New Directions and Therapeutics in Surgical Spine Treatment

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14.1 INTRODUCTION

Spine therapeutics and surgery for spine diseases have undergone long development periods — spine surgeries, particularly laminectomies, have been performed for over a century. Hypotheses concerning spine diseases are now undergoing radical revamping based on new information about the pathogenesis of pain syndromes, basic biology of bone and disc tissue, cellular replacement therapy and stem cells, development of the potential for arthroplasty instead of joint fusion, and refining of knowledge about spine biomechanics and appropriate forms of stabilization.

Additionally, concepts about origins of mechanical and axial pain (as opposed to spinal cord or nerve or root-mediated pain) are continuing to evolve, as is the role of surgery in treatment of axial spine discomfort. Spine surgery developed primarily as an empiric set of treatments for both axial and neurogenic pain and deficit, and is now subjected to more hypothesis-based testing and rationalization of existing therapies for validity. Judgment questions about when to suggest surgery and how to adequately inform patients of possible treatment options continue to resist agreement among spine specialists, particularly because essentially all spine surgery is considered optional and appropriate or helpful only for symptomatic relief under limited clinical circumstances.

This chapter will review many of these new concepts in the treatment of spine diseases, particularly treatments involving surgical approaches. In addition to advances in understanding of spine biology and development of new procedures, judgment decisions about when to perform spine surgery will be reviewed, as will clinical trial needs and formats, particularly the differentiation of clinical trials for device approval versus trials for rationalization of therapy. Chapter 16 will discuss clinical trials further.

14.2 NEW CONCEPTS IN BIOLOGY OF NORMAL DISC TISSUE AND BONES OF THE SPINE

As magnetic resonance imaging (MRI) scans become more ubiquitous, new aspects of the natural history and evolution of spine appearance have evolved. The appearance of a “normal” spine involves well-hydrated disc joints with intact height that appear bright on T2-weighted scans, cylindrical vertebral body appearance, a triangular-shaped spinal canal posterior to the vertebral body with sufficient room for spinal cord and peripheral nerve roots, and specific alignment in both the sagittal and coronal planes. The alignment includes a cervical lordosis, thoracic kyphosis and lumbar lordosis, and various indicators can be used to indicate appropriate overall alignment as well.

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Significant medical and radiological knowledge has accumulated regarding development of the spine (for example, in abnormalities such as spinal schism, spina bifida, and myelomeningocele) and growth of the spine in childhood (growth plates, etc.). However, much of this knowledge continues to be challenged by newer hypotheses and clinical findings, particularly concerning the discs and facet joints and their relationships to clinical disorders of the spine. While MRI scans and radiographs show excellent detail of bones, joints, some ligaments, and nervous elements of the spine, in many cases little or no correlation exists between the findings and patient discomfort or neurological abnormalities.

14.2.1 DISC CELL BIOLOGY

Because most of the spine is developed from notochord, it is natural to consider what remnants of notochord persist through development.\(^2,3\) Chordoma, the most prominent neoplasia associated with notochord, may develop at any time and usually at the midline of the vertebral and cranial axes as a remnant of notochord that has transformed into a fast-growing tumor. One current concept is that initially (until mid-childhood) remnant non-neoplastic notochordal cells remain within the nuclei of disc joints, and these cells contribute to disc hydration. However, after these notochordal cells are no longer present (presumably based on a developmentally regulated schedule), the discs may slowly begin to desiccate due to the lack of cells that enhance and promote hydration. This desiccation may lead to one of the prominently noted MRI features of the spine, namely that exuberant disc hydration (usually visualized on a T2-weighted image) decreases substantially with age. By the age of 40, many patients have highly desiccated discs that appear dark on MRI scans.

Interestingly, much is known about collagen, extracellular matrices, and other structural aspects of discs and how these elements are involved in a slow process of degeneration over a lifetime. Disc cells (including both notochordal cells and chondrocytes) prefer a three-dimensional matrix culture growth system instead of a flat two-dimensional culture system. They respond to both mechanical and osmotic shock in culture and \textit{in vivo}.\(^2,3\) Ongoing work suggests that replacement of notochordal cells (or some equivalent from stem cells) may in some ways be able to repair disc joints biologically.\(^4–11\)

This repair may be limited by vascular changes in endplates with the development of arthritis and perhaps by more limited diffusion of metabolic substrates into disc nuclei as a function of age. Thus, degeneration involves changes in the cellular composition of discs, alterations in diffusion, blood supply to the endplate, collagen disruption, and dehydration, all of which eventually lead to the dark disc appearance on T2-weighted MRI scans and then to narrowing sufficient to give rise to typical osteoarthritic appearances of the endplates.

Any of these alterations could potentially be subject to treatment. Treatment of discs at most levels can be accomplished via percutaneous needle approaches that have been used for many years for various treatments such as chymopapain and percutaneous discectomy approaches.
14.2.2 SPINE BONE BIOLOGY

For most fixation approaches to the spine (such as pedicle screws), the quality of bone may be the limiting feature affecting hardware attachment. For example, in osteoporosis, the pull-out strength of screws is markedly reduced, limiting the ability to provide adequate fixation of the spine in some instances. Many new medical treatment approaches are now used to enhance bone density in osteoporosis, as well as enhance bone healing in fusion (discussed next). One interesting quality of bone is the need for stress and pressure to augment healing. Presumably bone healing follows minute electrical gradients created by stress; small electrical currents can substantially enhance fusion rates.12–14

Many different types of bone fusion electrical stimulators (external to the body and internal near the bone graft) are commonly used because of this enhanced healing process. Likewise, if a hardware construct is too rigid, it is possible that a bone graft may not be subject to sufficient stress (because of shielding by the hardware) for adequate healing. New constructs that allow some slipping with time are touted as potentially increasing bone fusion rates due to persistent steady pressure placed on grafts, theoretically enhancing healing and graft incorporation.

Medical treatments to increase bone density and quality include daily or weekly dosing of bisphosphates. Future options are annual injectable dosing and parathyroid hormone (PTH). Both can stabilize bone density (but not necessarily increase it beyond the baseline) or restore it.

