Cervical Spine

Minimally Invasive and Open Surgery

Pier Paolo Maria Menchetti
Editor

Second Edition

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“To my family”

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Anatomy of the Cervical Spine

1

Rosario Barone, Fabio Bucchieri, Giulio Spinoso, Lawrence Camarda, and Francesco Cappello

Introduction

The anatomy of the region of the cervical spine is one of the most complex among the topographical regions of the human body (Fig. 1.1). The aim of this chapter is to provide an overview about it, without any claim to be exhaustive in a few pages. Therefore, we invite the readers to refer to specialized anatomy textbooks for further, necessary insights.

The vertebral column, or spine, is divided into cervical, thoracic, lumbar, sacral and coccygeal regions and consists of 32–35 vertebrae, separated from each other by intervertebral discs (except for the first cervical segment, the atlas, and the sacrococcygeal segments) [1, 2]. The cervical region consists of seven vertebrae, the thoracic region of 12 vertebrae, the lumbar region of five vertebrae, the sacral of five vertebrae, which are fused together, and the coccygeal segment comprises four or five vertebrae. Functionally, the vertebrae form a single structure designed to maintain an upright posture and balance countering gravity, enabling locomotion and every other kinetic movement against applied force and resistance [3, 4]. Therefore, the two basic requirements of the spine are rigidity, for static efficiency and protection of the spinal cord and spinal nerves, and flexibility, for the kinematics of the spine.

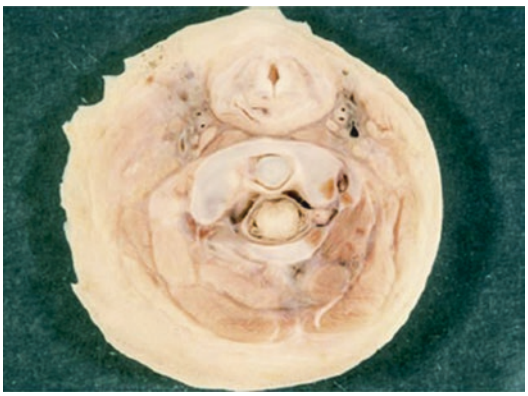

Fig. 1.1 Cross section of the neck. The greatest part of the section is occupied by muscles. The anterior part houses the viscera. Vertebrae are in the central part. See text for further details

The human spine consists of physiological curves, cervical and lumbar lordosis, thoracic and sacral kyphosis, which greatly increase the resistance to axial compression, compared to a rectilinear column (up to ten times). The cervical region (cervical vertebrae C1–C7), whose length varies from 15 to 16 cm in women and from 18 to 19 cm in men, of which 1/4 is represented by the

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intervertebral discs, presents a lordotic and mobile anteriorly convex curvature of about 36° that varies according to the conformation of the other spinal curves, and is more accentuated in the elderly [5–7]. The cervical vertebrae support the head, while allowing great freedom of movement and providing protection to the upper section of the spinal cord, vertebral arteries, and cervical and brachial plexus.

Cervical vertebrae (Fig. 1.2), according to their anatomical and functional characteristics, can be grouped into:

- A superior segment made up by vertebrae C1–C2
- An inferior segment made up by vertebrae C3–C7

Superior Cervical Spine

The C1 is also known as atlas and the C2 as axis, and their characteristics differ greatly from those of the other vertebrae. Atlas is a ring-shaped vertebra with no body, consisting of two lateral masses, an anterior arch with a roughened anterior tubercle and a posterior arch with a posterior tubercle as a rudimentary spinous process. Both lateral masses present a concave superior articular facet, which articulates with occipital condyles, and a flat inferior articular facet, which articulates with the axis. The medial side of the lateral masses presents a minute tubercule to which the transverse ligament of the atlas attaches and divides the vertebral foramen into two parts: the anterior part holds the dens of the axis and the posterior one holds the spinal cord. Axis is the second cervical vertebra, whose structure is similar to the inferior vertebrae. Axis' most distinctive characteristic is a prominent conic process, called odontoid process or dens. It is located vertically on the superior surface of the vertebral body and presents an anterior articular facet and a posterior one. The anterior articular facet articulates with the articular facet of the anterior arch of the atlas, and the posterior articular facet articulates with the transverse ligament of the atlas. Its triangular vertebral foramen is smaller than that of the other cervical vertebrae.

Inferior Cervical Spine

The inferior cervical spine is composed of five vertebrae (C3–C7) with similar morphogenetic characteristics. They consist of a smaller articular

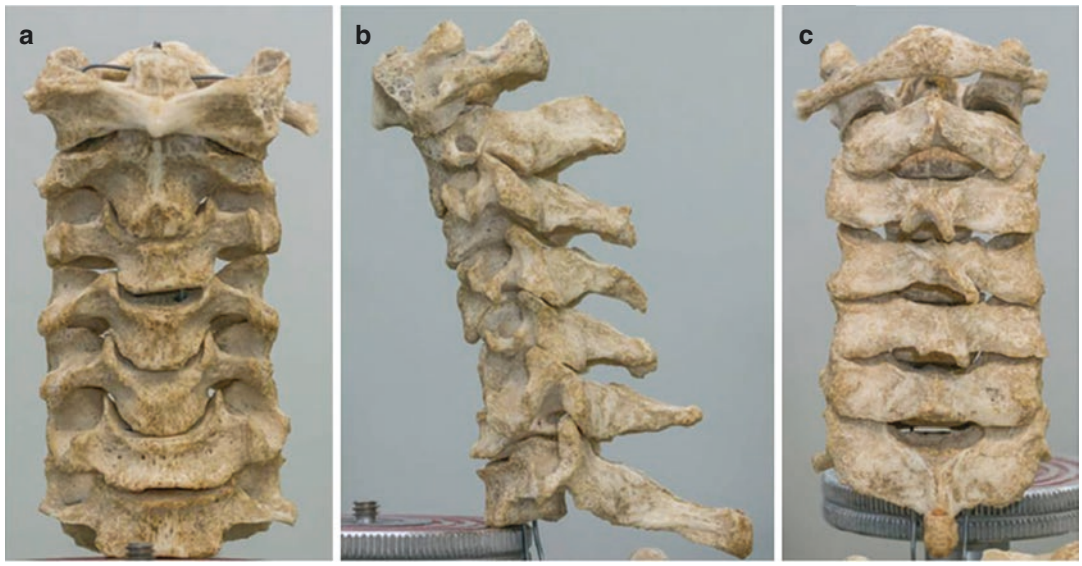

Fig. 1.2 Cervical vertebrae: anterior (**a**), lateral (**b**) and posterior (**c**) view. See text for further details

body developed in a transversal direction. The body has two facets, superior and inferior. Two uncinated processes are located at the lateral extremities of the superior surface, facing upwards. Two pedicles are directed backward, and transverse processes are situated anteriorly. Each transverse process consists of ventral and dorsal bars, which are linked by a bony lamina called costal (or intertubercular) lamella and terminate as tubercles. The transverse foramen is a hole formed by the costal lamellae and the bars of the two transverse processes. The transverse foramina form the transverse canal, crossed by vertebral vessels and vertebral nerve. Superior and inferior articular processes are located posteriorly to the pedicles and articulate with the upper and lower vertebra. The superior articular process ends with a backward-facing articular facet, while the inferior one ends with a superoposteriorly oriented articular facet. Spinous processes are short and bifid, except for the seventh cervical vertebra which is called "prominent", and whose spinous process is long, not bifid, and palpable at the base of the neck. It is an important landmark for locating the upper and lower vertebrae. The seventh vertebra also has a smaller transverse foramen through which the vertebral vein passes. The sixth cervical vertebra is characterized by the anterior tubercle of the transverse process, which is more developed and prominent (Chassaignac tubercle): an anatomical landmark for the common carotid (ligature), the inferior thyroid artery and the vertebral artery.

Cervical Spine Joints and Muscles

The function of the joints located between vertebrae is to allow for spine mobility. Vertebrae forming the different parts of the spine have joints that allow diverse spine movements, such as rotation, inclination, flexion, and extension of the head. The cervical spine can be divided into upper cervical spine, which topographically includes the inferior edge of the occipital bone, atlas and axis, and lower cervical spine, which extends from the inferior edge of the axis to the superior edge of the first thoracic vertebra.

The atlanto-occipital joints allow flexion-extension movements on the sagittal plane and little inclination on the frontal plane. They encompass the occipital condyles and the concave superior articular facets on the lateral masses of the atlas. These joints, called bicondylar joints, have two planes of movement and two degrees of freedom, and are composed of two bones and a fibrous capsule which attaches to the edges of the occipital condyles and of the superior articular facet of the atlas, and is covered by a synovial membrane. The articular capsule is thicker posteriorly and enforced by the anterior (and posterior) atlanto-occipital membrane. The anterior atlanto-occipital membrane connects the anterior margin of the *foramen magnum* to the upper border of the anterior arch of the atlas, while the posterior atlanto-occipital membrane connects the posterior margin of the *foramen magnum* to the upper border of the posterior arch of the atlas [8]. The anterior atlanto-occipital membrane comprises a fibrous band from which the anterior longitudinal ligament originates. The posterior atlanto-occipital membrane is crossed by the first cervical nerve and by the vertebral artery. The first pair of spinal nerves emerge between the occipital condyle and the atlas, forming the cervical plexus. This joint enables about 50% of the flexion and extension movements of the head by itself.

The atlas-axis joint consists of three synovial joints with no intervertebral disc between C1 and C2. It is formed by the atlas, two axis lateral joints, an atlas-axis medial joint and the dens. The lateral atlas-axis joint is a diarthrosis of arthrodial type (planar joint), formed by the inferior articular facets of the lateral masses, which are slightly concave, and by the superior articular facets of the axis, which are slightly convex. The articular capsules are inserted on the lateral edges of the articular cartilages and enforced anteriorly by the anterior longitudinal ligament and posteriorly by the *ligamenta flava*. The medial atlas-axis joint is a pivot joint between the posterior facet of the anterior arch of the atlas, covered by articular cartilage, and the articular facet of the dens, also covered by articular cartilage. The joint is stabilized posteriorly by a fibrous lamina, the trans-

verse ligament, which surrounds the dens and extends between the two lateral masses of the atlas, forming an osteo-fibrous ring consisting of the anterior arch of the atlas anteriorly and the transverse ligament posteriorly. The superior longitudinal band arises from the upper margin of the transverse ligament, inserting on the basilar part of the occipital bone. The inferior longitudinal band arises from inferior edge of the transverse ligament, attaching onto the posterior face of the axis. The transverse ligament and both the longitudinal bands compose the cruciform ligament [9, 10].

The articulations of the inferior cervical spine are plane joints (arthrodial joints) where intervertebral discs are located between the vertebral bodies. This region is specialized in flexion–extension movements and lateral flexion: lateral flexion is allowed by the C3–C5 joint, while flexion-extension is allowed by the C4–C6 joint. The inferior cervical spine joints have the same characteristics along the entire spine, except for the sacrum. The junctions between vertebral comprise intervertebral discs and zygapophyseal joints between the superior articular processes of a vertebra and the inferior articular processes of the one below. The joints between vertebral bodies are synarthroses of the symphyses type, formed by the articular surface of two adjacent vertebral body, covered by both hyaline cartilage and fibrocartilage, and the intervertebral disc. The discs of the cervical tract are thicker anteriorly, thus contributing to form the cervical lordosis and enabling the flexion-extension and lateral flexion of this section. Discs and vertebral bodies are linked and stabilized by the anterior and posterior longitudinal ligaments. The anterior longitudinal ligament is a fibrous tape which arises from the basilar part of the occipital bone and from the anterior tubercle of the atlas. It runs down along the anterior surface of the vertebral bodies to the anterior surface of the sacrum. The posterior longitudinal ligament arises from the body of the axis, running down along the posterior surface of the vertebral bodies to the sacrum.

The intervertebral disc is composed of a central part called nucleus pulposus and a peripheral part called annulus fibrous. Nucleus pulposus consists of a deformable and incompressible gel composed of mucopolysaccharides and water. The hydrophilic properties of proteoglycans depend on quantity and quality of mucopolysaccharides. The characteristics of the nucleus pulposus enable vertebral resistance to mechanical loading, whilst the fibrocartilaginous ring, which is made up by annular fibres, allows for flexion movements. These structural features of the discs are very important, especially following spinal trauma because hernias of the nucleus pulposus into the *specus vertebralis* may occur with compression of nerve roots. The zygapophyseal joints are arthrodial joints that enable slipping movements between the superior and inferior vertebral processes of two contiguous vertebrae. The superior articular processes, covered by hyaline cartilage, run up and backward, whilst the inferior ones run down and forward, and are covered by a thin articular capsule that connects to the edge of the articular cartilage.

The Table 1.1 shows the organization of the cervical muscles. The muscles of the head and neck execute movements of the head and the neck: flexion, extension, lateral deviation, and rotation. Different positions and types of insertion allow these muscles to accomplish different movements. Another role of the neck muscles, with the thoracic ones, is to maintain an upright position of the head and neck.

Vessels

Arteries

Arterial supply to the neck is provided by the external carotid and subclavian arteries [11].

1. External carotid artery branches into:
   (a) Occipital artery, which surrounds the external edge of the mastoid process, sliding under the sternocleidomastoid, *longissimus capitis*, *latissimus capitis*, splenius and semispinalis, ending on the occipital muscle; the occipital artery passes medially to the hypoglossal and laterally to the accessory nerve.

Table 1.1 Spine muscles

Intrinsic Muscles of the Cervical Spine: attached to the vertebrae only	Extrinsic muscles: attached into both the cervical spine and other skeletal segments	Neck proprii muscles (excluding cervical spine)
Interspinales muscles	Spinalis capitis muscle	Suprahyoid muscles: – Digastric – Stylohyoid – Mylohyoid – Geniohyoid
Intertransversarii cervici muscles	Semispinalis capitis muscle	
Multifidus muscle	Longissimus capitis muscle	
Brevis rotator muscles	Iliocostalis muscle	
Longus rotator muscles	Rectus capitis posterior major muscle	
Semispinalis capitis muscle	Rectus capitis posterior minor muscle	Infrahyoid muscles: – Sternohyoid – Omohyoid – Thyrohyoid – Sternothyroid
Spinalis cervicis muscle	Obliquus capitis superior muscle	
Longissimus cervicis muscle	Rectus capitis anterior muscle	
Longus colli	Rectus capitis lateralis muscle	
Obliquus capitis inferior muscle	Levator scapulae muscle	Sternocleidomastoid muscle
	Splenius capitis muscle	Platysma muscle
	Splenius cervicis muscle	
	Serratus posterior superior muscle	
	Rhomboid minor muscle	
	Trapezius muscle	

(b) Superior thyroid artery, which reaches this gland.

2. Subclavian artery branches into:
   (a) Vertebral arteries, which originate between the scalenus anterior and longus colli, running back into the *foramen transversarium* of the sixth cervical vertebra, and through the transverse channel, and arise from the hole of transverse process of the atlas forming a medially concave curve, surrounding the lateral mass creating a second anteriorly concave curve, then running through the posterior occipital-atlas membrane, dura mater, arachnoid and finally reaching the cranium, crossing the foramen magnum. The second curve is located in a triangle surrounded by the *rectus capitis posterior major* and *obliquus capitis superior* and *inferior* muscles. At its origin, the vertebral artery is crossed by the inferior thyroid artery while the seventh cervical transverse process, the inferior cervical ganglion and ventral rami of the seventh and eighth cervical spinal nerves lie posteriorly. In addition, the vertebral arteries pass by the spinal nerves at the opening of the intervertebral holes. In fact, osteoarthritis of uncinate processes can compromise normal functions of both the arteries and nerves.
   (b) Thyrocervical trunk, one of its most important collateral branches being the ascending cervical artery. This artery passes by the *scalenus anterior* muscle and the phrenic nerves; and from it arise muscular branches and segmental medullary arteries; the ascending cervical artery ends at the third cervical vertebra.
   (c) Costocervical trunk, one of its most important collateral branches being the deep cervical artery. This artery runs between the transverse process of seventh cervical vertebra and the neck of first rib to end in the deep muscles of the nucha.
   (d) Transverse cervical artery, the outermost of the subclavian collaterals. It arises from the interscalene portion and contributes with its branches to supply the muscles of the neck and nucha, as well as the trunks of the brachial plexus.

Veins

The venous network of the neck comprises, superficially, the anterior jugular veins system, posterior jugular veins system and external jugular veins system, and in the deeper layers, the thyro-linguo-pharyngo-facial trunk of the internal jugular and subclavian veins.

Lymphatics

The lymphatic network of the cervical spine is composed of a superficial lymphatic network that receives afferents from superficial cervical lymph nodes and of a deep system that form the jugular trunk. The right jugular trunk ends in the jugulo-subclavian junction between the internal jugular and subclavian veins, also called the venous angle. On the left side it usually joins the thoracic duct, or it may enter the internal jugular or subclavian vein.

Innervation

The cervical spine is mainly innervated by the cervical plexus. The cervical plexus is composed of the anastomosis of ventral branches of the first four cervical nerves and by an anastomotic branch of fifth one, forming the *ansa cervicalis*. The plexus is located deeply close to the transverse process of cervical spine. It is surrounded by: laterally, the vessels and nerves of the neck; anteriorly, the deep lymphatic nodes of the latero-cervical chain; and medially, the glossopharyngeal, vagus, accessory and hypoglossal nerves, and superior and middle cervical ganglia.

From the cervical plexus arise:

- Superficial branches that make up the superficial plexus; one of them is a small occipital nerve that arises from C2 to C3 and innervates the skin of the lateral portion of the occipital region.
- Deep muscular branches that compose the deep cervical plexus. In particular, the descendent cervical nerve (C1–C2–C3), which is near the descendent branch of the hypoglossal and phrenic nerve, by the scalenus nerve. This is a landmark to locate the phrenic nerve to perform surgery.

The nerves of the nape include the posterior rami of eight cervical nerves. The first cervical ramus, called suboccipital nerve, is a motor nerve. This nerve emerges between the posterior arch of the atlas and the vertebral artery, then enters into the occipital triangle delimited by the *rectus capitis posterior major*, *obliquus capitis superior* and *inferior* muscles. It also contributes to form the cervical plexus with an anastomotic branch directed towards C2: in the triangle, this nerve passes by the vertebral artery and its branches. The second ramus arises above the lamina of the axis. This nerve, once it reaches the inferior edge of *obliquus capitis inferior* muscle, divides into two branches, one more lateral and thinner, the other one ticker and more medial which innervate the muscles close to them. The medial branch, running up, ends in a gap between the *semispinalis capitis* and trapezius muscles. After going over the nuchal line of insertion of the trapezius, it runs superficially under the name of greater occipital nerve, innervating the skin of the occipital region. The greater occipital nerve is involved in a syndrome called greater occipital neuralgia. In particular, an anatomical variation of the suboccipital nerve, which gives off a cutaneous nerve that connects to either the greater or lesser occipital nerve, may pay a role in this condition. The lateral branch of the second cervical dorsal ramus innervates muscles. The third cervical dorsal ramus and its branches contributes to the innervations of nuchal muscles. The branches from the fourth to the eight are thinner than the others and arise from the trunk by the exit of the intervertebral foramen and are divided into lateral motor and medial mixed branches. The medial branch of the fourth ramus, after giving rise to the motor branches, supplies the *splenium capitis* muscle and trapezius, and becomes the third occipital nerve providing cutaneous sensation to a small portion of the skin of the nape.

Nerve branches originating from the brachial plexus also contribute to innervate this region (Figs. 1.3 and 1.4). The brachial plexus is formed by the last four cervical nerves, one anastomotic branch of the fourth cervical nerve and an anastomotic nerve of the first thoracic nerve. Some cranial nerves also contribute to the innervations of the neck: the hypoglossal nerve forms an anastomosis

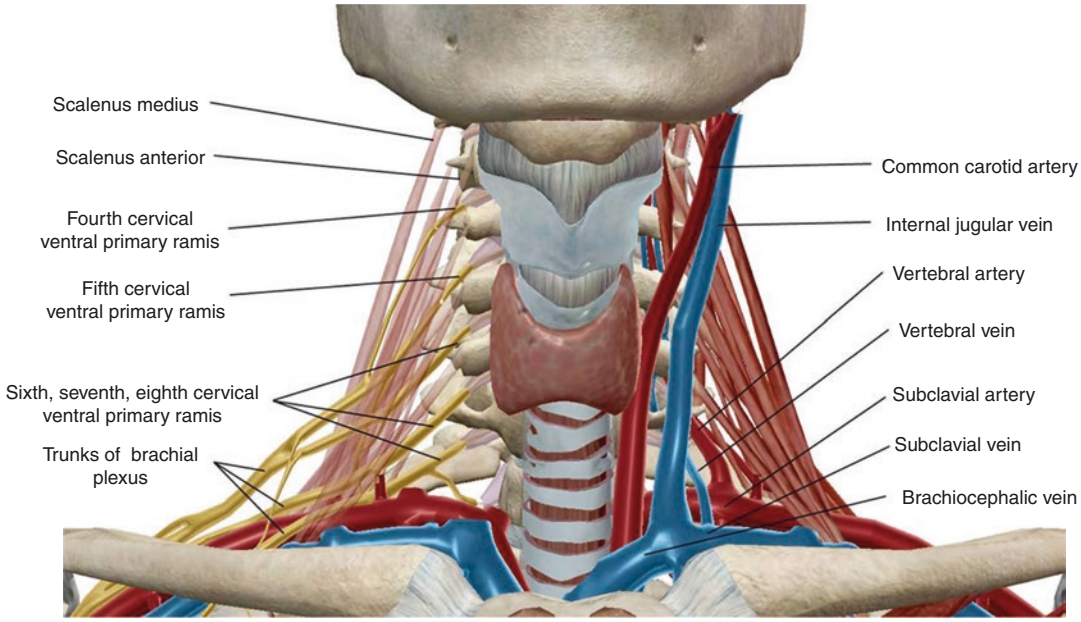

Fig. 1.3 3D reconstruction of the anterior view of the neck. On the right, most of the deep relations of some branches of the brachial plexus with the scalene muscles (in fade). On the left, the scalene muscles and the course of some arteries and veins. This figure was created with an educational 3D medical app "Visible Body, Human Anatomy Atlas"

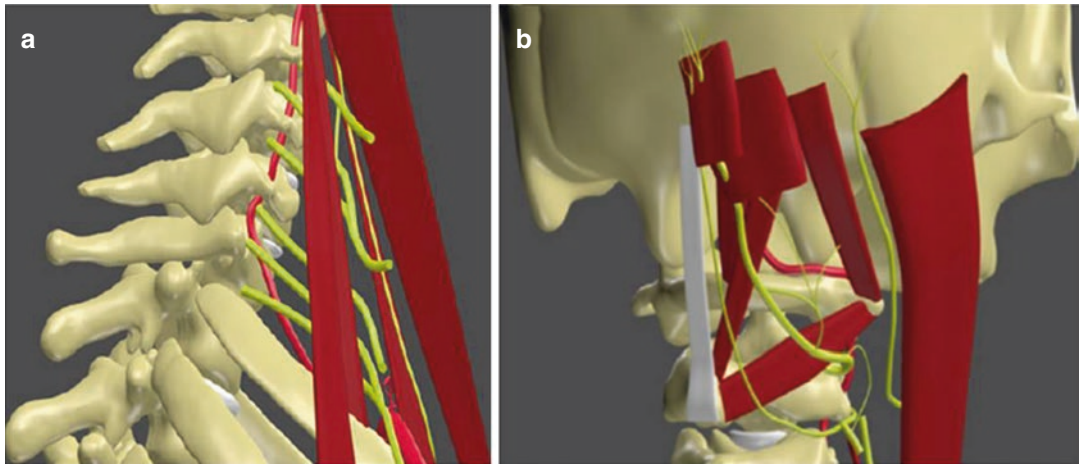

Fig. 1.4 3D reconstruction of the brachial plexus and its relationship with subclavian and dorsal scapular arteries. (**a**) Lateral view of the cervical spine, (**b**) Posterior view of the cervical spine and skull. See text for further details. This figure was obtained from the previous edition of this book

with the discontent cervical nerve. From this anastomosis branches for the subdeltoid muscles and the accessory nerve arise. After arising from the jugular foramen, it divides into an inner branch, which is near the vagus nerve, and into an external branch that runs down laterally in an oblique direction. After reaching and innervating the posterior face of the sternocleidomastoid muscle, it continues its path in the upper clavicular region, reaching the anterior edge of the trapezius.

Vertebral Canal

The neural space that contains the spinal cord and its cover membrane can be found across the osteo-fibrous plane. One of the ways to access the vertebral canal is laminectomy.

The epidural space lies between the spinal dura mater and the tissues which surround the vertebral canal. It is closed cranially by the fusion of the dura mater with the periosteum, which surrounds the occipital hole, and caudally by the sacrococcygeal ligament which encloses the sacral hiatus. The roots of the spinal nerves with vessels and epidural nerves run into the epidural space. The epidural adipose tissue spreads around the dural sac and accumulates mostly laterally and posteriorly in the recesses between the *ligamenta flava* and the dura, where the epidural space is wider. The dura mater is a very strong fibrous membrane that extends like a cylindric sac from the occipital hole to the second sacral vertebra, where it ends as the *conus medullaris*, and continues as the *filum terminale externum* that inserts on the coccyx.

Arachnoid mater surrounds the spinal cord and is separated from the dural sac by a tiny space called the subdural space. The arachnoid mater includes the subarachnoid space that separates it from the pia mater. The subarachnoid space extends for all the length of the spinal cord and is filled with fibrous filaments where vessels run. This space contains cerebrospinal fluid, and it is crossed by the roots of the spinal nerves which are separated by the denticulate ligaments. Pia mater is a very thin fibrous membrane that covers the spinal cord and from which denticulate ligaments and anterior and posterior septa arise. Pia mater is located near the epineurium of the spinal nerves and it is rich in blood vessels, lymphatic vessels and sensitive nerve terminations which arise from sensitive corpuscles.

The spinal cord is divided into neuromeres from which spinal nerves originate. These nerves are covered by dura mater and come through the intervertebral foramen. Spinal cord is made up peripherally by bundles of myelinate nerve fibres, which are organized in the anterior, lateral and posterior cords that are delimited anteriorly by the anterior median fissure and the dorsal median sulcus, and laterally by the ventral nerve rootlets and the dorsal nerve rootlets. Centrally, the spinal cord presents the neural component organized in two symmetric lateral masses that are linked centrally by the grey commissure which is crossed by the central canal or ependymal canal. Two lateral masses present a ventral horn that contains motor neurons and a dorsal horn that contains sensitive afferents. In the thoracic-lumbar region, there is a lateral protrusion that contains neurons of the sympathetic system. Cervical cord presents a bulge in C4–T1, where the brachial plexus is located. Here, the anterior horn is larger than the ones in the superior neuromeres, whereas the posterior horn is thinner than those of the superior ones [9, 10].

Topographic Organization

The structural components of the neck are covered by a system of fasciae: the superficial, medial and deep cervical ones. These fasciae surround the structures along their path, contributing to form spaces in the neck in which the laryngopharyngeal channel, tracheal channel and the vascular space with the vagus nerve and neck vessels (carotid and internal jugular vein) are located. The distribution of fasciae on different planes allows to delimit some regions with specific features. The antero-lateral region is located below the cutaneous and subcuticular plane and is formed by two different planes. The first one is composed of the sternocleidomastoids and suprahyoid muscles surrounded by superficial cervical fascia. The second one is made up of omohyoid and infrahyoid muscles, covered by medial cervical fascia. Posteriorly can be found the prevertebral, deep fascia surrounding vertebral muscles: *longus capitis*, *longus colli*, *rectus capitis anterior*, *rectus capitis lateralis*, *scalenus*, *splenius capitis* and *splenius cervicis*. In the posterior region of the nape, under the skin and on the subcutaneous plane, five different planes can be found (Fig. 1.5): the first one is made up of the trapezius muscle covered by superficial cervical fascia, the second one is made up of the *splenius*

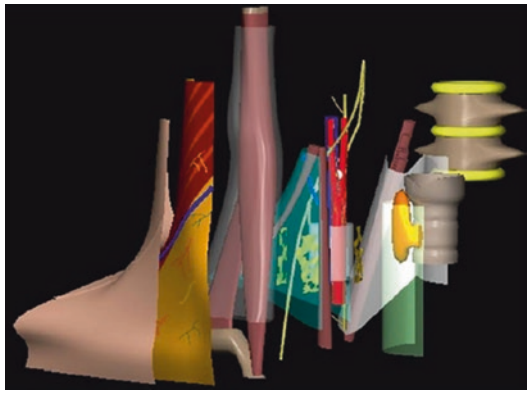

Fig. 1.5 3D reconstruction of the layers, from the skin to the vertebrae, that can be found during a dissection of the neck. See text for further details. This figure was obtained from the previous edition of this book

capitis, *splenius cervicis* and *levator scapulae* muscles and by the superior fascia of the rhomboid and *serratus posterior* muscles; the third one is made up of three muscles which are orientated in a longitudinal direction: laterally the *longus colli*, with the longus capitis in intermedial position and the *semispinalis capitis* located medially. The fourth plane is made up of the *rectus capitis posterior minor*, *rectus capitis posterior major*, *obliquus capitis superior*, *obliquus capitis inferior* and cervical spine intrinsic muscles. Finally, the fifth plane is made up of the occipital bone and the cervical spine with its junctions. This plane is connected with the cervical part of the sympathetic system comprising the sympathetic branches of the superior, medium and inferior cervical ganglia, located near the deep cervical fascia.

The superior cervical ganglion lies anteriorly to the transverse process of the second cervical vertebra; the middle cervical ganglion may be missing in some subjects, but when present it lies anteriorly to the fifth and sixth cervical vertebra; the inferior cervical ganglion lies anteriorly to the 7th cervical vertebra and it may be fused with the first thoracic cervical ganglion, forming the stellate ganglion. The nerves which form the visceral plexa of the neck arise from all these ganglia: the superior cervical ganglion corresponds to the transverse processes of the second and third cervical vertebrae, laterally to the pharynx, anteriorly to the longus capitis muscle and posteriorly to the vessels and nerves of the neck. The medium cervical ganglion and the stellate ganglion contribute to form the *ansa subclavia* of Vieussens.

Dissection Anatomy

When performing a dissection or surgery on the muscle-fascial planes of the neck, one must pay close attention, when the skin and the underlying plane are prepared, to the third occipital nerve, the great occipital and the occipital artery that appear on the top of the trapezium muscle: upon reaching the second and the third plane in the space between the trapezium and splenium, one must take great care to identify the small occipital nerve which is located laterally to the splenium muscle and the third occipital nerve, next to the nuchal ligament. In this space, the great occipital nerve and the occipital artery can be easily found between the *splenium capitis* and *semispinalis capitis* muscles. When the underlining plane is prepared, attention must be paid to the vertebral artery, the suboccipital nerve and the dorsal root of the second cervical nerve with its ganglia. Another space that should be highlighted is the one located between the trapezium and the elevator of the scapula, where the vascular pedicle and the accessories nerve run. Finally, when scalene muscles are prepared, attention must be paid to the trunks of brachial plexus, subclavian artery and dorsal scapular arteries.

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2 Functional Anatomy and Biomechanics of the Cervical Spine

Alessandro Ramieri, Giuseppe Costanzo, and Massimo Miscusi

Introduction

This chapter reviews for the second time the function and biomechanics of the cervical spine after the first edition of the book published in 2016. Starting from the basic concepts, it analyzes in detail the normal cervical motion and the spine stability under physiological conditions. Thereafter, there has been few new researches on these topics. But, we were able to search more recent papers on upper cervical ligament functions [1], musculoskeletal models [2, 3], finite element models applied to the functional spine unit [4] and range of motion of the intervertebral discs [5]. Last but not least, another important topic has been more deeply focused in recent years: the cervical sagittal balance/alignment and its influence on the spinal range of motion. This fundamental issue will be specifically addressed.

Summary of Biomechanical Terms Used in the Text

Translation: motion of a rigid body in which each straight line through any pair of its points remains parallel to itself.

Rotation: motion of a rigid body in which each straight line does not remain parallel but develops an angle of rotation between initial position (A1–B1) and final position (A2–B2) (Fig. 2.1).

Centre of Rotation or instantaneous axis of rotation (IAR): It is a fixed point obtained by the intersection of the line perpendicular to the

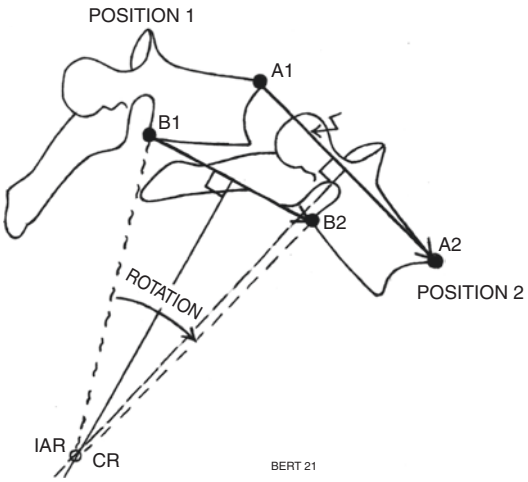

Fig. 2.1 Vertebral motion, defined by translation vectors A1–A2 and B1–B2, is a rotation about the instantaneous axis (IAR). IAR is obtained by the intersection of the lines perpendicular to the motion plane and the translational vectors

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motion plane and the translational vector (e.g. A1–A2 see Fig. 2.2).

Degrees of freedom: They define the position of an object in the space by a number of independent coordinates organized in a coordinate system (i.e. Cartesian system).

Range of motion (ROM): extent of physiological movement, measured from a neutral position of the spine, when the internal stresses and the musculature effort to hold the posture are minimal. Physiological ROM can be divided into two parts: neutral zone and elastic zone.

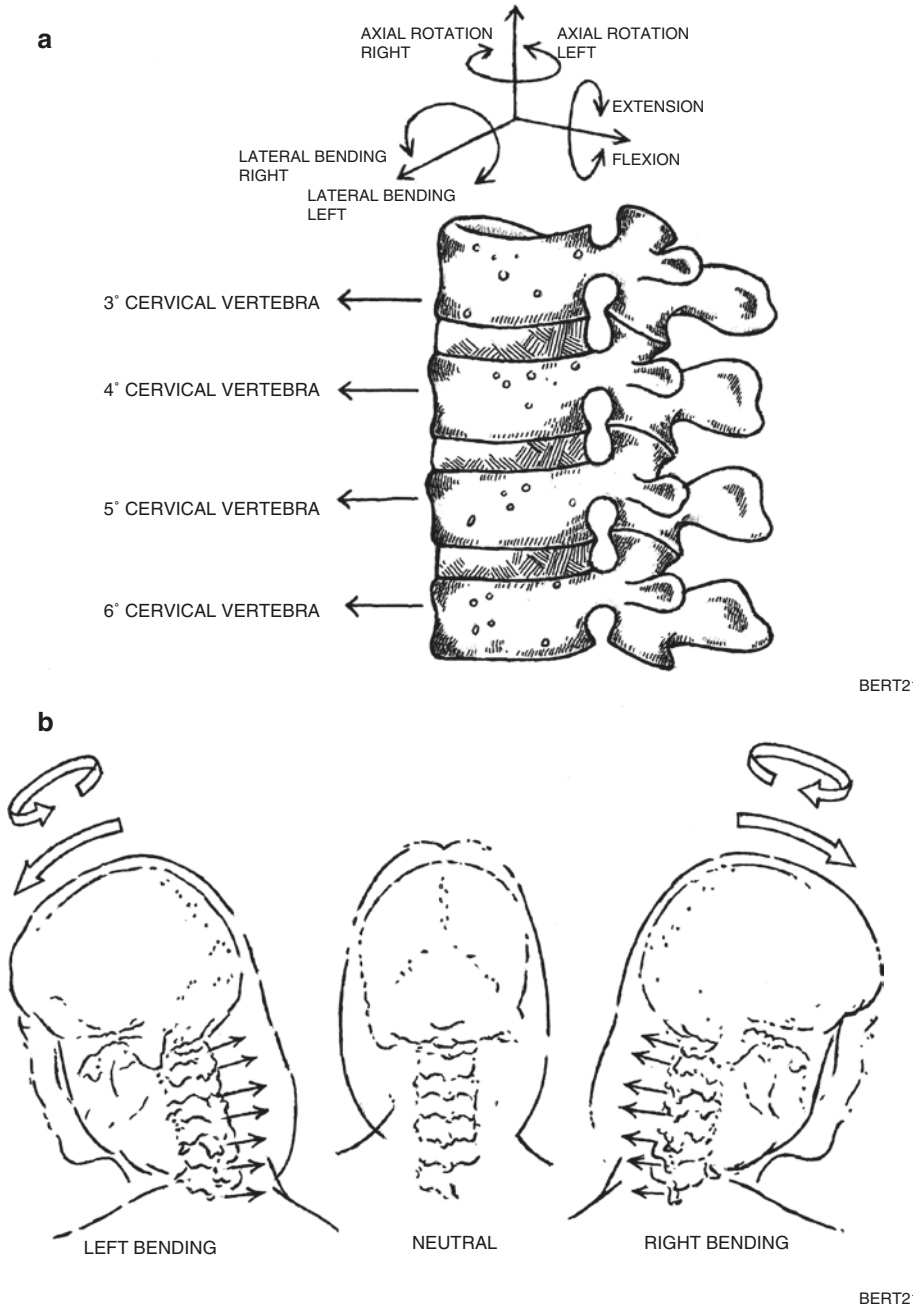

Fig. 2.2 (**a**) Lower cervical finite element and forces applied. (**b**) Coupling phenomenon i.e. axial rotation of the spinous processes away from the concave side of the direction of the lateral bending

Neutral zone (NZ): first part of ROM within which displacement of a biological tissue is produced against minimal internal resistance. The NZ is defined by flexibility of the tissue.

Elastic zone (EZ): That part of ROM, measured from the end of the NZ up to the elastic limit, in which displacement is produced against internal resistance. The EZ represents the stiffness of the biological tissue.

Plastic zone (PZ): It is the zone of trauma and failure of the biological tissue. When the elastic limit is reached, permanent deformation/displacement can occur. The tissue will fail if further forces are applied.

Force: any action that tends to change the state of rest or motion of a body to which it is applied. Force is a vector quantity that has magnitude and direction. The unit of measure for the magnitude of force is newtons (N).

Work and Energy: work is the product of force time distance and energy is the work done. The unit of measure is newton-meter (N-m) or joule (J).

Stress: it is the force applied to an object (load).

Strain: it is the response of the object to the stress (deformation).

Viscoelasticity: It is the time-dependent property of a such material to rate of loading or deformation. Bones, ligaments, tendons, passive muscles demonstrate viscoelastic behavior. Because of this, their stress-strain curves are dependent on the rate of loading.

Elastic modulus (Young's modulus): it is the ratio between stress and strain, representing the elastic properties of a body that is stretched or compressed.

Coupling: It is the phenomenon whereby a movement of the spine on a plane obligates a separate motion about another axis (see Fig. 2.1).

Basic Concepts

To analyze, understand and correct the various malfunction of the spine, it is essential recognize his normal function. The head-neck system consists of seven cervical vertebrae and has a unique anatomy and motion to accommodate the needs of a highly mobile head-torso transitory zone. From a kinematical point of view, this system is very complex. Normally, the spine mainly functions as a coupled unit, and neck kinematics can be analyzed by studying head movement relative to the upper body. Cervical motion in every plane is checked by anatomic restraints that protect the spinal cord and accompanying vascular structures. The head can be regarded as a platform that houses the sensory apparatus for hearing, vision, smell, taste: the cervical spine constitutes a device that support this sensory platform, moving and orientating it in the three-dimensional space. Any disturbance of anatomy and mechanical properties can lead to clinical symptoms. Also age-related changes can modified cervical anatomy and alignment, drastically reducing range of motion [6, 7].

Principles of Kinematics

While physical principles and laws rule the entire spine, kinematics examines the normal range of motion (ROM) of each segment in the three-dimensional space, without the influence of other internal or external forces. Normally, this range is expressed by translation and rotation in three planes. Too much motion should be considered as structural damage of the spine, while too little motion may accompany stiffness and pain. Motion segment is the "Functional Spine Unit" or FSU that consists of two adjacent vertebrae and the interconnecting soft tissue, devoid of musculature. To ameliorate the study of the FSU function in the lower cervical spine, finite element models were generated. More recently, some authors [4], using CT, developed a three-dimensional finite element model (FE model) from C3 to C6 level. Applying a force of 1 Newton/metro (Nm) and a flexion-extension analysis, they evaluated range of motion of the lower cervical spine and the load distribution across the intervertebral discs (Fig. 2.2a), comparing their outcomes with the literature values. Some years ago, we studied the same issues in the thoraco-lumbar and lumbar discs by the von

Mises criterion or von Mises stress [8]. In flexion, the greatest flexible behavior was recorded in C5–C6, while C3–C4 and C4–C5 were stiffer. In extension, C3–C4 was flexible while C4–C5 very stiff and C5–C6 slightly stiff. In the lateral bending, all levels were very flexible, conversely during the axial rotation. In flexion, disc stress distribution was lower in all levels, in extension was similar, in the lateral bending was higher as during the axial rotation. In summary, in flexion and extension loading, it was observed that the C3–C4 level and C5–C6 level exhibit more range of motion in comparison with C4–C5 level. In the lateral bending, all the level from C3 to C6 contribute the same physiological motion. In the axial rotation, the range of motion from C3 to C6 levels were observed and it was found that the C4–C5 level is little higher in comparison with the C3–C4 level. This FE model will be useful for future studies on the disc stresses during physiological or extreme motion.

Forces applied to the spine can always be separated into component vectors: indeed, a vector defines the force oriented in a fixed and well-defined direction in the three-dimensional space. If a force vector acts on a lever, known as "moment arm", a bending moment is generated. This bending moment applied to a point in the space causes rotation about an axis: this axis is defined as "the instantaneous axis of rotation" or IAR. Using the standard Cartesian coordinate system for the spine (X,Y and Z axes), 12 potential movements about the IAR can be detected: 2 translational and 2 rotational along or around each axes. When a cervical segment moves, there is an IAR passing through or close to the vertebral body (*see below*). In other terms, 6 degree of freedom exist about each IAR, i.e. each FSU has 6 degrees of freedom. When an FSU is loaded, the motion behavior is affected by the choice of the point at which the load or torque is applied. Balance point is achieved when an axial load creates nearly pure compression and the out of plane is minimized. Any loading out of this point causes a moment and induces bending. More specifically, if an axial load is applied at the point of the IAR, the result is an equal (in magnitude) but opposite (in direction) reaction force (Newton third's law) that may symmetrically deform the vertebral body. Instead, if the load is applied in a plane at some distance from the IAR, bending moment is generated by an interaction of forces and asymmetric deformation of the vertebral body can occur in any plane. This phenomenon introduces the concept of "couple", a pair of forces, equal and opposite, having a lines of action that are parallel but that do not coincide. If the resultant is zero, no translational movement occurs and the FSU is in equilibrium. Rotation can occur if the couple is unopposed. As stressed by Benzel [9], couple is different from "coupling". This term indicates the phenomenon whereby a movement of the spine obligates a separate motion about another axis. In the lower cervical spine is typical that the lateral bending results in axial rotation of the spinous processes away from the concave side of the direction of the bend. This is due to the orientation of the facets and the presence of the uncovertebral joints (Fig. 2.2b).

The IAR can be considered similar to the COR (centre of rotation), first described by Penning [10] and more recently used by Smith [5]. This method describes the motion behavior of the vertebral body respect to the adjacent one, defining the axis and the point about which vertebrae rotate. IAR or COR should be considered dynamic because nearly any motion of the FSU is a coupled motion. Infact, as a spinal movement occurs, the point about which adjacent vertebrae rotate varies during the motion. An extension of the COR approach provides the helical axis of motion (HAM) that defines a three-dimensional movement when rotation is superimposed on translation. The resultant component of motion is described by the translational movement vector called HAM.

Functions of the Cervical Spine

The craniovertebral junction (C0–C1), the upper (C1–C2) and the lower cervical spine (C3–C7) have distinct anatomic and kinematic features and must be described separately. Fundamental to understanding the behavior of the cervical

spine is an appreciation of how each segment contributes to the total function in relation to its specific characteristics. For descriptive purposes, the cervical spine can be divided in five units, each with unique morphology that determines its kinematics and its percentage of contribution to the entire function. In anatomical terms, the units are: the occipito-cervical junction (C0–C1), the atlas (C1), the axis (C2), C2–C3 junction, C3–C7 levels. Main anatomical characteristics of the upper compared to the lower cervical spine include the absence of the intervertebral disc, the absence of the ligamentum flavum, and the distinct shape between C1 and C2.

Occipitoatlantoaxial Complex (C0–C2)

Biomechanically Relevant Anatomy

The foramen magnum (FM) is located in the occipital bone, which has three parts:—the squamosal portion in the dorsal aspect;—the clival portion located anteriorly; the condylar part, connecting these two portions, that includes the occipital condyle, posterior margin of the jugular foramen and the hypoglossal canal. Occypital condyle receives the C1 lateral mass. The most posterior margin of the foramen magnum is called "opisthion", while the "basion" represents its most anterior midline. C1 differs from the other cervical vertebra by being a ring shape and lacks a vertebral body and a spinous process. It has two thick lateral masses which are situated at the anterolateral part of the ring. C2 has many attributes of the more caudal cervical vertebrae, but its transitional nature dictates a complicated anatomy configuration. Odontoid process represents its rostral extension: this fundamental structure originates by the developmental fusion process between the caudal part of the C1 somite and the cranial part of the C2 somite. The odontoid process begins to fuse with the body of C2 at 4 years of age and at 7 years of age the fusion is completed. In about one-third of adults, a remnant of cartilaginous tissue will be present between the odointoid and the C2 vertebral body. The pars interarticularis projects from the lamina in a rostral and ventral direction to attach to the lateral masses. C1 allows the odontoid process of C2 between its lateral masses. In other terms, odontoid occupies the usual position of the vertebral body [11, 12]. Odontoid articulates with the dorsal aspect of the ventral portion of the C1 arch by an anterior oval facet and posteriorly with the transverse ligament that is attaches to the tubercles on the medial aspect of the C1 ring. The lateral masses of C1 articulate with the occipital condyles and C2 by kidney-shaped articulations, while C2 is directly connected to the occiput by the alar and apical ligaments and the tectorial membrane. In a sense, C1 functions as an intermediate "fulcrum" that regulates movement between the occiput and C2 [13]. The special arrangements of the occipitoatlantoaxial ligaments are remarkable to allow for complex motion, yet provide stability to this area. Infact, the capsules of the C1–C2 lateral facets surround the articular surfaces and are reinforced by ligaments and lateral fibers that pass in a rostral direction from the tectorial membrane [14]. There are ligaments between the C1 anterior arch and the odontoid and behind it: the cruciate ligament that has a vertical component from the rim of the FM to the midportion of the C2 vertebral body; the apical ligament from the rim of the FM to the tip of the odointoid process; the alar ligaments from the lateral anterior rim of the FM to the dorsal aspect of the odontoid. The cruciate ligament is considered one of the most important ligament of the human body and its rupture, identified by high resolution MRI, can lead to craniocervical instability. As stated by Quercioli [15], pioneer of occipito-atlanto-axial biomechanics, the integrity of the transverse and occipitoaxial ligaments is the essential condition for maintaining a stable odontoid process in the axis.

Normal Kinematics

The occipitoatlantoaxial complex is the most mobile of the axial skeleton [16]. This functions as a single unit, considering C1 as a *cradle* for the occiput and C2 as a *washer* between the skull and

the cervical spine. This complex is responsible for 40% of total cervical flexion-extension and 60% of total cervical rotation.

C0–C1 Joint

The atlanto-occipital joint allows flexion-extension and minimal degrees of lateral flexion and rotation, while the atlanto-axial joint works in coupled, rotation plus minimal lateral bending (Table 2.1). C1 flexion-extension (e.g. nodding movements) are possible because the C1 superior articular surfaces are concave whereas the occipital condyle are convex. Flexion is achieved by the condyles rolling forwards and sliding backwards across the anterior walls of the notches. A converse combination of movements occurs in extension. Axial forces apply by the mass of the head and the muscles prevent upward displacement, maintaining the condyles nestled on the floor of their cavities. The total normal range of flexion-extension at the atlanto-occipital joint has been described as having a mean value between 14° and 35°, a range from 0° to 25° or a mean value of 14° with a standard deviation of 15° [17, 18]. During these movements, a minimal anterior or posterior translation was observed [19]. Moreover, other restraints to flexion are fixed by the impaction against the skull base, tension of the posterior muscles and capsules and contact of the submandibular tissues agaist the throat. Extension is limited by compression of the sub-occipital muscles against the occiput. Rotation and lateral flexion of atlanto-occipital joint are extremely limited, approximately 5°, due to the depth of the atlantal notches in which the occipital condyles rest. In biomechanical terms, during axial rotation to one side, the contralateral occipital condyle contacts the anterior wall of its atlantal notch, while ipsilateral condyle impacts the corresponding atlantal posterior wall. Therefore, joint stability stems largely from the depth of the C1 notches: their side walls prevent lateral translation, the front and back walls prevent anterior and posterior dislocation.

The IAR for the C0–C1 articulation has not been defined, although x-axis is considered to pass through the mastoids and the z-axis to be 2–3 mm above the tip of the odontoid process [20].

Table 2.1 Movements allowed in the craniocervical region, according to Benzel [9]

Joint	Motion	ROM (degrees)
C0–C1	Flexion/extension	25
	Lateral bending (unilateral)	5
	Axial rotation (unilateral)	5
C1–C2	Flexion-extension	25
	Lateral bending (unilateral)	5
	Axial rotation (unilateral)	40

C1–C2 Joint

The atlanto-axial complex is composed by two lateral facet joints, the unique atlantodental articulation and the joint between the posterior surface of the odontoid and the transverse ligament. Stability at this highly mobile articulation is primarily dependent on ligamentous structures, because the lateral joint capsules, in contrast to that of the atlantooccipital joint, are loose. Its foremost rule is to bear the axial load of the head and atlas and to transmit this load into the remainder of the cervical spine. For this function, C2 laterally presents wide superior articular facets that support the lateral masses of C1 and form the lateral atlanto-axial joints. The centrally-placed odontoid process acts as the "pivot" and forms the atlanto-axial median joint. In order to achieve axial rotation, the anterior arch of the atlas spins and glides around the pivot. Therefore, this movement is anteriorly restrained by the median atlanto-axial joint and inferiorly by the lateral atlanto-axial joints, that also subluxate. In particular, the ipsilateral lateral mass of C1 slides backwards and medially, while the contralateral lateral mass slides forwards and medially (Fig. 2.3a). During axial rotation, the lateral atlanto-axial joints glide across their osseous flat surfaces. But the articular cartilages both of the atlantial and the axial facets are convex in the sagittal plane, rendering the joint biconvex in structure. In addition to these anatomical features, the spaces formed anteriorly and posteriorly by the detachment of the articular surfaces,

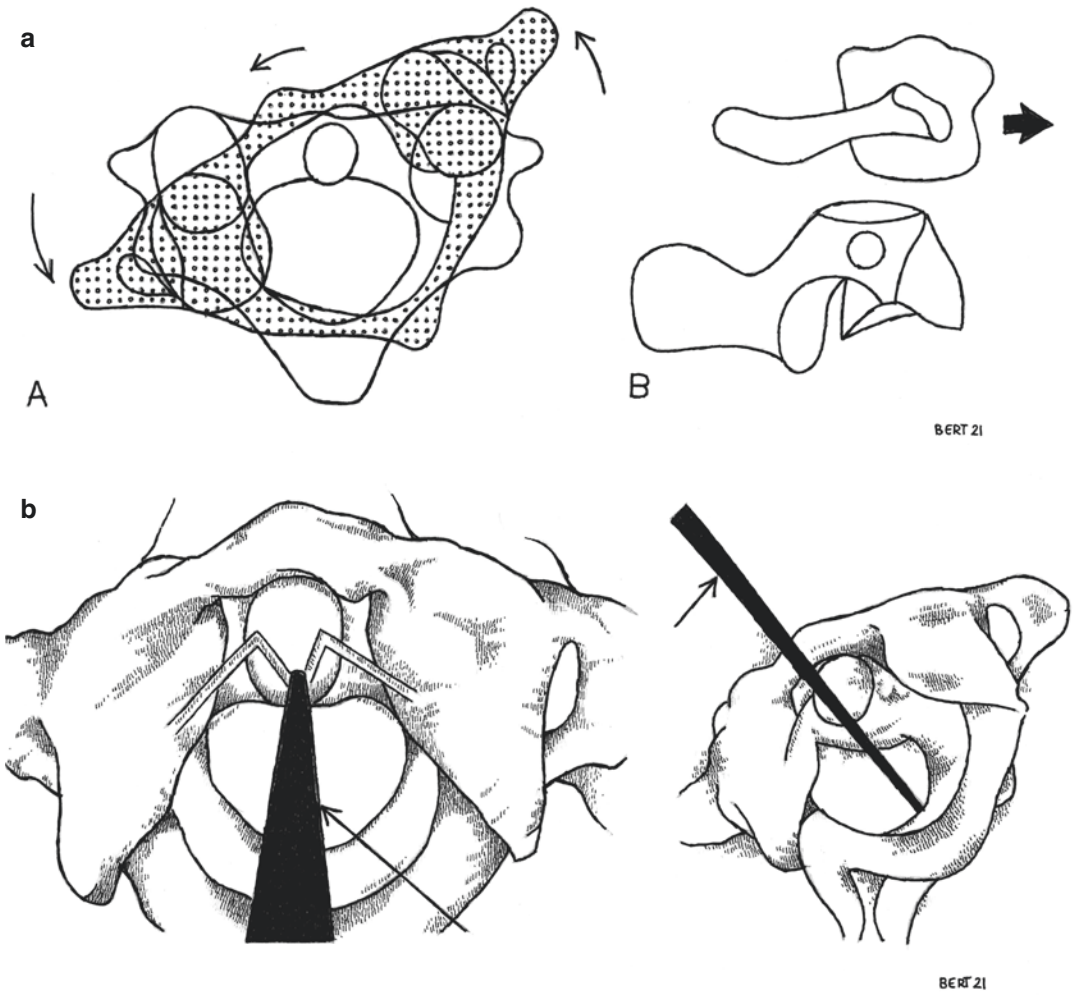

Fig. 2.3 (**a**) C1–C2 axial rotation. A (axial view): the anterior arch of C1 glides around the odontoid process; B (sagittal view): the lateral mass of C1 subluxates forwards across the superior articular process of C2. (**b**) Length and moment arm (arrows) of the AL ligaments in neutral position and their variations during left AR

are filled by large intra-articular meniscoids: these serve to keep a film of synovial fluid on articular surfaces. In the neutral position, the summit of the atlantial convexity rests on the convexity of the axial facet, i.e. the apex of the C1 inferior facets is balanced on the apex of the C2 superior facets. As the C1 rotates, the ipsilateral atlantial facet slides down the posterior slope of the respective axial facet, while the contralateral one slides down the anterior slope of axial facet. Upon reversing the rotation, C1 rises back onto the summit of the facets. In conclusion, C1 axial rotation requires anterior displacement of one lateral mass and a reciprocal posterior displacement of the opposite lateral mass. If the articular cartilages are asymmetrical , a small amplitude of lateral bending may accompany axial rotation: the side of coupling depends on the bias of asymmetry [21], but however this movement is considered negligible [22].[1] Principal structures that restrain axial rotation are the alar ligaments and

[1]Although not a physiological movement, lateral bending at the C1–C2 joint is assessed by some manipulative proceedings. While C2 superior articular facets slope inferiorly and laterally, C1 lateral translation must be accompanied by ipsilateral side bending. Minimal lateral translation can occur during lateral flexion of the entire cervical spine. Restraints to this motion are the contralateral alar ligament and the impaction of the contralateral lateral mass onto the lateral aspect of the odontoid process.

the joint capsules: at the limits of rotation, the lateral atlanto-axial joints are almost subluxated. The normal ranges of rotation of C1 on C2 are varied (see Table 2.1): 32° and 56.7 in cadaveric studies [23, 24], over 75° using x-ray [25] and 43° using CT [26] in healthy adults. Recently, some authors [27], measuring in vivo by MRI normal kinematics of the upper cervical spine in neutral position and during Dvorak's flexio-rotation test, reported respectively 77.6° and 65° of C1–C2 segmental rotation. Sagittal plane motion (flexion-extension) in C1–C2 has been reported by several authors to be on average of 11° and may be facilitated by the rounded tip of the odontoid process [28–30]. More recently, this value has been confirmed by a descriptive study based on computer-aided measurements from lateral flexion-extension radiographs [31]. The biconvex nature of the atlanto-axial articulation means that cervical spine flexion and extension often create motion in the direction opposite that being experienced in the atlas [32]. In other terms, when the entire cervical spine is flexing, C1 extends and when the cervical spine extends, C1 flexes. This paradoxical coupling motion is possible because C1 is sandwiched between the head and C2, undergoing a passive movement. Infact, in neutral condition, C1 is balanced precariously on the convexities of its articular cartilages, but when an axial compression load is applied, C1 starts to move. If the line of compression is anterior to the balance point, C1 moves into flexion. On the contrary, when the line is posterior, C1 will extend. This paradox is governed essentially by the muscles acting on the head and it can be observed even if the rest of the cervical spine is flexed. The restraint to C1 flexion/extension have never been formally established. No ligaments are disposed to limit this motion: essentially C1 is free to flex or extend until the posterior arch hits the occiput or the neural arch of C2, respectively. C1 backward sliding is limited by the impaction of its anterior arch against the odontoid process, while forward slipping is prevented by the transverse and the alar ligaments. Subluxation or dislocation implies destruction of both ligaments. Up to 3 mm of anterior translation of C1 on C2, as measured by anterior atlanto-dental interval (AADI), is considered normal. As the AADI increases to 5 mm or greater, the transverse and accessory ligaments are disrupted. When the transverse ligament is damaged, also rotary dislocation can occur at 45° of rotation, rather than 65° in normal condition.

The IAR for the C1–C2 sagittal plane motion is located in the region of the middle third of the odontoid. During axial rotation, it is located in the centre of the odontoid.

Because of the little data available regarding several suboccipital ligaments such as occipito-atlantal, atlantoaxial, and cruciform ligaments, Beyer et al. [1] recently used in vitro anatomical models of the upper cervical spine to identify the suboccipital ligaments, trying to assess their biomechanical characteristics and changes during sagittal flexion-extension or transversal axial rotation-lateral bending displacements. New data regarding the C0–C1, C1–C2 and C0–C2 range of motion were added (Table 2.2). Ligaments data on length variations and moment arm amplitude during flexion-extension (FE), neutral position (NP) and axial-rotation (AR) were also available: length alteration was >25% in FE, while a greater moment arm variation was found for the posterior atlanto-occipital ligament (OAMP); Considering the overall AR range (right and left) the anterior and posterior atlanto-

Table 2.2 Upper cervical spine: Range of motion values during flexion-extension and axial rotation reported by Beyer et al. [1]

	C0–C1	C1–C2	C0–C2
Flexion			
Middle	5.8 (3.2)	4.4 (3.8)	9.7 (3.1)
Maximal	11.0 (3.9)	6.3 (4.9)	15.4 (7.4)
Extension			
Middle	4.1 (1.5)	3.6 (2.9)	10.8 (5.6)
Maximal	8.3 (3.8)	7.6 (3.5)	19.2 (5.7)
Axial rotation			
Left			
Middle	1.1 (0.9)	15.2 (3.1)	16.8 (3.9)
Maximal	2.1 (1.8)	24.8 (3.7)	27.6 (5.0)
Right			
Middle	1.5 (0.9)	13.0 (8.3)	15.9 (6.4)
Maximal	4.0 (1.6)	25.0 (7.6)	27.7 (8.7)

axial ligaments (AAA and AAP) and the alar ones (AL) displayed the largest length changes (Fig. 2.3b). The main findings of this study suggest that suboccipital ligaments, other than alar and transverse ligaments (TR), may play a substantial role in the function and stability of the upper cervical spine in FE and AR. Suboccipital ligaments are associated with the mechanical stabilization of the C0–C2 segment, mainly in the sagittal and in the transversal planes. In particular, AL injuries can occur with rotation attitude of the neck, whereas transverse ligament and posterior atlanto-occipital membrane are more affected during frontal collisions. Length alteration would be accounted as a substantial factor during the clinical examination as well as the therapeutic procedure such as manual mobilization or post-traumatic immobilization positioning of the upper cervical spine. Length increase occurred more likely in axial rotation (in both directions) for AAP, from ipsi-to contra-lateral rotation for AAA and from contra-to ipsi-lateral rotation for AL. For sagittal motion, length increases from extension to flexion for OAMP, AAP and TR, and in the opposite direction for AAA, AL, tectorial membrane (TM), and anterior atlanto-occipital ligament (OAMA).

C2–C3 Junction or Vertebroaxial Joint [33]

Although the C2–C3 junction is often considered together with the rest of the lower cervical spine, this joint offers some peculiar differences in morphology. A pillar view of the region[2] reveals that the body of the axis looks like a deep "root" into the typical cervical spine (Fig. 2.4), securing the upper cervical spine in the remaining cervical column. Moreover, in such view, the unique orientation of the C2–C3 zygoaphophysial joints is seen: they are inclined medially, by about 40° [33], and downward [34], while they are typically transversal at lower levels. The processes of both sides form a notch, cradling the inferior articular processes of the axis. This architecture implies that C2–C3 joints operate in a different manner from that of lower cervical segments, nevertheless further differences are open to discovery. The main kinematic expression occurs during axial rotation plus lateral bending. According to Mimura et al. [25], C2–C3 axial rotation is similar to that of the lower segments, with mean value of 7° compared to 5, whereas lateral flexion is significantly different, with mean value of −2° at C2–C3 compared to 6 at C3–C4 and C4–C5 levels. In other terms, instead of tilting towards the same side, C2–C3 joint rotates towards the direction of the side bending (Fig. 2.5). The IAR for the C2–C3 sagittal motion is located lower than in the other cervical levels due to the lower location of the superior articular process of C3 (see below Fig. 2.7).

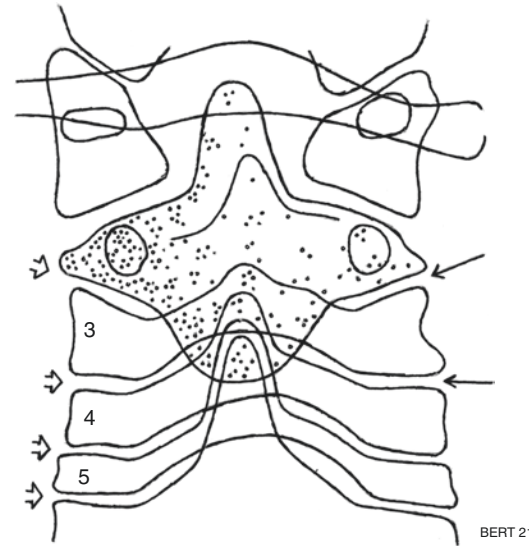

Fig. 2.4 Pillar view of the upper cervical spine, showing the unique morphology of C2 and architecture of the C2–C3 joints (see text)

[2]The "pillar view" is a cervical postero-anterior radiographic projection achieved by directing the beams upwards and forwards essentially along the planes of the lower zigoapophysial joints.

Fig. 2.5 (**a**, **b**) (coronal and sagittal views): axial compression force is applied during lateral bending of the head; (**c**) (sagittal views): the inferior articular process of C2 slides downward and backword along the superior articular process of C3; (**d**) (coronal view): C2 rotates towards the direction of the side bending due to the backward articular displacement

Mid and Lower Cervical Spine (C3–C7)

Biomechanically Relevant Anatomy and Kinematics

The middle and lower cervical spine segments have essential similar anatomic and functional features and can be effectively represented by the FSU: two vertebral bodies, the disc, the facet joints with associated ligamentous and capsular structures. Each vertebra consists of three pillars that forms three parallel columns for the load-bearing functions of the cervical spine. The anterior pillar is the vertebral bodies, which are united by interposed discs to form the anterior column. The two posterior columns are formed by the articular pillars: the superior and inferior facets are opposed to one another and united by a joint capsules. Their specific orientations allow to bear the weight of the segments above and prevent dislocation. The facet joints are the principal restraints against forward translation. End-plates of the vertebral bodies, that are stacked on one another, separated by the intervertebral disc, are not flat as in the lumbar spine. In the sagittal plane, they appear gently curved, tilting greatly downwards and forwards. The anterior inferior border of each vertebral body forms a lip that hangs, like a hook, towards the anterior superior edge of the vertebra below. As a result, the plane of intervertebral disc is not perpendicular but somewhat oblique and supports flexion-extension motion as cardinal movement of these typical cervical segments. The body supplies the strength and support for two-thirds of the vertebral compression load. The upper surface is typically concave from side to side and convex in the antero-posterior direction. On its lower surface, it is convex from side to side and concave in the antero-posterior direction. Also, the upper projection on the lateral superior surface of the vertebra below is called "the uncus". These bilateral uncinate processes are related intimately with the convex lateral inferior surfaces of the upper vertebral body and form the uncovertebral joints or joints of Luschka. The exact rule of these joints is not known: they would seem to prevent posterior dislocation and limit lateral bending.

The "saddle shape" structure thus described is clearly visible in the sagittal plane, while, by a section taken obliquely through the posterior end of vertebral body along a plane parallel to the plane of the facet joints, the concave superior surface formed by the body and its uncinate processes that receives the convex inferior surface can be assessed. The appearance is that of an ellipsoid joint and suggests that rocking could occur side to side between two adjacent vertebral bodies. But, regarding a section achieved through the uncinate region and facet joints along a plane perpendicular to the latter, it is clear that any attempt of lateral rotation is immediately prevented by the facets. On the contrary, if sections are taken along a plane parallel to that of the facet joints, rocking of the vertebral bodies is not precluded because the facets glide freely upon one another (Fig. 2.6).

These observations indicate that the cervical interbody joints are a saddle joints, meaning that in the sagittal plane the vertebral body is free to rock forwards and backwards around a transverse axis, while in the plane of the facets its rotation is allowed around a perpendicular axis and cradled by the uncinate processes. Motion around an oblique axis is precluded by the orientation of the facets. Since their orientation is about 45°, also the pure axial rotation is 45° in the plane of the facet joints [34]. Horizontal axial rotation is inexorably coupled with lateral flexion and viceversa. If horizontal rotation is attempted, the inferior articular process rises up the slope of the superior facet of the vertebra below and, as a result, a tilt to the side of rotation occurs. A reciprocal combination of events happens when lateral flexion is tested: the inferior process slides backwards down the slope of the superior process and the vertebra rotates to the side of lateral flexion. By CT scanning, some authors [35] tried to estimate the range of axial rotation of the typical cervical

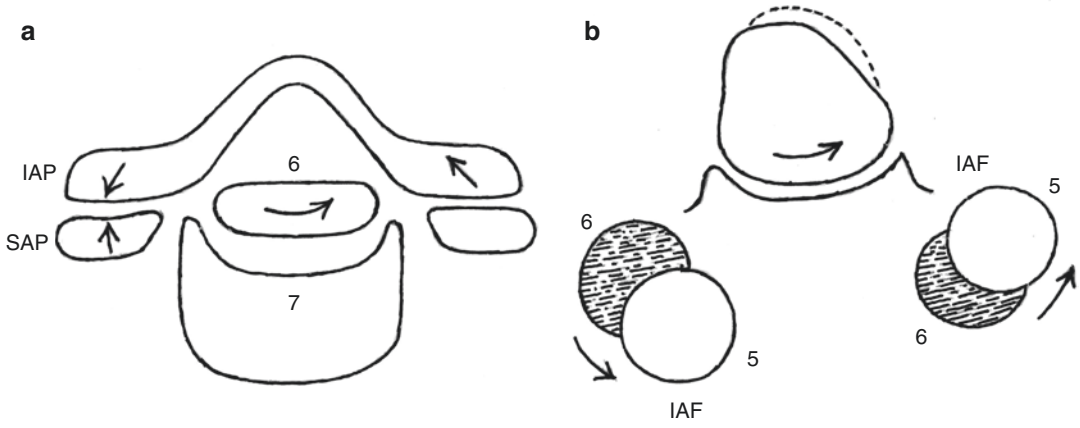

Fig 2.6 (**a**): axial section of a C6–C7 intervertebral joints along a plane perpendicular to the facets. In this plane, during left C6 vertebral body rotation, the right inferior articular process (iap) of C6 immediately impacts into the superior articular (sap) process of C7, preventing lateral rotation of C6; (**b**): axial section of a C5–C6 intervertebral joints along a plane parallel to the facets. In this plane, if the C5 vertebral body rotates, its iap is bilaterally free and can glide across the surface of articular facets of C6

Table 2.3 Mean values and ranges of axial rotation of the typical cervical vertebrae, according to Penning and Wilmink [35]

	ROM (degrees)	
Level	Mean	Range
C2–C3	3	0–10
C3–C4	6.5	3–10
C4–C5	6.8	1–12
C5–C6	6.9	2–12
C6–C7	2.1	2–10

vertebrae (Table 2.3). However, this kind of study was conducted with the CT scanning orientated across the conventional horizontal plane, failing to disclose the pure axial rotation. The axis of rotation in the plane of the facet joints passes through the anterior end of the moving vertebral body. During rotation, the anterior edge pivots about the axis without gliding, while the posterior margin is able to swing. The structure of the intervertebral disc supports this kinetics. The disc is the major compressive component of the spine. At low load rates, the disc deforms ad is more flexible, but at higher load it becomes stiff. Degenerative changes affect its viscoelastic properties and ability to tolerate mechanical stresses. The annulus is well developed and thick anteriorly, but thinner in the region of the uncinate processes. Its tensile properties are related to the orientation of the collagen fibers that converge upwards, towards the anterior portion of the upper vertebral body. This arrangement appears as an inteosseous ligament, disposed like an inverted "V", whose apex points to the axis of rotation so that the vertebra can pivot about its anterior end. The annulus is lacking posteriorly [36] and tapering towards the uncinate processes, with few fibers and about 1 mm thick. It is covered by the posterior longitudinal ligament (see below). In the absence of the posterior annulus, with the progressive formation of posterior transverse discal clefts, the posterior end is free to swing. As it swing, its posterior inferior border can glide up and down the concavity of the uncinate processes, while its inferior facets slip on the superior facets of the vertebra below.

Axial rotation and side bending can be regarded as secondary coupled movements at the typical cervical segments. The primary motion at the lower cervical spine is flexion and extension in the sagittal plane. Flexion is composed by an anterior sagittal rotation and anterior translation to various extent. While, in the past, the slope of the articular facets was postulated as the major determinant of patterns of segmental sagittal motion, more recently the height of the superior articular processes has been shown as the main

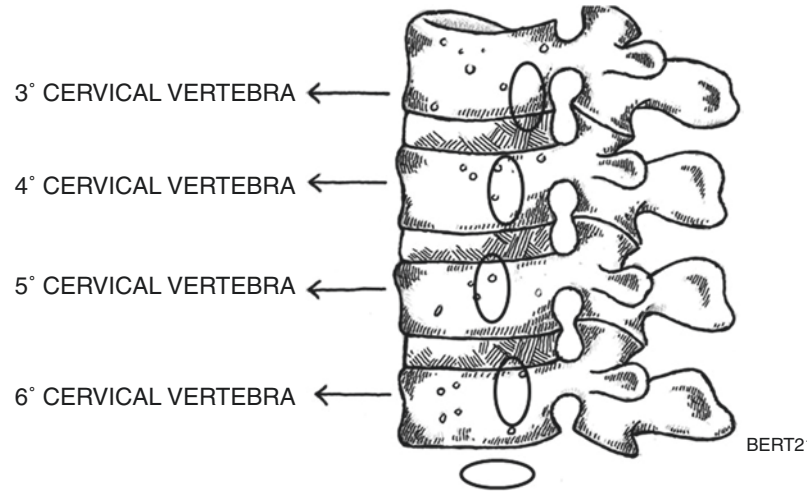

Fig. 2.7 Instantaneous axes of rotation (IAR) during maximal flexion-extension of the cervical spine. Dots indicate the IAR for each level, whereas an oval symbolizes the standard deviation (SD)

factor. Infact, regardless of its slope, the taller the superior articular process, the more it impedes anterior translation for any degree of anterior sagittal rotation. In other terms, this height determines the extent of coupling between sagittal rotation and translation [34]. Considering the IAR, it is located close to the intervertebral disc space of the FSU at the lower levels due to the greater height of the superior articular processes. On the contrary, since the articular processes are lower at the upper cervical levels, the IAR lies below more than disc of the segment in question (Fig. 2.7). The first description of the centre of rotation in healthy adults was derived from Penning's measurements [10], obtained by flexion-extension x-ray. With the aid of CT scan, the average centre of rotation for each level was determined [29]. Lysell [37] described the top angle or "arch of motion" from C2 to C7, as being flat at C2 and steep at the lower cervical spine. This means that the motion of the upper segments during flexion-extension is quite horizontal, whereas it is like an arch at the lower segments. The greater distance of the vertebra to the center of rotation in the upper region produces more flat motion, whereas smaller distance provides a sharper top angle. Ultimately, from above downwards the IARs are located progressively higher and closer to the intervertebral disc of their FSU. A critical determinant of this progression is the height of the articular pillars. These are lower at C2–C3 and progressively higher towards C6–C7. The height of the superior articular process at a given level predicts how much sagittal rotation must occur in the segment in relation to a specific and physiological amount of translation. Tall processes prevent an anteroposterior translation higher than 2.7 mm. Abnormal location of the IAR was proposed as a marker of poor quality of cervical motion in presence of pain, headache or previous trauma. The study by Amevo et al. [38] on 109 patients with post-traumatic neck pain showed an abnormally located IAR in 77% of cases and this relationship axis location-pain was highly significant statistically.

Generally, flexion is resisted in concert by the posterior longitudinal ligament (PLL), the yellow ligament, the capsules and the posterior ligamentous complex, while extension is principally limited by the anterior longitudinal ligament (ALL) and the annulus and by impaction of the posterior arches. This spinal architecture introduces the importance of the soft tissues in motion and stability of the cervical spine.

Soft Tissues

Ligaments, discs, fibrous capsules of the zigaphophysial joints and muscles represent the soft tissues of the cervical spine. These soft tissues render the spine compliant in that they allow for movement between vertebrae. They are also

responsible for limiting the range of many motion under physiological loads. Ligaments of various types connect the vertebral bodies and the posterior elements and span one or more segments. Ligaments consist of various amounts of collagen and elastina, arranged in an uniaxial manner, so they are able to resist tension forces. At each segmental level, the anulus fibrosus of the intervertebral disc binds the adjacent vertebral bodies. Posteriorly, as see above, in the region of the uncinate processes, the connection is interrupted by transverse clefts of the anulus. The intervertebral discs consist of proteoglycan nucleous designed to sustain compression loads, whereas the collagen fibers of the anulus resist tension, shear and torsion. The rule of the soft tissues in the biomechanics of the human cervical spine can be assesses using mathematical model (e.g. finite element models), investigating the external and internal responses of the spine under loads. As clarified by Yoganandum et al. [39] "external responses can be defined as measurable parameters of the spinal structure under an externally applied load" like moment-rotation curve produced by sagittal rotation under flexion-moment loading. In contrast, "internal responses can be defined as intrinsic parameters" like tensile stress of the disc: "Because of the complex nature of spinal architecture, internal responses are not direct measurable quantities in an experiment".

However, the biomechanical roles of the various soft tissues are different and each type must be discussed in terms of individual mechanical, geometrical and material properties.

Ligaments and Joint Capsules

Ligaments are monoaxial structures that resist tensile or distractive forces. The capsular ligaments are an important local stabilizer of the facet joints. Generally, ligaments are more effective when distracted along the direction of the fibers. But, because of their variable and complex orientation, some ligaments are be able to contrast external tensile forces in a wide range of directions. The anterior longitudinal ligament is resistant to an extension bending moment, whereas interspinous and sovraspinous ligaments (posterior complex) are more effective during flexion forces. Posterior longitudinal ligament, which lie close to the IAR, responde with less resistance than anterior and interspinous ligaments. The internal response of the ligaments secondary to loading depends on the severity, magnitude and application of load vector, but also on the individual mechanical properties: for example, ligamentum flavum, which is rich of elastina, is more elastic than the other. To quantify the geometry of the different ligaments of the cervical spine (origin and insertion=length; cross-sectional area), various methods of investigation have been adopted [39]. In summary, for length purposes, the longitudinal ligaments span the mid-height of adjacent vertebrae, ligamentum flavum and interspinous ligaments span the superior and inferior points of attachment of the two vertebrae and joint capsules span from the superior tip of the caudal facet to the inferior tip of the cephalad facet. Maximum cross-sectional area occurs midway between the two spinous processes for interspinous ligaments, mid-disc height for the two longitudinal ligaments and mid-capsule height for joint capsules. The ligaments are deformation sensitive: under axial tensile loading (traumatic force), the load-deformation response is achieved. The typical force-displacement and stiffness displacement responses of a ligament is shown by a non-linear curve which defines neutral, elastic and plastic phases (Fig. 2.8). So, for each ligament, an individual tensile force-deformation, energy and stiffness are calculated [39]. These properties are influenced by age, sex and loading rate [40]. Same biomechanical informations have been reported for stress, strain, stiffness and energy of joint capsules.

Intervertebral Discs

Intervertebral discs, in contrast with the uniaxial response of the ligaments, recognize multiple load vectors. Under any external loading, except tension, discs restrain essentially compressive forces in association with other components. Thus, the fundamental functional mechanical role is to respond to some degree of compressive loading, applied when the weight of the head (approximately three times the weight of the neck) is transmitted to the C2–T1 discs. Like

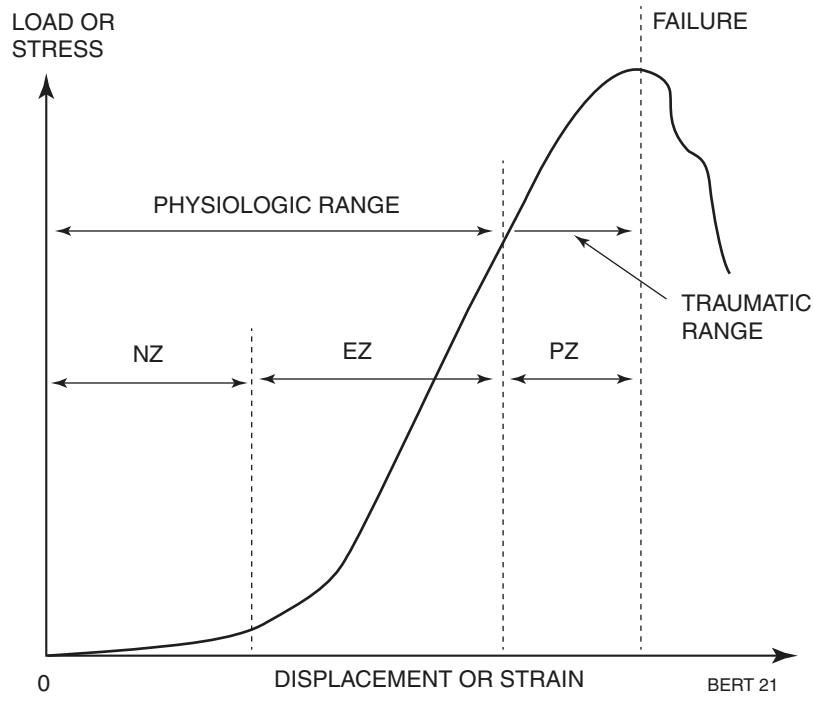

Fig. 2.8 The nonlinear load-displacement curve of the spine can be divided into physiological and traumatic ranges. The first part is the neutral zone (NZ) in which the displacement beyond the neutral position is achieved by application of a small force. The second part is the elastic zone (EZ) in which more load is required against an internal resistance. The last part, the plastic zone (PZ), is the displacement beyond the EZ to failure

Table 2.4 The mean changes (%) of the disc deformation between max flexion and extension of the neck

	Tensile def.	Tensile def.	Tensile def.	Shear def.	Shear def.	Shear def.
	Anterior	Central	Posterior	Anterior	Central	Posterior
C3–C4	70.3	13.2	37.5	68.3	57.8	45.9
C4–C5	61.9	17.2	50.9	78.5	76.7	60.5
C5–C6	75.9	25.4	40.4	48.3	46.0	42.9
C6–C7	39.1	21.5	34.4	33.1	30.9	34.6

ligaments, the internal response of the disc depends on the magnitude and nature of loading. The eccentrical anatomy of the nucleous polposus contributes to the dissimilar proportions of anterior and posterior anulus internal load-sharing during bending moment, as compression, flexion and tension. Three-dimensional geometrical data of disc nucleous and anulus have been reported in relation to height and cross-sectional area, but studies are in progress to capture intervertebral discs responses in tensile-compressive cycling loading and develop finite element models that may be applied in future [41]. The range of the disc deformation under loads was investigated by Yu et al. [5]. In particular, dynamic flexion-extension forces were applied in vivo on the subaxial cervical spine. A three-dimensional model, achieved by MRI technique, indicated that the range of disc deformation (anterior, central and posterior modifications under tensile and shear forces) is segmental level dependent and the anterior region experienced larger changes of deformation than the center and posterior regions, except for the C6/7 disc. These results would explain why disc degeneration affects other levels more than C6–C7 (Table 2.4).

Material properties, such as force-displacement, stiffness and stress-strain, must be achieved in more than one mode because of the multi-modal behavior of the disc, anulus and fibers. Using a single FSU and applying a traumatic compression or tension load, failure of the disc is identified as the point on the load-deflection curve at which an increase of compressive or distractive displacement results in a decrease of the resistive force. The force-displacement is non-linear and the post-traumatic phase indicate discal damage (see Fig. 2.8).

Muscles of Neck and Shoulders

The static and dynamic control of the head and neck is managed by a complex arrangement of about 20 muscles that enclose the cervical spine. The muscles at the upper cervical spine have individual unique structure, enabling lateral bending in C0/C1 and side rotation in C1/C2. Normally, the first 45° of rotation occurs in C1/C2, and then the lower cervical spine becomes involved. On the other hands, the muscles in the lower cervical spine are linear or interwoven, with every muscle activating several segments. This causes the segments of the lower spine to act as one unit. Anatomically, the deeper muscles are related intimately with the cervical osseous and articular elements, performing stabilizing functions, whereas the superficial muscles have no attachments to the cervical vertebrae. The deep musculature has a very high spindle density. The muscle spindles mediates the proprioceptive inputs from the cervical musculature and have an important role in head-eye coordination and postural control. The musculature involved in head and neck movement and stability is presented in Table 2.5.

Table 2.5 Musculature of the head-neck-shoulders system, involved in motion and stability of the cervical spine, according to Tortora and Grabowski [42]

Muscles of the neck, Mm. colli	***Function***
Sternocleidomastoideus	Supports the head
	Extension C0/C1
	Side rotation
Lateral vertebral muscles	Lateral bending
Scalenus anterior	
Scalenus medius	
Scalenus posterior	
Anterior vertebral muscles	Flexion, Lateral bending, Side rotation
Longus colli	
Longus capitis	
Suboccipital muscles	Extend, Rotate, Flexion, Side bending
Rectus capitis	
Obliquus capitis	
Muscles of the back, M. dorsi	
Upper trapezius	Elevates the scapula
	Function together with other muscles;
	Seldom as a single unit
Superficial erector spinae muscles	Erect posture
Ilicostalis cervicis	Lateral bending
Longissimus cervicis	Extension
Longissimus capitis	
Spinalis cervicis	
Spinalis capitis	
Superficial muscles	Rotates the head
Splenius capitis	Rotation and lateral bending
Splenius cervicis	
Deep transverso-spinales muscles	Supports the head
Semispinalis cervicis	Extension of head (C0/C1) and spine
Semispinalis capitis	
Mm. Multifidi	Stabilize individual segments
Mm. rotares cervicis	Lateral bending Side rotation

Normal Global Motion of the Cervical Spine

Data about the segmental motion of each cervical FSU have been reported in detail in vivo (Table 2.6) and in vitro (Table 2.7). But, the measurement of global ROM in the cervical spine is a routine part of the clinical examination of patients with neck disorders. The knowledge of normal age and sex-related ROM is the basis to analyze a pathologic motion patterns as well as decreased or increased ROM. In 1992, Dvorak et al. [45] tested 150 healthy asymptomatic volunteers to obtain normal values. Each subject, seated on specially designed chair, was requested to perform active motion, which is followed by passive examination by the physician. Flexion-extension, lateral bending, axial rotation were evaluated. In addition, axial rotations during full flexion and full extension were measured. The volunteers were divided into five groups according to age decades. The overall tendency was for ROM to decrease as age increased: the most dramatic decrease in motion occurred between the group aged 30–39 and 40–49. Axial rotation with cervical spine in full flexion is the only motion that remained the same or increased slightly with age.

Substantially, less motion was evident in the active tests and women showed greater ROM but only before age 60. Also, the measurement data for rotation out of maximum flexion suggested that the rotation of the C1–C2 joint did not decrease with age but rather remained constant or increased slightly, perhaps to compensate for the reduced motion of the lower cervical spine. In 1999, Feipel et al. [46] evaluated the normal global motion of the cervical spine by an electrogoniometric study. In 250 asymptomatic volunteers, aged 14–70 year, motion range and patterns between the first thoracic vertebra and the head were analyzed for flexion-extension, lateral bending, rotation in neutral sagittal plane position and in full flexion. Average motion range in the sagittal plane was 122° (Standard Deviation-SD 18°). Flexion was slightly more important than extension. Global bending was 88° (SD 16°), left and right bending being comparable. Homolateral rotation was associated with lateral bending: its extent was approximatively 40% of the bending range. Global rotation range in neutral sagittal plane position was 144° (SD 20°), without difference between right and left rotations. During rotation in flexed head position, global range was comparable to the one in neutral flexion for values of 134° (SD 24°). Finally, significant reduction of all primary motions with age was recorded, whereas sex had no influence on cervical motion range. Recently, the influence of the different functional structures on the normal cervical kinematics and ROM was investigated by Jonas et al. [3]. On cadaveric specimens, they tested the biomechanical reaction of the cervical spine, compared to the baseline (intact state of the specimen), after the resection of six structures: interspinous ligament, ligamentum flavum, facet capsule, vertebral arch, posterior longitudinal ligament, and anterior longitudinal ligament. Each state of induced anatomical damage was tested and each test sequence included 3.5 quasi-static motion cycles in all three bending directions using pure moments of 1 Nm. The overall range of motion was increased in all loading directions. Flexion-extension developed changes related to the resection of ligaments and joint capsules and the motion segments C2–C3 were most affected over the course of all performed resections. Lateral bending and axial rotation showed great changes, particularly in the presence of a vertebral arch resection Concerning the lateral bending, all resections had a significant impact on the respective change in ROM regarding all tested motion segments, while during axial rotation always C2–C3 showed the stronger increase in ROM. These observed changes in the overall kinematic behavior of each specimen due to the performed resections, give reason to believe that every single resection could potentially have an effect on the patients' individual motion pattern, which in return may provoke accelerated degeneration. Uncinate processes were reported as fundamental structures to be preserved as much as possible during anterior surgical procedures.

Table 2.6 ROM measurements in vivo for maximal flexion-extension of each cervical FSU, in degrees (± standard deviation), in normal subjects, according to A [43] and B [44]

	Flexion/extension	
Level	A	B
C0–C1	Not studied	
C1–C2	Not studied	
C2–C3	10 (3)	11 (3.4)
C3–C4	15 (3)	15 (4.0)
C4–C5	19 (4)	17 (4.6)
C5–C6	20 (4)	17 (6.1)
C6–C7	19 (4)	14 (4.7)

Table 2.7 ROM measurements of each cervical FSU, in degrees (± standard deviation), in human cadavers, according to the Multidirectional Flexibility Testing [31]

	C0–C1	C1–C2	C2–C3	C3–C4	C4–C5	C5–C6	C6–C7
Flexion	7.2 (2.5)	12.3 (2)	3.5 (1.3)	4.3 (2.9)	5.3 (3)	5.5 (2.6)	3.7 (2.1)
Extension	20.2 (4.6)	12.1 (6.5)	2.7 (1)	3.4 (2.1)	4.8 (1.9)	4.4 (2.8)	3.4 (1.9)
Axial rotation	9.9 (3.3)	56.7 (4.8)	3.3 (0.8)	5.1 (1.2)	6.8 (1.3)	5.0 (1)	2.9 (0.8)
Side bending	9.1 (1.5)	6.6 (2.3)	8.6 (1.8)	9.0 (1.9)	9.3 (1.7)	6.5 (1.5)	5.4 (1.5)

Alignment, Sagittal Balance and ROM Disorders

Cervical sagittal balance explains how the cervical spine is postured in the plane of sagittal and malalignment is associated with symptoms and health-related of life. Sagittal parameters are very important assessment indicators of the spinal alignment and are widely employed in the evaluation of disorders and surgery. They are age and gender dependent. A number of cervical spine parameters were presented to assess the sagittal balance in asymptomatic, but the ideal values are still debated. Among the most important and used, Azimi et al. [47] reported in their latest systematic review and meta-analysis:

- the *T1 slope* that is the angle between the horizontal line and the superior endplate of T1
- the *spino-cranial angle* (SCA) is the angle between the C7 slope and the straight line joining the middle of the C7 end plate and the middle of the sella turcica;
- the *cervical sagittal vertical axis* (cSVA) is the horizontal distance from a vertical plumb line dropped from the center of the C2 vertebral body to the posterior superior corner of the C7 vertebra (or C2–C7 SVA, according to Patwardhan et al. [48]

By the systematic review, considering the general population with or w/o cervical disorders, the reported mean values (Standard Deviation) of the T1 slope, cSVA, and SCA respectively ranged from 12.8 (7.9) to 42.6 (11.6) degree; from 4.5 (2.6) to 53.3 (15.7) mm; and from 83(9) to 75.6 (10.3) degree. By the meta-analysis, in the healthy population only, the mean T1 slope was 24.5 (range 22.6–26.4), the mean cSVA 18.7 (15.3–22.1) and the SCA 79.5 (72.6–86.5). The ranges of three parameters above mentioned for a good clinical condition were: T1 slope average ideal value must be 20° and not be higher than 40°; cSVA must be less than 40 mm (mean value 20 mm); SCA must stay at 83° ± 9°.

Le Huec et al. [49] also considered other two parameters. Dividing the cervical shape into two parts, they distinguished: the high cervical angle

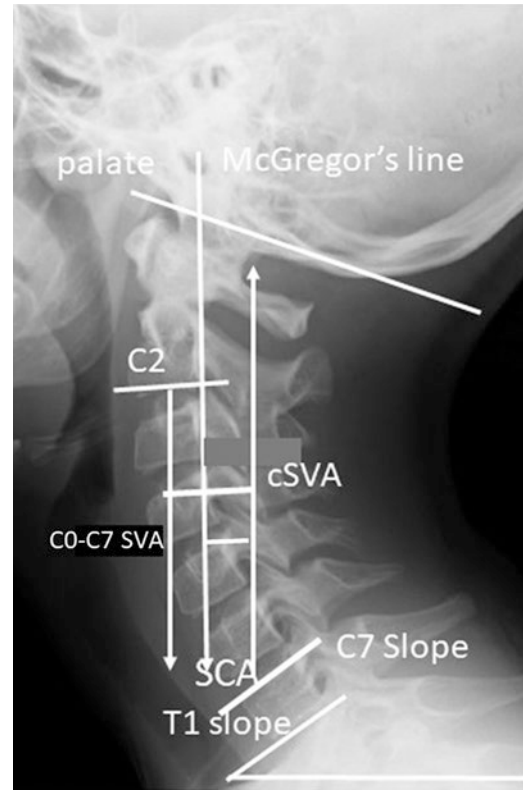

Fig. 2.9 Radiographic parameters to evaluate cervical alignment

Occcipito-C2 (O-C2) between the McGregor line and the lower C2 endplate. The McGregor line connects the posterior margin of the bony palate to the low point of the occipital bone. This angle has an average value of 15.81° (±7.15°), always lordotic; and the low cervical angle C2–C7 between the C2 endplate and the lower C7 endplate which is variable from kyphosis to lordosis in normal population. O-C2 and C2–C7 angles work inversely: When one is increasing, the other one is decreasing (Fig. 2.9).

The cSVA (or C2–C7 SVA) and the O-C7 SVA define the alignment of the cervical spine. The forehead head posture (FHP) is an important compensatory positioning of the cervical spine allowing to keep the cervical foramen size open and allowing to keep the gaze horizontal using the O-C2 hyperlordosis. A larger ROM of the craniocervical junction for kyphotic deformity and FHP has been clearly demonstrated by a multi-positional MRI [50]. In other terms, an increase of the

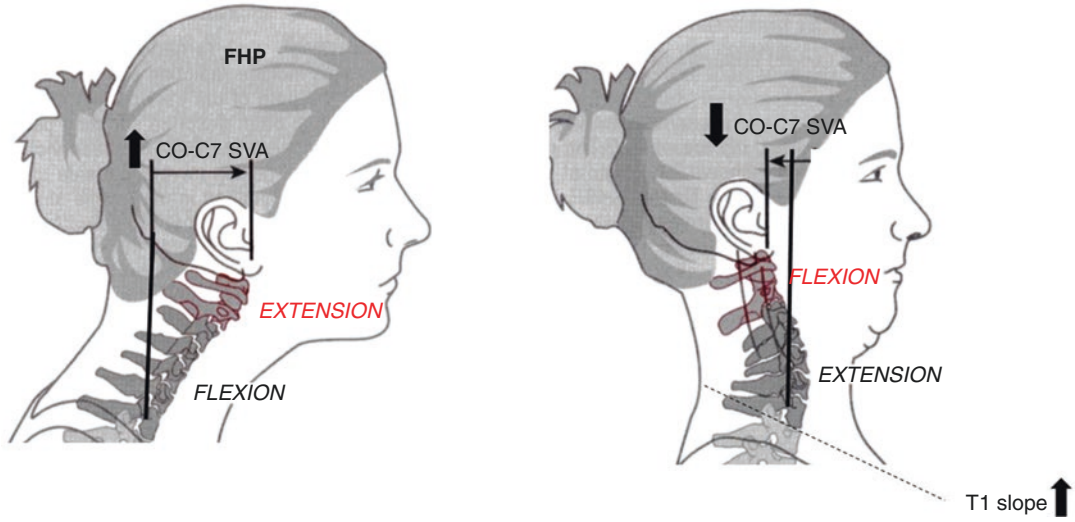

Fig. 2.10 Variations of the cervical shape and C0–C7 SVA due to compensatory mechanisms in FHP (left) or T1-slope increase (right)

C2–C7 SVA (or O-C7 SVA) causes flexion of C2–C7 segments and extension in O–C2, while a higher value of the T1-slope causes extension in the lower cervical segments and flexion in the O–C1 and C1–C2 segments (Fig. 2.10). Also, there is an inverse relationship between the neuroforaminal areas and changes in T1-slope angle. When the T1-slope angle increases, as in the high thoracic hyperkyphosis, a progressive decrease in the foraminal area can be observed due to the extension-hyperextension of the subaxial cervical segments. The peak of neural foraminal area narrowing occurs at C5–C7. When the T1-slope decreases, C2–C7 segments are in flexion (enhanced cSVA) and the foraminal area at all mid-to-lower cervical segments is larger. The C5–C6 level has the largest increase. The FHP is generally adopted by adult patients as compensatory mechanism to open a constricted foramen and relieve radiculopathy in the presence of a rigid thoracic hyperkyphosis. Another compensatory mechanism in the presence of FHP is the hyperextension of the O-C2 segment to maintain horizontal gaze that develops a progressive shortening of the sub-occipital muscles. Their chronic abnormal tension and effects on the Greater Occipital nerve can explain neck pain ad headache associated with a cervical kyphotic misalignment.

Neutral Zone and Cervical Spine Stability

When a spinal specimen is under a physiological load, the specimen does not return to its initial position. In other terms, a certain residual displacement remains. This displacement, measured from the neutral position, defines the neutral zone (NZ). NZ is the first part of ROM within which displacement of the spine is produced against minimal internal resistance. The NZ is defined by spinal flexibility or laxity. The elastic zone (EZ) is obtained simply as the difference between ROM and NZ. EZ is the part of ROM, measured from the end of the NZ up to the elastic limit, in which displacement is produced against internal resistance. The EZ represents the stiffness of the spine. Panjabi et al. [22] and White and Panjabi [51] reported in detail average values of NZ, EZ and ROM for the upper, middle and lower human cadaveric cervical spine and the nonlinear load-displacement curve of an FSU. In summary, with flexion-extension moment loading, coupled translations in the sagittal plane were anteriorly directed for flexion and posteriorly directed for extension in all intersegmental levels. With axial loading, the cervical spine exhibited the largest main rotation at C1–C2 and the largest coupled

extension at C0–C1. Coupled lateral bending was present at all levels, in the same direction of the applied torque. Coupled axial rotation was in the same direction as the lateral bending at all intersegmental levels. The NZ proved to be more sensitive than ROM in characterizing spinal instability. Infact, the NZ increased for injuries and fractures, whereas it decreased during muscle actions. An increase of the NZ can exceed the pain-free zone and may disclose the loss of spinal integrity. Post-traumatic failure of the spine occurs when the elastic limit is reached and further forces are applied (see Fig. 2.8).

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3 Diagnostic Imaging in the Degenerative Diseases of the Cervical Spine

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Introduction

Degenerative changes of the cervical spine, both physiological and pathological, proceed jointly with the age and can be easily identified and characterized by modern radiological techniques. The aging of the cervical spine, in particular, involves all its structures (osteo-discal-ligamentous complex); however, the intervertebral joints are the earlier and more conspicuously involved targets, being also the most specifically linked to the symptoms determined by the involution process [1]. Imaging can also distinguish degenerative diseases from other causes of radiculo-mielopathy, (i.e. infection or neoplasms).

In this scenario, magnetic resonance imaging certainly represents the best imaging modality in the evaluation of degenerative disease, especially in the cervical segment, where other methods of investigation (radiography, computed tomography) do not have a high diagnostic accuracy because of the peculiar anatomical features of the cervical spine. However, imaging findings must be considered clinically relevant only if correlated to the patient's symptomatology, as degenerative changes of the cervical spine can be easily found in asymptomatic patients older than 30 years [2]. In fact, imaging findings alone do not justify an aggressive therapy, particularly because some acute soft disk herniations can significantly decrease in size over time with conservative therapy [3]. This chapter is an attempt to help the clinician with a daily imaging reference in the treatment and management of patients with cervical spine degenerative disease.

Basic Anatomy

Two anatomically and functionally distinct components could be recognized in the cervical spine. The upper cervical spine (or suboccipital spine) consists of the first two cervical vertebrae, atlas and axis, articulating with the occipital bone, forming the craniocervical junction (CCJ). The lower cervical spine (or subaxial cervical spine) extends from the C2–3 to the C7–T1 joints [4].

Cranio-Cervical Junction

The atlas is ring-shaped; it is formed by a thick anterior arch, a thin posterior arch, two lateral masses, and two transverse processes. In the transverse process there is a foramen, through

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which passes the vertebral artery (transverse foramen). Lateral masses have a superior and an inferior articular facet which form the zygapophyseal joint.

The axis is composed by the vertebral body (which contains the odontoid process), large pedicles, laminae, and transverse processes; the odontoid process has an anterior articular facet that articulates with the anterior arch of the atlas.

The craniocervical junction includes six synovial joints: a pair of atlo-occipital joints, the anterior and posterior atlo-odontoid joint and a pair of atlo-axial lateral joints. The atlo-occipital joints are determined by the effacing between the occipital condyles and the superior articular facets of the atlas. The atlo-odontoid joint takes place between the dens and a osteofibrous ring formed by the frontal arc of the atlas and the transverse ligament. The atlo-axial lateral joints articulate the facet joints of the axis and of the atlas.

The craniocervical junction is held in place by extrinsic and intrinsic ligaments. The extrinsic ligaments include the nuchal ligament, which extends from the external occipital protuberance to the posterior portion of the atlas and of the cervical spinous processes and fibroelastic membranes that replace the anterior longitudinal ligament, intervertebral disks and the flaval ligaments.

The intrinsic ligaments, located within the spinal canal, provide the majority of joint stability. From the dorsal to the ventral side, they include the tectoria lmembrane, the cruciate ligament and the odontoid ligaments (apical and alar ligaments). The tectorial membrane connects the back of the axis body to the front of the foramen magnum and represent the cephalic continuation of the posterior longitudinal ligament. The cruciate ligament lies anterior to the tectorial membrane, behind the odontoid process; it is formed by longitudinal fibers, which extend from the anterior margin of the foramen magnum to the body of the axis, and by the transverse ligament, a sturdy fibrous tape stretched between the internal surfaces of the atlas masses. A synovial cavity is located between the dens and the transverse ligament. The transverse ligament is the most important ligament to avoid abnormal anterior translation. Odontoid ligament secure the axis dens to the occipital bone through the apical ligament and two alar ligaments, which prevent excessive lateral and rotational motion [5].

Subaxial Cervical Spine

Subaxial cervical spine includes vertebrae C3–C7. Vertebral bodies are concave on their superior surface and convex inferiorly. On the superior surfaces of the bodies arise processes, or hooks, called uncinate processes, each of which articulates with a depression on the inferior endplate of the superior vertebral body (Luschka joints, not considered true articulations) [6]. In most cases the spinous processes of C3–6 are bifid, while the spinous process of C7 is not.

Each vertebra has two superior and two inferior zygapophyseal joints, a disco-somatic joint and two, as we have just mentioned, Luschka joints. The facet joints are diarthrodial synovial joints with fibrous capsules.

The anterior longitudinal ligament (ALL) and the posterior longitudinal ligament (PLL) are found throughout the entire length of the spine; the former is not well developed in the cervical spine and is more closely adherent to the disks than the latter. ALL and PLL are the caudal extension, respectively, of the anterior atlanto-occipital membrane and of the tectorial membrane in the lower cervical spine. The supraspinous ligament, the interspinous ligaments, and the flaval ligaments (posterior ligamentous complex) maintain stability between the vertebral arches. The flaval ligament is the most important: runs from the anterior surface of the cephalic vertebra to the posterior surface of the caudal vertebra and, aided by the interspinous ligament, control the excessive flexion and anterior translation. The flaval ligament also connects to and reinforces the facet joint capsules on the ventral aspect.

Intervertebral disks are located between the vertebral bodies between C2 and C7 and are

made of four parts: the nucleus pulposus, the annulus fibrosus and two endplates attached to the superior and inferior vertebral bodies. The disks are thicker anteriorly: with the physiological process of aging the disks become progressively dehydrated and show height reduction.

The foramina progressively decrease in size from C2–3 to C6–7; the spinal nerve, which is the result of the union of the anterior and posterior nerve roots, occupy about one third of the foraminal space. The foramen is bordered anteriorly by the uncovertebral joints, posterolaterally by facet joints, superiorly by the pedicle of the vertebra above, and inferiorly by the pedicle of the underlying vertebra.

Technical Approach

Diagnostic workup in the assessment of degenerative cervical spine disease has the aim to identify the pathology of the spinal osteo-discal-ligamentous complex (i.e. spondylosis, hernias, etc.) and the consequently determined alterations of the "content" (spinal cord). We will briefly describe the most important imaging modalities (radiography, computed tomography, magnetic resonance imaging) in the evaluation of the effects of degenerative diseases that should be considered in advance to any therapeutic planning [7].

Radiography

Even if radiography is considered the "first step" technique in the study of degenerative cervical spine examination, nowadays it has undergone critical re-evaluation and its role is currently controversial [8, 9]. In the assessement of brachialgia, radiography can only provide information about the degenerative changes of bone spinal structure, but it is limited in the evaluation of stenosis of the central canal and disk herniation, the most frequent causes of pain and neurologic symptoms. The only indisputable use of radiography is confined to assessement of the instability, performing a flexion-extension radiograms [10]. However, the functional radiological study itself can't demonstrate the most frequent cause of instability represented by ligament laxity/injury.

Computed Tomography

The introduction of new multidetector computed tomography (CT) scanner has completely changed the accuracy and diagnostic capabilities of CT in the evaluation of degenerative cervical spine disorders. A slice thickness of 0.6–0.7 mm with 1 mm reconstruction and increases of 0.5–0.6 are recommended parameters in order to achieve an optimal visualization of degenerative changes. Contrary to radiography, CT is capable to visualize not only the bony structures but also some soft tissues features (e.g. disk herniations). In the last years the advent of new method of dose optimization, like ASIR (Automated system for Iterative Reconstruction), that could reach up to 50% of dose reduction, made the CT less invasive, especially when studying bone structures. However the overall quality of the images worsen, especially in the evaluation of soft tissues.

CT is inadequate in the study of ligaments and bone marrow changes, which almost exclusively done with MR imaging. Multiplanar and 3D reconstruction may be a useful integration to the axial examination, especially in surgical planning [11]. The use of contrast media nowadays should be strictly limited to the cases in which the Pt is not feasible for an MRI study (i.e. intensely claustrophobic and not willing to do on sedation, bearer of non MRI compatible devices etc.). In every case it is necessary to highlight the absolute uselessness of iodine contrast when evaluating the bone structures: in fact the increase in density provided by contrast media would not change the bone intrinsic hyperdensity. Eventually, iodine could be used, in these Pts, for the differentiation between hernia relapse and granulation tissue. Finally, the most significant limitations of CT results from its inability to demonstrate spinal cord disease, making MRI the modality of choice in patients with clinical evidence of myelopathy.

Magnetic Resonance Imaging

Cervical spine MR examination should be acquired with high-field equipment (≥−1.5 T), using powerful gradient systems and phased-array coils: with the progressive spreading of the 3T MRI, these systems should be considered as the new gold standard. These images offer several advantages over those obtained on the lower-field scanners, including improved image quality (higher spatial and contrast resolution) and clinical efficiency (higher temporal resolution). However the higher magnetic field lengthen the T1 and T2 relaxation times, with the consequent need to adjust the imaging sequences and, in some ways, the semiotic. These imaging protocols, incorporating the so called "driven equilibrium", SPACE readout and parallel imaging, have demonstrated its effectiveness in evaluating degenerative disease in the cervical but also in the thoracic and lumbar spine. The combination of high contrast and improved spatial resolution allows the radiologist to characterize disc pathology, assess for presence of cord and nerve root impingement, and evaluate neural foraminal stenosis.

The T1- and T2-weighted (T1-w and T2-w) images in sagittal and axial planes, which represent the baseline examination, should be completed with 2D–3D GRE T2*-w axial and sagittal images, in order to optimize the contrast between the bony and the discal/ligamentous structures. However, in some cases, more specific sequences and scanning planes could be added, to complete the study and optimize the diagnosis (i.e. oblique planes for studying nerve roots course).

Fat-sat sequences, such as fat-suppressed (fat-suppressed T2-weighted [FST2W] or short tau inversion recovery [STIR] should be routinely comprised in every study protocol: they are of paramount importance in evaluating every kind of signal changes in the bone marrow (i.e. Modic changes, traumatic injures with or without morphological modifications, but also other alterations related to degenerative spinal diseases).

The use of contrast media is limited to selected instances, i.e. to differentiate between degenerative, inflammatory and neoplastic diseases; in these instances the post contrast images must be acquired using fat sat T1w sequences. On the conventional T1 images in fact the gadolinium uptake could hide lesion, whose signal, hypointense in basal conditions and increased by the contrast media, become not distinguishable from the natural high signal of the bone marrow, mainly represented by fat.

In the latest years the overall technical improvement of MRI system resulted in a notable increase in the spatial resolution of the diffusion weighted images (DWI), making them feasible for a more routinely use in the diagnostic of the cervical spine. Different DWI sequences have been developed in the different MRI system. As an example DWI demonstrate good accuracy in differentiating benign from malignant fractures and in diagnosing pyogenic collections.

Finally, it must be taken into account that MR imaging can directly demonstrate, with high sensitivity, the lesions of spinal cord, nerve roots and meningeal sheaths that are in some cases determined by degenerative changes of the osteodiscal structures.

Basic Findings in the Degenerative Disease of the Cervical Spine

The Disk

Disk degeneration starts early in life and frequently progresses relentlessly. The elderly frequently show disk degeneration of the cervical and lumbar tract.

The pathogenesis of intervertebral disk degeneration is unclear: multiple factors working separately (hereditary factors, age related vascular changes, vertebral endplate changes such as calcification), may lead to the impairment of the discal trophism. Mechanical factors as trauma, sports, or working related, may play a role.

Altough the disk degeneration has to be considered a multi-factorial event, four are the elementary imaging features [12, 13] (Fig. 3.1):

- Loss of signal intensity of disk (MR imaging)
- Loss of height (all imaging modalities)
- Bulging (CT or MR imaging)
- Herniation (CT or MR imaging)

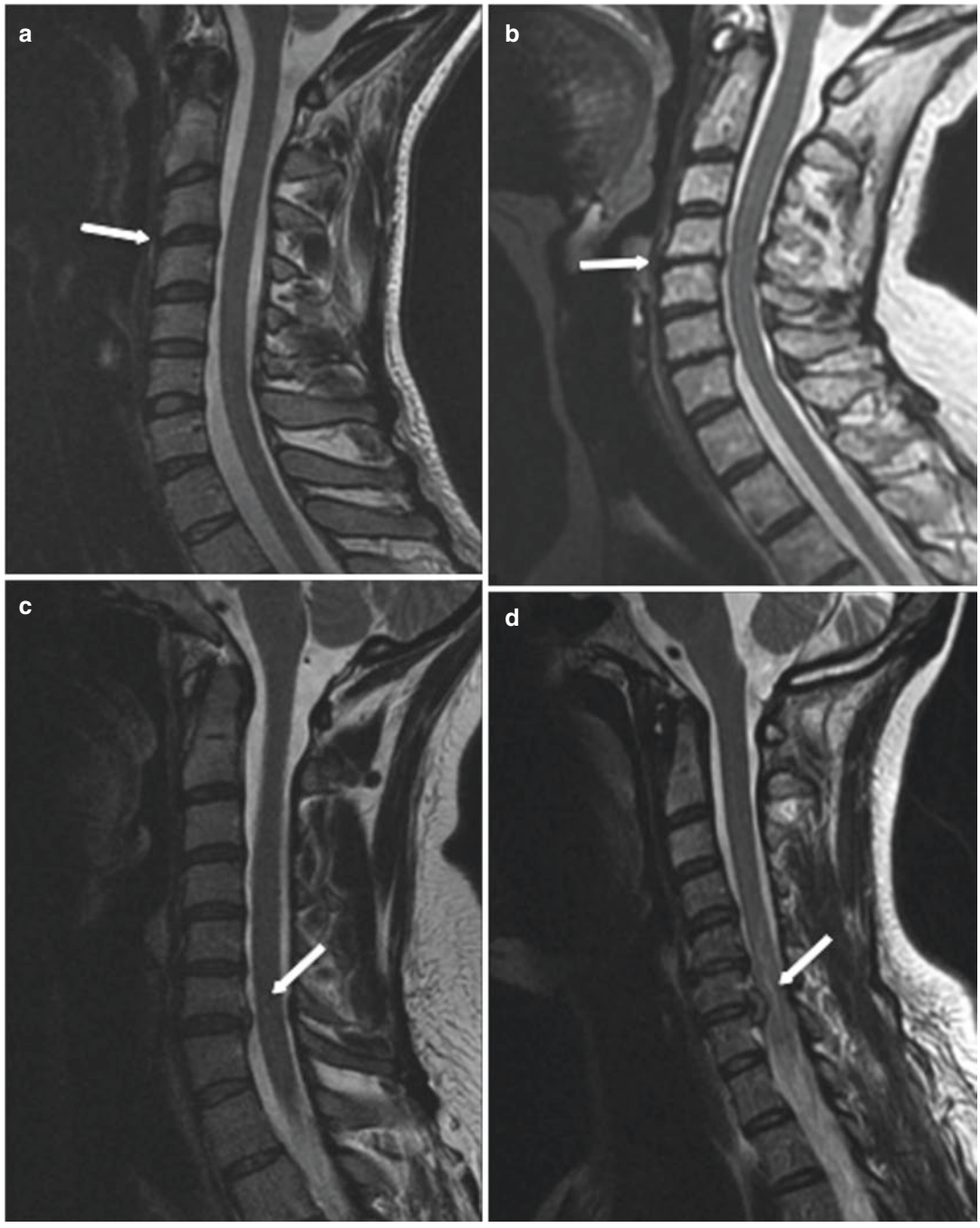

Fig. 3.1 Age-related disk modifications, disk bulging and disk herniation shown on sagittal FSE T2 images. Patient 1 (**a**): Minimal disk dehydration at C3–4 level (arrow), as demonstrated by low intensity signal on T2 images. Patient 2 (**b**): With the progression of degenerative changes, disk height is reduced and associated with mild spondylotic alteration at C4–5 level (arrow). Patient 3 (**c**): Posterior disk bulging at C6–7 level (arrow). Patient 4 (**d**): Disk herniation at C6–7 level (arrow)

The radial tear of the annulus that is often strictly associated with the other features, has to be considered the primary failure of the annulus itself [14]. The radial tear involves all layers on the annulus fibrosus and it is well described in MR imaging as high signal intensity tissue in the region of the disk, normally characterized by low signal intensity [15].

The disk degeneration processes evolve in a progressively loss of water, with a compromised integrity of the annulus fibrosus.

On MR imaging these signs are well evident on T2-w fast spin echo (FSE) or gradient echo (GRE) images with a loss of normal signal hyperintensity and an associated loss of height (often a vacuum phenomenon is demonstrated in CT or radiography). Frequently the disk degeneration is associated with an alteration of adjacent intervertebral body endplates (intervertebral osteochondrosis).

Modic [16] distinguishes three progressive grades of alteration adjacent to the endplates on MR imaging (Fig. 3.2), partially corresponding to the sclerosis described in radiographic or CT examination:

- Type I: hypointense on T1-w and hyperintense on T2-w bands which represent the marrow edema
- Type II: hyperintense T1-w and iso/hyperintense T2-w bands which represent the replacement by fatty marrow
- Type III: hypointense T1-w and T2-w bands which are characteristic of bone sclerosis.

The endplates bony marrow changes associated with degenerated disks needs to be however distinguished from other diseases, such as infection and metastases.

Spondilosys

Dehydration and fibrosis of the disk mean that static and dynamic mechanical stress can no longer spread through the horizontal plane of the disk, without altering it structurally. The disk becomes the site of fissures, protrudes out and becomes thinner. Because of the displacement of disk material beyond the margins of the intervertebral disk space, a productive reaction is established, producing fibroblasts, in the adjacent vertebral margins: these phenomena represent the anatomic-pathological processes of spondylosis.

Osteophytes are the most characteristic sign of spondylosis and are more commonly found at levels C5–7; initially they are thin and have a horizontal course, then gradually enlarge until they weld in a “bridge” in the more advanced stages. Uncovertebral joints osteophytes characterize the framework of mono- or bilateral uncoarthrosis: they grow into the vertebral foramina and can compress the spinal roots and extend into the intertransverse space, where they take relationship with the vertebral artery [17].

Interapophyseal joints osteophytes that protrude into the foramina will generally occupy the upper part and are rarely able to cause a radiculopathy by themselves. Instead they contribute to cause it in the presence of lateral herniated disk or severe uncoarthrosis.

The development of anterior osteophytes in cervical spondylosis is usually modest and asymptomatic. Both radiography and CT can well demonstrate osteophytes. Even in the MR imaging, osteophytes can be studied with T2*-w sequences that well demonstrate bone structures, distinguishing from the adjacent degenerated disk.

Cervical spondilosys, both determined by age related degeneration or traumatic events, represents one of the most frequent causes of cervical instability and in late stages can determine nonspecific symptoms (e.g. dysphagia), that may also mislead the clinical diagnosis. Therefore some studies tried to assess quantitative methods to evaluate and establish a grading of the spondilosys, basing on RX or CT examinations. Alizada et al. explored a radiographic index method based on evaluation of some features (cervical spine lordosis, the full flexion to full extension ROM, horizontal displacement, and cervical instability) on neutral and flexion-extension radiographs

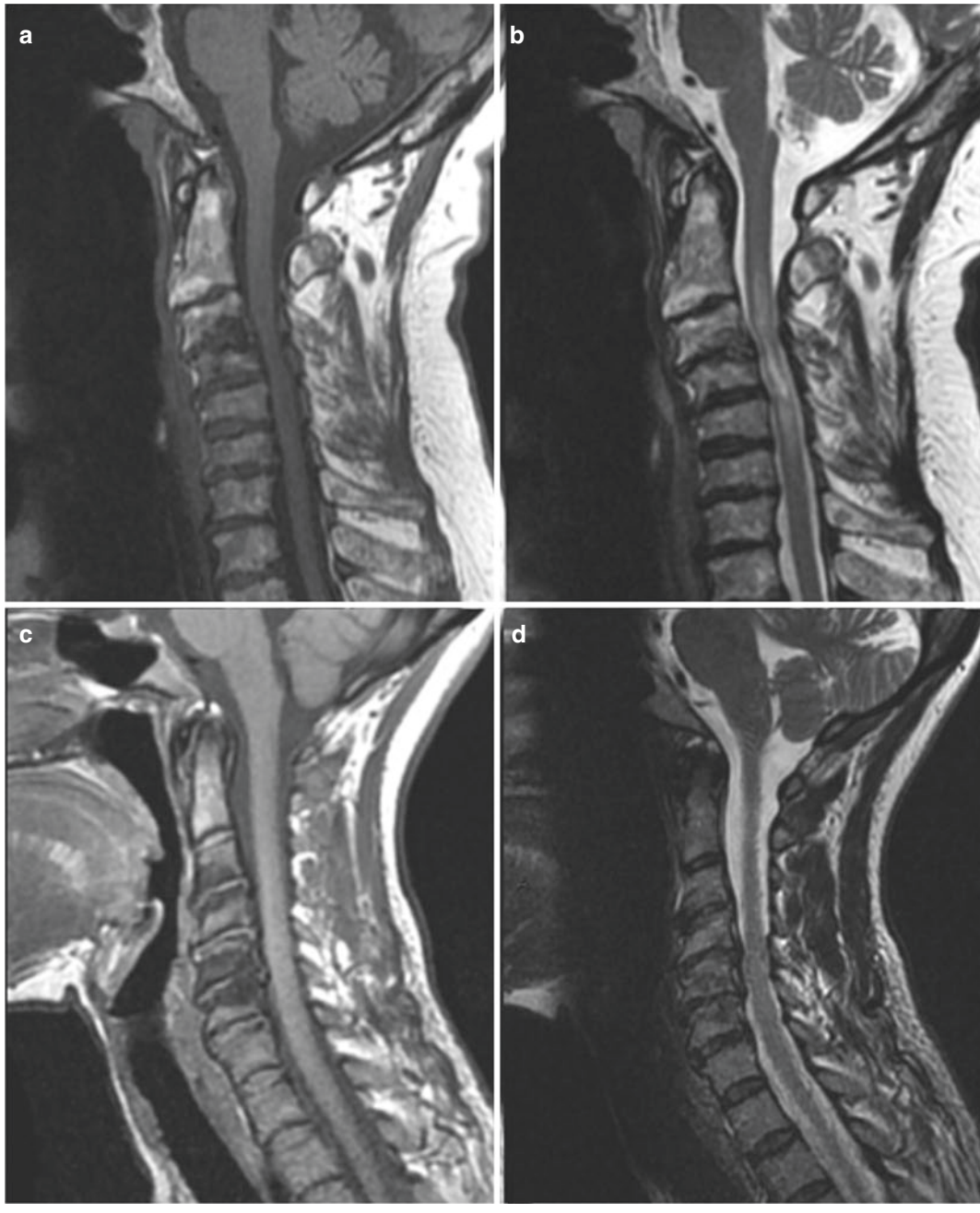

Fig. 3.2 Modic 2–3 alterations on sagittal FSE T1/T2 images. Patient 1: FSE sagittal T1 (**a**), FSE sagittal T2 (**b**). The vertebral endplates at C2–3 level show hyperintensity on both imaging sequences, due to fatty conversion of the normal bone marrow (Modic 2). Spondylosis results in spondylotic myelopathy as demonstrated by central high signal of the compressed spinal cord. Patient 2: FSE sagittal T2 (**c**), FSE sagittal T2 (**d**). The vertebral endplates at C5–6 show hypointensity on both sequences, representing subchondral bony sclerosis (Modic 3)

[18]. Rydman et al tested a CT based score system evaluating both disc and facet joint degeneration in a population of adult patients with a history of trauma of cervical spine and symptoms of neck pain [19].

