by rapid innovations, trials, failures, and often successes that astound even the most seasoned implanter. The majority of advancement arguably lies ahead. The expanding compendium of lead selection and power sources, refinement of new waveforms and high-frequency stimulation, percutaneous options for paddle lead placement, accelerometers for energy control, MRI compatibility, systems that sense their environment, and innumerable other innovations all seek to expand the role and efficacy of SCS in the treatment of pain. What will challenge physicians and patients most in the coming years, however, will be the shifting financial substrate on which all of medicine rests. Payers will demand more rigorous evidence of fiscal rationality, and all will ask for more compelling scientific data supporting efficacy. While it may appear that our immediate responsibility of individual patient safety and outcomes is our sole concern, we have a deeper, collective accountability to judicious use, adherence to safe practices, and an empiric substantiation of our claims that SCS is safe, effective, and when appropriately paired, life changing.

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Brain Stimulation for Pain

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Konstantin V. Slavin

Abbreviations

CCH	Chronic cluster headaches
CT	Computed tomography
DBS	Deep brain stimulation
DREZ	Dorsal root entry zone
ET	Essential tremor
FDA	US Food and Drug Administration
MCS	Motor cortex stimulation
MEG	Magnetoencephalography
MER	Microelectrode recording
MRI	Magnetic resonance imaging
OCD	Obsessive-compulsive disorder
PAG	Periaqueductal gray area
PD	Parkinson disease
PET	Positron-emission tomography
PNS	Peripheral nerve stimulation
PVG	Periventricular gray area
SCS	Spinal cord stimulation
STN	Subthalamic nucleus
TRD	Treatment-resistant major depression
VPL	Ventroposterolateral nucleus of thalamus
VPM	Ventroposteromedial nucleus of thalamus

Key Points

- Deep brain stimulation (DBS) in treatment of pain has a long and fascinating history that includes a decade and a half of its widespread use for variety of indications in the mid-1970s to the late 1980s.
- Use of DBS for pain greatly diminished after its approval for this indication was rescinded by FDA due to lack of conclusive evidence regarding its effectiveness.
- Most commonly used targets for DBS in treatment of pain include sensory nuclei of thalamus (primarily, ventroposteromedial and ventroposterolateral nuclei) and "central gray" matter (periaqueductal and periventricular gray areas).
- Currently, DBS is being explored as an option for otherwise refractory chronic cluster headaches, and the initial clinical results are quite encouraging.

Introduction

In the ever-advancing world of neuromodulation, use of electrical stimulation for pain relief has been a dominant theme – mainly due to wide acceptance of spinal cord stimulation (SCS) over the last four decades and, more recently, with rebirth of peripheral nerve stimulation (PNS) approach. The relative simplicity of these interventions resulted in a shift among practitioners who use it – and if in the beginning most neuromodulation procedures were done by neurosurgeons, vast majority of both SCS and PNS systems are now implanted by non-surgeons, primarily anesthesiologists and physiatrists who specialize in the field of pain medicine. Even those interventions that in the past required neurosurgical expertise – laminectomy for insertion of SCS paddles and nerve explorations for placement of PNS electrodes – are now frequently done by our orthopedic and plastic surgery colleagues.

The only target of neuromodulation where neurosurgeons proudly keep their surgical monopoly is the brain. And when it comes to indications for cerebral neuromodulation procedures, one immediately thinks of movement disorders, Parkinson disease (PD), essential tremor (ET), and dystonia,

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all of which have been successfully treated with stimulation of thalamic nuclei or basal ganglia. More recently, this approach of electrical stimulation of deep cerebral structures – both in the white and gray matter, usually referred to as deep brain stimulation (DBS) – has been used in treatment of psychiatric conditions, primarily obsessive-compulsive disorder (OCD) and treatment-resistant major depression (TRD); mixed motor and behavioral disorders, such as Tourette syndrome; and refractory epilepsy. Gradually, DBS has become a standard in surgical treatment of some of these conditions – essentially replacing destructive interventions that were commonly used in the past.

In addition to stimulation of deep cerebral structures, surgical neuromodulation may also target surface of cerebral convexity. This approach, through either epidural or subdural electrodes, is referred to as cortical stimulation. While cortical stimulation has been tried for treatment of tinnitus, depression, poststroke weakness, tremor, and Parkinson disease, one of the best known indications is chronic neuropathic pain for which the contralateral motor cortex is stimulated with implanted electrode. Motor cortex stimulation (MCS) for treatment of pain is a subject of separate chapter in this book. Here, we focus on DBS procedures and their applications in treatment of chronic pain.

DBS for pain has long and fascinating history [27, 40, 69]. First mentions of electrical stimulation suppressing pain sensation came from laboratory animals in the 1950s [51, 61], and right around that time, first clinical experience in humans was reported by Heath [29, 30] and Pool et al. [57] when they investigated brain activity in variety of subjects. Soon thereafter, multiple publications described stimulation of deep cerebral structures in patients with different clinical conditions [22, 47, 75], primarily with cancer pain and other refractory pain syndromes.

Instead of discussing different mechanisms of action that have been proposed to explain DBS effects in chronic pain, we will briefly go over the targets for DBS interventions, some basic procedural details, and the reasons why DBS is rarely utilized in contemporary clinical practice. Interested readers may gather more in-depth information from multiple recently published reviews [12–14, 25–27, 36, 40, 53, 69] as with decline in number of DBS procedures worldwide and almost complete abandonment of this approach in the United States, detailed literature reviews seem to outnumber original case series.

Targets for Deep Brain Stimulation in Treatment of Pain

Over the several decades since DBS was introduced, multiple targets have been explored – frequently with very encouraging initial results. Published reports concentrated on various distinct cerebral regions that represent different components of the pain-processing system including sensory pathways of the midbrain and their relays in thalamus, parts of the limbic system, and connections between the sensory and limbic areas.

Among the most commonly used targets are lemniscal system and thalamic nuclei that were explored as early as the late 1960s due to their known involvement in the processing of somatic pain [31, 45, 46, 50, 65]. Around the same time, the septal area [22, 66] and the internal capsule [3, 18] were successfully tried for pain control. Somatotopic organization of the posterior thalamic nuclei allowed one to selectively stimulate those parts that correlated with location of pain [73]. Production of paresthesias in the region of pain distribution supported use of thalamic DBS in cases of neuropathic pain, with medial locations (ventroposteromedial (VPM) nucleus) used in treatment of facial pain [31] and lateral locations (ventroposterolateral (VPL) nucleus) used for treatment of pain in the extremities [45]. Similar to other neuromodulation approaches (SCS and PNS), VPM and VPL DBS elicit paresthesias in the contralateral face or body areas, and as long as the paresthesia location matches location of the neuropathic pain, the pain relief is expected. In addition to that, medial thalamic nuclei were stimulated due to known involvement of this part of the thalamus in pain and emotional processing [8, 65, 72].

Although this approach was effectively used for neuropathic pain and associated phenomena, it was less effective for truly nociceptive pain conditions. For this group of indications, stimulation of periaqueductal gray matter (PAG) and periventricular gray matter (PVG) was suggested and tried. Since PAG and PVG (so-called central gray) are involved in descending modulation of pain, it is indeed conceivable that stimulation of this region would suppress nociception and produce pain relief through either monoaminergic [4] or opioid-mediated pathways [63]. The opioid hypothesis was supported by finding both endorphin-like [6] and enkephalin-like [7] substances in ventricular cerebrospinal fluid during PAG/PVG stimulation and by reversal of analgesia that it produced with administration of naloxone [2, 5, 32]. However, since these findings were rather nonspecific and not consistent, it was concluded that the mode of DBS action in generation and suppression of chronic pain is so far unknown [33, 48, 76].

Finally, the last target from the traditional era of DBS for pain (before its approval was rescinded by US Food and Drug Administration (FDA)) was the medial parabrachial area of the rostral dorsolateral pons, particularly the Kölliker-Fuse nucleus [78]. Stimulation of this area was reserved for the patients who failed to improve or improved only temporarily with either thalamic or PVG/PAG DBS procedures.

The aforementioned decision of FDA to rescind approval of DBS for treatment of pain was based on less-than opti-

mal results of two multicenter studies [13]. These studies were put together by Medtronic (Minneapolis, MN), the sole manufacturer of DBS equipment at that time, and failed to reach expected endpoints thereby negating positive findings reported in multiple large series published in the 1970s, 1980s, and 1990s [17, 26, 33, 35, 36, 41, 49, 50, 56, 60, 63, 64, 71, 77]. Nevertheless, the clinical experience continued to accumulate with several enthusiastic centers worldwide although most recent series came from outside of the United States [16, 28, 34, 53, 58, 59]. In addition to general series dealing with nonuniform cohorts of patients with neuropathic and nociceptive pain, there are now dedicated reports on use of DBS in treatment of poststroke pain [52], trigeminal postherpetic neuralgia [23], neuropathic pain in head and face [24], phantom limb pain [11], and pain due to spinal cord injury [58].

Low efficacy of DBS for pain and loss of its regulatory approval were not the only reasons for its gradual decline. The other treatment modalities such as improved nonsurgical means of pain control, more versatile spinal cord stimulation devices, and introduction of intrathecal opioids provided better choices for the patients and clinicians. In addition to that, not-so-low rate of complications made the entire modality less attractive, particularly when it is used exclusively on "off-label" status.

The concept of DBS for pain was reborn with discovery of discrete activation in hypothalamus during attacks of cluster headaches in 1998 [43]. Followed by discovery of similar pattern in patients with other painful conditions that involve face and head, such as short-lasting unilateral neuralgiform headaches with conjunctival injection and tearing, hemicrania continua, and paroxysmal hemicranias [42], a group of neurosurgeons implanted DBS into ipsilateral hypothalamus of a chronic cluster headache (CCH) patient [37]. This was followed by experience with bilateral implantation in a patient with bilateral symptoms [38] and then by several series of patients with intractable CCH [10, 19–21, 39, 67, 70] as well as other headache syndromes [9, 74]. Although the results were far from uniform with documented failure in some patients [55] – if anything, very similar to the past experience with DBS for other pain syndromes – and there was a mortality reported from DBS procedure in this otherwise nonfatal condition [67], hypothalamic DBS remains perhaps the most promising DBS application today, mainly due to severe disability and relative refractoriness of CCH and hemicranias to conventional, less invasive treatments.

Deep Brain Stimulation Procedure

Technically, DBS for pain uses very similar – or even identical – approach to DBS for movement disorders (PD and ET). The surgery usually consists of two parts with the first one done under local anesthesia and the second under general anesthesia. Stereotactic approach is used for implantation of DBS electrodes. The coordinates for stimulation target(s) are calculated based on MRI of the brain that is obtained prior to the surgery itself. Even though frameless DBS is gaining popularity, most centers continue using frame-based approaches for DBS when it comes to pain indications.

This means that the surgery starts with application of stereotactic frame. This is a metal contraption that is rigidly attached to the patient's head with several sharp pins. The frame serves as a reference for stereotactic coordinates and as a base for stereotactic surgical instruments. The pin insertion sites are anesthetized with local anesthetic, and then, once the frame is secured, the patient undergoes high-resolution stereotactic imaging, which may be either a brain MRI or a combination of CT scan with either MRI or ventriculography. In the past, ventriculography was the gold standard imaging modality, but it became replaced by CT and then by MRI as technology advanced. Currently, ventriculography is considered in surgical targeting for those patients who cannot have MRI and is used very rarely. The MRI may be done when the frame is already attached, or, alternatively, it may be obtained before the day of surgery and then "fused" with stereotactic CT of the brain. However, since the resolution of current MRI systems does not allow direct visualization of thalamic nuclei, the surgical planning is done based on the atlas coordinates that are referenced against classic landmarks. These landmarks include anterior and posterior commissures, height of the thalamus, and third ventricular width, all of which have been in use since the time of ventriculography. This atlas-based approach is expected to change once higher power MRI systems become available for clinical use as preliminary data from 7 T imaging indicate that direct visualization of thalamic nuclei is indeed feasible [1], similar to the change in DBS practice since the introduction of 3 T MRI allowed better direct visualization of subthalamic nucleus (STN) [68].

Once the imaging and subsequent surgical planning are completed, the electrodes are implanted using a standard approach, usually from pre-coronal burr hole, with trajectory planned in such a way that blood vessels and ventricles are avoided. Physiological confirmation of target correctness may include microelectrode recording (MER) depending on the target and the surgeon's preference, but must include macrostimulation in order to determine thresholds for desired effects and for side effects.

Once the physiological testing is completed, the DBS electrode gets inserted into desired location, and its position is routinely confirmed with intraoperative fluoroscopy and postoperative CT scan. The hardware for DBS is beyond the scope of this chapter – but it is worth mentioning that the originally used DBS electrode with four separate stimulating contacts (model 3380, Medtronic, Minneapolis, MN) was

discontinued in the early 1990s. The next model of DBS electrode (3387) was eventually approved by FDA for ET and PD treatment. With this approval, DBS electrodes remain available for other indications such as treatment of pain but only on an "off-label" basis [13].

DBS electrodes that are implanted into desired location are secured to the skull with cement, metal plates, or special locking devices. For the purposes of stimulation trial, a temporary extension cable is then connected to each electrode and tunneled under skin to a distant exit site. During this trial, the patient and surgeon determine whether DBS results in expected improvement and if there are any side effects that would prevent long-term DBS use. In case of implantation of multiple electrodes, a decision is made whether all of them are needed for best clinical effects. Following this trial that usually lasts a week or so, the implanted electrodes are either removed if the trial fails or get internalized if the trial succeeds. Internalization is performed under general anesthesia, and the permanent extension cables are tunneled toward the generator site which usually gets implanted in the infraclavicular region.

Postoperative DBS Management

The programming of DBS devices implanted for treatment of pain is similar to other neuromodulation applications, such as SCS for pain and DBS for movement disorders. The parameters of stimulation greatly depend on location of the DBS electrode contacts. In the early days, these electrodes were placed either in the thalamic nuclei, in the internal capsule, or in the central gray areas (PAG/PVG). More recently, it has become a common practice to put electrodes into both thalamic nuclei and central gray and then decide which one of them will be internalized or whether both areas need to be stimulated for optimal pain relief. The choice of the best contacts and stimulation parameters is determined by degree of pain relief, but since it may not occur immediately, attention is paid to location of paresthesias, particularly in the case of thalamic sensory nuclei, and to presence and tolerability of side effects that may be quite pronounced. At the same time, there is certain "insertional effect" where almost a half of patients in one series had a substantial improvement in pain severity in the absence of stimulation [28]. This may necessitate certain delay in the beginning of active programming following device implantation.

Most common side effects of DBS for pain are relatively minor. The transient headache occurs in more than half of all patients [36]. In addition to this, there are multiple issues related to the location of the electrodes – the proximity of PAG/PVG to oculomotor centers explains complaints related to double vision, blurred vision, and oscillation of objects in the visual field (oscillopsia), as well as sensation of nausea. Objectively, these patients may present with nystagmus and gaze palsy. Most of these phenomena, however, are transient and short-lasting. The stimulation-related sense of impending doom and severe apprehension are sometimes observed in PAG stimulation therefore limiting the patient's willingness to use the device [77]. PVG stimulation, on the other hand, may produce sense of diffuse warmth and/or well-being – and in several cases, this difference in associated sensations necessitated electrode repositioning [77].

Technical complications related to the insertion procedure and to the presence of implanted hardware include hemorrhages, sometimes fatal, ranging in incidence between 2 and 4 %, and infections in 3–13 % of cases [40]. Permanent neurological deficits were reported in 2–3.4 % of cases with mortality between 0 and 1.6 % [40]. Interestingly enough, duration of externalized trial did not correlate with the incidence of infections [36].

Inevitable and unavoidable risks associated with DBS appear to be another deterrent to its wide acceptance (and to its regulatory approval for this indication). One, however, has to take into consideration that the alternative treatments of severe and chronic pain are not absolutely safe either – and the recently reported incidence of mortality from intrathecal morphine in non-cancer pain patients reaching 3.89 % in 1 year [15] is an example of dangers associated with "less invasive" treatment modalities.

Future of Deep Brain Stimulation for Pain

It appears that despite its long history, DBS for pain will remain a rarely used modality in foreseeable future. Things may change if a new study performed in accordance with modern standards and expectations [14] shows its effectiveness and safety. However, with a general lack of enthusiasm among device manufacturers and, more importantly, in the neurosurgical community, the chance of such study happening anytime soon is rather low. An "off-label" status plays a major role in this – but one has to keep in mind that this situation is not the main reason for low DBS for pain utilization. Rather, this "off-label" status is the reflection of low efficacy and even lower enthusiasm toward this modality.

Despite this, there may be several incentives for DBS development. First, there may be a better definition of surgical indications and associated targets – similar to what we saw when DBS was explored for treatment of cluster headaches after an imaging-derived abnormality became a target for surgical intervention.

Second, the better understanding of DBS mechanisms in treatment of pain may strengthen a rationale for its clinical application. In the past, this was done with magnetoencephalography (MEG) [34] and positron-emission tomography (PET) [16, 44, 54] whereas pursuit of MRI-based investigations [62] was hindered by MRI incompatibility of implanted

hardware. With continuous strive toward development of MRI-compatible devices, it is conceivable that in the near future, we will be able to investigate DBS effects and perhaps define better responders during the stimulation trial or even preoperatively based on the imaging findings.

Lastly, new devices in the field of neuromodulation may be designed to specifically address needs of pain surgery – having multiple miniaturized contacts that may be stimulated simultaneously or independently from each other based on the patient's individualized and ever-changing requirements.

There is a definite need for more effective and safe pain interventions that may be used for a selected group of patients that are refractory to other modalities. As a part of busy pain surgery practice, I, like many others, frequently receive referrals for DBS or simply "brain stimulation," usually indicating that stimulation of everything "below the brain" has already been tried – and failed. Some of these patients, particularly those with intractable back pain, may qualify for intrathecal drug therapy. Others, like patients with brachial plexus avulsions and pain due to spinal cord injury, may require destructive interventions that include dorsal root entry zone (DREZ) and midline myelotomy. The patients with deafferentation pain including anesthesia dolorosa may be candidates for MCS. Similarly, some of the patients with intractable CCH and hemicranias may respond to PNS procedures that target their occipital and supraorbital nerves. Therefore, the resurrected DBS for pain will have to be compared with all these alternative approaches. And if DBS turns out to be safer and more effective, then it may replace some or all of them.

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Motor Cortex Stimulation

41

Chima O. Oluigbo, Mariel Szapiel, Alexander Taghva, and Ali R. Rezai

Key Points

- The management of central and peripheral neuropathic pain remains a daunting challenge for pain physicians in general and the functional neurosurgeon in particular.
- In spite of the increase in interest in motor cortex stimulation, its exact mechanism of action remains unknown.
- The main focus of preoperative planning is the localization of the motor cortex and its somatotopic arrangement and relationship to the relevant area of pain.
- Prediction of patient response to MCS is, at this time, based on response to a period of externalized trial stimulation. The development of techniques for predicting patient response to MCS noninvasively, such as the use of transcranial magnetic stimulation, will be an invaluable contribution to the management of these patients.
- Patients who have a successful trial are then returned to the operating room for internalization of the stimulator system. The scalp flap is only partially reopened during this second procedure to expose the MCS electrode lead that was coiled under the galea of the scalp at the first procedure.
- The outline of the precentral gyrus is projected onto the scalp using preoperative imaging fused with a frameless neuronavigation system. An appropriate incision centered over this region is made, and then, a 4-cm craniotomy, which is large enough to allow for epidural placement of a 4 × 4 electrode grid, is fashioned. The 16-electrode grid is then placed in the epidural space.

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Background

The management of central and peripheral neuropathic pain remains a daunting challenge for pain physicians in general and the functional neurosurgeon in particular. The reasons are manifold. Pharmacological advances in the management of neuropathic pain have been glacial with the only relatively new developments being the use of antiepileptics and antidepressants. Furthermore, the subset of these patients who present to the neurosurgeon have had this distressing pain for a long period of time and, having usually tried and failed numerous pain medications over this period of time, have developed psychological overlays such as depression, hopelessness, anxiety, personality disorders, and substance abuse issues.

The management of patients with intractable neuropathic pain can be of great challenge. A number of neurosurgical interventions involving various brain targets have been utilized to help these patients. These include deep brain stimulation (DBS), cranial nerve stimulation, lesioning,

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and motor cortex stimulation. DBS of the various regions of the somatosensory pathways has been performed, including the thalamic sensory relay nucleus – ventroposterolateral or ventroposteromedial (VPL/VPM) – periventricular and periaqueductal gray, internal capsule, and medial lemniscus. The outcomes have been mixed and in particular limited for central neuropathic pain. It was against this background that in 1991, Tsubokawa et al. first proposed the use of motor cortex stimulation for the treatment of central neuropathic pain [1]. Tsubokawa and colleagues were considering stimulation of the sensory and motor cortex as components of the somatosensory pathway and noted that stimulation of the motor cortex was more efficacious than the sensory cortex (REF). Tsubokawa's rationale for stimulation of the motor cortex was also based on observations in a cat model following deafferentation of the anterior spinothalamic tract. They initially noted burst hyperactivity of thalamic neurons recorded in these cats. However, complete, long-term inhibition of the burst hyperactivity was induced by stimulation of the motor cortex. Based on this experimental finding, they proposed that thalamic pain syndrome can be most effectively treated by chronic motor cortex stimulation. He then translated the procedure to seven human subjects with thalamic pain syndrome and reported "excellent" or "good" pain control in all cases without any complications or side effects.

Later, Tsubokawa et al. reported the use of motor cortex stimulation for the treatment of medically refractory central deafferentation pain in 12 patients with lasting pain improvement in 67 % of these patients [2].

In 1993, Meyerson confirmed the effectiveness of motor cortex stimulation in the treatment of neuropathic pain [3]. Importantly, he noted that all the patients with trigeminal neuropathic pain had significant improvement in their pain, while none of the patients with central neuropathic pain post-stroke improved, in distinct contrast to Tsubokawa's results.

In any case, since these reports, the interest in motor cortex stimulation grew rapidly as a result of the need for another therapeutic option in the challenging management of these patients with neuropathic pain. This interest is illustrated by a recent critical review of the literature on the efficacy and safety of motor cortex stimulation for chronic neuropathic pain in which Fontaine et al. reported 244 articles in the literature over a 15-year period (1991–2006) [4].

Mechanism of Action

In spite of the increase in interest in motor cortex stimulation, its exact mechanism of action remains unknown. Functional imaging studies are, however, providing insights into the mechanisms by which motor cortex stimulation (MCS) works to inhibit pain signal transmission in patients with central neuropathic pain. Positron emission tomography (PET) studies have highlighted the thalamus as the key structure mediating functional MCS effects [5]. Using PET, Garcia-Larrea et al. studied regional changes in cerebral blood flow (rCBF) in ten patients undergoing motor cortex stimulation for pain control [6]. They noted that the most significant MCS-related increase in rCBF was in the ventral-lateral thalamus, probably reflecting corticothalamic connections from motor areas. CBF increases were also observed in medial thalamus, anterior cingulate/orbitofrontal cortex, anterior insula, and upper brainstem; conversely, no significant CBF changes appeared in motor areas beneath the stimulating electrode. They therefore hypothesized that descending axons from the motor and premotor cortices are primarily activated by MCS, and these activate thalamic nuclei. The activation of these thalamic nuclei then initiate a downstream cascade of synaptic events in pain-related structures receiving afferents from these nuclei, including the medial thalamus, anterior cingulate, and upper brainstem. Through these connections, they reasoned that MCS could influence the affective-emotional component of chronic pain by way of cingulate/orbitofrontal activation and lead to descending inhibition of pain impulses by activation of the brainstem.

Recent evidence also points to a possible secretion of endogenous opioids triggered by chronic MCS. Using PET imaging and [(11)C]diprenorphine, an exogenous opioid receptor ligand, Maarrawi et al. studied the changes in opioid receptor availability induced by MCS in eight patients with refractory neuropathic pain. They noted significant decreases of [(11)C]diprenorphine binding in the anterior middle cingulate cortex (aMCC), periaqueductal gray (PAG), prefrontal cortex, and cerebellum which significantly correlated with pain relief. They concluded that the decrease in binding of the exogenous ligand was most likely explained by receptor occupancy due to enhanced secretion of endogenous opioids. This observation on the delayed release of endogenous opioids is consistent with the clinical effects of MCS, which may also last for hours or days after MCS discontinuation [7].

Indications

Motor cortex stimulation is finding increasing utility in the treatment of central and peripheral neuropathic pain. The main indications are central pain, especially pain related to a thalamic lesion, and trigeminal neuropathic pain since spinal cord stimulation is generally available for pain in the extremities or trunk. The central pain usually follows ischemic or hemorrhagic stroke in most cases but may be due to other rarer causes as multiple sclerosis and trauma. In a critical review of the literature on the efficacy and safety of

motor cortex stimulation for chronic neuropathic pain, Fontaine et al. reported that of 210 cases identified who had undergone MCS, the most common indication was central pain (117 cases) followed by trigeminal neuropathic pain (44 cases) [4]. Other indications reported in the literature include phantom limb pain, brachial plexus avulsion, spinal cord injury, postherpetic neuralgia, and peripheral nerve lesions including nerve root or nerve trunk pain related to previously excised neurofibromas in patients with neurofibromatosis [8–13].

Outcome

Fontaine et al. reviewed the outcomes in 210 cases of MCS implanted for different conditions in 14 studies published in the literature between 1991 and 2006 and reported that overall, 57.6 % of the patients had a "good" postoperative pain relief (defined as pain relief ≥40 or ≥50 % depending on the studies) while about 30 % of the patients had ≥70 % improvement [4]. In the 152 patients in the studies who had a follow-up of ≥1 year, 45.4 % had a "good postoperative outcome." Outcomes are best in patients with trigeminal neuropathic pain. It is generally suggested that outcome is related to the relative position of the MCS electrodes over the somatotopically relevant part of the motor cortex, but this has not been proven. In any case, patients with lower extremity neuropathic pain are known to have poorer outcomes with MCS, and this is felt to be related to the difficulty encountered with placing the MCS electrode over the medial surface of the brain [4].

Unfortunately, the literature on MCS is heterogenous, and the number of clinical series is still relatively low. There are very few double-blinded evaluations of the efficacy of MCS. This is in spite of the fact that MCS offers a unique opportunity for blinded evaluations as it does usually induce perceptible sensations. A randomized double-blinded trial by Velasco et al. reported pain improvement of ≥40 % at 1 year in all of eight patients who were implanted with MCS [14]. Rasche et al. noted that under double-blinded "on-off" conditions, a placebo response could occur in up to 35 % of patients undergoing MCS [15]. In any case, a detailed review of the literature to date suggests that MCS is effective and safe in the treatment of medically refractory neuropathic pain in select patients.

The ability to predict the outcome of motor cortex stimulation even before embarking on an externalized MCS trial will be invaluable. It will prevent a surgical misadventure with potential risks to the patient and save time and resources which is expended in planning and executing the procedure. To this end, various investigators have looked into means of predicting the outcome of MCS. Predictive factors that have been investigated include a system of pharmacological classification of pain [16], degree of motor impairment (which is felt to correlate to extent of intact thalamocortical connections) [17], degree of alteration of non-nociceptive sensory modalities within the painful area [18], and response to transcranial magnetic stimulation [19]. Unfortunately, larger studies have failed to confirm these findings [8, 20].

Procedure

Preoperative Evaluation

A detailed clinical history and physical examination is the first step in the evaluation of these patients. A history of the nature of the pain to confirm a neuropathic character, an identification of the etiology, and an evaluation of pain medications and other interventions undertaken to treat the pain are warranted. Sometimes, in the course of this evaluation, it may become evident that motor cortex stimulation is not indicated in the particular clinical scenario and that other simpler and less invasive interventions may be all that is warranted.

A neuropsychological evaluation should also be performed. Some of these patients, in the course of the long duration of their pain, have developed associated psychological overlays such as depression, anxiety disorders, and substance abuse issues that need to be addressed. Patients with personality disorders and those who have adopted a sick role or are deriving secondary gain from their condition generally tend to have poor outcomes. Detailed neuropsychological assessment will identify this subpopulation of patients who may sometimes be excluded.

The patient and family should have a clear understanding of the details and steps of the procedure and should have realistic expectations of the outcome. The patient should understand that the first stage of the procedure consists of an externalized MCS trial period which lasts typically between 3 and 7 days. A positive response consists of a 40–50 % reduction in pain, and the patient should indicate that this degree of reduction in pain will significantly improve his or her quality of life to justify this invasive procedure. Patient should also be aware of the prolonged stimulation sessions involved during the externalized MCS trial period and following the implantation of the permanent device and should have the mental fortitude to undergo this. Generally, a strong social and emotional support network from the patient's family is important in this regard. The patient should understand and be willing to accept the fact that a failure of the externalized MCS trial implies that the electrodes will be removed and no further treatment with regard to MCS will be pursued.

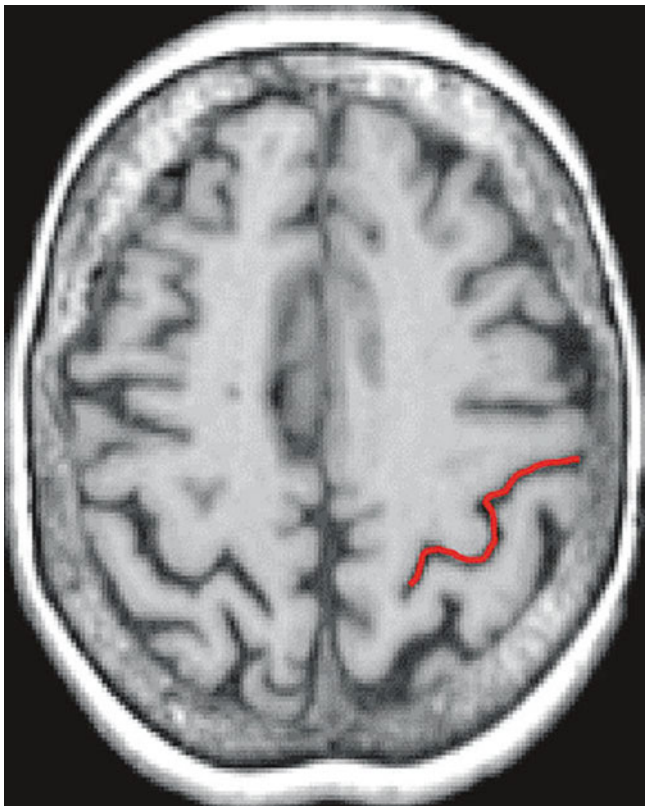

Fig. 41.1 MRI showing the central sulcus and the precentral gyrus

Surgical Technique

The specific surgical technique varies significantly between different institutions, but constant themes are maintained in the sequence of events. The sequence of events are preoperative localization of the motor cortex, intraoperative electrophysiological mapping of the motor cortex, and implantation of the MCS electrodes followed by a variable period of externalized MCS trial and then internalization of the system following a successful trial.

Preoperative Localization of the Motor Cortex

The main focus of preoperative planning is the localization of the motor cortex and its somatotopic arrangement and relationship to the relevant area of pain (Fig. 41.1). Fusion of preoperative imaging with frameless neuronavigation system enables anatomical localization of the motor cortex. Reformatted volumetric T1 magnetic resonance images are superior in this regard, but stereotactically acquired CT scans may also be used. Functional MRI (fMRI) may also be used to map the motor cortex and has sufficient spatial resolution to define somatotopic maps. Transcranial magnetic stimulation and the use of skull landmarks are other methods of localizing the motor cortex.

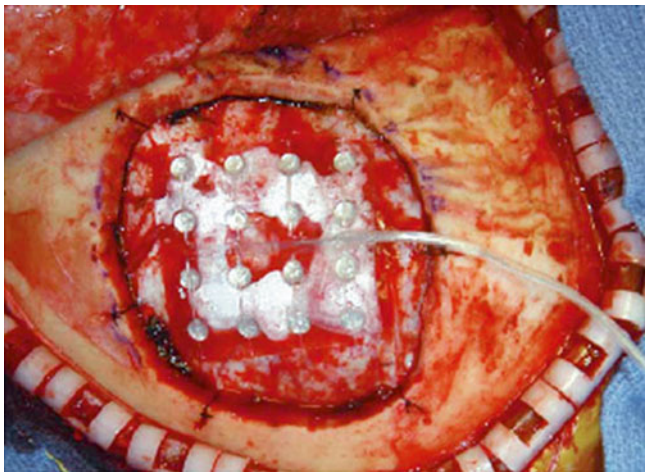

Fig. 41.2 16-Electrode grid placed in the epidural space

Surgical Procedure and Intraoperative Electrophysiological Mapping

The placement of the MCS electrodes may be performed through a burr hole or a small craniotomy. Our preference is to perform it through a small craniotomy centered over the region identified as the precentral gyrus during preoperative planning. This larger access allows for placement of epidural electrodes and optimizes intraoperative electrophysiological evaluation.

The procedure is performed under general endotracheal anesthesia while avoiding paralytic agents as these can interfere with electrical cortical mapping using electromyographic (EMG) responses. Some centers elect to perform awake procedures with monitored anesthesia care (MAC). The head is fixed with a three-pin head holder. The outline of the precentral gyrus is projected onto the scalp using preoperative imaging fused with a frameless neuronavigation system. An appropriate incision centered over this region is made, and then, a 4-cm craniotomy, which is large enough to allow for epidural placement of a 4 × 4 electrode grid, is fashioned. The 16-electrode grid is then placed in the epidural space (Fig. 41.2).

There are two main objectives of intraoperative electrophysiological testing – (1) the confirmation of the position of central sulcus (following earlier localization using preoperative imaging) and (2) the confirmation of the position of the motor cortex by stimulation.

The position of the central sulcus may be confirmed using somatosensory evoked potentials (SSEPs). The site and orientation of the central sulcus is identified based on N20-P20 wave shift (phase reversal) obtained during SSEP recordings (Fig. 41.3). Following this determination, the position of the motor cortex is then confirmed by stimulation via the electrode grid. In performing this test, stimulation of increasing intensity is applied while watching for motor contrac-

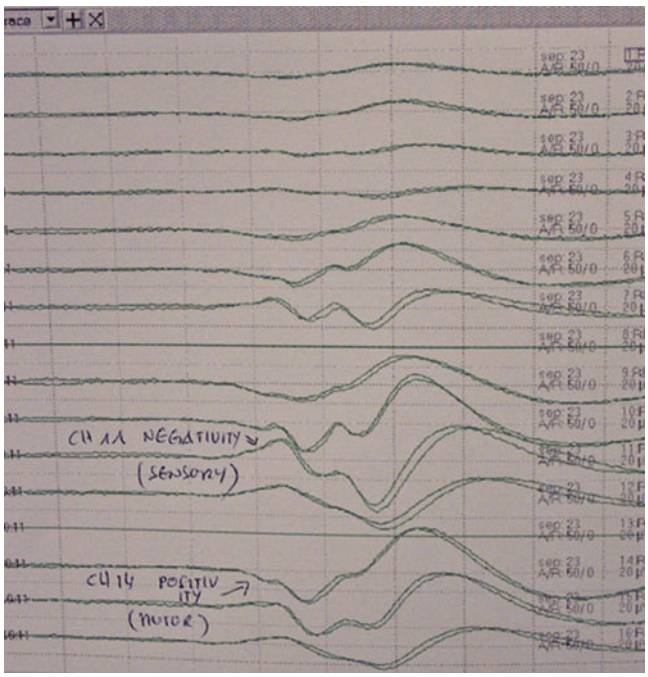

Fig. 41.3 The site and orientation of the central sulcus is identified based on N20-P20 wave shift (phase reversal) obtained during SSEP recordings

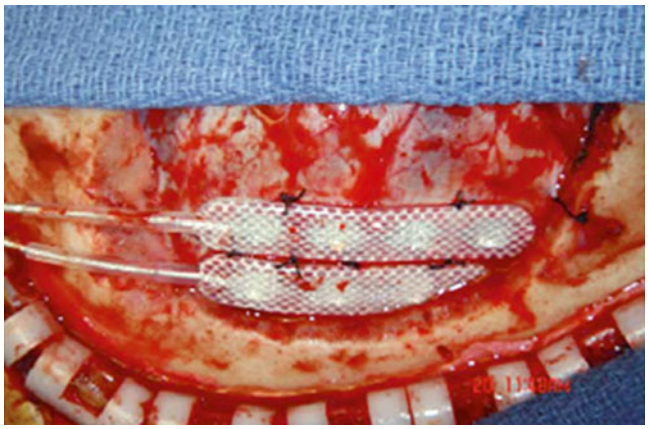

Fig. 41.4 Two two-plate Medtronic Resume paddle electrode arrays placed in the epidural space and oriented perpendicularly to the central sulcus and sutured to the dura

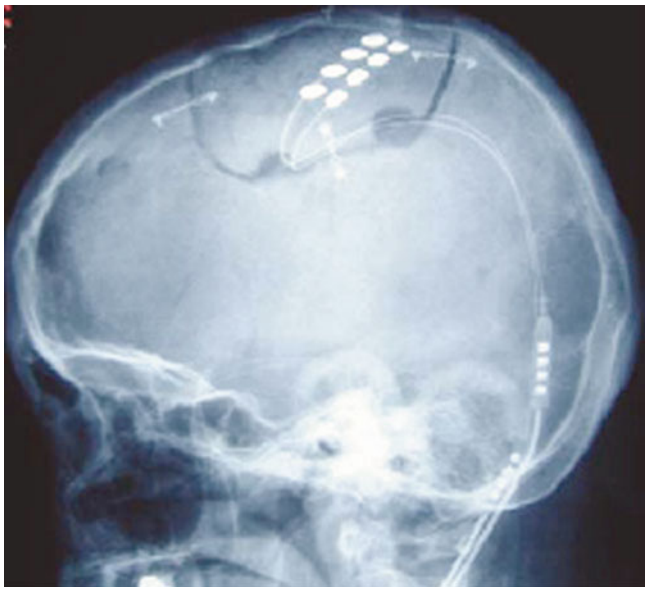

Fig. 41.5 The lead is connected to an extension wire which is tunneled under the skin and connected to an implantable pulse generator (*IPG*), which is typically placed in a subcutaneous or subfascial pocket created in the infraclavicular region

tions at the lowest stimulation threshold in the zone corresponding to the region of pain in the non-paralyzed patient. It is important to note that motor seizures can be provoked by the cortical stimulation. Cold saline or lactated ringer's solution should be immediately available for irrigation of the motor cortex in case of a seizure. The position of the stimulating electrodes which produced motor contractions at the lowest threshold in the appropriate region of the body is noted and marked on the dura. This position defines the optimal site for motor cortex stimulation.

Implantation of MCS Electrodes

Two two-plate paddle electrode arrays are then placed in the epidural space in the previously determined optimal position and are oriented perpendicularly to the central sulcus and sutured to the dura (Fig. 41.4). Alternatively, a four-plate Resume electrode array may be used, and in this case, the electrodes may be placed perpendicularly or parallel to the central sulcus. Some investigators have placed these electrodes in the subdural space [21]. Following placement, the electrodes are connected to extension leads, which are tunneled externally and connected to an external pulse generator for testing of the efficacy of stimulation over several days.

Externalized MCS Trial, Stimulation Parameters, and Internalization of Stimulation System

The externalized MCS trial stimulation is generally performed over 3–5 days. Patient should be monitored during the trial in an epilepsy monitoring unit, an intensive care unit, or the neurosurgical floor. During the trial, the stimulation amplitude is set at a value of 80 % of the threshold for motor contraction. Typical stimulation parameters used are amplitudes of 1–3 V, frequency of 40 Hz, and pulse width of 90 ms. A trial is considered successful if patients report at least 50 % pain relief with stimulation.

Patients who have a successful trial are then returned to the operating room for internalization of the stimulator system. The scalp flap is only partially reopened during this second

procedure to expose the MCS electrode lead that was coiled under the galea of the scalp at the first procedure. This lead is then connected to an extension wire which is tunneled under the skin and connected to an implantable pulse generator (IPG), which is typically placed in a subcutaneous or subfascial pocket created in the infraclavicular region (Fig. 41.5).

Conclusion

Motor cortex stimulation is safe and effective in the treatment of medically refractory neuropathic pain in select patients. Its main indications at this time are the treatment of medically refractory central and trigeminal neuropathic pain, but it is finding utility in other indications including treatment of phantom limb pain and complex regional pain syndromes. The mechanism of action is not yet fully elucidated, but may involve disruption of abnormal thalamic impulses by cortically mediated modulation.

Prediction of patient response to MCS is, at this time, based on response to a period of externalized trial stimulation. The development of techniques for predicting patient response to MCS noninvasively, such as the use of transcranial magnetic stimulation, will be an invaluable contribution to the management of these patients. Finally, more double-blinded randomized evaluations of this technique are indicated in view of its invasiveness and cost implications.

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Intrathecal Drug Delivery for Control of Pain

42

Brian M. Bruel, Mitchell P. Engle, Richard L. Rauck, Thomas J. Weber, and Leonardo Kapural

Key Points

- The utilization of intrathecal drug delivery has increased over the last two decades.
- Intrathecal delivery of analgesics provides another option for the treatment of both chronic and cancer-related pain.
- Appropriate selection of patients and competence in the implantation procedure are keys to successful therapeutic outcomes.
- There are numerous intrathecally delivered medications currently being utilized with different mechanisms of action for the treatment of pain.
- Guidelines for intrathecal drug delivery for pain are available, but further research is required in intrathecal pharmacology and physiology.

Introduction

Over the last two decades, the use of intraspinal drug delivery (ISDD) systems for the treatment of chronic pain and spasticity has increased [1]. The clinical practice varies from institution to institution as far as the utilization of different agents or routes of administration. The clinical approach for intraspinal drug delivery is influenced by the type of pain treated (e.g., chronic nociceptive vs. neuropathic). The choice depends on life expectancy as well as the planned time frame of treatment. Intraspinal catheter placement is frequently chosen for the treatment of cancer pain, spasticity (caused by cerebral palsy, multiple sclerosis, spinal cord injury, and other neurologic conditions), and intractable nonmalignant pain (severe post-laminectomy syndrome and arachnoiditis, vertebral compressive fractures resistant to other therapies, complex regional pain syndrome (CRPS), postherpetic neuralgia and other types of neuralgias), and the administration of intrathecal chemotherapy and CSF drainage [2]. Effective dosing through continuous intrathecal infusion is five to ten times less over 24 h when opioids are used.

Intrathecal (IT) drug delivery systems for the administration of opioids and non-opioids to treat intractable chronic pain have been used since late 1970s [3]. Technological improvements to intrathecal drug delivery systems throughout the 1980s and 1990s brought more sophisticated, totally implantable, and externally programmable devices [3]. The potential advantages of contemporary drug delivery systems include effective pain control by delivering opioids or non-opioids directly to the spinal cord, much lower doses of opioids and non-opioids required to control the pain, and fewer side effects in comparison with systemic drug delivery [3].

Brief History

In 1973, the opioid receptor was first identified [4]. This early research on the opioid receptor and its location in the dorsal horn of the spinal cord became the foundation for current intrathecal therapies. The first "permanent" catheter for intraspinal drug delivery was developed in the 1980s by Dupen and associates [5]. In the early 1980s, Coombs et al. pioneered the usage of continuous intraspinal morphine delivered by an implanted continuous system for chronic intractable pain. This small series of ten patients confirmed the efficacy of the sustained analgesic effects of the intrathecal route of opioids in treating cancer

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pain [6]. In 1991, Medtronic released the first FDA-approved externally programmable IDDS pump powered by batteries in the United States [3]. Since its FDA approval, more than 200,000 chronic pain patients have been treated with continuous intrathecal drug therapy.

Patient Selection and Workup

Proper patient selection is the cornerstone to successful intrathecal drug therapy. Appropriate patient selection is achieved by carefully choosing patients that may experience therapeutic success while experiencing minimal drug or procedural side effects. It is important to begin with a thorough history, physical exam, and psychological evaluation to develop an accurate diagnosis of the patient's pain condition. Another key step in successful implantable therapy is patient education. It is extremely important for the patient to have a thorough understanding of the procedure prior to implant and to have realistic expectations of pain relief post implantation.

Selection criteria for implantable therapies depend mainly upon the etiology of the patient's pain. It is important to differentiate between cancer pain and noncancer chronic pain. The strongest evidence in support of intrathecal therapy lies in the treatment of cancer pain patients [6–8]. Cancer pain is often associated with severe, debilitating pain. Oral opioid pain medications are often used in high dosages to treat cancer pain. Unfortunately, they are often associated with multiple side effects that negatively affect the patient's quality of life. Intrathecal opioids allow these patients to use lower overall amounts of opioids, allowing greater pain relief and the ability to minimize the side effects of excessive sedation, constipation, and respiratory depression, and to allow an improvement in overall function [7, 8].

In the United States, the most common indication for intrathecal therapy is chronic intractable noncancer pain that is not responsive to conservative therapy. Unfortunately, there are limited randomized controlled studies showing the long-term benefit of continuous intrathecal therapy in nonmalignant pain patients. Failed back surgery syndrome, spinal stenosis, intractable lower back pain, and other diseases of the spine are the most common indications for intrathecal therapy [2]. There is some general debate among pain physicians on who is an appropriate candidate for intrathecal therapy. Table 42.1 provides some general guidelines on selection criteria to intrathecal drug therapy [9].

Proper patient evaluation also requires knowledge of the contraindications of intrathecal therapy (see Table 42.2) [10, 11].

Prior to implant, it is important to perform thorough patient counseling on intrathecal therapy to ensure an appropriate chance of success. The counseling process begins with detailed instruction on the entire procedural process, the risks and benefits of the procedure, and discussion on realistic expectations from the therapy. The patient must understand the signs and symptoms of potential under- and overdosages to minimize potential life-threatening problems (Table 42.3). The patient must also be instructed to avoid any

Table 42.1 Selection criteria for intrathecal pump placement

Stable medical condition amenable to surgery	*
Clear organic pain generator	*
No psychological or sociological contraindication	*
No familial contraindication such as severe codependent behavior	*
Documented responsible behavior and stable social situation	*
Good pain relief with oral or parenteral opioids	*
Intolerable side effects from systemic opioid therapy	*
Baseline neurological exam and psychological evaluation	*
Failure of more conservative therapy including trials with non-opioid medications and nerve blocks	*
Constant or almost constant pain requiring around-the-clock opioid therapy	*
No tumor encroachment of thecal sac in cancer patients	*
Life expectancy >3 months	*
No practical issues that might interfere with device placement, maintenance, or assessment (e.g., morbid obesity, severe cognitive impairment)	*
Positive response to an intrathecal trial	*

Table 42.2 Contraindications for intrathecal (IT) therapy

Systemic infection
Coagulopathy
Allergy to medication being used
Inappropriate drug habituation (untreated)
Failure to obtain pain relief in a screening trial
Unusual observed behavior during screening trial
Poor personal hygiene

Table 42.3 Drug concentrations and dosages

Drug	Maximum concentration	Maximum dose/day
Morphine	20 mg/mL	15 mg
Hydromorphone	10 mg/mL	4 mg
Fentanyl	2 mg/mL	No known upper limit
Sufentanil	50 μg/mL (not available for compounding)	No known upper limit
Bupivacaine	40 mg/mL	30 mg
Clonidine	2 mg/mL	1.0 mg
Ziconotide	100 μg/mL	19.2 μg (Elan recommendations)

strenuous and high-impact activities. Scuba diving at a depth of 2 ATA (atmospheres absolute) may damage the pump. These activities may potentially damage the intrathecal catheter or pump reservoir. Intrathecal catheter or battery malfunction may require revision secondary to catheter kinking or occlusion.

There is no standard interpretation of the efficacy and utility of an intrathecal trial. In general, minimal expected outcome is a >50 % reduction in patient's pain and absence of side effects. Trial techniques are based on individual physician preferences and available resources. There is no convincing evidence that one technique is far superior to another; these include a single-shot injection of intrathecal opioids and non-opioids, multiple bolus injections, and continuous infusion of analgesics, either single or in combination, via an external catheter. There are pros and cons to each method.

A single intrathecal opioid injection involves the injection of intrathecal morphine or other opioids through a lumbar puncture. This is performed with a recommended 0.2–1 mg of intrathecal morphine or the daily equivalent intrathecal dose [12]. There are currently no standard conversion guidelines from systemic opioid doses to intrathecal dosing. Intrathecal boluses allow for a short trial period to evaluate the efficacy and safety of test medication. Long-term efficacy is not expected, and potential side effects of the therapy may occur but are usually short-lived. Multiple bolus injections can be performed through intrathecal or epidural injections, with or without the use of a catheter. This method allows the patient to experience a longer trial period to judge the efficacy of the therapy. The patient may also receive placebo injections to rule out any false positives or any underlying central mediated pain syndromes. The last method of trialing involves the use of continuous infusion of opioid therapy through an external intrathecal catheter. Continuous infusion occurs over several days at a low starting dose and increases every 6–12 h until pain relief is achieved [12, 13]. It is recommended that morphine be trialed in an inpatient or overnight setting to closely monitor for delayed onset adverse events, such as respiratory depression.

Non-opioids, such as ziconotide, may be trialed on an outpatient basis. Trialing of ziconotide is more complex and unpredictable mainly because of a narrow therapeutic window. Continuous infusion trials of ziconotide are traditionally utilized; however, some clinicians perform single bolus trials with varying dosages. Serious adverse side effects during a ziconotide trial, such as respiratory depression and death, are unlikely [13]. Although life-threatening adverse events are not expected with ziconotide, appropriate monitoring for cognitive and psychological effects, ataxia, nausea, and vomiting is recommended.

Psychological Evaluation for Implantable Devices

Currently, there is no large prospective study demonstrating positive predictive value of preoperative psychological testing prior to implantation of IT pump. However, most experts agree that psychological evaluations can improve the patient's chance of successful therapy by discovering untreated depression, anxiety, drug addiction, or/and underlying personality disorders. Patients with underlying personality disorders may have poor functional outcomes using implantable pain therapies [14]. Patients should understand possible outcomes and have realistic expectations for intrathecal therapy. A therapeutic partnership with the patient and physician should focus on adherence to the physician's recommendations and self-monitoring of efficacy and adverse events.

