Spinal Cord Stimulation

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Introduction

Spinal cord stimulation (SCS) has been used for several decades and just recently has been considered a superior treatment for patients with chronic, intractable pain. Currently, about 34,000 patients worldwide receive a spinal cord stimulator annually for any chronic pain. Spinal cord stimulation (SCS) leads are placed in the epidural space to deliver electrical stimulation to the dorsal columns of the spinal cord. Successful pain relief generally requires activation of dorsal column fibers that innervate the patient's painful area.

Historically, using traditional low-frequency (40–90 Hz) stimulation, the patient feels paresthesia located over the painful area and pain relief due to spinal and supraspinal mechanisms. However, only about 30–50% of patients respond to conventional low-frequency SCS therapy. Recent advances in SCS therapies are improving SCS outcomes. For example, continuous stimulation at a higher frequency (10 kHz) was shown to provide superior pain relief for low back and leg pain compared to traditional lower SCS stimulation frequencies. Additionally, prior studies have indicated that 1 kHz continuous stimulation or 500 Hz burst patterns of stimulation may provide an additional pain relieving benefit while reducing the stimulation energy required. More recently, both closed-loop and differential target multiplex types of SCS demonstrated, in well-conducted randomized controlled trials (RCTs), comparable outcomes to 10 kHz SCS in optimizing the overall outcomes of this therapy.

Mechanisms of Action

Traditionally, low-frequency, traditional type of SCS was thought to provide long-term pain relief by the activation of the gate control mechanisms, conductance blockade of the spinothalamic tracts, blockade of supraspinal sympathetic

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mechanisms, and activation or release of neuromodulators. When SCS is active, unmyelinated afferent fibers (A delta and C) are inhibited by the electrical stimulation of non-nociceptive, myelinated afferent fibers. Conductance blockade of the spinothalamic tract is accomplished by depression of the spinothalamic tract cells by SCS during thoracic or cervical stimulation of the ipsilateral dorsal columns. Such inhibition of actual transmission of electrochemical information can be accomplished anywhere along the spinothalamic tract. Blockade of supraspinal sympathetic mechanisms results in an increase of the peripheral blood flow in the skin which remains after the transection of the dorsal roots and after spinal cord section rostrally to the stimulating electrode. There is also transitory inhibition of sympathetic vasoconstriction documented in studies conducted in the early 1990s. Activation and release of neuromodulators included an induction of GABA release in the dorsal horn, glycine release in the extracellular space of the spinal cord, and reduction of glutamate and aspartate release in the dorsal horn.

Measured effects of SCS to heart function include reduction of intrinsic cardiac nervous system activity and preemptive suppression of marked increase in cardiac NSA following local occlusion of coronary blood flow which may inhibit local heart circuits and decrease frequency of arrhythmias in the ischemic heart. We do know that SCS has no effects on coronary blood flow during ischemic conditions, left ventricular function, or left ventricular blood flow distribution. However, positive and anti-ischemic effects include decrease of myocyte oxygen demand, significant increase of pacing tolerance, decreased ST segment depression, and improved myocardial lactate metabolism, which in turn results in pain relief and improvement in exercise tolerance.

SCS improves ischemic extremity pain providing vasodilator effect via peripheral release of calcitonin gene-related peptide (CGRP), prostacyclin release, and neuronal release of nitric oxide. During SCS, there is a decreased sensitivity to vasoconstrictive sympathetic stimuli mainly by suppression of efferent sympathetic activity. Such effect is inhibited after complete surgical sympathectomy and blockade of nicotinic transmission in the ganglia or postganglionic $[alpha]_1$ adrenoceptors. It has been determined that an increase in skin blood flow during SCS correlates with resulting pain relief, increase in transcutaneous partial oxygen pressure, and increased pulse-wave amplitude.

Other possible mechanisms of SCS were proposed recently when very specific types of SCS waveform are used, different than traditional low-frequency type of SCS. For example, recruitment of the dorsal horn with activation of inhibitory neurons was a proposed additional mechanism of action seen with 10 kHz. This is independent of any effect that SCS may produce on the dorsal columns. Such effect results in additional pain relief, not exhibited greatly when low frequencies (1–1200 Hz) of SCS were used.