14.2.3 BIOMECHANICS OF SPINE JOINTS

Abnormalities such as scoliosis, lack of maintenance of normal lordosis in the cervical and lumbar regions, and exaggerated kyphosis in the thoracic region have been known for years to change the biomechanical properties of the spine. If the upper torso is not centered over the spine and pelvis, the body may compensate with a secondary tilt at some level, to one side or in the anterior–posterior direction.

In recent years, sagittal balance has become recognized as important, particularly to maintain upright posture comfortably.15 The previous use of fixation devices that led to distraction of the posterior elements of the spine rather than compression in the lumbar region produced the now-recognized flatback syndrome with straightening of the lumbar lordosis.15 Guidelines now cover when to consider surgery for scoliosis and sagittal imbalance problems in terms of progression of abnormal curves over time and patient ability to compensate by using other joints. However, most adult cases of coronal or sagittal imbalance are primarily treated to relieve axial or extremity pain, rather than treating existing or threatened neurological impairments, leading to the elective (and optional) nature of most corrective deformity-related spine surgeries.

14.3 JOINT AND BONE DEGENERATION

The spine, like all other joints of the body, is subject to degenerative changes, usually termed osteoarthritis, degenerative joint disease (DJD), or spondylosis. These terms
imply a slowly progressive set of changes of bones and joints, as the wear and tear of daily life (and also trauma) take their toll on joint surfaces. The literature describes a large number of changes in disc joints, particularly changes in the end plates and associated vasculature, alterations in cell population in the discs, decreased hydration of discs (leading to decreased disc space height and laxity in the annulus), and eventual near-complete loss of discs that causes end-plate surfaces to grate on each other.\textsuperscript{16–18} Likewise, the facet joints (as synovial joints) undergo degenerative processes, possibly leading to loss of joint function that can facilitate the development of anterolisthesis or spondylolisthesis.\textsuperscript{19}

Although these changes are well documented from both radiological and pathological examinations of spine joints, what remains unclear is how these changes may lead to various types of discomfort in certain individuals. Clearly, from a patient standpoint, a wide range of variation in expression of pain related to joint degeneration exists. In some cases, radiology studies demonstrate severe arthritic changes without accompanying pain or discomfort. Even mild arthritis in some individuals may be associated with seemingly severe axial pain. This discrepancy between subjective complaints and objective studies remains unexplained, and is not commonly accounted for in clinical studies of spine surgery performed in many cases primarily to relieve axial discomfort. This topic is further explored in the following sections on disc changes and potential etiologies of back pain.

**14.3.1 Are Disc Changes Involution or Degeneration?**

The concept of development inherently includes a series of genetically programmed changes in cells, leading to growth, proliferation, and maturity. As part of this programmed series, many features such as puberty can be delayed many years, as can maturity of several parts of the brain, particularly the frontal lobes. In this sense of genetic programming of organisms, development is usually considered a “normal” process. However, it is now clear that many aspects of later life, particularly limitation of cell division (for dividing cells) through telomere control, are also genetically programmed in much the same way.

As part of development, cell populations change, and programmed cell death is a critical aspect of maturing and eliminating unwanted and unneeded cells, particularly in the nervous system. Thus, development, maturation, and in many ways the entire life spans of most organisms involve genetically programmed sequences of intrinsic alterations in cell populations, their birth and death, and expression of patterns of proteins. Programmed senescence is commonly termed “involution.” It represents a slow winding down of processes — the inverse of development.

Consider the hypothesis that the primary cells for disc maintenance may be remnant notochordal cells, particularly for hydration and extracellular matrices, and that the growth end plate is the crucial determinant of vascular supply and nutrient diffusion into the discs.\textsuperscript{2} If these crucial cells are programmed to disappear at an early age (perhaps before age 10), the subsequent disc changes popularly termed “degeneration” are inevitable and preset, but may take years to unfold. Perhaps subsequent wear and tear or trauma may partially influence this process of programmed disc changes, but if the basic process is already genetically mapped,
subsequent clinical influences may be minimal. The associated question is the degree to which these programmed changes really represent degeneration or are in fact normal processes akin to growing larger or developing typical frontal lobe properties, such as senses of timing, insight, long-term planning, and initiative that appear gradually over many years during childhood and early adulthood.

Regardless of whether disc changes are truly programmed or degenerative, many patients will want to reverse or treat the process, similar to the way they want to reverse many other aspects of human maturity and senescence. The drive to augment oneself and be normal appears to be inherently human and is universally accepted, as evidenced by the wide variety of medical and consumer products aimed at enhancing or maintaining function as we age. However, mixed with this philosophy of enhancement, is the ambiguity as to whether disc changes produce discomfort or limit function. This ambiguity is highlighted by current studies that indicate disc arthroplasty does not necessarily lead to improvement in axial pain, similar to many clinical studies on disc fusion that argue for careful patient selection. Thus, potential elements and structures within individuals and their spines that can lead to axial pain are still in dispute and often difficult to identify clinically, representing a considerable challenge for disc arthroplasty in general and its clinical role in particular.

14.3.2 What Causes Back Pain?

A recent review by Lutz assessed hypotheses of the origin of axial spine pain over the past 100 years and the evolution of related concepts. The main etiologies presupposed to lead to back pain included neural, muscular, osseous, disc-related, and psychogenic causes. The interesting finding was that at the turn of the 20th century, the most common causes presupposed in the medical literature were neural, muscular, and osseous. After the advent of discectomy in the 1930s, most attention has been directed to the disc joint as the main culprit. In this context, it is important to discriminate clear neurogenic pain due to nerve pressure or damage from axial pain. This distinction is not commonly made in the literature.

A practical rule to differentiate the two types of pain is to draw an imaginary parasagittal plane through the sacroiliac joint for the lumbar region, and similarly for the thoracic and cervical regions. Pain that is primarily medial to this plane may be considered as predominantly axial, and pain that is lateral to this plane (particularly in the sciatic notch and below) is usually predominantly neurogenic (related to the lumbosacral plexus or L5–S1 roots).