Intrathecal Delivery Systems Implantation Technique

The first step in the implant process is to appropriately prepare the patient for surgery. This begins by marking the potential pump reservoir site on the patient's abdomen. This should be performed with the help of the patient making sure that the site will not interfere with wheelchair use, patient's beltline, or any other activities of daily living. The most appropriate position in the abdomen would be below the lower costal margin and above the iliac crest and beltline and away from rectus abdominis muscle [15]. Chlorhexidine wash one night prior to implantation is recommended by some clinicians; however, there is no clear evidence that this reduces surgical site infection. After appropriate preoperative IV antibiotics are given, the patient is taken to the operating table and placed in the lateral decubitus position with the pump site in the nondependent position. Sterile prep and drape is then performed. A spinal needle is then placed at a shallow-angle (approximately 30° off the spine), paramedian oblique needle insertion trajectory (see Fig. 42.1). The entry point of the needle into the skin (or fascia if the needle insertion is performed through an open incision) should be approximately 1–1 1/2 vertebral levels below the interlaminar space selected for dural puncture and 1–2 cm lateral to the midline, on the side of the intended pump pocket.

The catheter guide wire is seated completely, with its hub against the proximal end of the catheter and remains in place during all maneuvers to insert or position the catheter. The needle bevel is oriented cephalad and the distal tip of the catheter is threaded through the needle to the desired location. One must be aware that if the catheter must be retracted during positioning, the needle tip can damage the catheter, requiring additional surgery to repair or replace the catheter.

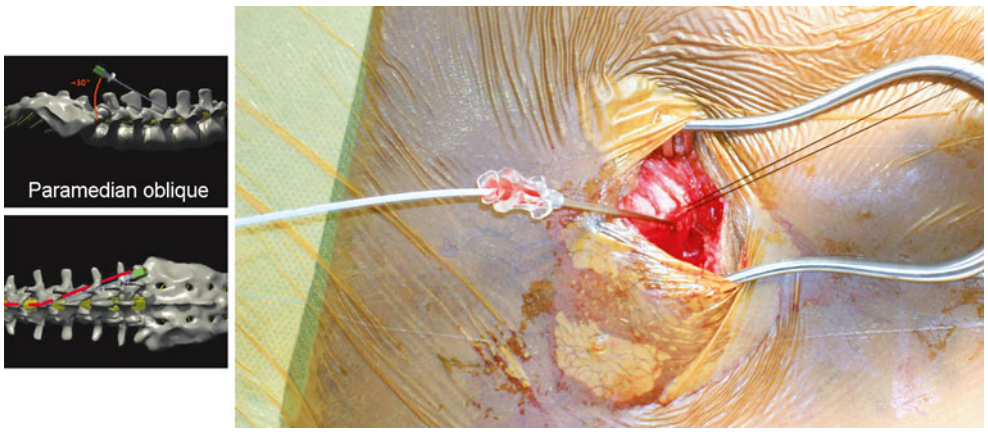

Fig. 42.1 Lateral and anterior-posterior model view of intrathecal needle placement using paramedian oblique approach. Note a significantly decreased angle to the lumbar spine. Such acute angle is needed to easily position catheter into posterior intrathecal space (Modified from the Medtronic IT implantation manual)

The needle is carefully removed, ensuring that the hub is orientated cephalad, with the guide wire removed simultaneously. To prevent catheter damage or dislodgement during guide wire removal, the catheter is held straight and securely at the exit site. Minimal traction to avoid catheter twisting helps prevent damage to the catheter. A purse string suture is then tied around the fascia surrounding the catheter, and then, an anchor is attached to the fascia via nonabsorbable sutures.

A subcutaneous pocket is prepared that is large enough to accommodate the selected IT pump. The pocket size should be close-fitting to prevent flipping or migration of pump. Expert implanters recommend that the pocket size should be no more than 20 % larger than the size of the pump. Using the appropriate size catheter passer, a subcutaneous tunnel is formed from the spinal incision site directed toward the pump pocket. The residual catheter length should be noted for accurate programming if a programmable pump is implanted. Strain relief loops at the spinal incision site and behind the implanted pump will allow for patient movements.

Nonabsorbable sutures are placed in the pump pocket fascia closest to four different corners of the pump pocket. The pump is then positioned inside the pocket so that the catheter is not twisted or kinked and securely anchored (Fig. 42.2). Skin and underlying fascia are closed with sutures.

Basics Concepts of Intraspinal Drug Delivery Routes

Epidural versus intrathecal modes of delivery influences distribution of the delivered drugs. Drugs delivered epidurally must cross the dura and arachnoid and then diffuse to their site of action. Drugs delivered intrathecally diffuse directly into the spinal cord [18]. However, the location of the catheter is important even for intrathecal drug delivery. Adjustment of intrathecal medications may be required to achieve therapeutic concentrations at target sites in the spinal cord if the catheter is distal to the targeted spinal level [16, 17].

The hydrophilic medications circulate throughout the CSF. Their duration of action is longer, have relatively slow onset, rostral migration may be more predictable, and is dose dependent [18]. Drugs deposited intrathecally reach high CSF concentration rapidly before reaching any significant serum level and are dose dependent [19]. Morphine and other opioids diffuse to the substantia gelatinosa in the spinal cord – their primary site of action – and bind to opioid receptors there. The required dose to achieve pain relief epidurally is much higher than intrathecally, and systemic absorption is much higher for the same level of analgesia. There is approximately five to ten times reduction of required dose when the route of morphine delivery is changed from epidural to intrathecal [20].

Lipophilic medications remain closer to the catheter tip. For these medications, slow migration of the drug in the spinal space, combined with the rapid uptake by intrathecal tissues, produces large drug gradients within the intrathecal space. Lipophilic opioids (fentanyl and sufentanil) when used for epidural analgesia have significantly higher plasma levels and exhibit less rostral spread. Their spinal mechanism of action is uncertain [21]. The dose for epidural injection is higher than for intrathecal administration, and drug pharmacokinetics is more complex. Dural penetration, epidural fat deposition, and systemic absorption occur [21]. The extent of systemic absorption for epidural infusion is thus higher than with intrathecal administration.

Recent animal studies provided the evidence that the position of the infusion catheter orifice and its relationship to the targeted spinal cord segment are crucial. There is limited capacity of the CSF to distribute drugs away from the distal lumen of the catheter [22–24]. Inadequate pain relief follow-

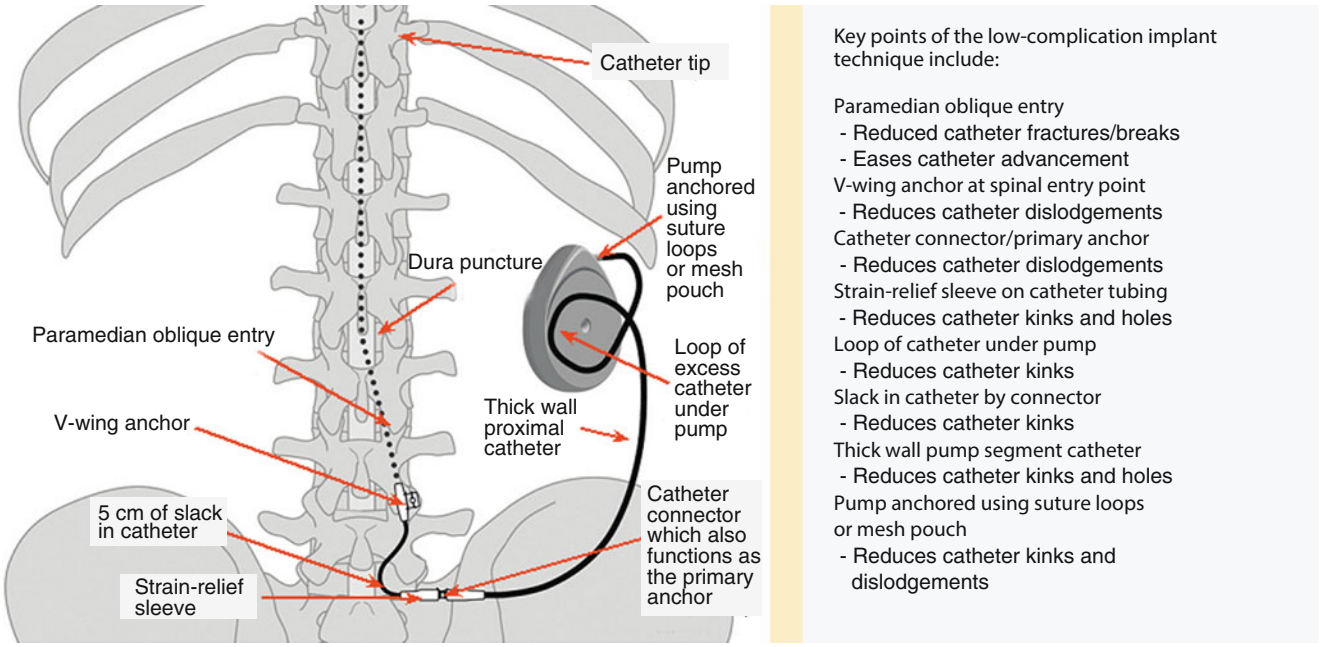

Fig. 42.2 Schematic and key points of what is called "low-complication implant technique" for intrathecal pump and catheter. Although such recommendations seem to represent common sense, there are no studies to support all of listed recommendations to prevent catheter kinks and migrations (Modified from the Medtronic IT implantation manual)

ing definitive pump implantation occurs frequently and often requires optimization, even after a successful trial.

The infusion velocity of the drug and the CSF motion are two elements that are critical in intrathecal pharmacokinetics. A bolus or a faster infusion rate shows wider CSF distribution compared with slower rates. The classic flow of CSF is caudad in the posterior surface of the spinal cord and cephalad along the anterior surface. However, this classic depiction is incorrect based on multiple MRI studies that have showed a to-and-fro rostrocaudal movement, driven by the cerebrospinal vasculature during the cardiac cycle. This flow pattern is greatest in the upper cervical segments and decreases progressively, becoming negligible at the cauda equina. There are three channels of CSF flow. These are medial-ventral, medial-dorsal and lateral, and the most valuable is the undetected circumferential motion in between the anterior and posterior sides of the spinal cord. The dorsal horn is the target. A well-positioned posterior catheter tip is important for dorsal column flow; however, targeting the anterior horn via ventral placement of the catheter tip may provide a better drug response [24].

Intrathecal Versus Epidural Delivery Route

When compared to epidurally placed catheters, intrathecal catheters may last longer with lower rates of complications [25, 26]. In addition, side effects related to drug infusion are less frequent (lethargy, respiratory depression, dysphoria) when intrathecal route is used [27]. The development of tolerance in patients with chronic pain is less frequent when intrathecal route is used [28]. Moreover, the major reason to select the intrathecal route for delivery of opioids came from cancer pain research. Patients who converted from epidural to intrathecal morphine have somewhat better pain relief [25, 26]. This trend was most obvious when long-term externalized epidural catheters were followed by externalized and internalized intrathecal catheters [26]. In regard to medications used, epidural opioids either alone or combined with epidural bupivacaine provided significantly less pain relief than intrathecal opioids or intrathecal opioids and bupivacaine [26].

Intrathecally Delivered Medications

Morphine

Morphine is the prototypical opioid analgesic. It is the only opioid currently approved for intrathecal administration by the FDA. Morphine is a highly hydrophilic compound that is poorly metabolized in the CSF, leading to prolonged duration of effect when delivered intrathecally. Morphine works through activation of opioid receptors, most specifically the μ-opioid receptor. These receptors are located in both the superficial laminae of the spinal cord and supraspinal sites such as the periaqueductal gray matter and the raphe nuclei [29]. Mu opioid receptors are G protein-coupled receptors

and are located at both pre- and postsynaptic sites in the spinal cord. On presynaptic terminals, activation of μ-opioid receptors leads to inhibition of voltage-gated calcium channels [30, 31]. In primary afferent neurons, this results in decreased substance P and excitatory amino acid release [32, 33]. Agonism of postsynaptic μ-opioid receptors activates G protein-coupled inwardly rectifying potassium (GIRK) channels leading to neuronal hyperpolarization [34, 35].

Hydromorphone

Hydromorphone is a semisynthetic derivative of morphine. Like morphine, it is a μ-opioid receptor agonist, but it also activates δ- and κ-opioid receptors. Hydromorphone is commonly used as a first-line drug for intrathecal delivery. In addition, due to its different chemical properties and receptor pharmacology, it is also used as a second-line agent when morphine fails to provide sufficient analgesia [36]. There is some evidence that hydromorphone is more lipophilic than morphine which may account for decreased distribution to supraspinal sites resulting in less side effects [37]. The potency of hydromorphone is five times that of morphine.

Fentanyl and Sufentanil

Fentanyl and sufentanil are synthetic anilinopiperidines that are μ-opioid receptor agonists. They are both highly lipophilic which results in segmental analgesia near the catheter tip due to rapid diffusion out of the CSF into the systemic circulation. Anilinopiperidines have higher intrinsic receptor activity than morphine, indicating that less receptors need to be occupied to generate the same physiological response [38, 39]. This property is likely related to the decreased tolerance seen with anilinopiperidine opioids compared to morphine. Relative to morphine, the potencies of fentanyl and sufentanil are 100 and 1,000 times greater, respectively.

Clinical Evidence for Intrathecal Opioids

Intrathecal opioids are currently used in the treatment of a broad spectrum of clinical conditions. Despite an extensive clinical literature detailing the usage of intrathecal opioids, only a relative handful of controlled prospective studies exist on the topic. The strongest evidence for the use of intrathecal opioid comes from the treatment of cancer pain. Rauck and colleagues published a multicenter prospective study of 119 cancer pain patients with data reported out to 16 months. Intrathecal morphine reduced the VAS from 6.1 to 4.2, and this effect continued through month 13. In addition, the patients had a reduction in both oral opioid consumption and the opioid complication severity index. The authors reported clinical successes of 83 % at 1 month and 91 % at 4 months with success defined as ≥50 % reduction in VAS, use of systemic opioids, or opioid complication severity [40]. Smith and colleagues published an important prospective multicenter randomized clinical trial comparing comprehensive medical management (CMM) versus CMM plus implantable drug delivery system (IDDS). With clinical success defined as ≥20 % reduction in VAS or equal VAS with ≥20 % reduction in toxicities, the CMM plus IDDS success rate was 84.5 versus 70.8 % for CMM alone. At 4 weeks, the CMM plus IDDS VAS was reduced by 52 versus 39 % for the CMM alone group. In addition, the CMM plus IDDS group had significant reductions in fatigue and depressed levels of consciousness. Finally, the CMM plus IDDS group had a trend toward increased survival at 6 months [7]. Collectively, these studies indicate a strong role for intrathecal opioids in managing cancer pain.

Evidence for the use of intrathecal opiates in noncancer pain is not quite as clear as with cancer pain in part because of a lack of randomized controlled trials. That said, several high-quality prospective studies have evaluated the effect of intrathecal opioids on neuropathic, nociceptive, and mixed noncancer pains [41–47]. Deer and colleagues reported a multicenter prospective registry of 136 patients with low back and leg pain who were implanted with intrathecal drug delivery systems. At 1 year, numeric pain ratings dropped by 47 % for back pain and 31 % for leg pain. In addition, there was a significant improvement in the Oswestry Low Back Pain Disability scores in implanted patients. Patients who had successful trials but were not implanted did not have similar improvements [48]. Thimineur and colleagues reported a prospective three-armed study of chronic nonmalignant pain. The first arm (N = 38) were implanted with pumps, the second (N = 31) either failed a trial or declined implantation, and the third (N = 41) were newly referred patients. All participants filled out extensive questionnaires at baseline and every 6 months for 3 years. Intrathecal therapy had significant benefits on pain scores, functionality, and mood. The nonimplanted group declined in these functions despite escalation of oral opioids and injective therapies. Neither of the first two groups advanced as well as the new referral group indicating that although intrathecal therapy is associated with significant pain, functional, and mood improvements, the disease pain burden remains high [49]. Although ample evidence exists demonstrating the ability of intrathecal morphine to provide analgesia for chronic noncancer pain, randomized trials need to be conducted before it is considered standard care.

Non-opioids

Bupivacaine

Bupivacaine is the most commonly used local anesthetic for intrathecal administration. The drug is an amino amide that binds the intracellular portion of the α-subunit of voltage-gated Na^+ channels, inhibiting Na^+ influx into the neuron. This ultimately decreases the rate of neuronal depolarization,

inhibiting action potential initiation and signal transduction [50]. For continuous intrathecal infusion therapy, bupivacaine is commonly combined with other agents and is rarely used alone. The drug is generally selected for neuropathic pain or when analgesic doses of opioids produce intolerable side effects. The data regarding the efficacy of intrathecal bupivacaine are mixed. In a retrospective analysis of 109 patients with failed back surgery syndrome or metastatic cancer, Deer and colleagues reported that patients with intrathecal opioids plus bupivacaine had better pain control, fewer physician visits, and higher overall satisfaction than patients with intrathecal opioids alone [51]. A single randomized, double-blind placebo-controlled crossover study has evaluated the effect of adding bupivacaine to intrathecal opioid therapy. Mironer and colleagues utilized 24 patients with chronic nonmalignant intractable pain and found no difference in mean pain scores with the addition of bupivacaine; however, there was a statistically significant improvement in quality of life scores [52]. Additionally, one prospective study in cancer patients by van Dongen and colleagues demonstrated that the addition of bupivacaine to morphine attenuated the dose progression of morphine over time, indicating a likely synergistic effect between the two drugs [53].

Ziconotide

Ziconotide is a selective N-type calcium channel blocker that was formerly known as SNX-111. It is a synthetic analog of the ω-conopeptide derived from the venom of the giant marine snail *Conus magus* [54, 55]. Ziconotide inhibits presynaptic N-type calcium channels, leading to decreased excitatory neurotransmitter release in the dorsal horn. Ziconotide is a permanently charged molecule with a molecular weight ten times that of morphine which provides relative confinement to the CSF. In addition, the molecule is relatively resistant to CSF peptidases. As such, clearance of the drug is mediated by CSF bulk flow and not by metabolism [56]. Common side effects include amblyopia, dizziness, nausea, nystagmus, urinary retention, and vomiting, which appear to be in part dose and titration schedule dependent. Ziconotide is approved for intrathecal administration by the FDA.

Three double-blind placebo-controlled studies examining the efficacy of ziconotide in the treatment chronic pain have been conducted. Staats and colleagues evaluated 111 patients with cancer or AIDS-related pain over an 11-day span. The study included a 5–6 day titration phase followed by a 5-day maintenance phase. The placebo group was crossed over into the ziconotide group after 5 days. Mean VAS reduction at the end of the titration phase was 53 % for ziconotide versus 18 % for the placebo group [57]. Wallace and colleagues evaluated 169 with nonmalignant mostly neuropathic pain over 11 days. Mean VAS reduction was 31 % for the ziconotide group versus 6 % for the placebo-treated group. Although both of these studies had significant reductions in pain scores with ziconotide therapy, they also had higher rates of serious adverse events and discontinuation [58]. Rauck and colleagues enrolled 248 patients with neuropathic, nociceptive, and mixed pain for randomization into either intrathecal ziconotide or placebo treatment. Unlike the previous two studies, the dose of ziconotide was gradually increased over 3 weeks to a low maximum dose. At week 3, the VAS decreased by 14.7 % in the ziconotide group compared to 7.2 % in the placebo group ($P = 0.036$). Discontinuation rates for adverse events and serious adverse events were similar between the groups [59]. Collectively, these results demonstrate that intrathecal ziconotide is an effective analgesic for both cancer and noncancer pain and that the adverse effects of the drug can be limited by careful titration and dosing.

Clonidine

Clonidine is a relatively selective α-2-adrenergic receptor agonist that produces dose-dependent analgesia when delivered intrathecally. It is FDA approved for epidural use in the treatment of cancer pain [60, 61] but is commonly used for intrathecal therapy [62]. Alpha-2-adrenergic receptors are located on both pre- and postsynaptic neurons in the dorsal horn [63–65]. The mechanism of action is mediated through inhibition of substance P and excitatory amino acid release from the primary afferent neurons and direct inhibition of second-order neurons [29, 66]. Clonidine synergistically augments the effect of morphine. It does not cause respiratory depression and does not potentiate opioid induced respiratory depression [67]. The major side effects of clonidine are bradycardia and hypotension. These effects tend to be dose related [68]. Abrupt cessation of intrathecal clonidine therapy may produce severe rebound hypertension [62]. Several studies have prospectively documented the efficacy of intrathecal clonidine in humans, particularly in the treatment of neuropathic pain. A small, prospective, randomized, double-blind, placebo-controlled trial in complex regional pain syndrome demonstrated significant benefit of epidural clonidine over placebo [69]. Eisenach and colleagues utilized a placebo-controlled trial to evaluate the efficacy of epidural clonidine for the treatment of severe cancer pain. Successful analgesia was more common in the clonidine (45 %) than saline group (21 %), with the effect being most pronounced in individuals with neuropathic pain [60]. Hassenbusch and colleagues evaluated intrathecal clonidine in the treatment of predominantly neuropathic pain at a large cancer center. Long-term success, defined as 50 % or greater reduction in pain intensity scores, was reported in 42 % of all patients enrolled in the study [62]. Taken together, these data indicate that intrathecal clonidine produces clinically significant analgesia, particularly with neuropathic pain.

Baclofen

Baclofen is a γ-amino butyric acid analog that is the prototypical $GABA_B$ receptor agonist. The receptor is expressed in the superficial laminae of the dorsal horn, appropriately situating it to modulate nociceptive information [70]. In rodent models, baclofen produces significant antinociception and analgesia [71, 72]. Unfortunately, the results in humans are less robust. A double-blind, randomized, placebo-controlled trial by Herman and colleagues reported the effect of intrathecal baclofen on pain associated with multiple sclerosis and spinal cord injury. Dysesthetic and spasm-related pain was significantly reduced, while pinch-induced pain was not [73]. In another study, intrathecal baclofen decreased painful muscle spasms in a population of women with complex regional pain syndrome [74]. Interestingly, intrathecal baclofen may augment the response to spinal cord stimulation [75]. The most common clinical utilization of intrathecal baclofen is for treatment of spasticity. However, in selected circumstances, intrathecal baclofen may be beneficial in managing centrally mediated pain. One concern of note with intrathecal baclofen is the life-threatening withdrawal that occurs with abrupt discontinuation of therapy. Physicians using intrathecal baclofen should be aware of this risk and understand appropriate treatment if accidental discontinuation should occur.

Adenosine

Adenosine is an endogenous purine nucleoside that is involved in multiple biological processes such as energy transfer and signal transduction. It activates four types of receptors in the spinal cord to modulate nociceptive transmission [76–78]. Several studies have examined the efficacy of intrathecal adenosine in humans. Following a dose-escalating phase I safety trial [79], Eisenach and colleagues reported a double-blind placebo-controlled study on the effects of intrathecal adenosine in 40 subjects. Adenosine did not modulate the response to acute thermal or chemical stimulation, but it did reduce mechanical hyperalgesia and allodynia following intradermal capsaicin injection. This effect lasted for at least 24 h even though adenosine levels in the CSF return to baseline by 4 h [80]. Belfrage and colleagues delivered intrathecal adenosine to 14 patients with chronic neuropathic pain, primarily of traumatic origin. The injection caused transient (<60 min) back pain in five patients. Spontaneous pain scores decreased by 63 %, while evoked pain scores dropped by 83 %. In addition, the area of allodynia and hyperalgesia decreased [81]. These studies indicate that intrathecal adenosine may be an effective treatment for neuropathic or centrally mediated pain syndromes, although further toxicity work is needed before adenosine can be recommended for widespread clinical use [37].

Gabapentin

Gabapentin is a γ-amino butyric acid analog that was originally approved for the treatment of epilepsy. Although initially thought to produce its pharmacological effect through GABA receptors, it has now been shown to bind the α2δ1 subunit of voltage-gated calcium channels, inhibiting channel function [82]. Gabapentin has both spinal and supraspinal effects. In the dorsal horn, it decreases the release of substance P [83] while supraspinal gabapentin activates descending inhibitory norepinephrine neurons [84]. Together, these effects are situated to dynamically modulate nociceptive transmission at the level of the spinal cord. Although gabapentinoids have increasingly diverse clinical indications, they have historically been a first-line treatment for neuropathic pain. Several recent rodent studies have demonstrated increased expression of the α2δ1 subunit in primary afferent neurons following nerve injury that is associated with allodynia [85, 86]. This upregulation may contribute to the initiation of neuropathic pain by altering voltage-gated calcium channel function and presents a putative mechanism for efficacious use of gabapentin in neuropathic pain. The intrathecal delivery of gabapentin has particular theoretical advantages. Following oral administration, the absorption of this drug is transporter dependent in the gastrointestinal tract and at the blood–brain barrier. As such, a "ceiling effect" is commonly seen clinically. Intrathecal delivery of gabapentin will bypass issues of absorption, possibly leading to less systemic side effects. Preliminary results of the phase II clinical trial of intrathecal gabapentin did not produce significant reduction in pain in humans.

Emerging Drugs

The field of emerging intrathecal drug therapies is continually expanding. Several drugs with particular promise include the ultrapotent capsaicin analog resiniferatoxin (RTX), the NMDA receptor antagonist ketamine, the synthetic analog of somatostatin octreotide, the COX inhibitor ketorolac, the benzodiazepine midazolam, the cholinesterase inhibitor neostigmine, the weak μ-opioid receptors agonist and serotonin/norepinephrine reuptake inhibitor tramadol, and the partial μ-opioid receptors agonist and κ-opioid receptors antagonist buprenorphine. For a more in-depth discussion of these compounds, we would refer the readers to the following reviews [37, 56].

The Polyanalgesic Consensus

In 2007, an expert multidisciplinary panel of clinicians convened to develop consensus guidelines for intraspinal therapy for pain. The panel convened on two separate occasions prior

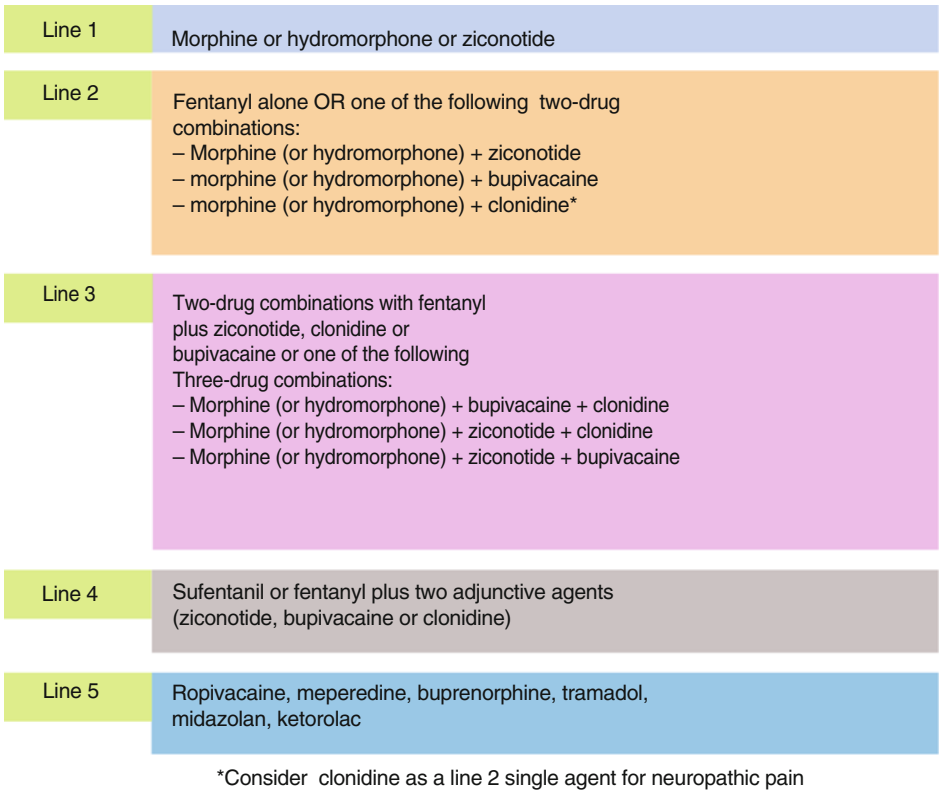

Fig. 42.3 Latest (2007) polyanalgesic consensus guidelines for management of pain by intraspinal drug delivery

to 2007, and the latest published algorithm is shown in Fig. 42.3. Review of published preclinical and clinical data led to the development of these guidelines. This publication was not meant to be the "standard of care" for intrathecal therapy for pain. The document was composed to serve as a guide for safe and effective therapy based on available evidence at the time. In 2007, the panel upgraded ziconotide to a first-line therapy based on relevant literature and collective clinical experience. Catheter tip granulomas (intrathecal inflammatory mass) were identified as an ongoing clinical problem, and steps to mitigate and correct this issue were identified. Recommended concentrations of intrathecal medications were also published in the consensus paper (Table 42.3).

Complications

Most of the drug-related complications were already detailed in respective paragraphs; however, there are some general complications related to route of drug delivery, technique of implantation, maintenance of the IT pump, and characteristics of the spinal fluid.

Intrathecal continuous infusion is safer than epidural infusion if the treatment exceeds 20 days [25, 26]. A comparison of complications between these two routes of opioid delivery suggests more problems with the subarachnoid route in the first 20 days of infusion (25% versus 8%). However, long-term epidural delivery of analgesia is associated with catheter failure, possibly due to epidural fibrosis [26]. The incidence of this complication ranges from 19–41 % [87, 88]. After the 20th day to about 1 year, 55% of patients who received epidural morphine experienced complications compared to 5% in the subarachnoid group. On this basis, the subarachnoid route is preferred for patients expected to live longer than 1 month [25].

Leakage of cerebrospinal fluid (CSF) during the first weeks of intrathecal treatment and formation of a CSF hygroma are possible complications after implantation of an intrathecal drug delivery device. In most patients, symptoms abate within 2 weeks. Symptoms can range from mild postdural puncture headache to a severe postural headache and additional complications related to extensive external loss of cerebrospinal fluid.

Intrathecal infections are more frequent when an underlying disease process is present. Also, externalized catheters may result in more infections compared to internalized systems. Noninfectious fever spikes are possible within 72 hours of implantation, occasionally associated with mild neck stiffness. Normal white blood cell count and some leukocytosis from CSF drawn from the pump side-port are common findings. Krames suggests that the management of these cases should be guided by the CSF analysis [11].

Conclusion

Intrathecal drug delivery for control of pain is an effective therapy for well-selected patients. Clinical experience, scientific investigations, and published reports have helped to elucidate practices that optimize intrathecal pain control while mitigating complications related to therapy. Current evidence supports intrathecal therapy for cancer-related pain, but there continues to be limited evidence for nonmalignant pain. Ziconotide has been added to the pharmacologic arsenal available for intrathecal infusion in the last decade. The introduction of ziconotide, a non-opioid analgesic, and the ongoing use of intrathecal opioids have led to a better understanding of pain modulation at the spinal level. Refinement of surgical techniques and early identification of potential complications of intrathecal therapy, such as the formation of inflammatory masses at the catheter tip, will improve overall safety of this important modality for pain control. Currently, there continue to be abundant unknowns in intrathecal therapy for pain, and the opportunity for further research will extend for many decades to come.

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Clinical Applications of Neuromodulation: Radicular Pain and Low Back Pain

43

Thomas L. Yearwood

Key Points

- It is crucial to understand and appreciate the clinically relevant neuroanatomy of intraspinal and extraspinal components of the sensory nervous system in order to achieve therapeutic and durable neuromodulation in the treatment of neuropathic pain.
- Neurostimulation is a "surface" phenomenon, and in general, penetration of the neuronal tissues is limited to less than 0.5 mm of depth.
- The nervous system is characterized by a somatotopic arrangement of sensory fibers and tracts, each of which offers a statistically relevant population density of targets suitable for stimulation. The more "focal" the need for neurostimulation, the more important it becomes to find access to the CNS by way of these suitable targets, moving peripherally from the dorsal columns toward the dorsal root entry zone (DREZ), nerve roots, dorsal root ganglion (DRG), and named peripheral nerves. The more "regional" the need for neurostimulation, the more important it becomes to find access to the CNS centrally, beginning with the dorsal columns. The somatotopic arrangement of fibers and tracts greatly enhances appropriate targeting for neurostimulation.
- The important "tools of the trade" for neurostimulation therapy are contact placement, complex programming, blending of neurostimulation targets, and integration of neurostimulation therapy with all the other therapeutic modalities in a cohesive and complementary fashion.
- The ultimate goal of neurostimulation is not targeting a specific anatomical area of neuropathic pain with paresthesias, but targeting those locations within the CNS where the neuropathic pain is perceived and interpreted and results in a response. There are numerous "portals of access" to those locations in the CNS from the periphery, and these neuronal pathways provide our opportunities for therapeutic neurostimulation.

Introduction

Neuropathic pain in the upper or lower extremities, and axial spine, can result from numerous and diverse disease states and are some of the most difficult conditions to treat effectively. Neuropathic pain is particularly resistant to opioid therapy and at a minimum requires the balanced integration of polypharmaceutical techniques, functional rehabilitation (physical and occupational therapy), behavioral medicine, and other conservative techniques such as fluoroscopically guided spinal injections techniques. The addition of electrical neurostimulation to this overall treatment plan has proven to be of substantial benefit in reducing pain and restoring physical function for patients with debilitating neuropathic pain of one or more extremities.

As technology for the treatment modality has matured, the practical applications of physician-prescribed electrical fields to excitable neural targets within the spinal canal and in the periphery have expanded. For example, in the spinal canal, technological limitations of lead construction and implantable pulse generator (IPG) programmability and power capabilities limited the application of electrical fields to the largest targets, and the terms "spinal cord stimulation" (SCS) and "dorsal column stimulation" (DCS) were synonymous. However, recent technological advances in lead and IPG design, allowing the development of sophisticated programming of the areas' electrical field parameters (pulse width, frequency, intensity, and polarity: wide ranges of cathode and anode combinations), have enabled the clinician

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to effectively target a greater variety of sites within the intraspinal canal. This has resulted in extending the indications for this treatment modality. These targets now include the dorsal root entry zone (DREZ), the dorsal root ganglion (DRG), and the spinal nerve roots as well as the dorsal columns. Thus, the more appropriate term would be *intraspinal neurostimulation*. In the periphery, the largest targets were the "named" nerves and the early neurostimulator systems produced what is now called peripheral nerve stimulation (PNS). With more advanced technologies, smaller and more discrete targets can be activated; this has allowed the evolution of peripheral nerve field stimulation (PNFS), stimulation of small "unnamed" nerves. These small "unnamed" nerves may come from more than one "named" nerve, and thus, a "field" of neurostimulation can be achieved.

Etiology of Neuropathic Axial and Extremity Pain

Neuropathic pain represents the principal clinical manifestation of neuronal injury. It can involve peripheral mechanisms, which become centralized over a period to produce a clinical state of pain and impairment without regard to ongoing tissue damage or insult. Any disease process can result in a neuropathic pain phenomenon depending on the neurophysiologic status. Table 43.1 summarizes some of these disease processes relative to neuropathic axial and extremity pain with examples of typical clinical conditions.

In each of these scenarios, some pathological mechanism for peripheral or central nerve injury has created an ongoing, self-sustaining pain process. This involves processes imbedded within the central nervous system such as "central sensitization" and "windup," which can be substantially influenced by normal sensory signals resulting in painful sensations, dysesthesias, and paresthesias. The involvement of the sympathetic nervous system in response to these phenomena adds another layer of complexity and pain pathology, as alterations in global and local sympathetic tone can amplify the pain experience.

Typical manifestations of neuropathic extremity pain include burning, throbbing, aching, and boring pains accompanied by allodynia, dysesthesias, hyperalgesia, and temperature or blood flow alterations. These can result in abnormalities of perspiration and piloerection, and episodic muscle cramping and twitching [1, 2], ipsilateral blockade of the sympathetic ganglia of the affected extremity (for neuropathic extremity pain), or bilateral blockade of the sympathetic ganglion of the affected intervertebral disc level (for neuropathic axial pain) will often result in pain relief and a normalization of vascular abnormalities. This includes enhanced blood flow to distal sensory neurons (with an increased sensitivity to light touch) and to muscle groups (with a relaxation of cramping and spasm). Those patients who respond well to sympathetic blockade tend to respond well to intraspinal neurostimulation, and many of these same features can be seen clinically.

Table 43.1 Disease processes relative to neuropathic axial and extremity pain with examples of typical clinical conditions

Congenital	1. Tethered cord syndromes
	2. Spina bifida
	3. Dural ectasia
	4. Spinal stenosis
Metabolic and inflammatory	1. Diabetic peripheral neuropathy
	2. Hyperthyroidism, hypothyroidism
	3. Ankylosing spondylitis
	4. Paget's disease
	5. Sarcoidosis
	6. Arachnoiditis
Traumatic	1. Traumatic disc disruption
	2. Complex regional pain syndrome (CRPS) types I and II
	3. Postsurgical nerve entrapment:
	(a) Post-laminotomy syndromes
	(b) Post-carpal tunnel/tarsal tunnel release-related CRPS-II
	(c) CRPS-II of the ulnar nerve postsurgical transposition
	(d) Chronic piriformis syndrome (sciatic neuralgia)
	(e) Brachial plexus avulsion
	(f) Electrical injury
	4. Traumatic amputation
Neoplastic	1. Chemotherapy-related peripheral neuropathy
	2. Peripheral nervous system malignancies
	3. Intraspinal malignancies
Infectious	1. Herpes zoster
	2. Epidural abscess
	3. HIV-related peripheral neuropathy
	(a) Primary
	(b) Secondary, related to antiretroviral chemotherapy
	4. Lyme's disease

Neuroanatomy and Neurostimulation

Nociceptive and neuropathic pain is carried to the central nervous system (CNS) from the periphery via sensory neurons, directly or indirectly. Beginning in small, microscopic ("unnamed") nerves, sensory information is transmitted to larger nerves and then to spinal nerves. These sensory neurons are incorporated into spinal nerves directly into the CNS by way of the dorsal root ganglia (DRG) and the dorsal root entry zone (DREZ) and, from there, into the dorsal horn to be incorporated into elements of the central nervous system. Sensory neurons can also enter the CNS indirectly by way of the autonomic nervous system (sympathetic or parasympathetic ele-

ments). At the level of the DRG, the spinal nerves are separated into ventral motor and dorsal sensory components before entering the spinal cord. The majority of sensory neuronal systems enter the spinal cord via the dorsal root entry zone (DREZ) and are distributed within the dorsal horn to ascending pathways in the dorsal columns (ipsilateral) and tracts of the ventrolateral quadrants (ventral spinothalamic tract and lateral spinothalamic tract) in both ipsilateral and contralateral manners via numerous interneuronal synapses [3, 4].

It is extremely important to understand that different ascending tracts within the spinal cord carry *qualitatively* different aspects of sensory information; this can have a bearing on the appropriate targeting for intraspinal neurostimulation. The dorsal columns carry the sensations of vibration, touch, proprioception, and pain to the thalamus; the lateral spinothalamic tract (part of the ventrolateral quadrants) carries sensations of pain and temperature, while the ventral spinothalamic tract carries sensations of visceral pain and temperature. Because of the profound neuroplasticity often associated with neuropathic pain, it is entirely possible that different qualitative pain sensations can be modulated with neurostimulation along tracts not traditionally associated with neuropathic pain. If this were not the case, it might very well be that neurostimulation of the dorsal columns alone would have minimal effect on neuropathic pain [4].

Since neuropathic pain frequently incorporates elements of both touch and temperature, it is often necessary to provide neurostimulation to both the dorsal columns and the ventral and lateral spinothalamic tracts in order to achieve optimal therapy. However, neurostimulator leads must be placed dorsally (e.g., dorsal columns and dorsal root entry zone), in order to avoid the motor stimulation that occurs with more ventral placements, and this substantially impedes access to the ventral and lateral spinothalamic tracts. The lateral spinothalamic tract is located too deeply within the spinal cord to be influenced directly by neurostimulation fields on the surface of the cord. The ventral spinothalamic tract is more superficial, and it can be influenced with neurostimulation. However, precise lead placement in this area can be quite difficult, dangerous, and complicated by motor recruitment. Thus, traditional dorsal column lead placement alone may miss some of the opportunities to adequately and more thoroughly affect the modulation of neuropathic sensory information traversing all three spinothalamic tracts.

Directly stimulating the DRG, or combining dorsal stimulation of the traversing and exiting spinal nerves (at the level of the neuroforamina), with/without DREZ stimulation, added to the more traditional approach of dorsal column stimulation (DCS), takes advantage of the neuroanatomy by incorporating additional spinal tracts in the total neuromodulation scheme of neuropathic pain. By appropriately targeting the DRG, individual spinal nerves, or the DREZ, electrical neuromodulation of fibers can be achieved before they are anatomically distributed and reorganized within the dorsal horn to the various spinothalamic tracts. This can greatly augment the efficacy of neuromodulation achieved with DCS alone and can be referred to as *multi-target stimulation*.

It is thus extremely important for the implanter to have a thorough understanding of cranial, spinal, and peripheral neuroanatomy to appropriately take advantage of the wide variety of neuronal targets that are available for efficacious neurostimulation.

Lower amplitudes of stimulation than that needed for the dorsal columns are required for stimulation of the nerve roots and the DRG, because the CSF layer is quite thin at these locations. Thus, contact separation from the targeted tissues is quite small, and significantly less energy is required for activating the nerve fibers at these locations [5, 6]. The amplitudes involved to generate a "therapeutic window" for pleasant and efficacious neurostimulation in the general region of nerve roots and the DRG are extremely small. (This phenomenon is present in the periphery as well, where the distance of separation from the electrical contact to the targeted nerve, and local tissue electrical impedance, determines the amount of energy (amplitude of stimulation) required to obtain clinically relevant neuromodulation.) With the presence of a disease state creating neuropathic pain, these same neuronal pathways may actually be much more sensitive to stimulation as a result of "primary hypersensitivity". Thus, these exquisitely sensitive neuronal pathways may be recruited with even lower levels of amplitude than their adjacent, somatotopically arranged neighbors, and thereby provide more focal targeting of specific anatomical areas. This could have significant clinical ramifications for selective neurostimulation of peripheral nerves, spinal nerves, the DRG, traversing nerves, nerve rootlets and the DREZ.

The optimal contact locations that enable field exposure to a sufficiently wide range of sensory fibers suitable for stimulation tend to cluster in the dorsal aspects of the spinal canal and are the preferred region for therapeutic neurostimulation. To avoid motor stimulation when nerve root or ganglion stimulation is desired, the individual lead electrodes need to be placed quite dorsal to the targeted structure. At this location, the therapeutic effects of both sensory and subsensory stimulation can be obtained with greater precision and success.

Electrical neurostimulation is a surface phenomenon, and the depth of penetration into neural tissue is remarkably small (less than 0.25–0.5 mm) compared to the spread of the stimulating electrical field across the surface of the targeted structure [6]. The more superficial the individual neuron is to the surface of the neural structure being targeted, the greater will be its sensitivity to electrical stimulation. In view of this, it is important to take advantage of the neuroanatomical differentiation between motor and sensory fibers in the spinal nerve roots in the area of the dorsal root ganglion and between the DREZ and the dorsal columns in the cord itself. Precise anatomic placement of the electrical field is essential,

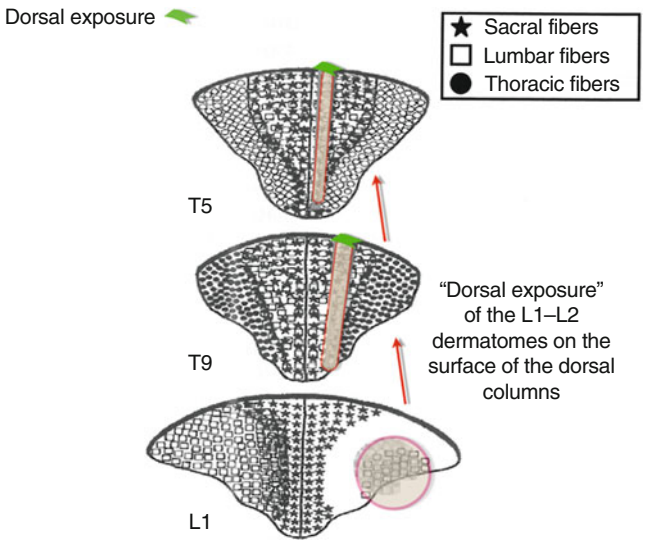


Fig. 43.1 Somatotopic representation of the dorsal columns. Note that after appearing in the deep tissues of the dorsal columns at lower spinal levels, the L1 and L2 dermatomes gradually develop a "dorsal exposure" at more cephalad spinal levels. This creates a superficial "rim" of somatotopic tissue for those specific dermatomes, which can respond to applied electrical fields. This rim of "dorsal exposure" migrates medially from the lateral edges of the dorsal columns along the borders of the dorsal root entry zone DREZ. They then "migrate" medially, as they ascend toward the foramen magnum, becoming thinner as the fibers decrease in size (Adapted from Smith and Deacon [7], with permission)

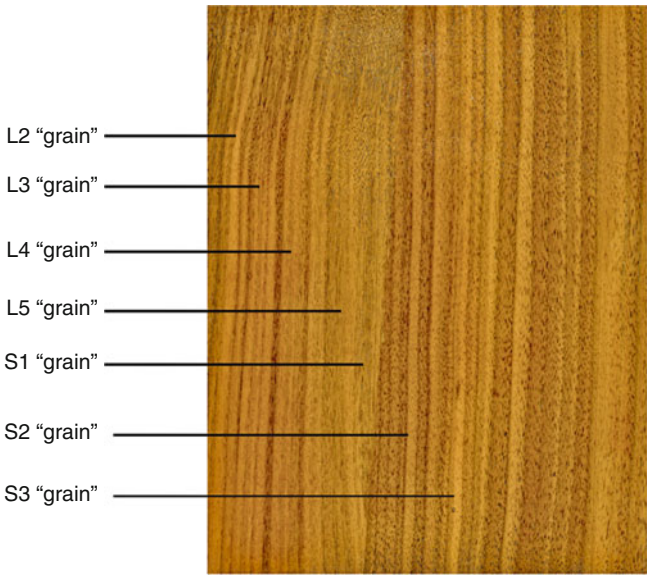


Fig. 43.2 Somatotopic representation of the dorsal columns. The striations of the dermatomes across the surface of the dorsal columns, moving lateral to medial, may well be a bit similar to the grain of wood as seen in this image of a walnut panel. Very little in nature is perfectly parallel, and individual variation between subjects appears to be the "norm." This concept helps to account for the high degree of variation between patients in programming neurostimulator leads over the Dorsal Columns, the DREZ, the DRG and even in the periphery

and the tools to be used include amplitude, frequency, pulse width, and contact configuration of cathodes and anodes. Appropriate attention to the use of all of these tools is necessary to create a therapeutic electrical field.

Further features of the neuroanatomy of the dorsal columns also bear consideration in the clinical application of electrical fields. They include the concepts of somatotopic organization, surface area, fiber types, sizes, and speeds of conduction, and thickness of the dorsal CSF layer.

Somatotopic Organization

There is considerable somatotopic organization within the dorsal columns [7], and fibers consistent with a particular dermatome tend to ascend within an organized scheme. After entrance into the dorsal horn, fibers synapse with interneurons and are distributed to the various ascending tracts. Within the dorsal columns, fibers associated with individual dermatomes appear in the ventral areas, deep within the gray matter of the fasciculus gracilis (thoracic, lumbar, and sacral spine) or the more lateral fasciculus cuneatus (in the cervical spine). From there, these fibers ascend toward the thalamus and migrate dorsally within the lateral aspects of the fasciculus to gradually develop a "dorsal exposure at the lateral border with the DREZ (Fig. 43.1)" [7].

The dorsal exposure on the surface of the dorsal columns is extremely important, as the electrical field does not penetrate greater than 0.25–0.50 mm within the gray matter of the cord. Thus, until a particular dermatome has a "dorsal exposure," it cannot be affected by epidural neurostimulation. The electrical impedance of the CSF is so much greater than the conductivity of the gray matter of the cord that electrical current will more readily be shunted (following the "path of least resistance") into the CSF, away from penetration of gray matter. This causes the electrical field to extend into the area of the dorsal roots (producing "flank" stimulation), and motor activation can occur as stimulation amplitude is further increased.

As shown in Fig. 43.2, this somatotopic organization of dermatomes across the surface of the dorsal columns creates a "grain," much like what one would see within a plank of wood. Clearly, the geometry of the electrical field needs to be parallel to the "grain" to induce the greatest electrical influence over the parallel fibers ascending to the thalamus. Interestingly enough, the majority of neurostimulator leads have contacts with the long axis parallel to the "grain" of the dorsal columns.

This somatotopic organization in the dorsal columns also helps to explain the ability to recruit fibers to create therapeutic paresthesias in the lower extremities from distal sites of stimulation such as the cervical spine (fasciculus gracilis). This is demonstrated by the ground-breaking work by Barolat et al. [8], shown in Fig. 43.3.

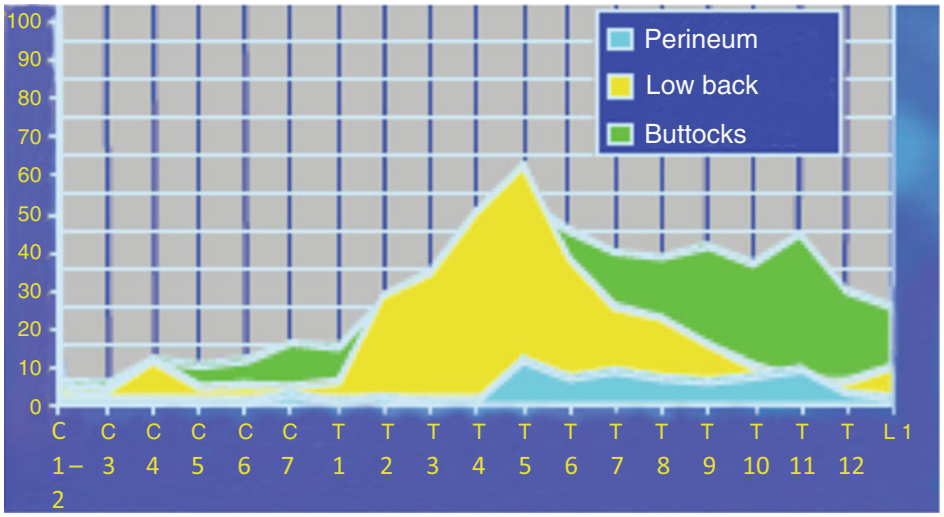


Fig. 43.3 Distribution of paresthesia from the dorsal columns. The ability to recruit stimulation of the lower extremities from cervical levels is well demonstrated in these figures. Barolat et al. noted that roughly 30 % of their subjects could obtain foot stimulation at C7 and nearly 60 % of their subjects could obtain stimulation of the low back at T5 under the right conditions (From Barolat et al. [8], with permission)

Somatotopic sensory organization is seen at all levels in the hierarchy of the nervous system, from the homunculus of the sensory cortex [9] to the ascending tracts in the cord [7], to the DRG [10–12], and within the peripheral nerves [13, 14]. Slipman et al. [15] carefully demonstrated with highly selective, fluoroscopically guided neural stimulation of cervical dorsal root ganglia the wide range of overlapping dermatomal stimulation associated with each DRG. This is a consequence of sensory input from multiple sensory nerve roots into adjacent and nearby dorsal root ganglia and enables a significantly robust interpretation of the sensory environment by the CNS. Thus, the whole concept of "two-point discrimination" is really a subtle and somewhat complex integration of sensory stimuli within the thalamus and higher centers. Obviously, this phenomenon is present throughout the peripheral nervous system, and while the classic dermatome maps are helpful, they are not to be interpreted in absolute terms. While there does appear to be a somatotopic distribution of dermatomal fibers within the DRG at any given level, for neurostimulation to be truly "focal" to a specific anatomic location, it is necessary to be "local" [16]. A conceptual schema of this is shown in Fig. 43.4.