Cervical Facet Arthropathy

The degenerative facet disease or arthropaty has to be considered an osteoarthritis of sinovially lined apophyseal joints. Each apposing facet is composed of a thin uniform layer of dense cortical bone, and an overlying layer of cartilage. The facet joint is lined by synovium.

The degenerative process is not different from other synovial joints. It starts with hypertrophic degenerative inflammatory changes, followed by subluxation, that may produce gas (vacuum phenomenon). Lately there is a cartilage erosion with narrowed joint space. Mid and lower cervical spine represent the most common site.

Radiologically the early degenerative signs maybe difficult to demonstrate, while the later changes are well shown in radiography (facet arthrosis, vacuum phenomenon, mushroom caps facet appearance, sclerosis). Altough CT with soft tissue window level well demonstrates the thickening and inflammatory changes of soft tissue, MR imaging obviously allows a much better visualization of the inflammatory changes and the facet effusion (linear T2-w images hyperintensity), but tends to overestimate, with the T2*-w images, the degree of foraminal and central canal narrowing. The gold standard about this topic should be represented by combination of fat-sat T2, standard T1 and post-contrast fat-sat T1w images (Fig. 3.3).

Ligament Degeneration

Cervical ligaments also undergo degenerative changes, represented by calcium deposits with the subsequent appearance of new bone forma-

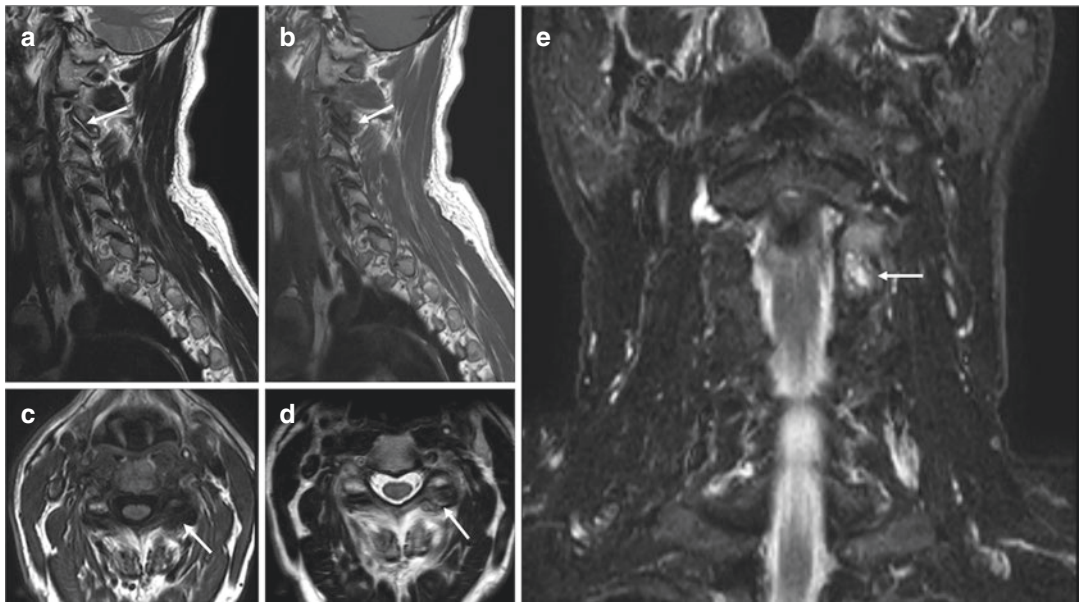

Fig 3.3 Cervical Facet Arthropathy. (**a**, **b**) Left parasagittal T2 (**a**) and T1 (**b**) w.i. (**c**, **d**) Axial T1 (**c**) and T2 (**d**) w.i. (**e**) Coronal T2 STIR. In this case of a Pt presenting with cervical pain on the left side at the level of the craniocervical junction the multiplanar T2w almost failed in demonstrating clear anomalies, showing only a minimal effusion in the C2–C3 lateral articular space [white arrow in (**a**) and (**c**)]. The T1w better demostrated a diffuse hypointensity of the medullar bone in the articular facets [white arrow in (**b**) and (**d**)]. The bony edema is finally evident on the coronal STIR images, both directly and in comparison with the hypointensity of the contralateral facets, due to the suppression of the fat signal, often high in the T2 FSE unsaturated slices [white arrow in (**e**)]

tion which compromise their firmness and elasticity. It should also be remembered that the involvement of disks and/or synovial joints is sufficient to induce ligamentous laxity, and consequently make alterations that entails the functional spinal unit (FSU). A FSU consists of two adjacent vertebrae, the intervertebral disk and all adjacent ligaments between them.

The calcified depositions and ossification are most frequently found both in the flaval and, especially, in the anterior and posterior longitudinal ligaments.

Degenerative Cervical Spine Instability

Stability can be defined as the ability of the vertebrae to maintain normal relations between them and to contain their mutual displacements, under the action of various postures and physiological loads. In normal conditions, the geometric characteristics of the vertebrae, a normal intradiscal pressure, the configuration of the facet joints and, above all, a correct ligament tension, are able to maintain correct motion between the FSU. When the above conditions are not preserved, the spine becomes unstable.

Despite the efforts of numerous authors to define the spinal instability, there is not a commonly shared definition; one of the biggest problems is represented by the fact that the concept has different meanings in various areas of clinical radiology and bioengineering. However, a reasonable definition has been proposed by White and Panjabi [20] that, supporting a bio-mechanical approach, define instability as a loss of "stiffness" of the motion segment in correspondence of which, under the action of a load, the motion determine abnormal displacement. In the biomechanical view, the "stiffness" is defined as the ratio between the loads applied to the structure and the resulting movement. The spine instability may therefore be the consequence of a trauma, of a degenerative disease and/or various other causes.

This premise is fundamental to allow an interpretation of cervical degenerative instability not as a mere list of topographical radiological signs but as an alteration of the spinal disk-ligamentous complex as a whole. The various degenerative changes must be categorized in well-defined pathological successive phases according to Kirkaldy-Willis [21], which are:

- Phase of functional derangement
- Phase of instability
- Phase of fixity

Phase of Functional Derangement

Early degenerative changes (disk fissures and apophysis' synovitis) determine an inter-apophyseal joints stress that leads to a modest hypermobility of the vertebrae. Consequently, the hypermobility causes a repeated stress of nerve fibers with the onset of cervical acute pain. Facet joints subluxation can be associated with a disk herniation or a symptomatic synovitis.

At this phase the radiography is negative, so in the suspicion of a herniated disk it is necessary to acquire CT or MR imaging.

Phase of Instability

With the advance of functional derangement, degenerative phenomena worsen both on disco-somatic complex (i.e. reduction of disk space, vacuum phenomenon, intervertebral osteochondrosis) and on zygapophyseal joints (sclerosis, "mushroom" deformation of articular pillars, articular effusion). Consequently radiculopathy or myelo-radiculopathy may emerge at this phase as a result of disk herniations; also a spondylolisthesis of the vertebra affected (degenerative spondylolisthesis) may result in dynamic narrowing of central canal and/or foraminal stenosis. The radiographic study, when made in LL projection, in flexion and extension (dynamic study), is able to detect not only the degree of listhesis but also to determine if it is fixed or unstable (Fig. 3.4).

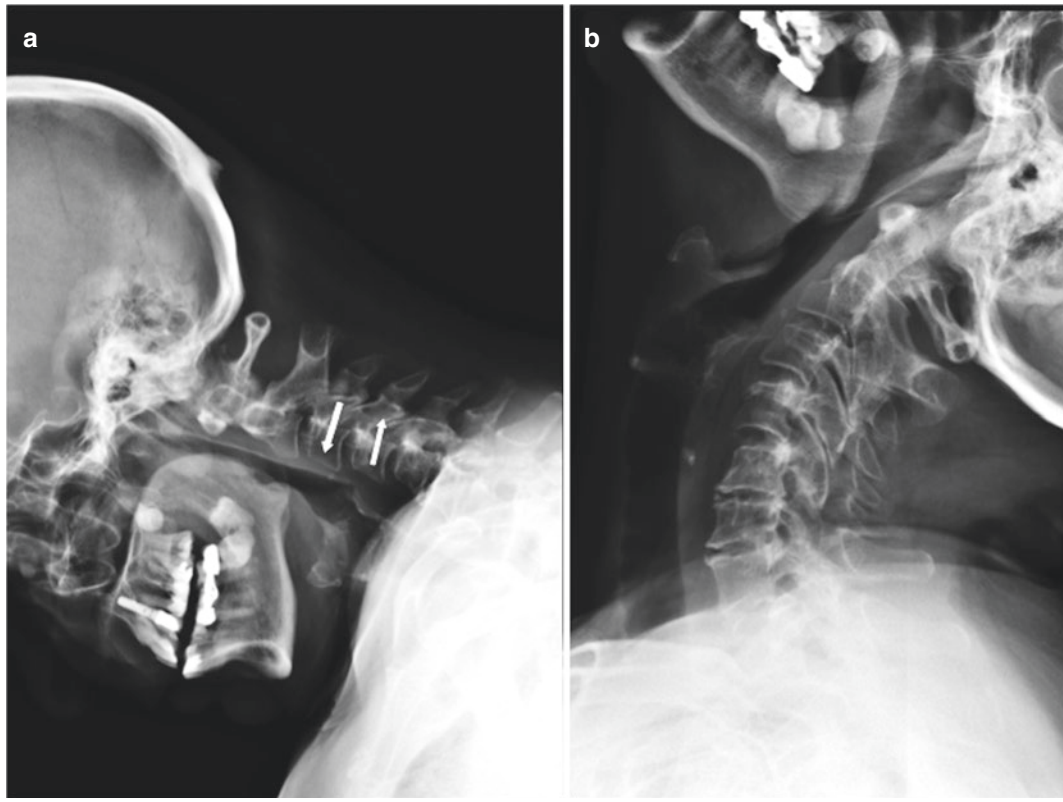

Fig. 3.4 Degenerative instability on flexion/extension radiography. Flexion (**a**) and extension (**b**). Minimal degenerative spondylolisthesis C3–4 evident on the flexion radiogram (arrows, "phase of instability" according to Kirkaldy-Willis) with complete reduction on extension radiogram

Phase of Fixity

The findings are those of advanced osteoarthritis, with loss of motion, joint deformation and above all an increase in osteoproliferative phenomena (osteophytes and hypertrophy of the articular pillars); these alterations may lead to central canal stenosis. Conventional radiology is able to highlight osteoproliferative changes but not to assess their effects on neurovascular structures, and therefore they should be investigated with CT and MR imaging.

Cranio-Cervical Junction Degenerative Disease

The joint most frequently subject to degenerative changes in the craniocervical junction is the atlanto-odontoid. Atlantoaxial advanced degenerative changes are the main cause of the onset of symptoms (headache), with concomitant reduction in mobility. Also, it has been suggested that the onset of vertigo can be referred to a strict relation between upper cervical spine afferent fibers and vestibular and oculomotor nuclei [22].

Sometimes degenerative changes can lead to the formation of abundant inflammatory reactive tissue, mainly posterior to the odontoid process, that could determine an encroach on the ventral surface of the spinal cord (inflammatory pseudotumor).

Imaging

CT and MR axial images, as in the subaxial cervical spine, provide a good evaluation of the spinal canal stenosis, which is often associated with

the degenerative changes in the cranio-cervical junction; MR imaging is also capable to evaluate compression on the medulla oblongata and the subsequent onset of myelomalacia (characterized by hyperintensity on T2-w images). Moreover, the MR imaging can differentiate hypertrophic pseudotumoral changes of the CCJ (Fig. 3.5). Post-contrast images are useful to exclude/identify inflammatory changes (pannus).

Subaxial Cervical Spine Degenerative Disease

Cervical Disk Herniation

Terminology

The general term of "herniated disk" means the displacement of disk material beyond the margins of the intervertebral disk space and repre-

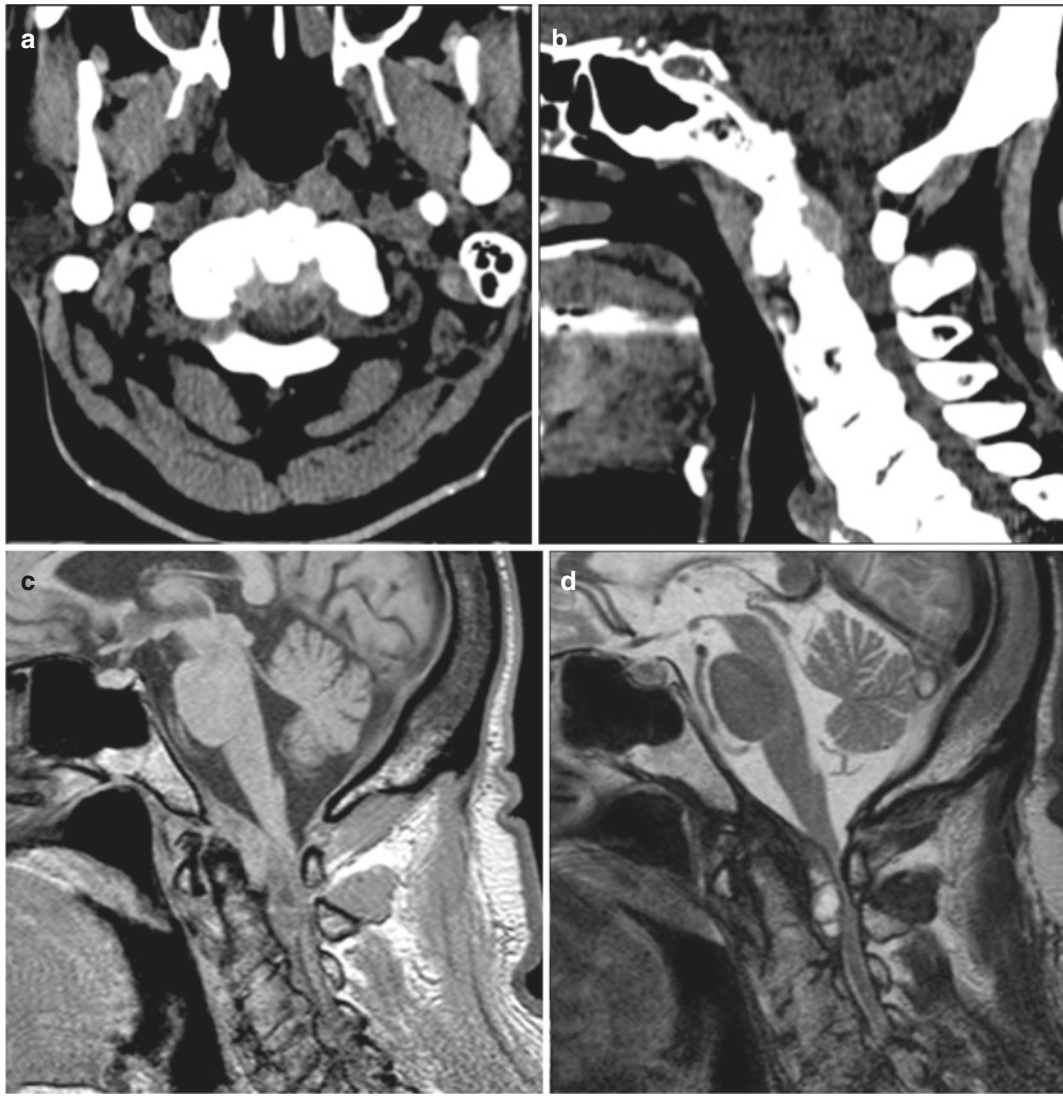

Fig. 3.5 Pseudotumor of the CCJ; CT and MR imaging. CT axial (**a**) and sagittal (**b**) images, sagittal GRE T1 (**c**) and FSE T2 (**d**) images. Abundant retro-odontoid inflammatory tissue at C0–C1 level, resulting in severe spinal cord compression

sents one of the major causes of neck pain. There are not universally accepted terminology and classification to define various pattern of disk herniation; different definitions are often used to describe the same type of hernia. A purely pathological classification of disk herniation is not suitable in daily radiological practice; i.e., the terms disk prolapse or disk herniation, respectively indicating that a portion of the nucleus pulposus has made its way through a fissure that involves only the innermost fibers of the annulus (prolapse), and the disk material that has gone through the whole annulus fibrosus, but not the posterior longitudinal ligament (disk herniation). However, since these two pathological conditions are not differentiable from each other even with MRI (both can manifest as focal contour deformities of disk), it is better not to make such a distinction. Morphologically we can distinguish protruded from extruded hernias: a disk protrusion is a herniated disk in which the distance between the edges of the disk herniation is less than the distance between the edges of the base; conversely, a disk extrusion is a herniated disk in which the distance between the edges of the disk material is greater than the distance at the base [23, 24].

Even if a universally accepted classification is not forthcoming yet, the differentiation between the "bulging disk" and the "hernia" is necessary in the clinical practice.

Bulging Disk (Fig. 3.6)

The "bulging disk" is characterized by wide/diffuse displacement of disk material beyond the normal limits of the intervertebral space, while the herniated disk is a focal dislocation. For wide/diffuse dislocation is meant a dislocation that affects more than 50% (180°) of the circumference of disk, while a dislocation is defined focal when interesting not more than 25% of the circumference of the disk. It is important to emphasize that the "bulging disk", a common finding in people over the fourth decade, may be associated with reduction in disk height and does not necessarily represent a pathological condition.

In the presence of a bulging disk, the posterior dislocation of the disk tissue is typically symmetrical and maximum on the median line, but occasionally it is possible to observe also a focal disk displacement on one side or, even more rarely bilateral focal protrusions. In a relatively narrow spinal canal, the bulging disk can flatten the dural sac surface, but only rarely and in the

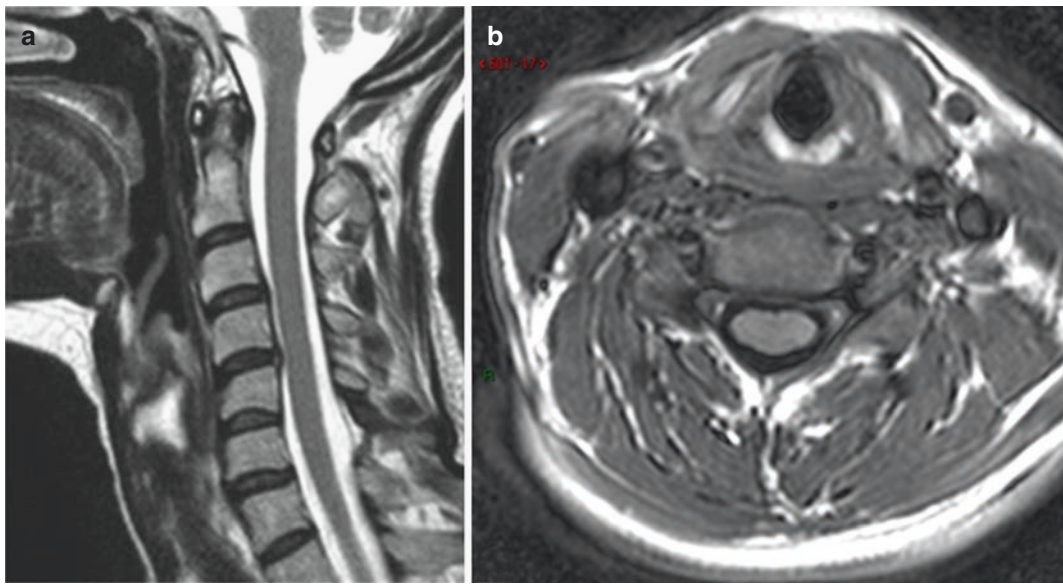

Fig. 3.6 Bulging disk. Sagittal FSE T2 (**a**) and axial FSE T1 (**b**) images. The C4–5 disk presents minimal diffuse bulging of its margins, with subtle effect on the ventral surface of the thecal sac

presence of a marked stenosis, it results in a true compression of the spinal cord or nerve roots.

Cervical Herniation: Subtypes

A herniated disk can occur in any direction, although those that have clinical relevance occupy the spinal canal or radicular canal and encroach the dural sac and/or nerve roots.

According to the location they are divided as follows (moving from central to lateral):

- "Central" hernia: extends into the spinal canal along the midline, compresses and deforms the epidural surface of the dural sac and sometimes, according to its size, is so voluminous that may cause a bilateral radiculopathy and/or myelopathy (Fig. 3.7);
- "Lateral/Paramedian" (Right/Left) hernia: not on the median line, but does not extend into the lateral recess. The herniated material displaces the epidural fat and may occupy the lateral recess, at the origin of the nerve root. It is responsible for a unilateral radiculopathy (Fig. 3.8);
- "Foraminal/extraforaminal" hernia: occupy the radicular (foraminal) canal, or extends beyond the corresponding foramen (foraminal/extraforaminal). Only the foraminal component has clinical relevance due to compression on the nerve root (Fig. 3.9).

By definition the herniated material, which can migrate upward or downward, is always in continuity with the intervertebral disk. The hernia can be more analytically described, in a MR study, as trans-ligamentous or sub-ligamentous, depending on the integrity of the posterior longitudinal ligament (PLL).

When a fragment of disk tissue is located in the central canal not in continuity with the disk, we use the term of free fragment. This fragment can migrate cranially or caudally and can thus impress a nerve root above or below the level from which it originated.

Although they may have, like all other disk herniations, an acute post-traumatic onset, are generally the result of degenerative processes of intervertebral disks such as the reduction in height of the intervertebral space and osteophytes that encroach the medulla or nerve roots. The evaluation of the relationship between herniated tissue and osteophytes is very important; in particular, we must distinguish between hernias where the disk component prevail ("soft hernia")

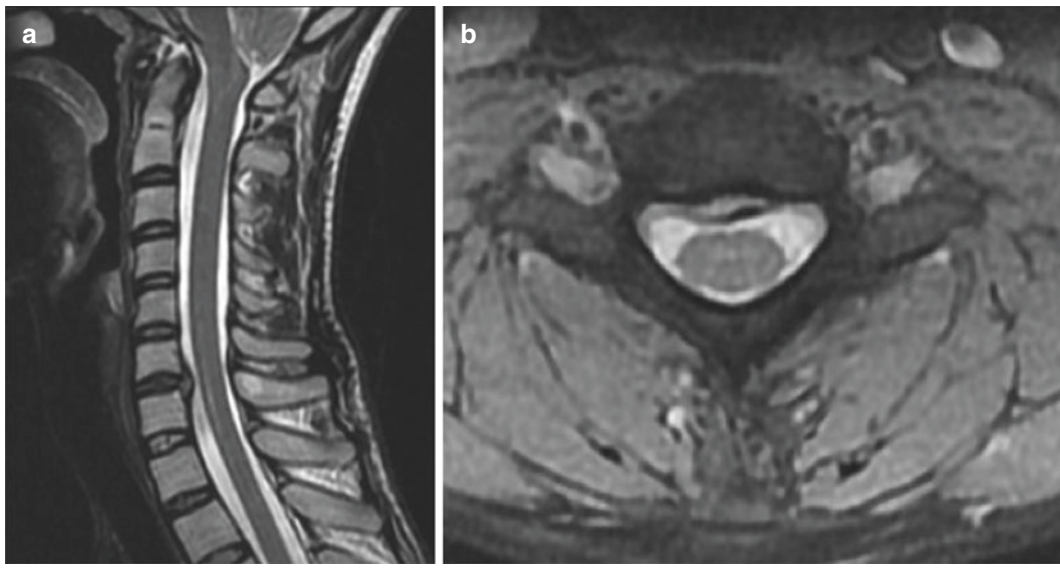

Fig. 3.7 Central disk herniation. Sagittal FSE T2 (**a**) and axial GRE T2 with fat suppression (**b**) images. It is evident a focal C6–7 protrusion/herniation of disk material deforming the ventral surface of the thecal sac on the midline

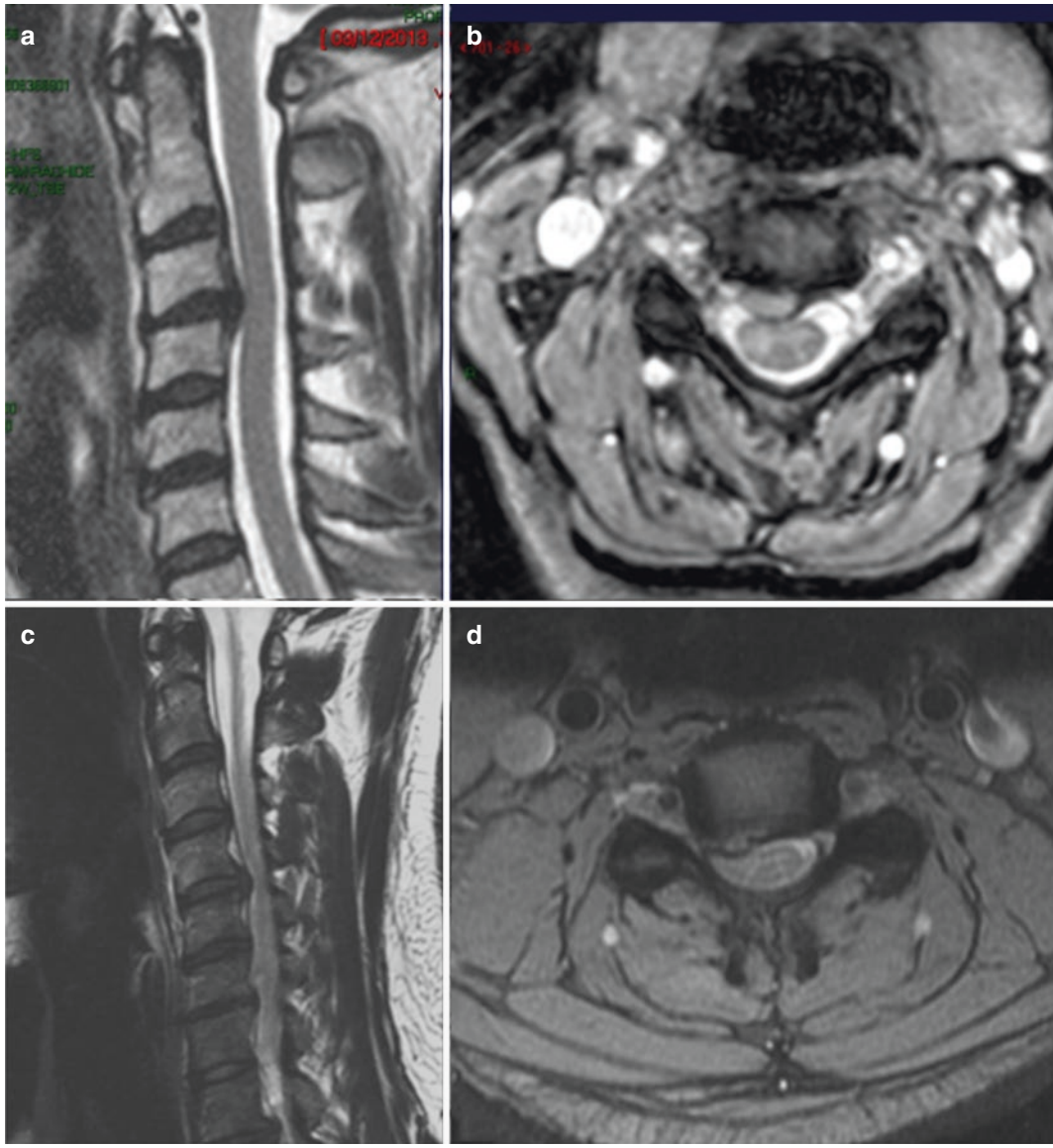

Fig. 3.8 Lateral disk herniations (posterior paramedian/posterolateral). Patient 1: Sagittal FSE T2 (**a**) and axial GRE T2 with fat suppression (**b**) images. The C3–4 paramedian disk herniation results in minimal impingement on the right hemicord. Patient 2: Sagittal FSE T2 (**c**) and axial GRE T2 with fat suppression (**d**) images. The C4–5 posterolateral disk herniation occupies the right lateral recess with compression of the C5 nerve root

from those that are completely contained in a shell bone ("hard hernia"). In the latter, the surgical outcome is generally worse.

Cervical disk herniations are less frequent than lumbar because the cervical disks and vertebrae substain less weight and the uncinate processes play an important role in containing the herniated material. The cervical hernia is more common laterally, because in that location the posterior longitudinal ligament is less tough. Cervical herniations most commonly occur at the C5–6 and C6–7 levels.

Cervical Herniation: Imaging

The peculiar anatomy of cervical spine, where intervertebral disks are thinner, radicular canals

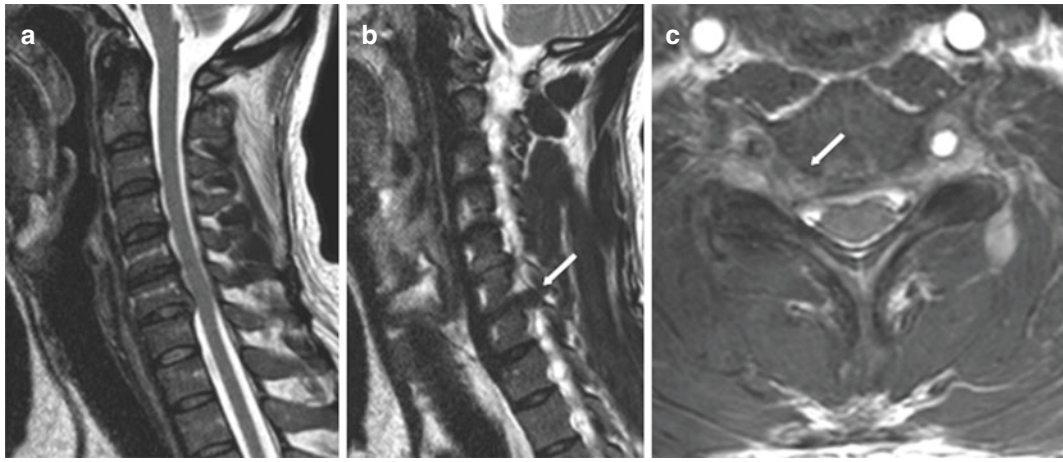

Fig. 3.9 Foraminal C6–7 disk herniation. Sagittal FSE T2 on the midline (**a**), right parasagittal FSE T2 (**b**) and axial FSE T2 (**c**). On the midline there is only minimal disk bulging while the large disk herniation [arrow in (**b**) and (**c**)] completely occupies the right neuroforamen

and foramina are shorter and there is much less epidural fat, should always be taken into account while executing a CT scan. CT is typically used to detect the different hernia components ("soft" from "hard" hernias) and in the evaluation of bony structures. The multiplanar oblique reconstructions perpendicular to the major axis of the radicular canals provide, for example, an excellent assessment of the size of the foramina and their possible stenosis due to the presence of uncovertebral osteophytes.

The detection of a small disk herniation may however be difficult for the scarse representation of epidural fat or, in patients with short and thick neck, for the superposition of the shoulders and the rib cage. The use of intravenous contrast medium can evidentiate the conspicuity of disk herniation thanks to the enhancement of epidural veins and of the associated granulation tissue. Although CT maybe useful in the diagnosis of cervical hernia, post-contrast examination are usually not required to make the diagnosis because of the clearcut superiority of MRI. Before scheduling a surgical procedure, however, it may be very important to evaluate the status of the bony walls of the central spinal canal and radicular canal, as shown by CT. In fact, disk herniation is often a contributing cause of the symptoms and may be associated, for example, to the stenosis of a radicular canal secondary to uncovertebral osteophytes, which are better visualized on CT.

MRI is definitely the examination of choice in patients with signs of radiculopathy or myelopathy caused by disk herniations. The MRI study should be executed using sagittal and axial SE T1-w images, the corresponding FSE T2-w images, and 2D/3D GRE T2*-w at the levels where there is a suspicion of disk disease. T1-w images provide detailed anatomical information; the disk appears hypointense, similar to the ligamentous structures and osteophytes. Because the cerebrospinal fluid (CSF) also presents low signal intensity and the epidural fat is scarcely evident, there is little contrast between extradural structures and CSF. It is therefore difficult, in axial T1-w images, to differentiate a small amount of herniated tissue from an osteophyte. Small herniated cervical disks are certainly easier to detect in 2D/3D T2*-w images, in which the bone is more hypointense, fluids are very hyperintense and therefore it is easier to differentiate the herniated disk from the bone and the adjacent osteophytes. Migrated fragments can sometimes mimics osteophytes, because of their low signal intensity, and are better visualized on GRE T2*-w images than on FSE T2-w images. The thinning and low signal of PLL on GRE T2*-w is characteristic of acute disk herniation [25] (Fig. 3.10).

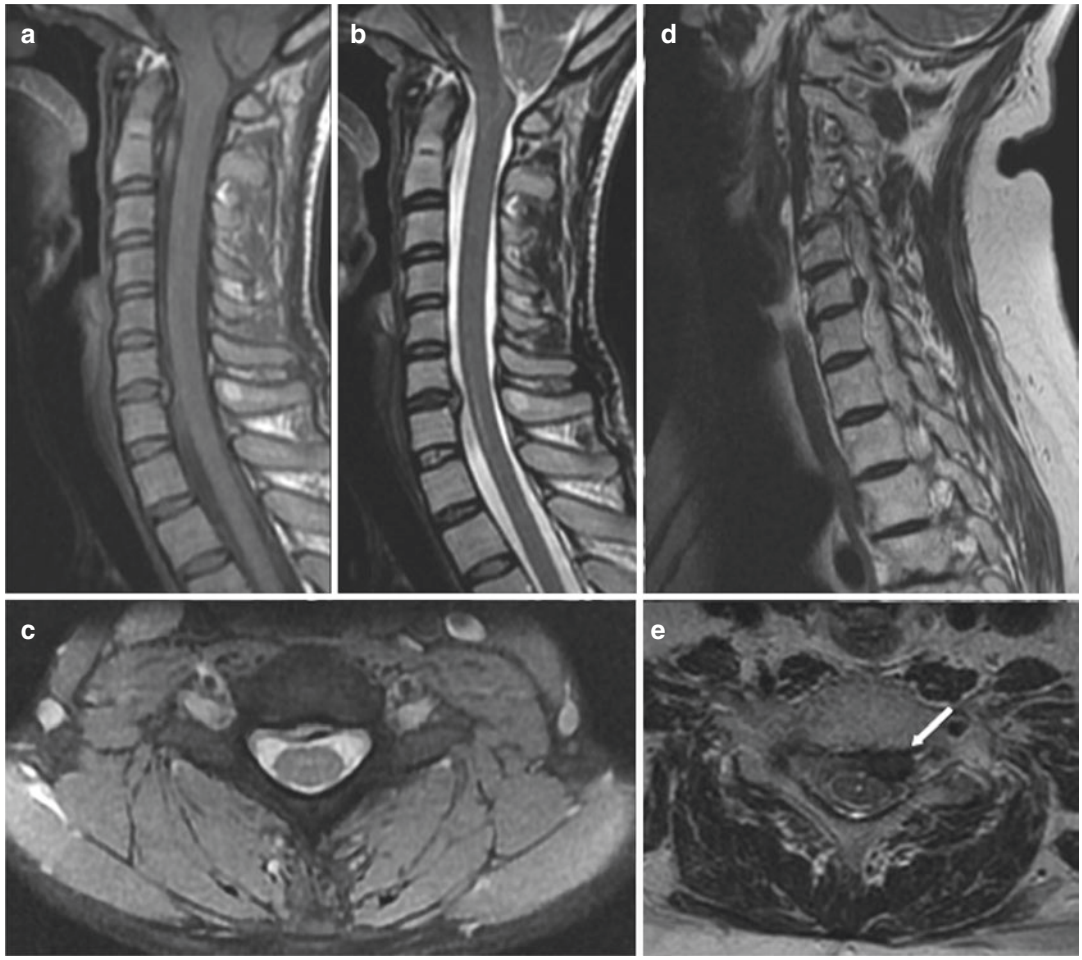

Fig. 3.10 Disk herniations, MR imaging. Patient 1: sagittal FSE T1 (**a**), sagittal FSE T2 (**b**), axial GRE T2 (**c**). Acute disk herniation with high signal intensity at C6–7 level. Patient 2: sagittal FSE T2 (**d**), axial FSE T2 (**e**). Lateral disk herniation with cranially migrated disk fragment [arrow in (**e**)] which shows low signal on T2 images

Stenosis

Central canal stenosis define the narrowing of the vertebral canal and/or lateral recesses and radicular canal, which can lead to compression of the nerve roots or spinal cord.

Patients with cervical stenosis have insidious symptoms onset, expression of mono or bilateral radiculopathy or myelopathy (e.g., upper limb paraparesis or dysesthesia).

The neck pain is often associated, but is not specific. Early diagnosis is essential, since there is no spontaneous regression of the process and the surgery prevents the progression of the symptoms and of the spinal cord damage.

Using etiological criteria it is possible to distinguish:

- Congenital stenosis (idiopathic, dysplasia, achondroplasia, mucopolysaccharidosis): characterized by short and stubby peduncles, shortness of the interpeduncular and sagittal diameter and hypertrophy and verticalization of the laminae; the central canal appears narrowed, as well as reduced, or completely absent, appears the epidural fat;

- Acquired stenosis: can be the result of surgery, traumatic lesions or neoplastic but, more frequently, derive from degenerative alterations of vertebral bodies (osteophytes), of articular pillars (hypertrophic degenerative osteophytes, subluxation), intervertebral disks ("bulging", herniated disk), of flaval ligament (hyperplasia, calcification) and/or of posterior longitudinal ligament ossification. The same reduction in height of the intervertebral space, due to disk degeneration, can determine the shortening and thickening of the intervertebral ligaments, resulting in the encroach on the dural sac;
- Mixed stenosis: are the most frequent in clinical practice and derive from the overlap of an acquired form on a condition of congenital stenosis; in this case, a disk protrusion and/or osteophytosis, even modest, may lead to severe nerve root or spinal cord compression.

Using topographic criteria, stenosis may be divided into:

- Central: characterized by a reduction in the size of the central canal, that in degenerative forms is supported by the "bulging" disk, hyperplasia and/or calcification of the flaval ligaments, osteophytes and degenerative articular pillars hypertrophy.
- Lateral: include lateral recesses and foraminal stenosis. Lateral recesses stenosis is due to uncinate process hypertrophy, degenerative enlargement of a superior articular facet and/or osteophytosis. Foraminal stenosis is mostly supported by congenital factors (shortness of peduncles), by degenerative pathology of the disk ("bulging") and posterolateral vertebral bodies osteophytosis.

Furthermore, measurement of the diameters of the canal is not very reliable, given the considerable individual variability. It is true, however, that at the cervical level there are two semeiological radiographic references that allow assessing the sagittal diameter of the central canal: the first coincides with the ideal line drawn along the posterior wall of the vertebral bodies; the second is the spinolaminar line. This imaginary line joins the convergence points of the laminae of each vertebral body on the midline. Normally, the spinolaminar line is convex forward and is at least 3–4 mm away from the posterior edge of the articular pillars. If the spinolaminar line is overlapped to the zygapophyseal joints, it is possible to infer that the sagittal diameter of the cervical central canal is reduced.

Another method to assess spinal stenosis is the central canal-to-vertebral body ratio, also called "Torg-Pavlov ratio". This is a ratio of the diameter of cervical canal to the width of cervical body. Less than 0.8 on radiography is consistent with cervical stenosis [26]. However, we can consider stenotic a cervical spinal canal with a width less than 13 mm [27]. CT better visualizes the causes of degenerative spinal stenosis, since it well demonstrates vertebral body and facet joints osteoproliferative processes, degenerative changes of intervertebral disks and calcification of flaval ligaments.

In case of degenerative spondylolisthesis, CT easily identifies subluxation of the zygapophyseal joints, the sign of "double arch" and, in the sagittal multiplanar reconstructions, dural sac impingement. CT also allows easier measurement of the diameter of the central canal, but it is not able to demonstrate the effects of the degenerative injury on the spinal cord. Moreover, in the cervical spine, the low amount of epidural fat and the relatively small size of the spinal canal is insufficient to assess a possible ligamentous hypertrophy.

Imaging

Good quality X-ray studies demonstrate the degenerative changes but not their compressive phenomena on the spinal cord, their extension (on sagittal images) and, above all, the direct effect on the nervous structures (edema, gliosis and myelomalacia). Because of these advantages, especially in the cervical spine, MR imaging represents the preferred imaging modality (Fig. 3.11). The root compression in the foramina is shown, in the sagittal T1-w images, by the dislocation or disappearing of periradicular fat; compression of the dural sac and disk degenera-

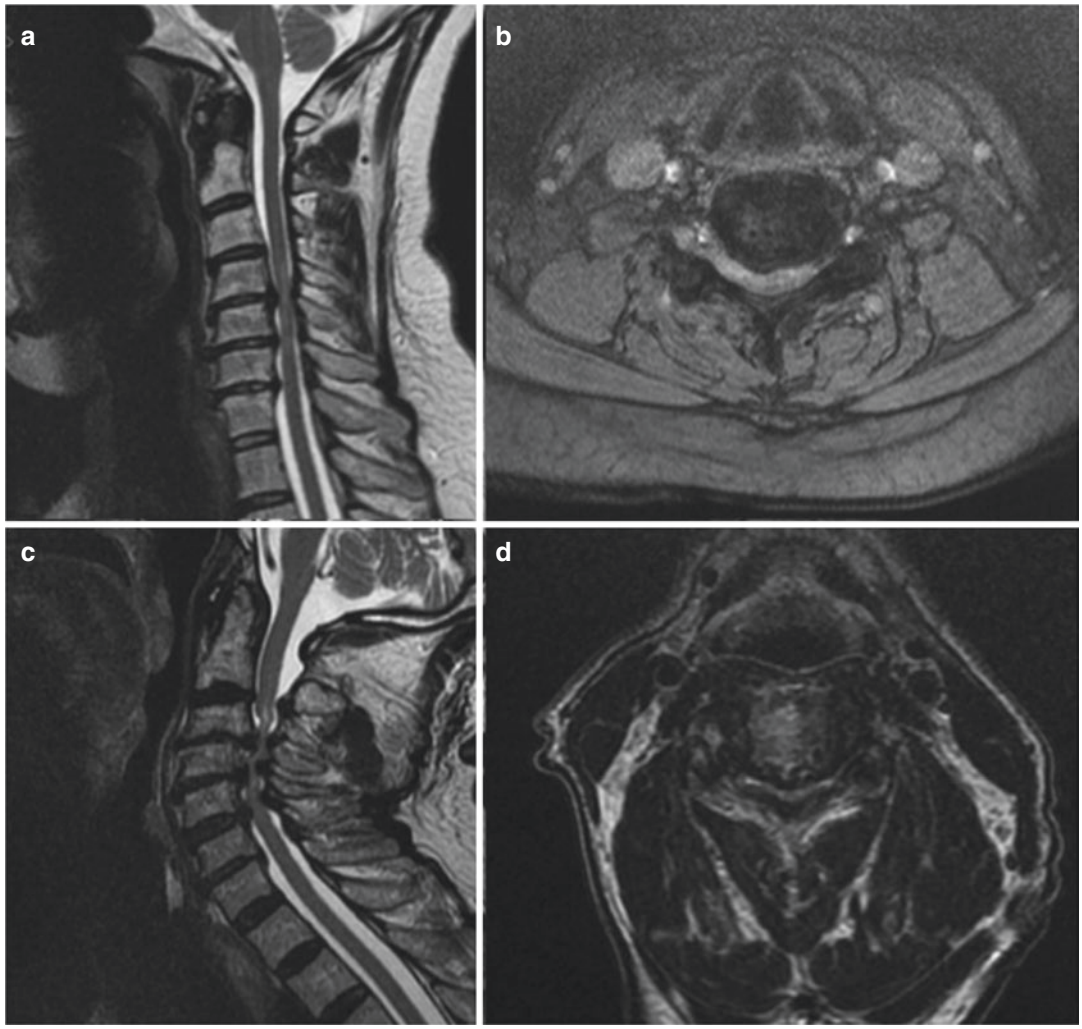

Fig. 3.11 Stenosis of the spinal canal, MR imaging. Patient 1: sagittal FSE T2 (**a**), axial GRE T2 (**b**). Posterior disk herniation associated to mild spondylosis at levels C4–5, C5–6 and C6–7 determine spinal canal stenosis with encroaching the spinal cord that presents intrinsic signal modifications. On axial images the degree of stenosis is better evaluated. Patient 2: sagittal FSE T2 (**c**), axial FSE T2 (**d**). Advanced stages of spondylosis and disk degeneration/herniation. The central canal is almost completely obstructed. Spinal cord is severely compressed with reduction of its sagittal diameter and intrinsic signal modifications

tion, however, are more evident in the T2-w images. Using volume 3D GRE techniques with thin sections (1 mm or less) it is possible to obtain the best evaluation of cervical neural foramina [28]. Although CT can be used to detect narrowed neural foramina, the MR imaging using axial GRE T2*-w or post-contrast MR scans usually offers better results. The T2*-w images allow identification of osteophytes and differentiate them from adjacent disk herniation. Furthermore, it clearly demonstrates the ossification of the posterior longitudinal ligaments and the flaval ligaments hypertrophy, due to the intrinsic high contrast that exists between these structures and the adjacent subarachnoid space. If the spinal cord is compressed from a long period, irreversible changes occur, namely myelomalacia and gliosis, with focal areas of high intensity signal in the cord on T2-w images [29], resulting in a more obvious reduction of the sagittal diameter of the spinal cord (atrophy) with increased evidence of the ventral fissure.

Specific Degenerative Diseases

Rheumatoid Arthritis

Even if Rheumatoid Arthritis is not a pure degenerative disease, we included this pathological entity in the chapter, because of the primary involvement of the cervical spine and the resemblance of its manifestations with those of the other degenerative diseases.

Rheumatoid arthritis (RA) is a chronic autoimmune disease that involves the small synovial joints leading to progressive destruction, with associated systemic involvement. The prevalence is 1% in general population, with female predilection (F:M 3:1), however males have a greater risk of developing advanced cervical involvement. The joint involvement in RA is symmetrical in the appendicular skeleton, while the axial skeleton is usually spared except for the cervical spine. The cervical spine is involved in up to 86% of patients and overall, RA is the most common inflammatory disorder that involves this rachidial segment. The synovial joints involved are the atlantooccipital and atlantoaxial joints. The progressive destruction of these joints leads to development of atlantoaxial instability (AAI) or forms of luxation or subluxation, in particular, atlantoaxial subluxation (AAS), vertical axis subluxation (VS) or cranial settling, and subaxial subluxation (SAS). The entity of cervical spine involvement is related to multiple factors (duration of AR, severity of peripheric arthritis, duration of corticosteroids therapy, presence of rheumatoid nodules, serum values of RF).

The pathologic primum movens is the synovial membrane inflammation, sustained by a cascade of events, with influx of immune cells, including neutrophils, mast cells, and macrophages into the synovium, and local release of proinflammatory cytokines and small-molecule mediators of inflammation. The inflammation of the atlantoaxial joint (Fig. 3.12), facet joints, uncovertebral joints, retrodental bursa, interspinous ligament and ligaments around the atlas leads to the formation of a periodonteum inflammatory pannus with progressive articular cartilage loss, formation of bony erosions and ligamentous destruction. Then follow cervical instability with ipermotility, while the successive step is the establishment of subluxations (atloaxial or subaxial) with consequent mechanical derangement of the segment (Fig. 3.13). The final consequences are the various compressive neurological and vascular manifestations.

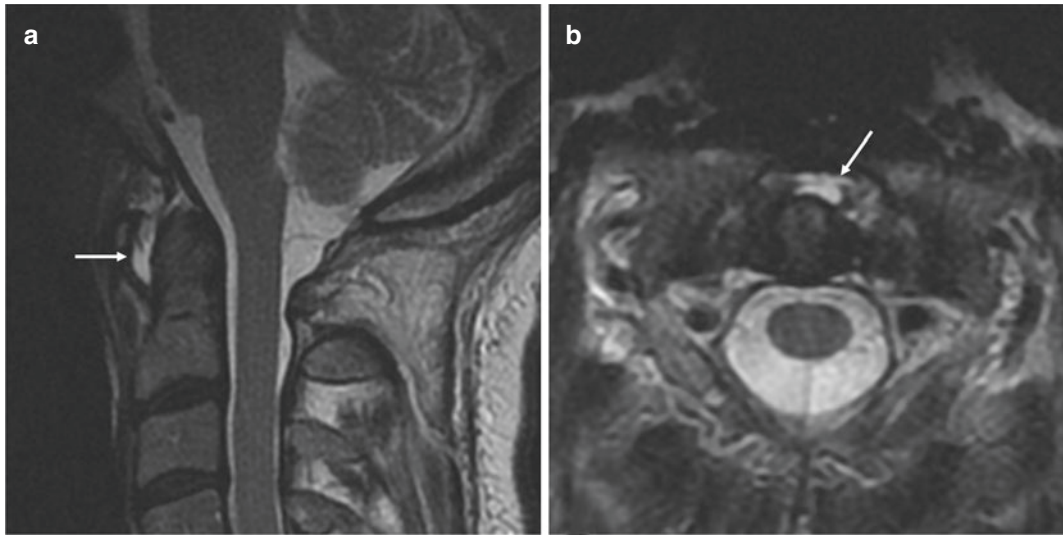

Fig. 3.12 Rheumatoid Arthritis, MR imaging. Sagittal FSE T2 (**a**) and Axial FSE T2 (**b**). Anterior subluxation, with presence of fluid and inflammatory tissue around the dens (in particular anteriorly), with high signal in T2 sequences [white arrow in (**a**) (**b**)]. No signs of erosions in this case

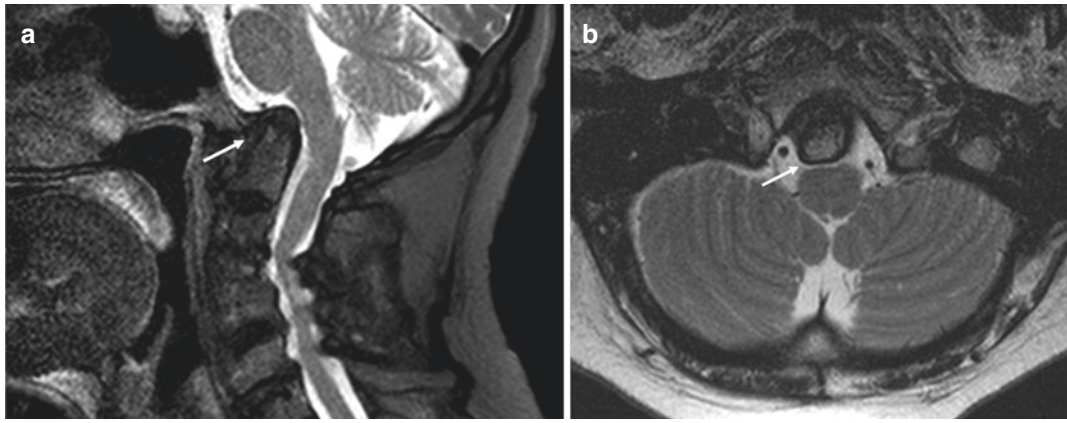

Fig. 3.13 Impressio basilaris in a Patient with rheumatoid arthritis, MR imaging. Sagittal FSE T2 (**a**) and Axial FSE T2 (**b**). (**a**) Vertical atlo-axial luxation; the apex of dens lies above the foramen magnum (white arrow); in (**b**) (white arrow) mild compression on the ventral surface of medulla oblungata is evident, without white matter involvement

The majority of patients with cervical involvement are asymptomatic at the moment of diagnosis. When symptomatic, the most common findings is neck pain, but there are multiple possible clinical presentations due to compression of cervical structures (cervical or cranial nerves, brainstem, spinal cord or vessels), or to cervical instability. Relatively common finding in symptomatic patients are different forms of pain, such as occipital headache (in case of cranial settling or AAI, due to compression of occipital nerves passing between the atlas and axis), migraines or neck, mastoid, ear, or facial pain (determined by the compression of the C2 spinal nerve or greater auricular nerve). The symptoms related to compression of the brainstem and/or vertebral arteries include tinnitus, vertigo, dysphagia, visual disturbance and diplopia. The symptoms related to cranial nerve compression are extremely variable: the most common are dysphagia (due to compression of the X or XI cranial nerves), dysarthria (due to the compression of the XII CN) and paresthesia, hypoestesia or facial pain (due to compression of the nucleus of the spinal trigeminal tract). The myelopathy symptoms (with variable combination of muscle atrophy, weakness, gait impairment, dexterity impairment, limb paresthesias, hyperreflexia, spasticity, loss of proprioception, bowel or bladder disturbance), that in the severe cases can lead to paralysis due to secondary syringomyelia, locked-in syndrome, or sudden death are related to the spinal cord compression. In physical examination Lhermitte's sign is reported in case of compression of the superior spinal cord and cervico-medullary junction. Cervical instability, in particular AAI, is related to sensation of the head falling forward upon flexion. Moreover, if the consequences of cervical instability determine kinking of the vertebral arteries, there is an increased risk of vertebrobasilar thromboembolism.

Pharmacologic therapy of RA is based on administration of glucocorticoids (GC), disease-modifying antirheumatic drugs (DMARD), and or biologic agents (BA). DMARDs and BAs decrease the incidence of cervical spinal involvement, but they are not effective in attenuating the progressive destructive disease course in the cervical spine when already present. This consideration highlights the necessity of an early diagnosis and treatment of cervical spine involvement in RA.

Imaging

Plain radiograph is usually the first examination, particularly in asymptomatic patients. The standard examination should include plain radiographs with dynamic flexion-extension and open

mouth views for odontoid. These projections are reliable in determining bone alignment and deformities. However, the assessment of instability of cervical spine based on plain films may vary. Moreover, some imaging features are not completely analyzable in plain radiographs, in particular bony erosions, the status of craniocervical junction and cervicothoracic junction and the characteristics of inflammatory pannus and spinal cord compression. In case of plain radiographs findings that confirm or pose a suspect for RA, or in case of symptoms (neck pain, neurological symptoms), computed tomography (CT) or magnetic resonance imaging (MRI) are indicated. CT scan with multiplanar reconstruction best depicts bony erosions and the presence of ankylosis or pseudarthrosis, and may be used in surgical planning. MRI has a specific indication on all patients with myelopathy or radiculopathy, because represent the best imaging modality for soft tissue and spinal cord assessment. The possibility to acquire dynamic flexion-extension MRI sequences is useful to diagnose subarachnoid encroachment that cannot be ruled out in static MRI.

Diffuse Idiopathic Skeletal Hyperostosis Syndrome

The Diffuse Idiopathic Skeletal Hyperostosis or DISH, (also known as Forestier disease, senile ankylosing hyperostosis and asymmetrical skeletal hyperostosis) is a not uncommon degenerative disorder in the elderly population, with a reported prevalence in some study of 10% in patients over 70 years [30, 31]. It is characterized by excessive ossification along the anterior longitudinal ligament of the spine, resulting in bridging osteophytes. In the 1970s, Resnick established specific radiological criteria for the diagnosis of DISH [32]: (1) presence of flowing calcification and ossification along the anterolateral aspect of at least four contiguous vertebral bodies; (2) relative preservation of intervertebral disk height in the involved vertebral segments without degenerative disk disease; (3) absence of apophyseal joints ankylosis and sacroiliac joint erosion, sclerosis or bony fusion [33]. Extra-spinal ossification in DISH may occur at the ligamentous attachments and para-articular soft tissues.

DISH is largely asymptomatic and it is usually incidentally detected. The exact etiology of the syndrome is unknown: the DISH could be considered an expression of the ossificans diathesis, typical of the advanced age, that leads to the production of bone tissue at the insertions of tendons and ligaments on the skeletal structures (entheses), to ligaments calcification and ossification, and finally to the formation of para-articular osteophytes [1]. The spine is the elective target of the disease, pointing out that other skeletal regions may also be involved.

The prevalence is highly variable (2.9–42.0%) and depends on different factors: the demographic background, the used diagnostic criteria and the presence of concomitant risk factors, such as older age, metabolic factors (hypertension, obesity, diabetes mellitus), and cardiovascular diseases [34].

Imaging

The radiological findings results directly from the histopathologic alterations of the spine. A characteristic aspect of the DISH is that the ossification of the ALL is more pronounced at the level of the disk spaces, creating a "bulky" aspect of the ventral spine profile.

In the first stages of the disease, radiography may show a fine ossification (with thickness of 2 mm or less); with the progression of the illness it is possible to observe the development of large syndesmophytes (a syndesmophyte is defined as a bony growth originating within a ligament). The typical site of syndesmophytes formation is the anterior aspects of vertebral body (because of the involvement of ALL).

Radiography is inadequate for evaluating the extent of the compression caused by the large syndesmophytes on trachea, bronchi, or esophagus. In this case, a CT study of the spine, with multiplanar reconstruction, would be helpful (Fig. 3.14).

CT play also a role in the evaluation of complications, such as fracture, spinal canal stenosis secondary to associated ossification of the poste-

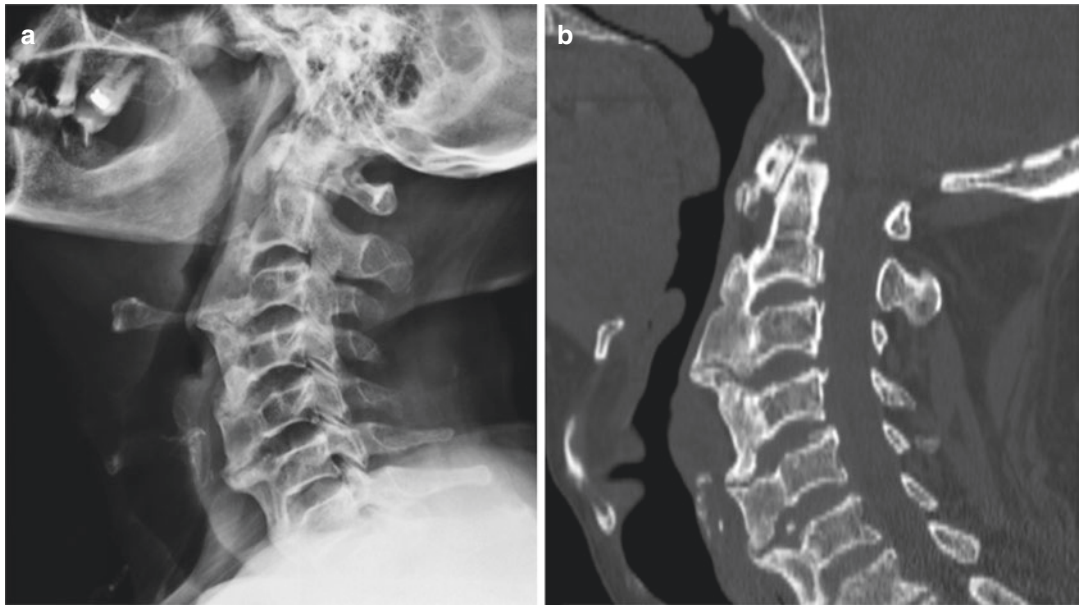

Fig. 3.14 Diffuse Idiopathic Skeletal Hyperostosis Syndrome (DISH), radiography and CT. Lateral radiogram in standing position (**a**) and CT sagittal images (**b**). Diffuse ossification along the ALL with bridging osteophytes from C2 to C7 is well evident, with preserved disk height. The findings are well demonstrated on CT examination, with a better visualization of the disease extension

rior longitudinal ligament, and pressure effects on the hypopharinx. The only indication for the MRI is to show/rule out cord compression when DISH is associated with an ossified PLL, as it is observed in a minority of patients [35].

The criteria most frequently employed to establish a diagnosis of DISH are those described by Resnick and Niwayama (bridging of four adjacent vertebral bodies by new formed bone, without severe loss of the intervertebral disc height and without degeneration of the apophyseal and sacroiliac joints probably reflecting findings related to the end stage of the disease [33]. Kuperus et al proposed the CT parameters to distinguish between no DISH, early DISH, and definite DISH in order to consider diagnostic criteria to establish the diagnosis in the early stage. The evaluated features were the presence and location of bone bridges, the degree of flow of the new formed bone and the location of new bone formation, giving points to each characteristic, thus realizing a score system [36].

Ossification of the Posterior Longitudinal Ligament

Ossification of the posterior longitudinal ligament (OPLL) is a spine disorder that usually affects individuals between the fifth and seventh decade of life, more frequently males; a higher incidence in the Japanese population has been reported [37]. The disease commonly involves the cervical regions of the spine and is clinically characterized by myeloradiculopathy, even if the OPLL may be often asymptomatic.

It has been proposed that pathogenesis of OPLL may be related to disk herniation and/or to a diffuse hyperostotic process [38].

OPLL can have a progressive course both in patient that underwent decompressive posterior surgery and in asymptomatic, not-surgically treated patients. Some studies focused on findings those risk factors. Lee et al found a greater risk for post-operative OPLL progression in patients that underwent posterior laminoplasty

for specific type of disc involvement and in case of increased range of motion (ROM) evaluated on dynamic plain radiographs; increased ROM is also a risk factor for development of cervical myelopathy [39]. Doi et al investigated the risk factors for OPLL progression in asymptomatic patients, finding that younger age, OPLL involvement of multiple vertebral levels, continuous type of OPLL and higher serum levels of uric acid represent higher risk of progression in this subset of patients [40].

Imaging

On plain radiography a continuous calcification along the posterior longitudinal ligament is observed, especially on the intermediate tract of the cervical spine (C3–5); the associated disk degeneration and facet ankylosis are often minimal.

CT has a higher sensitivity in the assessment of the calcification extension; in some cases the axial images can show specific patterns of calcification of the ligament ("upside-down T" and "bowtie"). MR imaging shows the spinal cord lesion that can be associated, particularly in those cases in which the ossification thickness is greater (Fig. 3.15).

In some patients with OPLL it is possible to detect an extensive calcification of the ALL or other signs of DISH; when it happens, differential diagnosis with inflammatory arthropathy is made possible by observing the absence of facet joint ankylosis and scarcity of associated disk degeneration [37].

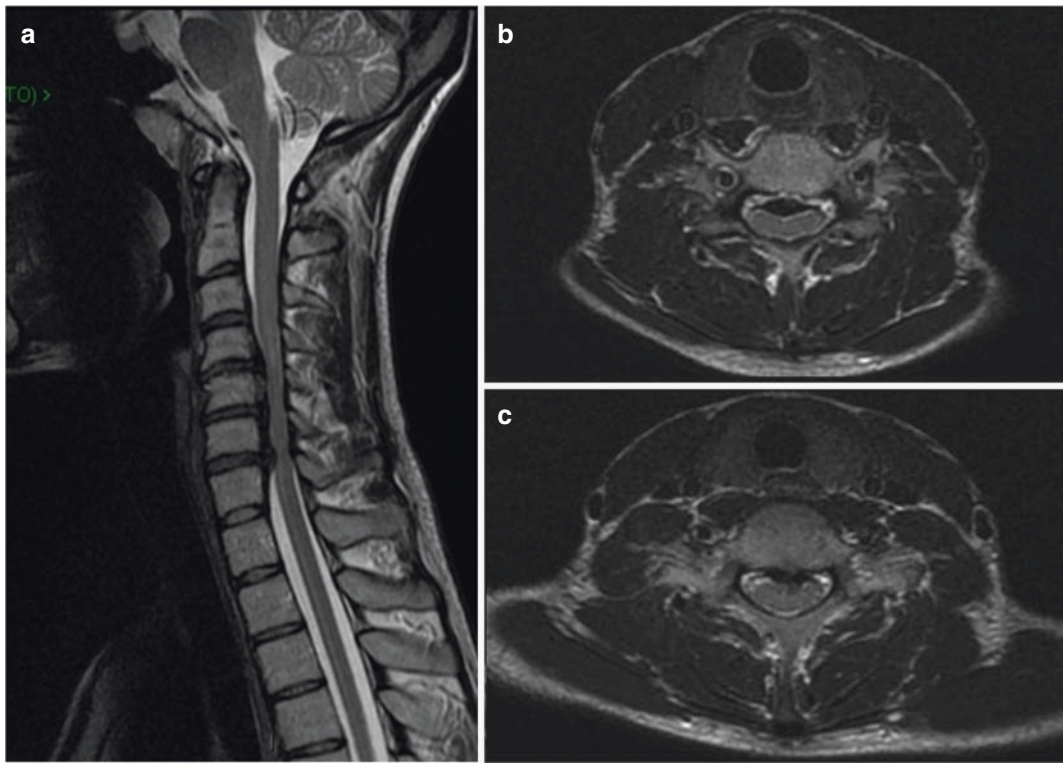

Fig. 3.15 Ossification of Posterior Longitudinal Ligament (OPLL), MR imaging. Sagittal FSE T2 (**a**) and axial FSE T2 (**b**, **c**). Ossification of the posterior longitudinal ligament is located at C3–C6 levels, in the intermediate tract of the cervical spine. The spinal cord shows mild hypertensity at that level (edema/gliosis) due to compression from the thickened ligament

Destructive Spondyloarthropathy of the Cervical Spine in Long-Term Hemodialyzed Patients

Destructive Spondyloarthropaty (DSA) is characterized on plain radiography by a notable reduction of the intervertebral disk space associated with erosions and cysts of the adjacent endplates and minimal osteophytosis. Typically, multiple vertebral bodies are involved: the lower part of the cervical spine (C5–7) is most frequently affected, though the CCJ may also be involved. Clinically, DSA can lead to medullary compression, which requires surgical decompression and stabilization. However, neurological symptoms are rare. The prevalence of DSA is difficult to establish: it varies from 5 to 25.3% in long-term hemodialyzed patients [41].

The exact pathogenesis of DSA is not well understood: it could be the direct consequence of the hemodialysis-related systemic amyloidosis. There are many risk factors associated with the onset of the DSA, such as the duration of renal failure, the age of onset, the duration of hemodialysis, dialysis membranes and the basic clinical condition of the patient, but to date the natural history of this syndrome is unclear and no effective treatments are available.

In a study of Nagamachi et al has been reported that the age at the onset of hemodialysis is also related with the progression of destructive changes, differently from the duration of hemodialysis that did not show such correlation [42].

Imaging

The radiographic signs of the syndrome include a severe reduction of the intervertebral disk space associated with erosions and/or cysts of the adjacent endplates, and minimal osteophytes formation.

On radiography, in the early stages of the DSA it is also possible to detect signs of enthesopathy, mimicking an early ankylosing spondylitis. As the pathology progresses, endplate destruction associated with a soft tissue mass is established, very similar to the spondylodiscitis appearance. These alterations lead to vertebral body collapse, subluxation or listhesis.

The degenerative process, with pseudotumors and bone erosions, can sometimes involve the CCJ, although it is uncommon. A relevant clinical problem is to rule out infections in symptomatic hemodialyzed patients (who present an increased risk of infective diseases) with destructive vertebral lesions. The radiologist should be able to distinguish DSA from spondylodiscitis; if the disks show low signal on T2-w and STIR (Short Tau Inversion Recovery) images, DSA is more likely.

Ossification of Flaval Ligaments

It is a degenerative disorder characterized by the ossification of flaval ligaments. The pathogenesis is unclear and probably associated with metabolic disorders (with hydroxyapatite or calcium pyro-phosphate deposition in ligaments).

Ossification of flaval ligaments appears as a linear thickening of flaval ligament similar to adjacent vertebral marrow ossification. The ossification is typically symmetric and bilateral; it is often diagnosed incidentally during imaging study ordered for other reasons.

Imaging

On radiography, when appreciable, ossification of flaval ligaments appears as a thin calcification located anteriorly to laminae.

CT is the best imaging modality to show ossification, but it is inadequate in order to determine the possible spinal cord involvement. On CT, ossification of flaval ligaments appears as a hyperdense thickening within the ligament, best shown on axial native scans with the characteristic V-shaped image.

MR imaging may easily detect not only ossification of the ligaments but also the secondary effect on the spinal cord. On T1-w images the ossification of flaval ligaments appears as a hypo- (thinner lesions) to hyperintense (thicker lesions) linear mass within the ligaments. OnT2-w images, it appears as a linear hypointensity associated or not with myelomalacia, due to cord compression. On GRE T2*-w images, the flaval ligaments appear as a thickened hypointense

band, and it is difficult to estimate the actual degree of canal narrowing due to susceptibility artefact [6].

Calcium Pyrophosphate Deposition Disease

Calcium pyrophosphate deposition disease (CPPD) is a metabolic arthropathy, also known as pseudogout, caused by a proliferation and deposition of calcium pyrophosphate dihydrate in and around the joints, especially in articular cartilage and fibrocartilage, with possible involvement of CCJ, namely the peri-odontoid structures. It is characterized by linear disk or ligament calcific deposits. The exact etiology of the syndrome in unclear; it may be associated with hyperparathyroidism, hemochromatosis, gout or hypophosphatasia.

Imaging

Radiography may demonstrate linear calcifications within the disk, and it is often associated with calcification of the pubic symphysis or triangular fibrocartilage of the wrist. CT is the best imaging tool for evaluating the calcifications, but the MR imaging, especially on the T2-w images, can demonstrate not only the calcifications but also the amount of granulation tissue and fibrosis [6].

Crowned Dens Syndrome

The "crowned dens" syndrome (CDS) is a clinical-radiological entity presenting tipically with acute onset of cervical-occipital pain, associated with fever, rigidity and general signs of inflammation, lasting from days to several weeks. The mean age at presentation is 60–70 years, with female prevalence.

The pathologic substrate is frequently associated to crystal deposits diseases, in most cases calcium pyrophosphate dihydrate (CPPD) but also hydroxyapatite (HA). Other articular inflammatory diseases may be associated with the CDS (RA, RA-DISH and other systemic connective diseases, as Systemic Sclerosis). Other conditions related to the occurrence of CDS are traumas, articular subluxations and tumors.

The syndrome could remain asymptomatic or cause chronic cervical pain and spinal cord compression; the classic onset, represented by a triad of symptoms (headache, fever and morning cervical pain) is aspecific, being related to different conditions, as infectious meningitis or also metastatic cervical spondylitis. Atypical clinical presentations include painful cervicobrachial syndrome (associated with shoulder stiffness and weakness) or occipito-temporal headache (similar to the symptom associated to atypical rheumatic polymyalgia or giant cell arteritis).

Imaging

CT scan represent the diagnostic gold standard: the findings that allow the definition of CDS (in the adequate clinical scenario) are calcifications of all odontoid articular structures (synovial membrane, articular capsule and ligaments); tipically the aspect of calcification is narrow and irregular, surrounding the odontoid process ("horseshoe appearance") with other smaller calcifications located at the apex of the dens surrounding the main calcification (Fig. 3.16).

CT also permit the evaluation of cortical bone, periodontoid calcifications and the presence of other smaller calcifications surrounding the odontoid process: moreover it can depict

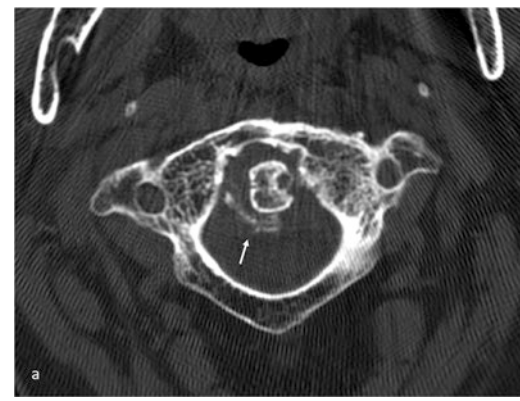

Fig. 3.16 Crowned dens, CT imaging. Axial. Mineralization of transverse ligament of the atlas, more evident in the right side (white arrow)

unknown fractures of the dens. However CT scan has some limitation in assessing CDS when performed tardily after an acute symptomatic attack (because the calcifications may have been reabsorbed or may migrate). This event is more often related to CDS associated with Hydroxy-Apatite Deposition Disease (HADD)-rheumatism [43].

Cranio Cervical Junction Pseudotumor

The retro-odontoid pseudotumor (ROP) represents a non-neoplastic proliferation of soft tissues at the atlantoaxial junction.

Retro-odontoid pseudotumor is commonly associated with atlantoaxial microinstability or subluxation: overtime the mass can determine compressive myelopathy on adjacent spinal cord. The symptoms may be variable, ranging from neck pain (the most frequent), headache and/or neck stiffness to paraparesis and paralysis (in the severe cases).

The retro-odontoid pseudotumor can be associated with several pathologic conditions;

RA is the most common disease associated to the development of retro-odontoid pseudotumor; a variable degree of retro-odontoid soft tissue thickening has been found in up to 83% patients [44], more frequently in patients with known peripheral arthritis; isolated retro-odontoid pseudotumor in this group of patients is rare [45].

The non-rheumatoid conditions related to retro-odontoid pseudotumor, with and without atlantoaxial instability, include: chondrocalcinosis, hemodialysis-associated amyloidosis, chronic odontoid fracture, gout, pigmented villonodular synovitis (PVNS) and ossification of the posterior longitudinal ligament. Other, less frequent conditions related to the growth of mass-like formations in the retro-odontoid region are represented by retro-odontoid synovial cysts, epidural hematoma and/or lipomatosis.

Surgical treatment of local instability is considered the best therapeutic option. Multiple cases reported in literature demonstrated volumetric regression of the pseudotumor after surgical stabilization of cranio-cervical junction.

Development of chronic atlantoaxial instability and resulting mechanical stress are treated surgically mostly with posterior fusion (with occipitocervical or atlantoaxial fusion): this procedure is an appropriate surgical strategy for retro-odontoid pseudotumor associated with atlantoaxial subluxation [46].

Kakutani et al. [47] analyzed the surgical outcomes of C1 laminectomy for retro-odontoid pseudotumor without atlantoaxial instability, finding an improvement in all the patients treated and included in the study.

Both Kobayashy et al. and Kakutani et al. studies evidentiated that the retro-odontoid pseudotumor that showed higher pre-operative MRI contrast enhancement, thus reflecting an higher neovascularization around the pseudotumor, had higher rates of regression after surgery.

Imaging

Neutral and flexion-extension radiographs are the primary imaging modality to evaluate cervical spine instability, with flexo-estension radiograph recommended in this clinical scenario.

Multidetector computed tomography is useful for identifying bony erosions, fracture, alignment, relationship of the joints and presence of pseudotumor: moreover the CT study easily evaluate the eventual mineralization within the retro-odontoid pseudotumor or in the peri-odontoid ligaments.

MRI represent nowadays the gold standard for the demonstration of retro-odontoid pseudotumor, allowing the identification of early pathological changes in case of early RA and the evaluation of tissue characteristics of the pseudotumor itself (determining the presence of hemorrhage, mineralization, fibrous tissue and, after contrast administration, the vascularity).

Some of the conditions related to the development of retro-odontoid pseudotumor present specific imaging characteristics.

In RA, ROP can show different histologic components (hypervascular, fibrous, or com-

bined), that reflects on different MRI appearance: high signal in T2-weighted images and enhancement in case of hypervascular pannus; intermediate signal intensity on T2-weighted images and absence of post-contrast enhancement in case of hypovascular pannus; and low signal intensity on T1 and T2-weighted sequence, without enhancement in case of fibrous pannus.

In CPPD the MRI signal would be usually low in T1 and variable-heterogeneous in T2-weighted imaging, due to the presence of calcium pyrophosphate dihydrate crystals deposits into hyaline and fibrocartilage.

Hemodialysis-associated amyloidosis can show cystic changes and erosions within the bony structures, better identified by CT.

In PVNS, histologically characterized by infiltrations of mononuclear histiocytes and multinucleated giant cells, the MRI signal is variable and heterogeneous in T1- and T2 weighted imaging, with "blooming" in gradient echo imaging determined by the presence of hemosiderin deposit.

The Gout rarely involves the cranio-cervical junction; the tophus, that can also cause well delineated bony erosions, are characterized by different grades of calcifications that determine a variable signal in MRI, not easily differentiable from a deposit of calcium hydroxyapatite crystals; dual-energy CT can be a useful diagnostic tool, allowing to differentiate between urate and calcific mineralization (that show different attenuation on the 80- and 140-kVp acquisitions).

In OPLL the ossification of posterior longitudinal ligament and its longitudinal extension can be better ruled out with CT, while on MRI the signal of the ossification is the same of the cortex.

Other conditions such as epidural lipomatosis or hematoma show tipically high signal in T1-weighted imaging due to the presence of fat tissue and blood clots, respectively. Retro-odontoid synovial cysts, related to degenerative changes involving the ligamentous structures, can show non equivocal MRI findings (a structure with fluid signal) if simple, nevertheless the signal may vary in case of complicated cysts [48].

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4 Anesthesia and Perioperative Care in Cervical Spinal Surgery

Angelo Chierichini and Marco Rossi

Anesthetic Management and Prevention of Complications

Preoperative Assessment

The preoperative conditions of the patients scheduled for CSS, and consequently the anesthetic technique chosen, may heavily affect the risks and the outcome of the procedure.

General indications about the most common and important coexisting diseases will be illustrated, underlining some peculiar aspects that need to be evaluated in this kind of surgery.

The most used method for the preoperative risk assessment is the stratification resulting from the American Society of Anesthesiologists Physical Status Classification System (ASA class). ASA score could be also used, together with the burden of the proposed surgical procedure, in order to properly assign the patients to an outpatient protocol, when allowed. With respect to the past, recent studies show that patients ASA III can be treated as outpatients without significant increase in perioperative complications while ASA IV patients are generally addressed for an inpatient treatment.

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However, most authors are now focusing their attention on the single comorbidities and on their grade of stabilization, rather than on the ASA class.

A careful evaluation is needed for patients suffering from diabetes, cardiovascular diseases and/or chronic obstructive pulmonary disease (COPD). Also, patients with already diagnosed or suspected Obstructive Sleep Apnea (OSA) deserve special attentions, in particular if a fast-track treatment is proposed. Untreated or poorly stabilized situations should suggest delaying the surgery or deciding for an inpatient treatment [1].

Obesity, with a body mass index (BMI) ≥ 35 kg/m^2 and two major comorbidities or a BMI ≥ 40 kg/m^2, represents a serious challenge for the surgeon and the anesthesiologist while undergoing CSS. Most of the possible complications are worsened and more frequent in the obese patient, including mistakes in the level of intervention, wound infection, position related injuries [2].

For diabetic patients, it's greatly advisable to assess the level of control of the disease, based on the history, the number of experienced hospital admission for hypo-hyperglycemia, and so on. It's also important to assess the level of compliance of the patient with his disease. Commonly, a good compliance consists in his ability to perform blood glucose test and to detect the early symptoms of hypoglycemia by himself.

Patients using insulin often take a combined therapy with a basal component (a single dose of long-acting insulin) and a postprandial correction

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with a short acting insulin. Usually, if the patient didn't experience preprandial hypoglycemia in the previous months, it is safe and advisable to administer 75–100% of basal-dose long-acting insulin the morning of surgery. However, the first target is to avoid hypoglicemia, so it's advisable to control blood glucose levels and to be ready to administer 5–10% glucose solutions i.v. perioperatively when needed.

Oral antidiabetics should not be assumed on the day of surgery, and avoided until normal alimentation is resumed.

The preoperative evaluation of glycosylated haemoglobin A1c (HbA1c) could help to identify patients with poor control of the disease. Levels of HbA1c lower than 7%, representing the ideal therapeutic target according to the American Diabetes Association Guidelines [3], were found associated with a significantly lower rate of postoperative infections [4]. A recent study showed that poorly controlled diabetic patients had a mean hospital stay 5 days longer than normal stay, while well controlled diabetic patients only 1 day longer [5]. Poorly controlled glucose levels are associated with worse mean outcome in diabetic and non-diabetic patients [6]. Some non-diabetic patients may have undiagnosed high levels of HbA1c, that is associated with a higher risk of complications undergoing spine surgery. Therefore, it could be advisable to include the HbA1c as a routine preoperative test for elective spine surgery [7]. Diabetic patients are more often burdened with ischemic complications due to the potential presence of microangiopathy, particularly in case of hypotension or hypovolemia.

Patients affected by coronary artery disease (CAD) should be carefully investigated, particularly when instability or recent modifications in the appearance of symptoms are present. Adverse cardiac events following CSS are not uncommon (4/1000) and their rate increases significantly in older patients (>65 y.o.) with greater comorbidities, particularly cardiovascular diseases [8].

Important studies suggest that Congestive Heart Failure (CHF) is actually the most important risk factor for perioperative morbidity and mortality [9]. CHF leading to a NYHA class (New York Heart Association) higher than II, recommends an inpatient treatment.

There is general agreement to continue chronic cardiovascular medications for cardiac patients until the morning of surgery. However, possibly some antihypertensive drugs could be remodulated: recent reviews suggest a short preoperative suspension for all the antagonists of renin-angiotensin-aldosterone system. These drugs have been involved in increasing the rate of significant hypotension episodes after the induction of anesthesia or during neuraxial blocks, and of postoperative development of acute renal failure [10].

The perioperative continuation of antiplatelet drugs should be carefully considered. While it's commonly accepted, in the presence of a bleeding risk, to suspend the therapy in primary prevention, many reports suggest that the antiplatelet withdrawal during secondary prevention for ischemic diseases may lead to serious complications [11]. When surgery is performed in an area where the development of a hematoma could lead to severe complications (e.g. the anterior region of the neck), or in closed spaces as the spinal canal, the risk of bleeding should be carefully evaluated. When a double antiplatelet therapy is indicated, elective surgery should be postponed. The average increase in bleeding risk in non-cardiac surgery is about 20% with aspirin or clopidogrel alone [12]. The risk rises up to 50% over the basic risk when aspirin and clopidogrel are used together [13]. In such particular situations, a multidisciplinary approach involving surgeon, anesthesiologist and cardiologist or neurologist is advisable to customize clinical decisions [14].

COPD is a frequent condition, especially among the older patients, and is often associated with obesity and higher rates of postoperative bronchopulmonary complications [15]. If general anesthesia or deep sedation are needed for elective surgery, when a severe or poorly compensated COPD is present, with increase in bronchial secretions and clinically relevant bronchial reactivity, a preparation with aerosol therapy and a short course of antibiotics is advised [16]. In addition, in the compliant patient smoke banning at least 6–8 weeks before surgery has signifi-

cantly lowered the rate of bronchopulmonary complications and improved surgical wound healing and bone fusion [17]. If possible, local anesthesia and Monitored Anesthesia Care should be preferred in patients with COPD. However, if tracheal intubation is mandatory, the early weaning from invasive ventilation and the adoption of lung-protective ventilation protocols help prevent pulmonary complications [18, 19].

In particular in the elderly, smokers and obese patients, OSA is not uncommon and is often underdiagnosed. The frequent association of anatomical abnormalities in the upper airway could advice a careful evaluation for suspected difficult intubation, and the availability of all emergency airway equipment [20]. In the last years, quite simple questionnaires with the aim to detect patients with suspected OSA have been proposed, compared with others and validated [21].

Patients with already diagnosed and treated OSA can be managed in OP or DS setting if they are able and skilled in the use of their own Continuous Positive Air Pressure (CPAP) device (possibly bringing their own device at the admission to the hospital). Patients with suspected OSA and without comorbidities, with a low risk emerging from clinical evaluation and from the questionnaire results, could be treated in OP or DS setting only if the postoperative pain can easily be controlled without opioids. In patients with high risk for suspected OSA, when other comorbidities are present or when postoperative opioid use is very likely, it is safer to decide in any case for an inpatient treatment [22].

Airway Assessment

As in every kind of surgery, a proper airway evaluation is mandatory before the induction of anesthesia, even if recent surveys show a poor accuracy of the clinical prediction of a difficult direct laryngoscopy (DL) [23].

A simple definition of "difficult airway" could be: a clinical situation in which a meanly skilled anesthesiologist experiences difficulty with facemask ventilation and/or with tracheal intubation [24].

Table 4.1 Components of the preoperative airway physical examination airway [24]

Examination component	Nonreassuring findings
1. Length of upper incisors	Relatively long
2. Relationship of maxillary and mandibular incisors during normal jaw closure	Prominent "overbite" (maxillary incisors anterior to mandibular incisors)
3. Relationship of maxillary and mandibular incisors during voluntary protrusion of mandible	Patient cannot bring mandibular incisors anterior to (in front of) maxillary incisors
4. Interincisor distance	Less than 3 cm
5. Visibility of uvula	Not visible when tongue is protruded with patient in sitting position (e.g., Mallampati class >2)
6. Shape of palate	Highly arched or very narrow
7. Compliance of mandibular space	Stiff, indurated, occupied by mass, or nonresilient
8. Thyromental distance	Less than three ordinary finger breadths
9. Length of neck	Short
10. Thickness of neck	Thick
11. Range of motion of head and neck	Patient cannot touch tip of chin to chest or cannot extend neck

The presence of one or more of the common findings that could hinder an easy direct laryngoscopy or facial mask ventilation must be detected, in order to establish a proper behavior (Table 4.1). All other things being equal, when a patient is scheduled for cervical spine surgery, and mostly if the stability of the spine could be impaired, a more cautious approach is needed. A collective evaluation with the surgeon regarding the preoperative neurological status, the spine stability and the intervention proposed is surely the best approach to choose the more suitable behavior and even to avoid legal issues [25]. Moreover, if an awaken intubation is finally chosen, the psychological compliance of the patients should be appraised, and however a proper information to the patient must be given.

Thanks to the improvement of electronics and glass fiber technology, many devices has been

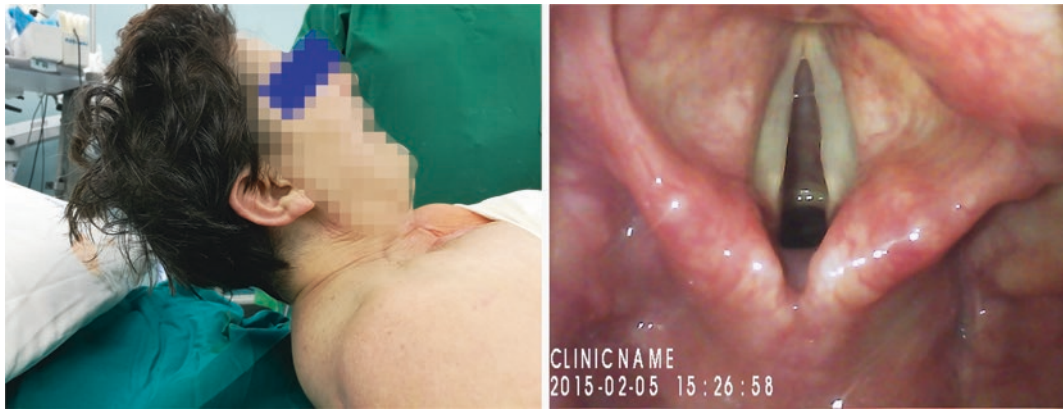

Fig. 4.1 Videolaryngoscopy in a "difficult airway" using a Glidescope®

proposed in the last few years to overcome difficult intubation (Fig. 4.1). These devices have been compared with the classical MacIntosh laryngoscope and also with the fiberoptic bronchoscope or laryngoscope for their efficacy in improving visualization and in reducing neck movements and mechanical stress of cervical spine [26, 27].

Awake fiberoptic intubation can be performed using topic anesthesia with a conscious sedation in order to minimize coughing and neck movements. This has been the favorite technique for most practitioners in patients scheduled for general anesthesia with anticipated difficult intubation [28]. However, awake fiberoptic intubation is not without risks. In a closed claims analysis 12 cases of failed awake intubations, for technical causes or for lack of patient cooperation, or development of airway obstruction for the sedation or edema, resulted in death or brain damage in 9 cases (75%) [29]. When awake intubation is advised and mouth opening is not too limited, awake videolaryngoscopy, being faster and simpler than fiberoptic bronchoscopy, should probably be considered [30].

Intraoperative Neurological Monitoring

Iatrogenic injury to the spinal cord and peripheral nerves could occur during CSS, caused from wrong positioning, surgical or anesthetic maneuvers or poor hemodynamic control; some lesions are often permanent and very disabling [31]. The blood supply to the medulla is granted from the anterior and posterior spinal arteries. The anterior spinal artery feeds approximately the two thirds of the cord mainly in the anterior and central area and the flow is centrifugal. The posterior spinal arteries feed the posterior part of the gray matter of the posterior horns and the more external portion of the anterior-lateral and posterior white matter, and its flow is centripetal. With the exception of the posterior half of the posterior horns, supplied only from the posterior spinal artery, the two systems have a discrete grade of overlapping. Unfortunately, the real efficiency of the interconnections is generally poor and not truly compensatory in case of obstruction of one of the two systems. Moreover, blood supply of the spinal cord is not homogeneous; the cervical tract is more vascularized with a good supply from both anterior and posterior systems, while thoracic and lumbosacral tract have respectively a weaker anterior and posterior flow [32].

In order to early detect neurologic modifications during spinal surgery various neurophysiologic techniques have been proposed and used. Somatosensory-evoked potentials (SSEPs) were the first to be studied and adopted. The registration of cortical or subcortical potentials after administration of peripheral stimuli and the evaluation of variations in amplitude and latency of the responses, helps in detecting possible functional impairment of the posterior afferent

pathways. Typically, the stimulating electrode are applied over the median nerve in the arm or over the posterior tibial nerve distally to the knee. The stimulation site is chosen depending of the site of surgery; when CSS is proposed the median nerve is generally used, while for surgery distal to the cervical segment the tibial nerve is stimulated [33].

Moreover, the technique in most cases gives indirect information about the functional situation of the anterior regions of medulla.

However, a recent review suggests that SSEPs changes during CSS are highly specific but not very sensitive in predicting poor outcomes after surgery [34]. Also for the anatomical and functional reasons described above, SSEPs may fail to detect spinal cord injury in the anterior-lateral area involving only the descending motor pathways without impairment of the posterior columns and gray matter.

TcMEPs monitoring was introduced to overcome these false negative records. The electrical or magnetic stimulation of the precentral motor cortex with the peripheric recording under the surgery level of the muscular response can help to assess the integrity of the anterior descending pathways.

Moreover, during CSS, TcMEPs and SSEPs seem to have different patterns of sensitivity: while TcMEPs are more useful to detect hypotension and cord hypoperfusion related injuries, SSEPs may be more helpful in preventing brachial plexus injuries [35].

Literature highly recommends continuous recording of both SSEPs and MEPs for the high sensitivity and specificity of the responses they can give when used together, allowing the recovery of situations otherwise probably with very poor outcome. Despite the lack of large studies, recently multimodal approaches have been proposed, involving clinical and radiological data with electrophysiologic findings, with the aim to predict surgical outcome. When pedicle screws are used, the intraoperative EMG is also recommended [36, 37].

Special anesthetic care is needed when monitoring of somatosensory-evoked potentials (SSEPs) and/or motor-evoked potentials (MEPs) is planned, in order to detect intraoperative functional impairment of the spinal pathways. Anesthetic agents can heavily affect the quality of the monitoring, particularly for cortical SSEPs for cortical direct depression. Moreover, general anesthesia causes also a depression of intrinsic spinal cord activity, which is more evident when nitrous oxide or halogenated agents are used. Even if the use of trains of stimuli rather than single stimuli tends to overcome this poor excitability, the depressive effects is however significant.

Hence, the simultaneous monitoring of a cortical and a subcortical site of SSEPs may help, when necessary, in the interpretation of a decrease in cortical SSEPs amplitude and/or increase in latency, because the subcortical response is far less impaired from the anesthetic effect. Generally, the first choice should be a Totally IntraVenous Anesthesia (TIVA), because of the impact of inhalational anestetics on evoked potentials even at low concentrations. Propofol suppresses the activity of the anterior horn cells, but significantly less than halogenated anesthetics [38]. Also intravenous drugs should be chosen carefully: benzodiazepines and barbiturates produce CMEPs depression at lower doses than those affecting the SSEPs and this effect lasts for several minutes. Ketamine, instead, has shown an increase in cortex magnetic excitability, leading to larger CMEPs amplitude [39]. Recent studies showed that dexmedetomidine when used during a TIVA at a clinical dose may affect some IONM parameters and without any advantage [40].

Opioids are an important component of anesthesia for evoked potentials monitoring: they produce only minimal changes in spinal or subcortical SSEP recordings, and only a mild decrease in amplitude and increase in latency for cortical SSEPs and myogenic responses from MEPs [41].

Recently it has been noted that remifentanil, when used at higher doses, can affect SSEPs monitoring, acting particularly on the amplitude of signals [42].

Spinal MEPs (stimulating cranially to the level of surgery) or pedicle screw testing during spinal instrumentation (EMG recording) are vir-

tually insensitive to anesthetic agents, while could be hindered from muscle relaxant drugs. Most anesthesiologists prefer to use even a little dose of rocuronium (i.e. about 0.3 mg/kg) to facilitate tracheal intubation and normally the residual neuromuscular blockade at the beginning of surgery has little impact on the quality of tEMG. When necessary, small doses of sugammadex (i.e. about 1–2 mg/kg) can be administered to achieve a better TOF response and abolish the interference with IONM [43].

In any case, due to the complex pattern of interference between anesthesia and intraoperative neurophysiologic monitoring, a continuous exchange of information among all the practitioners involved can improve the interpretation of data and the outcome of the patient [41, 44].

Patient Positioning and Related Complications

Positioning in CSS is potentially challenging. A study on 75 patients undergoing CSS with IONM showed a sudden worsening during positioning of trans cranial MEPs in three cases and both MEPs and SEPs in two cases. Despite the immediate adjustment of the position and the stabilization of an adequate blood pressure, in one case evoked potentials remained depressed during surgery and the patient presented delayed neurological impairment in the postoperative (tetraparesis), but fortunately with a complete recovery after 2 weeks. The other four patients gradually showed improvement of evoked potentials after repositioning with no neurological deficits at the end of surgery [45]. A recent series of 103 cases showed a 10.7% incidence of IONM significative changes during head positioning for CSS in cervical myelopathy, with complete or partial signal restoration after repositioning in 10 cases and poor signal improving in 1 case. Only in this patient a postoperative deficit was observed [46].

Neurological impairment, mostly transient, is reported even after non-cervical surgery particularly in the elderly patients in which unsuspected cervical stenosis are often present. This suggests always cautious positioning of the head and possibly, in any case of supposed spinal cord compression, a proper maintenance of mean arterial blood pressure that may have potential benefit in improving the blood supply to ischemic areas [32].

Peripheral nerve injury is a rare complication after surgery generally caused from bad patient positioning with an overall rate ranging from 0.03 to 0.1% [47]. The complication seems more frequent in patients with some comorbidities such as diabetes mellitus, alcohol dependence and vascular disease, and particularly in the elderly and in the extreme ranges of body mass index [2]. Literature data are poor and missing in randomized trials about the matter; no guidelines are available to address the correct positioning in any kind of surgery; only some advices have been proposed based on expert opinions, case reports and consensus surveys. The abduction of the arm seems to be more tolerated in the prone rather than in the supine position, though it's advised not to exceed 90° [47]. In the supine position with the arm abducted the ulnar nerve is better protected with the forearm in supine or neutral position; when the arm is tucked beside the trunk the forearm should be in neutral position and in any case pressure on the ulnar groove at the elbow and on the radial spiral groove of the humerus must be avoided. Flexion of the elbow may increase the rate of ulnar impairment, while excessive extension beyond the range preoperatively assessed as comfortable may stretch the median nerve. During surgery the position of the upper extremities should be periodically reassessed. Gel or foam padding are advised but they must be used carefully from experienced staff. A wrong use of padding can even increase rather than decrease the rate of postoperative neuropathy [48]. Fortunately, these nerve lesions are more often incomplete and deficits and symptoms tend to heal spontaneously, even if sometimes after weeks or months [49].

One of the most devastating complications in non-ocular surgery is the Peri-Operative Visual Loss (POVL), in some cases caused from wrong position. POVL is rare if considered in the whole population of surgical patients, ranging from 1:60,000 to 1:125,000, but is more frequent after spine surgery (3.09:10,000); only cardiac surgery has a higher risk of POVL (8.64:10,000). The

causes of POVL are mainly two: the Central Retinal Artery Occlusion (CRAO) and the Ischemic Optic nerve Neuropathy (ION). The CRAO leads to the ischemia of the entire retina, while the less severe obstruction of a branch of the artery (BRAO) causes an impaired function only in a sector. While during cardiac surgery the more common mechanism involved is the arterial microembolism, during spine surgery the complication derives mainly from an improper head position, leading to mono or bilateral ocular compression [50]. The mechanisms underlying the development of ION are not completely known, but the pathogenesis seems to be multifactorial [50]. The occurrence of ION seems to be strictly correlated with surgery duration. In a survey of 83 ION after spine surgery the majority of cases (94%) occurred for 6 h anesthetic duration or longer, while only one case was associated with surgery lasting less than 4 h [51]. Other risk factors for ION were detected such as obesity, male sex, Wilson frame use, greater estimated blood loss, and decreased percent colloid administration. Recently, a task force of the ASA has proposed some practical advices for POVL prevention in spine surgery [52]. For the prevention of CRAO and other ocular damage direct pressure on the eye should be avoided, the eyes of prone-positioned patients should be assessed regularly and documented [52]. ION is less rare than CRAO, accounting for about 89% of cases of POVL after spinal surgery. The pathogenesis of ION is not clear. The most popular theory involves the elevation of venous pressure and the development of interstitial edema leading to deformation and obstruction of the vessels feeding the optical nerve. All the factors able to increase the venous pressure in the head, such as the prone position with abdominal compression in obese patients or the head position lower than the heart, or to decrease the oncotic pressure, such as a significant blood loss with consequent hypoalbuminemia and the inadequate administration of colloids, could predispose to ION [53].

Other complications deriving from improper positioning should be prevented using gel or foam-made dedicated devices or even normal pillows assembled with the active contribution of the surgeons, the nurses and the anesthesiologist. The final result must ensure the distribution of the pressures as more as possible over larger extensions of tissues, avoiding excessive and localized compressions, and excessive stretching or flexion of elbows, shoulders and neck. Abdomen compression should be avoided to facilitate intermittent positive pressure ventilation and limit barotrauma. Moreover, the reduction of the intrathoracic mean pressure leads to improvement of venous return and helps in lowering surgical bleeding. This is particularly important in CSS, where a deliberate arterial hypotension must be generally avoided to ensure a proper blood perfusion to the spinal cord. As discussed above, the head and the face should be frequently controlled (Fig. 4.2) to avoid harmful compressions on the eyes and ears (Fig. 4.3).

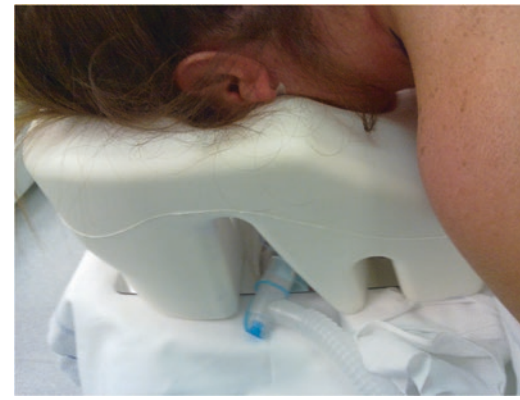

Fig. 4.2 A head-rest for prone positioning. The mirror allows eye and face control

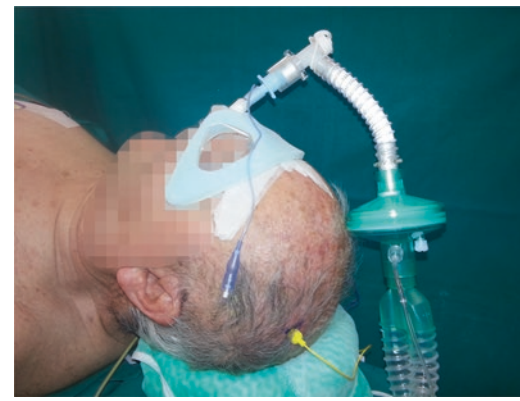

Fig. 4.3 Nasotracheal intubation for ACSS at C3 level. The eyes are protected by a shell-shaped device

Prophylaxis of Surgical Site Infection

Surgical site infection (SSI) is a dreadful and costly complication in spinal surgery. One retrospective study regarding 90 patients undergoing PCSS showed no infections in upper cervical surgery (all infected patients were operated at C3 level or below) while underlines the use of a rigid collar in the postoperative as an important risk factor for infections of the wound in subaxial cervical surgery [54]. Other known risk factors were investigated, such as smoke with an odds ratio (OR) = 2.10 and perioperative steroids (OR = 3.42), but neither resulted statistically significant. A larger series of 318 patients undergoing posterior cervical decompression, showed an incidence of 1.6% for SSI needing reoperation (five cases) with a statistically significant correlation between postoperative infection and the number of levels decompressed [55]. In a retrospective study on 1615 lumbar spine fusions (1568 patients), the overall rate of infection was 2.2%. Risk factors detected were diabetes (×6), smoke (×2) and positive history of spinal surgery (×3.7). Moreover, risk increased with the number of levels fused [56]. A recent study in a series of 264 patients undergoing posterior cervical decompression and fusion showed a significant correlation between the incidence of SSI and the variability of glycemic levels in the postoperative [57], and the importance of the optimization of glycemia is also highlighted by the recent guidelines for SSI prevention indicating with strong level of recommendation a blood glucose target value less than 200 mg/dl in the perioperative [58]. Besides the other indications, the guidelines suggest a particular attention to the maintenance of normothermia and the optimization of tissue oxygen delivery, not only by increasing the fraction of inspired oxygen (FIO2) in the perioperative but also optimizing blood volume and oncotic pressure.

Literature data support the efficacy of perioperative antibiotic prophylaxis in all the orthopedic spinal procedures with or without instrumentation, with a grade A in the strength or recommendation [59]. The standard recommended agent is cefazolin 2 g i.v. for adult patients (3 g in patients weighting over 120 kg, 30 mg/kg for pediatric patients), administered within 60 min before skin incision (Table 4.2). Clindamycin or vancomycin should be used as alternative agents in patients with β-lactam allergy. If organizational SSI surveillance shows that gram-negative organisms are associated with infections or if there is risk of gram-negative contamination of the surgical site, as for the transoral approach [60], clindamycin or vancomycin should be used in addition to cefazolin if the patient is not β-lactam allergic, or to aztreonam, gentamicin, or single-dose fluoroquinolone if the patient is β-lactam allergic. In patients who are known to be colonized with methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin should be added to cefazolin. For agents requiring a slow infusion over 1–2 h, as fluoroquinolones or vancomycin, the administration should begin within 120 min before skin incision. For patients with renal or hepatic impairment, the dose often does not need to be modified when given as a single preoperative administration before surgical incision. In order to maintain an adequate blood and tissue drug concentration, intraoperative redosing is recommended when the duration of the procedure exceeds two half-lives of the drug or there is excessive blood loss [61].

Table 4.2 Doses and redosing intervals for commonly used antimicrobials in adult CSS

Agent	Preoperative dosing	Redosing interval (h)
Cefazolin	2 g (3 g if body weight >120 kg)	3–4
Clindamycin	900 mg	6
Gentamicin	5 mg/kg	–
Ciprofloxacin	400 mg	–
Vancomycin	15 mg/kg	–

In clean non-instrumented procedures there is large consensus on discontinuing antibiotic prophylaxis in the postoperative. For instrumented spinal surgery, a 72-h antibiotic administration was associated with significantly less incidence of SSI than observed after a single preoperative dose (3.6 vs. 7.1%) [62].

Local antibiotics used as powder on the surgical site or to irrigate the wound are generally not

recommended because their usefulness is uncertain and may select resistant bacteria even becoming harmful [58, 63].

Deep Venous Thrombosis and Pulmonary Embolism Prevention

DVT complicates CSS meanly with a rate ranging from 0.5 to 4%, with a higher incidence after posterior fixation (1.3%) than after ACSS or posterior decompression (<0.5%), with a higher risk in male sex, pulmonary disorders, surgery in teaching-hospital. Despite this low rate of occurrence, when DVT is present the hospital stay increases by 7- to 10-fold over normal, and mortality rates increase by 10- to 50-fold [64–66]. In a prospective clinical trial in patients undergoing CSS, mechanical prophylaxis with intermittent pneumatic compression was equally effective as unfractionated heparin or low molecular weight heparin for the prevention of DVT and PE, but avoided the risk of postoperative hemorrhage [67].

The 9th edition of the Antithrombotic Therapy and Prevention of Thrombosis Guidelines from the American College of Chest Physicians suggests mechanical prophylaxis, preferably with IPC, over no prophylaxis or pharmacological prophylaxis. For patients undergoing spinal surgery at high risk for Venous ThromboEmbolism (VTE), including those with malignant disease or those undergoing surgery with a combined anterior-posterior approach, the guidelines suggest adding pharmacologic prophylaxis to mechanical prophylaxis once adequate hemostasis is established and the risk of bleeding decreases [68].

Postoperative Pain Management

Pain after spine surgery is often more severe than in other surgical settings. Skin incision involves more frequently multiple adjacent dermatomes and painful anatomical structures are often involved as periosteum, ligaments, facet joints, muscular fascial tissue. Among the deep somatic structures, periosteum seems to be one of the most painful tissues having the lowest pain threshold nerve fibers [69]. Complex mechanisms of peripheral and central sensitization of pain receptors and spinal cord pathways are also involved in explaining the resistance to treatment and the tendency to persist even after days. In addition, patients scheduled for spine surgery are often under preoperative chronic pain therapy. In some patients, a large use of opioids in the preoperative creates serious therapeutic challenges in the postoperative, making pain less responsive to incremental doses of opioids [70].

When minimally invasive techniques are adopted, pain could be milder for the generally small skin incisions and the reduced damage for muscles and deep tissues. However, among the postoperative "side effect" of surgery, pain represents one of the most common causes of hospital re-admission or delayed discharge, especially when an outpatient (OP) or day surgery (DS) treatment is planned [71]. Nowadays, the multimodal approach to pain therapy is considered the best model of treatment, leading to reduce the doses of the single drugs used and minimize the potential side effects. The multimodal or balanced treatment consists in combining, since the preoperative period, opioid and non-opioid analgesics with additive or synergistic actions sometimes with nonpharmacologic approaches [72].

Other techniques can be adopted together with drug therapy to help to decrease postoperative pain. Skin and tissues infiltration with a long-acting local anesthetic added with epinephrine before the surgical incision is a common practice, reducing intraoperative bleeding and analgesics requirement, at least in the earlier postoperative period, reducing the hospital stay and also the occurrence of PONV [73]. Continuous postoperative wound infiltration with local anesthetics through microcatheters of various length is also available, but not so widely used, though the efficacy and the slow rate of complications have been demonstrated [74]. In the last years, an overwhelming interest is arising about the use of Erector Spinae Plane Block (ESP Block) in order to provide good perioperative analgesia in spine surgery (Fig. 4.4). The risk/benefit ratio of the

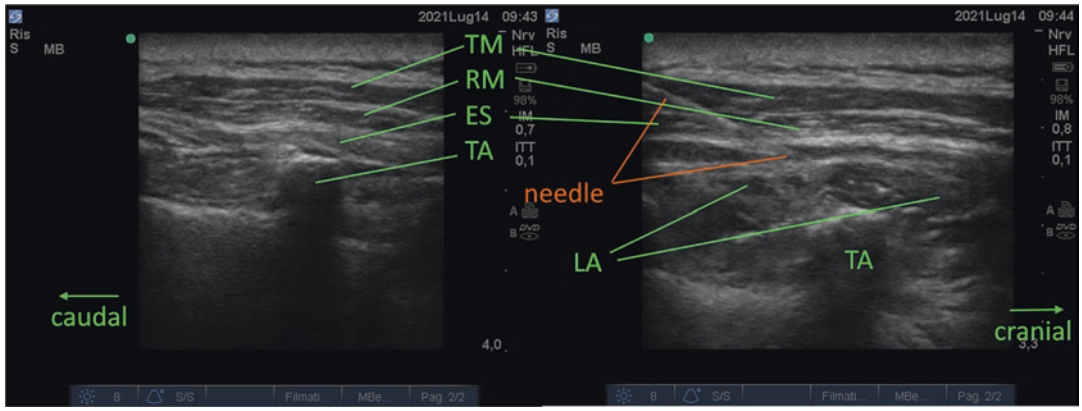

Fig. 4.4 High-thoracic ESP block for posterior CSS. *TM* trapezius muscle, *RM* rhomboid muscle, *ES* erector spinae muscles, *TA* transverse apophysis of T3, *LA* local anesthetic spreading cranially and caudally from the site of injection

technique at a cervical level is still unclear. While the first studies reported very encouraging data [75–77], after the findings of a specific cadaver study some Authors warned against the potential occurrence of bilateral phrenic nerve block after a bilateral cervical ESP block [78, 79].

Due to the wide safety margin and the very rare complications, acetaminophen has a special place in the management of pain after CSS. Acetaminophen alone or in combination with other NSAIDs or weak opiates, can control efficiently a moderate pain or significantly reduce the consumption of other analgesics in the post-operative period. The availability of oral and intravenous (iv) preparations makes it suitable both for perioperative and postoperative use, and also allows to continue the support therapy easily after patient discharge [72].

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and cyclooxygenase-2 inhibitors (COX-2) lead to increased risk of non-union after spine fusion surgery, but this adverse effect seems limited to prolonged use (>14 days) or high doses. The use of ketorolac at a dose of more than 120 mg/day even for few days or the use of more than 300 mg of diclofenac in all significantly affect the risk of non-union [80]. When used at lower doses and for few days, these drugs surely help in postoperative pain treatment.

Opiates still have an important role in the treatment of moderate-to-severe postoperative pain, but because of the important side-effects, it's advisable to reduce the doses in a multimodal protocol. The association of NSAIDs or celecoxib with a slow-release oxycodone given in the preoperative period, when compared with intravenous morphine, improved outcome in spine surgery, providing earlier recovery of the bowel function [81]. Patients treated preoperatively with opiates for chronic pain could necessitate large opiates doses in the perioperative period. The use of intraoperative ketamine infusion in these patients has significantly lowered opiates consumption even over 6 weeks after spine surgery, particularly after CSS [82]. The clinical benefit in terms of reduction in opiate-related PONV has been higher for CSS than for lumbar surgery, while the ketamine related side-effects such as disturbing dreams and hallucination were more common after lumbar surgery [83, 84].

The gabapentinoids (gabapentin, pregabalin) have also been used in association with other drugs for multimodal postoperative pain treatment, but their role remains uncertain as some studies failed in demonstrating a reduced opioids consumption. Furthermore, the side effects as somnolence and sedation, dizziness, ataxia, and visual blurring could slow the physical and psychological recovery, especially in the elderly [72, 85].

PONV Prevention and Treatment

Even if the topic is quite important in patients undergoing CSS, for the particular discomfort deriving from the association between PONV

and the frequently required supine position with limited neck movements, only few studies are reported in the specific field [73]. Postoperative nausea and vomiting affect heavily the grade of satisfaction of the patients and in some patients may increase the risks for other severe complications as pulmonary aspiration. After ambulatory or 1 day surgery PONV represents, after pain, the second cause of hospital readmission or delayed discharge. Several studies have been dedicated to the problem and guidelines have been established to help physicians in clinical decisions [86, 87].

Detecting preoperatively risk factors is crucial to provide a correct PONV prevention for each patient. A simple way to assess the risk of PONV after general anesthesia has been proposed; it's based on the evaluation of only four characteristics: female gender, history of motion sickness or PONV, non-smoking status, need of postoperative opioids [88]. When none of the risks is present, no prophylaxis is recommended. Higher risk scores suggest prophylaxis with one or more drugs, and/or the adoption of specific anesthetic techniques. When general anesthesia is needed, Totally Intra-Venous Anesthesia (TIVA) is associated with lower PONV incidence than inhalational anesthesia, especially in the first hours after surgery [89].

The protective effects of adequate preoperative and intraoperative hydration against PONV, drowsiness and dizziness, if not contraindicated, is generally accepted [87]. For the same reason, allowing oral intake of clear fluids until 3 h before surgery, may help prevent postoperative nausea while is considered safe for the risk of inhalation [90].

Dexamethasone is a long-acting glucocorticoid with a largely demonstrated activity in reducing PONV [91]. The mechanism of action, probably multifactorial, is still unclear. When administered iv during anesthesia induction at a dose ranging from 0.05 to 0.1 mg/kg, it significantly lowered the rate of PONV in various surgical setting and is considered safe in terms of side effects [92, 93]. Although many authors suggest that rescue medication should not involve dexamethasone, when added to ondansetron or droperidol it has been associated with a significant reduction in established PONV [94].

5-Hydroxytryptamine-3 (5-HT3) receptor antagonists are widely used in the common practice for the prevention of PONV and of the side effects of chemotherapy. Ondansetron is the most famous drug of the family, normally used at a dose of 4 mg iv at the end of surgery. Palonosetron, a 5-HT3 antagonist with a longer half-life and a higher receptor-binding profile, seems very promising especially for the prevention of PDNV. Even if more effective and safer than ondansetron (lack of action on QT interval), the use of palonosetron is still limited [92, 95, 96].

Transdermal scopolamine is effective and the side effects are quite frequent although generally mild and well tolerated [97]. In the elderly, however, the occurrence of confusion or an excessive sedation could be observed, suggesting to remove the patch. The patch is applied the evening before surgery or at least 2 h before the induction of anesthesia, because the onset of the effect is about 2–4 h [98].

D_2 receptor antagonists are also used for PONV treatment and prevention. Metoclopramide alone or in association with dexamethasone or other drugs has been studied and its efficacy has been questioned. Recent reviews suggest that metoclopramide 10 mg i.v. is effective in preventing PONV after general anesthesia when given preoperatively [99, 100], but may worsen extrapyramidal symptoms, constipation, visual disturbances [93]. Droperidol is very effective in the prevention of PONV even at very low doses (0.625–1.25 mg iv 5–15 min before the end of anesthesia) with a Number Needed to Treat (NNT) of 5, and highly effective in the prevention of nausea during patient-controlled analgesia with opiates (NNT = 3). In the last years, however, the use of droperidol has been greatly limited after the Black Box Warning issued from the Foods and Drugs Administration in the USA in 2001. Droperidol has been associated with adverse cardiac events as prolongation of QT interval and *torsades de pointes*. Several authors suggested a revision of that decision, for the lack of evidence supporting the black box warning [101, 102]. The warning is still active, restricting the use of droperidol to the treatment of patients who fail to show an acceptable response to other adequate treatments. Recently amisulpride 5 mg

iv administered few minutes before the anesthesia induction was approved for PONV prevention and at a dose of 10 mg iv for PONV treatment, with the recommendation to avoid use in patients with congenital long QT syndrome and in patients taking droperidol. It seems highly effective in PONV prevention and treatment with low side effects [103, 93].

More recent drugs, the Neurokinin-1 receptor antagonists and particularly aprepitant, appear very interesting for the prevention of PONV. Aprepitant, casopitant and rolapitant showed better results when compared in clinical trial with ondansetron in patients at high risk for PONV, even if the reduction in vomiting is more evident than the reduction of nausea [93].

Acupuncture has been proposed as a non-pharmacological tool for PONV prevention and treatment, with lack of side effects when compared with traditional approach. A recent meta-analysis of 14 RCTs that included 1653 patients concluded that the transcutaneous electrical acupoint stimulation is a reasonable modality to be considered into a multimodal approach for PONV prevention with a low incidence of adverse effects [104].

Other Complications

Postoperative Airway Compromise

Airway obstruction complicates ACSS with a rate varying from 1.2 to 6.1%. The situation can rapidly worsen and require emergent reintubation. The obstruction, mainly inspiratory, can cause a pulmonary edema due to the development of a markedly negative intrathoracic pressure. Fortunately, this kind of edema tends to resolve rapidly with the resolution of the obstruction and the oxygenation of the patient [105].

The obstruction is more frequently due to edema of the pharynx, prevertebral tissues and larynx and could be eventually worsened by direct trauma during a difficult intubation. Less common is the development of a hematoma in the wound or the involvement of the recurrent laryngeal nerve, with vocal fold palsy. The occurrence of a hematoma is evaluated between 0.4 and 1.2% in studies involving more than 40,000 patients, with a death reported for mechanical asphyxia [106]. Acute postoperative airway obstruction has been also reported for cervical cage displacement [107]. The obstructive events are more frequent when surgery involves more than three vertebral bodies or high cervical levels (c2–c4), with blood loss >300 ml, surgery lasting more than 5 h or combined anterior plus posterior. The incidence is increased in obese patient, with OSA and other respiratory comorbidities [108, 109]. These considerations could help in detecting the cases that deserve a more cautious clinical monitoring and management. Cases with high risk of postoperative airway obstruction for the characteristics of surgery, especially if other patient-related factors are present, need the admission in an intensive care unit (ICU), better with the head elevated about 30% just as for an intracranial postoperative [108]. Extubation must be delayed for 24–36 h and performed only after a fiberoptic inspection or a cuff leak test [110]. Furthermore, these cases need some hours of observation after extubation; recent studies demonstrated a good specificity but only a moderate sensitivity for the cuff leak test in the prediction of post-extubation airway obstruction [111, 112].

Dysphagia, Laryngeal Palsy and Aspiration

Early dysphagia is more frequent after anterior cervical spine surgery (ACSS), and is more common when a plate is used and in the elderly [113], but it's not so rare also for posterior approaches. After 2 and 6 weeks from surgery dysphagia was present respectively in 11 and 8% of PCSS vs. 61.5 and 44% of ACSS ($p < 0.0001$). No difference among the two surgical approaches was observed after 12 weeks with rates nearly 12% [114]. Many different strategies have been proposed to reduce the incidence and the lasting of postoperative dysphagia, mostly regarding surgical aspects such as choosing a thinner plate and avoiding plate prominence, limiting the duration of surgery, limiting retraction [115]. In the anes-

thetic field, the pressure or the ETT cuff was invoked in worsening an eventual nerve injury due to surgical retraction. In a series of 900 consecutive patients who underwent ACSS with plating, Apfelbaum observed a significant reduction in the incidence of temporary vocal fold paresis from 6.4 to 1.7% ($p = 0.002$), since when the systematic adjustment of the pressure of the ETT cuff after the positioning or repositioning of the surgical retractors was adopted. The acceptable cuff pressure of 20–30 cm of water is often exceeded when manual inflation of the cuff is adopted using a 10 or 20 ml syringe [116, 117], and the use of surgical retractors for ACSS may further increase the pressure. In this type of surgery it could be advisable to adopt routinely an automatic cuff pressure control device [117], even if the gradual and continuous pressure readjustment may not allow the ETT detaching from the trachea.

Apfelbaum supposed that the majority of the laryngeal nerve injuries during ACSS could derive from an asymmetric vocal fold compression. The ETT is anchored distally from the cuff and proximally from the tape; when trachea is retracted the tube compresses the homolateral vocal fold, with possible injury for the compression on the endolaryngeal segment of the nerve. The cuff deflation distally releases the ETT allowing the passive adjustment towards a "neutral" position between the vocal folds, and the release of compression over the ipsilateral nerve [118].

Many of the factors causing dysphagia and hoarseness are generally involved also in another severe complication after CSS affecting about 0.5% of all procedures: the aspiration pneumonia. However, even if the anterior approach is more commonly associated with risks of laryngeal nerves and esophagus injury, and neck tissues swelling that could predispose to swallowing disorders, unexpectantly aspiration is more frequent after PCSS (about 1 vs. 0.4%). Other risk factors are weight loss, fluid-electrolyte disorders, congestive heart failure, neurological disorders respectively with OR of 8.3, 6.2, 3.1 and 2.1. Moreover, it's more frequent in the elderly (>65 y.o.) and in patients with comorbidities [119]. When aspiration pneumonia occurs, the overall mortality rate in CSS dramatically increases from the basal 0.07 to 3.44%.