Can disc joints be responsible for axial or neurogenic pain? Clearly, many cases of herniated disc can lead to nerve pressure and hence cause radiating arm or leg pain that is adequately treated with discectomy. In many patients, axial pain continues after discectomy, so discectomy is not commonly considered a sufficient treatment for axial spine discomfort. However, some studies suggest that much axial pain can be related to other structures. For example, lumbar discectomy procedures have been done with local anesthesia so that the ability of individual structures to cause discomfort can be specifically addressed. In these procedures, significant back pain can be caused by pressure on or incision of the spinal fascia adjacent to the spinous processes, and some by muscle tension, whereas minimal discomfort is associated with removal of the lamina.
Interestingly, pressure on normal discs (those without previous injury or herniation) does not lead to discomfort; pressure on discs associated with damage or herniation can lead to leg pain (in the absence of nerve root pressure or touch). These now classic human experiments have led to the concept of radicular nerve ingrowth into the annulus after damage (from small collaterals as the ganglion passes the disc joint lateral to the facet), leading to a referred pain syndrome associated with disc pressure. This referred pain syndrome can simulate true nerve pressure, but without nerve pressure signs consisting of motor, reflex, and sensory alterations specific to that nerve root.

Additional studies have used hypertonic saline injections into the spinal fascia adjacent to the spinous processes, to initiate severe axial pain, similar to that associated with a typical episode of acute myofascial strain of the cervical or lumbar region. Likewise, local anesthetic blocks of trigger points within the fascia can at times relieve paraspinal discomfort, suggesting that ligamentous damage can certainly lead to severe pain. This is similar to the incisional pain near the midline associated with even small laminectomy incisions. Thus, from several types of studies, significant back pain appears to be associated with stretch, damage, irritation or contusion of spinal fascia and other soft-tissue mechanical structures, and less with posterior bony structures. Clearly, however, significant axial pain can be associated with vertebral body collapse (as in compression fractures) or with metastatic disease involving and expanding vertebral bodies. This discomfort can be relieved in some cases by vertebroplasty (injecting methacrylate cement into the vertebral body for stabilization)\textsuperscript{28–30} or by radiation treatment of bones involved in metastatic disease.

Because axial pain can be clearly associated with neural, ligamentous, and osseous causes in some cases, what about discogenic discomfort? The standard diagnostic test for assessing discogenic pain is the discogram — placing a small needle laterally through the annulus into the nucleus and injecting a small amount of saline to expand the disc. Presumably this expansion then places tension on the annulus. Unfortunately, this test has proven to be highly nonspecific. Many patients (and volunteers) develop axial pain with the saline injection, making it difficult to differentiate degeneration-associated axial pain from spontaneous discomfort associated merely with the injection of a normal disc. Likewise, spine fusions (usually done anteriorly to avoid the incisional-related back pain of a posterior procedure) may or may not relieve axial neck or back pain, and outcomes vary widely and are highly subjective.\textsuperscript{4,25} Presumably the advent of disc arthroplasty may clarify the role of disc degeneration in the treatment of axial pain but results of preliminary studies to date are mixed at best.\textsuperscript{24,25}

Thus, the conclusion remains that all the major possible etiologies for axial pain can lead to significant axial pain under some circumstances including neural, ligamentous, soft tissue (including muscular), osseous, discogenic, and psychogenic causes. The clinical ability to differentiate these entities has been helped somewhat by the high sensitivity of MRI, but MRI also has a great lack of specificity. In many cases, asymptomatic abnormalities are treated as symptomatic because the two types of abnormalities are difficult to separate.
14.3.3 Differentiation of Axial and Extremity (Neurogenic) Pain Syndromes

If axial spine discomfort is hard to sort out and usually multifactorial, what about neurogenic causes of extremity pain? In most cases, radiculopathy due to nerve root pressure can be reliably determined clinically, and approximately 80 to 85% of extremity pain can be relieved by simple nerve root decompression. Common causes of nerve root compromise include herniated discs and lateral recess stenosis. However, many patients may report referred pain syndromes with extremity pain, but without clear localizing deficits; nerve root decompression is often not helpful.

Additionally, patients with long-standing nerve root pressure or those whose pressure has been spontaneously relieved (i.e., resolved herniated discs) may still experience radicular pain despite demonstrated nerve decompression. In these patients (at least 15% of the population), it is commonly presumed that internal or intrinsic nerve root changes or secondary alterations of the central nervous system (CNS) are responsible for the persistent pain. Subsequent treatments include medicines that function primarily at CNS level (e.g., amitryptiline or neurontin) and direct CNS stimulation.

In these cases, the classic neurosurgery hypothesis of mass effect (i.e., pressure on the affected nerve root) fails and an alternative hypothesis of internal damage or CNS conditioning and retention of the pain memory is required. The latter is clearly demonstrated by nerve root section proximal to the area of damage — an older technique that was very unreliable in relieving long-term radicular pain syndrome.

14.4 Existing Spine Operative Procedures

Operative procedures fall into two main groups: (1) those directed at treatment of extremity pain or involving central decompression of nervous elements, and (2) those directed at spine stabilization or treatment of axial pain. Examples of these will be discussed, primarily as the context to exploring new treatment options currently being assessed. Because of the nature of surgical procedures and the fact that U.S. Food and Drug Administration (FDA) approval applies only to drugs and devices, surgical approaches are not submitted for FDA approval; surgeons are generally free to experiment with surgical techniques.

14.4.1 Laminectomy and Anterolateral and Posterolateral Decompression

The spinal canal is roughly round or triangular on cross-section and bounded anteriorly by the vertebral body, laterally by the pedicles and facets, and posteriorly by the lamina and ligamentum flavum. Depending on the location of an offending lesion, these separate bony elements may be removed to gain access to the spinal canal. By trial and error, the least invasive of these approaches has proven to be laminectomy, which involves unilateral or bilateral (and often spinous process) removal from a posterior approach. While this procedure has the theoretical disadvantage of removing the posterior interspinous ligament (a tension band), the joints (anteriorly the
disc joint, laterally the paired facet joints) appear to provide sufficient mechanical stability. The incidence of postlaminectomy instability varies from 5 to 15% in multiple series, depending on the reason for the laminectomy, position and angulation of the facets, and presence of degeneration, particularly of the facets. Laminectomy has been used for over 120 years to gain access to the spinal canal and remains one of the most common spine operations performed.