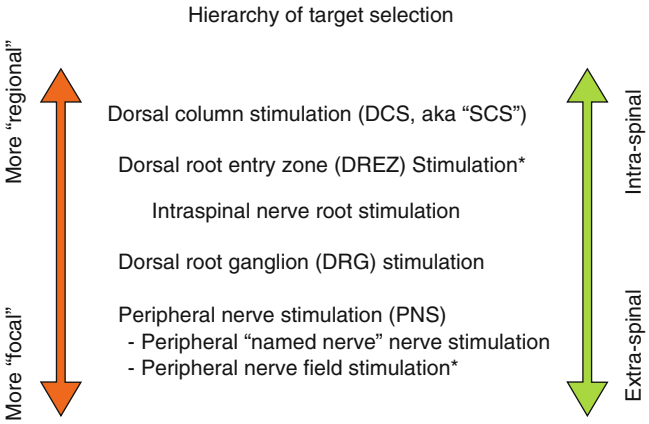


Fig. 43.4 Hierarchy of target selection in neurostimulation. As one moves from intraspinal to peripheral, the targets for neurostimulation change in complexity and specificity. There are always exceptions, especially with tremendous individual variation in patients. Two general exceptions are notable: (a) occasionally somewhat "focal" stimulation can be obtained with small electrical fields placed over rootlets at the DREZ and (b) peripheral nerve field stimulation (*PNFS*) is considerably broader than "named-nerve" peripheral nerve stimulation (*PNS*), as a result of the overlap of small branches from various separate "named-nerves"

Surface Area

The spinal cord varies in its cross-sectional area as it ascends from the conus medullaris to the foramen magnum. There are several remarkably important areas to be considered: the lumbosacral enlargement, the thoracic cord, the cervical enlargement, and the cervical cord. The lumbosacral and cervical enlargements are created by the immense number of additional neurons associated with motor, sensory, and autonomic functions within the lower and upper extremities, respectively, entering the spinal cord. This additional neuronal tissue enlarges the cross-sectional area of the cord over a portion of its distance, and thus, the total surface area of the dorsal columns is also increased. With this increase in the total surface area of the dorsal columns, a statistically greater opportunity exists for stimulating neurons within the dermatomal "grain."

Of particular interest is the fact that within the thoracic cord, above the lumbosacral enlargement, the cross-sectional area diminishes and the ability to stimulate sacral elements almost diminishes considerably. It is reasonable to conclude

that the width of the "grain" for the sacral dermatomes becomes quite small for most patients and is thus potentially quite difficult to recruit from surface stimulation. The opportunity to stimulate sacral and lower extremity dermatomes reappears at the cervical enlargement and continues some distance toward the foramen magnum [17]. It is almost as though fiber tracts "hidden" from an applied electrical field of stimulation within the fold of the dorsal median sulcus have blossomed back out onto the surface where they are again susceptible to stimulation. In many patients, there appears to be a slight contraction of the surface area of the dorsal columns within the cervical cord cephalad to the cervical enlargement, but in general, the surface area of the dorsal columns within the cervical cord is much greater than seen in the thoracic cord below the cervical enlargement. The cross-sectional geometry of the thoracic cord is virtually circular, whereas the cross-sectional geometry of the cervical cord resembles that of a lima bean, having a broader dorsal surface. With the cervical enlargement, the fasciculus cuneatus is formed lateral to the fasciculus gracilis, between which is the dorsal intermediate sulcus, and carries a "dorsal exposure" for dermatomes representing the upper extremities.

Fiber Types, Sizes, and Speeds of Conduction

There are different fiber types and sizes of fibers populating the dorsal columns. Both myelinated and unmyelinated fibers are found within the superficial layers of the dorsal columns, and they vary in size. Feirabend et al. [18] have shown by histological studies that Aβ-fibers having larger fiber diameters are found to recur more frequently along the lateral edges of the dorsal columns and near the center. Roughly 85 % of all fibers in the superficial dorsal columns are smaller than 7 μm, and only 1 % is larger than 10 μm, but these larger fibers occur with much greater frequency in the more lateral portions of the dorsal columns [18]. Aβ-fibers from a laterally placed dermatomal "grain" become smaller and migrate medially as they ascend toward the thalamus.

Of course, not all of the fibers are of a uniform size, nor are all the fibers myelinated. This has important consequence in neurostimulation because smaller fibers require greater amplitudes of stimulation intensity to trigger a response than larger fibers. This is demonstrated by a typical strength-duration curve shown in Fig. 43.5. Longer pulse width values promote the activation of smaller diameter fibers relative to larger diameter fibers, as found in other neurostimulation applications [19]. Thus, in dorsal column stimulation, longer pulse widths tend to increase the number of fibers activated, recruiting more of the smaller fibers toward the midline in the dorsal columns, where more sacral fibers are to be found, and producing a "sacral shift" in the perceived stimulatory pattern (Fig. 43.6) [20].

Also of note is the fact that the sensations created by neurostimulation of the dorsal columns traveling in myelinated fibers will reach the thalamus prior to those traveling in unmyelinated fibers. This is true whether the number of fibers recruited by any stimulatory pulse is sufficient to create a perceptible sensation within the thalamus, or remain as an imperceptible or "subliminal" influence upon the global sensory processing within the thalamus. Such a situation could perhaps block painful and erratic neuropathic signals

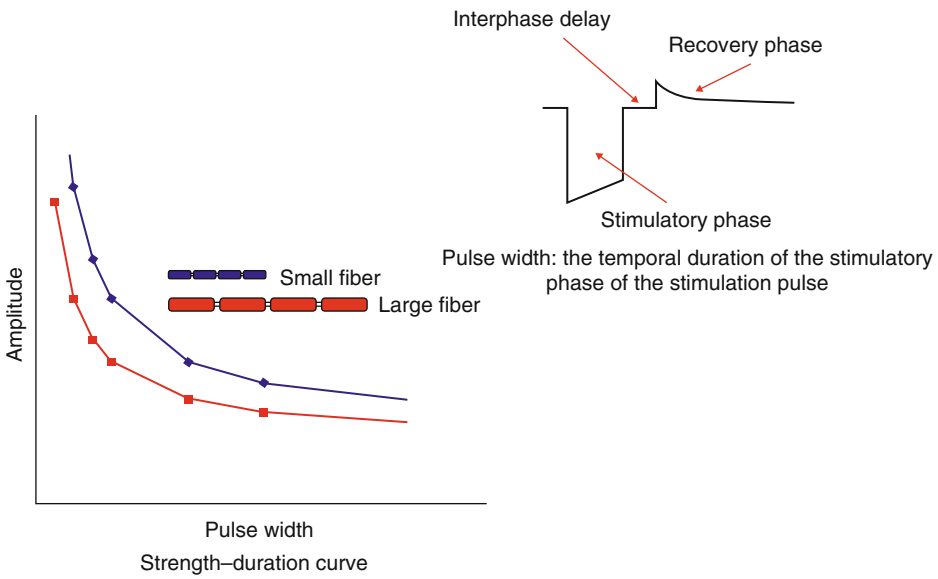


Fig. 43.5 Strength-duration curve. Larger diameter neuronal fibers are activated by applied electrical fields more easily than smaller fibers. Fiber sizes tend to be smaller nearer the midline of the dorsal columns. Increasing the pulse width of the stimulatory phase of the applied electrical field recruits more of these smaller diameter fibers and increases the area of perceived stimulation. *Inset*: A typical stimulation pulse for a neurostimulator contact

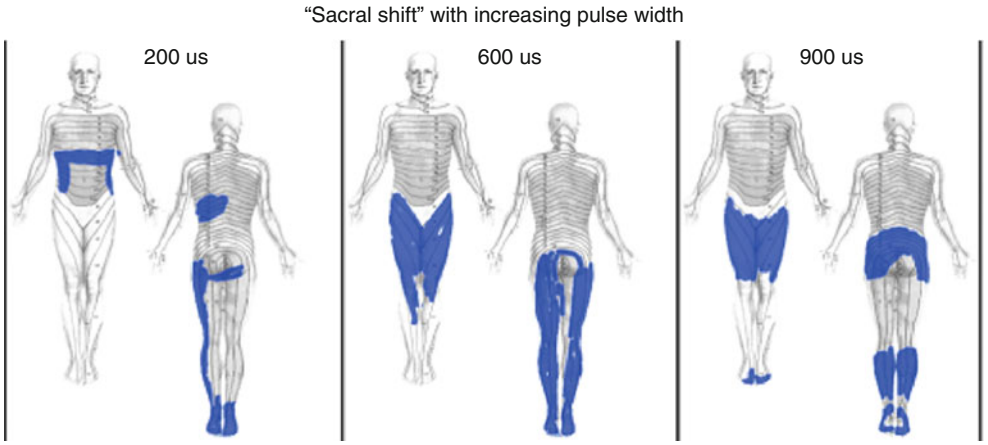


Fig. 43.6 Clinical example of the "sacral shift." The clinical effect of increasing pulse width in the stimulation pulse is often to increase the incorporation of smaller, more medial fibers (typically in greater abundance in the midline of the dorsal columns: sacral dermatomes primarily) (From Yearwood et al. [20], with permission)

from traversing the same individual neurons. With higher frequencies of stimulation, a greater number of fibers could potentially be slowly driven into a relative refractory phase, effectively rendering these fibers unavailable for pathologic signal transmission.

Finally, the absolute and relative refractory periods of the targeted neurons are in the time range of milliseconds, whereas stimulation duration and recovery phases of a typical neurostimulation system are in the time range of microseconds. This means that a typical neurostimulation system can deliver a number of stimulatory pulses of different contact configurations much more quickly than the CNS can process the individual signals. The typical speed of cinema is roughly 24 frames/s. This enables the CNS to appreciate perceptions of smooth motions from rapidly displayed individual "still-shot" frames. Thus, it is not surprising that the neurostimulation systems presently available are able to provide considerable sophistication in perceived and subliminal signals to interrupt the interpretation and CNS response of painful stimuli resulting from neuropathic processes. A typical rate of 40 stimulatory pulses/s is certainly above the CNS processing speed, as noted by the sensation of constant stimulation by most patients and this frequency. As in cinema, however, it remains to be seen if even higher rates of stimulation (400–800 Hz) provide a sense of "high definition (HD)" to the CNS that could have therapeutic benefit.

Thickness of the Dorsal CSF Layer

The thickness of the CSF layer between the implanted epidural contacts and the surface of the dorsal columns or other neuronal structures varies considerably within each individual patient based on posture and location within the spinal canal [21]. With increasing thickness of the CSF (dCSF) between individual contacts and neuronal surfaces, there is increasing influence of the electrical impedance of the CSF, requiring increased intensity of stimulation to achieve paresthesias. However, with increased distance from the contact, coupled with increased amplitude, the size of the electrical field across the surface of the targeted neuronal structures becomes larger and optimal target stimulation is easily compromised. In transitioning from prone to supine, there is a dorsal movement of the spinal cord within the dural and the dCSF can decrease remarkably. Unless the amplitude of the stimulation is decreased concomitantly, the patient may feel too intense a stimulation, and be uncomfortable, or the patient may experience too wide a field of stimulation, with collateral paresthesias that are similarly uncomfortable. Alterations in the local dCSF are also seen with transitioning from laying to sitting, sitting to standing, extending and flexing the spine, and lateral bending or twisting. All these considerations are important during the programming of the implanted device to assure optimal therapeutic benefit to the patient.

In summary, the efficacy of neurostimulation is dependent upon two fundamental concepts: appropriate placement of the electrode array (lead) in order to electrically modulate the bioelectric phenomena of the targeted neuronal tissue and the appropriate programming of the electrical neurostimulator system to control the style and character of the neuromodulation of the neuronal surfaces.

Lead Placement

Careful lead placement near the appropriate neuronal target(s) is essential in order to achieve the greatest likelihood of therapeutic stimulation within the superficial layers of the neuronal structure: peripheral nerve, DRG, dorsal roots, DREZ, dorsal columns, superficial motor cortex stimulation (MCS), or deep brain stimulation (DBS). It is crucial to remember the principle that the *ultimate target* of all of our neurostimulation efforts is the thalamus and that portion of the CNS involved in the perception of painful signals, and the response to pain.

Electrical Field Shaping (Programming)

Contact configuration and amplitude determine the size and shape of the stimulatory field. Pulse width can exert an influence on the total number of fibers stimulated by a specific stimulatory pulse by causing the stimulatory field to "linger" over the neuronal target, recruiting a greater number of fibers. Frequency can alter the repetition of activation and at higher rates (>1,000 Hz) can theoretically create a situation in which many fibers in the superficial layers of the dorsal columns can become relatively refractory.

Therapeutic Goals

The goal of therapy in electrical neurostimulation is to alter the pain state of the patient in such a way as to enhance the capability of achieving success with functional rehabilitation. Neuropathic pain in the extremities is often accompanied by abnormal muscle tone, usually episodic in nature, as well as autonomic dysfunction: decreased blood flow to connective tissue, muscles, and neuronal tissues; temperature abnormalities; and perspiration dysfunction. To achieve improvement in physical function, these autonomic features must be addressed along with the underlying pain complaints, to improve the metabolic state of the affected extremity. For this reason, it is often not sufficient for the patient to "feel stimulation" in the affected area and yet still have the autonomic dysfunction.

It is quite important to realize that the role of electrical neurostimulation is not limited to "pain relief" per se but should serve as an important tool in the rehabilitation of the patient. As such, it becomes a part of the overall plan of therapy for the patient to be integrated with functional rehabilitation, oral medication management, behavioral therapy, and conservative spinal injection techniques.

Clinical Examples: Treatment of Radicular Pain Syndromes

The term "radiculitis" is from the Latin *radix* – root – and is defined as the inflammation or irritation of the nerve root between the spinal cord and the exit of the nerve root from the canal [22]. As such, any irritation of a lumbar nerve root would be expected to create sensations (often painful) that "radiate" from the axial spine to the periphery. But note that the emphases of the definition are on the nerve "*radix* – root"– and not on the concept of radiating (from Latin *radiare* – "to emit rays"). Thus, painful sensations perceived along the axial distribution of the spine can result from a radiculitis or a radiculopathy of the nerve roots. That can be a significant clinical challenge. It can also provide a significant advantage for the clinical application of neurostimulation.

As noted by Malik and Benzon [23], the clinical syndrome of radicular pain in a predictable dermatomal pattern, characterized by *subjective* reports of sensory disturbance (paresthesia, dysesthesias, numbness, hyperalgesia, allodynia, etc.), and typical *objective* signs of weakness, decreased reflexes, and positive dural tension signs is referred to by a variety of terms: radiculopathy, radiculitis, and radicular syndrome. However, as they point out, the term *radiculopathy* inappropriately implies the presence of objective signs of pathological nerve root damage, including loss of sensation, muscle weakness, and diminished reflexes. But all of these objective signs can occur without objective evidence of anatomical or pathological nerve damage. In a similar fashion, *radiculitis* inappropriately implies an inflammatory process as the sole etiology for the causation of the radicular signs and symptoms. The term *radicular pain syndrome* appears to be most appropriate and correctly suggests a constellation of clinical signs and symptoms of variable etiology secondary to pathology or dysfunction of the sensory nerve roots or the dorsal root ganglia (DRG).

Thus, a radicular pain syndrome can be axial in distribution, or it can be manifested as radiating into an extremity, or a distribution of pain can occur in both the spinal axis and in the extremities concurrently.

Cervical Radicular Pain Syndrome

Post-laminotomy syndrome of the cervical spine s/p anterior cervical discectomy and fusion (ACDF), also known as failed neck surgery syndrome, often manifests itself with continued cervicogenic headache (CHA) [24–26], primary discogenic pain above and below the level of the fusion, axial neck pain, and upper extremity radiculitis/radiculopathy. Little is known about the neuropathic nature of primary discogenic pain in the cervical spine, but it has been well studied in the lumbar spine and has been found to have a nociceptive etiology with heavy autonomic nervous system transmission of sensory signals [27]. Thus, perceived pain within the axial spine, centrally and laterally, may have a neuropathic-like component susceptible to neurostimulation therapy; it is not necessarily always due to nociceptive facet arthropathy. Because it is neuropathic in nature, neurostimulation efforts can be of substantial benefit in treating this form of pain. Additionally, chemical radiculitis secondary to a disrupted cervical disc annulus can provoke tremendous neuropathic discomfort of the nerve roots, also suitably treated with neurostimulation. (This pattern of pain pathology is frequently seen with patients having a relatively normal MRI appearance of the cervical disc, but to exhibit significant leakage of radiocontrast material injected during provocative discography into the nucleus of the disc.)

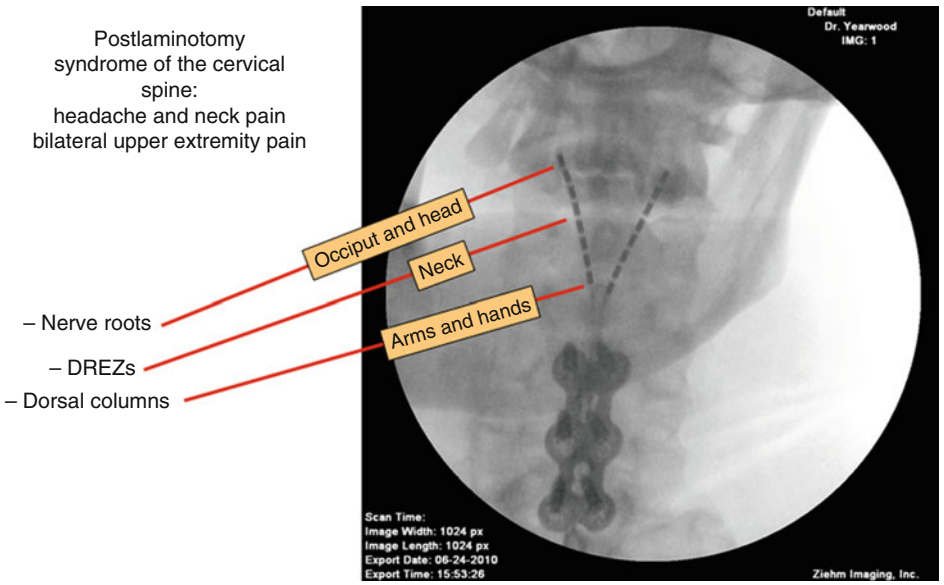


Fig. 43.7 Antegrade leads for post-laminotomy syndrome – cervical. Leads have been advanced in such a way as to curve laterally from the area of the dorsal columns (proximally) to the area of the nerve roots at C2 and C3 (distally), traversing the dorsal root entry zone (*DREZ*) along the way. Thus, in this single-lead array, three different types of neuronal targets are available for therapeutic stimulation

In the example shown below (Fig. 43.7), neurostimulator leads have been placed in such a way as to garner the greatest degree of therapy for the various pain areas in this particular patient: cervicogenic headache (CHA), axial neck pain, and bilateral upper extremity radicular pain. Stimulation of the nerve roots at C2 and C3 by the most cephalad contacts places sensory stimulation into that part of the thalamus and CNS that processes pain interpreted as deriving from the occipital nerves bilaterally. Clinically, this pattern of stimulation over the C2 and C3 nerve roots has the ability to provide excellent control of suboccipital headache pain, remarkably similar to that seen with peripheral occipital nerve stimulation (ONS).

More proximal along the leads, the neurostimulator contacts diagonally traverse the bilateral dorsal root entry zones (DREZ). Contact configurations can be along each lead individually, or between the leads, to achieve lateral and posterior axial stimulation of the neck. This pattern of stimulation can often cover the lateral neck, posterior neck, and shoulder girdle area: posteriorly (to the spine of the scapula) and anteriorly (to the infraclavicular area). Activation of the more caudal and medial contacts produces a dorsal column stimulation, affecting the upper extremities. Thus, all portions of the leads are used in a highly efficient manner.

An entirely different approach to the same clinical problem is shown in Figs. 43.8 and 43.9. In this case, retrograde C1–C2 cylindrical leads (euphemistically known as "percutaneous leads") have been placed over the area of the DREZ bilaterally, using an approach similar to that described by Whitworth and Feler [28]. In this case, the same results have been obtained. The advantages to this particular lead arrangement are the relative stability of the lead positions and their resistance to migration with active and dynamic movement of the head and neck. Migration of antegrade-placed cylindrical leads in the cervical spine can be a frequent clinical complication, because anchoring to the supraspinous ligament to the level of T2 or T3 allows too large a range of motion for the cervical spine relative to the leads. While paddle lead placement is associated with less lead migration, the lack of lead flexibility encourages greater encapsulation than is seen in more flexible "percutaneous" leads and can create a greater degree of spatial "occupation" in an area of the spine at risk for spinal stenosis secondary to degenerative disc disease. Furthermore, with factory-specified contact configurations, the surgical-lead implant is less versatile for selection of neuronal targets within the cervical spine.

Thoracic Radicular Pain Syndrome

Thoracic radiculitis can arise from a number of pathological conditions, including trauma, surgical trauma, infection (most notably herpes zoster), chemical radiculitis from degenerating discs, mechanical nerve impingement related to discopathy, metabolic disease (i.e., diabetic mononeuritis), degenerative scoliosis, degenerative stenosis, and peripheral intercostal nerve trauma. Figure 43.10a, b show the lead configuration for a patient suffering from three-level intercostal neuralgia secondary to trauma. The patient has had open reduction and internal fixation (ORIF) of two ribs at T8 and T10 and a complete resection of the T9 rib, all on the right. The patient's neuropathic pain was widely distrib-

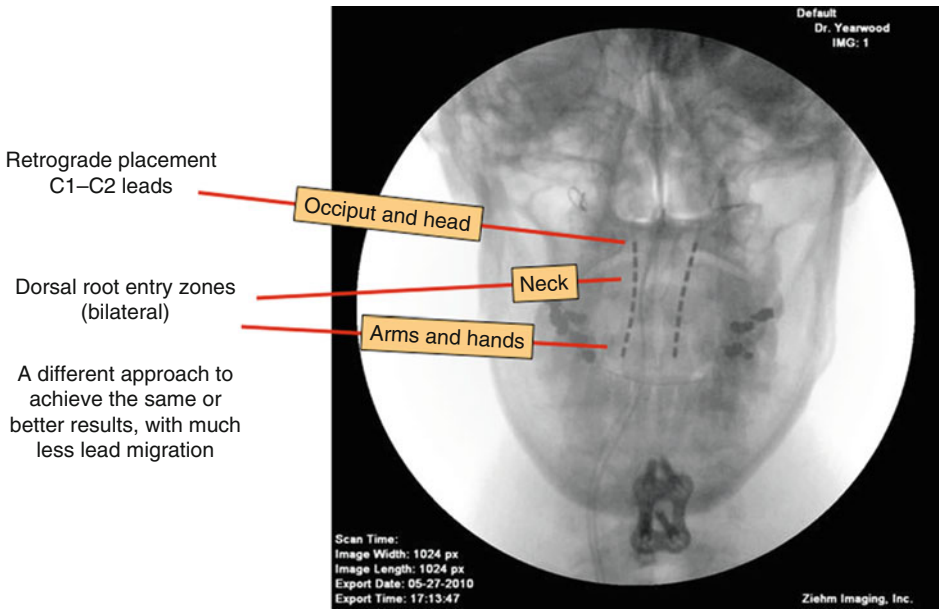
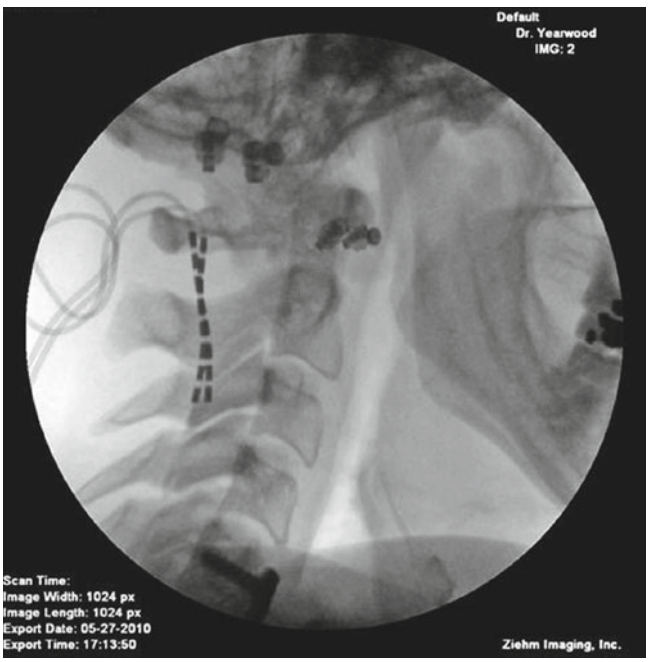


Fig. 43.8 Retrograde C1–C2 cylindrical leads ("perc" leads) for post-laminotomy syndrome – cervical (AP view)

Fig. 43.9 Retrograde C1–C2 cylindrical leads ("perc" leads) for post-laminotomy syndrome – cervical (lateral view). Note that the leads have been surgically placed over the arch of C1, to which they have been anchored. The leads remain posterior and experience very little migration with this configuration



uted along the lateral chest wall and toward the upper abdomen. Repeated intercostal injections provide the patient with an excellent pattern of pain relief, but were not durable, and the patient went on for implantation of neurostimulation therapy. Because of the secondary hyperalgesia involved in this neuropathic pain problem, it was clear that dorsal column stimulation was needed to provide "regional" therapy, with nerve root/DREZ stimulation more "focal" intercostal nerve therapy.

"Multimodal" Targeting for Neurostimulation at Different Levels of the Sensory Processing Hierarchy

This particular case serves to illustrate the concept of combining the more direct *focal* therapy achieved by modulating nerve roots/DREZ (creating a pre-dorsal horn modulation of sensory signals) with more diffuse *regional* therapy achieved by modulating dorsal column fibers directly (post-dorsal

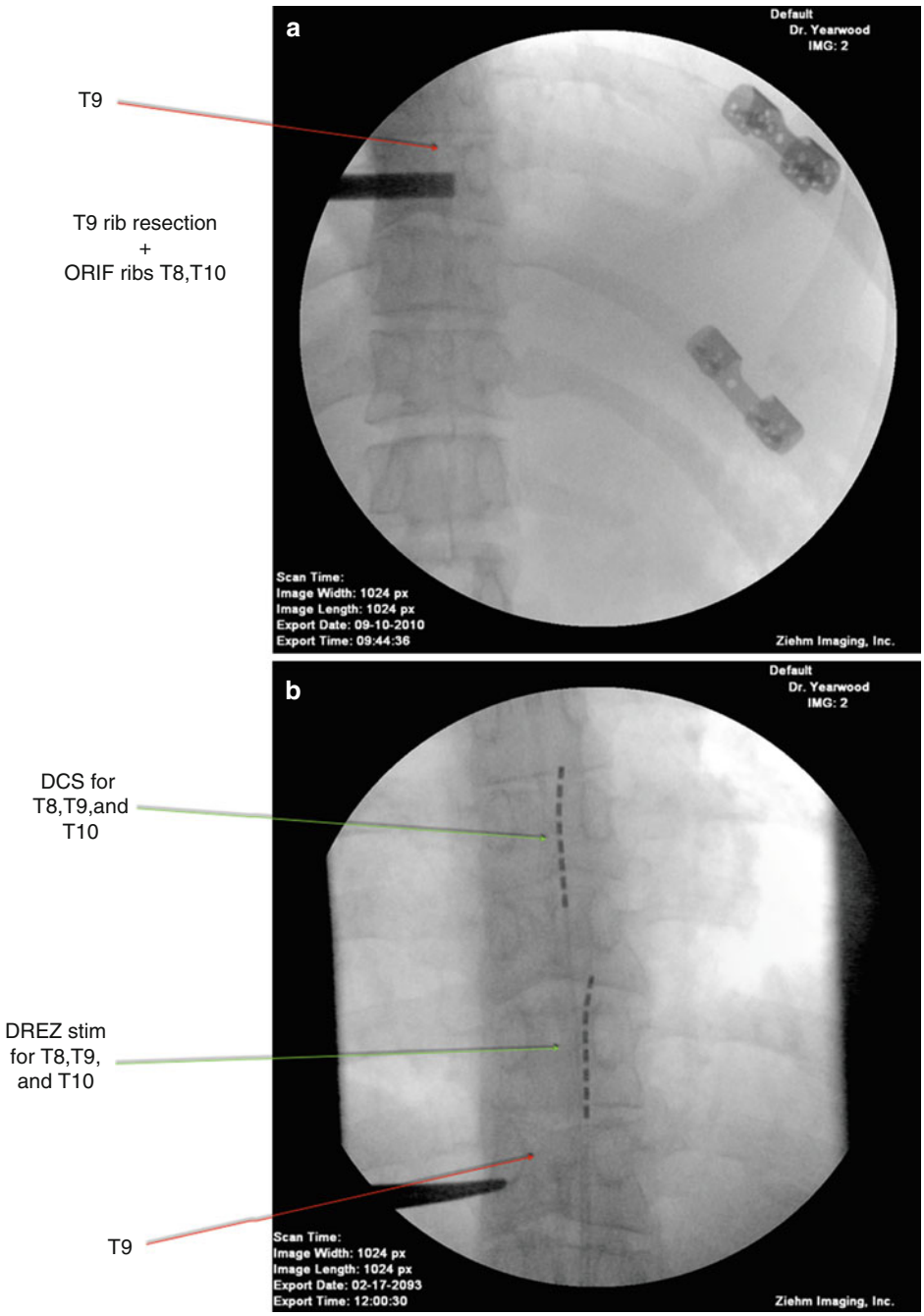


Fig. 43.10 (**a**) Radiological view of rib pathologies leading to intercostal neuralgia in a young male patient after a motorcycle accident. (**b**) Staggered thoracic leads for intercostal neuralgia

horn modulation). This combination of nerve root/DREZ and dorsal column stimulation fields can be highly effective, especially in more difficult cases of radiculitis where a strong component of neuralgia is present in addition to the more diffuse aching and burning pain associated with secondary hyperalgesia. This technique can often succeed in other cases throughout the spinal canal where there is a strong component of peripheral neuralgia coupled with a more regional field of neuropathic pain (e.g., CRPS-II). In the thoracic spine specifically, this technique has proven to be highly effective for postherpetic neuropathy pain and intercostal neuralgia associated with post-thoracotomy syndrome [29–33], which can be quite refractory to dorsal column stimulation alone [34].

An excellent example of this situation is shown in Fig. 43.11. This patient sustained an electrocution injury of the right upper extremity and right chest wall while speaking on the telephone during a lightning storm. He developed severe

Electrocution injury, right upper extremity and right chest wall

1. Neuropathic pain in right upper extremity ≈ CRPS-II ulnar nerve presentation

2. Large area of neuropathic pain in right chest wall ≈ CRPS-I presentation

DCS plus NRS creates greater efficacy in CRPS-II, allowing a greater influence over multiple spinothalamic tracts: lateral, ventral and dorsal

DREZ stimulation across a wide swath of nerve rootlets influences larger areas of pain:
- Sympathetic fibers involved
- Total surface area is much greater than at the neuroforamen

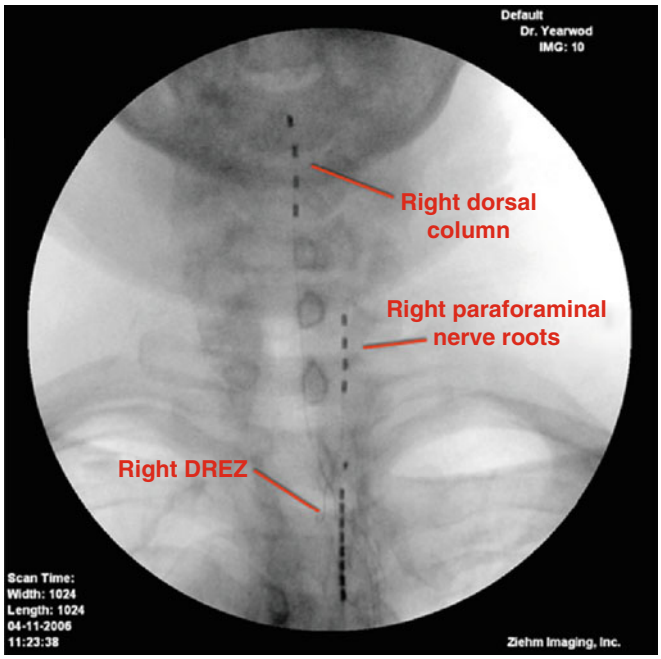


Fig. 43.11 Clinical application of "multimodal" neurostimulation at three different types of neuronal targets in the same patient

neuropathic pain that was consistent with a CRPS-II ulnar nerve presentation, coupled with a large area of neuropathic pain in the right chest wall having a CRPS-I presentation. His ulnar nerve-related neuropathic pain spread over several dermatomes, but his trial with dorsal column stimulation alone failed to relieve him of the obvious and persistent neuralgia associated with the ulnar nerve. Thus, he required not only dorsal column stimulation (DCS) but also nerve root stimulation (NRS) for more durable and efficacious therapy in his right upper extremity. The ability to stimulate along neuronal traction specific to the ulnar nerve on the right with NRS enabled "focal" therapy to be added to "regional" therapy from the DCS. In addition, he required neurostimulation therapy over the dorsal root entry zone (DREZ) in the thoracic spine to achieve suitable therapeutic efficacy of a very "focal" region of secondary hyperalgesia over multiple dermatomes. This is demonstrated by the right DREZ lead over the T2 and T3 spinal levels in Fig. 43.11. Thus, three different levels of the sensory processing hierarchy are involved in providing the patient with suitable pain relief.

Axial thoracic spine pain from degenerative disc disease and chemical radiculitis, as would be expected from incompetent thoracic annuli fibrosis (as demonstrated by significant leakage of radiocontrast material during thoracic discography), is notoriously difficult to treat with neurostimulation. However, optimal lead placement and creative programming can be effective in this area as well. Figure 43.12a, b demonstrate lead placements over the lateral edges of the DREZ for a young male patient with debilitating thoracic axial pain and rather modest radicular pain secondary to chronic degenerative disc processes believed to be associated with sports injuries (football). Dorsal column stimulation alone proved to be very inadequate in covering this patient's pain problems. A more lateral DREZ placement proved necessary, in order to obtain suitable therapeutic stimulation for his axial pain. Optimal programming for this lead involved the use of an "over-intensified anode" stimulation scheme.

"Over-intensified Anode" Stimulation Scheme

This case demonstrates the application of a single anode (+) coupled with seven cathodes (−) at three locations within a single stimulation program (Fig. 43.13). By carefully adjusting the amplitude and the pulse width of stimulation within these multiple, encompassing cathodes, "over-intensification" of the anode is achieved. This produces an area of hyperpolarization, surrounded by a very small area of the cathodic stimulation known as anodic "side lobes." This phenomenon is described in more detail by Rattay [35] and Struijk et al. [6]. As shown in Fig. 43.14, the highest current density is located at the anode. Fibers traversing "away" from the contacts with anodic side lobes are most responsive to this cathodic stimulation. The effects of the region of hyperpolarization may include denied access for neuropathic sensory signals along the neuronal structures in that "somatotopic grain." With this area surrounded by a very narrow field of cathodic activation, the net result arriving at the level of the thalamus is an interruption of neuropathic sensations with rather significant

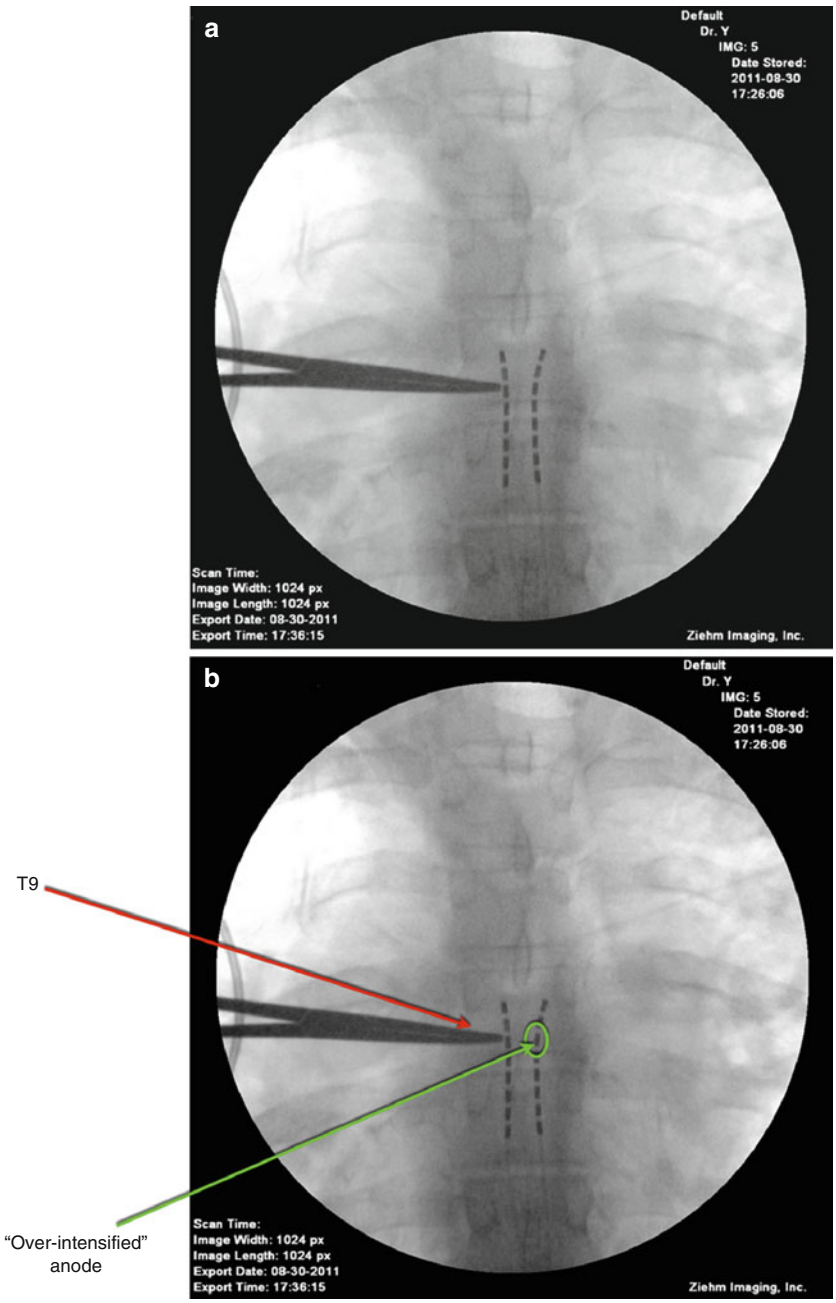


Fig. 43.12 (**a**) Bilateral DREZ placement for axial mid-thoracic primary discogenic pain. (**b**) "Over-intensified" anode in thoracic DREZ lead for axial thoracic pain

insertion of therapeutic, neuromodulating sensations. Clearly, stimulation from the caudal aspects of the cathodic field, which surrounds the area of hyperpolarization, will be partially blocked from the thalamus, but they may play a dual role in retrograde (antidromic) interference with ascending neuropathic signals [36]. Considerably, more work is needed to tease these aspects out in detail, but multiple clinical applications of this programming scheme are currently under investigation. This programming scheme is also quite effective for other targets within the spinal canal:

(a) The C2–C3 nerve roots (for stimulation within the distribution of the occipital nerves), where recruitment of high cervical fibers beyond the "reach" of standard cathode field stimulation
(b) The S2 and S3 nerve roots and the dorsal root ganglia in the sacrum (for stimulation within the distribution of the pudendal nerve).

Lumbar Radicular Pain Syndrome

Lumbar radicular pain syndrome is a very common pain problem because of degenerative or traumatic structural changes in the lumbar spine. As a portion of the spine with

the greatest biomechanical stresses imposed throughout a normal day of activity, the structures are generally larger, thicker, and more bulky and are held in alignment with some of the most structurally durable fascia anywhere to be found in the body. Because of the interrelatedness of these structures and the profuse neural supply that accompanies them, a physiologic or anatomic failure in any member of this articulated, weight-bearing complex of hard and soft tissues can have widespread consequences. Further, with the wide distribution of sensory neurons throughout this highly complex structure, the problems of referred pain can be tremendous. But, referred pain patterns can also offer an advantage to the clinical application of neurostimulation.

The appropriate intraspinal neuronal targets for the treatment of radicular pain syndrome with neurostimulation are as follows: the dorsal columns, the dorsal root entry zone, the nerve roots (traversing and exiting), and the dorsal root ganglion. These can be targeted individually, or more commonly, in combination. At nearly every target, the somatotopic distribution of sensory pathways offers opportunities and challenges.

Lower extremity radicular pain syndrome is easily addressed with dorsal column stimulation (DCS). The dermatomesof the lower extremities are L3, L4, L5, and S1, with portions of L2 and S2 that may be more pronounced or less pronounced within individual patients. The somatotopic distributions of these dermatomes are easily obtainable in most individuals between the superior endplate of T8 and the inferior endplate of T10. At these vertebral levels, midline placements of the contact arrays provide them with multiple available targets over the surface of the dorsal columns medial to the dorsal root entry zone (DREZ). If there is any correlation between the size of the homunculus and the density of the corresponding sensory neurons traversing the superficial layers of dorsal columns, it would be expected that there would be many more neurons available for stimulation of the lower extremities than for stimulation of the low back.

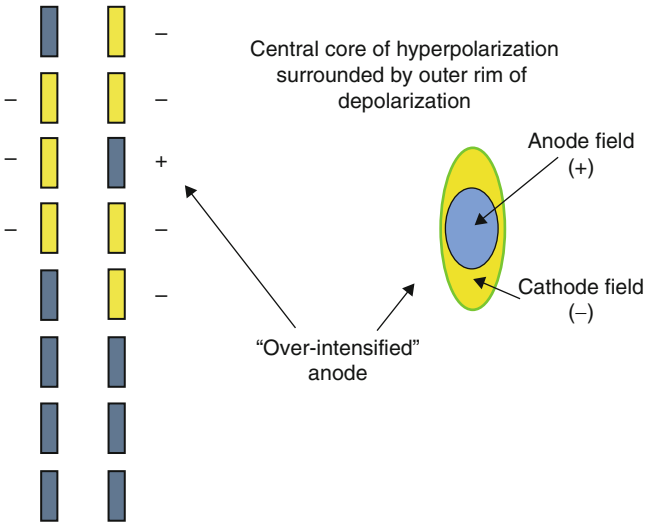


Fig. 43.13 Contact configuration for "over-intensified" anode programming scheme

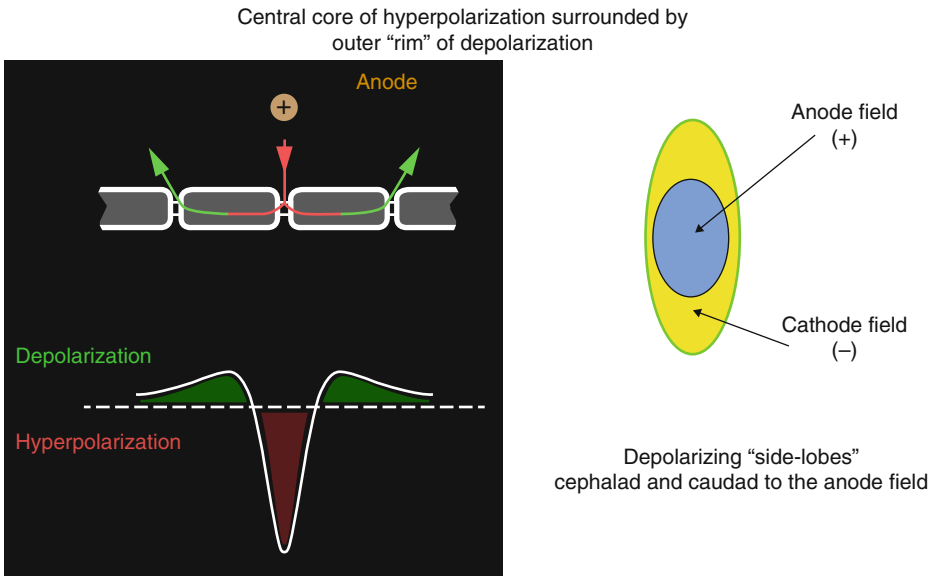


Fig. 43.14 "Side lobes" of depolarization associated with an "over-intensified" anode. Note that the rectangular geometry of the neurostimulator contacts, coupled with a decreased electrical impedance along the "grain" of the dorsal columns, causes the width of the electrical field on the surface of the spinal cord to be elongated in the cephalad-caudad dimension and narrowed laterally. This can be used to move the area of depolarization under the cathode away from the DREZ when attempting to avoid "flank" stimulation with the thoracic epidural lead placement (Adapted from Rattay [35], with permission)

Dorsal column stimulator (DCS) lead placement for complex, unilateral left lower extremity pain

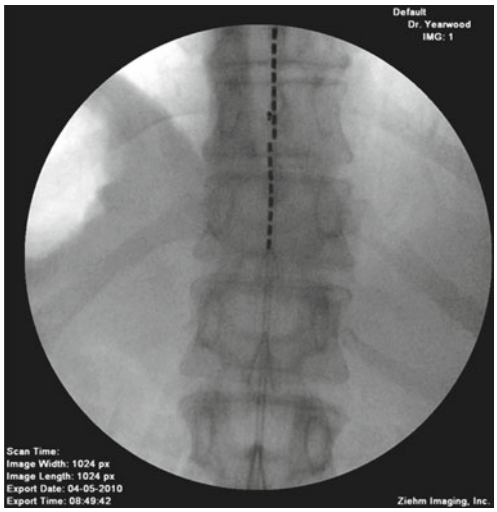


Fig. 43.15 Lead placement for multilevel dorsal column stimulation to an isolated lower extremity

Lead placement for plantar surface pain

Exiting L5 and traversing L4 nerve roots

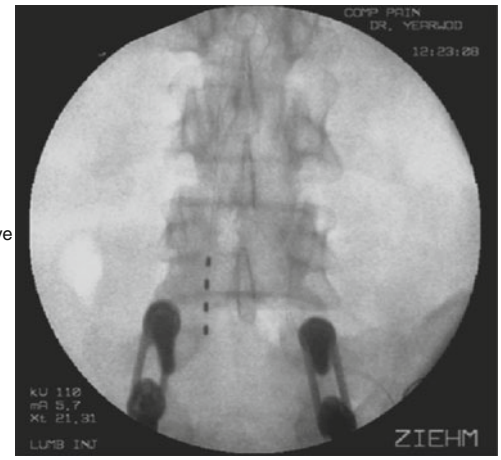


Fig. 43.16 Retrograde lead for plantar surface pain. This lead captures targets from the exiting L4 nerve and the traversing L5 and S1 nerves to provide stimulation to the plantar surface of the foot, achieving durable access to the CNS for neuromodulation of a specific anatomic location not well accessible in this particular patient from the dorsal columns

Multiple programming techniques can be highly useful in obtaining discrete areas of neurostimulation within this broadly distributed field of targets. As noted above, increasing pulse width can cause recruitment of smaller, more medial fibers associated with more sacral dermatomes (the sacral shift [14]). Discretely placed "over-intensified" anodes [30] can provide remarkable precision in obtaining relatively small areas of focal neurostimulation from the dorsal columns.

Figure 43.15 demonstrates lead placement for single lower extremity neuropathic pain secondary to post-laminotomy syndrome of the lumbar spine. In this clinical situation, the patient had severe neuropathic pain, responsive to lumbar sympathetic blockade, isolated to the entirety of the left lower extremity. The leads were place in such a manner to obtain the maximal stimulation over the available dermatomes based on the somatotopic organization of lower extremity fibers in the dorsal columns. The more caudal lead is slightly more laterally placed than the cephalad lead, and multiple vertebral levels are covered from the T9–T10 disc to the T11 vertebral body. This configuration provides neurostimulation across the full width of the left dorsal column, in the area of dorsal surface exposure of the dermatomes of the lower extremity. The patient experiences paresthesias throughout all areas of his leg, foot, and toes.

It is not always possible to obtain and maintain suitable stimulation of the foot from a dorsal column lead placement (Barolat personal communication, 2002; unpublished). From the discussion above, it should be apparent that this may be due more to the individual variations in the presence of sensory fibers that specifically represent the foot. A statistically sufficient number of targets within the area of "dorsal exposure" are required for those specific neuronal tracts on the surface of the dorsal columns specific for the foot to be available for DCS. Thus, it may be important to employ multi-target stimulation techniques, as described above, in order to achieve a more "focal" stimulation pattern.

Figure 43.16 shows lead placement for nerve root stimulation (NRS) to obtain suitable neurostimulation of the foot (plantar surface) for treatment of neuropathic pain. This patient had dorsal column neurostimulation leads for post-laminotomy syndrome but required supplemental stimulation of the L4 and L5 nerve roots in order to fully recruit efficacious paresthesias to areas of the foot. This lead was placed in a retrograde manner from the L1–L2 level, with entrance into the epidural space from the right, and dorsal placement maintained over the midline of the spinal canal, until the region of L4 was reached, at which point the lead was gradually steered into the dorsal aspects of the lateral recess on the left.

Despite the excellent clinical results achieved by this method of neurostimulation in the short term, there has been at least one report in the literature to suggest that nerve root stimulation may ultimately prove to be nondurable solution [37]. Nevertheless, clinical experience indicates that nerve root stimulation can offer substantial benefit to the patient and has been maintained for over 5–6 years with sophisticated reprogramming (Yearwood, (2010) personal communication not published). When there has been progression of discopathy, creating further central and neuroforaminal stenosis, the encapsulated lead itself can create a mechanical compression of the nerve root, evidenced by clinical signs of increased radicular pain. Judicious removal of the neurostimulation lead is then advised. This appears to be a rare phenomenon.