Particularly in the revision cases of ACSS surgeons might prefer a contralateral approach to avoid scar and altered anatomy. For these patients, and however in any patient with suspected laryngeal disfunction, a preoperative otorhinolaryngologist consultation is mandatory to prevent the dramatic event of a bilateral laryngeal nerve damage. For patients with monolateral laryngeal paresis surgery must be performed ipsilateral to the preexisting damage, to avoid acute airway obstruction and/or severe swallowing impairment with pulmonary complications [115].

Postoperative Delirium

Postoperative acute delirium (POD) is the third most common complication after cervical spine surgery, occurring in more 5% of cases. More frequent in patients with preoperative dementia, age over 85 year, history of stroke or transient ischemic attack [120]. Delirium has been observed even in elderly patients when immobilization of cervical spine is indicated with or without surgery. In this setting it's quite challenging to evaluate and balance the risks of an oversedation against the risks of an insufficient immobilization with cervical orthoses [121]. Practice guideline has been proposed from the American Geriatrics Society for the management of POD in older adults [122]. Special attention should be paid to nonpharmacologic measures for the prevention and treatment of POD, beginning from the information and training of the physicians and other healthcare professionals. Important nonpharmacologic interventions include early mobilization, orientation, physiotherapy, communication and practical actions as returning as soon as possible glasses, hearing aids and dentures. Also protecting the sleep-wake cycles is advisable, for instance avoiding the postoperative in ICU if not mandatory [123].

Anesthesia depth should be monitored in order to avoid excessive depression of electric brain activity; the intraoperative use of Bispectral

Index Monitoring has been associated with significantly reduced risk of postoperative delirium and long-term cognitive dysfunction [124]. Pain control is crucial in delirium prevention, preferably with an opioid sparing protocol. Antipsychotic or benzodiazepine medications should not be used for the treatment of older adults with postoperative delirium who are not agitated and threatening substantial harm to self or others. Only if the patient is severely agitated and when any attempt of behavioral measure has failed antipsychotic drugs can be used titrating the lowest effective dose and for the period as short as possible. Benzodiazepines should only be used if strictly indicated, as for the treatment of alcohol or benzodiazepine withdrawal, and however for the shortest possible duration and at the lowest effective dose. Some anticholinergic and antihistaminic drugs and meperidine should be avoided because can increase delirium risk as the drugs that contribute to serotonin syndrome. The prophylactic use of antipsychotic medications or cholinesterase inhibitors to prevent delirium in postoperative patients is not recommended [122].

Intracranial Complications

Remote IntraCranial Hemorrages (RICHs) are rare complications observed after spinal surgery performed at any level [125]. These events may evolve subtly. If they develop during surgery, they can simulate a simple delayed emergence that could be ascribed to persistent anesthetic effect or to cerebral edema due to prolonged prone position [126, 127]. More often the complication appears 10 or more hours postoperatively, with headache, nausea, vomiting; sometimes other symptoms may appear such somnolence, altered consciousness, dysarthria, ataxia, and motor or visual deficits. In a recent review all the eight described cases had intraoperative CSF leakage and postoperative drains with moderate serosanguinous output. RICH may be caused from an excessive CSF loss resulting from incidental or intentional durotomy or dural leakage for the action of a drain. This could cause a caudal prolapse in the cerebellum and encephalus, with traction and lesion of some bridging veins. The positioning of a surgical drain in patients with clear or suspected dural lesion should be carefully considered, and however any change in the neurological status deserves to be investigated with cranial imaging [128]. This kind of hematoma is more frequent in the posterior fossa, but sometimes can develop in the supratentorial region [127].

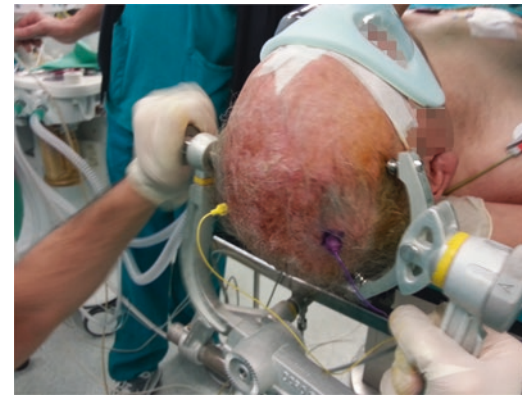

Fig. 4.5 Positioning of a 3-pin Mayfield clamp for ACSS

Another rare cause of intracranial hematoma during spine surgery is the possible penetration in the skull of a pin when a Mayfield clamp (Fig. 4.5) is adopted for the positioning [129].

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5 Clinical Neurophysiology of the Cervical Spine: Indication for Surgery

Rodolfo Quadrini, Chiara Lepre, and Antonio Luzzo

Introduction

The success of surgery rests on the surgeon's skills and on many other factors, too, the most important of which is the correct diagnosis, a fundamental prerequisite for a proper surgical indication. An appropriate diagnostic process includes a first clinical phase and a subsequent instrumental one. The first step is the detection of symptoms during which the clinical reasoning begins and the diagnostic hypotheses are formulated. These are subsequently assessed by the physical examination that filters the initial hypotheses and defines the diagnostic suspects for the differential diagnosis. Once the clinical phase is completed, the instrumental diagnostic phase begins, applying appropriate tests to confirm or discard the clinical suspicion (Fig. 5.1).

Radiculopathy and myelopathy, which often coexist, are the main cervical spine diseases of surgical relevance. The causes can be varied (trauma, neoplastic process, etc.) but spondylosis is the most prevalent cause [1]. Imaging and neurophysiological studies are the main examinations in cervical spine diseases. Imaging, particularly magnetic resonance imaging (MRI), is the first choice. Introduction of MRI has made it possible to examine the spinal cord and spinal roots for the first time in a reliable and non-invasive way, revolutionizing spinal diagnostics. MRI has many advantages, but, like any investigation, it also has limitations. Paradoxically, the high morphological sensitivity of MRI can lead to easy as wrong diagnoses if an adequate clinical judgment is neglected [2].

A case of our observation is given as an example: a young patient had developed a paraparesis associated with sphincter disorders and sensory disturbances of the lower limbs. MRI had shown a massive C5–C6 disc herniation and spinal cord deformation. Surgery was proposed, but the patient asked for a reassessment. Neurological examination showed painful and thermal hypoesthesia discordant with the hernia's localization. Further investigations, including a lumbar puncture, had identified cytomegalovirus transverse myelitis.

Furthermore, MRI provides an exhaustive exploration of the spinal morphology, but does not provide any function information and therefore, despite its high diagnostic value, it must always be combined with clinical and neurophysiological assessment. Often, indeed, radiological data are discordant with clinical status in cervical spondylotic myelopathy [3]. A correct interpretation of morphological findings is only achieved if they correlate with function data [4]. It is likely that, in the future, also MRI will be able to provide function evaluations of the spinal cord, as it

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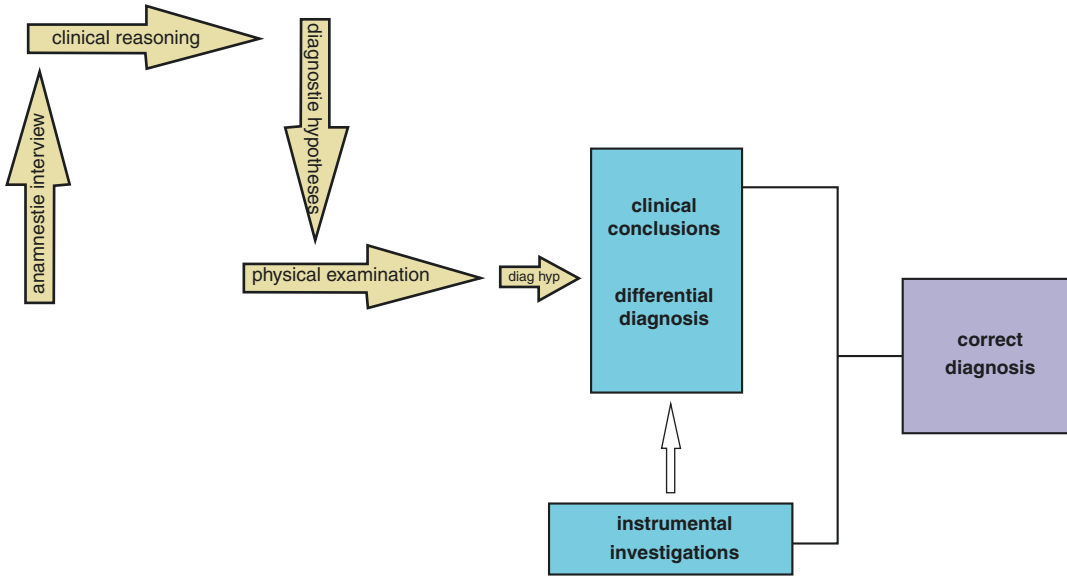

Fig. 5.1 Clinical process for proper diagnosis

already happens today in the brain with functional MRI. However, at the moment the function evaluations of the spinal cord can be provided only by neurophysiological studies. In some cases, a radiological alteration is not associated with functional impairment and therefore is not pathological. Well-known examples are nonspecific MRI cerebral foci of gliosis.

Conversely, spinal cord functional damage may not be detected by MRI. For instance, most degenerative diseases do not show radiological changes. Only in some cases of very advanced degeneration of the spinal cord, MRI can show non-specific atrophy. These diseases are studied very well with the neurophysiological study.

Neurophysiological studies play a crucial role in diagnosis and management of cervical spine disease, particularly in cases when the radiological data are discordant with the clinical status. Furthermore, they can be helpful for prognostic assessment and for surgical effects evaluation.

Neurophysiological studies are historically considered as an extending to the neurological examination. Let's consider, for example, the assessment of muscle strength during the neurological examination. When a person raises his arm, we analyze the ability of cortical areas to plan the movement so that only the necessary muscles are activated and those that would hinder movement are inhibited; also we analyze the capability to transfer the nerve impulse, made by the cerebral cortex, along the pyramidal tract until the spinal motor neurons; the functional capacity of the nerve roots, nerve trunks and the motor end plate interposed between nerve and muscle; finally we analyze the functional integrity of muscles. Damage of any of these structures can cause arm lift deficiency. The lesion could be located in the supplementary motor cortex for movement planning and manifest as apraxia (inability to perform a movement, although strength is normal, usually as a result of a stroke), in the primary motor cortex (stroke, amyotrophic lateral sclerosis), in the pyramidal pathway of the brain (for a stroke or a tumor), in the spinal cord (for cervical stenosis), and in the spinal root, nerve, motor endplate, and muscle.

Continuing the examination, neurologist searches for other associated signs that help determine the damage localization. In rare cases, the clinical evaluation alone establishes the localization of the damage with certainty. However, clinical practice shows that diagnosis can be difficult for several reasons: unclear signs, signs that mask a deficit, evaluation of the patient at an early stage of the disease with signs not yet shown, etc. Neurophysiological studies contribute to correct diagnosis as they confirms or contradicts the clini-

cal conclusions, identifies clinically undetectable dysfunctions, localizes the damage and establishes whether the alteration of the imaging is congruent with the clinical picture. Motor Evoked Potentials (MEPs) and Somatosensory Evoked Potentials (SEPs) test the function of central sensory and motor nerve pathways; electromyography (EMG) and nerve conduction study (NCS) test the function of the peripheral nervous system; the repetitive stimulation test allows to recognize a damage of the muscle end plate (myasthenia) and finally a primary damage of the muscle can be recognized by the EMG (muscular dystrophy, myositis). Eventually, precise localization of neurological damage in particular cases contributes to the determination of the etiological diagnosis as some neurological diseases prefer particular localizations. Thus, neurophysiologist plays not just a fundamental role in the diagnosis definition, but also helps the surgeon to determine when surgery is necessary, but also when an intervention could be harmful as well as not indicated.

Clinical Approach to Cervical Spine Pathology

The diagnosis of cervical spine disease is often difficult due to the complexity of the symptoms, to some symptoms in common with pathologies of the nearby anatomical structures and to the numerous pathologies that could mimic the cervical spine pathology such as amyotrophic lateral sclerosis, carpal tunnel syndrome and many others. For this reason, the application of an adequate diagnostic process is fundamental for a correct diagnosis. This approach is the only one that could guarantee therapeutic success and reduce the risks of legal disputes.

A proper diagnostic process involves a thorough clinical examination followed by instrumental researches. Taking a comprehensive health history plays a crucial role in the diagnostic process. However, often it is overlooked because of the time it can take and difficulties the patient have, describing the symptoms. It is important to ensure the patients' ease. To avoid misleading data, sometimes is necessary to ask the same questions several times, what increases the chances to obtain important information. It is a common experience to receive on our question "what are your problems?" the answer "I have a cervical hernia". Only after repeating the same question several times we reveal such complain as discomfort in the arm, neck or hand. Just in very rare cases the patients are able to provide an adequate description of the pain type, its location and duration. About four of ten patients with carpal tunnel syndrome report feeling discomfort in the first three fingers of the hand, the other six report discomfort in the whole hand; only one in ten distinguishes that the paresthesias are in the radial half of the fourth finger but not in the ulnar half. The most hardly detectable symptoms are pain and sensory ones. Nevertheless, even the adequate identification of motor disorder's characteristics often requires great efforts. A patient can easily indicate a lack of strength in the lower limbs, but hardly knows to specify whether he falls due to weakness in the knee or ankle or because of inability to balance himself after a displacement in his center of gravity.

Spondylotic radiculopathy and myelopathy will be treated as they are predominant in cervical spine surgery.

Because of the complex clinical picture of diseases, it is strongly recommended to know the notions of spinal cord anatomy and pathophysiology that underlie the clinical manifestations of spinal cord pathology.

Spinal Cord Anatomy and Pathophysiology

The spinal cord has a small diameter (1–1.5 cm) and a length of about 45 cm. It is located inside the vertebral canal, dipped in the cerebrospinal fluid of the subarachnoid space and also protected by epidural fat, epidural vessels and meninges.

The axial section shows two distinct structures, one deep and one superficial. The deep portion is called gray matter due to its color, has an H shape with two anterior and two posterior horns (spinal horns), and is mainly formed by the soma of neurons. The anterior horns contain the motor neurons. The posterior horns contain the sensory neurons. The superficial portion is called

white matter and consists of ascending and descending nerve fibers (Figs. 5.2 and 5.3).

Spinal motor neurons receive the motor fibers descending from the brain. Their axons come out of the spinal cord and form the anterior motor root and subsequently the brachial plexus and peripheral nerve. The axons of the posterior sensory root, which originate from the sensory neurons of the spinal ganglion, penetrate the spinal cord and ascend to travel mainly to the thalamus and finally to the sensory cortex (Fig. 5.3).

Fig. 5.2 Spinal cord axial section

The cervical cord is divided into eight segments called myelomeres, from C1 to C8 (one more than the number of cervical vertebrae). Each myelomere has a segmental organization for muscles and skin innervation. C1–C4 innervate the neck muscles; C5–C7 innervate the muscles of the arm and forearm and C8–T1 the intrinsic muscles of the hand. The skin segments pertaining to each myelomere are called dermatomes. Up to C4 the dermatomes have a belt distribution in the neck and part of the head. The C5–T1 dermatomes are distributed to the upper

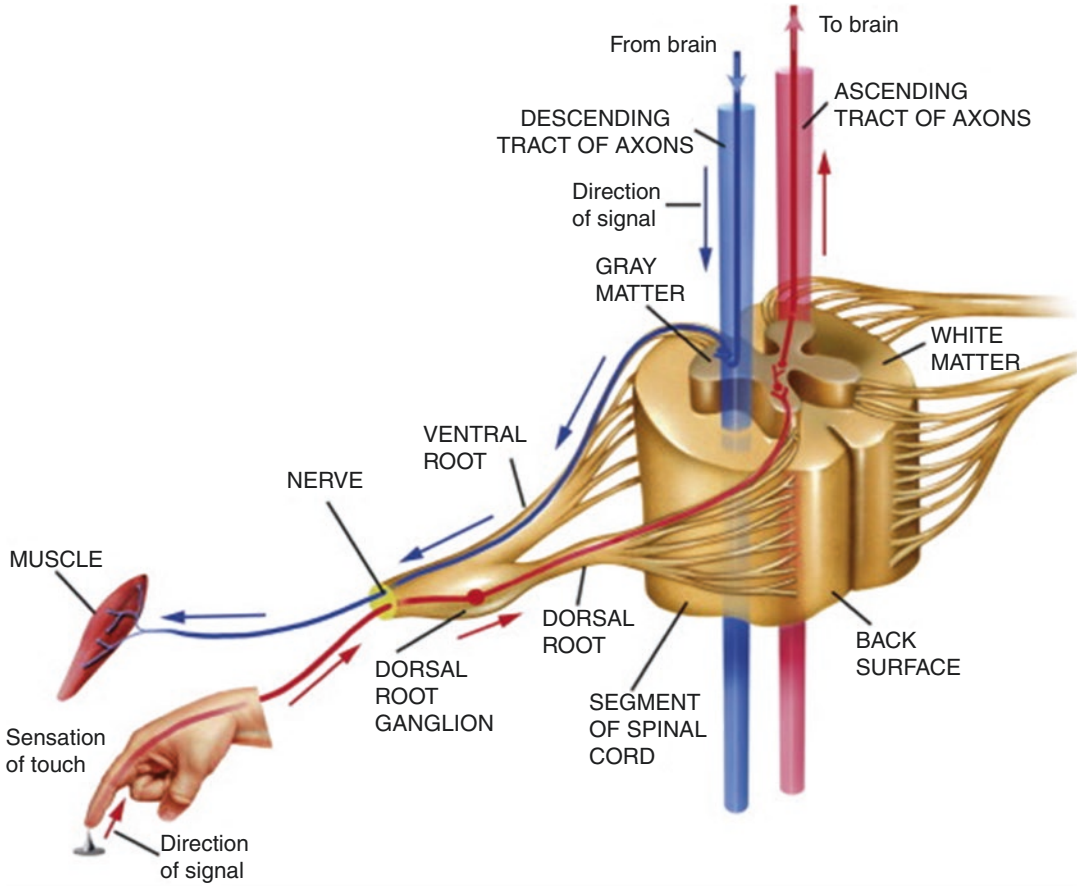

Fig. 5.3 Spinal cord anatomy and physiology

limb in the form of parallel descending strips along the major axis of the limb. C5 innervates the skin of the lateral region of the arm and gradually the skin regions are innervated in the centripetal direction until T1 which innervates the axillary region.

There is no precise correspondence between the level of the myelomere and the homonymous vertebra due to the different length between the spinal cord and the rachis. The distance becomes greater the further one descends towards the lumbosacral segments. In clinical practice, this phenomenon results the localization of spinal cord damage at a lower level than the vertebral level (e.g. voluminous central hernia C6–C7 compresses the spinal cord at the level of the C8 myelomer) (Fig. 5.4).

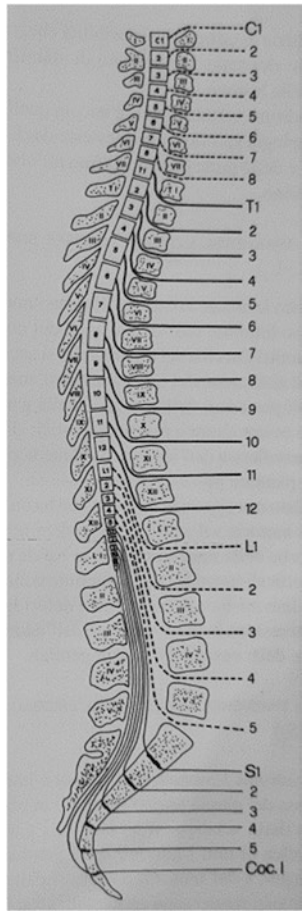

Fig. 5.4 Spinal segments and homonymous vertebral body relationship

Motor Functions of the Spinal Cord

The spinal motor neuron is controlled by the pyramidal pathway originating from the cortical motor neurons. Its activity is also regulated by other descending brain pathways, activators and inhibitors, with the intermediation of spinal circuits, including the spinal reflex arc. A lesion in any point of the descending motor pathways deprives the spinal motor neuron of the commands for carrying out the movements and therefore the patient loses muscle strength. The same motor neuron is also deprived of inhibitory descending controls so it remains activated even in resting conditions, due to the normal function of the spinal reflex arc which becomes hyperactive. This causes spasticity, a condition that further reduces an already weak movement. In this way, a condition of spastic paralysis (weakness, spasticity, increased tendon reflex) is determined (Fig. 5.5).

The spinal motor neuron axons emerge from the spinal cord and participate in the formation of the anterior root, the brachial plexus and finally the peripheral nerve. Damage to the motor neuron soma and/or its axon at any level (intraspinal tract, spinal root, brachial plexus, peripheral nerve) causes a loss of strength and also a loss of muscle tone, resulting in a flaccid paralysis due to the lesion of efferent arc of the spinal reflex (weakness, hypotonia, reduced reflex) (Fig. 5.5).

Sensory Functions of the Spinal Cord

Spinal sensory afferents are divided into two groups: (1) protopathic system (from the Greek πρῶτος = primitive) phylogenetically older, which includes coarse tactile sensibility, thermal and pain sensibility and (2) epicritic system, phylogenetically more recent and therefore more specialized in sensory discrimination, which includes discriminative tactile and proprioceptive sensibilities (sense of position and movement of the body segments, sense of pressure and vibration).

Ascending sensory fibers in the spinal cord are arranged in distinct bundles. Protopathic sensitivities go through the spinothalamic tract. Epicritic sensitivities ascend into posterior funiculus.

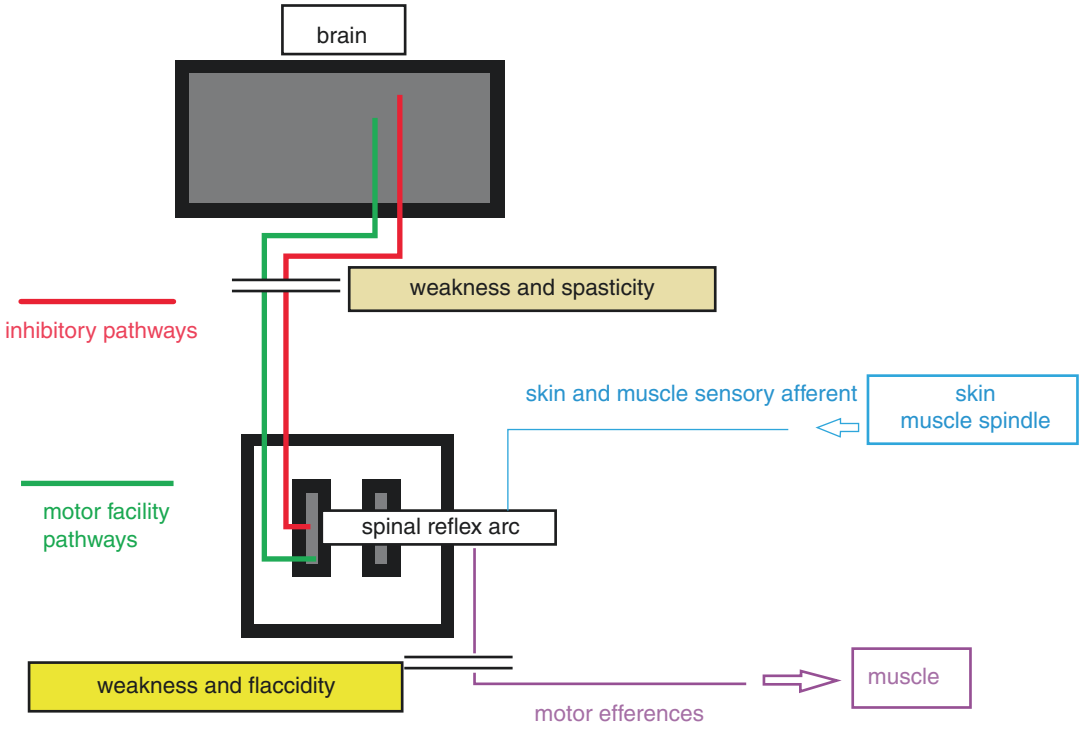

Fig. 5.5 Pathophysiology of spastic and flaccid paralysis

The fibers for the protopathic sensitivities, after going across the sensory root, penetrate the spinal cord, go up a little and connect with the sensory neurons of ipsilateral posterior horn of some more proximal segment. The axon that originates from the second neuron crosses and moves contralaterally, constitutes the spinothalamic tract and ascends to the thalamus, where a third neuron sends its axon to the sensory cortex which is contralateral to the stimulated body region (Fig 5.6).

Epicritic fibers form the posterior funiculus and ascend remaining on the same side of entrance into the spinal cord. Once in the spinal bulb they connect to neurons located in two sensory nuclei (nuclei of Goll and Burdach) whose axons cross to reach the nuclei of the contralateral thalamus and sensory cortex (Fig. 5.6).

Both sensory pathways carry information from one half of the body to the opposite half of the brain. A brain injury, e.g. in the right cerebral hemisphere, damages the sensory and motor pathways of the opposite half of the body and clinically a motor and sensory deficit is established on the left.

In most cases, a spinal injury causes damage to a large part or the entire spinal segment, due to its small size and the clinical manifestations in the underlying body segments are bilateral.

However, although rarely, an injury can affect only half of the spinal cord, resulting in a particular neurological condition called Brown-Sequard syndrome.

As already mentioned, both sensory pathways carry the sensibility of one half of the body to the contralateral half of the brain. However, due to the different place in which the spinothalamic fibers and the fibers of the posterior funiculus cross, a lateral injury of the spinal cord can determine a dissociation in the distribution of the sensory deficit.

For an example, an injury of the right half of the spinal cord causes the interruption: (a) of the right pyramidal pathway, (b) of the right posterior funiculus (both connected with the right half of the body). It also causes the interruption of: (c)

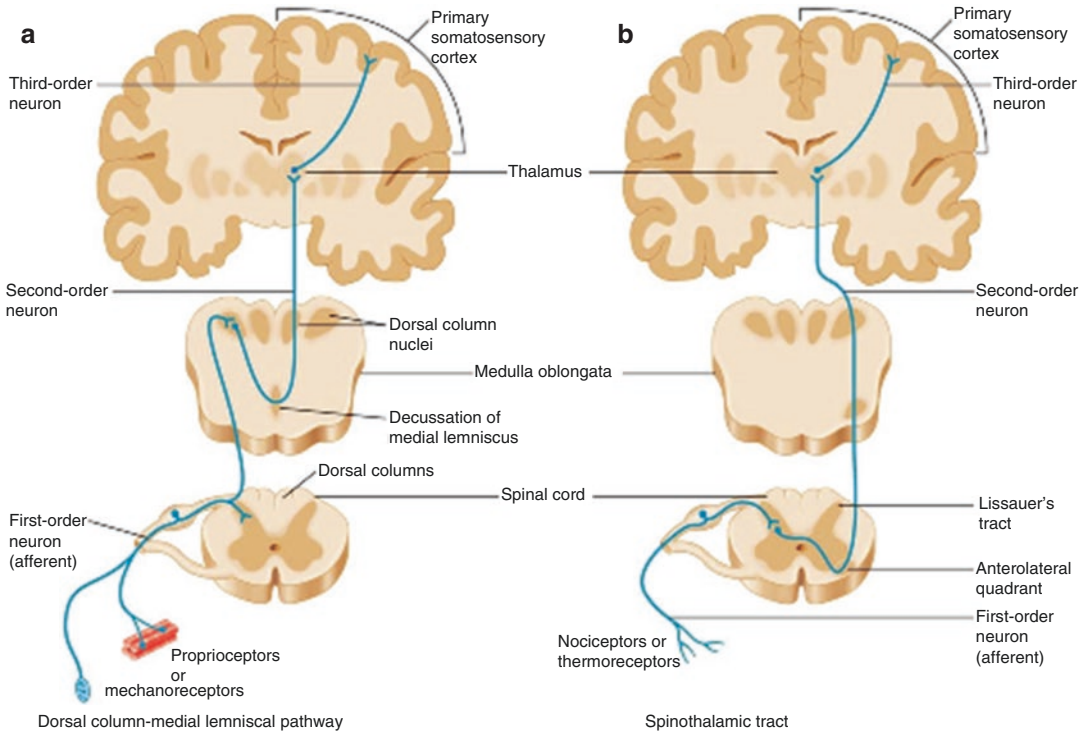

Fig. 5.6 Pathways of epicritic (**a**) and protopathic (**b**) sensitivity. a - Dorsal column - medial lemniscal pathway

the spinothalamic tract, which carries the sensibility of the left half of the body.

The consequences of this phenomenon are: epicritic anesthesia and motor damage to the right, homolaterally to the lesion, while the left half of the body has thermal and pain anesthesia. This rare phenomenon is called dissociation of epicritic and protopathic anesthesia (Fig. 5.7).

Another peculiarity of the spinal cord injury is the level of protopathic hypoesthesia always lower than the level of spinal damage. This is due to the ascent for some segments of the protopathic fibers after entering the spinal cord, before connecting to the posterior horn.

It should be noted that the sensory exam is difficult and requires time and patience. It cannot be clinically objectified as it is only based on the patient's subjective ability to perceive stimuli. It is susceptible to individual variations, cultural and intellectual factors and influenced by the ability to concentrate. However, if properly performed, it provides useful information for a precise localization of the level of injury, even better than the motor examination.

Spondylotic Cervical Radiculopathy

Cervical spondylosis is a very common disorder and spondylotic cervical radiculopathy (SCR) is one of the most common patterns, accounting for about 60–70 % of all cervical spondylosis. A 2012 US Army study found an incidence of 1.79 per 1000 people/year [5]. SCR is caused by the mechanical compression of nerve roots.

Spondylotic radiculopathy is the most frequently subjected to surgery cervical spine pathology.

Pathophysiology of Spondylotic Cervical Radiculopathy

The most frequent cause of SCR is spondylosis, followed by herniated disc and, lastly, trauma [1]. Spondylosis is a degenerative phenomenon that progresses with age. It causes a thinning of the intervertebral disc with the consequent narrowing of the intervertebral foramen. The thinning and reduction of disc cushioning results a functional overload on the intervertebral joints and vertebral body. These phenomena cause a hyper-

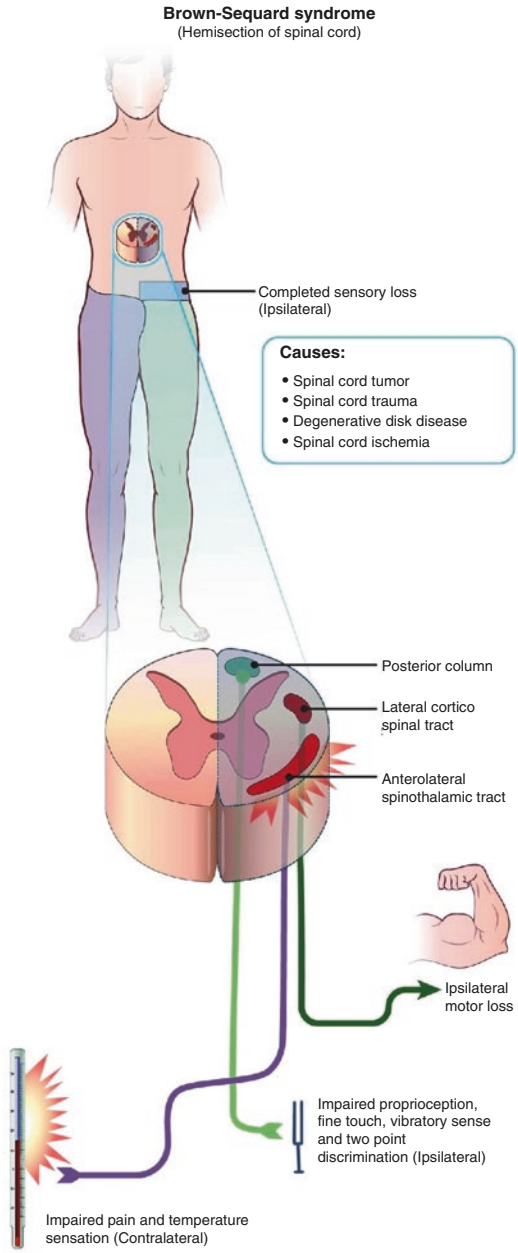

Fig. 5.7 Brown-Sequard syndrome representation

trophic bone reaction (osteophytes) and a further narrowing of the intervertebral foramen (foraminal stenosis).

Foraminal stenosis and herniated disc induce nerve root damage in two ways—mechanical and chemical. The mechanical one is represented by (1) stretching of the nerve fibers which causes damage to the myelin and, for greater compressions, also to the axon, and (2) focal ischemia due to compression of the vasa nervorum. In addition, the nucleus pulposus of the intervertebral disc, in contact with the nerve root, results also chemical damage through the activation of a pro-inflammatory cascade, mediated by tumor necrosis factor alpha (TNF-a), interleukin-6 and matrix metalloproteinase [6, 7].

C7 is the most frequently damaged root by C6–C7 disc herniation, following, in order of frequency, the root C8 (space C7–T1), C6 (space C5–C6) and C5 (space C4–C5). Differently common thought, trauma is a relatively rare cause of cervical radiculopathy. Patients often report the onset of pain while standing or sitting or while walking [8].

Symptomatology of Spondylotic Cervical Radiculopathy

Root compression can cause: (a) irritative symptoms (pain, paraesthesia), (b) sensory deficit (hypoesthesia) and (c) motor deficit (weakness).

Radiculopathy due to disc herniation has a sudden, unilateral onset, can cause functional neck scoliosis with convexity towards the painful side and abduction of the painful limb (reflex phenomena to reduce root tension). Radiculopathy due to foraminal stenosis generally has a slow onset but otherwise the two forms do not differ.

The pain affects the homonymous dermatome (Figs. 5.8 and 5.9). It involves the neck and upper limb, but often predominates or is limited in the distal region. It is throbbing, continuous, intense, often associated with paresthesia and dysesthesia. It is accentuated by movement that stretches the root and also by any cause of increased endorachid pressure, such as evacuation, which, causing increased abdominal pressure, also involves the spinal structures.

In C5 radiculopathy the pain and hypoesthesia affect the lateral region of the shoulder and arm. In C6 radiculopathy, the lateral region of the forearm and first two fingers. In C7 the posterolateral portion of the arm and the back of the forearm up to the middle finger. In C8 the distal medial region of the forearm and last two fingers.

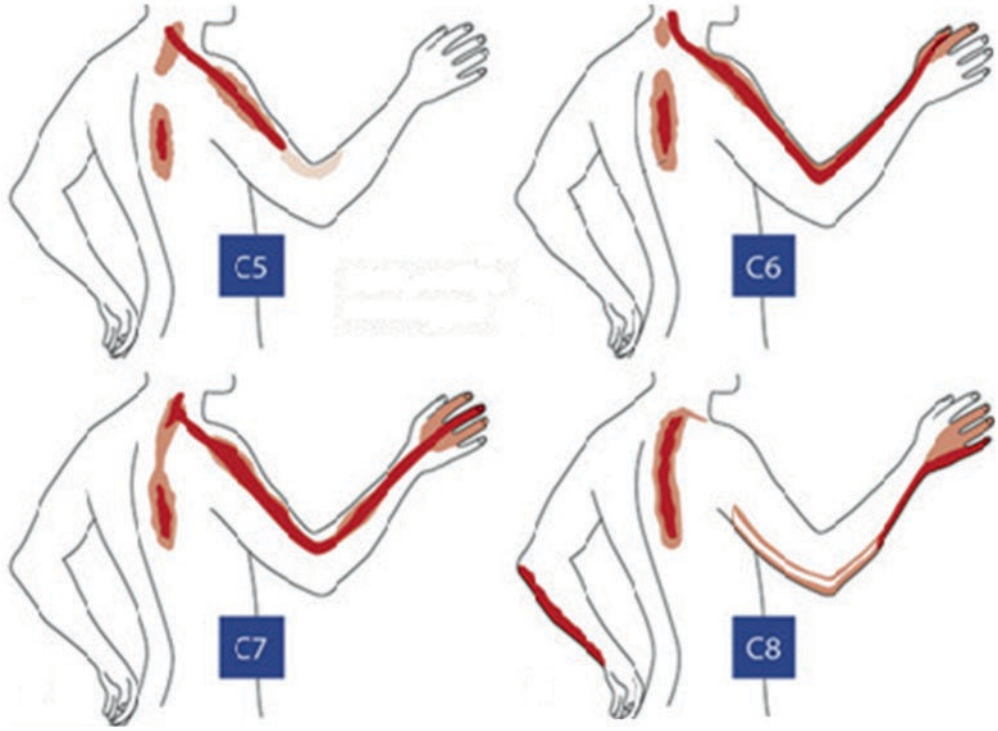

Fig. 5.8 Areas of pain and hypoesthesia distribution in the most frequent radiculopathies (C5, C6, C7 and C8)

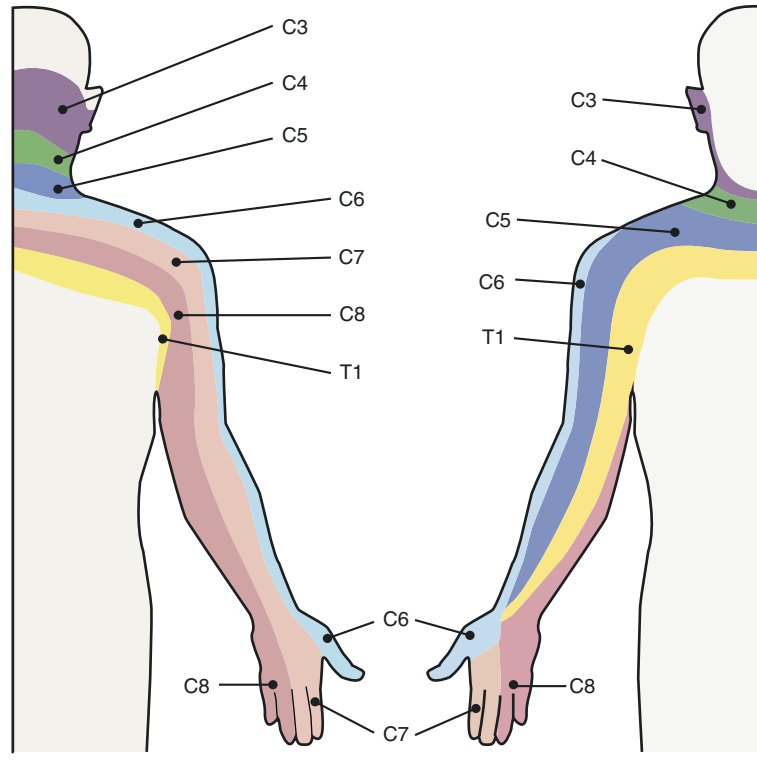

Fig. 5.9 Cervical dermatomes

The hypoesthesia has the same metameric distribution of the pain, but generally less spread due to the functional overlap of the adjacent roots (hypoesthesia due to damage of one root is partially compensated by the adjacent roots by overlapping the innervated areas).

Muscle deficits have a metameric distribution: C5 damage mainly causes abduction and elevation deficits of the arm, C6—forearm flexion weakness, C7—forearm and hand extension deficit, C8/T1—finger flexion deficit and weakness of intrinsic muscles of the hand. The metameric innervation, as well as the dermatomal one, has no clear boundaries and therefore in most cases, each muscle is innervated by at least two roots. For example, the deltoid muscle is innervated by C5 and C6 root. Multiple muscle innervation has been maintained over the course of evolution as it allows a functional advantage: in case of a nerve root injury, the muscle can continue functioning even though in a reduced way. The complex innervation of the majority of the muscles increases diagnostic difficulties in both clinical and instrumental settings. Only the rhomboid muscle is innervated exclusively by C5. This feature facilitates the diagnosis of C5 or C6 radiculopathy. In fact, if the neurological and electromyographic examinations show a deficit of the deltoid, biceps, supra, and infraspinatus muscles, innervated by both C5 and C6, it is enough to examine the rhomboid muscle and, if in case it is injured, C5 is the root damage. Conversely, if the rhomboid muscle is spared, the diagnosis of the site is C6. The lesion site diagnosis, causes greater difficulties in case of damage to the remaining cervical roots. It is necessary to examine several muscles with different innervations and, as in the construction of a "puzzle", to place the various pieces together to determine the potentially most damaged root (Table 5.1).

Spurling test and shoulder abduction test are the most commonly used clinical tests for the cervical radiculopathy diagnosis [9]. In the former one, the head is flexed towards the painful side by pressing on the head from top to bottom, thus causing further narrowing of the intervertebral foramen and consequently worsening of pain. The second is based on the reverse phenomenon: abduction of the arm widens the intervertebral foramen and compression of the root is reduced, with relief of symptoms (Fig. 5.10). The arm compression test, which is performed in the middle third of the arm, is another test used; the onset of intense pain is highly indicative for radiculopathy [9].

Table 5.1 Muscles supplied by cervical spinal cord segments and roots

Spinal segments/ Roots	Muscles with single innervation	Muscles with multiple innervation
C2–C4		Neck muscles, trapezius, diaphragm
C5	Rhomboids	Serratus anterior, supraspinatus, infraspinatus, deltoid, biceps, brachioradialis
C6		Serratus anterior, supraspinatus, infraspinatus, deltoid, biceps, brachioradialis
C7		Serratus anterior, pectoralis, triceps, extensors and flexors of the hand and fingers
C8–T1		Intrinsic muscles of the hand

Only the rhomboid muscle receive innervation from a single cervical root. This feature facilitates the diagnosis of C5 and C6 radiculopathy

Differential Diagnosis of Spondylotic Cervical Radiculopathy

Before starting the discussion on the differential diagnosis, should be emphasized that in any case of cervical radiculopathy, signs of myelopathy must also be sought as both pathologies have the same cause.

The diagnosis of SCR is generally quite simple, but in some cases it can be confused with other pathologies, particularly with some peripheral neuropathies (carpal tunnel syndrome, ulnar nerve entrapment) and shoulder pathology. Less frequent but insidious pathologies are thoracic egress syndrome and Parsonage Turner syndrome due to their diagnostic difficulty.

Differential Diagnosis of Radiculopathy and Carpal Tunnel Syndrome (CTS)

Both C6–C7 radiculopathies and CTS can manifest with paresthesia and pain in the first three fingers. Furthermore, in CTS, the disorder often

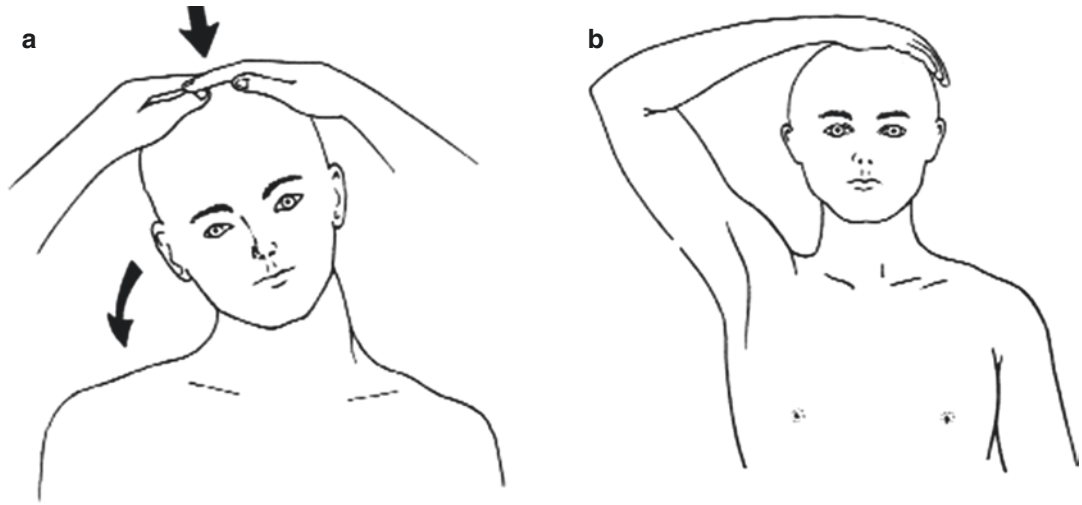

Fig. 5.10 Spurlin test (**a**) and shoulder abduction test (**b**)

radiates to the elbow, sometimes to the shoulder, causing further confusion with a radiculopathy. However, the spatial distribution of the pain is the only common element for both pathologies. The temporal presentation of pain is an important difference, mostly inconstant in CTS, but incessant in the SCR. In the early stages, CTS causes paresthesia during awakening, predominantly in the third and fourth fingers. After that, CTS presents during sleep in the night. As the damage progresses, it causes daytime disturbances, especially during repetitive wrist flexion or hand elevation, such as driving or holding a telephone for a long time. In the most severe cases, the pain is present permanently. Patients often wake up because of pain and shake out their hand to obtain relief. This is known as the flick sign [10]. Head movements do not affect CTS pain unlike SCR. CTS is frequently bilateral, although often asymmetrical. In CTS the tendon reflexes are not altered while in SCR they can be reduced. Severe CTS is easily recognized due to muscle atrophy limited to the thenar eminence. CTS and SCR can coexist as both pathologies are frequent, complicating the diagnosis. If both pathologies are confirmed with clinical and instrumental examinations, it is necessary to determine which one is the prevalent cause of the symptoms. For this reason, the neurophysiological study assumes the most important role in choosing the most urgent treatment.

> The nocturnal prevalence of symptoms, the sensory involvement of the fourth finger limited to its radial half, the flick sign, failure to worsen the pain with head movements are the symptoms and characteristic signs of carpal tunnel syndrome that help to distinguish it from a spondylotic cervical radiculopathy.

Differential Diagnosis of Radiculopathy and Shoulder Pathology

C5 radiculopathy can easily be confused with a shoulder disease, and vice versa, as both have shoulder pain in common [11]. The risk of misdiagnosis is particularly high if the patient is unable to identify adequately the painful area. Diagnostic difficulties also increase due to the frequent association of shoulder pathology and cervical radiculopathy. It is reported that painful shoulder impingement may occur in up to 24% of patients with cervical radiculopathy [12]. Concordance studies have shown that approximately 1 in 10 patients referred for cervical radiculopathy has comorbid shoulder pathology [13]. In addition, pain reported in the neck may

represent referred pain from the shoulder girdle and vice versa [14, 15].

Radicular pain can be distinguished from shoulder pain by its characteristics and factors that relieve or worsen it. A dull pain is more consistent with shoulder pathology, whereas burning or electric type pain is more likely of neurologic origin [16]. If the head is tilted to the side opposite to that of the pain, it is likely a radiculopathy [17]. In fact, the head inclination contralaterally to the pain widens the neural foramen and reduces the compression of the root. Arm abduction worsens the shoulder pain, but relieves radicular pain [18, 19]. Localization of pain at rest is generally less useful in distinguishing pain from shoulder disease or C5 radiculopathy. However, if the pain is accurately localized in a small area of the deltoid region, it is almost certainly due to shoulder pathology. Muscle strength can be misleading as its assessment often causes pain in both pathologies. Hypoesthesia in C5 dermatome and radio-flexor and bicipital reflex reduction indicate the radiculopathy. Character of pain at night, which generally worsens in the case of shoulder pathology, can contribute to the differential diagnosis. Pain arising after physical exertion or trauma is mostly resulted from a shoulder injury, post-traumatic radiculopathy being quite rare [20]. However, in the case of a traumatic shoulder injury, particularly in violent trauma, a possible association of root injury must always be sought.

A special case is the suprascapular nerve entrapment which must be suspected in any case of shoulder weakness and scapular atrophy without pain. The cause can be direct trauma or a ganglion cyst [12].

Nocturnal prevalence of pain and its worsening with abduction of the arm are the main features that distinguish shoulder pathology from radiculopathy.

Differential Diagnosis of Radiculopathy and Parsonage Turner Syndrome

Parsonage Turner syndrome (PTS), also know as neuralgic amyotrophy or brachial plexus neuritis, is an inflammatory dysimmune disease affecting the brachial plexus. The patient experiences sudden, very intense and relentless pain in the shoulder girdle, almost always unilateral [21] that can radiate to the crest of the Trapezius, arm, forearm and hand [22].

PTS is a rare syndrome, but the diagnosis is probably underestimated due to the difficult distinction with the cervical radiculopathy. Unlike radiculopathy, pain in PTS is not modified by the position of the limb or head, and usually increases at night. Activities that increase endorachid pressure do not accentuate pain.

In some cases the pain progressively decreases after 1 or 2 weeks and after complete ceasing a progressive muscle weakness, an alteration of sensibility and reduction of tendon reflexes occur. Muscle hypotrophy is evident within a month. Winged scapula may occur in case of long thoracic nerve affection.

A distinctive feature of PTS that can help its diagnosis, but, at the same time, requires very thorough examination, is the uneven muscles involvement, which does not follow the classic pattern of brachial plexus or radicular distribution.

For example, PTS can damage the suprascapular and/or thoracic long nerves and spare the deltoid and biceps muscles, although they share the same root and the same brachial trunk [23]. This is probably due to an extreme irregularity in the spatial distribution of nerve lesions in PTS.

The main traits of PTS are the typical two-phase progression: a first phase with intense pain, but without notable strength deficit and a second phase in which the pain disappears and the strength deficit occurs; the irregular distribution of muscle deficit that does not follow the classic brachial plexus pattern.

Differential Diagnosis of Radiculopathy and Thoracic Outlet Syndrome

The thoracic outlet is an anatomical corridor between the supraclavicular region and the armpit. It is crossed by structures coming from the neck and chest, crucial for the function of the upper limb. In particular, it is crossed by the subclavian artery and vein and brachial plexus.

The thoracic outlet syndrome (TOS) is characterized by the compression of the neurovascular bundle within the canal. Repetitive motions can cause muscle hypertrophy and contributes to compression. It can happen particularly in some sports or jobs, which require muscular effort with the upper limb extended (swimmers, baseball players, body builders, warehouse workers). Furthermore, several anatomical variants can cause compression of the neurovascular bundle. Among them is the cervical supernumerary rib with an estimated prevalence of 1–2% in the general population, remaining asymptomatic for most people. TOS is caused by a cervical rib in 20% of cases [24]. Congenital muscle variants that cause TOS, such as a supernumerary scalenus muscle, have also been reported [24]. Malignant or benign tumors such as Pancoast tumor or osteochondromas, causing compression, are another well-documented etiologies of TOS [25, 26].

Lower primary trunk which originates from C8 and T1 roots, is the most affected segment of the brachial plexus. Shoulder pain, often in the armpit, along the inner region of the arm, forearm and last two fingers and a motor deficit of the intrinsic musculature of the hand are the most common symptoms.

Distinction from cervicobrachial symptoms may prove challenging [27]. Palpation of the supraclavicular region can be painful. A positive Adson maneuver can be helpful in the diagnosis (disappearance of the radial pulse with extended shoulder and laterally rotated limb). Neurophysiological study and Doppler ultrasound have a fundamental role in the diagnosis of TOS.

TOS diagnosis is difficult, but a thorough clinical examination can reveal the disease. Practitioners must consider TOS in their differential diagnosis for shoulder and upper extremity pain symptoms, so that patients are directed appropriately to timely therapeutic interventions.

> Intense pain in the armpit, painful waking up at night with the upper limb raised above the head, pain caused by pressure on the supraclavicular region are the traits that may suggest the diagnosis of TOS.

Cervical Spondylotic Myelopathy

Cervical spondylotic myelopathy (CSM) is the most common spinal cord disease [1]. Its onset is insidious and progresses gradually, rarely "stepwise", generally begins after the fourth decade and prevails in males [28]. The clinical manifestation is complex as mixed motor disorders (both central and peripheral), sensory and sphincter disorders are associated. The most common symptoms are sensory disturbances of the upper and/or lower limbs, neck stiffness, feeling of "heavy legs", clumsy gait, bladder and bowel dysfunction.

Degenerative spondylotic phenomena affecting the vertebrae, intervertebral discs, facet joints and ligaments cause damage to the spinal cord either by direct compression or by ischemia due to blood vessel compression [29].

Spinal cord injury and the resulting functional damage are irreversible. For this reason, its timely identification is essential to provide an effective treatment before irreversible damage and permanent disability develop [30]. In recent decades, the number of patients undergoing CSM surgery has significantly increased due to better diagnosis for technological advances. On the other hand, the progressive increase in the average age and, consequently, in people with cervical spondylosis, is an important cause of the increase in cervical myelopathy diagnoses. For the same reason, it is likely that CSM will become even more widespread in the coming decades. Therefore, it is imperative for the physicians to identify CSM early, especially in the initial phases that are not yet disabling.

Cervical Myelopathy Symptoms

The clinical picture of CMS is complex due to the particular spinal cord anatomy and physiology.

The symptoms are due to: (1) focal damage of somas in the spinal gray matter (2) focal interruption of the ascending and descending spinal tracts.

Damage to the spinal motor neurons causes flaccid paralysis of the muscles innervated, similarly to what happens in the lesion of the homonymous root. In fact a flaccid paralysis occurs either from peripheral nerve, motor root, or spinal motor neuron injury. For the same reason, tendon reflexes are diminished. These symptoms may differ from patient to patient and vary according with the harmed myelomere.

At the same level, the descending fibers towards the underlying myelomeres are also damaged. This lesion causes a paresis, this time spastic, of all the muscles innervated by the segment just below the damaged one up to the Conus medullaris. The focal damage to the ascending sensory fibers causes anesthesia of the underlying body region with a limit corresponding to some lower dermatome. These symptoms are common in all the cases, regardless of damage site and are: lower limb stiffness and weakness, characteristic changes in gait, including slower gait speed, decreased step length, longer stride time, and increased step width [31], hyperreflexia of the lower limbs, Babinski sign, urinary and intestinal transit disorders.

The cervical spinal cord can be divided into a high sector (C1–C4 myelomeres) and a low sector (C5–T1). The upper myelomeres supply the neck muscles, diaphragm and the sensibility of the posterior region of the head, neck and upper chest. The lower segments control the upper limbs.

Cervical High Spinal Lesions

It is very difficult to accurately establish the damage site in the upper cervical tract due to the overlapping of muscle and skin innervated by the spinal segments. Help can only be provided by the electromyographic examination.

C1–C4 spinal lesions cause neck muscles, Trapezius and Diaphragm flaccid paresis (Table 5.1), spastic tetraparesis from C5 down, anesthesia up to the clavicle and the other symptoms in common in all cases of CSM.

High segment myelopathies are the most dangerous due to the involvement of the diaphragm and the risk of respiratory failure.

Low Spinal Lesions

C5 spinal lesion causes a flaccid paresis of deltoid, biceps, rhomboid, supra, and infraspinal muscles (abduction and external rotation of the arm and flexion of forearm deficit) + symptoms in common. The patient shows scapular, deltoid and biceps hypotrophy, bicipital and brachioradialis areflexia, triceps, pronator teres and lower limbs hyperreflexia, hypoesthesia up to the upper chest.

C6 spinal lesion causes a prevalent flaccid paresis of biceps and brachioradialis muscles (flexion of forearm deficit) + symptoms in common. The patient shows biceps hypotrophy, bicipital and brachioradialis areflexia, triceps, pronator teres and lower limbs hyperreflexia, hypoesthesia up to the upper chest.

C7 spinal lesion causes a prevalent flaccid paresis of triceps, fingers and wrist extensor muscles (forearm, fingers and wrist extension deficit) + symptoms in common. The patient shows triceps muscle hypotrophy, bicipital and brachioradialis normoreflexia, triceps areflexia, pronator teres and lower limbs hyperreflexia, hypoesthesia up to the mammary region and hypoesthesia of the C7 dermatomes.

C8 spinal lesion causes a prevalent flaccid paresis of the intrinsic muscles of the hand + symptoms in common. The patient shows hand hypotrophy, bicipital and brachioradialis normoreflexia, triceps hyporeflexia, pronator teres areflexia and lower limbs hyperreflexia, hypoesthesia up to the mammary region and hypoesthesia of the C8 dermatomes.

CSM has been shown to affect respiratory function not only in high spinal cord injuries due to diaphragm impairment, but also in C5–T1 injuries. It is believed that this occurs due to the involvement

of the autonomic and sensorimotor structures of the upper thoracic metamers and consequent reduction of respiratory exchanges [32].

Differential Diagnosis of CSM

Amyotrophic lateral sclerosis (ALS), Multiple Sclerosis, Syringomyelia, spinal tumors, vitamin B12 deficiency myelopathy (combined subacute degeneration) are the diseases most frequently confused with CSM.

ALS develops due to degeneration of the 1st cortical motor neuron and 2nd spinal motor neuron. Similarly to CSM, it debuts in the fourth-sixth decade. Patients have generally symmetrical strength deficits; muscular atrophy and fasciculations affecting all the musculature, including the cranial one, unlike CSM, where they are present only in the upper limbs. Pain is always absent, sensibilities and sphincters are not involved.

The fasciculations in the EMG study in ALS, involving all the musculature, including the cranial one, is the most important difference compared to the CSM.

Multiple Sclerosis occurs in young adults (second to fourth decade); a debut over 60 years is very rare. Similarly to CSM it can cause spastic tetraparesis or paraparesis, sensory and sphincter disorders. Unlike CSM, it has a mostly relapsing-remitting evolution (however, some cases evolve progressively), often causes vision disturbances (diplopia and visual field deficit) and other cranial nerve lesions. Psychic disturbances are often present.

Syringomyelia is easily confused with CSM due to its pathophysiology. It is due to a cystic cavitation within the spinal cord that maintains a continuity with the liquor circulation and tends to enlarge due to a valve effect, determining a progressive intraspinal compression. Therefore, it presents an insidious onset and symptoms very similar to those of the CSM: atrophy of the upper limbs, spastic paraparesis, sensory disorders, sphincter disorders. Only MRI allows diagnosis.

Similarly to CSM, *subacute combined degeneration due to vitamin B12 deficiency* occurs with sensory and motor disorders including gait ataxia, motor deficits, Babinski sign. It differs from CSM for tendon reflexes which are generally absent due to the severe sensory involvement of the peripheral nerves and for the frequent psychic symptoms of which the main one is dementia.

Spinal tumors can cause compression of the spinal cord in a manner similar to spondylosis and therefore determine a clinical picture that cannot be differentiated.

Numerous other pathologies have a clinical picture similar to spondylogenic myelopathy: epidural abscesses or hematomas, Arnold-Chiari malformation, vasculitis and spinal cord infarction, inflammatory and dysimmune myelitis, rheumatoid arthritis, vascular malformations [33]. Some pathologies of the peripheral nervous system can mimic myelopathy or radiculopathy such as multifocal motor neuropathy, tomacular neuropathy, multineuropathy.

Fasciculations spread to all the muscles, including the cranial ones, normal sensory and sphincters, are the main features that clinically distinguish ASL from CSM.

The signs that clinically distinguish Multiple Sclerosis from MSM are the evolution, mostly relapsing-remitting, and frequent involvement of the ocular nerves.

The clinical distinction of syringomyelia or neoplasm is almost impossible.

Subacute combined degeneration should be suspected if tendon reflexes are absent and psychic disturbances are associated.

Chronic Neck Pain

Before discussing the neurophysiological studies, it is pertinent to treat the chronic neck pain (CNP). This disorder deserves special attention due to its high frequency in the population. Two thirds of the population has suffered from neck pain of any kind at some point in their life [34]. The prevalence of chronic neck pain varies between 1.7 and 11.5% [35]. CNP leads to reduced work productivity, increased work absenteeism, and has a high health cost [36].

Patients complain of dull pain, muscle tension or stiffness of the cervical muscles, lasting more than 3 months. The course of CNP is irregular, with large intensity fluctuations. The patients rarely have temporary relief from pain. The pain intensifies during stress and decreases during sports activities. In some cases, CNP originates from an acute neck pain and lasts for months or years years but, in most cases, the patients identify the onset of the pain with a stressful event, if properly questioned. In fact, rarely he reports spontaneously an onset of the disorder during stress and, if stress is suggested as a possible etiology, in the first place the patient often recognize the stress secondary to continuous pain.

Although neck pain can be attributed to traumatic disorders (e.g. whiplash-associated disorder) or inflammatory disorders [37], the majority of chronic neck pain does not have a discernible cause and is considered idiopathic [38]. However, in recent decades, studies on the pathophysiology of chronic pain have multiplied, including those, which identify the alteration of the central modulation of pain as one of the most important causes of chronic pain [39]. The evidence of the efficacy of some antidepressant and anxiolytic drugs seems to confirm this hypothesis. In fact, it is known that the central pathways of pain are closely connected with anxiety and mood brain circuits and that they share the use of some neurotransmitters, the best known of which are serotonin and noradrenaline. It has been shown that these neurotransmitters are reduced both in chronic pain and in depression and anxiety. For this reason, mood alterations are frequently accompanied by alterations in the perception of pain [40]. Therefore, unlike what is often thought, pain does not that cause stress or vice versa, but these two phenomena are often associated due to a common neurotransmitter alteration. However, it is true that the two phenomena feed each other, creating a vicious circuit.

In patients with CNP the radiological images often show spondylosis. However, these findings are common in asymptomatic patients. Moreover, in spondylotic myelopathy, cervical pain is absent or very mild [1, 28, 30], although spondylosis is generally severe.

Alterations of the vertebral facet joints are also indicated among the causes of CNP. According to this theory, the profuse sensory endings of these structures are activated by the stretching of the articular membrane for spondylotic bone modifications and for altered joint relationships. However, this hypothesis seems to contrast with the relief patients often feel when the neck is snapped, even though this maneuver induces a sudden and extensive stretching of the joint membranes.

Straightening of the cervical spine is a common radiographic finding in CNP. It is characteristic for whiplash and is secondary to the contracture of the paravertebral musculature. However, there are few CNP patients with whiplash in the anamnesis.

Feeling of cervical tension, diarrhea, tachycardia and sweating during a stressful event is common. The widespread manifestation in the population of muscle tension in stressful conditions is the expression of a physiological phenomenon, due to an archaic defense reflex in which the muscles are activated in preparation for the motor response to a dangerous event. In most cases this contracture is limited to the persistence of the stressful anxiety-inducing event. However, in cases of pathological anxiety the patient continually perceives a feeling of danger even without a recognizable triggering event. Under these conditions, the brain circuits of anxiety are persistently activated and there is an imbalance between inhibitory and anxiety-inducing neurotransmitter.

A pharmacological intervention that restores the balance between these neurotransmitters determines the reduction of the stress state and its physical consequences. For this reason, most

CNP patients benefit from taking an SSRI and tricyclic drugs that regulate the functions of serotonin and noradrenaline.

However the therapeutic approach, used more frequently in patients suffering from chronic neck pain, includes anti-inflammatory drugs, physiotherapy, massotherapy, anesthetics or steroid infiltrations. The results of these treatments are temporary and do not significantly affect the patient's health conditions. Often after a long period of frustration due to the limitations of these treatments, the patient sometimes visits the neurologist and starts a tricyclic or SSRI treatment with a rapid and persistent effectiveness and stops consulting several specialists.

The tensive nature of most chronic neck pain is likely to be commonly underestimated due to a tendency to disregard stress disorder as a pathology. Probably this approach is secondary to the deep-rooted belief that everything that belongs to the mental sphere does not have "a body", is not "made of matter" and therefore cannot cause the dysfunction of a physical system. To understand that thinking is not abstract, it is enough to study the functional MRI studies of a subject undergoing to mental activity that shows the functional activation of brain areas. It is therefore possible to "see" the thought taking shape (Fig. 5.11).

It should therefore not be a surprise, if suffering from anxiety or depression person with constantly present weird fear that something is about to happen, even if he does not know what, has a persistent contracture of the spinal muscles and neck pain often associated with low back pain.

For the above, if a patient suffers from chronic neck pain, tension-type pain should be suspected. This benefits the patient with an effective, lasting treatment to control pain.

Cervical Spine Pathology: Neurophysiological Approach

The risk of an incorrect or incomplete electrophysiological conclusion is very high if the test is not preceded by a clinical evaluation. The neurophysiological study must be considered as an extension of the neurological exam, to confirm or refute the diagnostic suspicion and, like all other instrumental examinations, it is of little value if is separated from the clinical context. It is useful in identifying any functional deficits that are not clinically evident. The choice of the method and the districts to examine is guided by symptoms and physical examination.

The first step in diagnosing a disease is to suspect it. A disease can remain undiagnosed if it is not researched. For example, to avoid confusing brachial neuritis with radiculopathy, it is essential that both diseases are suspected and that appropriate tests are used to distinguish them.

An example that confirms the importance of a thorough clinical examination is the case of a patient with upper limb weakness and MRI showing cervical spine stenosis. The neurophysiologist has to determine if MRI findings are congruent with the clinical picture. The patient may suffer from spondylotic cervical myeloradiculopathy and be a candidate for surgery or, conversely, MRI findings do not reflect the clinical picture. He may suffer from amyotrophic lateral sclerosis (ALS), multifocal motor neuropathy (MMN), multineuropathy, neuropathy with susceptibility to pressure paralysis (HNPP). For this reason, the neurophysiologist must perform a neurological examination in search of the characteristic signs of each pathology that enters the differential diagnosis and finally apply the most suitable neurophysiological tests.

Further examples are useful to clarify the fundamental role of clinical evaluation.

In case of hand muscle atrophy associated with hyperactive pronator teres reflex, both related to the C8–T1 roots, amyotrophic lateral sclerosis should be suspected. In fact, a characteristic of this pathology is the spasticity of the hypotrophic muscles, contrary to what happens in radiculopathies and myelopathies. This phenomenon is due to the coexistence of spinal motor neuron degeneration, responsible of muscle atrophy, and cortical motor neuron degeneration leading to spasticity of atrophic muscles. Once this diagnostic suspicion has emerged, the neurophysiologist performs an electromyographic examination, first choice for the diagnosis of ALS.

A patient with multifocal motor neuropathy or polyneuropathy may have an MRI picture of stenosis or multiple hernias that can mistakenly lead

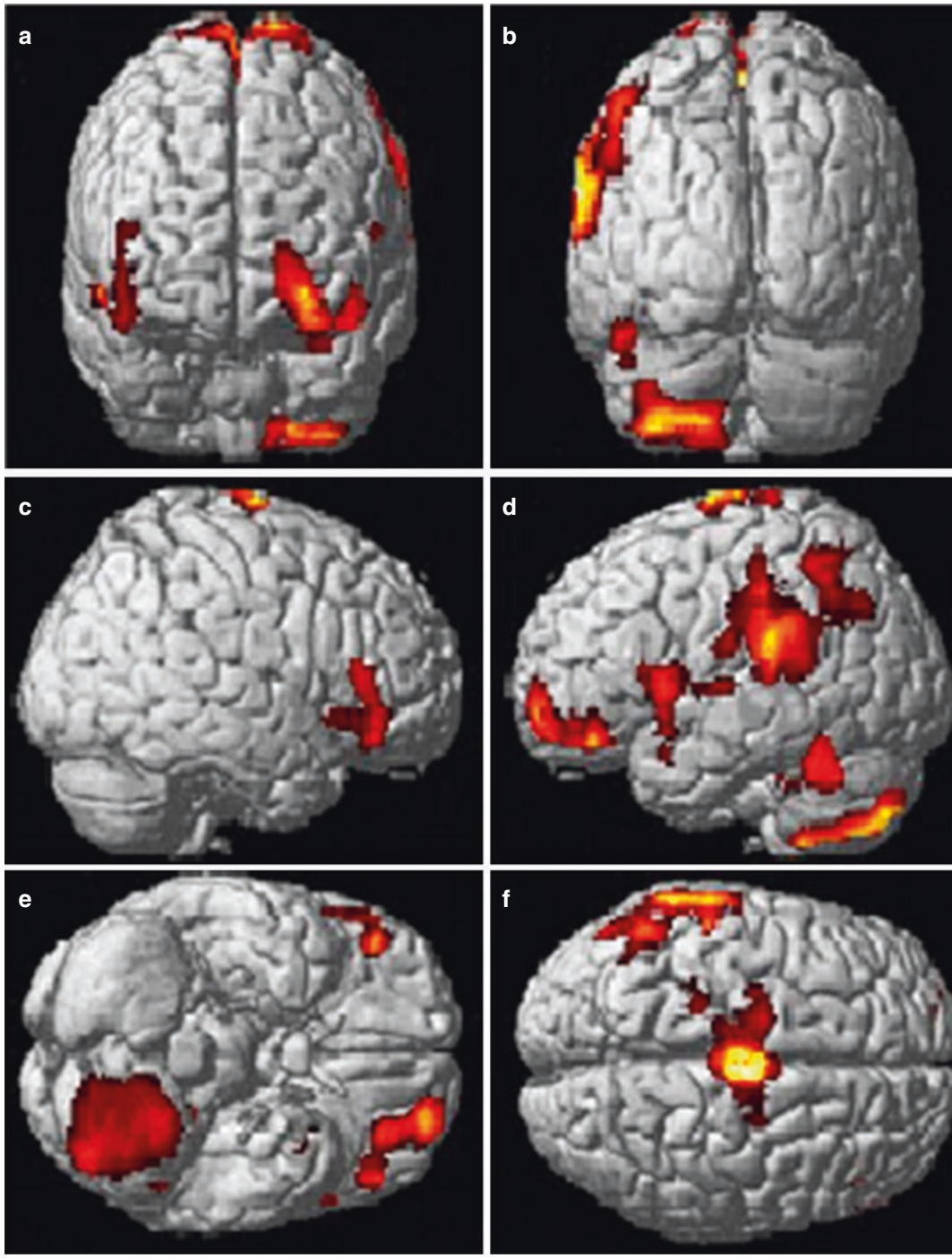

Fig. 5.11 Functional MRI of a normal subject during imagining their own body representation. Brain areas activated during the task (**a**–**f**)

to surgery. MMN shows typical motor conduction blocks on electrophysiological exam. In polyneuropathy the test shows the widespread damage of the nerve trunks.

The coexistence of these diseases and cervical myelopathy is possible. In this case the role of the neurophysiologist is even more important due to the complexity of the clinical picture. He

provides for establishing the role of each of these pathologies in the clinical picture and provide an indication of the most appropriate treatment.

Neurophysiological studies can provide a precise spinal damage site, but also a quantification of the functional damage. The electromyographic exam can also distinguish a recent damage (e.g. from a herniated disc) from chronic damage, present for many months or years (as in stenosis radiculopathy) and, finally, can determine whether the damage is previous, now stabilized and therefore no longer responsible for active symptoms (outcome of an old lesion). These distinctions allow to choose the correct treatment approach and to reduce the possible risks of medico-legal implications.

An example is the case of a patient with an acute brachialgia and MRI reports of foraminal stenosis, which may appear congruous with the pain. If the electromyographic exam reveals signs of previous root damage, now stabilized, it is unlikely to be the cause of the patient's acute pain and therefore, other causes of pain must also be sought (e.g. brachial neuritis, shoulder pathology), avoiding the risk of performing ineffective surgery which can also cause possible complications.

Neurophysiological studies can provide prognostic judgments on the expected outcome of surgical treatment, important for both surgeon and patient. In case of very painful radiculopathy with small damage EMG findings, the probability of pain resolution without significant functional deficits following surgery is very high. In fact, in radiculopathies, the intensity of the pain often does not correlate with the damage. Likewise, it is important to know before surgery if there is a serious root damage to inform both surgeon and patient of the high probability of persistent functional damage after surgery, despite the resolution of the pain. This information is of great importance as the patient always expects complete resolution of the ailments after surgery while failed expectations can lead to legal disputes.

The comparison of electrophysiological findings before and after surgery provides indications on the treatment effectiveness, important in cases of slow clinical recovery because neurophysiological improvement may appear earlier than clinical ones.

Finally, neurophysiological tests are increasingly requested by surgeons for intraoperative monitoring to highlight incipient nerve structures' damage and to modify the surgical procedure in order to reduce possible complications.

Neurophysiological Studies

The neurophysiological studies used in cervical spine diseases are: electromyography (EMG) , nerve conduction study (NCS), somatosensory evoked potential (SEP) and motor evoked potential (MEP).

Electromyography

EMG studies the electrical activity of muscle fibers. It provides a functional assessment of the muscle and nerve.

> EMG studies only the motor nerve fibers. EMG does not give information on sensory fibers.

EMG can be performed with a needle-electrode introduced into the muscle or with a surface electrode placed on the skin overlying the muscle. The first method is minimally invasive, but provides the best information; the surface electrode does not cause any disturbance but provides insufficient information. Therefore, only the needle-EMG examination will be described.

EMG studies the motor unit (MU). It is an anatomo-functional unit consisting of: (1) the soma of a single spinal motor neuron, (2) its axonal extension along the spinal root and nerve trunk, (3) motor end plate, (4) the set of muscle fibers innervated by the single motor neuron (Fig. 5.12).

The muscle fibers of each individual MU are scattered and mixed with muscle fibers belonging to other MU. Mixture of muscle fibers of different

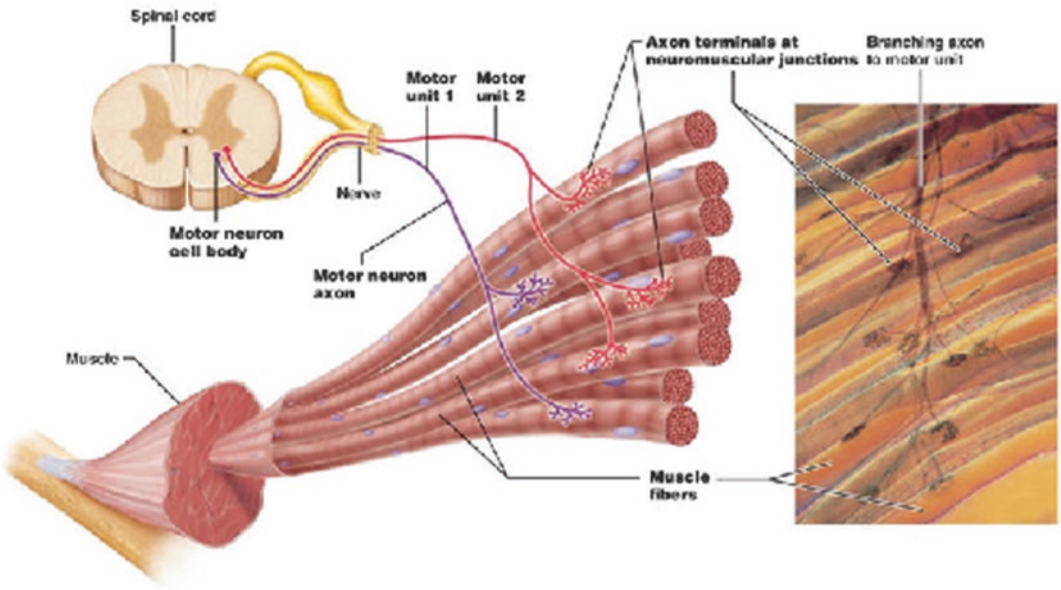

Fig. 5.12 Schematic representation of motor unit and the mixing of the muscle fibers of various motor units

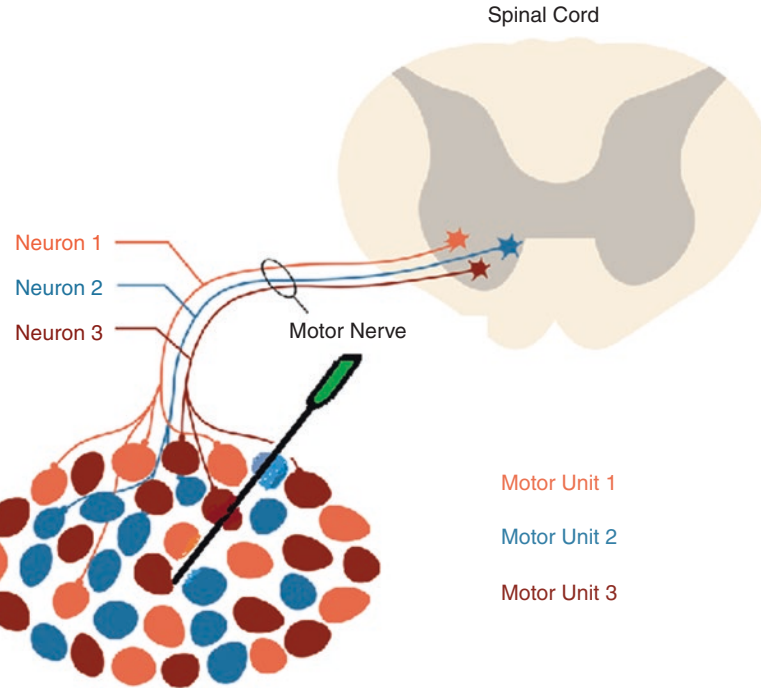

Fig. 5.13 Needle electrode examines more motor unit at each insertion point

MU ensures maximum linearity and homogeneity of muscle contraction and allows to examine more MU at each insertion point of the needle (Fig. 5.13).

The electrical signal recorded by the needle is sent to an amplifier, which is essential to make visible the small electrical signals recorded, which are filtered and isolated from other environmental electrical signals. A converter transforms the analog into digital signals, suitable for displaying and recording with computerized systems.

EMG provides information of the muscle's condition and, in case of disease, allows distin-

guishing a primary pathology (dystrophy, myositis, etc.) from a damage to the spinal motor neuron, spinal root or nerve.

The electrical activity of the muscle fibers of a single motor unit is recorded as an electric potential called motor unit potential (MUP).

The parameters examined during EMG are: (1) electrical activity of the muscle at rest; (2) morphological features of MUPs; (3) degree of muscle activation.

1. At resting, the normal muscle does not receive nerve impulses and the needle-electrode does not register any electrical activity: *normal electrical silence at rest*. If the spinal motor neuron, spinal root or nerve is injured, a small electrical activity is recorded even at rest, defining *spontaneous activity at rest*, which manifests as *fibrillation and sharp wave* (Fig. 5.14). These originate in the muscle fiber membrane suffering from lack of nerve impulses and trophic support from the nerve fiber. The affected membrane becomes electrically unstable and autonomously produces pathological electrical potentials.

   Fibrillation appears at least 2 weeks after muscle fiber denervation and is very important for the temporal dating of the damage. If EMG is performed earlier, less than 2 weeks have passed, no fibrillation potential is recorded. However, even so it can provide useful information: if few MUPs with normal morphology are recorded during muscle contraction and if no spontaneous electrical activity is present at rest, it can be concluded that the damage began no more than 2–3 weeks before and the lesion is defined *acute*.

   When spontaneous activity appears, the lesion is called *subacute*. Spontaneous activity persists until the muscle fiber returns to normal functioning or until it dies.
2. The electrical potentials of normal motor units have well-defined characters. They have a polyphasic morphology with no more than five positive and negative phase peaks, a duration between 6 and 16 msec and amplitude between 0.5 and 5 mV (Fig. 5.15). Damage to an axon or spinal motor neuron causes the denervation of muscle fibers, which remain "orphaned". For stimuli not completely known, branches begin to appear from the axons of the survivors UM, that "adopt" the orphan fibers. This phenomenon takes many weeks and, when completed, the adoptive motor units possess a greater number of muscle fibers and become larger with increased amplitude and duration and polyphasic morphology. This is due to the increased fibers' number that now form the motor unit (increase in amplitude), the enlargement of the innervated area (increase in duration) and the increase of fibers with various speeds of conduction of the nerve impulse (polyphasic potentials) (Fig. 5.16). Recording potentials with such characters allows dating the damage to a not recent time.

   If the damage continues over time, as in foraminal stenosis, different nerve fibers can be damaged at different times and therefore fibrillation potentials can be observed in association with enlarged and polyphasic potentials. This phenomenon is called *chronic-active denervation* as at the same time there are signs of long-lasting damage in some fibers and recent damage in others.
3. The denervation of a muscle determines a reduction of the motor units for which few MUPs are recorded during the voluntary contractions.

   Fibrillation and morphology of MUP are the most important parameters in EMG evaluation. Voluntary activation is a parameter with poor diagnostic value because of the patient's frequent inadequate response to perform a maximum voluntary contraction, which causes discomfort as the needle inserted into the muscle.

EMG in Cervical Spine Pathology

The target of EMG is the motor unit. Therefore, it does not provide information on sensory nerve conduction. For this reason, in cervical-spine diseases, EMG can diagnose lesions of the anterior spinal root only but not of the posterior root.

EMG records in spinal root pathology vary based on:

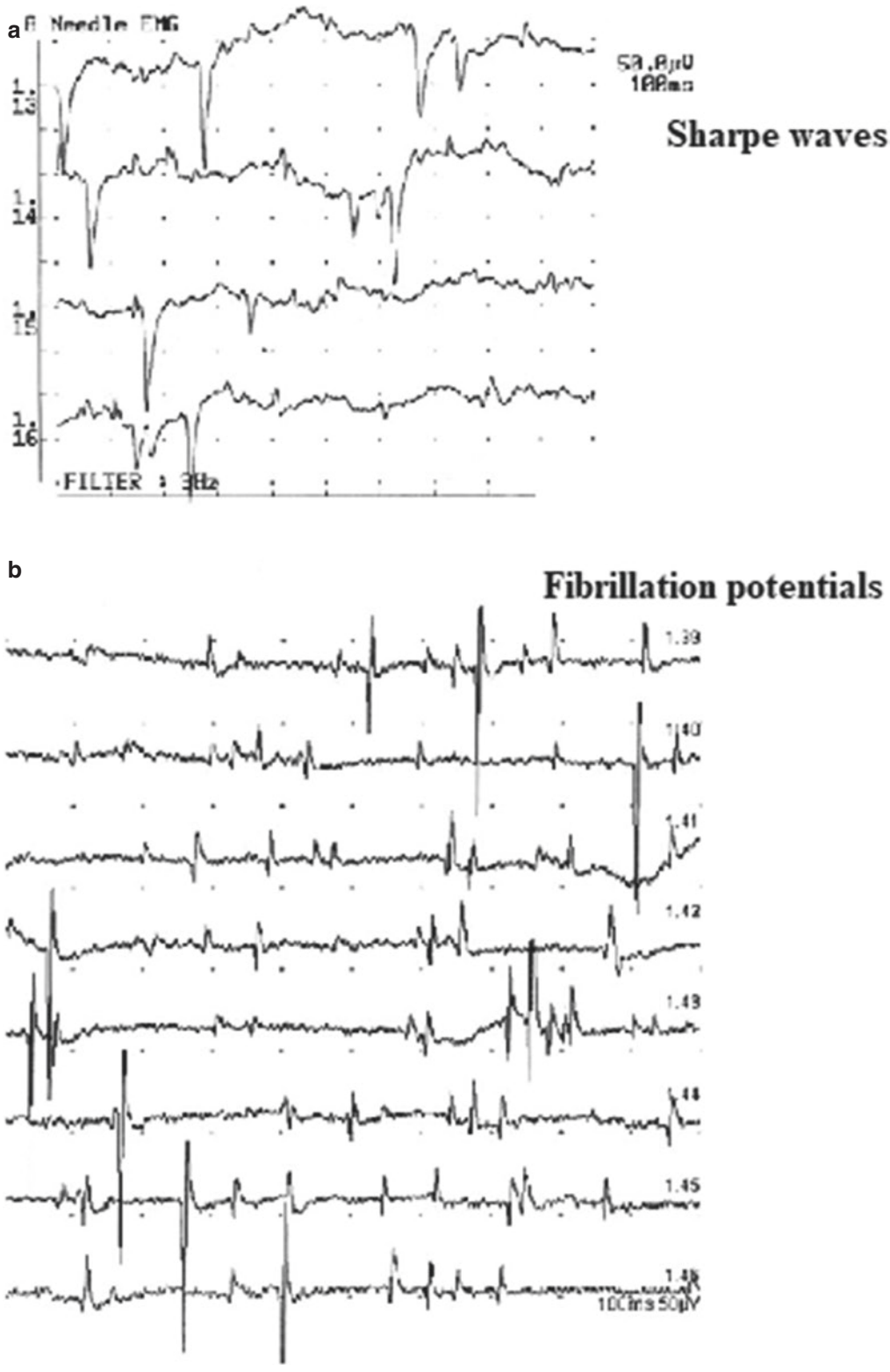

Fig. 5.14 Spontaneous activity of denervated muscle. (**a**) sharp waves and (**b**) fibrillation potentials

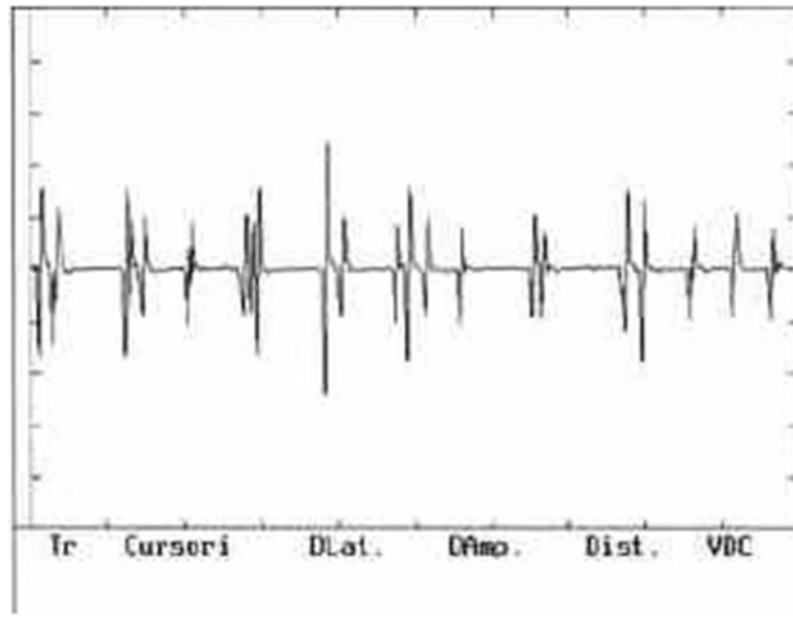

Fig. 5.15 Normal motor unit potentials

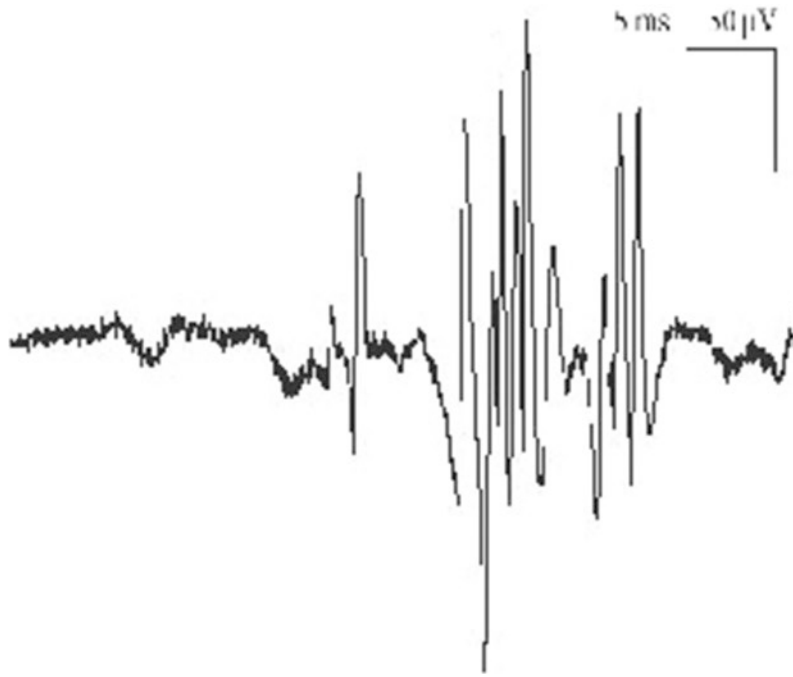

Fig. 5.16 Polyphasic motor unit potentials

1. damage mode of onset (acute e.g. from herniated disc or slow and progressive e.g. foraminal stenosis)
2. damage severity (complete root lesione e.g. radicular avulsion or partial lesion)
3. interval between the onset of damage and examination

Acute Complete Injury of the Motor Root

In acute and complete injury of the motor roots, such as in traumatic avulsion, if the examination is performed within 2 weeks, there is no fibrillation potential and, despite the patient's efforts to activate the muscle, no MUPs are registered.

After at least 2 weeks, there is abundant fibrillation and the MUPs are absent.

After a few months there will be a complete fibrous replacement of the dead muscle fibers and no electrical activity will be recorded, at both rest and attempts at voluntary contractions.

Partial Acute/Subacute Motor Radiculopathy

Almost all cases of acute root damage are caused by a herniated disc.

If EMG is performed within 2 weeks of damage, no spontaneous activity at rest is recorded, number of MUPs are below normal and MUPs maintain normal morphology (*acute partial damage*) Subsequently, fibrillation potentials are recorded, which are all the more abundant the greater the damage; the reduction in recruitment and the normal morphology of MUPs remain unchanged. The distinction between acute and subacute damage is determined just by the presence or absence of fibrillation and allows us to establish whether the lesion occurred within 2 weeks or later.

In summary, the typical EMG picture of acute motor radiculopathy at least 2 weeks after the onset of the disorders is the association of fibrillation potentials and reduced recruitment of motor unit potentials that maintain a regular morphology. This phenomenon is called *subacute partial root damage* and is the most interesting for the surgeon (Table 5.2).

Surgical Indications of Acute and Subacute Radiculopathy

In case of acute partial radiculopathy, the surgeon can follow a conservative wait-and-see approach as a rapid clinical improvement is possible. The only surgical emergencies for a herniated disc are the acute compression of the spinal cord and cauda equina. The compressive effect of the hernia can be reduced in a short time with drug therapy. Rapid shrinking of hernia is even more likely in the case of sequestered hernia, which losses the continuity with the rest of the disc. This happens because, being no longer "fed" by the disc, the herniated fragment is easily destroyed by the macrophages. Furthermore, the conservative approach is allowed because in some cases the strength deficit is due to a momentary "daze" of the nerve (neurapraxia), which quickly regresses.

Finally, a vigilant waiting is also accepted because, once structural damage has occurred, the surgical decompression of the root hardly modifies the functional evolution of the damage, even if the cause is eliminated and although the pain quickly subsides. Hernia causes nerve root injury when it violently exits the disc inducing irreversible damage to the axon within a few hours. The functional recovery time cannot be modified, as it is determined solely by the time necessary for reinnervation. In these cases, the patient should clearly understand that the effect of surgical decompression is limited to the resolution of pain.

The indication for surgery varies from case to case. The intensity of pain, its duration and its work and social implications are considered the

Table 5.2 EMG findings in the different types of radiculopathy

EMG outcome	Acute radiculopathy	Subacute radiculopathy	Chronic active radiculopathy	Past radiculopathy
Electric silence at rest	✓			
Fibillation		✓	✓	
PUM normal morphology	✓	✓		
Polyphasic enlarged PUM			✓	✓
Normal recruitment				
Reduced recruitment	✓	✓	✓	✓

most important variables in the evaluation of the indication for surgery.

It is advisable to wait if pain is moderate or rapidly decreasing, but surgery can be indicated if the pain is severe disabling or if it is lasting. The pain duration of at the time of surgical evaluation is very important. It is advisable to wait in cases that started a few days ago. If disabling pain persists, surgery may be indicated.

However, the case of radiculopathy due to foraminal herniation is an exception from this rule. In fact, in these cases, surgery is generally required even for the recently begun forms. The foraminal space is very small and is not extensible, consequently, the possibility that the root remains pressed for a long time by a small protrusion of the disc is very high and therefore it is preferable to decompress early.

EMG in Chronic Active Motor Radiculopathy

Foraminal stenosis causes progressive and prolonged damage to the spinal root over time, therefore, at a given moment, there are some motor fibers that have recently been damaged and others that have been suffering for a long time (*chronic active damage*). The EMG therefore records fibrillation potentials (from muscle fibers with recent damage) and enlarged and polyphasic PUMs (from fibers with older damage, which remodeled due to the phenomenon of reinnervation). This EMG picture is present in numerous cases of surgical interest.

EMG in Elapsed Radiculopathy

EMG in elapsed radiculopathy shows electrical silence at rest (no ongoing damage) and reduction in the number of enlarged PUMs. This type of damage has no surgical indication.

Limits of EMG

EMG only studies the motor nerve fibers, but not the sensory ones. Therefore, it is possible that numerous cases of radiculopathy will not be detected.

Sensory fibers are less resistant than motor fibers and, therefore, compression effects differently on nerve fibers depending of its degree. In minor compressions the sensitive fibers suffer at first, manifesting only in functional alterations without any anatomical damage. This is clinically manifested by paresthesia and pain, which are signs of irritation phenomena of the sensitive fibers. For compressions of a greater degree, anatomical damage of the sensory fibers is determined with initial damage to the myelin and, for even greater compression, with damage to the axon as well; in both cases the damage is clinically manifested by pain, paraesthesia and hypoesthesia. Only for the largest insults, also the motor fibers are damaged and a motor deficit is associated with paraesthesia and hypoesthesia.

In conclusion, in the case of compressive radiculopathy, the damage can be on three levels:

(a) irritative/sensory stage, for cases of minor damage, determined by irritation only of sensitive fibers, without structural damage, which causes pain and paraesthesia, without sensory and motor deficit and normal the tendon reflex
(b) sensory deficit stage, due to damage of a greater degree, in which paresthesia and pain are associated with a sensory deficit, often with tendon hyporeflexia due to damage to the afferent-sensory arch of the spinal reflex
(c) motor deficit stage, due to even greater damage, in which the symptoms above described are associated with a motor deficit, tendon reflex is always reduced due to damage to both the afferent sensory arc and efferent motor arc of the spinal reflex.

Since EMG only studies motor fibers, it can show pathological results only in case *c*. For this reason, even with a clear clinical

picture of cervicobrachialgia with MRI congruous disc herniation, it can happed that unexpectedly the surgeon receives a normal EMG report. The neurophysiologist must clarify this apparent contradiction to the surgeon by explaining that the normality of EMG is due to damage limited to sensory fibers and sparing of motor fibers.

Nerve Conduction Study

The peripheral nerve consists of motor, sensory and vegetative fibers. The nerve conduction study (NCS) is predominantly used to examine motor and sensory fibers and is distinguished in motor nerve conduction and sensory nerve conduction study. This technique will be described less as only the study of sensory nerve conduction has a diagnostic value for the purposes of this work.

To understand the target of the sensory nerve conduction study, a brief anatomo-functional description of the peripheral sensory system is given.

The first neuron of the sensory system is located in the spinal ganglion. It is defined as pseudounipolar neuron because a single axon originates from the cell body which, however, immediately bifurcates into two extensions: (a) peripheral branch that forms the nerve and which carries the nerve impulse to the cell body and (b) central branch, which enters the root and then in the spinal cord.

Sensory nerve conduction is performed with electrical nerve stimuli and records of the electrical response along the nerve. For instance, for the routine study of the median nerve, metal rings are placed around a finger of the hand to stimulate the nerve endings; recording electrodes are placed on the wrist, elbow and armpit. The electrical impulses on the finger activate the nerve; the impulse rises towards the wrist and the other recording sites where the electrodes record the passage of the electric wave. Wave analysis provides an indication of the number of functional sensory electrical fibers (by the amplitude of the recorded response) and the integrity of the myelin (by the nerve conduction velocity). If the nerve is damaged between the stimulation and registration point, a reduced amplitude nerve potential is recorded due to the reduction of functional axons; furthermore, the nerve potential has a slowed conduction velocity due to myelin damage.

Some nerves can easily be examined in this way for long stretches (in particular the median and ulnar nerves) but, for obvious anatomical reasons, this method does not allow to investigate directly the more proximal sensory nerve tracts, particularly the spinal root.

Sensory NCS, anyway, provide important information of the functional state of the spinal root. In fact, under normal conditions, the sensory electrical impulse, originating from the peripheral receptors, rises along the nerve, reaches the neuronal soma in the spinal ganglion and continues along the central branch in the sensory root, up to the spinal cord. Due to the particular anatomy of the spinal ganglion neuron, if a sensory root is compressed, the central branch is damaged, while the peripheral branch remains intact. The latter in fact continues to receive trophic elements from the cell body and continues to function normally. The patient clinically presents an alteration of sensitivity, but sensory nerve conduction study is normal. This is the only case of peripheral lesion, in which there is a dissociation between sensory deficit and normal results of the nerve conduction study (Fig. 5.17). Therefore the NCS assumes a fundamental role in the localization of the damage in the spinal root. If EMG shows pathological outcomes, a normal NCS of the nerve with the same root innervation indicates with certainty that the damage is localized in the spinal root. If sensory conduction abnormalities are present, the damage is certainly downstream of the spinal ganglion (in the brachial plexus or nerve trunk).

The combined EMG and NCS study is fundamental for the differential diagnosis between cervical root disease and other peripheral neurological diseases. It allows the diagnosis of

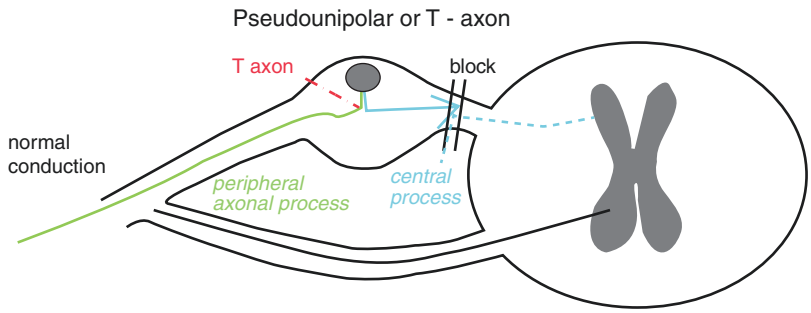

Fig. 5.17 Peripheral axonal branch in spared even if the central branch is damaged

root damage with good reliability, but only if the damage involves the motor root. Also, it gives a possibility to quantify the root damage, to date it and especially to define if a damage is recent and congruous with an acute symptomatology.

However, NCS allows studying the nerves only at the points, potentially suitable for directly recording the passage of the nerve impulse. The most proximal tracts of the peripheral nervous system (brachial plexus and spinal roots) and cervical spinal cord are not directly accessible to electromyographic and neurographic evaluations but can be effectively examined with Evoked Potentials.

Evoked Potentials

Evoked potentials (EPs) are electrical responses, evoked by external stimulus and recorded in the central nervous system or in muscles. They can be recorded by different structures of the brain (sensory, visual and auditory) after stimulation of the appropriate afferents (somatosensory evoked potentials SEP; visual evoked potentials VEP; auditory evoked potentials of the brainstem BAEP) or be recorded from the muscle by stimulating cerebral motor cortex and spinal cord.

In cervical spine disease, SEP and MEP are used.

EPs study the integrity of the entire sensory or motor pathway. By electrical stimulating the median nerve it is possible to follow the nerve impulse up to the sensory cerebral cortex (SEP). By stimulating the motor cortex with electromagnetic stimuli we can follow the nerve impulse to the muscle (MEP).

SEP

SEP examine the function of the entire somatic sensory pathway (peripheral nerve, nerve plexus, spinal roots, spinal cord, brain stem, deep brain structures, cerebral cortex). This test provides an objective and quantifiable measurement of sensitivity, hardly assessable because of the need for full patient cooperation and due to the variability and poor reliability of patient responses. Furthermore, SEP can provide localization of damage, detect subclinical sensory disturbances or sensory damage not detectable with radiological studies, such as in degenerative diseases. A disadvantage of the method is the long time it takes to perform the study.

Anatomo-Physiological Premises for the SEP Study

SEP studie the proprioceptive sensory pathway. Peripheral nerve is electrically stimulated with surface electrodes. The electrical stimulation of the nerve activates the proprioceptive fibers of large diameter and produces an action potential conducted at high speed due to the high myelination of the proprioceptive fibers. These fibers are the peripheral branch of the pseudounipolar neuron of the spinal ganglion. The impulse transmits along the nerve until it reaches the neuron in the spinal ganglion and activates the central branch that transmits along the sensory root and enters the spinal cord. Shortly after entering the spinal cord, the central branch sends collateral branches to the posterior horn and then moves upward to form the posterior funiculus. After reaching the spinal bulb, the axon connects to the neurons of the cuneate nucleus (for the upper limbs) or of the gracilis nucleus (for the lower limbs). The

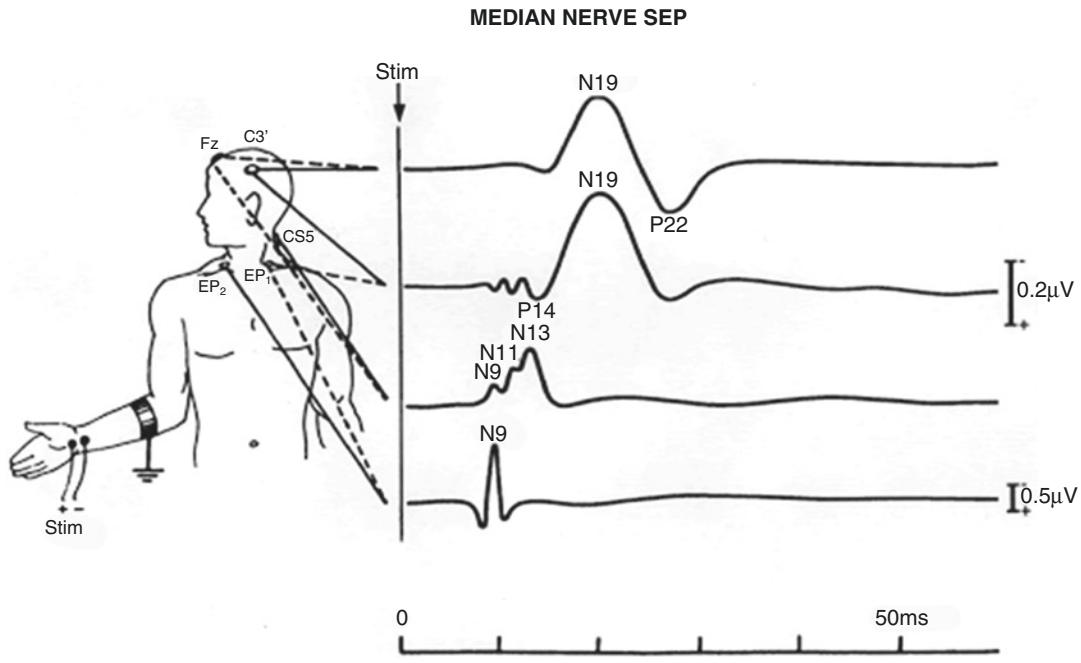

Fig. 5.18 SEP waves from Erb point, spinal cord and parietal cortex

axons departing from these neurons decussate and form the medial lemniscus that rises towards the nuclei of the contralateral thalamus, from which the thalamo-cortical pathway starts.

For the upper limbs, the most examined nerves are the median and the ulnar, stimulated on the wrist. A surface electrode, positioned at Erb's point, records the passage of the evoked potential along the brachial plexus, represented by a wide wave called P9 (P means positive polarity, 9 is the average normal latency in msec.) A surface electrode positioned at the spinous processes records the activation of the cervical spinal structures. One electrode on the spinous process C7 and one on C2 are applied to study cervical spine pathology. The entrance of the nerve impulse into the spinal cord gives rise to N11 wave. The impulse then reaches the posterior horn and gives rise to the N13 wave. An electrode on the parietal region opposite to examined limb, corresponding to the cortical representation of the hand, records the N20 wave. N13 and N20 are the most important SEP waves in cervical spine pathologies (Fig. 5.18). The amplitude of the evoked potential and latency intervals between the recording sites Erb-C7 and C7-scalp are the used parameters.

SEP studies spinal cord and roots function.

SEP in Cervical Radiculopathy

Injury of the sensory roots does not cause alterations of the nerve transmission in the peripheral branch of the T axon and, accordingly, the brachial plexus is undamaged. Therefore SEP registers a potential of normal amplitude and normal latency at the Erb's point (P9). Conversely, the interruption of the nerve impulse in the cervical root causes a reduction in the amplitude of all the waves originating from the remaining nervous structures up to the cortex and, therefore, both the spinal waves N11 and N13 and the cortical wave N20 have a reduced amplitude. The potential is small but not absent because the stimulated nerves derive from more than one root. Only in case of multiple root avulsion, as in road trauma, N13 and N20 can be absent.

SEP in cervical root lesions is characterized by a normal response to the Erb point and by reduced amplitude of the potential recorded at the spinal cord and cerebral cortex.

SEP in Spinal Cord Injuries

SEP can distinguish the damage of the more rostral portions (C1–C5) from the caudal portions (C6–T1) of the cervical spinal cord. For this purpose, it is necessary to apply electrodes recording on the spinous process C7 and C2. By stimulating the median nerve, lesions up to C7 are better studied while C8/T1 lesions are better studied with the ulnar nerve [41].

"Low" Myelopathy: Between C6 and T1 The conduction of the nerve impulse is unhindered in the brachial plexus and the P9 wave at Erb's point is normal. The impulse remains unhindered along the cervical roots and reaches the spinal cord, but, at this point, the nerve impulse stops, due to the damage of the myelomeres between C6 and T1, from which the roots that form the median nerve originate, and the N13 wave is low or absent from both electrodes C7 and C2.

In "low" myelopathy with damage between C6 and T1, N13 wave is small or absent from both the C7 and C2 spinous process.

"High" Myelopathy: Between C1 and C5 The electrode on C7 records a normal N13 wave. In fact, the posterior horns of myelomeres underlying the injured region are normally activated. However, further up, the impulse is interrupted and the posterior horns of the higher myelomeres are poorly activated and the N13 wave is significantly smaller or absent from the C2 electrode.

In "high" myelopathy C6–T1, N13 wave is normal at C7 level, but it is small or absent from the C2 recording electrode.

Contribution of SEP to Myelopathy Treatment

SEP identifies functional damage to the spinal cord with good sensitivity and therefore makes a major contribution to the treatment of myelopathy. It is common, in clinical practice, to find multiple cervical hernias or multilevel central stenosis. In these cases, the surgeon needs to know the most affected level of the spinal cord, to limit the invasiveness of surgery. SEP can identify the most damaged spinal level and indicate the correct site for surgery.

The high sensitivity of SEPs provides a substantial contribution to the diagnosis of myelopathy, particularly when used in combination with MEPs. The sensitivity of SEPs and MEPs is 60–70% if performed individually, but reaches 83% if both performed. The combination of both techniques facilitates the early diagnosis of CSM [4].

MEP

The studies on the human corticospinal motor pathway originates in 1874 when Bartholow demonstrated that the cerebral cortex could be stimulated through electrical impulses during neurosurgery. Subsequent attempts at diagnostic applications of non-invasive stimulation of the cerebral cortex by electrical stimuli on the scalp have failed due to technical (e.g., excessive dispersion of the electric current) and ethics (pain, high risk of activation of epileptogenic mechanisms) issues.

These problems were overcome much later, in 1985, when Anthony Barker of the University of Shieffield presented a non-invasive, safe and painless method of transcranial magnetic stimulation (TMS). This technique is based on the

electromagnetic induction principle of Faraday's law, according to which a moving electric field is able to generate a magnetic field. Barker produced a prototype of a magnetic stimulator consisting of a coil in which he passed a short duration and high intensity electrical impulse, what allowed the generation of a magnetic field capable of reaching the cerebral cortex without attenuation through the scalp and the theca cranial, inducing a secondary ionic current in the brain, capable of activating the motor pathway.

The studies deriving from TMS have rapidly found a wide diagnostic and therapeutic application in a wide range of pathologies, including neoplasms, vascular diseases, Parkinson's disease and other degenerative nervous diseases, headaches, mood disorders and other psychiatric pathologies.

For the purposes of this work, only the application of TMS in the study of nerve conduction along the central cortico-spinal pathway and the peripheral motor pathway will be examined.

As MRI, MEP is contraindicated in patients with pacemakers, subcutaneous infusion pumps, metal clips or stents.

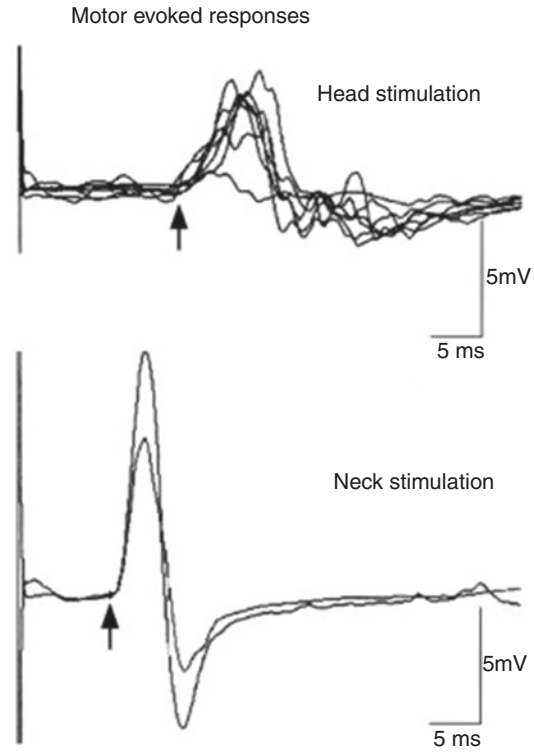

Fig. 5.19 Motor evoked responses

Instruments and Methods

The MEP device consists of a central unit with a control panel and a dispensing device, a circular coil. Surface electrodes are applied over the belly of the muscle which, for our purposes, are the deltoid and thenar or ipothenar muscles. The magnetic stimulus is delivered on the scalp, in correspondence with the motor region for the upper limb, and subsequently at the spinal level.

The magnetic stimulation activates the cortical pyramidal cells and an impulse is transmitted along the corticospinal pathway, reaches the spinal motor neuron, the spinal root, the brachial plexus, the nerve trunk and finally the muscle.

Deltoid and hand musculature are recorded simultaneously. After the stimulus to the scalp, the following parameters are evaluated: (a) brain—muscle deltoid conduction time; (b) brain—eminence thenar conduction time; (c) the difference between these two times.

Then the magnetic stimulus is applied to the cervical spine and the spinal cord-muscle conduction time is detected. By subtracting this conduction time from the brain-muscle time, a Central Brain-Spinal cord Conduction Time is obtained, which coincides with the conduction time of the motor pathway up to the myelomere of the recorded muscle (Fig. 5.19).

Using these parameters it is possible to localizate the spinal cord damage.

If the damage is proximal to myelomere C5 MEP records are:

1. increased both Brain-Muscle Conduction Time and Central Brain-Spinal Cord Conduction Time from both deltoid and hand muscles
2. normal interval between MEP latency from deltoid and hand since the spinal cord section between the two myelomeres is well functioning

In cases of injury between C6 and T1, the MEP recorded by the deltoid muscle presents normal

Brain-Muscle Conduction Time and Central Brain-Spinal Cord Conduction Time as the motor impulse does not encounter obstacles as the spinal cord lesion it is more distal. The evoked potential recorded by the hand is slowed down and both the Central Brain-Spinal Cord Conduction Time and Spinal Cord-Muscle Conduction Time are increased, as well as the latency interval between the MEP recorded by the deltoid muscle and the hand-recorded MEP.

MEP can indicate the site of functional spinal cord damage by distinguishing a site between C1 and C4 from a site between C5 and T1.

Contribution of SEP + MEP to Myelopathy Treatment

Unlike cervical radiculopathy, myelopathy always requires surgery.

Spinal cord injury causes irreversible functional damage. Timely diagnosis and treatment of myelopathy are essential to prevent disabling neurological deficits. Therefore it is necessary to apply all the procedures useful to provide an early diagnosis.

As already mentioned, MRI is the first choice method. If the site of MRI signal alteration is clearly consistent with the clinical manifestations, it is possible to immediately give the surgical indication without waiting for the Evoked Potentials if they delay surgery.

MRI is widely used. The evidence of compression of the cervical spinal cord with deformity of its profile but without alterations of the MRI signal, is increasingly frequent.These cases are of great significance for the complex implications they determine on therapeutic decisions.

Clinical practice shows that in these cases there are two possible occurrences: (a) the patient does not complain of neurological deficits and does not show alterations to the neurological examination; or (b) the patient complains of slight difficulty in walking and the neurological examination shows signs of mild pyramidal damage, for istance, hyperexcitability of the tendon reflexes of the lower limbs and normal reflexes in the upper limbs.

In the former case, a wait-and-see approach may be suitable, as there are no clinical signs of functional damage to the spinal cord and there are no MRI signal alterations. In fact, deformities due to compression of the spinal profile can remain such for a long time without becoming functional or anatomical damage.

However, it is possible that the patient has a subclinical spinal cord damage. In this case the therapeutic approach changes and the patient must be operated on. The only tests capable of highlighting a spinal subclinical damage are the SEP and MEP which therefore become decisive for the indication for surgical treatment. In case of normality of the Evoked Potentials it is suitable a wait-and-see approach, for example, with repetition of the Evoked Potentials and MRI after a few months. If the Evoked Potentials provide signs of functional damage in a congruous location, the indication for surgical intervention should be made also in absence of MRI alteration.

In consideration of the pejorative evolution of spondylotic myelopathy, the conditions of subclinical functional damage and paucisymptomatic pictures represent the most favorable cases for surgical indication as the patient does not yet have a deficit and surgery would prevent their establishment.

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6 Role of Radio Frequency for Cervical Facet Pain: Indication and Results

Luigi Manfrè, Allan Brook, Georgy Bassem, Joshua Adams Hirsch, and Adrian Kastler

Introduction

Neck pain is a very frequent and disabling condition affecting up to 20% of the worldwide population [1]. Among possible sources of pain, cervical zygapophyseal joint dysfunction is hypothesized to result from trauma and/or degeneration of the cervical facet joints. Facet pain may generate both chronic neck and referred pain in the upper arm [2]. However, as has been reported in the lumbar spine, correlation between symptoms and imaging data may be discordant. History and physical examination may suggest but not confirm FJ's as the source of pain and performing injection block to confirm facet syndrome is commonly performed. Denervation techniques such as radiofrequency have become widely performed due to their mini invasiveness and positive outcome [3].

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Epidemiology and Clinical Features

Although the prevalence of facet joint pain is difficult to know, it has been estimated that between 25 and 40 of neck pain may be attributed to facet syndrome, rising to 55% in case of a history of whiplash. Other causes of cervical facet syndrome include computers workers, postural impairment, trauma and degenerative disorders [2, 4].

Cervical facet pain is often characterized by axial neck pain, which may radiate suboccipitally to the shoulders or midback and does not present the characteristics of a neuropathic radicular pain present in case of radicular pain. Topography of pain is represented in the Fig. 6.1.

Anatomy of Facet Joints (FJs)

Each spinal segment consists of an intervertebral disc and, posterior paired synovial joints (FJ) comprising a "three-joint complex", where each component influences the other two, with degenerative changes in one joint affecting the biome-

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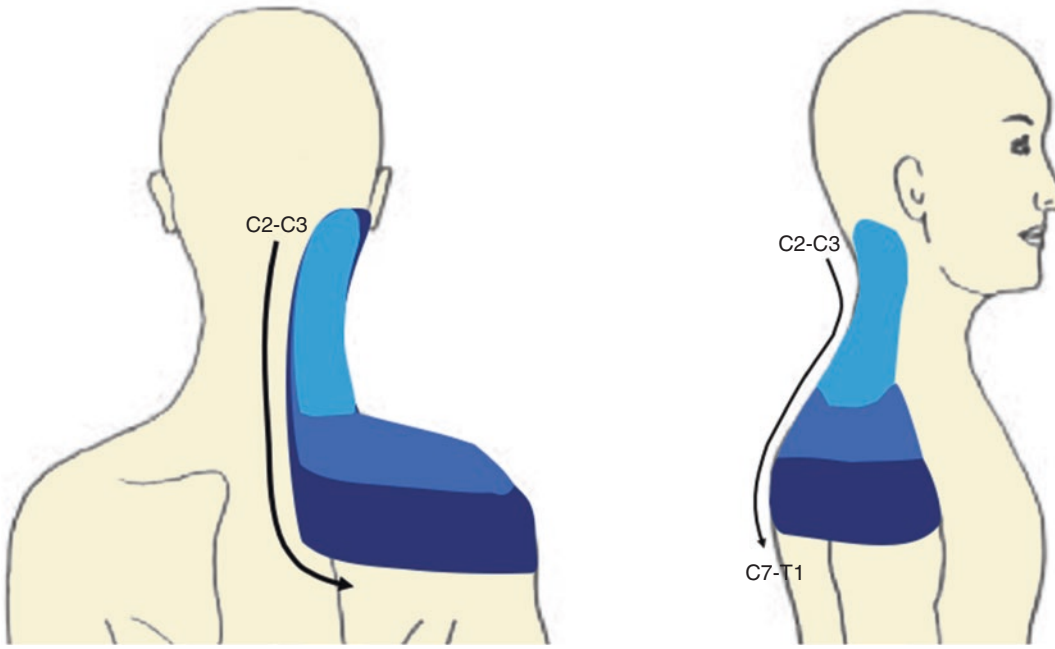

Fig. 6.1 Topography of cervical facet pain

chanics of the whole complex. FJs constitute the postero-lateral articulation connecting the posterior arch between vertebral levels. Cervical facet joints are diarthrodial joints formed by the articulation of the superior articular process with the corresponding inferior articular process. Each facet joint is surrounded by a fibrous capsule, lined by a synovial membrane, and contains articular cartilage and menisci. The innervation of the cervical facet joints was described by Bogduk [5]. From C3–4 through C8–T1, the joints are innervated by the posterior medial branches of the cervical dorsal rami above and below the joint as these branches course around the waist of the articular pillars Fig. 6.2.

Interventional Management

First line therapy consists in conservative multimodal management such as pain medication (acetaminophen, nonsteroidal anti-inflammatory drugs, muscle relaxants, antidepressants), physiotherapy, acupuncture, and if necessary psychotherapy.

As mentioned above, because radio clinical correlation is not reliable in patients with neck pain, the diagnostic and therapeutic role of interventional procedures targeting the FJ have been reported in chronic spinal neck pain in patients who have failed conservative management. Steroid injection into the zygapophyseal joint may also be performed but in cases of refractory patient to conservative management, necrolysis of the medial branch may be proposed. The first step in this interventional management is to perform an injection block and select the accurate level based on both physical examination and imaging. Indeed, FJ level can be deducted by comparing the patient's pain to FJ pain referral maps, and MRI or SPECT CT imaging data, which may help to identify painful joints.

Blocks

Because no clinical features or diagnostic imaging studies can determine whether a FJ is painful or not, controlled blocks are the only reliable tool in the diagnosis of FJ pain as a cause of LBP [6].

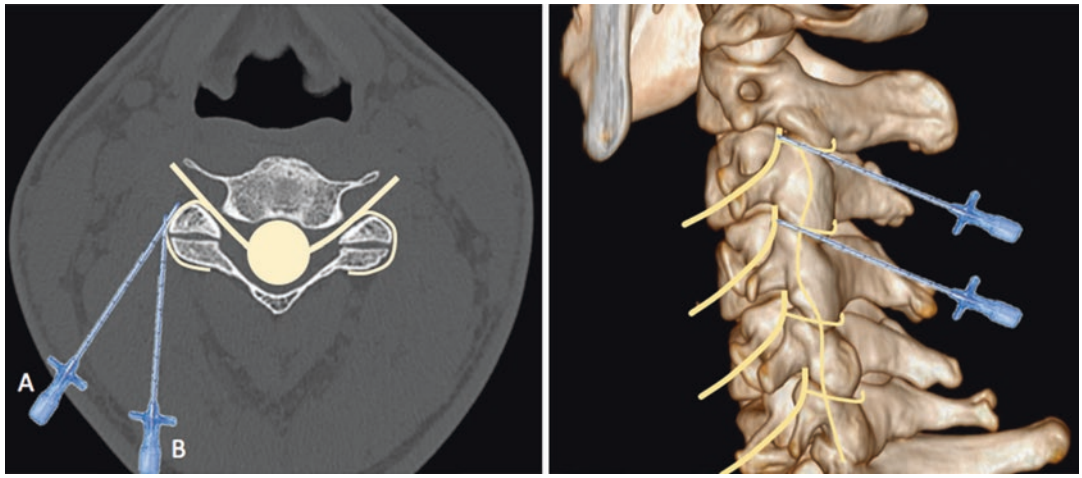

Fig. 6.2 Anatomical description of the facet innervation and needle placement according to the oblique (A) or parasagittal (B) needle placement

Diagnostic blocks of nervous structures that are suspected to generate pain can be performed to evaluate the role of the target structure in the painful syndrome. However, several debates exist on the technique and the definition of the performed block.

