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New Horizons in Spine Treatment

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A multidisciplinary journal for patients and spine specialists

THE JOURNAL OF THE SPINAL RESEARCH FOUNDATION
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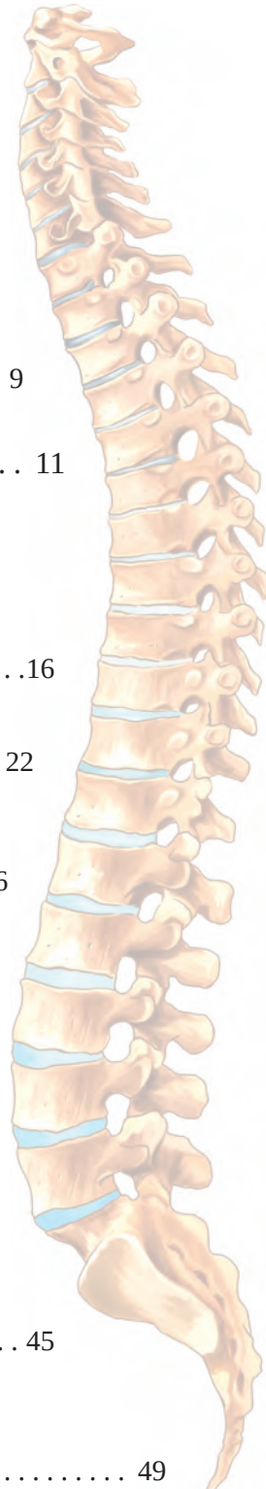
Table of Contents



From the Editor

Brian R. Subach, M.D., F.A.C.S.

I am excited to present to you this *Journal of the Spinal Research Foundation* which focuses on new horizons in spinal surgery. In shaping this issue, we brought together experts from various fields to present their thoughts and ideas about the future of spinal health care and to comment on the techniques that are shaping the future of spinal surgery.

In referring to new horizons, I believe that there are three aspects of spinal surgery which will continue to evolve. The first is the use of minimally invasive techniques. Such approaches to decompression and fusion of the spine have made significant improvements secondary to advances in imaging technology. Computer systems which combine CT scan, MRI data, or x-ray into three-dimensional images increase the accuracy of identifying the critical structures, making the procedures both safer and less uncomfortable for the patient. One such example is the Mazor robotic technology. This computer platform allows CT scan images to be mapped to the patient's x-rays while that patient is on the table. This gives unparalleled accuracy and precision in identifying critical structures and placing hardware in sensitive areas of the spine.

The second advance which deserves comment is the advent of motion-preservation approaches. Typically for degenerative conditions, arthrodesis, or fusion procedures, have been performed to stabilize segments which were painful or unstable. Now using arthroplasty, or artificial disc techniques, there are real and proven alternatives to fusion technology. Although only FDA approved for single-level cervical and single-level lumbar disease, surgeons across the globe have been pushing the envelope and performing multiple arthroplasty procedures in the same patient. In some cases, a hybrid technique using both arthrodesis and arthroplasty (fusion and motion preservation) in the same patient seems to work optimally.

The third and final area which represents a new horizon has to do with regenerative strategies for the spine. As we are all well aware, the aging process causes discs to deteriorate, cartilage to wear away, and bone spurs to form. This progressive wear and tear is unavoidable as one ages. Many times, based upon body weight or choice of exercise regimen, these degenerative changes can be accelerated. It is possible to utilize injection therapy to stabilize unstable ligaments. In a technique known as prolotherapy, using either salt water or sugar water to cause an inflammatory response, ligaments will actually scar, tighten, and stabilize. Additionally, research is being done using bone marrow aspirate, autologous fat grafting, and cartilage-forming stem cells. These materials can be taken from the patient and injected directly into a degenerating disc. The hope is that the aging process, which causes the loss of the vital cellular elements of the disc, will reverse. By populating a disc with new cellular elements, it is possible to turn back the clock of aging and avoid an open surgical procedure.

I would also like to draw your attention to the upcoming Spinal Research Foundation's, "We've Got Your Back" Race for Spinal Health, to be held May 18, 2013 in Reston, Virginia. The website at www.SpineRF.org has a listing of all of the race sites and dates around the country.

Finally, I would like to call special attention to our Spinal Hero, Dr. Thomas Schuler. Dr. Schuler is an expert in the non-operative and operative care of spinal disorders who takes excellent care of his patients, but he is also an advocate for spinal health care, both on a national and local level. It is heroes like Dr. Schuler who make a difference in patients' lives every day.

From the President

Thomas C. Schuler, M.D., F.A.C.S.

Monopolies in Health Care are Limiting Patients' Options

Spinal health care has advanced immensely, especially in the past twenty years. Through advancements in knowledge and technology, we are able to help heal people rapidly with minimal down time and maximum restoration of their normal activity levels. This is all accomplished through improved diagnostics and therapeutic agents, improvements in surgery (both open and minimally invasive), and improved rehabilitation. We have disc arthroplasties, motion preserving devices, biologics to accelerate fusions, improved spinal instrumentation, minimally invasive surgery, and more. This is all exciting and great news. The problem is that an individual American's access to these life-changing interventions is diminishing because of changes in health care reimbursements. Insurance companies are searching for ways to deny treatments in order to save their dollars and improve their profits. The government is doing the same. The problem is that we are on a rapid course to a single-payer system, in function if not in form. There has been extreme consolidation in the health care market, and the public is not aware of it.

When I founded The Virginia Spine Institute over twenty years ago, there were greater than twenty insurance companies willing to offer up to thirty different types of insurance policies for the employees of my organization. In 2012, while we were negotiating our insurance renewal, there were only four companies, each offering a maximum of three different policies. This consolidation has been fueled by market forces, as well as legislation.

Wall Street and government policy led to the housing crash of 2007. Wall Street created significant, bad investments by combining toxic assets with reasonable assets. Once the housing bubble burst, Wall Street could no longer make money in that sector. Since that time, Wall Street has moved on to other sectors to pillage. One significant focus in the past five years has been the health care sector. During this time, a significant increase in mergers and acquisitions has occurred amongst hospitals, insurance companies, and various provider organizations. The result of these monopolies is a decrease in the number of options available for consumers. As the number of insurance providers dwindles, it is easier for the remaining insurers to deny coverage for a service for which they, unilaterally, choose to not pay. This problem is exacerbated by the fact that the government and these private insurers are cross-sharing their denial information, all leading to decreased access to life-improving interventions. This is what we have been living with at an accelerating rate during 2012, and it will only greatly worsen over the next several years as the new health legislation is further implemented, resulting in one large monopoly.

The difficulty in surgical fields is to meet what some of these rationing forces interpret as scientific proof that a treatment works. The insurance companies have hired for-profit companies to create policies to determine which care will be reimbursed. These hired guns are requiring human experimentation to validate surgical procedures, thereby enabling insurers to use unobtainable standards to create policies which deny care.

It is very difficult in surgical procedures to effectively and ethically perform randomized, blinded trials. Herein lies the catch-22 that exists in modern health care. Although we know with great certainty and great outcomes data that certain procedures work, insurance companies and the government choose to disregard this data since they claim it has not been validated in a randomized, blinded prospective fashion. In addition, if any corporate funding has been involved in the research, which meets their arbitrary requirements, then any data that meets these strict criteria is disregarded because, again, it is unilaterally viewed as biased. The problem only worsens because, where is the funding for these costly research projects supposed to come

from, if not from the companies invested in selling their advances?

Denial of service is the easiest cost-saving maneuver for insurers and the government. Failure to provide access to appropriate interventions, surgeries, and therapies will greatly decrease the quality of life for millions of Americans, as well as prevent their ability to be gainfully employed and be active members of their families and society. It is critical as we move forward that we continue to understand the miracles of modern medicine that are possible when competent spinal specialists are allowed to perform their technical abilities as determined by their educated assessments of each individual's situation. Spinal surgery is the most complex area of health care, and there is great variability in the individualized treatment that is required to resolve each person's specific pathology, anatomy, and social situation. No prospective, randomized studies will give us the answer to all of the situations or even to most of the situations in spinal health care. Large outcome studies can show us trends and ideas, but individual decisions will need to be made. Because of the rapid consolidation of the health care market, we will end up with one government insurer, through CMS, covering the government insured and one to three private insurers covering the rest of the country. Decision making will become centralized, thus removing it from the hands of the physicians and patients. Bureaucrats and "professors of evidence-based medicine" will dictate standard care or one-size-fits-all care. This will cause loss of access to care for Americans who require these life-changing and, more specifically, life-improving interventions.

We must restore the sanity of evidence-based medicine (comparative effectiveness) back to the true intent: that a physician integrates individual clinical expertise with the best available external clinical evidence from systematic research to determine what is in the best interest of an individual patient.

Neck and Back Pain Affects Millions

The Spinal Research Foundation is a non-profitorganization dedicated to improving spinal health care through research, education, and patient advocacy. Located in Reston, Virginia, the Foundation collaborates with spinal research partners across the country to prove the success of traditional approaches, as well as develop new techniques and technologies. These results are shared with both the medical profession and the general public to improve the overall quality and understanding of optimal spinal health care.

More than 85% of the population will suffer from severe neck and/or low back pain during their lifetime. Eight percent of these people develop chronic pain, which means that at any given time, around 25 million people in the United States are directly affected by this condition and many more indirectly. Techniques to cure, manage, and prevent this limiting and disabling condition need to be developed. Educating the public, health care providers, and insurance providers is the firststep in advancing spinal health care.

The Spinal Research Foundation has made remarkable progress in scientific research associated with neck and back pain. The Foundation collects data relative to patients' treatments and outcomes and has embarked on projects designed to better understand the biochemistry of neuropathic pain and develop new drug and surgical regimens to address it. The Foundation continues to expand its research efforts, partnering with other research institutions to further the advancement of spine related research. The Spinal Research Foundation has been involved in numerous studies:

- ***The use of novel perioperative drug therapy to improve surgical outcomes.***
- ***The evaluation of medical devices for relief of back pain.***
- ***The evaluation of analgesic drug regimens.***
- ***The development of non-operative techniques to resolve disabling neck and back pain.***
- ***Investigating the use of BMP (Bone Morphogenetic Protein) in minimally invasive spinal surgery to minimize post-operative pain and dysfunction.***
- ***The development of cervical and lumbar disc replacement technologies.***
- ***The development of disc regeneration technology through the use of stem cells derived from bone marrow.***
- ***The investigation of lactic acid polymers to prevent fibroblast in-growth in surgical wounds.***
- ***A nation-wide multi-center prospective spine treatment outcomes study.***

You can help!

The Spinal Research Foundation is America's leading non-profit health organization dedicated to spinal health. Friends like you have made it possible for us to make huge strides and groundbreaking research discoveries. Join us in our mission to improve spinal health care. Support cutting edge research by making a donation to the Spinal Research Foundation.

Support Cutting-edge Research

- Visit www.SpineRF.org to make a secure online donation.
- Call (703)766-5404 to make a donation over the phone.
- The Spinal Research Foundation is a non-profit 501(c)(3) organization. Donations are tax deductible.

Stay Informed

- Visit our website often to keep up-to-date on the Foundation's activities and research breakthroughs.

www.SpineRF.org

Overview

Marcus M. Martin, Ph.D. and Anne G. Copay, Ph.D.

Every day, scientists make advancements that bring us closer to overcoming the diseases which plague humanity. Through research efforts in academia and in philanthropic and private enterprises, we are steadily moving closer to a time when many of the diseases which now afflict mankind will be mere fodder for our historical archives.

Spinal disease affects millions in the United States and across the globe. Consequences range from mild discomfort to extreme pain and physical disability. The lifetime incidence of spinal pain has been reported to be 80% to 85% of all adults.[1] Around the world, researchers and spinal care practitioners are relentlessly working to develop new treatments for spinal ailments. The current issue of the *Journal of the Spinal Research Foundation* aims to highlight some of these advances and upcoming developments in the field of spinal disease treatment. We have tapped into the experts from various specializations to provide the reader with an update on some of the major advances in the field of spinal care.

Robotic technology is expanding in scope and applicability. This technology is rapidly and dramatically revolutionizing modern life. It is now also being utilized in spinal surgery. The Mazor robot, for example, is a guidance system for surgeons performing spinal procedures. Its precise mapping of human anatomy enables it to act as a surgeon's extra sense during surgical procedures. Dr. Good, a spine surgeon who utilizes robotic technology, provides an expert overview of the workings of the device.

The use of biologics to enhance spine treatment is highlighted in an article by Dr. Coric. He explains the utility of cell therapy in the treatment of degenerative disc disease, a condition that affects all aging humans.

For many who have been confined to wheelchairs, regaining the ability to walk upright has long been considered an implausible dream. However, this dream is now becoming a reality through technological advances. The ReWalk system does just that. In an informative article about this system, Dr. Esquenazi explains how this walking assistance device has literally changed the lives of those crippled as a result of spinal cord injury.

Advances in the realm of conservative spinal therapy are reflected in both physical therapy and pain management. Dr. Nguyen provides an overview of current pain management approaches, while Jessica Stepien, DPT, presents a review of dry needling, a therapeutic approach that is rapidly gaining popularity as a means of treating myofascial trigger points.

The sacroiliac (SI) joint is considered by many therapists as an under-recognized pain generator. Dysfunction of this joint is often addressed by immobilization through joint fusion. The traditional approach to SI fusion requires a large incision and the use of muscle-splitting techniques. New approaches to SI joint fusion and their significant benefits, compared to the traditional approach, are highlighted by Dr. Hasz.

The article 'Advances in Bone Grafts and Fusion Augmentation' examines an assortment of bone growth adjuvants. It covers the use of specifically engineered anchor proteins (P-15) to induce cell anchoring and bone formation. This relatively new product is explained and contrasted to the traditional bone morphogenetic proteins which are also designed to enhance bone fusion.

Harnessing the fundamental principles of physics, the 4WEB technology combines stronger structural support with more space for bone ingrowth and osteoinductive surfacing to create a revolutionary new approach to interbody spinal cages. The material and the structural characteristics of this novel approach to spinal implants are underscored by Dr. Gainey in his informative review.

The current issue highlights advances in minimally invasive approaches to surgery which allow for smaller incisions, less tissue injury, shorter hospital stays, and often faster recovery times. In an insightful article by Dr. Orndorff et al., readers are exposed to the process and benefits of minimally invasive spine surgery.

[1]WHO The burden of musculoskeletal conditions at the start of the new millennium. *World Health Organ Tech Rep Ser*. 2003;919:1–218.

The future of spinal therapy is bright. The advances outlined in this issue give emphasis to some of the major frontiers in the field of spinal research. As you read this current issue, know that, at this very moment, thousands of scientists and physicians and millions of support staff are working tirelessly toward the goal of freeing patients from the debilitating condition that is spinal disease.

Marcus M. Martin, Ph.D.

Dr. Martin's research interests include neuroimmunology, virology, and immunology. He is engaged in collaborative research through The Spinal Research Foundation with the Medical University of South Carolina Children's Hospital, geared toward the development of neuroprotective and neuroregenerative compounds for the treatment of nerve pathology. Dr. Martin's current research collaborations include research initiatives to apply stem cell therapy for tissue preservation, the development of regenerative therapies for intervertebral discs, and the development of novel methods of enhancing bone fusion.

Anne G. Copay, Ph.D.

Dr. Copay studies the outcomes of surgical and non-surgical spine treatments. She published several articles on the outcomes of spine fusion. She has ongoing research projects concerning the effectiveness of new spine technologies and the long-term outcomes of surgical treatments.

Past Issues of the
Journal of the Spinal Research Foundation

The Crisis of Osteoporosis
Fall 2008

The Genetics of Spinal Disease
Spring 2009

Obesity and Spinal Disease
Fall 2009

The Evolution of Spinal Health Care
Spring 2010

The Success of Spinal Health Care
Fall 2010

Spine Support:
Muscles, Tendons, and Ligaments
Spring 2011

Trauma and Tumors of the Spine
Fall 2011

Spines of Service
Spring 2012

Spines in Motion: Biomechanics of the Spine
Fall 2012

Please follow this link to access previous journal issues:
http://www.spinerf.org/education/journal.php

Ask the Expert

Jonathan R. Slotkin, M.D.

How are stem cells used in spine treatment?

There are three sources of stem cells: from the patient (autologous), from cadavers (allograft), and from living donors (allograft). Without doubt, the most successful stem cell product is cadaveric derived stem cells within a bone matrix. Seven years ago, the first cadaveric-based stem cell products came to market. Given that no adverse events have been reported so far, these allograft-based stem cell products are increasingly considered to be safe and reliable sources of growth factors.

Stem cells may be used to promote bone formation and, hence, improve the fusion of bones in the spine. Stem cells may also be used to generate new cells inside an intervertebral disc and allow us to heal a degenerated disc. Autologous and allograft biologic strategies are increasingly attractive avenues of innovation. Between 30–40% of all spine and neurosurgeons are now incorporating stem cell treatments in their practice.

What are the benefits of minimally invasive spine surgery versus traditional approaches to spine surgery?

The term "minimally invasive" has been used in a less than genuine manner. Some procedures are called minimally invasive because they are performed through a smaller incision. However, these procedures may still be very invasive if they involve cutting through muscles and removing bone.

In a traditional approach, the removal of a disc herniation relies on cutting through muscles and removing pieces of bones to access the disc. In a truly minimally invasive surgery, it is now possible to avoid muscle dissection and bone removal. A small nano probe is inserted through the skin with an incision as small as a freckle. This incision does not require any stitches and is covered by a Band-Aid after the surgery. The probe is guided between the vertebrae to the herniated disc. Nano tools are then used through the hollow center of the probe. The nano tools can be used to remove disc fragments and small bone spurs. A traditional surgery cuts through skin, muscles, and bones; this creates scar tissue and potentially lingering pain. It also requires longer recovery time and longer hospital stay. A truly minimally invasive surgery avoids damage to surrounding tissue and decreases the recovery time.