Recently, much work was done on neuromodulation, mainly SCS, involving glial cells in addition to neurons. These cells (microglia, astrocytes, and oligodendrocytes) are abundant in the spinal cord and carry ratio of about 12:1 to neurons in the gray matter and 20:1 in the white matter. While glial cells support normal brain function by cleaning damaged areas and regulating neurotransmitters, in chronic disease conditions, they can become "activated" and contribute to a pathological state, such as chronic pain. Glial cells respond to electrical field application by depolarizing, releasing neurotransmitters, and communicating with each other. Differential target multiplex (DTM) type of SCS is directed toward modulation of glial cell response. In an acute neuropathic pain model in rodents and mammals, DTM type of SCS provided superior thermal and mechanical hypersensitivity suppression compared to low and high (1000 Hz) type of SCS. During DTM SCS in an animal model of neuropathic pain, gene expression is better restored toward the baseline, non-pain state, when compared to low- and high-frequency SCS, including the genes related to neuroinflammation.

Finally, a recent development in spinal cord stimulation waveform optimization is a closed-loop stimulation. During closed-loop stimulation, data regarding the spinal cord response to stimulation, measured as evoked compound action potentials (ECAPs), is recorded in real time. This allows the spinal cord stimulator system to adjust its stimulation parameters to maintain ideal therapeutic response.

Spinal Cord Stimulator Trial Technique

As opposed to any other interventional therapy for control of chronic pain, patients can undergo temporary SCS trial. Time interval of SCS trial may vary between 3 and 30 days (in the United States, most frequently 7–10 days). Based on NACC guidelines, patients who have been identified by the physician as potential SCS candidates should be screened for risk factors that may predispose them to complications from SCS, referred for psychological evaluation to rule out any prohibitive psychological disorders that may hinder successful response to neuromodulation, and thorough history and physical examination must be performed. Vital questions for the SCS candidate include whether or not they are anticoagulated, have a history of poorly controlled diabetes, are current smokers, or have a history of surgical site infection/poor wound healing. If the patient is anticoagulated, American Society of Regional Anesthesia and Pain Medicine (ASRA) guidelines should be strictly adhered to in order to minimize the risk of catastrophic epidural hematoma formation or any other bleeding. Attention should be given to the patient's body habitus, as increase in body mass index may affect procedural technique and predispose the patient to postoperative

infection. Spine imaging should be carefully reviewed in order to rule out structural instability that would warrant surgical attention, as well as central canal stenosis that may preclude the safe insertion of SCS leads.

The patient is brought to the fluoroscopy suite and positioned prone with adequate padding under the abdomen to minimize lumbar lordosis. Weight-based antibiotics are administered 30–90 minutes prior to epidural space access. Sterility should be maintained while prepping and draping the patient. If sedation is required, it should be minimal in order to facilitate patient-physician communication throughout the procedure. AP fluoroscopy is centered over the intended epidural entry point, most commonly L2–L3 to T12–L1 for thoracolumbar SCS (back and leg pain). The image is optimized with fine oblique adjustments to center the spinous processes between the pedicles and cephalad or caudal tilt to square the endplates of the vertebral body at the intended level of epidural entry (Fig. 72.1).