Procedure can be done under fluoroscopic or CT guidance. Our preference is to use CT guidance with medial branch block. The patient is placed in prone position. An initial, non-enhanced planning CT is performed from the subsequent level in order to determine target and the safest needle pathways. Tip of the needle should be placed at the lateral aspect of the facet at the level of the foramen (Fig. 6.3). A mixture of fast and slow acting anaesthetic (1 ml mixture of lidocaïne hydrochloride 1%, and of ropivacaïne chlorhydrate 2 mg/ml). Patients are then asked to report pain relief in the following 12 h, both with by self-reported improvement (percentage of pain decrease) and VAS score. Pain should significantly frop after the block

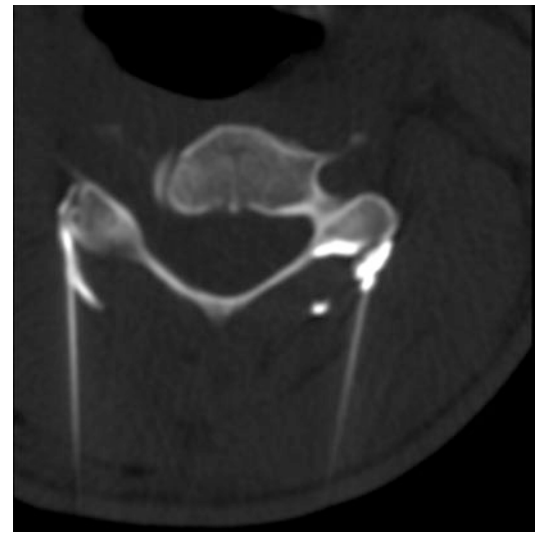

Fig. 6.3 Example of a block performed under CT guidance at the lateral aspect of the C4–5 facets

Physical Neurolysis

A: Principle

RFA consists in the placement of electrodes under imaging guidance, delivering a sinusoidal current (400–500 kHz). Regions crossed by the current undergo an ionic agitation which leads, through particle friction, to tissue heating. The sought purpose is to expose nerve cells to a temperature >45 °C causing an irreversible cellular denaturation. A wide range of temperature (70–90 °C) has been reported in the literature with good results. Another possibility is the use of pulsed RF (application of RF energy with pulsed time cycles at temperatures not exceeding 42 °C).

The rationale for the use of pulsed RF is to avoid any potential inadvertent damage to adjacent nerve roots as well as possible secondary spinal instability due to muscle denervation. However, the use of this technique appears to be less effective in the long term. Therefore pulsed RF does not appear as a substitute for conventional thermal lumbar medial branch neurotomy.

B: Technique

Lord et al. underlined the importance of patient selection and the use of a properly performed technique [3]. Because of the dual nerve supply to a zygapohyseal joint, radiofrequency neurolysis may be performed at the supposed pain level and the level above, and Bogduck suggested to perform a double pass at the same level, para sagittal and oblique, in order to enhance the chances of success [3, 7] (Fig. 6.2). Moreover, operators should not rely on single placement of the electrode, and multiple placements may be required in order to cover all possible variations of the nerve.

The needle insertion should be very carefully performed and accurate needle placement is the rule. CT helps with accuracy and once needles are inserted (Fig. 6.4), sensitive stimulation is performed at a frequency of 50–100 Hz which should reproduce a tingling sensation in the painful area. Motor stimulation (frequency 2–5 Hz) is then performed and should not provoke arm muscle contraction. Caution is necessary in case of sedation as stimulation threshold are biased by the neuroleptanalgesia. In case of RFA 1–3 cycles (90 s) between 70 and 90 °C may be performed, with slight needle repositioning between each cycles. Local anesthesia may be needed in case of pain during the heating process. A steroid injection may be added to avoid secondary neuritis.

C: Adverse Events

Possible reported complications secondary to facet neurolysis include: neuritis (increased pain), radicular damage, muscle atrophy in case of frequent repeat treatments. However, cervical facet RFA remains a very safe and effective treatment.

D: Results

The available data render the evidence for long-term improvement with cervical radiofrequency neurotomy as a Level II with moderate strength of recommendation, when perormed after the diagnosis of cervical facet joint pain [4]. The average pain release in higher than 75% and 12 months is usually the average pain improvement reported period.

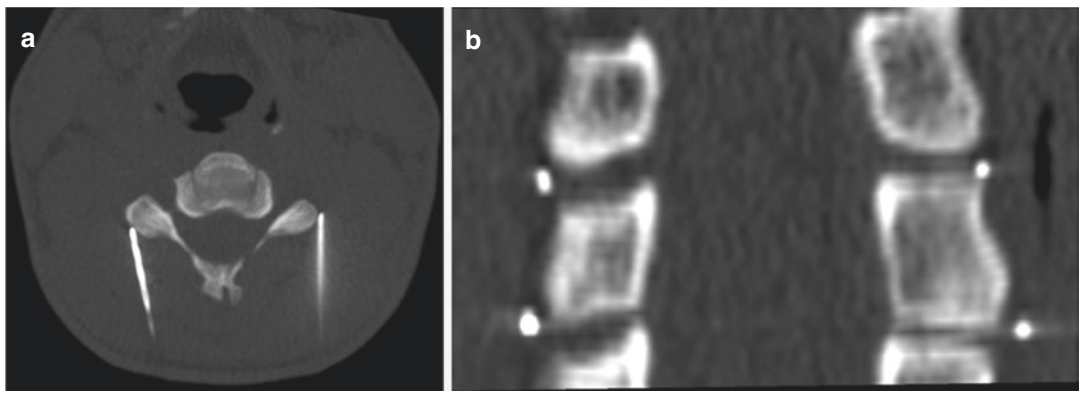

Fig. 6.4 Example of a cervical C3–4 and C4–5 RFA in a young 32 years patient with neck pain following trauma, and two positive block tests. Needle were placed at the lateral aspect of the facets at each level and three cycles at 70–75 and 80 °C were performed at each level. Pain improvement was obtained for 2 years following procedure. (**a**) axial view; (**b**) coronal reconstruction

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7 Biomechanical Approach to Stability of Intersomatic Implants in Cervical Spine

Stefan Freudiger

Introduction

It is being explained, that for compatible strain at an implant-bone interface not only the modulus of elasticity of the implant material is of importance, but also the properties of its geometrical shape. For axial stiffness it is the cross section area and for bending stiffness the cross section area moment of inertia. Furthermore, for an interface in axial compression, also lateral strain ($\varepsilon_q = \nu \times \varepsilon$) might need to be taken into consideration.

With a conceptual model of a head and its cervical spinal column, it is being shown, that the loads on a cervical motion segment in the activities of daily living do not seem to be critical in view of the vertebra's strength. While subsidence is still a predominant complication, other reasons than statically overload need to be looked for. One reason might be shear not transferred by the facet joints due to lost balance or a tilted implant with stress concentration or simply not enough immobilization during bone remodeling.

Natural Vertebral Endplate

The natural vertebral endplate is an extraordinary structure. It incorporates a thin shell made of compact bone over an elastic foundation made of cancellous bone [1, 2] (Fig. 7.1). The shell is connected to the walls of the vertebral body and together with the elastic foundation, is capable to carry high compressive loads and impacts [3]. These compressive loads are optimally distributed, as these loads are applied through the nucleus pulposus with hydrostatic properties (i.e. uniform pressure load). Across the vertebral body the loads are further transferred by the trabeculae, the scaffold of the cancellous bone.

Though the understanding of the endplate's function is still considered controversial [4–7]. From a biomechanical point of view however, the function of the endplate can be explained. According to Mosekilde [8] the endplate's bone should be considered as condensed trabecular

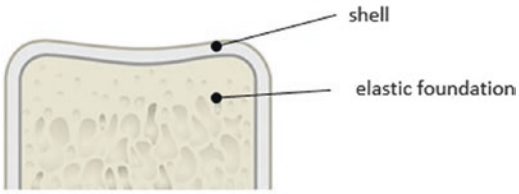

Fig. 7.1 Vertebral plateau

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Fig. 7.2 Truck on road

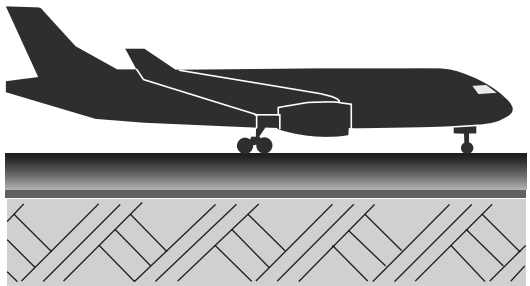

Fig. 7.3 Aircraft on runway

bone rather than cortical bone for histological reasons. The combination of the endplate as a shell and the underlying spongious bone as an elastic foundation can be compared with a road (Fig. 7.2) or a runway (Fig. 7.3), which also are combinations of top layers with substructures. Combined, they are capable to carry considerable high loads, such as trucks and aircrafts, respectively. But at their own, none of them could carry such loads. Many searchers suggest, that endplates should not be sacrificed for the accommodation of implants due to loss of structural integrity. A minimal opening of the endplate is although considered necessary for reasons of vascular supply to any bony implants. This leads to a trade-off between maintaining maximum mechanical strength and necessary biological interaction [4, 5, 9, 10].

Since from a mechanical point of view, the endplate is to be considered a shell, where numerical analysis of such shells could not reliably be carried out with linear finite-element methods as often done. Since a basic property of a shell is its deflection and since deflection results in altered loading patterns (ref. theory of second order) geometrical non-linear finite element code is required to properly consider redistribution of reactions (e.g. tension in sagging rope rather than bending in flat plate). According to Jackman et al. [7] an endplate can anyhow deflect up to 0.9 ± 0.6 mm.

Vagueness exists over the load sharing between the endplate and the cancellous bone underneath. Literature data suggests that the endplate contributes 33% [9], 45–75% [11], 44–52% [12] and 50% [6] to the vertebra compressive load bearing capacity.

Illustration of Endplate's Sensitivity

To illustrate the sensitive behavior of a vertebral endplate, an own experiment is mentioned. At the time of laser nucleotomies, ideas came up to refill the nucleus voids with filling material to prevent a loss of disc height. One idea consisted in small balls (diameter 6 mm made of Polycarbonateurethane) (Fig. 7.4).

Human vertebrae were excised from lumbar vertebral columns (e.g. L4, male, 30 years) with the cranial endplate left perfectly intact (including the cartilaginous layer) (Fig. 7.5). The natural annulus was replaced by a synthetic ring (micro-

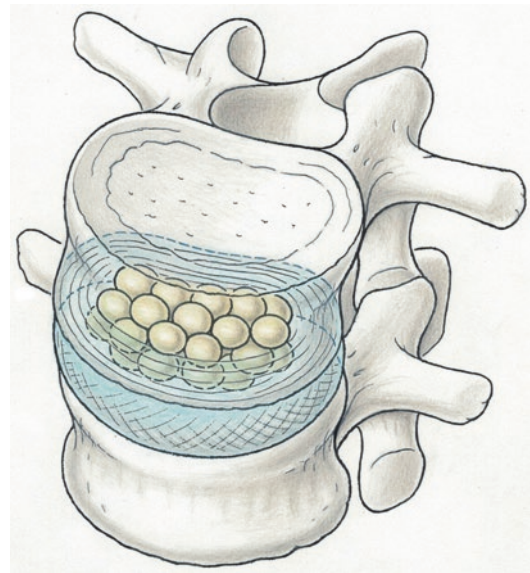

Fig. 7.4 Nucleoplasty

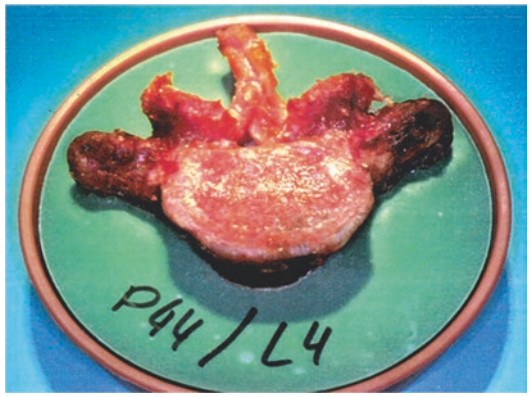

Fig. 7.5 Specimen potted in cup

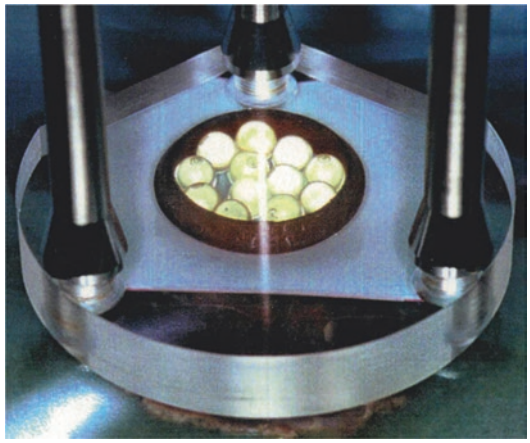

Fig. 7.6 Transparent pressure plate

cellular polyurethane) in order to carry the hoop stress and to keep the balls in place.

A thin protective film was laid over the vertebra and a pressure sensitive film (Fuji prescale) underneath the balls. For applying the load on the set-up, a transparent pressure plate (polycarbonate) was used in order to have direct insight in the dynamism of the nucleus replacement (Fig. 7.6). The load applied was 3375 N (75% of 4500 N on the nucleus in elderly persons) [13] using a universal testing machine (Zwick 1456). The prescale film yielded a total area of contact of approx. 150 mm^2 and the pressure taken from the Fuji pressure charts yielded approx. 22.5 MPa (Fig. 7.7).

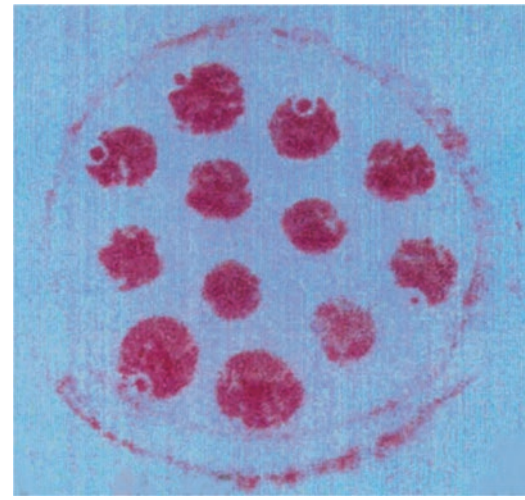

Fig. 7.7 Imprints in pressure film

Interestingly, this pressure provoked local damages to the endplate. Best remedy consisted in leaving residual nucleus material in the cavities between the balls, which restored normal unified nucleus pressure on the endplate, preventing any damage to the endplate.

Natural Vertebral Disc

The characteristic of the vertebral disc is the compressibility and extendibility of the annulus fibrosus due to the diagonal arrangement of its fibers. Consequently the annulus fibrosus is capable to transfer rotational loads while allowing lateral bending as well as flexion and extension movements. Simultaneously it acts as the seal of the nucleus pulposus providing uniform pressure at arbitrary inclination angles (Fig. 7.8).

Surgical Treatments

Whenever a natural discs has undergone severe degeneration with loss of normal performance it will normally be removed partially or entirely. As replacement two procedures are generally used. One procedure intends to preserve motion

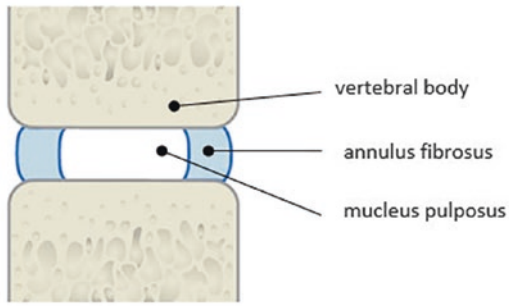

Fig. 7.8 Vertebral disc

whereas the other procedure intends to achieve the fusion with the adjacent vertebrae [14, 15].

(a) Implantation of a prosthetic disc

Two types of disc prostheses are distinguished. First, disc prostheses which move along a geometrical hard sliding core (Fig. 7.9) (also called "ball and socket") mostly made of *UHMWPE* (ultra high molecular weight polyethylene) and two endplates made of titanium alloy. One endplate is sliding over the other imposing an ICR (instantaneous center of rotation) when the adjacent vertebrae undergoes flexion and extension movements. This ICR is often far from the natural ICR. This concept is further subject to wear of the polyethylene core against the metal endplates. This concept does not provide axial elasticity along the vertebral column axis, since the sliding core is too stiff, in comparison with the natural intervertebral disc. Second, disc prostheses which move as a result of the elasticity of an elastomeric core (Fig. 7.10) (also called "silent bloc"). The materials used shall mimic a vertebral disc and have therefore a pronounced elasticity. The mostly used material is the PCU (polycarbonateurethane) (e.g. *Bionate*®) possibly blended with silicone (e.g. *Carbosil*®). The elastomer core does not impose any cinematic constraints. It allows motion according to its elasticity in the specific loading axis. The elastomer core is able to absorb axial loads and to provide axial elasticity along the vertebral column axis.

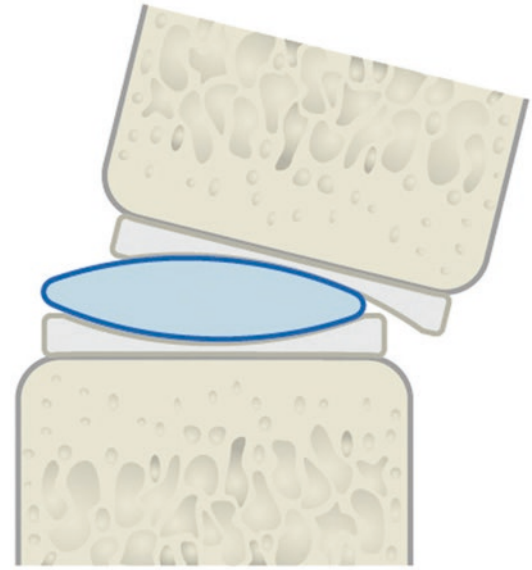

Fig. 7.9 Prosthetic disc with sliding core

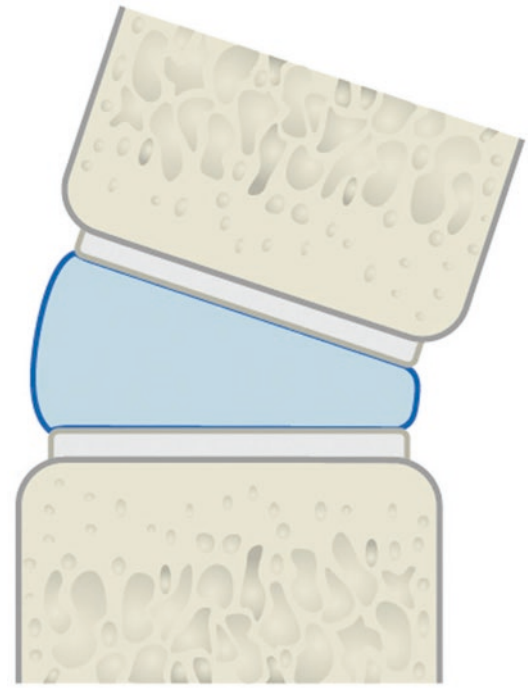

Fig. 7.10 Prosthetic disc with elastomer core

(b) Fusion of the segment

The fusion of two adjacent vertebral bodies is often assisted by the insertion of a body to maintain height. Such body can be autolo-

gous bone, a cage or a combination of both (Fig. 7.11).

Great care must be given to the load transfer from the implant to the vertebra. As soon as the natural endplate is resected or otherwise damaged, the maximum loading capacity may be reduced down to its half. It is generally recommended, that implants, whether disc prostheses or cages, should cover as much surface of the vertebra as possible [16–18]. If the contact area would be lower, strong bone adherence with consecutive bone remodeling [19] would be required.

Cages

A basic feature of an implant material is the stiffness and a basic characteristic of the stiffness is the elastic modulus (also called Young's modulus) (denoted as E). But when comparing stiffness from one body to another, the modulus of elasticity is only half of the truth. For comparing stiffness, beside the material constant, also a geometrical parameter needs to be considered, which depends on the type of loading. For axial load (Fig. 7.12) the geometrical parameter is the cross section area (denoted as A) and for bending (Fig. 7.13) the cross section area moment of inertia (denoted as I). Consequently the axial stiffness is given by $E \times A$ and the bending stiffness is given by $E \times I$.

Typical materials used for cages are *PEEK* (polyetherehterketone), *Titanium*, *carbon fiber composites*, *PMMA* (polymethylmetacrylate) and *TCP* (tricalciumphosphate) as a filler material.

The cage typically has a frontal contact with the bone and is subject to compression loads. As a consequence the cage is principally exposed to lateral strain (Fig. 7.14), which in the worst circumstances may produce micromotion against the bone, if the interface shear characteristics do not comply with each other. Furthermore, the vertebral endplate would only be loaded on a limited surface, where the endplate itself is being surrounded by compact bone along its periphery; both limiting lateral strain.

Lateral strain (denoted by ε_q) is given by the longitudinal strain (denoted by ε) multiplied with Poisson's ratio (denoted by ν) [3] where the longitudinal strain ε equals the stress (which is the

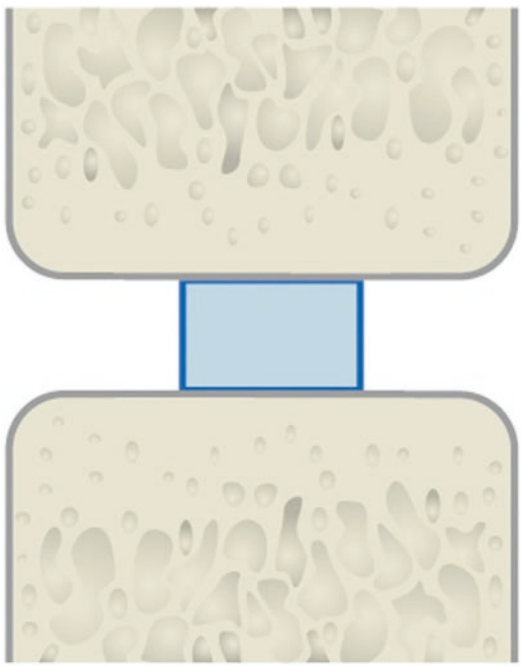

Fig. 7.11 Intersomatic body

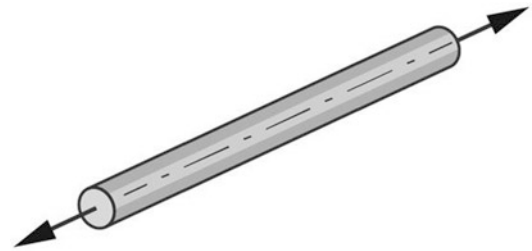

Fig. 7.12 Axial load

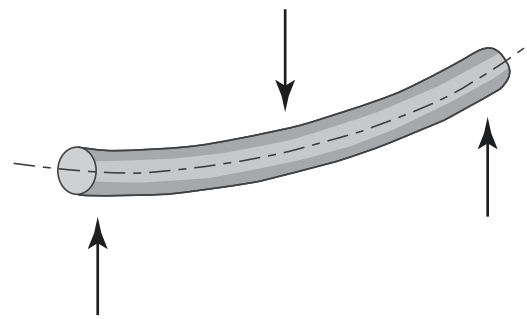

Fig. 7.13 Bending load

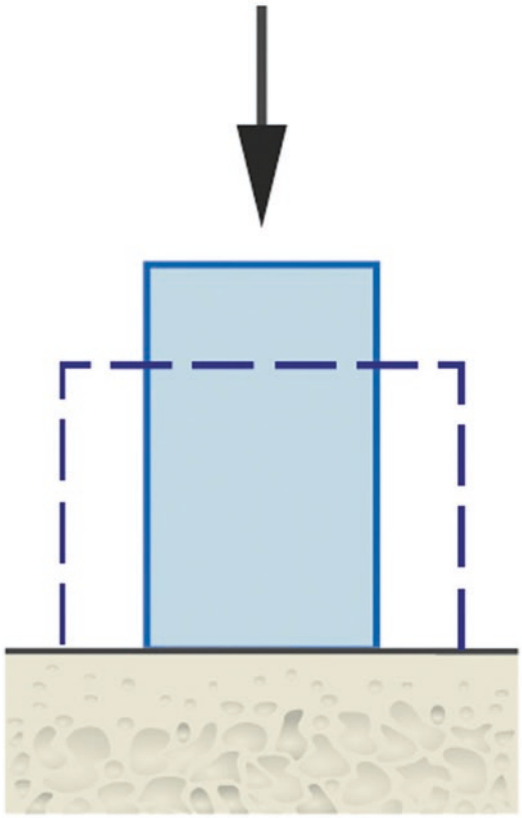

Fig. 7.14 Lateral strain

force divided by the surface, denoted by σ) divided by the modulus of elasticity (E). If the force and the surface are the same for the cage and the bone, the lateral strain becomes proportional to the quotient of the Poisson's ratio and the modulus of elasticity or $\varepsilon_q \approx \nu/E$.

Cages must cover a sufficiently large area of the (resected) vertebral body, since the strength contribution of the natural shell is being sacrificed. Cages need to achieve a good bone adherence for successfully transmit the expected loads. If the cage surface is not sufficiently osseoinductive it will need to undergo a surface treatment with an adequate coating.

Basic Engineering Approach

In order to make a rough stress analysis, a conceptual model is proposed in Fig. 7.15, representing the head's flexion in the course of activities of daily living (ADL). The weight of the head is derived from literature where absolute numbers of this order of magnitude or percentages of body weights are given [21–23]. The lever arm of the head's center of gravity as well as the inclination of an exemplary C5 vertebra are assumed. The so found bending moment of 3.7 Nm (Fig. 7.16) is in the range of the findings of Harms-Ringdahl et al. [23] who found 4.3 Nm at the level of C7/Th1 when the head as well as the cervical spinal column are both flexed. Non equidirectional movements of the spine and the head are called "paradoxical motion" by White and Panjabi [24].

A schematic cross section of the neck's structures is taken from anatomy atlases and is given in Fig. 7.17 with an estimated lever arm from the disc center to the center of the cumulative posterior muscles net cross sections of 40 mm. The resolution of this load arrangement yields a total compressive load perpendicular to the vertebral plateau of 131 N and a shear load parallel to the vertebral plateau of 32 N (Fig. 7.18). While these loads represent a 1 g (gravity) case, higher loads in ADL can be achieved during walking. According to Hwang et al. [25] and Kavanagh et al. [26] the head may experience an accelera-

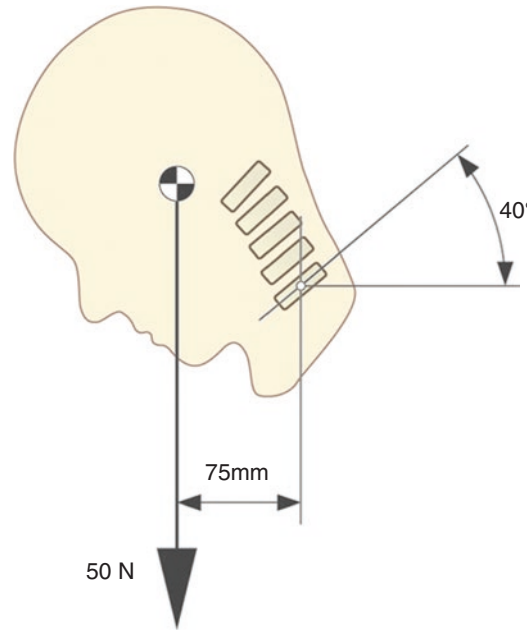

Fig. 7.15 Conceptual model head and spine

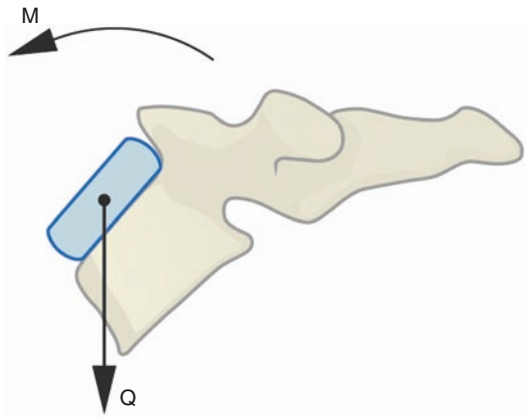

Fig. 7.16 Overall load on vertebra

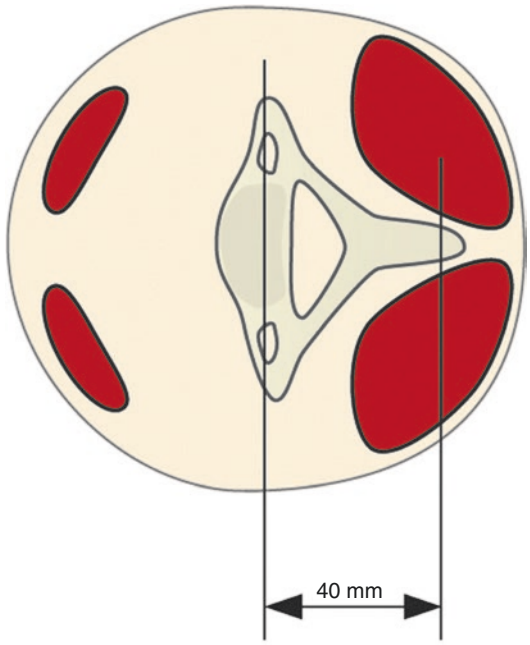

Fig. 7.17 Conceptual model neck cross section

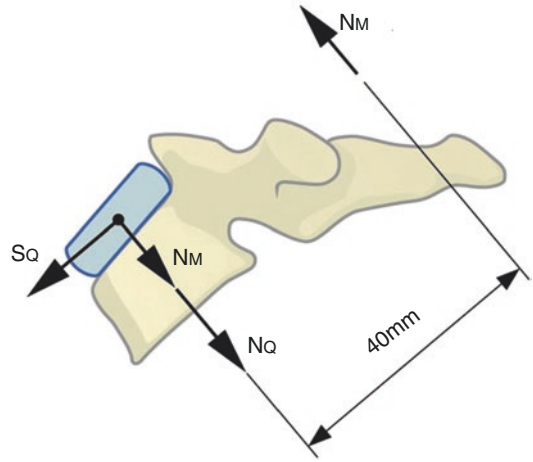

Fig. 7.18 Load breakdown on vertebra. N_M = 3.7/0.04= 93 N; $N_Q = 50 \times \cos 40° = 38$ N; $S_Q = 50 \times \sin 40° = 32$ N; $N = N_M + N_Q = 131$ N

tion of approx. 1.4 g yielding 183 N normal and 45 N shear load.

This normal load is surprisingly small, since it would lead to rather low compressive stress. Assuming an intersomatic implant with a contact surface of as few as 100 mm^2 only (unrealistic worst case), 1.83 MPa would result. This stress is far below most published strength data for a complete vertebra as well as for a vertebra with a resected bony endplate. Literature data range from 6.3 MPa up to 56 MPa [10, 12, 18, 27] for elderly cervical vertebrae. These high variations may be due to following reasons: diameter of testing indenter in respect to the bone's morphology (e.g. trabecular spacing), speed of indentation, definition of failure criteria, location on the vertebral plateau, etc. Consensus exists however as to the location of the strongest parts on the vertebral plateau which are more lateral and posteriorly than anteriorly and centrally [4, 9, 12, 27–29].

Neglected in this conceptual model is although any permanent muscle tonus, which anyway should rather be low in view of the natural concept of energy minimization. Furthermore it is assumed that antagonist muscles would not simultaneously contract according to the principle of reciprocal innervation. Moroney et al. [22] have also addressed this assumption.

Complication Subsidence

Despite the fact, that a worst case maneuver of ADL is not critical to a vertebrae even, if its loads are transferred through an implant with a mini-

mal contact area, subsidence is still the most frequent complication after inserting implants between vertebrae [4, 5, 9, 10, 12, 16–18, 21, 27, 29]. Understanding and explaining this outcome represents a real challenge to biomechanical and clinical searchers.

Subsidence needs to be more precisely documented. The major question is whether it is a true subsidence with sinking only at right angle to the vertebral plateau while strictly maintaining the implants footprint or whether subsidence is accompanied by any transversal destroyment of bone parallel to the vertebral plateau. In addition, the zone of bone damage must be investigated, since damage may also occur below the zone of implant to bone contact [15], a mechanism which is called Hertzian pressure.

In the first case, it might have to do with a weakening of the bone during the bone remodeling phase [19]. Or adjacent vertebrae continue to incline differently with tilting the implant and modifying a uniform support to an edge support with corresponding stress concentration. A remedy could be in efficiently protecting the implant site with a brace during the remodeling time until sufficient bone ingrowth is reached. In the case of a stand-alone cage, also additional means of securing (e.g. screws, anchor, plate, etc.) may help.

In the second case, shear loads may be at the origin. Due to the pronounced forward and downward inclination of the lower cervical vertebrae, any compressive load is automatically coupled to anterior shear loads. Shear loads from one vertebra to another should basically be transferred by the facet joints, provided that after implantation the load shearing is still fully balanced. Otherwise a form- or friction fit need to be achieved, where the surface of the implant can "hook" into the bony structure or where sufficient friction can be rapidly enough built-up by implant surfaces with high bone growth stimulus, such as Titanium or Hydroxyapatite for example. Thereafter sufficient bone adherence is required to prevent incompatible strain resulting in micromotion with implant loosening.

Comparison of Materials

The considered materials are biomaterials with a proven biocompatibility which must have demonstrated compliance with the relevant international standards (e.g. ISO 10993).

For overview the mechanical properties of the materials of interest are listed in Table 7.1.

Data are order of magnitudes for reference. Especially polymer characteristics may vary with strain rate, body temperature and environment.

For illustration, the initial stiffness ($E = \sigma/\varepsilon$) of the materials of interest are plotted in Fig. 7.19. The curves are highly idealized. Other slopes using other databases are possible. The TCP curve had to undergo a coordinate transformation for comparison. For ease of illustration, tensile and compressive data are shown in the same quadrant.

However, UHMWPE, Bionate® and Carbosil® are not expected to be used in direct contact with bone. They are rather used as core material for disc prostheses.

TCP is also not expected to be used as stand-alone cage, because of its resorbable behavior. TCP is rather be used to fill voids in hollow cages to accelerate bone-ingrowth.

Table 7.1 Overview of biomaterials of interest

Material	Strength [MPa]	Mod. of elast.[a] [MPa]	Ultim. strain [%]	Poisson ratio	Lat. strain[b] [%]	Ref.	Note
Cancellous Bone	2.37(c)	352.00	1.19	0.20	0.057	[20, 30]	
PEEK	107.00(t)	2853.00	20.00	0.36	0.013	[31]	
Ti6Al4V	950.00(t)	113,800.00	14.00	0.34	0.000	[32]	
Carbon fiber	1315.00(t)	235,000.00	0.56	see note	0.000	[33]	1
Bionate® 80A	46.61(t)	8.74	531.00	0.50[c]	5.721	[34]	2
Carbosil® 80A	35.03(t)	9.70	473.00	0.50[c]	5.155	[35]	2
TCP	21.13(c)	1198.00	2.24	0.28	0.023	[36]	
PMMA	100.00(c)	2700.00	5.10	0.40	0.015	Var.	
UHMWPE	21.00(t)	770.00	350.00	0.42[c]	0.055	Var.	

[a]Secant modulus (first distinctive segment—idealized)
[b]Lateral strain with unit stress
[c]Ex: http://ocw.mit.edu/courses/materials-science-and-engineering/3-11-mechanics-of-materials-fall-1999/modules/props.pdf
(c): Measured in compression
(t): Measured in tension
Notes:
1. Mechanical properties of carbon fiber implants depend also on the orientation of the fiber in the composite and the axis of loading. Exact fiber orientations within spinal cages are not disclosed. Data shown are averages of ref. [13]
2. Bionate® and Carbosil® are also available in other grades. Exact grades used in the prosthetic discs are not disclosed
3. Bionate® and Carbosil® are trademarks of DSM

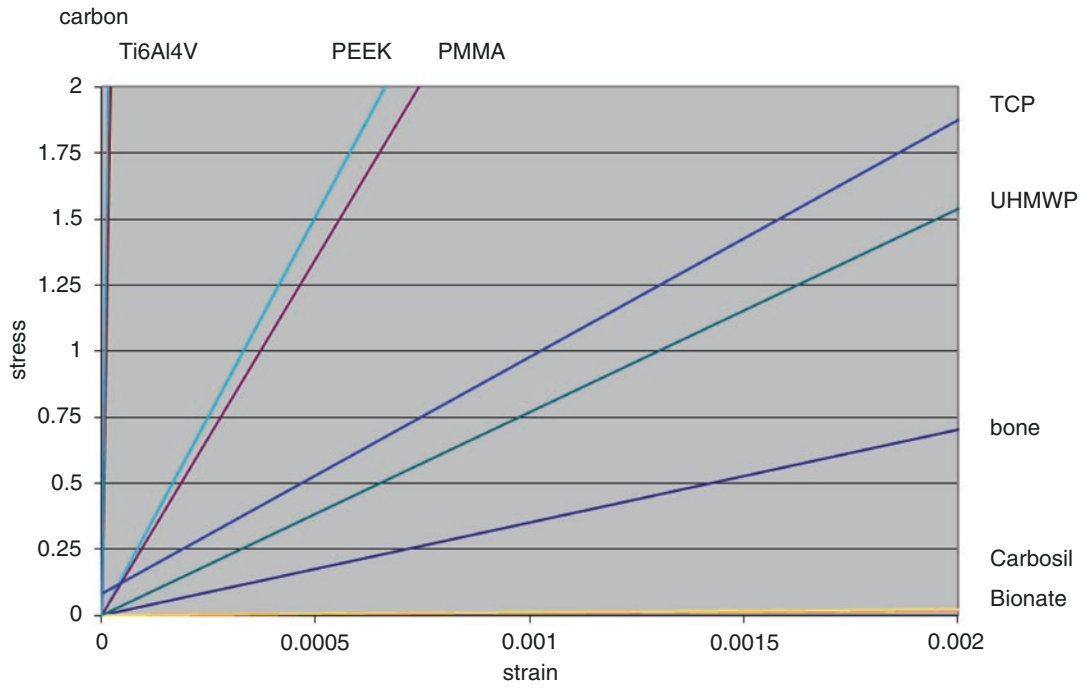

Fig. 7.19 Stress/strain plot of specific biomaterials

Conclusion

It is generally assumed that the predominant complication of subsidence has to do with the contact surface of the implant with its resulting pressure on the vertebra and the preparation of the implant's seat. Particular attention is given to the preparation of the vertebral plateau where minimal resection of the bony endplate is generally recommended.

A rough stress analysis with a flexed head in the activities of daily living reveals, that the stress on the vertebra is rather low, compared to the strength of the vertebral plateau with or without its bony endplate. Consequently other mechanisms leading to subsidence must exist. From a mechanical point of view, they might be found in the way how shear is transferred (transversal or rotational through facet joints or implant) or the risk of tilting the implant resulting in local stress concentration. From a biological point of view, the violation of the well balanced endplate-disc-endplate system would need to be further investigated.

The reason why a natural motion segment is apparently designed for much higher loads, than those of activities of daily living, can probably be found in extraordinary high margins of safety or in a reasonable high protection from accidental loads.

Finally, another mechanism of Mother Nature seems worth to be mentioned, which is the oncotic pressure, managing the water content in the nucleus pulposus. Where antagonist muscle contraction with elevated loading of a motion segment is rather improbable, keeping pretension on motion segments passive structures such as the annulus fibrosus or the various ligaments, appears to be much more appropriate, in order to steadily provide adequate stability. Another mechanism which although would be sacrificed, when removing a degenerated disc.

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Role of Materials in Cervical Spine Fusion

8

Carlo Doria, Francesco Muresu, Fabio Milia, and Andrea Baioni

Introduction

Degeneration of the cervical spine is present in over 50% of middle-aged people and is the most common cause of neural dysfunction. Usually, the first approach is conservative; however, surgery is indicated for symptomatic patients who are unresponsive to conservative management [1].

Spondylosis is the most common cause of neural dysfunction in the cervical spine. The degenerative changes of ageing typically herniated disc, osteophyte formation and hypertrophied ligament may compress the spinal cord to present symptomatically as neck pain, radiculopathy, myelopathy or radiculo-myelopathy [2].

Anterior cervical corpectomy and fusion (ACCF) and anterior cervical discectomy and fusion (ACDF) are common surgical procedures for patients suffering pain and/or neurological deficits and unresponsive to conservative management [3]. When compression is limited only to the disc level, ACDF is superior to ACCF because it entails less blood loss, short hospitalization, and fewer postoperative complications. Nevertheless, when the compression is extended to the vertebral body levels, ACCF is much preferred over ACDF because it can achieve satisfactory decompression at the vertebral body levels [4–6].

However, ACDF is the gold standard for the treatment of degenerative disc disease and cervical spondylosis associated with radiculopathy or myelopathy, hitherto the ideal implant from the biological and biomechanical points of view has yet not been determined and it depends largely on the surgeon's preference and training [7–10].

Several authors, including Smith-Robinson [11], Cloward [12], Bailey and Badgley [13], and Simmons [14], have described various methods of anterior cervical fusion. These methods were developed in the 1950s and 1960s and serve as the historical foundation for modern reconstruction techniques. Robinson et al. described the use of a horseshoe shaped tricortical graft removed from the anterior iliac crest; in their technique, the bony endplates are preserved during discectomy and the tricortical graft is impacted into the disc space. Cloward described a technique using a cylindrical drill to create a round hole centered at the disc; fusion was achieved by impacting a slightly oversized cylindrical dowel of bone into the hole. Simmons et al. described the use of a keystone shaped graft for anterior cervical fusion; the keystone graft was developed to increase graft stability and provide a larger surface area of cancellous bone to enhance bony fusion. Bailey and Badgley described a method of anterior fusion of the cervical spine using a strut of iliac crest bone placed into a trough prepared in the cervical vertebra.

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The success of these procedures relied on a thorough decompression and development of a solid osseous fusion [15, 16]. The advantages of fusion include: maintaining cervical lordosis, achieving indirect decompression through enlarging the diameter of intervertebral foramen, stabilizing surgical segment, and preventing the progression of posterior lesions [17–19].

For single level discectomy with autogenous bone fusion, anterior cervical discectomy and fusion can achieve a 92–100% fusion rate [20] and 70–90% neurologic and symptomatic improvement [21, 22]. However, in multilevel discectomies or somatectomies, the success rate declines as the number of levels increase [23]. In cervical degenerative diseases, the literature supports a consistent rate of 10–12% non-fusion (pseudoarthrosis) for single level anterior discectomy and autogenous bone fusion, 20–27% for 2-level, and approximately 30–56% for 3-level fusions [24, 25]. Non-fusion accounts for 80% of spinal surgery failures [26]. Graft collapse with autogenous bone is also reported in 20–30% of multilevel fusion [27]. Even with solid fusion, kyphosis of spinal curve often develops in multilevel discectomies with autogenous iliac crest graft fusion [28, 29].

Some surgeons prefer to add an anterior plate in fusion procedures to decrease the micromovement of the cervical spine, increase stability, enhance the fusion rate and correct spinal curve to physiologic lordosis (Fig. 8.1a, b) [30]. Nevertheless, the addition of a plate is not without side effects: despite the profile of current anterior plates being thinner than that of earlier designs, plate complication rate varied from 2.2 to 24% and included screw pullout and breakage [31, 32], injury of laryngeal nerve [33], injury of

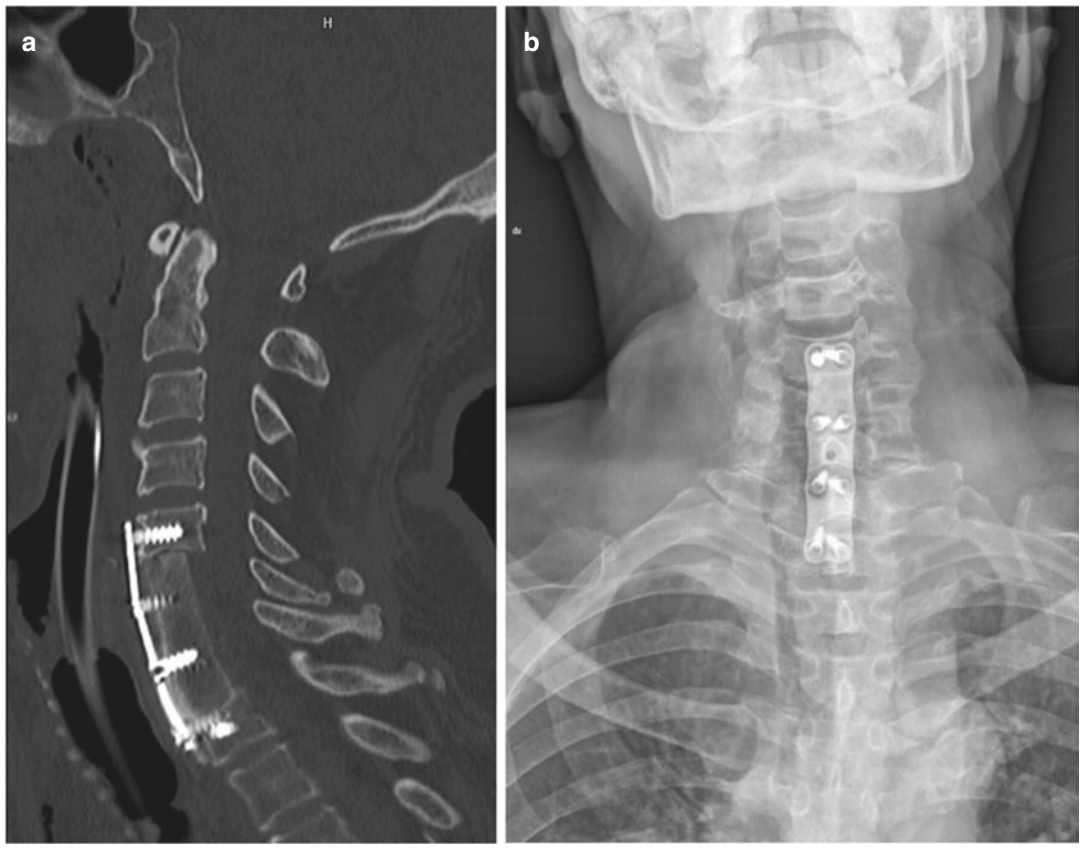

Fig. 8.1 CT scan sagittal view showing C6–C7 somatectomies and tri-cortical iliac strut graft and anterior plating (**a**). Postoperative posteroanterior X-ray view of the same patient (**b**)

esophagus, injury of spinal cord or root, injury of vertebral artery, wound infection [34, 35], stress-shielding and adjacent-level affection [36, 37]. In the early postoperative period, 2–67% of the patients may complain of dysphagia [38]. During the first 3 months after surgery most of these symptoms disappear spontaneously, however complete recovery does not occur in all patients and not all patients recover completely from swallowing problems [39].

Generally, complications reported for ACDF are adjacent segment disease (8.1% rate, range 0.9–52.2%), dysphagia (5.3% rate, range 0.2–87.5%), C5 palsy (3.0% rate, range 0.1–7.7%), graft or hardware failure (2.1% rate, range 0–50.0%), pseudarthrosis (2.0% rate, range 0–55.0%), recurrent laryngeal nerve palsy (1.3% rate, range 0.1–60.9%), infection (1.2% rate, range 0–16.7%), hematoma (1.0% rate, range 0–12.5%), cerebrospinal fluid leak (0.5% rate, range 0.03–7.7%), new/worsened neuro deficit (0.5% rate, range 0–25.7%), Horner syndrome (0.4% rate, range 0.1–2.5%), vertebral artery injury (0.4% rate, range 0.2–2.2%), esophageal perforation (0.2% rate, range 0–0.46%) [40].

To address these complications, stand-alone interbody cages were designed to provide stability and facilitate fusion between cervical vertebrae without necessitating the use of an anterior plate [3, 41]. This technique, however, has its own complications, such as cage subsidence, cervical dislocation, and cervical kyphosis [17]. Past studies have compared the two techniques, but a consensus has not yet been reached about the superiority of one technique over the other. To date, two meta-analyses have been published comparing the use of a zero-profile device versus a cage and plate technique in ACDF [42, 43]. Cheung et al. [44] in their systematic review and meta-analysis demonstrated that ACDF with a cage-only technique was associated with decreased incidence of postoperative dysphagia, intraoperative blood loss, and ASD compared with a conventional cage-plate technique. However, a cage-only technique was found to have increased rates of cage subsidence, decreased postoperative disc height, and less restoration of cervical lordosis.

Bone graft in anterior cervical surgery is used to achieve several goals. Structural grafts are used to reconstruct anterior column defects and restore the load-bearing capacity of the cervical spine. Bone grafts may be shaped to restore the normal lordotic posture of the cervical segment. Bone graft also performs a biologic role in promoting a bony fusion, which spans the spinal defect and achieves long-term stability. To be successful, bone grafts must be able to successfully fulfill the dual role of providing structural support and achieving a solid fusion [45].

Various materials have been used for interbody grafts in anterior cervical fusion [46]. To supplement the bone graft, several fusion devices have been developed over the past decades for stand-alone use or in conjunction with anterior or posterior instrumentation (Fig. 8.2a, b).

Cervical Spine Devices

In the past decades, autologous tricortical iliac bone graft had always been the preferred bone grafting material. Although this demonstrates high fusion rate, because the potential donor-site complications of autografts [47, 48] and low bony fusion rate and graft collapse of allografts [24], surgeons focus their attention on other graft materials [42, 49].

In 1988, a cage fusion technology was proposed by Bagby et al. [50] and since then stand-alone cage designs, with or without additional fixation, have become the mainstay of ACDF, achieving excellent safety, primary stability and long-term fusion without the limitations and morbidity associated with graft options. Cage interbody implants have improved biomechanical properties, designs having improved year by year with to maximization of biocompatibility and osseointegration [51]. The basic design of cage implants is a small, hollow implant featuring lateral, upper or lower windows or both to a central cavity filled with either autologous bone,

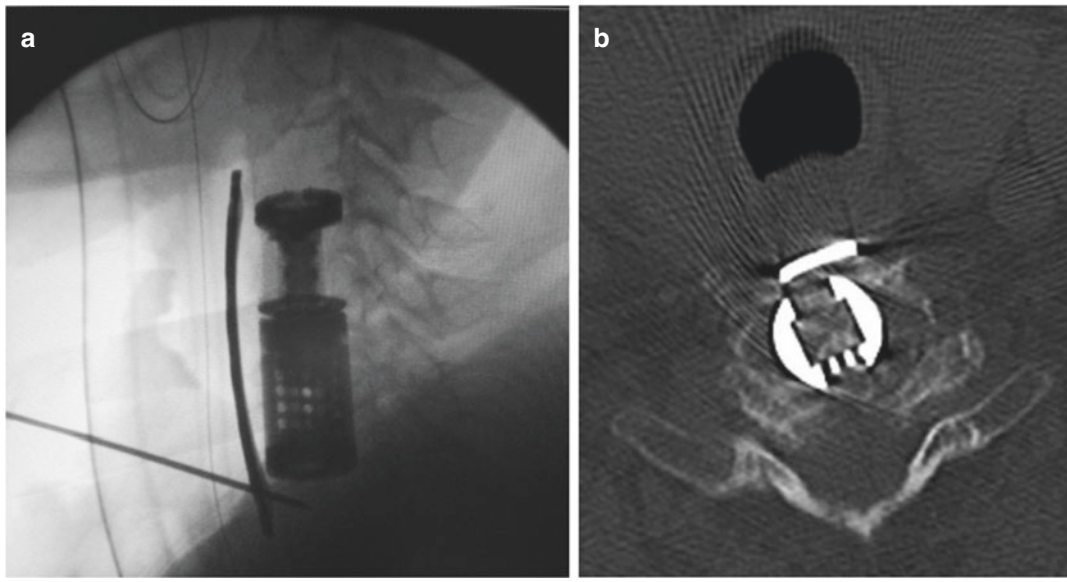

Fig. 8.2 Intraoperative X-ray image showing anterior plating after multilevel somatectomies and positioning of expandable vertebral bodies substitute (**a**). CT scan axial view showing mature bony trabeculae inside the expandable device of the same patient (**b**)

allograft bone or osteoinductive materials [52]. Historically, cage designs varied, both threaded and non-threaded designs being available. Since their introduction, optimization of ACDF procedures has been achieved by research in broad fields encompassing ideal shape, dimensions, materials and enhancement with biological growth factors.

An ideal cage design would restore healthy alignment and disc height and achieve immediate post-operative stability, high-fusion rates and low complication rates. Historically, three main materials have been utilized in the creation of cervical cages: Titanium (Ti) and its alloys, polyetheretherketone (PEEK), carbon fiber and carbon fiber-PEEK [53]. A lot of clinical research and biomechanical testing exhibited excellent performance and effectiveness; however, for each device, there are inherent deficiencies of raw materials [54, 55].

The objective of these spinal devices is to immobilize the unstable degenerated motion segment so that bony fusion can occur. Currently three types of spinal fusion devices are available: horizontal cylinders, vertical rings and open box cages (Fig. 8.3).

Fig. 8.3 Intraoperative picture showing expandable vertebral bodies substitute inserted into the corpectomy defects

Carbon Fiber Implants

Carbon Fiber Cages were introduced in the early 1990. In their study, Brantingan et al. [56] demonstrated that carbon is preferable to titanium, first because it is radiolucent and, second because it also does not induce any kind of bone corrosion

or inflammatory reaction [57, 58]. Moreover, the advantages offered by the high elasticity of carbon fiber implants, almost equal to that of cortical bone, are the redistribution of load-sharing to the bone graft inside the implant, thus stimulating bone formation improving the quality of fusion and reducing stress on the adjacent vertebral level. Potential drawbacks include fracture as a standalone device without anterior plating or a reactive inflammatory response to carbon [59].

Several studies have investigated the feasibility of using carbon fiber cages in the cervical spine with autograft, allograft and hydroxyapatite graft material. Few randomized studies that compare carbon fiber cages with a standard procedure exist [60]. Preliminary experience with cervical carbon fiber cages reported by Brooke et al. [61] reported improvement in 14 of 17 patients with neck pain and bony fusion in all 19 reviewed cases. Agrillo et al. [62] implanted 57 cages packed with coralline hydroxyapatite and reported no implant-related complications and complete fusion in all patients at 12 months. Tancredi et al. [63] also reported 119 carbon fiber cages packed with autograft, allograft or hydroxyapatite. All scans after 6 months demonstrated fusion. To avoid donor site complications altogether, empty carbon fiber osteoconductive polymer cages were placed by Payer et al. [64], who reported segmental stability in all 25 patients and bone fusion in 24. Hacker et al. [65] reported nearly 100% fusion rates with threaded carbon fiber cages and autograft versus 90% for non-instrumented bone graft alone. Salame et al. [66] reported 98% fusion in 100 patients with the interbody fusion carbon cage. However, these fusion results differ from the fusion results of a trial reporting only 62% fusion for carbon fiber cages and 86% for the Cloward procedure with mean 36-month follow-up [67]. The authors argue that the reason for this discrepancy is based on the criteria by which fusion is determined.

In the study of Marotta et al. [68] that the use of carbon fiber cages containing hydroxyapatite is apparently a safe procedure with a favorable clinical and radiological outcome. In this study, a good fusion rate (87%) was achieved in accordance with the literature using carbon fiber cages while the non-fusion rate was 13%. The study is the first one to deal with ACDF employing carbon fiber cages with such a long follow-up (77 months, range 54–90 months) and the only one to evaluate the rate of interbody fusion using CT scan.

Cawley et al. [69] demonstrated a fusion rate of 92.8%. Loosening or breakage of screws occurred in 11 cases, including two with pseudarthrosis.

Their experience with carbon fiber cages suggests that these devices represent a valid option for restoring the intervertebral disc space and promoting arthrodesis in cervical disc surgery while their elastic properties minimize the risk of kyphosis, subsidence, and adjacent level disease [70].

Polyetheretherketone (PEEK)

PEEK is a semi-crystalline polyaromatic linear polymer having a good combination of strength, stiffness, toughness and environmental resistance. PEEK cages were introduced in the 1990s by AcroMed as an alternative to titanium cages; they are biologically inert and have high versatility and out-standing mechanical properties, including high strength in all directional planes, elasticity close to that of bone, impact and fatigue resistance. In addition, PEEK is radiolucent, allowing a better radiographic assessment of bone fusion than titanium; the position of the cage can be assessed by radiopaque lines incorporated within the cage. PEEK cages are MRI and CT compatible and cause no relevant artifacts that would reduce the clarity of imaging. Moreover, PEEK cages do not induce a corrosive reaction to contiguous vertebral bodies and show excellent properties at pull-out and mechanical compression tests [71].

The major drawback of PEEK is that it is bioinert and limits host bone integration [72]. Various strategies have been proposed to improve the biologic integration of PEEK, including augmenting PEEK devices with graft extenders, such as demineralized bone matrix or cellular products, as well as modifications to the PEEK device

[73, 74]. Proposed modifications include surface enhancements, such as increased surface porosity or titanium coating, and impregnation of PEEK with bioactive materials such as hydroxyapatite [75]. The effects of these modifications on fusion success and clinical outcomes are unclear.

A majority of studies have reported improved fusion rates, lower subsidence rates and radiolucency with PEEK than with Ti cages [76], one long-term study by Chen et al. [77] reporting minimal differences in the early postoperative period, but better maintenance of intervertebral height, cervical lordosis and clinical outcomes by PEEK cages over a 7-year follow-up.

Jain et al. [78] conducted a systematic review of the literature to compare fusion rates of structural allograft versus PEEK interbody devices in patients with cervical spine degeneration who underwent ACDF. Of the 14 studies included in their review, the overall fusion rates were 82–100% for structural allograft and 88–98% for PEEK interbody devices.

Suess et al. [79] followed a cohort of 356 patients who underwent ACDF with PEEK interbody devices without any osteopromotive fillers and without additional anterior instrumentation. Complete radiographic fusion occurred for 43% of patients at 6 months, 73% of patients at 12 months, and 83% of patients at 18 months. The authors recommended against using PEEK interbody devices alone without fillers because of delayed fusion.

Ahmed et al. [80] in their review found that filled PEEK cages was associated with high fusion and low subsidence rates compared with empty PEEK cages, as empty cages had fusion rates of 81.3–100% and subsidence rates of 0–48.3%.

The use of bone graft extenders or biologic materials in addition to PEEK cages has been reported and advocated to improve fusion success [81]. However, the reported fusion rates with materials such as hydroxyapatite are approximately 85%, which is similar to the rate achieved with structural allograft or PEEK alone [82].

Although PEEK provides good biocompatibility and strength, it is unable to bond directly to bone and to osseointegrate [83]. Modifications to PEEK designed to address the issue of osseointegration have gained popularity. These modifications include hydroxyapatite-coated PEEK, porous PEEK, titanium plasma– coated PEEK, carbon fiber–reinforced PEEK, and polyetherketone [84].

A meta-analysis including six studies comparing anterior cervical discectomy and transforaminal interbody fusion found no difference between fusion rates of PEEK cages and titanium cages but noted that there was a higher subsidence rate with the titanium cages [85]. PEEK cages can be combined with ceramics for additional osteoconductive effects and have been shown to be a suitable substitute for autograft in anterior cervical discectomy and fusion.

Future studies examining the influence of interbody devices on fusion rates should adjust for use of bone graft extender and fusion augmentation materials.

Titanium

The list of titanium benefits is lengthy; this makes it incredibly useful for several different industries, including the automotive, aerospace and architectural worlds. But because titanium resists corrosion, is biocompatible and has an innate ability to join with human bone, it has become a staple of the medical field, as well. From surgical titanium instruments to orthopedic rods, cages, mesh, pins and plates, medical titanium has truly become the fundamental material used in medicine. Titanium Ti 6Al-4V and Ti 6Al-4V ELI, alloys made of 6% Aluminum and 4% Vanadium, are the most common types of titanium used in medicine. Benefits of medical titanium are strong, lightweight, corrosion resistant, cost-efficient, non-toxic, biocompatible (non-toxic and not rejected by the body), long-lasting, non-ferromagnetic, osseointegrated (the joining of bone with artificial implant), long range availability, flexibility and elasticity rivals that of human bone. Two of the greatest benefits of titanium are its high strength-to-weight ratio and its corrosion resistance. Couple this with its non-toxic state and its ability to fight all corrosion

from bodily fluids and it's no wonder titanium has become the metal of choice within the field of medicine.

The use of titanium mesh cages (TMCs) was first introduced in 1986 [86]. Since then, TMCs have been used widely for spinal reconstruction. TMCs are fixed cylindrical devices that can be filled with autologous bone to provide structural support for the anterior column and reconstruct the natural alignment of the spine. Due to the immediate load-bearing ability of TMCs, when the vertebral body is involved, resected vertebral fragments will fill into TMCs, and if the lesion is limited to disc level, a smaller quantity of autologous bone graft from the iliac crest and other autograft bone regions will be put into TMCs instead of a structural bone graft piece.

In 2001, Kandziora et al. [87] introduced some designs of titanium cages, including screw-design titanium cages, box-design titanium cages, and cylinder titanium mesh cages. By comparing their biomechanical characteristics in a sheep model after ACDF, they suggested that cylinder-design TMCs were able to contain extension and lateral bending more effectively than cages with other designs. The traditional cylinder-design TMCs are still used widely in cervical surgery [88–90]. Besides these traditional TMCs, more kinds of TMCs were introduced to be used in degenerative cervical diseases.

Many previous studies have reported on the efficacy and safety of traditional TMCs used in treating degenerative cervical diseases [91, 92]. Although it avoids the donor-site morbidities and achieves a solid bony fusion, complications such as TMC subsidence still occur at follow-up [93]. In recent years, a new type of TMC was designed to reduce the subsidence rate of TMCs [94]. Although these new types of TMCs differ from each other, the first principle is to match the anatomy of the TMC design with the adjacent endplates and increase the contact area between them. Yu et al. [95] and Liu et al. [96] compared the radiological and clinical outcomes of new types of TMCs and traditional TMCs, showing the subsidence rate is significantly lower in new-type TMCs.

Considering the sufficient biomechanical stability of TMCs and advantages of the TMCs in avoiding donor-site complications and achieving a high fusion rate, TMCs are worth promoting for use in degenerative cervical pathologies.

Additive manufacturing enables the construction of 3-D printed porous titanium implants to potentially facilitate bony ingrowth throughout the cage instead of just surrounding the cage such as in PEEK and solid titanium implants. Arts et al. [97] compared patients receiving 3-D porous titanium cervical cages with patients receiving PEEK cages with autograft. Their study was able to demonstrate an increase rate of fusion, at earlier timepoints. In the 3-D printed titanium cages, fusion was achieved in 84% of the patients at 3 months and 89% of the patients at 6 months, over the PEEK control group in 67% and 72%, respectively. Although there is no statistical difference between the groups for fusion at 1 year, the speed of solid fusion in 3-D printed porous titanium cage is faster.

Tantalum

Tantalum is a biocompatible, relatively inert transition metal whose first reported use was as a component of surgical sutures by Burke in 1940 [98]. Since its introduction, it has successfully been used in various orthopedic fields, dentistry, hernia repair, vascular anastomoses, neural reconstruction and cranio-facial fields [99]. Porous tantalum is an open-cell structure composed of tantalum in a repeating dodecahedron pattern creating an appearance similar to cancellous bone [100]. Scaffolds of porous tantalum have been manufactured to have a small elastic modulus (3–25 GPa) [101]. Porous tantalum's elastic modulus is similar to that of cancellous bone (3.78 GPa) and cortical bone (14.64 GPa), thus reducing shielding, while having a ten-fold higher bend strength [102]. Tantalum has also been shown to have relatively high frictional characteristics, which allows it to maintain a strong initial stability against bone compared to other materials [103]. A sign of the high biocompatibility of tantalum is seen by its excellent cor-

rosion resistance [104]. This resistance is provided by a stable oxide (Ta2O5) coating the surface of the metal which is occasionally accompanied by macrophages but is associated with little to no inflammatory reaction.

One of the most appealing aspects of porous tantalum is its high porosity, with 75–80% of the material's volume composed of pores [105]. Porous implants, through their ability to allow bone, vascular and other tissue infiltration, are effective in providing stability for implants secondary to biological fixation. A recent study by Wang et al. [106] showed that osteoblasts cultured on porous tantalum samples adhered to the surface and pore walls by day 3. By week 12 the surface and pores were fully covered by interwoven bone, demonstrating that tantalum is an ideal material for adhesion and proliferation of osteoblasts as well as infiltration of nutrients.

Anecdotal reports of osteointegration of porous tantalum in human subjects has been reported in acetabular shells, femoral stems, tibial trays and patella specimens, showing variable levels of bone ingrowth [107]. One report of ingrowth in a cervical spine porous tantalum specimen explanted 7 months post-operatively showed primarily lamellar bone surrounding vascular channels in approximately 50% of the pores, with 83% of the bone having been formed de novo and no inflammatory response [108]. Additionally, porous tantalum implants have a low rate of infection [109]. These biologic properties of tantalum make it a favorable metal to utilize in spinal fusion surgery.

However, several studies reported the divergent clinical outcome and fusion rate with porous tantalum device in ACDF, which leads to contradictory views among spine surgeons.

The review of Patel et al. [110], the systematic review and meta-analysis of Wang et al. [111] and the meta-analysis of Li et al. [112] analyzed several studies.

The King et al. [113] study retrospectively looked at ten patients treated with ACCF using tantalum stand-alone cages. They found stable cervical lordosis and 100% fusion rates at 2-year follow-up.

Fusion rates were similar in both the Fernandez-Fairen studies [114, 115] between the tantalum and autograft groups (2018: 96 vs. 100%, 2008: 89.3 vs. 84.4%, respectively, neither was significantly different). The Lofgren et al. study [116] found a significant difference in fusion rates at 2-year follow-up with the tantalum group showing 69% fusion and the autograft group showing 92% fusion.

Three studies looked at tantalum stand-alone in ACDF treatment that further provide strong support for the use of tantalum in cervical spine fusion. Tomé-Bermejo et al. [117], Mastronardi et al. [118] and Papacci et al. [119] had a fusion rate between 97.7 and 100%. Mastronardi et al. also noted differences in fusion rates for smokers and non-smokers in their tantalum treated ACDF group; they saw a fusion rate of 87.8 vs. 48.9% after 6 months in their non-smokers vs. smokers, respectively. Although, both groups reach 100% at 12 months.

The studies of Kasliwal et al. [120] and Wigfield et al. [108] looked at tantalum stand-alone cages in ACDF placement in addition to autograft control and tantalum ring (filled with iliac crest autograft) groups. The most significant result from the Kasliwal study is their low fusion rate. Whereas, they found 100% fusion in their autograft group, their tantalum groups were only 38% fused at 2-year follow-up. The authors do not provide any explanation for their poor fusion rates. This sharply contrasts what was found in the Wigfield study, which had to halt study recruitment when they saw low fusion rates in the tantalum groups initially, where they found 100% fusion rate at 24-month follow-up for both tantalum groups and an 85.7% fusion rate for their control group. They attribute this late fusion to two factors. First, a study done by AO ASIF Research Institute that observed bone remodeling initially might be a temporary porosis associated with necrosis due to periosteal damage or interruption of blood supply. Once the blood supply is restored, bony ingrowth can proceed [121]. Their second reason is due to difficulties in radiographic interpretation of fusion. They state that the high radiopacity of tantalum makes it easily

visible on radiographs but makes it difficult to assess the bridging trabecular bone for assessment of fusion. A study done by Levi et al. [122] found that tantalum produced more streak artifact on CT, but less on MRI, permitting MRI reading to be better able to image surrounding bony structures to assess fusion [123]. Blumenthal et al. [124] suggested that plain radiographs might underestimate the degree of fusion in 1 out of 5 cases, with different thresholds of accepted angulation leading to vastly different rates of fusion.

Further randomized trials are needed to tease out the timing and criteria of fusion with the implementation of tantalum in the cervical spine.

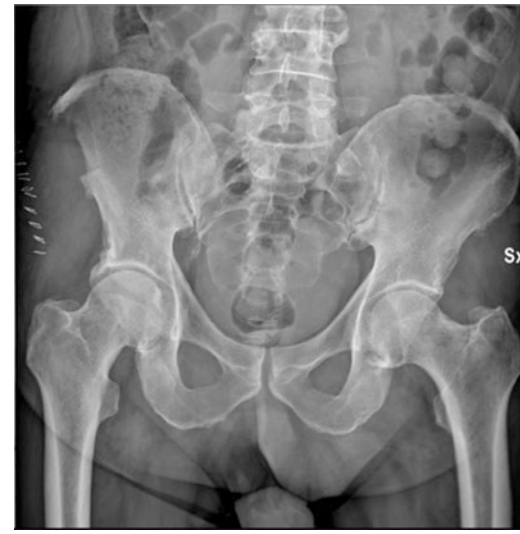

Fig. 8.4 Posteroanterior X-ray of pelvis after the harvest of tri-cortical iliac strut graft on the right side

Bone Graft Substitutes

Bone grafts and bone substitutes are indispensable for achieving and maintaining fusion in stability in spine surgery. Autologous bone has long been regarded as the gold standard for obtaining reliable spinal fusion, mainly because of its micro-architecture and biological properties, which make it osteoconductive, osteoinductive and osteogenic. However, the reserve of autologous bone graft is limited. Moreover, issues of sub-optimal bone quality in osteoporotic patients and donor site morbidity after graft harvest have led orthopaedics to look for alternatives: Allografts, Demineralized bone matrix (DBM), Ceramics (hydroxyapatites, tricalcium phosphate, biphasic calcium phosphate], calcium phosphate cements, bioactive glass), Osteogenic growth factors (namely Bone Morphogenic Proteins), Autologous growth factors (AGFs) (Platelet derived growth factors), Stem cell products and Synthetic peptides [125].

Autograft

Cortico-cancellous bone harvested from the iliac crest is widely used for the cervical spine (Fig. 8.4). A systematic review of the literature reported autograft to have a mean arthrodesis rate of 77% [45]. In one-level non-instrumented procedures, autograft fusion rates are a reported 83–99% [126] but decreases with number of levels fused [127]. Autograft experiences relatively few incidences of graft complication, such as graft collapse or migration, poses no risk of disease transmission and is non-immunogenic [58]. Autografts also have the advantage of having all three of the pillars of bone regeneration, including osteogenic, osteoinductive, and osteoconductive capabilities that other grafts may or may not offer. For these reasons, autograft remains the standard of care for cervical spinal fusion [128]. Autografts can be further classified by bone type: cortical and cancellous. Cortical bone is described as an extremely dense bone with limited porosity, while cancellous bone is the opposite and is extremely porous. While cortical bone provides the advantage of early stability due to its high density, early revascularization and osteoinduction may be sacrificed. Osteoclasts are required to first reabsorb bone, making way for the formation of cavities to the osteonal canal. Upon reaching the canal, osteoblasts are then able to start bone formation. Eventually, this results in complete resorption of graft and replacement with new bone. In contrast, cancellous bone is very

osteogenic due to its large surface area. Osteoblasts can rapidly incorporate new bone and revascularization happens relatively quickly when compared to cortical grafts. Although early mechanical strength is limited, the ability to rapidly begin producing new bone generally outweighs the risks in most patients [128]. While the advantage of being able to promote strong fusion with complete histocompatibility has firmly established its widespread usage, autografts are not without drawbacks. The quality of individual grafts can vary according to age and metabolic activity [129].

Historically, for ACDF the iliac crest is the most commonly cited source of autologous bone graft. However, while iliac crest bone graft (ICBG) is considered the gold standard for harvesting, unfortunately the stipulation of a second surgical site not only increases operative time and blood loss but introduces significant donor site morbidity. Although the risk of harvest site morbidity has been suggested to be overstated, it is generally accepted within the literature to be of significant concern [130]. A retrospective study of one-level anterior cervical fusion found 26.1% of patients suffered persistent pain and 15.7% experienced numbness at the harvest site [47].

Functional assessment revealed impairment in ambulation (12.7%) and other daily activities. Many other complications have been observed including infection, hematoma, bruising, pelvic fracture, peritoneal perforation, hernia, gait, ureteral injury, reoperation and poor cosmesis [131]. Rawlinson reported 31% of patients felt donor site pain caused them to remain in hospital longer than if they had not had that procedure [132]. Finally, there are inherent limitations with supply and occasionally, autograft quality. Some authors have investigated the harvest of autograft from alternative locations, such as the fibula [133], cervical vertebrae, clavicle [134], and the manubrium [135], so as to retain the advantages of autograft whilst circumventing its associated morbidity, to varying success. Others have explored the effectiveness of iliac crest reconstruction using synthetic materials in alleviating postoperative pain, with mixed results [136].

Allograft

Allograft is the most used non-autogenous grafting material in spinal surgery, and 35% of all bone transplantations involve the use of human allograft tissues [137]. Aside from being readily available, allografts have an additional advantage of lacking the need for multiple incision sites from the patient to harvest the graft. Mineralized allograft is primarily osteoconductive, with weak osteoinductive capacity and no osteogenic potential because graft cells do not survive processing and transplantation. Allograft used for orthopedic applications is fresh frozen, freeze-dried, or demineralized [138]. The method of preparation has significant effects on graft strength, immunogenicity, capacity for incorporation, and potential for disease transmission. Fresh-frozen allografts retain much of their original mechanical strength, while freeze-drying can reduce graft strength up to 50% [139]. The freezing process also reduces immunogenicity of allografts [140]. The effect of immunogenicity in compromising graft incorporation may be significant [141]. Transmission of disease from donor to recipient is a problem with human allografts. The principal pathogens involved are human immunodeficiency virus (HIV) and hepatitis viruses B and C. The risk of disease transmission is determined by the rigor of screening procedures for donors and tissue, and the only cases of disease transmission in musculoskeletal allografts from the method of graft preparation to date have involved frozen, unprocessed grafts. Tissue processing techniques include high pressure lavage to clear out marrow elements and donor cells and chemical treatments to eliminate viruses and reduce immunogenicity of the graft. The standard method to eliminate the risk of disease transmission by destroying microorganisms involving gamma radiation which have been widely proven to be able to effectively inactivate pathogens, while ideally having the lowest possible impact on structural integrity of the tissues [142]. However, the sterilization process can damage the molecular structure of fragile biologics such as cytokines, chemokines, and growth factors which can

alter the biomechanical properties of bone. Gamma radiation has several advantages of other methods that include better penetration, greater certainty of sterility, and effectiveness that is independent of temperature and pressure [143]. The combination of donor screening, tissue testing, and tissue processing reduces the risk of viral transmission to less than one event per million grafts [144]. However, there are some disadvantages to allografts. Because allografts are also derived from human origin, they are both osteoconductive and weakly osteoinductive. However, because of the sterilization process, allografts lack viable cells and have no osteogenic properties [145]. Allograft is available in many preparations. However, the majority are composed of primarily cancellous or cortical bone. Cortical allografts provide significant mechanical stability and structural support, while cancellous bone lends little mechanical stabilization on implantation but has a faster rate of incorporation. Cancellous allograft and particulate allograft preparations (cancellous or cortical) incorporate with new bone forming on the surfaces of trabeculae, with a large surface area available for new bone formation. In contrast, cortical incorporation occurs slowly via a process of periosteal new bone formation around the allograft as an external callus derived from the host bone. Particulate and structural grafts demonstrate significant differences in the histology of incorporation. Particulate grafts demonstrate more rapid and complete revascularization than structural grafts. Particulate bone remodels completely with time, while cortical bone remains a mixture of necrotic and viable bone. The process of creeping substitution is also differing significantly between these forms of allograft, with new bone formation occurring appositionally followed by resorption in cancellous bone, which process is reversed in cortical allografts [146]. These differences in biologic capacity between graft types lead to significant differences in optimal clinical applications. The use of bone allografts in the spine has been reviewed previously by the senior author [147]. Structural cortical allografts are most useful in interbody arthrodesis of the lumbar and cervical spine, with low rates of graft tricortical allograft may be as effective as iliac crest in promoting anterior arthrodesis of the spine [148]. Crushed cortical or cancellous allograft may be useful as an autograft extender in posterior spinal fusion. In thoracolumbar deformity, cancellous allograft with instrumentation may give satisfactory results in the pediatric population but yields inferior results in adults. The conclusion from the senior author's experience is that successful use of allograft bone in the spine is dependent on the type of allograft bone used, the anatomic site of fusion, and patient age. A review of other clinical applications of allograft compared with autogenous bone in spinal surgery is useful. In cervical spine, the use of allograft vs. autograft has been debated since the first anterior discectomies and interbody fusions. Smith and Robinson used autogenous iliac crest graft and reported radiographic union in 18/21 patients [149]. Concurrently, Cloward reported resorption of only 3/46 grafts using his dowel technique with fresh-frozen allograft [150]. More recent reviews demonstrated similar fusion rates using autogenous and allogenous grafts in single level cervical surgery but significant differences in multilevel cervical fusions [151]. Park et al. [152] compared cortico/cancellous composite allograft with autoiliac bone graft: the fusion rates of two groups were similar on plain radiographs and CT.

Graham et al. [153] in a prospective randomized control trial comparing glycerol preserved versus freeze dried allografts for anterior cervical fusion reported fusion rates greater than 95% in both groups, which were not statistically different. In another prospective semirandomized comparative study, Suchomel et al. [154] evaluated freeze-dried fibular allografts versus autologous iliac crest grafts in 80 patients undergoing instrumented anterior cervical fusions. In single-level procedures, there was no significant difference in fusion rates (100 vs. 93.3%, $p = 0.197$) between autograft and allograft, respectively. In two-level procedures the differences were also insignificant: 90.9 vs. 93.5% fusion rate ($p = 0.709$) for autograft and allograft, respectively; however, fusion took a longer time to occur in the allograft group. The number of levels fused per case did not have any significant effect on outcome mea-

sures. More recent studies using instrumentation to augment allograft constructs also reported high fusion rates, ranging from 91.9 to 94.3% [155–157].

Demineralized Bone Matrix (DBM)

Demineralized bone matrix (DBM) is derived from human allograft bone which has been acid-treated in order to remove the mineral matrix, while maintaining the organic matrix and growth factors such as bone morphogenetic protein (BMP) [158], insulin growth factor (IGF), transforming growth factor (TGF), or fibroblast growth factor (FGF) [159]. In proportion, 93% of a DBM is represented with collagen and 5% with growth factors. Since some growth factors are maintained, DBM can show osteoinductive capabilities and osteoconductive properties by the presence of a collagen structure [160–162]. Nevertheless, a large rate of the osteogenic capacity of bone is lost during its processing. DBM shows no immunological rejections because the antigenic surface structure of the bone is destroyed during its demineralization by acid [163]. The use of DBM avoids donor site morbidity, and studies showed a comparable pain intensity after the surgical procedure compared to autograft procedures [164]. It presents suitable availability, but this substitute is more expensive than an iliac crest bone autograft procedure and its mechanical properties are quite low. Thus, DBM is only used for filling purposes and generally not as a stand-alone bone substitute. A variety of DBM preparations have been made commercially available in the form of powders, granules, gels, putties, and strips.

A prospective study by An et al. [165] evaluated the use of DBM (Grafton DBM™) in combination with allograft for cervical disc disease. In this study involving un-instrumented fusions, radiologic pseudarthrosis was found in 33.3% of treated cervical levels in the allograft-DBM group versus 22% of levels in the autograft group ($p = 0.23$). Others studies [166–169] reported acceptable to good fusion rates (ranging from 88.9 to 97%) and comparable clinical outcomes using a combination of DBM and interbody cages for cervical fusion.

Synthetic Bone Graft Substitutes

Ceramics

Ceramics represent one of the most studied groups of bone substitutes in spine surgery and are mainly used as bone graft extenders in combination with autologous bone or bone marrow aspirates and interbody devices. Ceramics provide a scaffold for bone growth and a showing osteoconductive properties without any osteogenic or osteoinductive potential [170, 171]. Hydroxyapatite (HA), beta-tricalcium phosphate (β-TCP), calcium phosphate (CaP), calcium sulfate, and bioactive synthetics such as silicate-substituted calcium phosphate (Si-CaP) and bioglass (BAG) are among the most notable ceramic scaffolds that have been studied for use in human spinal fusions. In newer generation of ceramics, bioactive synthetics go beyond osteoconductive role, and they have osteoproductive characteristics which promote cell stimulation towards osteogenesis and growth factor production. Ceramics are an attractive alternative given that they are an inert substance that is non-toxic, non-immunogenic, and without risk of infection. They are fully customizable, easily stored, and available in virtually unlimited supply. Lastly, when compared with other graft materials, they are also a less expensive option [172]. The main disadvantage is the inherent lack of mechanical strength. Ceramics are brittle with low fracture resistance and tensile strength limiting their use as a standalone bone substitute [173]. Therefore, they are commonly protected until bone ingrowth has occurred.

Beta Tricalcium Phosphate (βTCP)

Beta tricalcium phosphate (βTCP) was one of the earliest calcium phosphate compounds to be used as a bone graft substitute. βTCP is a synthetic bone graft substitute similar to normal bone [174]. It is composed of 39% calcium and 20% phosphate [171]. βTCP shares the same osteoconductive properties of other ceramics, enabling it to function as an effective carrier for both cells and growth factors. In 1920 Albee and Morrison reported that the rate of bone union was increased

when βTCP was injected into the gap of a segmental bone defect [175]. Beta tricalcium phosphate is available in porous or solid form as either granules or blocks. Structurally porous βTCP has a compressive strength and tensile strength like cancellous bone [176]. Similar to other calcium phosphate preparations, it has been found to be brittle and weak under tension and shear, but resistant to compressive loads [177].

Typically, it has been used in its granular porous form. Porous granules tend to migrate less than solid granules due to earlier fixation by fibrovascular ingrowth [178]. Beta tricalcium phosphate undergoes reabsorption via dissolution and fragmentation over a 6–18-month period. Unfortunately, the replacement of βTCP by bone does not occur in an equitable way. That is, there is always less bone volume produced than the volume of βTCP reabsorbed [179]. For this reason, the clinical use of βTCP has been as an adjunctive with other less reabsorbable bone graft substitutes or as an expander for autogenous bone graft.

Dai et al. [180] concluded that interbody fusion cages containing β-TCP following one- or two-level discectomy proved to be an effective treatment for cervical spondylotic radiculopathy and/or myelopathy, with successful fusion seen in all patients at 6 months follow-up ($p < 0.05$). In a retrospective cohort review, Sugawara et al. [181] reported on the use of β-TCP (Osferion ™) compared to Hydroxyapatite packed in cylindrical titanium cages for ACDF procedures. The complete fusion rate at 6 months and 1 year was significantly superior in the β-TCP group (46% at 6 months and 69% at 1 year) than in the HA group (24% at 6 months and 49% at 1 year) ($p < 0.05$) Other available studies report good efficacy and satisfactory outcomes with β-TCP use when compared to autologous bone grafts [182].

Hydroxyapatite (HA)

HA [Ca10 (PO4)6 (OH)2] is a hydroxyl compound of calcium phosphate and is the main component of natural mineralized bone. The synthetic form is highly crystalline, produced through a high-temperature reaction and is like the natural HA chemically and crystallographically. Such chemical similarity to natural bone and the subsequent biocompatibility and osteoconductivity is the exceptional property of HA [183–185].

The chemico-physical characteristics of the HA graft allow to induce a rapid and complete interbody fusion but also restore the physiological lordosis and maintain the intervertebral and foraminal height.

The process of mixing these materials leads to porous ceramics with high osteoconductive properties. The graft can be invaded by newly formed bone that grows directly into the pores [186].

Hydroxyapatite grafts have the advantages of osteoconductive properties, good resistance to collapse, simplicity of use, and a physiological shape [187].

In experimental studies and, in particular, those in which electron microscopy observations are made, the authors have demonstrated the bioactive properties of HA grafts and their apparent ability to be directly bonded to bone, reproducing the natural bone-cementing mechanism [176].

Unlike other synthetic grafts, however, there is no interposition of fibrous tissue between implant and bone [188].

In their study Senter et al used synthetic, dense, no resorptive HA spacers on 84 patients, although the HA spacer was similar to iliac crest autograft in terms of symptom relief, spinal alignment and stability, superiority was demonstrated in terms of long-term relief of symptoms, lower need for reoperation and the absence of resorption with subsequent collapsed disc space [189].

Unlike autografts and allografts, HA is not amenable to absorption by the host cells. Resorption of HA is very limited in both cell and solution-mediated processes, in contrast to tricalcium phosphate compounds, which are rapidly resorbed [190]. Preliminary clinical results were published in 1986 by Koyama and Handa [191] and then by Senter et al. [189] in 1989 and by Böker et al. [192] in 1993. These studies report the use of the HA graft combined with plate placement and demonstrated that this graft material is very effective in inducing cervical interbody fusion. The first step of fusion was always a remodeling of the bone–graft interface.

Progressively, a bone bridge appeared around the graft, mainly posteriorly, and enlarged until total incorporation of the graft occurred.

In a retrospective study Kim et al. [193] analyzed clinical and radiological outcomes of anterior cervical interbody fusion using hydroxyapatite spacer. They enrolled 29 patients in the study and 40 segments were involved and all patients were performed anterior cervical interbody fusion using HA spacer and plating system. Indications for surgery were radiculopathy caused by soft-disc herniation or spondylosis in 18 patients, spondylotic myelopathy in 1 patient, and spinal trauma in 10 patients. Cervical spine radiographs were obtained on postoperative 1 day, 1 week, and then at 1, 2, 6, and 12 months in all patients to evaluate intervertebral disc height, and the degrees of lordosis. Cervical computed tomography was done at postoperative 12 month in all patients to confirm the fusion status. The mean period of clinical follow-up was 17 months. Kim et al obtain complete interbody fusion in all patients enrolled in the study, preoperative kyphotic deformities were corrected in all cases after surgery, intervertebral disc height was well maintained during follow up period. There were no cases of graft extrusion, graft deterioration and graft fracture. They conclude that HA spacer is very efficient in achieving cervical fusion, maintaining intervertebral disc height, and restoring lordosis.

Vukic et al. [194] in their study evaluate the efficacy of hydroxyapatite grafts in multilevel cervical interbody fusion during the 1-year follow-up. They enrolled 86 patients with DCDC and underwent all together 224 cervical interbody fusion procedures. HA graft was used in patients with or without plating. The pathology treated were radiculopathy in 38 cases, myelopathy in 20 cases and myeloradiculopathy in 28 patients. Clinical results were excellent in patients suffering from radiculopathy (86% of cases), while less satisfactory clinical results were obtained in patients with myelopathy (54% of cases). In no clinical case a graft collapsed was noted and a complete bony bridge interposed in the graft between two adjacent vertebral plates was obtained. Vukic et al identified five grafts mobilizations and one graft fracture, two grafts extruded in non-instrumented patients and required repeated surgery. At the radiographic control carried out 1 year after the surgery the fusion rate obtained at 86% for two-level discectomy, 80% for three-level surgery and 74% for four-level discectomy. The results of this study show how HA can be a very effective synthetic material for cervical arthrodesis as it allows a high fusion rate and a small risk of complications, especially when the arthrodesis is followed by plating. Other studies [195–197] reported good results with a fusion rate ranging from 92.50 to 100% and concluded that HA was an effective alternative to autologous iliac crest graft.

HA has been used extensively since its discovery and over the years, cages of different materials, such as titanium and peek, have been used which have been added with hydroxyapatite in order to obtain an ACDF. For example, this mode of use of HA can be evaluated in the study by Papavero et al. [198]; they used a rectangular fenestrated titanium cage filled with a porous HA cylinder soaked with vertebral bone marrow aspirate (BMA) from a vertebra in 78 patients. The results of the work were obtained by studying the graph through quantitative CT scan (qCT) because the radiopaque implant limits the radiographic assessment, they performed an arthrodesis analysis 6 months after surgery and quantitative computed tomography showed up to a 14% increase in the HA mass in the core of the implant, which was statistically significant. Two years after the surgery they saw an increase to 24% of the newly formed hydroxyapatite mass without any slippage or fracture occurring, also all 71 patients undergoing surgery achieved excellent clinical results and no revision surgery was necessary.

If we analyze different materials compared to titanium cages, we can appreciate the peculiarity of radiolucent materials such as PEEK and carbon fiber-reinforced polymer allow us to analyze much better the degree of fusion and to remove those difficulties related to radiopaque materials

that do not allow us to fully evaluate the degree of arthrodesis obtained after surgical ACDF [62, 68, 199].

In the literature it is possible to identify many works in which the peek cages are filled with hydroxyapatite. Chang et al. [199] in a clinical study analyze 45 patients that underwent to ACDF using PEEK cages containing either autologous bone or HA. They carried out a follow-up from 2 to 10 years and did not find any radiographic complications, they also underlined the fact that both groups analyzed had obtained an excellent degree of fusion and concluded by stating that the PEEK cages added to HA have an excellent safety and represent a suitable alternative to autologous transplantation.

Yi et al. [73] in a recent prospective randomized clinical trial compare bone union rate following ACDF using a PEEK filled with a mixture of Hydroxyapatite/B-Tricalcium phosphate versus Hydroxyapatite/demineralized bone matrix. One year after surgery they analyzed complete arthrodesis in 87% of patients, in both groups through the use of dynamic radiographs, while through CT scans the degree of fusion was respectively equal to 87% for the group that received the HA/TCP mixture and 72% for those who received the HA/DBM mixture. Yi et al concluded that the HA/DBM mixture as a fusion material in a PEEK cage would provide noninferior outcomes compared to the HA/β-TCP mixture, therefore clinical and radiological results are comparable in both treated groups.

Coralline Hydroxyapatite

Coralline-derived hydroxyapatite is manufactured from the Porites and Goniopora species of sea coral by the hydrothermal chemical conversion of calcium carbonate to hydroxyapatite [200]. These two products have porous microstructures similar to human cortical and cancellous bone [201]. Zdeblick et al. [202] reported the results of cervical interbody fusion in a dog model using coralline-derived hydroxyapatite. In the non-instrumented group, fewer than half the grafts incorporated, 14% extruded, and 29% collapsed. Extrusion was eliminated, and the fusion rate increased to 71% with non-rigid anterior plating. However, graft collapse was reduced to only 24%. In a retrospective study Thalgott et al. [203] reported the results of cervical interbody fusion in 26 patients using the same implants associated with rigid anterior cervical plating. At the 2-year follow-up assessment, there was an average of 75.8% reduction in pain, and 100% of the grafts were reported as incorporated on radiograph evaluation. Thalgott et al. concluded that coralline-derived hydroxyapatite is a promising material for bone replacement in the cervical spine and suggested that future studies should compare this new material with autograft in prospective randomized trials. In a prospective randomized trial McConnell et al. [51] demonstrated a high rate of radiographic fragmentation, collapse, and loss of alignment of the coralline-derived hydroxyapatite that appears structurally inferior to iliac crest bone for cervical interbody fusion. In this study graft fragmentation occurred in 89% of the hydroxyapatite grafts versus 11% of the autograft ($p = 0.001$). Plain AP and lateral radiographs at periodic intervals and CT images for the final status were used to evaluate interbody fusion rates. Significant graft settling was also reported in 50% of the HA grafts, as compared to 11% of the autograft patients ($p = 0.009$).

Calcium Sulfate

Calcium sulfate has long been used as a bone substitute, particularly in orthopedic trauma, and has been praised for its availability, low-cost, and osteoconductive properties [159]. The crystalline structure of calcium sulfate is similar to that of cancellous bone, providing architecture for the introduction of capillaries and mesenchymal stem cells [161]. The lack of osteoinductive or osteogenic properties, as well as quick resorption time (1–3 months), hinders the use of calcium sulfate as a standalone graft and mandates the use of additional substances such as demineralized bone matrix or local allograft for maximized effect.

Previous reviews have demonstrated similar results between calcium sulfate and autologous graft for lumbar fusion across multiple studies [204]. However, more recent clinical investigations of calcium sulfate for spinal fusion are lim-

ited. In a prospective study of 68 patients with cervical degenerative disc disease being treated with one- or two-level discectomy, Xie et al. showed comparable results between polyether-ether-ketone (PEEK) interbody cages with calcium sulfate/demineralized bone matrix (CS/DBM) and those with autogenous iliac cancellous bone. At 12-month follow-up, the CS/DBM group showed 94.3% fusion compared with 100% in the ICBG group. Both groups had 100% fusion at final follow-up (24 months). No significant difference was found in follow-up clinical symptom score or lordotic angle between the two groups. The complication rate for the ICBG group (18.2%) was significantly higher than the CS/DBM group (8.6%) [18].

Calcium Phospate

The calcium phosphate family of synthetic bone grafts has both osteointegrative and osteoconductive properties. Osteointegration results from the formation of a layer of HA shortly after implantation. The Ca^{2+} and $PO4^{2-}$ ions required to establish this layer are derived from the implant and surrounding bone. The pathways of both Ca^{2+} and $PO4^{2-}$ ions have been traced in serum and urine without any significant elevation in serum levels from which it can be concluded they are handled as part of the normal body ion pool. They have an excellent record of biocompatibility with no reports of systemic toxicity or foreign body reactions [205].

Literature on calcium sulphate products is limited to their use in lumbar fusion surgeries.

Silicate Substituted Calcium Phosphate (Si-CaP)

Silicate substituted calcium phosphates (Si-CaP) are a novel sub-class of ceramic bone substitutes which, in addition to exhibiting osteoconductive properties, are purported to be osteoinductive as well. This newer generation ceramic material, as the name implies, is prepared by partially substituting silicate for phosphate in a controlled manner. This substitution is typically 0.8% by weight for the commercially available product Actifuse™. The presence of silicate increases the negative charge of the ceramic scaffold, which is hypothesized to attract more osteoblasts to the material surface, thus conferring osteoinductive effects [206]. Si-CaP has also been shown to exhibit an increased in vivo resorption rate compared to the more traditional hydroxyapatite ceramics [207].

Studies evaluating the efficacy of Si-CaP versus autologous bone grafts are currently lacking: two prospective randomized studies [208, 209] compared Si-CaP with rhBMP in lumber interbody fusion; two retrospective studies by Jenis et al. [210] and Nagineni et al. [211] reported fusion rates from 76.5 to 90% with the use of Si-Cap in cervical and lumbar fusion procedures. Alimi et al. [212] reported a fusion rate of 92.6%.

Bioactive Glass Ceramic (BGC)

Developed for the first time by Hench et al. in the 1970s [213], bioactive glasses (or bioglasses) are originally silicates that are coupled to other minerals naturally found in the body (Ca, Na2O, H, and P). The original bioglass composition is 45% silica (SiO2), 24.5% calcium oxide (CaO), 24.5% sodium oxide (Na2O), and 6% phosphorous pentoxide (P2O5) in weight percentage [214]. The main clinically-used bioactive glass formulations is the 45S5 which have a long history of successful clinical use as a bone graft material in both the spine and general orthopedics [215, 216]; it is composed of 46.1 mol% SiO_2, 24.4 mol% Na_2O, 26.9 mol% CaO and 2.6 mol% P_2O_5.

One of the key properties of bioactive glasses is the ability to form an in vivo layer of bone-like mineral [hydroxy-carbano-apatite (HCA)] on surface of the glass material. As the glass resorbs through in vivo exposure to an aqueous solution or body fluids, surface of bioglasses converts to a silica-CaO/P2O5-rich gel layer that subsequently mineralizes into hydroxycarbonate in a few hours [217, 218]. This bioactive layer enables the glass to chemically bind with adjacent bone and improves the overall ability of the material to support bone growth on its surface (osteoconductivity) [219]. Originally, the improved bone healing seen with bioactive glasses was attributed to

this bioactive property. However, further research revealed that the ionic by-products of glass dissolution had positive effects on the surrounding cells; once this HCA layer is formed, dissolution of calcium and silica ions stimulates attachment of osteoblasts, cell division, and up-regulation of osteogenic genes that is dose dependent to ion release [220, 221]. Bioglasses are biocompatible, osteoconductive and, depending on their processing condition, offer a porous structure which promotes their resorption and bone ingrowth [222–224]. The use of bioglasses does not induce an inflammatory response, and their resorption is complete in 6 months for silica-based bioglasses [225].

Early animal model studies found bioactive glass to induce either comparable rates of fusion or higher volumes of fusion mass than autograft [226, 227]. Ilharreborde et al. [228] conducted a comparative study of bioglass vs. iliac crest autograft for spinal fusion in adolescent idiopathic scoliosis and found complete fusion with both graft materials in 88 patients. A study by Frantzen et al. [229] found a higher fusion rates with bioglass with a higher silica content than 45S5 BAG (53.9 vs. 46.1 mol% for 45S5) in patients undergoing L4/5 and L5/S1 spinal fusion for spondylolisthesis. A recent study by Barrey et al. [230] assessed 30 patients with a wide range of degenerative and traumatic conditions of the cervical or lumbar spine who underwent spinal fusion with bioactive glass and found an overall fusion rate of 93% at 1-year postop. A new format of bioactive glass bone graft putty (BioSphere® Putty) is now available: this product utilizes 45S5 bioactive glass particles with a unique, spherical shape. The spherical glass particles in BioSphere Putty are specifically sized and engineered to selectively control the ion release profile during glass dissolution. The radiographic assessment showed evidence of complete fusion in all patients. Bone formation was seen within the cervical spacer graft area and was fully integrated with the inferior and superior cervical endplates [231]. Kim et al. [232] compared the effectiveness and safety of BGC cages to allograft bone for ACDF: they not found differences in the rates of bone fusion (on reconstructed CT images) in the two groups at 1 year ($p = 0.07$) and 2 years ($p = 0.54$) after surgery. The fusion rates in the BGC cage group were 73% (38 segments) at 1 year and 94% (30 segments) at 2 years after surgery; however, they were 87% (31 segments) and 91% (20 segments) at 1 year and 2 years after surgery, respectively, in the allograft bone group. According to these results, BGC cages may be considered a feasible alternative to allograft bone, with comparable radiological outcomes and rates of fusion.

Biphasic Calcium Phosphate (BCP)

β-TCP is mostly used in association with HA [159, 233]. Synthetic HA can be made by the precipitation of calcium nitrate and ammonium dihydrogen phosphate. This association presents all the advantages of its two components (osteoconductivity [234], biocompatibility, safe and nonallergen use, and promotion of bone formation). The major gain of using biphasic ceramics (HA and β-TCP mixture) concerns their resorption. Indeed, the resorption of β-TCP is faster than the resorption of HA,but mechanical properties of HA are slightly better than β-TCP's (average compressive resistances are, respectively, of 160 and 100 MPa). Thus, the association of β-TCP and HA enables a faster and higher bone ingrowth rate than using HA alone while offering better mechanical properties than β-TCP alone. Indeed, 12 months after the implantation of the material, 60% of the β-TCP resorbs compared to only 10% for the HA. HA and β-TCP ceramics form a strong direct bond with the host bone. They can be found with different HA/β-TCP ratios and can be associated with bone marrow aspirate which then provides enhanced osteogenic properties to the material.

Biphasic calcium phosphate (BCP) is a composite of HA, which is less soluble, and b-TCP, which has greater solubility [235]. Thus, the factor determining solubility in the biphasic ceramics is the HA/b-TCP ratio; the lower the ratio, the greater the solubility and osteoclastic resorption. However, osteoclastic resorption does not always enhance as solubility increases. Yamada et al. [236] demonstrated that, although pure b-TCP

had the highest solubility in acidic solution, a biphasic ceramic calcium with HA/b-TCP ratio of 25/75 was more extensively resorbed with osteoclasts than pure b-TCP. In the clinical setting, the biphasic ceramic used for ACDF is commonly composed of 60% HA and 40% b-TCP. The study by Cho et al. [237] involving 100 patients showed that PEEK cages containing BCP or autograft had 100% fusion rate at 6-month follow-up. Of note, the fusion rate was lower with cages containing BCP than autograft during the first 5 months after the operation. Spinal curve correction, neuroforamen enlargement, and neurological recovery were the same in both groups. Chou et al. [238] compared the results of BCP implants (9 with PEEK and 27 with titanium cages) with autograft (n. 19). After 1 year, the fusion rate was 100% in patients treated with PEEK cages or autograft and no subsidence or subluxation was reported in either, while the titanium cage fusion rate was as low as 46.5% and led to subsidence and subluxation in 26% and 3.7% of patients, respectively. The PEEK cage containing BCP was demonstrated to be a viable alternative to autograft. Another study using PEEK cages containing BCP was conducted by Mobbs et al. [239] involving 58 patients. They reported that the fusion rate was 100% at 6 months with anterior plating and 96.2% without plate fixation. In the non-plated group, delayed fusion, nonunion, graft subsidence, and graft migration occurred.

Polymer-Based Bone Substitutes

The limitations of current cages gave some impetus for the development of bioresorbable cages: their stiffness is comparable to that of bone, they are radiolucent, and they resorb over time. As such, they also have great potential as drug release systems [240]. Furthermore, biodegradable cage devices eliminate the risks of permanent implants. Bioresorbables, however, have their own drawbacks and pitfalls. First, their strength is usually considerably lower than that of metals or non-degradable polymers. Also, the brittleness of some frequently used polymers is worrisome. The main concern, though, is the concentration of degradation products like acids and crystals, because very high concentrations may lead to serious tissues responses like inflammation and osteolysis. The local concentration of degradation products depends on their rate of production and their rate of drainage. Therefore, good vascularization of the tissues around bioresorbable implants is of utmost importance. Degradation depends on many factors such as material properties (chemical species, molecular weight distribution, and permeability), implant design (bulkiness and porosity), handling (sterilization and thermal history), and environment (pH and mechanical loading). Slow degradation is desirable not only to maintain the mechanical function of the implant until fusion is obtained, but also to reduce the risk of tissue reactions. Such reactions may occur many years after implantation of the device [241].

Although bioresorbable polymers have been used in orthopedic surgery for more than 30 years, bioresorbable polymer implants have only recently been applied in spinal surgery [242].

Polymers are long-chain molecules derived from repeating units, typically with a carbon backbone. When the backbone is hydrolytically unstable, these chains will degrade when placed in an aqueous environment. This material property to degrade over time has led to a variety of medical applications [243]. The most commonly used biodegradable materials are polyesters that are derived from so-called poly(a-hydroxy acids), like poly(lactic acid) (polylactide, PLA), and poly(glycolic acid) (polyglycolide, PGA). Importantly, lactic and glycolic acid are present in the biochemical pathways of cells and organisms; PLA and PGA thus degrade to natural metabolic compounds. PGA, however, is very unstable and loses its strength within a month. Therefore, it is not a suitable material for a cage device, unless as a minor component in a copolymer. Its main application is in sutures, which only need to be strong for a few weeks [244].

The most useful and applied base material for spinal interbody cages is poly(lactic acid) or polylactide (PLA). PLA can be engineered to possess appropriate mechanical properties and is more resistant to hydrolytic degradation than PGA [245].

There are several parameters, though, that help to characterize polymers like PLA, the most important ones being crystallinity and average molecular weight (or, alternatively, inherent viscosity). Other relevant parameters are molecular weight distribution (polydispersity), impurities (such as residual monomers, water, and free radicals), and glass transition temperature.

Crystalline regions in the polymer have stronger secondary bonds between the chains of the polymer, and make it difficult for water to penetrate, which makes these regions degrade more slowly. Racemic polylactide, which is entirely amorphous, degrades within months, whereas high-crystalline PLLA has been reported to require more than 4 years to degrade.

The second factor that has major impact on the properties and degradation kinetics of polymers is molecular weight. Polymer strength increases with molecular weight by the formation of secondary bonds between the chains and by the entanglements in the structure. Degradation occurs more slowly because more secondary bonds have to be broken per chain.

Initially used as graft extenders [185], researches focus on synthetic polymeric bone substitutes, especially in the field of tissue engineering. Polyesters like poly (ε-caprolactone) (PCL), for example, can be synthetized by mimicking the collagenic matrix, offering a structural porosity and osteoconductive properties [246]. Most of the polymer-based bone substitutes are suitable to be used as bioactive molecules or growth factors carriers [247], potentially conferring osteogenetic properties [246]. Since PCL is soluble in a wide range of organic solvents, it is a promising polymer for continuous researches in tissue engineering [248].

Polymer-based bone substitutes are mainly scrutinized for their wide potential in tissue engineering, allowing their fabrication with macropores and micropores and in the shape of thick membranes (e.g. PCL or PLA). Clinicians should keep a close eye on outcomes of researches concerning polymer-based bone substitutes as scaffolds for regenerative medicine.

Factor and Cell-Based Approaches for Bone Graft Substitutes

Emerging adjuvant therapies have allowed surgeons the option of composite bone grafts. The addition of an osteoinductive and/or osteogenic substance provides theoretical benefits when combined with an osteoconductive substrate. The most potent and promising of these adjuvants are the highly osteoinductive bone morphogenetic proteins (BMPs), discovered by Urist [249] in 1965 following his observation of bone growth from animal demineralized bone matrix. BMPs are osteoinductive molecules belonging to the transforming growth factor beta (TGF-β) superfamily of proteins. Of the more than 20 types of BMPs described BMP-2 and BMP-7 (also known as Osteogenic protein-1, or OP-1), in their recombinant forms (rh), are the most widely used BMPs in clinical practice. Since BMPs are soluble proteins and may readily diffuse into the surrounding tissues, away from the site of application, they are used in combination with carriers to maintain effective concentrations at the intended fusion sites. Though efforts to identify the ideal carrier are ongoing, absorbable collagen sponges (ACS) and compression resistant matrix (CRM) are frequently used. Autologous and allogenic bone grafts, ceramics, DBMs and polylactic acids are other substrates that have been utilized for rhBMP delivery [125].

Less expensive alternatives include bone marrow aspirate (BMA) taken from the iliac crest and platelet rich plasma (PRP).

Platelet degranulation leads to the release of growth factors that contribute to both bone and wound healing. These autologous growth factors (AGFs) contain mitogenic properties for inducing proliferation of osteoblasts, fibroblasts, and mesenchymal stem cells [128]. Two of the most researched growth factors include platelet-derived growth factor (PDGF) and TGF-β. PDGF is thought to directly increase the replication and synthesis of matrix proteins, playing an important role in the remodeling and construction of new bone. Similarly, TGF-β regulates extracellu-

lar bone matrix synthesis and serves a crucial role of stimulating angiogenesis. These growth factors are extracted and prepared via the ultra-concentration of platelets, and theoretically can be used in combination with either autograft, allografts, or ceramics to increase rates of successful fusion. Further, platelet-rich plasma is utilized in a variety of other orthopedic procedures as well including rotator cuff tears, tendinopathies, osteoarthritis, and articular cartilage injuries [250].

Bone Morphogenetic Proteins (BMPs)

Bone morphogenic proteins (BMPs) were first isolated in 1965 by Robert Urist and have since been extensively studied for their clinical application in spinal fusion [128, 251]. The term BMP refers to over 20 known cytokines and growth factors of the TGF-family with osteogenic capabilities. Of this family, BMP-2, BMP-4, and BMP-7 (osteogenic protein-1) are the most studied [252]. BMPs have shown considerable promise in the human lumbar spine [253] and in animal models of anterior cervical fusion [254]. Recently, a number of clinical studies have focused on its appropriateness in the human cervical spine, with consistently reported fusion rates of 100% [255]. BMPs can be used either alone as bone graft substitutes with a synthetic collagen carrier or in addition to other autograft or allograft materials. The ability of BMPs to enhance bony fusion has been confirmed by comparative trials. A meta-analysis by Parajón et al. comprising of 40 studies found that fusion rates with the use of recombinant human bone morphogenetic protein (rhBMP) were slightly superior compared to fusions without the use of rhBMP (96.6% and 92.5%, respectively) [256]. They found the highest rate of fusion in cases where rhBMP was used in combination with local bone autograft (99.1%).

Baskin et al. [257] conducted the first prospective randomized controlled trial for anterior cervical interbody fusion, comparing recombinant human BMP-2 with iliac crest autograft, both placed within a fibula allograft and supplemented with anterior plating. All 33 patients from both groups were fused by 6 months. At 24 months, the rhBMP-2 group had significantly better improvement in neck ($p < 0.03$) and arm ($p < 0.03$) pain than autograft, had no complications attributable to rhBMP, and had avoided statistically significant pain ($p < 0.007$) from the harvest site at 6 weeks. Boakye et al. [258] in a retrospective review of 23 patients with one- to three-level procedures similarly found 1.05 mg/level of rhBMP-2 in PEEK cages induced solid fusion with good clinical outcomes and no significant morbidity. However ectopic bone formation was observed to occur in three patients who were early on in the series and had received twice that amount. However, many authors have elucidated the need for caution when using rhBMPs in the cervical area. Smucker et al. [259] performed a multivariate analysis and found patients receiving rhBMP-2 to have a 10.1-fold increase in risk for swelling complication compared to those that did not receive rhBMP-2. In a retrospective review of 151 patients undergoing anterior cervical fusion using rhBMP-2 with plating, Shields et al. [260] found 23.2% had suffered complications including hematoma, swelling, dysphagia, and increased hospital stay. The authors noted their three-and-a-half fold dose of bone morphogenetic protein (2.1 mg BMP/level) compared to Baskin et al. (0.6 mg/level) as a possible reason, perhaps causing an excessive inflammatory response in the initial phase of bone healing. Tumialan et al. [261] noted a decrease in dysphagia with a dosage reduction from 2.1 mg/level down to 0.7 mg/level, and from multilevel compared to single-level procedures. In a prospective non-randomized study Buttermann [262] compared BMP-2 with allograft against iliac crest autograft in anterior cervical discectomy with fusion. Using 0.9 mg BMP/level he found that although both groups demonstrated similar clinical improvements, 50% of the BMP group suffered dysphagia caused by neck swelling compared to 14% autograft. Khajavi et al. [263] also supported rhBMP use for ACDF. In a letter, Dickerman et al. [264] reported clinical success

with a dose of 1.05 mg/level insulated by a DBM putty and delivered in PEEK cages, as these measures provide containment of the BMPs.

In the meta-analysis and systematic review of Wen et al. [265], for the better fusion rate, rhBMP-2 was recommended to ACDF, even in the dose of <0.7 mg/level. Their analysis showed that although rhBMP-2 could improve fusion, rhBMP-2 may induce higher complication rates compared to that in non-rhBMP-2, especially at high and middle doses of rhBMP-2 (>0.7 mg/level). rhBMP-2 improved fusion rate especially in multi-level ACDF, but the influence did not show any level dependence. Therefore, when an ACDF due to the multi-level has a high risk of nonunion, rhBMP-2 may be an option of increasing the fusion.

In a study that contained rhBMP-2 using thrombin glue and bioabsorbable spacers, no graft-related complications occurred [266]. Vaidya et al. [267] reviewed the cases of 22 patients who received 1 mg rhBMP-2/level contained in polyetheretherketone (PEEK) cages and 24 patients who received allograft spacer with demineralized bone matrix. BMP performed well radiographically with probable fusion in 100% of patients at 12 months. Allograft attained similar results. BMP had statistically significant dysphagia associated with anterior swelling, with severity observed to be dose dependent. Compared to allograft, the BMP procedure was three times more expensive, and so was ceased. In another study by the same lead author [268], rhBMP-2 with allograft for cervical fusion was ceased despite 100% fusion, due to a 33% incidence of graft subsidence. Costs associated with the implementation of BMP for anterior cervical fusion may be prohibitive, however it remains to be seen how cost-effective they are compared to autograft and other alternatives long-term. Further investigation is required in determining the optimal dose and delivery method of BMP for anterior cervical fusion, whether a measurable clinical advantage is produced, and if so, in whom these procedures should be performed.

Platelet Rich Plasma (PRP)

Platelet-rich plasma (PRP) is generally obtained from the patient's blood [159]. Blood is centrifuged through gradient density, and the resulting blood platelets are mixed with thrombin and/or calcium chloride. Hence, PRP includes an important concentration of platelets and fibrinogen, and is believed to contain several growth factors including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), transforming growth factor (TGF), insulin-like growth factor (IGF), epidermal growth factor EGF), epithelial cell growth factor (EGR), and hepatocyte growth factor (HGF) [269–272]. Even if PRP shows limited infectious risks and adverse effects by its origin (autologous blood), it does not present any mechanical resistance and is not validated as a stand-alone bone substitute [273]. PRP is rather used as a supplement to other materials [274–276].

Recently, the use of PRP in spinal fusion surgery was investigated; several systematic reviews have evaluated the effectiveness of PRP for spinal fusion. The use of PRP has been very successful in enhancing spinal fusion in an animal model [277] but the use of PRP to augment bone fusion after spinal deformity correction in humans is still controversial; Kubota et al. [278] in their prospective randomized control trial of posterolateral lumbar fusion surgery found a high fusion rate in the PRP group compared to control. Tarantino et al. [279] in their prospective cohort study of 21 patients who underwent posterolateral arthrodesis with implantation of cancellous bone substitute soaked with PRP found that PRP increases the rate of fusion and bone density adding osteoinductive and osteoconductive effect. Also, Hartmann et al. [280] in their 15 controlled cohort patients who underwent anterior spinal fusion after suffering lumbar or spinal injury found that PRP increased the rate of fusion and high-density value within the region of fusion compared to control. On the other hand, Feiz-Erfan et al. [281] in their double-blind randomized study with platelet-gel concentrate or control

group of 50 patients undergoing anterior cervical microdiscectomy, allograft fusion, and plating found that platelet-gel concentrate had no consistent effect in promoting early fusion in cervical disc disease relative to control. Carreon et al. [282] in their retrospective cohort study of 76 patients who underwent posterolateral lumbar fusion with autologous iliac crest bone graft mixed with autologous growth factor (AGF) and control found a high nonunion rate in the AGF group compared to control. Also, Jenis et al. [283] in their prospective study of patients undergoing lumbar spinal fusion using iliac crest autograft and allograft combined with autogenous growth factors (AGF) found a similar outcome in terms of bone fusion, pain, and functional improvement between the two groups. Elder et al. [284] concluded that there is insufficient evidence to recommend the widespread use of PRP in spinal fusion surgery. Park et al. [234] reported that PRP might promote human spinal fusion if the platelet count or the concentration of growth factors in the PRP increases. The meta-analysis of Cai et al. [285] concluded that PRP promotes bone fusion and new bone formation well within 6 months of implantation, and after 6 months, the effect normalizes. Also, a minimum concentration of platelet in PRP, 5 times higher than that in the peripheral blood, has a stimulatory effect on bone fusion. The review of Manini et al. [286] also considered PRP to have a positive effect on the early fusion of the spine. However, because of the limited data, they not concluded that PRP treatment would stimulate a shortened time of fusion.

Future studies to focus much on the stable carrier of PRP which allows the continuous release of growth factor to the local tissue for a long period, optimal implantation time, frequency of implantation, and bioavailability of the growth factors. More high-quality RCTs are needed to further evaluate the effect of PRP on fusion rate especially in cervical spine.

Mesenchymal Stem Cells (MSCs)

In recent years, there has been a rising interest in the use of stem cells products as bone graft substitute for spine fusions and other orthopedic procedures [287–293]. Stem cells or progenitor cells are a renewable population of undifferentiated cells, resident within their niche in most adult tissues, which can give rise to the various types of mature cells and they can be driven toward specific tissue or cellular differentiation with growth factors and mitogens [294, 295]. For spine procedures, mesenchymal stem cells (MSCs) and osteogenic progenitor cells may be differentiated into osteoblasts that can help achieve fusion by providing cells that participate in bone formation and may also produce osteoinductive molecules [296, 297]. They can be isolated from autologous and allogeneic sources then expanded to provide a constant and viable source of bone graft substitute alternative to ICBG. Autologous sources for MSC include the iliac crests, vertebral bodies, and adipose tissues. Iliac crest remains an optimal source of autologous MSCs, with MSCs representing 0.0017–0.0201% of the cell population [298]. Unlike other bone graft substitutes available in the market today, mesenchymal stem cells and progenitor cells are believed to possess the osteogenic and osteoinductive properties of ICBG. In addition, when mix with other bone graft extenders as carriers or fillers, they can add osteoconductivity to the final stem cell products [299].

In animal models, high concentrations of cultured autologous bone marrow MSCs produced similar rates of posterolateral fusions compared to autograft when combined with a hydroxyapatite-granule carrier [300].

Perhaps the most common source of MSCs is bone marrow aspirate (BMA) that is harvested by aspirating the vertebral body or iliac crest bone marrow. The aspirate is then typically concentrated to allow for the isolation of MSCs that can then be implanted for use in spinal fusion. It is believed that the autologous MSCs isolated from BMA can provide osteogenic and osteoinductive properties like ICBG without the morbidity of harvesting ICBG. Despite existing animal data and the wide availability of BMA harvesting systems today, it is still unclear if autologous BMA can provide similar spine fusions rates and clinical outcomes compared with ICBG, particularly in the setting of cervical spine fusion.

Hsieh et al. [301] identified six case series that evaluated the use of autologous BMA in conjunction with various types of graft materials [198, 302–306], and two retrospective cohort studies that evaluated the effectiveness of autologous stem cells harvested from the iliac crest (unconcentrated bone marrow aspirate [BMA] in one study [307] and cancellous bone marrow [CBM] in the other [199]) compared with hydroxyapatite for use with anterior cervical discectomy and fusion (ACDF). Solid fusion was achieved in 84% to 100% of patients across six case series with follow-up periods ranging from 6 months to a mean 36 months. At final follow-up (range 6 months to mean 36 months), similar proportions of patients (0–3% across studies) had evidence of radiographic pseudarthrosis across five studies [198, 302, 304–306]; one study reported a pseudarthrosis rate of 16% at 12 months (1 of the 5 patients was symptomatic) [303]. Revision was required in 0–4% of patients across four studies [198, 303, 304, 306]. Barber et al. [307] reported a significantly greater fusion rate, defined as the percentage of levels fused per month, in patients treated with autologous BMA compared with HA collagen sponge (9.8 vs. 6.1%, p = 0.003); evidence of pseudarthrosis at latest radiographic follow-up had a similar proportion of patients in both groups (24.1% overall). In the cohort study comparing cancellous bone marrow (CBM) versus hydroxyapatite [199] the proportion of patients with pseudarthrosis was similarly low in both groups at final follow-up.

Hsieh et al. [308] evaluated also the use of allogenic stem cells in cervical spinal fusion and they identified five studies: one retrospective cohort comparing Osteocel with allograft [309] and four case series. The case series include one case series using Osteocel Plus [310], two case series using Trinity Evolution with local autograft [311, 312], and one using Vivigen allograft [313]. Anterior cervical discectomy and fusion (ACDF) was performed in three of the four series; a variety of procedures was used in the fourth case series. In the retrospective cohort study (N. 114), overall fusion rates were somewhat lower in the Osteocel group compared with the Verigraft allograft controls (88 vs. 95%), but statistical significance was not achieved; a similar pattern was seen for those receiving intervention at one level (86.2 vs. 96.6%) only. Fusion between the treatment groups was similar for 2-level procedures. Across case series, criteria and definitions of fusion varied and fusion frequency varied across timeframes and intervention products. At 6 months, they varied with rates in two series of Trinity Evolution of 66% and 79%, respectively, and of 100% in the Vivigen series; by 12 months, fusion was seen in 89 and 94% of Trinity Evolution recipients. At 24 months, the series of Osteocel reported fusion frequency of 87%. The comparative retrospective cohort study reported more nonunion for Map3 recipients compared with allograft recipients (12.3 vs. 5.3%) at 12 months, but results did not reach statistical significance [309]. Across case series, rates of nonunion varied substantially: at 6 months, the two series of Trinity Evolution reported nonunion rates of 34.4% [311] and 21.4% [312], with lower rates by 12 months (10.6 and 6.5%). While the small series of Vivigen reported no nonunion [313], the series of Osteocel reported 18% at 24 months with 13% at >24 months [310]. No revision surgeries were reported across three series [310–312].