Other approaches require different access routes, such as lateral extracavitary, anterolateral (i.e., thoracotomy in the thoracic spine), or anterior. In these cases, more bone must usually be removed for access into the spinal canal. In some cases, the planned bone removal is clearly sufficient to warrant considering a stabilization procedure as part of the primary procedure, including placement of bone, hardware, or both to add stability to the spine. Such stabilization is usually done to maintain normal spine alignment rather than correct a spine deformity, and is usually labeled in situ fusion. In the future, arthroplasty of the involved joint may be performed, although facet joint replacements lag far behind anterior disc joint replacement prostheses. All these procedures are commonly performed and well documented in contemporary spine texts, including details of the technique.

14.4.2 Midline versus Lateral Spinal Canal Syndromes

Spinal canal approaches include those primarily for access to nerve roots laterally or for access to the central aspect of the canal. Two primary syndromes of involvement are well recognized. The first syndrome is lateral impingement on a nerve root, which is likely to give rise to radicular pain and loss of function (motion and sensation). Extensive dermatome maps were compiled in the 1930s from root sections for relief of cancer-associated pain. These dermatome maps include common sensory patterns and motion loss associated with a root section, and can be extended to many forms of root involvement. Common mechanisms leading to lateral syndrome include herniated discs, lateral recess or foraminal stenosis, and nerve root tumors.

The second syndrome is central and consists of myelopathies in the cervical and thoracic regions (due to spinal cord involvement) and multiple root pressure in the lumbar region (as is noted in neurogenic claudication). Common reasons for spinal canal involvement include stenosis from degenerative changes, intramedullary (within the spinal cord) or extramedullary (outside the spinal cord) tumors, and internal conditions within the cord or nerve roots.

14.4.3 Mechanics and Principles of Spine Fusion

Spine fusion without instrumentation dates back to the 1940s, when healing fractures only with immobilization was insufficient. The period of immobilization was often 3 to 6 months, usually in an in-patient setting. Fusion was considered to augment healing. The advent of anterior cervical spine and anterior lumbar spine fusion procedures in the 1950s brought on an era of fusion of degenerated joints not previously subjected to trauma. That development led to fusion of degenerated joints both for neurological decompression and also to treat axial pain.
For a time, posterior fusion alone was considered an alternative to posterior laminectomy and discectomy, based on the hypothesis that immobilization of the segment would eventually lead to improvement of the radiculopathy. As treatment of severe scoliosis and other spine deformities became common, it was realized that external bracing and noninstrumented fusion had severe limitations and relapses ensued. Therefore, Harrington and others developed instrumentation for spine fixation.

Between 1980 and 1990, a large number of new instrumentation devices to augment fusion arrived on the market. Interestingly, many were used without specific FDA approval for the spine indication — most of the hardware for posterior instrumentation, such as thoracic and lumbar pedicle screws and lateral mass cervical screws. These screws were adapted from long bone use, together with plates and rods with which to connect them. However, because of the policy of “grandfathering,” many types of anterior instrumentation such as anterior cervical plates, and anterior thoracic and lumbar instrumentation became FDA-approved. More recently, lumbar pedicle screws have become approved for limited indications such as severe L5–S1 spondylolisthesis. However, for many years, the use of instrumentation for nonapproved uses was somewhat in limbo legally, even though it was commonly used clinically.

The general principle of instrumented fusion is to provide internal support for vertebrae, thus improving fusion rate and providing stability while healing occurs, or correcting a deformity so a fusion occurs in a better anatomic position. For example, noninstrumented lumbar lateral fusion (intertransverse process) appears to show a radiographic fusion rate of 65%; the same fusion approach with pedicle screws shows a 95% radiographic fusion rate. Pedicle screws also demonstrate another principle, that of 3-column support, since the screws traverse the posterior elements into both posterior and anterior aspects of the body. This support, depending on bone quality and degree of fixation, offers considerable initial rigidity. However, another principle is that if the bony fusion fails to fully develop, the hardware will eventually loosen and/or break. Thus, assessing hardware stability can determine whether or not fusion has occurred. In addition to the hardware implanted in the spine, an external orthosis such as a cervical collar, lumbar corset, or brace may be used for additional support. Bone stimulators also may augment fusion, either as implantable or externally applied devices. Since bone growth follows lines of stress and secondarily generated electrical force lines, the addition of an artificial electrical field, even of small magnitude, appears to augment bone growth. These general principles will be elaborated further in the sections on novel treatment.

Current spine instrumentation measures approved by the FDA include the anterior cervical plate, posterior Harrington and other devices for deformity correction, anterior thoracolumbar plates and devices (Z-plate and Kaneda instrumentation), and pedicle screws for spondylolisthesis at L5–S1. Additionally, a variety of horizontal and vertical cages are available for implantation in the disc space. All these devices achieve immobilization to augment fusion instead of joint replacement devices to augment motion.

Because these devices by nature provide rigid constructs with immobilization, the inevitable force usually transferred through joints (now removed or immobilized)
must be transferred to adjacent segments. Adjacent segment stenosis may affect all spine segments, in which potentially degenerative changes may progress faster next to immobilized segments because of the need to shoulder more stress of motion. Theoretically, spine arthroplasty should alleviate this accelerated degenerative change through augmentation of motion.  

14.4.4 KYPHOPLASTY AND VERTEBROPLASTY

Interventional procedures are available to treat collapsed and painful vertebral bodies. Common indications include osteoporotic compression fractures associated with severe axial pain and metastatic cancer involvement of the vertebral body.  

Vertebroplasty involves bilateral injection of methacrylate into vertebral bodies via a transpedicular percutaneous approach. Kyphoplasty requires placement of a balloon into a vertebral body for restoration of height, then insertion of methacrylate to maintain height. Both procedures are usually done under fluoroscopic control. Complications include transfer of emboli of methacrylate into the lungs and posterior extrusion of methacrylate into the spinal canal if a posterior vertebral body defect is present. These procedures are commonly performed to treat subjective indications of severe axial pain, usually a few weeks after a fracture to allow the initial pain to resolve, but less than 6 months after the fracture. A possible (and fortunately very rare) complication is infection in the methacrylate that requires removal of the entire body, presumably through drilling away the dense plastic. While the approaches are well established, few controlled studies have focused on their clinical value and usefulness. Newer substances for injection such as hydroxyapatite cement and bone morphogenetic protein (BMP) are future directions for these techniques.