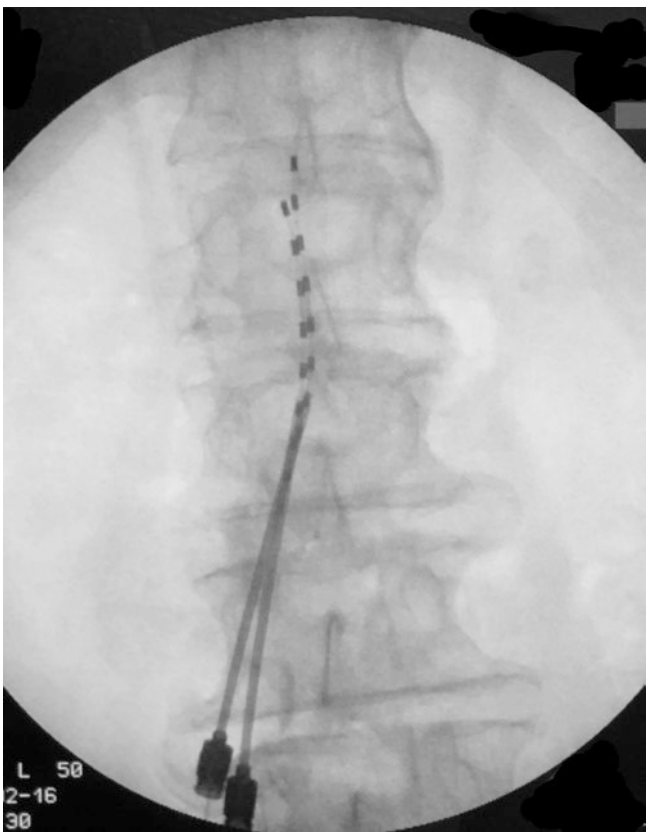

Fig. 72.1 Anterior-posterior fluoroscopic view of an entry point to the lumbar epidural space. Notice that both Tuohy needles are placed next to each other within the same lumbar interspace. Final advancement of the needles was achieved in lateral view (see Fig. 72.2a) and after the confirmation of an epidural space, and leads accessed epidural space in lateral view, further advancement of the leads is commenced in anterior-posterior fluoroscopic view as shown in Fig. 72.2b

Once the optimal AP image has been obtained, needle entry point must be determined. The goal is to enter the epidural space at a relatively flat angle of 30–45°. Individual patient body habitus greatly impacts the proper skin insertion point. The greater the amount of subcutaneous tissue, the further the skin entry point will be from the intended interlaminar target. In a patient of average BMI, local anesthetic is injected in the skin overlying the medial border of the pedicle one level caudad to the interlaminar epidural target. Deep local anesthetic infiltration may be achieved using a spinal needle along the intended trajectory. Next, the 14-gauge Tuohy needle is directed toward the midline of the intended interlaminar space. Note that the necessary length of the Tuohy needle may vary based on point of skin entry.

Utilizing frequent AP fluoroscopy, contact should be made with the cephalad aspect of the lamina immediately below the intended epidural target. This serves as a depth gauge and minimizes the risk of inadvertent entry into the epidural or intrathecal space. Once contact has been made, a lateral fluoroscopic image is obtained.

The angle of approach is further reduced, and the Tuohy needle is advanced anteriorly toward the epidural space. As the needle approaches the base of the spinous processes under lateral fluoroscopy, a loss of resistance technique is utilized to safely identify the epidural space. Once loss of resistance is obtained, the SCS lead is slowly advanced into the epidural space. A lateral image is obtained to confirm the lead is positioned posteriorly in the spinal column (Fig. 72.2a, b).

The lead is advanced superiorly through the epidural space under continuous fluoroscopic guidance to the desired vertebral level. This target varies based on the diagnosis being treated and various device manufacturer recommendations.

Once the first lead has been advanced to the intended target site, attention is directed to the placement of the second Tuohy needle. This can be inserted ipsilateral to the first needle at the same interlaminar level, at the level above or the level below the insertion site of the first needle. It may also be inserted from the contralateral side aiming toward the intended interlaminar entry point. After entering the epidural space, the second lead is advanced alongside the first lead until it reaches its target vertebral level (Fig. 72.3).

After satisfactory lead location has been established, the Tuohy needles are removed with intermittent fluoroscopy to ensure they do not advance or withdraw during needle movement. Once the needles are removed, the leads are secured in a fashion that suits the physician's preference. This may include suturing in place using manufacturer provided anchoring devices, suturing to the lead itself, securing it using Steri-Strip, and dressing only or tunneling leads for possible prolonged trials (Fig. 72.4).