Do you foresee the development of a preventative treatment for spinal degeneration?

The new frontier in biologics involves both trying to regenerate the disc and preventing degenerative disc disease. Currently, numerous companies and basic science labs are working on these issues. Many things are being tried, including growth factors, different genes, and injecting stem cells into the disc. There are on-going studies where OP-1 (BMP-7) is injected into the degenerated disc. I think that the OP-1 growth factor injection is probably not going to be the final treatment. It is a great first step, but growth factors won't survive long enough inside the disc to continue to prevent disc arthritis; repeated injections would be needed. The environment in the disc itself is harsh. The pH level is low and there is no blood supply, so the injected cells are short-lived. This harsh environment makes it hard to grow new cells and regenerate the disc. As degeneration progresses, the biomechan-

ics of the disc change, the disc space collapses, and there is more instability. Once we identify the proper growth factor, we may be able to inject the gene for the growth factor in the disc. Theoretically, the gene for the growth factor will remain active for a longer period of time inside the disc. It is widely believed that in the future, success will mean a combination of the right genes, growth factors, and stem cells, and even using biomechanical devices for later stages of disc degeneration when the disc biomechanics are altered.

Have you used robotics in your treatment? How has this enhanced your surgical practice?

Yes, I started to use robotics for my more complex surgeries. It allows me to both plan and execute the complex surgery cases with more precision. The robot 3D software creates a blueprint of the procedure that I intend to perform. This blueprint is specific to the patient's anatomy and condition.

In the operating room, I use the guidance of the robot, that is, the robot guides my tools according to the blueprint to place the implants safely and accurately in the exact pre-planned locations. The average accuracy of implant placement by spine surgeons is about 90%. With the help of the robot, the accuracy increases to 98.3%. While in surgery, I also rely on the robot to check the position of the pedicle screws that I implant. The robot creates a 3D axial view of the spine showing the exact location of each pedicle screw and its relationship to the spinal canal. I can immediately evaluate the positions of the screws and, if need be, correct them. This takes no more than five to ten minutes of additional OR time. Without the robot, surgeons have to wait for a post-operative CT scan to verify the placement of the screws. Significant misplacements of the instrumentation would have to be revised with a second surgery.

Jonathan R. Slotkin, M.D.

Jonathan Slotkin, MD is director of spinal surgery at Geisinger Neuroscience Institute and the director of spinal cord injury research. He has clinical interests in brain tumor surgery and complex spinal surgery, including degenerative conditions, spinal oncology, spine trauma, surgical back pain, adult deformity, minimally invasive approaches, and artificial disc replacement technologies. He also has an interest in sports-related spine and neurological injuries. Dr. Slotkin is an active researcher and is currently focusing on spinal cord injuries, neural regeneration, and nanotechnology. He has been published in peer-reviewed publications and co-edited a two volume publication on spine surgery. Dr. Slotkin is also a member of the scientific advisory board of In Vivo Therapeutics Corporation.

"We've Got Your Back" Race for Spinal Health

Laura A. Bologna, Spinal Research Foundation National Program Coordinator

San Francisco, CA
September 15, 2012

San Francisco's famous fog burned off in time to kick off the third annual "We've Got Your Back" Race for Spinal Health at scenic Lake Merced.

As this event continues to grow, we welcomed more participants, more volunteers, and most excitingly, more Spinal Champions at this year's event. Almost 200 participants, 30 volunteers, and many friends and family were in attendance to run, walk, and provide support.

The Daly City Police SWAT team made a big impression on the event, returning after their participation in last year's race to support their colleague Mike P. The presence of the official SWAT truck was an exciting addition to the event.

Dr. Paul Slosar gave a heartfelt thanks to all of the patients who were able to participate in the run or the walk and acknowledged our generous sponsors.

The host for this event was the SpineCare Medical Group, whose staff made up the core group of volunteers. Thanks again to all of our national sponsors and local donors for their generosity, which ensured the success of this 3rd annual event. And a very special thanks to Dr. Slosar and his wife who make this entire event possible.

New Orleans, LA

January 6, 2013

The first annual New Orleans "We've Got Your Back" Race for Spinal Health was held this past January. The inaugural event was a great success and attracted over two hundred New Orleans area residents who braved the pouring rain to support this event. Our goal was to to increase community awareness about the devastating effects of back and/or neck pain and to get people involved in our efforts to battle its effects. This was the first event of its kind in New Orleans.

Dr. Thomas addressed the crowd and got them excited to take part in this event. He spoke of the importance of research and development in spinal surgery, emphasizing how each attendee's support allows for progress to be made every day.

The event's primary purpose was to celebrate the achievements of patients who have overcome debilitating back or neck pain to regain their lives and share their successes with the community. We celebrated several Spinal Champions and their successes at this event.

The host for this event was Southern Brain and Spine. Thanks again to all our national and local sponsors for their generosity, and to our race volunteers for their willingness to be involved in our first event. A special thanks to Denise Crawford and Michelle Jacob for making this event a success.

Upcoming Races

We are excited to announce seven upcoming races in 2013. Five of these races are being hosted by new locations this year as our event continues to grow and gain national presence. The upcoming races are: 1st annual race in Freehold, New Jersey, hosted by Princeton Brain and Spine Care on April 6th; 1st annual race in Carmel, Indiana, hosted by Indiana Spine Group on April 27th; 1st annual race in Coos Bay, OR, hosted by South Coast Orthopaedic and Bay Area Hospital on May 4th; 6th annual race at our flagship race site in Reston, VA, hosted by The Virginia Spine Institute on May 18th; 1st annual race in Durango, CO hosted by Spine Colorado on June 15th; 3rd annual race in San Francisco, CA on September 14th; and 1st annual race in Peoria, IL hosted by Midwest Orthopaedic in October. Show your support and join us at one of our upcoming events. For registration and volunteer opportunities, please visit www.spineRF.org/race.

Spine Tale
Silvana Masood

Brian R. Subach, M.D., F.A.C.S.

Silvana Masood had known about spinal disease for years having watched her husband go through physical therapy, spinal injections, and pain medications with little benefit. When he eventually underwent spinal fusion surgery with excellent results, she became a believer.

Silvana first came to The Virginia Spine Institute in 2008. She was experiencing disabling low back pain with both pain and numbness in her entire right leg. The pain had been bothering her intermittently for the past ten years, but she had never really sought medical attention until years later when her pain progressively worsened.

On initial evaluation, Silvana had tremendous low back pain and tenderness overlying multiple joints of her lumbar spine. There was muscle spasm and numbness in her entire right leg. She was prescribed physical therapy and anti-inflammatory medications for the pain and numbness while considering her options for her lumbar degenerative disc disease. The MRI scan that she had in 2008 demonstrated one disc showing signs of moderate degeneration without any compression of the sciatic nerves. She continued to maintain her core strength and took anti-inflammatories, dealing with the pain fairly well until she had her daughter. Both the pregnancy and the child care significantly worsened her pain. She found that not only her life, but also her career and her family were being affected by the pain. In discussions with her husband, she decided to undergo spinal fusion. An updated MRI scan demonstrated worsening of the disease at L5/S1, with progressive loss of height and bone spur formation. She had clearly done everything possible to avoid surgery.

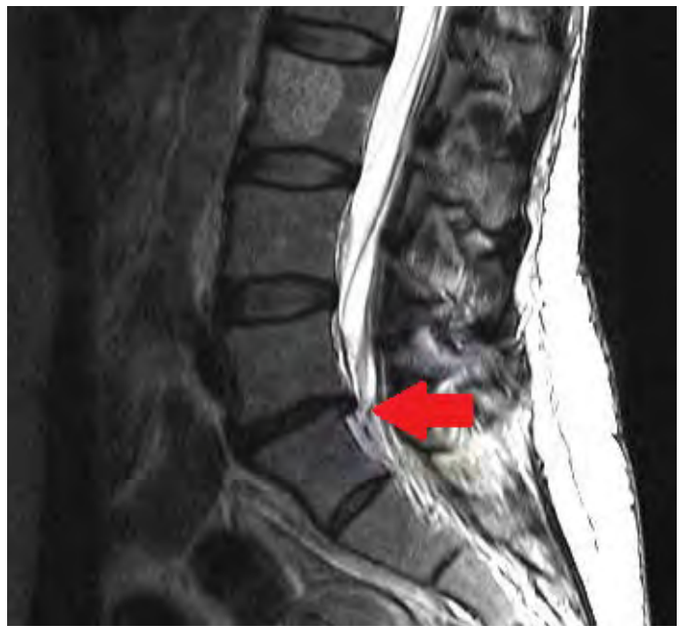


Figure 1. Lateral view of the pre-operative MRI: the red arrow indicates a herniated disc at the L5-S1 level.

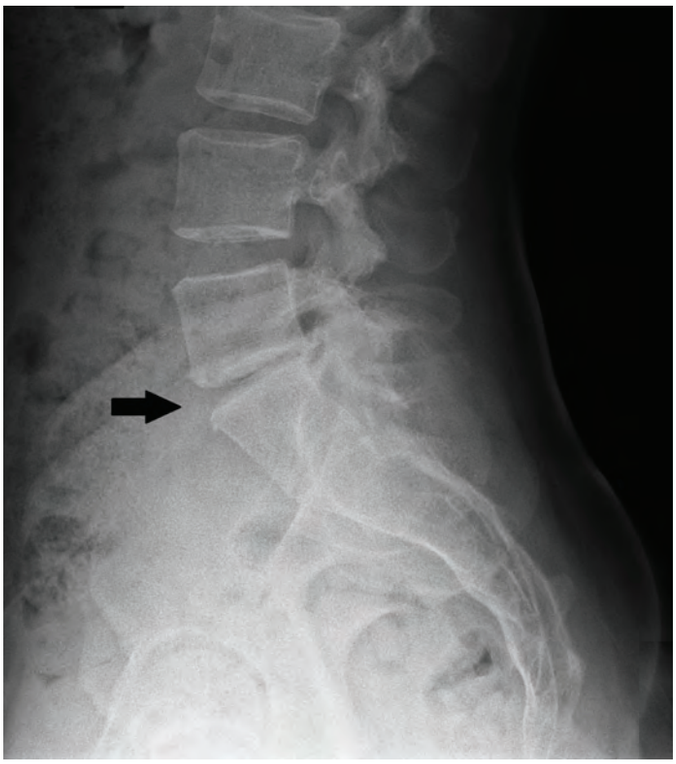


Figure 2. Lateral view of the pre-operative x-ray: the arrow identifies the L5/S1 disc with loss of disc height and bone spur formation.

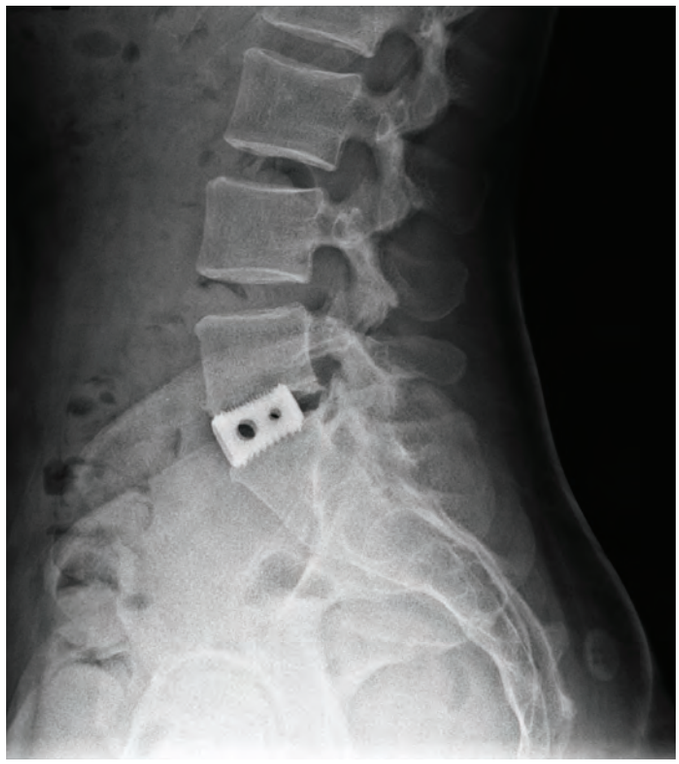


Figure 3. Lateral view of the post-operative x-ray shows restored disc height and posture at L5/S1 following a minimally invasive anterior lumbar interbody fusion using two LT cages.

In April 2012, she underwent anterior lumbar interbody fusion at L5/S1. Two large LT cages were placed through a small abdominal incision into her L5/S1 disc space. (Figure 3) Those cages restored the height and posture of the disc space and gave it immediate stability. There had been such collapse at the disc space that the cages wedged firmly in place, obviating the need for any further surgery. (Figure 2)

At her follow-up visit two weeks after surgery, her pain level was down to a two (on a scale from one to ten), and she had noticed an immediate difference. She felt that her spine was stronger, her leg symptoms had resolved, and she was ready to begin physical therapy.

Silvana is presented as a Spine Tale in this issue of the *Journal of the Spinal Research Foundation* because she had lived with degenerative lumbar disc disease for a decade. When things finally worsened despite nonoperative care, she decided to do something about it. With a minimally invasive intervention, instead of being disabled by pain, she now has her career, her life, and her family back.

Spine Tale
Daisy Cher

Brian R. Subach, M.D., F.A.C.S.

Daisy Cher is a 43-year-old woman with a history of neck pain and right upper extremity weakness. She had previously been operated on in 2011, undergoing anterior cervical fusion from C4 through C7. Her x-rays from February 2011 demonstrated excellent posture, alignment, and healing; however, repeat x-rays done in August 2012 demonstrated evidence of subsidence or collapse of the C7 screws into the vertebral body, causing a kyphotic (leaning forward) posture. She had also developed spondylolisthesis, or forward slippage, of bone C7 on bone T1. Her EMG study done in September 2012 demonstrated an acute C7 radiculopathy (ongoing nerve damage).

Daisy was suffering from severe pain as well as progressive weakness in her upper extremities. Subsequent x-rays demonstrated evidence of kyphosis and progression of collapse at C7. Daisy returned to the operating room for a combined anterior and posterior reconstruction of her cervical spine. (Figure 1)

The primary goal of the reconstruction was to bring her posture back to normal. Her posture was forward flexed, causing her to hunch or lean forward. By entering the front of the spine first, it was possible to remove the previous plate and to redo the anterior cervical fusion, restoring her posture to normal. Given the kyphosis, or forward flexed posture, which was occurring at the junction of the cervical and thoracic spine, she needed a posterior decompression and fusion extending from the cervical spine through the upper thoracic spine.

She underwent the revision anterior cervical fusion in October 2012. The previously placed plate was removed, as well as most of the fractured C7 bone, and then additional fusion was performed at both the C6/7 and C7/T1 disc spaces. A new anterior cervical plate was placed in Daisy's neck with excellent posture and alignment. (Figure 1)

The day following the surgery, she underwent a fine-cut CT scan to evaluate her alignment as well as the room available for the spinal cord. That CT scan and the Mazor robot were used to plan and perform the posterior screw fixation from C3 through T3. The robotic technology enhanced the surgeon's accuracy and precision as well as the safety of the operation. Daisy underwent an uncomplicated second stage operation, placing Vertex lateral mass screws in the upper cervical spine and Solera screws into the upper thoracic spine. The use of Vertex technology in combination with Solera, as well as robotic guidance, represents a true new horizon in spinal surgery.

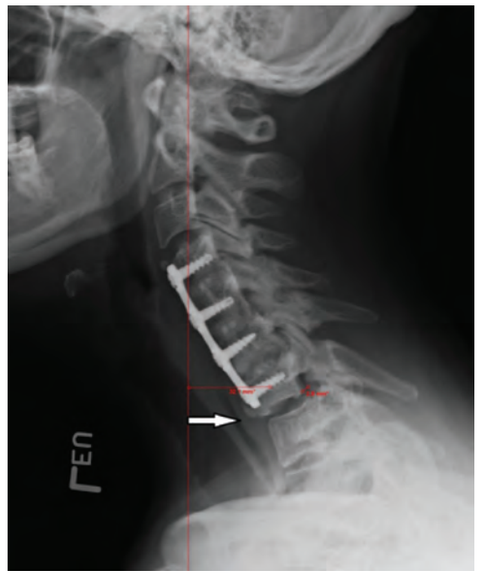


Figure 1. Lateral view of the pre-operative x-ray: the arrow points to the collapse of the C7 screws into the vertebral body of C7 (below the prior fusion) causing a kyphotic posture and spondylolisthesis of C7 on T1.

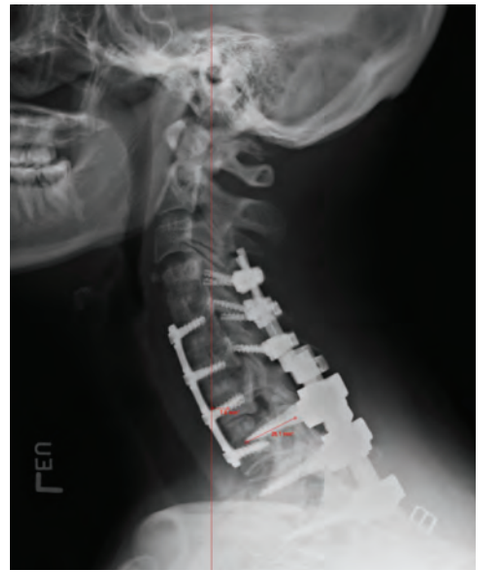


Figure 2. Lateral view of the post-operative x-ray: revised fusion from C4 through C7 and additional fusion at C6/C7 and C7/T1.