Low Back Pain: Lumbar Radicular Pain Syndrome Limited to the Axial Distribution

The treatment of axial pain that is predominantly centered about the lower lumbar and lumbosacral area has proven to be a considerable challenge. Many patients are able to experience therapeutic neurostimulation in this area from epidural lead arrays placed over the dorsal columns, yet often find that the pain is inadequately treated, and suffer from persistent "breakthrough" pain. Many patients cannot maintain an efficacious stimulation of this area, after having experienced substantial benefit initially, and only continue to receive paresthesias in the lower extremities. This all too often encountered clinical experience has led to increasingly sophisticated technologies to target the lower back from the epidural space. Some of these technologies are still "emerging" and have yet to prove themselves in the long run: subthreshold and high-frequency stimulation (Nevro Corporation, Menlo Park, CA), a new way to "program" epidural neurostimulation, and dorsal root ganglion stimulation (Spinal Modulation Inc., Menlo Park, CA), a new *location to target* from within the epidural space.

Deep spinal pain originating in the disc results from the transmission of nociceptive pain of inflammatory etiology by way of the sinuvertebral nerves. The sinuvertebral nerves also supply innervation to the longitudinal ligament and notably cross the midline of the posterior disc and ligament complex [38, 39]. Thus, right-sided annular disruption can at times be perceived as pain on the left lower back, as the depth and height of the annular tear progresses under the normal "wear and tear" of the activities of daily living. The primary nociceptive afferent fibers of the sinuvertebral nerve travel to the spinal cord by a dual pathway [40]: one route travels with fibers of the DRG and thus presents a segmental pattern of innervation from the disc to spinal cord. The other route travels in a non-segmental fashion with the sympathetic system by way of the gray ramus communicans to the sympathetic chain. From here, primary nociceptive afferent fibers ascend to the L2 level (and possibly to some other levels more cephalad), returning via the white ramus communicans nerve to the join the sensory fibers of the DRG and ascend into the cord in that manner (Fig. 43.17). Thus, the character and mechanisms of lumbar discogenic pain suggest it is a type of "visceral pain" (as suggested by others [27, 41, 42]) unique to the musculoskeletal system

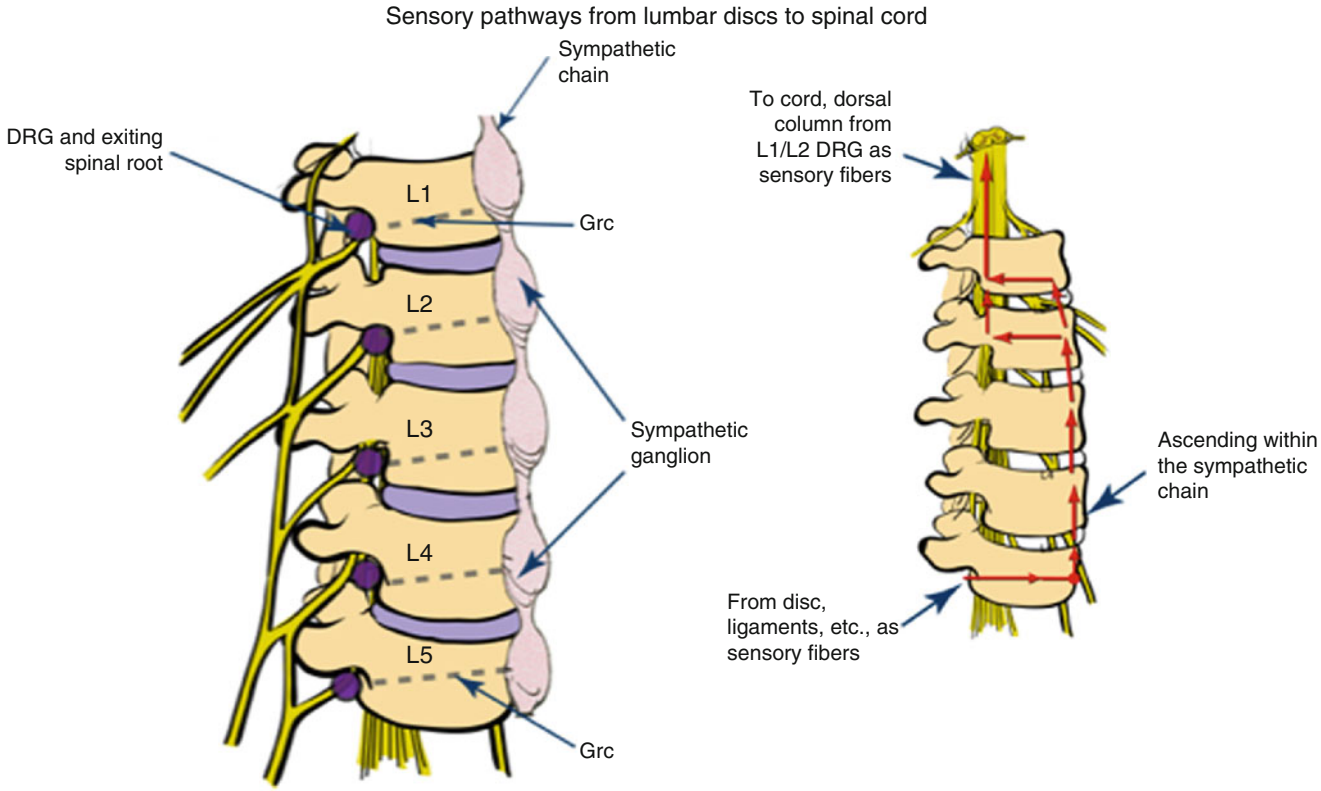


Fig. 43.17 GRC pathways for intradiscal nociceptive pain. The argument can be made that primary discogenic pain, secondary to inflammatory mechanisms within the disc annulus, is a type of "visceral" pain because of its close association and escort to the CNS by way of the sympathetic nervous system. This association gives discogenic pain an entry into a very wide distribution of influence within the dorsal horn, allowing a spread of sensory information over a relatively wide number of levels and producing a flood of neuronal signals to the CNS consistent with a very broad, diffuse anatomic location of the perceived discomfort. This is quite characteristic of "visceral" pain in general [27]

that is subject to "peripheral sensitization" and "central sensitization," leading to its chronic nature in an anatomically widespread presentation.

Clinical Applications of Central (Dorsal Column) Neurostimulation for Axial Low Back Pain

Two features of the neuroanatomy of lumbar discogenic pain lend itself to epidural neurostimulation as a reasonable therapeutic modality: the somatotopic distribution of dermatomes across the dorsal columns and the apparent concentration of afferent sensory fibers in association with L2 sensory input. This suggests that placement of electrical contacts over the region of the L2 "grain" should enable suitable neuromodulation along the sensory tract most associated with primary discogenic pain. Clinically, the dorsal exposure of the L2 "grain" can be found between T7 and T9, and this correlates very well with the work of Smith and Deacon [7].

Figure 43.18 demonstrates placement of dual neurostimulator leads over this area of the dorsal columns. Placed more cephalad, the targets for low back pain are lost in the midline and become too narrow; placed too caudal and the targets are too close to the DREZ to obtain efficacious paresthesia without stimulating flank. The somatotopic dermatomes of S1, L5, L4, and L3 already have a "dorsal exposure" by the time L2 develops one (in the region of T9). The width of this L2 "dorsal exposure" decreases in size as it ascends, as a result of fiber diameter contraction, and it migrates toward the midline. Thus, at all levels of the L2 "dorsal exposure," "leg" fibers greatly outnumber "back" fibers along the narrow L2 strip. For many patients, the physical dimensions of their L2 "grain" appear to be quite narrow, and the perceived paresthesia patterns appear to "jump" from flank stimulation to hip and thigh stimulation, without traversing the low back. This is due to individual variation, and many patients can achieve excellent stimulation of the lower back. The proximity of the L3, L4, and L5 fibers create an environment in which therapeutic stimulation of the low back is quite difficult to achieve without collateral stimulation of the lower extremities to some extent, and patient satisfaction will depend on the degree of that collateral stimulation.

Clinical Applications of Peripheral Neurostimulation for Axial Low Back Pain

Neurostimulation in the periphery appears to be most appropriate for peripheral nerve pathology which presents clinically as a neuralgia, and very "focal" neurostimulation is needed. When secondary hyperalgesia accompanies the

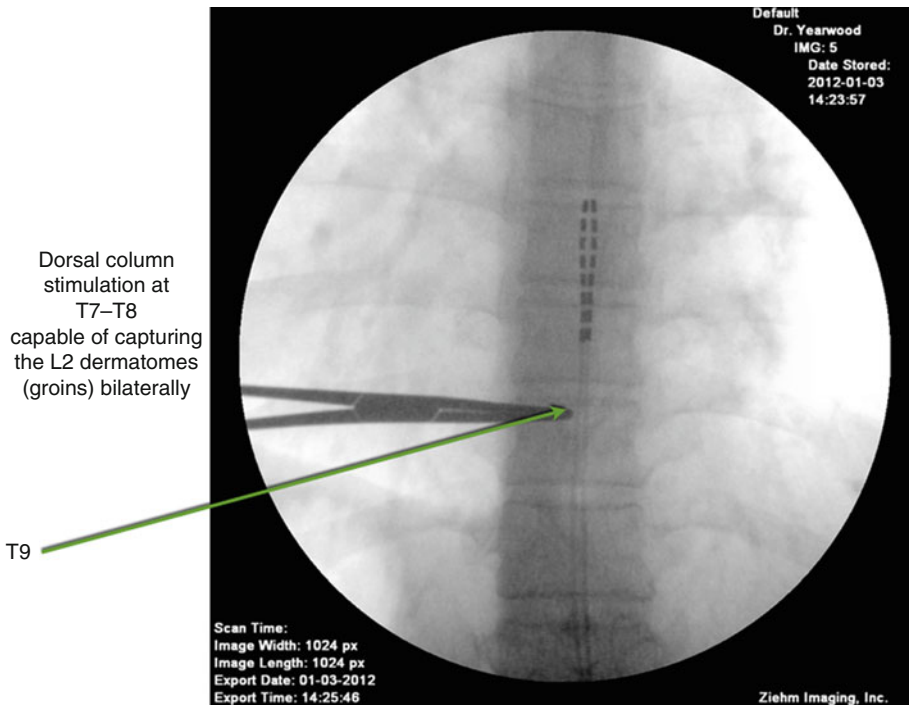


Fig. 43.18 Dorsal column stimulation at T7–T8 for primary discogenic pain. The L2 dermatomal "grain" runs along the surface of the dorsal columns in most patients and can be accessed with this lead arrangement. When sensations of electrical paresthesias cannot be achieved in the lower back, it is occasionally possible to obtain relief of low back pain using subsensory stimulation of the L2 dermatomal "grain." Targeting the L2 dermatomal "grain" is accomplished by obtaining sensory paresthesias in the groins (See Yearwood and Foster [45])

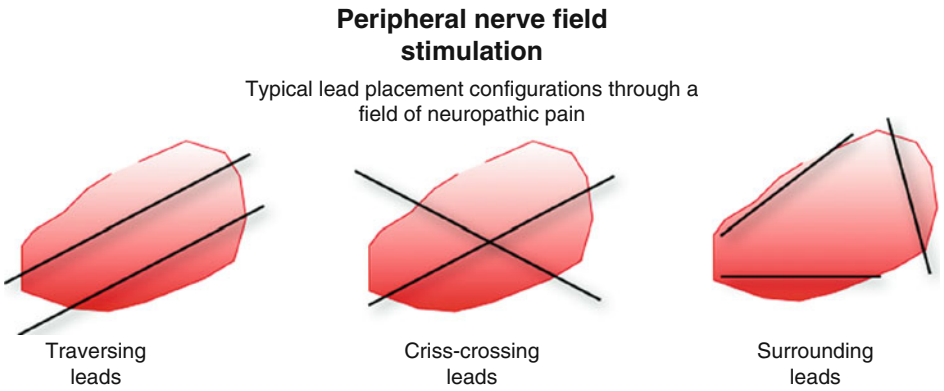


Fig. 43.19 Typical subcutaneous lead placement schemes for peripheral nerve field stimulation (*PNFS*) to a "field" of neuropathic pain

neuralgia, the patient experiences a field of neuropathic pain that extends beyond the distribution of the identifiable nerve [43]. For example, in the case of CRPS type II, dorsal column stimulation (DCS) in conjunction with peripheral neurostimulation (PNS) appears to be indicated, as discussed above (multi-target stimulation). Recognition of this fact has given rise to the increased interest in the clinical applications of peripheral nerve stimulation (PNS) of "named," macroscopic nerves, and peripheral nerve field stimulation (PNFS) of "unnamed" and microscopic nerves (assumed to be branches of one or more anatomically identifiable peripheral nerves).

The "unnamed" nerves most frequently targeted using this technique are in the subcutaneous tissues. But a major question has been exactly "where" and in what arrangement to place the leads to achieve optimal results. Typical lead arrangements relative to the geometry of a "field" of neuropathic pain are shown in Fig. 43.19. Clearly, each of these lead arrangements takes advantage of garnering stimulation from many branches of one or more peripheral nerves as these branches ascend into the subcutaneous tissues from deeper levels. Optimal lead depth has also been studied [44], and it has been reported to be the best location for stimulating Aβ "fast adapt" and appears to be roughly 10–12 mm below the surface. The neuroanatomy of the dermis and subcutaneous tissue is such that Aδ fibers tend to concentrate closer to the dermis and within the dermis and produces a sensation of "sharp pain" and "stinging" by electrical fields. The Aβ "fast adapt" fibers are modestly deeper within the subcutaneous tissue and produce sensations of "tingling" and "tickling" (see Table 43.2). For programming algorithms utilizing subsensory stimulation, this is less important [45]. But for programming algorithms utilizing sensory stimulation, this can be quite important. It is essential to understand that the main goal is pain relief per se and not simply the production of sensory paresthesias. As with any other neuronal target suitable for neurostimulation, even the "unnamed nerves" provide a portal of entry for neuromodulation of the central nervous system. It is just a matter of finding most suitable "on-ramps" to the "interstate" to arrive at the optimal location within the CNS.

Table 43.2 Fiber types and associated sensation

Fiber types	Associated sensation
Aβ "fast" adapt	Tingling, tickling
Aβ "slow" adapt	Vibrating
Aδ	Sharp pain, stinging
C fibers	Burning, aching

Of particular interest to peripheral neurostimulation for low back pain are the superior and middle cluneal nerves. These nerves are each derived from two spinal nerves: superior cluneal nerves (principally arising from L1, L2, and L3) in three separate branches over the posterolateral iliac crest and middle cluneal nerves (principally arising from S1, S2, and S3) in three separate branches about the posterior superior iliac spine (PSIS). Their locations relative to the bony ilium have been studied in detail by Tubbs et al. [46]. Figure 43.20 shows their distribution relative to the iliac crest. This is an area that is subject to surgical trauma during harvesting of bone for spinal fusions at L4 and L5 [47–49]. Further, the postsurgical biomechanics of the investing fascial layers become altered with spinal surgery, deconditioning, loss of range of motion about the lumbosacral junction, and fascial degeneration [50]. As shown in Fig. 43.20, these nerves must penetrate the lumbosacral and sacroiliac fascial layers in order to pass over the iliac crest. Because of this, they are subject to any biomechanical alterations in these layers, and this can lead to biomechanically induced neuralgia and even neural entrapment. Cluneal nerve entrapment has been reported in the literature [51–53], as a clinical symptom characterized by persistent low back pain, aggravated by activity [50].

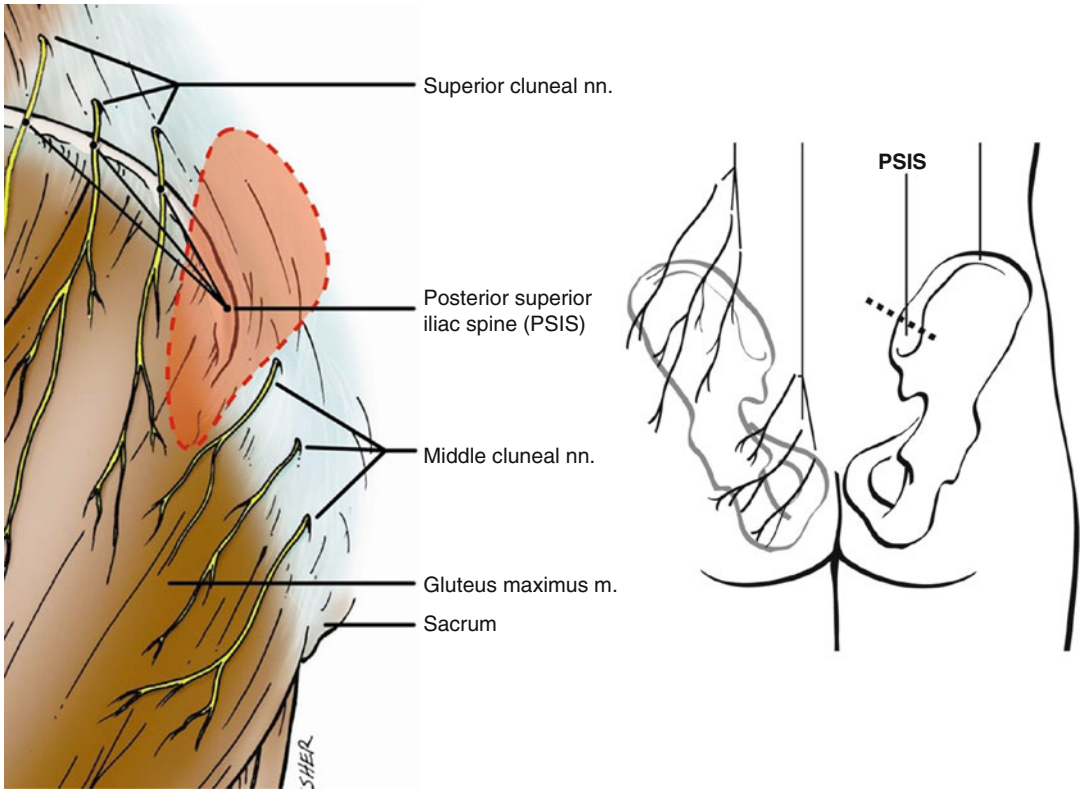


Fig. 43.20 Anatomical drawing (a) and Schematic drawing (b) of the cluneal nerves in the left gluteal region. The relative "safe zone" for bone harvesting is shown in *light red*. *M* muscle, *nn* nerves (Adapted from Tubbs et al. [46], with permission)

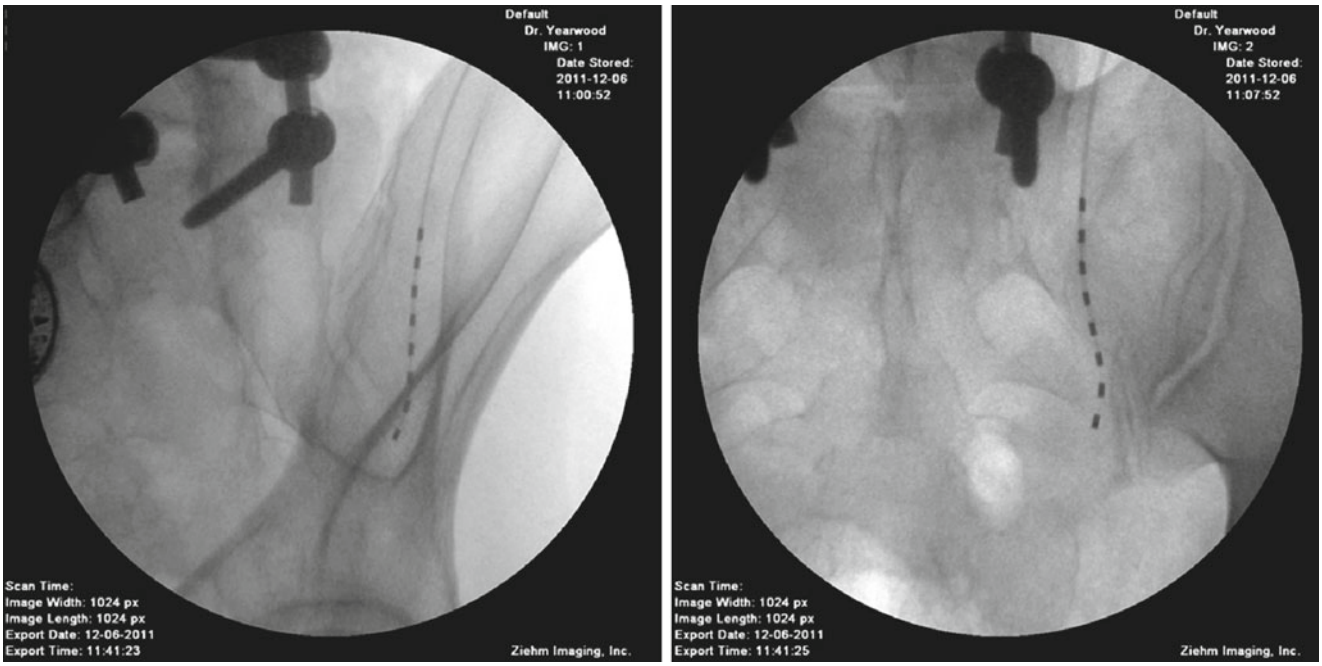
Thus, as noted by Vora et al., the discs, facet joints, and posterior spinal elements are interwoven in a dynamic biotensegrity network of ligaments, muscles, and fascia [50]. When this condition is chronic, there is potential for "central sensitization" within the dorsal horn of the spinal cord. Stretching exercises, which may keep these fascial layers and tissues flexible, are well noted to provide a reduction in low back pain [55] in patients who have not been treated by spinal fusion at the lumbosacral junction.

There are numerous reports in the literature of neuroablative efforts at relieving chronic low back pain within the distribution of the superior and middle cluneal nerves and their medially and laterally displaced branches. Neurostimulation along the anatomic pathways of the cluneal nerves is thus a highly rational approach to treating a peripheral neuralgia involving these nerves.

As of this writing, a retrospective study of ten patients with previously implanted epidural neurostimulator leads for failed back surgery syndrome (FBSS) is currently underway in our clinic, in which a combined technique of fluoroscopy and ultrasound guidance was employed for PNS of the cluneal nerve lead placement. This configuration appears to demonstrate excellent pain relief in patients with and without previous iliac bone harvesting. Figure 43.21 demonstrates a typical lead placement along the iliac crest to a level slightly caudal to the PSIS. The fact that not all patients had previously undergone iliac crest bone harvesting for fusion underscores the potential for disuse atrophy and disruption of the dynamic biotensegrity network of ligaments, muscles, and fascia in the lumbosacral junction to create a peripheral neuralgia in this area that is resistant to epidural neurostimulation alone.

Sacroiliac joint dysfunction syndrome [57, 58] has a remarkably similar clinical presentation and is not well treated with epidural-based neurostimulation techniques. PNS stimulation of the primary dorsal rami of L5, S1, S2, and S3 gives an entirely similar pattern of stimulation, providing one with a suitable axial low back pain relief at the lumbosacral junction, hips, and buttocks. This is identical to the peripheral neurostimulation seen with PNS over the middle cluneal nerves described above and has been a target for recently developed "cooled-RF" neuroablative techniques in the treatment of sacroiliac joint dysfunction syndrome [59]. Figure 43.22 shows a typical arrangement of the leads in this case. Once again, this stimulation is much more "focal" in nature than can be achieved with epidural neurostimulation, even in cases where a previously implanted epidural system provides some degree of paresthesia coverage to this difficult and hard-to-reach anatomical area.

PNS of the right middle cluneal nerves
s/p Iliac crest bone harvesting

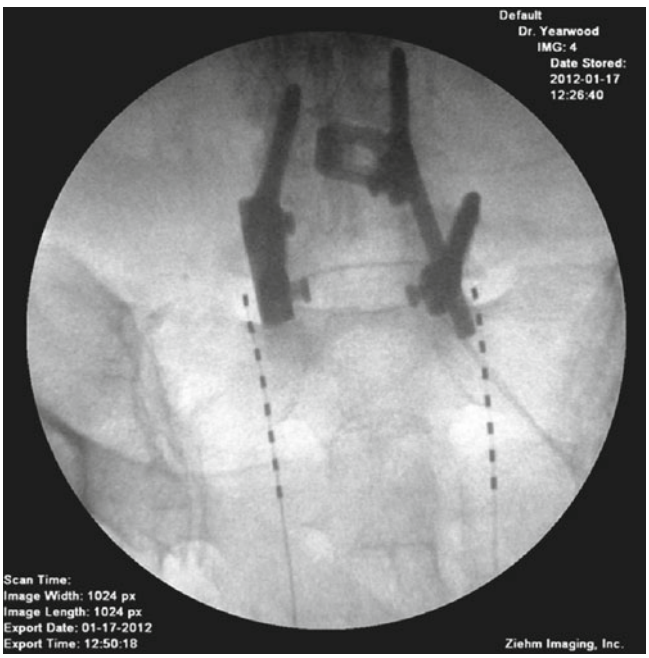


Oblique view AP view

Fig. 43.21 PNS stimulation of the middle cluneal nerves on the right. Neurostimulation along the anatomic pathways of the cluneal nerves is thus a highly rational approach to treating a peripheral neuralgia involving these nerves

Fig. 43.22 PNS stimulation of the primary dorsal rami of L5, S1, S2, and S3

PNS stimulation of the primary dorsal rami of L5, S1, S2, and S3



Peripheral nerve field stimulation (PNFS) in the more superficial layers of the low back would appear to derive its success from utilizing anatomic pathways to the dorsal horn which are similar or identical to those used in PNS and intraspinal neurostimulation (DCS, DRG stimulation, and nerve root stimulation) for neuromodulation of painful neuropathic signals. The primary difference between PNS and PNFS appears to be the "focality" of the stimulation. PNFS offers access to the CNS for neuromodulation that is conceptually larger than PNS, as it may involve multiple

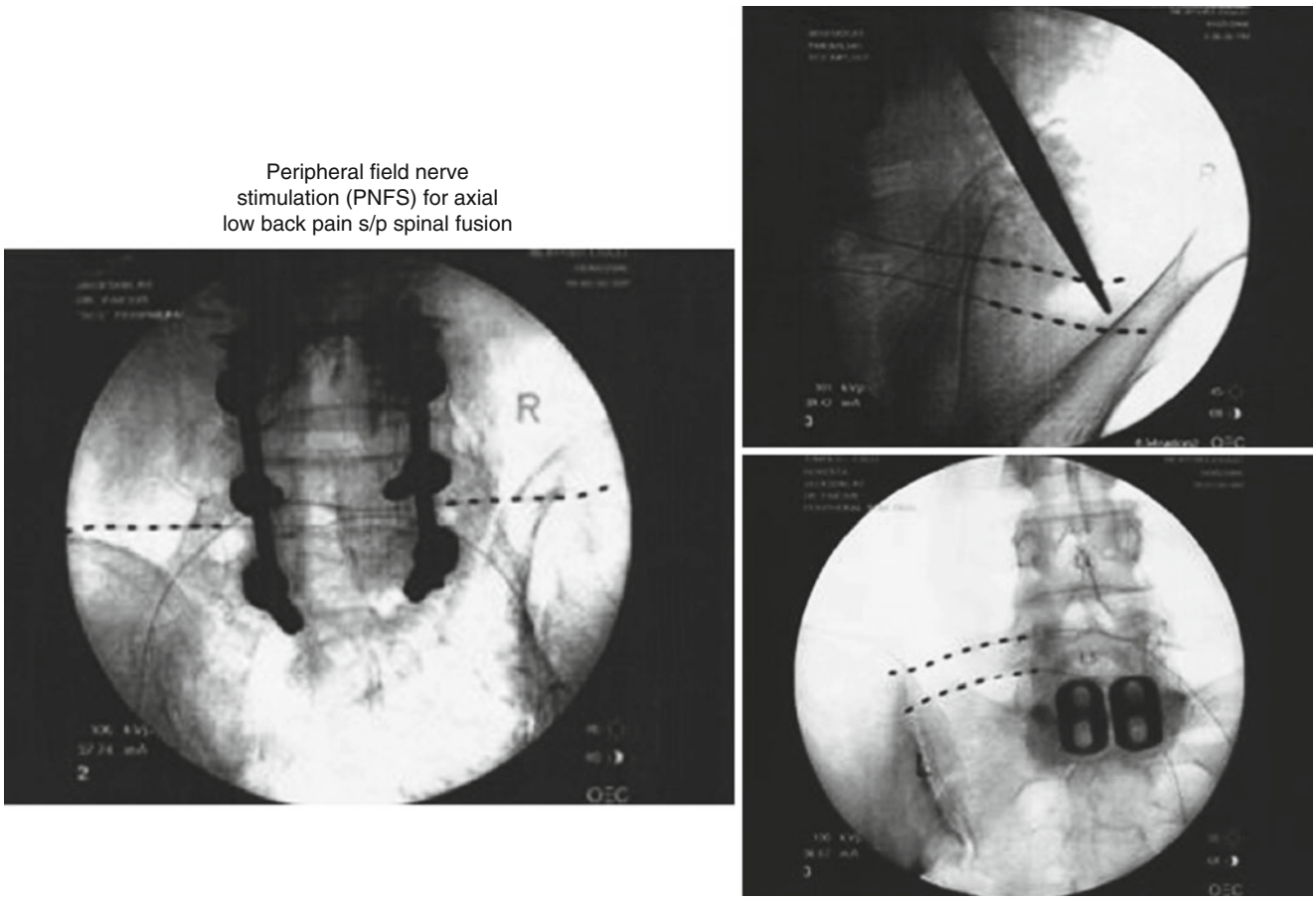


Fig. 43.23 Peripheral nerve field stimulation for low back pain in post-laminotomy syndrome ("FBSS") (From Paicius et al. [61], with permission)

"named" nerves, as noted above. This is an exploding area of interest, and excellent results have been reported for its use in many conditions, including chronic low back pain [60]. Figure 43.23 [61] shows typical lead placements for PNFS leads in treating axial low back pain. It should be noted that in each of these cases, the patient has undergone fusion of the L5 disc. Specific mention of bone harvesting was not made in this report, but direct surgical trauma to the iliac crest is not needed to produce chronic low back pain in this area, for biomechanical reasons noted above. Indirect effects can certainly result in cluneal neuralgia, and this is precisely the area where superior and middle cluneal involvement would be expected and where PNS stimulation of the primary dorsal rami of L5, S1, S2, and S3 is also effective.

PNFS has also been combined with intraspinal neurostimulation for the treatment of low back and leg pain [62]. This technique derives its clinical benefit from the advantages of multi-target stimulation, providing a modestly "focal" stimulation pattern when epidural-based "regional" DCS proves inadequate. It could be that similar neuroanatomical "conduits" of neurosensory input by these two different approaches result in modulating areas of the dorsal horn where wide dynamic range neurons play a role in central sensitization and "wind up" in chronic low back pain from both nociceptive and neuropathic sources.

In summary, neurostimulation can have significant benefit in treating radicular pain syndromes of the cervical, thoracic, and lumbar spine, including particularly difficult pain problems such as low back pain. Recognition of the capabilities of and limitations of each style of neurostimulation is necessary, as determined by the pathology of the targets involved, in achieving optimal clinical results. If secondary hyperalgesia and other "centrally mediated" neuropathic pain processes predominate in a given clinical situation, dorsal column stimulation may suffice. Where a peripheral neuralgia is superimposed on this clinical picture, combined techniques of intraspinal neurostimulation and peripheral neurostimulation (PNS, PNFS) may be required. The ultimate goal is to modulate those sensory signals that reach the thalamus which are disruptive to CNS as a whole and, in so doing, enable the patient to have a substantially greater clinical capacity for physical function and social engagement.

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Clinical Applications of Neuromodulation: Neurostimulation for Complex Regional Pain Syndrome

44

Michael Stanton-Hicks

Key Points

- Complex regional pain syndrome (CRPS) is defined, and criteria necessary to be satisfied for this diagnosis are addressed.
- A review of recent literature describing the use of spinal cord stimulation (SCS) in the management of CRPS is provided.
- The risk–benefit analysis, patient criteria, and conditions should be met before consideration of SCS is addressed including the need for psychometric testing and instruments that are used for this purpose.
- The multidisciplinary management of patients with CRPS is emphasized including how SCS may be introduced as either a temporary adjunct to functional restoration or its permanent implantation in cases that require the ongoing attributes of SCS as it serves to ameliorate pain and improve the microcirculation and functional improvement of motor function is emphasized.

Introduction

Complex regional pain syndrome (CRPS), formerly termed reflex sympathetic dystrophy (RSD), was introduced in 1994 by the International Association for the Study of Pain (IASP) [1, 2]. CRPS comprises two syndromes: type I, representing reflex sympathetic dystrophy, and type II referring to causalgia [3]. The hypothesis of sympathetically maintained pain (SMP), introduced by Roberts in 1986, represents a phenomenon that may be present in both syndromes and can be confirmed, when present, by sympathetic blockade [4].

As set forth by the IASP, the diagnostic criteria that must be satisfied comprise pain, impaired function in the region, trophic changes involving the nails, hair growth, and sudomotor dysfunction [2]. Sensory abnormalities such as hyperesthesia, hyperalgesia, and mechanical or thermal allodynia (or both) are also present (Table 44.1).

The fundamental signs and symptoms of CRPS entail sensory, motor, autonomic, and trophic changes. The IASP requires that these clinical features be identified under these four categories. No supportive clinical tests are included in the IASP classification. However, tests of sudomotor dysfunction, e.g., the quantitative sudomotor axon reflex test (QSART), quantitative sensory testing (QST), skin biopsy, and the use of sympathetic blocks to determine whether any significant autonomic dysfunction is evident, can be undertaken.

The differential diagnosis of CRPS requires the elimination of other clinical syndromes which share clinical features with CRPS but which are clearly distinct by virtue of their own unique constellation of signs and symptoms. Clinical features similar to those of CRPS include the pain, edema, and temperature asymmetry characteristic of trauma patients, but who nevertheless do not develop CRPS. Table 44.2 describes the clinical diagnostic criteria of CRPS, termed the "Budapest Criteria" and published in 2010.

Movement disorders, not previously associated with CRPS, are now well recognized (see Table 44.3) [8]. They include weakness, tremor, muscle spasms, dystonia, and inability to initiate movement. Occasionally sympathetic blockade, when undertaken soon after the onset of CRPS, may eliminate the movement disorder.

Contemporary thinking accepts that the initial clinical features of CRPS resemble a significant inflammatory disorder. However, this thinking has been shaped by studies revealing that free O_2 radical expression can sensitize activity in C and A-δ fibers. Continuous excitation of these nociceptors will in

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Table 44.1 Diagnostic criteria for complex regional pain syndrome (CRPS)

Factor 1	Factor 2	Factor 3	Factor 4
Hyperalgesia signs (0.75)	Temperature asymmetry symptoms (0.68)	Edema signs (0.69)	Decreased range of motion signs (0.81)
Hyperesthesia symptoms (0.78)	Color change signs (0.67)	Sweating asymmetry signs (0.62)	Decreased range of motion symptoms (0.77)
Allodynic signs (0.44)	Color change symptoms (0.52)	Edema symptoms (0.61)	Motor dysfunction signs (0.77)
			Motor dysfunction symptoms (0.61)
			Tropic symptoms (0.52)
			Trophic signs (0.51)

From Harden and Bruehl [5]. With permission

Table 44.2 Budapest clinical diagnostic criteria for complex regional pain syndrome (CRPS)

1. Continuing pain, which is disproportionate to any inciting event
2. Must report at least one symptom in *three of the four* following categories:
Sensory: reports of hyperesthesia and/or allodynia
Vasomotor: reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry
Sudomotor/edema: reports of edema and/or sweating changes and/or sweating asymmetry
Motor/trophic: reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
3. Must display at least one sign at time of evaluation in *two or more* of the following categories:
Sensory: evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or deep somatic pressure and/or joint movement)
Vasomotor: evidence of temperature asymmetry and/or skin color changes and/or asymmetry
Sudomotor/edema: evidence of edema and/or sweating changes and/or sweating asymmetry
Motor/trophic: evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
4. There is no other diagnosis that better explains the signs and symptoms

From Harden et al. [6]. Used with permission

Table 44.3 Prevalence of movement disorders in complex regional pain syndrome (CRPS)

N	Weakness (%)	Akinesia (%)	Dystonia (%)	Spasms (%)	Tremor (%)	Reference
200			22			Schwartzman and Kerrigan (1990)
829	95		36[a]	25	49	Veldman et al. (1993)
181	89	80			45	Blumberg and Jänig (1994)
123	75/76[b]				24/94[b]	Harden et al. (1999)
145	79	45	30[c]		48	Birklein et al. (2000)

From van Hilten et al. [7]. Used with permission
[a]Reflects involuntary movements
[b]Symptoms/signs
[c]Including myoclonia

turn sensitize first-order and higher neurons in the central nervous system (CNS). Central sensitization can be demonstrated not only in the spinal cord but also at the supratentorial centers in the brain [9].

Rationale for the Use of Neurostimulation

Most pharmacologic treatments of CRPS target neurologic dysfunction. The treatments include membrane stabilizers, antidepressants, norepinephrine reuptake inhibitors, and NMDA antagonists—all of which are used to support a return of function by means of physiotherapeutic measures [10]. Two other measures used to support rehabilitation are (1) epidural infusions of local anesthetics with or without opioids and (2) the addition of alpha-2 agonists like clonidine. These techniques have proved very effective but are associated with a low incidence of infection as well as technical failure of the infusion system. They are also expensive because they require home health-care support and associated pharmaceuticals.

When sympathetically maintained pain (SMP) has been demonstrated by a sympathetic block, with almost complete

symptomatic relief, a comparatively long duration of effect can be achieved by segmental radio frequency ablation (RFA) of the sympathetic trunk.

Increasing evidence now supports the use of neuroaugmentative procedures such as spinal cord stimulation (SCS) or peripheral nerve stimulation (PNS) [11–13]. This evidence includes randomized controlled trials (RCTs), several long-term studies, and several case studies. The first RCT, conducted by Kemler et al., was published in 2000 [14]. The patients in this study met the IASP diagnostic criteria for CRPS and were unresponsive to conventional medical management (CMM). Two randomly assigned groups comprised patients who undertook spinal cord stimulation (SCS) plus physical therapy and patients who received only physical therapy. All patients who successfully completed their trial underwent implantation of the neurostimulator. The subsequent intention-to-treat analysis demonstrated a significant reduction in pain in the SCS/physical therapy group [15]. Other measures showed that the SCS/physical therapy group experienced improvement both in the global perceived effect (GPE) and in quality of life (QOL). All patients underwent implantation of their SCS. The same authors demonstrated long-term improvement in pain relief and GPE among the SCS/physical therapy group, in comparison to the patients who received only physical therapy at 2 years. At 5 years, the GPE remained better than in patients who had received only physical therapy, although the "expressed" pain relief did not differ between the two groups. However, all the patients who had received an SCS stated they would repeat the treatment should the need arise.

In one study, carbamazepine and morphine were compared in patients previously implanted with an SCS [16]. This study, divided into two phases, investigated the effect of administering carbamazepine or placebo in phase I and morphine and placebo in phase II after the patient's SCS system had been deactivated. Carbamazepine was superior to morphine in reducing the level of pain. However, only 2 of the 38 patients preferred to continue their treatment with carbamazepine; the remaining 36 preferred to continue their treatment with SCS. These results clearly demonstrated the successful symptomatic management of either neuropathic pain or CRPS.

Although most of the papers during the past 35 years have been case studies or retrospective reviews, a common thread of success runs through these works. The latest publication that supports the use of SCS is probably the 2009 Health Technology Assessment report, issued by the National Institute for Health and Clinical Excellence (NICE). This report reviewed 6,000 citations, including 11 RCTs of neuropathic pain and eight of ischemic pain [17], and concluded that SCS effectively decreases chronic neuropathic pain, and the results are more effective than those of conventional medical management (CMM). With regard to cost containment, the incremental cost-effectiveness ratio (ICER) described a range of $25,000–$30,000 per quality-adjusted life year (QALY), and if based on device longevity of 4 years, these figures were reduced to $20,000 per QALY.

It should be emphasized that most of the data reported so far have been obtained with comparatively unsophisticated systems. However, the efficacy of SCS, and in particular its effect on CRPS, has been improved by means of more modern neurostimulation systems with computerized programming capabilities, multiple arrays, and dual or multiple electrode systems. When the results of these latest systems are carefully studied, it becomes clear that early intervention is responsible for a much greater success rate in reversing or suppressing the symptoms.

The temporary use of SCS to provide analgesia in support of a physiotherapeutic program or a more comprehensive interdisciplinary treatment program was advocated by Prager and Chang in 2000 [18]. In this study, the authors described a triple-lead (tripolar) system that was temporarily implanted, and an "extended trial" was used to facilitate exercise therapy. The system was retained for 4 weeks, and if the patient required further analgesia after that time, it was implanted. A second set of 16 patients, who had failed 4 weeks of comprehensive therapy, underwent permanent implant of SCS with continuing interdisciplinary treatment. Patients who no longer felt that SCS was necessary underwent explantation. Five of the original eight patients showed improvement in their symptoms sufficient to warrant removal of the system. The authors noted that SCS is a fairly inexpensive treatment compared to CMM or multiple sympathetic blocks. Finally, it should be noted that an implanted SCS lead with an externalized pulse generator could always be converted to a totally implanted system, circumstances prevailing.

Patient Selection

Appropriate selection of patients for SCS is essential to a successful outcome [11]. Most published treatment algorithms describe the use of SCS after simpler and more conservative therapies have been tried in a stepwise fashion although usually in support of an exercise therapy treatment program [19]. Conventional wisdom would suggest that any patient who is likely to need an implantable device such as an SCS must undergo a satisfactory behavioral assessment [20]. Such an assessment is essential for precluding those patients who might believe that a simple or rapid intervention such as SCS is most likely to cure their clinical problem, or who may have unrealistic expectations regarding the management of their syndrome. Although SCS is a minimally invasive procedure, it should always follow an adequate screening trial. The trial should demonstrate to the patient and to the treating physician that the activities of daily living (ADLs) can be improved and that notwithstanding improved symptoms, the patient should maintain their exercise therapy (Table 44.4).

In this respect, convention requires a 50 % reduction of pain. If other comorbidities, or the possible anatomic anomalies, are suggested, preradiologic screening with MRI or CT scan is imperative. Additional selection criteria have been developed by several authors (see Table 44.3). In an effort to standardize criteria for the selection of patients for SCS, several scientific bodies, including the International Association for the Study of Pain (IASP), the International Neuromodulation Society (INS), the North American Neuromodulation Society (NANS), and the American Academy of Pain Medicine (AAPM), are involved in the education and dissemination of guidelines to be met before patients are selected for neurostimulation. The requirement for psychological pretesting is addressed by the Centers for Medicare Services (CMS), the industrial commissions and state bureaus of workers compensation (BWC), and most health insurance agencies. Most contemporary psychological evaluation is based on an inventory of risk factors which, together with behavioral management, play a significant role in patient care that supports the use of SCS in selected patients [23, 24].

Table 44.4 Selection criteria for spinal cord stimulation in complex regional pain syndrome (CRPS)

Oakley [11]	
Inclusion	Exclusion
Diagnosis of CRPS	Absence of initial CMM
6-month pain duration	Previous failed SCS trial
Psychological clearance	Untreated axis I psychiatric disorder
Informed consent	Certain psychoses
Contraindications	
North et al. [21]	
Relative	Absolute
Medication dependence	Coagulopathy
Unresolved psychiatric disorder	Immunosuppressive therapy
Nonorganic signs (Waddell's)	Unacceptable surgical risk
Inconsistent history	Conflicting therapy diathermy
Anticoagulation therapy	Serial MRI requirements
Alternative therapy with lower risk/benefit ratio	Occupational risk

Minimally adapted from Prager [22]. Original used with permission

Risk–Benefit Analysis

The potential benefit of SCS as a treatment modality for CRPS has been described in the supporting literature. Table 44.5 identifies several observations that underscore the value of SCS; however, pain relief remains the most significant reason to consider SCS. For more than 30 years, success has been defined as a reduction of 50 % in pain [30]. However, pain reduction is subjective, and the level of pain is assessed by means of arithmetic scales such as the visual analog scale (VAS), verbal rating scale (VRS), and numerical rating scale (NRS). Unfortunately, because pain is subjective and is an exponential function, the values, expressed arithmetically, bear little resemblance to the constellation of symptoms about which the patient complains. Furthermore, chronicity and environmental factors materially impact the number chosen on any one of the above scales. Function should become the standard by which the impact of pain can influence a variety of functional markers (Table 44.5).

The Neuromodulation Therapy Access Coalition identified studies that demonstrate the ability of patients to undertake

Table 44.5 Potential benefits of spinal cord stimulation in treating complex regional pain syndrome (CRPS)[a]

Benefit	Comments
Pain relief [25, 26]	The primary outcome measure of SCS success is patient-reported pain relief, generally using a standard pain scale such as the visual analog scale (VAS), functional rating index, McGill Pain Questionnaire [21]
	A majority of patients may experience at least 50 % reduction in pain
Increased activity levels or function [12, 26, 27]	As demonstrated by activities of daily living, such as walking, climbing stairs, sleeping, engaging in sex, driving a car and sitting at a table [28]
	Measured by the Oswestry Disability Index (specific for low back pain), the Sickness Impact Profile (for general health), Functional Rating Index, Pain Disability Index
Reduced use of pain medication (Harke et al. 2005)	Patients in whom SCS is successful should be able to reduce or eliminate their intake of pain medication [21]
Improvement in quality of life [21, 27]	Would repeat treatment to achieve the same result [21]
Patient satisfaction with treatment (Alo et al. 1999; Bennett et al. 1999; [12, 21, 27])	
Fewer symptoms of depression [12, 21, 27, 29]	Measured by the Beck Depression Inventory

From Prager [22]. Used with permission

[a]Original author's note: Consult "practice parameters for the use of spinal cord stimulation in the treatment of chronic neuropathic pain" [21] for a comprehensive bibliography of studies that support the benefits of spinal cord stimulation in treating complex regional pain syndrome (CRPS) Selected long-term or seminal studies are cited here; short-term studies and case reports are not

their activities of daily living (ADL) and to improve quality of life (QOL). Although there are quite extensive data from patients in whom failed back surgical syndrome (FBSS) has been treated by SCS, other functional markers used are the Oswestry Disability Index and the Hospital Anxiety and Depression (HADS) Scale [27]. All measures showed significant reduction. In the single RCT on CRPS by Kemler et al., the QOL improved by 11 % [14]. Although patient satisfaction has never been standardized, several authors have indirectly described patient satisfaction as those patients who choose to cross over from CMM to SCS, or who choose to repeat implantation to achieve the same result, indicating the success of SCS [25, 31]. An interesting aspect of SCS that often escapes comment is its effect on depression. Several authors have noted that SCS patients manifest fewer symptoms of depression such as those measured by the Beck Depression Inventory (BDI) [29, 32, 33].

The greatest impediment to successful treatment stems from complications due to technical failure, or from infection, which occurs in as many as 30 % of all cases [34].

Under the best of circumstances, the incidence of perioperative infection is between 4 and 5 % of all cases [11, 34]. North, describing 20 years of experience with spinal cord stimulation, found 0 incidence of spinal cord injury, meningitis, or other life-threatening infection. An incidence of spinal fluid leak, neurologic injury, or hemorrhage has been reported in 0–42 % of cases [11].

Electrode displacement occurs in approximately 24 % of cases [34]. The subsequent loss of therapeutic stimulation requiring surgical revision occurs in approximately 50 % of cases. However, many of the foregoing data have been derived from older and simpler systems. Modern multichannel systems with computerized implanted pulse generators (IPGs) are significantly more reliable. Accordingly, the future of SCS should markedly improve as a result of technological advances in contemporary equipment.

In a review of 126 cases, Oakley found that 26 patients (20 %) requested that their system be explanted or discontinued [11]. The main reasons for failure were progression of disease, loss of therapeutic paresthesia, and discomfort at the implant site (primarily IPG). On the other hand, four patients (3 %) experienced such successful analgesia that they no longer used their system. When patients are being prepared to consider SCS, the relative merits of its use should be placed in the context of their treatment to date. It is critical that the patient be informed of the shortcomings associated with SCS (as described above), of the nature of the screening trial, and the reasons for it. The specific endpoints a patient should assess during a trial are (1) the degree of pain relief, (2) what functional improvements are experienced on the affected side, (3) whether activity is facilitated, and (4) whether circulation, as determined by temperature change and skin color in the region, is improved. It is also important to allow the patient to continue their routine medical management—in particular, medication—so that any reduction in use may definitively reflect successful SCS. Finally, patients should be encouraged to increase daily activities and, if appropriate, maintain their exercise program.

Obviously, a detailed description of the risk–benefit aspects of SCS that can be experienced should be discussed with each patient. Moreover, long-term efficacy should be placed within the context of our cumulative experience of SCS.

Multidisciplinary Care: The Role of SCS

Experience gained during the past 20 years has clearly highlighted the need for multidisciplinary or interdisciplinary management of patients with CRPS. It has been determined that neurostimulation, in its various forms, is the single most successful modality to use in most patients. In 2002, a physiotherapeutic continuum involving multidisciplinary management for CRPS was published (see Fig. 44.1) [35]. This algorithm underscored that psychological, rehabilitative, and interventional pain management should be implemented in a time-contingent manner—sequentially, or at times simultaneously. The various behavioral and/or interventional approaches are introduced only if or when progress slows or stalls during the course of psychotherapeutic measures. "Time contingency" as proposed by the international group that participated in the development of this algorithm was considered to be the sine qua non for promoting physical therapy and, when adopted, underscored the need to incorporate neurostimulation as a major component of therapy. In fact, during rehabilitation, desirable functional effects (e.g., vasodilatation and motor improvement) are most often conferred when interventions such as SCS are incorporated [36]. These effects obviously require validation.

Although SCS is usually introduced as an intervention during the course of treating neuropathic pain, contemporary experience would suggest that in some cases, because of its significant attributes, SCS should be introduced much earlier [37–42]. This point is already addressed in the treatment algorithm.

One thing is certain that previously used ablative measures such as sympathectomy—whether pharmacologic or surgical—have little part to play in the modern management of CRPS.