Mesenchymal stem cells and osteogenic progenitor cells can be derived from patient's own bone marrows or adipose tissues. However, the quantity and quality of the autogenic stem cells may be limited by the patients' age and biology similar to ICBG [314]. On the other hand, allogenic stem cells can be derived from a donor and expanded in cultures then optimized for osteogenic differentiations in a controlled process [295]. This process may circumvent the concerns about quantity and quality of the cells that can implanted in spine fusion surgeries.

Evidence for the efficacy of autologous or allogenic MSCs to promote cervical arthrodesis is severely limited due to the poor quality of existing evidence. Small sample sizes, inconsistencies between studies in outcome measurements, lack of comparative interventions, and an overall substantial risk of study bias, prevent any firm conclusions from being drawn at this time. High-quality clinical studies are clearly needed to evaluate the efficacy, safety, and cost associated with MSCs for cervical spine fusions.

Synthetic Peptides

The combined use of bioactive peptides and porous implants or materials has led to a new generation of fusion extenders [315]. Perhaps the most well-known, P-15™ is a 15-residue synthetic polypeptide which acts as a binding factor for osteogenic cells on a domain of type I collagen [316, 317].The P-15™ peptide has been studied in a variety of animal models and is reported to enhance cell migration, induce osteoblast differentiation, and influence a pathway which results in new bone formation [318].

It has been used in dental applications for over a decade and has recently been adopted for use in the spine. I-Factor™ (Cerapedics, Inc., Westminster, CO) is a proprietary composite consisting of P-15 adsorbed to anorganic bovine bone mineral (ABM). ABM consists of smooth, porous particles of "pure" deproteinated hydroxyapatite [316]. This bone graft combination of ABM and P-15 is claimed to facilitate bone formation. IFactor™ is indicated for use in skeletally mature patients for reconstruction of a degenerated cervical disc at one level from C3–C4 to C6–C7 following single-level discectomy for intractable radiculopathy. I-Factor™ peptide enhanced bone graft putty must be used inside an allograft bone ring and with supplemental anterior plate fixation [319]. One report was available describing a single blind randomized non-inferiority control trial [320]. This study compared i-Factor™ (N = 165) to iliac crest autograft (N = 154) for use in single-level ACDF procedures for cervical radiculopathy. At 12 months follow-up both groups demonstrated a high fusion rate (88.97% for i-Factor and 85.82% for autograft, non-inferiority $p = 0.0004$) and equivalence with respect to the other clinical outcomes. The authors concluded that i-Factor met all FDA non-inferiority criteria and demonstrated safety and efficacy in this patient group.

Conclusion

There are several acceptable and promising material options for anterior cervical spine fusion. Although many studies have investigated the effectiveness of these substrates, currently, no option is conclusively superior to strut iliac crest bone autograft combined with rigid anterior plate fixation. Autograft remains the standard of care for anterior cervical spine fusion, allowing a good stability with higher incidence of radiographic fusion rate, near to 100% and excellent clinical outcomes. For this reason, the autograft technique is still considered the gold standard between a high number of materials and techniques in cervical spine fusion. Moreover, the use of autograft avoids the risk of infection, disease transmission, and histocompatibility differences associated with allograft. Allograft is somewhat substandard in comparison to autograft due to increased graft complication and reduced fusion rates, but it's still an acceptable option especially when combined with plating. Allograft works well as an osteoconductive scaffold with some degree of osteoinductive properties. Demineralized bone matrix is associated with variable outcomes and is dependent upon the formulation used and differences in factors such as product batch.

Other bone graft substitutes may offer a viable alternative, in fact the use of alternative devices avoids the harvest of strut iliac tri-cortical graft without complications at the bone donor site. Titanium may offer a satisfactory alternative, with good fusion rates and low rate of complications. Ceramics achieve acceptable fusion rates and clinical outcomes at a reasonable price and is thus another acceptable alternative to autograft; they appear to be a promising group of bone graft extenders, especially when combined with bone marrow aspirates. Bone morphogenetic proteins (BMPs) are an unrefined graft technology with developing guidelines on dosage and delivery. Although BMPs demonstrate impressive osteoinductive properties, the most published and extensively studied group of rhBMPs likely came closest to dethroning iliac crest autograft, when promising early reports emerged over a decade ago. However, their complication profile, as well recent studies re-evaluating the risks/benefits with BMP use, require physicians to reconsider their routine application in spinal fusion procedures. Data on stem cell-based products and the synthetic peptides is currently very limited, hav-

ing only recently popped up on the horizon. More better quality studies are required comparing these substitutes and extenders not just with autografts, but also with each other.

New research is being conducted to find materials with increased bone grafting properties (by doping existing materials or developing new materials), improving strength/Young's modulus, and developing novel ideas to prevent further postoperative complications by improving range of motion, decreasing pain, distributing anatomic forces to decrease adjacent segment disease, and minimizing the necessity for additional spinal surgery. New developments in biomaterials for spinal implants and the advent of new technologies, like 3D printed patient-specific implants, have made incredible progress in biocompatibility of spinal tools. Spine surgeons should remain vigilant regarding the current literature and technological advancements in spinal materials and procedures.

Nevertheless, with such a plethora of available options, and with such diversity in the data on their application under different scenarios and in different combinations, it becomes necessary for spine surgeons to scrutinize all options carefully before adopting them in clinical practice.

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Endoscopic Cervical Spine Surgery

9

Joachim M. Oertel and Benedikt W. Burkhardt

Introduction

History of Spinal Endoscopy

The purpose of this section is to give the reader a comprehensive overview of the process of endoscopic spine surgery with a special emphasis on the cervical spine.

Since the early nineteenth century, when P. Bozzini developed his "Lichtleiter" the endoscope is under continuous evaluation and evolution to become a fundamental tool of the surgical armamentarium. Another major step in this evolution was the invention of rigid rod lens telescopes by H. Hopkins in 1965. Karl Storz, founder of Karl Storz Company in Tuttlingen, Germany collaborated with Hopkins and replaced the light source from the tip of the endoscope with an external device [1]. Further development included the introduction of video cameras for imaging. Direct observing was not necessary any longer because of external monitors and new light sources enabling the surgeon to view images on a screen. However, video cameras were very large in the initial phase of endoscopy with very low resolution. Nowadays, image quality is not in standard definition (SD) anymore. It is available in high definition (HD) with approximately 2,000,000 pixels which are superior to SD in identifying anatomical structures and endoscopic data is collected digitally [2]. Recently even 4K technology was introduced. Thus, at present, the endoscope offers distinct advantages in many different surgical fields, such as gynecology, urology, neurosurgery, ENT and many others.

It took some time for this new technology to arrive in spine surgery. The origin of endoscopic spine surgery dates back to the 1970s. In 1975, Hijikata et al. from Japan performed an indirect lumbar decompression procedure via resection of disc material via a posterolateral approach using a Craig cannula. In those procedures, the surgeon had to rely on the intraoperative discography and the ideal position of the cannula. Intraoperative visualization of the disc material via an optic device was not available. The overall clinical success rate reported by Hijikata was 64%.

Inspired by the study performed by Hijikata, Schreiber and Suezawa from Switzerland published their experience using a series of cannulas with an increasing inner diameter of up to 8 mm facilitating a faster nucleotomy. In the following years, different concepts were introduced to this new field of minimally invasive spine surgery. A key step was the central nucleotomy which could be either performed chemically, mechanically or by laser vaporization. However, none of these techniques for nucleotomy prevailed its relevance for the majority of spine diseases.

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It was Kambin and his colleagues who extensively studied the anatomical relationship of the vertebral body, the disc space, the transversing, and the exiting nerve root to define a safe zone to perform endoscopic lumbar disc procedures, the "Kambin triangle". In the 1990s, Kambin et al. and Mathews were the first surgeons who independently reported their experience in using an endoscope for visualization of the surgical field via an extraforaminal approach. At the early stage of endoscopic spine surgery, the image quality was far inferior compared to the operating microscope. This disadvantage and the fact that endoscopic instruments were very different from standard open or microsurgical instruments led to a lot of criticism for endoscopic spine surgery.

It became evident that endoscopic spine surgery offers several advantages, and one of those was the minimal trauma to the muscle and soft tissue during the approach. Patients reported less postoperative pain and required less pain medication. However, the surgical technique and instruments were different compared to the open or microsurgical technique. With the philosophy of minimally invasive spine surgery in mind, surgeons overcame the issue of the instrument and combined microsurgical techniques, and used tubular retractors. Magnifying loupe and microscope were used for visualization. In the late 1990s, it was Destandau from France and Foley from the USA who developed a tubular retractor system with integrated endoscopic visualization. At that time, this technique allowed to surgically treat a bigger spectrum of spinal disorders compared to the percutaneous endoscopic techniques. In 2006, Oertel reported his results using the EasyGO system, which was the first endoscopic tubular retractor system that offered HD visualization of the surgical field [2–4].

The percutaneous endoscopic technique and systems were also refined throughout the years. The current systems consist of a working channel with integrated rigid optics and a variety of instruments including drill and Kerrison to approach the spine either via a transforaminal, posterolateral, or interlaminar approach.

Most of these techniques were applied in the lumbar spine. The first endoscopic cervical procedures were reported in the late 1990s. At this time anterior endoscopic procedures were attempted, but due to technical limitations of the equipment and serious complications, this technique was not taken up widely. The posterior approach to the cervical spine for circumscribed laminectomies and foraminectomies was a well-established concept using open microsurgical techniques. In 2002, Fessler reported his experience using an endoscopic assisted tubular retractor system for the treatment of cervical radiculopathy [5]. In 2008, Ruetten reported clinical results of two separate series of patients who were either treated via an endoscopic anterior cervical transdiscal approach or an endoscopic posterior cervical foraminotomy [6]. Since then endoscopic cervical procedures were constantly refined. Main focus of the present chapter is on the current status of these techniques. Other surgical techniques which address the cervical spine such as endoscopic assisted transoral odontoidectomy, endoscopic transnasal resection of the odontoid, or endoscopic posterior fixation also evolved and are continuously refined but are not addressed in this chapter.

Terminology of the Endoscopic Cervical Spine Equipment and Techniques

Endoscopic cervical spine techniques depend highly on the endoscopic equipment, and the surgical technique enabled by this specific equipment.

Frequently spine surgeons differentiate between so called "full-endoscopic" and "endoscopic assisted" surgery. The exact meaning of this terminology is variable between surgeons. Also it is frequently used in an inaccurate way.

The term "full-endoscopic" refers to a surgical technique/procedure which is performed under continuous endoscopic visualization. No others tools for visualization such as microscope or magnifying glasses are applied. An example of a full-endoscopic procedure is the endoscopic third ventriculostomy or the laparoscopic cholecystectomy.

The term "endoscopic assisted" refers to a technique on which the majority of the procedure is performed without endoscopic visualization. The endoscope for example is used sequentially during the procedure to inspect a certain area of the surgical field or to manipulate under endoscopic visualization partially. An example of this would be the microsurgical resection of a vestibular schwannoma. The majority of the procedure is performed under microscopic visualization, the endoscopic assisted part is when the surgeon inspects the nerve and the intrameatal area using the 30° angulated telescope. An additional manipulation and tumor resection under endoscopic visualization might be performed at this stage of the procedure.

In spine surgery, frequently the terminology is used in a different context. According to the property of the endoscopic equipment, three different concepts are available.

The *percutaneous full-endoscopic* system (see Fig. 9.1) is characterized by a single tube which consists of an integrated telescope channel, a separated working channel and a separate channel for irrigation and light conduction. Many different "full-endoscopic" systems are available. All use continuous saline irrigation throughout the procedure. The outer diameter of the working tube is, in general, less than 9 mm which allows a very small incision with a single stich closure.

The *tube based endoscopic systems* are often also referred as "microendoscopic" procedure. These systems combine the use of a tubular work sheath and a rigid endoscope (see Fig. 9.2). The endoscope is inserted into the tubular retractor once the tubular retractor is in place and it can be

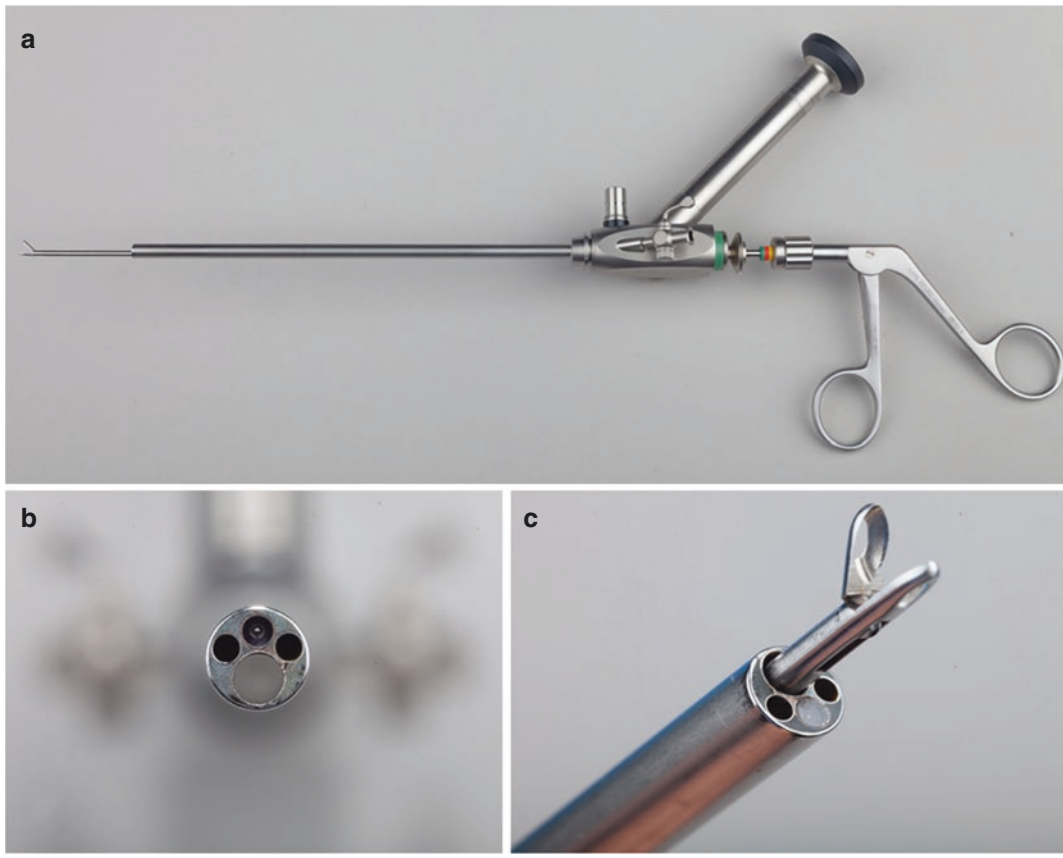

Fig. 9.1 (**a**–**c**) Example of a full endoscopic system. Please note the single working tube with incorporated telescope, irrigation, suction and working channels

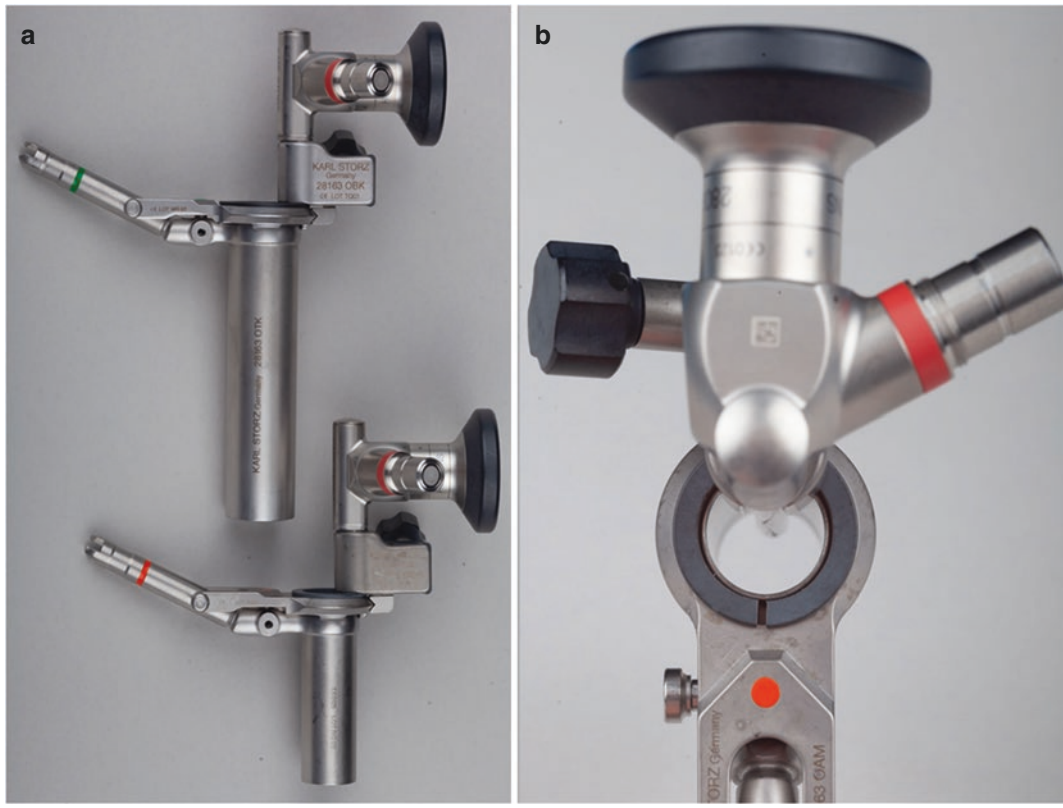

Fig. 9.2 (**a**, **b**) Example of a tube based endoscopic system. Please note the working tube which gives space for telescope and bimanual surgical instrument manipulation within one channel

removed during the procedure at any time. In contrast to the "full-endoscopic spine systems", these procedures are performed "under air" without continuous saline irrigation and allows the use of standard microsurgical instruments in a bimanual fashion which facilitates a steep learning curve [7]. From the point of visualization, these procedures are also full endoscopic procedures. However, particularly in the beginning of the application of these systems the optical quality of the endoscopes was poor. So the majority of procedures were performed under microscopic visualization through the working tube. This is the reason why this surgical technique is still frequently called "microendoscopic".

Biportal endoscopic systems are characterized by the use of two separate working portals. One portal is used to place the endoscope and a separate working channel is used to bring instruments close to the pathology. During surgery, constant saline irrigation is applied for clear visualization of the instruments.

Selection of Surgical Approach and Surgical Technique

While in the lumbar spine, the techniques can grossly be divided in transforaminal and interlaminar approaches, the options in the cervical spine are more diverging. Many pathologies in the cervical spine can be approached by different routes and by different surgical techniques. The authors of this chapter try to give a comprehensive overview which does not mean that alternative surgical techniques are excluded.

In general, the posterior approaches are better described and characterized in the cervical spine. According to the surgical technique, one has to consider the underlying disorder. At the cervical spine, three major disorders can be addressed via endoscopic procedures: disc herniation, cervical spinal canal stenosis, and osseous foraminal stenosis. Depending on the exact position of the structure that compresses the nerve root or spinal cord the surgeon chooses the approach for the procedure.

Strictly posterior spinal canal stenosis such as in hypertrophy of the ligamentum flavum, a posterior approach is preferred.

For lateral disc herniation and osseous foraminal stenosis, a posterior approach is more suitable, because the trajectory of instruments and tissue manipulation will not conflict with the thecal sac and spinal cord. It is a very easy straight forward technique in these indications. Most of the endoscopic spine surgeons will favor a posterior route for these cases.

However, some experienced endoscopic surgeons favor an anterior approach by selective uncoforaminectomy and report very high success rates.

A central or mediolateral localized pathology might not be addressed safely via a posterior approach this would require manipulation and traction at the spinal cord. In these cases, an anterior approach is preferred.

There are different surgical techniques for the nerve root and spinal canal decompression which can be performed via an anterior or posterior approach.

There are two main surgical technique which can be performed via an endoscopic posterior approach: posterior cervical foraminotomy (EPCF) and cervical laminoplasty and laminectomy (EPCL).

The two main surgical techniques which can be performed via an endoscopic anterior approach: microendoscopic discectomy and fusion, and full-endoscopic discectomy via transdiscal or transcorporal approach.

Posterior Approaches

Posterior Cervical Laminoforaminotomy (PCLF)

In the hands of the authors of this chapter, the posterior endoscopic foraminectomy is by far the most frequent endoscopic procedure in the cervical spine.

In 1951, Frykholm was the first who described the posterior foraminotomy. The procedure was performed for surgical treatment of patients who complained about cervical radiculopathy. Frykholm performed a partial resection of the medial margin of the facet joint to decompress the cervical nerve root [8]. At that time, this new technique was novel compared to the well-established operative techniques such as laminectomy with and without chiseling of retrospondylophytes, which was performed for dorsal decompression of the cervical spine. Conventional posterior approaches have the disadvantage of detaching the extensor cervical muscles from the laminae and the spinous process. Detaching of the paraspinal muscles can cause severe muscle trauma and can come along with postoperative complications like axial neck pain, shoulder pain, loss of lordosis, or even spinal instability [9, 10]. The posterior cervical laminoforaminotomy technique applied microsurgical principles to the dorsal approach to the cervical spine for the first time. It enables bony decompression of the nerve root in cases of foraminal stenosis or removal of a lateral disc herniation with the advantage of less risk of injuries to the spinal cord. It does not allow the removal of medioventral nerve compressing lesions. Nonetheless through the development of the anterior approach to the cervical spine (ACDF) by Smith and Robinson and modified by Cloward in 1955 eluded the problem of the spinal cord being in the way of access to the pathology [11, 12].

The anterior approach became the gold standard for the treatment of degenerative cervical

disc disease and cervical stenosis within the next decades because it offered the option to perform bilateral nerve root decompression, restoration of disc height, and realignment of the cervical spine. The posterior approach became obsolete by the time. However, ACDF has some drawbacks which became evident within the years after its first introduction. Accelerated degeneration of the segments adjacent to the fusion was seen following the ACDF procedure. The loss of a motion due to fusion was considered the main cause for this finding, even though there is still no consensus. Also, ACDF is associated with approach-related morbidity and graft-related complications. A widespread movement came into the development of new techniques for the treatment of degenerative cervical diseases. Besides alternative to segmental fusion in the anterior approach which mostly centred in artificial disc replacement, the posterior foraminotomy was rediscovered and improved upon [13]. The aim to reduce iatrogenic trauma related to the surgical approach has led to the evaluation of new retractors and endoscopes in spinal surgery. Endoscopic lumbar discectomy has been shown to produce comparable results to standard microsurgical discectomy with the advantage of less muscular trauma and thereby less back pain [4]. However, till today there is still no consensus about the ideal surgical approach for the treatment of cervical radiculopathy. Depending on the individual morphology of the pathology, advantages and disadvantages of both approaches and surgical techniques have to be kept in mind when deciding which approach is ideal. In cases, in which the cause of compression is located lateral to the thecal sac, or intraforaminal, the posterior cervical foraminotomy has shown to be effective and safe [14]. This paragraph presents an overview of the endoscopic posterior cervical laminoforaminotomy (EPCLF). It will address the surgical technique and equipment that is necessary to perform EPCLF and gives a short review of clinical results.

Indications

- Persistent or intolerable radicular pain and/or neurological deficits due to
- Lateral disc herniation [15–17]
- Osseous foraminal stenosis [15, 18]
- Zygapophyseal joint cysts with compression of the cervical nerve root [19]
- Rare unilateral pathologies: bleeding, epidural empyema
- Mono or bisegmental unilateral pathologies
- Nerve root compression and contraindication for anterior approaches (e.g. tracheostomy, cervical radiation therapy before surgery)

Contraindication

- Isolated neck pain
- Medial localized disc herniation with spinal cord compression
- Osseous central spinal canal stenosis
- Evidence of instabilities and/or deformities
- Discogenic pain resulting in neck pain and none-radicular arm pain

Surgical Equipment for Full-Endoscopic PCLF

- General equipment for endoscopic surgery: monitor, camera unit, light source and cable, documentation system, irrigation fluid including feed system
- Motor for the bone cutter
- Radiofrequency generator for the usage of a bendable bipolar radiofrequency electrode
- Rod lenses with a 20°–30° angled view and an external diameter of 5–8 mm depending on the system used
- Access instruments with a dilator and working tube with an external diameter of 5–8 mm depending on the system used
- Endoscopic surgical instruments: rongeurs, scissors, punches, dissector, and various bone cutters with a diameter of less than 5 mm
- Fluoroscopy (C-arm)

Surgical Equipment for Tube-Based PCLF

- Tubular dilatation system
- Tubular retractor which can be connected to a table-mounted holding arm
- 30° Hopkins® Forward-Oblique telescopes which can be inserted into the tubular retractor (i.e. EasyGO- system Karl Storz GmbH & Co KG, Tuttlingen, Germany)
- Video digital endoscopy unit with a monitor, camera, and data archiving system (e.g.

AIDA® compact NEO, Karl Storz GmbH & Co. KG, Tuttlingen, Germany)
- Microsurgical instrument and high-speed diamond burr
- Fluoroscopy (C-arm)

Surgical Technique for Posterior Endoscopic Cervical Laminoforaminotomy

The main steps of the full-endoscopic and microendoscopic procedures vary regarding nuances of approach, tissue dilation, and the instruments used to decompress the nerval structures. The overall principle to perform decompression is the same.

After the induction of general endotracheal anaesthesia, the patient is placed in a prone position or a sitting position and preoperative antibiotics are administered. In a prone position, the head is fixed in a three-point Mayfield headrest, slightly inclined, and elevated above heart level to reduce venous congestion. Reduced blood loss results in better visualization of the surgical field and a shorter operative time. Therefore, the sitting position is preferred by some surgeons. However, the sitting position is discussed controversially, even though the risk of air embolus is reduced due to the minimally invasive approach and short operative time. Further, the ability to identify the cervicothoracic junction via fluoroscopy is improved in sitting position. In any endoscopic approach, it is of crucial importance to identify exactly the level of the surgical target.

Because of the limitations of the semisitting approach, most surgeons prefer the patient in prone position. For an optimal position, the patient is put in prone position, the abdomen is decompressed and the head with the surgical field is elevated to reduce venous congestion. The screen is positioned opposite to the surgeon and after application of sterile draping, the surgical table is prepared (Fig. 9.3).

The affected segment is identified via lateral fluoroscopy. For ideal identification, the shoulders may be pulled down and fixed by using medical duct tape in a prone position. After identification of the ideal trajectory towards the diseased segment, the skin incision is marked. The skin incision is placed about 2 cm parallel to the midline. Depending on the endoscopic system, it may vary from 7 to 14 mm and should not be made too small because of the risk of skin

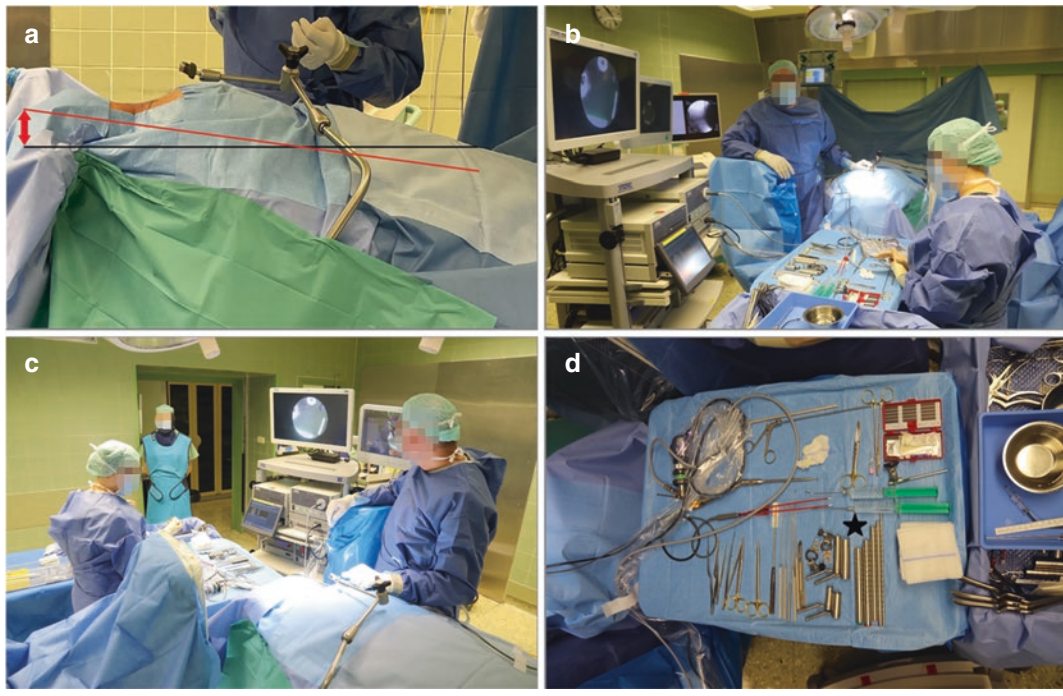

Fig. 9.3 (**a**–**d**) The patient is put in prone position with the head and cervical spine elevated to avoid venous congestion. The surgical table is prepared and the screen is positioned opposite to the surgeon

ischemia. In the case of a single-level surgery, the skin incision is planned in a fashion that the centre of the working sheath points in a direct way at the pathology, i.e. neuroforamen of the affected segment. In case of a two-level surgery, the skin incision is recommended to be made halfway between the two affected segments. The working sheath could be adjusted in its angle towards both facet joints. In the rare case of a three-level surgery, the skin incision is at the middle segment.

In contrast to standard open approaches, the surgical planning of an endoscopic approach is of utmost importance. If the skin incision is made too far cranial or caudal or medial or lateral, the success of the whole surgical procedure might be at risk. If the skin incision is too far medial, the spinous process might force the endoscope too far lateral. If the skin incision is too far lateral, the decompression of the nerve root might only be possible with a complete facetectomy. If the skin incision is too far cranial or caudal, the decompression of the nerve root might be slowed by significant amounts of subcutaneous fat tissue since the work sheath remains in suboptimal contact to the lamina. Also exposure of the epidural veins which are usually anterior to the nerve roots might be required. Thus, the surgical procedure should be planned far ahead and then the skin incision should be at an optimal position (Fig. 9.4).

By the skin incision, the muscle fascia is opened too. The next step of the procedure is the dilation of the muscle with a single dilator or a set of dilators in case of the microendoscopic procedure. Beginning with the smallest dilator the vertebral arch was punctured. The tip of each dilator should have firm contact with the vertebral arch respectively the facet joint. While holding the dilator(s) in place a particular working sheath is

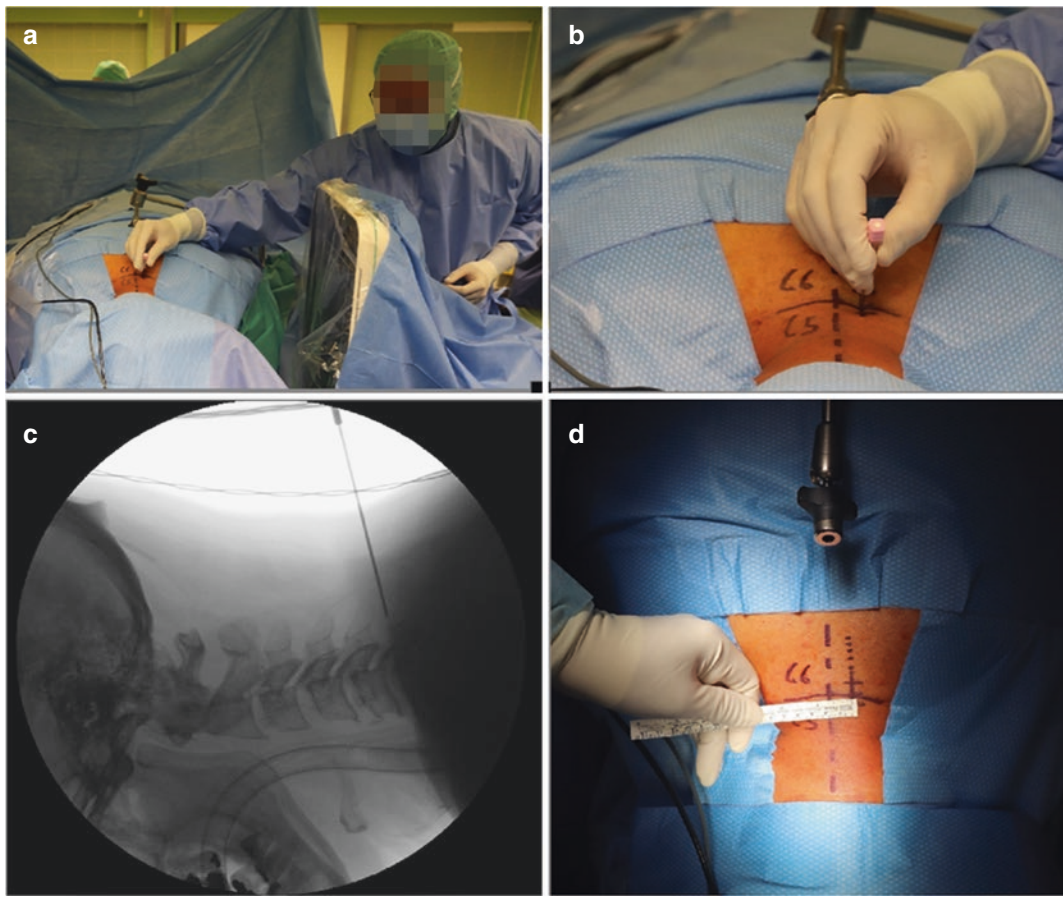

Fig. 9.4 (**a**–**d**) Positioning of the puncture needle in the direct straight approach to the target area. Marking of the skin insicion 2 cm lateral to the midline to avoid problems with the spinous processes

introduced. The whole process of muscle dilation and insertion of a working cannula is done under the control of lateral fluoroscopy. In a microendoscopic procedure, the working sheath is connected to a table-mounted holding arm and fixed in its ideal position. In the case of a full-endoscopic procedure, the working cannula is not fixed and held by the surgeon (Fig. 9.5).

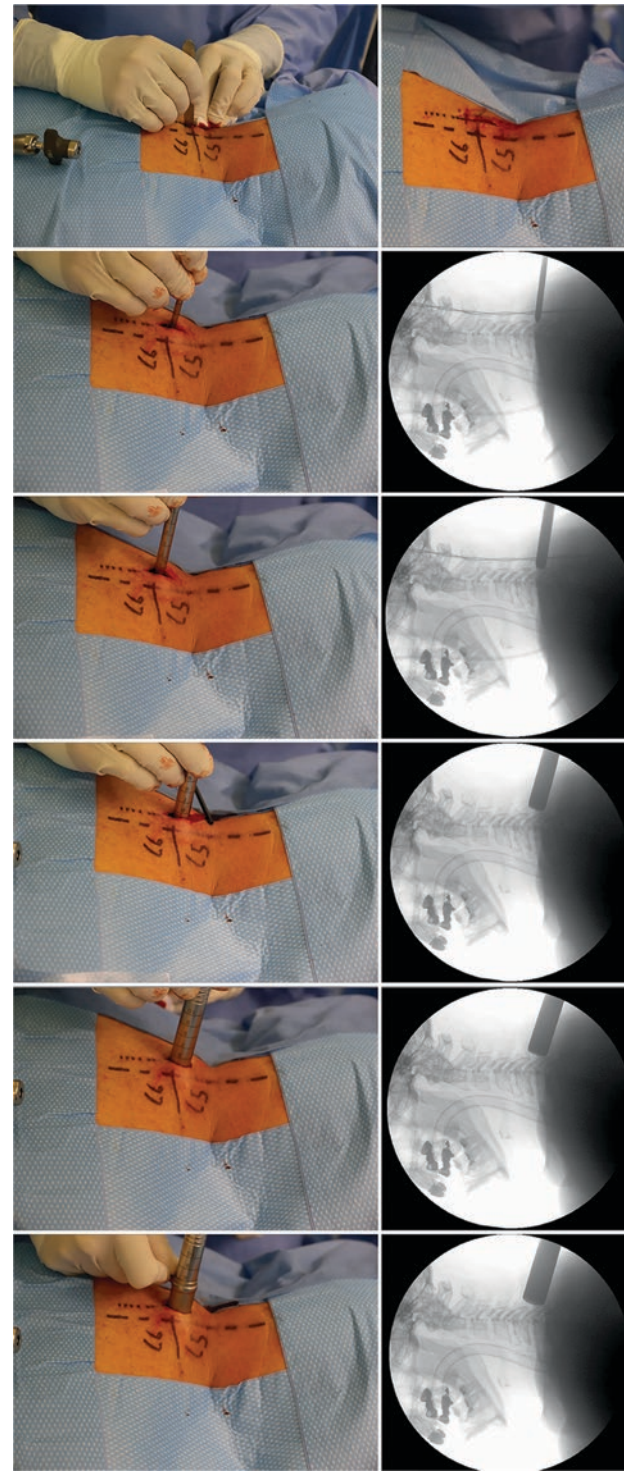

Fig. 9.5 The skin incision is done paramedian, the muscle fascia is dissected. The dilators are used to subsequently dilate the muscle tissue and insert the work sheath. On the right side, the position of the dilator and work sheath in relation to the cervical spine is shown by lateral fluoroscopy

Once the working cannula/sheath is in an ideal position, the endoscope is inserted to visualize the surgical field. The optic points towards the midline. Remnant muscle and fat tissue is removed and the lamina and the facet joint are exposed. The next step is the removal of the soft tissue and the exposing of the vertebral arch and the facet joint. A radiofrequency probe, bipolar forceps, or grasping forceps can be used for this step of the procedure. The superior lamina and medial portion of the facet joint are thinned out with a diamond drill before the ligamentum flavum is resected. Through this technique, the lateral section of the dural sac with its outgoing nerve root is depicted (Fig. 9.6).

The nerve root is decompressed from medial to lateral towards the neuroforamen by removing the medial half of the facet joint. Heavy bleeding can be caused by compressed epidural veins at the junction of nerve root and thecal sac. To control the intraoperative bleeding coagulation gently, compression via sponges and cotton, a combination of both or surgical hemostatic agents for hemostasis is recommended. After successful decompression of the nerve root, the surgical field is irrigated and the working sheath carefully pulled out. The wound is closed by fascia-, subcutaneous- and subcuticular sutures.

Clinical Success of EPCLF

- The overall clinical success rate of treatment of cervical radiculopathy due to lateral disc herniation or osseous foraminal stenosis is 93.6% for full-endoscopic procedures and 89.9% for microendoscopic procedures [16, 20, 21].
- The difference is not statistically significant between the two procedures.
- Patients with prior cervical spine surgery have a lower clinical success rate [22].

Possible Complications of EPCLF

- EPCLF is associated with few complications. According to the existing body of literature, the following complication might occur: epidural hematoma if the origin of bleeding is

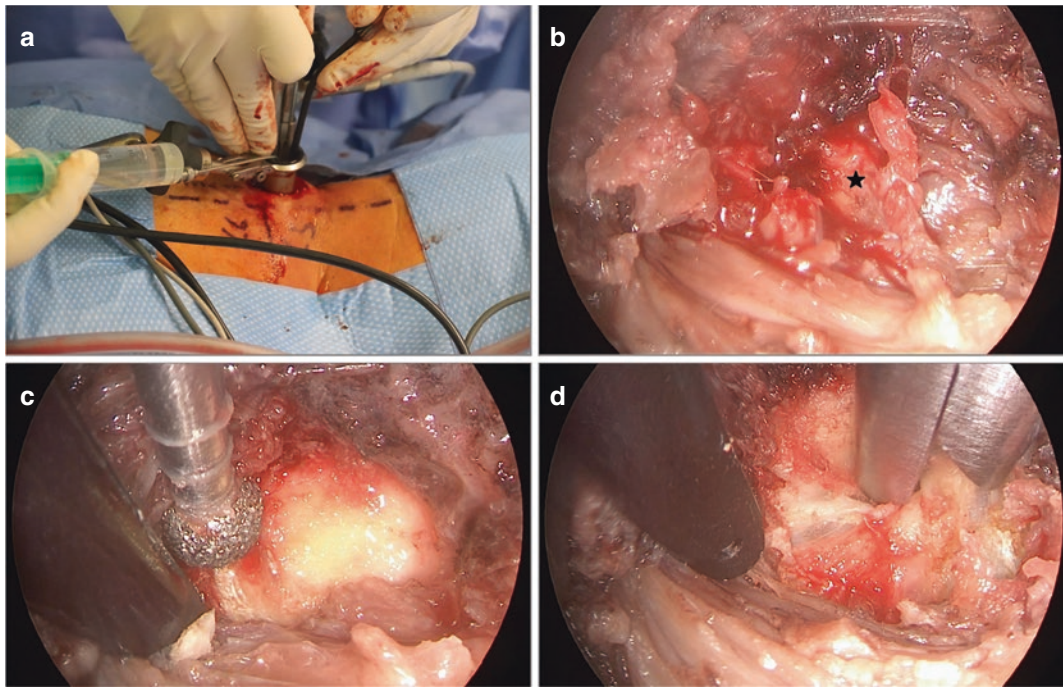

Fig. 9.6 The inserted tube with endoscope. Subsequent exposure of the bone, the ligamentum flavum and resection of the lateral part of the ligamentum flavum to expose the nerve root. (**a**) Bimanual handling of instruments through the seath. (**b**) Soft tissue to be removed. (**c**) Bone decompression via drill. (**d**) Fat removal with punch

inaccessible, dural injury, CSF fistula, contralateral neurogenic thoracic outlet syndrome, recurrent dis herniation, transient nerve root palsy, superficial wound healing problems,
- The overall complication rate is 3.0–6.1% for full-endoscopic procedures, and 3.5% for microendoscopic procedures [23, 24].
- The difference is not statistically significant between the two procedures.

Reoperation Following Endoscopic PCLF

- The overall reoperation rate is 6.1% for full-endoscopic, and 5.3% for microendoscopic procedures.
- The reoperation rate is higher in a patient with previous cervical spine surgery [22]
- The difference is not statistically significant between the two procedures [23].

Advantages of Endoscopic PCLF Compared to Open PCLF

There is significant heterogeneity in studies comparing the open procedure to endoscopic PCF, but it appears that EPCF offer

- Decreased hospital length of stay
- Postoperative analgesic usage
- Reduced blood loss

Microendoscopic Cervical Laminotomy and Hemilaminectomy

Cervical spinal stenosis is one of the common causes of cervical spondylotic myelopathy (CSM). It is the natural result of degenerative compression on the spinal cord. CSM is a common disorder in people more than 55 years of age. Patients often experience a progressive and stepwise deterioration of neurological function such as ataxia and problems with fine motor skills, dexterity, and signs reflecting upper motor neuron disease [25]. Intervention is often controversially discussed, especially when symptoms are absent or minimal [26]. However, surgical intervention is often pursued as symptoms progress but controversy still exists over the optimal choice of surgery for spinal cord decompression [27, 28]. Posterior laminectomy decompression has been described as a treatment for CSM since the 1940s. It requires the stripping of the posterior cervical muscles and detachment of supraspinous and interspinous ligamentous structures (posterior tension band) from the bony parts of the cervical vertebra. Patients may experience postoperative neck pain from iatrogenic muscle injury and muscle spasms. Multilevel laminectomies are associated with an increased risk of 6–47% for postlaminectomy kyphosis [9, 29]. Fusion may be required if kyphotic deformity or instability is existing before decompression.

Postoperative instability and iatrogenic morbidity have forced spine surgeons to explore more efficacious ways of decompression. Cervical open-door laminoplasty allows for adequate posterior decompression of the spinal cord while retaining the posterior elements it was described by Hirabayashi and Satomi first [30]. This technique minimizes the amount of removal of the posterior tension band and, hence, decreases the risk for postoperative instability and kyphosis and therefore the risks of posterior cervical fusion. Multiple techniques for performing a cervical laminoplasty have been described such as expansive "open door," a midline "French Door," En Bloc resection, spinous process splitting, and Z-Plasty [31–34].

The comparative outcomes, however, are still a matter of controversy no definitive literature shows its superiority to laminectomy in conjunction with a posterior cervical fusion. Minimally invasive techniques have been refined constantly. The goal of these techniques is to achieve comparable clinical outcomes as traditional open surgeries but through smaller incisions and with less muscle dissection and tissue traumatization. Minimized muscle trauma and devascularization favors low rates of wound infections, less blood loss, less postoperative pain, and a shorter hospitalization time [35]. Different techniques for microendoscopic cervical laminoplasty and laminectomy (MECL) have been reported in the literature. Minamide reported a bilateral decompression technique via a unilateral approach [36]. Yakubi described a technique for a

partial laminectomy by performing two paramedian approaches for ipsilateral decompression [37]. Dahdaleh performed single or multilevel hemilaminotomies for the treatment of CSM [38]. Recently Oshima reported about a midline approach for interlaminar decompression.

The following sections will give a short introduction to these techniques.

Indications

- Cervical stenosis due to hypertrophy of the ligamentum flavum

Contraindications

- Cervical myelopathy due to tumor, trauma, infection
- Severe ossification of the posterior longitudinal ligament (OPLL)
- Deformity due to rheumatoid arthritis,
- Destructive spondylo-arthropathies
- Cervical kyphosis (preoperative)

Surgical Equipment for MECL

- Tubular dilatation system
- Tubular retractor which can be connected to a table-mounted holding arm
- 30° Hopkins® Forward-Oblique telescopes which can be inserted into the tubular retractor (i.e. EasyGO- system Karl Storz GmbH & Co KG, Tuttlingen, Germany)
- Video digital endoscopy unit with a monitor, camera, and data archiving system (e.g. AIDA® compact NEO, Karl Storz GmbH & Co. KG, Tuttlingen, Germany)
- Microsurgical instrument and high-speed diamond burr
- Fluoroscopy (C-arm)

Surgical Technique for Microendoscopic Cervical Laminotomy and Hemilaminectomy

Microendoscopic Laminoplasty: The procedure is performed in general endotracheal anesthesia. The patient is placed in the prone position and the head is fixed in a Mayfield head clamp. The neck is fixed in a neutral position. The fluoroscopic C-arm is recommended to be positioned into the surgical field so that lateral fluoroscopic images can be obtained intraoperatively. The level of interest is marked on the side of the approach. A skin incision of approximately 18 mm in length is made at the spinal level which has to be decompressed. The muscle fascia is split before the tubular dilation system is introduced. The paravertebral cervical muscles are gently dilated before the working channel is then passed over the dilators and connected to the flexible holding arm mounted to the table side rail. Confirmation of correct working channel position has to be obtained by lateral fluoroscopy before removal of dilators. The tubular retractor is pending perpendicular to the lamina and facet joints and points parallel to the intervertebral disc space. The endoscope is introduced into the working channel and bipolar cautery is used to remove any residual muscular and soft tissues overlying the lamina and facet joints. After depicting the bony edges of the lamina a small angled dissector is used to confirm inter-lamina space and the medial aspect of the facet joint. First, the lamina near to the ligamentum flavum is thinned out whit a highspeed diamond drill and then resected with a Kerrison punch. After identifying the attachment of the ligamentum flavum of the superior lamina the drilling and resection are continued by identifying the superior attachment of the inferior lamina. The ligamentum flavum is left intact. The working channel is then turned medially and downward to obtain a contralateral view (see Fig. 9.7). Next, the basis of the spinous process is drilled before laminotomy can be performed. The angled endoscopic view in combination with a turn of the working channel allows for excellent visualization to the contralateral side. Again, the ligamentum flavum is left intact to protect the dura while laminotomy is performed. When all bony structures are removed from the ligamentum flavum the loose ligamentum flavum was inspected. Attention is paid to removing the ligamentum flavum gently without applying too much pressure on the underlying dura or causing a dural tear. A small angled curette or nerve hook is ideal to mobilize it from its attachment. Decompression is finished when dural pulsation is visible. In the case of a two-level procedure, the working channel can be turned towards the

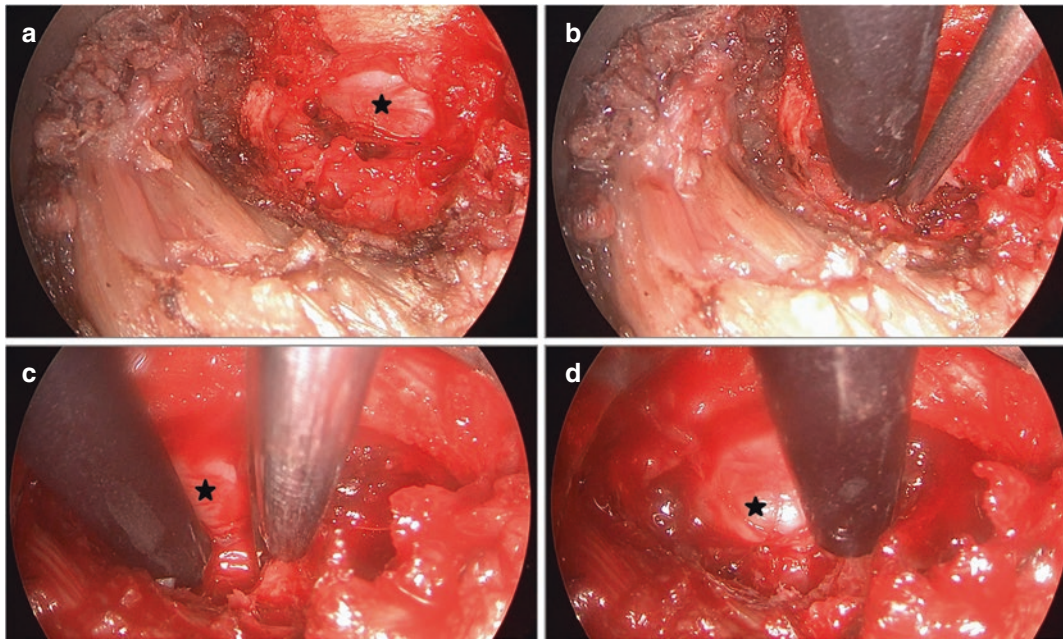

Fig. 9.7 Exposure of the lateral dura. Decompression of the nerve root from medial to lateral until the nerve root is completely decompressed. (**a**) Endoscopic view. (**b**) Laminotomy. (**c**) Flavectomy. (**d**) Dural exposure completely decompressed

adjacent segment either cranially or caudally. For a four-level procedure, two separate skin incisions are necessary to reach all segments sufficiently. The placement of a drain is optional before wound closure.

Clinical Success of MECL

- The JOA score increased from 10.1 to 14.3 points at 5 years of follow-up.
- The JOA recovery rate was 58.6
- The pain intensity decreased from 5.1 to 2.0 points.

Possible Complications of MECL

- EPCLF is associated with few complications. According to the existing body of literature, the following complication might occur: epidural hematoma if the origin of bleeding is inaccessible, temporary nerve root palsy, dural injury, superficial wound healing problems,
- The overall complication rate is 6.0% for microendoscopic cervical laminotomy.

Advantages of MECL Compared to Open Cervical Laminotomy

- Postoperative axial neck pain is significantly lower following MECL compared to open procedures. Less intraoperative blood loss compared to open procedures [39].
- At 5-year follow-up, cervical alignment showed increased lordosis and is favorable in the MECL compared to open cervical laminotomy which was associated with postoperative kyphosis [39, 40].

Anterior Approach

Cervical Microendoscopic Discectomy and Fusion

Anterior cervical discectomy and fusion (ACDF) was first described in the 1950s. Since then it became the standard treatment for degenerative cervical disc disease [11, 12, 41]. However, ACDF is associated with certain disadvantages graft sub-

sidence, nonfusion with consecutive pseudarthrosis, recurrent laryngeal nerve palsy, esophageal injury, and dysphagia [42, 43]. Anterior cervical discectomy without fusion (ACD) offers good clinical results but has a higher risk of postoperative segmental kyphosis and postoperative axial pain [44]. Minimally invasive techniques were developed to reduce tissue trauma while approaching the spine. It has been proved that minimally invasive techniques for approaches to spinal pathologies preserve healthy tissue and reduce surgical associated morbidity, shorten the operative time, decreased complication rates, reduces hospital length of stay, cause less postoperative use of narcotics, enable faster patient recovery and offer lower costs [45, 46]. Depending on the material, minimally invasive techniques can be limited to certain pathologies and indications. The percutaneous endoscopic cervical discectomy as an alternative to ACD is considered to be indicated in cervical disc herniations which have to be soft and contained or non-contained but without sequestration and contained by the posterior ligament [47, 48]. Cervical microendoscopic discectomy and fusion (CMEDF) is an alternative technique for ACDF that reduces the surgical morbidity of conventional surgery but without limited indications for the treatment of cervical degenerative pathologies. This chapter will deliver an impression of the endoscopic technique and equipment that is necessary to perform CMEDF and gives a short review of clinical results.

Indications

- Central and lateral cervical disc herniations or osteophytes associated with a neck injury
- Discogenic radiculopathy
- Discogenic myelopathy
- Spondylotic myelopathy
- Discogenic myeloradiculopathy [49–51]
- Axial neck pain, lost cervical lordosis, reduced disc space height
- Magnetic resonance image (MRI), computed tomographic (CT) scan, or post myelogram CT-scan that is positive for spinal cord or nerve root compressing pathologies consistent with dermatome of clinical symptoms
- Failed improvement of symptoms after conservative treatment for 12 weeks
- Surgery can be performed from mono- to trisegmental pathologies that involve the levels C3–4, C4–5, C5–6, and C6–7

Contraindications

- Compressive pathology located behind the vertebral body (OPLL)
- Severe spinal canal stenosis

Surgical Equipment for MECDF

- Tubular retractor which can be connected to a table-mounted holding arm
- (e.g. METRx, Sofamor Danek, Memphis, USA/EasyGO- system Karl Storz GmbH & Co KG, Tuttlingen, Germany)
- Different endoscopes (i.e. 0°-optic and 30° Hopkins® Forward-Oblique telescopes which can be inserted into the tubular retractor).
- Video digital endoscopy unit with a monitor, camera, and data archiving system (e.g. AIDA® compact NEO, Karl Storz GmbH & Co. KG, Tuttlingen, Germany)
- Microsurgical instrument and highspeed diamond burr
- 5-mm osteotome
- Cage (e.g. Polyetheretherketone (PEEK)/titanium)
- Fluroscopy (C-arm)

Surgical Technique for Microendoscopic Cervical Discectomy and Fusion

The MECDF procedure is performed under general anesthesia with orotracheal intubation. Occasionally the procedure can be performed under local anesthesia in younger patients. Preoperative antibiotics are admitted and dexamethasone might be administered to minimize airway and esophageal edema. The patient is positioned supine with the neck slightly extended. The head might be rigidly affixed via pins in a Mayfield holder. The shoulders are gently tapped down to enhance visualization of the lower cervical spine with intraoperative lateral fluoroscopy. The segment(s) to be operated on can be identified by intraoperative C-arm fluoroscopy. In case

of a two- or three-level procedure, a small (18–20 mm) transverse skin incision is recommended to be placed at the midpoint of the operative distance. The prevertebral anatomical structures have the characteristics to be movable. Skin incision has to be made deep to the platysma before subplatysmal structures can be dissected by the index and the middle finger. The larynx is pushed toward the opposite side with the index and middle fingers while muscle and the carotid were held laterally. Next fingers were slipped inside towards the front of the vertebral body until the anterior cervical spine and edge of the disc is palpated. Optional artery forceps are placed through the skin incision between both fingers with its blunt tip kept at the vertebral leading edge by creating an access path. Next step the endoscopic tubular dilators were introduced sequentially under fluoroscopic guidance between the carotid artery and the esophagus. A working trocar with an outer diameter of about 18–20 mm is introduced at last and fixed to a mechanical flexible holding arm that is attached to the operating table. After confirming the correct level via lateral C-arm-fluoroscopy the dilators are removed and an endoscope system of choice is installed. The annulus fibrosus of the disc is incised by using a micro-knife before the nucleus pulposus is removed. Osteophytes can be removed by a Kerisson punch or diamond drill. Continuous irrigation with saline solution is recommended to remove the remaining fragment and to prevent thermal nerve damage in case of drilling. An arterial or any kind of source of bleeding from paraspinal muscular can be controlled by bipolar forceps. Micrograsper, micro forceps, dissectors, and small curettes are used to remove the rudiment of the disc of the vertebral body. Special curettes are available to dissect the remnant cartilage endplates and enlarge the intervertebral space. Since distraction screws are not placed manual cervical distraction is performed to widen the interbody space by pushing up the head gently and pulling down the arms at the same time. Another technique for distraction is placing a 5 mm osteotome in the disc followed by its twisting. A cage of choice is placed under fluoroscopic guidance and optionally filled with bone graft substitutes (see Fig. 9.8). After removal of the tubular retractor, the subcutaneous tissue is closed in standard fashion with a skin adhesive and steristrips the placement of a suctions drain is optional.

Clinical Success of MECDF

- The JOA score increased from 7.2 to 13.1 points at 3 years of follow-up.
- Disc height after fusion showed minimal subsidence from 7.9 to 7.8 mm
- The pain intensity decreased from 2.8 to 0.6 points.
- Clinical success according to Odoms was noted in 86–91% of patients at 3-year follow-up [49–51]
- Increased disc height and high fusion rates [51]

Possible Complications of MECDF

- EPCLF is associated with few complications. According to the existing body of literature the following complication might occur which are equivalent to the complications of the traditional open approach [49, 50]
- Vascular injury
- Esophageal injury
- Trachea injury
- Thyroid injury
- Laryngeal nerve injury
- Postoperative hemorrhage

Advantages of MECDF Compared to Open ACDF

- Less traction on the soft tissue.
- Less manipulation at the trachea and esophageal
- Lower self-reported laryngopharyngeal complications such as dysphonia and dysphagia [49–51].
- Less usage of postoperative analgetic doses

Anterior Percutaneous Endoscopic Cervical Discectomy via Transdiscal or Transcorporeal Approach

The standard treatment for cervical soft disc herniation in spine surgery is anterior cervical discectomy and fusion ACDF. The majority of

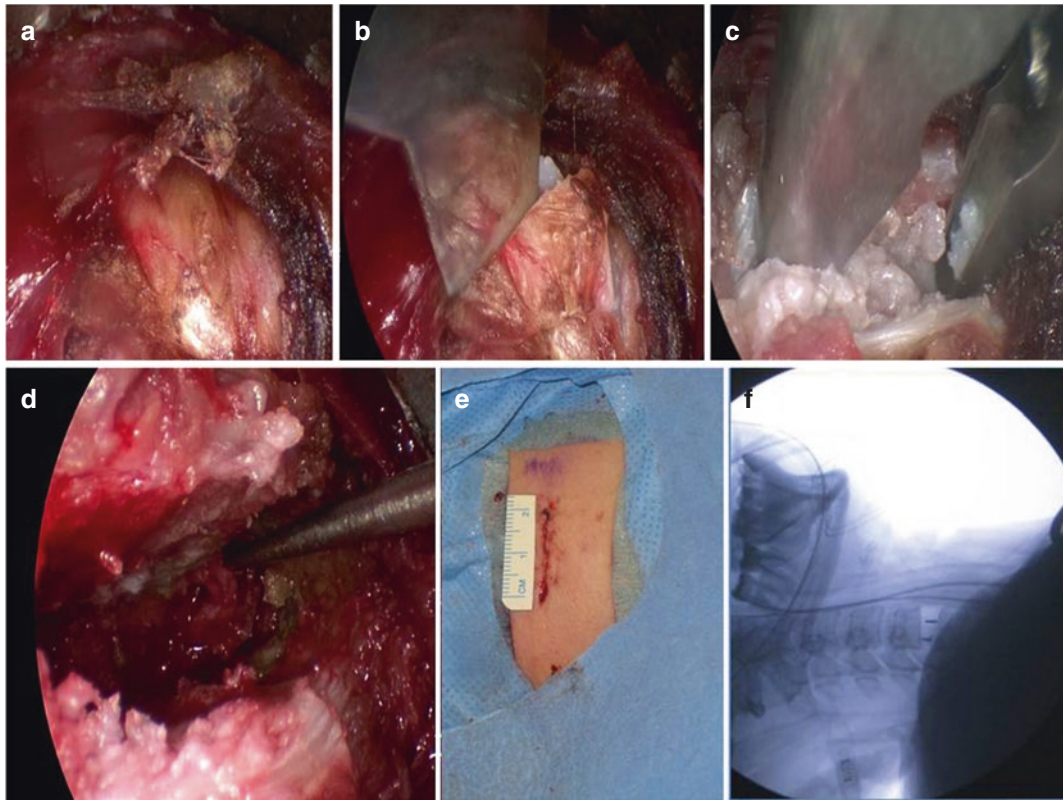

Fig. 9.8 (**a**–**d**) Intraoperative images of a MECDF procedure [51]. Consecutive numbers are in clockwise order, orientation of intraoperative images is up = cranial, right = left side of the body. (**a**) Exposure of the anterior ligament. (**b**) Incision of the disc annulus. (**c**) Removal of disc material with Pituitary forceps. (**d**) Removal of sequester with hook. (**e**) Size of skin incision. (**f**) Lateral Xray after cage insertion

surgeons perform ACDF because the theory behind it is that fusion prevents segmental instability and kyphosis due to reconstruction of empty disc space by implanting a graft out of an autologous iliac crest, a cage (e.g. PEEK, titan), or disk prosthesis. Surgeons are concerned that cervical alignment would be distorted due to a collapse of the operated segment without fusion which could result in axial neck pain and radicular arm pain in case of a compromised neuroforamen. In the past decades, there was less discussion about the imperative of fusion. Little research about the outcome after ACD compared to ACDF although postoperative clinical results seem similar [52, 53]. Since the first description of cervical percutaneous discectomy by Tajima et al. many minimally invasive techniques were developed to treat cervical spine disease [54]. Anterior percutaneous cervical procedures for decompression of the nerval structures can be divided into techniques with endoscopic visualization and non-visualized techniques. The objective of both techniques is to reduce the nerve compressing volume. Nonvisualized techniques can reduce the volume either via aspiration of the nucleus pulposus [55, 56], via radiofrequency [57, 58] or via radiofrequency [59]. The success of surgery depends on adequate decompression of the nerve root. Therefore, the non-visualized techniques are criticized for their lack of identifying free disc fragments and assessing the status of decompression intraoperatively. The anterior percutaneous endoscopic cervical discectomy (APECD) combines the advantages of a minimally invasive approach via a needle and the inspection of the intradiscal space via endoscopic visualization.

Further holmium: Yttrium-Aluminium-Garnet (YAG) laser can be used via this technique for decompressive and thermoannuloplasty. Although a percutaneous cervical stabilization with an expandable holder can be performed via this approach.

A loss of disc height was noted for the transdiscal approach due to the iatrogenic disc space damage, therefore the transcorporeal approach was developed to preserve the disc while approaching the nerve root or spinal cord compression pathology. While the initial transdiscal approach was mainly used for the treatment of soft disc disease the transcorporeal approach enlarged the spectrum of pathologies to cervical myelopathy.

The idea behind it is to maintain the disc height after decompression. This chapter will deliver an impression of the endoscopic technique and equipment that is necessary to perform APECD and gives a short review of clinical results.

Indications

- Soft cervical disc herniation at any zone of the cervical disc causing unilateral radiculopathy.
- Cervical radiculopathy and myelopathy unresponsive to conservative management over 12 weeks [60]
- Magnetic resonance imaging (MRI) computed tomography (CT) that is positive for mediolateral localized monosegmental contained or non-contained soft disc herniation
- Segments C3–Th1;
- Ventral and posterior disc height must be at least 4 mm [6, 48, 61, 62]

Contraindication

- Osseous foraminal stenosis
- Intraforaminal disc herniation
- Calcified disc or disc height of less than 4 mm
- Central canal stenosis with broad disc bulging
- Craniocaudal dis sequestering of more than half of the vertebral body
- Evidence of instability and/or deformity
- Isolated neck pain
- Foraminal stenosis without disc herniation
- Previous operation at the same segment
- Severe osteoporosis for transcorporeal approach

Surgical Equipment for APECD

- Endoscopic system (e.g. Karl Storz GmbH & Co KG, Tuttlingen, Germany) Outer diameter 4.0 mm/working length 12 cm/central working channel 1.9 mm
- Video digital endoscopy unit with a camera
- 0° endoscopic optic
- Special endoscopic instruments (micro forceps, trephine, etc.)
- Discography: Telebrix (Guerbert, France), Contrast agent: Indigo carmine (Korean United Pharma, Seoul, Korea)
- Holm-yttrium aluminum garnet YAG) laser (e.g. Trimedyne, Inc., Irvine, CA)
- Fluoroscopy (C-arm) [47, 48, 62]

Surgical Technique of Anterior Transdiscal Percutaneous Endoscopic Cervical Discectomy

The patient can be operated on under local anesthesia with light sedation so the surgeon can talk to the patient and be aware of any neurological changes. However, if preoperatively there is a sign that the patient may suffer from intraoperative psychological or physical stress because of the introduction of the endoscopic system, general anesthesia can be used as an alternative instead. Preoperative antibiotics are admitted and dexamethasone might be administered to minimize airway and esophageal edema. The patient is placed in a supine position with the neck mildly extended on a radiolucent table. Intraoperatively fluoroscopic guidance (C-arm) the segment of operation is carefully identified in lateral and a.p. X-ray using a radiopaque instrument. The skin incision is marked and with a felt-tipped pen and the skin and subcutaneous tissue were infiltrated with local anesthetic (e.g. 1% xylocaine, 1% lidocaine). Generally, the approach is at the contralateral side about 2–5 mm paramedian from the midline. The anatomical structures are very mobile due to the compartmentalization and ideal for an anterior percutaneous approach. The goal is to displace the trachea and esophagal medially

and the carotid artery and internal jugular vein laterally. First, the pulsation of the carotid artery should be felt, then the visceral structures (thyroid, trachea, larynx, and esophageal) can be mobilized to the opposite side with the index finger. The middle finger is then slipped inside towards the cervical spine till the protruding ring of the disc is felt between both plane forefronts of the vertebral bodies. Under continuous fluoroscopy an 18-gauge puncture needle is then carefully inserted in the space between the visceral and vascular compartment into the disc space close to the posterior body line of the posterior part of the disc, trying to preserve the longus coli muscle. A next step of the surgery a discography (e.g. 10 mL Telebrix and about 0.5 mL of contrast media e.g. indigo carmine is injected to specify the posterior part of the disc) is performed to determine the annular tear, to confirm the presence of soft disc herniation, and to stain the nucleus pulposus into blue in contrast with the neural tissue. Then a guidewire is inserted to replace the puncture needle and is skin incision of 3 mm is made to allow the dilation of the skin and soft tissue via serial progressive dilator (2–5 mm). By this technique, soft tissue is prevented from trauma and the approach-related pain is reduced. Finally, the tip of the working cannula is firmly placed to reach the posterior part of the disc. Its correct position is confirmed via fluoroscopy. The distance between the tip of the working cannula and the end of the posterior longitudinal ligament represents the working depth for the endoscopic instruments. Next, the endoscope is inserted into the working cannula. Continuous saline mixed with antibiotics (e.g. cefazolin) is used as irrigation. First endoscopic images of the intradiscal cavity are visible on a monitor. Under endoscopic visualization, the herniated disc fragments are removed with micro forceps and trephine without injuring the spinal cord. The risk of instability or local kyphosis may be avoided by leaving the anterior fraction of the disc intact while removing the posterior aspect. If necessary the endplate and parts of the posterior edge of the vertebral body are ablated via Holmium yttrium–aluminum–garnet (Ho: YAG) laser. Further, the laser can be used to shrink the remaining disc herniation and to vaporize abnormal annular structures. A low dose of energy for laser with 2 J and 10 Hz is recommended, therefore YAG-laser is about 0.3–0.5 mm deep. The laser may be useful to create an intradiscal cavity for the exploration of adequate decompression. At the end of decompression, the posterior longitudinal ligament or dura should be visible. Discoplasty of the working cannula surrounding disc tissue may be performed by YAG-laser before removing the working cannula. The position of the laser should be frequently checked via endoscope and fluoroscopy to prevent spinal cord or nerve root injury. Further, an expandable holder or autologous iliac bone graft can be introduced for stabilization [63]. The initial diameter of the holder is 3.3 mm while it is inserted into the intradiscal cavity. It can be expanded up to 7.0 mm in diameter inside the disc by rotating the expander rotational handle. It is then fixed to the disc. The correct position is controlled under fluoroscopic guidance. If the procedure is performed under local anesthesia the surgeon can interact with the patient and ask whether the preoperative pain has disappeared or was relieved during surgery. The endoscope and working cannula were carefully pulled out. The remaining irrigation and blood are drained before the wound is closed in a standard fashion.

Surgical Technique of Anterior Transcorporeal Percutaneous Endoscopic Cervical Discectomy

Of note, there are several modifications of the transcorporeal approach, which will not be addressed in the chapter. The following paragraph should give the reader an overview of this surgical technique.

The patient is operated on under general anesthesia with the head in a neutral position. Preoperative antibiotics are administered and dexamethasone might be administered to minimize airway and esophageal edema. The patient is placed in a supine position with the neck mildly extended on a radiolucent table. For better visualization of the C6–T1 segments, the shoulders are pulled caudally and affixed to the bedside rail with tape. Intraoperatively fluoroscopic guidance

(C-arm) the segment of operation is carefully identified in lateral and a.p. X-ray using a radiopaque instrument. The cervical level of interest is marked, most surgeons prefer to approach the lesion from the affected side. After determination of the incision site, a 10 mm transverse incision is performed medial to the sternocleidomastoid muscle slightly below the diseased level. After blunt dissection, a stepwise transcorporeal approach is performed. At first, a blunt puncture-needle is inserted in a cranially and medially trajectory on the anterior border of the vertebral body. After confirmation of correct positioning via fluoroscopy, the blunt K-wire is replaced by a sharp stylet. The puncture-needle is then advanced until the tip reaches the posterosuperior edge of the vertebral body. The sharp stylet is replaced by a blunt guidewire before a dilator is inserted. The trephine is inserted and endoscopic working sheath. Under endoscopic visualization, a diamond high-speed drill is then used to enlarge the hole using the former trajectory A blunt hook is used to inspect whether the posterior wall of the vertebral body is opened. In case of intractable bleeding from cancellous bone, bone wax is smeared on the endoscopic burr to facilitate hemostasis. After the opening of the posterior wall of the vertebral body, the disc herniation is identified using a nerve hook. The herniated nucleus pulposus is then removed with a rongeur, inspection of the surface of the dura is performed to ensure whether the neural decompression is adequate. After hemostasis is achieved the instruments and endoscopic working sheath are removed. The skin is closed subcuticular suturing and skin clue [64].

Clinical Outcome of APECD

- Excellent or good functional recovery according to MacNab Criteria by the self-reported outcome in 74–97% of patients [6, 17, 20, 47, 48, 61, 65–69]
- Significant decrease in arm- and neck pain on the visual analog scale (VAS)
- Significant improvement concerning Neck Disability Index (NDI)
- The average time before returning to work 10–28 days
- Significantly decrease in disc height
- Postoperative development of segmental kyphosis and instability remains unclear
- About 2% of patients need additional open surgery

Possible Complications of APECD

- Vascular injury: Carotid artery or jugular vein injury (dissection, rupture) [47]
- Esophageal injury
- Trachea injury
- Thyroid injury
- Laryngeal nerve injury [70]
- Dysphagia [71]
- Postoperative temporary headache due to prolonged high irrigation pressure [17, 47]
- Decreased disc height (decreased via transcorporeal approach)
- Discitis [70]
- The overall rate of complications for the transcorporeal approach is 5.3–8.6% [72, 73]
- The overall rate of complications for the transdiscal approach varies from 0 to 15% [17, 20, 70]

Advantages of APECD Compared to Open ACDF

- Less traction on the soft tissue.
- Less manipulation at the trachea and esophageal
- Lower self-reported laryngopharyngeal complications such as dysphonia and dysphagia.
- Less usage of postoperative analgetic doses

Disadvantages of APECD Compared to Open ACDF

- Loss of disc height
- Progressive segmental kyphosis
- Loss of vertebral body height in case of transcorporeal approach

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Arthroplasty in the Cervical Spine

10

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Introduction

Cervical spine consists of seven vertebral bodies with intervening discs. The discs and the unique configuration of the posterior zygoapophyseal joints allow a full 3D positioning of the head in the space, while the vertebral bodies provide a protective passage for the spinal cord and vertebral arteries. Degenerative changes in intervertebral discs due to aging or trauma can alter significantly the biomechanics of the cervical spine and lead to compression of nerve roots (i.e. cervical radiculopathy) or spinal cord (i.e. cervical myelopathy). For many years, the only available treatment option for cervical radiculopathy and/or myelopathy has been either discectomy (*anterior cervical discectomy*, ACD) or discectomy and fusion (*anterior cervical discectomy and fusion*, ACDF). Over the past 15 years cervical disc arthroplasty (or *cervical disc replacement*, CDR) has emerged as a viable alternative to fusion and the development of new artificial disc devices has been an area of intense research. The aim of this chapter is to present the current state of this technique, including the results of the best available outcome studies of the most common devices.

Anterior cervical discectomy and fusion (ACDF) surgery was pioneered by Cloward and Smith—Robinson in early 1950s. Following the early encouraging results, the new technique rapidly became the gold standard in treatment of cervical spondylosis and disc degeneration. Numerous recent studies have reported good to excellent results in 70–90% of patients, and a fusion rate of 89% in single level operation [1]. However, despite being a successful and widely used procedure some important drawbacks of this technique have become apparent as more fusions are performed every year throughout the world.

Adjacent segment degeneration is defined as the radiographic appearance of degenerative changes at a level above or below a fused segment. The reported incidence of this phenomenon varies greatly in literature (ranging from 51.1 to 92%) [2]. Despite the very common occurrence of adjacent segment degeneration, only a minority of patients will require surgery at an adjacent level. For this reason, a clear distinction exists in literature between *adjacent segment degeneration* (*ASDegeneration*) and *adjacent segment disease* (*ASDisease*). Adjacent segment disease is defined as adjacent segment

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Table 10.1 Classification of adjacent segment degeneration

	Disc height	Anterior osteophyte formation
Normal	Same as adjacent disc	No anterior osteophyte
Mild	75–100% of normal disc	Just detectable anterior osteophyte
Moderate	50–75% of normal disc	Clear anterior osteophyte <25% of AP diameter of the corresponding vertebral body
Severe	<50% of normal disc	Clear anterior osteophyte >25% of AP diameter of the corresponding vertebral body

degeneration with clinical symptoms (pain or neurologic disorders or both), whilst *adjacent segment degeneration* (*ASDeg*) only refers to the presence of radiographic degenerative changes in the absence of clinical symptoms (Table 10.1).

In 1999, Hilibrand et al. [3] reported on the long-term outcome of 374 patients after single and multiple-level ACDF surgery and observed a constant yearly incidence of ASDisease of 2.9% (range, 0.0–4.8% per year) during the first 10-years after the operation. The Kaplan-Meier survivorship analysis developed by the authors suggested that 13.6% of patients with ACDF will develop ASDisease within the first 5 years after surgery and that 25.6% will have new disease within 10 years after the index procedure. Although the actual reported figures, 11.7% prevalence of ASDisease at 5 years and 19.2% prevalence at 10 years, are slightly lower they provide a good overview of the real extent of the problem. Other authors [1, 4, 5] have confirmed these findings reporting an incidence of ASDis of 25% at 5–10 years after surgery [2].

Although reported data suggest a strong correlation between ACDF surgery and higher risk of ASDisease, this is most likely a multifactorial process. The incidence of degenerative changes in the cervical spine increases with aging. In a seminal study, Boden et al. [6] studied the prevalence of degenerative changes in the cervical spine of 68 asymptomatic volunteers and found that abnormalities were present in 14% of the subjects less than 40 years old and in 28% of those who were older than 40. In a different study on cervical disc herniation and radiculopathy, Henderson et al. [7] noted new radiculopathy at a different level in 9% of 846 patients after posterolateral foraminotomy without fusion at an average of 3 years after surgery. This study is frequently cited by authors who believe that ASDegeneration/ASDisease is part of the normal aging process of the cervical spine and the higher incidence observed in patients treated with ACDF is to be related to an intrinsic genetic predisposition of these patients.

Other factors can also contribute in determining the risk of ASDegeneration. As shown by Nassr and co-workers [8] the insertion of a marking needle during surgery in a disc at the wrong level determined a threefold increase of risk of disc degeneration at that level. Similarly, placement of an anterior plate within 5 mm from the adjacent segment has been shown to be a significant risk factor for adjacent level ossification and degeneration [9, 10]. On the other hand, intrinsic mechanical factors are also involved in the degeneration process. According to Hilibrand et al. [11] the relative risk of ASDis is 3.2 times higher at the C3–C4 and C4–C5 levels than C2–C3 level and 4.9 times higher at C5–C6 and C6–C7 interspaces. Biomechanical analyses have shown an increase of intradiscal pressure (stress) at the levels adjacent to a previous fusion and led to the concept that levels adjacent to a fusion have to compensate for the loss of motion in the fused segment [12]. Finally, more recently a lot of research efforts have been placed in elucidating the role of spinal sagittal alignment on the incidence of ASDegeneration and ultimately ASDisease. Yang et al. have shown that patients with higher values of the occipito-cervical angle are at increased risk of ASDegeneration [13]. On the other hand, other authors have failed to recognized a clear definitive role of cervical spine sagittal alignment on the risk of ASDegeneration and ASDisease [14, 15].

The ultimate goal of cervical disc arthroplasty is to preserve segmental motion in order

to prevent development of ASDisease, thus reducing incidence of secondary surgery. The typical candidate for cervical disc replacement is the young active adult with single level soft disc herniation and intact zygapophyseal joints. Motion preservation at the index level avoids stress raise at the adjacent levels and prevents later adjacent segment degeneration/disease (ASDegeneration/ASDisease). By not achieving fusion, cervical disc replacement also avoids the morbidity of bone graft harvest and typical complications of ACDF surgery, such as pseudoarthrosis, issues caused by anterior cervical plating, and prolonged cervical spine immobilization.

History and Implant Design

Some basic understanding of the history of CDR is of pivotal importance in interpreting present clinical results and evaluating future devices. Many new implants have been developed in recent years, reflecting an increased interest on non-fusion technologies by industry and clinicians. However, over the last 40 years, three fundamental designs have emerged in TDR [16]. These three design philosophies have led to the development of three different prosthetic devices: the PRESTIGE (Medtronic, Inc.), the BRYAN (Medtronic, Inc.), and the ProDisc-C (Synthes-Spine, Inc.). These three implants will be discussed here and will serve as base knowledge to evaluate other available implants.

Early attempts at developing an artificial substitute of the intervertebral disc with stainless steel balls are credited to Ulf Fernstrom and date back to 1960s. The early clinical follow-up of the new technique, however, showed unacceptably high rates of implant migration (88%) and subsidence and led many surgeons to direct their interest towards fusion procedures [17]. Twenty years later, in 1989, B.H. Cummins at the Frenchay Hospital in Bristol, UK, developed the first model of a modern cervical disc arthroplasty. This new device consisted of two pieces of 316L stainless steel with a metal-on-metal ball-and-socket design. The anchoring system consisted of two anterior screws that fixed the device to the vertebral body. Unfortunately, early implants were plagued by high incidence of screws pull-out, dysphagia and implant mobilization [18].

A second-generation device was developed from the original Cummins prosthesis with the name of Frenchay artificial disc in 1998. The anterior profile of the device, the locking screw system and the articulating surface were all completely redesigned and following acquisition by Medtronic, Inc., renamed PRESTIGE I Disc. Several redesigns of the implants have led to the fourth-generation system, PRESTIGE ST, and more recently to the fifth-generation PRESTIGE LP (low profile) disc. Although the metal-on-metal design has not been modified, the articulating mechanism of the PRESTIGE ST has been changed into a coupled, semiconstrained system. The newer PRESTIGE LP model is made of a titanium-ceramic composite and incorporates two endplate rails for extra fixation strength in the vertebral body.

The BRYAN cervical disc (Medtronic, Inc.) was designed by the American neurosurgeon Vincent Bryan from Seattle in 1990s. The concept and design of the BRYAN disc is completely different from the Bristol/PRODISC series. This device consists of two titanium alloy endplates articulating with a polyurethane core. The two titanium endplates are fixed to the bone by a porous titanium layer and stability is achieved through a tight fit of the prosthesis in the milled cavity. The implant has been extensively tested in Europe and received US FDA approval in May 2009.

The third alternative to metal-on-metal implants is represented by the ProDisc-C device (Synthes, Inc.) which has recently obtained the approval for use in the United States. The ProDisc-C system was developed by Dr. Thierry Marnay in France and consists of two cobalt-chrome-molybdenum (CCM) endplates with an UHMWPE articulating surface. It is a ball-and-socket constrained prosthesis and has a central keel for extra fixation in the vertebral body.

Other devices have recently joined the market of cervical TDR. Kineflex-C disc (Spinal Motion, Inc.) and CerviCore disc (Stryker Spine, Inc.) are metal-on-metal implants, whilst PCM (CerviTech, Inc.), DISCOVER (DePuy Spine, Inc.), and the MOBI-C (LDR, Inc.) are metal-on-UHMWPE implants. More recently, the SIMPLIFY disc (Nuvasive, Inc.) gained FDA approval for single and double level disc replacement procedures.

Indications for Use and Contraindications

The rationale of considering CDR rather than a standard fusion procedure (i.e. ACDF) lies in the aim of maintaining the motion of the treated segment and preventing adjacent-segment degeneration and disease. The typical candidate patient for CDR is the young active adult patient with single level symptomatic disc disease (i.e. radiculopathy) from C3 to T1 with intact posterior facet joints. General contraindications are marked reduction of the disc space (<3 mm or <50% of normal disc height) with loss of motion at that level [19, 20], zygapophyseal joint osteoarthritis, significant deformity in the sagittal and coronal plane, clear segmental instability, and infection. Other relative contraindications include rheumatoid arthritis, renal failure, osteoporosis (T-score values < 1 SD), cancer, and preoperative corticosteroid use [21].

Evaluation of sagittal alignment, presence of zygapophyseal joint osteoarthritis and instability is of paramount importance and should be undertaken as routine preoperative assessment in every patient. Standard X-ray films (i.e. AP and lateral view) of the cervical spine and flexion-extension studies are usually sufficient in clarifying the extent of residual movement at the index level and the presence of osteoarthritic changes in the posterior joints.

The role of CDR in patients with axial neck pain has not been clarified yet and therefore disc pathology with no neurological symptoms should not be considered an indication for CDR. European and US trials have enrolled patients 1- or 2-levels cervical radiculopathy due to disc herniation (soft or hard), foraminal osteophytes as well as cervical myelopathy. In our clinical experience the presence of a hard disc herniation should be considered a relative contraindication to TDR due to frequent need of a more extensive disruption of the endplate for a satisfactory clearance of the canal. In both European and North American trials, there has been a strong prevalence of patients enrolled with radiculopathy (77–93%) rather than cervical stenosis/myelopathy. The role of TDR in cervical myelopathy remains controversial [22–24]. According to the authors' clinical experience cervical TDR should be avoided in patients with cervical myelopathy. Complete clearance of the spinal canal and wide decompression of the spinal cord are top priorities in cervical myelopathy surgery and the achievement of a solid and stable fusion if the best single guarantee for a long term success of the decompression.

A summary of the most common indications and contraindications for cervical TDR is shown in Table 10.2. In a recent analysis of 464 consecutive patients undergoing cervical spine surgery treated at a single center by three surgeons specializing in CDR, the rate of CDR eligible patients was 76.7%. The most common reasons for not performing CDR were: anatomy (i.e. severe compromise of disc height and less than 2° ROM at the index level) that may compromise segmental stability and/or CDR functionality (13.79%), insurance denial of coverage (3.23%), and deformity/kyphosis not addressable with CDR (2.80%). Osteoporosis also was considered a contraindication in 0.43% of cases. Two cases were reported with unplanned intra-operative conversion of CDR to ACDF due to: (1) poor ver-

Table 10.2 List of indications and contraindications for TDR

Indications for cervical TDR	*Relative* indications for cervical TDR	Contraindications for cervical TDR
Radiculopathy caused by soft disc herniation	Radiculopathy caused by hard disc herniation	Osteoarthritis of the zygapophyseal joints
	Myelopathy caused by disc herniation	Sagittal malalignment of the cervical spine
	Radiculopathy caused by foraminal osteophytes	Segmental instability
		Infection
		Previous posterior surgery
		Ossification of the Posterior Longitudinal Legament (OPLL)

tebral body endplate quality, (2) anterior inferior vertebral body bevelling with high risk of implant migration [25].

Clinical Studies

BRYAN Disc

The BRYAN disc has the longest clinical and radiological follow-up among cervical TDR devices. The first multicentre study on this device was published in 2002 by Goffin and co-worker as part of a European prospective multicentre trial [26]. The study enrolled 60 patients with cervical radiculopathy or focal myelopathy non responsive to at least 6-weeks of conservative treatment. Exclusion criteria were the presence of sole axial neck pain, malalignment of the cervical spine, previous neck surgery and cervical instability. Only single level implants were used for this study and clinical success rates at 6 months and 1 year were 86 and 90%. Because of the lack of a control group, the authors assumed from the literature a target level of success rate of 85% for ACDF surgery. The number of patient lost at follow-up was significant with only 30 patients available at the 1-year follow-up. No complications directly related to the implant were detected. However, three patients underwent revision operation for prevertebral hematoma drainage, posterior foraminotomy for residual compression, and posterior laminectomy for residual myelopathy.

In a second study, Goffin and colleagues [27] expanded their original study with a second group of patients treated with two levels TDR. The study reported the results for 103 patients in the single-level group and 43 patients in the two-level group at 2 years follow-up. Success rates for the single-level group were 90%, 86%, and 90% at 6 months, 1 year and 2 years follow-up respectively. Patients in the two-level group had success rates of 82% at 6 months, and 96% at 1 year. No device failure or subsidence was reported in this second study and an average postoperative range of motion of 7.9° per level in flexion-extension was recorded. Movement was maintained in 87.8% of the single-level patients and 85.7% of two-level patients. Four complications were reported including one case of prevertebral hematoma, one case of epidural hematoma, one case of pharyngeal and oesophageal injury, and one case of residual nerve root compression.

The first extensive report on North American experience with the BRYAN disc has been published by Sasso and co-workers in 2007 and 2008 [28, 29]. The authors conducted a prospective, three-center, randomized trial on 115 patients randomized in a 1:1 ratio to disc

replacement and ACDF and plate surgery. Inclusion criteria were similar to the European studies and included patients with cervical radiculopathy and focal myelopathy due to single-level disc degeneration with symptoms non responsive to conservative treatment. Follow-up was 2 years for 99 patients. The authors reported a longer operative time for the arthroplasty group (1.7 vs. 1.1 h) but a significantly lower NDI for the disc replacement group at 12 months and 24 months (11 vs. 20, p = 0.005). Analysis of arm pain at 1 and 2 years also favoured the arthroplasty group with significantly lower VAS scores (14 vs. 28, p = 0.014). The reported average range of motion per level in the disc replacement group was 7.9° in flexion-extension at 24 months, whilst it was 0.6° in the fusion group. No complications related to the implants were noted, as well as no heterotopic ossifications. Six patients underwent additional operations during the follow-up period, four patients in the control group and two patients in the BRYAN group. Four patients (two in the control group and two in the BRYAN group) underwent a new ACDF surgery for adjacent segment degeneration.

Results of the FDA IDE approval trial of the BRYAN disc was published by Sasso et al. in 2011 [30]. The study was designed as a non-inferiority trial and randomized a total of 582 patients into two arms (i.e. ACDF vs. CDR). Overall success rate at 4 years was significantly better for BRYAN disc (85.1%) vs. ACDF surgery (72.5%, p = 0.004). Also, neck disability index improvement was higher for BRYAN disc (mean NDI at 4 years, 13.2) than ACDF (mean NDI at 4 years, 19.8, p < 0.001). Up to 48-months follow-up, nine patients (3.7%) in the arthroplasty group and ten patient (4.5%) in the fusion group had to undergo secondary surgical procedures; the difference between the two groups was not statistically significant. Interestingly, the rate of adjacent segment surgery in the two groups was also similar and not statistically significant (4.1%) [30]. Ten-years outcomes of the same group of patients were reported by Lavelle et al. in 2019, although only 232 patients out of the initial 582 patients were available. Overall success rate was significantly higher for the BRYAN group (81.3 vs. 66.3%, p = 0.005), and the rate of secondary surgery at adjacent levels was lower for the BRYAN group (9.7 vs. 15.8%, p = 0.146). ROM at the index level in the BRYAN group was 8.7° [31].

In a more recent work, 18-year follow-up data for BRYAN disc were reported by a single center [32]. At the time of the latest follow-up, residual movement at the index level was noted in 56% of patients, the average range of motion decreased from 10.1° preoperatively to 6.1° at the time of the last follow-up. Rate of ASDegeneration and heterotopic ossification was 77.1% and 73%, respectively, at the time of the latest follow-up; no data is provided in terms of reoperation rate in this cohort [32].

ProDisc-C

The ProDisc-C implant has received the US FDA approval for use in single-level disc arthroplasty due to the good results reported by the IDE study by Murrey and colleagues [33]. An earlier study by Bertagnoli et al. [34] reported on the results of 27 patients treated with single-level ProDisc-C implantation at 1 year follow-up. Patients experienced sustained improvement of their symptoms at 1 year follow-up with decrease of NDI and VAS scores. No device complications were reported.

The actual FDA approval study was published in 2009 [33]. It was a prospective, multicenter, randomized controlled trail conducted on patients with single-level pathology. A 1:1 randomization scheme was adopted, 106 patients were randomized into the ACDF group and 103 patients in the arthroplasty group. VAS, NDI, and SF-36 scores were recorded at 3, 6, 12, 18, and 24 months after surgery. Clinical outcome measures significantly improved in both groups after surgery and results were maintained at final follow-up. Arthroplasty

group maintained range of motion at the index level in 84.4%. Overall, the ProDisc-C group showed results equivalent or slightly superior to the ACDF group although there was a statistically significant difference in the complication rates. In the fusion group, 8.5% of the patients needed re-operation, revision, or supplemental fixation compared with 1.8% of the ProDisc-C group ($p = 0.033$).

Long term results with ProDisc-C prosthesis have been recently published by two independent groups [35, 36]. Zhao et al. reported results of 27 patients treated with single-level ProDisc-C arthroplasty at 10-year follow-up. The average range of motion at the index level was 6.6° ± 3.5° at final follow-up. Seventy-four percent of patients developed heterotopic ossification (12 levels were classified at grade III according to McAfee's classifications). Three patients (11.1%) developed ASDisease with recurrent radiculopathy and/or myelopathy and underwent reoperations (i.e. two cases of CDR surgery and one case of cervical laminoplasty) [35]. Zigler et al. reported reoperation rate of 535 patients who underwent single-, two-level, and hybrid (i.e. ACDF and adjacent level CDR) with a median follow-up of 77 months. Reoperation occurred in 30 out of 535 patients (5.6%) and included 3 conversions to ACDF, 1 arthroplasty repositioning, 21 ASDisease, 1 non-union, 1 wound infection, 1 hematoma, and 2 patients who received stimulators for pain control. No reoperations were performed for issues related to device failure [36].

PRESTIGE Disc

The Cummins/Bristol device was the precursor of the PRESTIGE series of disc arthroplasty. The Cummins disc was developed to address the problem of disc degeneration in patients with previous fusions or with Klippel-Feil syndrome. The first study on this device enrolled 20 patients and showed, at 5 years, significant clinical improvement and preservation of the movement in 88.9% of the patients. Unfortunately, a high rate of complications was reported, including screw loosening, mobilization of the implant, dysphagia and transient hemiparesis.

The PRESTIGE I and II discs were developed as an evolution of the original Cummins disc. Clinical results of the PRESTIGE I disc were published by Wigfield and coworkers in 2002. A total of 15 patients were enrolled in a prospective non randomized trial [37]. Inclusion criteria encompassed patients with cervical radiculopathy or single level myelopathy secondary to cervical disc herniation or foraminal osteophytes. No significant complications were reported by the authors and all patients showed preservation of motion at the index level at 2 years after surgery. Mean flexion-extension ROM was 6.5° and mean antero-posterior translation was 2 mm. Clinical improvement was documented by ODI, NDI, and SF-36 but no valuable statistical analysis was undertaken because of the small number of patients.

The best available data on clinical safety and efficacy of the PRESTIGE ST disc has been published in 2007 by Mummaneni and colleagues [38]. Data from this report have also served as the basis for the current FDA approval of this device in the United States. The study consisted in a prospective 1:1 randomized trial with patients undergoing either single level disc arthroplasty or single level ACDF. A total of 541 patients were enrolled, 276 patients in the PRESTIGE ST group and 265 patients in the ACDF group. The study showed a two-point greater improvement of NDI in the investigational group at 12 and 24 months. Improvement in SF-36 questionnaire scores was higher in the arthroplasty group at 12 and 24 months, as well as the VAS score. The rate of revision surgery was lower for the interventional group (5 revision surgeries) vs. the fusion group (23 revision surgeries). No device failures or complications were reported, the average motion preservation at 2 years was 7°. The PRESTIGE LP disc

arthroplasty has received FDA approval for use in patients in July 2014.

Outcomes at 10 years of the PRESTIGE LP disc arthroplasty were reported by Gornet et al. in 2019 [39]. Scores of patient reported outcomes and neurological function remained stable for the CDR group. The rate of revision surgery at the index level was 10.3% (nine patients), while four patients (7.8%) reported serious implant adverse events. The rate of secondary surgery at adjacent level was 13.8% for the CDR group, and incidence of heterotopic ossification increased from 1.2% at 2 years to 9.0% at 10 years [39].

McAfee and colleagues have summarized best available evidences about the use of cervical total disc replacement in clinical practice. The authors looked at the reported results of four prospective randomized controlled FDA IDE trials using BRYAN, PRESTIGE, ProDisc-C, and PCM implants. Data from 1226 patients at 24 months were available for the analysis. Results showed an overall success rate of 70.8% in the ACDF patients and 77.6% in the arthroplasty group ($p = 0.007$), thus favouring this last treatment. The analysis of all clinical subcomponents (i.e. neck disability index, neurological status, and survivorship) also favoured arthroplasty over ACDF surgery at 24 months. Survivorship ranged from 90.9% in the PRESTIGE group to 98.1% in the ProDisc-C group. Survivorship was achieved by 96.6% of the cervical arthroplasty group on average and by 93.4% of the ACDF patients. Some criticism has been raised regarding the poor results of the ACDF surgery (70.8% overall success rate) in the reported FDA IDE trials. As pointed out by the authors of the study a common perception of a much higher success rate in fusion patients undermines confidence in the results of these trials. FDA criteria for definition of *success* are much more stringent than what has been traditionally reported in observational studies on ACDF surgery. This may account for the lower than expected results of the control fusion groups; taken together these data suggest that cervical disc arthroplasty is at least as clinically successful as fusion at 24 months [40].

Complications

Complications following CDR surgery can be grouped as: surgery related; implant related; or changes in physiological biomechanics of the cervical spine. CDR surgery shares with ACDF surgery the same risks related to the surgical approach. In a recent meta-analysis by Hui et al. including a total of 3223 patients the pooled prevalence of post-operative complications following CDR was low, ranging from 0.8 to 4.7% [41]. The most commonly reported complications included, intraoperative dural tear (0.9%), post-operative dysphagia (5.4%), neurological adverse events (5.0%), and intraoperative vascular injury (1.1%) [41]. In a retrospective review by Fountas et al. of 1015 cases of primary one, two, and three level ACDF and plating, reported mortality was 0.1%; 9.5% of the patients suffered from postoperative dysphagia, 3.1% had recurrent laryngeal nerve palsy, 2.4% prevertebral hematoma, 0.5% had dural perforation, 0.1% hardware failure, and 0.1% wound infection [42]. Most recent evidence suggests that the rate of surgery related complications between ACDF and CDR surgery is similar [43].

Implant related complications are specific to CDR and have been reported by several authors. Goffin and colleagues reported a total of four implant complications (three cases of subsidence and one case of implant migration) in a series of 146 patients. Implant failures were related to an improper milling of the endplates and implant positioning [27]. General advice is to avoid CDR in osteoporotic patients because of the increased risk of implant subsidence and supposedly stress shielding effect of the implant on adjacent bone. The largest available and possible implant footprint should also be used in each patient in order to increase the load sharing area of the implant. It is important to notice that no cases of posterior migration and neurological compromise due to cervical arthroplasty have been reported so far to our knowledge. On the other hand, some keeled implants, carry the risk of vertebral body fracture during implant insertion. Datta and co-workers reported a case of C6

Table 10.3 McAfee grading of heterotopic ossification (HO) in cervical disc arthroplasty [46]

Grade 0	Absence of HO
Grade 1	Presence of HO in front of vertebral body but not in the anatomic disc space
Grade 2	Presence of HO in the disc space, possibly affecting the prosthesis's function
Grade 3	Bridging HO with prosthesis's motion still present
Grade 4	Complete fusion of the segment with absence of motion in flextion/extension

vertebral body fracture during insertion of a keeled implant [44]. Similarly Shim and colleagues described a case of an avulsion fracture [45]. In a more recent meta-analysis involving 3223 patients implant related complications between Prestige-LP (2.0%, range 0–4.1%), Bryan (1.3%, range 0–2.9%), Discover (5.1%, range 2.2–8.1%), ProDisc-C (0.9%, range 0–2.6%), and Mobi-C (2.0%, range 0.4–3.6%) arthroplasties were compared. Pooled implant related complications at short term (i.e. <2 years) was 2%, at mid-term (i.e. >2 years, and <5 years) was 1.5%, and at long-term (i.e. >5 years) was 1.7%. Overall, no significant differences were noted between different types of implant.

Heterotopic ossifications (HO) and anterior ankylosis is a known and dreaded complication of cervical disc replacement surgery. HO is commonly classified according to McAfee et al. in four grades (Table 10.3) [46]. Early reports from Leung et al. showed an incidence of 17.8% (16 patients) of HO in a multicentre study on BRYAN disc arthroplasty [47]. Similarly, Mehren et al. reported an incidence of moderate (grade III) HO of 10.4% at 4 years after surgery in a case series of 54 patients treated with ProDisc-C, whereas seven cases (9.1%) had spontaneous fusion of the treated segment at 1 year after surgery [48]. According to more recent meta-analysis the cumulative incidence of HO following CDR is 32.5% [49]. Prevalence of grade 1 HO was estimated at 5.4%, grade 2 at 8.4%, grade 3 at 5.6%, and grade 4 at 3.8%. Kineflex-C (pooled prevalence 62.4%) and Secure-C (pooled prevalence 74.2%) prostheses demonstrated higher overall rates of HO. In contrast, M6-C (pooled prevalence 1.7%), Prestige ST (pooled prevalence 1.7%), and PCM (pooled prevalence 0.4%) exhibited lower rates of HO compared to the overall prevalence of HO. An overall increasing prevalence of HO with length of follow-up was also reported [49]. Aetiology of this complication of CDR remains unknown. Some authors speculate that the extensive dissection of the longus colli muscle could be a contributing factor, while others think that extensive endplate milling should be taken into account. Risk factors for development of HO include male sex, single level CDR, and age [47]. The influence of age on the risk of HO is still controversial. Hui et al. in a meta-analysis involving a total of 3223 patients reported an inverse relationship between age and risk of HO [41]. Non-steroidal anti-inflammatory drugs (NSAIDs) have been shown to be effective in preventing HO in hip arthroplasty and similarly some authors have advised their use for prevention of this complication in cervical TDR as well. Standard protocol requires administration of NSAIDs for 2 weeks after surgery although this practice is still not supported by solid evidence [50, 51].

"Aseptic loosening" or failure of a total joint arthroplasty is a very well-known phenomenon of polymer-bearing implants in general orthopaedics. Peri-implant osteolysis has been reported for CDR surgery as well [52–55]. The aetiology is most likely multifactorial, such as chronic infection, immune-mediated inflammation, vascular compromise, and stress shielding. Most patients showing post-operative peri-implant osteolysis are asymptomatic. A minority of patients though can present with new onset of pain, neurological deficit, and or spinal deformity (e.g. kyphosis at the index level). Reported incidence of cervical osteolysis following CDR ranges from 4.2 to 63.7%, and incidence seems to be higher with a larger number of operated levels [53, 54, 56]. In a recent meta-analysis, two clinical patterns of cervical osteolysis were identified. A first pat-

tern has reported in which mild osteolysis is observed early after surgery but rarely progresses beyond 1 year. A second pattern is observed whereby osteolysis is more pronounced and can progress up to 4 years after surgery. Cavanaugh and co-workers reported a case where a revision of CDR was performed and a local chronic inflammatory reaction was noted, the patient also developed a delayed hypersensitivity reaction to metal ions [57]. More recently, Guyer and colleagues reported on four cases of early failure of metal-on-metal CDR presenting with worsening pain and/or radicular symptoms. There were three cases of lumbar CDR and one case of cervical CDR, all patients underwent posterior decompression and anterior removal of the implant. In the cervical case the authors observed the presence of a gray-tinged soft-tissue surrounding the implant suggestive of metallosis [58]. Goffin also reported on a similar case with a BRYAN prosthesis where a chronic inflammatory reaction led to osteolysis and loosening of the implant. Lebl et al. recently published a case series of 30 ProDisc-C implants removed and analysed using light stero-microscopy, scanning electron microscopy and x-ray. Posterior endplate-endplate impingement was present in 80% of the implants. Although no backside wear was observed, third-body wear occurred in 23% of the implants [59]. Based on current evidence, in cases of asymptomatic early osteolysis following CDR surgery, a watchful approach should be used and no surgery performed. In cases on symptomatic (i.e. neck pain, cervical radiculopathy) and progressive CDR osteolysis, revision surgery should be performed with removal of the implant and ACDF or corpectomy with definitive fusion.

The aim of cervical arthroplasty is to preserve movement at the index level and avoid mechanical overloading of adjacent segments. Sagittal alignment of the spine is of paramount importance in determining load distribution on discs and posterior joints. Multiple studies have reported post-operative kyphosis as an adverse event of cervical CDR [60, 61]. Troyanovich and co-workers have shown that adjacent segments to a kyphotic level develop compensating hyperlordosis and accelerated degeneration [62]. Kyphosis may be caused by preoperative loss of physiological lordosis of the cervical spine but also by asymmetric milling of the endplates, wrong insertion angle of the implant, or undersizing of the prosthesis [63]. Several meta-analysis comparing the rate of ASDegeneration and ASDisease between ACDF and CDR sugery have been performed in recent years with contrasting results. Two recent meta-analysis have shown that CDR is superior to ACDF in reducing the rate of ASDegeneration at short and midium-term follow-up [64, 65], while other authors have found that CDR can significantly reduce the rate of ASDisease compared to ACDF [66, 67]. The reported prevalence at 5 years follow-up of ASDegeneration following CDR is 36% and pooled prevalence of secondary surgery of the cervical spine at long follow-up (i.e. >5 years) is 4.5%. Main indications for surgery at the index level are pseudoarthrosis, and new onset myelopathy or radiculopathy; whereas indication for adjacent level surgery is manly ASDisease [41]. The overall risk of reoperation at the index or adjacent level is lower for CDR surgery (6%) than ACDF (12%), accounting for a 50% reduction of reoperations [68].

Biomechanics

The main aim of cervical CDR is maintenance of segmental motion at the index level and avoidance of adjacent segment degeneration. Several studies have shown that segments adjacent to a fusion develop increased compensatory movement and higher intradiscal pressure [12, 69, 70]. These changes are thought to be the basis of increased incidence of ASDeg/ASDis after fusion. Therefore, the most important aim of cervical CDR is to restore the physiological segmental motion of the treated level. Each cer-

vical motion segment consists of three joints, the disc in the front and the two zygapophyseal joints in the back. Ligaments provide extra stability to the motion segment and help prevent extreme motions. The normal cervical spine exhibits flexion-extension movement as well as some anterior translation. The centre of motion is mobile during flexion-extension in order to accommodate for the anterior and posterior translation. Motion constraints also change with flexion-extension. In flexion, load is applied to the disc and posterior joints "unlock" reducing their constraining effects. In extension, load is applied on the posterior joints which also "lock" and limit the amount of possible movement. Therefore, from a mechanical point of view, it is extremely important to achieve a correct balance between posterior joints and intervertebral disc.

In vivo and in vitro studies have confirmed these ideas on the motion of the cervical spine. TDR has been shown to maintain index-level sagittal motion, translation, coupled motion in lateral bending with rotation, disc-space height, and centre of rotation, as compared with preoperative or intact states [71]. However, many artificial discs are available for CDR and not all artificial disc designs will behave the same mechanically because of the distinctiveness of each implant design. Disc designs vary widely in terms of translation of the axis of rotation (constrained vs. semiconstrained vs. unconstrained), range of motion (flexion/extension, rotation and lateral bending), materials (titanium, hydroxyapatite coating, cobalt-chrome alloy, ultra-high molecular weight polyethylene, and polyurethane), number of moving pieces, and encapsulation of the overall design (open vs. closed). Biomechanical studies have shown some important differences in the design of the implants that can significantly affect the in vivo biomechanical behaviour of the prostheses. The three most common and widely studied designs are: (1) the Prestige LP, an open two-piece, semi-constrained design with metal-on-metal articulation, (2) the ProDisc C, an open two-piece, semi-constrained design with polymer-on-metal articulation, and (3) the Bryan disc, a closed one-piece, unconstrained (no fixed core or center of rotation) design with a saline-lubricated polyurethane core. In a recent in silico study all three designs were compared [72]. Prestige LP and ProDisc C were shown to increase motion to a supraphysiologic range and increase facet joint forces at the index level. In contrast, the Bryan disc was shown to reduce forces in the facet joints at the index level but also a reduced flexion movement compared to a physiologic disc at the index level and supraphysiologic movement at the adjacent levels [72].

Cost Analysis

A total of seven cervical disc replacement (CDR) systems have been FDA approved following completion of the FDA investigational device exemption (IDE) studies, and CDR is becoming an increasingly popular technique for treatment of cervical radiculopathy [16, 73]. A common criticism is that novel surgical techniques and devices tend to be more expensive than traditional techniques, while their efficacy is unproven. Ideally, the best interventions will not only optimize outcomes but will also help curb health care spending in the long term. Average cost of a single-level cervical total disc replacement implant is about $4000, whilst the cost for a cervical interbody cage and anterior plate is $2500 in the US [74]. The target market for CDR technologies is huge. In US only, a total of 450,000 cervical and lumbar fusion procedures are performed every year and conservative estimations are that 47.9% of these patients would be good candidates for a motion preservation procedure. The estimated yearly revenue from this segment of the market was $2.18 billion in 2010 [74].

Since the length of hospital stay, therapy protocol, medication usage, imaging, perioperative

complications, and readmission rates are comparable between ACDF and CDR, the largest driver of cost savings in CDR surgery is the reduced rate of secondary surgery due to adjacent segment disease [75]. Early cost-analysis studies comparing ACDF and CDR used data gathered from difference sources. In 2013, Qureshi et al. conducted a cost-effectiveness analysis of single-level CDR vs. ACDF surgery using outcomes data from the Nationwide Inpatient Sample and Medicare reimbursement data. The authors assumed an average failure rate (pseudoarthrosis or hardware failure) of ACDF at 1 year of 5%, and incidence of ASDis of 3%. Failure rate of disc arthroplasty at 1 year was assumed in the range of 0–2%. Supported by a recent meta-analysis of four randomized trials on CDR vs. ACDF the authors also assigned a utility value to CDR of 0.9 (scale 0–1) as compared to ACDF which was assigned a slightly lower value of 0.8. According to the authors disc replacement surgery generated a total lifetime cost of $11,987, whilst ACDF lifetime cost was $16,823. Cervical disc replacement resulted in a generation of 3.94 QALY, whereas ACDF resulted in 1.92 [76]. On the other hand, Warren et al. using data from the ProDisc C IDE study found ACDF surgery to be more costly than CDR ($16,162 vs. $13,171) but more effective in terms of QALY increase at 2 years [77].

Although real cost estimation is extremely difficult and varies greatly in different health care systems and settings, cost-effectiveness studies comparing CDR vs. ACDF have become increasingly sophisticated in the past decade. In 2016, Radcliff et al. conducted a cost-minimization analysis using a single dataset from a health care payer (Blue Health Intelligence). The authors found reduced rates of expenditure by the payer on the index surgery costs and the posthospital health care resource use in CDR vs. ACDF patients ($29.679 vs. $42.486, $p < 0.05$ through 7 years). Even excluding index-level surgery costs, the expenditure per member per month was lower in CDR patients through 36 months. Additionally, the reoperation rate was lower in CDR patients [78]. Additionally, interventional pain procedures and postoperative physical therapy outside of the normal course of treatment were also documented. The authors found that the cumulative costs of ACDF and CDR at 7 years were $42.486 and $29.697, respectively. Utility score measurements demonstrated an improvement in QALY in CDR over ACDF (4.36 ACDF vs. 4.52 CDR) at 7 years. Thus, CDR was a dominant strategy, as it was found to be less expensive but also more effective [78]. As it becomes clear that the largest driver of cost savings of CDR is the reduced rate of secondary surgery; it is likely that with longer-term follow-up study, the financial benefits of CDR will likely be magnified.

Conclusions

Cervical disc arthroplasty has progressed over the last three decades from a merely hypothesis to a clinical reality. The concept of artificial substitution of cervical discs has been embraced by many spinal surgeons and centres throughout the world. Early failures and complications have fostered more research in cervical spine biomechanics and design of better implants. Biomechanical studies have also confirmed that disc replacement decreases the amount of stress posed on adjacent motion segments and on this observation is based the promise of this technique of reducing the incidence of adjacent segment degeneration and disease. Available long term clinical studies have shown that cervical arthroplasty offers similar, and in some cases, better results than the commonly accepted "gold standard" of fusion. Nevertheless, debate is still open as to whether the impact of CDR on reduction of adjacent segment surgery is significant in the long term. As interest for non-fusion technologies from spinal surgeons, industry, and patients increases, cervical total

disc replacement will remain an active and fruitful area of research of spinal surgery in the years to come.

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11 Cervical Spine Fractures and Dislocations, Classification and Treatment

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Introduction

Epidemiology

Subaxial Cervical spine fractures and dislocations represent rare events accounting for approximately 7% of traumatic cervical injuries but often result in significant morbidity and death [1].

The mortality for patients with traumatic spinal cord injury (SCI) is markedly high, with rates ranging from 4 to 16.2% and 21.7 to 32.3% within 30 days and 1 year from admission respectively [2, 3].

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The total frequency of SCI is estimated from 27 to 47 per million in the entire population and approximately 6% in polytraumatized patients; about 40% of patients may present some degree of neurological deficit due to spinal cord or nerve root injury [4]. In the literature a lower mortality was reported for surgically treated patients respect those conservatively treated [5].

There is generally a higher prevalence of cervical fracture among males, and significant predictors of cervical fracture seems to be: pelvic fracture, pelvic fracture combined with a fall and/or concurrent head injury, injury severity score >15, and age over 40 years [6, 7]. The main injury mechanism reported was a motor vehicle accident (MVA) followed by falls from height. Wang et al. [8] reported the most common mechanisms to be MVA in 33.1%, falls in 50.6%, and sports in 0.8%. Young et al. [4] sustained MVA, falls, motorcycle, bicycle, and pedestrian accidents as significant independent predictors of cervical spine injury and fractures.

Despite the overall low incidence of severe subaxial cervical fractures-dislocations, the correct classification and treatment of these patients still represents a topic of debate in literature. Therefore, the purpose of this chapter is to discuss the role of classifications to offer an easy and reliable method to establish the severity of injuries, and thereafter, to assist spinal surgeons in a correct treatment planning (conservative and/or surgical).

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Classification Systems

Care protocols for polytraumatized patients (Prehospital Trauma Life Support and Advanced Trauma Life Support) that recommend maintaining a cervical collar until the presence of cervical injuries can be excluded, have been revealed strategically to reduce the incidence of complications after cervical injuries.

A correct injury pattern identification and classification could play a crucial role on the traumatized patient's outcome. However, a proper evaluation, especially in a minor and peripheral hospital, is not always possible often due to poor equipment and the lack of a spinal surgeon available. In this scenario, an ideal classification system should be simple and reproducible, and able to transmit comprehensive information about diagnosis, prognosis and clinical/surgical management. Besides, it must allow the practitioners (often from different hospitals) involved in the multidisciplinary treatment of a polytrauma patient to speak a common language [9, 10].

Despite many systems were proposed to classify subaxial cervical spine trauma based on different criteria (morphological and/or pathogenic) [11, 12] to date, none of the classification was universally accepted; furthermore, many studies in the literature revealed the variability in severity assessment and management of traumatic spine injuries [13].

In the last decades, Magerl's classification was most often used [14]. This classification exploded in a dizzying international success in the late 1990s, and rapidly replaced the older classification of Allen-Ferguson (AF) [15].

The most common classifications currently used are:

- the **S**ub-axia**l** **I**njury **C**lassification (SLIC) and Severity Scale.
- the AOSpine Subaxial Cervical Spine Injury classification system that represents, an upgrade of Magerl's classification based on quite similar morphological features [16, 17].

Allen and Ferguson Classification

Firstly, published in 1982, Allen and colleagues devised a cervical spine injury classification system based on the traumatic mechanism they called *mechanistic classification*. The authors described six common patterns of indirect injury to the lower cervical spine, named phylogenies, based on radiographic pictures and supposedly involved traumatic forces (flexion/extension/compression/distraction). Each phylogeny was named according to the presumed attitude of the cervical spine at the time of failure and the initial, dominant mode of failure. Compressive flexion, vertical compression, distractive flexion, compressive extension, distractive extension and lateral flexion were the six phylogenies identified (Fig. 11.1).

Each pattern could be divided into stages according to the severity of musculoskeletal damage. A close correlation appeared to exist between the neurologic and musculoskeletal injury in each pattern [18].

The authors also point out that ligament injuries cannot always be evaluated with standard radiological examinations. However, such injuries can be indirectly detected by residual spinal displacement. In most cases the ligaments are injured by tension and/or shear forces but hardly by those in compression [19–23].

Among the various factors to be evaluated in case of cervical spine trauma, there were: residual malalignment and presence of neurologic injury. In contrast to instability, which indicates abnormal movement, malalignment implies a fixed abnormal relationship.

Another novelty introduced by this classification unlike the previous ones, in which it was argued that there was no strict correlation between the type of fracture and neurological injury [24]. Allen and his colleagues claim that higher stages are reflective of a more severe injury to the spine and predictably show a more severe cord involvement.

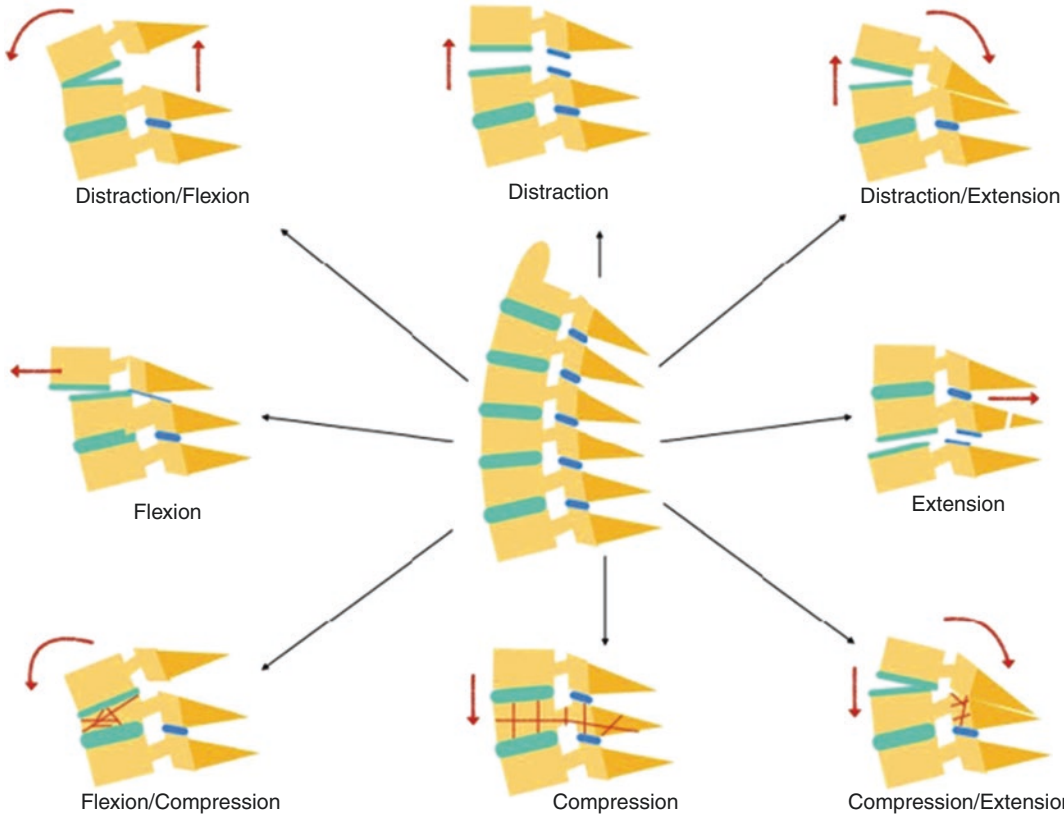

Fig. 11.1 Allen and Ferguson classification: illustrative image of the six aetiopathogenic mechanisms described in the classification

Magerl's Classification

Unlike the previous one, Magerl's classification was based on injury pathomorphological characteristics. Categories were settled according to the main mechanism of injury pathomorphological uniformity, and in consideration of prognostic aspects regarding healing potential.

The three main categories have a typical fundamental injury pattern defined by a few easily recognizable radiological criteria [14].

Emphasis was placed on the extent of the anterior and posterior elements involvement, with particular attention to soft-tissue injury, as well as ancillary bony lesions. Analysis of the injury pattern provides information on the pathomechanics of the injury and, at least, regarding the main mechanisms. In this classification, the loss of stability represents the key point for injuries classification, and the choice of treatment depends on it. The risk of neural injury seems to be primarily linked to the degree of mechanical instability. The dichotomous division between disco-ligamentous injuries and osseous lesions was set due to important prognostic and treatment differences in the two lesions. Because disco-ligamentous injuries had a poor healing potential, surgical stabilization and tension should be considered to avoid chronic instability [25].

The three main types of injuries are type A injuries, primarily caused by compression, type B by tension, and type C by axial torque corresponding to an increasing degree of injury instability. Thus, the severity of the injuries in terms of instability is expressed by its ranking within this classification system.

Subaxial Injury Classification (SLIC)

In 2007 a novel classification was published with the purpose to establish a system easy to remember and to apply in clinical practice guiding treatment decision-making in an objective and systematic manner.

Three main categories (injury morphology; disco-ligamentous complex integrity; and neurological status) were identified as important to injury description and a score were assigned according to the overall injury severity. Treatment options were assigned based upon threshold values of the severity score.

Three major injury characteristics were identified:

1. injury morphology as determined by the pattern of spinal column disruption on available imaging studies.
2. integrity of the disco-ligamentous complex (DLC) represented by both anterior and posterior ligamentous structures as well as the intervertebral disc.
3. neurologic status of the patient.

Within each of the three categories, subgroups were identified and graded from the least to the most severe.

This is done according to the following categories:

1. Spinal level,
2. Injury level morphology,
3. Bony injury description,
4. Status of DLC with descriptors, i.e., presence of a herniated nucleus pulposus,
5. Neurology,
6. Confounders.

Bony injury descriptors include fractures or dislocations of the following elements: transverse process, pedicle, endplate, superior and inferior articular processes, unilateral or bilateral facet (subluxation/dislocation), lamina, spinous process, lateral mass, etc. Confounders include the following factors: presence of ankylosing spondylitis, diffuse idiopathic hyperostosis, osteoporosis, previous surgery, degenerative disease, etc.

This classification identifies three components of injury which represent the *major* and largely *independent* determinants of prognosis and management.