Spine Tale
Sean O'Neil

Brian R. Subach, M.D., F.A.C.S.

Sean O'Neil is a 52-year-old tennis professional who initially presented to his neurologist in 2011 complaining of numbness in both of his hands. He felt that he was losing some grip strength and slowly but progressively worsening. According to his neurologist, he had a normal neurologic examination of both arms, including strength and reflexes. This was followed by an EMG study (nerve test) of his arms, which only showed mild carpal tunnel syndrome in both hands. When he arrived at The Virginia Spine Institute in December 2012, he was still complaining of numbness in both hands. He felt that there was no obvious positional component, but that the numbness was worse if he used his hands. He noted decreased fine motor control, but he was still active in his profession.

The x-rays of Sean's cervical spine demonstrated evidence of mild degenerative changes involving the discs. There were some bone spurs that were forming across the front of the spine, consistent with someone in his early 50s. However, the reflexes in both his arms and legs were extremely hyperactive or jumpy. He had a positive Hoffmann's sign in his thumb and evidence of clonus in both ankles, both consistent with someone who has pressure on his cervical spinal cord.

An urgent MRI scan of the cervical spine was ordered. The radiologist called from the MRI scanner to comment about the severity of Sean's disease. Sean essentially had three discs which were bulging and had significant arthritic changes, but more importantly, his spinal cord was being compressed to approximately half of its normal diameter. There was some signal change seen within the cord itself, indicative of swelling or bruising of the spinal cord.

The most common operation carried out for cervical degenerative disease and bone spur formation is an anterior cervical fusion. In the setting of an elite athlete, such a cervical fusion can irreparably alter his ability to use his neck, meaning he would lose significant range of motion in flexion, extension, and lateral bending. Such motions are generally necessary for a tennis professional. A second option, much less frequently performed, is a cervical laminoplasty. The operation essentially cuts the bone in the back of the neck and then repositions it so the spinal cord is no longer compressed. It does not change the arthritic disease in the spine, meaning it will not alter his range of motion, nor would it alter any pain that he may have from the arthritis. Sean considered his options and chose to undergo a posterior cervical laminoplasty procedure designed to give his spinal cord the normal amount of room.

On January 7, 2013 he underwent the laminoplasty procedure in which small titanium plates were placed in the back of his neck, securing the cut bone to the adjacent spine. This was not a fusion operation, but rather a surgery designed to give him the room necessary for his spinal cord to avoid further injury and also stabilize his spine using its own intrinsic ligaments and muscular support. (Figure 2)

When Sean returned approximately two weeks after surgery, he was complaining of soreness in the back of the neck. However, his range of motion was excellent. He stated that he had already noticed improvement in the numbness in his hands. He still has carpal tunnel syndrome which will become obvious with repetitive use of his hands; however, his spinal stenosis has been completely cured.

Although his hyperreflexia will remain, further surgery may not be necessary. By doing the laminoplasty procedure, his range of motion was spared and Sean is able to maintain the high level of function necessary in his sport.

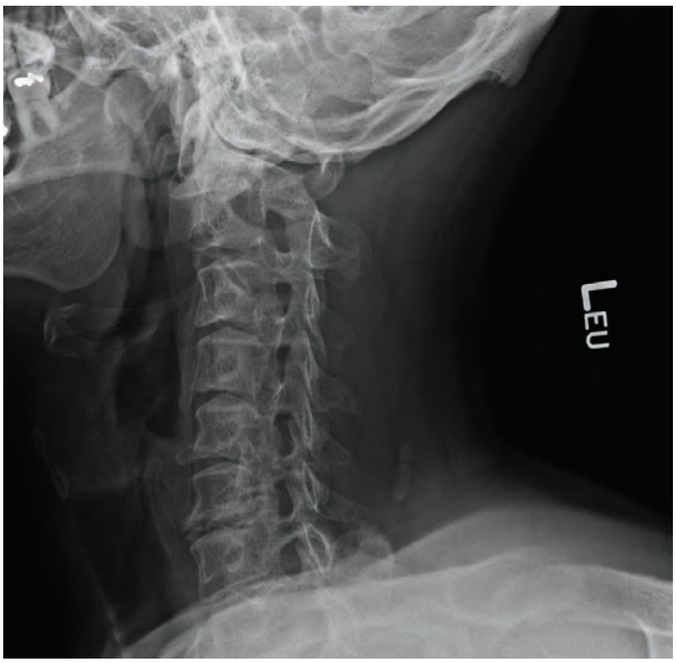


Figure 1. Lateral view of the pre-operative x-ray.

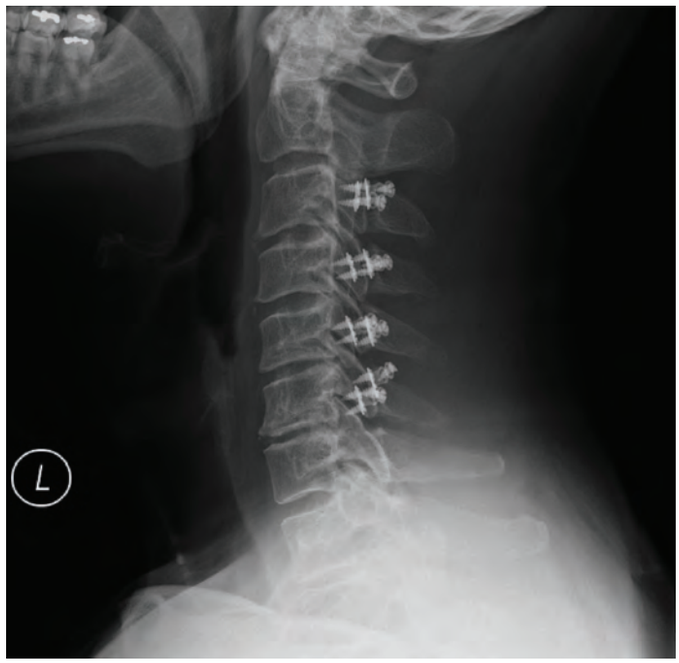


Figure 2. Lateral view of the post-operative x-ray shows the small titanium plates placed in Sean's neck during the laminoplasty procedure.

Brian R. Subach, M.D., F.A.C.S.

Dr. Subach is a spine surgeon and the President of The Virginia Spine Institute. He is a nationally recognized expert in the treatment of spinal disorders and an active member of the American Association of Neurological Surgery, the Congress of Neurological Surgeons, and the North American Spine Society. He is an invited member of the international Lumbar Spine Study Group and a Fellow in the American College of Surgeons. He lectures extensively regarding the management of complex spinal disorders in both national and international forums. He is the Director of Research and Board Member for the non-profit Spinal Research Foundation (SRF) and Editor-in-Chief of the *Journal of the Spinal Research Foundation* (JSRF). He has written 15 book chapters and more than 50 published articles regarding treatment of the spine.

Robot-Guided Spine Surgery

Christopher R. Good, M.D., F.A.C.S. and Blair K. Snyder, P.A.-C.

The goals of modern spinal surgery are to maximize patient function and accelerate a return to a full life. As spinal surgery has evolved, more focus has been placed on minimizing trauma to the body during surgery and expediting a return to function through the use of minimally invasive techniques. The era of modern spinal surgery has blossomed over the past 15 to 20 years as a result of scientific advancements including minimally invasive surgery, genetic testing, next generation spinal implants, stem cell research, and the use of biologic agents to promote spinal healing.

Robot-guided spinal surgery offers many potential advantages to patients and surgeons including improving the safety of both minimally invasive and complex surgical procedures, improving the accuracy of spinal instrumentation placement, and minimizing the use of radiation during surgery. Robot-guided spine surgery utilizes highly accurate, state-of-the-art technology for the treatment of many spinal conditions including degenerative spinal conditions, spine tumors, and spinal deformities.

Figure 2. The Mazor Robot is attached to the spine of the patient. The robot arm helps guide the surgeon's hand during a minimally invasive surgery. *Image courtesy of Mazor Robotics.*

How It Works

The Mazor Robotics' Renaissance system is one of the only robotic guidance products in the United States used for implanting devices during spine surgery. The Mazor Robotics system allows the surgeon to use the images from a computerized tomography scan (CT scan) that is taken before surgery to create a blueprint for each surgical case. The CT scan information is loaded into a computerized 3D planning system which allows the surgeon to plan the surgical procedure with a high degree of precision before ever entering the operating room (Figure 1).

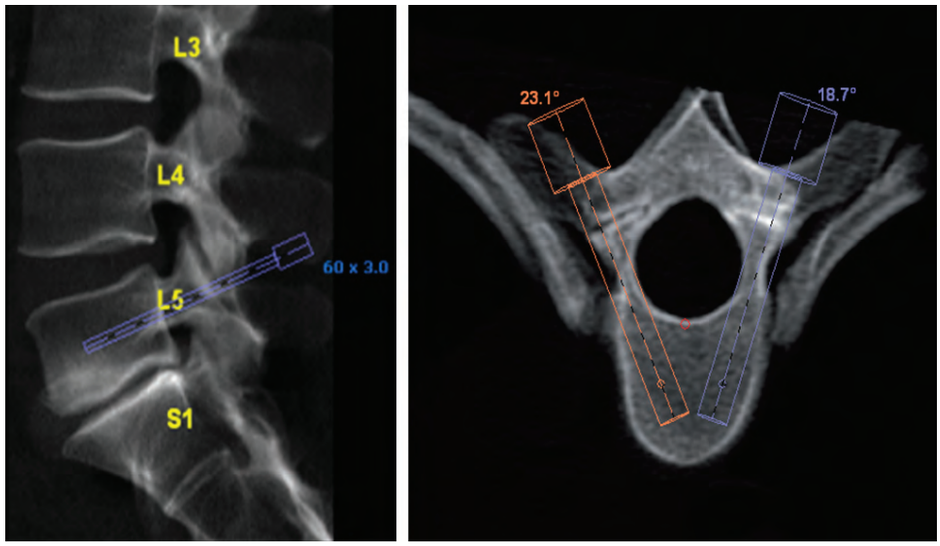


Figure 1. CT scan images of the spine are taken prior to surgery, and the exact location of spinal implants is blueprinted with 3D software. The orange and purple lines represent screws that are to be placed into the bones of the spine.

In the operating room, the surgeon does all of the physical work of the surgery. The robot-guidance system is a tool that helps to guide the surgeon's instruments based on the highly accurate pre-operative planning of spinal implant placement. During the surgery, the robot is placed near the patient either by attaching it to the bed or directly anchoring it to the spine of the patient. The robot is approximately the size of a 12 oz. beverage can with a small arm attached. The robot has the ability to bend and rotate in order to place its arm on the spine in a very specific location and trajectory (Figure 2). This ultra-precise guidance can improve

C.R. Good and B.K. Snyder/Journal of the Spinal Research Foundation 8 (2013) 16–21

the surgeon's ability to safely place implants, particularly when working through very small incisions (minimally invasive surgery) or when dealing with complex anatomy (spinal deformity or previous spine surgery).

Minimally Invasive Spine Fusion

One common technique presently used by spine surgeons to correct spinal conditions is spine fusion. The purpose of a spinal fusion is to create a rigid union between two separate segments of the spine to correct malalignment or instability. Spine fusion has traditionally been performed using "open surgery" with an incision that is big enough to expose the entire area being treated. Open surgical techniques are beneficial and necessary for many conditions; however, in some cases minimally invasive surgery (MIS) can be utilized to safely obtain a similar result. MIS uses smaller incisions which usually result in less damage to surrounding healthy tissue, less post-operative pain, and faster recovery.

In many situations, MIS requires an increase in the use of intraoperative x-rays in order to compensate for a surgeon's inability to directly visualize the spine. In some cases, this lack of visualization could decrease the surgeon's accuracy when compared to open surgery. In addition, the increased radiation exposure during surgery is a concern for the patient as well as the health care team, as previous studies have shown an increased rate of cancer among spine surgeons, compared to the general population.[1]

Robot-guided surgery technology allows the surgeon to perform MIS in a very precise fashion while minimizing the need for radiation during the surgical procedure. Robot-guidance technology guides the surgeon's tools during MIS to ensure accuracy while also decreasing tissue trauma, resulting in less bleeding, smaller scars, less pain, and faster recovery (Figure 3).

A recent study reviewed 635 surgeries involving the placement of 3,271 spinal implants and found a

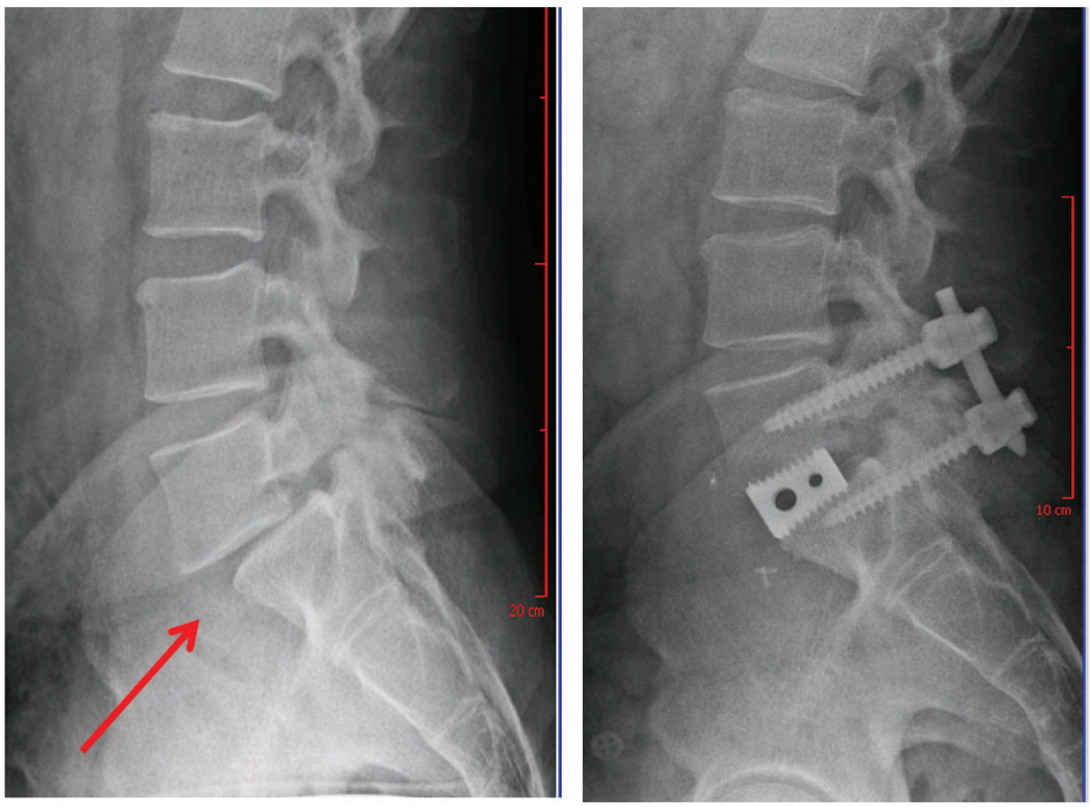


Figure 3. X-rays of a patient before and after minimally invasive correction of spondylolisthesis of the lumbar spine. Progressive disc collapse and slippage of the bone (red arrow) has been corrected using minimally invasive techniques. Using robot-guidance, the screws were placed in the back through an incision one inch in length.

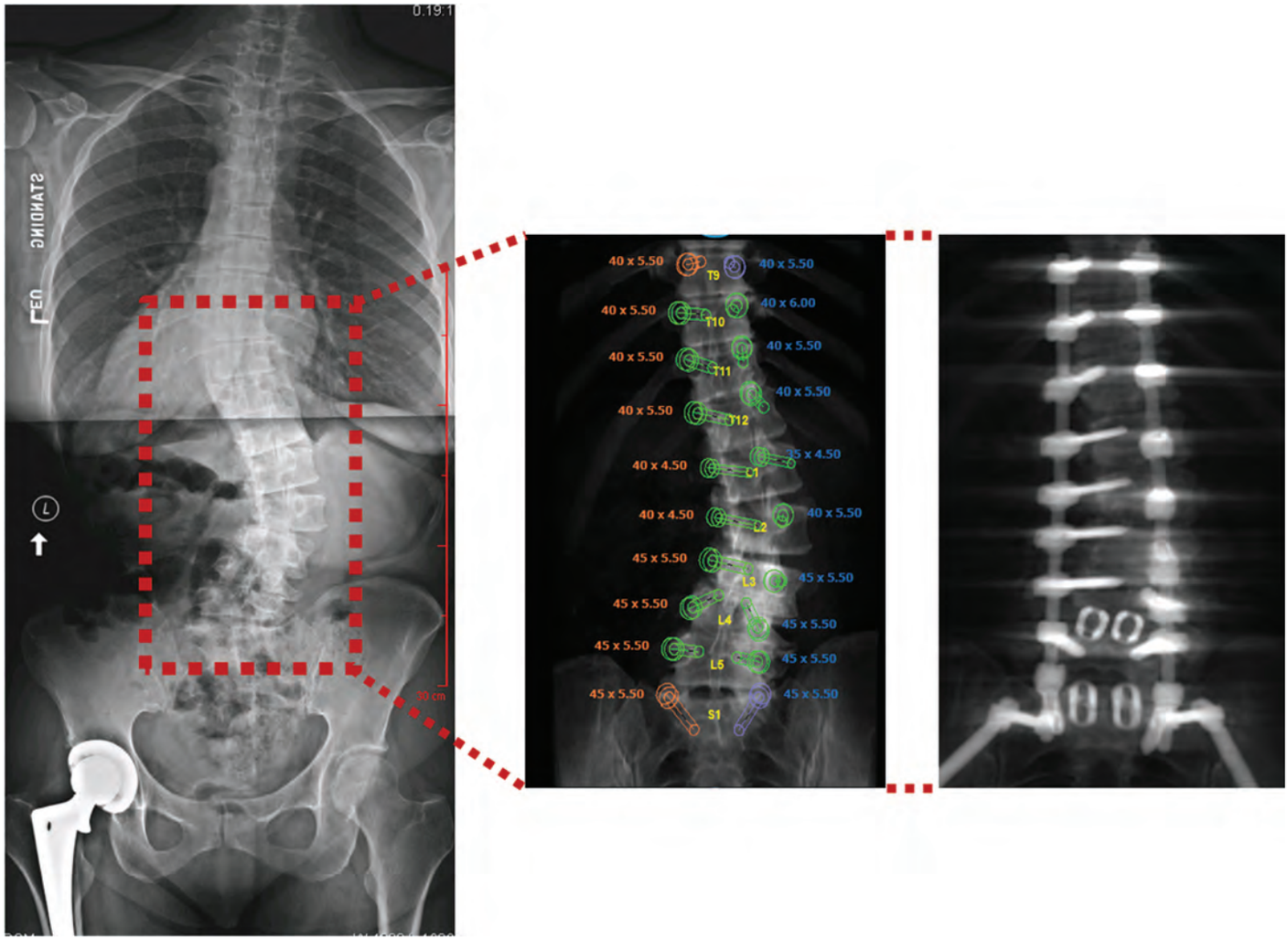


Figure 4. Left: x-ray of patient with thoracolumbar scoliosis. Center: pre-operative blueprint showing the location where screws will be placed during scoliosis correction surgery. Right: final location of the implants after surgical correction.