The SCS Trial

A trial of SCS offers patient and physician the opportunity to determine whether the patient's therapy can be continued without the restrictions of their disability and at the same time

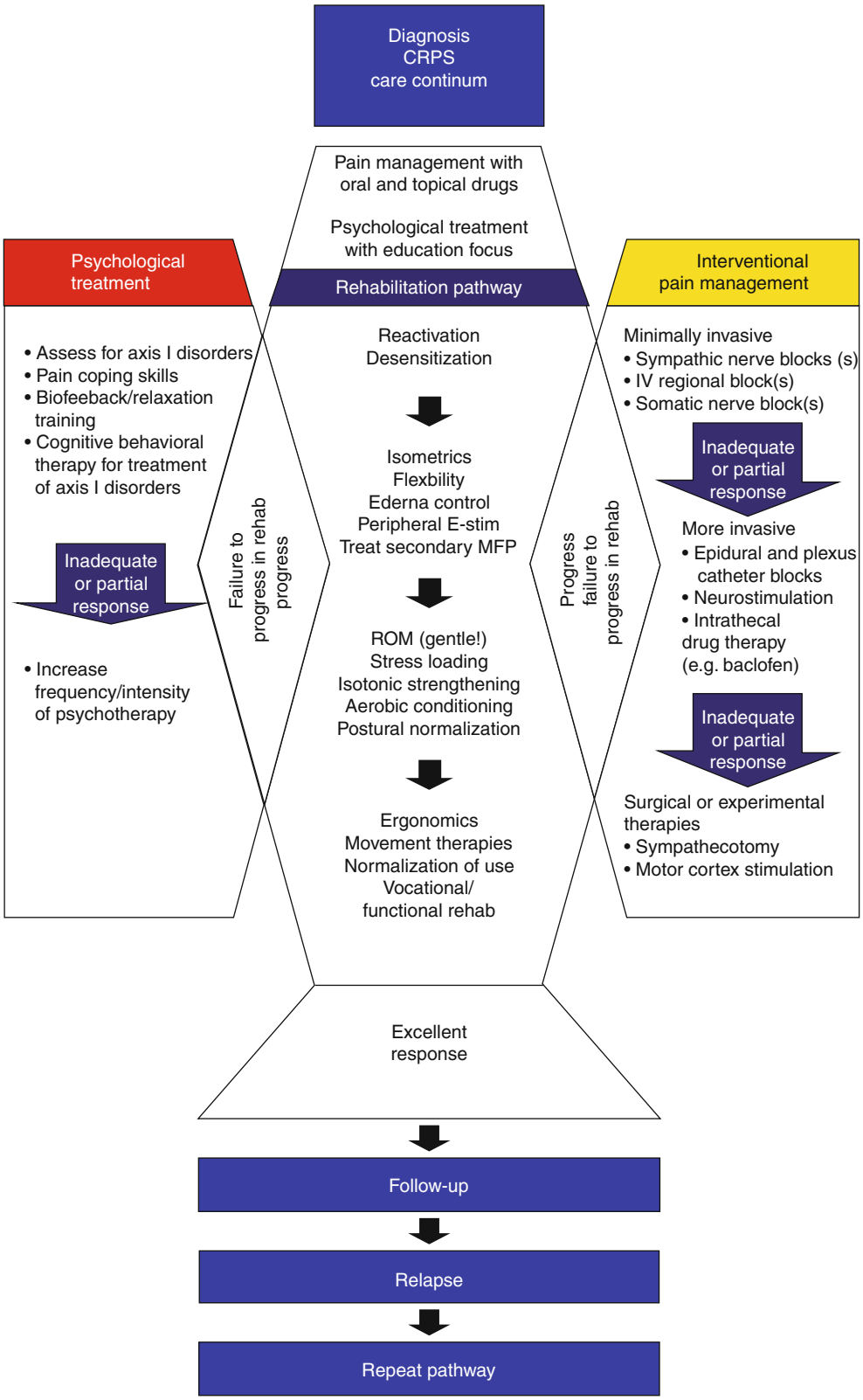

Fig. 44.1 Treatment algorithm suggested for the restoration of function using a stepwise approach and the introduction of behavioral or interventional measures that should be introduced in order to facilitate progress in treatment. With demonstrated improvement, the physiotherapeutic measures may be increased in intensity and frequency in order to achieve a final remission of this syndrome

allows the physician to assess whether the patient might be able to successfully discontinue their medications if any. The trial should assess goals that the treating physician has proposed, and it should also aim to reduce pain symptoms by at least 50 %, while functional rehabilitation is still being undertaken [26, 29].

In addition to psychological assessment, a physical examination should be performed; this is also including a complete neurologic assessment to detect and evaluate other possible comorbidities [28]. Although many screening protocols are followed, a trial of SCS will be influenced by the site (upper vs. lower extremity), the patient's overall medical condition, the practice resources, geographic proximity to the patient's home, and economic issues related to the patient's reimbursement for their trial, e.g., private insurance, Medicare, BWC.

If the patient has certain anatomic abnormalities and/or prior adverse experience with neurostimulation, these aspects may require consultation with a neurosurgeon so that a percutaneous trial [28, 43, 44]. The customary duration of an SCS trial is 1 week, which is usually long enough for the patient and physician to evaluate the merits of SCS as a therapeutic modality. Longer periods are customary if a patient doubts the efficacy of their trial.

In certain cases, a so-called "extended" SCS trial is used to facilitate either rehabilitation or a comprehensive outpatient or inpatient multidisciplinary pain program [45, 46]. In such cases, the trial electrode is left in situ for periods of 6–8 weeks. In many of these cases, it is not intended that an SCS system be subsequently implanted; the trial merely serves as a means for facilitating their exercise program.

Surgical Implantation

Because SCS represents a radical departure from CMM, the patient should regularly be made aware that SCS will reduce, but in most cases will not completely eliminate, their pain. Patients must also understand that SCS will be a component of other therapies. Whenever practicable, patients should be followed at intervals of 3, 6, and 12 months so that any adjustments can be made prospectively or in response to the loss of therapeutic stimulation. Patients who are to undergo laminotomy placement of their SCS must be informed that greater discomfort and some morbidity are associated with the procedure but that within a reasonably short time, these symptoms should resolve [47]. Patients should also be counseled that lifelong exercise therapy will be needed to maintain optimal therapeutic support from the SCS. Moreover, they should be cautioned that over a 2-year period there will be about a 10 % loss in efficacy; after which, there will be no further loss for the life of the neurostimulator [48]. Finally, at no time should the relationship between the patient and the implanting physician be disrupted; for maintenance of the relationship allows subsequent technical issues or a breakdown in SCS efficacy to be addressed in a timely manner.

Cost-Effectiveness

Several studies in the USA, the Netherlands, the UK, Germany, and Canada have evaluated the cost of SCS treatment. Evidence from RCTs confirms the cost-effectiveness of SCS for treating CPRS. In the Netherlands, the 12-month cost of CRPS treatment by SCS was $4,000 greater than that for CMM but in an analysis over a lifetime; SCS was found to be $60,000 less than CMM per patient. In the UK, the lifetime cost savings was $60,800 for SCS compared to physical therapy alone. In Canada, Kumar et al. found that in a group of 104 patients, the cumulative cost of SCS was $29,123 compared to $38,029 for CMM [21, 48–53].

Summary

SCS is successful as an adjunct in the treatment continuum for CRPS. A trial of SCS is always necessary before implantation is considered or implemented. Not only analgesia but also improvement in function and in the ability to tolerate physical therapy should be determinants of a successful trial. Over the past 30 years, during which SCS has been used in the treatment of CRPS, no adverse effects have been reported on the central nervous system or neuroendocrine systems. SCS is cost-effective. Continuing improvements in the understanding of its mechanism of action, as well as improvements in technological developments, should anchor this modality as one of the most successful treatments for neuropathic pain. Thus, it plays a unique role in the management of and supportive of rehabilitation for CRPS.

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Clinical Applications of Neuromodulation: Section on Angina and Peripheral Vascular Disease

45

Marte A. Martinez and Robert D. Foreman

Key Points

- The gate control theory of Melzack and Wall provided the backdrop for developing various forms of neuromodulation including spinal cord stimulation, but the exact mechanisms remain controversial.
- Spinal cord stimulation for treatment of ischemic conditions activates mechanisms that are fundamentally different from those activated for neuropathic pain.
- Every year, patients are treated worldwide with spinal cord stimulation to alleviate peripheral arterial occlusive disease and chronic refractory angina pectoris.
- The principal indication for using spinal cord stimulation to treat peripheral arterial occlusive disease is severe ischemic pain at rest (Fontaine classification stage 3).
- Spinal cord stimulation for ischemic pain is primarily mediated by suppressing efferent sympathetic activity and antidromic activation of the dorsal roots innervating blood vessels that release calcitonin gene-related peptide.
- Spinal cord stimulation is indicated for patients suffering from angina pectoris (NYHA classes III–IV or Canadian Cardiovascular Society classifications I–IV) and refractory to conventional treatment.
- Basic science research has suggested that angina pain is reduced because pain transmission is reduced in nociceptive pain pathways and cardiac function is improved as a result of stabilizing neurons of the intrinsic cardiac nervous system, activating adrenoreceptors that reduce infarct size, and reducing atrial arrhythmias.

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Background

Clinical neuromodulation refers to the use of electrical stimulation of a peripheral nerve, the spinal cord, or the brain for relief of pain. For centuries, physicians have been interested in deriving therapeutic benefit from the use of electrical impulses to treat a variety of diseases. In fact, the first medical use of electricity is credited to a Roman physician named Scribonius Largus who described the use of the electric torpedo fish in the treatment of headaches and gouty arthritis. In his work titled *Compositiones Medicae* [1], Scribonius described the placement of a fish across the forehead or affected area to deliver a shock that alleviated pain much like a modern transcutaneous electrical nerve stimulators (TENS). As human understanding and utilization of electricity evolved so did its use in the treatment of various disease states.

In the early twentieth century, Head and Thompson proposed the theory that certain discriminative sensations including touch could exert an inhibitory effect on pain impulses; furthermore, that this facilitation or inhibition of sensory impulses was mediated in the posterior horn before the signal was relayed to secondary interneurons [2]. The idea that chronic pain involved an imbalance between the epicritic and the protopathic components of pain in which the epicritic sensory system exerted an inhibitory influence over the protopathic sensations led, in part, to the modern era of neuromodulation [3]. This era moved forward with the first trials of sensory electrical thalamic stimulation via implanted electrodes for treating severe neuropathic pain conditions that were performed in Paris [4]. Mazars and col-

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leagues hypothesized that sensory thalamic stimulation could compensate for a deficit of epicritic information by artificially enhancing the epicritic level [4].

In a 1965 *Science* article entitled "Pain Mechanisms: A New Theory," Melzack and Wall [5] proposed the gate control theory which allowed for significant advancement of our understanding about pain control over the next decades. This theory proposed that the balance of activity between large and small nerve fibers in the peripheral nervous system determines whether signals are transmitted centrally. According to the theory, small-diameter fibers, which carry nociceptive (pain) signals, impede inhibitory cells located in the dorsal horn (DH) and when small fiber input is dominant leads to central transmission of nociceptive stimuli ("open gate") to areas of the brain that interpret this information as painful. However, when large-diameter fiber input dominates, inhibitory cells are stimulated and hence "close the gate." Since electric stimulation depolarizes large-diameter fibers before small fibers are affected, Melzack and Wall stated that selective stimulation of larger-diameter fibers could have therapeutic implications in the treatment of pain. Based on this study, Shealy [6] delivered current directly to the spinal cord of a terminal cancer patient via an implanted electrode and an external pulse generator that he called a "dorsal column stimulator" successfully relieving the patient's otherwise intractable pain. Today, we refer to "dorsal column stimulation" as spinal cord stimulation (SCS).

The gate control theory was heavily criticized throughout the 1970s and remains controversial because of apparent inconsistencies noted during clinical experience. For example, according to the gate control theory, all pain should be inhibited by electrical stimulation; however, clinical studies have demonstrated that although SCS clearly demonstrates benefit in the treatment of neuropathic pain, acute and nociceptive pain signals are only minimally affected [7, 8]. Moreover, *large fiber activity* can itself signal pain during sunburns, for example, which is opposite with the view that all large/diameter fibers stimulate inhibitory cells and prevent central transmission of painful stimuli [9]. Although the gate control theory was not completely novel and has remained controversial, it is impossible to overstate its importance and impact on modern pain research [10]. In fact, today, neuromodulation involves the placement of a SCS for the treatment of neuropathic pain for which there may be only a few alternative therapies.

It is estimated that each year over 18,000 new SCS implantations are performed worldwide for a variety of conditions including peripheral arterial occlusive disease (POAD) and chronic refractory angina pectoris [11–13]. SCS implantation is a minimally invasive, reversible procedure that offers its candidates the advantage of undergoing a screening trial with a temporary SCS system to ensure efficacy of treatment before permanent implantation is performed. Unlike other surgical procedures that aim to ablate pain pathways, SCS implantation results in minimal anatomic changes. As such, SCS is expected to ameliorate but not eliminate neuropathic pain and can provide sustained pain relief for decades in some patients. The application of SCS at various levels along the dorsal aspect of the spinal cord has been found to have different effects and to affect function in different organ systems. For example, evidence suggests that mechanisms involved when SCS is utilized for treatment of ischemic conditions are fundamentally different than those for neuropathic pain [14, 15].

Spinal cord stimulation is a safe and effective therapy for a variety of patients; however, the lack of knowledge of its clinical usefulness and underlying mechanisms especially for treating cardiac diseases and peripheral vascular disease has deterred its dissemination into mainstream practice. The initial high cost of SCS implantation has been considered an initial deterrent, but recent studies have demonstrated the cost-effectiveness of SCS versus coronary artery bypass grafting in conditions such as cardiac ischemia [16]. One additional hurdle to mainstream acceptance of the use of SCS in conditions such as PAOD and refractory cardiac ischemia is a consistent referral of these patients from primary care and internal medicine physicians to a cardiologist. While cardiologists have used electrical stimulation for more than 50 years for cardiac rhythm management, the idea that SCS can alter and improve coronary blood flow and functional status is a novel idea [17]. To date, hesitance in referring patients to physicians who specialize in neuromodulation reflects a lack of knowledge and understanding of the therapy. Strides must be made to implement education programs that promote a shift in awareness that would allow primary care physicians, cardiologists, cardiovascular surgeons, and pain physicians to work hand in hand for the benefit of the patient [17].

Spinal Cord Stimulation for Peripheral Arterial Occlusive Disease (PAOD)

PAOD is responsible for the majority of ischemic conditions in the limbs [18]. In addition to its impairment of activity of daily living (ADL) and quality of life (QOL), PAOD is a major cause of disability, loss of work, and lifestyle changes in the United States [18, 19]. It is estimated that PAOD affects two million Americans with an incidence of 2 % in men under 50 years old and 5 % in men over 70 years old; although the incidence in women is similar, on average onset of disease is delayed by 10 years [20]. SCS has been used for the treatment of PAOD and vasospastic conditions, such as Raynaud's syndrome, for over 30 years and was originally described by Cook et al. in 1976 [21].

PAOD is usually caused by atherosclerosis leading to an imbalance between oxygen supply and demand. PAOD begins as intermittent claudication with only 1–2 % of cases progressing to critical ischemia classified as Fontaine stage III or IV (Table 45.1). With major advancements made in vas-

Table 45.1 The Fontaine classification of symptoms in peripheral vascular disease

Stage	Clinical features
I	Arteriosclerosis with no symptoms
II	Intermittent claudication with no symptoms at rest
IIa	Intermittent medium claudication (after 200 m of walking)
IIb	Intermittent severe claudication (before 200 m of walking)
III	Claudication, symptoms at rest and night pain without tissue involvement
IV	Grade III + tissue loss (ischemic ulceration; gangrene)
IVa	With local inflammation
IVb	With widespread inflammation

cular surgery techniques allowing longer bypass grafting procedures, SCS implantation is considered only after vascular surgery and medications have failed to prevent the progress of PAOD. The principal indication for the use of SCS is severe ischemic pain at rest (stage III). SCS is not likely to relieve neuropathic pain associated with injury to peripheral nerves cause by ischemia and diabetes. Likewise, SCS is also not expected to alleviate peripheral nociceptive pain associated with ulcerations or edema from venous insufficiency. The patient should be made aware that only deep aching ischemic pain may respond to treatment [22]. Transcutaneous oxygen pressure ($TcpO_2$) measured on the diseased extremity should range between 10 and 30 mmHg; additionally, a $TcpO_2$ gradient of supine to sitting position measurements exceeding 15 mmHg predicts a greater benefit [22–24]. Patient ulcerations should not exceed 3 cm in diameter although benefit of SCS for arresting tissue loss may be the primary goal with the aim of permitting a more distal amputation site [25].

Exclusion Criteria (Adapted from [26])

1. Life expectancy <3 months.
2. Lack of patient compliance.
3. Ischemic ulcerations >3 cm.
4. Wet gangrene.
5. Presence of infection.
6. Imminent acute obliteration requiring emergency amputation.
7. The use of SCS in the presence of an on-demand pacemaker is relatively contraindicated.
8. MRI with body coil is absolutely contraindicated after SCS implantation.

Mechanism of Action

Ischemic pain is the only nociceptive pain that is proven to respond to SCS. As opposed to mechanisms involved in neuropathic pain attenuation, beneficial effect of SCS on ischemic pain involves attenuation of tissue ischemia as a result of increasing and/or redistributing blood flow to ischemic area or by decreasing tissue oxygen demand to the ischemic area. SCS has been shown to improve microcirculation in an animal model [27]. These effects appear to be mediated by two mechanisms: (1) suppression of efferent sympathetic activity (via nicotinic ganglionic receptors and mainly alpha-1 adrenoreceptors in the periphery) and (2) antidromic mechanisms involving the dorsal roots that stimulate the release of calcitonin gene-related peptide (CGRP) [15]. The balance of these mechanisms depends on a variety of factors including the tone of the sympathetic nervous system, patient factors (diet, genetic differences, etc.), and intensity of SCS [29]. Figure 45.1 illustrates the mechanisms and neurotransmitters known or hypothesized to be involved in the effects of SCS in PAOD. A thorough review of the putative mechanisms behind the effects of SCS on peripheral vascular disease is found in Wu et al. [29].

Spinal Cord Stimulation for Angina Pectoris

Angina usually occurs during episodes of vasospasm or occlusion of the coronary vessels that results in an imbalance between the supply and the demand of oxygen in the heart due to decreased blood flow to the heart. Patients with angina pectoris are often managed effectively through pharmacological treatment with beta-receptor blocking agents, long-acting nitrates, and calcium antagonists, by revascularization procedures such as coronary bypass surgery (CABG) or by percutaneous transluminal coronary angioplasty (PTCA); however, a segment of patients suffering from chronic angina pectoris does not respond to conventional treatments [30]. Many patients suffering from severe disabling angina (New York Heart Association (NYHA) classes III–IV) suffer from concurrent comorbidities, making them unsuitable for major invasive procedure. Other patients suffer from widespread obliteration or distal lesions that do not permit successful surgical interventions. Regardless of the etiology, these patients suffer from what is termed treatment refractory angina and have a low quality of life, limited physical capacity, and frequent hospital admissions representing a large costs for society [31]. Patients suffering from treatment refractory angina led clinicians to develop alternative strategies such as neuromodulation to provide pain relief. In European estimates, refractory angina is a common condition with a prevalence of 100,000 patients [32]. SCS has been used to treat such therapy-resistant angina pectoris since the mid-1980s [33, 34]. The first ten cases of SCS directed specifically at the treatment of angina were reported in 1987 by Murphy and Giles [34].

Patient selection involves specific criteria that maximize the likelihood of clinical success and eliminates patients that are not likely to benefit in an effort to prevent these patients

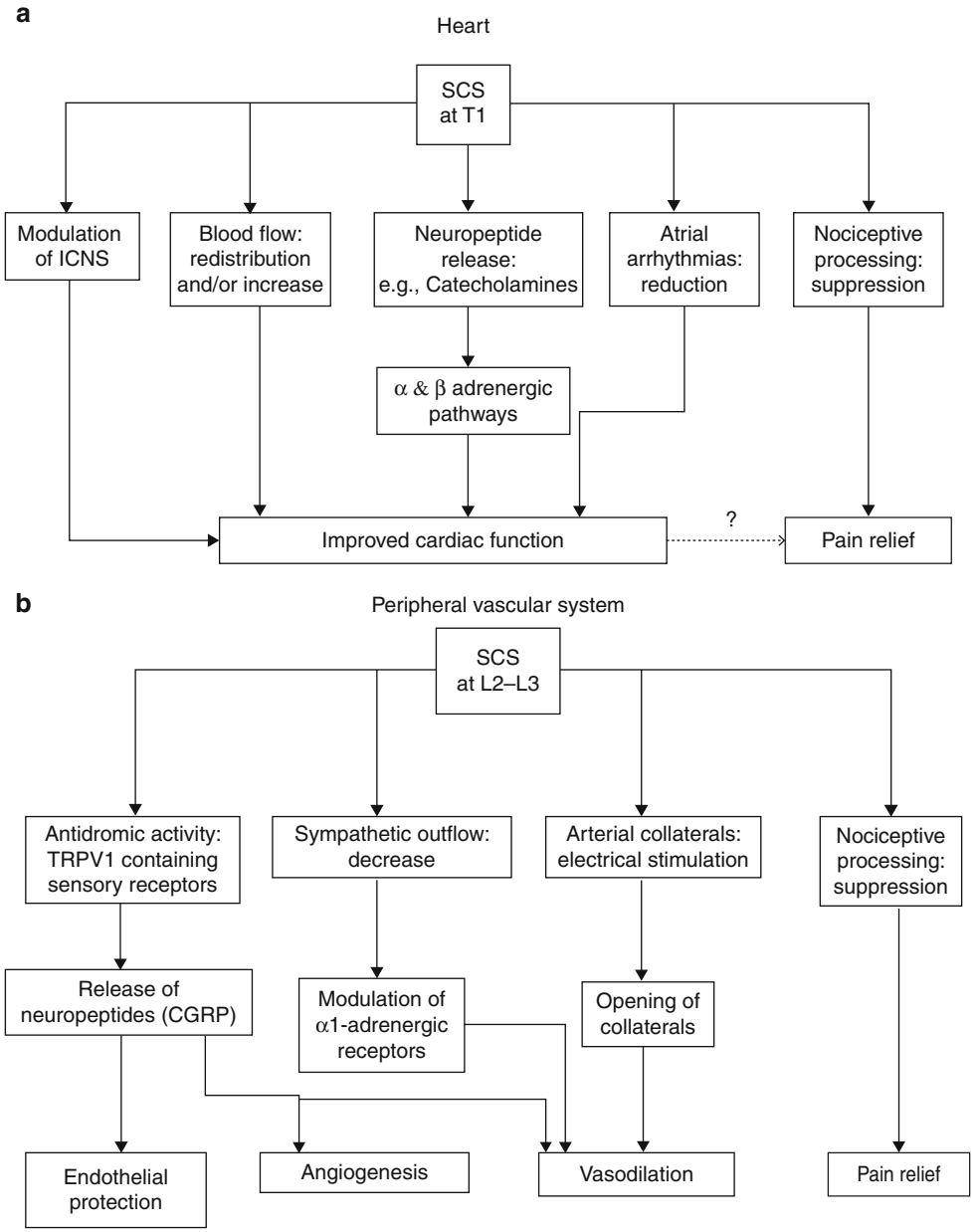

Fig. 45.1 (**a**, **b**) Illustrates the mechanisms and neurotransmitters known or hypothesized to be involved in the effects of SCS in PAOD

from undergoing an unnecessary procedure in lieu of their multiple comorbidities. The following inclusion and exclusion criteria are adapted from [26].

Inclusion Criteria

1. Severe angina pectoris (NYHA classes III–IV or Canadian Cardiovascular Society classifications I–IV) refractory to conventional treatment. Patients who have been subjected to thoracotomy may present with post-thoracotomy syndrome or intercostal neuralgia, so a careful pain assessment is mandatory. Efficacy of treatment is related to angina that is due to a reversible cardiac insult.
2. Significant coronary artery disease.
3. Demonstrated reversible myocardial ischemia as a cause of patient's symptoms.
4. Patients diagnosed as suffering from syndrome X.
5. Success of TENS in pain alleviation indicates a high likeliness for a positive response to SCS.

Exclusion Criteria

1. Acute myocardial infarction.
2. Presence of other ongoing heart diseases such as pericarditis or myocarditis.
3. Presence of on-demand pacemaker (relative contraindication).
4. MRI investigation with body coil is an absolute contraindication after implantation.

Mechanism of Action

Ischemic heart disease often presents as shortness of breath and angina pectoris, described clinically as an extremely intense substernal crushing pain and that usually radiates to the chest, shoulder and left arm, and occasionally to the neck and jaw [33, 35]. This nociceptive information is transmitted by sensory afferent fibers that enter the C7–T5 spinal segments and synapse on spinothalamic tract cells, and cells of other ascending pathways, that also receive converging cutaneous and muscle input from the overlying somatic structures such as the chest and upper arm [35]. This nociceptive information is also transmitted in nociceptive vagal afferent fibers that converge on spinothalamic tract cells in the upper cervical segments that also receive somatic convergent input from the neck and jaw [35].

Although investigators disagree about the mechanisms responsible for the alleviation of angina pain by SCS, human studies have shown that SCS reduces ischemia by redistributing coronary blood flow [36, 37] and also by decreasing cardiac myocyte oxygen demand [38]. Patients also benefit from increased time to angina in exercise tests [37], increased resistance to critical ischemia [38], and modulation of cardiac neurons leading to decreased dysrhythmias [14, 39]. Of particular importance is that SCS does not mask myocardial infarction [40, 41]. Animal studies have shown that SCS suppresses pain transmission in nociceptive pathways and improves cardiac function by stabilizing neurons of the intrinsic cardiac nervous system, reducing infarct size via adrenoreceptors, and reducing ST segment changes during ischemic episodes, and reducing atrial arrhythmias [42] (for review see Foreman et al. [43]; Wu et al. [29]). Figure 45.1 illustrates the mechanisms and neurotransmitters known or hypothesized to be involved in the effects of SCS in angina.

Preoperative Considerations

Careful preoperative evaluation of patients with PAOD and angina pectoris is mandatory since these patients often have an assortment of coexisting comorbidities that makes even a minimally invasive procedure a challenge. SCS requires active patient participation to ensure proper placement of electrodes with the goal of covering the patient's pain with a comfortable level of paresthesia that completely covers the affected area. During preoperative evaluation, a psychological evaluation performed by a psychologist or a pain-oriented psychiatrist may reveal certain psychological conditions that may exclude patient's from SCS treatment including major personality disorders, deficient capacity to collaborate and to communicate their pain, and drug-seeking behavior or abuse. A thorough analysis of the patient's pain is mandatory since many mixed pain conditions (i.e., coexisting neuropathic and nociceptive pains) may not respond to treatment and may result in clinical failure. Risks and benefits including spinal cord or nerve injury, dural puncture, epidural hematoma, headache, and infection should be discussed with the patient, and all questions and concerns should be answered or addressed appropriately.

Patients with chronic pain conditions are usually being treated with multiple pain medications, and in general, all pain medications should be continued until 2 h before the procedure is performed. Transdermal patches may be continued throughout the procedure. A majority of chronic pain patients do not respond well to increased or additional pain and are seemingly immune to normal doses of systemic analgesics. Caution should be used with liberal dosing of opioids as these patients remain vulnerable to overdose and oversedation may lead to difficulty in communicating with patient to ensure proper electrode placement. Copious use of local anesthetic may be utilized; however, the maximum dose of local anesthetic should be calculated preemptively to avoid toxic dosages. Patients on antipsychotic medications are at risk for developing neuroleptic malignant syndrome.

Chronic pain conditions are associated with numerous physiologic abnormalities of which the practitioner should remain vigilant. Patients will often be deconditioned and have a decreased respiratory reserve due to decreased physical activity caused by pain. As with all procedures involving prolonged immobility, a careful neurologic evaluation should be performed to detect preexisting deficits. Chronic opioid users have decreased gastric emptying and GI motility with superimposed chronic constipation. These patients are at an increased risk of aspiration, and care should be taken if emergency tracheal intubation becomes necessary. It is prudent to administer aspiration prophylaxis including 10–20 mg of intravenous metoclopramide 30 min before transport to the operating room and 30 mL oral Na citrate on transport to operating room.

Intraoperative Considerations and Technique

Following the placement of standard monitors and an intravenous catheter, sedation with midazolam is initiated as the patient is placed in the prone or lateral position. Antibiotic coverage with 1–2 g of cefazolin is administered.

The majority of percutaneous SCS electrodes are placed in the prone position with the aid of frontal fluoroscopy. Sterile technique is mandatory as infection in the epidural space can lead to catastrophic consequences if an epidural abscess should develop. As previously discussed, the procedure is performed under copious local anesthesia.

Epidural puncture is usually performed 20 cm below the target level (C7–T2 for angina [usually slightly to the left] and T10–11 for PAOD); however, desired position of the active electrodes and the length of the leads must be taken into account. Thoracic SCS placement mandates a lateral-oblique approach that is also used for lumbar SCS placement. A loss-of-resistance technique with air or saline using a Tuohy needle is used to locate the epidural space. Fluoroscopic guidance may aid in determining correct location of the epidural space if location proves difficult. The lead is manipulated using fluoroscopy until desired position is obtained. Intraoperative test stimulation is used to finalize placement of the lead over the target area. The goal of stimulation should be to completely cover the painful area (or at least 75–80 %) with a tolerable level of paresthesia, which requires patient cooperation and interaction. Some clinicians recommend testing the electrode position in the sitting position because it may provide a more stable electrode position. Frequency of stimulation ranges between 50 and 120 Hz, with a pulse width between 100 and 500 μs. The effective amplitude can vary but usually falls in the range of 2–6 V. The effective amplitude should ultimately be set to produce comfortable effective stimulation. There are a variety of electrode designs and configurations to choose from, and ultimately, clinicians should use equipment which with they feel comfortable. To date, there is little evidence supporting that superiority of technically more advanced types of SCS over simple quadripolar, transcutaneously implantable electrodes [44].

Electrodes can migrate leading to loss of appropriate paresthesia coverage. Plate electrodes are less likely to dislocate; however, many physicians reserve plate electrodes for clinical situations in which a cable lead has been dislodged, dislocated, or when scar tissue creates technical difficulty in threading cable electrode to target area [25]. Occasionally, pain can change location leading to clinical failure; however, SCS systems allow postimplantation adjustment of stimulation parameters to recapture coverage or "steer" paresthesia to a new location [25]. Surgical intervention for readjustment of SCS is only occasionally encountered. Some patients do not tolerate or dislike paresthesia and do not continue SCS therapy.

Trial stimulation should be performed via temporary electrodes or via temporary, percutaneous connections with potentially permanent electrodes for PAOD [45]. Moreover, many health-care systems mandate a trial stimulation period as a requirement for reimbursement. Data on the predictive value of trial stimulation for long-term outcome of PAOD are conflicting, and there are no systematic, well-designed studies demonstrating the improvement of long-term outcome after success of trial stimulation. Trial stimulation period is performed for 1–2 weeks, and pain scores using visual analogue scale (VAS), opioid consumption, value for their daily life activities, as well as objective measures of peripheral blood flow should be assessed to indicate success of SCS. Because of the high success rate when SCS is applied for angina pectoris, systems can be applied in one session when being used for this purpose.

Postoperative Considerations

Postoperative complications include spinal cord injury, epidural hematoma, or abscess/other infection and require prompt postoperative neurologic assessment if suspected. Postoperative pain scores range from 3 to 8 on a VAS, and patients may require increased pain medication dosages as they are frequently intolerant of postoperative pain. Opioids should be used with caution as patients remain susceptible to narcotic overdose including respiratory distress in response to the patient's usual opiate dose if relief is achieved. If SCS has produced significant pain relief, patients may experience drug withdrawal symptoms from a rapid decrease in their opioid usage and may need to be tapered. A 50 % reduction in pain is generally considered as an accepted clinical goal of SCS treatment; however, most single measures of clinical success have limitations [46]. Hence, pain reduction needs to be coupled with functional capacity increase as well as improved quality of life to demonstrate success.

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Clinical Applications of Neuromodulation: Spinal Cord Stimulation for Abdominal Pain

46

Leonardo Kapural and Marc D. Yelle

Key Points

- Proper patient selection may result in better outcome when SCS is used to treat visceral abdominal pain.
- Team work with referring gastroenterologist and continued collaboration helps to elucidate main cause of the patient's pain and prevents us to conceal any serious symptomatology.
- Diagnostic retrograde differential epidural block can identify those patients who have predominantly visceral abdominal chronic pain.
- Careful placement of the epidural needle and lead is of greatest importance in thoracic area as of presence of the spinal cord.
- Most frequent tip of the lead positioning is around T5 area to achieve paresthesias within the area of abdomen.
- Further studies are needed to explain possible mechanisms of pain relief when spinal cord stimulation is used to treat painful gastrointestinal disorders and to provide more evidence that such treatment would produce long-term improvements in patients' chronic pain.

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Introduction

Chronic abdominal pain poses significant challenges to patients and physicians alike. For patients, pain can limit both professional and personal quality of life [1]. It results in increased doctor visits, imaging and surgery interventions that frequently fail to find a cause or provide relief [2, 3]. For physicians, identification of etiology is fraught with difficulty, largely due to the fact that visceral pain is frequently diffuse and is poorly localized and referred to somatic structures [4, 5]. Abdominal pain is one of the most common complaints for primary care visits [6] and is the leading reason for gastroenterological consultation. These challenges taken together with the high prevalence, frequent office visits and extensive work-up, as well as decreases in productivity, work hours [1, 3], and socioeconomic status, make chronic abdominal pain a significant burden on the patient, physician, healthcare system [1, 3], and society as a whole. In the United States alone, between 20 and 45 % of Americans will suffer from chronic visceral pain [7], of these only 50–70 % will have a definitive etiology of their pain identified [8]. Recent research has provided data helping to better elucidate visceral pain pathways and the dorsal column's role in not only transmission but also amplification of visceral pain. Exciting data in both animal models and human subjects has demonstrated that spinal cord stimulation of the dorsal horn can provide analgesia for chronic visceral pain and improve both quality of life and functional status.

Mechanisms of Abdominal Pain

Data from multiple disciplines have shown that the integration of peripheral (sensory, motor, and autonomic) and central nervous system (spinal cord as well as midbrain and cortex) input to end organs (GI mucosa, glands, muscles, etc.) is essential to normal gastrointestinal physiology. This bidirectional neural circuit has been referred to as the "brain-gut axis" [9, 10]. Imbalance within this system that links visceral

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sensation with intestinal function is fundamentally linked to both functional GI disorders as well as chronic visceral pain [11–14]. Chronic visceral pain has been classically thought of as simply a nociceptive sensory disorder, but new evidence suggests that it may not only be entirely organic to the viscera but also neuropathic pain disorder [15, 16].

Peripheral Pathways

Visceral pain is not only difficult for patients to specifically localize to structures within the abdomen; the pain is frequently referred to various somatic structures. This is largely due to complex neurobiology of the visceral pain pathways. Visceral nociceptors are frequently polymodal and can respond to mechanical, thermal, and chemical stimulation [15], but are not uniformly distributed around the abdomen.

Autonomic and spinal nociceptors project on unmyelinated C- or lightly myelinated Aδ-fibers. Like somatic sensory afferents, the cell bodies of visceral afferent fibers are located in the spinal (or dorsal root) ganglia, with the exception of vagal afferents that have cell bodies located in the inferior ganglion of the vagus nerve (nodose ganglia). On their path to the dorsal horn, visceral spinal afferents project collaterals to both prevertebral and paravertebral ganglia allowing for modulation of autonomic response to sensory stimuli. Visceral spinal fibers then enter Lissauer's fasciculus followed by the dorsal gray matter, synapsing on second-order neurons in mostly the substantia gelatinosa (lamina II) and nucleus proprius (laminae IV–VI). These same second-order neurons also receive somatic sensory input. This convergent input explains, in part, why visceral pain is frequently referred to somatic structures [17–19].

Dorsal Horn: Neuromodulation and Hypersensitivity

Data from animal models as well as humans have long demonstrated alterations in activity of dorsal horn neurons in response to peripheral tissue injury [1, 3]; nerve damage [20, 21]; frequent, repeated sensory input [22]; and descending modulation (facilitatory and inhibitory) from midbrain and cortex [23]. Functional plasticity within dorsal horn neurons following sensitization results in enlargement of receptive fields, increased recruitment of peripheral fibers, increases in suprathreshold responses (both in intensity and duration) to sensory input, and even vigorous activation of neurons that are usually silent with normal nociceptive input. In somatic pain, central sensitization in the dorsal horn leads to leftward shift in the stimulus/response curve where normally innocuous stimuli cause painful responses (allodynia) and previously painful stimuli result in an exaggerated response (hyperalgesia). It seems that similar patterns of stimulus/response occur in visceral sensitivity and in functional bowel disorders [24] where exaggerated responses are not only intrinsic to the viscera but also get referred to somatic regions. In animal studies, repeated colonic distension results in the enlargement and convergence of visceral afferent receptive fields, demonstrating the central nervous system involvement in visceral hypersensitivity [25, 26]. In normal human subjects, repeated distension of the viscus results in increased reported pain intensity and referred somatic pain as well as changes in the reported quality of the sensation [27]. These data demonstrate how peripheral visceral input to the CNS can result in hypersensitivity and pain. This hypersensitivity has been shown to be involved in the pathophysiology of chronic visceral pain [28, 29].

Spinal Pathways of Visceral Pain: Spinothalamic Tract and Dorsal Column Pathway

Second-order neurons in the dorsal horn relay afferent (nociceptive) sensory information to thalamus mainly through two ascending pathways, the spinothalamic tract and the spinoreticular tract. Projection neurons, mostly in the substantia gelatinosa and nucleus proprius, project fibers across midline and ascend to thalamus and brainstem in the contralateral, anterolateral spinal cord. The spinothalamic tract is regarded to be the relay primary pathway for visceral nociceptive information [30]. However, dorsal column has been shown to not only transmit some visceral nociceptive information [31] but also modulate (amplify) visceral pain transmission [31]. Lesions in dorsal cervical spinal cord in primates altered responses to colorectal distension, demonstrating that nociceptive information ascends in not only the anterolateral spinal cord (STT) but also the dorsal column pathways [32], which usually thought to transmit purely innocuous sensory information. Anatomical studies identified fibers in both the STT and DC were activated by visceral peripheral nerve stimulation [30]. Other studies have carefully described the dorsal column pathway involvement in modulation of visceral sensory information. With chronic stimulation and/or inflammation of peripheral visceral nerves, plastic changes in receptors and signal transduction occur in postsynaptic dorsal column neurons [33–37].

In several animal studies, visceral pain caused by direct stimulation of organs including the ureter, pancreas, stomach, and colon diminished after DC lesion [30, 38, 39]. This hypothesis is supported by substantial clinical data. In a study conducted in patients with visceral pain related to colon cancer, small midline lesions (either mechanical or radio-frequency myelotomy) relieved pain in 71.5 % (10 or 14) patients [40]. This data has been replicated by multiple surgeons for chronic visceral pain from multiple locations

within the abdomen (stomach, liver, pancreas, bowels) and pelvis with considerable success and few complications [4, 41–46]. Patient not only had reductions in reported pain but also decreases in opioid use [46]. Investigations into the exact role of the DC in the processing of visceral information have shown that while the STT tract is central to the relay of sensory information, the DC pathway appears more important than the STT in the modulation of this information [42, 46–48]. These studies suggest that such pathway is an excitatory and central to the visceral pain processing; it may play a critical role in mediating the changes in sensory processing associated with peripheral inflammation and central sensitization. Moreover, it seems likely that the neurons in this DC pathway comprise the ascending arm of the amplification loop by activating descending facilitatory influences from the rostroventral medulla [48]. While surgical lesions have provided significant improvements in patients with cancer-related abdominal and pelvic pain, less invasive treatment options would benefit a larger patient population with more varied and benign pain etiologies.

Spinal Cord Stimulation for Visceral Pain

The use of electrical stimulation of the dorsal horns has been for years to treat numerous chronic pain syndromes [49], originally indicated for back and extremity pain including radicular low back pain, post-laminectomy syndrome [50], complex regional pain syndrome [51, 52], and peripheral vascular disease [53, 54]. Spinal cord stimulation involves delivery of the low current from implantable generator to the epidural leads and contacts, protecting a small electrical field into and around the spinal cord at that level. The mechanism of SCS neuromodulation resulting in pain relief is not completely understood; however, a number of hypotheses have been proposed [49, 55]. Activation of supraspinal pain modulatory pathways by SCS could account for its analgesic effects [56]. It is possible that the SCS modulates the afferent signal in the dorsal horn by "closing the spinal gate" by activating large, myelinated that inhibit small nociceptive fibers [57] or by the release of inhibitory neuromodulators, such as GABA [58, 59]. Alternatively, SCS could provide blockade of nerve conduction [60, 61], possible by antidromic activation. Neurosurgical data (discussed above) suggests that lesioning the postsynaptic DC pathway via midline myelotomy interferes with the generation and maintenance of chronic visceral pain by removing the ascending limb of a facilitatory pain loop. It is possible that the electrical field from SCS also interrupts this ascending limb without physical lesioning of the pathway. Another possible mechanism for SCS is downregulation of intersegmental or supraspinal sympathetic outflow [59, 62–64]. Regardless of the exact mechanism of SCS, the resultant neuromodulation in the dorsal horn provides great potential for the treatment of chronic abdominal pain.

Basic Science

SCS has been studied in rats with and without post-inflammatory visceral hypersensitivity during colonic distention. The visceromotor response (VMR) elicited by colonic distention was suppressed by SCS in both normal and sensitized rats [65]. In addition, the authors reported that the effect of SCS on VMR continued to be observed for a prolonged duration, even after SCS was discontinued. These data are consistent with previous SCS data for treatment of refractory angina pectoris [66] and suggest that SCS may result in persistent, complex alterations of the neural activity and neurotransmitter release. SCS electrodes placed in either cervical or lumbar regions have been shown to inhibit lumbosacral neural responses to colonic distention in rats [67]. These data lead the authors to hypothesize that SCS may cause antidromic activation of peripheral sensory fibers negating the afferent input [67].

Clinical Evidence in Humans

At this time, there is very compelling yet limited data demonstrating the significant improvements, both in reported decreased pain intensity and increased functional capacity in patients with a wide variety of chronic visceral pain syndromes. Level A clinical evidence and recommendations remain years away; still numerous case reports and case series have demonstrated significant clinical improvements and positive treatment outcomes for chronic visceral syndromes including mesenteric ischemic pain [68], esophageal dysmotility [69], gastroparesis [70], IBS [71], chronic pancreatitis [72–75], familial mediterranean fever [76], posttraumatic splenectomy [74], generalized chronic abdominal pain [74], and chronic pelvic pain [62]. While these studies provide encouraging results, the full significance of their findings needs to be validated.

The first reported use of SCS in the treatment of chronic abdominal pain was in an elderly patient with refractory pain secondary to chronic mesenteric ischemia. Transient relief of severe postprandial pain was reported after celiac plexus block; however, the pain quickly returned. In order to provide a long-term relief, SCS system was trialed. Leads were placed in the epidural space at T6 spinal level. Following the procedure, the patient reported paresthesia across her abdomen and complete relief of the pain [68]. Thoracic SCS was also used to treat visceral pain related to inflammatory bowel syndrome (IBS). The patient reported a robust initial reduction in pain. However, this effect was not sustained. The patient experienced paresthesias in distal extremities, but not in the region of her abdominal pain [71]. While the pain relief was transient, immediate and sustained relief of frequent diarrheal episodes was achieved. These data taken together with case

studies in esophageal dysmotility [69] and gastroparesis [70] suggest that, in addition to providing visceral pain relief, SCS may improve dysmotility of the functional gastrointestinal disorders. Khan and colleagues [74] reported significant pain relief (mean VAS decrease of 4.9) in long-standing chronic pancreatitis patients using less than half the narcotics required prior to the procedure. These findings were corroborated a later case study of a 38-year-old female with a 13-year history of recalcitrant, chronic pancreatitis [73] who had undergone multiple surgeries and frequent [22] endoscopic retrograde cholangiopancreatography without relief.

Recently, a several much larger case series provided evidence that chronic pancreatitis, but also multiple other chronic abdominal pain and dysmotility syndromes, could be controlled using SCS. Those treatable causes of chronic abdominal pain studied included gastroparesis, mesenteric ischemia, post-gastric bypass chronic epigastric pain, and chronic visceral pain after various intra-abdominal surgeries with present evidence of abdominal adhesions [72, 77, 78].

A first larger study examined 35 patients with chronic visceral pain who underwent SCS trial [72]. The etiology of these patients' pain was confirmed to be visceral (n = 32) or mixed visceral and central (n = 3) in origin by retrograde differential epidural block. Five of these patients failed SCS trial. The 30 remaining patients reported at least a 50 % reduction in their pain with significant reductions in pain scores (average pretrial VAS rating of 8.1 ± 1.6 to 3.1 ± 1.6 cm) and an average opioid use (110 ± 119 to 70 ± 68 mg morphine sulfate equivalents). Nineteen patients were followed for 1 year; the remainder were either followed for less than a year (n = 3); had the SCS removed due to infection or lead migration (n = 4), were lost to follow-up (n = 1), or passed SCS trial, but did not have improvement at 6 months and requested explant (n = 1). The 19 patients that were followed for 1 year following SCS implant maintained low pain rating (VAS of 3.8 ± 1.9 cm and opioid use (38 ± 48 mg morphine equivalents)) [72].

To elucidate further specifics of the technical aspects of SCS when used for chronic abdominal pain, survey was conducted across the United States. Twenty-two physicians reported 70 cases of SCS for various chronic abdominal pain syndromes [77]. The technical characteristics of SCS when used to achieve the optimal spinal cord stimulation in this study were consistent with the data that we collected in above-described retrospective study on 35 consecutive patients [72]. The most frequent placement of the lead (mainly two octrode leads) was posterior epidural midline, and the most frequent vertebral level where the lead tip was positioned was T5 (see Figs. 46.1 and 46.2) [77].

Most recently reported was a clinical experience using SCS in 30 patients with chronic pancreatitis [78]. Patient population was somewhat different, as there were 9 out of 30 patients with previous alcohol or opioid abuse. Similar SCS lead placement was required to achieve appropriate paresthesias (T5 (N = 10) or T6 (N = 10)). Twenty-four patients (80 %) had >50 % pain relief during the trial. Improvements in VAS pain scores were substantial: from 8 ± 1.6 to 3.6 ± 2 cm at 1 year (same as decrease in opioid use from 165 ± 120 to 48.6 ± 58 mg of morphine equivalents). SCS was very useful therapeutic option for >70 % of trialed patients with severe visceral pain from chronic pancreatitis [78].

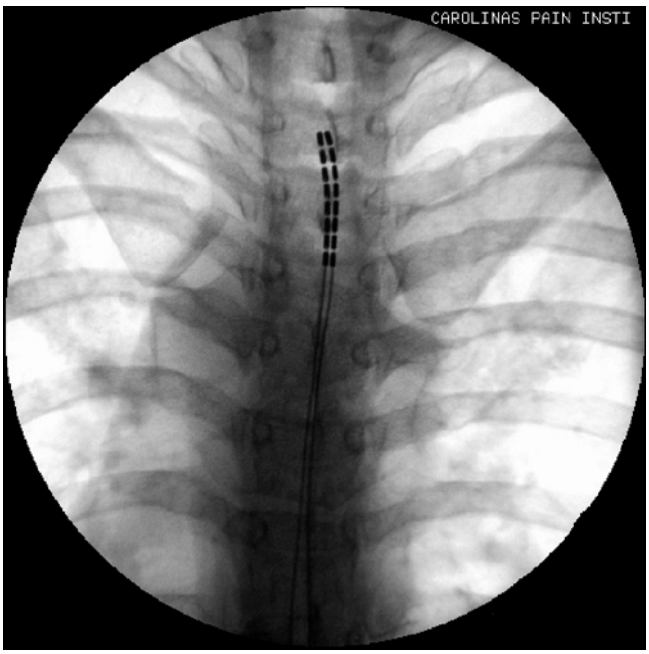

Fig. 46.1 Fluoroscopic anterior-posterior (*AP*) radiograph of thoracic spine with appropriately positioned two octrode leads midline and with the tips positioned at T5. This is the most frequent lead positioning when used for the SCS in painful gastrointestinal disorders

Conclusion

When SCS is used in the animal models of colorectal distension and irritant-induced colonic sensitization, data suggest that the SCS may suppress visceromotor reflex in rats [65]. Recent study results suggest that SCS may be a very useful therapeutic option when trialed in patients with various chronic visceral pain conditions [72, 77]. In order to elucidate mechanisms behind such modulatory effect, additional basic science research is required. In addition, prospective, randomized studies are needed to determine the long-term clinical efficacy of SCS (Fig. 46.3).