In this way, the SLIC severity scale is the first sub-axial trauma classification system to give up the anatomical and mechanical elements characterizing the other classifications in favor of injury morphology and clinical status. By building the system on injury patterns less severe to more severe, the SLIC severity scale helps to objectify both diagnosis and optimal management.

Practically, SLIC generates a score of severity that is helpful for the surgeon in the decision-making process. Score between 1 and 3 suggests conservative treatment while 5 or more recommends operative treatment.

Within the three categories of the SLIC system, integrity of the DLC is the most difficult to objectify. The Sub-axial Injury Classification (SLIC) and Severity Scale provides a comprehensive classification system for sub-axial cervical trauma, incorporating pertinent characteristics for generating prognoses and courses of management.

See Fig. 11.2 for calculating the score according to the SLIC system score.

AO Spine Subaxial Cervical Spine Injury Classification System

This classification was developed according to the criteria already used for AO group thoracolumbar (TL) junction fractures classification. The goal was to develop a comprehensive and simple classification system with high intra- and interobserver reliability [26].

The classification system describes injuries based on four criteria:

1. morphology of the injury,
2. facet injury,
3. neurologic status,
4. any case-specific modifiers.

Injuries are described by their level, followed by the morphologic type of the primary injury. The secondary injuries and modifiers are placed in

	Parameter	Description	Points
1	Injury Morphology	Compression	1
		Burst	2
		Distraction	3
		Rotation/translation	4
2	DLC [1] Integrity	Intact	0
		Suspected disruption	1
		Disruption	2
3	Neurological Status	Intact	0
		Nerve root injury	1
		Complete cord injury	2
		Incomplete cord injury	3
		Persistence cord injury#	+1

Total points	Management
1-3	Non-surgical
4	Surgical or Non-surgical
5-10	Surgical

Fig. 11.2 Subaxial Injury Classification (SLIC) and Severity Score. *DLC* discolegamentous complex; *# neuromodifier* continuous cord compression in the setting of a neurologic deficit

parentheses (facet injury, neurologic status, and case specific modifiers).

According to morphology of the injury, AO Spine study group described three types:

> "Type A" injuries are fractures that result from vertebral compression with intact tension band divided into five subtypes of increasing severity.
>
> "Type B" injuries include failure of the posterior or anterior tension band by distraction forces with physical separation of the subaxial spinal elements while maintaining the alignment of the spinal axis without translation or dislocation.
>
> "Type C" includes those injuries with displacement or translation of one vertebral body relative to another in any direction: anterior, posterior, lateral translation, or vertical distraction.

The second element analyzed was the morphology of facet injury according to an increasing grade of

severity. The evaluation is strategic given the role of facet complex as a dominant stabilizer for axial rotation, and overall stability in association with the capsule, disc, and ligamentous structures [27, 28]. In case of multiple injuries of the same facet (for example, a small fracture and dislocation), only the highest injury is classified (dislocation). If both facets on the same vertebrae are injured, the right-sided facet injury is listed before the left sided injury if the injuries are of different subcategories. The "Bilateral" (BL) modifier is used if both facets have the same type of injury. If only facet injuries are identified (no A, B, or C injury), they are listed first after the level of injury. (*For details of the main categories and subgroups, see AOSpine subaxial cervical spine injury classification system*).

Neurological status is graded according to a six-part system like the system described for the TL classification:

- N0—neurologically intact
- N1—transient neurologic deficit that has completely resolved by the time of clinical examination (usually within 24 h from the time of injury)
- N2—radiculopathy
- N3—incomplete spinal cord injury
- N4—complete spinal cord injury
- NX—neurology undetermined—used to designate patients who cannot be examined due to head injury or another condition which limits their ability to complete a neurological examination such as intoxication, multiple traumas, or intubation/sedation.
- The symbol "+" is the only difference with TL classification introduced to identify ongoing cord compression in the setting of incomplete neurologic deficit or nerve injury.

Additional modifiers created to describe unique conditions relevant to clinical decision making are as follows:

- M1—posterior capsuloligamentous complex injury without complete disruption,
- M2—Critical disk herniation [29],
- M3—Stiffening/metabolic bone disease [i.e., Diffuse Idiopathic Skeletal Hyperostosis (DISH), Ankylosing Spondylitis (AS), Ossification of the Posterior Longitudinal Ligament (OPLL) or Ossification of the Ligamentum Flavum (OLF)]. This modifier describes conditions that may argue either for or against surgery for those patients,
- M4—Signs of vertebral artery injury [30].

Treatment

The choice of best treatment in case of cervical spine injury is the logical consequence of estimation of severity of the lesion according to the correct evaluation of many clinical, morphologic elements. All the proposed classification has been aimed to give the most reliable system of grading the severity of the lesion and suggest an algorithm of treatment. Suspicion of traumatic spinal instability due to cervical injury should guide spinal surgeons throughout the diagnostic process. Underestimating potential cervical spine instability could cause devastating spinal cord injury [31]. In fact, spinal surgeons are generally less worried of serious but stable bone lesions rather than soft tissue injuries (disc-ligamentous complex), potentially responsible for traumatic instability.

In case of cervical severe cervical trauma, it should be advisable to take a multidisciplinary approach from the emergency department to the final treatment decisions [32].

The first step is to accurately classify the injury according to the preferred classification system, estimate the severity of the lesions and differentiate between surgical and non-surgical cervical lesions. When surgical treatment is required, a careful assessment of priorities (polytrauma patients) and timing is essential, especially in the case of concomitant neurological injuries. Last, but not least, is the choice of the surgical approach and technique [33].

The goals of a surgical treatment must be neurologic decompression (in case of neurologic injury) and mechanical stabilization of the spine, to provide a correct spinal alignment and to obtain a solid spinal fusion [34]. Given the complexity of the issue, several methods of reduction-fixation of fractures and dislocations have been published in the literature. However a

clear and universally accepted consensus on uniform or standardized methods of surgical approaches and techniques does not exist [35–37].

In this regard, classifications can play an important role in suggesting an anterior rather than a posterior or combined approach but are not useful for guiding the choice of specific surgical techniques. Therefore, even today, it is the surgeon's experience and confidence with one approach over the other that guide and justify the final choice [38].

The timing of decompressive surgery, defined as the time elapsed from the trauma until the operation, and its influence on recovery after a neurologic damage deserve special considerations. In fact, the old concept that timing could be the most important factor for neurologic recovery remains a topic of debate. For many years, there have been no statistical differences in neurological outcomes after spinal cord injury in patients undergoing early or late surgery and, to date, a clearly accepted definition of early or late surgery is still lacking [32, 39]. Recent studies underlined that the difference between early and late surgery and their consequences on postoperative outcome are closely related to the physiopathology of SCI. In the literature there is no surgical procedure that can limit the primary damage while it is mandatory to prevent the secondary SCI, represented by vascular and biochemical changes (electrolytes modification, free radical production, serotonin, and catecholamine accumulation), edema formation and inflammation that appear within 72 h after spinal trauma [40, 41]. Therefore, on the basis of the data of the literature, it seems wise and appropriate to state that the neurological patient should be treated surgically as the general clinical condition and comorbidities can allow it and in any case within 72 h of the trauma [42].

Anterior Approach

The main advantages of the anterior approach to the cervical spine with respect to posterior are minor surgical trauma, reduced infection rate, minor bleeding, and minor postoperative pain. In addition, the anterior surgical approach frequently does not need long fusions which could be limited to one segment of motion, while the posterior approach often requires longer fusions [43].

One of the best indications for anterior approach is the presence of spinal cord compression due to posterior dislocation of bony fragments or disc hernia that allows surgeons to decompress the spinal canal by directly removing them.

Discussed is the anterior approach for facet dislocations with or without previous attempts to closed reduction. An attempt to close reduction for unilateral facet dislocations is sometimes recommended with gentle maneuvers in awake, alert, and cooperative patients.

According to the literature, approximately 50% success rate of a closed reduction has been reported. In the past, some cases of neurologic deterioration have been reported soon after closed maneuvers in which MRI was able to detect disc material inside the spinal canal.

After the first reports of dramatic neurologic complication, even though the occurrence of this event is quite rare, MRI has become strongly recommended for its high sensitivity for soft tissues [44]. Of course, based on the previous statement, any attempt of closed reduction should be performed only after MRI confirmation of the absence of any possible compression of the spinal cord due to disc herniated fragments or epidural hematoma [45, 46]. Spinal epidural hematoma frequently occurs in patients with spondylopathy, particularly in ankylosing spondylitis, after blunt trauma of the cervical spine so MRI is strongly recommended in these patients where the risk of spinal cord compression is very high and an urgent decompression of the spinal cord may be required [47].

Much more dangerous and not recommended are the attempts to reduce bilateral dislocations of the facets due to the simultaneous lesion of the disc and of the anterior and posterior longitudinal ligaments.

Recent literature has shown that in the case of bilateral facet dislocation, the anterior approach

alone may not be sufficient due to the high risk of late kyphosis or hardware failure even years after surgery [48].

In these cases, due to the high instability of the lesion, the best indication is that of a combined anterior and posterior approach, in a single phase or, when contraindicated, in two phases, preferably starting from the posterior one.

The posterior approach is mandatory in the case of locked (irreducible) cervical facet dislocations, in the case of late or incorrect diagnosis, or in the case of failed attempts of reduction both closed and open.

Among disadvantages and complications of anterior approach, many patients complain transient laryngopharyngeal discomfort that disappears within 1–2 weeks, while permanent lesion for iatrogenic laryngeal nerve damage is reported as frequent complications of anterior approach especially with right access mostly used by neurosurgeons [49]. Radcliff et al. reported a 61.5% incidence of dysphagia after anterior surgery [50].

Posterior Approach

The most common and used worldwide posterior cervical column fixation technique is lateral mass screwing while the most demanding pedicle screwing technique is still limited to selected cases [51].

An effective cervical internal fixation system for lower cervical fracture-dislocation should provide immediate stabilization of the spine, correction of spinal deformity and limitation of use of external orthosis [52, 53]. Some posterior instruments widely used in the past (such as spinous process wiring, sublaminar wires and laminar hooks) are now completely abandoned due to the lower stability obtainable with these implants compared to those made with the screwing of lateral masses or pedicles [54, 55].

The lateral mass screw, nowadays, represents the gold standard in posterior cervical fixation for its relative safety and reliability in ensuring stability to the damaged spine. However, in a purely posterior column fixation, the resistance to pull-out forces may be limited. To reduce the risk of postoperative implant failure which, occasionally, can occur before fusion is achieved, some authors are used to apply a temporary external rigid collar after surgery. Rarely, stronger external immobilization, such as a halo vest, may be needed to protect the implant from failure particularly when, due to local factors, such as poor bone quality, it is difficult to make a strong and rigid structure [56].

Recently, the increasing availability of neuronavigation systems has given a new impulse to the use of cervical pedicle screw fixation [56]. Abumi et al. [54] first reported the results of pedicle screw fixation for traumatic lesions of the cervical spine in 1994.

Cervical pedicle screw fixation is a three-column fixation system with many biomechanical advantages. The results of biomechanical research demonstrate that the stability of cervical pedicle screw fixation is significantly higher than that of the lateral cervical mass and even superior to combined anterior and posterior fixation. Although cervical pedicle screws have a significantly lower loosening rate at the bone-screw interface as well as increased strength after fatigue testing, the main concern of surgeons is the accuracy of screw placement and the high risk of neurovascular injury. Currently, computer-assisted navigation systems are increasingly used to maximize the accuracy of screw placement [57]. which, in the literature, is between 16.8 and 97% [58] and minimizes the neurovascular damage that remains, however, the main concern in the use of this technique [59].

Unfortunately, given the high cost of navigation, its use is still limited and available only in the best equipped and reference centers for spinal surgery. Despite the lack of a clear guideline, shared among surgeons, the main indications for pedicle screwing are all cases where stronger fixation is required (i.e. osteoporotic patients), in case of major correction of severe traumatic deformities and in case of traumatic floating mass.

Combined Approach

The aim of a combined approach, in a single or two steps, is to achieve superior biomechanical stiffness by providing additional stability to the implants. Circumferential reconstruction has been found to provide maximum stability when applied in the subaxial cervical spine and cervicothoracic junction in case of severe disc-ligamentous complex lesion [60]. In literature, posterior fixation is recommended in case of previous anterior approach after extended corpectomy at more than two levels. In rare cases of severe spinal cord compression, when anterior and posterior decompression is required, the combined approach becomes mandatory despite the inevitable increased risk of complications due to the complexity of the procedure.

The decision to perform a combined approach is not an easy one and requires teams of experts, a proper preoperative assessment of the patient's general condition capable of supporting a longer intervention and the availability of postoperative intensive care units because of greater surgical trauma, blood loss and increased risk of infection. It has also been reported that the change of patient's position between the two steps of surgery can increase the risk of nerve injury [61].

Even the study of Yang and colleagues, states that in case of injuries that have a score equal to greater than 7, ranked according to score SLIC, it is advantageous to perform a double treatment [49].

Illustrative Cases

Case 1 Car accident. 45-year-old man arrived in hospital unconscious (GCS 3) and intubated for head trauma with skull fracture and subdural hematoma. Upon arrival the SLIC severity score was 5 suggesting an unstable lesion, as shown in CT scan (Fig. 11.3a). The widening of

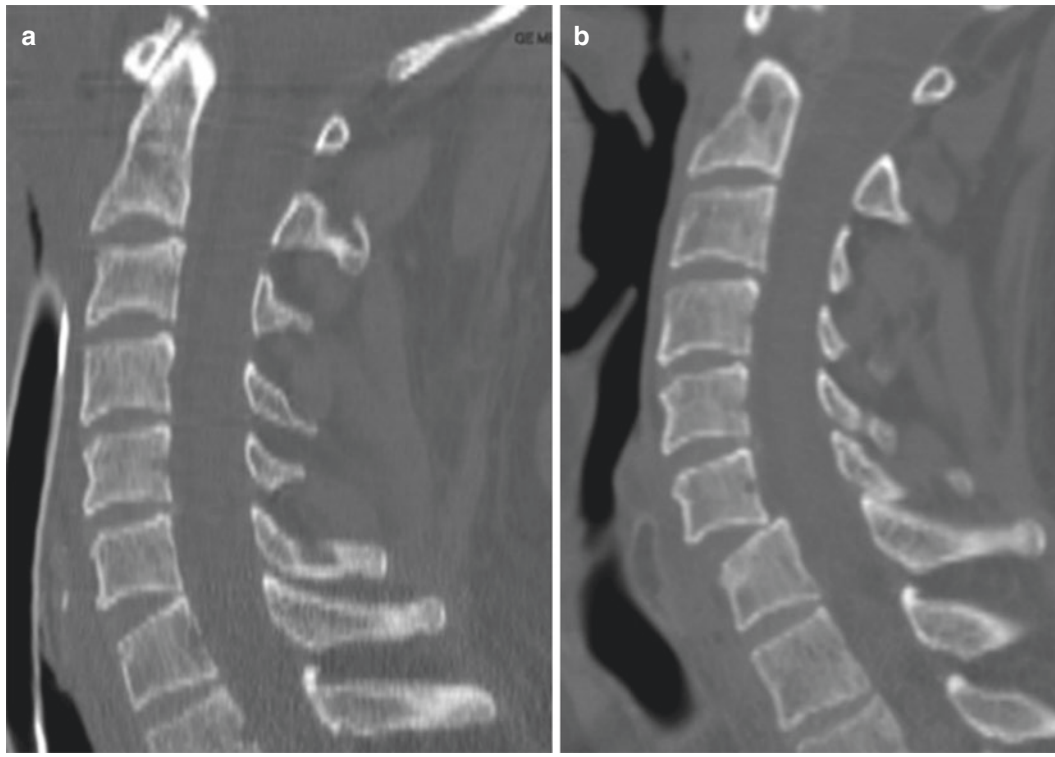

Fig. 11.3 (**a**) CT scan at arrival. SLIC SCORE: Morphology 3 (hyperextension injury), integrity of DLC 2 (disruption of anterior longitudinal ligament and intervertebral disc), neurological status 0 (intact). AO C6–C7: B (C7:A1) (BL, F4, N0); (**b**) CT scan after 2 weeks

the anterior part of the intervertebral space suggests the disruption of the anterior longitudinal ligament and disc, without the need for MRI. For the coexistence of comorbidities, planned mono-segmental anterior arthrodesis was delayed and an external orthosis was applied. A new CT, carried out 2 weeks later, showed progression of the C6–C7 listesis (Fig. 11.3b) which confirmed the involvement of the whole disc-ligamentous complex. The careful interpretation of the images, acquired with high resolution CT, has allowed the recognition of clear signs, even if initially slight, highly suggestive of serious cervical injuries without the need of further investigation. An anterior approach was carried out (Fig. 11.4c, d). At surgery, the anterior longitudinal ligament was broken, and disc disrupted (Fig. 11.4a, b) as shown in intraoperative image.

Case 2

A 26-year-old woman hit by a vehicle was transferred to the hospital with no neurologic deficit. She reported cervical and thoracic trauma with pulmonary contusion. A chest drainage was applied for hemothorax. During the CT, she became tetraplegic. Behind the C6 vertebral body, a huge round mass was recognizable only on the soft tissue sequences (Fig. 11.5b). While no evidence of mass occupying space inside the spinal canal was recognizable on bone sequences, as show in Fig. 11.5a. No additional bony lesions were recognized. With the suspicion of epidural hematoma, in absence of more lesions, the patient underwent urgent anterior decompression surgery. Surprisingly, a complete tear of the anterior longitudinal ligament and intervertebral disc was detected. After the corpectomy, a huge disc fragment, compressing

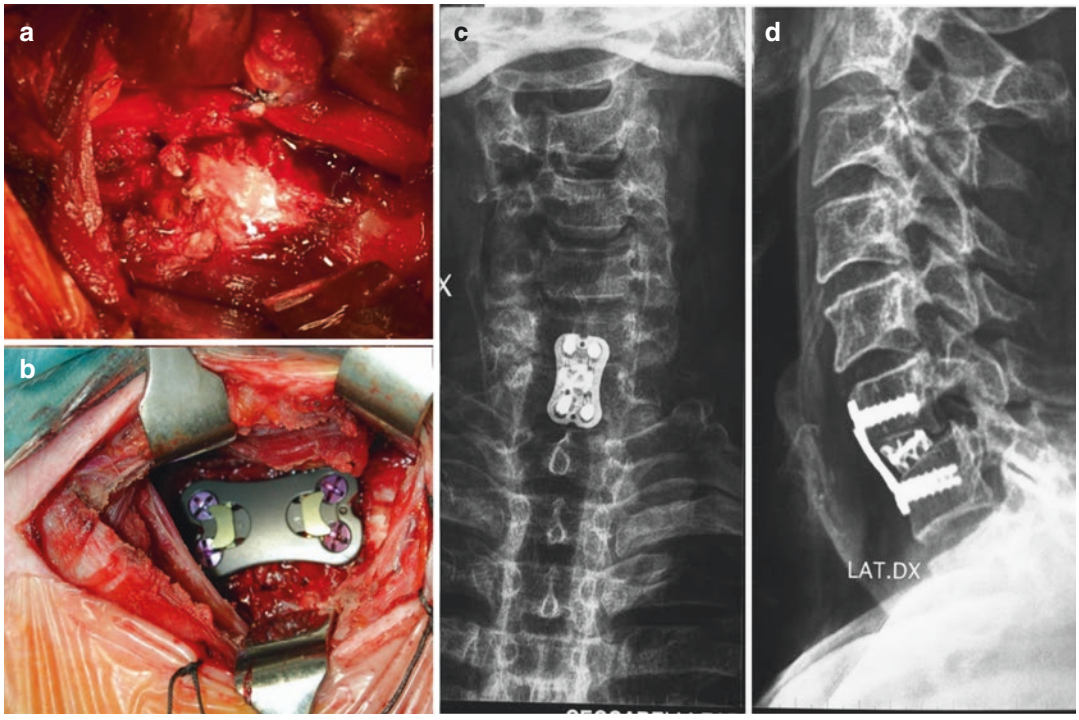

Fig. 11.4 (**a**) Anterior approach. Intraoperative images of the broken anterior longitudinal ligament (**b**) and of the plate (**c**, **d**) postoperative X-Ray in AP and lateral view. A titanium mesh has been inserted in the intervertebral space to fill the gap and maintain the lordotic alignment. A plate has been carefully shaped to adapt the segment morphology and fixed to the vertebral bodies with screws

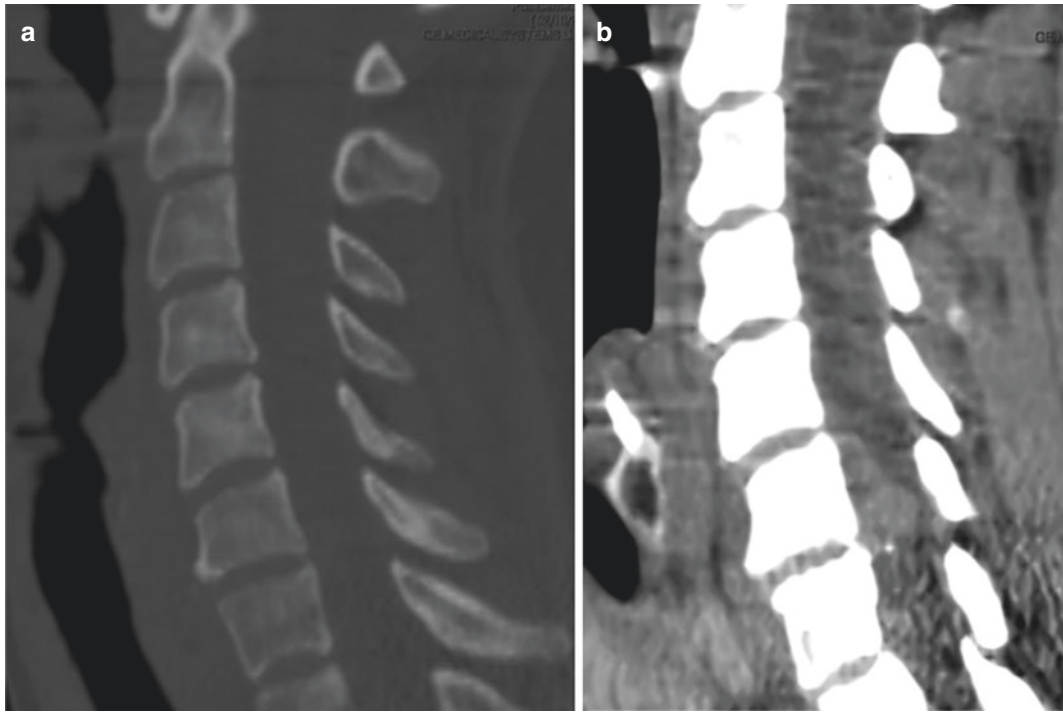

Fig. 11.5 CT scan in bone (**a**) vs. soft tissue sequences (**b**)

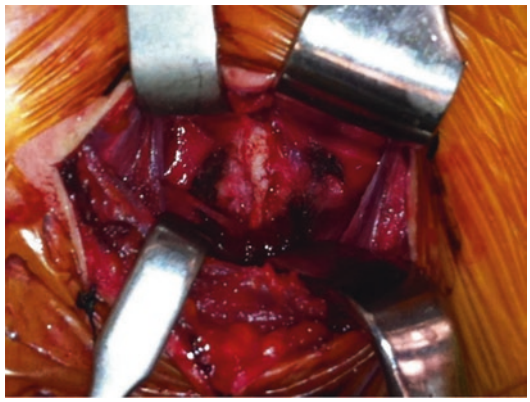

Fig. 11.6 Anterior approach: disc fragment and anterior longitudinal ligament disrupted

the spinal cord, was found, and removed (Fig. 11.6). A titanium MESH was used to replace the C6 vertebral body and stabilization was performed with a plate between C5 and C7. As the stabilization resulted not stable enough, an urgent, postoperative MRI was than requested of whole spine. MRI surprisingly demonstrated the coexistence of a serious damage of posterior tension band and, probably of the disc. Lesion of all ligamentous, which required a posterior decompression and arthrodesis (Fig. 11.7). After the results of MRI (Fig. 11.8a) all CT sequences acquired before the operation were reviewed (Fig. 11.8b). Underestimated facet subluxation of more than 50% of the joint were recognized despite they may be a sign of possible major injury to the disc-ligament complex. Assuming a major spine instability, a posterior cervical and thoracic stabilization was carried out 12 h after the first step. Lateral mass screw implant was performed in the cervical spine and a stable fixation was then carried out in the thoracic spine. During the operation a clear instability of the spine was detected with complete lesion of the supra- and inter-spinous ligaments, both joint capsule and subluxation of the facet joint. There was also, a hidden Dural lesion and a right foraminal vascular lesion with leakage of CFS fluid and bleeding with the acts of breath. A temporary mono-segmental fixation deter-

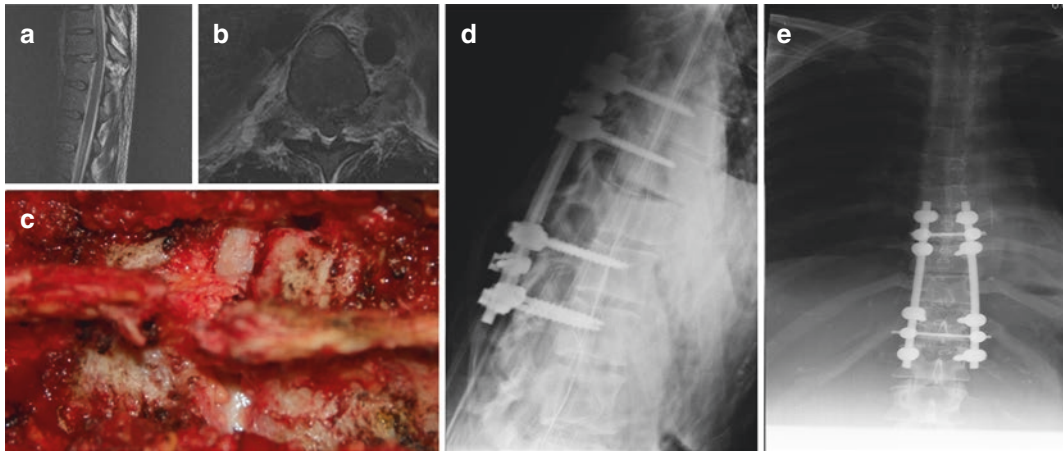

Fig. 11.7 Dorsal spine involvement: (**a**, **b**) dorsal spine's MRI imaging (**c**) surgery (**d**, **e**) After surgery X-rays

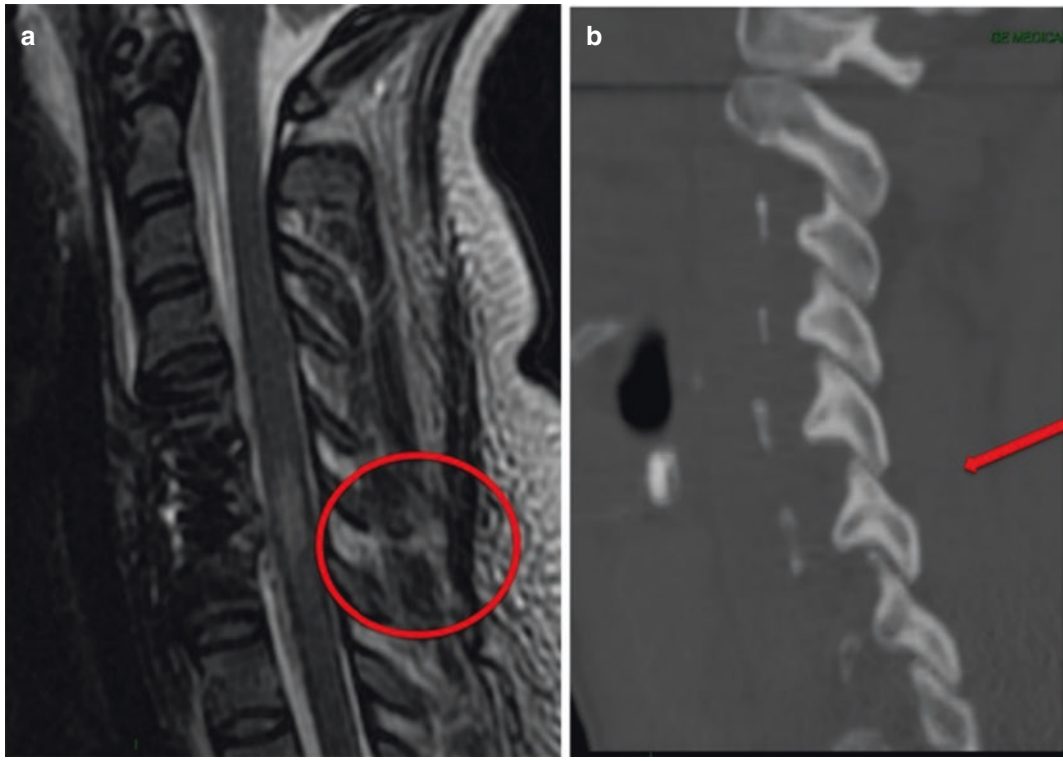

Fig. 11.8 (**a**) MRI vs. CT scan: the involvement of the posterior component was conceivable by paying attention to the facet joints (**b**)

mined immediate cessation of the CFS leakage and bleeding. Finally, a definitive pedicles fixation, two levels above and below, was performed (Fig. 11.9). The patient fully recovered in a few months later.

Case 3 67-year-old male, who fell from 3 m in height, arrived at the ER without neurological deficits despite slight numbness in the arms. CT showed C6–C7 spondylolisthesis (Fig. 11.10a) and bilateral dislocation of the facet (Fig. 11.10b, c). The lesion

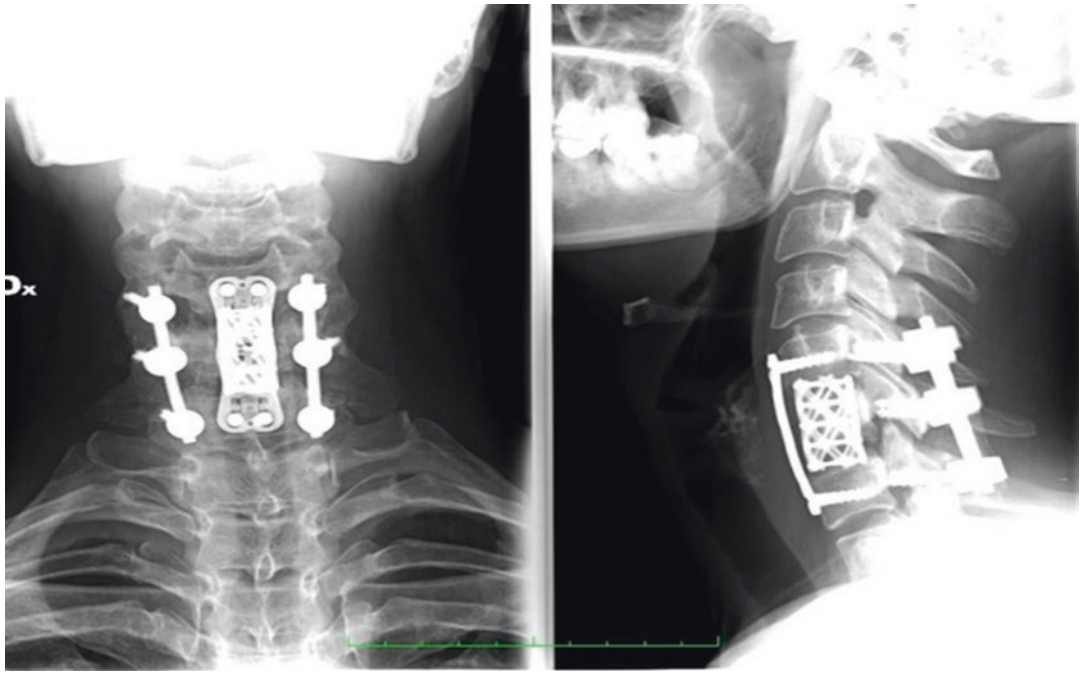

Fig. 11.9 X-ray scan at the 1-year follow-up

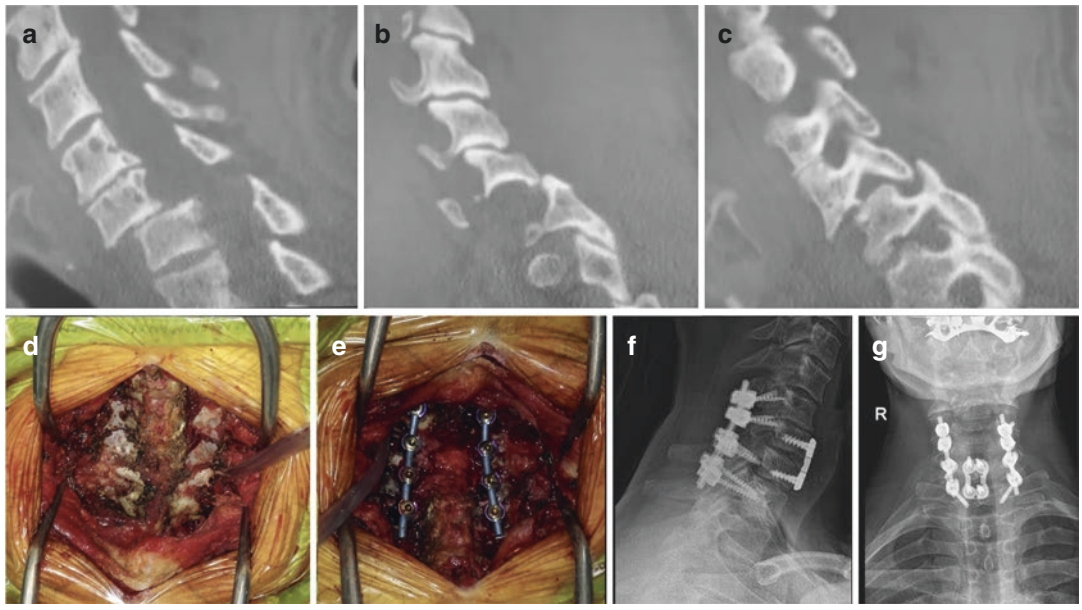

Fig. 11.10 (**a**–**c**) CT scans at the arrival. The SLIC severity score was 5 (Morphology—distraction pt 3/Disc-ligament complex—disruption pt 2 and AO C6–C7:C (F4, BL, N0). (**d**, **e**) first stage with posterior approach. (**f**, **g**) C5–T1 posterior fixation and C6–C7 anterior arthrodesis

was judged to be severely unstable, and a posterior approach was performed a few hours after arrival (Fig. 11.10d, e). Although an attempted closed reduction is suggested in literature, as soon as possible after cervical injury. A surgical reduction was preferred due to the low collaboration of patient. Despite the open surgery, displacement reduction resulted particularly difficult requiring a partial resection of the lower facets. A long, multilevel fixation was carried out from C5 to T1 and given the optimal clinical condition of the patient, A single level of anterior arthrodesis (Fig. 11.10f, g) was performed 3 days later to accelerate clinical recovery.

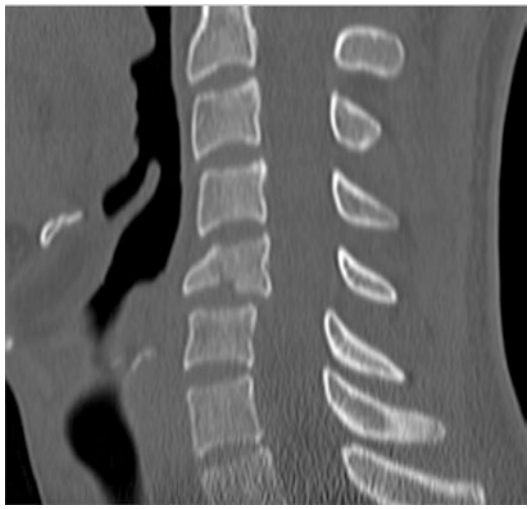

Fig. 11.11 CT image in which it would appear that the fracture is only of the C5 soma

Case 4

A 19-year-old boy, victim of a car accident, had suffered a dislocated C5 fracture (Fig. 11.11). On arrival in the emergency room, he had no strength or sensory deficits. The trauma mechanism was flexion-distraction, according to the Allen & Ferguson classification. Classifying the fracture according to SLIC the score was 5 pt. From the axial and coronal CT images the facet joint diastasis lesion is clear (Fig. 11.12a–d). The surgery was done via an anterior approach. Due to the young age of the patient, it was decided to perform surgery using autologous bone grafting to support rapid fusion. The alternative could have been a corpectomy of the C5 soma with expansion cage implantation. The X-ray at 3 months follow-up shows an excellent reduction of the fracture and good fusion of the bone graft (Fig. 11.13a, b).

Discussion

Subaxial cervical spine injury represent one of the most frequent cause of fracture-dislocations, which when not promptly treated can result in important cord lesions that reduce the quality of patients' life. The incidence of neurological complications has been reduced thanks to first-aid rules on the scene or during transportation to the ER and thanks to the multidisciplinary management of patients with multiple injuries.

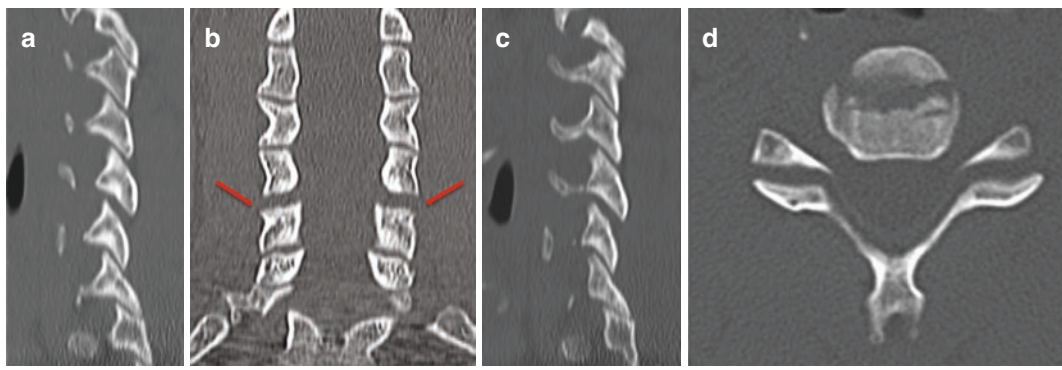

Fig.11.12 (**a**, **c**) even in sagittal CT sequences it is possible to see that there is more than 1/3 loss of contact between the joint surfaces; (**b**) in the coronal scan the diastasis of the facet joints is clearly evident (**d**) facet joint diastasis is equidistant on both sides of the vertebrae

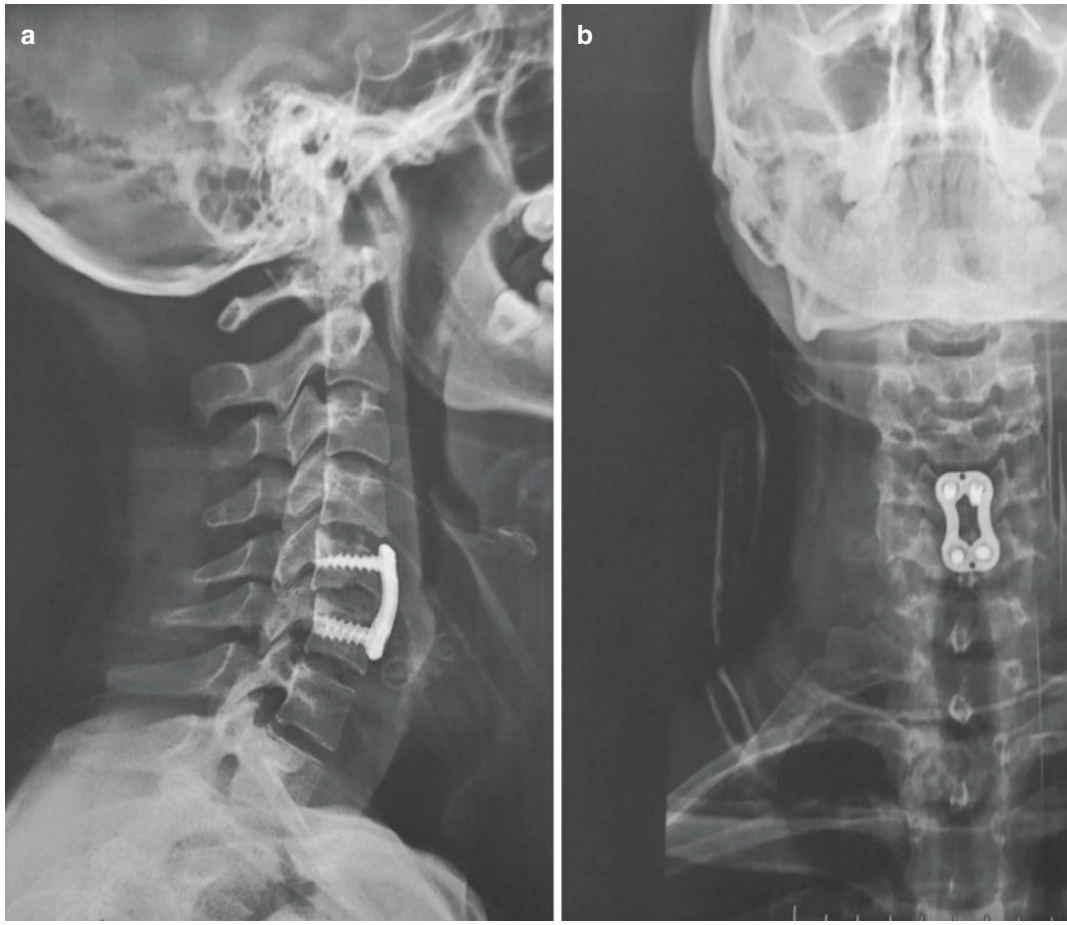

Fig. 11.13 X-ray at 3 months follow up, (**a**) lateral view, (**b**) antero-posterior view

Further reduction of patients' morbidity and mortality is due to the improvement of spine surgery, acknowledgement of spine's injury anatomy, biomechanics and classifications that permitted more appropriate diagnosis and stadiation of the injuries.

Classifications' common element is presenting the injuries in increasing order of severity, defined by a sum of various features.

There's an amount of classification: during the last decades they became easier, more reliable and easier to reproduce.

Allen Ferguson (AF) classification, dating back to 1982, drew the attention to spine's biomechanics and six different common mechanisms of trauma, so much to gain the definition of "a mechanistic classification". It was extremely simple, based on X-rays, the only analysis available in that time, which, inevitable, tends to underestimate the severity of the injuries. Furthermore, there was no mention of neurologic involvement, so the authors concluded that medullary lesions' risk increases with injuries' gravity. Despite the absence in literature of a clear definition of instability, defined as "ethereal subject badly in need of rigorous definition", in AF classification, instability was the main factor in treatment decision-making. They concluded that there was not enough instrument to decide whether to go for surgical or conservative treatment, despite being aware of ligaments' low healing capacity. Surprisingly AF is still widely used in the world, in the common practice. Comparative studies with more recent classifica-

tions, showed AF has a good or even better reliability, despite its was conceived and based on x-ray only. Chhabra, in a questionnaire survey on expert opinion worldwide, observed that 38% declared they were using AF, 35% SLIC and only 5% CPISS [62].

SLIC classification and AO classification are the most used nowadays, both stressing out interpretation of lesions' morphology.

In SLIC classification major emphasis has been put on the disk-ligament complex (DLC), considered as the main stabilizer of the joint, in fact facet subluxation >50% increases the injuries' score. The involvement of DLC is not always clear using gold standard thin-layer CT, but MRI is sometimes helpful. The initial reliability assessment of the SLIC score was substantial but, among the three components of the classification, the lowest ICC was that of the DLC that confirms the difficulty in its assessment. The highest ICC was that of neurologic status.

Reproducibility is on the limits of every classification: inter and intra observer studies were conducted to demonstrate it. In 2010 Stone et al. [63] and later in 2013 Van Middendorp et al. [64] reported conflicting results on SLIC reliability: first authors reported an excellent inter and intrarater agreement for SLIC and a moderate interrater to an excellent intrarater agreement for AF, while Van Middendorp showed a moderate agreement on SLIC by internal validation studies, but an external validation study yielded a poor agreement.

So, worldwide multicentric studies show that the SLIC's limit is reproducibility, instead of AF which seems to have a better reliability according to Kanagaraju [65].

In a recent study on multicenter observational survey on reliability and reproducibility for lower cervical spine injuries classification systems, an excellent agreement regarding management was observed among the experienced surgeons using SLIC while agreement among less experienced neurosurgeons was found 2 times less than that of experienced [66]. As advocated also by Vaccaro et al. [67], results showed that higher levels of experience may improve agreement of SLIC.

Subaxial cervical spine injury have heterogeneous morphologic features hence selecting the best surgical approach remains controversial. According to the perspective of many surgeons, they prefer to have a classification comprehensive, easy to use but more oriented to suggest the surgical indication. To achieve this aim, a further classification has been proposed recently with the aim to predict the failure of only anterior approach, called PLICS and measure the intra-interobserver reliability [49]. Anterior only approach is widely used but hardware failure and late cervical deformity are not rare and acceptable complications. In these cases, unstable injury due to not well recognized and estimated posterior elements lesion (bone and ligamentous complex) is the responsible of the complications. The issue is not new. Kotani et al. [68], Lee et al. [69] recognized the strategical importance of zygapophyseal joint and ligaments in conferring stability to the segment of motion. Longitudinal ligament lesion (anterior and posterior) and disc disruption were significantly associated with facet joint fractures and dislocation. The subtype analyses of lateral mass fractures demonstrated high rates of anterior translation in separation, split, and traumatic spondylolisthesis, as well as significant coronal malalignment in comminution and split types [62].

Unlike SLIC, AO classification is easier and with a better reliability and validity, again with the increasing gravity's levels using a morphologic valuation. Urrutia et al. in 2016 compared agreement between AF and AO. The study demonstrated a significantly better inter-observer agreement with AO while the AF had insufficient inter-observer agreement and did not reach the minimum limit of agreement ($k = 0.55$) [70].

Nowadays, there's the introduction of smartphone apps which are helpful to applying classification in clinical practice [71].

In 2021 Schroeder shows that treatment choice depends on experience and origin even in highly unstable injuries [72]. In fact, according to the literature, and also in our experience, there is no classification that includes all the elements that the therapeutic choice requires. Each of the classifications has some peculiar aspects that help the

choice of the surgeon. Furthermore, the experience and preference of surgeons are still a bias in the choice of treatment, surgical approach, and techniques.

There is a need for further studies to improve the reliability of existing classifications by aiding communication between healthcare professionals, assisting in treatment decisions, and reducing errors due to misdiagnosis.

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12 Tissue Sparing Posterior Fixation as a Treatment Option for Degenerative Disc Disease

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Background on Cervical Spondylosis

Cervical spondylosis is the age-related degeneration of cervical discs that results in symptoms of neck pain, radiculopathy and/or myelopathy. The chemical composition of the nucleus pulposus and annulus fibrosis changes and is associated with a progressive loss of the disc's viscoelastic properties. Disc height decreases, the disc bulges posteriorly, and the adjacent vertebral bodies collapse onto one another. Failure of the disc causes secondary changes: buckling of the ligamentum flavum, thickening of the facet joint capsules, osteophyte formation, and vertebral subluxations. These secondary changes contribute to a decrease in size of the central canal and neuroforamina. The above events are collectively described as degenerative disc disease and result in spinal stenosis. Spinal stenosis causes direct mechanical pressure on the nerve roots and/or spinal cord. The exact pathogenesis of cervical radicular pain is multifactorial. It is understood to be a result of a combination of direct nerve root compression, movement at the stenotic level, and an inflammatory response [1, 2]. Intrinsic blood vessels of the compressed nerve have been shown to demonstrate increased permeability, which results in nerve root edema. As the edema becomes chronic, fibrosis and scar ring ensue, contributing to an altered response threshold and increased sensitivity of the nerve root to pain. Pain mediators released from the nerve cell bodies, intervertebral disc, and surrounding tissue play a role in initiating and perpetuating the inflammatory response [3].

Age related degenerative disc changes often lead to symptoms of neck pain, arm pain, shoulder pain, numbness, weakness, and changes in gait. When degenerative changes result in pinched nerves in the cervical spine, the resulting painful condition is commonly referred to as cervical radiculopathy. Globally, the reported annual incidence of cervical radiculopathy is 83.2/100,000 persons [4], while the reported prevalence is believed to be 3.5/1000 persons [5].

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Posterior Microendoscopic Foraminotomy

Posterior cervical foraminotomy has been indicated in patients with unilateral radiculopathy, absent significant neck pain with maintained cervical lordosis [6–8]. Further, it is a desirable option in cases presenting with laterally herniated disc and lateral stenosis [6]. The surgical objective of a foraminotomy is to decompress the nerve roots while maintaining motion at the affected level. Fessler and Adamson were among the first to describe clinical outcomes utilizing a microendoscopic approach [6, 9]. A meta-analysis of posterior cervical foraminotomies performed by McAnany et al. and a clinical study by Kim et al. showed a significant improvement in pain and return to normal life [10, 11]. In some cases, axial neck pain, and less commonly, instability may ensue because the motion segment is not stabilized [12].

Decompression and Fusion

A surgeon may prefer to decompress and fuse the spine when there is instability, bilateral radicular symptoms, and/or symptomatic spinal cord compression. Anterior cervical discectomy and fusion (ACDF) is currently the most common approach for decompressing and stabilizing the spine, accounting for 68% of all cervical spinal surgeries [13].

Despite the numerous benefits associated with ACDF, there are risks that could lead to a surgeon recommending against it. The most well-documented post-operative complication tied to ACDF is dysphagia, a serious complication that has been reported to be as high as 31% following multi-level ACDF [14]. Access to the upper anterior cervical spine can be challenging due to position of the jaw, while exposure of C6–T1 is variable and may be problematic in some cases. Injury to the esophagus or vertebral and carotid arteries are rare but can be life threatening. Another concern with ACDF is the risk of pseudarthrosis. When treating multiple levels with an ACDF procedure, Bolesta et al. reported rates of solid arthrodesis to be as low as 47% [15].

A surgeon may consider a posterior (PCF) or a combined anterior and posterior (circumferential, CCF) option. Of the three common methods of cervical fusion, CCF is currently the least commonly performed [16, 17] however the frequency of CCF has been increasing at a greater rate than ACDF or PCF (CCF:182%, ACDF:139%, PCF:177%, between years 2001 and 2010) [16]. One contribution to the increase in CCF is that surgeons are opting to perform fusion and decompression procedures in patients previously deemed high-risk for revision following ACDF or PCF procedures alone.

The inclusion of supplemental posterior fixation most commonly involves lateral mass screw and rod fixation, laminectomy, and fusion of the posterior lateral mass [18]. This approach is preferred when there is posterior neural compression, a congenitally narrowed canal, or pathology at three or more levels. Posterior instrumentation increases rigidity of the construct and improves fusion rates [19]. Accessing the spine with this method comes with a cost via extensive paraspinal muscle dissection, detraction, and retraction. The combined trauma to muscle, increased incision size, and prolonged surgical retraction are a few explanations for why posterior fusion surgeries are associated with a longer surgery time, greater blood loss, and longer hospital stays compared to ACDF [20].

A tissue-sparing approach for posterior cervical fusion was developed [21] that preserves the normal muscular and ligamentous attachments to the posterior cervical spine. This technique has been shown to reduce the length of stay, blood loss, and operative duration to be comparable to that typically seen following ACDF [22] and shorter than that typically seen following PCF with lateral mass fixation [23].

When decompression is deemed necessary, which co-morbidities or risk factors are most relevant in determining approach? We briefly highlight some of the most prevalent risk factors for revision: nicotine use and advanced age.

Nicotine Use

Smoking has been shown to negatively affect the cervical spine by contributing to the onset of osteoporosis, reducing osteoblast activity, increasing cortisol levels, decreasing vascular oxygen

supply to bone, and decreasing calcium absorption [24]. This altered bone metabolism contributes to the increased risk of pseudarthrosis, infection, dysphagia, and adjacent segment disease, as well as decreases the rate of fusion observed in smokers [24–27]. Smokers receiving multi-level treatment exhibited lower rates of fusion and higher rates of complications, particularly postoperative wound infection [24, 25, 27]. A circumferential approach may benefit patients who use nicotine through improved stability during fusion.

Advanced Age

The majority of ACDF procedures are performed on people over the age of 45 [28]. Advanced age at time of cervical spinal fusion has been well documented as a predictor of complications [29–31], poorer surgical outcomes [29, 32], and increased length of stay [30]. Moreover, the prevalence of comorbidities such as diabetes and cardiovascular diseases significantly increase with advancing age [33], with these individuals now representing a greater population of patients being treated with surgery [34]. Patients with an average age over 54 that have opted for circumferential fusion have shown high fusion rates and comparable complication rates to ACDF [35, 36]. Thus, we can conclude that advanced age increases possibility of postoperative complications or disease progression following ACDF, but these risks can be mitigated with the inclusion of supplemental posterior fixation.

DTRAX System

Tissue sparing posterior fixation can be performed using instrumentation available on the market. One such system is the DTRAX® Spinal System (Providence Medical Technology, Inc.). The spinal system is composed of specialized instruments that carry out the novel technique and placement of the cervical facet implants and decortication/fusion of the lateral mass (Fig. 12.1). In the U.S., the spinal system and

Fig. 12.1 (**a**) Instruments of DTRAX/CORUS Spinal System. (**b**) Detailed views of instrument tips. (1) Access Chisel (2) Trephine Decorticator (3) Guide Tube (4) Rasp Decorticator (5) Rotary Decorticator (T) Bone Graft Tamp

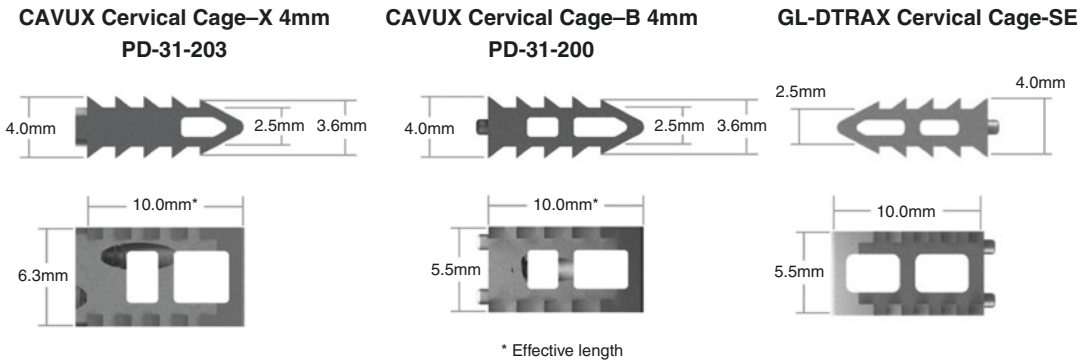

Fig. 12.2 Cervical cage configurations

cages are referenced under separate product names; the CORUS Spinal System and CAVUX Cervical Cages.

DTRAX Cervical Cages are manufactured from implant grade titanium alloy. They are available in three configurations (Fig. 12.2): the DTRAX Cage-SE, CAVUX Cage-B, and CAVUX Cage-X. A hollow design in all cages enables packing of bone graft. The teeth on superior and inferior surfaces are designed to resist expulsion. The surfaces of the cages are acid-etched and textured at the cellular level to facilitate osseous integration. The CAVUX Cages -B and -X are not available in CE approved markets, but are available in the U.S.

Indications and Contraindications

The indications differ between the U.S. and EEA markets and are therefore both presented below.

EEA Market

Indications The DTRAX System is indicated for use in skeletally mature patients for posterior cervical treatment at C3–C7 (inclusive) spinal levels for patients with single level radiculopathy due to degenerative disc disease (DDD) as defined by back pain of discogenic origin with degeneration of the disc confirmed by history and radiographic studies and/or degenerative disease of the facets.

US Market

Indications The CORUS Spinal System is a set of instruments indicated to be used to perform posterior cervical fusion in patients with cervical degenerative disc disease.

The CAVUX Cervical Cage is indicated for use in skeletally mature patients with degenerative disc disease (DDD) of the cervical spine (C3–C7) with accompanying radicular symptoms at one disc level. DDD is defined as discogenic pain with degeneration of the disc confirmed by patient history and radiographic studies. Patients should have received at least 6 weeks of non-operative treatment prior to treatment with the device. Devices are intended to be used with autogenous bone graft and supplemental fixation, such as an anterior plating system.

Surgical Technique

Operating Room and Patient Preparation

After routine intubation, place the patient in a prone position on bolsters with face supported by a donut or foam support, holding the neck in a neutral position. Use tape or a cervical visualization harness to pull the patient's shoulders inferiorly (Fig. 12.3). Rotate the table to allow positioning of the two C-arm machines.

Fig. 12.3 Patient preparation involves prone positioning, head support and pull-down of shoulders

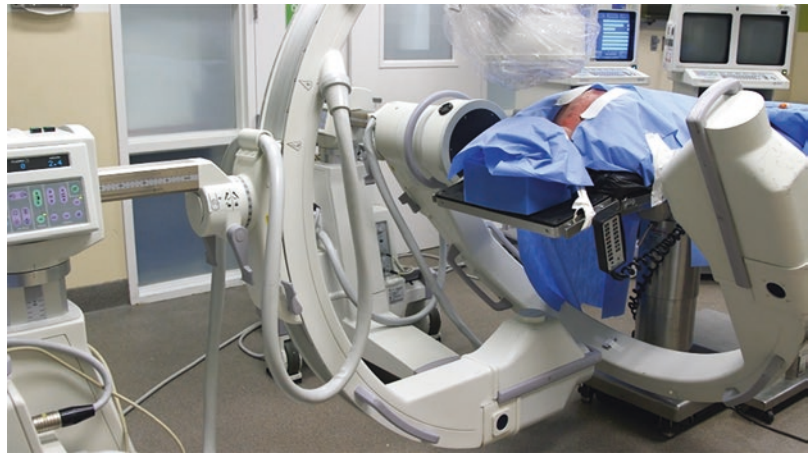

Fig. 12.4 The use of two C-arms for lateral and AP views concurrently is recommended

C-Arm Preparation and Tips

Set up the C-Arm at the side of the table in AP with the arm fully retracted. Find a clear AP view. Advance the C-Arm while rotating the detector back to find the lateral view. A fully retracted C-Arm allows for finding the lateral view by advancing the arm of C-Arm instead of moving the whole machine. Returning to the AP position only requires rotating the detector forward while fully retracting the C-Arm. This C-Arm set up allows clear imaging to be retained while rapidly switching between views.

The use of two C-Arms is recommended for ease of imaging which can improve safety and significantly reduce the time length of the procedure. If a second C-Arm is used, leave the first C-Arm in the lateral position. Rotate the first C-Arm 20°–30° so that the arm is under the patient's shoulders. This provides room for the second C-Arm under the patient's neck. Place the second C-Arm at the head of the table and with the arm fully advanced to find the AP view.

Finding the AP view with the arm of the second C-Arm fully advanced allows the arm portion to be retracted during the procedure to create working space for tools, then fully advanced to quickly restore AP imaging. On the second C-Arm add approximately 25–30° caudal/cranial inclination; this adjustment, along with the flexion of the head, allows an en face or near en face view of the target facet joint (Fig. 12.4).

Skin Markings and Sterile Field

Images clearly demonstrating facet joint anatomy are essential for proper preoperative skin markings. Use fluoroscopic guidance to identify surgical border and level to be treated. Identify and mark the medial and lateral borders of the facets using AP view on fluoroscopy, a slender, straight

metallic instrument (e.g., K-wire or Steinman pin), and surgical pen (Fig. 12.5). Identify the target facet joint level using the same method and mark it with a transverse line (Fig. 12.6). Mark the approximate skin incision and entry point by measuring two finger widths caudally from the target level.

Prepare and drape the patient's posterior neck in a routine sterile fashion. It is recommended the C-Arm(s) remain in place during this portion so that the radiological markers are not lost. Open the sterile-packaged tray containing the surgical instruments and the sterile-packaged pouches containing the implants and their delivery instruments.

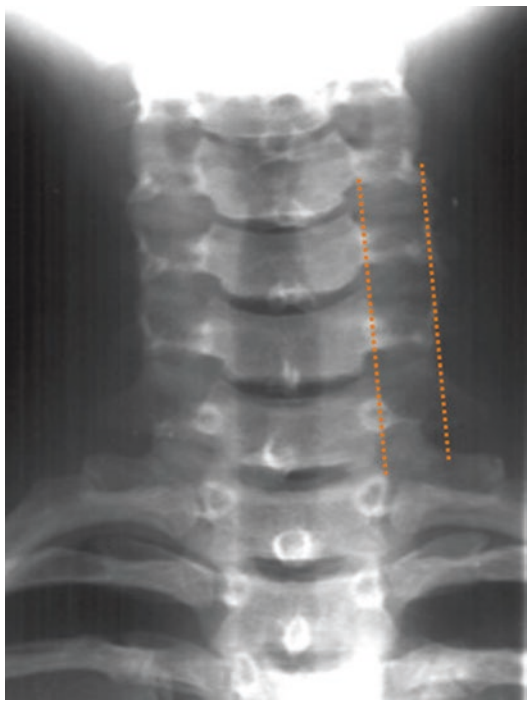

Fig. 12.5 The medial and lateral borders of the facets are identified using AP view

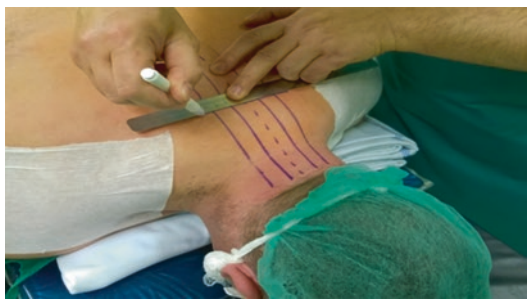

Fig. 12.6 The operative level is identified and marked on the patient

Establish Trajectory and Access the Facet Joint

Use a spinal needle to confirm the trajectory under fluoroscopic guidance. Due to the acute angle of the facet joint the trajectory often results in the entry point being located approximately two finger widths below the target level. Reinsert or reposition the spinal needle as needed until the correct entry point and trajectory is confirmed. The correct trajectory will match the angle of the facet joint (Fig. 12.7). Repeat this process for the contralateral side. If desired the needles may be used to administer local anesthesia and/or epinephrine for pain or bleeding control. Remove the first spinal needle while leaving the contralateral needle in place to provide a guidance reference. Make initial longitudinal incision by the confirmed entry points and carry through the subcutaneous tissue and the fascia. Use a hemostat to

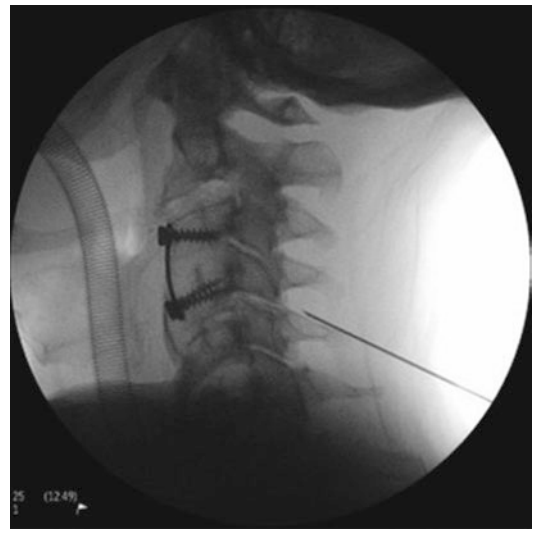

Fig. 12.7 The spinal needle confirms trajectory under fluoroscopic guidance and is positioned to match the angle of the facet joint

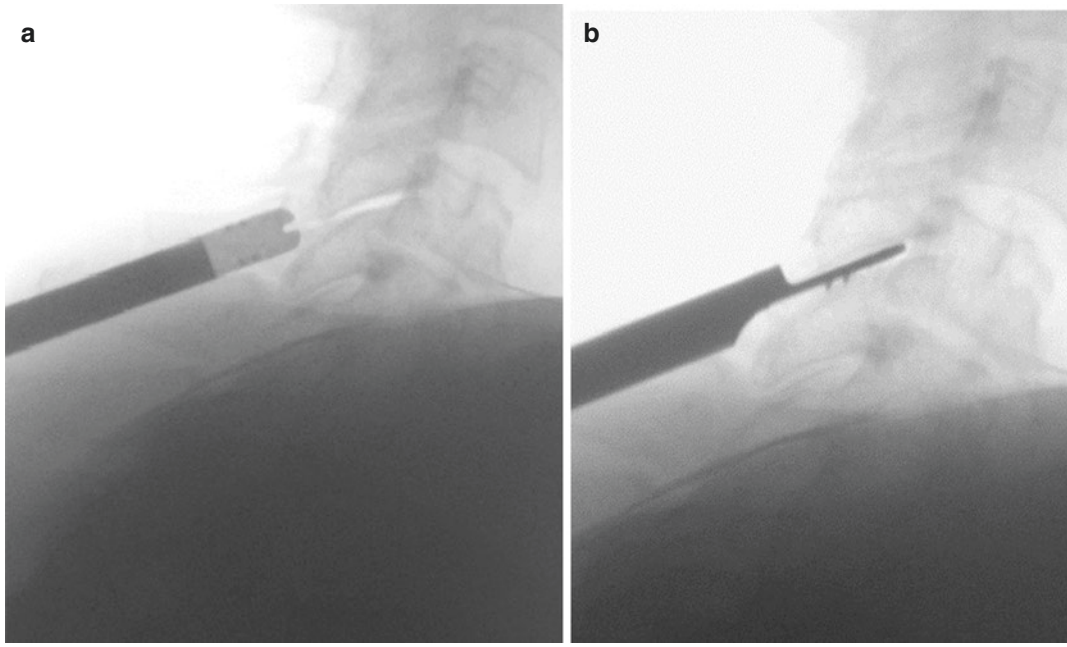

Fig. 12.8 (**a**) The Access Chisel is advanced with a flat end in a cranial/caudal orientation until bone is reached. (**b**) Upon reaching bone, the chisel is rotated 90 degrees and advanced into the facet joint. The positive stop should be facing the inferior articular process of the level above

spread the fascia laterally. Carry the dissection down as needed to achieve desired level of direct visualization.

Under AP fluoroscopic guidance, advance the Access Chisel through the incision using a slight medial to lateral trajectory in AP view with its distal tip in the cranial-caudal orientation until bone is reached (Fig. 12.8a). Confirm the Access Chisel is centered medial to lateral on the lateral mass. Rotate the Access Chisel 90° so that its positive stop feature is oriented cranially, i.e., towards the inferior articular process of the level above. Orientation markers on the Access Chisel indicate the orientation of the instrument. Using control in AP and lateral fluoroscopy, find the superior portion of the facet joint, lower Access Chisel tip to find and cut the capsule of the joint. Use the Multi-Tool to lightly mallet the Access Chisel to advance it into the facet joint (Fig. 12.8b). Advance the Access Chisel until its positive stop feature abuts the inferior articular process of the level above. Once positioned, pull back on the Access Chisel handle's orange trigger to release the Access Chisel handle. Remove the handle. Maintain gentle downward pressure on the Access Chisel to retain its placement within the facet joint.

Decorticate the Lateral Masses and Establish Working Channel

Advance the Decortication Trephine over the Access Chisel while rotating in an alternating clockwise/counterclockwise motion to aid its advancement through soft tissue until its distal tip contacts bone (Fig. 12.9). Align the Trephine Decorticator so that its teeth are positioned against the superior lateral mass. Decorticate the superior lateral mass and the medial portion of the lamina by moving the Trephine Decorticator in a windshield wiper motion of 10° rotations. This action will strip the muscle subperiosteally and create bleeding from the bone. Do not apply excessive pressure while decorticating as over decortication may compromise the biomechani-

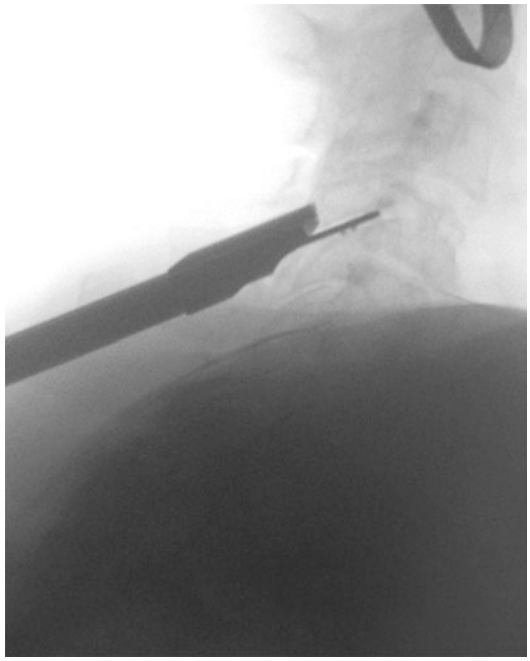

Fig. 12.9 The Trephine Decorticator is advanced over the Access Chisel until the distal tip contacts bone

cal integrity of the inferior articular process of the level above. Remove Trephine Decorticator while applying gentle downward pressure on the Access Chisel to prevent the Access Chisel from dislodging from the facet joint.

To establish the working channel, slide the Guide Tube over the Access Chisel with the tines of the Guide Tube in a cranial/caudal orientation to ease insertion over the proximal end of Access Chisel. Then rotate the Guide Tube 90° to align its tines with facet joint. Because the Guide Tube is a unidirectional tool ensure its correct orientation in the facet joint. Align the head arrow icon on Guide Tube handle with the orientation markers on Access Chisel shaft. The head arrow icon and orientation markers should be facing cranially.

Confirm the distal tines are aligned with the facet joint. Place the Multi-Tool over the Access Chisel. The Multi-Tool should be placed with its pry feature faced down. Lightly impact the Multi-Tool to advance the Guide Tube into the facet joint. Advance the Guide Tube until its positive stop feature abuts the inferior articular process of the level above (Fig. 12.10). Verify Guide Tube placement on both lateral and AP views. Proper and final Guide Tube depth is achieved when its positive stop feature abuts the inferior articular process of the level above. Center the Guide Tube between the medial and lateral borders of the facet joint on AP view. Remove the Access Chisel while maintaining downward pressure on the Guide Tube.

Decorticate the Facet Joint

Insert the Rasp Decorticator through the Guide Tube and advance using the Fork Mallet until the upper handle of the Rasp Decorticator is flush with the handle of the Guide Tube. Lightly mallet the Rasp Decorticator with the Multi-Tool to decorticate the interarticular surfaces of the facet. Retract the Rasp Decorticator by inserting the Multi-Tool into the Rasp Decorticator notch and rotating the Multi-Tool to release the Rasp Decorticator handle. This allows for the controlled removal of the Rasp Decorticator while maintaining the position of the Guide Tube in the facet joint. Lift the Rasp Decorticator, rotate it 180°, then lightly impact it to advance it and further decorticate, achieve bleeding of the bone, and remove joint material. Repeat this step until the Rasp Decorticator can be retracted out without resistance. Remove the Rasp Decorticator while maintaining downward pressure on the Guide Tube.

Insert and advance the Rotary Decorticator through the Guide Tube by hand while rotating its handle in a clockwise motion until it reaches a hard stop against the Guide Tube. Once the Rotary Decorticator is fully inserted in the Guide Tube, apply caudal pressure to the Guide Tube and rotate the Rotary Decorticator clockwise 360°. Caudal pressure on the Guide Tube helps the Rotary Decorticator decorticate the inferior facet. Remove the Rotary Decorticator while continuing to rotate it clockwise.

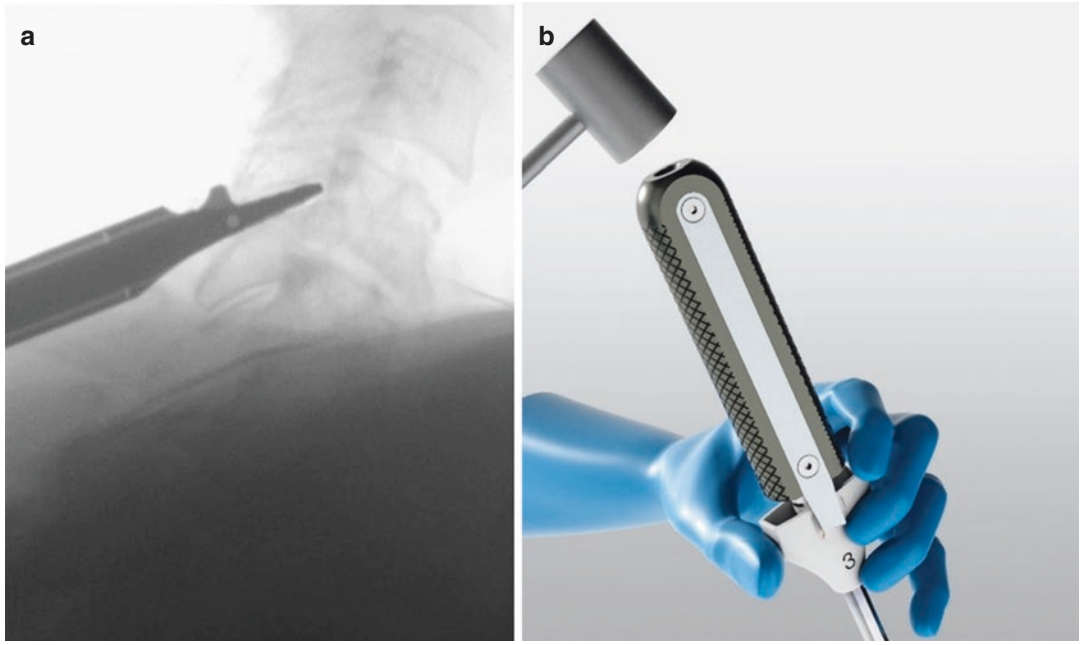

Fig. 12.10 (**a**) The Guide Tube is advanced into the facet joint using the (**b**) Multi-Tool

Implant the Cervical Cage

Prepare the Cervical Cage by packing it with autogenous and/or allogenic bone graft prior to placement. The Cervical Cage is preloaded on its delivery instrument (Cage Delivery Instrument). Align the Cage with the facet joint by orientating the head arrow icon on the handle of the Delivery Instrument cephalad, i.e., toward the patient's head. Under AP and lateral fluoroscopic control mallet the Cage Delivery Instrument through the Guide Tube until its handle locks with the handle of the Guide Tube in order to advance the Cage into the facet joint.

Use AP & Lateral fluoroscopy to confirm proper placement of the Cage. The Cage should be in the middle of the facet joint, centered between the medial and lateral borders of the facet joint as identified by fluoroscopic views (Fig. 12.11). The anterior margin of the Cage should be aligned with the anterior margin of the lateral mass.

Deploy the Inferior Bone Screw (Cage-B and Cage-X Only)

Once proper cage position is confirmed, introduce, and advance the bone screw into the hole at the top of the handle of the Cage Delivery Instrument while maintaining downward pressure on the Cage Delivery Instrument. When resistance is encountered, rotate the Bone Screw Handle clockwise while applying downward pressure to advance it into the Cage. The laser-mark line on Bone Screw Shaft indicates the screw position relative to the Cage. When the laser-mark line is visible above the Cage Delivery Instrument the Bone Screw is contained within the Cage Delivery Instrument. When the laser-mark is no longer visible above the Cage Delivery Instrument the Bone Screw Tip has reached the Cage. Continue to rotate the Bone Screw Handle until a snapping sound is heard and there is no resistance rotating the handle (Fig. 12.12). This indicates full Bone Screw

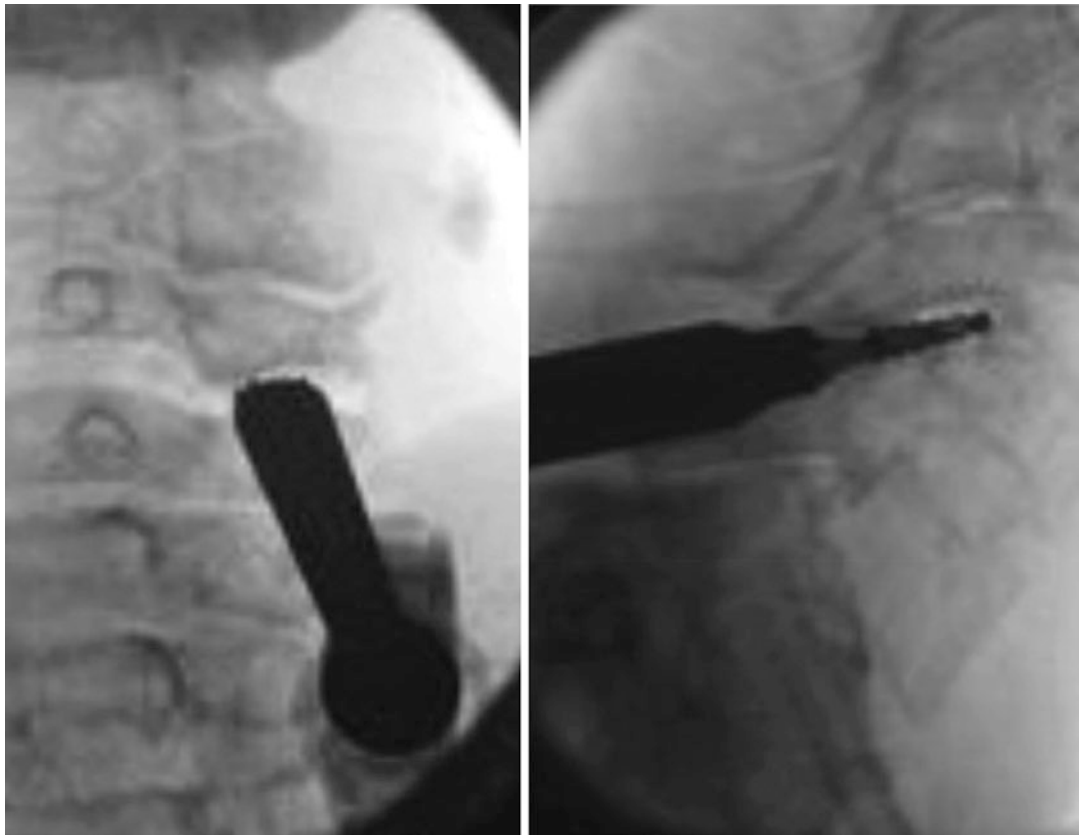

Fig. 12.11 AP and lateral fluoroscopy is used to position cage in facet

Fig. 12.12 The screw will break away from the delivery mechanism after enough resistance from advancing into the bone

deployment and that the release feature of the Bone Screw has been activated. Once deployed, remove the Bone Screw Shaft and Handle by pulling it out of the Cage Delivery Instrument. Turn the gray Release Knob on the Cage Delivery Instrument counterclockwise until the Cage is fully released.

Deploy the Superior Bone Screw (Cage-X Only)

Remove the Release Knob and Retention Wire Assembly from the Cage Delivery Instrument to reveal the superior bone screw hole. This is the larger hole on the handle of the Cage

Delivery Instrument. While maintaining downward pressure on the Cage Delivery Instrument, introduce and advance the Bone Screw into the Superior Fixation Screw Hole until the black marker line is no longer visible above the handle of the Cage Delivery Instrument. Deploy and release the Fixation Screw by repeating the process described in the section above. Remove the Release Knob and Retention Wire Assembly from the Cage Delivery Instrument, then remove the Cage Delivery Instrument. Use AP and lateral fluoroscopic views to verify the correct placement of the Cage and Bone Screws.

Apply Bone Graft Material to Decortication Bed

Insert bone graft material such as demineralized bone matrix, into the top of the Guide Tube (Fig. 12.13). Introduce the Bone Graft Tamp into the Guide Tube and advance to push the bone graft material into the prepared bony surfaces, i.e., the decorticated lateral masses. Final control and verification of Cage positioning using AP and lateral fluoroscopy is recommended (Fig. 12.14).

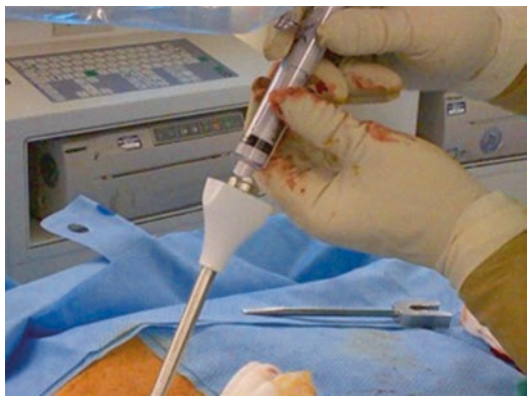

Fig. 12.13 Bone graft material is placed into the top of the Guide Tube

Sutures, Contralateral Procedure, and Final Patient Preparation

Close the paraspinal muscles, approximate tissues, and skin in layers with sutures. Repeat the full procedure for the contralateral facet joint of the target level. Apply a sterile dressing. Apply external immobilizing collar according to surgeons' post-operative protocol.

Clinical Evidence for Decompression and Fusion When Using Posterior Cervical Stabilizers

The capability of the DTRAX system to provide decompression and fusion at the cervical spine has been described both when performed as a stand-alone posterior procedure as well as when used as supplemental fixation as part of a circumferential procedure.

A prospective, multi-center, single arm clinical study was performed to assess clinical and radiographic outcomes of patients with cervical radiculopathy treated with DTRAX cages using a tissue sparing decompression and fusion posterior procedure at one level. The patients were followed over a period of 2 years following surgery [37]. The study hypothesis was that indirect root decompression with the DTRAX Cage would provide clinical relief of radiculopathy in patients with spondylosis with straight or lordotic cervical spines that do not present with symptomatic central canal stenosis necessitating an anterior approach.

Sixty patients were initially enrolled into the study, and 53 of them (88%) were available at 2-year follow-up. The mean age at the time of surgery was 52.8 years (range: 40–75 years). The treated level was C3–C4 in three patients (5.7%), C4–C5 in 6 (11.3%), C5–C6 in 36 (67.9%) and C6–C7 in 8 patients (15.1%). A significant decrease was reported in the mean values of Neck

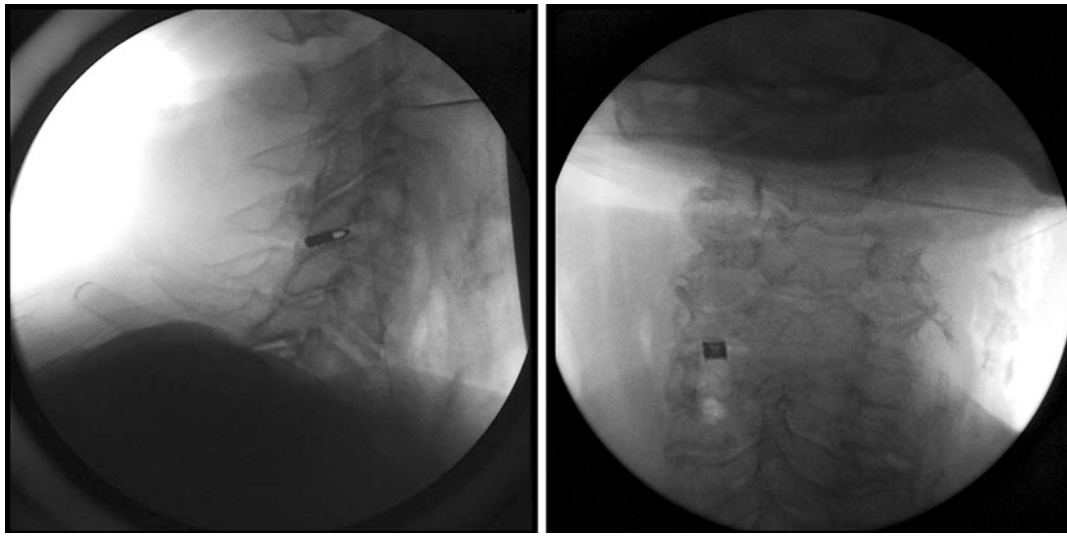

Fig. 12.14 Final cage positioning is confirmed in AP and lateral fluoroscopy

Disability Index (NDI) and Visual Analogue Scale (VAS) for the neck and arm pain as well as an increase in SF-12v2 physical and mental scores at each follow-up out to 2 years comparing to the preoperative values. There were no significant differences in clinical outcomes between 1-year and 2-year follow-up.

All patients showed improvement in the NDI when compared to preoperative and this improvement was maintained at 2 years. Of the 53 patients, 2 patients had an increase in arm pain and 2 had an increase in neck and arm pain that was reflected in VAS scores. Three patients had no change in neck pain and one had no change in neck and arm pain scores for VAS.

The most common device-related adverse events were shoulder pain and paresthesia. The most common procedure-related adverse events were postoperative pain, nausea, pain from bone graft harvest site, and shoulder pain. Severe adverse events included shoulder pain, shoulder/elbow weakness, bilateral sciatica, flank pain, mid-back pain, recurrence of neck pain, recurrence of arm pain, and acute exacerbation of osteoarthritis in the knee. No procedure or device-related serious adverse events were noted during the 2-year follow-up. One patient reporting right shoulder pain was noted as a severe adverse event, which was reported as procedure-related. No revision surgeries were reported at the index level or at adjacent levels. Finally, there were no device migrations, expulsions, or breakages at the 2-year follow-up.

The radiographic fusion rate was reported in 52 of 53 patients (98.1%). Radiographic fusion was defined by less than a 2 mm change in interspinous distance measured on flexion extension radio- graphs taken at 24 months. The overall change in interspinous distance was 0.78 ± 0.58 mm with a range of 0.04–2.16 mm. Translational motion at the treated level of less than 2 mm were noted for all 53 patients. There were no radiographic signs of implant loosening, breakage, migration, or screw back-out. CT scans revealed evidence of bridging bone in 93.3% of patients at 12 months.

In the United States, the DTRAX system is commonly used in conjunction with ACDF to improve fusion rates. Good clinical outcomes were observed by Kramer et al. [38] when using DTRAX Cages to augment an ACDF procedure in 35 high-risk patients (mean age, 55 years). In their report, they defined high-risk as either addressing three or more levels, two or more levels with concomitant comorbidities (osteoporosis, nicotine use, arthritis), or two or more levels

with history of pseudarthrosis. Of their cohort, 16 were smokers and 27 had three or more levels treated.

Including both anterior and posterior procedures, average blood loss was 70 ml and the average length of stay was 1.03 days. As of last follow up (range 102–836 days), VAS scores improved on average 4.86 points or 64.70%. Two patients were treated for complications consisting of superficial wound infections and resolved with antibiotics. There were no reoperations or readmissions nor were there any recorded neurological or vascular complications.

A multi-site prospective randomized clinical trial is currently underway in the United States to evaluate the safety and efficacy of the DTRAX system when used as supplemental posterior fixation to an ACDF in patients treated at three levels.

Biomechanical Performance of DTRAX Cervical Cages Alone and When Integrated with Anterior Constructs

The efficacy of the DTRAX facet cage is due to a decreased range of motion at the instrumented level, foraminal distraction, and maintenance of its deployment position during repeated bending motion and loading.

A study by Leasure and Buckley was conducted to evaluate the biomechanical efficacy of the DTRAX cervical cage in vitro [39]. Three aspects of device performance were addressed, including acute stabilization, neuroforaminal distraction, and migration of the implant over time due to repeated loading. The results of this study indicate that a stand-alone cage substantially increases intervertebral stability, does not loosen within the cervical facet joint during repeated bending loads, and maintains decompression of the cervical nerve roots through extension.

The biomechanical performance of the DTRAX Cages were further tested by Voronov et al. [40]. In their study they measured flexion-extension range of motion, lateral bending, and axial rotation across three conditions; intact, with anterior plate, with anterior plate and DTRAX Cages. This progression of constructs was tested for one level (C6–C7) and two levels (C3–C5). As expected, adding an anterior construct stabilized the cervical spine. When the anterior plate was supplemented with posterior stabilizers, all three measures of stability further improved significantly. By the authors estimation, the addition of facet cages to a ACDF increased stiffness six-fold compared to the anterior construct alone. Havey et al. [41] observed similar changes on stability using a zero-profile anterior cage with DTRAX Cages. In addition, their results showed that when both anterior and posterior constructs were used together, there was no change in lordosis observed when compared to the intact condition. Conservation of lordosis in the absence of an anterior construct was summarized by Laratta et al. [42], who in their review of DTRAX literature, found no evidence of kyphosis at follow-up visits ranging from 12 to 24 months.

Conclusion

Technological advancements in tissue sparing PCF have shown this technique can improve outcomes when compared to a traditional open approach in select patients with symptomatic radiculopathy, particularly when used as an adjunct to ACDF. The presented clinical, radiographic, and biomechanical evidence for minimally invasive posterior cervical facet cages should encourage surgeons to consider their full armamentarium when designing a treatment plan for patients presenting with increased risk for non-union. Moreover, we call for future work to determine which additional risk factors increase chance of revision and to establish subsequent treatments to best mitigate these risks, providing better outcomes for this growing pool of patients.

Disclaimer This Chapter contains information about DTRAX® Spinal System and the CORUS Spinal System and CAVUX Cervical Cage product lines, manufactured by Providence Medical Technology, Inc. Other manufacturers' products may be available to treat or degenerative disc disease. One of the contributing authors of this Chapter, Erik Summerside, is an employee of Providence

Medical Technology, Inc. Information about the DTRAX Spinal System is provided herein for educational purposes and is not to be construed as promotional in any manner. Prescribing decisions should be made based on DTRAX Spinal System indications and labeling by trained medical professionals. This Chapter may contain information that is not in the labeling approved by the U.S. Food and Drug Administration or another applicable regulatory body.

Conflicts of Interest Dr. Heller has acted as a consultant for Convatec, Nuvasive, Providence Medical Technology, SI Bone, Stryker, Zimmer Biomet, and RTI. He receives royalties from Nuvasive, has personal investments in Portola, ATEC, and SpineBiopharma, and provides research support for Ethicon. Dr. Glenn has consulted for Providence Medical Technology. Bruce McCormack and Erik Summerside have an ownership stake in Providence Medical Technology (see disclaimer).

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13 Anterior Cervical Decompression and Fusion with Autologous Bone Graft

Paolo Perrini, Davide Tiziano Di Carlo, and Nicola Di Lorenzo

The anterior approach to the cervical spine was conceived and promoted in the early 1950s by the seminal investigations of different pioneers [1–3]. In 1952, Bailey and Badgely performed an anterior decompression and fusion utilizing an autologous onlay strut bone graft in a patient with a cervical lytic lesion [1]. In 1955, Robinson and Smith reported anterior cervical discectomy and fusion for spondylosis utilizing a tricortical horseshoe-shaped iliac crest graft [3]. Subsequently, Ralph Cloward described his technique for cervical discectomy with removal of ventral osteophytes and fusion using a dowel-shaped iliac crest graft, and popularized the anterior approach for the treatment of degenerative, neoplastic, traumatic and infective pathologies exerting a ventral compression of the spinal cord and/or cervical roots [2]. Since these original descriptions, the progress of available grafting options proposed allograft-, synthetic- and factor/cell-based technologies for bone graft substitutes [4, 5]. However, the autologous bone graft is still considered the gold standard for anterior cervical fusion after anterior cervical discectomy (ACD) or corpectomy because is the only graft with the properties of osteogenesis, osteoinduction and osteoconduction [4, 6]. In addition, the corticocancellous architecture of the autologous bone graft enhances interface activity with bony ingrowth and provides load-bearing capacity, which is extremely relevant in avoiding a kyphotic change across fused segments.

This chapter describes the technical nuances of anterior cervical decompression and fusion with autologous bone graft.

Surgical Techniques

Anesthesia and Positioning

Patients are positioned supine on the operating room table for orotracheal intubation. Awake fiberoptic nasotracheal intubation is required only in selected myelopathic patients in which spinal injury as a result of neck extension during intubation must be avoided. A single dose of intravenous prophylactic antibiotics is administered half an hour before the time of incision. The head is slightly extended without rotation on the radiolucent operating table and a rolled towel is placed under the neck to improve the cervical lordosis. Alternatively, the head is placed on a horseshoe headrest. The shoulders are pulled caudally using wide adhesive tape to allow

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visualization of the lower cervical spine on fluoroscopic images. The knees are slightly flexed to prevent stretch injuries. Electrophysiological monitoring is not necessary in routine cases.

Incision and Soft Tissue Dissection

Diversity of opinions among neurosurgeons exists regarding the effect of approach side on the incidence of recurrent laryngeal nerve (RLN) injury after anterior approach to the cervical spine. Anatomical arguments have been proposed to support one side of approach over the other. Because the left RLN is longer and enters the tracheoesophageal groove at a less steep angle it has been argued that a left-sided approach would minimize the incidence of RLN palsy [7, 8]. However, several clinical investigations reported that the side of approach has no significant effect on the incidence of RLN injury [9, 10]. In addition, a left-sided approach theoretically places the thoracic duct at risk of injury [11]. It is our practice to operate mostly from the right side for ease of surgery for right-handed surgeon, reserving a left-sided approach in patients with previous left-sided neck surgery and resultant vocal cord dysfunction.

The incision is localized using fluoroscopy. A horizontal skin incision beginning at the midline and extending laterally to the medial border of the sternocleidomastoid muscle is suitable to expose up to two intervertebral discs or one vertebral body (Fig. 13.1). A longitudinal incision following the medial border of the sternocleidomastoid muscle is performed for more extensive procedures. The platysma muscle is sharply divided in line with the incision and a subplatysmal release is performed to relax the wound edges and to facilitate further dissection. Careful dissection and accurate release of fascial planes allow optimal exposure with minimal retraction. The superficial layer of the deep fascia which envelopes the sternocleidomastoid muscle is sharply divided exposing the middle layer of the deep fascia. This layer is incised anterior to the anterior border of the carotid artery, which remains on the lateral side of the surgical field. Transection of the omohyoid muscle that runs obliquely across the field at the level of the C6 vertebral body can be usually avoided through extensive fascial release. At this point the vertebral bodies can be palpated with a finger under the deep cervical fascia also known as alar fascia. The trachea and esophagus, which are contained in the middle layer of the deep fascia, are gently retracted medially whereas the carotid sheath and the sternocleidomastoid muscle remain laterally. The alar fascia is incised to obtain access to the anterior cervical spine. A needle is placed on the anterior anulus of the disc space and a lateral fluoroscopy is obtained for level confirmation. After fluoroscopic confirmation, blunt dissection is used to expose the ventral aspect of vertebral bodies. Identification of the midline is obtained exposing the longus colli muscles bilaterally, which are generally equidistant from the midline. In presence of anterior osteophytes, their removal is necessary for the identification of the midline. The insertions of the longus colli muscles are coagulated and lateral retraction blades are placed bilaterally under their medial edges. When a long segment construct e second retractor with blunt blades is placed in the cranio-caudal direction to enhance the surgical exposure and to protect soft tissues from injury.

Smith-Robinson Technique

The anterior longitudinal ligament and the anulus fibrosus are incised flush from the edges of the vertebral bodies with a No. 11 scalpel (Fig. 13.2). The anterior osteophytes, when present, are removed with a curved osteotome or rongeurs. The anterior longitudinal ligament lying on opposing vertebral bodies is removed to clearly expose the bony surface. Interbody distraction is obtained by placing distracting pins into the mid-portion of the vertebral bodies above and below the interspace to be treated. After distraction, the disc and the cartilaginous plates are progressively removed with curette. High-speed drill and Kerrison pounch are used to complete the discectomy and to remove the posterior osteophytes under microscopic view. The posterior

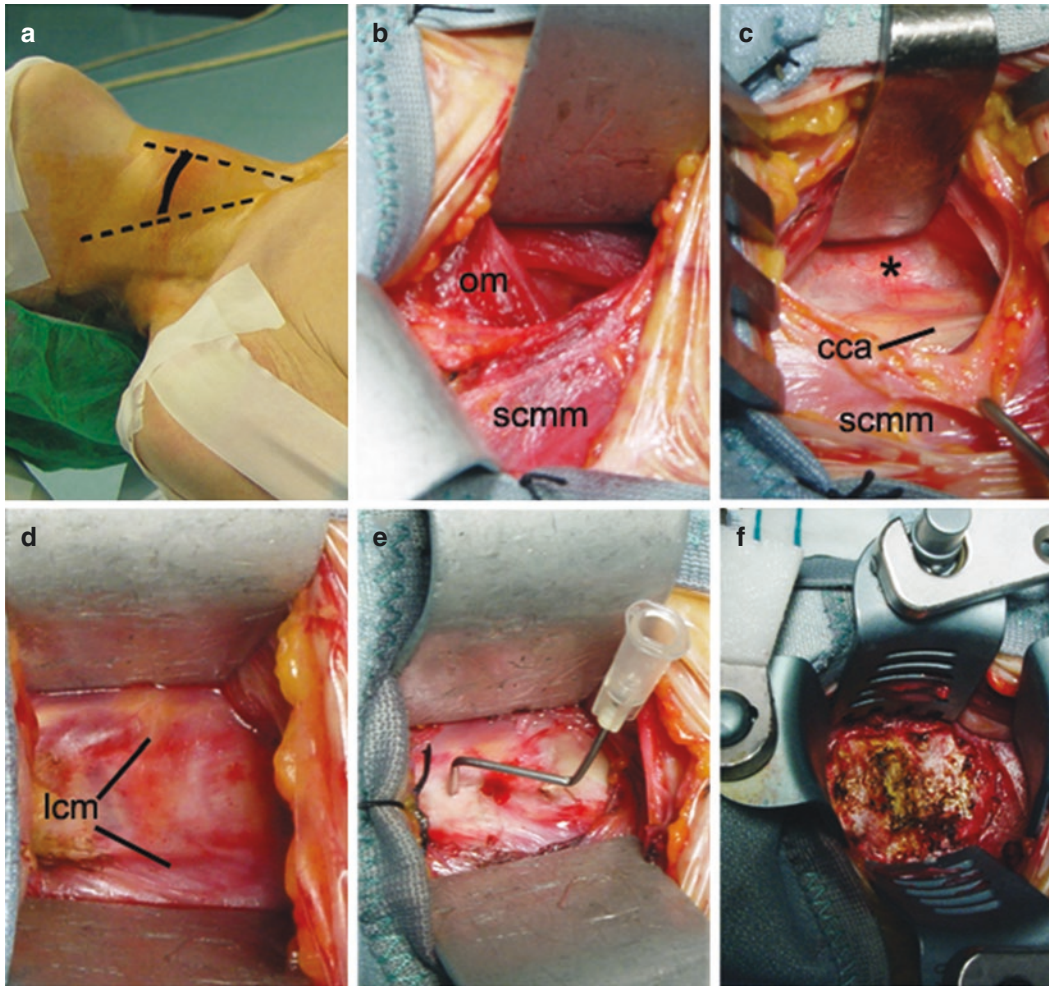

Fig. 13.1 Incision and soft tissue dissection. (**a**) A transverse skin incision extending from the midline to the medial border of the sternocleidomostoid muscle is adequate to expose up to two intervertebral discs or one vertebral body. An oblique incision along the anterior border of the sternocleidomastoid muscle is used in more extensive procedures. (**b**) After incision of the platysma and subplatysma dissection, the superficial layer of the deep cervical fascia is entered with exposure of the sternocleidomastoid muscle. Dissection of the middle layer allows exposure of the omohyoid muscle. (**c**) The carotid artery can be palpated posterior to the sternocleidomastoid muscle. The alar fascia (asterisk) covers the longus colli muscles and separates the vertebral bodies from the trachea and esophagus. (**d**) the longus colli muscles are clearly exposed and help to identify the midline. (**e**) a right-angle bent needle is inserted in the disc and a lateral x-ray is obtained to confirm the level. (**f**) the longus colli muscles are dissected and the retractor blades are inserted. The anterior longitudinal ligament and the anulus fibrosus are incised and removed. *cca* common carotid artery, *lcm* longus colli muscle, *om* omohyoid muscle, *scmm* sternocleidomastoid muscle

longitudinal ligament (PLL) is generally opened widely to expose the dura and to verify complete removal of disc herniation and optimal resection of osteophytes. We use a nerve hook to open laterally the PLL, which is elevated from the dura and progressively resected with kerrison pouch. When foraminal stenosis is present, the medial aspect of the uncovertebral joint is resected using a No. 1 or 2 Kerrison punch. Bleeding from epidural veins in the neural foramen is controlled with small pieces of surgical and gentle pressure with cottonoid.

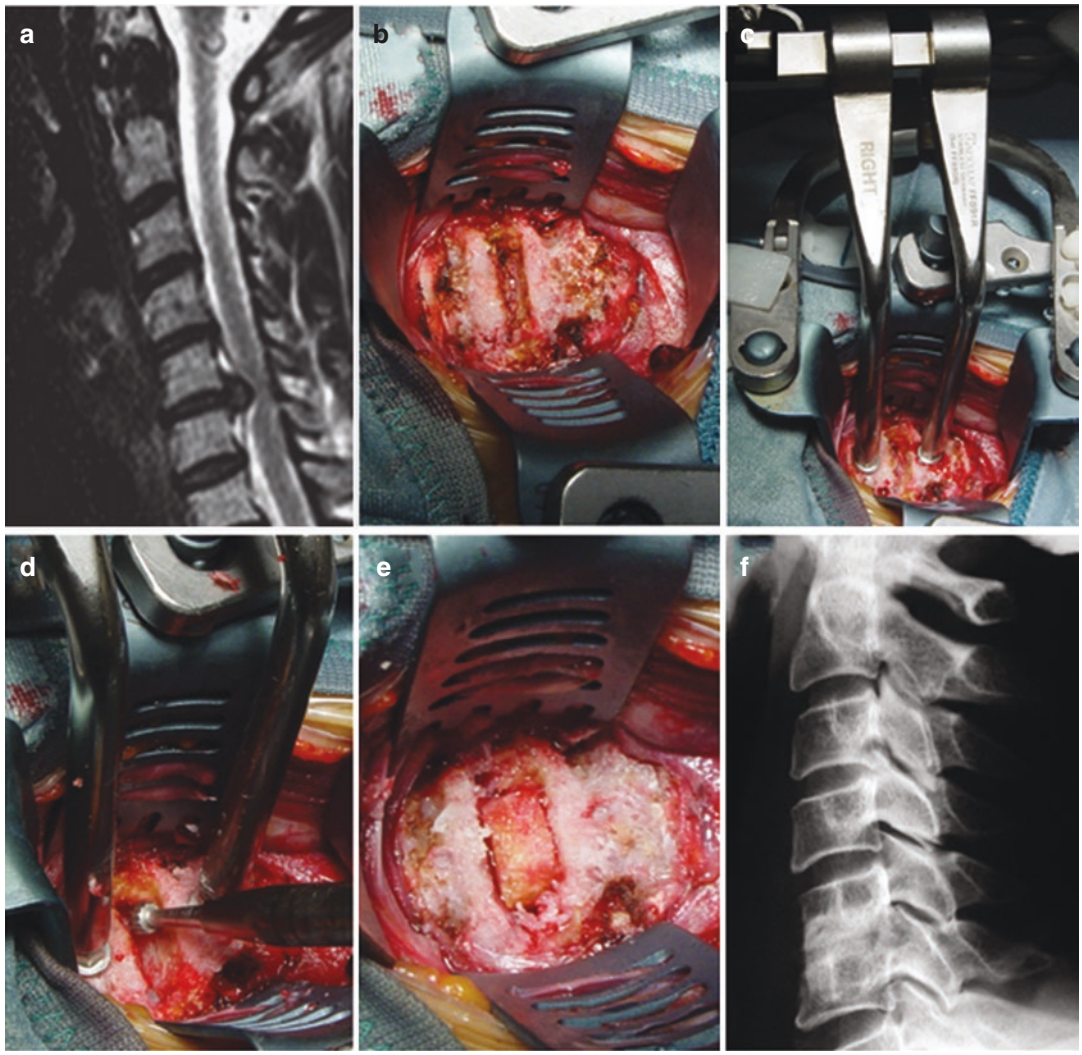

Fig. 13.2 Interbody fusion with Smith-Robinson technique. (**a**) preoperative midsagittal T2-weighted MRI scan discloses C5–C6 disc herniation with severe compression of the spinal cord. (**b**) After exposure of the cervical spine the anulus fibrosus is incised and the anterior longitudinal ligament is removed at the C5–C6 level. (**c**, **d**) the disc space is opened with Caspar distraction pin device and the discectomy is completed microsurgically. (**e**) after complete removal of soft disc herniation, a tricortical autologous iliac crest graft is tapped into place and the distraction is released. (**f**) lateral x-ray obtained 6 months after surgery demonstrated solid fusion between C5 and C6

Cloward Technique

This technique increases the space available while the surgeon performs ostheophytes removal and consists of drilling a circular opening in the region of the intervertebral disc, into which a dowel of bone is inserted (Fig. 13.3). After a standard discectomy, measure is taken, and the drill depth is determined. The hand-held drill with a guard is applied to the midpoint of the cervical motion segment and drilling of the adjacent vertebral bodies to the desired depth is performed. The guard prevents penetration of the posterior cortical bone, which is removed with high-speed drill and rongeurs. The decompression is completed with microsurgical

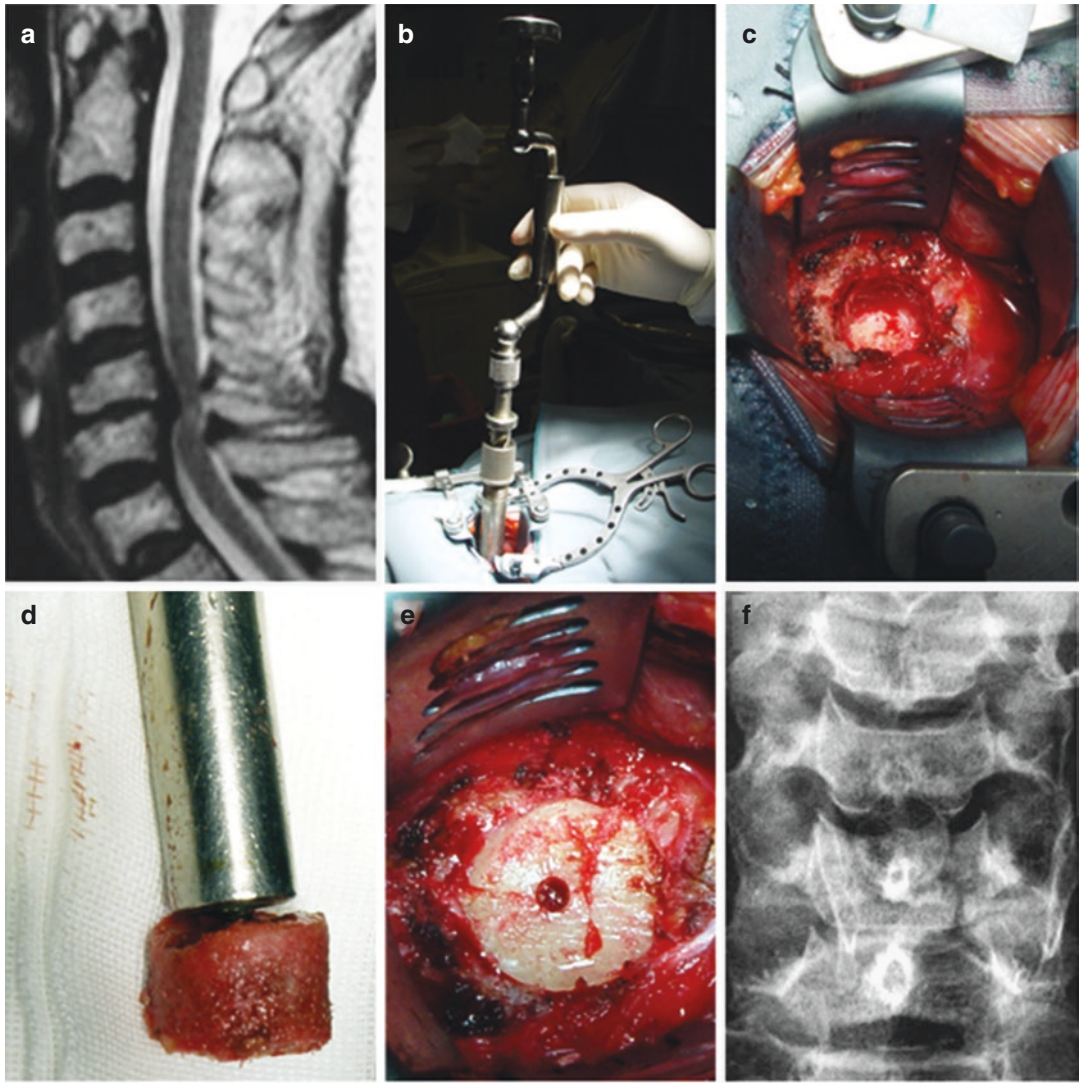

Fig. 13.3 Interbody fusion with Cloward technique. (**a**) preoperative midsagittal T2-weighted MRI scan discloses C5–C6 spinal cord compression with high signal changes in the spinal cord as a result of herniated disc associated with osteophytes. (**b**) after standard discectomy, a hand-held drill is used to drill the adjacent vertebral bodies. (**c**) the remaining cortical bone is removed microsurgically. (**d**, **e**) a bicortical dowel graft of iliac crest bone is tapped into place. (**f**) antero-posterior x-ray obtained 6 months after surgery discloses fusion between C5 and C6

removal of the PLL, osteophytes and disk herniation, when present. A slightly larger, cylindrical, bicortical autologous dowel graft is harvested from the anterior iliac crest and impacted into the drilled defect. The limitations of this approach consist in the decreased compression strength of the bicortical graft, the extensive exposure of cancellous bone and the impossibility to perform multilevel contiguous fusions [12]. Due to these limitations, the Cloward's technique is nowadays seldom utilized.

Corpectomy

When a corpectomy is planned, the anterior longitudinal ligament over the vertebral body to be

resected and over the contiguous portions of the adjacent upper and lower vertebrae is removed (Fig. 13.4). Anterior osteophytes are resected to ensure that the cervical plate will lie flat on the vertebral body. The discetomies above and below the chosen corpectomy site are performed first to evaluate the depth of the spinal canal and to carefully define the limits of bony resection. The majority of the vertebral body is removed under direct visualization to maintain midline orientation and obtain a symmetrical bony decompression. We use a 6-mm cutting burr to rapidly remove the vertebral body to the posterior cortical margin. The location and course of the vertebral arteries is noted on preoperative CT and MRI scans and the distance separating them is mea-

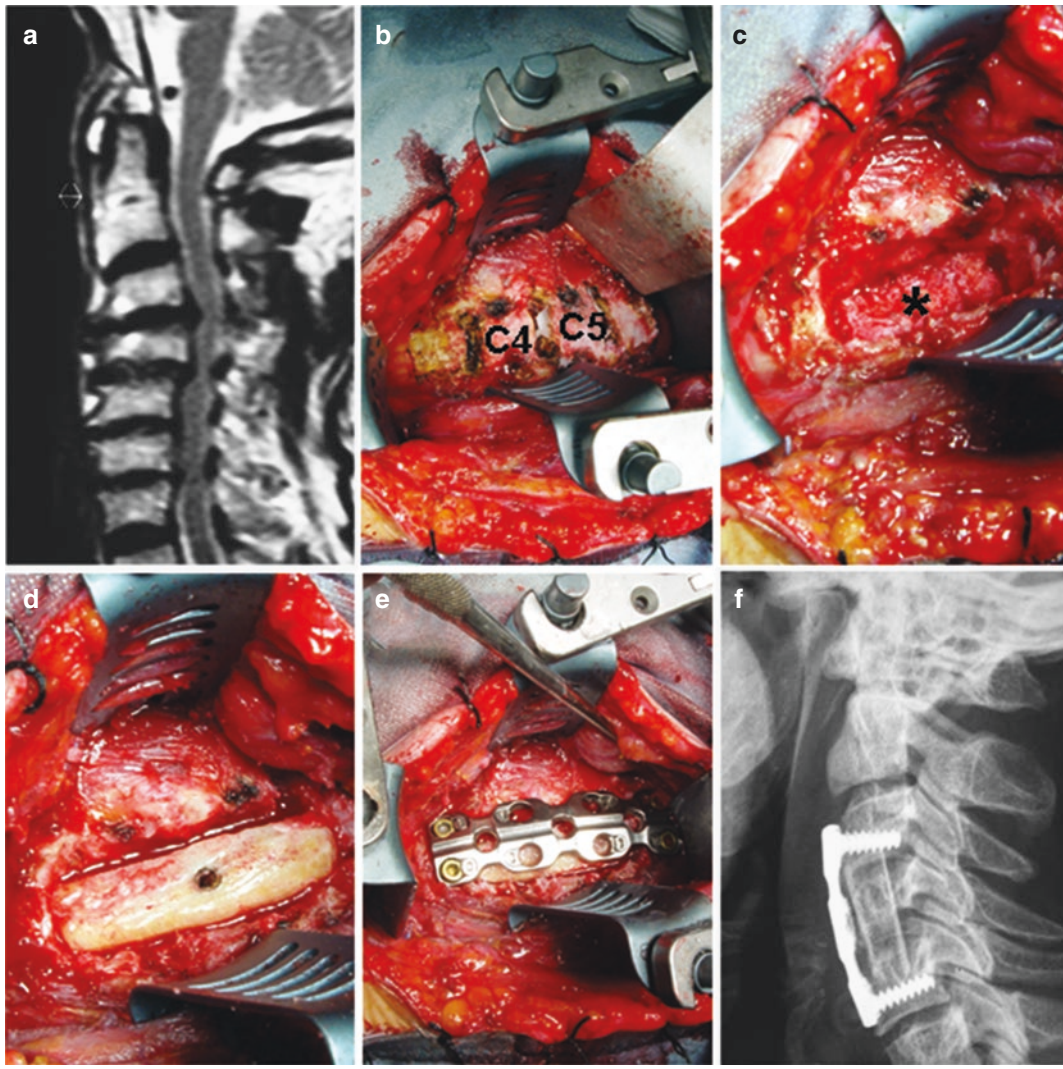

Fig. 13.4 Interbody fusion after corpectomy. (**a**) preoperative midsagittal T2-weigheted MRI scan shows cervical spine stenosis C3–C5 and kyphotic deformity. (**b**, **c**) after wide exposure of midportion of the cervical spine, discectomies are performed above and below the corpectomy site and the vertebral bodies of C4 and C5 are removed using high speed drill. The posterior longitudinal ligament and the osteophytes are resected exposing the decompressed dura (asterisk) (**d**, **e**) a tricortical iliac crest graft slightly oversized is tapped into place under distraction and internal fixation is obtained with plate and screws. (**f**) lateral x-ray obtained 6 months after surgery demonstrates solid fusion and restoration of focal lordosis

sured. Generally, the mean distance separating the medial borders of the transverse foramina is approximately 26–30 mm [13]. According to these findings, we do not extend bony decompression more than 10 mm from the midline to avoid injury of the vertebral artery. Under microscopic view the posterior cortex is removed with a 2-mm Kerrison pouch. The posterior osteophytes are resected with an up-going curette and Kerrison pouch. A matchstick-type burr is used to resect completely the cartilage from the endplates of edjacent vertebrae while maintaining the bony endplate to prevent graft subsidence. The PLL is entered with a nerve hook, incised and widely removed using kerrison pouch. Bone wax is avoided because it prevents bony fusion.

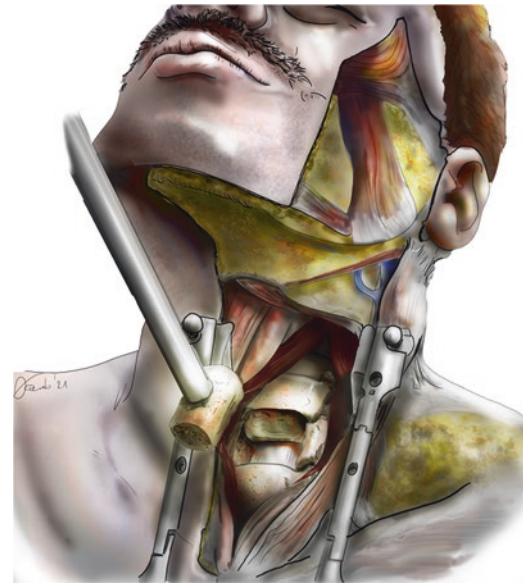

Fig. 13.5 Artist rendering depicting the bony reconstruction with autograft after cervical corpectomy

Bony Reconstruction with Autograft

Autologous bone grafts can be classified according to tissue composition (cortical, corticocancellous, cancellous), anatomic origin (iliac crest, rib, fibula) and blood supply (vascularized, nonvascularized). Autografts such as fibula and tricortical iliac crest graft bear the mechanical compression loads applied to the anterior column of the spine due to their strength from their cortical bone composition [14]. These grafts can be fashioned as tricortical or bicortical struts or dowel according to the technique used. Rib grafts are weak mechanically because provide a limited volume of bone and are characterized by a thin cortex. While autologous rib grafts can be used as source of cancellous bone or can wired to the occiput during an occipitocervical fixation, they are not generally used for bony reconstruction of the cervical spine. Vascularized corticocancellous autograft such as vascularized fibula grafts are used in irradiated and devascularized fusion beds. The main limitation of fibula graft is the mismatch of the densities with that of the vertebral body with resultant penetration of the fibula through the vertebral body, i.e. the "pistoning effect". For bony reconstruction of the cervical spine we use autologous bone graft obtained from the anterior iliac crest (Fig. 13.5). Surgical technique plays a pivotal role to ensure proper bone healing and reducing postoperative complications (Table 13.1). The bone graft is harvested after the anterior approach and stored in saline-soaked sponges until used. A short (5 cm) skin incision is made parallel to the anterior iliac crest starting at least 2 cm behind and lateral the anterior superior iliac spine (ASIS) (Fig. 13.6). A limited use of electrocautery is required during superiosteal dissection to avoid injuring the ilioinguinal, iliohypogastric and lateral femoral cutaneous nerves, which course along the medial surface of the ileum. Care is taken to cut through the fascia avoiding the muscles. The periosteum of the iliac bone is progressively elevated from the inner and outer bone surfaces with a Cobb periosteal elevator. A bone graft of the measured size is harvested from the ilium using a single-bladed oscillating saw under irrigation for tricortical or, more rarely, bicortical bone. The graft site is measured with caliper and the graft is cut slightly oversized (2–3-mm longer than the rostrocaudal length of the corpectomy). Both ends of the graft are flat-surfaced to increase the surface area for fusion. It is our preference to exert distraction of the cervical spine by having the assistant pull on the angle of the mandible on the long axis of the patient's body. Alternatively, distraction can

Table 13.1 Summary of the studies describing post-operative complications after anterior cervical decompression and fusion with autologous bone graft

Study	Year	Techinque	N.patients	ASD	Failure	Kyphotic angle worsening	Infection	FU (years)
Liu et al. [15]	2017	ACDF	31	–	–	–	2	2
Burkhardt et al. [16]	2016	ADCF	95	11 (11.6%)	3 (3.1%)	–	1 (1.5%)	28
Perrini et al. [17]	2015	Corpectomy	20	0	0	–	0	1
Iwasaki et al. [18]	2014	ACDF	16	0	0	–	0	0.5
Lied et al. [19]	2008	ACDF	278	–	4 (1.5%)	–	1 (0.3%)	0.5
Rajshekhar et al. [20]	2003	Corpectomy	93	–	–	33 (35%)	–	2

ACDF anterior cervical discectomy and fusion, *ASD* adjacent segment disease, *FU* follow-up

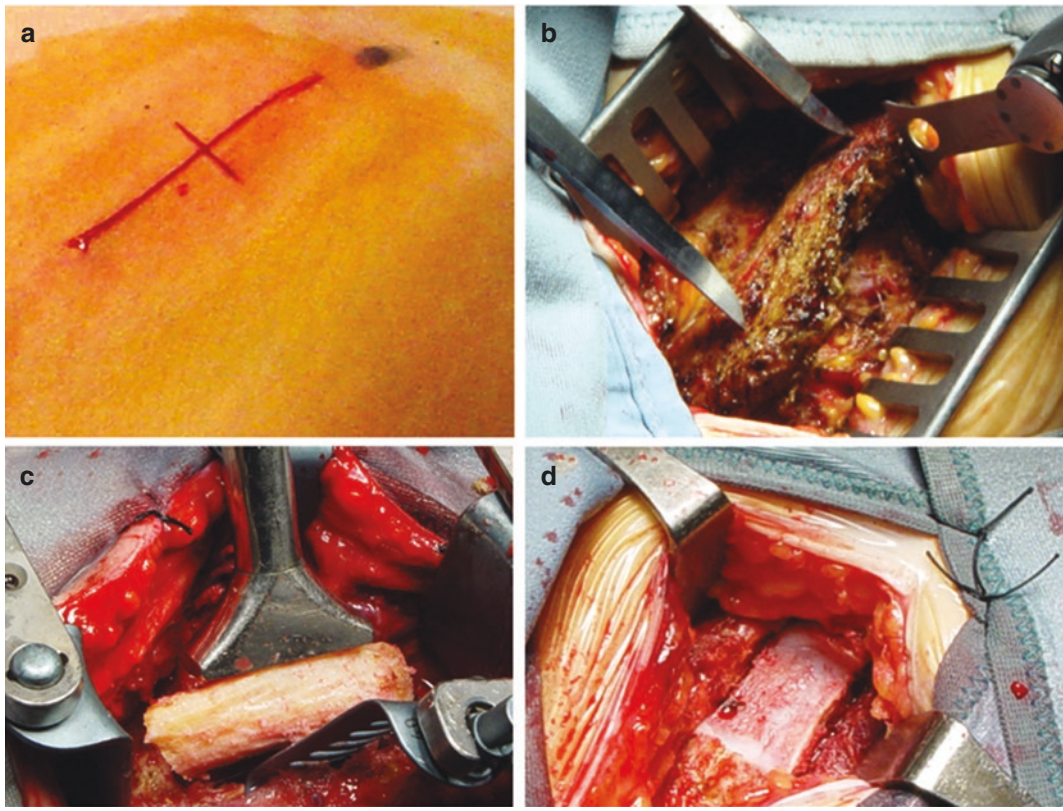

Fig. 13.6 Bone graft-harvesting from the iliac crest. (**a**) a skin incision of approximately 5 cm is made at least 2 cm behind the anterior superior iliac spine. (**b**) after subperioteal dissection, a tricortical bone graft of the measured size is harvested from the ilium using an oscillating saw (asterisk). (**c**) a pin-headed Cloward impactor is used to place the graft into the corpectomy defect. (**d**) meticulous hemostasis of the ilium is done with bone wax and the soft tissues are closed in separate layers

be obtained by placing distracting pins into the vertebral bodies above and below the corpectomy site. Excessive distraction due to a graft that is to long for the length of the vertebrectomy should be avoided because can lead to postoperative interscapular pain. When the anterior decompression is performed using the Cloward approach, a hand-held drill with a guard is applied on the lateral surface of the ilium at least 2 cm behind the anterior superior iliac spine and a bicortical, cylindrical dowel graft is harvested (Fig. 13.7).