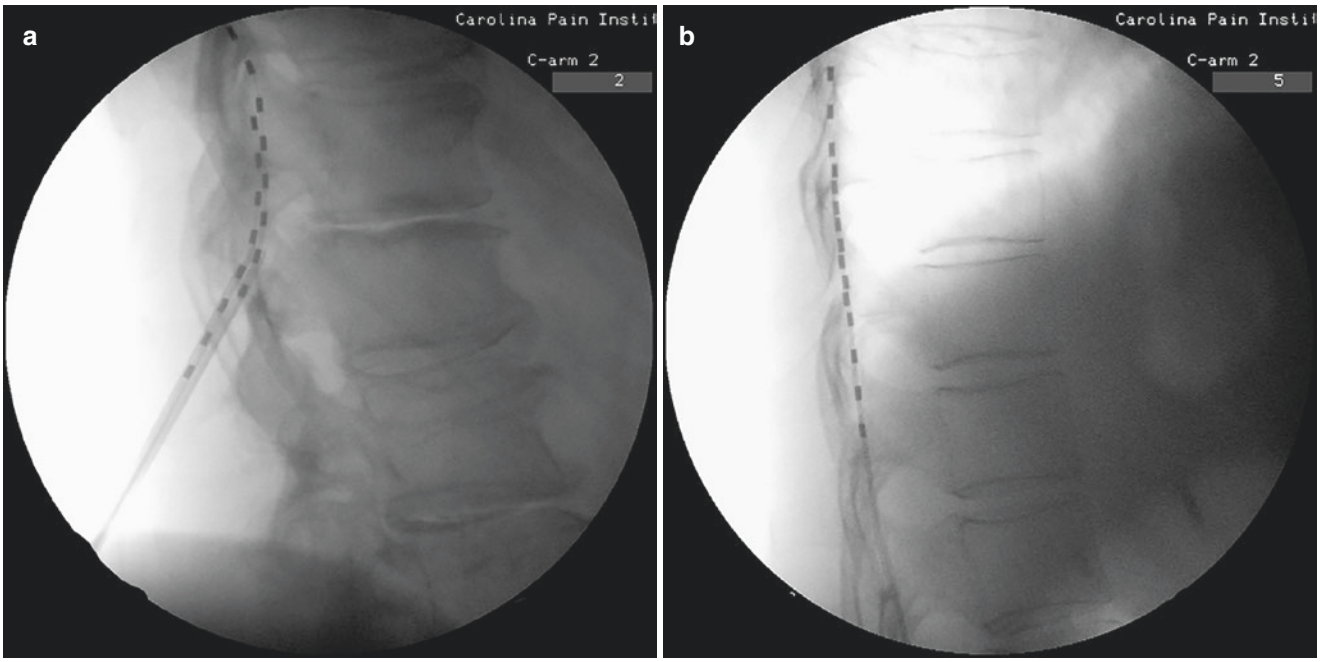

Fig. 72.2 Lateral fluoroscopic views during Tuohy needle and lead insertion in the epidural space. (**a**) Needle insertion level, typically upper lumbar, for the lead placement that would be used for back and leg chronic pain. Notice that both needles are inserted at the same ligamentum flavum level and leads with eight contacts each were just confirmed to be positioned in the posterior epidural space. (**b**) A final position of two 8-contact leads in the posterior epidural space. In this example, leads were stacked from the top of T8 vertebral body to mid vertebral body of T11

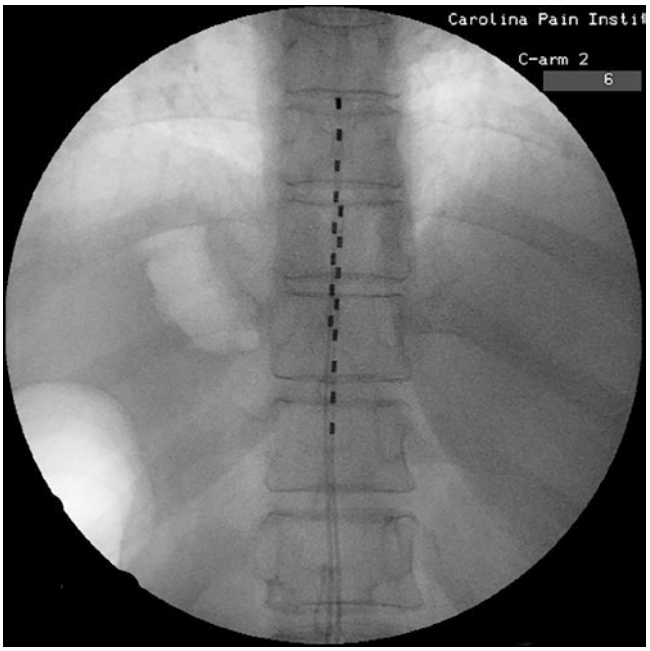

Fig. 72.3 Final positioning of two Octrode leads in the anterior-posterior view. One lead reached top of T8 vertebral body, the other one top of T9

The duration of the trial may range from 3 to 10 days depending on patient response and physician preference. Beyond a 10-day trial period, the risk of infection increases, but could be mitigated by tunneling leads (Fig. 72.3b).