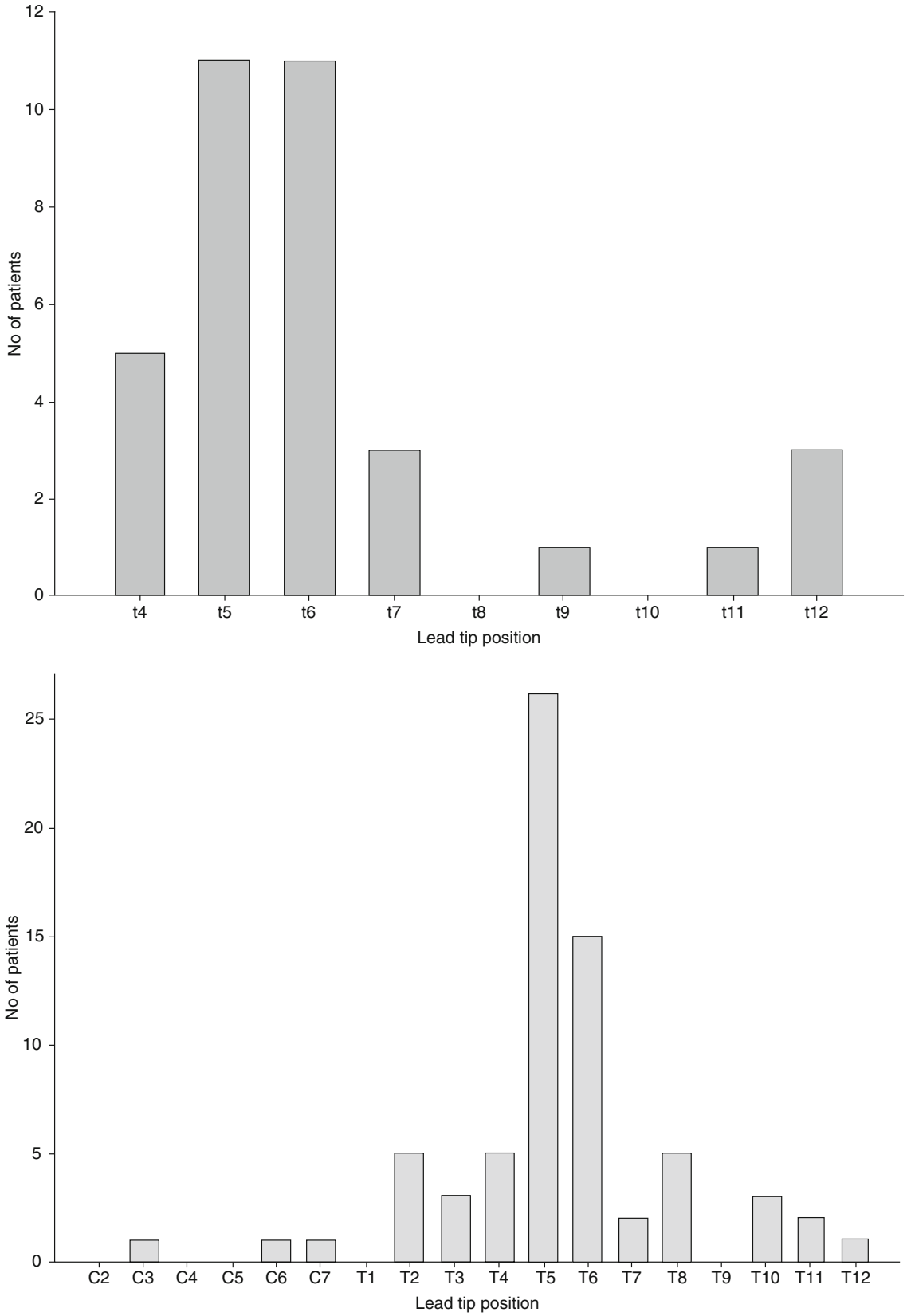

Fig. 46.2 Two graphs below illustrate distribution of the lead tip positions when SCS used for treatment of chronic visceral hyperalgesia. Graphs shown are from two published studies: (**a**) a retrospective larger case series on 35 patients with various causes of abdominal pain and (**b**) survey that collected data on 70 SCS cases. More than two-thirds of the patients were able to achieve optimal paresthesias to cover the area of abdominal pain when leads were positioned midline and up to T5 or T6 vertebral level (With permission from *Pain Medicine* [72, 77])

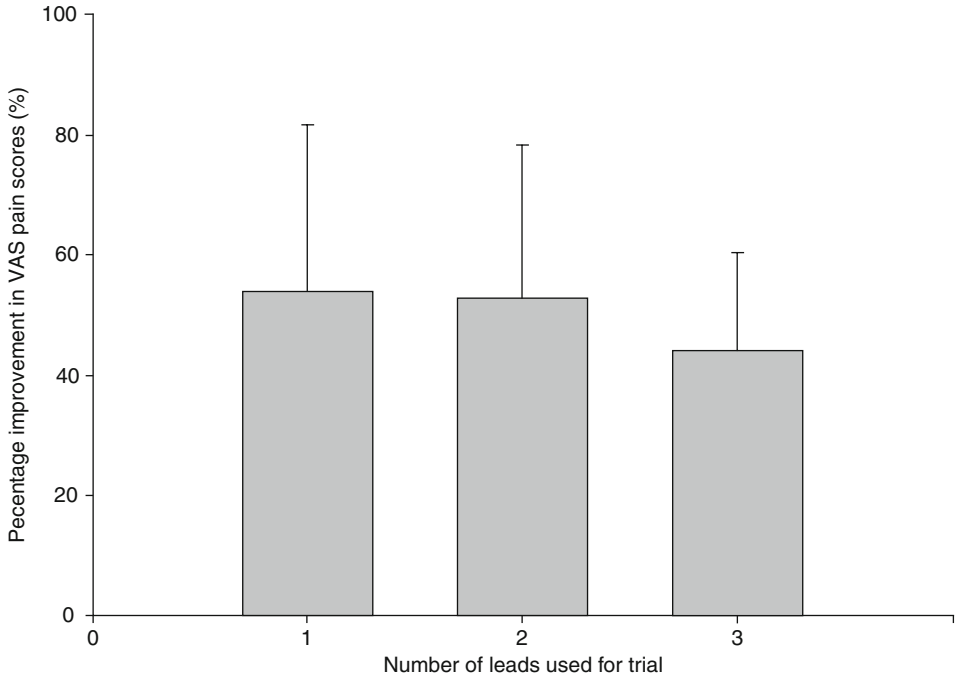

Fig. 46.3 Additional published data on spinal cord stimulation for chronic abdominal pain. It appears that the number of leads used does not influence improvements in pain relief, at least not in below-presented small study. If one, two, or three leads are used in order to provide an optimal trialing, pain relief was comparable at the end of the trial (With permission from Kapural et al. [72])

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Cost-Effectiveness of Interventional Techniques

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Key Points

- Intrathecal drug therapy (IT) and spinal cord stimulation (SCS) therapy are robust, cost-effective therapies for management of chronic pain and are superior to conventional medical management (CMM).
- From a cost-effectiveness standpoint, it is better to have failed SCS and IT than to be maintained on CMM alone.
- An integrated approach to the treatment of chronic pain will result in improved utilization of limited health-care resources.
- Technological advances that increase hardware lifespan and improve catheter and electrode design will reduce complication rates, further bolstering the already favorable cost profile of these interventions.

Introduction

The field of neurostimulation has matured over the past decade to emerge as an important modality for the treatment of intractable chronic pain. Despite relatively high initial costs, a breadth of evidence exists, and extensive clinical experience suggests that spinal cord stimulation and intrathecal drug delivery systems are safe, effective, and economical. The benefits of neuromodulation are manifested in improved functional capability, health-related quality of life (HRQoL), and reduced demand for health-care resources. This results in long-term economic benefit and cost saving. Neuromodulation is a viable option for the early treatment of patients with intractable pain syndromes.

This chapter profiles the development, clinical utility, and cost-effectiveness of two popular neuromodulatory modalities: intrathecal drug therapy (IT) for the management of intractable chronic nonmalignant pain (CNMP) and the role of spinal cord stimulation (SCS) in the treatment of failed back surgery syndrome (FBSS).

Spinal Cord Stimulation

Background

SCS is a safe, reversible, cost-effective, and minimally invasive intervention capable of generating superior outcomes for the treatment of neuropathic pain [1–17]. A large body of evidence supports the application of SCS in a diverse array of clinical scenarios [18–21]. The role of SCS is well established in the treatment for pain resulting from FBSS, complex regional pain syndrome, diabetic neuropathy, and peripheral vascular disease. The beneficial effects of SCS on pain, function, and depression are widely acknowledged [3–5, 22, 23]. It is now recommended that SCS be considered earlier in the treatment continuum in order to maximize

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patient outcomes and improve the opportunity for successful rehabilitation [2, 13].

Low back pain is extremely common, trailing only hypertension and diabetes as the reason behind most physician office visits [24]. It accounts for a large proportion of healthcare expenditure without clear evidence of improvement in health status. Ten to forty percent of patients undergoing lumbosacral spinal surgery for low back pain (with or without radicular symptoms) fail to achieve satisfactory outcomes and develop persistent or recurrent pain – referred to as FBSS [25]. In this scenario, SCS has proven superior to reoperation, both in terms of pain relief and cost [8, 9].

At present, only three published, randomized, controlled trials have evaluated the impact of SCS in management of FBSS and CRPS [4, 5, 8, 26]. These investigations demonstrate that SCS offers superior pain relief, HRQoL, and functional capacity and is cost-effective compared to conventional medical management (CMM).

Technological innovation, in terms of leads (type and variety), pulse generators (rechargeable and non-rechargeable), and programming capability, facilitates enhanced pain control and outcomes. This has improved the management of axial pain, which has historically defied harnessing.

Scientific Rationale

Through epidural electrode placement, SCS electrically stimulates dorsal columns of the spinal cord. The exact mechanism(s) by which SCS achieves pain control remains unclear. Several experimentally supported theories have been propagated. Initially, the effects of SCS were explained on the basis of Melzack–Wall's gate control theory [27]. However, this explanation proved inadequate and does not fully account for the differential success of SCS in neuropathic pain management.

Mechanisms at play during stimulation may include (1) suppression of the hyperexcitability of wide dynamic range neurons and high-threshold nociceptive-specific spinothalamic neurons in the dorsal column, (2) activation of interneurons at or in close proximity to the substantia gelatinosa which consequently inhibits the deeper laminae III–V in the dorsal horn, and (3) excitation of supraspinal sites such as the pretectal nucleus which in turn produces analgesia by inhibiting nociceptive dorsal horn neurons. The long-lasting effects are thought to be mediated via the dorsolateral funiculus because sectioning of this tract abolishes this beneficial effect. Moreover, SCS is known to produce electrical and chemical alterations as it induces the release of neurotransmitters such as adenosine, glycine, and 5-hydroxytryptamine, while also activating gamma-aminobutyric acid beta-receptors, which in turn decrease excitatory amino acids at the level of the dorsal horn cells [28–32].

Early SCS employed the use of unipolar electrodes. Technological advances have led to the introduction of multichannel quadripolar and octapolar leads which enable bipolar stimulation and are superior to single-channel devices. Single-electrode arrays have been used successfully to produce pain relief, in both unilateral and bilateral pain of the upper or lower extremities [33–40]. At present, dual-electrode arrays (either percutaneously implanted (placed parallel to each other on either side of the midline) or surgically implanted) are more often used in this role. Clinical reports indicate that patients with FBSS, experiencing predominant radicular symptoms, respond well to dual quadripolar or octapolar lead arrays [4, 5, 34, 35, 41]. Computer modeling suggests that patients with predominant axial pain may benefit from the enhanced current steering capabilities offered by tripolar lead configurations [33]. Lead choice primarily depends on surgeon preference taking into consideration underlying pathology. The octapolar lead has an advantage over the quadripolar lead in cases where migration occurs resulting in loss of stimulation-induced paresthesia and recurrence of pain. In these circumstances, pain relief can be restored by reprogramming rather than resorting to surgical intervention. Advances in lead and pulse generator technology have improved clinical outcomes by enabling programming of each individual contact which allows for more accurate and consistent stimulation of the desired body region [36, 37].

In the mid-1970s, the first fully implantable pulse generator (IPG) was introduced and was powered by a non-rechargeable primary cell battery [38]. The disadvantage of this system is that battery life is limited to 2–5 years. When battery exhaustion occurs, a surgical procedure is required for replacement. The first rechargeable IPG was approved by the Federal Drug Administration (FDA) in 2004 (Advanced Bionics, Valencia, California, USA). Bench testing reveals that rechargeable IPGs could last 10–25 years, necessitating fewer replacements and consequently improving morbidity and resulting in cost saving [38].

Intrathecal Drug Therapy

Background

In 1979, Wang, Nauss, and Thomas reported the first human study demonstrating safe, effective intrathecal administration of morphine [42]. Soon thereafter, Behar and associates [43] and Lund [44] demonstrated the efficacy of epidural morphine in pain management. Since the 1980s, IT has been successfully used for the management of CNMP and spasticity [45–64]. IT becomes a valuable tool for patients who have failed multidisciplinary, multimodal treatment algorithms. Over the lifetime of IT, some patients develop tolerance or experience disease progression and have to contend

with drug dosage escalation and associated side effects in an attempt to maintain adequate pain control. In these situations, polyanalgesic regimens become necessary [65–68].

As several delivery systems exist, the choice of system is dictated by patients' clinical need. A percutaneous catheter (tunneled or not tunneled) or a catheter with a subcutaneous injection port, connected to an external pump, is suitable for patients with limited life expectancy. However, percutaneous catheters require frequent monitoring for infection and migration. This mode of delivery also restricts patient mobility. For long-term use, a fully implantable system is required. This has the advantage of retaining mobility and functional activity. Fixed-rate delivery systems are less expensive than variable-rate systems but lack flexibility of drug delivery. In fixed-rate systems, dosage adjustments require that drug concentration be changed, which necessitates an additional pump refill. In contrast, programmable systems allow for easy dose alteration without invasive intervention and enable bolus programs (practitioner and/or patient-activated) [62, 63].

The first fully implantable and programmable infusion pump (Medtronic Inc., Minneapolis, MN, USA) became available in 1988 [64]. Technological advances have been paralleled by the availability of pharmaceutical agents for IT use, resulting in the expansion of this field. Presently, opioids are used as single agents or in combination with adjuvant pain medications such as anesthetic or antispasticity drugs [62].

Presently, there are no standard guidelines for patient selection [46, 47]. Common indications for IT include CNMP due to FBSS, mixed neuropathic–nociceptive pain, complex regional pain syndrome, and certain neuropathies including diabetic and small-fiber neuropathy. IT is also utilized to control severe spinal and supraspinal spasms and rigidity which may occur with multiple sclerosis, cerebral palsy, stroke, brain injury, or spinal cord injury [49–61]. It is safe, effective, and cost-efficient [46, 54–58, 69–73].

In 2000, the first expert panel convened to develop basic guidelines for administration and use of IT pharmacotherapy [65]. The consensus statements for intrathecal drug delivery were revised in 2003 and again in 2007 to incorporate new evidence, recently approved medications, and safety warnings [67, 68]. To date, only morphine, ziconotide, and baclofen acquired FDA approval for intrathecal use [68]. However, other agents are used frequently and are done so "off-label."

Scientific Rationale

IT primarily relies on an implantable (programmable) pump which is connected to an intrathecal catheter. This system allows the administration of analgesics directly into the intrathecal space at a specified concentration and rate. The advantage of IT being that analgesia may be obtained at dose levels significantly below those needed if oral therapy is used. This is accompanied by a reduction in dose-related side effects. For instance, subarachnoid delivery has a two orders of magnitude (100-fold) dose advantage over oral delivery [74].

Opioid receptors were originally identified in the spinal cord in 1973 [75]. Cousins in 1979 used the phrase "selective spinal analgesia" to describe the phenomenon that spinally administered opioids could produce a specific analgesic effect with few motor, sensory, or autonomic side effects [76, 77]. Intrathecal opioids exert their analgesic effect pre- and postsynaptically by reducing neurotransmitter release and by hyperpolarizing the membranes of neurons in the dorsal horn, thus inhibiting pain transmission [78].

Intrathecally, local anesthetics exert their effect by sodium channel blockade, which inhibits the action potential in neural tissue in the dorsal horn, producing a reversible analgesic effect. Intrathecal clonidine, an α2 agonist, modulates pain transmission by depression of the release of (1) C-fiber neurotransmitters, (2) substance P, and (3) calcitonin gene-related peptide. It has been hypothesized that clonidine also suppresses preganglionic sympathetic outflow [79].

Ziconotide is a calcium channel antagonist specific to the presynaptic terminals in the dorsal horn of the spinal cord. Intrathecal ziconotide is thought to produce its analgesic effects by blocking neurotransmitter release in primary nociceptive afferent fibers [80].

Polyanalgesia is therapeutically beneficial and modulates the various components of pain, with each agent serving to attenuate a specific mechanism involved in producing the pain state. Combinations of different drug classes such as opioids plus local anesthetics (±clonidine) are currently being used in clinical practice. The basis for polyanalgesic therapy includes the following: (1) Multiple agents with different mechanisms of action can more effectively combat clinical pain states which are themselves an amalgam of several mechanisms implicating both central and peripheral neuronal circuits. (2) There is strong evidence that several agents may attenuate the tolerance otherwise associated with an equipotent dose of a monodrug regime. (3) Even if various pain states are produced by a single underlying mechanism, agents acting on different elements of the system may exhibit a synergistic interplay that improves the therapeutic effect [79–81].

Methods

At our multidisciplinary pain clinic, we maintain a database of more than 500 patients. Our present analysis is based on the results of earlier studies in which we compared intervention (SCS or IT) to CMM [4, 5, 16, 72, 73]. A decision analytic model was constructed to examine the cost-effectiveness of intervention versus CMM. We have updated financial data to reflect current economic realities. Additionally, we reexamined patients' charts to verify accuracy of outcomes and utilization of health-care resources.

Tabulation of Costs

The cost basis for each group was calculated by tabulating costs of the initial evaluation, physician visits, diagnostic procedures, adjunctive therapies, medications, and hospital stays for the treatment of breakthrough pain. In addition to this common base cost, the intervention groups incurred additional expenses including the costs of hardware, hospital, and surgical fees for implantation, complications related to the implant procedure and its maintenance, and pharmacotherapy.

All actual costs are based on the year 2011 Canadian dollar which is presently trading at par with the US dollar (March 29, 2011: $1 CDN = $1.02 US). As this study was conducted in Regina, Saskatchewan, Canada, all cost references are taken from that province's fee schedule. The costs of the implantable devices were obtained from the manufacturer's price list for the year 2011 (Medtronic of Canada, Ltd., Brampton, ON). Markup of these products is not permissible under Canadian law. The costs for each category were calculated on an annual basis, extrapolated for the 10-year study period, applied to each group, and then compared. Cost data were organized into the following categories:

1. Pre-implant costs: including professional fees and diagnostic procedures such as magnetic resonance imaging (MRI), computed tomography (CT) scanning, myelography, and lumbar spine x-ray films.
2. Implant procedure costs: including professional surgical fees, operating room fees, hospital stay, and equipment costs.
3. Maintenance costs: consisting of nursing contact, physician consults, medication, associated complications (for intervention groups), and hospitalizations for acute exacerbation of pain.
4. Adjunctive therapy costs: such as acupuncture, physiotherapy, massage, and chiropractic therapy.
5. Pharmacotherapy costs include drug and dispensing costs.

Personnel Cost Analysis

Health-care professional fees are determined through negotiations between various professional groups and the provincial health department. Professional fees calculated in this study are based on the actual year 2011 payments. The costs associated with nursing contacts were calculated according to the hourly wage earned by the neuromodulation nurse. Similarly, costs calculated for contact with physiotherapists, chiropractors, massage therapists, and acupuncturists reflect actual therapy costs.

Diagnostic Costs

The frequency of the imaging procedures performed was extracted from all patients' charts. The cost of each imaging procedure was derived from the actual costs incurred to the hospital as determined by the finance department of the Regina Qu'Appelle Health Region.

Hospitalization Costs

Hospitalization costs at the Regina General Hospital, where the study was based, are $1,500/patient/day.

Oral Pharmacotherapy Costs

The commonly used drugs prior to and following implantation were opioid, antidepressant, nonsteroidal anti-inflammatory, analgesic, or muscle relaxant agents. Costs of pharmacotherapy for each patient were calculated according to the Saskatchewan Health Formulary, allowing a predetermined government-approved pharmacist markup schedule and a flat rate for dispensing according to pharmaceutical standards. From this, we calculated a monthly and subsequently yearly cost, which was then extrapolated to a 10-year period.

Decision Analysis Model

We constructed a Markov-based decision model to simulate the course of events for patients undergoing intervention. We applied the cost–utility guidelines developed by the United Kingdom's National Institute of Clinical Excellence to compare the cost-effectiveness of intervention versus CMM [82]. In each case, the model assumes that CMM remains available as an adjunct treatment. Cost-effectiveness analysis (CEA) was performed to optimize (maximize) effectiveness and minimize cost.

We conducted probabilistic sensitivity analysis (PSA) to account for underlying parameter uncertainty. In a PSA, each parameter is given a probability distribution, and uncertainty in all model parameters was then explored simultaneously using 100,000 Monte Carlo simulations. Medical treatment decisions are subject to uncertainty. Thus, Markov models are preferred over conventional decision trees to avoid unrealistic simplifying assumptions.

The variables we subjected to PSA include clinical success, resource use, complication rate, and hardware failure rate over time. We calculated the cost-effectiveness of each strategy and ranked them accordingly. We also plotted the results as acceptability curves, sensitivity analyses, and net monetary benefit (NMB) graphs and judged them to be cost-effective on the basis of maximum willingness to pay (WTP) thresholds of $20,000/quality-adjusted life year (QALY). We discounted costs and QALYs at an annual rate of 3.5 %.

Spinal Cord Stimulation

All patients were initially managed in a multidisciplinary pain clinic where CMM failed to provide adequate relief. In the previous study, data of 122 consecutive patients with FBSS was utilized. The data were derived from chart reviews and follow-up appointments, supplemented with telephone interviews. The patients were then subdivided into two groups.

The groups were matched with respect to age, sex, mean number of operations performed before enrollment into the study (3.3 operations), and time away from work since injury (minimum of 1 year). All patients were evaluated by the same multidisciplinary pain specialist group.

All patients underwent a SCS trial and received permanent implants if they reported ≥50 % pain relief on the visual analogue scale (VAS). While these patients were awaiting trial stimulation, 18 patients either moved or refused to participate in the study and thus were lost to follow-up. These exclusions left a working group of 104 patients who were monitored for a minimum of 5 years. The SCS group consisted of 60 patients (57.7 %; 28 female patients [47 %] and 32 male patients [53 %]), with a mean age of 52.3 years. The CMM group included 44 patients (42.3 %; 21 female patients [48 %] and 23 male patients [52 %]), with a mean age of 51.4 years [16].

At our center, the neuromodulation nurse is responsible for device programming. The cost of SCS is predicated, in part, on the longevity of the IPG which is approximately 4 years in the case of non-rechargeable systems and 9 (Medtronic Inc.), 10 (St. Jude Medical), and 5 (Boston Scientific) years for the various rechargeable IPGs as conservatively provisioned by the FDA. It should be noted that bench testing of the Boston Scientific IPG reflects a lifespan of 10–25 years [38]. In our present analysis, we subsume the cost of IPG replacement at 4 years postimplantation for non-rechargeable systems, and at 9 years for rechargeable ones, these costs are amortized accordingly.

To reflect the current trends in lead choice for implantation, we reviewed our current implant practices over the past 3 years. Accordingly, we apply the present breakdown: 50 % receive a percutaneous octapolar or a 16-contact paddle lead. The remaining 50 % receive dual octapolar leads. Similarly, half of patients are now receiving rechargeable IPGs while the other half have new generation non-rechargeable IPGs such as the Prime-Advanced™ (Medtronic Inc., Minneapolis, MN, USA). These trends are influenced by patient need and choice as well as by budgetary constraints as the hardware is financed through the publically funded Canadian health-care system.

Decision Analytic Model

The model was developed by using software (Excel, Microsoft, Seattle, WA). A decision tree reflects possible initial responses to SCS and a Markov model which simulates costs and QALYs over a 10-year time span (Fig. 47.1).

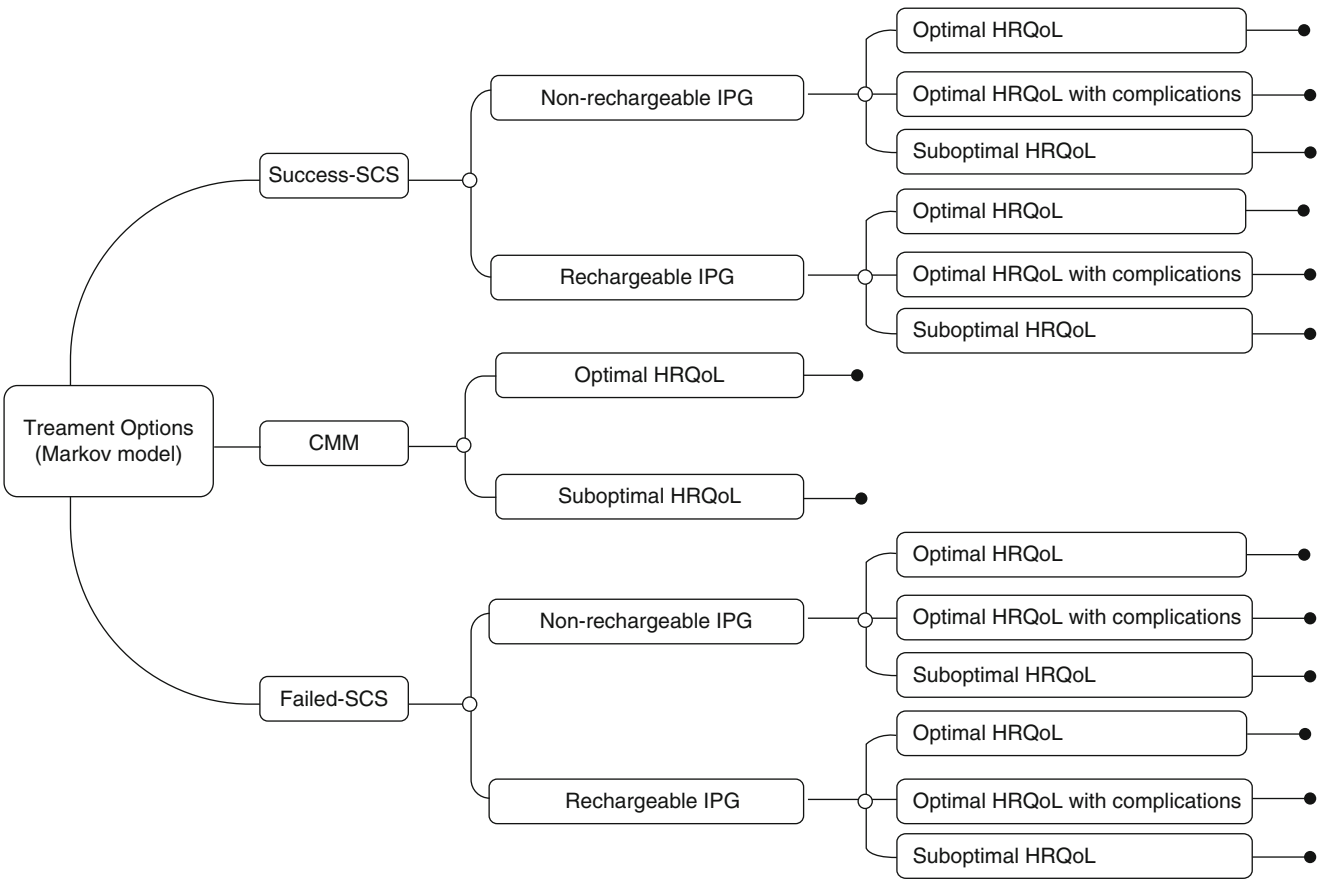

Fig. 47.1 Markov model, SCS analysis

In this model, patients were divided into three cohorts, each undergoing a different strategy:

1. Successful treatment with SCS (success-SCS).
2. Failed SCS after 3 years of intervention had hardware explanted and were subsequently maintained on CMM (failed-SCS).
3. CMM.

During the simulation, there were four mutually exclusive health states in which patients could exist: optimal HRQoL (with or without complications), suboptimal HRQoL, or death. Each health state was associated with a utility value and probability taken from the literature [7–10]. In health economics, a utility value is a number that represents a given quality of life or state of health. An individual with a medical condition can be assigned a utility value between 0 (death) and 1 (perfect health) depending on how substantially the disease affects quality of life. Patients first undergo a screening trial. Those who achieve optimal pain relief proceed to a permanent implant, and the rest receive CMM.

During each 1-year Markov cycle, patients allocated to SCS are assumed to remain in their health state unless they (1) experience a complication or (2) move from optimal to suboptimal HRQoL [7–10]. Table 47.1 indicates the values assigned to model probabilities, utilities, and costs. EuroQoL-5Dimension (EQ-5D) scores were 0.598 for optimal pain relief without a complication, 0.258 for suboptimal pain relief (with or without complications), and 0.168 for no pain relief. In calculating the results of the failed-SCS group, we utilize the success-SCS group data for the first three cycles and CMM results for the remaining cycles. The model assumes that long-term SCS complications will occur at a rate of 18 % per annum [14]. It is assumed that any complications incurred in the CMM strategy do not impact cost or quality of life. We also modeled the impact of non-rechargeable versus rechargeable IPGs (Table 47.1).

Table 47.1 Costs, utility, and probability distribution pertaining to SCS analysis

Procedure	Cost	Sensitivity analysis range	
SCS			
Implantation			
Rechargeable system	$23,160	$18,528	$27,792
Non-rechargeable system	$29,162	$23,330	$34,994
Annual maintenance			
Rechargeable system	$2,786	$2,229	$3,343
Non-rechargeable system	$3,732	$2,985	$4,478
Trial	$1,930	$1,544	$2,316
Explantation	$529	$423	$635
Adjunct drug therapy with SCS	$1,692	$1,354	$2,030
CMM	$7,988	$6,390	$9,586
Utility score (*EQ-5D*)			
Optimal HRQoL			
Success-SCS			
Without complications	0.598	0.478	0.718
With complications	0.528	0.422	0.634
CMM	0.396	0.317	0.475
Suboptimal HRQoL			
Success-SCS			
Without complications	0.258	0.206	0.310
With complications	0.258	0.206	0.310
CMM	0.205	0.164	0.246
Probability			
Complication rate (SCS)	0.180	0.144	0.216
Complication rate (CMM)	0.000	0.000	0.000
Death rate	0.009	0.007	0.011
Optimal HRQoL			
Success-SCS	0.585	0.468	0.702
CMM	0.100	0.080	0.120
Suboptimal HRQoL			
CMM	0.900	0.720	1.000
Strategy			
Success-SCS			
Cost	$104,197	$83,357	$125,036
Effectiveness (QALY)	5.63	4.50	6.76
Cost/effectiveness	$18,504	$14,803	$22,205
CMM			
Incremental cost	–$7,197	–$5,757	–$8,636
Incremental effectiveness	–3.51	–2.81	–4.21
Cost/effectiveness	$46,180	$36,944	$55,416
Failed-SCS			
Incremental cost	$67,628	$54,103	$81,154
Incremental effectiveness	–1.34	–1.07	–1.60
Cost/effectiveness	$39,998	$31,998	$47,997

Modified from Kumar et al. [83]

Intrathecal Drug Therapy

To investigate IT cost-effectiveness, we utilized the data of 88 patients with FBSS who underwent SCS and subsequently failed to achieve satisfactory pain relief. These patients had their SCS electrodes explanted. The 88 patients were randomly divided into two groups of 44 patients each and were matched, in the same manner described earlier. Patients in the IT group received an IT morphine trial. Twenty-three patients (11 female [48 %] and 12 male [52 %]) were selected to undergo implantation of a permanent SynchroMed™ pump (Medtronic of Canada Ltd., Brampton, ON, Canada) as they met the outcome criteria of ≥50 % pain relief. The remaining 21 patients were excluded from study. In the original investigation as in the current study, anticipated costs of these patients were not factored, as they received no further treatment of any kind and thus incurred no further expenses [72].

Pump refills are performed by a neuromodulation nurse, the frequency of which is dictated by the medication dose and concentration. The dose escalation required with time for each patient was averaged. In this study, we found that

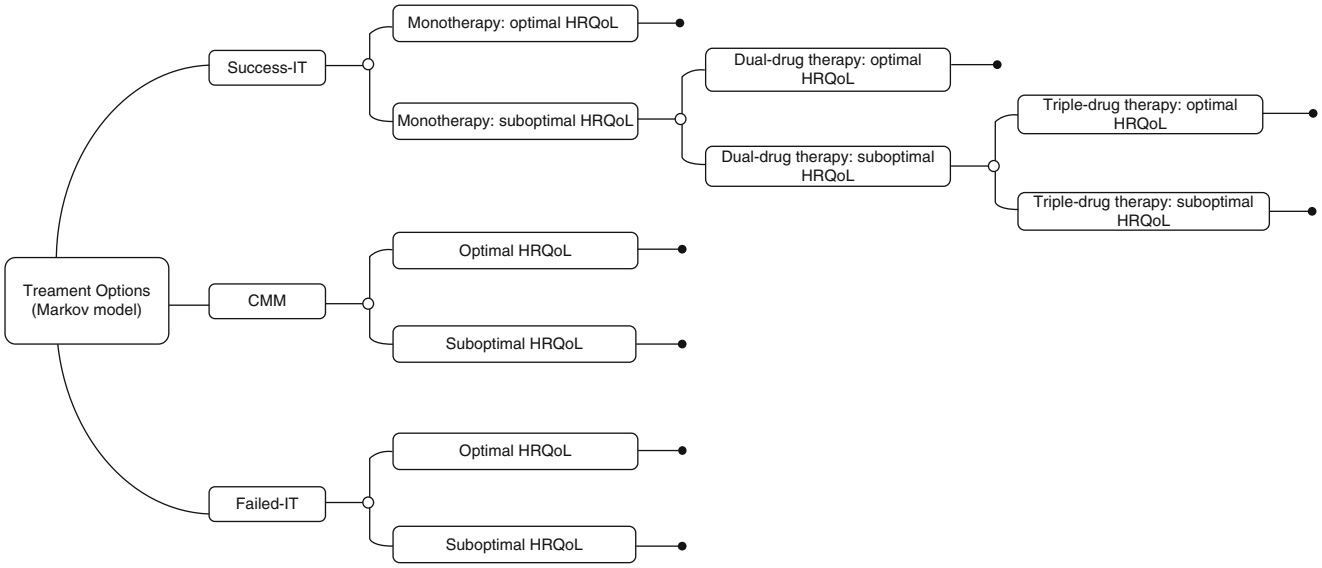

Fig. 47.2 Markov model, IT analysis

the pumps had to be replaced in the sixth year of life due to battery depletion and amortized the cost accordingly. In the context of IT, costs include those associated with intrathecal agents, pharmacy costs for compounding and dispensing, refill costs, and physician contacts for dose adjustment.

Decision Analytic Model

This model was developed to compare costs and outcomes over a 10-year span for three strategies and is structured similarly to the abovementioned Markov process for SCS (Fig. 47.2). It is assumed that a patient always exists in one discrete health state during each 1-year Markov cycle. In this model, patients were divided into three cohorts, each undergoing a different strategy:

1. Successful treatment with IT which is initiated by monotherapy. If monotherapy results in suboptimal pain relief, the patients are sequentially advanced to dual- and triple-drug admixtures (success-IT).
2. Failed IT after 3 years and subsequent maintenance on CMM (failed-IT).
3. CMM.

During the simulation, patients could exist in three mutually exclusive health states, optimal HRQoL, suboptimal HRQoL, or death. Each health state was associated with a utility value and probability taken from the literature and patient chart reviews [72, 73]. Patients first undergo a screening trial. Those who achieve optimal pain relief proceed to a permanent implant, and the rest receive CMM.

Utility values were 0.521, 0.617, 0.603, and 0.405 for optimal improvement in HRQoL with IT mono-, dual-drug, triple-drug therapy, and CMM, respectively. EQ-5D scores for suboptimal improvement were 0.250. In calculating the outcomes of the failed-IT group, we utilized the success-IT group data for the first three cycles and CMM results for the remaining cycles. Our model assumes that the pump will remain functional for an average of 6 years, after which a replacement will be necessary. Furthermore the model assumes that CMM complications will not impact cost or quality of life. The model subsumes an overall rate of 24 % per annum for IT-related complications (Table 47.2) [84].

Interpretation

Spinal Cord Stimulation

Cost-Effectiveness

The analysis confirms that success-SCS is the most cost-effective strategy with a cost-effectiveness ratio (CER) of $18,504 followed by failed-SCS (CER: $39,998). Clinically, even if the effectiveness of SCS dissipates over 3 years requiring hardware removal and reversion to CMM, it is a more acceptable alternative to CMM which is least cost-effective (CER: $46,180) (Table 47.1). The CER for successful SCS therapy is well below the societal WTP thresholds of $20,000–$50,000.

In addition to the Markov model, we re-tabulated cumulative costs for a 10-year period by updating our previously published 2002 analysis [16] to reflect 2010 values. Costs are calculated as described above in methods: tabulation of costs (Fig. 47.3). The graph reflects that the higher initial cost of SCS, due largely to hardware costs, is recovered by 2.25 years after which CMM becomes more costly than SCS.

Table 47.2 Cost, utility, and probability distribution pertaining to IT analysis

Procedure	Cost	Sensitivity analysis range	
IT			
Implantation	$16,140	$12,912	$19,368
Annual maintenance			
Polyanalgesia and supplemental oral drug costs	$6,157	$4,926	$7,389
Monotherapy and supplemental oral drug costs	$3,700	$2,960	$4,440
Trial	$4,535	$3,628	$5,442
Explantation	$636	$509	$763
CMM	$7,988	$6,390	$9,586
Utility score (EQ-5D)			
Optimal HRQoL			
Success-IT	0.527	0.422	0.632
CMM	0.400	0.320	0.480
Suboptimal HRQoL			
Failed-IT	0.310	0.248	0.372
CMM	0.205	0.164	0.246
Probability			
Complication rate – IT	0.240	0.192	0.288
Complication rate – CMM	0.000	0.000	0.000
Death rate	0.009	0.007	0.011
Optimal HRQoL			
Success-IT			
Monotherapy	0.571	0.457	0.685
Dual-drug therapy	0.797	0.638	0.956
Triple-drug therapy	0.789	0.631	0.947
CMM	0.150	0.120	0.180
Suboptimal HRQoL			
Failed-IT			
Monotherapy	0.429	0.343	0.515
Dual-drug therapy	0.203	0.162	0.244
Triple-drug therapy	0.211	0.169	0.253
CMM	0.850	0.680	1.000
Strategy			
Success-IT			
Cost	$92,798	$74,239	$111,358
Effectiveness (QALY)	5.01	4.01	6.01
Cost/effectiveness	$18,532	$14,825	$22,238
CMM			
Incremental cost	$1,414	$1,131	$1,696
Incremental effectiveness	−2.75	−2.20	−3.30
Cost/effectiveness	$41,772	$33,418	$50,127
Failed-IT			
Incremental cost	$14,958	$11,967	$17,950
Incremental effectiveness	−1.87	−1.50	−2.25
Cost/effectiveness	$34,363	$27,490	$41,236

The one-way sensitivity analyses (using CMM, failed-SCS, or success-SCS as baseline) revealed that the cost-effectiveness of success-SCS was exceptionally resistant to parameter uncertainty, as it remained cost-effective compared with the other two strategies (i.e., CER < $20,000/QALY) throughout all of the sensitivity analyses.

Net Monetary Benefit

A positive NMB implies that the cost of a new therapy is less than the value of the additional benefit achieved. Conversely, a negative NMB implies that an intervention should be rejected, as its costs are higher than the value of the benefit achieved. The NMB analysis showed substantial savings over a relevant range of WTP for a QALY in the case of success-SCS where the NMB becomes positive at a WTP of $18,501. For failed-SCS and CMM, the NMB thresholds were much higher at WTP of $40,000 and $48,000, respectively. For all commonly accepted values of WTP, SCS represents the optimal strategy (Fig. 47.4).

Impact Analysis

The tornado diagram shows the impact of the most influential individual parameters on the incremental CER for base-case analysis. Impact analysis determined that the most significant factor affecting the model was IPG costs.

Acceptability of Treatment

The acceptability curve represents the probability that the intervention is cost-effective, given a varying threshold for the willingness to pay for each QALY gained. The success-SCS strategy had a 50 % probability of being cost-effective even under the conservative assumption that there exists no WTP ($0) for a gain of one QALY which subsequently increases to 99 % at a WTP of $5,500.

Rechargeable Versus Non-rechargeable IPG

One-way sensitivity analysis shows that the rechargeable IPG is relatively less costly than a rechargeable one. However, both strategies are cost-effective with a CER of $15,672/QALY for the rechargeable system and $16,439/QALY for the non-rechargeable IPG.

Future Directions

Advances in hardware technology and surgical technique will ensure that both clinicians and patients continue to benefit. Computer-interactive programming is gaining popularity, especially due to the increasing sophistication of implanted devices. Spinal cord stimulators now offer the ability to independently stimulate individual contacts as well as multiple arrays of electrodes [33]. This allows for accurate direction of current flow and more consistent overlapping paresthesia, resulting in better pain control and improved clinical outcomes [38]. SCS will undoubtedly move up several steps in the treatment ladder of chronic pain conditions as new applications are realized [40].

The limitations of current literature present an opportunity for researchers to generate robust, hypothesis-driven studies. This is a challenging and potentially rewarding undertaking.

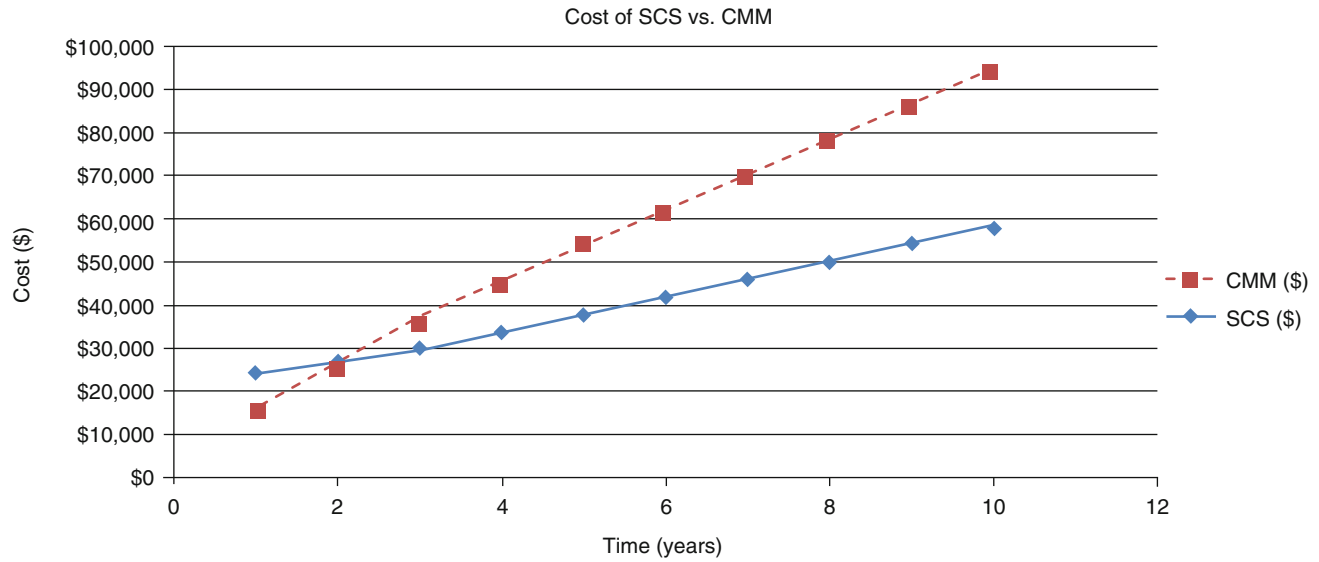

Fig. 47.3 Cumulative cost comparison SCS and CMM over a 10-year period. The 2.25-year payoff period should be noted

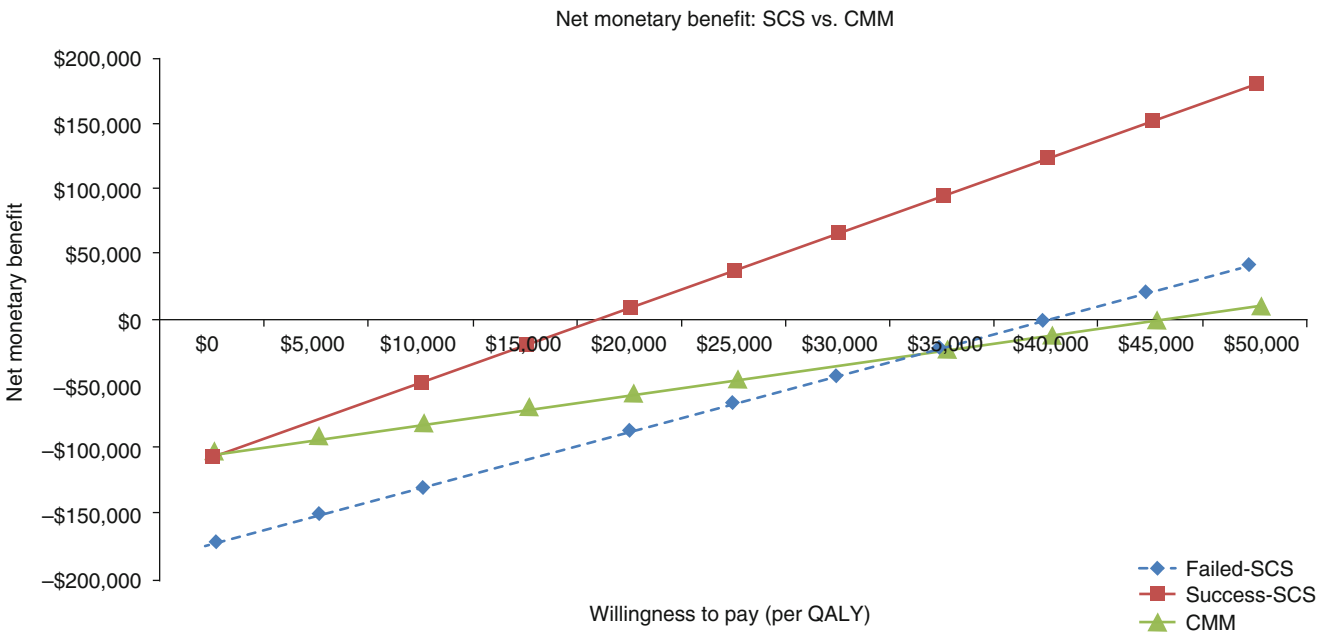

Fig. 47.4 Net monetary benefit (*NMB*), SCS versus comparator treatment. In the case of success-SCS, the NMB becomes positive at a WTP of $18,501. For failed-SCS and CMM, the NMB thresholds were much higher at WTP of $40,000 and $48,000, respectively. Thus, success-SCS represents the optimal strategy

To date, most studies with SCS are not controlled. It is difficult to find a control group, let alone perform adequate randomization, because by definition the patients have often failed all other available treatments and are reluctant to enroll. A sham procedure presents its own set of ethical predicaments. Similarly, investigations are virtually impossible to blind because the patient can detect the stimulation-induced paresthesia created by the system.

Intrathecal Drug Therapy

Cost-Effectiveness

The analysis confirms that success-IT is the most cost-effective strategy with a CER of $18,532 followed by failed-IT of $34,363 and CMM of $41,772 (Table 47.2). Clinically, even if the effectiveness of IT dissipates over 3 years requiring hardware removal and reversion to CMM, it is a more

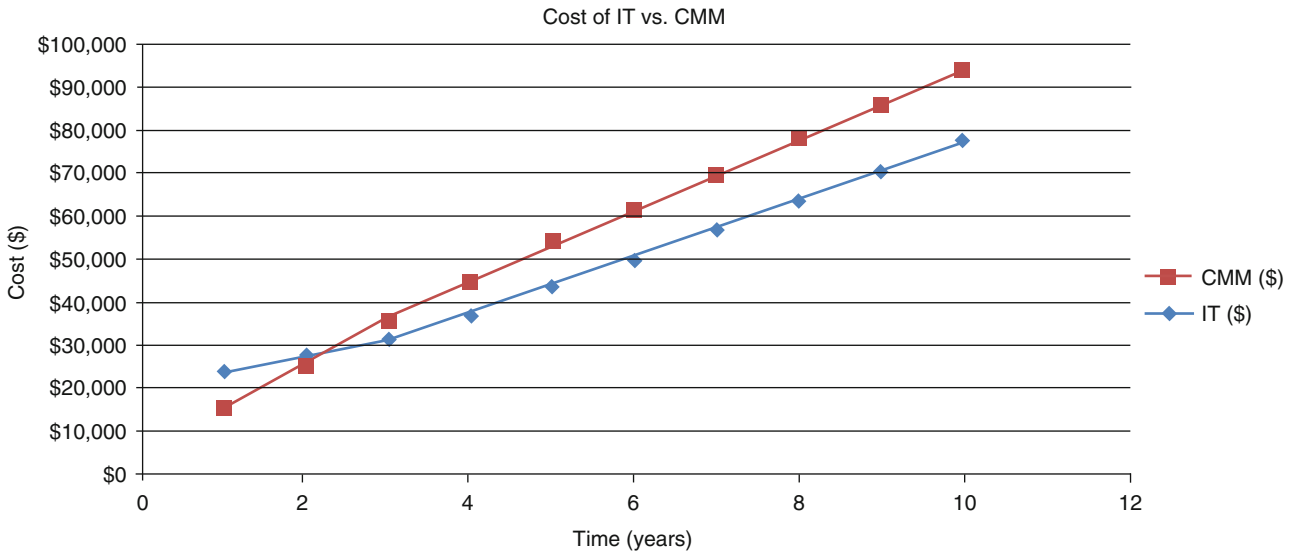

Fig. 47.5 Cumulative cost comparison IT and CMM over a 10-year period. The 2.5-year payoff period should be noted

acceptable alternative to CMM which is least cost-effective. The CER for success-IT is well below societal WTP thresholds of $20,000–$50,000/per QALY.

In addition to the Markov model, we re-tabulated cumulative costs for a 10-year period by updating our previously published 2002 analysis [72] to reflect 2010 values. Costs are calculated as described above in methods: tabulation of costs (Fig. 47.5). The graph reflects that the higher initial cost of IT, due largely to hardware costs, is recovered by 2.5 years, after which CMM becomes more costly than SCS. The one-way sensitivity analyses (using CMM, failed-IT, or success-IT as baseline) demonstrated that the cost-effectiveness of success-IT was exceptionally resistant to parameter uncertainty, as it remained cost-effective compared with the other two strategies (i.e., CER < $20,000/QALY) throughout all of the sensitivity analyzes except in the single case when the probability of obtaining optimal HRQoL in the success-IT arm is less than 10 %. Failed-IT was more cost-effective than CMM when the probability of an optimal outcome with CMM is less than 30 %.

Net Monetary Benefit

Single-drug IT generates the greatest NMB. The success-IT NMB is positive for WTP > $18,500. For failed-IT and CMM, the NMB threshold is much higher at WTP > $39,000 and >$42,000, respectively (Fig. 47.6). The difference between the averages of NMB between two strategies is equivalent to the incremental NMB. The incremental NMB for IT is approximately 2.9 times WTP.

Impact Analysis

Impact analysis determined that the most significant factors affecting the model were costs for success-IT and the probability of optimum pain relief with intrathecal monotherapy.

Acceptability of Treatment

The acceptability curve shows that the success-IT strategy had a 100 % probability of being more acceptable than the comparator condition (CMM) from a cost-effectiveness point of view, even under the conservative scenario that there is no ($0) WTP for a gain of one QALY.

Future Directions

Considerable progress has been made in the field of IT since the 2000 Polyanalgesic Consensus Conference (PACC) survey [65]. Ziconotide was approved by the FDA in 2004, making it the first new IT analgesic in more than a decade to gain approval. Today, it is considered first-line therapy. IT drug selection algorithms developed by the 2000, 2003 PACCs, and again updated in 2007 have aided physicians in choosing the safest and most effective drugs and their dosages for their patients [65–68]. Strides have also been made in the prevention and treatment of granulomas [67]. In 2011, the American Pain Foundation will publish new consensus guidelines.