14.4.5 OUTMODOED FDA-APPROVED PROCEDURES

A large number of outmoded approaches and devices, often with FDA-approved indications, are no longer routinely performed. Examples include chymopapain, most of the percutaneous discectomy approaches (such as laser discectomy), and many types of instrumentation including various cages. Once a device is approved for use by the FDA, its manufacturer rarely stops production except in cases of significant safety concerns. With many of these approaches such as percutaneous discectomy, only safety studies were performed. Few or no efficacy studies were required (see Chapter 1).

The efficacy studies were all performed after introduction to the market. After 2 to 3 years of use and study, the approaches were by and large abandoned. Thus, FDA approval is only the initial step in gaining true market approval of a device or approach because FDA approval studies are performed usually by a manufacturer or clinical enthusiast and are usually poorly controlled. After FDA approval is obtained, the clinical skeptics can perform independent studies if a clinical need exists. In many instances, these secondary studies are marginal at best in terms of demonstrating efficacy.
Another reason devices become outmoded is replacement by better ones. Several generations of anterior cervical plates are now available. The newer versions offer easier use, locking mechanisms to prevent screw back-out, lower profiles, and assorted sizes — often at increased cost. The newer versions clearly eclipse many older versions, including the original Caspar plate that was difficult to apply in practice and led to many complications.

14.5 NEW SURGICAL PROCEDURES IN DEVELOPMENT

Evolution of surgical procedures is natural, and in general such transformations do not require FDA approval (only devices or instruments do). In addition, many new procedures have been modified or enhanced by the availability of novel devices and instrumentation. Recent introductions to the market include frameless, fluoroscopically guided computer systems to aid hardware placement. Examples include the Stealth Medtronic, Fluoro-Nav, General Electric and InstaTrak systems.

Since these devices are surgeons’ aids and not therapeutic devices in their own right, they require a different category of FDA approval. The evolution of devices for stabilization has been constant. Devices on the market now include a full series of occipital-to-cervical fusion sets, cervical plates, adjustable screws, anterior plates, improved thoracic and lumbar posterior instrumentation, and a large variety of horizontal and vertical cages. Such devices will not be further detailed, but there is now an evolution from fixation and fusion hardware to arthroplasty for maintenance of motion.\(^{1,8,17}\) Interestingly, the spine is one of the last bastions of fusion treatment of joint malfunction because decreased motion at one or a few segments usually does not detract significantly from overall spine function.

Several orthopedic concerns have transformed bone and joint surgery: advanced knowledge of joints including degeneration and replacement, bone and fusion biology and enhancement of both, and outcome measures to estimate whether surgical procedures are worthwhile. The surgical procedures and advances introduced earlier will be discussed in sequence.

14.5.1 IMPROVEMENTS AND RATIONALIZATION OF LAMINECTOMY

Technical aspects of laminectomy have been debated for many years. One of the current discussions centers on what may be considered a minimally invasive laminectomy. One suggestion is a bilateral hemilaminectomy for lumbar stenosis, sparing the spinous process and interspinous ligament, but resecting part of each facet to achieve bilateral lumbar decompression. This is in contrast to a facet-sparing laminectomy, where the spinous process and medial aspect of the lamina are resected, but the facets are only undermined rather than trimmed.

This is one example of the small, technical changes that are constantly debated, although the outcome from overall surgery may still require further studies to fully define. As is common in many surgical disciplines, this differential approach lies in the category of surgeon preference, rather than relying on substantive biomechanical or clinical outcome studies to support one approach or another.

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Most laminectomy procedures are performed to treat degenerative changes such as cervical or lumbar stenosis to achieve root or central (spinal cord or cauda equina) decompression. In general, laminectomies are elective procedures with usually subjective endpoints. An excellent example is decompression for cervical stenosis associated with cervical myelopathy. Treatment of this disorder has a long history. Over time, the recognition of the syndrome and MRI diagnosis have consistently improved, but no natural history studies have accompanied the improvements.\(^{31-33}\)

Earlier studies in patients with severe myelopathies indicate progressive worsening over time, but the degree of worsening and the influence of surgery on the disorder remain poorly characterized. In addition, many surgeons now suggest decompression for asymptomatic cervical stenosis without clinical signs suggestive of myelopathy. As in the case of carotid stenosis and associated symptoms of either transient ischemic attacks or stroke, a clear delineation is required to assess how patients fare without surgery and determine the impacts of surgical decompression over the short and long runs, especially compared to the risks of surgery.

Preliminary randomized studies suggest that, at least in milder myelopathy patients, surgery produces no net benefit.\(^{37}\) Although practitioners agree on the need for a full randomized study of all forms of cervical myelopathy,\(^ {38}\) the format and mechanisms of such a study remain highly contentious. This is one area where rationalization of the need and outcome for surgery is important to obtain. However, market forces and lack of collaboration among surgeons tend to forestall such a common multicenter action.

There is a perceived need among surgeons for increased information about outcomes from surgery and what types of surgery to perform. For example, when should a fusion be added to a laminectomy? Additional questions relate to improved patient education: which symptoms are really treatable with surgery and how can we optimally advise patients on surgical outcomes and risks?\(^ {39}\)

### 14.5.2 New Developments in Fusion Technology

The outcomes of surgical fusions have dramatically improved with advanced hardware over the past 20 years. Further improvements are expected with the use of bone-specific growth factors, particularly BMPs.\(^ {35,40,41}\) Most of the large number of growth factors are involved with promoting bone growth and development. Currently approved forms of BMPs involve rigid applications such as within cages to avoid dispersion to tissues where bone growth is not wanted.\(^ {42}\) New formulations for posterior lateral (intertransverse process) fusions to replace the onerous iliac crest autograft placed on the transverse processes to enhance fusion are in clinical trials.