Spinal Cord Stimulator Permanent Implant

Permanent implantation of a SCS system is performed in a sterile operating room setting. The patient is positioned prone in a similar fashion as described for the SCS trial procedure, with adequate padding to reduce normal lumbar lordosis (or cervical lordosis for cervical SCS implant). Anesthesia is administered and the patient is prepped and draped in a sterile fashion. Intravenous antibiotics have been administered within 1 h of incision. AP fluoroscopy is utilized to identify the intended interlaminar target. A vertical incision site is marked starting at the level of the intervertebral disc immediately inferior to the intended interlaminar insertion site and extending inferiorly 3 to 4 cm.

The skin and subcutaneous tissue is anesthetized with 1% lidocaine containing 1:200,000 epinephrine. A vertical incision is made using a scalpel blade. Careful dissection is per-

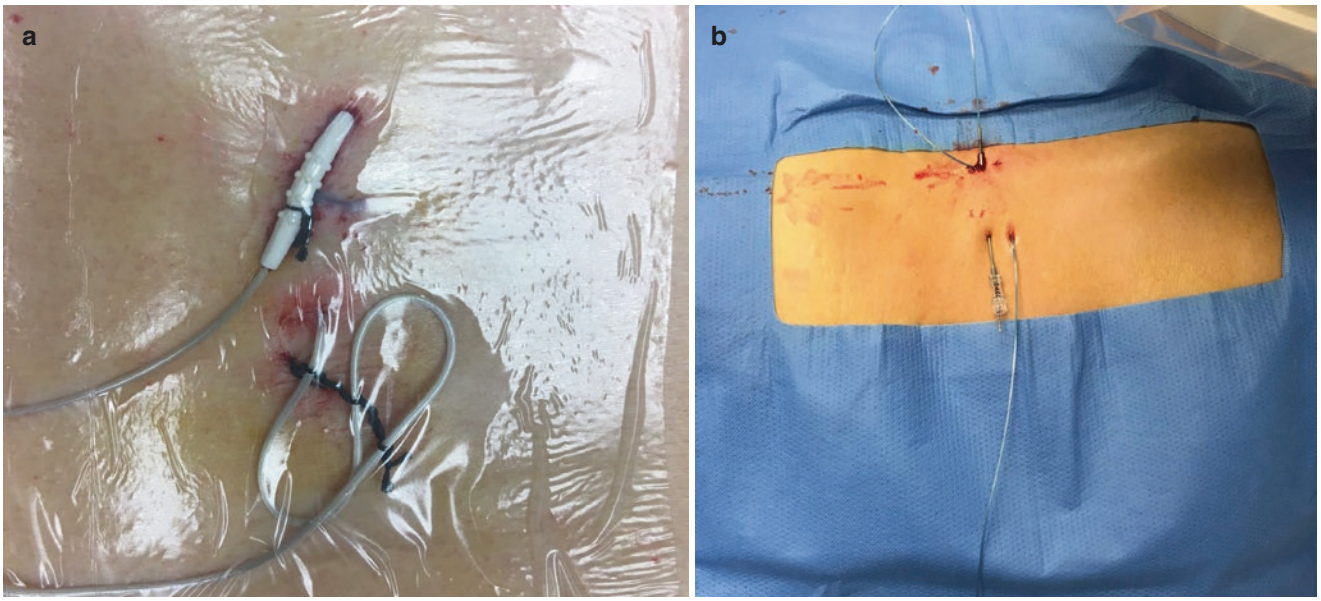

Fig. 72.4 Photographs of various externalized lead skin anchoring techniques at the conclusion of lead placement. (**a**) Examples of industry-offered anchor secured to the skin (left) vs directly tied lead in number-eight-shape form to prevent migration. (**b**) Two epidural leads tunneled about 4–5 cm under the skin for possible prolonged trial. Notice that second epidural needle is inserted in a small stab wound to facilitate tunneling

formed, assisted by electrocautery to achieve hemostasis, until the fascia overlying the spinous processes/supraspinous ligament is exposed. A Weitlaner retractor may assist during the dissection as well as Tuohy needle placement.