98.3% accuracy rate for implants placed with robot-guidance. In this study, 49% were defined as minimally invasive surgeries. Neurologic issues were noted in 4 cases, but following revision surgery, no permanent nerve damage was encountered. The study reported an improvement in accuracy of instrumentation placement and lower risk for neurologic issues compared to previous studies.[2] Robot-guidance has been directly compared to open surgical techniques, and in one retrospective study demonstrated an improvement in implant accuracy by 70%, reduction in radiation dose by 56%, and decrease in hospital stay by 27%.[3]

Scoliosis Correction Surgery

Scoliosis is an abnormal curvature of the spine that affects approximately seven million people in the United States. Adolescent idiopathic scoliosis is most commonly diagnosed between the ages of 10 to 12 years old and may be discovered by parents, during school screenings, or at pediatric visits. When scoliosis is suspected, patients are referred to orthopedic scoliosis specialists who evaluate the patient to determine the severity of the patient's curvature. Symptoms of scoliosis may include back pain, uneven shoulders or hips, abnormal gait, breathing issues, and neurologic problems.

C.R. Good and B.K. Snyder/Journal of the Spinal Research Foundation 8 (2013) 16–21

Treatment options for idiopathic scoliosis include observation, bracing, and surgery. In general, bracing is recommended for curves between 25–30 degrees in patients with significant growth remaining, and corrective surgery is generally reserved for progressive scoliosis curves greater than 45° or curves that do not respond to bracing treatment. The goals of scoliosis correction surgery are to amend the spinal curvature and to prevent the curve from progressing further during the patient's life (Figures 4 and 5).

Surgery for scoliosis involves the use of spinal instrumentation such as screws, rods, hooks, and wires which are placed along the spine. Surgery treats but does not cure scoliosis; it corrects the abnormal curvature and prevents further progression of the disease. Surgical treatment of scoliosis requires a high degree of planning and precision. Each specific curve pattern is unique, and many patients with scoliosis have atypically shaped vertebrae, making the surgery more challenging.

Robot-guided scoliosis correction offers increased precision of instrumentation placement and therefore, an increase in the safety of the surgical procedure. It offers the surgeon the ability to carefully plan ahead before entering the operating room and design the ideal procedure for each patient. Studies have validated superior clinical results for adolescent scoliosis reconstruction with robotic technology based on improved accuracy of implant placement and safety. In a recent study of 120 teenagers with scoliosis, robot-guided surgery was found to achieve 99.7% accuracy of 1,815 implants placed.[3]

Vertebroplasty

Vertebroplasty is an outpatient procedure commonly performed for the treatment of osteoporotic compres-

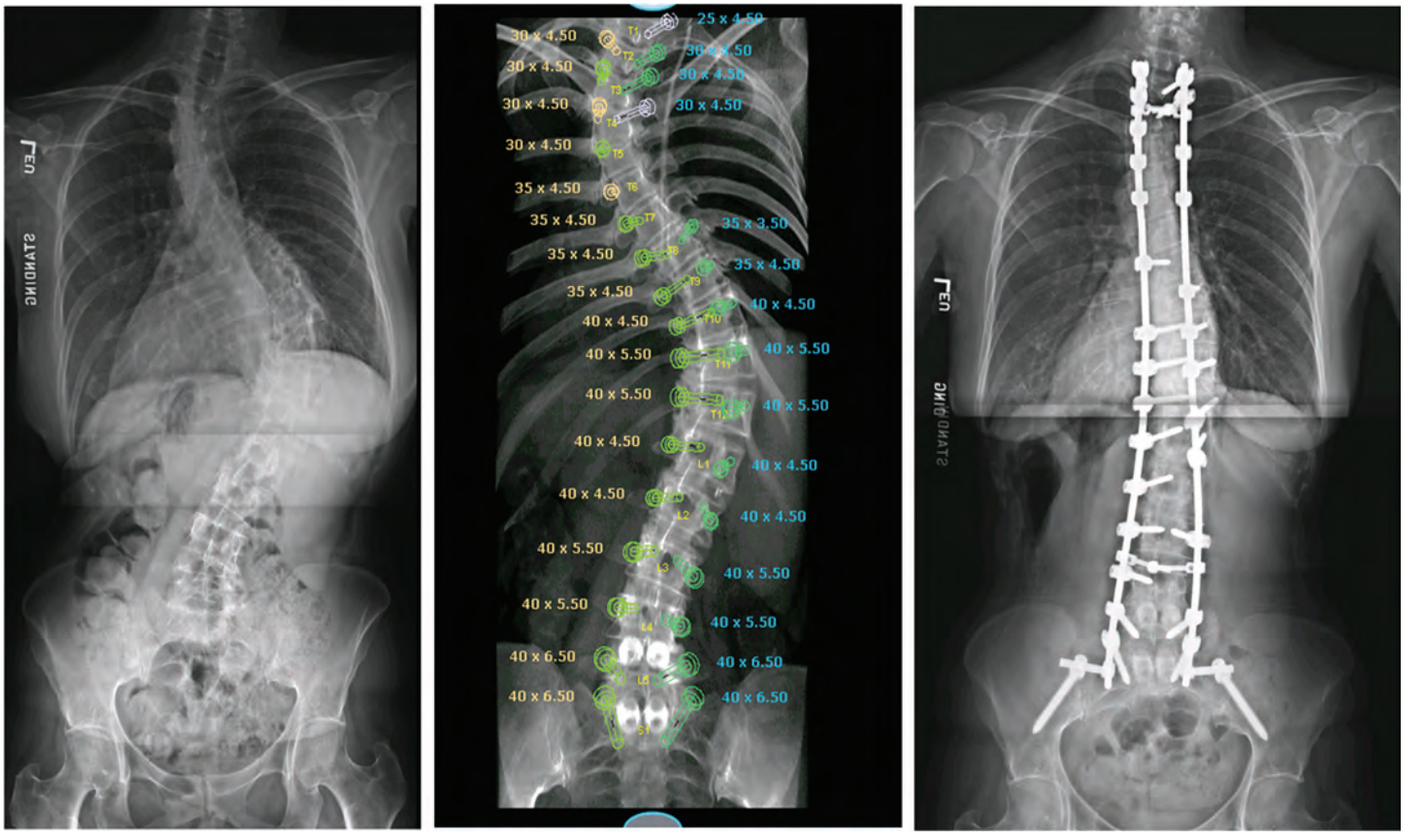


Figure 5. Left: x-ray of patient with large thoracic and lumbar scoliosis which is affecting heart and lung function. Center: pre-operative blueprint, showing the location where screws will be placed during scoliosis correction surgery. Right: final location of the implants after surgical correction.

sion fractures. During the procedure, synthetic bone cement is injected into a broken spine vertebra through a needle. This cement hardens a few minutes after it is injected which stabilizes the fractured vertebra, thereby decreasing pain and the potential for the bone to break further. (Figure 6)

Vertebroplasty requires a high level of precision because a needle is guided through the vertebra near the spinal cord or nerves. Additionally, the accuracy of the needle location is important to prevent the bone cement from flowing into the area around the nerves in the spine. Robot-guidance allows the surgeon to position the needle precisely to minimize the risks surrounding vertebroplasty procedures. In a recent study of osteoporotic compression fractures, robot-guidance was shown to yield improved accuracy over traditional methods, which reduced the total time needed for the procedure and in some cases, allowed the procedure to be performed on patient's who would not have been able to be treated conventionally.[4] The use of the robot has also been reported to decrease radiation exposure to the patient and operating room staff by 50–70% in vertebroplasty procedures[5] (Figure 7).

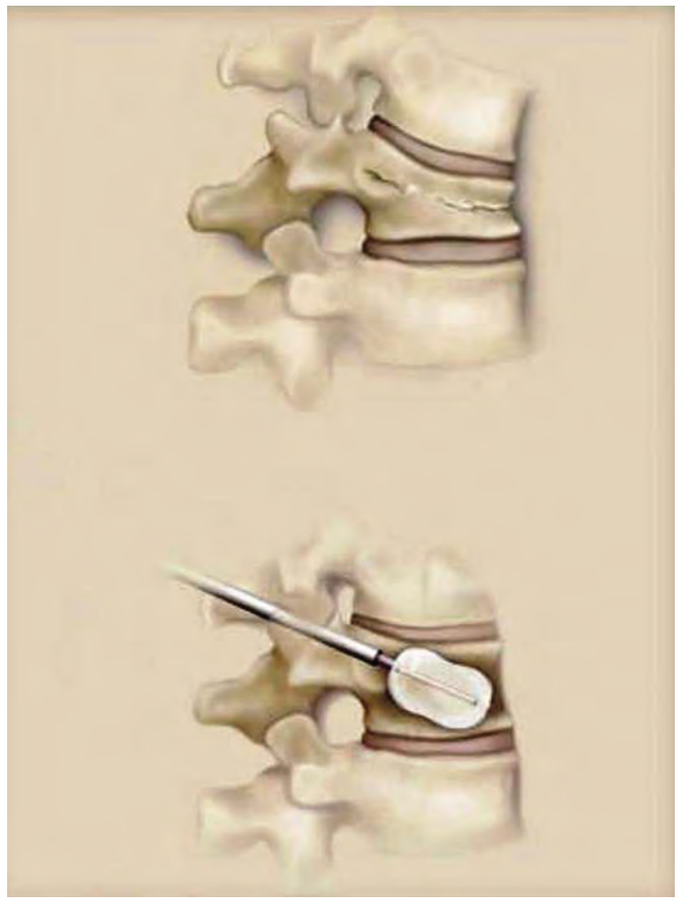


Figure 6. Example of a balloon Kyphoplasty. *Image courtesy of Medtronic.*

Spine Biopsies

In some cases, it is necessary to obtain a small piece of tissue from the spine in order to perform microscopic studies to understand a patient's disease or make a specific diagnosis. This is particularly true in cases of spinal tumors when it is imperative to determine if a lesion is benign, malignant, or infected. Biopsies are usually taken with a needle through a small incision without direct surgeon visualization of the tumor. In many cases, surgeons use CT or x-ray images to guide the needle into the correct location. This process involved additional radiation and in some cases, it can be difficult to find the right spot for the biopsy. Robot-guidance allows the surgeon to pinpoint the exact location the biopsy is to be performed and can decrease the time needed for the procedure and the duration of radiation (Figure 8).

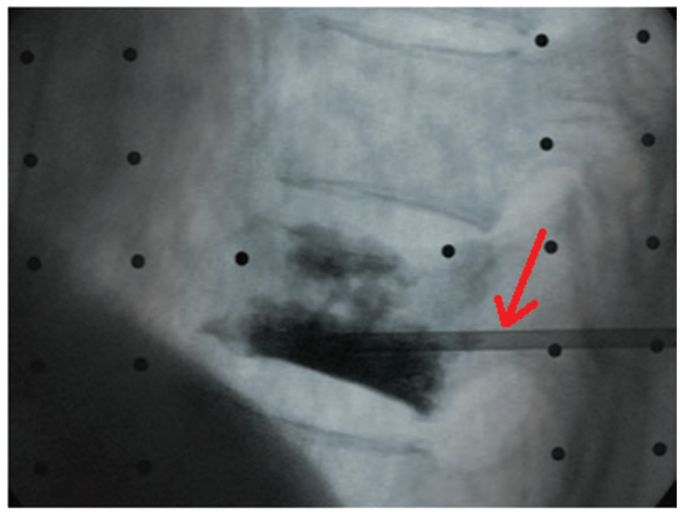


Figure 7. X-ray taken during vertebroplasty with robot-guidance. The compressed bone has been accessed by a needle (red arrow) and filled with synthetic bone cement for stabilization.

Conclusion

Robot-guided spine surgery is a promising new technology that has many advantages and may allow sur-

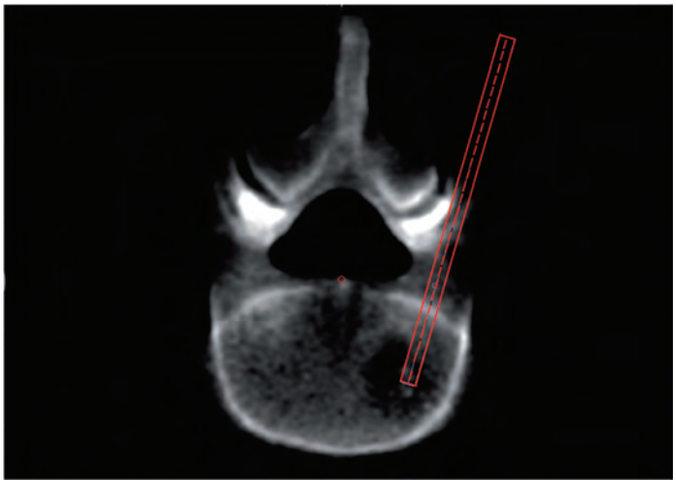


Figure 8. Pre-operative blueprint showing the trajectory of biopsy needle accessing a lesion in the bone.

geons to perform less invasive surgical procedures with smaller incisions, less bleeding, faster recovery, and shorter hospital stays. Robot-guidance also can increase the accuracy and safety of surgical procedures and allow these procedures to be performed with less intra-operative radiation exposure to patients and health care providers.

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Cell Therapy in Intervertebral Disc Repair

Domagoj Coric, M.D.

Low back pain (LBP) is a common condition affecting tens of millions of Americans yearly. Fortunately, the vast majority of LBP cases respond well to non-surgical management. A small, but still sizable percentage of patients are plagued by recurring, severe discogenic LBP triggered by simple activities such as sitting, standing, or walking. These patients are notoriously difficult to diagnose, as well as treat, and can become debilitated by their symptoms. Ultimately, a significant number of these patients turn to chronic, long-acting narcotic therapy, repeated invasive procedures, such as epidural steroid injections or facet rhizotomy, and major surgical procedures, such as fusion or total disc replacement.[4,6,8] (Figure 1)

The intervertebral disc is a fibro-cartilaginous structure that consists of two parts: (1) an outer annulus fibrosus which consists of fibroblast cells and type I collagen, and provides tensile strength and (2) an inner nucleus pulposus with disc or chondrocytic cells and type II collagen which resists compressive forces. Therefore, the predominant native disc cell type is a cartilage-like disc cell that produces extracellular matrix (ECM). ECM consists primarily of proteoglycans, such as aggrecan and versican. These proteoglycans are hydrophilic molecules consisting of protein stems surrounded by highly negatively charged glycosaminoglycan (GAG) side chains. The two most abundant GAGs in ECM are chondroitin sulfate and keratin sulfate which serve to attract and hold water molecules. Degenerative disc disease (DDD) compromises the native disc cell's ability to produce and maintain ECM. The subsequent loss of proteoglycans and GAG side chains causes disc desiccation and loss of disc height with increased mechanical loads on surrounding vertebral bodies. These increased stresses ultimately manifest themselves radiographically as annular tears, endplate sclerosis (or Modic changes), and disc dehydration (or 'black disc disease'). These structural changes to the disc can be manifested clinically as mechanical LBP. In this somewhat simplified view, DDD and mechanical LBP can be viewed as the result of the disc cell's inability to produce and maintain ECM.[4,6] (Figure 2)

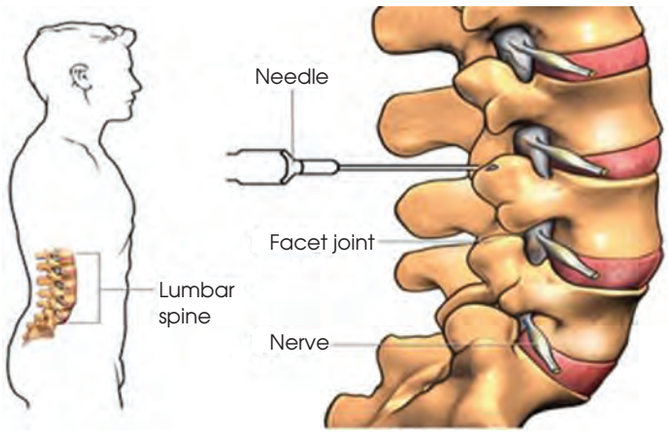

Figure 1. Facet rhizotomy: heat is conducted through a needle to destroy the medial nerve branches of the spine in order to interrupt the pain signal transmission. *Image courtesy of Twin Cities Pain Clinic.*