Because one of the issues with instrumented fusions is rigidity, and hence the tendency to transfer stress to adjacent segments, one consideration is the return to noninstrumented fusions with enhanced rates of fusion augmented by BMPs. Other new techniques include gene therapy for transfection of BMPs and other growth factors, again with the primary goal of enhancing fusion.\(^ {41,43}\) Such approaches do not restore motion unless there is consideration of joint enhancement, such as with stem cell replacement of chondrocytic joint surfaces or replacement of notochordal stem cells for disc replacement.\(^ {17,8}\) Clearly, a large number of possibilities exist.
because mesenchymal stem cells are readily available and likely easier to induce to specific fates than neural stem cells due to the markedly fewer fates possible.\textsuperscript{10}

14.5.3 Cervical Arthroplasty

The primary consideration for joint replacement has focused on disc joints because they are more accessible and larger than the facet joints, which are synovial. Synovial joint replacements are available for small joints, such as finger joints in rheumatoid arthritis. They have also been considered for additional replacement of a disc joint at a single segment and also the two facet joints. The Frenchay artificial cervical joint has now been in use in clinical trials for several years, but has not yet received widespread approval.\textsuperscript{44}

As with many prototypes, certain issues must be resolved: anchoring the artificial joint within adjacent bodies and long-term functioning of the joint, but it is expected that further prototypes will be developed. Ideally, an artificial joint would be used with every anterior cervical procedure, instead of allografts or autografts, to preserve motion segments and prevent or forestall the long-term progression of degenerative changes at adjacent levels.

14.5.4 Lumbar Disc Arthroplasty

Lumbar disc joint replacement likewise is primarily under consideration for early disc degeneration — a condition treated presently with anterior lumbar fusion.\textsuperscript{25} A disc replacement should be as easy to insert as an anterior cage. It should tightly hold into adjacent endplates and be able to withstand considerable wear and tear over time due to the large stresses imposed on lumbar disc joints. Current prototypes are not yet ready for widespread clinical use and they need revisions and better clinical trials to achieve full clinical integration.\textsuperscript{24,25}

14.5.5 Stabilization without Fusion

To provide stability while avoiding the complications of fusion surgery, a pedicle screw system with an elastic synthetic compound is used to control motion. Early studies are promising, but long-term results are not yet available. One indication for this type of nonfusion fixation is segmental instability with stenosis.\textsuperscript{45}

14.6 Judgment Decisions and Patient-Informed Consent

Because most spine surgery falls into the elective and optional category of medical treatment, considerable judgment about when to propose a procedure is required on the part of a surgeon. Judgment and sufficient understanding are also required of a patient so that he or she can truly give informed consent. Clearly, different surgeons have different indications as to when they propose various procedures. Wennberg initially demonstrated the wide variation that exists even on a small scale by performing a regional analysis of the rates of spine surgery.\textsuperscript{46}
Subsequently studies of large Medicare regions throughout the U.S. showed less variation due to averaging across multiple practitioners within each region.

It is clear that some surgeons may consider a procedure worthwhile if 90% of the patients to whom it is offered may benefit; another surgeon may view a 60% likelihood of improvement as an adequate measure. Although most surgeons assess such decision making on a patient-by-patient basis, the preference can persist over many patients to create an average. One factor in such decision making relates to patients who do not improve with operative intervention. The larger the percentage in this group, the more a surgeon will be challenged by poor results and over time will likely adjust his or her judgment. However, the origins of judgment tend to be based partly on training and experience, so such adjustment may not necessarily occur.

14.6.1 What Spine Problems Are Susceptible to Operative Procedures?

Spine surgery is clearly very common in the U.S., particularly compared to the U.K., suggesting that different standards and indications are applied in the two regions. Thus, the question arises: is spine surgery in the U.S. suggested too often and for less than reasonable indications? Since most surgery is for relief of pain (clearly a subjective outcome), does the frequency also reflect the tendency in the U.S. for a desire among patients to be completely pain-free? These are thorny ethical issues that many spine surgeons in the U.S. find uncomfortable to contemplate, although they relate to other forms of optional medical care such as plastic surgery or enhancement of bodily functions.

14.6.2 Appropriate Patient Information and Basis for Informed Consent

Patients commonly have misconceptions regarding spine surgery and these misconceptions are rarely discussed. One approach has been to develop a patient video that provides both information and describes surgery from a patient’s perspective. Two common misconceptions were identified. The first was that “the MRI scan will tell the doctor what is wrong with me.” Patients do not appear to recognize the high number of asymptomatic abnormalities and may not understand that clinical interpretation of MRI scans requires integrating patient symptoms with MRI findings. The second misconception was that “surgery is 98% effective for back pain.” Thus, patients commonly perceive that MRI scans are critical. In reality, for most evaluation purposes, an MRI scan represents one piece of clinical information that may or may not be concordant with the patient’s symptoms.

These results highlight the nearly ubiquitous use of MRI scans for assessing spine abnormalities due to common availability and a low degree of invasiveness. However, from a surgeon’s perspective, it is common now for patients to treat MRI findings as their primary concerns instead of subjective symptoms such as back and leg pain. In other words, considerable patient concern surrounds even asymptomatic findings on MRI scans, particularly osteoarthritis and age-appropriate degenerative changes.
The video presentation developed to educate patients involves an unbiased explanation as to which symptoms actually improve with surgery and the realistic likelihood of improvement. Because spine surgery is optional and best considered helpful for specific problems, this likelihood can be estimated for each predominant symptom such as radicular pain or axial pain, depending on the specific surgery. The likelihood of worsening (risk) can also be explained. An excellent aspect of the video presents various patients’ perspectives indicating whether their symptoms were sufficiently bothersome to make surgery worthwhile. Contrasting views are presented. In the example of lumbar stenosis with walking-related pain, the ability to walk only a limited distance without pain may be a severe disability for one patient while another may not be bothered by this limitation. Presenting opposite patient perspectives regarding interest in elective surgery for the same basic problem allows a patient to understand that (1) surgery is not necessary in an absolute sense but can be helpful for certain problems and (2) surgery involves a certain rate of helping and a certain rate of worsening from unexpected problems. Thus, a balanced approach to making a surgical decision includes placing a patient’s symptoms (and underlying condition) into perspective. A patient should understand that the surgical treatment is not perfect but can be helpful, depending on the symptoms and the patient’s underlying concerns regarding the procedure.