Next, the first epidural needle is inserted lateral to the palpable spinous processes at a 30–45° angle, directed toward the midline of the target interlaminar space. This insertion site should be within the superior one third of the incision in order to allow adequate space below for the insertion of the second needle. Contact may be made with the lamina just caudad to the intended interlaminar space in order to gauge depth. The needle is further advanced utilizing lateral fluoroscopy and a loss of resistance technique until the epidural space is reached. The stimulator lead is then advanced through the needle into the epidural space, which is confirmed by posterior location of the lead on lateral fluoroscopy. The lead is then advanced under continuous AP fluoroscopy to the intended vertebral level. Next the second epidural needle is placed either ipsilateral and inferior to the first needle or on the contralateral side (Fig. 72.5). Proper entry into the epidural space is confirmed as described for the first needle, and the second lead is advanced in parallel to the first lead.

The epidural needles are removed leaving the leads in place. The leads are then secured to the underlying fascia using the SCS manufacturer provided anchoring devices and non-absorbable suture (Fig. 72.6). A final fluoroscopy image is captured to ensure no lead migration occurred with needle removal and anchoring of the leads.

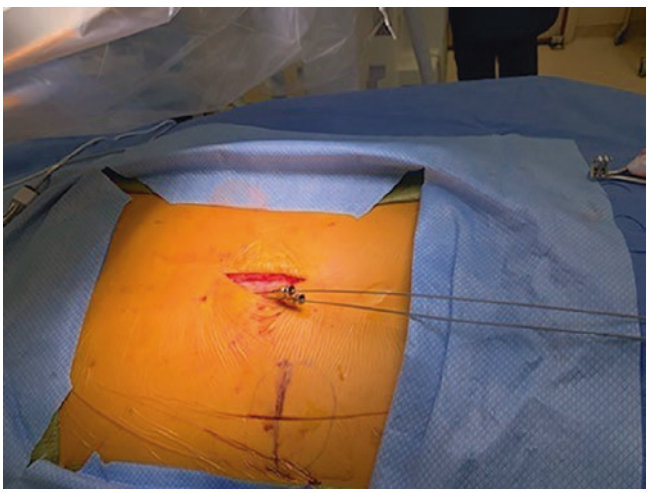

Fig. 72.5 Tuohy needles and epidural lead placement during the percutaneous SCS system implantation. Two needles in final position, inserted ipsilaterally and vertical to one another, with SCS leads advanced through those needles

It is essential to discuss IPG location with the patient prior to implantation. It is vital to examine the potential site of implantation while the patient is in the sitting position, paying attention to the location of the iliac crest, the inferior aspect of the ribs, as well as the level at which the patient's belt-line typically lies to avoid postoperative discomfort. The desired site is marked preoperatively before proceeding to the operating room.

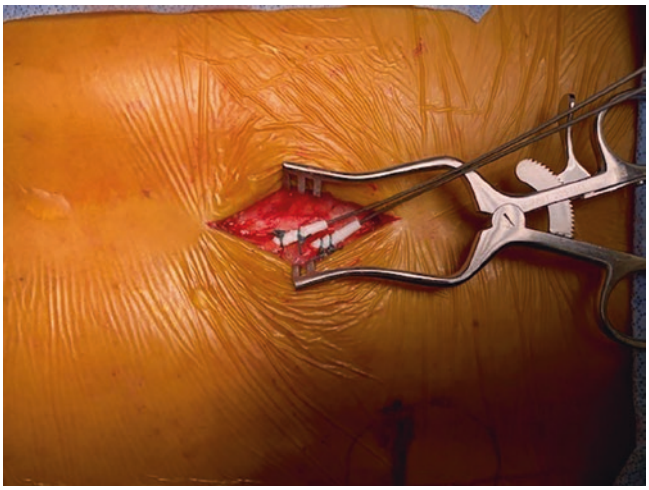

Fig. 72.6 Two cylindrical leads anchored utilizing manufacturer provided anchor devices and non-adsorbable suture