Surgery for patients with chronic, severe LBP is generally viewed as a treatment of last recourse and has traditionally involved removal of the majority of the intervertebral disc followed by instrumented fusion of the adjacent vertebral bodies. Currently, the most common fusion techniques involve instrumented interbody fusion via various approaches, such as anterior (ALIF), posterior (PLIF or TLIF), or lateral (LLIF) approaches. Minimally invasive techniques may decrease operative morbidity, but still involve loss of segmental motion and increased adjacent level stresses. Total disc replacement (TDR) was developed to maintain motion, but still represents a major surgical procedure with removal of the majority of the disc, including the annulus and nucleus.[6,8] (Figure 3)

Recently, novel technologies have focused on less invasive procedures seeking to maintain or enhance the structure and function of the disc. These disc repair procedures can be broadly categorized as: (A) nucleus augmentation and (B) nucleus repair. There are currently no FDA-approved devices/drugs for disc repair, but there has been extensive preclinical and some clinical research into these areas. Nucleus repair involves introducing biologically active material into the disc to replenish cells or increase production of ECM. Nucleus augmentation involves adding a synthetic or biologic material to the disc. Nucor, an injectable silk/elastic polymer, and Biostat Biologix, an injectable form of fibrin sealant, are examples of nucleus augmentation that have been studied clinically.[3,5,6,15]

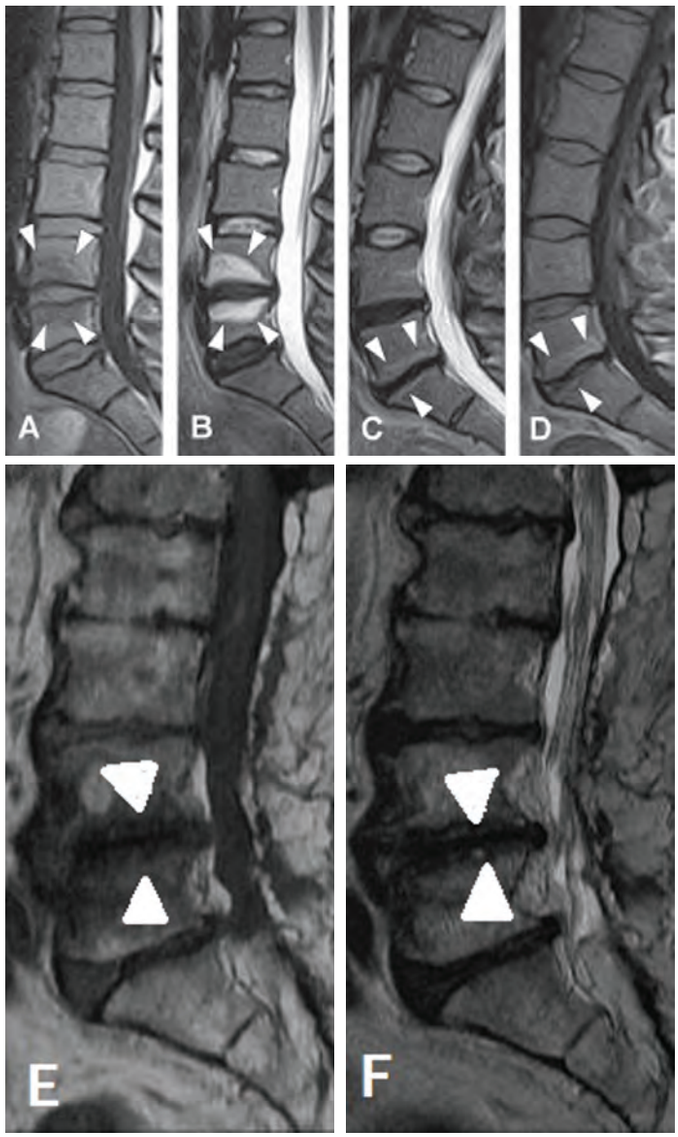

Figure 2. T1 & T2 MRI showing Modic changes. (A&B) Type 1 modic changes: the endplates are black in T1 and white in T2 (edema). (C&D) Type 2 modic changes: the endplates are white in both T1 and T2 (fat). (E&F) Type 3 modic changes: the endplates are black in both T1 and T2 (sclerotic). *Images A and B courtesy of Medical Hypotheses, retrieved from* Albert, H.B., et al. Modic changes, possible causes and relation to low back pain. *Medical Hypotheses* 2008; 70(2):361–368.

Nucleus repair procedures can be subdivided into three categories: (1) growth factor therapy, (2) gene therapy and (3) cellular therapy.[6,7] Growth factors are small peptide cytokines with cell regulatory function that can increase the existing disc cell's ECM production. Bone morphogenetic proteins (BMPs) are examples of growth factors, and BMP-7 (OP-1) and BMP-14 (GDF-5) have been used in clinical trials.[7,10] Gene therapy involves the transfer of genetic material to enhance the disc cell's native production of ECM. Gene therapy requires vectors, either viral or nonviral, to transfer genetic material into host cells. There have been no clinical trials of gene therapy for disc repair to date.[16] Tissue engineered cell therapy actually introduces new cells into the disc to produce more ECM. Cellular therapy for disc repair has focused on chondrocyte and stem cell replacement therapy.[6,13] (Figure 4)

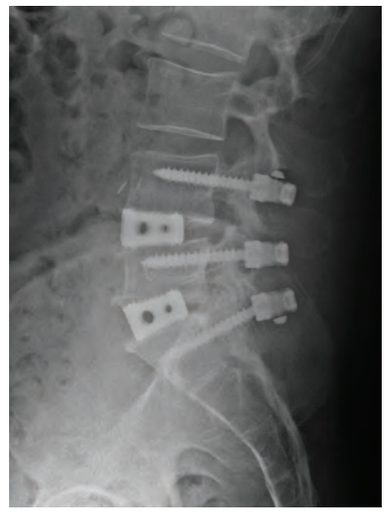

Figure 3. Lateral x-ray of a two level anterior lumbar interbody fusion.

Some anatomic factors favorably predispose the disc to cellular therapy. The nucleus is contained by the annulus and has a limited blood supply, limiting cell migration and providing a relatively immunologically privileged environment.[13,14] There has been extensive basic research and animal studies investigating nucleus repair, but there have been few clinical studies.[1,2,9] Both Yoshikawa et al. (2010),[17] two patients, and Orozco et al. (2011),[12] ten patients, published small series on patients with LBP treated with expanded iliac crest derived mesenchymal stem cells. Meisel and associates (2006) reported on 12 patients who underwent discectomy with harvest of autologous disc chondrocytes which were subsequently expanded in culture and re-injected into the disc space after twelve weeks (Eurodisc Study).[11] The preliminary results were promising with post-discectomy patients treated with autologous chondrocytes showing greater pain reduction at two year follow-up.[6,11]

Clinical study into these disc repair procedures have been classified by the FDA as Investigational New Drug (IND) studies, as opposed to the Investigational Device Exemption (IDE) studies of spinal device implants. Recently, two different IND studies

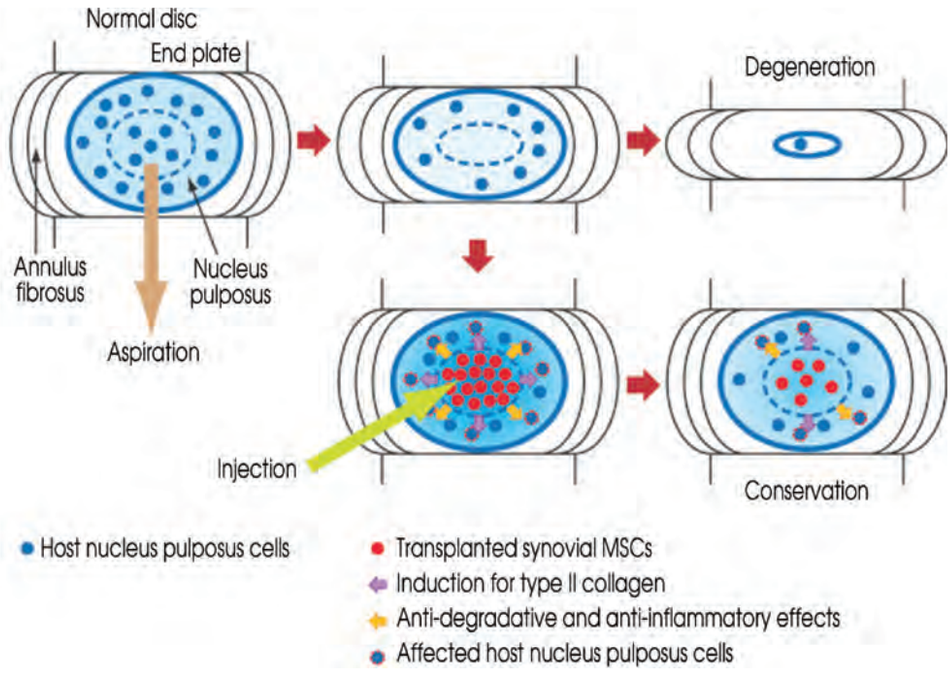

Figure 4. Proposed mechanism for cell therapy using mesenchymal stem cells (MSC) to preserve intervertebral discs. *Image courtesy of Arthritis Research and Therapy, retrieved from* Miyamoto, T., et al., Intradiscal transplantation of synovial mesenchymal stem cells prevents intervertebral disc degeneration through suppression of matrix metalloproteinase-related genes in nucleus pulposus cells in rabbits. *Arthritis & Research Therapy* 2010;12(6):R206.

have completed enrollment evaluating chondrocyte and stem cell procedures for disc repair, respectively: (1) 15 patients were treated prospectively at two sites with NuQu juvenile cartilage cells in 'An Open Label I/II Pilot Study to Evaluate the Treatment of Degenerative Lumbar Discs with Allogenic Cultured Chondrocytes' and (2) 100 patients were enrolled in a prospective, randomized study comparing Mesoblast stem cells to placebo in 'A Prospective, Multicenter, Double-Blind, Controlled Study Evaluating Safety and Preliminary Efficacy of a Single Injection of Adult Allogeneic Mesenchymal Precursor Cells Combined with Hyaluronan in Subjects with Chronic Discogenic Lumbar Back Pain.' A second multicenter trial utilizing NuQu juvenile chondrocyte cells is currently actively enrolling: 'A Phase II, Randomized, Double Blind, Placebo Controlled Study Evaluating the Treatment of Degenerative Lumbar Discs with Allogeneic Cultured Chondrocytes.' The research department at Carolina Neurosurgery and Spine Associates (CNSA) has been involved in all three studies, serving as the lead investigative site for both the NuQu studies.[6] (Figure 5)

Both NuQu (allogeneic juvenile chondrocyte cells) and Mesoblast (allogeneic mesenchymal stem cells) are investigational cellular therapies that involve harvest of cadaveric cells that are subsequently expanded in cell culture and frozen. Prior to use, the cells are thawed and combined with a carrier (commercial fibrinogen and thrombin, for the chondrocyte cells, and hyaluronic acid, for the stem cells). Finally, 5–10 million viable cells/cc are injected into the center of the disc space under fluoroscopic guidance during an outpatient procedure using 22-gauge needle. Generally, 1–2cc are injected into the disc over a period of 5–45 seconds.[6]

The results of the Phase I NuQu study have been published.[6] Fifteen patients (6 female, 9 male) were treated at 2 investigational sites with a single delivery of NuQu juvenile chondrocytes (levels: L3-4 = 2, L4-5 = 1, L5-S1 = 12, Pfirrmann grade III = 12; grade IV = 3). Mean age was 40 years (range 19–47). Fourteen of the 15 patients

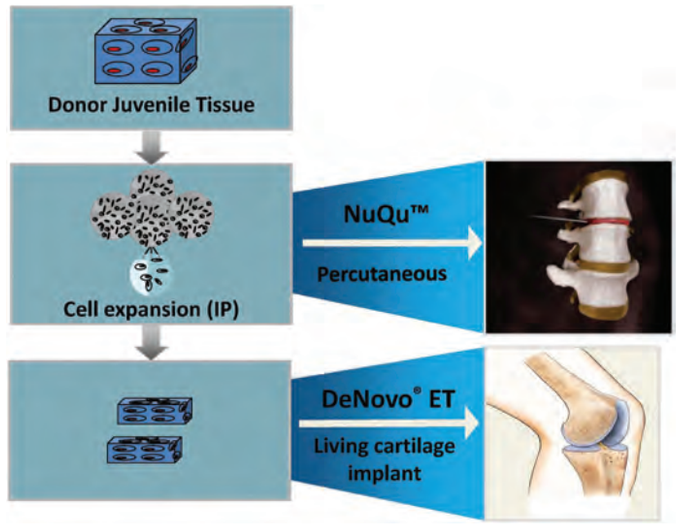

Figure 5. Examples of cell therapy using cadaveric chondrocytes as an allograft for regenerative intervertebral disc cell therapy and cartilage tissue transplant. *Image courtesy of ISTO Technologies, Inc.*

(93%) completed a minimum of 1 year follow-up. The pre-procedure morbidity of this patient population is reflected by the relatively high baseline disability (ODI = 53.3) and pain (NRS = 5.7) scores comparable to the baseline disability and pain scores of patients in the Charite and ProDisc-L IDE surgical trials. The clinical results showed statistically significant improvements from baseline on all clinical scales (ODI-disability scale, NRS-pain scale, and SF-36). The majority of radiographic parameters were unchanged; however, there was improvement in 10 of 13 patients imaged at 6 months and 8 of 13 patients imaged at 12 months. Improvements were primarily seen in posterior annular tears. Safety was also demonstrated; no patients experienced neurological deterioration, there were no disc infections, and there were no serious and unexpected adverse events. Lab studies indicated that there was no immunological response to the chondrocyte treatment.[6]

Biologic disc repair represents a minimally invasive and motion-preserving treatment to address LBP due to early lumbar DDD. Early results have been promising, but remain preliminary. Further investigation with prospective, randomized, blinded, placebo-controlled study design is necessary, warranted, and ongoing.

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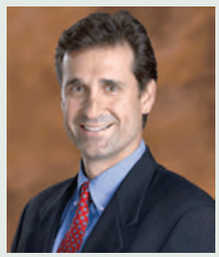

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New Bipedal Locomotion Option for Individuals with Thoracic Level Motor Complete Spinal Cord Injury

Alberto Esquenazi, M.D.

Until now, wheelchair propulsion has been the most common mode of locomotion for individuals with a motor complete thoracic level spinal cord injury (SCI).[1] Using a wheelchair, individuals are often able to navigate around a properly modified home and workplace environment, perform many activities of daily living, and engage in some social and recreational activities. However, wheelchair seating posture reduces the opportunity for eye to eye social interaction with able bodied adults, does not load the legs in a normal manner, can promote joint contractures, lead to pressure sores, and increase the risk of shoulder overuse.

Other modes of locomotion such as knee-ankle-foot orthoses (KAFOs) have come up far short of even the standard set by the wheelchair. Difficulty donning/doffing, high energy consumption and potential for increased upper limb overuse can all be identified as causes for KAFOs' limited use only as a therapeutic intervention.

Functional Electric Stimulation (FES) systems may enable patients to ambulate for very limited distances. This technique also has many limitations including requiring functioning lower motor neurons (LMNs) for neuromuscular excitability and complete sensory loss to tolerate the significant electrical stimulus needed to achieve muscular contraction. In addition, electrical stimulation differs greatly from the physiological nerve impulse because in FES all motor units in a muscle group are stimulated simultaneously. This rapidly induces muscle fatigue and results in high-energy consumption. The functional performances of all these methods remain quite modest in comparison to normal gait due to very low walking speed and high-energy utilization.

An alternative here described is the use of an externally powered orthosis that facilitates independent walking and in some cases stair climbing.

Description of the ReWalk™ Exoskeleton Suit[2,3]

The ReWalk is a lower extremity, battery powered exoskeleton that allows individuals with thoracic or lower level motor complete SCI to walk independently. ReWalk contains independently computer-controlled bilateral hip and knee joint motors, rechargeable batteries, and a computerized control system carried in a backpack. ReWalk users fully control their walking through subtle trunk motion and changes in center of gravity positions. A sensor registers these changes, determines the angle of the torso, and generates a preset hip and knee displacement (angle and time) that results in stepping. The ankles are supported using simple double action orthotic joints that have limited motion and spring assisted dorsiflexion, adjustable through screw tension. ReWalk currently exists in two versions, ReWalk I for use in institutional set up and ReWalk P for use at home and in the community. ReWalk I is easily adjustable in height and width, has padded interfaces for calves and thighs, and a rigid pelvic frame linking the limbs. Padded

The ReWalk suit enables ambulation for those with thoracic level motor complete spinal cord injury. *Image courtesy of Argo Medical Technologies.*

A. Esquenazi/Journal of the Spinal Research Foundation 8 (2013) 26–28

Velcro closures, shoes, and a waist belt are used to secure the user in the exoskeleton. ReWalk P is available in 4 sizes and multiple colors and is fitted by the manufacturer to match the patient anatomy. The same system, as previously described for ReWalk I, is also used to secure the user in the ReWalk P exoskeleton. Crutches provide standing stability, and the subject can interact remotely with the computer system handling a user-operated wrist pad controller that can command sit to stand, stand to sit, and walk activation.