The critical knowledge needed for an individual to make a good decision regarding surgery varies considerably from patient to patient and a surgeon’s recommendation may weigh heavily in the decision. The basic principles upon which the surgeon must touch to obtain a fully informed consent include describing patient-specific outcomes in specific terms the patient can fully understand, the salient risks of the surgery (in basic categories, using the concept that certain individuals may be affected if a problem arises), the lack of guarantee (except that the surgeon, of course, will try to avoid problems), and the need for recovery time.

Included in this discussion should be the patient’s perception about the surgery (some patients are very worried about “going under the knife”) and the underlying disorder. These are all complex factors that feed into the decision. One critical feature of the decision to elect or decline surgery that should be emphasized to patients is that surgery is irreversible, so both the patient and surgeon must be committed to caring for any postoperative problems. Likewise, the possibility that a positive benefit from surgery may or may not occur, depending on the outcome identified preoperatively, is a difficult principle to explain to patients who always expect to be fully relieved of their problems.

Figure 14.1 illustrates facets of the problem of a lumbar herniated disc. The patient’s perspective involves two main concerns: the resulting leg pain and whether the underlying disc problem (regardless of pain) could lead to future back problems (i.e., is the problem serious?). From the patient’s perspective of surgery, residual back pain (not considered to be helped by the procedure) may be the most troubling problem, and far outweigh the relief of leg pain at a later date. From the surgeon’s perspective, a lumbar discectomy is considered an excellent procedure, but caveats are usually relayed to the patient in terms of relative relief of back versus leg pain. From society’s perspective, the surgery may or may not be worth performing, depending on whether the patient promptly returns to work and whether his or her
care will consume exorbitant resources. What is clear is that the same medical problem and the same surgical procedure are valued very differently by patients, surgeons, and society.

14.6.3 **WHEN IS A SURGICAL PROCEDURE “NECESSARY?”**

Patients often ask whether it is “necessary” to have surgery when it is suggested as an option. “Necessary” is defined medically as clinically indicated and implies serious consequences if the surgery is not performed. Examples of clearly “necessary” surgery include life-saving procedures to treat acute epidural hematoma with deteriorating mental status or performing a carotid endarterectomy with clear neurological symptoms and severe carotid stenosis. In both situations, the clinical condition is obvious or significant medical evidence has accumulated. Hence, the surgical procedure may be highly recommended and in some cases, life-saving.

Many conditions and diseases have obvious consequences if surgery is not done, for example, a severe infection that may worsen. Most spine surgery does not fall

![FIGURE 14.1](See color insert following page 146.) Multiple perspectives on lumbar disc herniation. The center component is one of the most common spine problems: lumbar disc herniation. There are three different perspectives on the disease and surgical treatment, depending upon the vantage point. The patient, the surgeon, and society all have different views of definition of outcome and whether a surgical procedure is worth undertaking.
into the “necessary” category based on obvious clinical criteria or medical evidence. The context into which most spine surgery clearly falls is optional, but clearly helpful under appropriate circumstances. In other words, options are available. Whether or not to opt for a surgical procedure depends on a balance of benefits, risks, and patient opinion. From a medical view, indications have been developed for medical conditions in which surgery may be appropriately considered an option and thus medically indicated. In this context, cervical decompression for spondylotic myelopathy is cited as a standard approach that most surgeons usually recommend. Even then, many patients demur, and no strong medical evidence indicates what the best course of action may be.

14.6.4 Is There a Role for Prophylactic Spine Procedures?

A high standard of evidence is required to perform surgical procedures for preventative purposes on otherwise asymptomatic individuals. Two neurosurgical conditions are examples where the evidence strongly points to performing procedures, the purpose of which is only to treat potential future (but likely) occurrences rather than make the patient symptomatically better. These examples are clip ligation of symptomatic (previous subarachnoid hemorrhage) cerebral berry aneurysms to prevent rerupture (and possibly worse consequences such as death) and treatment of symptomatic carotid artery stenosis to prevent stroke. Studies performed to show whether to treat these two conditions (berry aneurysms and carotid stenosis) in the absence of premonitory symptoms have been problematic.

The major factor determining whether the low rate of conversion of asymptomatic to symptomatic status is worth a procedure is the actual risk of the procedure. Thus, when the risk that a patient will become symptomatic is low and a procedure has tangible risks, considerable long-term data on the natural history of the disease and the impact of the disease on health status are required to make a convincing case for preventative surgery.

Asymptomatic cervical spinal stenosis and cervical spondylotic (compression) myelopathy with stenosis (symptomatic stenosis) provide an interesting contrast. Many patients have MRI scans that show degrees of spinal cord compression or deformity due to cervical degenerative (spondylotic) stenosis without clear myelopathic symptoms. In contrast, some patients who have abnormal MRI scans showing both stenosis and abnormal signals within the spinal cord usually demonstrate some forms of spinal cord-related symptoms. While we can argue for offering surgical decompression to patients with symptoms (to stabilize their symptoms), can the argument be extended to prevent an unknown event (development of cervical myelopathy) from occurring?

No natural history data are available on the progression of cervical stenosis, the likelihood of developing myelopathy, or the determination whether patients fare better than this natural history after undergoing cervical decompression. As in the case of asymptomatic carotid artery stenosis, a large randomized, follow-up study with a clear natural history arm would be required to delineate whether any net benefit would accrue from an aggressive (presymptomatic)
surgical approach to cervical stenosis. Because cervical stenosis and cervical myelopathy are common problems, such a study is feasible if interest among surgeons and a commitment for long-term follow-up to assess outcomes in patients are present.

14.7 WHEN SHOULD CLINICAL TRIALS BE PERFORMED AND BY WHOM?

Clinical trials in general and randomized clinical trials in particular remain very controversial in spine surgery, except for small studies evaluating new technology. Because spine surgery is very common, it produces a large impact on society in terms of costs and standard issues arise as to how to effectively perform unblinded trials of surgical treatments. Although other trial formats are possible (open label or cohort trials), randomized trials still offer the most efficient route (in terms of patients and money) to answer clinical questions provided sufficient interest and funding are available. Chapter 15 gives further information on possible clinical trial formats for making decisions about surgical procedures and outcome measures.