The past 20 years have provided significant advances in the systemic and spinal approaches to analgesic drug delivery. Since the initial description of the spinal action of opioids and alpha-2 agonists 25 years ago (and demonstration of human efficacy), many spinal targets have been elucidated;

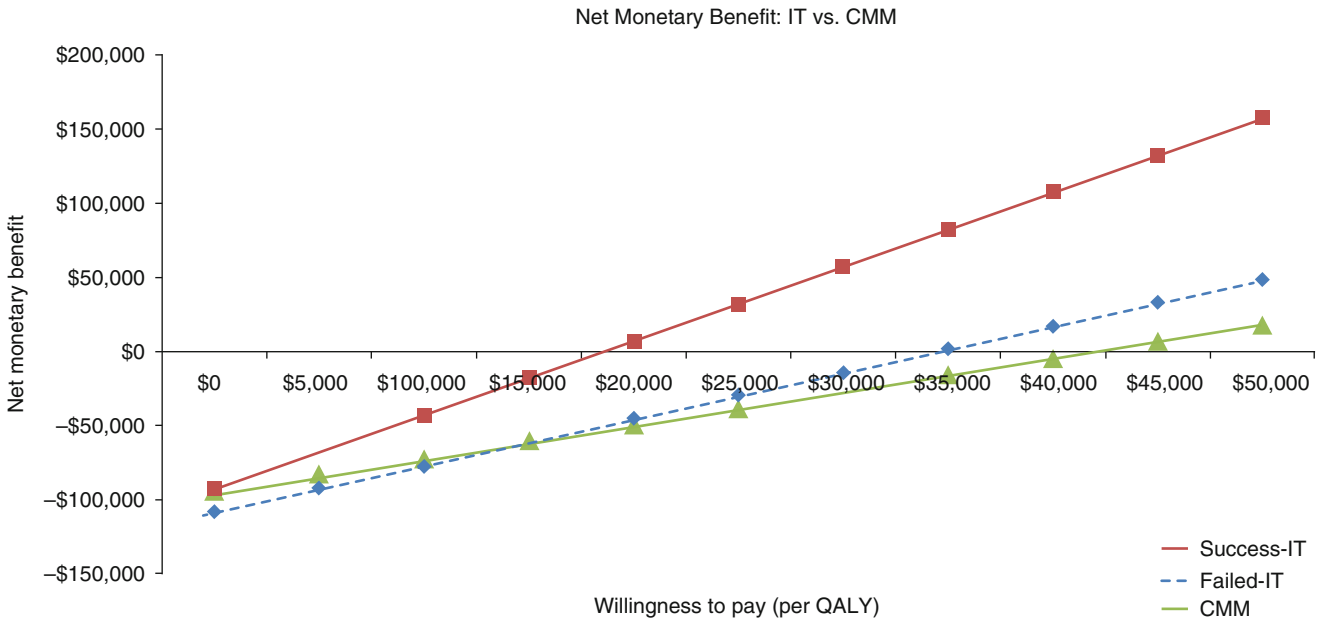

Fig. 47.6 Net monetary benefit (*NMB*), IT versus comparator treatment. In the case of success-IT, the NMB becomes positive at a WTP of $18,500. For failed-IT and CMM, the NMB thresholds were much higher at WTP of $39,000 and $42,000, respectively. Thus, success-IT represents the optimal strategy

some have been validated in human pain states [85]. Intrathecal delivery enables clinicians to target specific sites where nociceptive signals are encoded. However, the full potential of therapy is limited by the lack of clinical investigation of available agents. Researchers should prioritize the identification of new central targets and the development of new formulations and concentrations of known agents for intrathecal administration. The investigation of the stability and compatibility of single and combinations of multiple agents must be attuned to the physiologic conditions that exist in pump environment. Clinical inquiry should focus on well-designed randomized controlled clinical trials. In this context, multicenter collaboration and standardized clinical trials merit strategic priority.

In spite of significant advances on the therapeutic side, results of a recent survey suggest that economic and reimbursement difficulties continue to constrain IT use [86]. Clinicians, researchers, and advocacy groups must further evaluate the effects of economic trends on patient access to treatment [86].

Conclusion

IT and SCS are robust, cost-effective therapies. Significant cost savings can be attained with the use of these therapies in patients with CNMP secondary to FBSS when compared to CMM. Additional benefits may include an increased rate of return to work, better pain control, and quality of life. An integrated approach to the treatment of FBSS will result in improved utilization of scarce health-care resources. Technological advances that increase hardware lifespan and improve catheter and electrode design will reduce complication rates, further bolstering the already favorable cost profile.

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Neurosurgical Techniques for Pain Management

48

Hendrik Klopper and Kenneth A. Follett

Key Points

- Augmentative neuromodulation techniques have supplanted ablative procedures as treatments of choice for intractable pain.
- Augmentative techniques are effective in well-selected patients and are associated with a low risk of complications.
- Augmentative techniques are superior to ablative techniques in the treatment of neuropathic pain that has a continuous, dysesthetic component.
- Ablative techniques may be appropriate for individuals such as those with cancer-related pain who have short life expectancies, patients with a predominant nociceptive component of pain, and those with neuropathic pain with paroxysmal or evoked components.
- Ablative techniques are very useful for certain pain syndromes: rhizotomy for trigeminal neuralgia, DREZ lesioning for "end-zone" or "boundary" pain associated with spinal cord injury or phantom-limb pain associated with avulsion of cervical or lumbosacral spinal nerve roots, and cordotomy or myelotomy for treatment of intractable cancer pain in individuals with short life expectancies or who have failed treatment with neuraxial analgesics.
- Pain management physicians should be familiar with the variety of neurosurgical techniques available for the treatment of pain, the general indications, and the general outcomes, and incorporate these treatments in the care of their patients when appropriate.

Introduction

Surgical procedures have been important tools for the treatment of pain for many years. Until the 1980s, most surgical therapies for pain treatment were anatomic (e.g., decompressive or reconstructive) or ablative in nature. Ablative procedures, based on knowledge of the anatomy and physiology of nociception and aimed at interrupting pain pathways, were the mainstay of surgical treatment of intractable pain for decades. The past few decades have witnessed the introduction of the gate control theory and an awareness of intrinsic pain-modulating systems, leading to the advent of neuroaugmentative therapies. In most instances, neuroaugmentative therapies, including neurostimulation and neuraxial analgesic infusion, have supplanted ablative techniques as the procedures of choice for the treatment of chronic pain. These therapies are discussed in detail in Chaps. 39, 40, 41, 42, 43, 44, 45, 46, and 47 of this book. Although ablative therapies have largely fallen by the wayside, pain providers should retain a general familiarity with them because they may be procedures of choice for certain pain syndromes and certain patients. Unfortunately, as augmentative therapies increasingly supplant ablative neurosurgical techniques, fewer neurosurgeons have the expertise or equipment to perform traditional neuro-ablative surgeries. This requires that in some instances, patients may need to be referred to a neurosurgical center with special expertise in pain therapy. In this chapter, the authors discuss pain procedures provided primarily or exclusively in the neurosurgical domain

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Table 48.1 Anatomic procedures and their primary indications

Procedure	Indication
Spinal decompression and reconstruction	Progressive myelopathy or radiculopathy resulting from compression of neural structures (e.g., from intervertebral disk herniation, osteophyte, spondylolisthesis, ligamentous hypertrophy)
Microvascular decompression	Classical trigeminal, glossopharyngeal, or nervus intermedius neuralgia (i.e., paroxysmal, lancinating pain)

of pain treatment, including anatomic, ablative, and augmentative therapies.

As with all other pain treatments, the basic tenets of pain care must be observed during the delivery of neurosurgical pain therapies. The treatment offered should be selected according to the needs of each individual patient and the skills of the treating physician. Patient-related factors must be taken into consideration including the pain etiology, location, and characteristics (nociceptive or neuropathic); life expectancy; and psychological, social, and economic factors that could impact the pain complaint. The relative advantages and disadvantages of anatomic, augmentative, and ablative therapies should be weighed in view of these factors, and a choice between these three general approaches should be made before choosing a specific intervention.

Anatomic Therapies

The anatomic therapies are aimed at correcting underlying structural abnormalities that cause specific pain syndromes. These procedures include spinal decompressive or reconstructive techniques for spinal pain syndromes and microvascular decompression for cranial neuralgias (e.g., trigeminal neuralgia). The anatomic therapies and their primary indications are summarized in Table 48.1.

Spinal Decompressive and Reconstructive Procedures

This group of procedures encompasses a range of operations aimed at decompression of the spinal cord and spinal nerve roots for the treatment of structural abnormalities that result in neurological deficit or intractable pain. Procedures in this category include cervical, thoracic, and lumbar diskectomy, laminectomy, and spinal fusion. They are performed routinely in the practice of general neurosurgery with minimal morbidity and mortality and – provided treatment is directed at a structural abnormality that is concordant with the pain syndrome – are for the most part quite successful in relieving axial and/or radicular pain resulting from the structural abnormality. The discussion of these procedures is beyond the scope of this chapter, and the interested reader is referred to any of a number of general neurosurgical textbooks for a more detailed treatment of these operations and outcomes.

Microvascular Decompression

Microvascular decompression is one of the most important techniques for the treatment of intractable trigeminal neuralgia, glossopharyngeal neuralgia, and nervus intermedius neuralgia [1, 2]. It is indicated for the treatment of classical neuralgia (paroxysmal, lancinating pain, often described as "electrical shocks") that is refractory to pharmacological treatment. It is most appropriate for healthy patients, generally under the age of 65 or 70, with no medical contraindications to craniotomy.

The rationale of microvascular decompression is to eliminate compression of the affected cranial nerve by a blood vessel (usually an artery), which generally occurs near the entry of the nerve into the brainstem. Microvascular decompression has the advantage of the absence of a postoperative sensory deficit, which is an obligate outcome of percutaneous or open ablative procedures (e.g., radiofrequency rhizotomy or ganglionectomy for trigeminal neuralgia). Early pain relief is achieved in more than 90 % of patients. Pain may recur over the course of months or years, but microvascular decompression is regarded generally as providing the most durable pain relief of the various procedures, and most patients obtain lasting pain relief [1, 2]. Microvascular decompression is much less successful in treating atypical facial pain (i.e., constant, burning pain, typically not involving a clear trigeminal sensory distribution). In general, the less the degree of paroxysmal pain and the greater the degree of constant, burning, dysesthetic pain in a given individual, the less likely a good long-term outcome will be achieved with surgical intervention [3].

Ablative Therapies

Ablative therapies are often viewed as treatments of last resort for intractable pain, but in some instances, they remain the procedures of choice and should not be forgotten or overlooked by pain care providers. Important examples include dorsal root entry zone (DREZ) lesioning for treatment of phantom-limb pain following spinal nerve root avulsion or "end-zone" pain arising from spinal cord injury and cordotomy, which may be preferable to intrathecal analgesic administration for the treatment of cancer-related pain in a patient with a short life expectancy.

Table 48.2 Ablative procedures and their primary indications

Procedure	Indication
Sympathectomy	Visceral, cancer-related pain
Neurectomy	Identifiable neuroma following peripheral nerve injury (e.g., following limb amputation); meralgia paresthetica; inguinal pain syndromes (e.g., post-herniorrhaphy pain)
Dorsal rhizotomy/ganglionectomy	Cancer-related trunk/abdominal pain
Cranial nerve rhizotomy	Classical trigeminal and glossopharyngeal neuralgia when microvascular decompression is contraindicated
C2 ganglionectomy	Occipital neuralgia
DREZ lesioning	Localized neuropathic pain following spinal nerve root avulsion; "end-zone" pain following spinal cord injury
Cordotomy	Cancer-related pain below mid- to low cervical dermatomes
Myelotomy	Cancer-related abdominal, pelvic, perineal, or lower extremity pain

Ablative therapies have been developed which target almost every level of the peripheral and central nervous system: eripheral techniques that interrupt or alter nociceptive input into the spinal cord (e.g., neurectomy, ganglionectomy, rhizotomy), spinal interventions that alter afferent input or rostral transmission of nociceptive information (e.g., DREZ lesioning, cordotomy, myelotomy), and supraspinal intracranial procedures that may interrupt transmission of nociceptive information (e.g., mesencephalotomy, thalamotomy) or influence perception of painful stimuli (e.g., cingulotomy).

Ablative therapies tend to be most appropriate for the treatment of nociceptive pain rather than neuropathic pain. Neuropathic pain that is intermittent, paroxysmal, or evoked (e.g., allodynia and hyperpathia) may improve after an ablative procedure, but continuous, dysesthetic neuropathic pain tends to respond much less favorably in long-term follow-up [4]. The ablative therapies are summarized along with their primary indications in Table 48.2.

Sympathectomy

Sympathectomy is indicated for the treatment of visceral pain associated with certain cancers [5, 6]. It can alleviate non-cancer pain such as that associated with vasospastic disorders or sympathetically maintained pain (when sympathetic blocks reliably relieve the pain), but it has generally fallen into disfavor as a treatment for intractable pain of nonmalignant origin because of inconsistent results [5–8]. Some data indicate that SCS provides better long-term outcomes with lower morbidity and SCS may replace sympathectomy in the treatment of sympathetically maintained pain of non-cancer origin [9]. Sympathectomy is commonly and successfully used in the treatment of intractable hyperhidrosis.

Neurectomy

Neurectomy may be useful in individuals who develop pain following peripheral nerve injury, including that associated with limb amputation. If an identifiable neuroma is the cause of pain, its resection can provide significant relief [10]. In the absence of an identifiable neuroma, neurectomy is unlikely to provide pain relief. In this regard, neurectomy is not useful for treatment of nonspecific stump pain after amputation, and it is not generally useful for the treatment of other nonmalignant peripheral pain syndromes. The utility of neurectomy is limited because pain arising from a pure sensory nerve is uncommon, and sectioning of mixed sensory-motor nerves is associated with significant risk of neurologic deficit and resultant functional impairment. There may be several exceptions to this rule. For example, section of the lateral femoral cutaneous nerve has been reported to provide long-lasting relief of meralgia paresthetica [11], and section of the ilioinguinal and/or genitofemoral nerves has been reported to provide relief of certain inguinal pain syndromes (e.g., post-herniorrhaphy pain) in properly selected individuals [12].

Dorsal Rhizotomy/Ganglionectomy

Dorsal rhizotomy and ganglionectomy serve similar purposes in denervating somatic and/or visceral tissues, but ganglionectomy may produce more complete denervation than can be accomplished by dorsal rhizotomy. Some afferent fibers enter the spinal cord through the ventral root [13] and are not affected by dorsal rhizotomy. In contrast, ganglionectomy effectively eliminates input from dorsal and ventral root afferent fibers by removing their cell bodies, which are located within the dorsal root ganglion.

Rhizotomy and ganglionectomy can be used to treat pain in the trunk or abdomen. Neither procedure is useful for treatment of pain in the extremities unless function of the extremity is already lost because denervation removes proprioceptive as well as nociceptive input and produces a functionless limb. Limited denervation (e.g., a single level) does not generally provide adequate pain relief because segmental innervation of dermatomes overlaps with adjacent levels. Therefore, these procedures typically must be performed at several adjacent spinal levels. Multilevel denervation increases the sensory loss and risk of functional impairment of an extremity.

These procedures are most useful for the treatment of cancer-related pain, as non-cancer pain does not improve consistently [14, 15]. When used for treatment of neuropathic pain (e.g., postherpetic neuralgia of the trunk), lancinating, paroxysmal, or evoked pain may improve but continuous dysesthetic pain does not typically improve. In the setting of cancer, these procedures can be useful for thoracic or abdominal wall pain; for perineal pain in patients with impaired bladder, bowel, and sexual function; or for the treatment of pain in a functionless extremity. Multiple sacral rhizotomies can be performed (e.g., to treat pelvic pain from cancer) by passing a ligature around the thecal sac below S1 [16].

Cranial Nerve Rhizotomy

Rhizotomy is especially useful as a treatment of cranial neuralgias, especially trigeminal and glossopharyngeal neuralgia [17, 18]. Classical trigeminal and glossopharyngeal neuralgia are unique among neuropathic pain syndromes in their uniformly good response to ablative procedures. This reflects the general utility of ablative techniques in relieving lancinating, paroxysmal pain. In contrast, atypical facial pain syndromes (constant, burning, dysesthetic pain) do not improve with ablative techniques and may be worse following denervation by rhizotomy or other ablative techniques, either from worsening of the pain, per se, or superimposition of potentially unpleasant sensory loss on the original pain.

Percutaneous trigeminal rhizotomy can be accomplished with thermal radiofrequency (RF), glycerol injection, or balloon compression. These techniques are performed on an outpatient basis, are well tolerated, and have high success rates in relieving paroxysmal pain of cranial neuralgias. Early pain relief is almost universal, but pain can recur over months or years (in which case the same procedure or another surgical treatment can be offered) [18]. These techniques are especially useful in treating elderly, medically infirm patients who are not good candidates for craniotomy for microvascular decompression of a cranial nerve. Postoperative sensory deficit is an obligate outcome of successful rhizotomy, so candidates should be counseled accordingly. Postoperative sensory loss may render this procedure undesirable for treatment of pain around the eye because corneal sensory loss may lead to keratitis and impaired vision. Open rhizotomy (i.e., via craniotomy or craniectomy) is usually performed for treatment of glossopharyngeal and nervus intermedius neuralgia and may be useful for treatment of some trigeminal neuralgias.

Stereotactic radiosurgery rhizotomy for the treatment of trigeminal neuralgia is an alternative to percutaneous or open rhizotomy or microvascular decompression for some individuals [19]. Radiosurgery is performed on an outpatient basis as a single procedure. In contrast to percutaneous rhizotomy and other surgical treatments for cranial neuralgias, which have a high likelihood of providing immediate postoperative pain relief, pain relief may not occur for several weeks following radiosurgical treatment. Radiosurgery is, therefore, not appropriate for individuals with severe acute pain that cannot be controlled adequately with medications. Pain may recur over months or years in some patients, but relief is maintained in many patients [17, 18]. Unlike percutaneous or open rhizotomy, sensory loss after radiosurgery is uncommon. Radiosurgery is most useful for individuals who desire a relatively noninvasive treatment and whose pain is sufficiently well controlled that they can tolerate the postprocedure delay in pain relief.

C2 Ganglionectomy

C2 ganglionectomy is indicated for the treatment of occipital neuralgia. It is especially effective for individuals with posttraumatic occipital neuralgia who have no migraine component to their headache [20]. Pain relief may be comparable to that achieved with occipital nerve stimulation (see Chaps. 40 and 47) but without the need for implanted devices and long-term follow-up.

Dorsal Root Entry Zone (DREZ) Lesioning

DREZ lesioning of the spinal cord (for trunk or extremity pain) [21–23] or nucleus caudalis (for facial pain) [22, 24] can provide significant relief of neuropathic pain in properly selected individuals. The rationale of DREZ lesioning is to disrupt input into and outflow from the superficial layers of the spinal cord dorsal horn, which are the sites of termination of afferent nociceptive fibers and sites of origin of some of the nociceptive fibers that ascend within the spinal cord. DREZ lesioning may also disrupt spontaneous abnormal activity and hyperactivity that develops in spinal cord dorsal horn neurons in the setting of neuropathic pain.

DREZ lesioning is best reserved for localized pain with a neuropathic component. Certain types of cancer pain can be treated effectively with DREZ lesioning (e.g., neuropathic arm pain associated with Pancoast tumor). The most successful applications are related to treatment of neuropathic pain arising from spinal nerve root avulsion (cervical or lumbosacral) and "end-zone" or "boundary" pain following spinal cord injury. These pain syndromes sometimes respond to spinal cord stimulation or intrathecal drug infusion, but DREZ lesioning can provide a similar result without the need for long-term maintenance required by an augmentative device.

DREZ lesioning has been used for the treatment of other neuropathic pain syndromes (e.g., postherpetic neuralgia), but good pain relief is not achieved consistently. DREZ lesioning of nucleus caudalis can provide relief of deafferentation pain affecting the face (including postherpetic neuralgia), but outcomes are inconsistent. It is less helpful for facial pain of peripheral origin (e.g., traumatic trigeminal neuropathy). As with other ablative procedures, DREZ lesioning is most effective for relieving paroxysmal or evoked neuropathic pain rather than continuous neuropathic pain [23].

Cordotomy

Cordotomy can be an effective method of pain control, especially when pain is related to malignancy, and especially for individuals with short life expectancies for whom it is difficult to justify the costs of implantation of drug infusion systems. The rationale of cordotomy is to disrupt nociceptive afferent fibers ascending in the spinothalamic tract in the anterolateral quadrant of the spinal cord. Cordotomy offers the advantage, compared to neuraxial analgesic administration, of being a onetime procedure with no required long-term follow-up or maintenance. This is important for individuals who may find it difficult to return to a medical facility for refilling of an infusion system or for whom costs of ongoing medical care can become burdensome. Cordotomy is used most commonly for the treatment of cancer-related pain below mid- to low cervical dermatomes. It is not generally used for treatment of patients with pain of non-cancer origin because pain typically recurs over months to years in patients with long life expectancies, and there is significant risk of postcordotomy dysesthesias or neurological complication [25]. Cordotomy can be performed as an open [25] or closed (percutaneous) [26, 27] procedure. Percutaneous techniques are less invasive, but open techniques remain viable options because most surgeons lack the expertise and equipment required for percutaneous procedures.

Pain relief varies with pain characteristics and location. Laterally located pain responds better than midline or axial pain (e.g., visceral pain). Midline and axial pain may require bilateral procedures to achieve pain relief. Lancinating, paroxysmal neuropathic pain and evoked (allodynic or hyperpathic) pain that sometimes occurs following spinal cord injury or as part of peripheral neuropathic pain syndromes can improve following cordotomy, but continuous neuropathic pain does not improve [26].

There is a significantly greater risk of complication with bilateral procedures, including weakness, bladder, bowel, and sexual dysfunction, and respiratory depression (if the procedure is performed bilaterally at cervical levels) [25, 26]. Bilateral percutaneous cervical cordotomies are usually staged at least 1 week apart to reduce the likelihood of a serious complication. The risk of respiratory depression subsequent to a unilateral high cervical procedure mandates that pulmonary function be acceptable on the contralateral side. For example, a patient who has undergone a previous pneumonectomy for lung cancer should not be subject to cordotomy that would compromise pulmonary function on the side of the remaining lung [26].

Cordotomy provides good pain relief in approximately 60–80 % of patients [26, 28], but loss of pain relief tends to occur over time. Approximately, one-third of patients have recurrent pain in 3 months, half at 1 year, and two-thirds at longer follow-up intervals [28, 29].

Myelotomy

As with many other traditional ablative neurosurgical therapies, myelotomy has become an uncommon procedure since the advent of neuroaugmentative therapies, but it can provide significant pain relief in properly selected individuals, including some who fail treatment with intrathecal analgesia [30]. Commissural myelotomy was developed to provide the benefits of bilateral cordotomy without the inherent risks of lesioning both anterior quadrants of the spinal cord [30–32]. This is accomplished by sectioning spinothalamic tract fibers from both sides of the body simultaneously with one lesion where they decussate in the anterior commissure. The advantage compared to cordotomy is that bilateral and midline pain can be treated with a single operative procedure, with lower morbidity and mortality.

Clinical observations revealed that a limited midline cordotomy (a lesion of a few millimeters in length vs. the several centimeter length lesion of commissural myelotomy) [33] or high cervical myelotomy [28, 34] can be as effective as classical commissural myelotomy in relieving abdominal, pelvic, and lower extremity pain. Identification of a dorsal column visceral pain pathway has lead to the development of punctuate midline myelotomy [32].

These procedures are indicated primarily for the treatment of cancer-related pain, generally in the abdomen, pelvis, perineum, and legs. They are most effective for nociceptive rather than neuropathic pain. Early complete pain relief is achieved in most patients (greater than 90 %), but pain tends to recur over time such that approximately 50–60 % of patients have good long-term pain relief [28]. The risk of bladder, bowel, and/or sexual dysfunction is less than that associated with bilateral cordotomy, but still remains sufficiently high that use of these procedures is restricted in most instances to patients with cancer-related pain who have preexisting dysfunction.

Table 48.3 Brainstem ablative procedures and their primary indications

Procedure	Indication
Mesencephalotomy	Cancer-related pain involving the head, neck, or upper extremities
Thalamotomy	Widespread cancer-related pain (e.g., diffuse metastatic cancer); midline, bilateral, or head/neck pain with contraindications to other procedures (e.g., cordotomy, neuraxial analgesic infusion)

Brainstem Ablative Procedures

Ablative neurosurgical procedures directed at the brainstem are not in widespread use, in part because relatively few patients require such interventions and because relatively few neurosurgeons have the expertise to perform these interventions. These procedures are mostly of historical interest, but rarely may be considered for patients who fail more conservative therapies or who are not candidates for less invasive procedures. These procedures and their indications are summarized in Table 48.3.

Mesencephalotomy

Mesencephalotomy is indicated for the treatment of intractable pain involving the head, neck, shoulder, and arm [4, 35]. Most commonly, the procedure is used for the treatment of pain related to cancer. The rationale for mesencephalotomy is disruption of nociceptive fibers ascending in the brainstem, in which sense it can be viewed as a supraspinal version of cordotomy [4]. Early pain relief is achieved in 85 % of patients [28]. It does not provide consistent long-term relief of central neuropathic pain [35]. Side effects and complications are common, especially oculomotor dysfunction [4, 28, 35].

The utility of mesencephalotomy has diminished subsequent to the advent of neuraxial analgesic administration. Intraventricular morphine infusion can provide good relief of head, neck, shoulder, and arm pain with a lower incidence of complications. Mesencephalotomy may be preferable for some individuals, for example, those with short life expectancies or for whom the costs or long-term follow-up required with neuraxial analgesic administration become a burden.

Thalamotomy

Thalamotomy has been used for the treatment of cancer-related and non-cancer-related pain [36, 37]. In the setting of cancer, thalamotomy is most appropriate for individuals who have widespread pain (e.g., from diffuse metastatic disease) or who have midline, bilateral, or head/neck pain, for which other procedures may not be likely to provide relief [36].

The success rate of thalamotomy in relieving pain is slightly lower than that achieved with mesencephalotomy, but the incidence of complications is lower with thalamotomy [38], so thalamotomy may be preferable for the treatment of head, neck, shoulder, and arm pain in individuals who are not candidates for neuraxial analgesic administration. It can also be useful for individuals who are not candidates for cordotomy, for example, those with pain above the C5 dermatome or with pulmonary dysfunction [38]. The procedure can be accomplished via stereotactic radiofrequency [4, 28, 38, 39] or radiosurgical techniques [37]. Medial thalamotomy appears most effective for treating nociceptive pain (e.g., cancer pain), with acceptable long-term pain relief obtained in approximately 30–50 % of patients [4, 36, 39]. Overall, neuropathic pain syndromes respond less consistently to thalamotomy, with only about one-third of patients improving long term [4, 39]. As with other ablative procedures, paroxysmal, lancinating neuropathic pain or neuropathic pain with elements of evoked pain (i.e., allodynia and hyperpathia) may improve following thalamotomy, whereas continuous neuropathic pain tends not to improve [4].

Cingulotomy

Cingulotomy is used less commonly for treatment of intractable pain than for management of psychiatric disorders. It is applied most commonly to the treatment of cancer pain but has been used for non-cancer pain as well [28, 40, 41]. Approximately, 50–75 % of patients benefit from the procedure, at least short-term. In the cancer population, pain relief is maintained generally at least 3 months. The utility of cingulotomy for chronic non-cancer pain is less certain, with some studies indicating relatively good long-lasting pain relief [28, 41] and others indicating only 20 % long-term success [36]. Because cingulotomy is performed for treatment of psychiatric disease and carries the stigma of "psychosurgery," formal review by institutional ethics committees may be warranted if this procedure is being considered as a treatment for intractable pain.

Hypophysectomy

Hypophysectomy (surgical, chemical, or radiosurgical) can provide good relief of cancer-related pain. It is traditionally felt to be most effective for hormonally responsive cancers (e.g., prostate, breast cancer) but may relieve pain associated with other tumors as well. It is indicated primarily for the treatment of diffuse pain associated with widespread disease. Pain is alleviated in 45–95 % of patients. Pain relief is inde-

pendent of tumor regression, and the specific mechanism of pain relief is unknown [28, 42–44].

Stimulation Therapies

Stimulation therapies provided by neurosurgeons include spinal cord stimulation, peripheral nerve stimulation, deep brain stimulation (DBS), and motor cortex stimulation (MCS). These therapies are presented in detail elsewhere in this chapter. A brief overview of intracranial stimulation therapies, which lie exclusively in the neurosurgical pain management domain, is presented here.

Intracranial stimulation therapies include DBS of the somatosensory thalamus, hypothalamus, and periventricular-periaqueductal gray [45–51] and MCS [52–55]. Deep brain stimulation and motor cortex stimulation are not approved for use by the United States Food and Drug Administration, but have been incorporated into pain management strategies in some centers. DBS and MCS are used primarily for treating pain of nonmalignant origin, such as pain associated with failed back surgery syndrome, neuropathic pain following central or peripheral nervous system injury, or trigeminal pain or cluster headache.

Stimulation sites for DBS are chosen generally on the basis of the pain characteristics. Nociceptive pain and paroxysmal, lancinating, or evoked neuropathic pain (e.g., allodynia, hyperpathia) tend to respond to PVG-PAG stimulation. Continuous neuropathic pain responds most consistently to paresthesia-producing stimulation of the sensory thalamus (nucleus ventrocaudalis) [48]. Because many pain syndromes (e.g., failed back surgery syndrome) have mixed components of nociceptive and neuropathic pain, some physicians offer the patient a screening trial using electrodes in both regions to determine which provides the best pain relief. A morphine-naloxone test has been used by some providers to clarify the extent of nociceptive and neuropathic pain components and facilitate selection of the best stimulation target [46].

Success rates of DBS for the treatment of intractable pain are difficult to determine because patient selection, techniques, and outcomes assessments vary substantially among studies. Approximately 60–80 % of patients undergoing a screening trial with DBS will have pain relief sufficient to warrant implantation of a permanent stimulation system. Of those who receive a permanent stimulation system, approximately 25–80 % (generally 50–60 %) [45] will gain acceptable long-term pain relief [45–49]. Patients with cancer pain [48], FBSS, peripheral neuropathy, and trigeminal neuropathy (not anesthesia dolorosa) [45, 46, 48] tend to respond to DBS more favorably than patients with central pain syndromes (e.g., thalamic pain, spinal cord injury pain, anesthesia dolorosa, postherpetic neuralgia, or phantom-limb pain) [45, 46, 48]. The incidence of serious complications of DBS is low, but the combined incidence of morbidity, mortality, and technical complications can approach 25–30 % [45, 48]. In contrast to reports that describe utility of DBS for treatment of chronic pain, others indicate little if any long-term benefit [51], and the procedure remains uncommon even in neurosurgical circles.

MCS has been proposed as an alternative to deep brain stimulation [52–55]. MCS is used primarily for treatment of neuropathic pain syndromes and seems most effective for certain types of facial pain (e.g., trigeminal neuropathic pain), in part because the cortical region of interest for treatment of facial pain is relatively easy to target [53]. Approximately 50 % of patients undergoing MCS have good long-term pain relief. As with DBS, MCS appears most effective in the absence of anesthesia in the distribution of pain being treated. Compared with DBS, the overall clinical efficacy of MCS is similar, but the complications associated with MCS might be less serious because the electrode is placed epidurally rather than within the brain parenchyma. MCS shows some promise, but long-term efficacy remains to be determined.

Summary

In general, augmentative neuromodulation techniques have supplanted ablative procedures as treatments of choice for intractable pain. The augmentative techniques are quite effective in well-selected patients, and the risk of complication is low, making them the first choice for many patients. They are also superior to ablative techniques in the treatment of neuropathic pain that has a continuous, dysesthetic component. Ablative therapies may be appropriate for some individuals, for example, individuals with cancer-related pain who have short life expectancies, patients with a predominant nociceptive component of pain, and those with neuropathic pain with paroxysmal or evoked components. Furthermore, ablative techniques are very useful for certain pain syndromes: rhizotomy for trigeminal neuralgia, DREZ lesioning for "end-zone" or "boundary" pain associated with spinal cord injury or phantom-limb pain associated with avulsion of cervical or lumbosacral spinal nerve roots, and cordotomy or myelotomy for treatment of intractable cancer pain in individuals with short life expectancies or who have failed treatment with neuraxial analgesics.

As attention is focused increasingly on augmentative therapies for the treatment of intractable pain, ablative therapies that might be appropriate for some individuals may be overlooked as treatment options. Pain management physicians should be familiar with the variety of neurosurgical techniques available for the treatment of pain, the general indications, and the general outcomes, and incorporate these treatments in the care of their patients when appropriate.

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Spinal Cord Stimulation in the Treatment of Postherpetic Neuralgia

49

Stanley Golovac and Louis Raso

Key Points

- Postherpetic neuralgia is a painful condition affecting your nerve fibers and skin.
- The burning pain associated with postherpetic neuralgia can be severe enough to interfere with sleep and appetite.
- Postherpetic neuralgia is a complication of shingles, which is caused by the chickenpox virus.
- Most cases of shingles clear up within a few weeks. But if the pain lasts long after the shingles rash and blisters have disappeared, it is called postherpetic neuralgia.
- The risk of postherpetic neuralgia increases with age, primarily affecting people over the age of 60. Effective treatment of postherpetic neuralgia is difficult, and the pain can last for months or even years.
- Cases in which pain persists can be treated with spinal cord stimulation.

Introduction

In the pain clinic setting, one of the most difficult pain syndromes to treat is postherpetic neuralgia (PHN). Recent advances in the treatment of an acute infection with the herpes zoster virus have lowered the incidence of PHN. The pain specialist needs to treat the acute episode aggressively and early, if he is to be successful in reducing the onset of PHN. It is well known that PHN continues to be a common reason for suicide in the elderly population [1]. In most patients with an acute herpes zoster infection, the disease is self-limiting, and the rash and pain disappear completely. In some patients, however, the pain can persist for many years. This chapter will review the cause, clinical course, and current treatments including the use of spinal cord stimulation in the treatment of PHN.

Epidemiology

Acute herpes zoster infection is a reemergence of the varicella zoster virus, or chickenpox virus, which has been lying dormant in the dorsal root ganglion of the nervous system since it became infected during childhood. The reactivation of the virus occurs with the loss of immune surveillance and cell-mediated immunity due to aging [1]. Therefore, the disease is one of the elderly. It starts as a ganglionitis and progresses to an inflammation of the sensory root with eventual skin involvement with the classic vesicular rash [2]. This classic vesicular rash that follows one or two dermatomes is so unique that once seen, it is easily recognizable in future clinical situations. The immune system is usually able to limit the disease process to one or two dermatomes. The most common area for the outbreak is the thoracic area followed by the ophthalmic division of the trigeminal nerve [3].

In patients of any age with a significant immune deficiency, the disease is more common. Examples of such include patients with AIDS, lymphoma, leukemias, corticosteroid dependency, and chemotherapeutic immune suppression. In patients with PHN, there is irreversible skin and sensory damage when the dorsal root ganglion and its processes are attacked by varicella zoster virus and may be severely damaged from the spinal cord to the epidermis [1–3]. Patients with PHN collectively describe three distinct components to their disorder:

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A constant, usually deep pain
A brief, recurrent shooting or shocking tic-like pain
A sharp, radiating dysesthetic sensation evoked by very light touching of the skin (allodynia)

The probability that an acute herpes zoster episode will result in PHN increases with increasing age. PHN occurs in less than 8 % of zoster cases in patients under age 30, 50 % in patients aged 50, 60 % in patients aged 60, 70 % in patients aged 70, etc. [3].

PHN is defined as pain lasting more than 6 weeks after the acute onset of zoster. In the past, with standard treatment, patients were generally not satisfied and they were unable to achieve any significant reduction in their pain levels and any improvement in their quality of life [3]. Generally, after an acute episode of zoster, only 5–8 % of patients will have a recurrence, implying that immune system is able to keep the virus in check for the remainder of the patient's life. Ten to 15 % of patients may present with the classic pain without the classic rash (sine herpete).

Generally, the pain precedes the rash, and it is not unusual for a patient to get a complete work-up prior to the emergence of a rash. There are many patients that have been treated for a herniated disk, acute cholecystitis, myocardial infarction, or other pain syndrome prior to confirming the diagnosis. If the patient is given any corticosteroid therapy, it can even further confuse the clinical picture [1–3].

Treatment of PHN

In a survey conducted in 2002 in 385 patients ≥65 years of age with persistent pain after shingles (PHN) and receiving prescription medication, only 14 % were highly satisfied with their treatment. A majority of patients had moderate to severe pain. Treatment of the acute phase with medical therapy has the ability to decrease viral shedding and the development of new lesions, while also it has the ability to potentially decrease the duration of the outbreak [4].

There have been numerous treatments for PHN cited in the literature. They have included corticosteroids, opioids, antiviral agents, and topical agents. They are tried after aggressive treatment of the acute phase has failed. Some of the common medications used in the past include the following:

- Anticonvulsants
- Antidepressants – tricyclics, serotonin-norepinephrine reuptake inhibitors (SNRIs)
- Opioid analgesics
- Dermal and topical treatments [5]

Recently, a chickenpox vaccine has been instituted into society to reduce both the acute and chronic episodes of varicella infection. As the population ages, we will see the impact of this vaccine [6]. The acute phase is mediated via the sympathetic nervous system and the chronic phase being a sympathetically independent phase. The chronic or PHN phase is very difficult to treat. Numerous treatments have been tried with a very low success rate and a low percentage of patient satisfaction. This ineffective therapy has led to the high incidence of suicide in the elderly population.

Interventional Therapy

It has been thought for a long time that if the sympathetic outflow could be disrupted to the nerves involved, the occurrence of PHN could be reduced. The interventional pain community has embraced this concept and is aggressive with neural blockade early in the treatment of the acute phase. There are numerous references as far back as 1938 continuing to the present day [7]. It has been proven in these studies that if you are able to intervene early during the acute phase, you can prevent the onset of PHN in up to 95 % of the patients. Dr. Alon Winnie published one of the largest studies that revealed the drop-off time in order to reduce the incidence of PHN at approximately 8 weeks. By instituting sympathetic blockade, you are able to reduce the duration of the acute phase and the progression to PHN [8]. PHN is thought to be due to neural ischemia and intraneural capillary blood flow, and by 8 weeks, the ischemic changes become irreversible, especially in the larger nerve fibers [9]. The large nerve fibers are more prone to the ischemic changes due to their higher metabolic rate. These changes result in the allodynia, resulting from activation of the nonmyelinated C-nociceptive fibers along with a loss of large myelinated fibers [9]. The large myelinated fibers normally suppress the activation of the small nonmyelinated and therefore the pain transmission. It is this loss of suppression that leads to the sharp lancinating pain and allodynia that is closely associated with acute herpes zoster and postherpetic neuralgia [9].

Evidence is scant for the value of surgical and procedural interventions in general, although there are numerous small studies supporting the use of specific interventions such as nerve blocks, neurosurgical procedures, and neuro-augmentation.

Conventional methods are used daily in order to blunt and force the viral entity that most patients desire to avoid. Many patients elect to apply creams with antiviral components, tricyclic antidepressants (TCAs), neuroleptic medications, and some unfortunately with opioid medications such as hydrocodone, oxycodone, and morphine sulfate [10]. Each of these forms of treatments may help to a degree, but without interventional treatments, procrastination is enviable.

Epidural steroids is a treatment form that helps reduce swelling, inflammation, and pain sensation from the nerve endings located at the dorsal root ganglion (DRG), where the varicella zoster virus is located.

Neurostimulation is the application of precise targeted electrical stimulation on nociceptive pathways. Electric stimulation has a long history in medicine for treating various ailments [11]. The nociceptive pathways are made

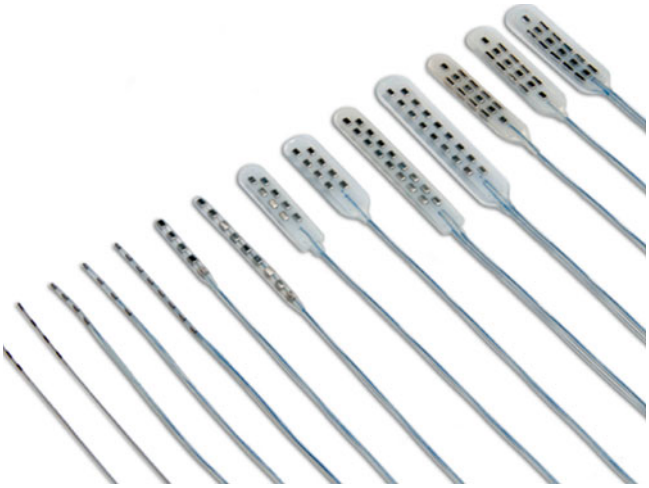

Fig. 49.1 Array of various leads from percutaneous to paddles

up of tracts in the central and peripheral nervous systems. The central nervous system includes nociceptive pathways in the spinal cord and brain, specifically the dorsal roots, dorsal ganglion, spinothalamic tracts, and all ascending neural tracts to the cerebrum. The peripheral nervous system includes pathways outside the spinal cord, specifically various plexuses and peripheral nerves.

Components of the System

Spinal cord stimulation involves the placement of an electrical system to block nociception. The system comprises the surgical placement of epidural electrodes, cables, and radiofrequency transmitter or battery. Much of this method has evolved from cardiac pacemaker technology. The minimal invasiveness and trialing has led to the success of this approach. Neurostimulation can be placed during an outpatient procedure, with local anesthesia and sedation. The patient experiences minimal discomfort when the system is placed and during the postoperative period [12–16].

Before the system is placed, a simple trial of percutaneous lead placement can be performed. In this case, the patient goes home with the lead connected to a screener box. No incision is necessary, and the procedure is performed using only local anesthesia. The purpose of the trial is to determine the effectiveness of the stimulation for relieving pain and improving the patient's quality of life. If this temporary method allows the patient to sleep better, use less pain medication, and sit and stand longer, then it becomes more convincing to place an internalized spinal cord stimulation system.

Leads of various types are commonly used by all three companies: Boston Scientific, St. Jude Medical, and Medtronic. There is an array of various leads from percutaneous to paddles (Fig. 49.1). Figure 49.2 demonstrates two leads placed slightly off the midline toward the left dorsal root entry zone. This allows segmental stimulation over the roots affected by the viral injury.

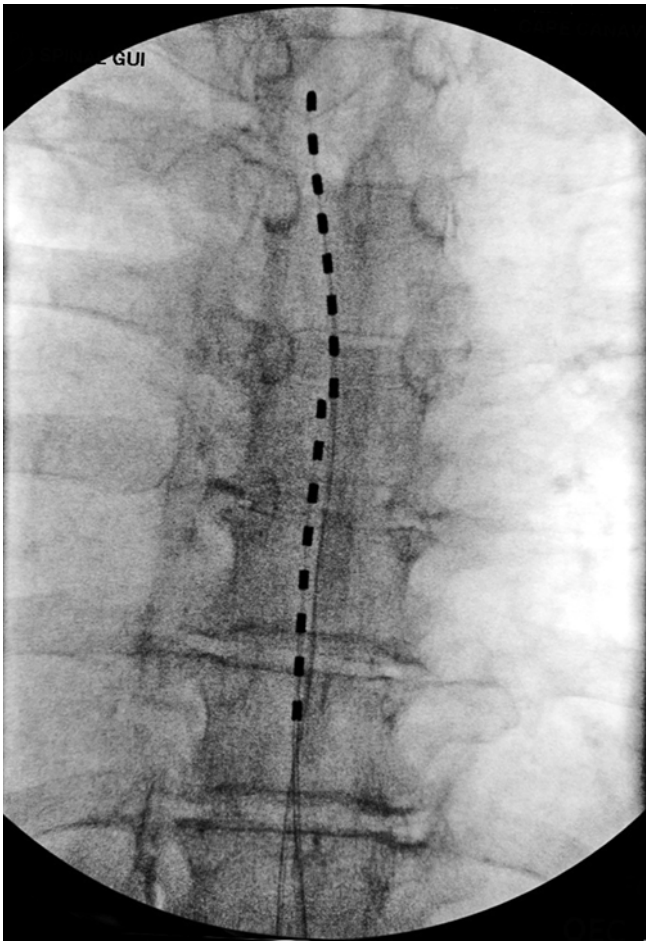

Fig. 49.2 Two leads placed slightly off the midline toward the left dorsal root entry zone. This allows segmental stimulation over the roots affected by the viral injury

Mechanism of Action

The mechanism of action of spinal cord stimulation is based on the placement of epidural electrodes along the dorsal columns. Originally, spinal cord stimulation was called dorsal column stimulation. It is thought that spinal cord stimulation works through the gate-control theory of Melzack and Wall [13] which theorizes that stimulating large nerve fibers (A beta fibers) can inhibit or modulate smaller nerve fibers (A delta or C fibers), transmitting nociceptive input possibly at the dorsal root or horn of the spinal cord. Strategically placed epidural electrodes stimulate the dorsal columns (A beta fibers) to inhibit or modulate incoming nociceptive input through the A delta or C fibers. Ongoing research suggests that spinal cord stimulation may inhibit transmission in the spinothalamic tract, activation of central inhibitory mechanisms influencing sympathetic efferent neurons, and release of various inhibitory neurotransmitters.

Pain Conditions

Spinal cord stimulation can be applied to treat neuropathic pain conditions, including arachnoiditis, complex regional pain syndrome (formerly called reflex sympathetic dystrophy), neuropathies, brachial and lumbosacral plexopathies, radiculopathies, deafferentation syndromes, phantom limb pain, and postherpetic neuralgia. Clinical studies and 30 years of clinical experience have continued to show efficacy in these conditions. Visceral syndromes such as interstitial cystitis, chronic abdominal pain, and chronic pancreatitis have been treated with limited success.

Most randomized controlled trials of chronic neuropathic pain have examined only two pain syndromes: PHN and diabetic neuropathy [17]. In the Practice Parameter: Treatment of Postherpetic Neuralgia, an evidence-based report of the quality standards subcommittee of the American Academy of Neurology, published in Neurology in September 2004, excellent overview of treatment options is provided. Overall, the group with the best efficacy with low side effects included gabapentin, lidocaine patch, pregabalin, and tricyclic antidepressants. Opiates remain a controversial option for treatment of PHN or any chronic pain syndrome. In severe cases of either shingles or PHN, epidural steroid injection can be helpful.

Limited success of spinal cord stimulation may depend on the extent of peripheral vascular disease. Based on one study, spinal cord stimulation does not reduce the incidence of amputation in the lower extremities. The same rationale for using spinal cord stimulation for treating peripheral vascular disease is now being applied in clinical trials of patients with intractable angina, including those with patent coronary vessels who continue to have intractable angina and patients who are not candidates for coronary bypass and stent procedures. It is theorized that these patients have a neuropathic condition and microvascular blood flow deficiency.

Some painful conditions cannot be stimulated along the spinal cord and therefore are not responsive to spinal cord stimulation. Thus, peripheral nerve and plexus stimulation has evolved as a complementary neurostimulation approach. The mechanism of peripheral nerve and plexus stimulation is unclear since the electrodes are not stimulating the dorsal columns. Some postulate that a variation of the gate-control theory is involved at the peripheral nervous system level. Moreover, peripheral nerve stimulation may activate central structures, leading to inhibition of various nociceptive pathways, similar to the way acupuncture results in somatosensory cortex activation.

Postherpetic Neuralgia

The effectiveness of SCS in postherpetic neuralgia remains controversial. Meglio et al. reported good success in six of ten implanted patients [17]. Other authors have been unable to reproduce this success rate. None of the published series contain more than a handful of patients with this condition. In the senior author's experience, postherpetic neuralgia has not been very responsive to stimulation. The stimulation-induced paresthesias are often felt as sharp and annoying and not tolerated by these patients.

Conclusion

Neurostimulation of the central and peripheral nervous systems is playing a vital role in the treatment of various intractable pain conditions, including conditions for which we have limited pathophysiologic understanding, such as complex regional pain syndrome. Until we develop treatments that truly eliminate pain, neurostimulation can play a major role in improving the quality of life for pain patients. These systems do not damage neural pathways and could be removed when curative therapy becomes available.

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Complications of Interventional Pain Management Techniques

50

Marco Araujo and Dermot More O'Ferrall

Key Points

- The most common reported complications are medication-related misuse, pneumothorax, spinal cord injury, and nerve damage.
- Intrathecal injection of 10 ml of preservative-free normal saline can reduce the potential for post-dural-puncture headache after a dural puncture.
- Other causes of headache following epidural steroid injection include intracranial or subdural hematoma, epidural abscess, meningitis, and pneumocephalus.
- Frequently, the ligamentum flavum is adherent to the dura above C5 spinal level.
- Injection of particulate steroids can lead to anterior spinal cord syndrome. Use of nonparticulate steroids and inferoposterior foraminal needle placement reduces the risk of paraplegia after transforaminal epidurals.
- The use of lateral fluoroscopic guidance for trigger point injections of the thoracic wall musculature reduces the risk of pneumothorax.
- Radiofrequency needle placement close to the nerve root can cause severe postoperative dysesthesia and nerve root and spinal cord injury.
- Right-sided SGB may cause sinus arrhythmias, while left-sided SGB can cause left ventricular dysfunction in patients with preexisting left ventricular disease.
- Contrast volume should be maximum of half (0.5) ml/disc in cervical discography.
- Warfarin should be stopped five (5) days prior to neuraxial procedure, and the INR should be less than 1.4 before proceeding.

Introduction

Several textbooks cover the techniques, indications, contraindications, and the mechanism of action of the interventional pain management techniques, but only few textbooks have focused on the complications and on their consequences. Interventional pain management has evolved tremendously since the first described therapeutic nerve block, performed by Tuffer in 1899 [1, 2]. The combination of Interventional Pain Physicians with small amount of experience in the field and the recent significant increase in the utilization of interventional diagnostic and therapeutic techniques raises the potential for increased complications.

Unfortunately, there are major limitations in the analysis of complications. Historically, physicians have a tendency to report no poor outcomes; therefore, only few complications are reported. Health privacy issues and fear of litigation prevent several physicians from reporting the complications of interventional techniques. Furthermore, the complications may be reported to different databases, making the analysis even more difficult.

The American Society of Anesthesiologists (ASA) Closed Claims Project Database can provide valuable information on the adverse outcomes in chronic pain management from 1970 through December 2000 [3]. During this time period, 284 chronic pain management claims were reported. 276 (96 %) claims were related to interventional pain management techniques including nerve blocks, epidural steroid injections, trigger point injections, tendon or joint injections, neuroablation procedures, and neuromodulation implant

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techniques. 78 % claims were related to nerve blocks and injections. The most common complications were pneumothorax and spinal cord-nerve injury [3]. There were 18 (6 %) claims for paraplegia or quadriplegia with four caused by epidural abscess, eight caused by chemical injury from injection into the spinal cord, and six caused by epidural hematoma. Even more alarming, 5 % of claims were related to brain damage, while 4 % were related to death.