Currently, there are two other commercial systems following on the tracks of ReWalk, but the unique manner in which the user is actively involved in controlling walking is only available in the ReWalk system. The specially designed software algorithm interprets a signal from the torso placed sensor and generates alternating limb coordinated motion to produce bipedal walking. As a safety feature, the system prevents two sequential steps of the same leg. During training, joint angle displacements for the knee and hip can be adjusted using an external computer to optimize the walking characteristics of the user. A manual training mode can be used to trigger steps bypassing the tilt sensor. The same mode of operation can be used to trigger sit-stand-sit transfers.

ReWalk is suitable for adults who have preserved bilateral upper extremity function after sustaining a SCI. Because the system is battery powered, completely untethered, and individuals are fully in control of when they step, ReWalk offers a real option to improve upon the current ambulation standard for individuals with thoracic level motor complete SCI. Moreover, because walking in ReWalk emulates upright bipedal walking, it may offer the potential to overcome some of the physical and psychosocial problems caused by the loss of natural walking. (Figure 1)

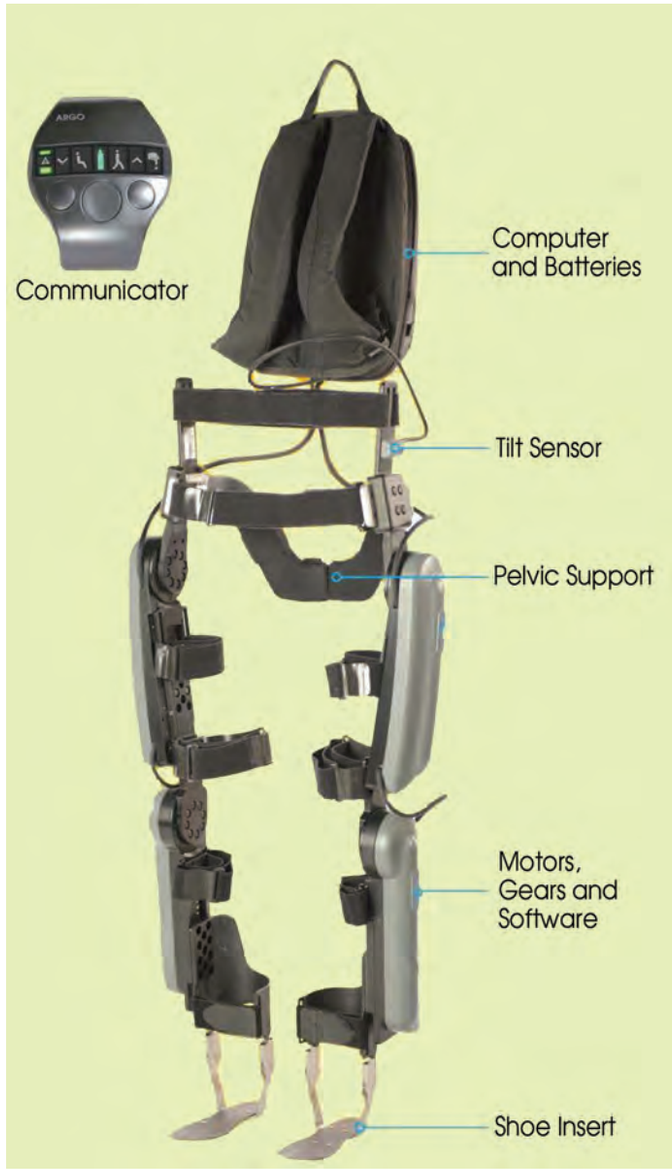

Figure 1. Components of Argo's ReWalk system. *Image courtesy of Argo Medical Technologies.*

Impact of the Loss of Walking for the SCI Population

Lack of standing, ambulation, muscle activity, weight bearing, and neuro-endocrine changes, all contribute to rapid and marked alteration in body composition. Individuals with SCI experience declines in muscle mass and bone density, as well as increases in adipose tissue. Additional complications, such as muscle atrophy, joint contractures, pressure sores, osteoporosis, increased spasticity, pain, edema, urinary and intestinal stasis, and carbohydrate, lipid and protein metabolism abnormalities may also be present.[4,5]

Non-recreational walking accounts for a significant fraction of activity for the average non-disabled adult. Lower physical activity levels have been observed after SCI resulting from lost motor function, lack of training during acute rehabilitation, decreased access to exercise facilities with adequate adaptive fitness equipment, limited time, and psychological factors. The physical de-conditioning resulting from largely sedentary lives of individuals with thoracic or higher level SCI is well documented.[5,6] Exercise has been shown to be an effective contributor to overall health maintenance, bone density, a proper level of muscle tone, cardiovascular fitness, regular bowel and bladder function, reduced risk for obesity, heart disease, and reduction of Type II diabetes for patients with SCI. Therapeutic exercise for individuals with SCI have several limitations. For example, they may have difficulty in exercise execution, insufficient cardiovascular stimulus, greater potential for injury, and they need specialized equipment. Individuals with thoracic level SCI who rely on wheelchair propulsion for locomotion and their arms for transfers may increase the likelihood of overuse of already taxed upper limb joints when performing upper body exercises including hand ergometry or weight lifting. Reduced work and leisure time after a SCI has been reported to reduce adherence to an exercise routine that is separate from, rather than a part of, the activities of daily living. Functional walking is an excellent means to accomplish exercise without requiring extra time commitments, but this is a difficult option—particularly for those with motor complete SCI at the thoracic or higher levels. ReWalk facilitates functional independent walking and may have a positive impact on many of the detrimental effects of spinal cord injury. In two recent publications, we have demonstrated the safety and tolerability of the device and some of the effects of training. Additional trials needed to demonstrate its impact on other physiological parameters are in the development stage.

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Pain Management

Thomas T. Nguyen, M.D., D.A.B.P.M.

The practice of pain medicine is multi-disciplinary in approach, incorporating modalities from various specialties to ensure the comprehensive evaluation and treatment of the pain patient. Today's pain specialists have sophisticated new treatments to provide pain relief including, but not limited to, newer effective drugs, implants, and electrical stimulation. These advances continue to emerge as researchers and clinicians gain further, greater understanding about the origin, mechanism, and perception of pain.

Pain specialists today have a better understanding of how the sensation of pain occurs within the human body from the periphery to the central nervous system, including the interaction between the spinal cord and the brain. Insights into the neurotransmitter system, where chemical messengers pass along signals of painful stimuli, have allowed for strategies to manipulate these painful messages to the brain, providing pain relief and analgesia. These discoveries have allowed pain clinicians to attack pain through different modalities, including using different classes of innovative medications targeted nerve ablative procedures, regenerative injections, different drug delivery systems, and neuromodulation within the spine itself. (Figure 1)

Medications

Medications are usually the first line of treatment for both acute and chronic pain for pain specialists. Since different types of pain, i.e., somatic or neuropathic, central or peripheral, can respond to different medications, it is most imperative to get the correct diagnosis and etiology of the pain. Subsequently, finding the most effective medications for your specific pain may be a trial and error process due to individual sensitivities and life exposures. There is no one best drug for everyone. Different drugs and drug combinations will be tested until the optimal goal of effective pain relief with minimal side effects is achieved.

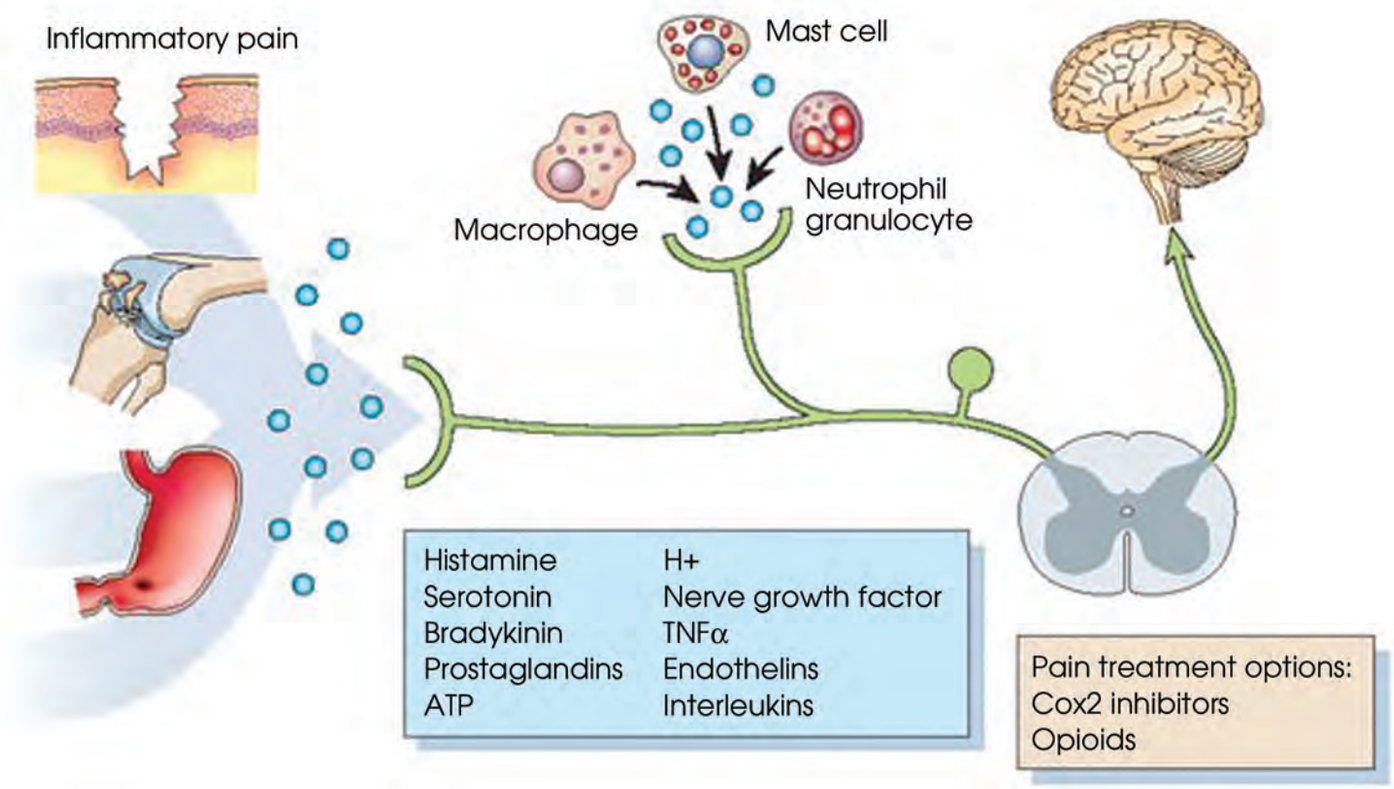


Figure 1. Cellular mechanism of inflammatory pain. Image courtesy of Nature Publishing Group, retrieved from Scholz, J. and Woolf, C.J., Can we conquer pain? *Nat Neurosci* 2002;5(Suppl):1062–7.

NSAIDs

When treating pain, physicians will typically start with oral nonsteroidal anti-inflammatory drugs that will address the pain from acute or chronic inflammation in cases of arthritis, bursitis, tendonitis and some cancer pain. Traditional NSAIDs are numerous and can have associated side effects of gastrointestinal discomfort especially with long term use. Newer, more selective NSAIDs known as COX-II inhibitors (e.g., Celebrex), increase tolerability by decreasing the chance of GI irritation. Other new medications (Arthrotec, Vimovo) come in a combination of a NSAID and a GI "protective" medication to negate the common adverse effects on the stomach. Albeit helpful, these newer NSAIDs still have potential to cause harm if not carefully monitored.

Antidepressants

For a long time, low doses of common antidepressants were being prescribed for many chronic pain problems. These drugs adjust levels of neurochemicals, which is thought to be their mechanisms for helping to control pain. Antidepressants are often used as analgesic adjuvants when patients don't get complete chronic pain relief from other treatments. They relieve pain regardless of whether the person is depressed or not. The doses needed to treat pain are usually lower than doses used for depression treatment. Tricyclic antidepressants (TCA) like amitriptyline (Elavil) and nortriptyline (Pamelor) have long been the mainstay antidepressants prescribed to help treat neuropathic pain like cancer pain, diabetic peripheral neuropathy, and postherpetic neuralgia (PHN) pain from shingles. They affect the brain concentrations of norepinephrine and serotonin. Their main disadvantage, which limited their use, was their strong side effects including, but not limited to, sedation, dry mouth, and orthostasis (low blood pressure upon standing).

More recently, new antidepressants have been developed with better side effect profiles and specific indications for certain chronic pain syndromes. Duloxetine (Cymbalta) and Milnacipran HCL (Savella) are in a class of antidepressants called serotonin and norephinephrine reuptake inhibitors (SNRI), which increases the availability of these chemicals in the brain. Cymbalta is FDA-approved for the treatment of diabetic neuropathy, fibromyalgia, and musculoskeletal pain like that of osteoporosis and chronic low back pain. Savella is FDA-approved for the treatment of fibromyalgia.

Topical Medications

Pain relief creams are increasingly becoming more popular to treat certain types of pain. Topical pain killers like Zostrix contain capsaicin, an ingredient found in peppers, which works by reducing transmission of a pain-relaying chemical called Substance P to the brain. Other products like Aspercreme and Bengay have ingredients like salicylate which decreases inflammation and relieves pain as well as counter-irritants like camphor, eucalyptus oil, and menthol, which relieve pain by causing either coolness or heat at the painful region. Topical NSAIDs are now available in gel (Voltaren Gel) and liquid (Pennsaid) form to address arthritic conditions.

There are also new types of transdermal patches that act to relieve pain. The Lidoderm patch contains lidocaine to offer local anesthesia. These patches are FDA-approved for chronic nerve pain from shingles, a condition known as postherpetic neuralgia. Qutenza is another pain patch that contains capsaicin to help relieve neuropathic pain. It is usually applied by your doctor and can be used every three months. A final type of pain patch is a transdermal NSAID patch (Flector) indicated for acute musculoskeletal strains and sprains.

Opiate Analgesics

When pain is severe, pain specialists may opt to try stronger pain medications. Opiate pain medications have been used since the beginning of human history. Narcotic pain medications like codeine, fentanyl, morphine, and oxycodone bind to central pain receptors and are very effective in controlling severe pain. Oxymorphone (Opana) is a newer synthetic opiate that is unique in its lack of CYP enzyme interaction with other drug metabolism (avoiding adverse drug interaction). Advances in opiate medication include

T. Nguyen/Journal of the Spinal Research Foundation 8 (2013) 29–35

extended release preparations that are longer in duration, ranging from a twenty-four hour extended release morphine pill (Avinza) to a seven day extended release transdermal buprenorphine patch (Butrans). Innovation in immediate release preparations include transmucosal fentanyl lozenges (Actiq), sublingual fentanyl sprays (Subsys) and sublingual fentanyl tablets (Fentora, Abstral); all of which are indicated for breakthrough cancer pain.

Procedures and Injections

Injections of medications to decrease pain and inflammation have long been used in pain medicine as additional, adjunctive treatment to medications. Traditionally, it has always been a combination of a steroid and a local anesthetic agent. The steroid acts to interrupt the inflammatory cascade that leads to pain and swelling. The local anesthetic provides immediate pain relief to provide diagnostic confirmation of the pain generator as well as to break the pain cycle in certain chronic pain syndromes like Complex Regional Pain Syndrome (CRPS) and trigger points.

Platelet Rich Plasma (PRP) Therapy

This is a revolutionary new treatment that relieves pain by promoting long lasting healing of musculoskeletal conditions. The body's first response to soft tissue injury is to deliver platelet cells. Packed with growth and healing factors, platelets initiate repair and attract the critical assistance of stem cells. PRP therapy channels the body's natural healing process to an injured region by delivering a higher concentration of platelets. To create PRP therapy, a small sample of blood is drawn (similar to a lab test sample) from the patient and placed in a centrifuge that spins the blood at high speeds, separating the platelets from the other components. The concentrated platelet rich plasma (PRP) is then injected into and around the point of injury, jump-starting and significantly strengthening the body's natural healing signal. Because the patient's own blood is used, there is no risk of a transmissible infection and a very low risk of allergic reaction.

Recent advances have also come in the area of injection technique. First came fluoroscopic imaging to assist with needle placement, which was previously done "blinded" or by "feel". Now, in an attempt to limit exposure to radiation, needle guidance and identification of structures is done with ultrasound. (Figures 2 and 3)

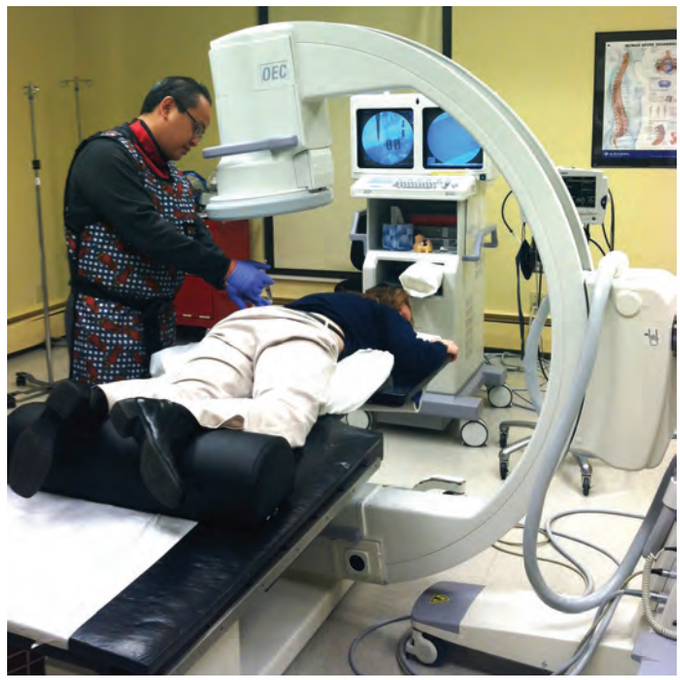


Figure 2. Fluoroscopic-guided procedure helps physicians visualize needle placement during injections.