Although objective outcome measures are known for many spine syndromes, in most cases spine surgery is performed for subjective relief of pain and quality-of-life measures are critical to determine whether a patient perceives the same benefit from the procedure as do surgeons (Figure 14.1). Thus, careful selection of objective, measurable outcome measures and issues related to quality of life (i.e., SF-36 [36 questions to assess general health status], etc.) are important for assessing the impact of a surgical procedure on a patient’s life.

14.7.1 CLINICAL TRIAL FORMATS

Randomized, effectively powered pivotal studies are usually not required for FDA approval of devices. Most devices achieve approval in other ways such as grandfathering and relating to older devices (see Chapter 1). The clinical trials performed for device approval are usually performed by “enthusiasts,” who have often been involved with development of the device and are interested in bringing it to market. Because enthusiasts believe strongly that their device is both efficacious and worth marketing (otherwise why would they do the work?), they are biased because of this outlook and also by substantial financial incentives. FDA approval studies ideally should be performed by clinicians who have no stakes in the outcome.

After a device is FDA-approved, secondary studies are commonly performed by “skeptics” who have no stakes in the results to assess more critically the worth of a device in practice. In many cases, devices become outmoded because of these secondary studies and overall lack of market approval. For example, percutaneous discectomy procedures have by and large been abandoned because of lack of efficacy. Thus, should efficacy and safety be determined by external, critical randomized trials before new hardware becomes FDA-approved?
14.7.2 FDA APPROVAL REQUIREMENTS

The FDA regulates marketing of devices and drugs, for considerations of safety and to assess manufacturing standards, to ensure that optimal practices are used in the initial testing and production. The FDA is particularly careful about surgical implants because of their permanent nature. All spinal instrumentation components are characterized as significant risk devices. The typical steps in device approval are that a company obtains an investigational device exemption (IDE) for initial clinical testing, which certifies that both appropriate animal studies and manufacturing requirements have been met (see Chapter 1).

After initial feasibility clinical studies, pivotal safety and efficacy studies are performed for final approval, unless a device is substantially equivalent to one already on the market. It is important to remember that the FDA does not regulate surgeons; it only regulates manufacturers and marketing. It can require labeling of any device or drug to indicate FDA-approved uses, however. It is important to explain to patients that nonapproved uses are not necessarily experimental and that it is up to the individual physician or surgeon to decide what is appropriate.

For many years pedicle screws (and other posterior instruments such as cervical screws) used for spine fixation (for fusion augmentation) were not FDA-approved for that purpose. The final consensus was to recommend them, indicating to patients that in the surgeon’s experience such devices (such as pedicle screws) were optimal for the condition even though they were not specifically approved by the FDA for such use. “Off-label” uses of drugs or devices by individual physicians or surgeons are common and accepted, but a practitioner should have a good rationale for such use if questioned.

14.7.3 ENTHUSIASTS AND SKEPTICS

Improvement in treatment is a natural extension of patient care and the perception of less-than-optimal treatment schemes in current practice (or less-than-optimal outcomes in patients) is a strong force for developing better or newer approaches to treatment. Such alternative approaches could be new surgical methods, new devices, or new treatment protocols.

Generally, one individual or a group of clinical investigators has sufficient energy or enthusiasm for development of a new concept in spine surgery, and tends to be the force behind development, clinical testing, and often FDA approval of a new device. However, in the process of developing a new approach or device, the enthusiasm is high because the new approach is better than conventional treatment (or else it would not be worth developing). This investigator enthusiasm could also extend to a new device from which the investigator may receive royalties or other financial compensation for development and eventual use. Clearly, the enthusiastic developer does not necessarily maintain an objective viewpoint on the overall worth of a new approach or device. However, in spite of this bias toward presumed usefulness or efficacy, the enthusiast is usually responsible for the FDA approval process in terms of providing data sufficient to ensure approval.

Thus, by the time the FDA has approved a new device (as opposed to a new drug), only one clinical trial may have been performed by the developer or enthusiast.
who has considerable subjective bias in favor of the device and who focuses more on safety than efficacy. It is then commonly left to the market to sort out (after FDA approval) the value of the new device. Usually at the time of product introduction, a consortium of independent investigators (skeptics) has begun to organize, and often they do not share the blind acceptance of the worth of the new introduction to the market. In many cases, clinical trials to assess the true worth of the approach or device will then be conducted by the skeptics, often leading to abandonment of the product (despite the existence of FDA approval). This has happened many times. For example, percutaneous discectomy approaches (such as chymopapain) are still FDA-approved and available, but are rarely used because of a lack of demonstrated efficacy or unacceptable side effects.

As noted, FDA approval data are usually insufficient to satisfy a skeptic’s thirst for both efficacy and safety information, although usually preliminary safety information may be known. One consideration may be to have skeptics (those not involved with the development of an approach or device) available to assess efficacy and safety prior to FDA approval. Another suggestion is for FDA approval to require scientific data beyond those provided by the company or enthusiasts, particularly a controlled trial performed by independent investigators.

### 14.8 CONCLUSIONS

There are many significant areas of conflict related to advances in spine therapy. For example, if arthroplasty were to become more widespread, interest in fusion enhancement might drop rapidly because of a decreased need for fusion procedures. Although many new devices are constantly in development, the actual value in practice of these new approaches and devices remains unknown, particularly in relation to existing therapies.51

In many cases, the enthusiasm for something new (and the equation of this enthusiasm to an improved outcome) can overbalance a rational approach to deciding value. Significant judgment questions remain about spine surgery in the United States, particularly procedures performed for treatment of axial pain syndromes. The answers in terms of how to decide the location and type of pain generator for subsequent surgical attack remain murky. Thus, spine surgery is at a very active point in its history. Because technology constantly provides new equipment and approaches, rational decision making based on the efficacy of new technologies is almost completely lacking.

Due to the rapid flux of devices, techniques, and surgical approaches, rationally designed clinical trials often are too cumbersome and cannot keep pace with technology development because the time requirements for initiating and concluding studies may range from 5 to 7 years. If a surgical technique or device under study is a “fad” and becomes rapidly outmoded, any trial is of historical interest only. As a result of this concern, few trials are performed and practitioners have scant data upon which to build clinical decisions for patients. Improved premarketing clinical trials may limit device development, but could bring more order into the highly complex clinical environment of spine surgery.
REFERENCES


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