While the overall incidence of significant complications in interventional pain medicine is low, some catastrophic complications do occur as ASA Close Claims Project Database shows. Physicians need to be familiar with current literature and to be aware of potential complications. With the advent of interventional pain medicine as a recognized subspecialty of medicine, more formal and standardized interventional training must occur in the academic setting, which will hopefully reduce the likelihood of complications [2–6]. This chapter will focus on procedure-specific complications and on ways to improve safety and minimize complications, by addressing issues pertinent to the patient, the physician, the nursing staff, the equipment, and the medications utilized.

Procedure-Related Complications

As the practice of pain medicine grows, there is a need for greater awareness of potential injuries to patients. Interventional pain management physicians and staff must explain clearly these complications in layman's terms to the patient in order to reduce the occurrence of claims. Written preoperative instructions explaining the procedure and potential complications should be given and signed by the patient prior to the procedure, allowing time for its review. The *informed* consent prior to all procedures should include a discussion about the indication, complications, risks, and available alternative therapies. Ideally, additional consent should also be obtained prior to utilizing medication for off-label, non-FDA (Food and Drug Administration)-approved use.

Epidural Injection

Absolute contraindications to epidural steroid injections include local or systemic infection and bleeding diathesis. Severe central spinal stenosis may be a relative contraindication, and caution must be taken if the injection is being performed interlaminarly at the severe spinal stenosis level. Pregnancy may be a contraindication if fluoroscopy is used.

The documented incidence of dural puncture is anywhere from 0.5 to 5 % in the literature, although this is unacceptably high, especially with the use of fluoroscopy [7–9]. Potential complications of dural puncture include spinal headache, subdural hematoma, and potential for spinal anesthesia or spinal-neural injury. When the rate of cerebral spinal fluid (CSF) loss exceeds CSF production, a downward shift of the brain in the skull may occur, placing traction on the meningeal nerves and subdural veins resulting in spinal headache or subdural hematoma, respectively. Post-dural-puncture headache may follow dural puncture in up to 75 % of cases [10].

If, while performing an interlaminar epidural injection, an inadvertent dural puncture is obtained and confirmed with injection of contrast, producing a myelogram, then without needle movement, an intrathecal injection of 10 cc of preservative-free normal saline can reduce the potential for post-dural-puncture headache significantly [11]. The injection should be performed at another level, or via a different route, such as transforaminal, but without local anesthetic because of the potential for spinal anesthesia.

One epidural blood patch can result in complete, almost instantaneous relief of spinal headache in up to 75 % of patients. If the first epidural blood patch was not successful, the second epidural blood patch can relieve the spinal headache in up to 95 % of patients [12]. Dural puncture brings the risk of subdural hematoma, which can be seen intracranially or spinally [13–15].

It is important to understand that there are many, potentially serious causes of headache following epidural steroid injection, including intracranial or subdural hematoma, epidural abscess, meningitis, pneumocephalus, and spinal headache from dural puncture. A thorough history and physical examination will usually yield a diagnosis, although occasionally imaging studies will be warranted. An epidural abscess, subdural or epidural hematoma resulting in spinal cord compression, needs to be recognized early, and surgical intervention within 8 h is mandatory in order to prevent a permanent neurological injury (Fig. 50.1a, b) [16–25]. Epidural abscess, bacterial meningitis, and aseptic meningitis have all been described [17, 23, 26, 27]. Pneumocephalus produces an immediate and severe headache when patient is allowed to sit. Pneumocephalus is diagnosed with CT scan, and the headache usually resolves as the air is absorbed, over a period of 5–7 days.

Other documented complications of interlaminar epidural injections include arachnoiditis, intrinsic spinal cord injury, spinal anesthesia, transient paralysis, arterial gas embolism, and transient blindness [28, 29]. Controversy exists over whether arachnoiditis can complicate epidural steroid injection [19, 20].

Anatomy

Understanding the anatomy of the epidural space is important. It is triangular in shape, and 1–2 mm in depth in the upper cervical spine, with 3 mm in depth in the lower cervical spine, this increases to up to 5 mm in the upper thoracic spine and is 5–6 mm in depth in the midlumbar spine. Thirty-four percent of the time, the ligamentum flavum is adherent to the dura above C5 [30].

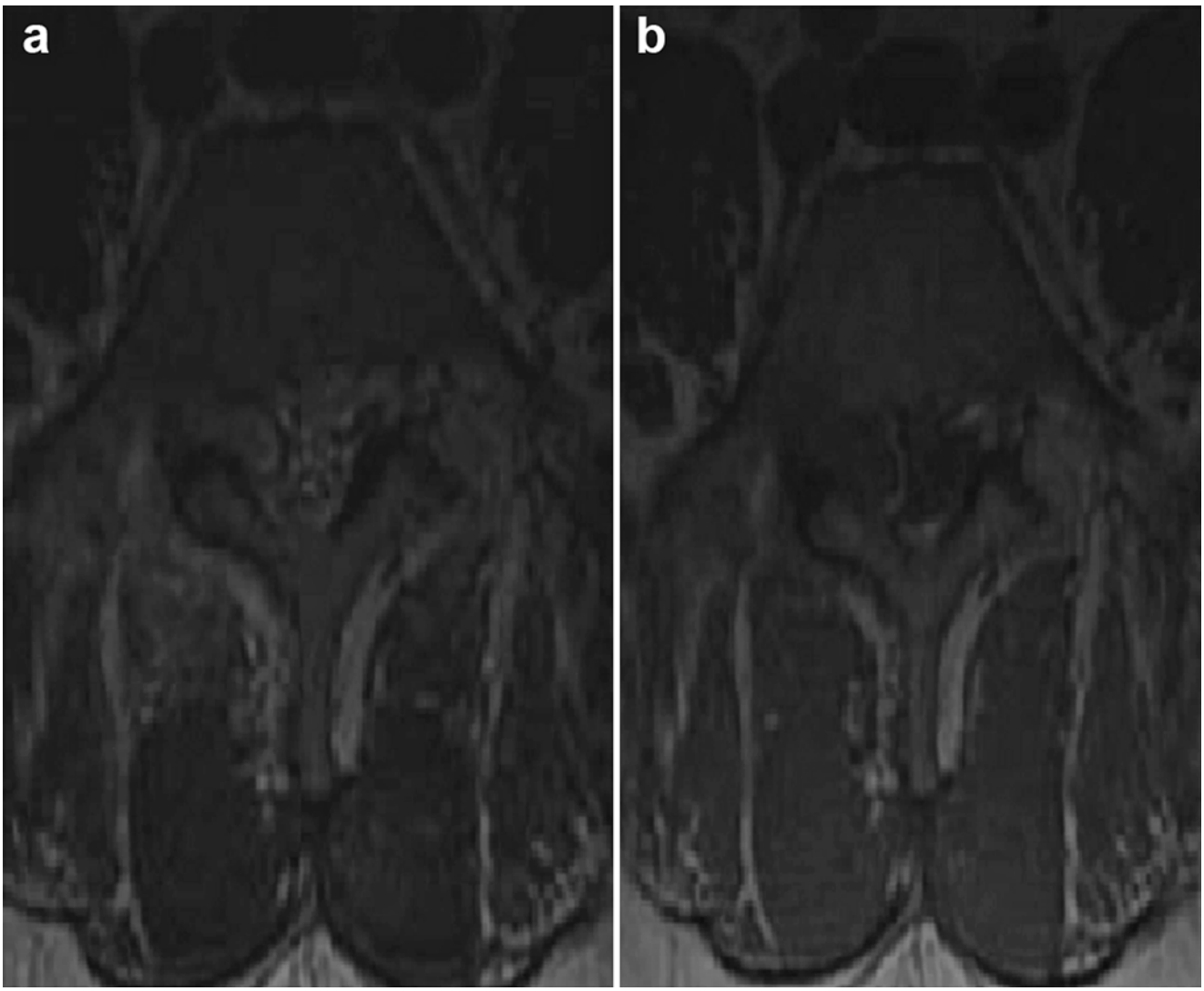

Fig. 50.1 (**a**, **b**) Epidural abscess seen on the above T2 and T1 axial images of the lumbar spine resulting in compression of the exiting right L5 spinal nerve. It occurred following a right L5/S1 intra-articular zygapophysial joint injection

Recommendation

The needle entry point for cervical interlaminar epidural steroid injections should be at the C7/T1 level or below, and the epidural space should be entered in the midline where depth is greatest. The needle should be anchored at the skin with the nondominant hand and advanced with the dominant hand.

When the epidural space is identified with the loss of resistance technique, a catheter should be thread to the appropriate level and contrast injected to confirm the correct level, no vascular uptake and an epidurogram (Figs. 50.2 and 50.3) [31–34]. One should minimize the volume injected to 2–3 cc, and the solution should be injected slowly. AP, oblique, and lateral fluoroscopic views should be taken to document unequivocal epidural spread of contrast prior to injection of medication. Contrast should be injected under live fluoroscopy to confirm no concomitant vascular uptake (Fig. 50.4). Sedation should also be minimized because oversedation may cause loss of communication and the ability to monitor the patient. Oversedation also increases the potential for unintentional patient movement or startle and increases the potential for cardiopulmonary complications. It is generally accepted in the pain medicine community that oversedation or deep monitored anesthesia care (MAC) should not be utilized because it increases the potential for catastrophic complications as spinal cord trauma.

The advantage of this technique is to reduce the chance of dural puncture, spinal anesthesia, and spinal cord injury. Entering the epidural space at the midline position, where there are fewer epidural veins, will also reduce the potential risk of epidural hematoma.

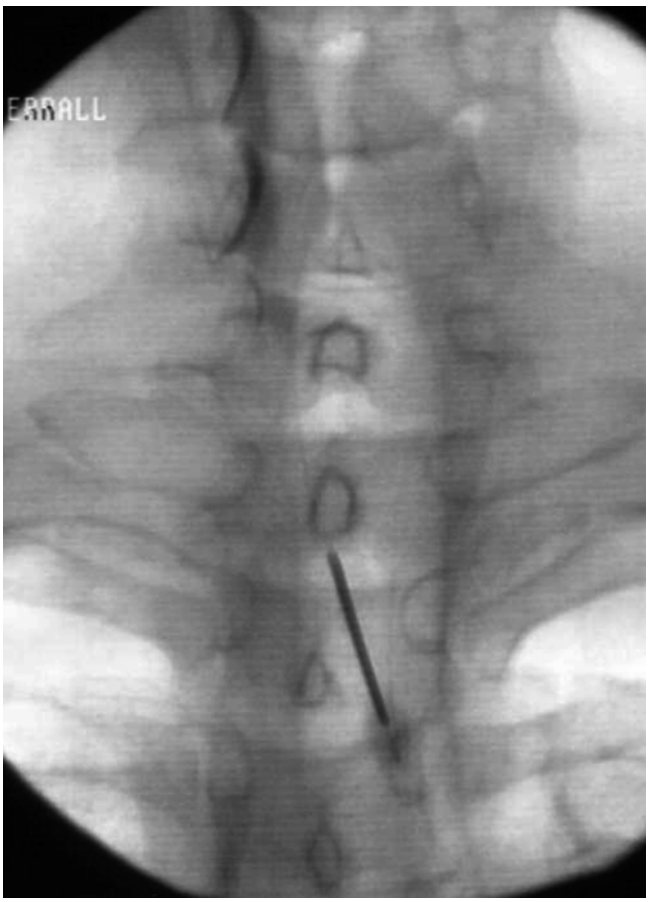

Fig. 50.2 AP fluoroscopic image of a cervical interlaminar epidural steroid injection with a catheter thread to C6/7 in a patient with a left C7 radiculopathy. Note needle entry at T2/3

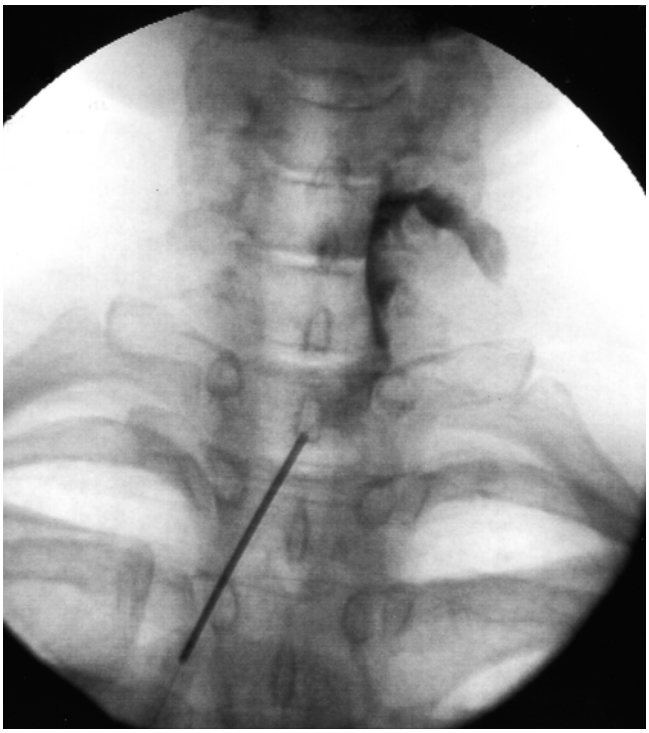

Fig. 50.3 AP fluoroscopic image of a cervical interlaminar epidural steroid injection with a catheter thread to C5/6 in a patient with a right C6 radiculopathy. Note needle entry at T1/2

Transforaminal epidural steroid injections are felt in general to be safe, although the prevalence of complications remains underreported [35]. Complications from the transforaminal approach are similar to interlaminar epidural steroid injections but also include the catastrophic complication of anterior spinal cord syndrome. This can follow inadvertent injection into the radiculomedullary artery (Adamkiewicz) in the lumbar or thoracic spine or cervical radicular artery in the cervical spine. Locked-in syndrome or brain stem infarct may follow unrecognized vertebral artery injection during cervical transforaminal injection (Fig. 50.4).

In the thoracic and lumbar spines, two unfortunate circumstances need to be present. Firstly, the artery of Adamkiewicz (radicular medullary artery) needs to be present at the symptomatic level and, secondly, undetected arterial penetration with subsequent injection. The artery of Adamkiewicz usually arises on the left between T7 and L4 but may be as low lying as S1 on the left or right. It runs with the spinal nerve in the anterosuperior aspect of the foramen and therefore may be penetrated inadvertently at this site [36, 37].

Proposed theories for this include intravascular injection of particulate steroid, resulting in spasm or thrombosis, which results in anterior spinal cord infarction because of the absence of collateral circulation. In the cervical spine, the sole vascular supply to the anterior spinal cord again comes from the anterior spinal artery, and the feeding radicular arteries are highly variable in number, location, and side. Similarly, the presence of a radicular artery at the symptomatic level, and undetected interarterial injection, can result in anterior spinal cord infarction and quadriplegia [38–47].

Strategies to reduce the chance of this catastrophic complication include the following: (1) understanding the fluoroscopic anatomy; (2) understanding contrast flow patterns; (3) optimizing interventional skills; (4) use of extension tubing and injection of contrast under live fluoroscopy to avoid the need to recannulate the needle after contrast is injected; (5) use of digital subtraction imaging; (6) use of nonparticulation solution such as dexamethasone and betamethasone; (7) in addition, some experts have recommended using blunt tip needles, as these are less likely to penetrate an artery [48, 49]; and (8) needle placement in the posteroinferior aspect of the foramen (lumbar, thoracic) to avoid the artery of Adamkiewicz which runs with the spinal nerve in the anterosuperior aspect of the foramen.

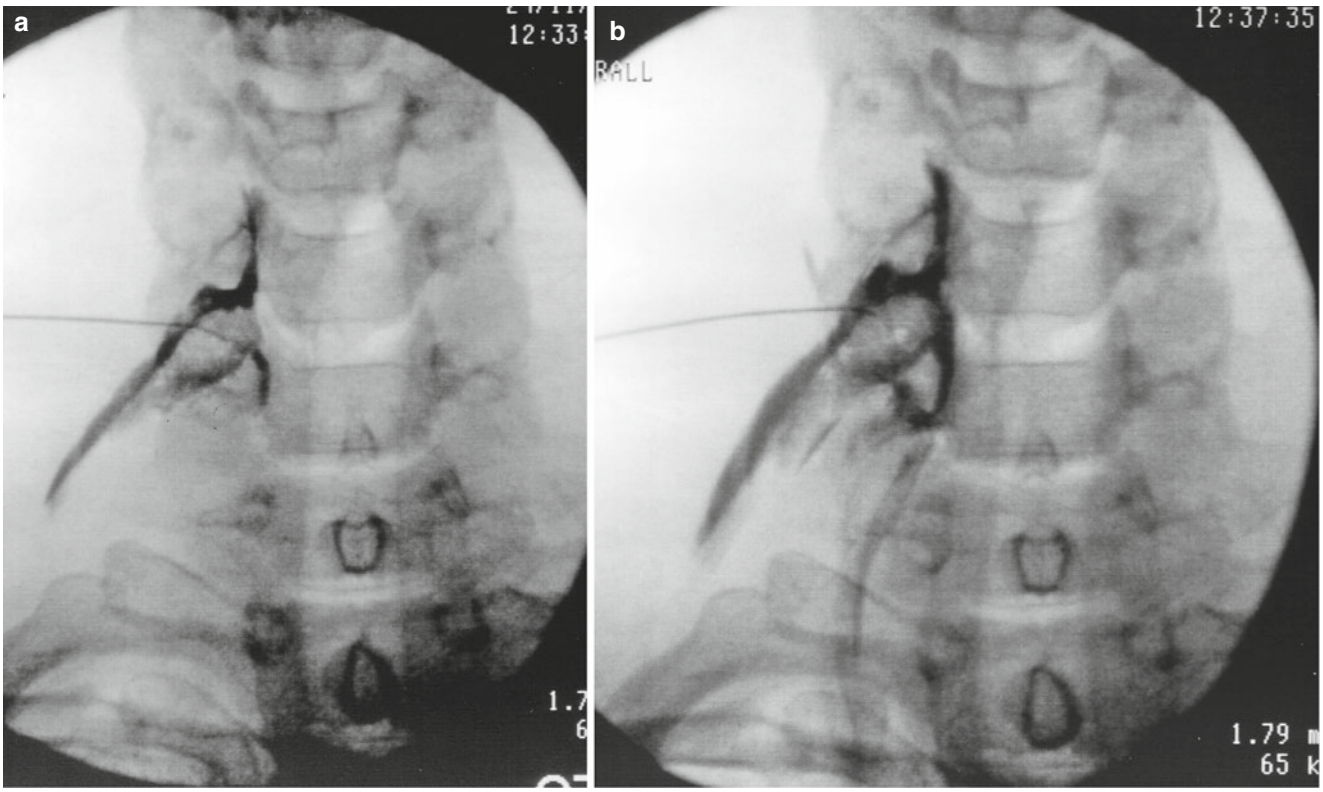

Fig. 50.4 (**a**) AP fluoroscopic image of a right C5/6 transforaminal epidural steroid injection. (**b**) AP fluoroscopic image of a right C5/6 transforaminal epidural steroid injection. Please note the vascular uptake not seen on the previous image is apparent with contrast injection under live fluoroscopy

Trigger Point Injection

Trigger point injections are generally considered to be fairly straightforward; however, some catastrophic complications have been described in cases without fluoroscopy. In a closed claims study, the second most common cause of pneumothorax behind intercostal nerve block was trigger point injection, being responsible for 21 % of cases [5].

Other documented complications include local infection, cellulitis, hematoma, epidural abscess, pneumothorax, spinal anesthesia, spinal cord injury, anaphylaxis, and death.

Use of fluoroscopy for trigger point injections in the cervical or thoracic area will help reduce needle misplacement, either into the epidural, subdural, subarachnoid space, or into the spinal cord, which has occurred with trigger point injections of paraspinal muscles. The use of lateral fluoroscopic guidance for trigger point injections of any posterior thoracic wall musculature will document needle depth and prevent pneumothorax by remaining superficial to the ribs [50–52].

Zygapophysial Joint Injection/Medial Branch Block

In general, lumbar zygapophysial (facet) joint injection is a safe procedure, although complications similar to epidural steroid injections have been described. These include infection with resulting cellulitis or epidural abscess, epidural hematoma, intravascular injection, dural puncture, spinal anesthesia, spinal cord trauma, neural trauma, chemical meningitis, and pneumothorax. Vertebral artery damage or injection is a potential risk with cervical facet joint injections [53–59]. With the use of fluoroscopy and contrast injection in experienced hands, serious complications should not occur. In the cervical spine, a posterior parasagittal approach to the medial branch nerves or posterior approach to the interarticular z-joint injection is safer than a lateral approach (Fig. 50.5). A lateral approach brings the contents of the spinal canal potentially into the path of the needle, especially if the clinician is unable to eliminate parallax and get a true lateral fluoroscopic image. Potential for going through and through a facet joint is real if needle depth is not checked frequently as the needle is advanced. Ideally, under tunnel

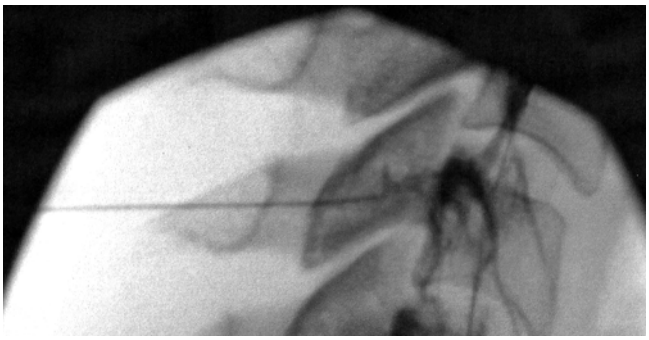

Fig. 50.5 Lateral cervical spine fluoroscopic image of C4 medial branch block showing vascular uptake

vision, the periosteum of the adjacent articular process should be intentionally contacted prior to entering the joint to confirm depth and then the needle rotated into the joint. This will help prevent the needle going through the joint to the adjacent tissue [60].

Stellate Ganglion Block

Many techniques have been described for stellate ganglion block, some of which are without fluoroscopic guidance [61–63]. Multiple complications have been described, most of which have occurred from nonfluoroscopically guided injections that have resulted in inadvertent needle placement into the vertebral artery, adjacent disc, neurotissue, esophagus, intrathecal space, or pleura. These complications have included seizures from intravascular injection, spinal anesthesia, cervical epidural abscess, brachial plexus block, intercostal neuralgia, locked-in syndrome, pneumochylothorax, pneumothorax, reversible blindness, hoarseness, dysphagia, and death [64–74]. These complications can be reduced or hopefully eliminated with a technique described by Abdi et al. [75].

Under ipsilateral oblique fluoroscopic guidance, the respective endplates are squared off, and the C-arm is obliqued until a crisp C7 uncinate process is visualized. Then a 25-gauge spinal needle is advanced down, under tunnel vision, to the base of the uncinate process at the junction of the vertebral body. Under live fluoroscopic guidance with extension tubing, injection of contrast is performed to confirm appropriate nonvascular contrast flow. The needle will lie anterior to the vertebral artery, posterior to the common carotid artery, and lateral to the esophagus. A total of 5 cc should be adequate to obtain stellate ganglion blockade.

Discography

In experienced hands, discography is safe, whether that be in the cervical, lumbar, or thoracic spine. Understanding indications and contraindications to discography is important. Coagulopathy and active infection are general contraindications, but central spinal stenosis, myelopathy, and large disc protrusion are contraindications to cervical or thoracic discography [76].

Potential and described complications pertinent to all three areas include superficial infection, epidural abscess, discitis, or nerve root injury. In the cervical or thoracic spine, the potential for spinal cord injury exists. Quadriplegia has been described following epidural hematoma, epidural abscess, and from subdural empyema [77–84]. It has also occurred secondary to cervical disc herniation from disc pressurization at discography. Keeping the contrast volume in cervical or thoracic discography to a minimum is also important, with less than 0.5 cc/disc usually sufficient for cervical discography.

While infection is a real concern, the administration of preoperative intravenous antibiotics, intradiscal antibiotics, and/or a coaxial needle technique has been described in the literature to be able to reduce the incidence of infection (Fig. 50.6).

A coaxial needle technique has been shown to reduce the chance of discitis from 2.7 to 0.7 % in 220 patients [85]. Preoperative intravenous cefazolin has been shown to reduce the chance of disc infection from 1 to 4 % down to 0 %. Utilizing cefazolin in a concentration of 1 mg/cc intradiscally resulted in no intradiscal infections of 127 patients [86, 87].

The prophylactic antibiotics commonly utilized do not prevent anaerobic discitis, which may occur with the anterior approach to cervical discography, where esophageal penetration is possible. Utilizing a right anterolateral (oblique) approach reduces the chance for esophageal perforation and consequent potential anaerobic discitis. Auscultation of the carotid artery should be performed and ultrasound ordered if carotid bruits are heard prior to discography if an oblique approach is utilized, because of the potential of the needle traversing the carotid and dislodging an unstable plaque.

Patients with discitis usually present with pain and fever, 3 days to 2 weeks post-discography. Erythrocyte sedimentation rate, white cell count, and C-reactive protein are usually positive within the first week. It may take anywhere from 2 to 5 weeks for a bone scan to become positive. MRI with or without gadolinium is now considered the gold standard imaging study. If discitis is suspected, infectious disease consultation, disc biopsy, and culture should be taken. IV antibiotics should be started, and consideration should be given for surgical exploration and/or bracing.

Many of the complications reported with lumbar discography were reported prior to 1970, with many of them in the 1950s. Today with preoperative intravenous antibiotics, intradiscal antibiotics, and a coaxial needle technique, with extrapedicular, extradural fluoroscopically guided approach, these complications should be minimal [88, 89].

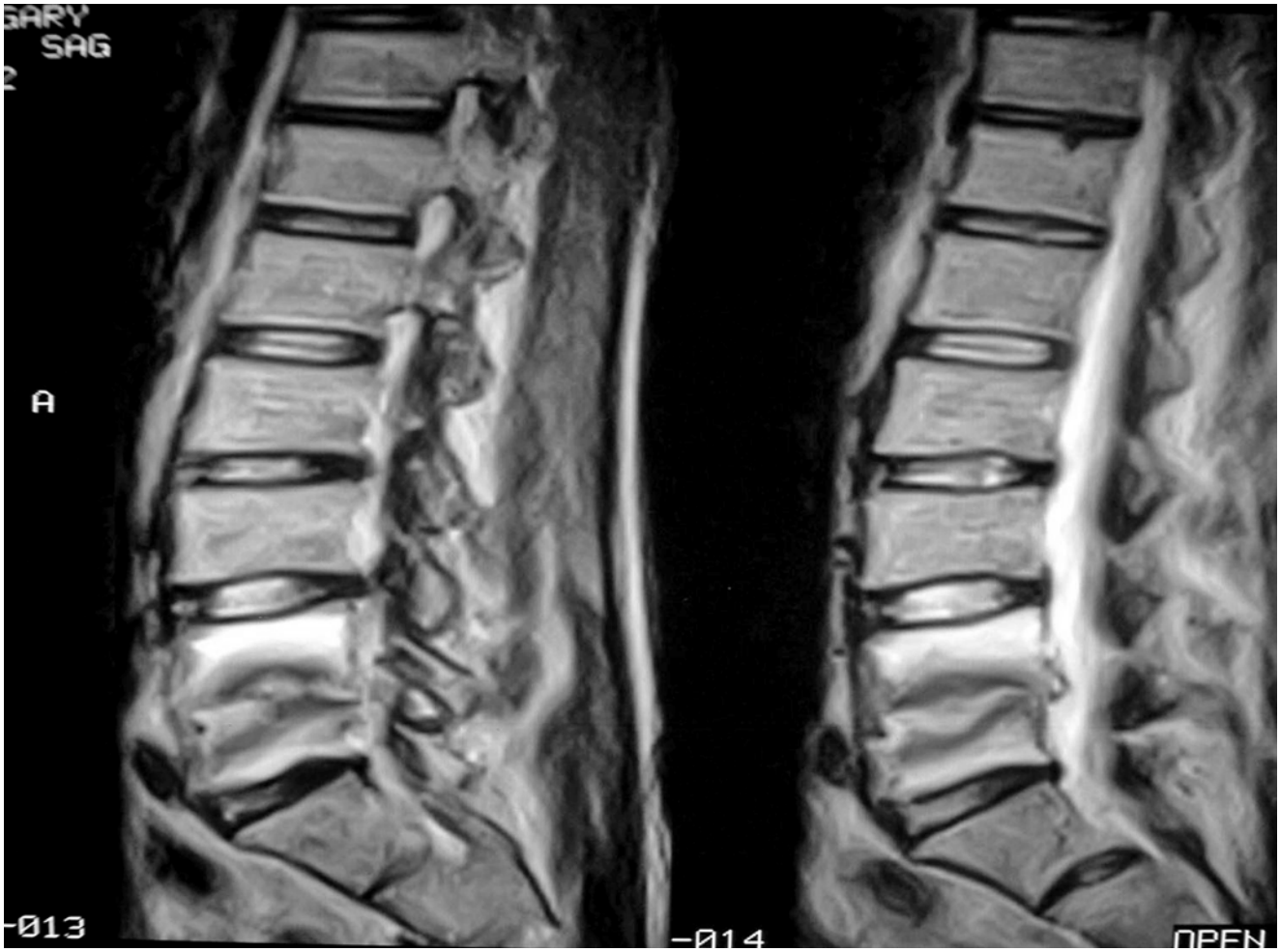

Fig. 50.6 T2-weighted MRI scan of lumbar spine demonstrating L4/5 discitis

If a posterior transdural approach to a disc is planned, then it is important not to utilize intradiscal cefazolin because of the potential for intractable seizures with inadvertent intrathecal cefazolin injection. Therefore, in a patient with previous posterolateral intratransverse bony fusion mass, when posterior transdural approach is considered, or if inadvertent dural puncture occurs with extrapedicular, extradural approach to the disc, then contrast should be mixed with another antibiotic besides cefazolin, such as ceftriaxone, gentamicin, or clindamycin [90].

Pneumothorax has been described as a complication of thoracic discography but could also occur with cervical discography at the C7/T1 level.

In general, cervical or thoracic discography, because of the more challenging technical aspects, and potential for more catastrophic complications, should only be performed by highly skilled and experienced interventionalists.

Summary

It is important to know the literature on current technical standards, modify practice accordingly, and understand that many complications are never published. History and physical examination should be performed on all patients prior to spinal injections. Physicians should review pertinent imaging studies, understand indications and contraindications of procedures, and obtain informed consent. Knowledge of regional and fluoroscopic anatomy is important before attaining technical expertise in a supervised training environment. Familiarization with all contrast flow patterns under live fluoroscopy is imperative. Above all, understand that complications are inevitable, and it is imperative to identify and treat these problems promptly to minimize their impact when they occur and communicate these issues with the patient.

Patient Pertinent Issues

A thorough history and physical examination is vital on all patients prior to neuraxial blockade, regardless of practice set-up or referral pattern. Important points of the history of a patient undergoing an interventional procedure will be addressed.

Past Medical History

This should include any bleeding diathesis, any immune suppressive disorder, history of allergy, anaphylaxis or asthma, and whether they have valvular heart disease.

Medications

It is important to note whether the patient is taking any oral steroid, antibiotics, anticoagulants, or Glucophage, as these will impact patient outcome. Glucophage is generally considered safe in patients with normal renal function when a small amount of nonionic contrast is utilized. It should be temporarily discontinued in patients with impaired renal function undergoing procedures requiring larger amounts of contrast, as it may result in the patient developing lactic acidosis.

Patients taking oral steroids will not only be immunosuppressed but also at increased risk of potential side effects from steroids [91].

Anticoagulants will clearly put patients at risk for hemorrhagic complications. Knowledge of prescription and over-the-counter medications and herbal remedies is important in risk-stratifying patients.

Neuraxial blocks on patients with an active infection requiring antibiotics should be postponed because of the potential for bacteremia and introduction of bacteria to the epidural space.

Allergies

Knowledge of patient allergic to medications that may be utilized in a procedure such as steroid, local anesthetic, or antibiotics is important in reducing the chance of anaphylactic reaction. It is also important to document any known allergy to shellfish or iodine if contrast is to be utilized and any latex allergy, as these procedures need to be done, first case of the day, in a latex-free environment. (Gadolinium may be used in iodine-allergic patients, although there is a documented cross allergy to gadolinium.)

Review of Systems

Thorough review of systems should help rule out any occult coagulopathy, infection, cord compression, malignancy, or pregnant state.

Social History

This should include any prior litigation as even more thorough documentation and informed consent may be required.

Physical Examination

A general but also procedure-specific physical examination should be performed. Attention should be paid to whether the patient is hemodynamically unstable or febrile, as elective procedures should be rescheduled in that event.

A thorough neurological examination is important to establish as a baseline, especially in the event of an adverse neurological outcome. Knowledge of a carotid bruit and subsequent Doppler study result is vital in patients undergoing procedures, in which the carotid artery may be penetrated, such as cervical discography, as the potential for dislodging a mobile thrombus is real. A thorough cardiopulmonary assessment is important in patients undergoing conscious sedation.

Imaging Study

Interventional pain physicians should be to the spine, what the cardiologist is to the heart. They should be comfortable with not only the medical and interventional management of these patients but as good, if not better, than the radiologist in interpreting pertinent spinal imaging studies. Reviewing the imaging prior to procedure in all patients is important [30, 76].

The Nurse

Time should be taken to train nursing staff and allied health professionals in interventional pain medicine, as they play a vital role in reducing significant complications.

Probably the most important *checklist* that medical assistants, nurses, and surgical technicians should review with all patients includes:

1. *Allergies* – Knowledge of nonmedication (shellfish, latex, iodine) and medication allergies is imperative as outlined above.

2. *Pregnancy* – Documentation of the last menstrual period and a pregnancy test if there is any concern should be required if fluoroscopy is utilized.
3. *Anticoagulants* – Prescription anticoagulation or over-the-counter medication or herbal remedies taken by the patient, which have potential for impairing normal coagulation, need to be known. This will be discussed in more detail later.
4. *Diabetes* – If the patient is a diabetic, knowledge of their finger-stick blood glucose is important, as they may be hypoglycemic if fasting or at risk of hyperglycemic complication if steroid injection is planned.
5. *Fever* – Elective spinal injections should be postponed in a febrile patient, as the risk of infectious complication increases.
6. *Fasting* – Knowledge of the last time a patient ate or drank is important if conscious sedation is anticipated.
7. *Side* – The side of the patient's symptoms should be marked with an X to help reduce one of the more common preventable surgical errors.

This *checklist* should be issued to all staff members who interact with the patient and should be communicated to the physician in the operating room prior to each procedure.

Nurse/Surgical Technician Preparation

If the physician is not drawing up the medications for injection, then appropriate education and training of the surgical staff is vital in reducing medication errors. Medication should be drawn up by a surgical technician with nursing supervision. All syringes should be labeled, and clearly, sterile precautions must be followed.

If you practice in a setting that is used by different specialists, such as a radiology suite at a hospital, it is important that the physician reviews all the medications prior to each procedure, to ensure no medication error. Specifically, that preservative-free local anesthetics are utilized (for epidural injections), and nonionic contrast that is safe for intrathecal use, such as Omnipaque or Isovue, and not an ionic contrast medium that may be used for urologic or gastrointestinal imaging.

Appropriate sterile preparation is mandatory and should include povidone-iodine preparation, allowing it to dry. In patients with iodine allergy, chlorhexidine gluconate and/or isopropyl alcohol may be used. For more invasive procedures such as implant or discography, some practices utilize a triple scrub, including isopropyl alcohol, chlorhexidine gluconate, and povidone-iodine. While sterile towels are adequate for draping an area for most procedures, in the case of more invasive spinal procedures, full-body draping with iodine-impregnated fenestrated adhesive biodrapes, sterile towels, and half sheets should be used [92, 93].

Patient Monitoring

Appropriate perioperative monitoring is important for all procedures and should include IV access, pulse oximetry, cardiac monitoring with ECG tracing, and blood pressure and heart rate monitoring. A fully stocked, regularly updated crash cart should be easily accessible. ACLS-trained personnel should be available. Mock codes should be run at least quarterly. This will help minimize the impact of an adverse reaction or complication.

In the postoperative patient recovery room, trained staff knowledgeable in recognizing post-procedural complications should be available. Such complications include hypotension, vasovagal reactions, sensory motor blockade, excessive somnolence, respiratory suppression, and cardiovascular complications.

Depending upon the procedure and the amount of sedation utilized, patients will be in a monitored postoperative setting, anywhere from 20 min to 8 h, until discharge criteria are met. These include an alert, oriented patient who is hemodynamically stable, with stable cardiovascular and neurologic examination and ambulating as well as expected, with someone else to drive them home if they have had sedation.

Physician

Physicians from numerous subspecialties have converged on the field of interventional pain medicine, all with varying levels of training and competence. Until recently, the standard interventional pain training occurred in the fellowship setting. Interventional pain medicine, now a recognized subspecialty of medicine, will soon have formal residency training programs.

There are still physicians performing interventional pain techniques that were learned at weekend courses. While these courses are helpful, they are by no means sufficient. A thorough understanding of spinal anatomy and how that relates to fluoroscopic anatomy is vital. Unfortunately, at these conferences, the optimum fluoroscopic image is already set, and physicians may struggle with reproducing this in their clinical practice. Contrast flow patterns are not generally taught, and therefore, the ability to recognize vascular uptake or to differentiate between a myelogram, epidurogram, or subdural contrast flow is not learned.

Physicians should be cognizant of all potential complications pertinent to a given procedure being performed. The mindset of anticipating complications will hopefully lead to earlier recognition, a more prompt and appropriate response, and minimize the effect of that complication. It is inevitable that a complication will occur to every interventionalist. How it is dealt with will frequently determine the outcome.

The physician should not be afraid to reschedule the procedure if difficulties are encountered with a particular procedure on a given day. If, for example, while performing a cervical transforaminal epidural steroid injection, vascular uptake is noted despite repositioning the needle multiple times in the foramen, the appropriate course of action may be to reschedule the patient or consider an interlaminar approach.

The minimum experience level required for certain procedures is somewhat controversial. Clearly the level of expertise required to perform an uncomplicated interlaminar lumbar epidural steroid injection on a healthy patient is far less than that required for a cervical transforaminal epidural steroid injection. Cadaver courses may help develop some of those skills, but supervised training in the clinical setting is strongly advised.

Equipment

The physician should be familiar with all equipment that may be required for a given procedure. They should be able to operate all the equipment independently and problem solve in the event of equipment malfunction. Reliance on company representatives or surgical technicians may result in operator error and avoidable complication. The physician should know how to run the fluoroscope and obtain optimal fluoroscopic images and minimize radiation exposure to all personnel.

Needle

Three basic types of needles are utilized in interventional pain practice, including a ramped needle such as a Tuohy needle which is utilized for interlaminar epidural steroid injections, a Quincke or standard spinal needle, which is used for most common spinal injections, and the third type, a pencil-point needle, which is used far less frequently (Fig. 50.7). The pencil-point needle was developed to reduce the incidence of post-dural-puncture headaches for patient undergoing spinal anesthesia and is not used frequently in interventional pain procedures.

Understanding the needle dynamics and bevel control is vital to facilitate precise needle placement. The direction of needle deviation is governed by the design of the needle tip (Fig. 50.7). Ramped needles (Tuohy) deviate away from the ramp. Pencil-point needles (Sprotte or Whitacre) only deviate a minimal amount, although not in a specific direction. Beveled needles (Quincke) consistently deviate away from the bevel. Experienced interventionalists usually accentuate this natural tendency of the beveled needle by placing a 15-degree curve, just proximal to the distal end of the needle.

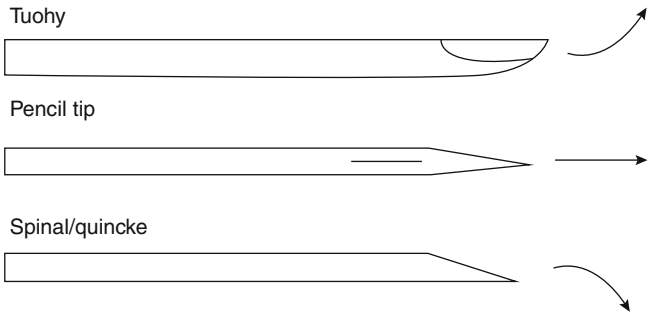

Fig. 50.7 Examples of needle types and deviation direction: Tuohy/ramped utilized for interlaminar epidurals. Pencil tip utilized for spinal anesthesia and lumbar punctures. Spinal/Quincke utilized for most interventional procedures

The degree to which a needle deflects depends on the density and distance of tissue traversed, the needle type and gauge, with 25-gauge needles deflecting more than 22 gauge [94–98].

Regardless of what needle is utilized, a two-handed needle technique should be used on all interventional procedures, with the nondominant hand anchoring the needle at the skin, and the dominant hand advancing the needle. Anchoring the needle at the skin will prevent inadvertent excessive needle advancement in the case of a patient making a sudden move which, in the case of a thoracic or cervical interlaminar epidural steroid injection, may result in spinal cord injury.

Complications resulting from interventional pain procedures have raised the issue of safety of blunt versus sharp needles for doing these procedures [45]. Some experts have recommended using blunt tip needles, rather than traditional sharp needles when performing transforaminal ESIs, with the hope of reducing the catastrophic complications of vascular penetration and anterior spinal cord infarction. This may occur with inadvertent and unrecognized injection of medication into an artery, such as radiculomedullary artery (Adamkiewicz), which may be encountered with thoracic or lumbar transforaminal injections. It may also occur with penetration of a cervical radicular artery with cervical transforaminal epidural steroid injections. Blunt needles have been unable to directly puncture the renal artery or penetrate the spinal nerve in animal models and are therefore felt by some to be safer [40, 99, 100].

Needle Placement

It is very important for the interventionalist to understand the concept of a three-dimensional object, such as the spine, being projected in two dimensions on the fluoroscope. The principle of direction, depth, direction is vital. Once the fluoroscopic working view is obtained and needle entry point determined, then the needle is directed in the sagittal or coronal plain with the needle advancing in the caudad/cephalad

or medial/lateral direction. Needle depth is then checked by switching the fluoroscope to a different view, for example, by switching from an AP view to a lateral view. After assessing depth, the fluoroscope is then changed back to the original working view and redirected. Frequent checks of needle depth are vital to avoid potential needle misplacement with resultant potential complication.

Medications

The interventionalist should be very familiar with all medications utilized, including various steroid formulations, and which ones are deemed safe and appropriate for epidural use. Understanding the appropriate dosage, duration of action, potency, and side effect profile is important [19, 20, 101, 102]. This is beyond the scope of this chapter. Utilizing the smallest particle size steroid may help reduce the potential for vascular thrombotic complications. Betamethasone is of smaller particle size than triamcinolone and dexamethasone, respectively. Ideally steroid in solution and not suspension should be used.

If compounded medications are being utilized, be aware of the practices of your pharmacy, as US Pharmacopeia guidelines should be followed. There have been numerous deaths throughout the United States linked to contaminated compounded betamethasone, resulting from meningitis, encephalitis, and septic shock. If compounding medications are being utilized, it behooves the interventionalist to check the pharmacy's practice and track record.

Contrast agents are used for accurate localization of needle placement, to confirm no vascular uptake and to delineate pertinent anatomy and appropriate contrast flow pattern. Nonionic and ionic contrast agents are available. Nonionic contrast agents are more hydrophilic, and this reduces subarachnoid and intravenous toxicity. They also have a lower osmolality and produce fewer adverse effects. All epidural and intrathecal procedures should be performed with nonionic contrast agents. Commonly used nonionic contrast agents in interventional pain include iohexol (Omnipaque) and iopamidol (Isovue).

For patients who are iodine allergic and who require contrast, either gadolinium or premedication and nonionic iodinated contrast can be utilized. Premedication should include corticosteroid and an antihistamine combination, such as prednisone, 50 mg by mouth, 13, 7, and 1 h before injection with diphenhydramine (Benadryl) 50 mg IV or by mouth, 1 h prior to the injection. Other experts also include H2 blockers such as Zantac taken 1 h before and following the injection. If premedication with steroid alone is utilized, methylprednisolone, 32 mg orally, 12 and 2 h prior to the contrast agent is sufficient [103, 104].

It is generally accepted in the radiology community that it is safe to administer gadopentetate dimeglumine in patients with a known allergy to an iodinated contrast agent. In one study, however, 6.3 % of iodine-allergic patients experienced an adverse reaction to gadopentetate dimeglumine, and therefore, some degree of caution is still warranted [105].

Knowledge of anesthetic type, whether it be an amino amide, such as lidocaine or bupivacaine or an amino ester such as 2-chloroprocaine, as well as the usual concentration, onset, duration of action, and maximal single dosage is required. Caution should be exercised not to exceed the maximum dose which could occur, especially with larger procedures such as spinal cord stimulation or perhaps multilevel bilateral radiofrequency medial branch neurolysis.

Toxic CNS effects include confusion, convulsions, respiratory arrest, seizures, and even death. Other potential adverse reactions include cardiodepression, anaphylaxis, and malignant hypothermia. The patient should be monitored for signs of toxicity including restlessness, anxiety, incoherent speech, light-headedness, numbness and tingling of the mouth and lips, blurred vision, tremors, twitching, depression, or drowsiness. Injections in the cervical spine require the utmost care, as even a small dose of local anesthetic injected intravascularly may result in significant systemic toxicity and deaths have been reported [106, 107].

All local anesthetics injected into the epidural space should be preservative-free.

Resuscitative equipment and medication should be immediately available when local anesthetics are being utilized. Central nervous system toxicity by 1 % lidocaine has an onset at plasma concentrations of 5–10 mcg/ml which equates to slightly more than 400 mg (40 cc) of total bolus. Bupivacaine is about four times more toxic than lidocaine, with a toxic bolus of 100 mg (10 cc) [108].

Volume and Rate of Injection

There is some controversy as to the optimum volume for epidural injection. As a general rule in a young patient with no central or foraminal stenosis, large volumes of contrast can be injected safely without any neurocompressive complications. However, in the cervical spine in someone with multilevel moderate to severe central and foraminal stenosis, where limited run off is available, then compressive complications may occur with as small volume as 3 ml, especially if injected quickly.

As a general rule, target-specific epidural injections delivered transforaminally at the symptomatic level or interlaminarly with a catheter advanced to the appropriate level can be achieved with volumes of 2 or 3 ml. High volume, rapid epidural steroid injection can result in large increases

of intraspinal pressure, with the risk of cerebral hemorrhage, retinal hemorrhage, visual disturbance, headache, and compromise of spinal cord blood flow. A retinal hemorrhage has been described and felt to be secondary to a sudden increase in intracranial pressure from a rapid epidural steroid injection, resulting in increase in retinal venous pressure [109–114].

Fluoroscopy

Fluoroscopy should be used for all spinal injections, including discography, diagnostic intra-articular facet joint injections, diagnostic medial branch blocks, diagnostic sacroiliac joint injections, radiofrequency medial branch neurolysis, and all transforaminal epidural steroid injections. For these, no controversy should exist. Surprisingly, however, controversy still abounds regarding the need for fluoroscopy with interlaminar or caudal epidural steroid injections. This, despite the fact that needle misplacement occurs 25–40 % of the time with caudal injections and about 30 % of the time with interlaminar lumbar epidural injections, and up to 53 % of the time with cervical epidural steroid injections without fluoroscopy [115–117]. Fredman reported more than 50 % of blind lumbar epidural steroid injections were performed at the wrong level [118–120].

Surprisingly, the results of a national survey of private and academic practices demonstrated that for cervical interlaminar epidural steroid injections, only 39 % of academic practice versus 73 % of private practitioners utilize fluoroscopy [121].

There are multiple studies showing that negative aspiration is unreliable for vascular uptake and the high incidence of vascular penetration with transforaminal lumbar and cervical epidural steroid injections which if unrecognized could result in catastrophic spinal cord infarction [122–124].

The use of fluoroscopy and contrast injection can demonstrate precise needle placement at the correct level and appropriate contrast flow. Injection of contrast under live fluoroscopy with extension tubing can help confirm there is no vascular uptake prior to injection of medication.

Many of the published complications of interventional pain procedures including sympathetic blocks and trigger point injections are because of needle misplacement with *blind* techniques and are eminently avoidable with fluoroscopy. These will be discussed in more detail later in this and other chapters.

Unrecognized inadvertent subdural injection may occur in close to 1 % of injections without fluoroscopy [125]. A hard copy confirming accurate needle placement can also be kept in the file. Fluoroscopy should be used for all interventional spine procedures except during pregnancy.

Anticoagulation

Significant bleeding following interventional pain procedures is extremely rare but may have catastrophic outcome. These procedures carry an inherent risk of bleeding, but the real extent of this risk is unknown. Bleeding complications will increase with poor technique, the presence of high procedure or patient-associated bleeding risk factors, and anticoagulation. Many prescription or over-the-counter medications and even herbal remedies such as garlic, ginkgo, ginseng, and ginger may impair coagulation [126].

Published guidelines from European and American Anesthesiology societies exist but only define the risk of significant bleeding complications for neuraxial procedures in the presence of anticoagulation [127–129]. The incidence of spinal hematoma is rare. In fact, the published incidence is 1/150,000–1/190,000 for epidurals, and 1/220,000 for spinals [130–132].

The authors as well as the German and the Spanish Society of Anesthesiology recommend that aspirin and nonsteroidal anti-inflammatory drug (NSAID) should be held prior to elective spinal injections. In the presence of increased procedure and patient-related bleeding risk factors, aspirin should be held 7 days and NSAIDs for 72 h prior to these procedures. The American Society of Regional Anesthesia and Pain Medicine (ASRA) states this practice as controversial.

In general, little controversy surrounds ticlopidine which should be held for 14 days and clopidogrel which should be held for 7 days prior to neuraxial block [130–132]. Warfarin should be stopped 4–5 days prior to neuraxial procedure, and the INR should be less than 1.4 prior to proceeding according to ASRA guidelines.

Prophylactic or therapeutic dose low molecular weight heparins should be held at least 12 or 24 h, respectively, before an epidural. Understand, however, that there are newer, longer-acting LMWHs that may need to be held longer [133].

COX-2 inhibitors such as celecoxib and valdecoxib do not need to be stopped perioperatively.

The ASA recommends discontinuing herbal medicines for 2–3 weeks prior to elective surgery. The authors suggest that vitamin E and herbal medications like garlic, ginseng, ginger, and ginkgo may increase the patient risk for bleeding, and consideration should be given to stop them, especially if there is other associated patient or procedure-related risk factors present.

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