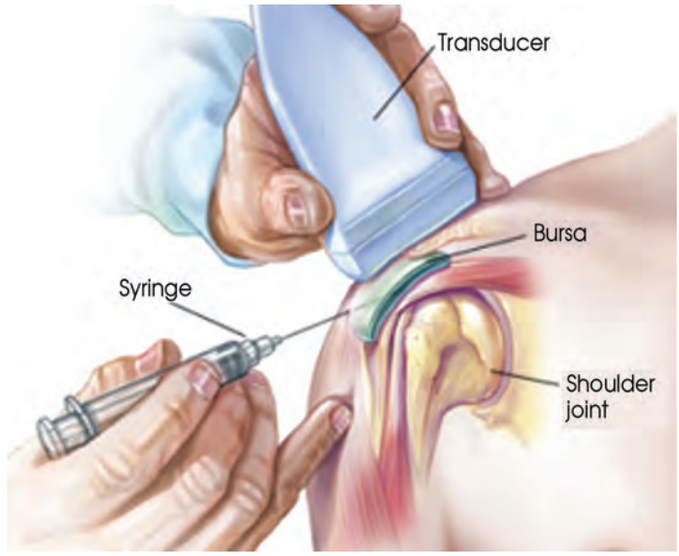


Figure 3. Ultrasound machines guide needle injections without harmful radiation exposure. *Image courtesy of the Mayo Clinic.*

Radiofrequency Ablation

A radiofrequency ablation (RFA) interrupts the sensory nerve pain signal to the involved facet or sacroiliac joint through the use of thermal denervation. After the skin is adequately anesthetized, the physician uses fluoroscopy (x-ray) guidance to place special radiofrequency needles alongside the nerves that supply the inflamed joint. After testing to ensure that the needle is in the correct position, thermal energy is applied, and the nerve is deadened. The goal of the RFA procedure is to provide more prolonged duration of relief for many months to years that is not achieved through standard steroid injections. This procedure is done as an outpatient. (Figures 4 and 5)

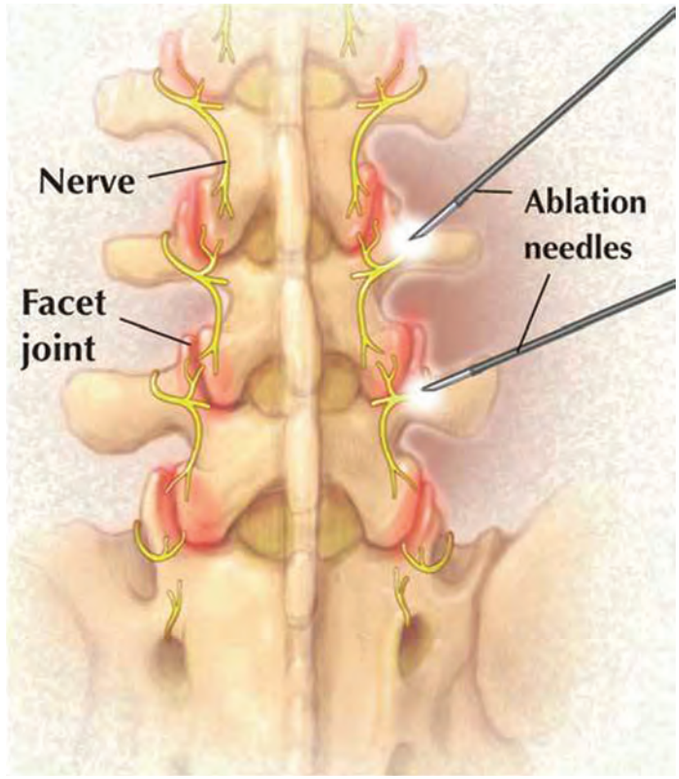


Figure 5. Facet radiofrequency ablation. Thermal energy is conducted through needles to destroy nerves surrounding the irritated facets in order to interrupt the painful stimulus. *Image courtesy of the Mayo Clinic.*

Interventional Therapies

Spinal Cord Stimulation

Spinal cord stimulation (SCS) is an innovative technology that addresses some of the most difficult pain problems experienced. Proven[1–3] as an effective treatment option for many chronic sufferers, SCS is most often used for neuropathic pain, including spinal radiculopathies, diabetic peripheral neuropathies, post-laminectomy syndrome (residual pain after back surgery), and Complex Regional Pain Syndrome (CRPS).[4] Neuropathic pain occurs when there is an injury, disease, or trauma to the central nervous system (spinal cord) or peripheral nervous system (any nerves outside the spinal column). Neuropathic pain symptoms can cause sharp, pricking, and/or stabbing pain. You may experience intense pain from a non-painful stimulus such as a light touch or a brush against the skin. You may also feel an exaggerated response to a painful stimulus. Spinal cord stimulation is an implanted device that transmits mild electrical impulses to the pain transmitting tracts on the spinal cord. The stimulation interrupts the message of feeling pain and substitutes it with a more pleasing sensation called paresthesia or "pleasant tingling". Spinal cord stimulation is often used

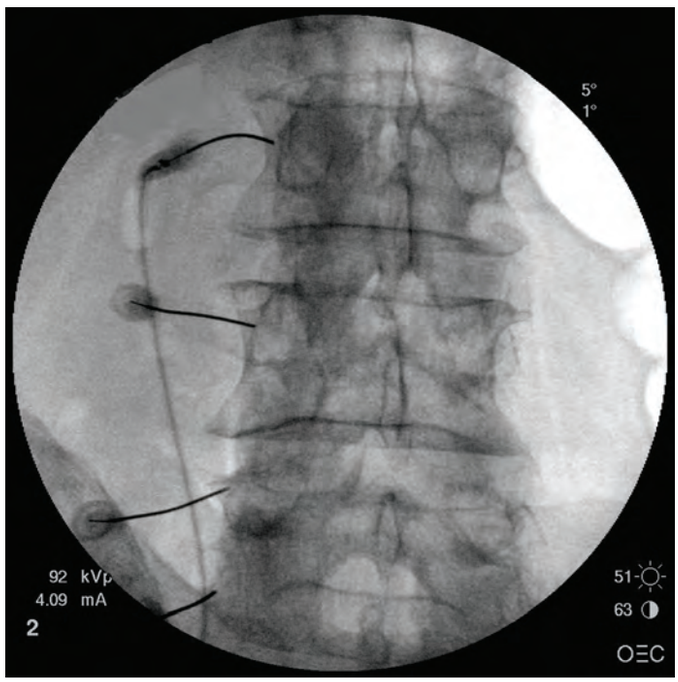


Figure 4. Fluoroscopic image of lumbar facet radiofrequency ablation procedure.

T. Nguyen/Journal of the Spinal Research Foundation 8 (2013) 29–35

when other treatments have failed. Recent new technology is focused on rechargeable, multi-programmable generators and various electrical lead arrays and configurations to provide maximal stimulation coverage. (Figure 6)

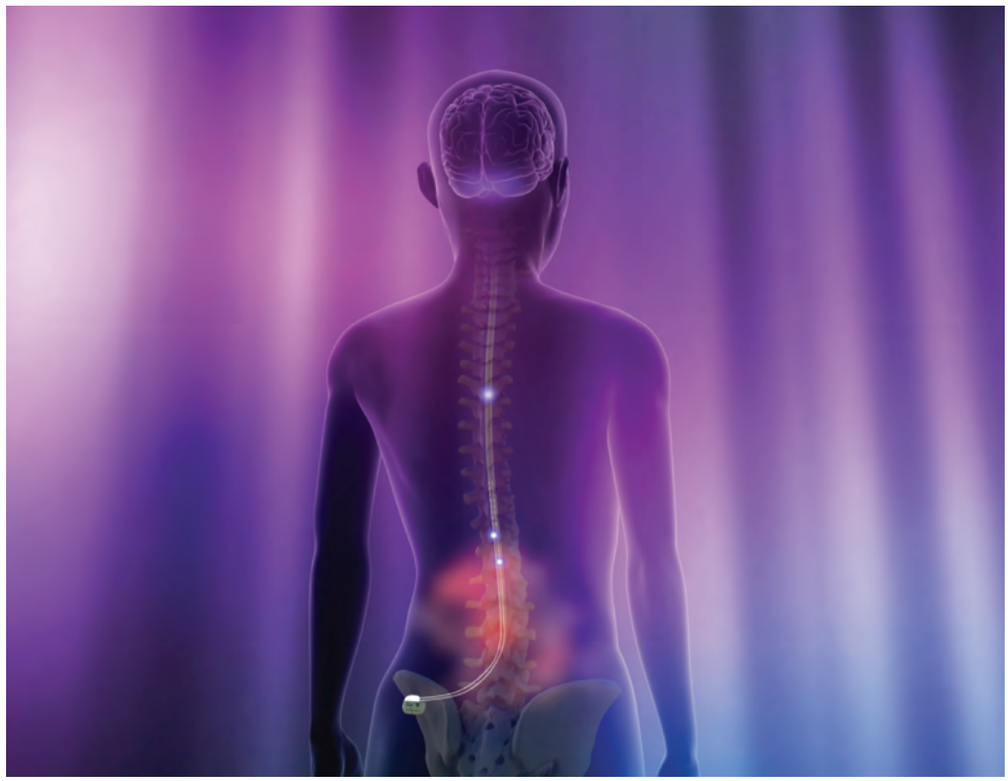


Figure 6. An implanted spinal cord stimulator device treats neuropathies by interrupting the painful nerve signal and replacing it with a more pleasant sensation called paresthesia. *Image courtesy of St. Jude Medical, Inc.*

Intrathecal Pumps

An intrathecal pain pump is a method of delivering pain medication directly to a patient's spinal cord. The system uses a small, programmable pump that is surgically placed under the skin of the abdomen and delivers medication through a catheter into the area around the spinal cord (similar to an epidural that women may have during childbirth). A pain pump may be a treatment option if all other traditional methods have failed to relieve long-term symptoms of chronic pain. Because the medication is delivered directly to the spinal cord, symptoms can be controlled with a much smaller dose than is needed with oral medication. The goal of an intrathecal pain pump is to better control a patient's symptoms while drastically reducing the side effects noted with oral medications. An intrathecal pain pump works much more efficiently than oral pain medication because it delivers medicine directly into the cerebrospinal fluid, bypassing the path that oral medication takes through the body. In fact, the potency of the medication is about 100–300x more with the pump than when taken orally. (Figure 7)

New Therapies on the Horizon

Deep Brain Stimulation (DBS)

The goal of deep brain stimulation and motor cortex stimulation is to restore function or relieve pain by stimulating neural activity through surgically implanted electrodes. DBS was developed in the 1980s principally to treat movement disorders associated with essential tremor (ET) and Parkinson's disease (PD). Today, its applications include other types of

Figure 7. This intrathecal pain pump is implanted under the skin of the abdomen and delivers pain medication directly to the spinal cord.

movement disorders and certain non-motor syndromes and pain conditions. Currently, deep brain stimulation is being studied to treat central neuropathic pain syndromes like trigeminal autonomic cephalgia and cluster headaches.[5]

Transcranial Magnetic Stimulation (TMS)

Transcranial magnetic stimulation is a tool that has been used in a wide variety of neurological disorders, including experimental, diagnostic, and therapeutic purposes. The TMS procedure produces a magnetic field that traverses the skull relatively unimpeded and induces an electrical field that yields actual brain stimulation. (Because TMS is noninvasive and painless, it can be easily performed in awake patients. Repetitive TMS has been investigated as a potential therapy in patients with medically intractable neuropathic pain and migraine headaches.[6] (Figure 8)

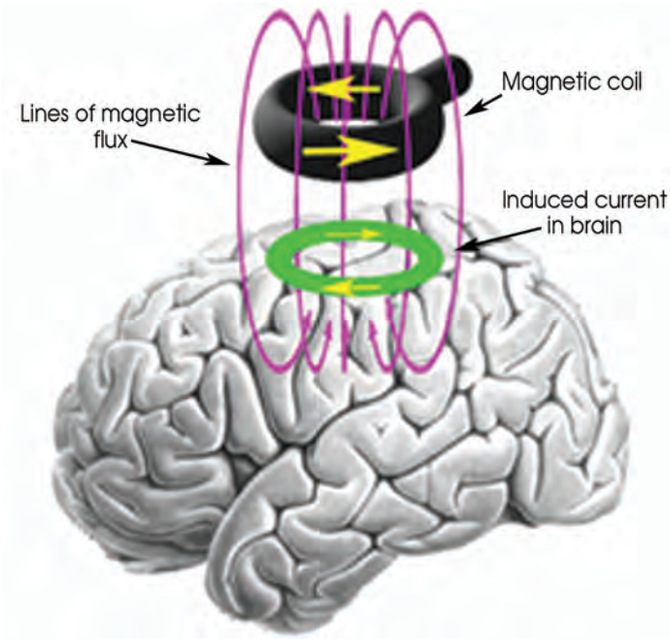
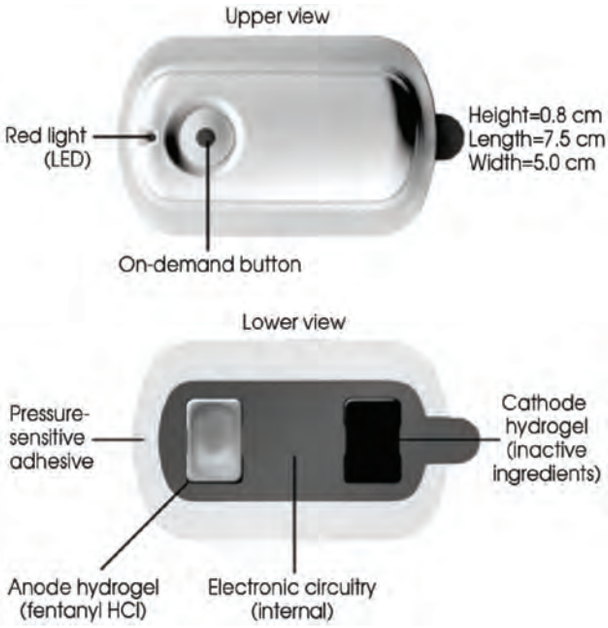
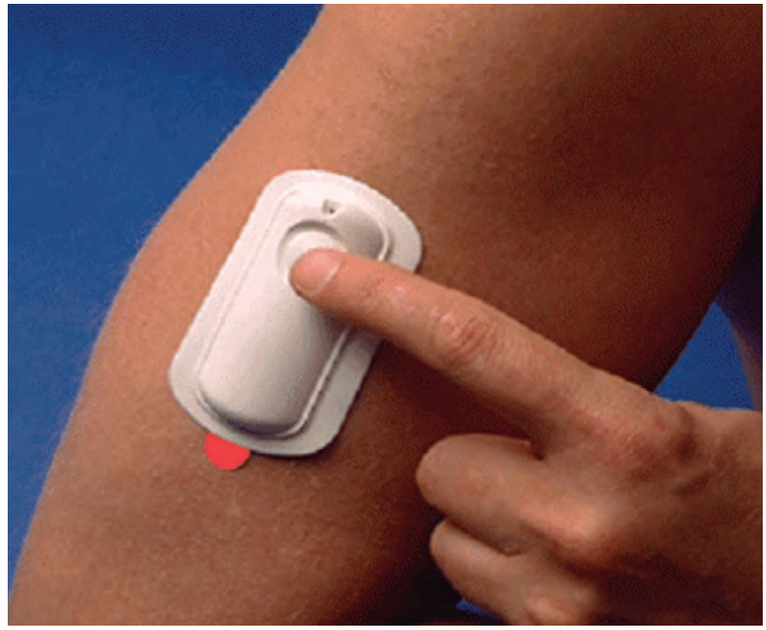


Figure 8. Transcranial Magnetic Stimulation (TMS) uses a magnetic coil to induce a magnetic field across the brain, yielding brain activity stimulation. *Image courtesy of the Laboratory for Cognition and Neural Stimulation, Neurology Department, School of Medicine, University of Pennsylvania.*

Fentanyl HCL Iontophoretic Transdermal System (Fentanyl ITS)

The use of patient-controlled analgesia (PCA) over the last few decades has resulted in vast improvement in management of postoperative pain control and patient satisfaction. PCA allows patients to self-administer pain medications according to their own personal requirements for pain relief. The common routes of





Figures 9 and 10. Iontophoresis. The patient controls drug delivery through the skin with low-intensity electric current. *Image courtesy of Janssen Pharmaceutica NV, Beerse, Belgium.*

administration for the PCA have been through the intravenous line or epidural catheter. Iontophoresis uses a low-intensity electric current to transport ionized drug molecules actively across the skin and into the systemic circulation. Iontophoretic drug delivery is more advantageous over passive transdermal administration as the drug delivery is strictly controlled by the application of electric current which offers precise control over the frequency of analgesic dosing with a non-invasive approach.[7] (Figures 9 and 10)

Conclusion

As the field of pain management evolves, scientists and clinicians from various specialties and medical fields work towards ever improving our understanding of the mechanism of pain and how to counteract it to provide excellent pain control. We look for new innovative medications, devices, delivery systems and surgeries. We aim to achieve satisfactory analgesia while limiting adverse effects from medications. We have only reached the tip of the iceberg.

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Thomas T. Nguyen, M.D., D.A.B.P.M.

Dr. Nguyen specializes in advanced, minimally invasive diagnostic and treatment modalities for acute and chronic pain syndromes. Dr. Nguyen has practiced pain medicine since finishing his pain fellowship at the Mayo Clinic in 1999. He was the founder and medical director of the Comprehensive Pain Management Center in Newport News, VA from 1999–2002. He is an active member of the American Academy of Pain Medicine, the International Spine Intervention Society, and the American Academy of Family Practice. Dr. Nguyen is involved in several national multicenter studies for the treatment of chronic back pain.