Donor Site Complications

The complication rate after harvesting bi- or tricortical iliac bone ranges from 4 to 39% [21, 22]. Donor site complications include acute and chronic local pain, nerve injury, infection, hemorrhage, hernia formation and exceptional iliac crest fracture. The most reported complication is acute postoperative pain at the donor site with resultant longer hospital stay. Several evidences suggest that donor site pain is the result of micro- and macro-fractures, hemorrhage and infection that trigger intact nociceptors adjacent to a nerve injury site [21, 23–29]. Accordingly, many reports suggest the use of synthetic or allogenic graft to obtain fusion without the risk of donor-site post-operative sequelae. Nonetheless, as demonstrated by a recent systematic review, no high-quality evidence arose in the recent years suggesting any significant difference or superiority in the use of allograft and synthetic graft in comparison to autologous bone [5]. Furthermore, the risk of donor site complications can be minimized with a careful standard technique [3]. A short skin incision, limited muscle retraction, subperiosteal dissection, and reduced use of electrocautery prevent the injury to the lateral femoral cutaneous nerve, ilioinguinal nerve and lateral cutaneous branch of the subcostal nerve. Performing the most anterior osteotomy at least 2 cm behind the ASIS avoids a stress fracture of the bone remaining anterior to the harvest site. In addition, some evidence suggest that graft harvesting using single-bladed oscillating saw reduces the risk of stress fracture of the ASIS when compared with the osteotome technique [3, 27]. Finally, careful hemostasis, moderate use of electrocautery and avoidance of muscle stripping help to avoid pain, fluid collection, and cosmetic dissatisfaction [24].

Anterior Instrumentation After Autologous Bone Graft

In single-level discectomy and fusion for degenerative disease, there is no strong support for

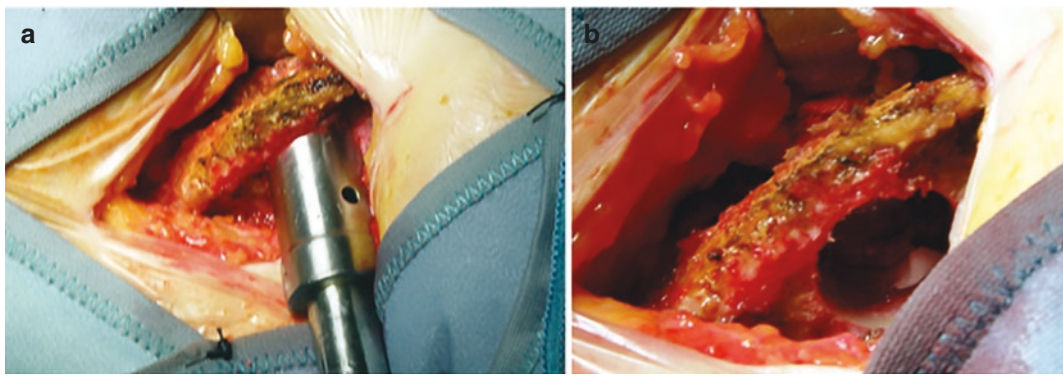

Fig. 13.7 Bone graft harvesting from the iliac crest according to the Cloward technique. (**a**, **b**) a hand-held drill provides a cylindrical, bicortical dowel graft that is impacted into the drilled defect

plate fixation in the literature [30]. In addition, some authors reported no graft extrusions in large series of patients treated with multilevel discectomy and fusion with autograft without supplemental instrumentation [31]. However, recent prospective studies comparing mono- or bisegmental cervical fusion with autograft with and without a plate found that graft quality (height of graft, dislocation and resorption) was significantly better in the plated group [32]. According to the literature, the rate of pseudoarthrosis increases with an increase in the number of segments fused suggesting that fusion over more than two segments is an indication for instrumentation [22].

The critical concerns of graft displacement, graft fracture, pseudoarthrosis, subsidence and kyphotic changes are particularly relevant in cases of corpectomy without plating. Although some authors still recommend uninstrumented corpectomy for cervical spondylotic myelopathy [20, 33] several classic clinical studies reported graft-related complications rates ranging up to 45% without plating [34–38]. Yonenobu et al. [38] reported nonunion rates of 5% and 45% after one- and three-level corpectomy and autograft without instrumentation, respectively. Internal fixation after cervical corpectomy and autograft provides several advantages including biomechanical improvements, immediate stability and improved fusion rates with acceleration of the fusion process. In fact, when corpectomy is not associated with internal fixation, rotational and translational forces in three dimensions increase complication rates and lower fusion rates. Rigid internal fixation allows immediate stability and fixed bone-to-bone contact under compression, that promotes successful incorporation of the autograft.

Conclusion

Autologous bone graft is still considered the gold standard for reconstruction of cervical spine after discectomy or corpectomy due to its properties of osteogenesis, osteoinduction and osteoconduction. A careful and standardized harvesting technique minimizes donor site complications and improves the clinical outcome.

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14 Anterior Cervical Approaches: Decompression and Fusion with Cages

Massimo Balsano, Andrea Vacchiano, Mauro Spina, Maurizio Ulgelmo, and Davide Calzi

Introduction

The preferred approach for fusion of the middle cervical spine (C3–C7) and cervicothoracic junction is the anterior one (presternocleidomastoid).

During 1950 a novel cervical spine surgical technique emerged: in 1955 Smith G.W. and Robinson R.A. developed a surgical technique concerning anterior removal of cervical disc and replace it with a rectangular bone graft.

Afterwards, Cloward in 1958 developed a different technique which consists in milling the anterior profile between two adjacent vertebras, filling it with a bone cylindrical autograft dowel, after the disc removal [1].

At today, Anterior Cervical Discectomy and fusion (ACDF), as Cloward or Smith Robinson designed, is worldwidely adopted (Fig. 14.1).

Nowadays, fusion is performed with cages, stand-alone, or reinforced with plates or with a posterior instrumentation. A new type of stand-alone cage, provided with lag screws, work as a cage-plate construct with a single implantable.

We personally prefer this new cages, manufactured with a low profile and biomechanically comparable to the standard cages with a separate plate.

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Indications and Limits

ACDF is the gold standard procedure for degenerative disc disease (DDD), radiculopathy, myelopathy, stenosis, deformity (e.g. excessive kyphosis), revision surgery. Relative indication is axial neck pain. Selection of the patient is essential to achieve an optimal outcom. Patients with higher neck disability index (NDI) scores, older age and working status show better post-surgery outcome at the physical and radiological follow-up [2]. Relative contraindications were multilevel congenital stenosis, prior anterior neck infection/scarring, voice worker, hypertrophy of the ligamentum flavum and vocal cord dysfunction.

Patient's Positioning and Draping

The patient is placed supine onto a surgical room table.

In our spine center, we prefer to use a radiolucent dedicated spinal procedures table for better fluoroscopy visualization. Alternatively, the head is placed onto a Mayfield frame or in a dedicated helmet for fulling control neck motion. We prefer to place the patient on the surgical bed without supports. Then we lock the head using adhesive bands. A rolled towel or equivalent placed transversely under the scapulae allow the neck to slightly extend increasing the chin-chest distance and anterior elongation of the intervertebral disc space (Fig. 14.2).

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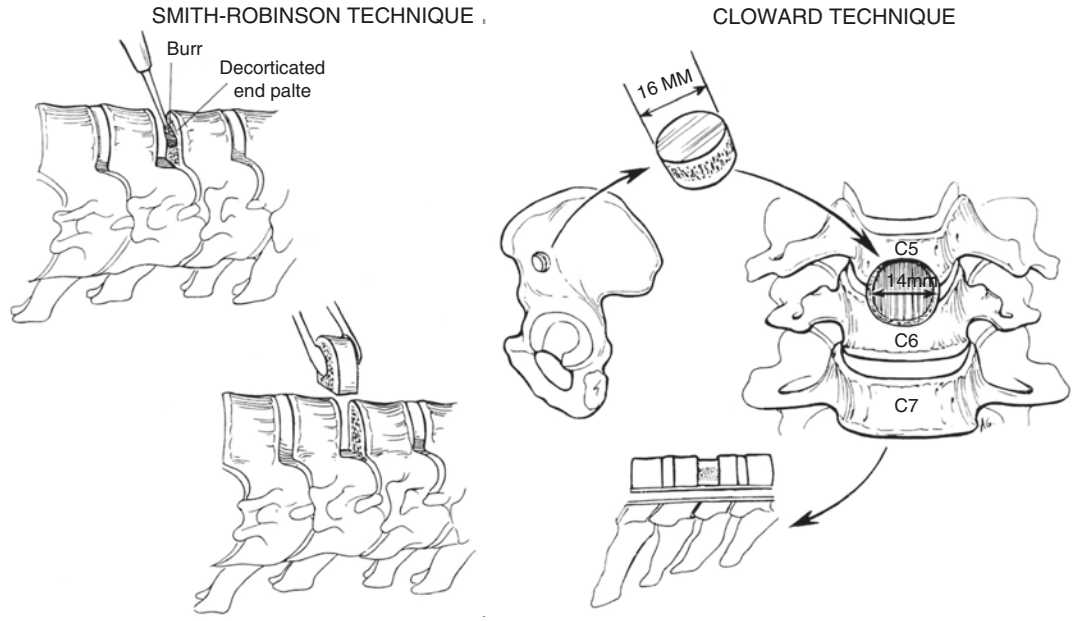

Fig. 14.1 Smith-Robinson and Cloward bone graft technique

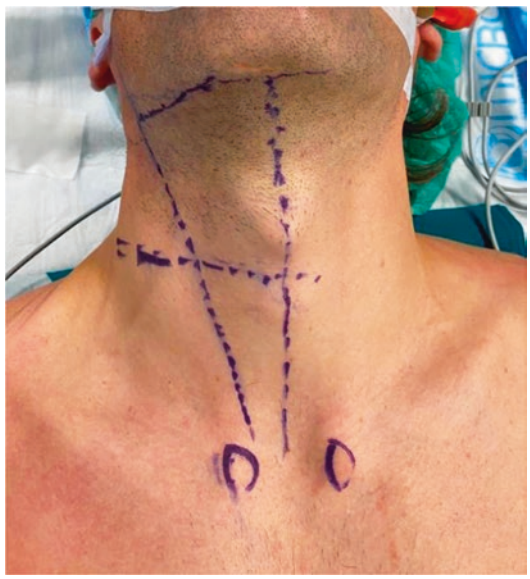

Fig. 14.2 Pre-operative marked skin

Side Making Decision

The current literature shows studies favor alternatively both for right or left side anterior cervical spine approach. Historically literature favored a left side approach due to the anatomy of the right and left inferior/recurrent laryngeal nerve (RLN) [3]. RLN is a branch of the vagus nerve, which originates in the thorax and the left RLN loop anterior to the aortic arch while the right RLN loop anterior to the right subclavian artery with a higher oblique angle. After looping both reach the tracheoesophageal groove continuing up the larynx. We prefer just only right side because our surgeon team is a right-handed with a finer control of the procedure. It should be noted that there are no clinical studies proving a higher risk of RLN palsy in a right-side approach [4]. However, there are some evidences suggesting that, a decreased endotracheal cuff pressure reduce the RLN damage risk. A left-side approach is suggested at C6–T1 levels (thoraco-cervical junction) due to close proximity of right RLN.

Anterior Cervical Approach

Smith-Robinson and Cloward procedures approach the neck by antero-lateral: this is the best way to place a cage in mid-cervical and thoracic-cervical junction spine [5]. After adequate disinfection and draping, the skin is marked on the pathological level/s with the help of fluoroscopy. Usually, a

3–6 cm transverse incision is performed following skin crease, for better cosmetic effect. Platysma is dissected in line with his muscular fibers alternatively with a blunt dissection. Following the medial border of the sternocleidomastoid a blunt dissection is performed dividing it from the strap muscles. Proceeding deeply the blunt dissection the carotid sheath is retracted laterally and the trachea and esophagus medially. Retract gently visceral structure and thyroid gland medially to preserve alternatively left or right RLN. The prevertebral fascia with the lying longus colli muscle is now exposed. Careful blunt dissection of longus colli, adopting bipolar electrocautery to avoid venous bleeding, eventually is reached the anterior vertebral body surface (Fig. 14.3). A valid exposure is mandatory. Nevertheless, a too lateral exposure leads at risk of damage the vertebral artery and the sympathetic chain which can lead to Claude-Bernard-Horner syndrome.

Discectomy and Decompression Technique

After carefully exposure of the pathological disc, the affected discectomy level is performed. To confirm the correct level a k-wire can be used as a fluoroscopic marker [6]. Thus, pins are placed cranially and caudal to the disc space and Caspar retractor is assembled in slight distraction (Fig. 14.4). Then an annulotomy can be performed with a desired scalpel. All the disc is then removed with microcurettes or dedicated Kerrison roungers, and also the posterior portion of the annulus fibrosus reaching the posterior longitudinal ligament (PLL) [7]. To make an adequate decompression is mandatory to open the PLL, which leads to visualize the dural sac. However, it is better to open the PLL when there is radiculopathy or myelopathy also if the MR or CT do not show that so clear [8]. In addition to finalize and complete the decompression is it necessary to remove antero-inferior osteophytes. Following the lateral border of uncinate process the uncus is partially removed with a burr. An internal foraminotomy is performed with a Kerrison roungers to expose and release the nerve root, proved when a nerve hook can easily pass into the foramen.

During these maneveurs it is important to avoid injuries to the vertebral artery, which is just lateral to the uncus, the venous plexus and, when detaching the PLL, the dural sac.

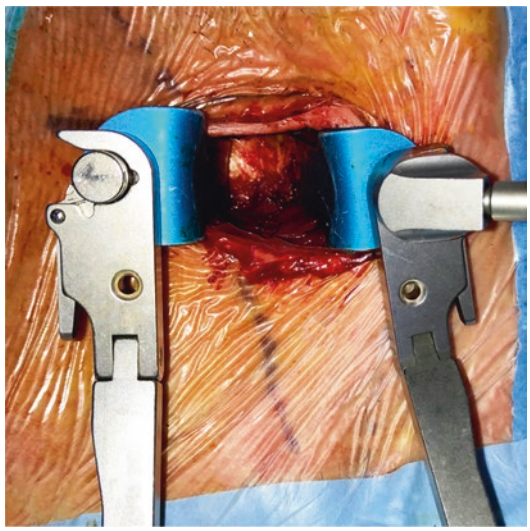

Fig. 14.3 Vertebral body is identified and soft tissues and visceral structures are retracted

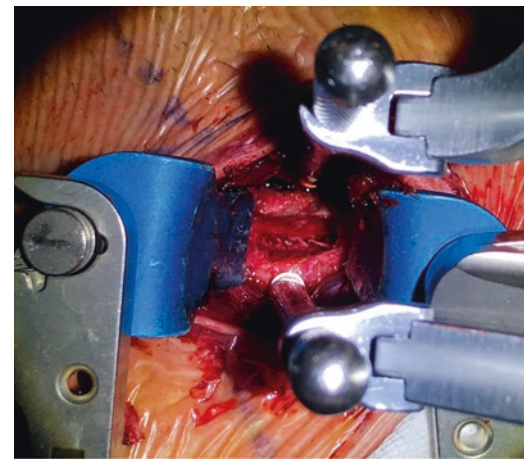

Fig. 14.4 Pins are inserted into the upper and lower vertebral bodies and the adjacent intervertebral disc is opened

Implant Selection

After performing the decompression and discectomy, filling the gap with an adequate device to obtain a solid fusion is mandatory. Smith-Robinson and Cloward for this purpose adopted solely a bone graft as a mechanical support. This was an excellent option; however, it did not allow adequate biomechanical stability, leading to long immobilization with a neck collar.

To increase stability two different options are used: the anterior plate, to support the bone implant, and the stand-alone cage. The adoption of the frontal plate improved the original ACDF technique, increasing the local stability [9]. However, several complications associated with the placement of an anterior plate construct are reported in the literature, probably because of their relatively "large" size compared to the cages and proximity to noble structures: esophageal damage, neurovascular injury and dysphagia [10].

The other type of implant to ensure adequate fusion is the stand-alone cage, positioned in place of the bone implant of the original ACDF technique, thus avoiding grafting of autologous bone from the iliac crest and local consequences.

The use of a stand-alone cage has a reduced risk of postoperative dysphagia, blood loss and adjacent segment disease (ASD) compared to the plate.

However, it leads to an increased risk of subsidence and a sligh correct realignment of cervical lordosis [11]. In 2009, to overcome these limitations, a new device has been designed: the locking stand-alone cage (LSC) [12]. It is usually a low-profile cage equipped with lag screws to anchor the vertebral plates. Although the risks of LSC are the same as those of stand-alone (risk of subsidence and poor restoration of cervical lordosis), they are nevertheless of lesser magnitude. Moreover, the literature is poor in clinical studies in this regard [13].

Locking Stand-Alone Cage Technique

After implant the dedicated Caspar pins, which are fixed inside into the vertebral bodies, adjacent to the pathological disc, discectomy/decompression is completed. The space is prepared to accommodate the cage. The endplates are shaved the necessary to ensure acceptable fusion and to avoid subsidence. Then modular trials are inserted to determine the appropriate size. The choice of the definitive implant is given by tactile feedback and fluoroscopy. The best fitting trial must be in the center of intervertebral disc in the AP x-rays image and maintain the disc height and stabilize the segment. After that, the final spacer is introduced with a mallet with fluoroscopy monitoring. Then the screws (number change depends on the model of adopted cage) are screwed into the upper and lower end-plates. When the procedure is finished, the mechanical stability of the cage is tested and a final fluoroscopy is made (Fig. 14.5).

Post-operative Cares

At the end of the surgery, we recommend the positioning of a small redon type drain with negative pressure, which we usually remove just after 24 h, unless there is excessive bleeding. We place a soft collar that we recommend to maintain roughly for 1 month; afterwards a control x-rays and clinical follow-up is made. Our perioperative antibiotic protocol is cefazolin 30 mg/kg during anesthesiologic induction procedure (about 30 min before the surgical incision), then cefazolin 30 mg/kg every 6 h until drain removal (in case of allergy clindamycin 10 mg/kg). We advise prophylactic low molecular weight heparin just after surgery until the next 2 weeks. The patient stands, with the soft collar, the day after surgery. During the second post-operative day a control x-ray LL and PA is made to confirm the

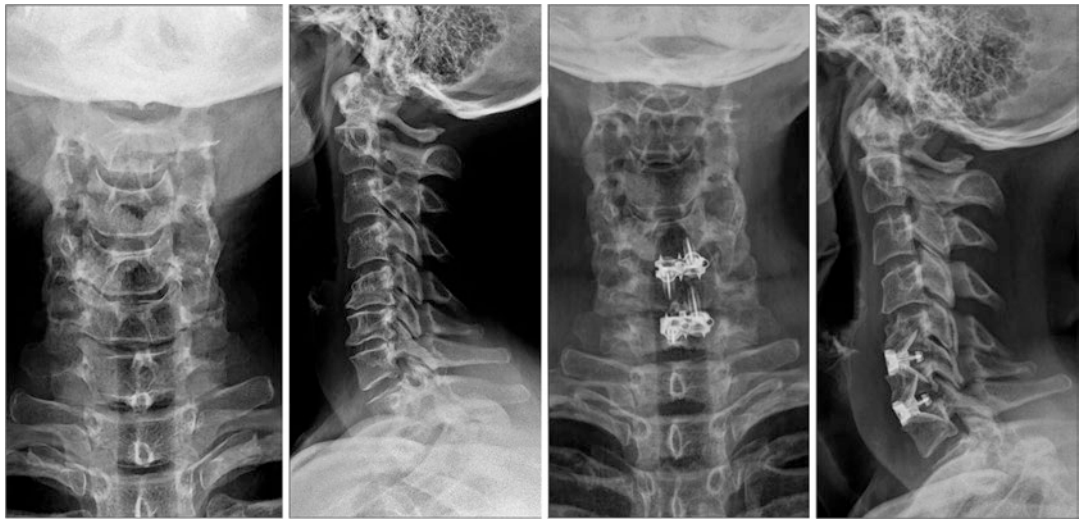

Fig. 14.5 A case of a 49-year-old female patient affected by C5–C6 and C6–C7 degenerative disc disease treated with two locking stand-alone cages. Pre and post operative x-rays

correct positioning of the device. In the third post-operative day, the patient is usually discharged, as there are no complications.

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Axial Instability of Cervical Spine: Posterior Surgical Approach

15

Alberto Maleci, Pier Paolo Maria Menchetti, and Nicola Di Lorenzo

Many pathologies can cause instability of the cranio-vertebral junction (CVJ). Among the most common diseases must be considered traumatisms [1], neoplasms [2, 3], inflammation [4], but also congenital malformations [5]. Instability of the CVJ is a potentially life-threatening condition and improper treatment can lead to severe neurological deficits as well as continuous, excruciating pain in the neck. Conservative treatments are often disappointing, and surgery must always be taken in consideration when approaching instability of the CVJ, being in many cases the only therapy that can provide satisfactory results.

Anterior approaches to the CVJ are usually limited to few and selected cases and, with the exception of type II C2 fractures, posterior approach must be considered the first choice to restore stability of the axial cervical spine.

History

Posterior sub laminar wiring of C1 and C2 was attempted in 1910 by Mixter and Osgood [6]. Foerster, in 1927, was the first to describe the use a peroneal graft to treat a trauma of the cranio-vertebral region [7]. However, the first widely used surgical technique to restore stability of the C1–C2 segment was posterior fusion with wires and autograft and was developed by Gallie et al. in 1939 [8].

Gallie's technique gained wide appreciation and has been used for many years; in 1978 Brooks and Jenkins [9] proposed a modification of the original technique. The development of the concept of posterior C1–C2 wiring and grafting is represented by clamps between the posterior arch of C1 and C2 laminae. Integrity of the posterior arch of the atlas was necessary and postoperative immobilization was strongly recommended. When the posterior arch of C1 was interrupted the occiput had to be involved in the fusion leading to a complete abolition of rotatory movements and severe limitation of flexo-extension of the head.

In 1987 Magerl and Seeman proposed the union of C2 to C1 by two screws that, passing through the C2 isthmus, were screwed to the C1 lateral masses [10]. The integrity of the posterior arch of C1 was no longer needed and the construct was so stable that also postoperative course did not require firm immobilization. In 1994 Goel and Laheri [11] published an original technique where two screws were placed in the lateral masses of C1 and two screws in the isthmus of C2. The screws were connected by plates realizing the stabilization of the C1–C2 segment. Some years later Harms and Melcher [12] proposed a modification of this technique that gained great

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popularity in the following years. In 2004 Wright [13] proposed a modification of the Harm's technique which avoided the risk of C2 isthmus perforation; the caudal screws were inserted in the laminae and connected to the lateral mass screws.

Conservative Treatment

Pathologies that can be treated by external immobilization are mainly traumatic: fractures of the atlas, fractures of the dens (reducible fractures type 2 and 3 according Anderson and D'Alonzo) [14]. The goal of an external fixation is to maintain an optimal alignment of the axis for a time long enough to provide healing and fusion (usually 3–4 months). The best way to obtain stability of the cranio-vertebral junction by non-surgical techniques is positioning a halo-cast or halo-vest [15, 16], even though a Philadelphia collar has been proposed to treat C2 fractures [17]. The sternal-occipital-mandibular immobilizer (SOMI)—brace has also been used in the past [18]. The most common traumatic lesion of the axis is the C2 fracture type II. Conservative treatment of this type of lesion has been reported by many authors [19], but a high percentage of non-union has also been reported. Unfavorable results are related to many factors, first of all the presentation of fracture. When translation was larger than 6 mm, the non-union rate was as high as 86% while the results were much better in the cases of dislocation inferior to 4 mm. Another crucial point is the age of the patients: non-union in patients older than 50 [20, 21] is frequently observed. Neurological status is also important; in the presence of progressive neurological deficits or serious impairment of functions as well as in non-cooperative patients, conservative treatment should be avoided. Finally, other lesions involving the cranial and facial bones and thoracic and pulmonary conditions can prevent the correct positioning of a halo vest.

Halo positioning requires insertion of four pins in anterior and posterior position, through the skin and secured to the skull. The direction is vertical, with a 90° angle with the skull, as a differently angled direction decreases biomechanical resistance [22]. The secure zone for the anterior pins insertion is quite small and is represented by an area of about 10 cm^2 1 cm above the orbital ridge on the external part of the forehead in order to avoid the arterial branch of the superficial temporal artery laterally and the supraorbitary nerve superiorly and medially.

Non-union is the most common but not the only complication following conservative treatments of cranio-vertebral junction. Cutaneous ulcers are quite common [23], but nerve palsy, particularly of the marginal mandibular nerve (terminal branch of the facial nerve) has also been reported [24]. As far as halo is concerned, loosening of the pins is a common complication [25]. Cutaneous infection can follow the positioning of the pins [26] but infections can involve also bone and intracranial structures [21, 27, 28] and subdural as well as epidural hematoma [29].

Presently conservative treatment should be restricted to axis traumatic lesions with minimal dislocations, in young patients without neurological abnormalities; patients with systemic diseases that carry high operative risk should be treated conservatively as well.

In all other cases surgical treatment should represent the first choice.

Biomechanical Analysis of Surgical Treatments

The goal of the surgical treatment is to provide a stabilization of the unstable segment (i.e. the axial part of the cervical spine) as strong as possible. On the other hand, as every posterior stabilization leads to loss of motion, the ideal treatment should be the strongest and the least invalidating.

Many biomechanical studies have investigated the ability of the different treatments of stabilizing the C1–C2 segments. According Sim et al. [30], who measured the range of movement and the neutral zone of cadaver specimens after different techniques of stabilization, posterior wiring (PW), trans-articular screws (TA) and screws in C1 lateral masses combined with C2 screwing (C1LM-C2 PS) are all able to stabilize an

unstable axis in flexion–extension. However, posterior wiring couldn't give enough stability at rotational and lateral bending tests, and were therefore considered insufficient. The three-point reconstruction, using TA and PW provided the best results in all the tests, but also the C1LM-C2PS achieved a sufficient stability in the three planes.

A recent review has been published by Du et al. in 2015 [31]. The authors found differences in the results of the single papers, but generally TA, C1LM-C2PS provided good stabilization in the three movements tested, while screwing C1 lateral masses and trans laminar C2 (C1LM-C2TL) were less effective in the lateral bending tests.

Posterior Wiring and Clamps

The original Gallie's technique utilized a single bone harvested from the iliac crest and placed on the C2 spinous process and the posterior arch of C1. The stabilization was then obtained by steel wires which passed below the C1 arch and around the C2 spinous process, keeping at the same time the autograft in place (Fig. 15.1a). In the Brooks and Jenkins technique two single grafts were used, shaped in order to be positioned between the posterior C1 arch and C2 lamina. The wiring was sublaminar both in C1 and C2 (Fig. 15.1b). Dickman et al. [32] furtherly modified the original Gallie's technique using a single graft, not only leaned on the posterior arch of C1, but wedged underneath the spinous process of C2 and C1. The wires to keep in place the graft and to provide stability passed below the posterior arch of C1 and a notch prepared on the spinous process of C2 in order to increase the stability of the construct.

The results of posterior grafting and wiring were satisfactory in a number of cases. Nevertheless, the non-fusion rate was still elevated [33], rotational stability was poor and immobilization for 3–4 months in a halo was mandatory in the postoperative course. Furthermore, sublaminar wires carried the risk of nervous injuries and dural tears.

Interlaminar clamps should decrease this risk: the hooks are placed underneath the posterior

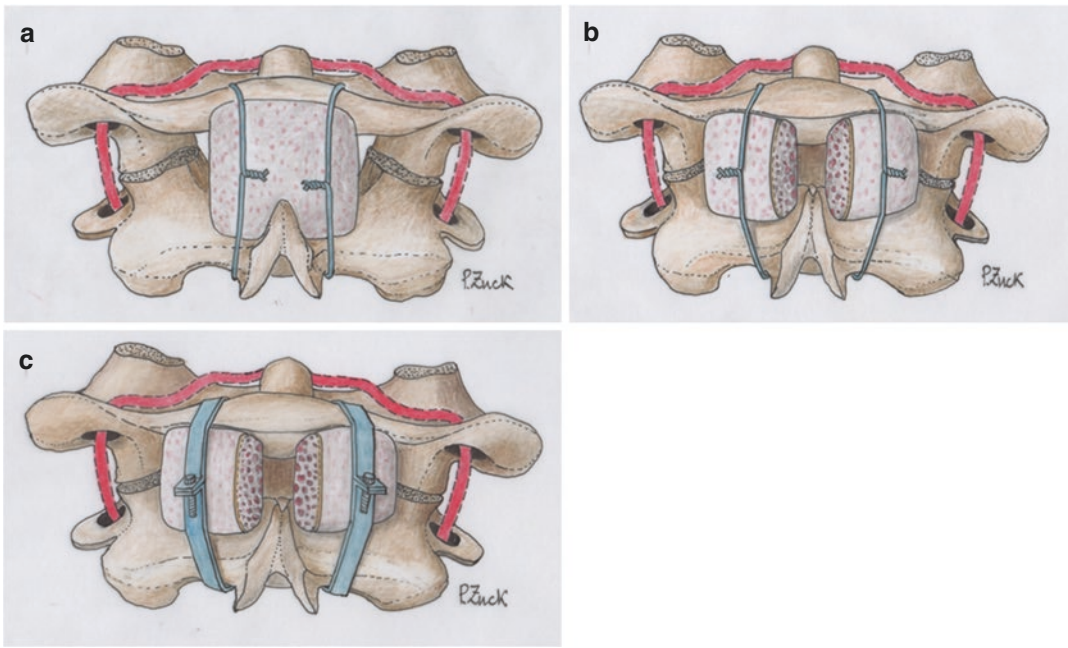

Fig. 15.1 Posterior C1–C2 wiring: (**a**) according to Gallie (**b**) according to Brooks and Jenkings (**c**) according to Dickman

arch of C1 as well as C2 lamina, and then tightened by different mechanism [34]; the autograft, harvested by the iliac crest, is compressed between the posterior aspect of C1 and C2 (Fig. 15.1c). Even though clamps are easier to be positioned than wires, they have good stability only in the flexion and extension movements, while in rotational motion and lateral bending the stability is very poor. Dislocation of the clamps are therefore not uncommon, needing for second surgery (Fig. 15.2). As for all the wiring techniques also clamps require an intact posterior arch of C1.

C1–C2 Trans-articular Screw Technique

This technique, described in 1987 by Magerl [20] gained wide acceptance in the following years, being the most effective technique to stabilize C1–C2 [35], especially if combined with posterior wiring or clamps [36]. This technique can be used also in cases where there is an interruption of the posterior arch of C1 but requires a good alignment of the axis.

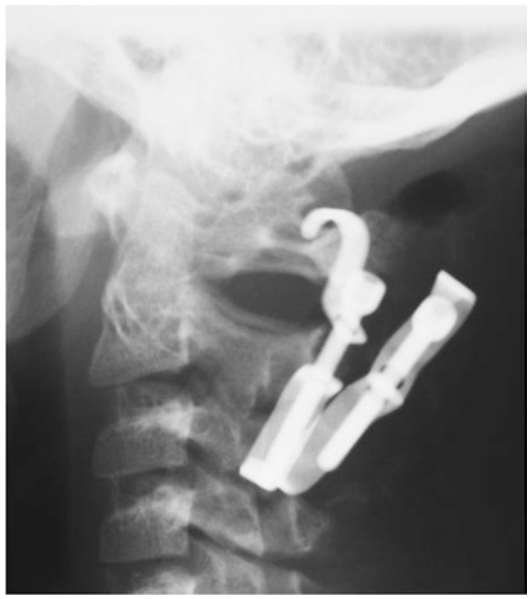

Fig. 15.2 Dislocation of Halifax clamps

The patient is placed in the prone position in a three-points head holder: a horse-shoe head holder can also be used, but, in this case, is more difficult to obtain the optimal alignment of the axis. With an external K-wire the ideal trajectory of the screws is identified before the skin incision. The entry point for the drill, in most cases, lies laterally to the spinous process of T1 or T2. The skin incision is on the midline from C0 to C3 and a careful dissection of the muscles is performed. During this step is important to maintain the midline to avoid bleeding from the muscles which are easily detached from the C1 and C2 posterior aspect, especially in young subjects. There is no need to extend dissection too far laterally, but identification of the C2–C3 joint is mandatory. Two small incisions are then made, and two guide tubes are placed along the ideal trajectory from the T2 level up to the C2–C3 joint. The direction is checked with X-rays and the entry point on C2 is identified: it lies just 3 mm medially and superiorly to the center of the C2–C3 joint. After decortication of the dorsal aspect of the joint a guide K-wire is drilled under x-ray control with a sagittal direction toward the anterior C1 tubercle and with a lateral medial inclination of about 0°–10°. If it is not possible to obtain a perfect C1–C2 alignment the trajectory should be a little superior to the anterior tubercle. The drilling is stopped 3–4 mm before reaching the anterior tubercle, preventing penetration of the retro-pharyngeal space and a cannulated screw is then screwed on the K-wire. A special attention must be paid to avoid the advance of the K-wire while the screw is positioned. Some systems have also the possibility to connect two hooks, embracing the posterior arch of the atlas, to the screws, creating a very strong stabilization of the axis (Fig. 15.3a, b). Bone autograft or allograft is finally positioned between C1 and C2. If any doubt arises, a small spatula can be inserted in the C1–C2 joint, after dislocation of the C2 nerve root, to check the presence of the screw crossing the joint.

The main problem of this technique is the risk of lesions to the vertebral artery [37]; a preoperative CT scan with reconstruction should always be performed to investigate the course of

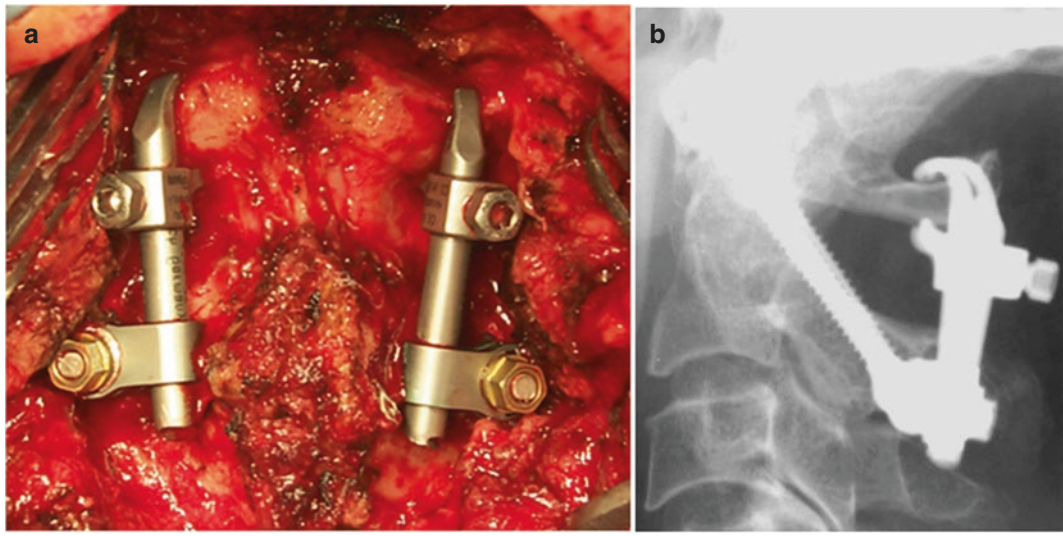

Fig. 15.3 C1–C2 stabilization by transarticular screwing and clamps. (**a**) Operative field (**b**) Post-operative control in LL

vertebral artery. Some studies have shown that anomalies of the vertebral artery anatomy or a large vertebral artery groove are present in more than 20% of the patients [38, 39]. In these situations there are two options: to change technique or to perform an unilateral trans-articular fixation.

C1 Lateral Mass Screws and C2 Pedicle Fixation

This technique was first described by Goel and Leheri in 1994 [11, 40], but gained popularity after its reappraisal by Harms and Melcher [12] some years later. The main advantage of this method is that the integrity of the posterior arch of C1 is not needed and also alignment of the axis is not necessary. With this technique a reduction and alignment of the C1–C2 complex can be obtained also in many cases considered non reducible at the pre-operative studies (Fig. 15.4a–c). At the same time the technique allows good results in terms of primary stability [31] and later fusion [40]. The technique is suitable also in mild cases of basilar invagination: by distraction of C1 and C2 the dens is pulled downward (or the skull is pushed upward), releasing compression on the ventral aspect of the brain stem, so that transoral decompression can be avoided [41].

The patient is in prone position with the head in a three-point or horse-shoe head holder. The skin incision is from C0 to C3 and the muscle of the neck are detached on the midline, exposing the posterior arch of C1 and C2 on both sides. In comparison with the trans-articular technique, the exposition is wider because the lateral mass of the atlas must be fully exposed; some bleeding can rise from the important venous plexus that surrounds the lateral aspect of the spinal cord, the C2 root and the vertebral artery, but it is usually easy to control with gel foam or other hemostatic agents; there is no need to fully expose the vertebral artery. The medial wall of the lateral mass is identified by a smooth dissector and the C2 root is also isolated. The entry point for the C1 screw is in the center of the lateral mass or at the union of the posterior arch with the lateral mass. In order to avoid conflict with the C2 nerve root, a little portion of the inferior aspect of C1 posterior arch can also be removed by drilling or rongeurs (Fig. 15.5). No drilling should be made above the junction of the posterior arch with the lateral mass because this area is too close to the vertebral artery. Under fluoroscopy a hole is drilled with a direction from 0° to 25° medially toward

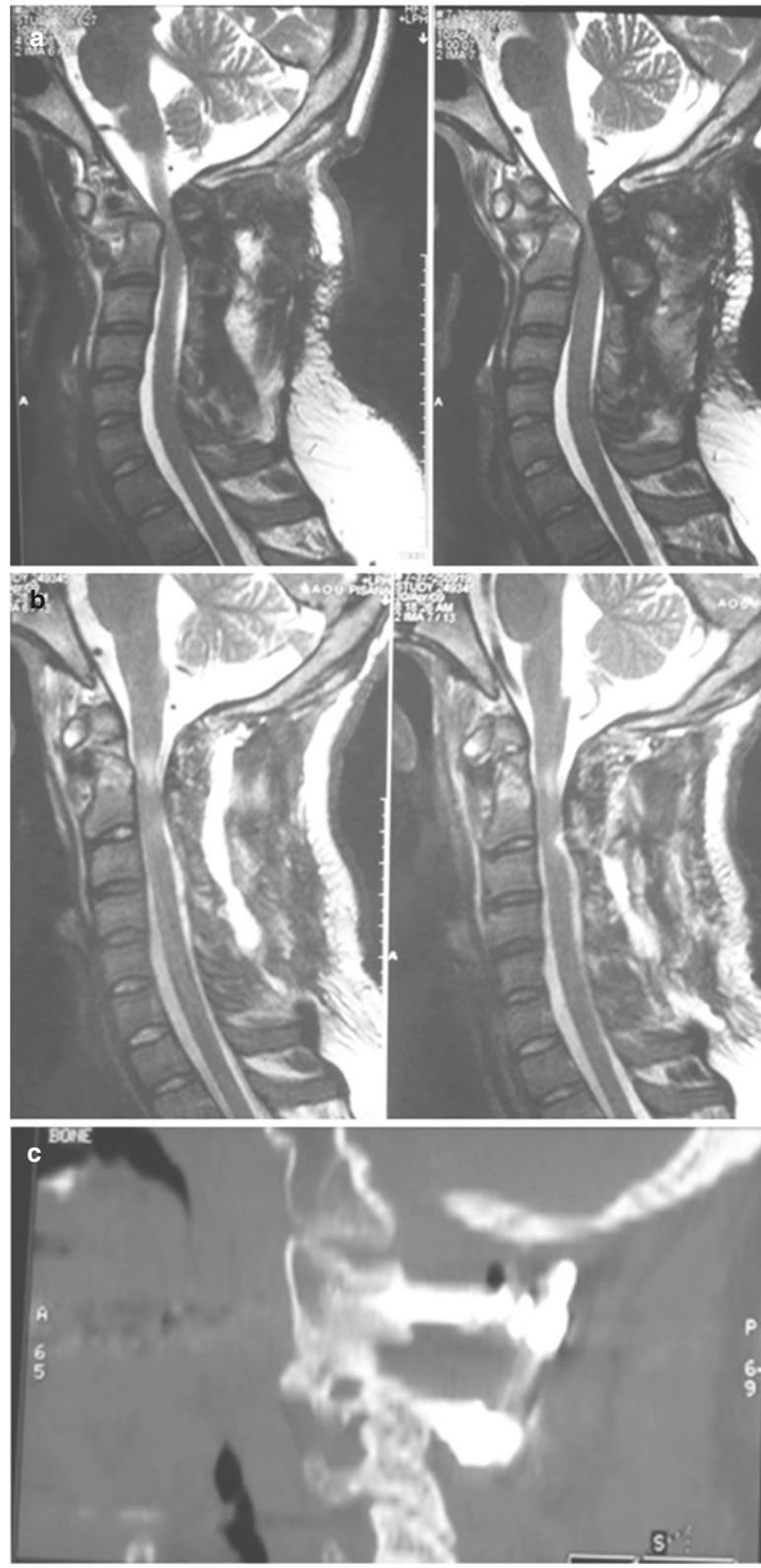

Fig. 15.4 Non-reducible os odontoideum. (**a**) pre-operative MRI (**b**) post-operative MRI following C1–C2 stabilization according to Goel and Leheri (**c**) post-operative CT reconstruction

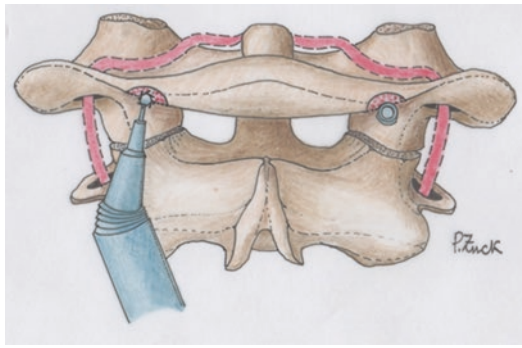

Fig. 15.5 Drilling of posterior arc of C1 before lateral mass screw insertion

the anterior tubercle. After tapping the hole, a screw (3.5 mm) is positioned.

The entry point of the C2 screw depends on the intention to place the screw in the pedicle or in the pars, knowing that there are not real differences from a biomechanical point of view [30, 42, 43]. Conventionally, the pars of C2 is that portion of the vertebra between the superior and inferior surfaces. The entry point and the direction of the screw are about the same as in the trans-articular technique (3 mm medially and 3 mm superiorly to the articular surface of C2 toward the anterior tubercle) with a latero-medial angulation of 15°. The screw is much shorter and the risk of injuries to the vertebral artery is lower. The pedicle of C2 is located anteriorly to the pars and trajectory is a little less angulated (about 20° on a sagittal plane and 15° medially). The entry point of a C2 pedicular screw is very little (about 2 mm) superior and more medial than the entry point for screwing the C2 pars. The C1 and the C2 screws are then connected to bars that allow reduction and stabilize the axis. As in the other techniques bone allograft or autograft are finally inserted between C1 and C2 in order to provide fusion.

Conclusion

Many techniques are available to restore stability of an unstable axis. The choice depends upon the pathology which caused the instability and the severity of damage to bone and ligaments. Posterior wiring and clamps are less demanding from a technical point of view and carry less risks to injuries to the vascular and nervous structures, but give less stability, which means the need for postoperative halo or collars and a significant rate of failures. Trans-articular screwing of C1–C2 is the best performing technique and should be seen as the gold standard, but carries the risk of life-threatening complications and it is not suitable in all cases. C1 lateral mass and C2 (pars or pedicle) screwing has a wider range of feasibility and is a little less risky than trans-articular screwing. The advantages are balanced by less stability.

Mispositioning of the screws, both when Magerl's technique and Goel's technique are performed, is not uncommon and navigation, when available, is recommended; nevertheless, must be said that clinical complications are exceptional also in case of a mistake in screw positioning [37].

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Lateral Mass Screw Fixation of the Subaxial Cervical Spine

16

Pier Paolo Maria Menchetti, Francesco Cacciola, and Nicola Di Lorenzo

Background

Efficient instrumented fusion of the cervical spine by means of screw and plate or screw and rod fixation represents a multifaceted and peculiar challenge to the spinal surgeon.

This is determined by a series of conditions that characterize this anatomical segment. On the one hand the cervical spine is the most mobile segment of the spinal column and exposed to a high risk of acceleration trauma, such as in whiplash injuries, as it serves as a carrying pillar for the relatively heavy skull and its contents. On the other hand it is the most delicate segment of the vertebral column with thin bony structures, especially in the posterior segments, and only a relatively small surrounding support structure given by the neck muscles when compared to the remaining spinal sections.

This peculiarity of the cervical spine, where high ranges of movement and potentially high acceleration forces on all three spatial planes encounter a delicate musculoskeletal structure, make a sound fixation in case of congenital or destructive destabilization absolutely mandatory. Being able to perform a 360° cervical spine fusion is therefore of paramount importance for the spinal surgeon who wishes to engage in treating complex cervical spine pathology. Posterior instrumented fixation with lateral mass screws has opened up the path for complex cervical spine surgery delivering the first technique to integrate from the posterior aspect the already further developed anterior approaches being both versatile and biomechanically sound.

Furthermore, in recent times a group of authors has published their long term results on posterior cervical fusion as the sole approach to treat degenerative spinal compression which appear to be very interesting and which could make this surgical approach even more widespread in terms of indications and frequency in the future.

Introduction

Lateral mass screw (LMS) fixation of the subaxial cervical spine has gained increasing diffusion in the spinal surgical community over the last two decades, thus integrating the anterior approaches already established for a longer time.

The first description of Roy-Camille using a technique of screw and plate fixation in the posterior cervical spine comes almost exactly 20 years after Orozco Delclos and Llovet Tapies describe an anterior cervical plate in 1970 and this, in turn,

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comes 15 years after the first description of Smith-Robertson's anterior cervical discectomy and fusion in 1955 [1–3].

It should, however, not be forgotten that the first approaches of fixation of the cervical spine involve the posterior aspect and date as far back as 1891 when Dr. Berthold Earnest Hadra first described a wire fixation technique using the spinous processes as anchoring points [4]. During the years the techniques of wiring and placement of hooks evolved having, however, the need for the presence of the posterior elements as a limiting factor in those settings where fixation is needed to integrate a posterior decompression. The absence of spinous processes and laminae makes wiring and hook techniques unfeasible.

With the advent of LMS and plate fixation the presence of the laminae and spinous processes was no longer needed making it therefore a very versatile tool in posterior cervical spine surgery and with the technical improvement of the hardware the possibilities of even complex correction surgeries have clearly evolved (Figs. 16.1 and 16.2).

While LMS fixation has gained through the years the most widespread diffusion in the spinal surgical community, recently published case series of Goel et al. [5] on posterior fixation of the sub axial cervical spine for degenerative disease via transfacet screws (TFS) have brought to our attention a technique that is at least as old as the LMS technique but which seems to have gotten less attention than it deserves.

We will now carry on to describe the surgical technique of the main LMS fixation procedures and of the TFS technique and discuss their differences subsequently.

Surgical Techniques

The LMS Techniques

Four techniques of LMS fixation have been more diffusely described and compared.

The original Roy-Camille procedure was modified by Magerl, Anderson and An. While all four techniques are conceptually the same, involving the placement of a screw in the width of the lateral mass, they differ in the entrance point for screw insertion and in the orientation of screw trajectory.

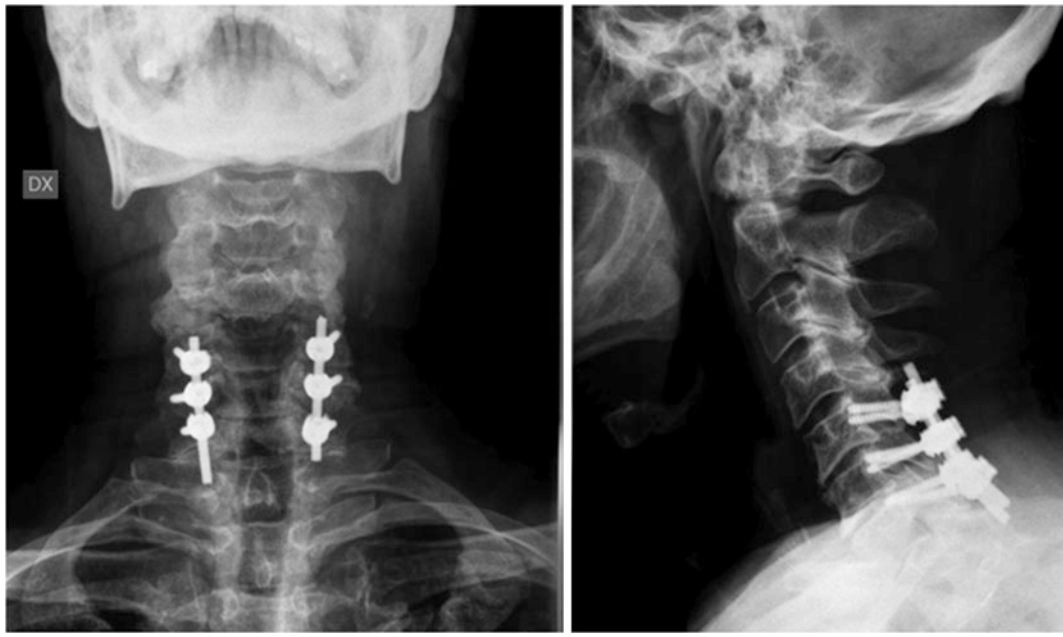

Fig. 16.1 Postoperative cervical spine x-rays in the anteroposterior and lateral projections of a C5–7 LMS fixation

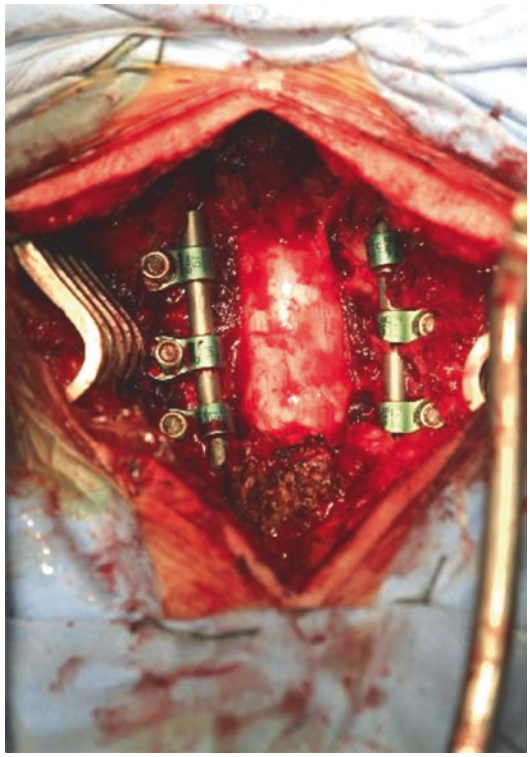

Fig. 16.2 Intraoperative photograph of a three level LMS fixation of the subaxial spine. Note the wide decompression and dural exposure with removal of all posterior elements

This is due to the attempt of the various authors to find the ideal combination of maximum screw purchase and minimum risk of injury to the exiting cervical nerve root and the vertebral artery in the transverse process of the cervical vertebra.

Approach to the Posterior Cervical Spine

While the initial exposure of the posterior aspect of the cervical spine is not specific to LMS instrumentation procedures it is worth underlining some peculiar steps from skin incision to muscle dissection that will facilitate the entire procedure.

In approaches to the posterior cervical spine, especially if only a single level fixation is contemplated, it is worth it to plan the skin incision with lateral fluoroscopic control. Particular attention should be paid not only to the rostrocaudal extension of the incision but also to the orientation of the deepening of the incision as muscle dissection procedes. This will help minimizing the extent of muscle dissection, bleeding and injury to the zygoapophyseal joint capsules not involved in the fusion. Contrarily to pedicle screw insertion techniques, LMS insertion requires a diverging screw trajectory, thus not requiring extensive muscle dissection rostrally and caudally to the instrumented levels for appropriate muscle retraction.

If instrumentation is confined to subaxial levels, attention should be paid not to dissect the rectii capitis and oblique muscles off the posterior aspect of C2 to avoid unnecessary destabilization of the craniocervical junction.

Holding to the midline after incision of the fascia and meticulous dissection of the paraspinal muscles off the spinous processes and laminae can help avoid excessive bleeding often encountered in the posterior cervical spine due to large paraspinal venous plexuses.

Finally, a clean dissection of the levels to be instrumented is mandatory to correctly identify the surgical landmarks which essentially consist in the midpoint of the lateral mass on its posterior aspect. Inferior, superior and lateral confines of the lateral mass to be instrumented should thus be clearly identified.

Once the midpoint of the lateral mass is identified, the four techniques proceed according to their specific indications.

Roy-Camille

The entry point for screw positioning is exactly in the center of the posterior surface of the lateral mass. On the sagittal plane the trajectory is obtained by aiming anteriorly with an inclination perpendicular to the posterior surface and on the axial plane by aiming laterally at 10° (Fig. 16.3).

Magerl

The entry point is two milimeters (mm) medial and 2 mm superior to the center of the posterior facet of the lateral mass. On the sagittal plane the trajectory is oriented cephalad at an angle so as to parallel the joint space and on the axial plane it goes laterally at an angle of 25°–30° (Fig. 16.4).

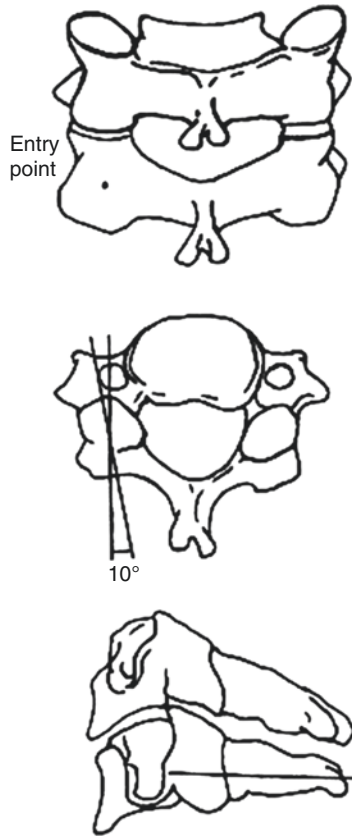

Fig. 16.3 Schematic drawing of cervical vertebrae depicting on top a view from behind. Note the entry point at the center of the dorsal aspect of the lateral mass. (Ebraheim NA, Klausner T, Xu R, Yeasting RA. Safe lateral mass screw lengths in the Roy-Camille and Magerl techniques. Spine 1998; 23 (16): 1739–1742. Reprinted with permission)

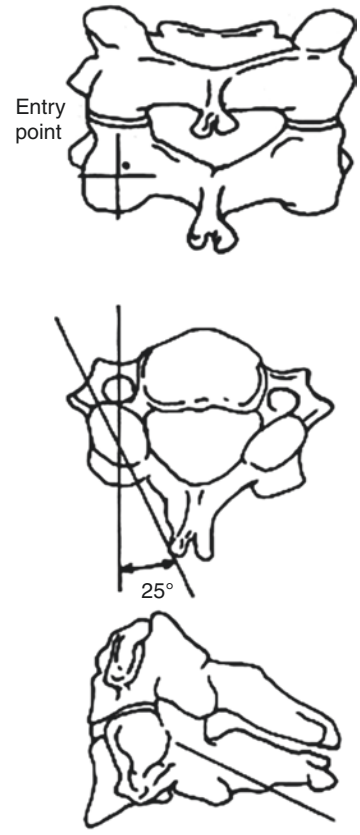

Fig. 16.4 Schematic drawing of the Magerl technique. Note that the entry point is slightly medial and cranial with respect to the center point. (Ebraheim NA, Klausner T, Xu R, Yeasting RA. Safe lateral mass screw lengths in the Roy-Camille and Magerl techniques. Spine 1998; 23 (16): 1739–1742. Reprinted with permission)

In this technique, given that the cephalad orientation on the sagittal plane parallels the facet joint, this landmark can be used in two ways to help guiding screw insertion: a thin straight dissector can be inserted into the joint space between two levels that need to be instrumented, thus guiding orientation, or lateral fluoroscopy can be used to plan the trajectoy, paralleling the cephalad and caudad facet joints.

An

The entry point is 2 mm medial to the midpoint of the lateral mass at the same height. On the sagittal plane the trajectory is oriented 15° cephalad and on the axial plane 30° laterally (Fig. 16.5).

Anderson

The entry point is again 2 mm medial to the midpoint of the lateral mass at the same height. On the sagittal plane the trajectory is oriented 30°–40° cephaladly and on the axial plane 10° laterally (Fig. 16.6).

Once the trajectories have been made according to one or the other technique, as far as screw diameter and length are concerned, nowadays most manufacturers have a cervical instrumentation kit in their program and standard screw diameter is 3.5 mm with a rod of the same measure. In terms of screw length, as we will see in the next section, bicortical purchase should be obtained in order to achieve the highest biome-

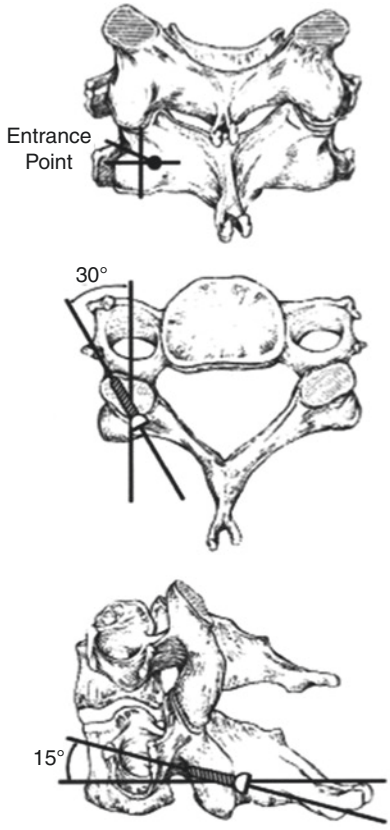

Fig. 16.5 Schematic drawing of the An technique. The entry point is slightly medial and at the same level of the center point. (Xu R, Haman SP, Ebraheim NA, Yeasting RA, The Anatomic Relation of Lateral Mass Screws to the Spinal Nerves A Comparison of the Magerl, Anderson, and An Techniques. Spine 1999; 24(19): 2057–2061. Reprinted with permission)

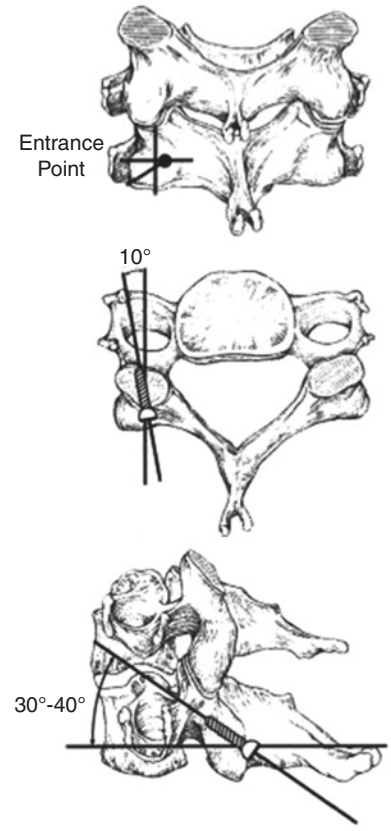

Fig. 16.6 Schematic drawing of the Anderson technique. The entry point is the same as for the An technique. (Xu R, Haman SP, Ebraheim NA, Yeasting RA, The Anatomic Relation of Lateral Mass Screws to the Spinal Nerves A Comparison of the Magerl, Anderson, and An Techniques. Spine 1999; 24(19): 2057–2061. Reprinted with permission)

chanical resistance of the implant. Average screw length, based on anatomical studies, is around 15 mm from dorsal to ventral cortex but this is just an indicative value.

Actual screw length is case specific and the authors suggest the use of a fine tip ball probe to explore the screw hole once probed. With some experience it can be quite reliably felt when the ball tip exits the breached ventral cortex and the position of the probe is then held just at that point while a small Mosquito clamp is attached to the probe flush with the dorsal cortex. Once retracted the distance between the Mosquito and the ball tip is then measured and this quite reliably gives an indication for the actual screw length. Some manufacturers offer specific depth gauges in their instrument kits to perform these measurements.

In any case it is important not to overpenetrate the ventral cortex too much as we will see further on.

The TFS Technique

The TFS technique had been described for the first time by Roy-Camille in 1972 [6] when it was presented as an alternative or adjunct to "standard" (LMS) techniques in the treatment of fractured lateral masses (Fig. 16.7). For some reason this technique has remained an alternative to

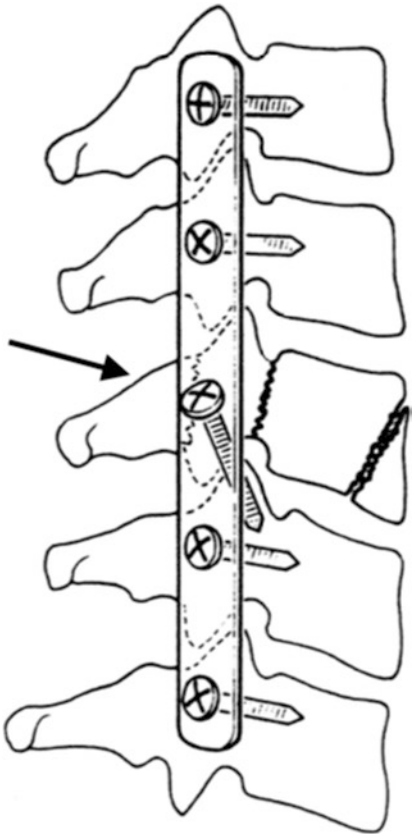

Fig. 16.7 Schematic drawing of the first description of a transfacet screw in the cervical spine by Roy-Camille. (Roy-Camille R, Saillant G. Chirurgie du rachis cervical: Luxation-fracture des articulaires. Nouvelle Presse Medicale 1972; 1:2484–5, Reprinted with permission)

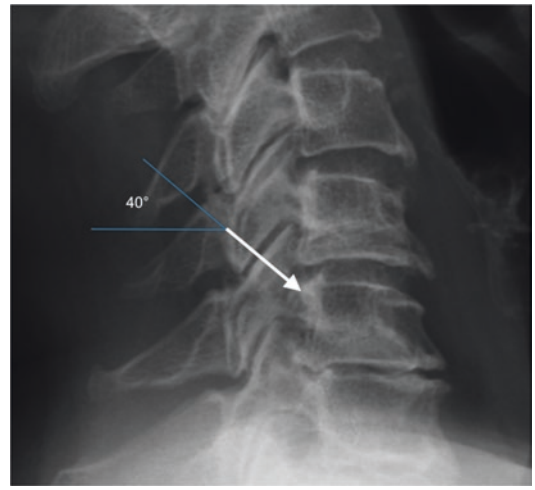

Fig. 16.8 Lateral cervical radiograph showing the trajectory and inclination (white arrow) of the transfacet screw. Note the course through the facet and the 40° angulation perpendicular to the posterior aspect of the facet

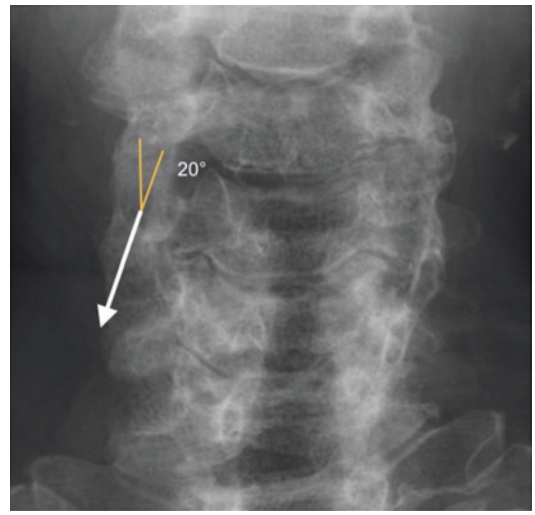

Fig. 16.9 Anteroposterior radiograph of the cervical spine showing the trajectory and inclination of the transfacet screw (white arrow). Note the 20° lateral angulation of the trajectory

LMS, so much so that it had almost been forgotten by the spinal surgeons even though it appears to be biomechanically even more stable than LMS as we shall see in the next section.

As far as the technique is concerned, the entry point of the screw is again the midpoint of the lateral mass but instead of directing the screw superior and out, it is directed inferior and out. The angles are 20° lateral with respect to the vertical line and 40° inferior with respect to the surface plane of the lateral mass (Figs. 16.8 and 16.9). Just as with LMS image guidance is recommended to confirm the direction that almost perpendicularly traverses the joint space. On its way the TFS engages with four cortical bone surfaces, that of the posterior lateral mass surface, the two joint surfaces and the cortex of the anterolateral aspect of the lateral mass at its exit point. Even though the appropriate lateral direction of the trajectory should avoid the exiting nerve root, as this exits the foramen in an anterior direction, care must be taken to engage the exit cortical layer with just one or two threads of the screw. The technique in order to achieve this and how to

select the appropriate screw length has been described in the previous section.

A downside and limiting factor of the TFS technique is the caudal inclination of the screw and the occiput which in some case might limit the downward angulation. This could become especially relevant and limiting in case where a long fixation construct has to be considered and where the appropriate degree of lordosis needed might bring the occiput into the way.

Comparison of the Four LMS and the TFS Techniques

LMS Techniques

Among the four LMS techniques illustrated, the Magerl technique seems to have gained the widest diffusion in the literature describing case series. This is most likely due to the fact that the cephalad orientation on the sagittal plane is indicated as having to be parallel to the joint spaces. This obviously furnishes the surgeon with a precise landmark, at least on this plane, that can be reliably identified either by insertion of a dissector into the joint space or by fluoroscopy as outlined above (Fig. 16.10).

While identification of the inclination on the sagittal plane is quite straightforward also in the Roy-Camille technique, where it should be oriented perpendicularly to the posterior plane of the lateral mass, on the axial plane the inclination of 25°–30° in Magerl's technique probably gives surgeons more confidence in knowing to avoid transverse foramen breaching and thus potential vertebral artery injury with respect to the 10° divergence in the Roy-Camille technique even though this inclination was obviously designed to avoid the vertebral artery just as reliably.

Vertebral artery injury does, in fact, not appear to be a concern in the literature, as we will see further ahead, and comparative anatomical studies that compare the safety of LMS techniques have looked at which technique represents the highest risk for nerve root injury.

Ebraheim et al. [7] have carried out an anatomical study comparing the Magerl and Roy-Camille techniques in order to identify maximum screw length and related hazard of injury to the exiting nerve root. In their paper they make the premise that bicortical purchase of the screws yields higher biomechanical stability, as stated in previous studies, and thus examined the location of the nerve root with respect to the screw tip once this has exited the distal cortex. Considering that anatomically, the spinal nerve exiting from the intervertebral foramen courses in an anterolateral and inferior direction and is situated directly in the front of the medial portion of the superior facet and the posterior ridge of the transverse process, they made the following observations: The cervical specimens from their study showed that the spinal nerve lies directly in front of the Roy-Camille screw's trajectory in all specimens. The spinal nerve will therefore be penetrated if the screw is too long, even though the screw's entrance point and trajectory are correct. The mean distance between the ventral or distal cortex of the lateral mass and the spinal nerve along the screw path measured 1.2–2.3 mm.

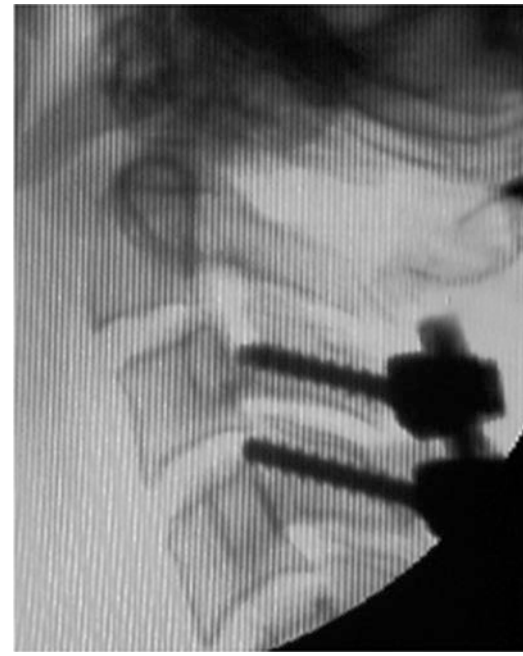

Fig. 16.10 Intraoperative fluoroscopic image of the cervical spine in the lateral projection. LMS fixation of C3–4 according to the Magerl technique. Note the trajectories of the screws parallel to the joint space

With the Magerl technique only in 21% of specimens the nerve root was located in front of the screw's trajectory, although most were located just below the screw's path. Risk of nerve root injury with Magerl's technique was highest in the lower cervical levels.

They therefore conclude suggesting that ideally penetration of the ventral cortex for bicortical purchase should not be higher than 1 mm as this would represent the safety zone in all instances.

Xu et al. [8], of the same group, 1 year later published another study comparing Magerl's technique with the An and the Anderson technique. In this study, which again is a cadaveric study, they placed 20 mm screws to overpenetrate the lateral mass on purpose in order to create a nerve root conflict. They then dissected the specimens and established the screw-nerve relationship in particular to the dorsal and ventral ramus.

In their series the overall percentage of nerve violation was significantly higher with the Magerl (95%) and Anderson (90%) techniques than with the An (60%) technique ($P > 0.05$). The largest percentages of nerve violation for the Magerl, Anderson, and An screws were found at the dorsal ramus (50%), the bifurcation of the ventral dorsal ramus (45%), and the ventral ramus (55%), respectively.

They conclude that the results of this study indicate that the potential risk of nerve root violation is higher with the Magerl and Anderson techniques than with the An technique.

While such studies are certainly highly important in order to establish in particular the amount of risk every single technique carries, it has to be kept in mind that they are performed with the use of measuring devices on a cadaver and that the in-vivo conditions generally entail the surgeon estimating the inclination based on his or her experience. Under such conditions a difference of 10° inclination in an angle can easily occur making it thus difficult to effectively differentiate between the techniques and to know whether the intended angulation is effectively being applied.

Pal et al. [9] have carried out a study starting from the assumption that estimation of the angle of inclination during LMS positioning remains arbitrary and would appear to be very much operator dependant.

The aim of their study was to assess how accurately the lateral trajectory angle of 30° is achieved by visual estimation amongst experienced surgeons in a tertiary spinal unit and to determine the likelihood of neurovascular injury during the procedure. They chose an anatomical 'sawbone' model of the cervical spine with simulated lordosis. The senior author marked the entry points. Five spinal consultants and five senior spinal fellows were asked to insert 1.6-mm K wires into the lateral masses of C3–C6 bilaterally at 30° to the mid- sagittal plane using the marked entry points. The lateral angulation in the transverse plane was measured using a custom protractor and documented for each surgeon at each level and side.

The overall mean angle of insertion was 25.15 (range 20.4–34.8). The overall SD was 4.78.

They concluded that a moderate but notable variability in trajectory placement exists between surgeons during insertion of cervical lateral mass screws. Freehand estimation of 30° appears therefore to not be consistently achieved between surgeons and levels and in patients with gross degenerative or deformed cervical spine anatomy, this may increase the risk of neurovascular injury.

The same group, in a paper of Bayley et al. [10], suggest the use of the ipsilateral lamina as a guidance for determination of the axial angle of insertion. They performed a CT based measuring study to determine whether alignment of the LMS trajectory parallel to the ipsilateral cervical lamina reliably avoids vertebral artery violation in the sub-axial cervical spine. They placed a virtual trajectory through the lateral mass parallel to the ipsilateral lamina and found that in all cases this would avoid vertebral artery injury while delivering a precise landmark that can thus help in determining axial inclination. Limitations of this technique are, however, that the length of lateral mass available for bony purchase ranges from 5 to 7 mm and could in some cases not encounter sufficient bone stock at the C3 and C7 level as, for example, in female patients.

Safety of LMS Techniques

Even though the potential hazards of vertebral artery or nerve root injury in LMS positioning would appear quite obvious, given the vicinity of these structures to the screw path traversing and exiting the lateral mass, the literature available shows quite consistently that it is a safe procedure with small complication rates.

Kim et al. [11] report in a prospective study on the evaluation of 1256 lateral mass screws positioned in 178 consecutive patients at their institution. Their technique, that appears to be a combination of Magerl's and An's in terms of entry point and inclinations, and is executed "freehand", with only an initial lateral radiograph for level determination, they describe an incidence of foramen transversarium (FT) violation of 0.876% with, however, no case of vertebral artery injury. FT violation was most common at C6 (6/11 violations). Mean divergent angle in cases of FT violation was 15.0° and was significantly smaller than that of safe cases. They report no violation of an intervertebral foramen and an ncidence of facet violation of 1.433%.

Coe et al. [12] have conducted a systematic literature review to describe the safety profile and effectiveness of LMS fixation. They found 20 articles (two retrospective comparative studies and 18 case series) that satisfied the inclusion and exclusion criteria.

Both of the comparative studies involved comparison of lateral mass screw fixation with wiring and indicated that the risk of complications was comparable between treatments (range, 0– 7.1% compared with 0–6.3%, respectively). In one study, the fusion rate reported in the screw fixation group (100%) was similar to that in the wiring group (97%). Complication risks following lateral mass screw fixation were low across the 18 case series. Nerve root injury attributed to screw placement occurred in 1.0% (95% confidence interval, 0.3–1.6%) of patients. No cases of vertebral artery injury were reported. Instrumentation complications such as screw or rod pullout, screw or plate breakage, and screw loosening occurred in <1% of the screws inserted. Fusion was achieved in 97.0% of patients across nine case series.

They conclude that the risks of complications were low and the fusion rate was high when LMS fixation was used in patients undergoing posterior cervical subaxial fusion.

TFS Technique

As far as comparisons in safety between the TFS and LMS techniques is concerned there are no available studies in the literature to the best of our knowledge. This is obviously due to the limited diffusion of the TFS technique but might just as well change if the technique rises to the importance it appears to have. What is available in the literature though, and what evokes even more surprise for those not familiar with the technique, is a paper published by Klekamp et al. in 2000, which is the first of a few of its kind [13, 14].

In this paper the authors have made a biomechanical comparison between TFS and LMS. They conclude that the pullout strength of TFS is equal if not superior to LMS. This is obviously down to the fact that TFS traverses four cortical layers and LMS only two.

As already mentioned, a limiting factor for TFS with respect to LMS is that the neck of the patient has to be positioned in slight flexion in order to bring the occiput anteriorly and keep it from interfering with the correct caudal angulation. This fact makes TFS less useful, and in some cases impractical, when it comes to long fusion constructs, even more so if they have to include the occiput. It could, however, be very useful in single level fixations, as in the case of a posterior 360° completion of an anterior fusion, where, furthermore, it also reduces the amount of screws from 4 to 2 and thereby halving the risk of potential injury due to screw placement, as well as eliminating the need for rods (Fig. 16.11).

Finally, should one really prefer TFS over LMS even in complex and long fixations, rectangular drills and screwdrivers could easily be implemented to eliminate the limiting factor of the occiput.

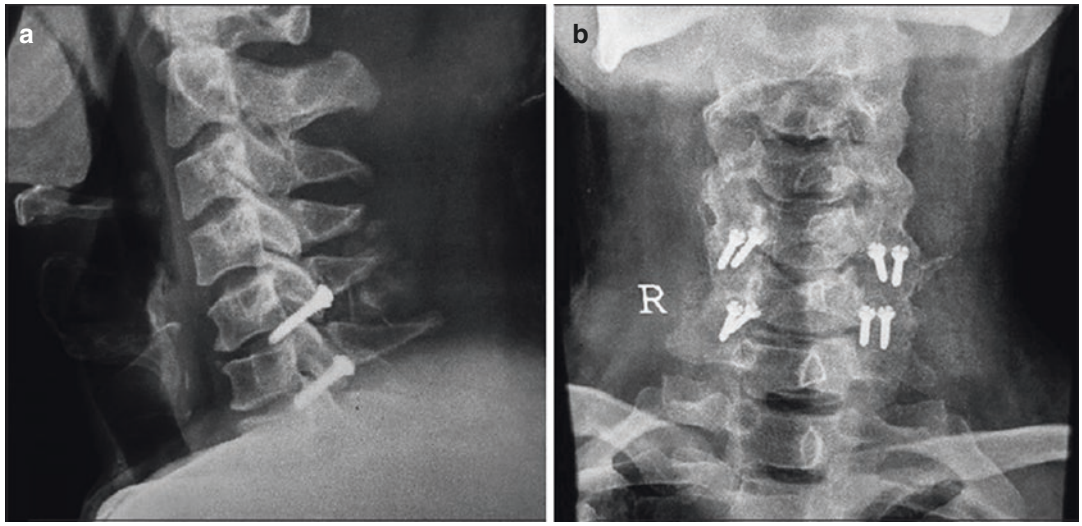

Fig. 16.11 Anteroposterior and lateral radiograph of the cervical spine showing multilevel fixation with transfacet screws. Note the direction of the screws on both planes and the choice of the authors two use two screws at each level which is a variation of the usual single screw technique. (**a**) Lateral projection. (**b**) Anteroposterior projection (Goel A. Camille's transarticular technique of spinal fixation: An underused surgical technique. J Craniovert Jun Spine 2019;10:197–8, Reprinted with permission)

Conclusions

LMS and TFS fixation has changed the face of surgery in the cervical spine. While similar to wiring techniques in terms of complication and fusion rates these techniques are, however, certainly more versatile and thus efficient. This is due to the fact that no lamina or spinous process are needed, therefore enabling the surgeon to associate fixation with wide decompressions or to employ it in case of revision surgeries where a decompression had already been performed [15]. Furthermore, the screw and tulip setup of modern systems deliver the possibility to associate subaxial cervical fixations easily with craniocervical fixations or dorsal fixations via appropriate transition rods or domino connectors due to the modularity that this technique permits with the appropriate systems.

The TFS technique, which biomechanically appears to be at least as sound as the LMS, represents a valid additional option and might possibly be mainly used in single or even multilevel fixations where the direct transfacetal placement of the screw eliminates the need for rods and thus complex screw constructs where a tulip for rod accommodation is needed. This brings along two further advantages of TFS over LMS, which are a major cost effectiveness, as only two screws are needed for a single level fusion with TFS instead of fours screws and two rods with LMS (REF) and TFS lends itself also to the option of placing the screw, and thus performing the fixation, percutaneously if needed [16–18].

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Craniocervical Anomalies: Chiari Malformation

17

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Introduction

The autopsy of a 17-year-old girl who died of typhoid fever was the first case of Chiari malformation described by Hans Chiari in 1891 [1]. Hans Chiari wanted to describe changes in the cerebellar region caused by hydrocephalus, she had however had no cerebellar or medullary symptoms prior to her death of typhoid fever; an incidental finding. Later on he went on to describe a case series consisting of 14 patients with Chiari malformation and speculated in other mechanisms such as insufficient bone growth or skull enlargement resulting in higher intracranial pressure [2]. He described the condition among other malformations of the craniocervical junction. Just 25 year later, in 1932, the first surgical attempt to correct the malformation was performed by Van Houweninge Graftidijk [3]. Much like the current surgical techniques he tried by resecting redundant cerebellar tonsils or resect the bone over the malformation and incise the dura. Given the early days of neurosurgery, his patients however didn't survive the procedure. By the end of 1930 and beginning of 1940 the condition had received further attention by several other publications in which adult cases of Chiari malformation was described either with or without hydrocephalus.

Today almost 1.5 century later we can still to some extent recognise the challenges and difficulties pioneers of neurosurgery faced and their struggle to find and refine surgical techniques to treat this condition. Our challenges have however changed in a fundamental way with overt use of imaging techniques leading to a surge in incidental findings with Chiari malformation being one of these findings. Just like Hans Chiari describing a condition that had to effect on the deceased girl and her symptoms, we can now face patients initially investigated for an unrelated condition or trauma and with no symptoms with a condition ultimately being an incidental finding.

It is fundamental to recognise that despite having varying degree of involvement of rhombencephalic derivate and hindbrain structures Chiari malformations are also a heterogeneous group of malformations with different underlying mechanisms and overlapping symptoms. Best treatment demands understanding of the various pathophysiological mechanisms involved in the specific case.

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Definition

Classic Chiari I malformation is a congenital condition with descent of cerebellar tonsils into foramen of magnum equivalent to or beyond 5 mm. Chiari malformation is found in 0.8–1% in hospital series [4, 5]. The prevalence seems to also be similar or lower among general population and is described as 0.2–1.7% in adults [6–8]. Asymptomatic cases are therefore almost always found among patients undergoing radiological imaging for various reasons specially among infants and young children. In children and infants, the extent of the caudal migration might decrease over time and asymptomatic children are therefore followed up until adulthood. There are also patients who do not have the classic descent of the cerebellar tonsils but who do have crowding in their posterior fossa with extensive syringomyelia and who do improve after decompression surgery of the posterior fossa.

In recent years the need to further describe the variety seen in Chiari I patients has led to description of two new entities within the Chiari I category namely Chiari 0 and Chiari 1.5. Chiari 0 describes the condition where a syringomyelia is present in absence of cerebellar herniation which resolves after posterior fossa decompression. Chiari 1.5 is a more severe form of Chiari I malformation in which the both the medulla and cerebellar tonsils are herniated below foramen magnum [9, 10].

Unlike Chiari I, patients with Chiari II suffer from neural tube defects such as myelomeningocele and encephalocele. Syringomyelia is common in this group as is hydrocephalus and a variety of other conditions involving the skull, bony spine, meninges, ventricles, spinal cord and various cerebral structures [11].

Pathophysiology

Early on it was hypothesized that hydrocephalus was related to and could cause Chiari malformation as evident in the early descriptions of Chiari. However later series found this association in less than 10% of the Chiari cases and hence a causal relationship between Chiari malformation and CSF disturbance has not been established [12].

Comparisons of posterior cranial fossa of Chiari I patients and normal population has shown that the posterior cranial fossa is smaller in Chiari I patients compared to normal controls [13, 14]. In a recent study these differences has been shown to be more prominent among men than women despite the higher prevalence of Chiari I malformation in women than men [15]. A smaller posterior cranial vault is also observed in Chiari malformation cases associated with other conditions such as multisuture craniosynostosis, platybasia, neurofibromatosis type I, familial vitamin D-resistant rickets and acromegaly [16–19]. It has been hypothesized that mesodermal defects can cause a smaller posterior cranial vault which in turn can cause cerebellar tonsillar herniation [20, 14].

Signs and Symptoms

Chiari I patients can be asymptomatic as Chiari I can be found as an incidental finding. Symptoms usually have a gradual onset and acute onset is unusual.

The most common type of symptom in both adults and children is occipital and or cervical headache or pain which is either exacerbated or elicited by Valsalva manoeuver or Valsalva-like strain such as laughing and coughing. The headache should typically be of short duration (seconds to minutes). The proposed mechanism for the headache is disturbed cerebrospinal fluid dynamics and raised intrathecal pressure and worsening of the crowding in posterior fossa [21]. In young children and infants this presentation can be in the form of irritability or inconsolable crying [22].

Headache is a very common symptom in general population and among children and adolescents and therefore a thorough investigation of the origin of the headaches are necessary if the history is inconsistent with strain-related headache. Aside from headaches, medullary symptoms can be found and be prominent in patients with syringomyelia. The symptoms are that of

classical medullary signs and symptoms with progressive limb weakness, hyperreflexia, balance- and gait disturbance. Paediatric patients may also present with failure to thrive, sleep apnoea, hoarseness, snoring or arching back [22]. Scoliosis can also be a manifestation of Chiari I in children and is usually accompanied by syringomyelia.

Other types of symptom include dizziness, swallowing difficulties, sinus bradycardia and autonomic dysfunction, difficulties with hand coordination, nystagmus and visual impairment [12].

Syringomyelia

Syringomyelia, a fluid filled cavity within the spinal cord, is one of the most common findings associated with Chiari I malformation. First description of syringomyelia has been accredited to Stephanus who in 1545 described a cavitation in "the interior substance of the marrow of the back" containing a red brown fluid. This description is more befitting of a post-haemorrhagic cavity than true syringomyelia. A cystic cavity in spinal cord found in connection with hydrocephalus was first described by Brunner in 1688. The term itself was first applied by Ollivier D'Angers in 1827 who thought of the central canal as a pathological finding [23].

Syringomyelia can have various different causes with different underlying pathophysiological mechanisms. The condition can be tumour related, congenital, inflammatory or traumatic in nature and treatment should always if possible treat the underlying condition such as in the case of Chiari malformation or tethered cord. As previously mentioned, patients with Chiari 0 are patients in whom a syringomyelia is detected without tonsillar herniation but with posterior fossa crowding. In these patients the treatment of the underlying cause which is believed to be a functional obstruction of the foramen magnum with posterior fossa decompression and duraplasty can typically resolve the underlying syringomyelias.

Surgical Treatment

The surgical treatment of Chiari I malformations is very much in line with what forefathers of neurosurgery once proposed. Suboccipital decompression and duraplasty is the standard surgical method for treatment of Chiari I malformations. The procedure is often combined with C1 laminectomy but laminectomy to achieve a good decompression of structures oftentimes pushed beneath the level of foramen Magnum. C1 laminectomy should however be limited to minimal manipulation of facet joints and their capsule to avoid future complications and swan neck deformity. In recent times the use of suboccipital decompression alone without duraplasty has been performed and advocated because of the procedure's low rate of complications and easy mobilisation and discharge of patients. CSF leakage remains the most common complication of suboccipital decompressions combined with duraplasty and is avoided with bony decompression alone. The so called "bony only" decompressions are however mostly used in children without syringomyelia [24]. The procedure is then combined with C1 laminectomy, resection of atlantooccipital membrane and scoring of the outer layer of the dura. A recent study found that this procedure also had a favourable long-term outcome in children [25]. For adults the matter remains controversial as no high quality study has been performed on adult patients comparing the two procedures [26]. The preferred surgical method for adults remain suboccipital craniotomy with duraplasty.

As an alternative to suboccipital craniotomy and duraplasty, an extra arachnoidal craniocervical decompression has been successfully practiced at the institution of the senior author [27]. Using this technique the arachnoid membrane is left intact and duraplasty is not performed. The dura is left open with the dural slits stiched laterally to the muscles. The technique is briefly described here, Figs. 17.1 and 17.2. Patients are positioned in sitting position for this procedure. A suboccipital craniotomy and C1 laminectomy of at least

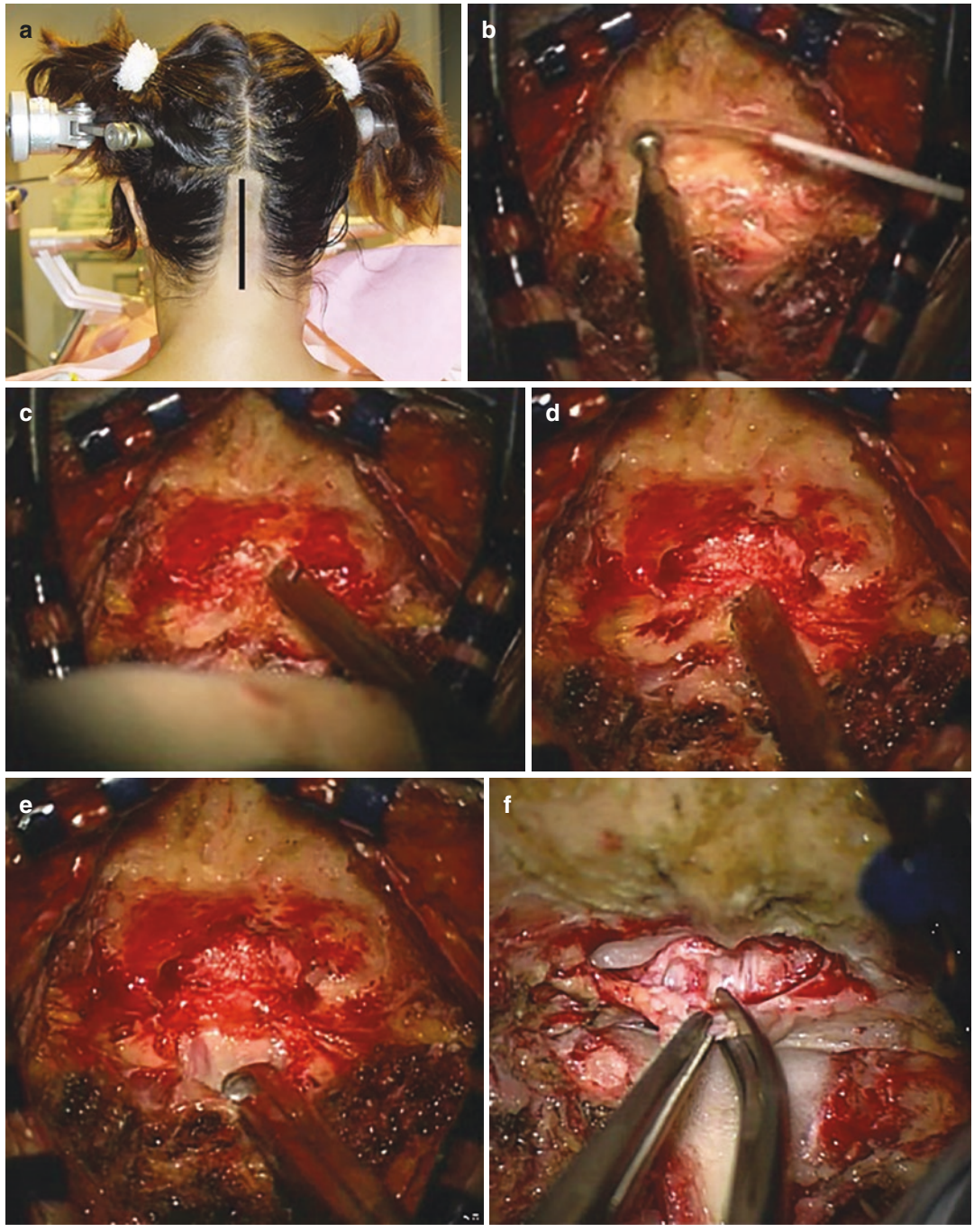

Fig. 17.1 (**a**) Patient is positioned in sitting position with a midline trichotomy. (**b**–**f**) Stepwise suboccipital craniotomy and opening of the posterior atlantooccipital membrane. (**g**) Opening of the dura with angled dural dissector. (**h**, **i**) Stiching of the dural to laterally to the muscles

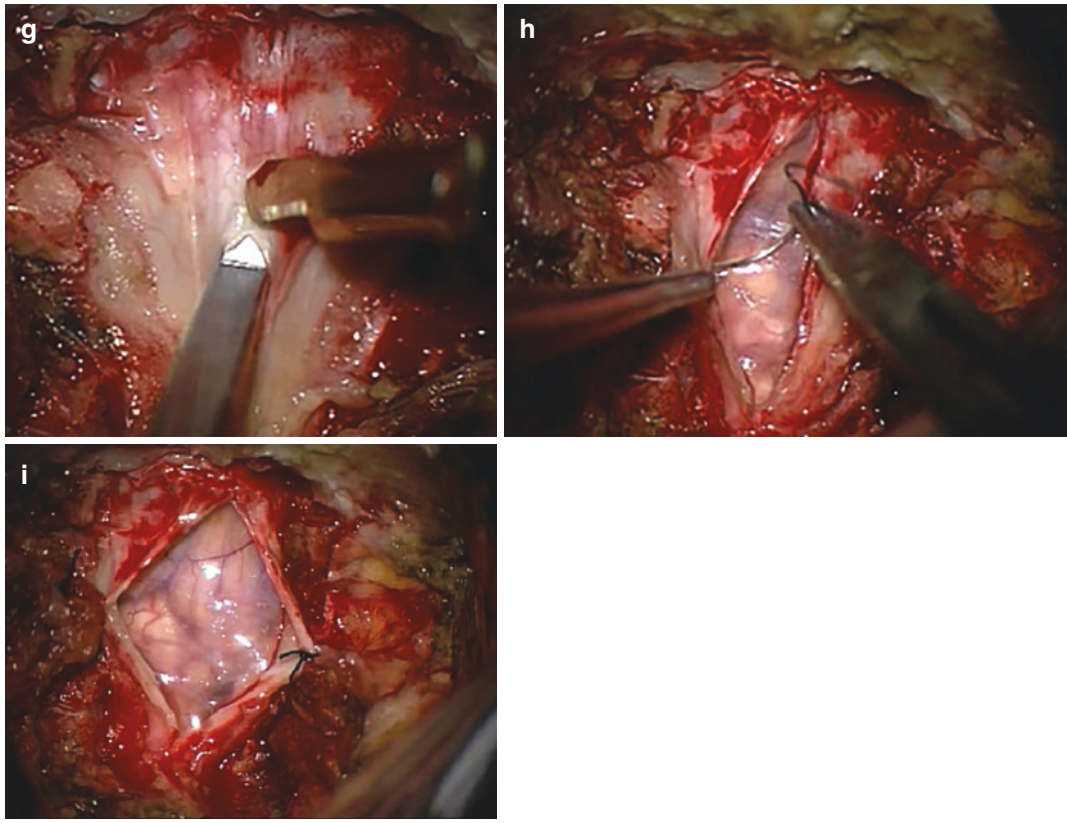

Fig. 17.1 (continued)

2 × 3.5 cm is performed after which the underlying posterior atlantooccipital membrane is opened. Underlying dura is opened meticulously using an angled dural dissector and paying attention to not violate the arachnoid membrane accidentally. The dura is then stitched to the muscles laterally and left open. In our series a resolution of the syringomyelia and good neurological outcome was found after a mean follow-up period of 44 months [27]. The senior author uses this procedure for younger adults due to its low risk of complications and good surgical outcome in that patient group.

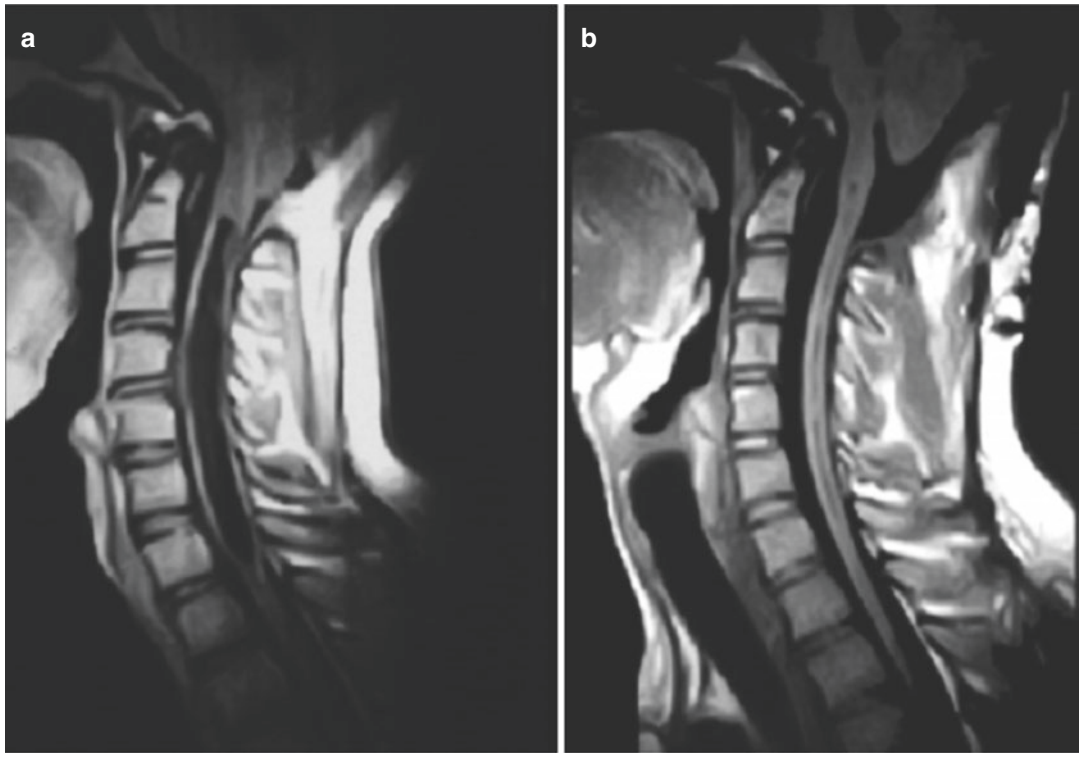

Fig. 17.2 (**a**) Preoperative images of the patient described in Fig. 17.1. (**b**) Postoperative imaging of the same patient

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18

Endoscopic Endonasal Odontoidectomy

Description of the Surgical Technique and Outcome

Felice Esposito, Filippo Flavio Angileri, Luigi Maria Cavallo, Fabio Cacciola, Antonino Germanò, and Paolo Cappabianca

Introduction

Anterior approach to the cranio-vertebral junction (CVJ) and, particularly, to the odontoid process of the second cervical vertebra has classically been performed, in neurosurgical settings, via a transoral route. Such technique is still considered the gold standard treatment for odontoid process diseases.

However, the advent of endoscopy in neurosurgery and the development and the refinement of the endonasal approaches to the entire midline skull base [1–5], has meant that also this field, once dominated by microsurgery, has become territory of exploration for neurosurgeons who have dedicated clinical and scientific efforts is this direction. As a matter of facts, the endoscopic endonasal approach to the cranio-cervical junction, and to the odontoid process, is among the areas of most interest to which endoscopic technique is developed.

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Indeed, several studies either anatomical and/or clinical have been reported showing the interest of approaching the CCJ through the nasal corridor [6, 7]. In fact, the availability of new technologies, such as endoscopes, high definition endoscopic cameras, navigation systems, ultrasound micro-Doppler, dedicated endonasal instruments and bipolar forceps have opened new horizons to manage pathologies involving this complex region using the natural nasal corridors; this way/approach has demonstrated a remarkable improvement of the quality of disease resection as well of the functional outcome with a lower morbidity.

The endonasal route provides a direct access to the surgical field, minimizing the mucosal and the neurovascular manipulation: it follows a natural path road that goes from the nostrils to the mucosa covering the rhynopharynx, the rhinopharyngeal muscles, the anterior arch of C1 and, finally the odontoid process. As a consequence, the surgical invasiveness, of the endoscopic endonasal approach is lower and does not require additional surgical maneuvers, such as (1) mouth retraction, (2) tongue compression or even splitting, (3) possible injury to the teeth, (4) injury to the uvula and/or the soft palate and velupendulum, (5) neurovascular manipulation through the oropharynx. Theoretically, such facts imply a lower rate of postoperative complications related to invasiveness with a lower rate of post-operative

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dysphagia and respiratory complications, which are due to the possibility that, with the endoscopic approach, extubation coincides with the end of the procedure. All this involves, consequently, a more rapid mobilization and a reduction of recovery times for natural feeding, which then is reflected, of course, on hospitalization time. Seen in this light, the endoscopic endonasal approach offers a viable alternative to the more established transoral approach, especially for the clear advantages that the endoscopic technique offers in cases where there is full indication to execute it. On the other hand, in case of dural opening, there will be an important risk of CSF leak and meningitis; as a consequence, the endonasal approach is associated with a difficulty of dural closure with the related higher risk of postoperative CSF leakage and meningitis. Given the intrinsic features of the endoscope, the endonasal route provides a wider, panoramic and multiangled view of the region favoring also a closer-up of the relevant anatomical structures of the surgical field.

Anterior Versus Posterior Approach

The decision making between an anterior or a posterior approach depends on different particular aspects: (1) the direction of the compression and, (2) the surgeon's confidence and experience with the approaches, and thus, the possibility to perform the reduction of the compression with anterior, posterior or a combined approach. In general, unreducible anterior subluxation associated with spinal cord compression requires anterior approach, whereas a reducible posterior compression a posterior surgical route. However, different complex diseases, acquired or congenital, can cause an alteration of atlanto-axial relationships and anterior cervico-medullary junction compression. In these cases, a fixation or a posterior stabilization could be not sufficient to resolve the ventral compression. As matter of facts, in these last years, the option of a combined, anterior and posterior, approach has become the best choice for many authors.

Transoral Approach and Transnasal Approach

Several surgical routes have been described for the cranio-vertebral junction (CVJ) region because of its complex anatomy and vital surrounding structures. During the last decades, the transoral approach with microscopic assistance has been proposed as the standard procedure to perform the anterior odontoidectomy, considering the etiology of the disease, the mechanism of compression and finally its reducibility [8–11]. The transoral approach has been considered the gold standard approach for the surgical treatment of pathologies at the anterior CVJ. Specifically, in the absence of spinal cord contusion or progressive myelopathy, the posterior decompression and fusion are sufficient alone to achieve an acceptable outcome. Odontoidectomy is necessary when there is a non reducible bony compression of spinal cord or soft tissue pannus, causing severe ventral compression and resulting in progressive myelopathy.

The risk of bacterial contamination, prolonged post operative intubation, nasogastric tube feeding, tongue swelling, and nasopharyngeal incompetence after transoral surgery have led authors to identify alternative routes to approach this region.

The anterior aspect of the cranio-cervical region can be exposed also via a transnasal despite the fact that some anatomical limits exist. In the transnasal route, the exposure of the C2 body below the odontoid process is limited by the posterior part of the hard palate; however, angled endoscopes, drills, and dedicated instruments provide access downwards to the lower edge of the C2 body [12–15]. On the other hand, the transoral approach is limited by the degree of mouth opening, the size of the patient's tongue, and the position of the uvula and the soft palate. The inferior limit of the access, usually the C3 vertebra, is determined by the degree of mouth opening, the size of the patient's oral cavity and the prominence of the incisors. However, also for the transoral approach, the use of angled endoscopes and instruments, directs the approach superiorly

increasing the rostral access above the anterior arch of the atlas to the lower clivus and C2 [16, 17]. One of the main anatomical landmarks to consider, especially in transoral route, is the course of vertebral artery (VA). The VA, after ascending through the transverse foramen of the axis and atlas, approximately 15 mm from the midline, courses medially along the upper surface of the posterior arch of the atlas to reach its dural entrance. It is mandatory to preserve the segment of the vertebral artery ascending between the C1 and C2 transverse processes.

Once the anterior arch of C1 is exposed, its drilling is necessary to expose the odontoid process of C2. Another difference between transoral and transnasal approach is the visualization of the ligamentous complex. For instance, the apical ligament, is easily visualized directly straight ahead of the endoscope in the transnasal route but is seen later, after removal of the odontoid, in the transoral approach. The main step of the anterior odontoidectomy is represented by the drilling of the dens. In the transnasal approach, the dens is seen directly ahead. The anterior cortical surface and core of the dens is drilled, whereas the cortical shell is removed. On the other hand, the base of the dens is more easily accessed for drilling by the transoral route. In addition, a different view is offered by these two approach regarding as the exposure of the upper, middle or lower clivus. The standard endoscopic transnasal transsphenoidal approach allows to reach the upper clivus, which corresponds to the posterior wall of the sphenoid sinus. Thus the middle and lower clivus are viewed directly straight ahead in the transnasal approach. The access to the middle and lower clivus generally does not require opening the sphenoid sinus. On the other hand, in the transoral approach the middle and the upper clivus are not usually accessible because of it would be necessary the soft and hard palates opening, the splitting of the tongue or mandible to gain an upward angulation. However, such maneuvers as using an angled endoscope, retracting sufficientlythe uvula, and widely opening the mouth provide a safe access to the lower clivus.

Indications

Odontoidectomy is a procedure that is necessary in all cases in which there is an impairment of the nervous structures of the cranio-cervical junction due to an irreducible alteration of the relations that the odontoid process contracts with neighboring neurovascular structures.

Various pathologies may cause atlanto-axial misalignment and bulbo-medullary junction compression, among them, congenital malformation—such as Arnold Chiari type II—, genetic degenerative transformation—such as in Down's syndrome—, chronic inflammation related to rheumatoid arthritis and/or metabolic disorders and, finally, post-traumatic alterations (Fig. 18.1).

The irreducibility is a crucial concept in the path that leads to the indication for surgery. In fact, several studies confirmed that, when feasible, the reduction of the compression by putting in traction the cranio-cervical junction and the subsequent fixation, as well as, in cases of compression due to the rheumatoid pannus, posterior stabilization of the cranio-cervical junction leads, in some cases, the improvement or even the resolution of the ventral compression.

Therefore, the indications for the odontoidectomy arise in all those cases in which there is irreducible atlanto-axial subluxation, associated with severe brainstem and/or spinal cord compression causing progressive neurological dysfunction. In most cases, the pathological process can be due to: (1) irreducible basilar impression [18–23]; (2) ventral compression, as in the cases of rheumatoid pannus, not resolved after posterior stabilization [24–26]; (3) significant retroflexion of the odontoid process or basilar invagination associated with Chiari disease; [27] (4) presence of *os*

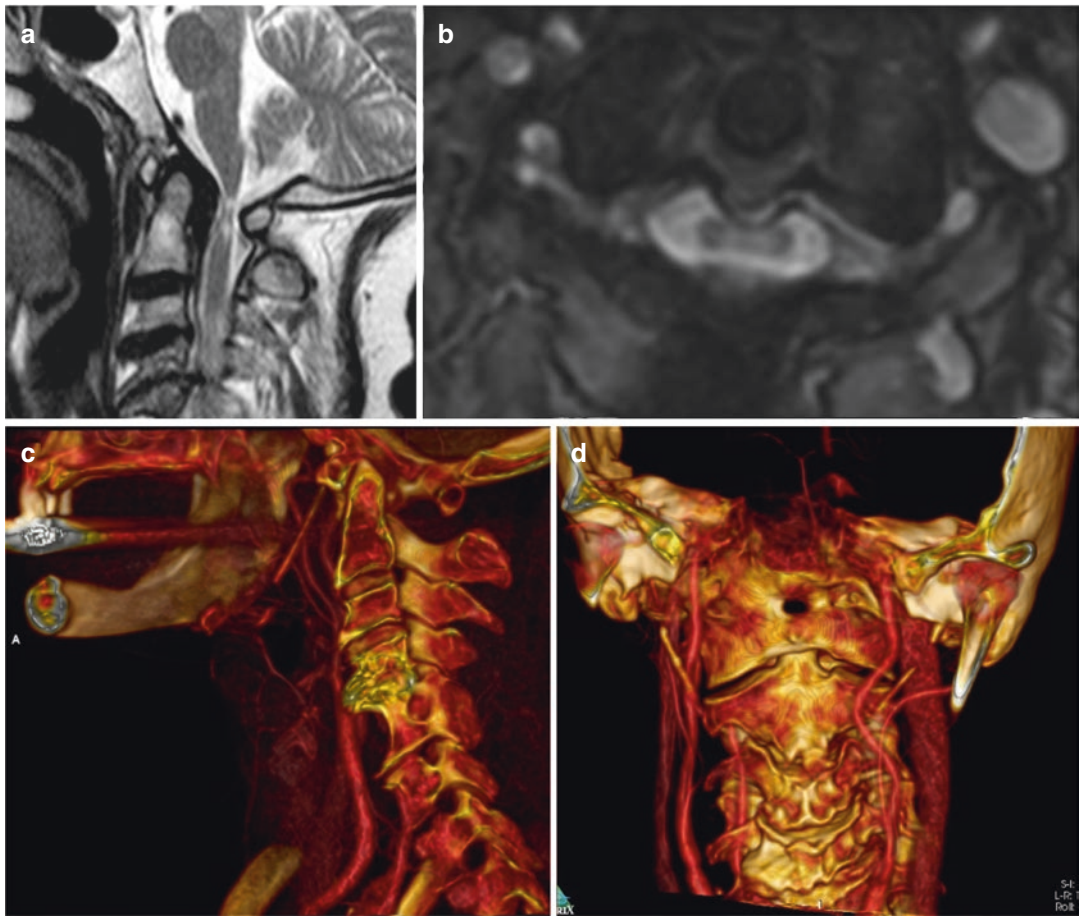

Fig. 18.1 Preoperative neuroimaging studies. T2-weighted sagittal (**a**) and axial (**b**) MRI of the CVJ showing a bulbomedullary compression by an extradural mass lesion of the odontoid process (rheumatoid pannus). (**c**, **d**) 3D reconstruction of an angio-CT of the same patient

odontoideum [28–30]; (5) post-traumatic pseudoartrosis or misalignment; (6) several recent experiences have enlarged the indications of endoscopic endonasal odontoidectomy for the treatment of intradural lesions [3, 5, 31–33].

Feasibility of the Endoscopic Endonasal Odontoidectomy

The goal of the surgical operation is to completely remove the odontoid process of C2 and obtain a sufficient decompression of the ventral brainstem and CVJ. In the debate between microsurgery and endoscopic technique, a remark is done to the eventuality, in the endonasal approach, to have difficulty in reaching the lower portion of the cranio-cervical junction and, namely, the base of the dens. To understanding this aspect, numerous studies on cadavers and on radiological images were performed, with the purpose of delimiting the limits and then the indications to endoscopic approach to the odontoid process pathology. However, leading authors widely reported the feasibility of the endoscopic endonasal approach (EEA) to the CVJ [3, 6].

In cases low junction, located far below the level of the hard palate, it could be quite difficult if not impossible to reach anterior arch of C1 and the base of the odontoid process. Such cases can represent still an indication for the transoral approach. On the other hand, in a higher junction,

the dens is more easily reachable and removable by the nasal route.

In order to preoperatively assess the feasibility of the odontoidectomy via an endoscopic endonasal route, in a midline sagittal CT slice with bone window, it's possible to draw four lines representing possible paths, to depart from piriform aperture of the nasal bones, which target the odontoid process and lead to assess the inferior limit for surgical exposure. Predicting the inferior limit of the CVJ is crucial to choose the appropriate approach in an aerea which is considered a transitional area between endonasal and transoral route.

Nasopalatine Line

One of the criticisms of the EEA to the upper cervical spine is the limited exposure inferiorly. Endonasal dissection of the upper cervical spine is limited superiorly by the nasal bones and soft tissues of the nose, and inferiorly by the hard palate and soft palate [34, 35]. The line created by connecting the most inferior point of the nasal bone to the posterior edge of the hard palate in the midsagittal plane is defined the naso-palatine line (NPL), and considered a limitation of caudal dissection with straight endoscopic instruments. The angle created by this line and the plane of the hard palate, the nasopalatine angle (NPA) provides the window of exposure to the skull base and upper cervical spine. The mean nasopalatine angle is $27.1° \pm 0.7°$. The mean point of intersection between the nasopalatine line and the vertebral column is reported to be 8.9 ± 1.8 mm above the base of the C2 vertebral body. The NPL is considered by several authors, a controversial predictor of the maximal extent of inferior dissection in endoscopic endonasal resection of odontoid process [34], considering that the inferior limit predicted by the NPL was found by a mean value of 12.7 mm, below the real inferior extent of surgical dissection. Various pathologic (basilar invagination) and physiologic factors (head positioning) affect the point of intersection of the NPL with the cervical spine. In order to improve caudal exposure, the use of angled instruments or drills may be of value. Additionally, the retraction of the soft palate and drilling the posterior edge of the hard palate may improve the exposure but may increase the risks of palatal dehiscence and velopharyngeal insufficiency.

Naso-Axial Line

The naso-axial line (NAxL) is defined as the line constructed in the midsagittal plane using a starting point that corresponds to the midpoint of the distance from the rhinion to the anterior nasal spine of the maxillary bone and a second point at the tip of the posterior nasal spine of the palatine bone. It is extended posteriorly and inferiorly to the cervical spine. Some authors, in order to predict more accurately, than using NPL,the lower limit of the EEA to reach the CVJ through the correspondence between CT measurements and the real surgical limit, performed a cadaveric study evaluating the predictive value of NAxL. Their findings supported the close correspondence between the NAxL, drawn in preoperative CT images, and the anatomic surgical extent [36].

Hard-Palate Line

The hard-palate line (HPL) is defined as the line that passes through the anterior and posterior edges of the hard palate (anterior nasal spine of the maxillary bone and posterior nasal spine of the palatine bone, respectively) and intersects the cranio-vertebral junction posteriorly. This line represents the long axis of the hard palate [37]. It is considered a realible marker of the inferior extension of CVJ especially in congenital abnormalities, such as platybasia with associated basilar invagination, where the tip of odontoid is often above the plane of the hard palate [38].

Rhinopalatine Line

The rhinopalatine line is defined as the line constructed in the midsagittal plane using a starting

point that corresponds to the two-thirds point of the distance from the rhinion to the anterior nasal spine of the maxillary bone and a second point at the posterior nasal spine of palatine bone. The line is extended posteriorly and inferiorly, ending to the cervical spine. There have been great efforts from different groups to study the inferior limit of the endoscopic endonasal approach (EEA) . De Almeida et al. [34] described the nasopalatine (NPL) as a good and accurate predictor of the inferior limit of the EEA, but in their study, the NPL resulted always below the inferior extent of surgical dissection with a mean value of 12.7 mm. Consequently, the naso-axial line was reported to predict more accurately and reliably the inferior caudal exposure of the EEA to the CVJ. Similarly, it was been found that the NAxL also overpredicted the lower limits of the approach [37]. The rhino-palatine line (RPL) seemed to be a most accurate predictor in several studies.

This predictor accounts also for patient anatomical variability, such as the presence of nasal and palatal osseous and soft structures, together with the hard palate's direction and length, which represent the most significant factors that limit the inferior extension of the EEA. The RPL cannot be used to predict the lateral limits of the EEA to the CVJ.

Operative Tecnique

According to different pathologies we perform an endoscopic endonasal odontoidectomy followed by posterior decompression and fusion in a single stage surgery.

In order to accurately choose the correct approach, we consider on sagittal CT scan the relationship between naso- and rhino-palatine line and the upper cervical spine.

We routinely use the neuronavigation system (StealthStation S7, Medtronic, Minneapolis [MN], USA), based on contrast enhanced MR with angiographic TOF sequences merged with a 1 mm layer CT of the brain and cervical spine in unique volume. Generally, we use the optical tracking of the StealthStation S7® in order merged with the angiographic TOF sequencesin order to provide feasible pre-operative images regarding the relationship between bone CVJ bone and vascular structures such as vertebral and carotid arteries. Somatosensory evoked potential neuromonitoring is routinely used.

Patient Positioning and Preparation

Following general anesthesia and oro-tracheal intubation, the patient is placed in supine position with the trunk elevated of about 20°. The head is slightly turned on the right of, maximum 10°, not flexed, and fixed in a radiolucent Mayfield-Kees three-pin head-clamp. The head is kept parallel to the floor and maintained without flexion or extension during the posterior fusion when the patient is turned by supine to prone position. In all cases we used the O-arm® system (Medtronic, Minneapolis [MN], USA) in the phase of posterior fusion. On this, the optical reference of the neuronavigator is mounted, should the optical system be used. On the contrary, the magnetic reference is positioned on the patient's head, in case the electromagnetic system is employed. We use antibiotic prophylaxis with Cefazolin 2 g 1 h before the procedure.

Nasal Phase

The nose is prepped with cottonoids soaked with diluted iodopovidone 5% solution inside the two nostrils. A 0° angled lens and 18 cm endoscope associated with an HD camera (Karl Storz, Tuttlingen, Germany) is introduced inside the right nostril. The identification of usual anatomical nasal landmarks is performed (inferior turbinate laterally and nasal septum medially). As a standard endoscopic endonasal procedure, above the inferior turbinate, the middle turbinate is identified and luxated laterally putting cottonoids soaked with diluted adrenaline between middle turbinate and nasal septum, to prevent bleeding of the nasal mucosa. The same maneuvers are carried out in the left nostril. The endoscope advances parallel to the floor of the nasal cavity until the choana is reached. With the aid of the neuronavigation system, the anatomical landmarks are verified. The mucosa over the posterior and inferior aspect of the nasal septum is cauterized with monopolar coagulation or, better, with bipolar forceps. We

do not routinely perform the removal of the anterior wall of the sphenoid sinus since a transsphenoidal corridor is rarely needed, unless an higher exposure should be required in case of the tip of the dens goes quite high or when more space is required for the surgical maneuvers, due to patient's individual anatomy. Afterwards, an inferior septectomy is performed, removing sufficiently the vomer bone and extending inferiorly, down to the hard palate. The most superior limit reached is the clivus-nasal septum junction. At this stage few important anatomical landmark should be identified, which guide the surgeons to stay oriented: (1) the clivus-septum junction superiorly, (2) the Eustachian tubes laterally, (3) the nasal floor/soft palate inferiorly as marked by the hard and soft palate. The neuronavigation will confirm the position of such surgical landmarks and give the correct direction for the subsequent surgical steps.

Nasopharynx Phase

The key points of the nasal phase allow the widest exposure of the rhinopharynx and to avoid any conflict among the instruments during the next surgical steps. The nasopharynx muchosa is incised on the midline (Fig. 18.2a) and the muscles are dissected bilaterally in order to expose the anterior arch of C1 (Fig. 18.2b). Several authors reported a reverse "U"-shaped flap of nasopharyngeal prepared with monopolar electrocautery, elevated and reflected caudally to the level of the soft palate in order to improve the surgical field.The cranio-caudal extension of the flap involves the inferior third of the clivus superiorly, the C2 vertebral body inferiorly, and the lateral margin of the operative exposure included the lateral masses of the C1 vertebra. The U-shaped nasopharynx flap extends the surgical corridor laterally, but on the other hand increases the risk of injuries to parapharyngeal carotids which are located laterally to the superior pharyngeal constrictor muscle. We prefer doing a straight midline opening of the nasopharynx because of guarantees a sufficient exposure and a lower risk of vascular damage. Then, we proceed with skeletonizing of the anterior arch of C1 and of the odontoid process in a subperiosteal fashion.