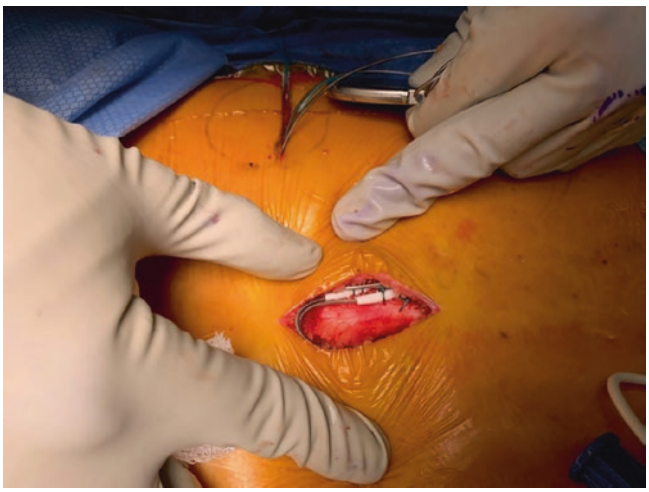

Fig. 72.7 Retention loop created within the midline incision intended to decrease/prevent incidence of lead migration

After injecting 1% lidocaine with 1:200,000 epinephrine, a 4 cm horizontal incision is made using a scalpel blade. Blunt dissection and electrocautery are utilized to create a pocket that is no more than 2 cm below the surface of the skin. This ensures the ability to effectively charge the device. A sizer may be utilized to check that the pocket size will fit the IPG.

Once the pocket has been created and hemostasis has been achieved, the leads must be tunneled from the midline incision to the pocket. The tunneling device may be bent slightly to ensure the ability to remain superficial while tunneling. It is inserted through the tissue at the inferior aspect of the midline incision and directed toward the IPG pocket. Care should be taken to palpate the tip of the tunneler as it is advanced to prevent deep penetration. Once the tunneler emerges in the IPG pocket site, the two SCS leads are fed into the tunneling device until they are visualized on the IPG pocket side of the tunnel. Enough lead may be left within the midline incision to create a retention loop in order to reduce the risk of lead migration (Fig. 72.7). The sheath is then pulled through the tunnel and removed through the IPG pocket incision.

Next, the electrodes are cleaned with a wet and dry Raytec and inserted into the IPG. An impedance check is performed, and the leads are locked into place.

Copious irrigation of both incisions is performed prior to closure. The excess length of SCS lead is looped behind the IPG as it is placed inside the pocket. Non-absorbable suture is utilized to secure the IPG within the pocket. The wounds are closed in a layered fashion using simple interrupted absorbable suture. The skin is closed using a running absorbable suture or staples.

Complications

SCS device-related infection rate has been estimated to be 3.11% based on a logistic regression (n = 6615) over a 12-month postoperative period. It is most commonly seen at the IPG pocket site. Lead migration has been reported as a possible complication of SCS, occurring at a rate of approximately 2.1–12% of implants depending on the reference source. Pocket site discomfort has also been noted with some frequency. Other less common complications that have been described include electrode fracture, IPG failure, and CSF leak following dural puncture, among others.

Clinical Outcomes

Traditional 0–1200 Hz

Traditional SCS has been demonstrated to be a superior treatment option for patients suffering from failed back surgery syndrome when compared to conventional medical management or reoperation. In addition to traditional SCS being more efficacious in improving pain scores and quality of life, it was also found to be less costly than long-term medical management or reoperation for failed back surgery syndrome. Low-frequency SCS has traditionally been reliant on paresthesia coverage overlapping the distribution of a patient's pain. However, some studies have demonstrated superior response to sub-perception stimulation at less than 1200 Hz when compared to traditional tonic stimulation. A multicenter, prospective, randomized controlled trial that enrolled 70 subjects and randomized to either receive supra-perception or sub-percep-

tion stimulation at less than 1200 Hz demonstrated non-inferiority to subthreshold stimulation. 39% of subjects with sub-perception settings and 29% with supra-perception settings had a greater than or equal to 50% reduction in their overall pain scores at 3 months post-activation as compared with baseline. Notably, there has been evidence to suggest the contrary that there is no significant difference between patient response to sub-perception versus supra-perception. Attempts have been made to elucidate the exact threshold frequency of stimulation at which patients have an improved response. In a prospective RCT, mean low back pain VAS scores were compared in patients suffering from failed back surgery syndrome who were treated with either sham stimulation, 1200, 3030, or 5882 Hz. There was no significant difference found between the sham stimulation group, 1200 Hz, and 3030 Hz groups. Patients in the 5882 Hz group did experience a greater reduction in VAS score. The overall trend in study results appears to be in favor of higher-frequency stimulation. However, the exact stimulation frequency threshold in which the greatest results are obtained has yet to be determined.