C1 Anterior Arch Preservation in Selected Cases

Recently, several authors reported their experience in matter of endoscopic endonasal odontoidectomy, focusing on the preservation of C1 anterior arch during the craniovertebral junction phase, avoiding the posterior fixation [32, 39]. Particularly, in case of rheumatoid arthritis or other inflammatory diseases, the anterior arch of the atlas is preserved by drilling the odontoid base, weakening its apical, and leading to the pulling downward of the dens in the working area. The following removal of the axis with other remaining compressive inflammatory lesions is performed using a combination of high-speed drill, ultrasonic bone curette and standard Kerrison's rongeurs [32, 39]. According to such authors, working above and below the C1 anterior arch and its preservation represent not only an element of stability, but also give an important opportunity for reconstruction and to reinforce the closure. Additionally, the same groups, in case of inveterate D'Alonzo II fractures or in the combination of odontoid fracture associated with fracture of anterior arch of C1, proposed their tecnique of anterior fixation and anterior C1 arch reconstruction [40].

Craniovertebral Junction Phase and Closure

In our tecnique, the anterior arch of the atlas is exposed and removed through the high speed drill with diamond burrs and Kerrison's rongeurs (Fig. 18.2c). Posteriorly, the odontoid process of C2, is exposed, separated from the alar and apical ligaments, dissected from the transverse ligament, thinned using the microdrill and finally removed (Fig. 18.2d). At this point, a wide surgical corridor is created. The odontoidectomy is performed carefully by using high speed drill,

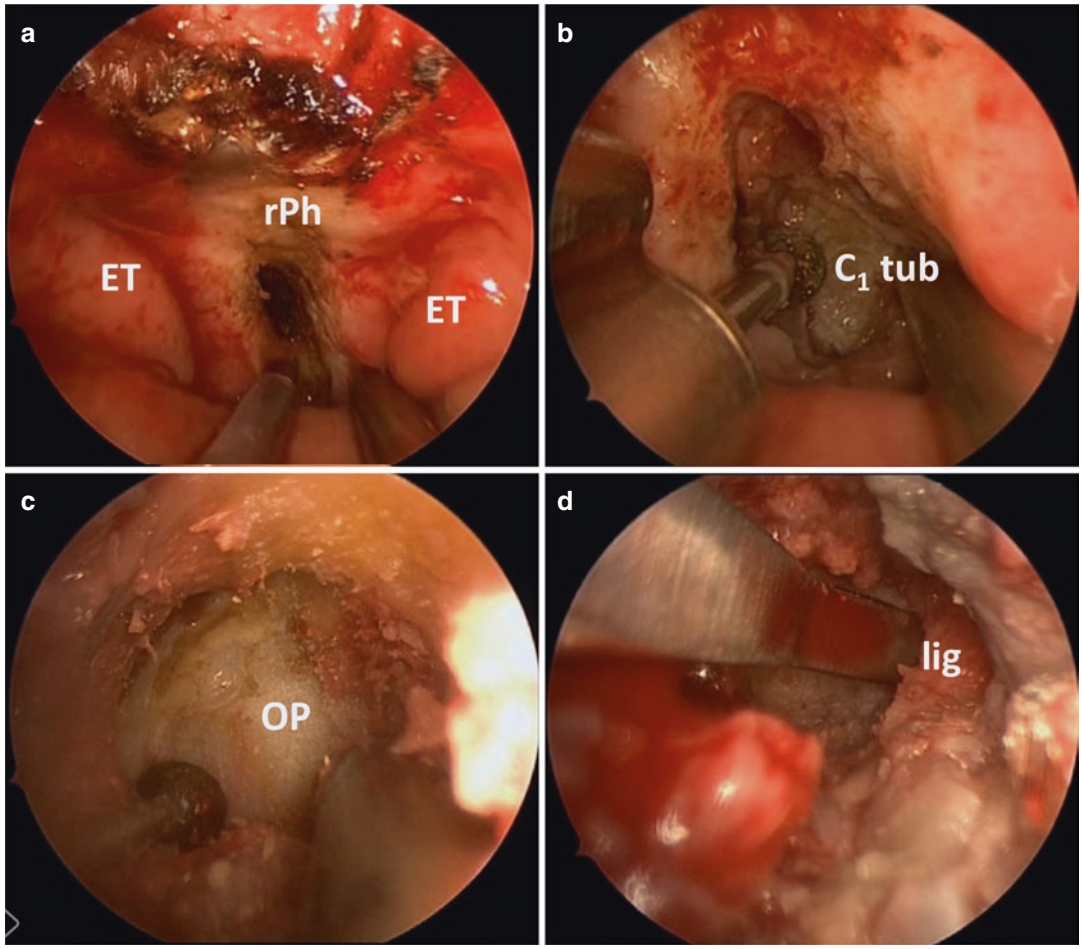

Fig. 18.2 Intraoperative pictures of the endoscopic endonasal approach. (**a**) Incision into the rhinopharynx; (**b**) drilling of the anterior arch of C1; (**c**) drilling of the odontoid process of C2; (**d**) freeing of the remaining part of the dens from the ligaments. *rPh* rhinopharynx, *ET* Eustachian tubes, *C1 tub* anterior tubercle of C1, *OP* odontoid process, *lig* ligaments

Kerrison's, and in case of lesions with soft consistency, curettes and pounches or ultrasound aspiration. When the removal is complete the dural plane appears pulsating and indicates an optimal decompression of the brainstem (Fig. 18.3a, b).

After having obtained a satisfying hemostasis, the closure is guaranteed with a layer of fibrin glue only in the absence of a possible dural tearing (Fig. 18.3c). In case of CSF leak, a packing with Gelfoam/Surgicel and fibrin glue is realized to reinforce the closure. In these cases we consider the possibility to position and extended lumbar drain (ELD) at the end of the operation. We close the nasopharynx muchosa by a single stich because of the median opening allows a faster closure of the muscles at the end of endoscopic time. Generally, we position a nasogastric tube under endoscopic control.

Posterior Fusion

The second step of the operation is characterized by the posterior occipito-cervical fusion. The patient, already fixed to the Mayfield-Kees three-pin carbon fibers radiolucent head-holder, is turned by supine to prone position with the head

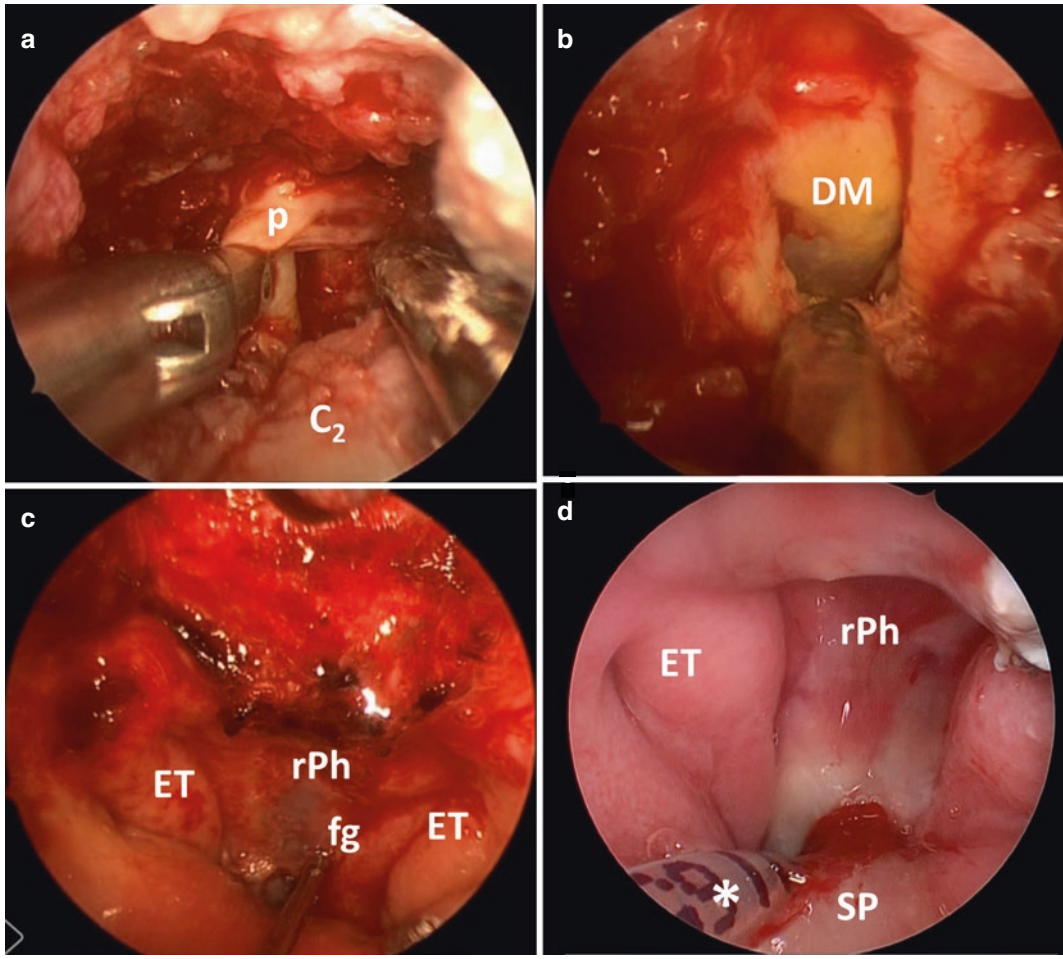

Fig. 18.3 Intraoperative pictures of the endoscopic endonasal approach. (**a**) removal of the pannus causing the compression; (**b**) dura mater of the CVJ; (**c**) closure of the muscle and mucosal incision with the aid of the fibrin glue; (**d**) endoscopic control of the surgical field 3 days later showing the optimal closure of the incision. *p* pannus, *C2* base of the dens (body of C2), *DM* dura mater of the CVJ, *ET* Eustachian tube, *rPh* rhinopharynx, *fg* fibrin glue, *SP* soft palate; asterisk: nasogastric tube

parallel to the floor and with a slight degree of extension. This position considers the C0–C2 angle which is formed by the posterior extension of the hard palate and the vertical line passing through the dens and avoids the breath impairment related to the flexion. A midline incision is performed starting from the inion to the spinous process of C6. The fascia is exposed and incised on the midline with monopolar cautery. The muscle dissection is performed along the raphe in a subperiosteal fashion from the basiocciput to the posterior complex of C5. The bone landmarks are clearly visible: (1) the occipital bone; (2) posterior arch and lateral masses of C1; (3) posterior complex from C1 to C5.

Generally, we remove the posterior arch of C1, because of, in most of our cases, it contributed to the bulbo-pontine compression. The lateral masses of C3 and C4 are identified and verified through the O-arm® system. The fixation system we used in all cases was the Vertex titanium system (Medtronic, Minneapolis [MN], USA). The high speed drill is used to prepare the position of the screws within the lateral masses of C3 and C4. The polyaxial screws are inserted according to Magerl technique [41] in order to

avoid vascular injuries. Differently, in the basiocciput the monoaxial screws are positioned 2 cm from the inion on both sides and 1 cm above the sinuses. The length of the screws we use is 8 mm. After screws are positioned, the two rods are pulled to obtain the correct alignment of the cervical spine, and finally fixed through the wrench of wing nuts. The bone fusion is improved with the addition of bone substitutes. The last verification with the O-arm® system is done at the end of the procedure. At the discharge we recommend the use of cervical collar for 2 months (Fig. 18.4).

Series Presentation

A series of five endonasal endoscopic odontoidectomies have been performed in our centers. Demographic, clinical, and management details are summarized in Tables 18.1 and 18.2.

All patients were female, ranging between 62 and 82 years (mean age 68.8 years). Four patients were admitted with a neurological onset characterized by tetraparesis; in one patient, motor deficits were prevalent on the right arm. Urinary incontinence was present in two patients. Was present in two patients. One patient presented severe dysphagia for either solids or liquids. In three patients, symptoms were related to the presence of a rheumatoid synovial pannus, while the other two cases showed signs and symptoms due to a complex malformation of the craniocervical junction and to a misalignment of the odontoid process following a previous non-fused Anderson-D'Alonzo type II frac- ture, respectively. Interestingly, the patient affected by the complex CVJ malforma- tion underwent previously to aoccipital-cervical stabilization to another institution. Subsequently, she underwent an attempt of transoral odontoidectomy, which

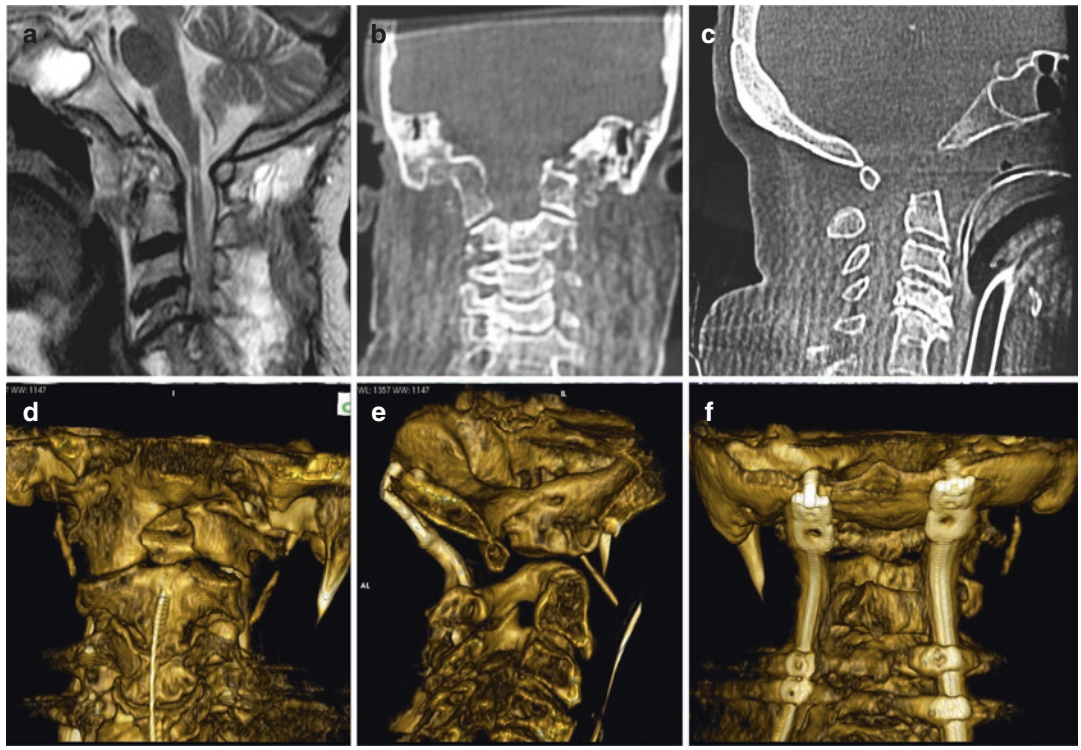

Fig. 18.4 Postoperative neuroimaging studies of the same patient of Fig. 18.1. The T2-weighted sagittal (**a**) MRI of the CVJ shows an optimal decompression of the bulbo-medullary junction. (**b**, **c**) intraoperative O-arm® images showing the removal of the odontoid process. (**d**–**f**) 3D reconstruction of the post-operative CT scan of the CVJ

Table 18.1 Demographic, etiological and clinical data

N°	Age (years)	Sex	Etiology	Symptoms	Post-operative outcome
1	62	F	Rheumatoid pannus	Right arm weakness Tetrahyperreflexia Urinary incontinence	Improved, oral feeding
2	64	F	Odontoid process misalignment in patient with previous type II Anderson-D'Alonzo fracture (not stabilized)	Tetraparesis Tetrahyperreflexia Urinary retention	Improved, oral feeding
3	82	F	Rheumatoid pannus	Tetraparesis	Improved, oral feeding
4	63	F	CCJ malformation	Tetraparesis Severe dysphagia Dysphonia	Improved, dysphagia not completly resolved
4	73	F	Rheumatoid pannus	Tetraparesis	Improved, oral feeding

Table 18.2 Management details

N°	Procedures	OR set-up	Post-op hospital stay (days)
1	Endoscopic endonasal odontoidectomy and occipitocervical stabilization at the same stage	StealthStation S7® with optical tracking + O-arm®	17
2	Endoscopic endonasal odontoidectomy and occipitocervical stabilization at the same stage	StealthStation S7® with optical tracking + O-arm®	13
3	Endoscopic endonasal odontoidectomy and occipitocervical stabilization at the same stage	StealthStation S7® with optical tracking + O-arm®	19
4	Endoscopic endonasal odontoidectomy	StealthStation S8® with optical tracking	9
5	Endoscopic endonasal odontoidectomy and occipitocervical stabilization at the same stage	StealthStation S8® with optical tracking + O-arm 2®	7

failed due to the higher position of the dens. She was referred in our clinic for an anterior decompression performed through an endoscopic endonasal odontoidectomy. In the remaining three patients, in the same single-stage surgery, anterior decompression and posterior stabilization were performed during the same operation.

The length of stay ranges from 9 to 19 days (including the first period of rehabili- tation). In all patients, there was an improvement of the neurological conditions, compared to the preoperative one. In one patient the swallowing dysfunction resolved, allowing an early oral feeding. In two cases an implementation with par- enteral nutrition was necessary for a few days.

Postoperative Management

In our practice, according to the general clinical condition of patient and the lenght of sedation, we preferred leaving the patient in our intensive care unit for 24 h. This occurred in two of the four cases treated. In our department, the primary aim is the early mobilization of the patient, to lower the risks of an extended bed rest. In addition, the use of the nasogastric tube guaranteed a sufficient patient's caloric intake, with the addition of parenteral nutrition, when required. We performed at least two endoscopic postoperative

controls: one in the first 24 h and one before the discharge (Fig. 18.3d). During such checks we verified the proper closure of the surgical wound and the possible presence of CSF leak, and thus we removed the nasogastric tube under endoscopic control. This maneuver can be performed only after testing the function of lower cranial nerves by and otolaryngologist. In our series, the removal of nasogastric tube occurred in three patients, in the eighth postoperative day, in two patients, and in the seventh postoperative day, in the other one. In our series patients performed before discharge, a CT scan of the head and cervical spine in order to assess the degree of the odontoidectomy and the correct position of screws and rods of the posterior fusion, and an MRI to evaluate the decompression of neurovascular structures. A further control was performed after 3 months. All patients started a physical rehabilitation program, which also continued after discharge.

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19 Basilar Invagination and Atlanto-Axial Dislocation

Paolo Perrini, Nicola Benedetto, and Nicola Di Lorenzo

Malformations of the craniovertebral junction (CVJ) encompass a wide range of different bony abnormalities involving the axis, the atlas and the occipital bone. Basilar invagination (BI) and chronic atlanto-axial dislocation (AAD) are the most common congenital anomalies of the CVJ, can occur combined and become symptomatic when produce a ventral cervicomedullary compression. BI consists in the congenital prolapse of the spinal column into the skull base and is radiologically defined as the occurrence of the odontoid tip more than 2.5 mm above the Chamberlain's line [1] (Fig. 19.1). The term platybasia refers to an angle greater than 140° between the clivus and the plane of the anterior cranial fossa (basal angle) and is an anthropological measure without pathological implications itself [2]. Platybasia can occur in association with BI. In this case shortening and horizontalization of the basioc-

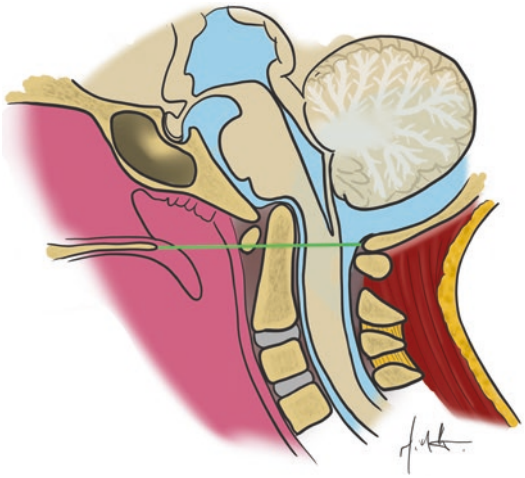

Fig. 19.1 Illustration depicting the Chamberlain's line (green line). Note the position of the invaginated odontoid peg above the Chamberlain's line and the compression of the cervicomedullary junction

ciput displace the foramen magnum cranially with subsequent anterior (ventral) invagination of the odontoid (Fig. 19.2). Basilar impression is a term often erroneously used as a synonym of BI and consists in an acquired BI related to bone-softening disorders such as hyperparathyroidism, Paget's disease, Hurler's syndrome, and rickets [3]. BI and AAD are usually irreducible on skeletal traction and require surgical treatment when cause progressive cervicomedullary compression resulting in disabling neurological deficits [4]. Although the transoral approach (TOA) to the

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CVJ was originally described by Kanavel in 1917 to remove a bullet lodged between the atlas and the clivus, it wasn't until the late 1970s that Menezes et al. proposed a rationale algorithm for the CVJ malformations based on the stability, reducible malformation and site of encroachment, that is still valid today [3, 5]. In this chapter, based on our experience with over the past four decades, we describe the surgical nuances of TOA that allow to achieve a satisfactory decompression of BI and AAD minimizing the postoperative complications [4, 6–10].

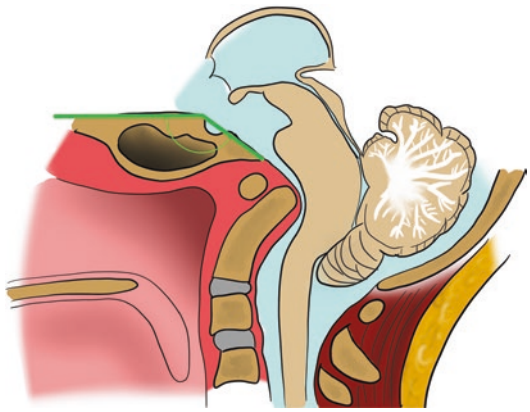

Fig. 19.2 Illustration depicting platybasia and basilar invagination. In platybasia basal angle exceeds 140°. The cranial displacement of the foramen magnum is generally associated with a ventral encroachment at the level of the nasopharynx

Treatment Algorithm for BI and AAD

The surgical strategy is dictated by extensive preoperative neuroradiological investigation including MRI, CT scan with flexion and extension views. In BI and AAD the site of encroachment is generally only anterior particularly when an associated atlas assimilation is present (Fig. 19.3). The detection of irreducible ventral compression is an indication for TOA [2–4, 6–17]. In our experience skeletal traction is not effective in congenital CVJ malformations and is poorly tolerated by the patients. In the rare instances of concomitant fixed posterior compression, an additional foramen magnum decompression can be considered [4]. Limitations of TOA are the limited mandibular excursion (i.e. interdental space ≤30 mm) and severe basilar invagination (odontoid tip projecting ≥20 mm above the Chamberlain's line) with a resultant neural compression at the level of the nasopharynx [4, 12]. In these cases, we selected transmaxillary approaches [4]. The Le Fort I osteotomy with down-fracture of the maxilla allows exposure from the sphenoid sinus to the middle clivus and can be required in patients with severe basilar invagination [18]. The Le Fort osteotomy with palatal split (transmaxillary palatal split approach or open door maxillotomy approach) increases the caudal exposure compared to Le Fort I oste-

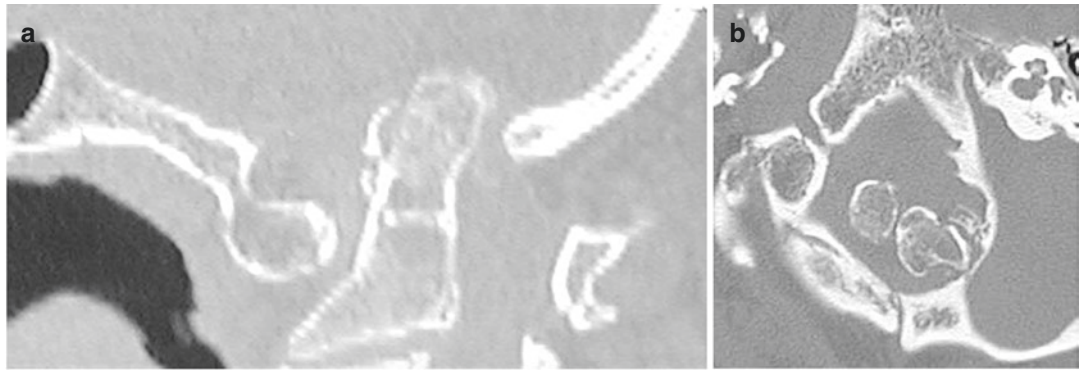

Fig. 19.3 Sagittally reformatted (**a**) and axial (**b**) CT scan domonstrating basilar invagination, atlanto-axial dislocation and atlas assimilation. Note the position of the offending odontoid peg in the posterior fossa

otomy and was used in patients with inability of sufficiently open the mouth [4, 19]. Over time, we moved away from performing transmaxillary approaches in cases of limited mandibular excursion and severe basilar invagination with neural compression at the level of the nasopharynx. In these situations, we now favor endonasal endoscopic approach (EEA) that allow a cranial exposure from the anterior fossa floor to the superior aspect of the clivus and a caudal exposure dictated by the nasopalatine line [12, 17, 20–23]. According to our experience, the standard TOA allows a satisfactory surgical exposure and decompression in more then 80% of patients with BI and AAD [4]. The rate of tonsillar prolapse in patients with CVJ malformations is between 33 and 38% [4, 16, 24–26]. The surgical treatment of this association is still matter of controversy. Several studies reported early deterioration or more often delayed worsening in patients treated with foramen magnum decompression due to postoperative angulation of cervicomedullary junction and progressive cranial settling [4, 27]. According to our experience corroborated by recent literature, transoral decompression is affective in removal of the CSF obstruction and the level of the cervicomedullary junction in most patients with fixed CVJ malformations and tonsillar prolapse [4, 27]. In these patients the tonsillar herniation is the result of reduced posterior fossa volume due to the infolding of the exoccipital bone which is exacerbated by the prolapse of the odontoid peg though the foramen magnum. After extensive anterior decompression, the ascent of cerebellar tonsils into the posterior fossa and the resolution of associated syringomyelia are generally observed and support the restoration to normal of CSF flow at the CVJ level [4, 27]. The occurrence of acute or delayed spinal instability (occipito-atlantal, atlanto-axial, or occipito-atlanto-axial instability) after transoral decompression is invariably high [7, 8, 28–30]. The single anesthesia transoral decompression and subsequent posterior fixation and fusion eliminate the risk of postoperative instability and allow to mobilize the patients as soon as possible [4, 8].

Transoral Approach

Preoperative Assessment, Anesthesiologic Considerations and Positioning

Careful assessment of preoperative neuroradiological investigations is required to establish the correct surgical strategy. TOA is indicated in patients with BI and/or AAD inducing fixed ventral compression of the cervicomedullary junction mainly located at the level of the oropharynx. According to our experience the standard TOA might expose the odontoid projecting ≤20 mm above the Chamberlain's line [4]. TOA can be performed in patients with an interdental working distance of at least 30 mm and without active nasopharyngeal infection [3, 4]. Fiberoptic nasotracheal intubation is routinely used in all transoral cases. We reserve tracheostomy only in patients with preoperative brain stem compromise and lower cranial nerve dysfunction [4]. The patient is positioned supine with the head fixed in a Mayfield headholder and extended 10°–20° according to the severity of the BI. In fact, the head extension improves the rostral exposure of the CVJ and is particularly effective in patients with severe BI. In addition, the intraoperative use of moderate Trendelenburg position can help the rostral visualization of the CVJ. Anatomical studies demonstrated that division of the soft palate provides nearly 10 mm of clival exposure [31]. However, to reduce postoperative rhinolalia and nasal regurgitation we avoid soft palate splitting and we retract the soft palate with two rubber catheters inserted through the nares and stitched to the uvula. A dedicated transoral system (Crockard transoral instruments, Codman Raynham, MA) including retractors and extra-long instruments is required for an effective surgery. Lateral fluoroscopy is reliable in confirming the location of anterior tubercle of the atlas, which is easily palpated transorally, and in providing information on the extent of cranio-caudal exposure during the operation. Frameless navigation systems provide additional information of the medial-lateral orientation. Neurophysiological

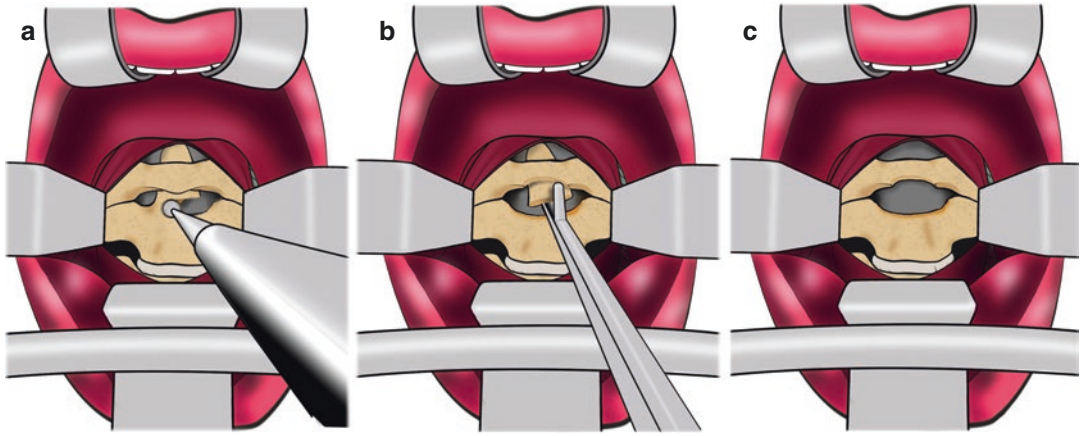

Fig. 19.4 Illustration demonstrating the transoral atlas-sparing technique. This technique is generally feasible in patients with mild basilar invagination and/or fixed atlanto-axial dislocation. (**a**) The base of the dens and few millimeters of the inferior half of the anterior arch of the atlas are resected with high speed drill. (**b**) When the base of the dens is transected, the ligaments are sectioned while the odontoid is grasped with an odontoid rongeur and pulled inferiorly without any pressure on the cervicomedullary junction. (**c**) Odontoid removal allows exposure of the cervicomedullary region which appears decompressed. (Modified with permission from Acta Neurochir (Wien) 2014;156(6):1231–1236)

monitoring is used throughout the procedure and allows functional assessment of spinal cord.

Incision and Soft Tissue Dissection

The surgical procedure is entirely performed with the aid of the surgical microscope while the surgeon is seated at the top of patient's head. The posterior pharynx is infiltrated with 1% lidocaine and epinephrine, and a midline incision along the median raphe of the posterior pharyngeal wall is carried through the mucosa and the pharyngeal muscles. The incision is extended cranially and caudally depending on the peculiar anatomy of the single patient. Monopolar cautery is used to dissect the pharyngeal constrictor, longus colli and longus capitis muscles which are elevated in a single layer and maintained laterally using tooth-bladed pharyngeal retractors. After dissection of the anterior longitudinal ligament, the anterior arch of C1, the inferior tip of the clivus and the ventral surface of the body of C2 are exposed.

Transoral Atlas-Sparing Technique

Preservation of anterior arch of C1 during the TOA minimizes postoperative instability of the CVJ and is usually feasible in the treatment of retro-odontoid pannus. However, it in can be achieved in patients with fixed AAD and in selected cases of mild basilar invagination (Fig. 19.4) [4, 9, 10, 29, 32]. When the C1 ring is preserved, the stability of the CVJ can be obtained with C1–C2 screw techniques instead of occipitocervical fusion [10, 32]. Biomechanical studies demonstrated that interruption of the anterior arch of the atlas can promote lateral spreading of C1 and subsequent cranial settling with resultant kinking of bulbo-medullary junction and progressive neurological worsening [28, 29, 33]. The atlas-sparing technique requires drilling the base of the dens and approximately 5 mm of the inferior half of the anterior arch of C1. After transection of the base of the dens, the odontoid is grasped with an odontoid rongeur and pulled inferiorly while the alar and apical ligaments are sharply dissected without pressure on the cervicomedullary junction (Fig. 19.5). This maneuver

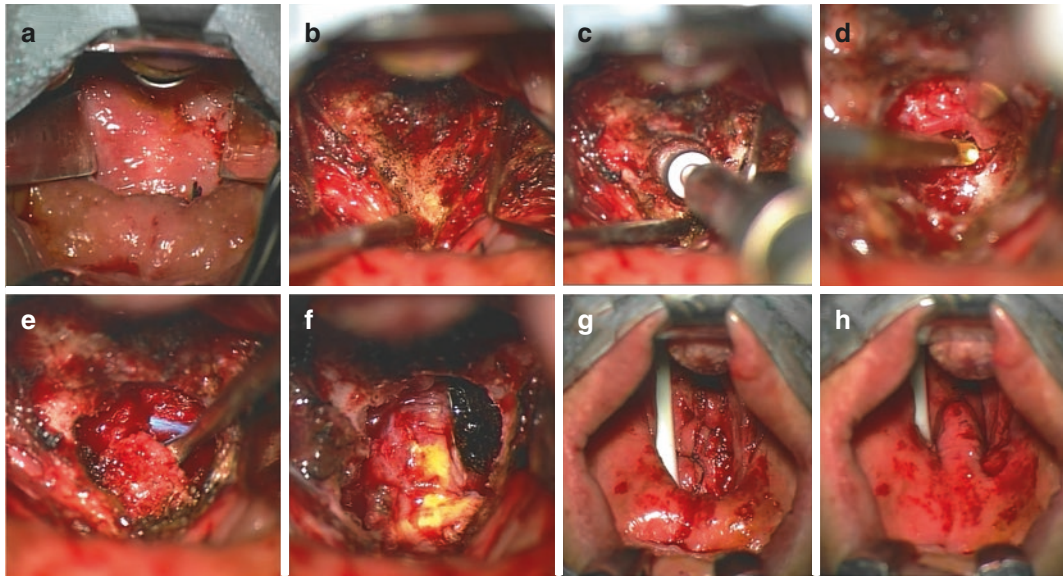

Fig. 19.5 Intraoperative photographs of the patient presented in Fig. 19.6. The tongue is oriented at the top of the photograph with the palate at the bottom. (**a**) The posterior wall of the pharynx is exposed after retraction of the soft palate into the rhinopharynx. The nasotracheal tube is mobilized laterally using the Crockard retractor. (**b**) After midline incision of the posterior pharyngeal wall and dissection of the longus colli muscles, the bony surface of the craniovertebral junction is exposed. (**c**) The drilling involves the dens and the inferior rim of the anterior arch of C1. (**d**) The remaining shell of the base of the dens is removed with Kerrison rongeur. (**e**) The offending odontoid peg (asterisk) is removed after section of the alar and apical ligaments. (**f**) After generous bony decompression the ventral surface of cervicomedullary junction is exposed. (**g**) The mucosa and pharyngeal muscles are closed in a single layer. (**h**) Normal appearance of oropharyngeal mucosa at the end of the transoral approach

allows the surgeon to remove the invaginated odontoid in an en bloc fashion without pressure on the cervicomedullary junction (Fig. 19.6). When AAD and BI are associated with atlas assimilation, preservation of the anterior ring of the atlas is not a concern. In this scenario after transoral decompression a posterior occipitocervical fixation and fusion is mandatory also in case of atlas preservation.

Transoral Trans-atlas Technique

In patients with severe basilar invagination transection of anterior arch of C1 is required to expose and resect the offending odontoid peg in a piecemeal fashion (Fig. 19.7). After atlas resection using a 3- to 4-mm diamond burr the odontoid is shaved until a thin sheet remains, which is removed with Kerrison and curettes (Fig. 19.8). The retro-odontoid ligaments are dissected only when appear thick and distorting the dura avoiding unintentional dural tearing. After decompression, hemostasis is achieved and the wound is closed in a single layer with 2-0 Vicryl sutures [4, 10]. It our policy to perform the posterior fixation and fusion during the same anesthesia session to eliminate the risk of acute postoperative instability and to mobilize the patients early in the postoperative period.

Postoperative Management

Postoperatively, patients are transferred to the intensive care unit where the endotracheal tube is maintained for 12–18 h, depending on soft tissue swelling and respiratory function. Nutrition is

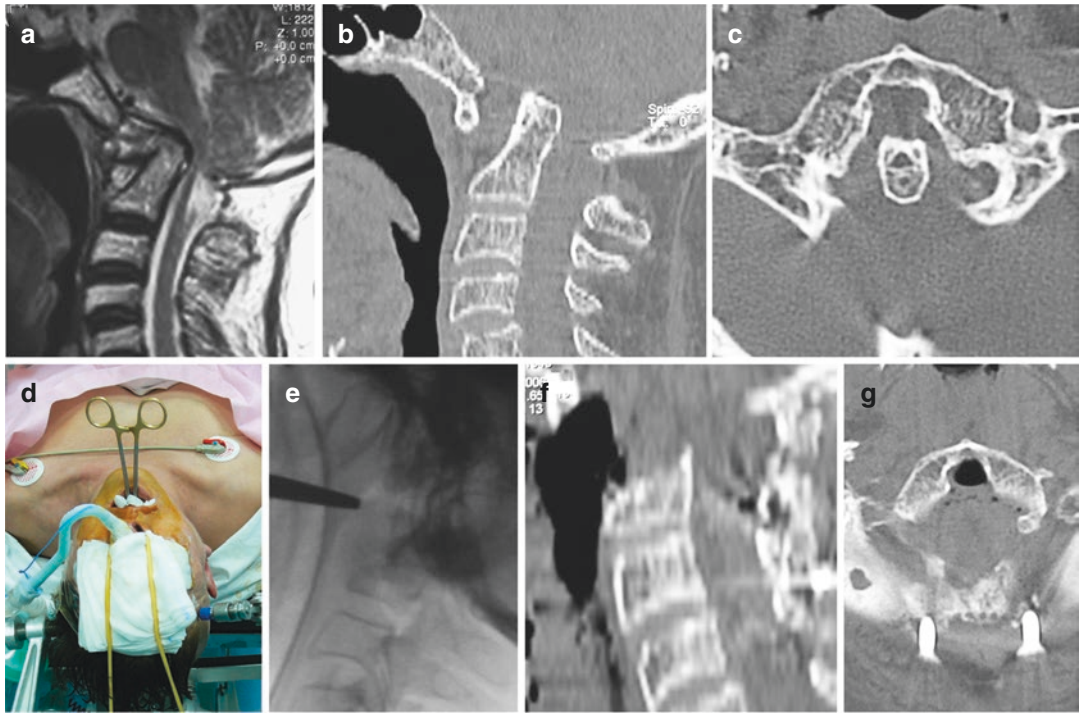

Fig. 19.6 Case illustration of a 64-year-old lady with craniovertebral junction malformation suitable for transoral atlas-sparing approach. Preoperative sagittal T2-weighted image (**a**) and sagittal reformatted (**b**), and axial (**c**) CT scan showing basilar invagination, atlas assimilation and atlanto-axial dislocation with severe compression of the cervicomedullary junction. The soft palate was retracted in the nasopharynx (**d**) and fluoroscopy confirmed the location of the anterior arch of the atlas (**e**). The altas-sparing technique allowed wide decompression and preservation of the atlas as seen on postoperative sagittal reformatted (**f**) and axial (**g**) CT scan images

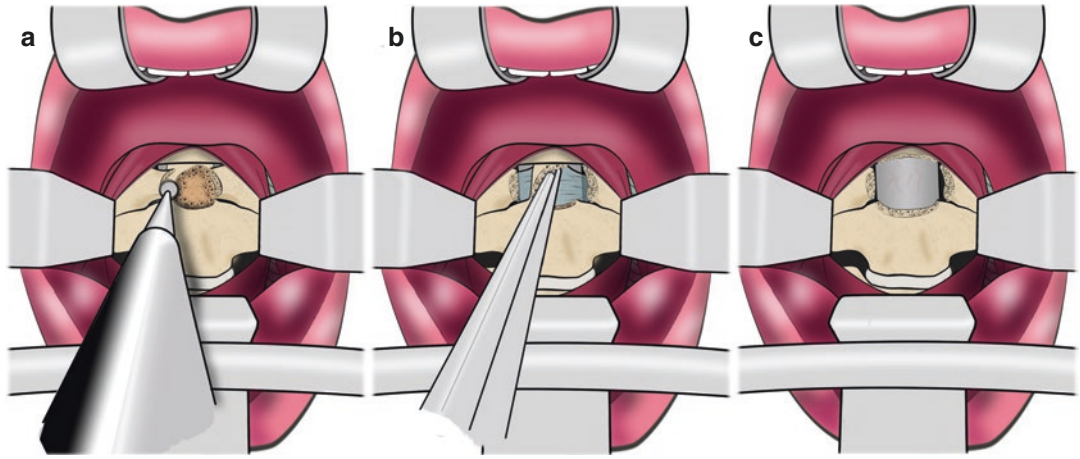

Fig. 19.7 Illustration demonstrating the transoral transatlas technique. This technique is required in patients with moderate basilar invagination (odontoid peg projecting ≤20 mm above the Chamberlain's line). (**a**) After transection of the anterior arch of the atlas, the odontoid is shelled out with high speed drill. (**b**) the residual shell is progressively removed with kerrison rongeurs. (**c**) After careful dissection of the retrodental ligaments the dura of the craniovertebral junction is exposed. (Acta Neurochir (Wien) 2014;156(6):1231–1236. Reprinted with permission)

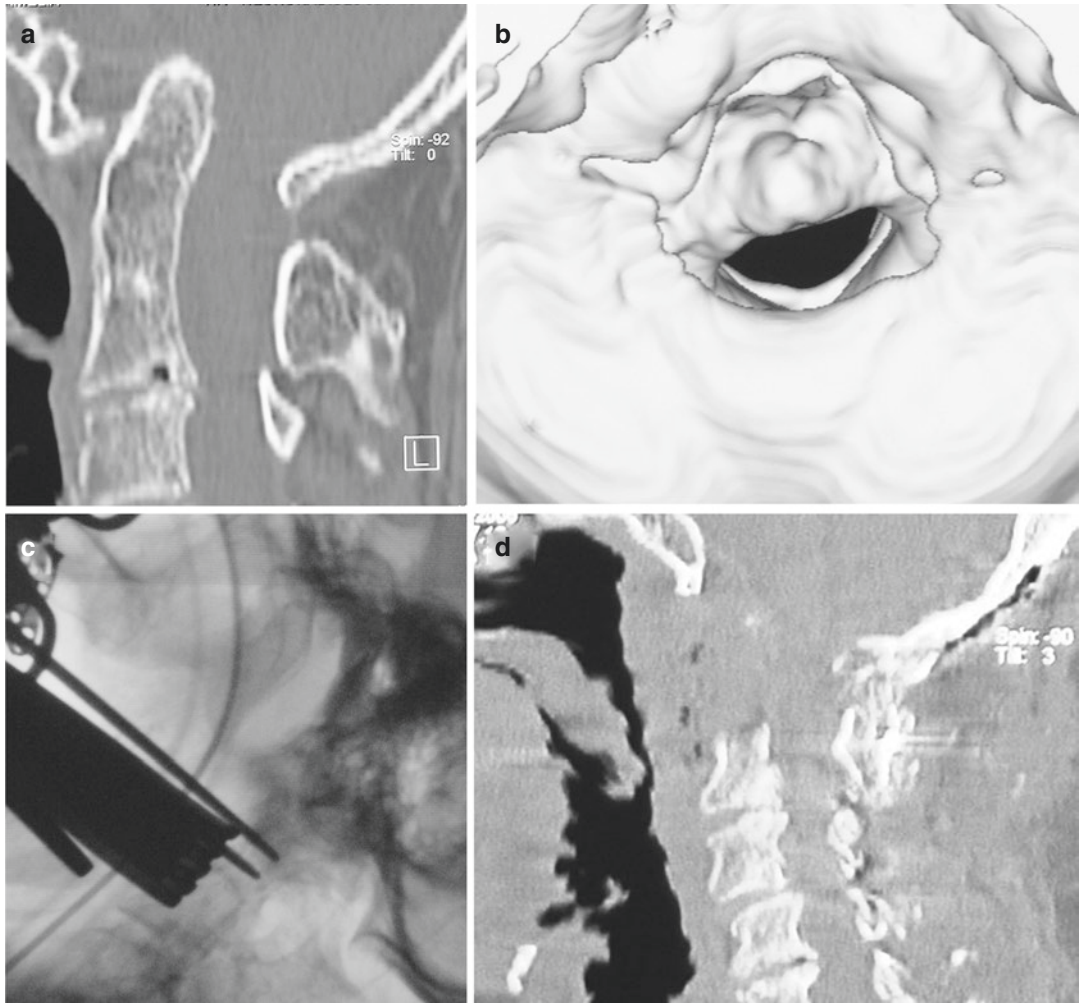

Fig. 19.8 Case illustration of a 72-year-old lady with craniovertebral junction malformation requiring transoral trans-atlas technique. Sagittal reformatted CT scan (**a**) and 3D CT reconstruction (**b**) domonstrating severe basilar invagination, atlas assimilation and fixed atlanto-axial dislocation. Intraoperative fluoroscopy (**c**) shows initial resection of the dens. Complete resection of the offending odontoid peg required transection of the anterior arch of C1, as seen on postoperative CT scan (**d**)

administered intravenous, and patients are allowed to sip cold fluids only after 3 days. Broad spectrum antibiotics are administered for 72 h. A CT scan of the cranio-cervical region with sagittal and coronal reconstructions is done before patients are mobilized to assess the extent of CVJ decompression and the correct position of posterior fixation system.

Postoperative Complications and Their Avoidance

In recent clinical studies complications after TOA are minimal ranging from 7 to 10% [15, 32]. Potential complications include CSF leak and meningitis, velopharyngeal dysfunction, neurological deterioration, vascular injury, pha-

ryngeal wound breakdown, and postoperative soft tissue swelling. CSF leak due to accidental dural injury can occur in the final stages of odontoid resection. When the dura is clearly lacerated a direct repair should be attempted followed by insertion of a lumbar drain for up to 5 postoperative days. Velopharyngeal insufficiency is the result of scarring and fibrosis of the soft palate, and causes hypernasality of the voice, nasal regurgitation and dysphagia [34]. Retraction instead of cutting the soft palate minimizes the occurrence of velopharyngeal dysfunction [4]. Neurological deterioration after transoral decompression occurs in roughly 1% of cases and is though to be the result of direct trauma during the operation or loss of spinal alignment during patient repositioning between anterior decompression and posterior fixation [32]. Careful evaluation of preoperative CT scan is required to avoid injury of the vertebral artery which can occur in case of rotatory subluxation of C1. Pharyngeal wound dehiscence occurs in 3% of cases [4] after TOA. In our experience the single-layer closure of the posterior pharyngeal wall with interrupted absorbable sutures minimizes the occurrence of this complication. When wound dehiscence occurs the pharyngeal wound should be revised under general anesthesia [4, 10, 30]. Although infection has long been considered a serious drawback of TOA, large clinical series reported rates of pharyngeal infection less than 1% [32]. In fact, local resistance of oral tissue to its own bacterial flora facilitates wound healing. The postoperative soft tissue swelling is common after TOA, generally subsides after 24–48 h and its occurrence is minimized by delicate tongue retraction and careful intraoperative handling of soft tissues.

Conclusion

TOA with or without transection of the atlas allows a direct and unobstructed corridor for the effective treatment of most patients with BI and AAD exerting irreducible ventral compression of the cervicomedullary junction. In cases of severe basilar invagination with the offending odontoind peg at the level of the nasopharynx, transmaxillary approaches or, more recently, endoscopic endonasal approaches, should be considered. After an adequate learning curve and following the basic tenets of skull base surgery, the approach related-morbidity in standard TOA is minimal.

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Cervical Spine Tumors

20

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Introduction

Among central nervous system tumors, only about 15% of tumors occur intraspinally. These are mostly benign tumors with 60% occuring extradurally (ED), about 30% occurring intradural extramedullarly (ID-EM) and only 10% occurring as true intramedullary spinal cord tumors (IMSCT).

Intramedullary Spinal Cord Tumors

Epidemiology

Intramedullary spinal cord tumors (IMSCTs) are rare neoplasms of the central nervous system (CNS) and have been a significant clinical challenge due to the lack of a clear standard of care, limited therapeutic options, and challenges of drug delivery. IMSCTs account for 2–4% of all CNS tumors, with ependymoma being the most common in adults and astrocytomas being the most common in children and adolescents [1]. Overall, ependymomas are the most frequent IMSCTs, followed by astrocytomas and then miscellaneous tumors including hemangioblastomas, gangliogliomas, germinomas, primary CNS lymphomas, and melanomas (Table 20.1). Although rare, IMSCTs can also develop as a result of metastasis from a primary malignancy.

While most IMSCTs are benign, low-grade (WHO Grades I and II) tumors, many vary in histology and 7–30% of astrocytomas are considered malignant [2, 3]. IMSCTs can be found in any location throughout the length of the spinal cord; however, they are most common at the cervical level (33%), followed by the thoracic (26%) and lumbar (24%) levels [4]. The higher incidence of IMSCTs at the cervical level may be related to the higher gray matter present at that level.

Genetic Factors

Several genetic factors are associated with IMSCTs. Understanding the various genetic mutations assists in illustrating the clinical manifestations, progression, and management of these tumors. The clinical syndromes currently associated with IMSCTs include neurofibromatosis 1, 2 (NF-1, NF-2) and Von Hippel-Lindau disease (VHL).

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Table 20.1 Intramedullary spinal cord tumors

Tumor	Incidence	Location
Ependymoma	Most common (50–60% of IMSCTs)	Cervical > thoracic > lumbar
Myxopapillary ependymoma	Rare	Filum terminale & conus medullaris
Astrocytoma	Second most common	Cervical > thoracic > lumbar
Hemangioblastoma	Very rare; increased incidence in VHL disease Patients	Cervical > thoracic > lumbar
GCT	Very rare	Cervical > thoracic > lumbar
Ganglioglioma	Rare	Cervical > thoracic > lumbar
CNS lymphoma	Rare	Cervical > thoracic > lumbar
Melanoma	Very rare	Cervical > thoracic > lumbar

GCT germ cell tumor

Neurofibromatosis

Neurofibromatosis is a common autosomal-dominant disorder with 100% penetrance in familial lines [5]. Two subtypes havebeen established: NF-1 and NF-2. Fifty percent of patients with neurofibromatosis possess a family history of the disorder with new mutations developing in the remaining constituents. The reported prevalence of NF-1 (also known as von Reckinghausen disease or peripheral neurofibromatosis) is 1 in 3000–4000 individuals [6]. Although the incidence of IMSCT in individuals with NF-1 is speculative, it has been suggested that almost 19% of subjects diagnosed with NF-1 develop IMSCT [7]. Expressivity varies due to the heterogenetic characteristics of the disorder. The mutation is located on the long arm of chromosome 17 (17q), which encodes for neurofibromin, a negative regulator of the RAS cellular proliferation pathway [8]. Neurofibromin is a tumor suppressor gene, whereby mutation disinhibits the RAS pathway leading to increased cellular division and proliferation and eventual tumor development [8]. In the presence of NF-1, multiple neurofibromas may appear. Although many tumors are associated with NF-1, in relation to IMSCTs, astrocytomas are the most likely to develop (Table 20.2) [7, 9]. Less prevalent than NF-1, NF-2 (also known as central neurofibromatosis) occurs in 1 in 40,000 individuals and represents 2.5% of patients with IMSCT [7]. The location of NF-2 has been identified as a mutation of the "Merlin" gene on chromosome 22q12 [8]. NF-2 is largely associated with ependymomas and occasionally meningiomas (extramedullary) [7]. The severe form of the condition exhibits multiple tumors with an earlier onset and a rapid clinical deterioration. The milder form is characterized by fewer tumors with a later onset and a gradual clinical progression.

Table 20.2 WHO classification of ependymal tumours

Ependymal tumours
Myxopapillary ependymoma
Subependymoma
Ependymoma Papillary ependymoma Clear cell ependymoma Tanycytic ependymoma
Ependymoma, *RELA* fusion-positive
Anaplastic ependymoma

Von Hippel-Lindau Disease

VHL is a rare autosomal-dominant disease with 90% penetrance. Moller first suggested that VHL was a genetic disorder in 1929 [10]. Briefly summarized, mutation of a tumor suppressor gene located on chromosome 3p25–26 is responsible for this condition [11, 12]. The VHL tumor suppressor proteins form a protein complex that interacts with elongins B and C and other proteins, marking them for degradation by the cell, which inhibits hypoxia-related cell transcription factors (HIF1a, HIF2a) [8, 13]. The VHL proteins also suppress the hypoxia-induced production of vascular endothelial growth factor, erythropoietin, and platelet-derived growth factor [8, 14]. Without the VHL protein present, an increased presence of these transcription factors occurs on the cellular level, eventually leading to tumor formation, and given the specifics of the transcription factors involved, these are often highly vascular lesions.

VHL is characterized by widespread formation of both benign and malignant tumors throughout the body. According to Melmon and Rosen, VHL is diagnosed if the following manifest: the presence of more than one hemangioblastoma of the central nervous system (CNS), the presence of an isolated lesion associated with a visceral manifestation of the disease, or the presence of one characteristic of the disease and a family history of the disease [15]. A wide array of tumors is associated with this disease, and especially common are retinal hemangioblastomas. Hemangioblastomas of the medulla oblongata and spinal cord as well as renal cell carcinoma may ensue and lead to significant mortality in 50% of individuals with the disease. Of CNS hemangioblastomas, 80% occur in the posterior fossa and 20% appear in the spinal cord. Furthermore, 10–15% of cranial hemangioblastomas are associated with VHL, whereas 25% of spinal cord hemangioblastomas are associated with VHL [16, 17]. In association with VHL, there is an earlier age of development of hemangioblastomas than in those of sporadic origin.

Clinical Presentation

IMSCTs present with a wide array of symptoms that vary in intensity and chronicity. The clinical features of each tumor are related to the growth rate, location, and longitudinal extent of the tumor [8]. The most common presenting symptom of IMSCT is neck pain, which may be diffuse or radicular in nature. This is hypothesized to result from dural distension and irritation. The pain is of constant intensity and varies between individual patients; it is classically worsened in the recumbent position. Nerve root compression can produce weakness, spasticity, and clumsiness [18]. Centrally located lesions can produce myelopathic symptoms. If the tumor extends cranially, cranial nerve involvement is possible. Paresthesias or dysesthesias can present unilaterally, often starting distally and progressing proximally before affecting the opposite side. Also, radiculopathy is implicated with lumbosacral involvement [19].

Diagnosis is especially difficult in children, where IMSCTs may remain asymptomatic for a long period of time or cause nonspecific complaints [20]. The character of the pain varies, but is commonly reported to worsen at night. IMSCTs can also impinge on somatosensory and motor systems, causing dys- and paresthesias, spasticity, and weakness. Loss of bowel and bladder function can also occur at a later stage and is the least common presenting symptom [21]. Symptoms in children may be perceived as clumsiness or attributed to trivial injuries, and scoliosis is present in one-third of patients [20]. Due to the late onset and sometimes non-specific nature of neurological symptoms, the diagnosis of these tumors is often delayed. The level of the tumor dictates the neurological symptoms. IMSCTs patients typically present with nonspecific symptoms progressing over years prior to diagnosis, although rare instances of intratumoral hemorrhage can provoke acute deterioration [20]. Common symptoms include neck pain, spasticity in the lower extremities, gait ataxia, sensory loss, and paresthesias. Cervical tumors can present upper or lower extremity symptoms if they affect the corticospinal tract or dorsal columns, respectively. Additional factors can contribute to the symptomology of IMSCT. Among them are age, degenerative changes of the spinal column, spinal canal size, medical comorbidities, and tethering structures, which may alter sensory and motor function. Tethering effects of the dentate ligament and dorsal and ventral roots occur as a response to cord distension by the tumor mass. Compromise of the corticospinal tract produces upper motor neuron deficit. Decrease in temperature sensation and pain results from spinothalamic tract encroachment. Compression of the dorsal columns can manifest with defects in proprioception and gait abnormalities. Tumors affecting the autonomic pathways produce disturbances of the sympathetic and parasympathetic system. Severe cord defects can also complicate respiratory, bowel, bladder, or sexual function [9, 10]. Damage to cranial nerves is also a possibility with tumors located in the upper cervical spine. The hypoglossal nerve

can be subject to compression by tumors located laterally at the foramen magnum leading to ipsilateral tongue paresis and atrophy. Arising from the C1–C5 anterior horn cells, the accessory nerve travels cephalad through the foramen magnum via the subarachnoid space between the ventral and dorsal rootlets and unites with its cranial counterpart. Thus, tumors around the upper cervical spinal cord can compress the accessory nerve, leading to weakness and atrophy of the sternocleidomastoid and trapezius muscles. Hydrocephalus occurs in 1–8% of patients with IMSCT [22, 23]. The hydrocephalus may result from tumoral obstruction of the subarachnoid CSF flow or impaired CSF absorption induced by non disseminated subarachnoid space tumors that increase CSF protein levels.85 Focal block of CSF flow by a tumor (or abscess formation) with increased CSF protein and presence of xanthochromia is known as Froin syndrome, which can lead to a "dry" lumbar puncture [24].

Histology and Clinical-Radiologic Correlation

Ependymomas

Ependymomas are rare, unencapsulated glial tumors of the brain, but they represent the most common form of IMSCT in adults and account for approximately 50–60% of all intramedullary tumors [25]. Ependymomas develop from ependymal cells, which are the epithelial-like cells lining the ventricles of the brain as well as the central canal of the spinal cord. Histologically, the 2016 WHO classification of CNS tumors includes five distinct entities of ependymal tumors [26]: subependymomas (WHO°I), myxopapillary ependymomas (WHO°I), classic ependymomas (WHO°II), anaplastic ependymomas (WHO°III), and *RELA*-fusion-positive ependymomas (WHO°II/III) (Table 20.2). Subependymoma WHO grade I is characterized by clusters of bland to mildly pleomorphic, mitotically inactive cells embedded in an abundant fibrillary matrix with frequent microcystic changes and dystrophic calcifications. Myxopapillary ependymoma WHO grade I is histologically characterized by cuboidal or elongated tumor cells forming fibrillary processes toward fibrovascular cores typically showing perivascular mucoid degeneration. Mitotic activity is low. Myxopapillary ependymomas account for up to 50% of ependymoma cases, typically arise from the filum terminale, and are usually located in the cauda equina while the other four subtypes follow the normal distribution of IMSCTs and are most often found in the cervical or thoracic spinal cord [27]. Ependymoma WHO grade II usually shows a solid, well-circumscribed growth and is composed of uniform cells forming perivascular pseudorosettes and, in some tumors, true ependymal rosettes. Mitotic activity is low while non-palisading necroses may be present in a fraction of cases. Three variants of ependymoma, each characterized by distinct histological features, are recognized in the WHO classification, namely papillary ependymoma, clear cell ependymoma, and tanycytic ependymoma. Ependymoma, *RELA* fusion-positive is a novel supratentorial ependymoma entity that is defined by the presence of a C11orf95-RELA fusion [28, 29]. It may correspond to WHO grade II or III, but patient outcome is worse compared with other types of supratentorial ependymomas [28]. Anaplastic ependymoma WHO grade III carries histological features of anaplasia, in particular high mitotic activity and microvascular proliferation. Pseudopalisading necrosis may also be observed. However, accurate histological distinction of WHO grades II and III ependymomas is challenging and its role in predicting survival has been disputed [30]. Hence, WHO grading is inadequate to reliably predict the outcome in individual patients, and molecular subgrouping or single molecular markers may offer new perspectives for improved prognostic stratification [28–31]. Most ependymomas are slow growing and display a benign pathology; however, anaplastic ependymomas tend to be rapidly growing and demonstrate more aggressive behaviour. Overall, ependymomas occur more commonly in males presenting with chronic back pain [18]. On MRI, ependymomas are centrally located and can be seen as a localized enlargement of the spinal cord

on T1- and T2-weighted images. Ependymomas will appear hyperintense on T2-weighted and FLAIR images and hypo- or isointense on T1-weighted images, although the use of FLAIR for imaging lesions of the spinal cord has been studied much less than that for lesions of the brain [18]. Myxopapillary ependymomas differ slightly in that they may appear hyperintense on T1-weighted images as well. All types appear to show heterogeneous enhancement with contrast, and cyst formation and syrinx are common especially at the cervical level [18].

Cysts form in both the rostral and caudal directions from the enhancing mass. Two different types of cysts have been described [18]: intratumoral cysts (ITC) which develop within the solid portion of the ependymoma and satellite cysts (SC), or peri-tumoral cysts, which were in contact with a cranial or caudal portion of the solid portion of the ependymoma. Syrinx was distinguished from SC by the presence of normal spinal cord tissue between the solid tumor and the cyst (Fig. 20.1).

Astrocytomas

Intramedullary astrocytomas are glial tumors responsible for approximately 60% of all spinal cord tumors in children and adolescents, despite affecting patients of all ages [18]. Most spinal cord astrocytomas are low grade (WHO Grade II) and generally considered to be less aggressive than those in the brain. Of a total of 86 studied astrocytoma cases, Raco et al. [21] found 48% to be WHO Grade II, followed by 31% to be WHO

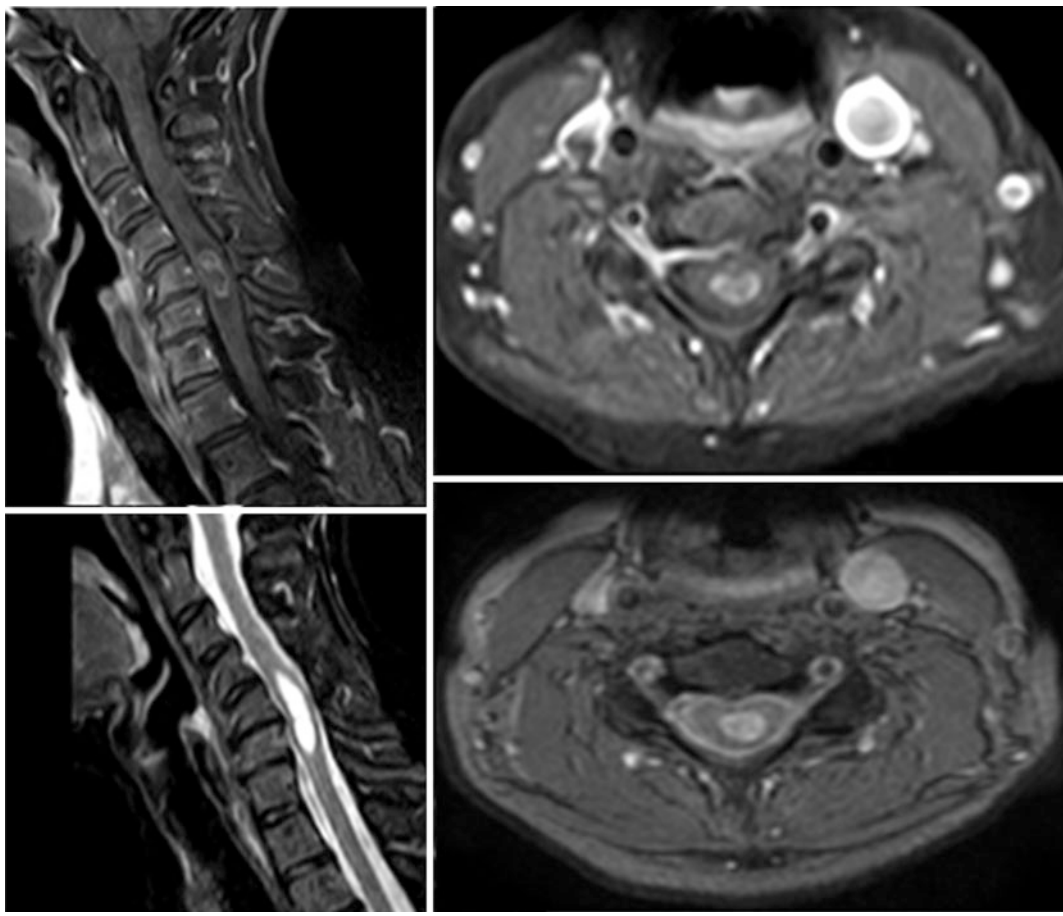

Fig. 20.1 MRI features of C4–C7 intramedullary ependymoma

Grade I, and 21% to be WHO Grade III to IV. WHO Grade I lesions represent pilocytic astrocytomas, a slow-growing tumor associated with cyst formation. Some studies have suggested that pilocytic astrocytomas represent the most common subtype in children, though these studies are limited by their sample sizes. Grade III and IV astrocytomas carried a poor prognosis with a mean survival of 15.5 months [21]. These lesions are the most aggressive and infiltrative class of astrocytomas. The presentation of these lesions varies, with pain being one of the earliest symptoms similar to ependymomas. Since these lesions tend to affect pediatric populations, certain symptoms in children are indicative of astrocytoma. These include children complaining of pain at night that wakes them up, abdominal pain, motor deficits or regression, and scoliosis [18]. Combined together, presentation in children is often nonspecific and may require extensive diagnostic workup to rule out other etiologies before suspecting astrocytoma. On MRI, astrocytomas are difficult to distinguish from other types of intramedullary tumors. While usually hypo- or isointense on T1-weighted images and hyperintense on T2-weighted images (Fig. 20.2), their asymmetry and slightly off-center location may help distinguish them from other tumor types [18]. Similar to ependymomas, astrocytomas show heterogeneous enhancement with contrast that makes it hard to distinguish between ependymomas and astrocytomas based on MRI alone.

For this reason, biopsy and histology might be considered the best methods for distinguishing astrocytomas from ependymomas and planning treatment options.

Hemangioblastomas

Intramedullary hemangioblastomas are rare, benign tumors of mesenchymal origin that originate from the vascular system within the spinal cord. Intramedullary hemangioblastomas account for 3–4% of all IMSCTs and are the third most frequent after ependymomas and astrocytomas [32]. Hemangioblastomas most commonly present in the posterior fossa (83%); however, approximately 13% are found within the spinal cord [32]. While they do not develop from the intrinsic cells of the spinal cord, their close association with the vasculature that nourishes the spinal cord can lead to the rare development of intramedullary tumor. For this reason, they tend to possess a high degree of vascularity and angiogenesis during growth. Hemangioblastoma is strongly associated with von Hippel- Lindau (VHL) disease, and approximately 10–30% of patients diagnosed with spinal cord hemangioblastoma will also have VHL disease [32]. Patients with VHL disease typically present with multiple hemangioblastomas in addition to other abnormalities such as renal cell carcinoma, pheochromocytoma, pancreatic cysts, and others [32]. The presence of multiple hemangioblastomas along with these other abnormalities may thus point toward VHL disease. In patients with VHL disease, gene mutation results in the enhanced transcription of several genes, including vascular endothelial growth factor (VEGF), which perhaps contributes to the development of vascular tumors such as hemangioblastomas [33]. Intramedullary hemangioblastomas tend to develop in the dorsal portion of the spinal cord and thus present with progressive sensory deficits, particularly proprioceptive deficits [1]. Due to the high vascularity of the tumor, there is also a risk of hemorrhage. Although rare, hemorrhage from hemangioblastoma can be subarachnoid hemorrhage (73%) or intramedullary hemorrhage (27%) [34]. Unlike astrocytomas, hemangioblastomas can be differentiated from ependymomas using MRI by the presence of hypervascularity along with tumor enhancement [1] (Fig. 20.3). Furthermore, due to the altered vasculature within the spinal cord, unusual enlargement of the spinal cord may be observed due to edema [35]. Similar to other IMSCTs, resection is the primary treatment for intramedullary hemangioblastomas.

Germ Cell Tumors

Germ cell tumors (GCTs) of the CNS are made up of cells similar to the germinal cells that develop in the gonads. GCTs represent approximately 1% of brain or spinal cord tumors in Europe and the United States, with higher rates of incidence in other geographical regions such

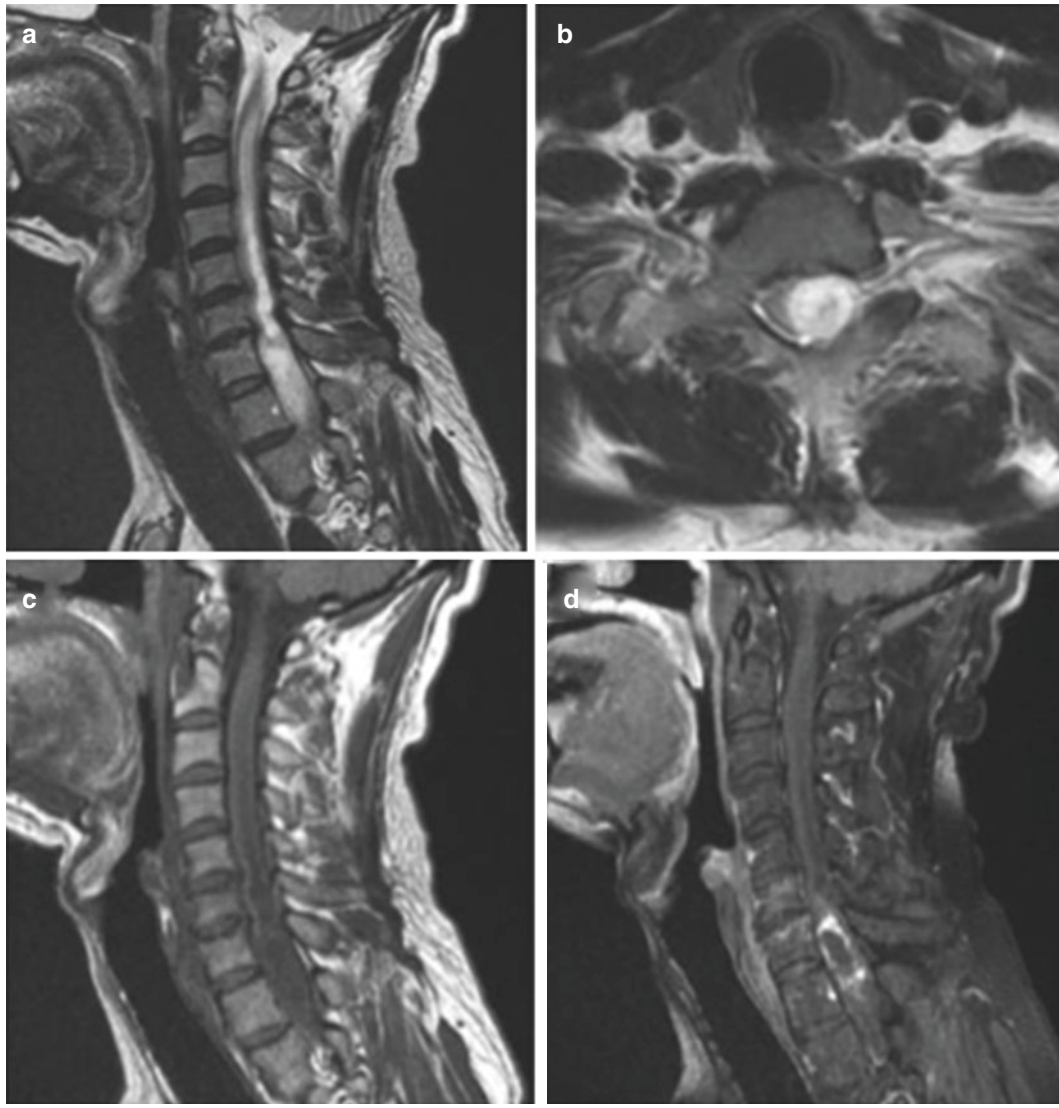

Fig. 20.2 (**a**–**d**) Cervical-thoracic astrocytoma. (**a**) Preoperative sagittal T2-weighted MR image shows a hyperintense lesion in the cervical-thoracic spinal cord with syringohydromyelia. (**b**) Axial T2-weighted MR image shows an eccentric growth pattern. (**c**) Sagittal T1-weighted MR image shows the tumor at hypointense signal intensity. (**d**) Sagittal contrast-enhanced T1-weighted MR image shows diffuse non-homogeneous enhancement of the tumor

as Japan (3%) and East Asia (12.5%) [36]. The rates of primary intramedullary GCTs are even lower. There are two types of GCT: non germinomatous GCT and germinoma. Patients with primary intramedullary germinomas typically present with sensory and motor deficits of the lower extremities that can progress to include gait disturbance and urological dysfunction [37]. MRI typically shows an expanding mass (often at the lower thoracic level), contrast enhancement with T1- and T2-weighted MRI can vary, and focal spinal cord atrophy may be an important sign [37]. Germinomas have been shown to be radiosensitive, with some studies suggesting 5-year survival rates of 65–95% with irradiation alone [38]. Germinomas are sensitive to chemo-

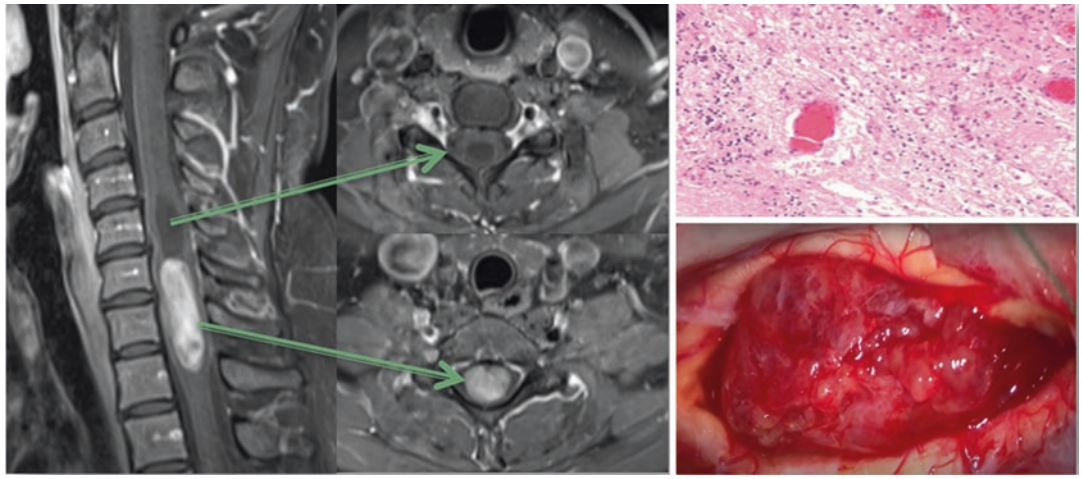

Fig. 20.3 Sagittal and axial T1-weighted MRI study obtained with gadolinium contrast showing an anterior hemangioblastoma with associated extratumoral pseudocyst

therapy as well [39]. In contrast, nongerminomatous GCTs show little sensitivity to radiotherapy alone and are often treated in combination with chemotherapy [38].

Intramedullary Metastases

Although intramedullary metastases are considered rare, they affect 0.4% of all patients with cancer and represent 1–3% of intramedullary tumors [39]. They are most commonly derived from primary tumors found in the lung (49%), breast (15%), and lymphoma (9%) [40]. The prognosis of patients diagnosed with intramedullary metastases is generally very poor, and thus prompt diagnosis and treatment are often crucial for survival. Recent studies have shown a median survival time of 4 months with 0 patients achieving complete remission [41]. Resection may be attempted, but the lack of a clear plane of dissection often prevents achievement of GTR.

Diagnosis

The differential diagnosis for intramedullary lesions, beyond neoplasms, includes vascular lesions, inflammatory conditions, infections, and syrinx. The most common vascular lesion is a cavernous malformation, which constitutes approximately 5% of intramedullary lesions in adults. MRI findings associated with cavernomas are typically sufficient for making this diagnosis due to the presence of distinct hypointense signal on T1-weighted image resulting from hemosiderin deposits [42]. Dural arteriovenous fistulas and spinal cord infarction with its associated edema must also be considered in the differential. Inflammatory and/or demyelinating conditions such as multiple sclerosis (MS), particularly when associated with pseudotumor formation, can often be mistaken for primary tumors [43]. In these cases, when cerebrospinal fluid (CSF) analysis is inconclusive, MRI images can be evaluated for the presence of "open" or incomplete ring enhancement on MRI, which are seen in up to 95% of subjects with spinal cord MS [44]. This finding may be used as a distinguishing characteristic for the acute phase of a demyelinating disease that is rarely seen in non-demyelinating conditions [43]. Transverse myelitis also should be considered in the differential for spinal cord tumor, although the time course and antecedent events that are typical of transverse myelitis make this a distinct clinical entity [44]. Spinal cord abscesses and neurosarcoidosis also can produce intramedullary masses. In most cases, distinct MRI T1- and T2-weighted signal characteristics detailed above as well as clinical

history and CSF characteristics (i.e., ACE levels for neurosarcoidosis, IgG, and oligoclonal bands in MS) are sufficient to distinguish between neoplastic and non-neoplastic entities [45]. In more ambiguous cases, advanced MR techniques such as diffusion tensor imaging (DTI) and perfusion imaging can assist in differentiating between these diagnostic entities. In a recent study evaluating IMSCT versus tumor-like lesions, the authors found elevated apparent diffusion coefficient (ADC) and peak height values in tumors compared to non-neoplastic entities [46].

Advances in MRI capabilities also have allowed for more precise imaging-based prediction of tumor histology. Arima et al. [47] have proposed a paradigm for assisting in the diagnosis of intramedullary lesions based on tumor-specific MRI findings, resulting in an average preoperative diagnostic accuracy of 89% [47]. The authors tested diagnostic accuracy using an algorithmic approach based on pattern of edema, T2-weighted signal intensity, distribution of contrast, and central versus eccentric location on axial images. Based on this paradigm, all IMSCTs demonstrate spinal cord swelling and high signal intensity on T2-weighted images; lack of these findings suggests a non-neoplastic entity. All IMSCTs with the exception of some astrocytomas demonstrate contrast enhancement. Strong homogenous enhancement strongly suggests a diagnosis of hemangioblastoma, whereas heterogenous enhancement with areas of necrosis is suggestive of ependymoma or astrocytoma. Finally, heterogeneously enhancing lesions located centrally are typically ependymomas, whereas eccentrically located lesions are more frequently astrocytomas. Interestingly, use of this elegant paradigm correctly identified 100% of astrocytomas and hemangioblastomas [47]. In differentiating ependymomas from astrocytomas, the presence of syringohydromyelia and a cap sign (hypointense hemosiderin ring at the pole of the tumor) are more frequently seen in ependymomas, with the presence of syringohydromyelia resulting in an accurate diagnosis in 86% of cases when used as the sole predictive variable [48].

Treatment

Evidence-based treatment of IMSCTs (Table 20.3) primarily involves resection, with radiotherapy and chemotherapy often reserved for tumor recurrence, high-grade and infiltrative tumors, or when resection is contraindicated. Preoperative neurological status and tumor histology are considered the best predictors of outcome, with tumor histology shown to be predictive of extent of resection, functional neurological outcomes, and recurrence [39]. Resection is generally considered a good predictor of outcome. Recent studies, however, have shown that surgical intervention for the management of astrocytoma is associated with higher rates of long-term neurological complications with no derived benefit for patients [39].

The standard of care for most cases of IMSCT is resection, which has improved with the development of modern neurosurgical instrumentation, use of the operating microscope, as well as the measurement of intraoperative motor and somatosensory evoked potentials. However, resection of IMSCT is generally dependent on the presence or absence of a clear plane of dissection. While ependymomas typically have a clear plane between the tumor and spinal cord parenchyma, astrocytomas tend to be more infiltrative, lacking a good plane of dissection. This limits the ability for gross-total resection (GTR) for intramedullary astrocytomas, as any attempt at GTR may damage spinal pathways, leading to postoperative neurological deficits involving both motor and sensory systems.

Adjuvant radiotherapy is recommended when resection is contraindicated, or for high-grade tumors that are not amenable to GTR. The role of radiotherapy, though, is controversial, as there have been reports that suggest a positive outcome while others suggest no benefit despite its routine use in the clinical setting [49]. Additionally, radiotherapy can have several adverse effects, including radiation myelopathy, impaired spine growth, spinal deformities, radiation necrosis, vasculopathy, changes to the normal spine parenchyma, and a 25% risk of secondary tumors in 30 years [1, 41]. These longer-term consequences

Table 20.3 Current evidence-based recommendations for the treatment of IMSCTs

Tumor	Treatment	[a]Evidence-based classification
Ependymoma	Primary: Resection Secondary: RT Secondary: Chemo	Class I, level of evidence: C Class IIa, level of evidence: C Class IIb, level of evidence: C
Myxopapillary Ependymoma	Surgical resection	Class I, level of evidence: C
Astrocytoma	Primary: Resection Secondary: RT Secondary: Chemo	Class IIb, level of evidence: C Class IIa, level of evidence: C Class IIb, level of evidence: C
Hemangioblastomas	Surgical resection	Class I, level of evidence: C
GCT	Primary: Resection Secondary: RT (germinomas) Secondary: Chemo (non-germinomatous GCT)	Class I, level of evidence: C Class IIa, level of evidence: C Class IIa, level of evidence: C
Ganglioglioma	Surgical resection	Class I, level of evidence: C
CNS lymphoma	Intrathecal chemo	Class IIb, level of evidence: C
Melanoma	Primary: Resection Secondary: RT	Class I, level of evidence: C Class IIb, level of evidence: C

Chemo chemotherapy, *RT* radiotherapy
[a]The American Heart Association Evidence-Based Scoring System

can be particularly adverse in children and adolescents. Since children are more sensitive to the adverse effects of IMSCTs, the role of chemotherapy has gained further appreciation. Chemotherapy has historically been used only when resection and adjuvant radiotherapy were contraindicated or unsuccessful [41]. Some of the limitations of chemotherapeutic agents include the inability of large molecules to bypass the blood–spinal cord barrier (BSCB), CSF pulsations, and the widespread systemic effects of the drugs.

Surgery

For IMSCT, safe entry zones into the cord have been described in detail [42–44]. The posterior midline myelotomy is feasible in most intrinsic spinal cord tumors with a central or slight paramedian extension. For lateralized IMSCTs posterior to the level of the attachment of the dentate ligament, the posterolateral sulcus (dorsal root entry zone) is feasible [42]. Anterior or anterolateral intramedullary tumors, which are very rare, may need an anterior approach when feasible with a paramedian anterior myelotomy (Fig. 20.4) [43]. Access to the spinal canal should be large enough in length (through laminotomy or laminectomy) and cover the extension of the solid tumor part in order to control protrusion of the cord and tumor into the dural opening by the immediate release of CSF and/or opening of a tumor cyst. Intraoperative ultrasonography helps to reconfirm sufficient exploration of the dura in relation to tumor extension and to identify an ideal starting point for myelotomy (at the center of the tumor). Myelotomy should respect the vasculature in general, but a draining vein over the posterior midline sulcus might be obliterated. Especially at the posterior midline, the sulcal microvasculature guides the microsurgical separation of the posterior columns down to the tumor. In cases of attempted maximum tumor resection, the myelotomy should be extended in length to the poles of the tumors for full visualization and preparation [44]. Myelotomy is performed by sectioning the arachnoid and bluntly dissecting within the plane while avoiding focal pressure on the adjacent tissue (by using, e.g., plated forceps or broad blunt bipolar but always preparing a shallow and long, but not deep and small approach). Preparation of the tumor-spinal cord interface depends on differences in color, texture, and vascularity and might be performed with microdissectors or ultrasonic aspiration under high magnification. Pial retention sutures at the posterior cord attached to the dura or sup-

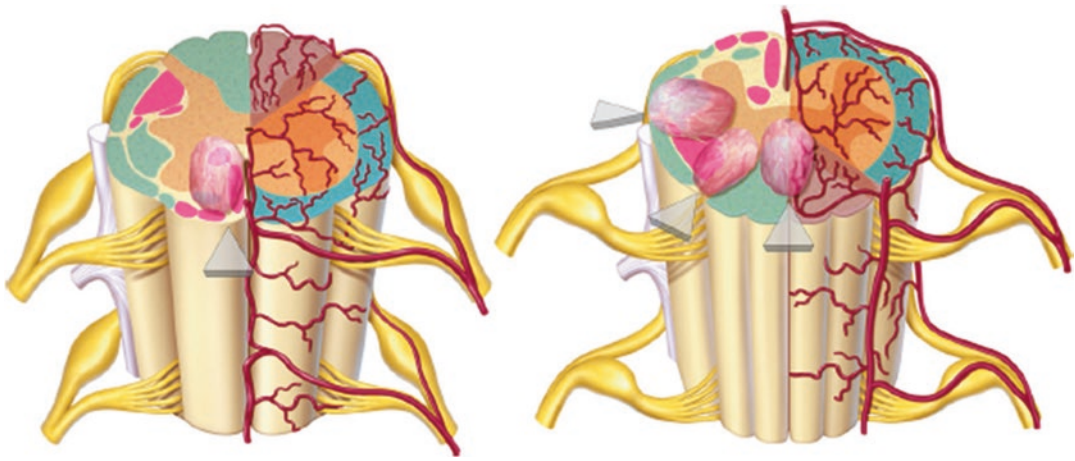

Fig. 20.4 Cross-section of the spinal cord showing ascending (pink) and descending (green) tracts, the ligamentum denticulatum (on the left) and the vascular supply (on the right). Left: anterior view with blood supply from the anterior spinal artery (predominantly supplying the motor area). The paramedian anterior myelotomy is indicated to resect tumors situated anteriorly or anteriolaterally. Right: posterior view showing one of two posterior spinal arteries and the surgical approaches to the spinal cord from right to left; posterior midline myelotomy, posterolateral myelotomy at the dorsal root entry zone (posterolateral sulcus), and lateral approach with entry point at the level of the dentate ligament

ported by weights (i.e., minibulldog clamps) might minimize repetitive alteration of the dissected surface of the cord, but stretching of the cord tissue by the pial sutures must be avoided. Surgery might start with debulking of the tumor by ultrasonic aspiration. A fast-stain histology evaluation is recommended. Identification of the tumor-spinal cord interface starts on the lateral tumor borders. Gaining early control of the anterior extension of the tumor at the tumor poles eases intraoperative orientation especially in cases of cystic tumor poles. The decision to aim for GTR might be based on two factors: malignancy verified by fast-stain histology and the continued identification of a plane of dissection. In cases of a non malignant or inconclusive grade of malignancy on fast stain, "smart" resection (relying totally on a distinctive tumor–cord interface with cessation of resection with loss of this guiding plane [6]) and IOM-guided resection are mandatory. Bipolar coagulation should be avoided to reduce the risk of spinal cord alteration. Identification and preservation of the anterior spinal cord artery or its tributaries to the anterior cord is absolutely mandatory and damage by traction, evulsion of tributaries, or direct coagulation must be avoided. Reconstruction of the cord by pial sutures is advised to minimize the risk of posterior tethering of the dorsal columns and formation of a secondary syringomyelia. Duroplasty should be used to expand the CSF space in cases with tumor remnants or residual cord swelling to improve CSF flow around the cord [44].

Adjuvant Therapies

Literature on adjuvant radiotherapy and chemotherapy is largely limited by the rarity of IMSCTs and the heterogeneity of treatment based on histology.

Radiosurgery

Surgery remains the first choice treatment for spinal intradural tumors. Radiotherapy has been used for years especially after STR in intramedullary ependymomas or astrocytomas with conventional fractionation and doses of 45–50 Gy, limited by the risks of radiation myelopathy and gastrointestinal or fertility compromise and with mixed effects on tumor control [45]. In recent

years, stereotactic radiosurgery for spinal lesions, first described by Hamilton et al. in 1995 [46], has become an effective alternative for patients with recurrent or residual disease or in cases where surgery is contraindicated. A recent systematic literature review on stereotactic radiosurgery for intramedullary spinal cord tumors concluded that the technique is safe and effective in selected cases [47]. However, long-term data are still lacking and because the therapeutic effect of radiosurgery sets in slower and is less pronounced than surgery, radiosurgery remains a first choice treatment alternative only in a select group of patients [48]. While radiosurgery on spinal tumors is an established and well-described procedure [38, 49], the associated treatment-related toxicity on adjacent organs which are at risk in about 25% of cases has to be taken into consideration [50]. The risk of spinal cord toxicity and radiation myelopathy has to be discussed with the patient. Nevertheless, radiosurgery will most likely be developed to play a more important role in the treatment of spinal intradural lesions as it has with cranial tumors.

Radiotherapy

While stereotactic radiosurgery seems to pose more importance in future treatment regimens, conventional radiotherapy (RT) has been used to treat spinal tumors, especially extensive intramedullary tumors, with satisfying results [51]. Adjuvant radiotherapy for primary IMSCTs is employed variably based on tumor histology, extent of resection, and recurrence [52]. It is used variably for ependymomas but, in other cases, is reserved for high grade tumors only [53, 54]. Postoperative RT has been shown decrease recurrence in high-grade astrocytomas [55] but is controversial in the treatment of low-grade astrocytomas [52]. It is employed more frequently in cases of incomplete resection [56]. Despite the use of adjuvant radiation, the prognosis for high-grade astrocytomas remains poor, resulting in variable findings of efficacy in this population [52, 57]. RT is also used as an adjunct for radiosensitive metastases such as small cell lung carcinoma, breast carcinoma, and lymphoma [58], although survival rates remain extremely low in these cases [59].

Chemotherapy

Chemotherapy is not widely used in the treatment of most IMSCTs but may be used on a case-by-case basis as an adjuvant therapy, particularly in the pediatric population [53]. Chemosensitive metastases such as small cell lung cancers and hematologic malignancies may have improved response to chemotherapeutic agents, particularly in cases of coexisting systemic metastases [58].

There is currently no well-described role for the use of chemotherapy in ependymomas. In a small prospective study of 10 patients with recurrent intramedullary ependymoma, oral etopside was used as an adjuvant therapy with 70% of patients had stable or partially responsive disease following a single cycle of etopside [35].

While there are no standard guidelines for spinal germinomas, the standard treatments for the highly chemosensitive CNS germinomas include platinum and alkylating agents such as cisplatin, belomycin, vinblastine, and etopside. Complications of combination regimens include sterility, renal and auditory toxicity. These treatments may be considered for spinal germinomas [1].

Chemotherapies for intramedullary astrocytomas most commonly include alkylating agents (temozolomide) and vascular endothelial growth factor (VEGF) inhibitors (bevacizumab) highlighted below. Hemangioblastomas that are multifocal, recurrent, or associated with VHL may be treated systemically with VEGF inhibitors such as bevacizumab or tyrosine kinase inhibitors [49].

Intradural Extramedullary Cervical Spine Tumors

Meningiomas and peripheral nerve sheath tumors (schwannomas and neurofibromas) are the most common neoplasms in intradural extramedullary compartment of cervical spine with very similar incidence. Other benign tumors like lipomas, hamartomas, dermoids, epidermoids, teratomas, fibrous tumors, and hematogenous or drop metastases are very rare in this location.

Meningiomas

Meningiomas are slow-growing benign tumors that arise from arachnoid cap cells adjacent to the dura or directly from dural fibroblasts. They usually present after the fourth decade of life with a striking female predominance. Tumors are generally located laterally in the spinal canal and occur more frequently in anterolateral position compared to those below C7, where posterolateral location dominates. Up to 15% involve both the intradural and extradural spaces or are purely extradural. Both, aggressive behavior and malignant degeneration, are rare. Meningiomas can be histologically classified as psammomatous, fibroblastic, or meningothelial. These generally well-circumscribed, slow growing lesions can be treated successfully with surgical resection. Nevertheless younger patients tend to develop more complex meningiomas with a mortality rate up to 10% even when treated [60]. GTR is the treatment of choice for spinal meningiomas. Yoon et al. reported the Simpson Grade of resection as a good predictor for recurrence with no recurrent disease seen in their series after Simpson Grade I to III resections [61]. Invasion of the arachnoid or pia is an independent negative prognostic factor [62]. Advanced age does not seem to be contradictive to a good outcome [63]. Minimally invasive approaches should be used where possible because they are associated with a better postoperative course. However, severe intratumoral calcification might lead to a more extensive approach in order to remove a hard tumor safely [64]. Radiosurgery is reserved for cases where surgical treatment is not possible or for cases with recurrent, residual, or multiple lesions, as with other benign intraspinal tumors [65]. Surgical treatment of spinal meningiomas has a favorable outcome in the majority of cases. When resected completely, functional outcome is excellent and recurrence rates are low [66].

Nerve Sheath Tumors

Nerve sheath tumors (NSTs) have the same incidence as meningiomas but occur equally in men and women and are mostly discovered during the third to fifth decades of life.

Schwannomas are slow-growing lesions that arise from the sensory dorsal rootlets in most cases. The majority of lesions are intradural but they can also grow extradurally (10%) or combined intra-extradurally (10–15%). Schwannomas tend to develop an hourglass shape due to bony impression at the neural foramen during their growth and are then called dumbbell tumors. They present first with radicular pain and later result in motor deficits. The recurrence rate after surgical resection is low. Malignant dumbbell tumors are rare (2.5%) and are more common in children under the age of 10 [67]. If associated with neurofibromatosis (NF), an autosomal dominant neurocutaneus disorder, nerve sheath tumors are likely to be neurofibromas. In this case, they incorporate other cells in addition to schwann cells, are unencapsulated, and tend to occur in multiple locations, engulfing the nerve rather than displacing it. The management of NF differs because the goal is to achieve control of symptoms and local disease. Therefore in most cases only symptomatic tumors are considered for resection. Intradural spinal tumors are more common in NF2 than in NF1. NF should be considered in pediatric patients with a nerve sheet tumor and in patients with additional spinal or cranial tumors (especially vestibular schwannomas and meningiomas), skin lesions (nodules, dermal neurofibromas, café au lait spots), or first degree relatives with NF. The workup includes ophthalmic examination, genetic studies, auditory evaluation, and MRI of the whole neuroaxis to rule out additional tumors. These patients should be managed by a multidisciplinary care team consisting of neurosurgeons, neurologists, geneticists, opthalmologists, dermatologists, plastic surgeons, and endocrinologists. Nerve sheath tumors are also primarily treated surgically in most cases. Tumors with large extraforaminal extension may require more extensive approaches and sometimes even stabilization. Therefore these tumors are associated with complications more often [68]. Nerve sheath tumors can be removed safely and effectively through microsurgery.

Surgical Technique

For intradural extramedullary tumors, the surgical approach should aim to control the origin of the respective tumor. Direct control after dural opening is feasible with a posterior or laterally located tumor matrix (e.g., highly vascularized tumors or tumors that are difficult to debulk such as partly calcified meningiomas) with no mobilization of the spinal cord.

Tumors with an anterolateral or anterior matrix might be accessible posterolaterally in cases with a sufficiently large lateral tumor extension, which in turn might allow debulking and reaching its anterior matrix without moving the cord medially or posteriorly. Sectioning of the dentate ligaments might further release the cord and enable some cord rotation (but not traction) to improve anterior control.

Without medial dislocation of the spinal cord by the tumor itself, a posterior or posterolateral approach might not suffice to control the tumor matrix (and its vascular supply, which might disturb a clear microsurgical field by constant oozing) and an anterolateral or anterior approach should be considered. Anatomical regions with obstacles for an anterior approach (i.e., craniocervical junction, upper thoracic spine, sacral region) might be addressed via a lateralized posterolateral approach, including facet joint resection, which warrants reconstruction by instrumentation at the end of the procedure in most cases. Schwannomas nearly exclusively originate from the posterior sensory root. Unless the tumor has extended into the dorsal root gangion, the anterior motor root might be decompressed and saved anatomically. A T-shaped dural opening towards the root sleeve improves visualization and root-sparing resection. Lateral dural defects at the radicular dural sleeve might be controlled by a pull-through soft tissue plug (i.e., autologous muscle or subcutaneous fat) from the dural inside to outside, which is attached to the epidural tissue/dura with a stitch. This technique supports a facets-paring combined intra-extraspinal approach in dumbbell-shaped tumors.

In case of resection of the dura, meticulous dural repair is absolutely mandatory. Synthetic duraplasty sutured into the dural defect by a non-absorbable monofilament suture (e.g., Prolene) might reduce the risk of secondary tethering of the spinal cord, but clearcut evidence in favor of one specific material is still missing. In spinal meningiomas, resection of dura is only recommended if it can be done without altering the risk for CSF leak or other complications [69, 70] and is feasible in the posterior or posterolateral attachment. Given that about three out of four spinal meningiomas are attached at or anterior to the level of the lateral dentate ligaments [71], spinal duraplasty is technically more demanding. The increased perioperative risk does not outweigh potential longterm benefits in PFS [70]. Reconstruction of a normal sized or even widened subarachnoid space is very important in order to reduce adhesions, tethering, and the risk of secondary syringomyelia as a rare complication [70].

Illustrative Cases

Surgical removal of all cases was performed by the Senion Author (PC).

Case 1

A 19-year-old boy developed weight loss and slowly progressing tetraparesis. Neurological examination revealed tetraparesis grade 4 MRC with spastic gait disturbance and brisk tendon reflexes. Severe cord compression from a dumbell-shaped tumor at C5 was seen on MRI (Fig. 20.5). The tumor was removed en bloc via a posterior approach with sharp dissection from the dura (Simpson Grade II). The patient regained full motor and sensory function. He had no tumor recurrence at long-term (10 years) follow-up.

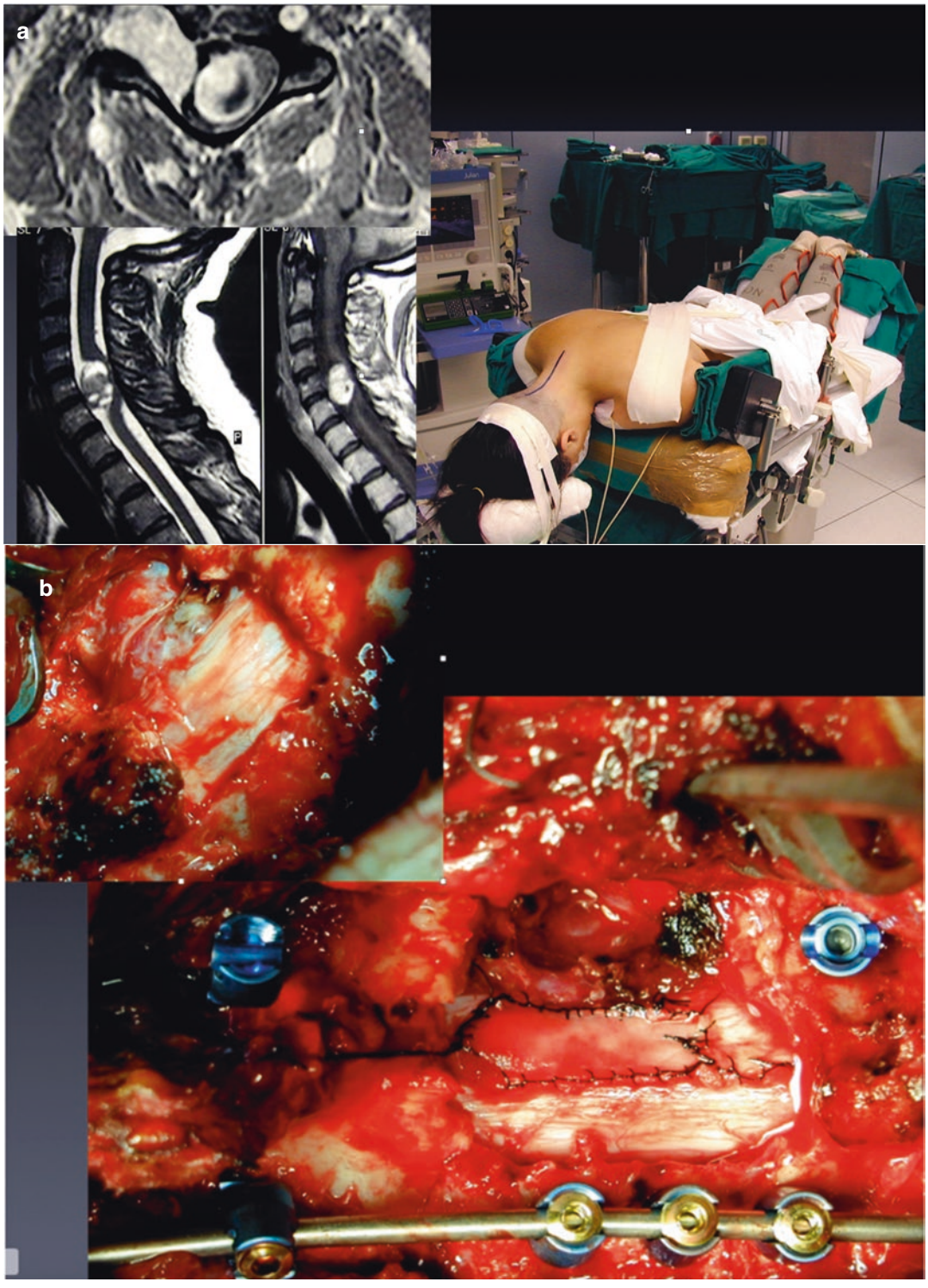

Fig. 20.5 (**a**, **b**) Cervical schwannoma. (**a**) Preoperative Imaging and setting (**b**) Intraoperative images

Case 2: Intradural Spinal Meningioma

A 52-year-old woman presented to our Neurosurgery department with headaches and neck pain not associated with any neurologic deficits. The MRI with contrast of the cervical spine showed a huge left-sided intradural extramedullary tumor suspicious for a meningioma at the level of C1/C2 with severe cord compression (Fig. 20.6). The surgery was planned with SSEP and mMEP monitoring. We performed a C1 laminectomy, C2 left hemilaminectomy, and bony widening of the foramen magnum on the left. The dura was opened in a C-shaped fashion to the left side. The dural entrance of the left vertebral artery was controlled and the tumor matrix at the spinal dura was sharply resected. The tumor was mobilized and removed en bloc (Simpson grade II). The patient was discharged home on postoperative day 6 with mild neck discomfort and normal neurological status. MRI revealed complete tumor removal.

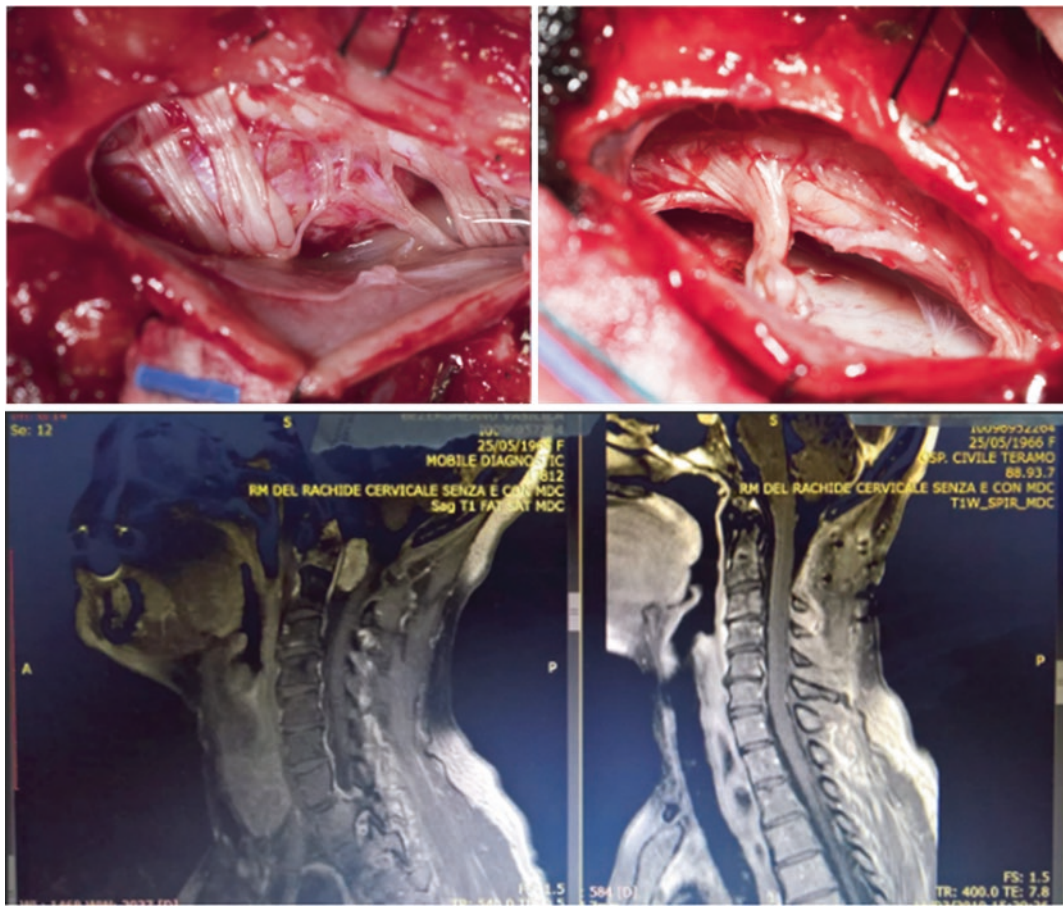

Fig. 20.6 C1/C2 Meningioma

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Neck Pain Rehabilitation

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'Neck Pain Rehabilitation'

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Neck Pain

Definition

According to the International Association for the Study of Pain (IASP), Neck pain is defined as a pain that comes from an area between the nuchal line and another imaginary line passing through the lower end of the spinous process of first thoracic vertebra and sagittal plans tangent to the side edges of the neck.

Indeed, Neck pain is the most common disorders of the musculoskeletal system, second only to low back pain. It constitutes 40% of all backache and is the fourth cause of disability, with an annual incidence of 83 per 100,000 individuals, aged between 13 and 91 years, in the US [1]. This pain may also radiate to the upper limbs if there is a nerve root compression, the distribution depends on the affected nerve root. The painful perception depends mainly on the nociceptive elicitation of the major structures innervated in the neck region, such as cervical muscles, ligaments, facet joints, and nerve roots.

The IASP's definition considers posterior pain, which can be divided into high pain, up to C3, and lower pain, down from C4, and, merely according to the time of onset, it can be divided into acute (lasts less than 3 months) and chronic (lasts longer).

In 50% of cases, neck pain resolves spontaneously or with pharmacological and physiotherapy treatment, however the remaining 50% will have recurrent or chronic neck pain [2].

Epidemiology

This musculoskeletal problem has significant effects in terms of economic and social costs, due to the considerable number of days of absence from work. It is estimated that its prevalence is 12.1–71.5% in the general population and 27.1–48.8% in workers, while the annual prevalence of disability is 1.7–11.5% [2]. It reaches its peak in middle age up to affect two-thirds of the population, mainly women [3]. It has been evaluated that the annual cost for neck and low back pain treatments is 72.2 billion euros in the US [2].

In 10% of cases, it tends to become chronic, affecting 30–50% of the general population every year.

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Functional Anatomy

The cervical spine represents the most mobile and at the same time most stable portion of the whole spine. It performs three important functions: acts as a support for head, enables head movements and provides protection to the spinal cord and the vertebral arteries flowing inside. It consists of two anatomically and functionally distinct parts:

- The upper cervical spine, which consists in atlas and axis, the first two vertebrae, is articulated through a three-axis with three degrees of freedom; it coordinates in space the position of the head and allows the alignment of the sense organs.
- The lower cervical spine, from the bottom plate of the axis to the top of the first dorsal vertebra, that allows flexion-extension and mixed rotation-tilt movements.

These two traits are functionally complementary and allow head rotation, tilt and flexion-extension movements. The posture of the head keeps the eyes parallel to the horizon, influences the TMJ static/dynamic occlusal scheme and body scheme, in order to maintain balance.

Etiology

Cervical pain can be fully considered a multifactorial disease. Indeed, its etiology is still misunderstood, or otherwise attributable to different triggers, except for post-traumatic events, such as whiplash [4]. In most cases, the etiologic mechanism is represented by dysfunctional source ("nonspecific" or "common" neck pain), in which coexist inflammatory, muscular, neurological, mechanical, and postural components [5].

It may be related to:

- specific organic problem (cervical uncarthrosis, zygapophysealarthrosis, facet joint syndrome, disk degeneration, spinal canal stenosis, myofascial syndrome, rheumatic diseases, cancer, etc.)
- psycho-social, "not organic" problems
- post-trauma, work, sports, etc.

Moreover, it is possible to identify risk factors and their possible causes [4].

About that, they can be divided in non-modifiable and modifiable risk factors. Among the first, we include age, gender (women are more affected), and genetic factors. While the latter are: smoking (active and passive), physical activity, poor posture, high demands at work, repetitive or precision work, low social esteem [6].

Many authors agree that neck pain can be defined as a clinical syndrome that occurs due to an imbalance between load conditions, load capacity and, especially, adaptation. A weakness of the craniocervical flexor muscles and a forward head posture, usually associated, seem to be the basis of the functional aspects of this disease. Also, hyperlordosis of the upper cervical trait and increased kyphosis of the lower trait result in a overload on the transition area between the two curves [6].

Classification

Neck pain can be classified into four grades:

- Grade I: absence of signs of major diseases and without interference in everyday activities.
- Grade II: absence of signs of major diseases, but with interference in daily activities (<10%).
- Grade III: neck pain accompanied with signs/symptoms of radicular pain. Requires specific tests and treatments.
- Grade IV: neck pain with signs of major diseases (instability or infection). It requires tests and urgent treatment.

According to the American Physical Therapy Association (APTA) neck pain can also be classified as:

– neck pain with impaired motility;
– neck pain associated with coordination disorders;
– neck pain associated with headaches;
– pain in the neck with irradiation of the upper limbs [6, 7].

Clinical Evaluation

Clinical evaluation of neck pain is the basis for diagnosis, treatment, and prognosis. A comprehensive history is a very important moment of the clinical investigation that can direct to/exclude a diagnostic hypothesis and especially allows you to suspect other diseases that have symptoms such as neck pain ("Red flags").

The main symptom is represented by pain in the cervical spine that can radiate to the occipital region, from the shoulders to the upper limbs (brachialgia); it can also affect the temporal and retronucal region or the anterior region of the thorax. In case it radiates to the arms we talk about "brachialgia", paresthesia and/or reduction of strength in the upper limbs may coexist.

The next step is the inspection, which begins with the patient's entry into the ambulatory. It includes the careful observation of head posture, shoulders, and upper limbs. It continues while the patient undresses and during all his natural movements. Moreover, presence of any scars, blisters, etc., need to be evaluated.

Thenit's advisable to put the patient on the supine position in order to release the deeper muscles and let us to begin palpating the bony prominences more attainable. In the front, you can palpate hyoid bone, thyroid cartilage, the first cricoid ring and carotid tubercle. In the posterior area, occiput, inion, superior nuchal line, mastoid process, spinous processes of the cervical vertebra and, moving sideways to 3 cm, the facet joints. Palpation of the soft tissues also identifies two zones: front, that includes sternocleidomastoid muscles, lymphatic chain, thyroid, parathyroid, carotid pulse and supraclavicular fossa, and rear, where we find trapezius muscles, occipital nerves and the superior nuchal ligament.

The range of motion of the cervical spine allows six degrees of freedom: flexion, extension, left and right rotation and tilt. About 50% of flexion and extension occurs between occiput and C1, the remaining 50% is distributed evenly among the other vertebrae; mind 50% of the rotations occur between C1 and C2, the other 50% involves the breaking 5 cervical vertebrae.

It's preferable to consider first active motility and then passive motility.

The neurological examination of the cervical spine has a very important role in case of brachialgia which underlies the involving of the brachial plexus. This evaluation consists of two phases: the evaluation of muscle strength of the intrinsic muscles of the cervical spine and peripheral neurological examination of the upper limbs (muscle strength, sensitivity and tendon reflexes). At the end of our evaluation, it's possible to execute some provocative tests such as Spurling's Neck Compression Test, Shoulder Abduction (Relief) Test, Neck Distraction Test, Lhermitte's Sign, Hoffmann's Sign, Adson's Test, and Valsalva Maneuver.

A very important step to monitor the effectiveness of treatment and the disease course is the administration of district-specific rating scales, as the Neck Pain, Cervical Radiculopathy, Neckache Scale, etc.

Recently, however, the World Health Organization (WHO) is trying to guide to abio-psycho-social vision of the patient that includes all aspects of the health in order to improve quality of life. This system has been identified in the ICFDH (International Classification of Functioning Disability and Health), around which you can build the evaluation/diagnostic process, pharmaceutical, rehabilitation, and subsequent outcomes.

Red Flags

In line with the 2011 SIMFER diagnostic and therapeutic recommendations for back pain, specific investigation is necessary to exclude serious cervical disease and evaluate alarm signals (red flags).

These red flags are: (tab)

- age <20 years/>50 years
- signs of systemic disease
- incessant pain at rest
- altered state of consciousness
- language disorders
- symptoms or signs of alteration of the central nervous system
- ligamental weakness
- sudden onset of acute neck pain or headache with unusual characteristics
- suspected carotid dissection
- suspected neoplasia
- suspected discitis, osteomyelitis and tuberculosis
- surgical outcomes
- structural deformities with progressive pain

Diagnostic Imaging

It's recommended to use diagnostic imaging studies not routinely, but only to confirm a clinical suspicion. More particularly, if symptoms persist for more than a 1 month and on suspicion of a specific disease the execution of the radiograph of the cervical spine in standard projections is recommended. Indeed, the MRI or CT are justified only in cases of documented neurological compression or in the suspicion of a serious condition (myelopathy, discitis, fractures). The aforementioned two examinations should be accompanied by EMG/ENG (herniated disks, spinal stenosis) [4] in order to identify the nerve root involved and the type of dysfunction or any possible plexopathies [7].

Prognosis

As we said before in most cases, neck pain resolves itself within a few days or weeks, however half of the patients develop a chronic disease and in 5% of cases it can cause severe disability. Unfortunately, early treatment, as well as the degree of degeneration, do not influence the prognosis. Furthermore, the prognosis is worse in women, in advanced age, in obese and smokers, in case of coexisting intense pain at baseline or radiculopathy [8].

Therapy

Medical Therapy

According to 2011 SIMFER guidelines of the diagnostic and therapeutic recommendations for neck pain, paracetamol/NSAID/Steroids are recommended for the reduction of the painful symptoms in the short term.

However, two systematic reviews show no evidence in the use of analgesics, NSAIDs, muscle relaxants and antidepressants for acute and chronic neck pain.

A study suggests that Eperisone hydrochloride (muscle relaxants) in synergy with physical therapy can be a valuable tool in the therapeutic management of cervicalgia [9].

Rehabilitation Treatment

Since it is not possible aetiological therapy, the main objective of rehabilitation treatment will be aimed at the reduction or resolution of pain, the global and segmental joint recovery, and especially the restoration of skills decreased from cervical disease.

The treatment consists in an integration of drug therapy and an individual rehabilitation program, tailor-made for each patient depending on the intensity of symptoms and the general clinical condition [4–7].

Despite there are several studies that describe multiple interventions, they are characterized by poor methodological quality and diversity of patient samples, so it can't be possible to identify a standard treatment.

Specifically, the intervention consists in reaching of short-term goals (pain control, initial joint recovery if there is a limitation), medium-term (full recovery of ROM, resolution of muscle contractures, reinforcement of the stabilizing muscles of the head), and long term goals (taking proper posture and prevention of relapse).

The rehabilitation program, will include different manual techniques, such as global postural re-education by Souchard, that arises from the assumptions of Mezieres and McKenzie techniques. However, unlike the Mezieres method, Souchard focuses on the diaphragm (respiratory muscle) and the phrenic nerve that supports it, as well as its synergistic action with the posterior back muscles chain and the ileo-psoas muscle.

The Souchard method distinguishes dynamic muscles from static muscles, considering that static muscles are exercised in an eccentric way and dynamic muscles in a concentric way. As a consequence, a shortening of the static muscles will lead to a retraction and an excessive resistance to elongation, while the dynamic ones can be freely shortened (contracted). The choice of the used posture is determined by functional evaluation of dynamic and static muscles, together with an examination of retractions. Moreover, Souchard believes that muscular chains can be summarized in two larger groups: anterior and posterior. Two morphological patterns depend on them: the first is called the 'anterior', in which patients have a forward position of the head, dorsal kyphosis, lumbar hyperlordosis, anteversion of the pelvis, femur internally rotated and valgus knees, heel and foot valgus; the second is named 'posterior', in which patients may present mainly the following characteristics: short neck, flat back, lumbar hypolordosis and subsequent diaphragmatic problems, retroverso pelvis, varus knees, heel and foot varus.

Indeed, the McKenzie method, is based on maintaining correct posture and how to perform specific exercises to treat some forms of back pain, mainly mechanically (related to the maintenance of posture or execution of harmful movements). The treatment, according to McKenzie, is based mainly on the involvement and active participation of the patient for symptoms resolution and to prevent a recurrence [2–10] (Fig. 21.1).

Therapeutic Exercise

Several studies support the role of therapeutic exercise for acute neck pain that involves strengthening and stretching of the stabilizing muscles of the cervical spine and shoulder girdle, improved mobility and proprioception, always respecting the pain threshold [10].

However, in case of chronic neck pain are recommended isometric strengthening exercises, with results maintained even in 3 years.

The execution of specific exercise depends on the local load capacity, while, for nonspecific exercises, individual general load capacity must

Fig. 21.1 Manual treatment of the patient. Mc Kenzie method. (**a**) Manual exercises (**b**) Postural exercises

be taken into account, and in particular the presence of comorbidity. It's recommended to choose exercises directed to the upper cervical spine, the lower spine and the cervicothoracic transition basing on the clinical presentation.

At the end of the treatment the specific gesture will be taken care of the patient will mimicwork gestures movements, or sport movements, in order to allow the full reintegration in its activities.

A systematic review by Hidalgo et al. shows that combining physical therapy with exercise enhances the effectiveness of the latter, but it also demonstrates that mobilization of the spine during the acute phase is absolutely contraindicated.

Manual Therapy

The aforementioned exercises seems to have a synergistic effect in combination with manual therapy, as it's recommended in the guidelines [11]. Manual therapy of the soft tissues and the joints is based on two different techniques: the first one is performed on the muscles, tendons and ligaments designed to restore the elasticity of the structure and the resolution of the pain of myofascial origin; the second one uses mobilization with and without impulse.

Mobilizations are carried out by applying different parameters of intensity and time, respecting the range of motion allowed. More specifically, they can be distinguished depending on the direction of the movement: direct mobilization, if is carried out towards the barrier of restriction, or indirect mobilization, if it takes place in the opposite direction. This technique is also distinct in primary, when it involves only the articulation to mobilize, and secondary, if it takes place through the mobilization of other joints [11].

Stretching

In case of post-surgery chronic neck pain, the painful component is partly attributable to the presence of the surgical scar, to the possible manifestation of adhesions and mainly to the onset of contractures. In this case it's recommended the stretching exercise of the scalene muscles, trapezius, scapulae, pectoralis minor and major, together associated with manual therapy and physical exercise [12].

Proprioceptive Exercise

A proprioceptive exercise program can be considered a valuable treatment in patients with neck pain, as Espi-Lopez et al. demonstrated in their study.

Cervical proprioception exercises (including balance exercises, somatosensory stimulation training and joint repositioning training) indeed have shown to decrease pain and disability and increase motility and quality of life in people with neck pain [13].

The sense of joint position depends on proprioception; the development of this sensitivity is responsible for the ability to stabilize a joint during static and dynamic functional tasks.

Physical Therapy

The effectiveness of physical therapy in the reduction of acute and chronic neck pain consists mainly in the use of magnetic therapy, analgesic electrotherapy, ultrasound and laser therapy in its various forms.

A single randomized trial demonstrated a modest short-term efficacy of magnetic therapy in the treatment of acute and chronic non-specific neck pain.

TENS and ultrasound instead, lacking systematic reviews, are recommended in combination with exercise therapy and other methods of physical therapy in chronic neck pain [14, 15].

Laser therapy is recommended for the reduction of neck pain in the short term in both acute and chronic phases [16].

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