Burst

Burst stimulation is another recently studied waveform with significant evidence to support its use. A "burst" is characterized by a five-pulse train with internal frequency of 500 Hz delivered at 40 Hz utilizing a passive recharge pattern and waveform. It was first described by De Ridder et al. in 2013. This early study examined 15 patients that were randomized to placebo, tonic, or burst stimulation groups. Patients receiving burst SCS experienced improvement in back, limb, and general limb pain VAS scores by 51%, 53%, and 55%, respectively, whereas the tonic SCS group and placebo group experienced 30%, 52%, and 31% and 18.9%, 11.7%, and 10.9% improvement, respectively. Deer et al. conducted a large RCT (SUNBURST) in which 100 patients were randomized to receive traditional or burst stimulation for 12 weeks. At the conclusion of the 12-week period, the patients were then crossed over to comparing stimulation group 12 additional weeks. Burst stimulation was found to be superior to traditional tonic stimulation, with slightly better average pain scores ($P < 0.017$). Of note, at 1 year post-implant, 68.2% of patients preferred burst stimulation.

10 kHz

There is substantial, Level 1 evidence to support the efficacy and durability of high-frequency (10 kHz) SCS for treating back and leg pain and superiority of high-frequency stimulation to traditional stimulation. In a large prospective randomized controlled trial published in 2015 (SENZA-RCT), the response rates of 171 patients who were implanted with either a 10 kHz or traditional low-frequency 2–1200 Hz SCS system to treat back and leg pain were compared. At 12 months post-implant, both groups had sustained response, but the 10 kHz therapy provided in 80% of patients more than 50% of pain relief, versus less than 50% responders in the traditional SCS group. Mean back pain was reduced from VAS of 7.4 ± 1.2 to 2.5 (67% decrease) in the 10 kHz group versus being reduced from 7.8 ± 1.2 to 4.3 (44% decrease) in the traditional SCS group. These results were noted to be durable through a 24-month follow-up, with 76.5% ongoing responder rate in the 10 kHz SCS group versus 49.2% responder rate in the traditional SCS group. Evidence for the efficacy of 10 kHz SCS has been further substantiated by two large randomized prospective studies on chronic nonsurgical back pain patient population and those with neuropathic pain in peripheral neuropathy in diabetes. Both studies substantiated superiority of 10 kHz SCS to conventional medical management in control of chronic pain with consistent responder rate exceeding 80% of treated patients. This therapy is currently the only SCS modality supported by three large prospective RCTs. Furthermore, a recent elegant retrospective study measured 10 kHz SCS's ability as rescue therapy in patients who were previously implanted and failed conventional, low-frequency SCS systems. Out of 105 patients analyzed, 81% of patients experienced greater than 50% pain relief after transitioning from the traditional (less than 1200 Hz) to 10 kHz SCS.

Closed Loop

Levi et al. conducted a multicenter, double-blind, parallel-arm, RCT which enrolled 134 patients. The participants were randomized to the control group which received fixed output, open-loop stimulation or the experimental group which received ECAP-controlled closed-loop spinal cord stimulation. The primary outcome measure was the percentage of patients that obtained greater than 50% pain relief in the back and legs at 3 and 12 months. The closed-loop group had 82.3% responder rate at 3 months, and 83.1% at 12 months, compared to the open-loop group, which had a 60.3% and 61% responder rate at 3 and 12 months, respectively (20). Closed-loop SCS stimulation is not currently available for commercial use, but preliminary data shows promising results for sustained and even improved response rates over time.

Conclusions

Spinal cord stimulation for control of chronic pain recently became the fastest advancing therapy in the area of neuromodulation. The main reason is an introduction of novel waveforms in SCS therapy providing better long-term out-

comes than long-standing traditional 0–1200 Hz SCS. Closed-loop, 10 kHz, and differential target multiplex therapies for the first time in well-conducted RCTs demonstrated in more than 80% of patients 50% or more pain relief and very few procedural or long-term complications of therapy. There is a strong interest and much ongoing basic science and clinical research exploring novel approaches and waveforms to simplify techniques of electrical stimulation and improve the outcomes. Currently, the future of SCS for control of chronic pain looks bright and very promising.

Suggested Reading

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