Sacroiliac Joint Stabilization

Michael W. Hasz, M.D., F.A.C.S.

Within the past few years, there has been a resurgence in the recognition of the sacroiliac (SI) joint as a potential source of low back pain. For instance, up to 25% of patients presenting to a spine clinic have been found to have significant pain contribution from the hip or SI joint.[1] Much of this resurgence is due to recent advances in the treatment options of sacroiliac joint dysfunction. The majority of patients can be treated non-operatively through anti-inflammatory medications, physical therapy, or SI joint injections. However, some patients will require surgical treatment. This review discusses two recent entries into the lateral approach for the stabilization and fusion of the sacroiliac joint.

Numerous techniques have been described for the surgical treatment of sacroiliac joint dysfunction with little agreement as to their relative advantages. One type of surgical technique involves the removal of a rectangular window of bone from the ilium immediately over the sacroiliac joint, allowing exposure of the articular surface of the joint. The articular cartilage is curetted from the sacrum and the ilium, then the bone block is reinserted. The joint is stabilized with the use of a T- or L-plate and screws. Patients have to remain non-weightbearing on the affected side for 3 months or until evidence of solid fusion is seen.[2]

Figure 1. SI-Bone's iFuse implant. *Image courtesy of SI-BONE, Inc.*

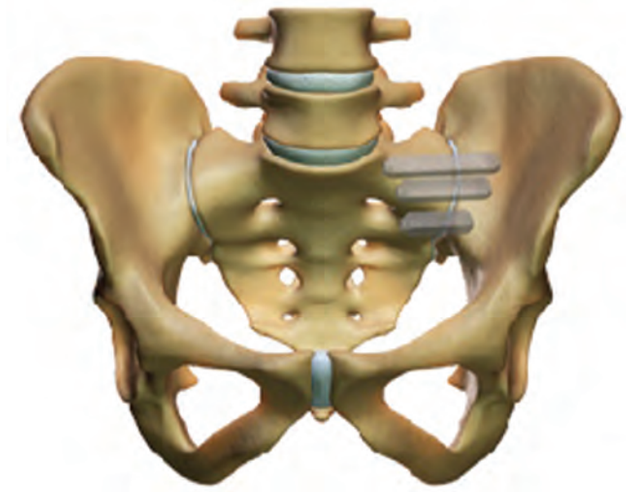

Figure 2. The iFuse implant inserted across the sacroiliac joint to reduce pain and give stability to the joint. *Image courtesy of SI-BONE, Inc.*

Another approach to the stabilization of the sacroiliac joint uses the percutaneous placement of cannulated screws across the joint. This procedure stabilizes the joint but does not fuse it. In my experience, reviewing patients who have had this procedure, the initial stabilization can afford some pain relief. However, often the continued micromotion across the sacroiliac joint lends toward eventual loosening of the stabilization, and the patient's symptoms often return.

Two recent techniques have been proposed to address the issue of late loosening. One is the *iFuse* implant system from SI-Bone (San Jose, CA). The other is the *SImmetry* system from Zyga Technologies (Minneapolis, MN). Both of these technologies afford lateral access to and offer stabilization of the sacroiliac joint. The initial stabilization is provided by the instrumentation.

M.W. Hasz/Journal of the Spinal Research Foundation 8 (2013) 36–37

In the case of the iFuse system, two to four, but usually three, triangular shaped titanium rods are placed across the sacroiliac joint, with the rod extending from within the ilium to within the sacrum (Figure 1). These rods afford initial stabilization and can provide significant initial improvement in the pain, postoperatively. The iFuse procedure also relies upon a surface technology on the implants (porous plasma spray) to encourage and/or allow bone in-growth into these devices. Both the triangular shape and the coating of the implant are designed to prevent rotation and motion of the SI joint, with the intention to give long-term stability to the joint (Figure 2).

The Zyga SImmetry system also affords initial stabilization across the SI joint via two large compression screws (Figure 3). Zyga's technology differs from that of SI-Bone in that it actually addresses a goal of obtaining a fusion of the SI joint. A device is placed directly into the SI joint to remove soft tissue and prepare the bony edges for actual fusion. Once the SI joint has been prepared, bone graft can then be placed within the joint. Two screws are placed across the joint for initial stability and the long-term goal of actual fusion of the SI joint (Figure 4).

Both technologies, from SI-Bone and Zyga, are muscle splitting, small incision approaches. They require fluoroscopic imaging or other image guidance for the procedure. They are a lateral approach to and across the sacroiliac joint, and both can allow the patient to be up and mobilized very rapidly.

Figure 3. Zyga Technology's SImmetry compression screws. *Image courtesy of Zyga Technology.*

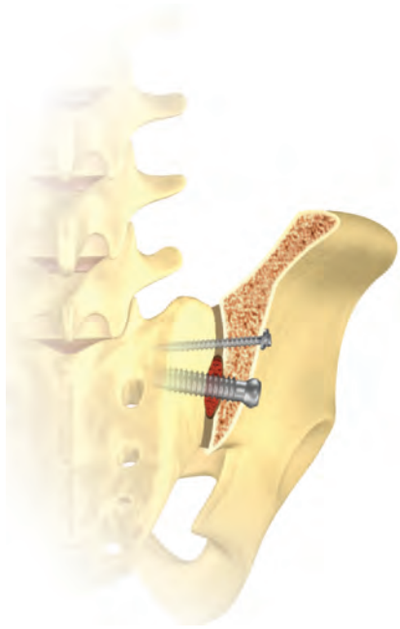

Figure 4. SImmetry screws implanted to fuse the sacroiliac joint. *Image courtesy of Zyga Technology.*

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Michael W. Hasz, M.D., F.A.C.S.

Dr. Hasz is a spine surgeon at The Virginia Spine Institute. He is board certified by The American Board of Spine Surgery, a Fellow in the American Academy of Orthopaedic Surgeons and a member of both the American Association of Orthopaedic Surgeons and the North American Spine Society. He was Chairman of the Department of Orthopaedic Surgery and Director of Spinal Surgery at the Andrews Air Force Base/Malcolm Grow Medical Center in Maryland. He currently holds an appointment as Clinical Instructor of Orthopaedic Surgery and Assistant Professor of Surgery at the Uniformed Services Health Science University in Bethesda, Maryland.

Trigger Point Dry Needling

Jessica Stepien, P.T., D.P.T.

Trigger point dry needling, also known as intramuscular stimulation, is a technique using a solid filament needle to treat hyperirritable spots of the skeletal muscle. These hyperirritable spots are called trigger points and are typically associated with palpable nodules in taut bands of tissue. (Figure 1) Physical therapists insert a dry needle, without medication or injection, in trigger points to treat myofascial pain.[1]

As far back as the 16th century, myofascial pain syndromes have been recognized by medical practitioners as causing sensory, motor, and autonomic symptoms and dysfunctions. Myofascial pain syndromes are associated with the palpable nodules or taut bands known as myofascial trigger points. Dr. Janet Travell is recognized for bringing attention to myofascial trigger points in the mid 1900's. Dr. Travell started her medical career in cardiology and later shifted to musculoskeletal conditions due to her interest in muscle pain and the impact of referred pain on patient's dysfunction. Myofascial origin of pain was discovered through an injection of hypertonic saline into trigger points which produced referred pain patterns. Initially, injection of an analgesic medication into the trigger points produced a decrease in a patient's symptoms, pain, and the sensitivity to touch of the trigger points.[2] After further research, it was discovered that the actual insertion and stimulation of the muscle with a dry needle produced pain relief without the need for medication. Thus, the development of trigger point dry needling began. (Figure 2)

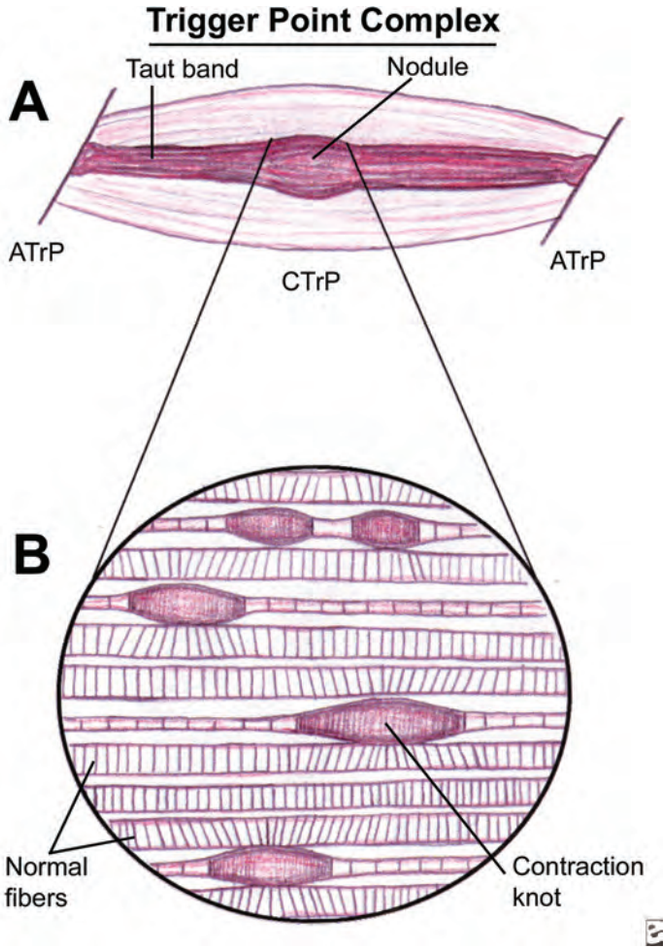

Figure 1. Trigger point complex. *Image courtesy of Medscape.com, 2011, available at http://emedicine.com/article/89095-overview.*

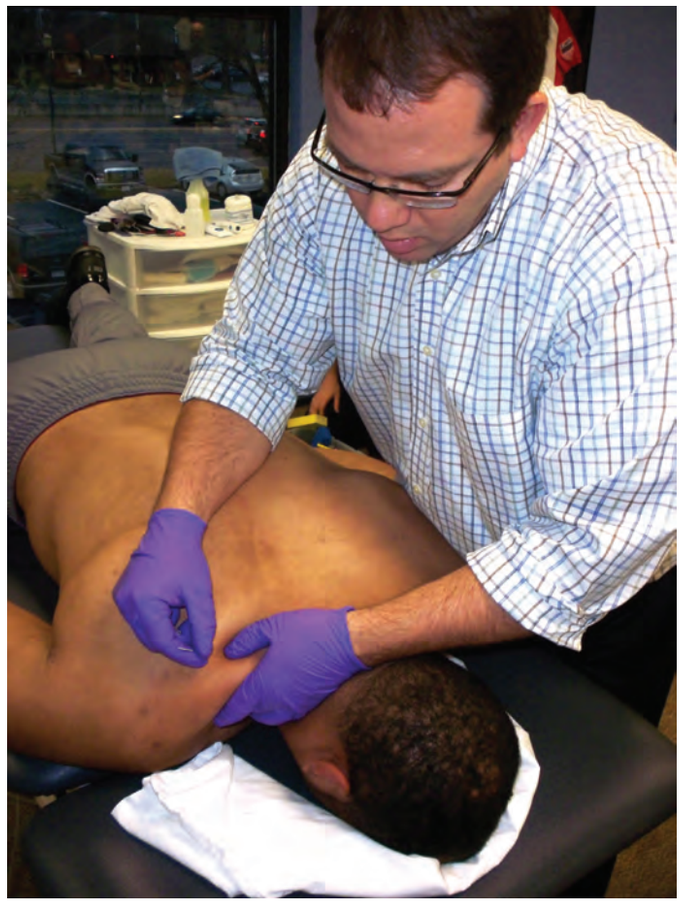

Figure 2. Trigger point needling.

J. Stepien/Journal of the Spinal Research Foundation 8 (2013) 38–40

The perpetuating factors of myofascial pain syndromes are low level musculature contraction, unaccustomed eccentric contraction, muscle overloads, and muscle fatigue. These factors can be caused by, but not limited to, mechanical dysfunctions such as forward head postures, joint hypermobilities, ergonomic stressors, poor body mechanics, and scoliosis.

Dry needling techniques are developed on various models, which are implemented in physical therapy practices on a daily basis. Dr. Chan Gunn contributed to the development of dry needling and introduced the term intramuscular stimulation (IMS), in which he described that myofascial pain syndromes are a result of radiculopathy or peripheral neuropathy, causing a disordered function of the peripheral nerve. This concept is referred to as the radiculopathy model and is based on the Cannon and Rosenblueth's *law of denervation*, which states that free flow of nerve impulses maintains innervated function and integrity of structures. When any neural flow is disrupted, all the structures that are innervated by that nerve, such as skeletal muscle, smooth muscle, spinal neurons, sympathetic ganglia, and sweat glands, are affected and can become atrophic, highly irritable, and hypersensitive. The trigger point model describes myofascial trigger points consisting of taut musculature bands due to the excessive release of acetylcholine. Myofascial trigger points are classified as active or latent. Active myofascial trigger points can cause local and referred pain, or other parasthesias, whereas latent myofascial trigger points may not produce pain without being stimulated. Active myofascial trigger points typically refer pain to a particular site, and these sites are not restricted to a single segmental or peripheral nerve distribution. Clinically, myofascial trigger points can cause motor dysfunction or muscle weakness as a result of motor inhibition, restricted motion, and muscular stiffness. Furthermore, sensory dysfunctions may be noted through localized tenderness, referral of pain to specific areas, hyperalgesia (extreme pain reaction to a painful stimulus), and/or allodynia (pain reaction to a non-painful stimulus).

The goal of the insertion of a fine filament needle into a trigger point is to produce a twitch response (short contraction) of the muscle being needled. The twitch of the muscle is the desired response; however, benefits can occur even without a twitch of the muscle. The simple insertion of the needle into the taut bands can interrupt the pathogenic process and produce mechanical changes in the tissue. (Figure 3) The insertion of a needle into the trigger point can produce a deep ache or cramping pressure that lasts only briefly. Reproduction of pain and referral of symptoms may also occur, and soreness may last up to 24–48 hours. Improvements in functional range of motion, decrease in complaints of pain, and ease of mobility may be seen after treatment.

Dry needling allows access to deep musculature that may never have been reached without the use of a needle. By releasing the myofascial restrictions through trigger point dry needling, a physical therapist is able to further enhance a patients care and return to function. Trigger point dry needling can disrupt the

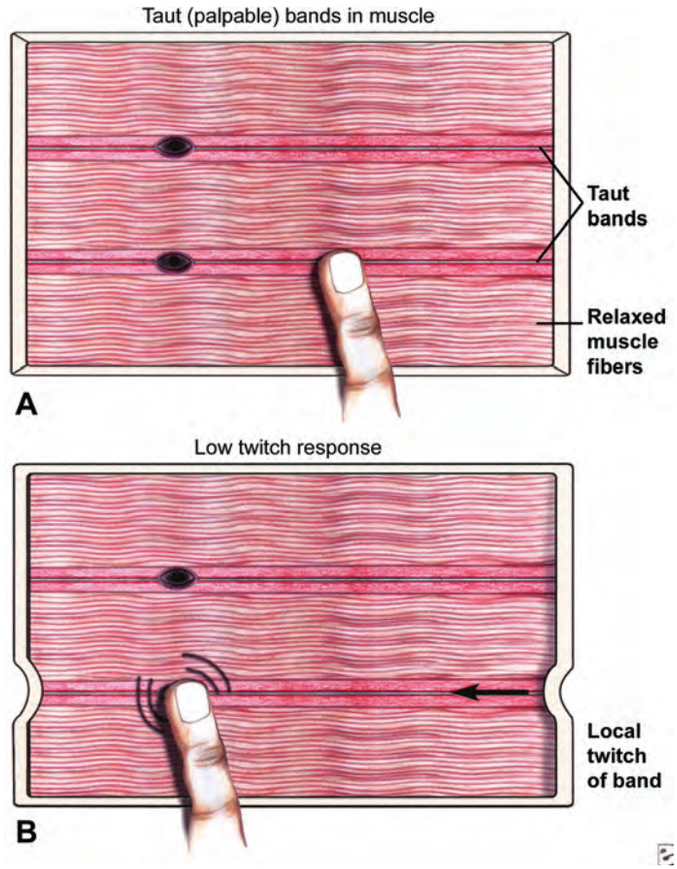

Figure 3. Identification of trigger by low-twitch response to palpation. *Image courtesy of Medscape.com, 2011, available at http://emedicine.com/article/89095-overview.*

neurological feedback loop eliciting pain in the musculoskeletal system.

Myofascial trigger point dry needling has no similarities with traditional acupuncture except for the tool being used during the process.[3] Traditionally, acupuncture is based upon Chinese medicine that seeks to regulate flow and stability of energy through subcutaneous placements of needles. Acupuncture points are points mainly along the paths of energy flow (or meridians). In contrast, trigger point dry needles are inserted into specific musculature, targeting tight muscles, and based on neuromuscular and biomechanical principles.

Trigger point dry needling is a novel technique in physical therapy.[4] Internationally, Australia, Belgium, Canada, Chile, Denmark, Ireland, The Netherlands, New Zealand, Norway, South Africa, Spain, Sweden, and Switzerland have recognized trigger point dry needling to be within the scope of practice for a physical therapist. In the United States, each state licensure board determines the appropriateness of dry needling within the state's scope of practice for physical therapy. In 1984, Maryland was the first state to approve dry needling as a technique within the scope of physical therapy practice. The acceptance of dry needling is rapidly spreading. As of 2012, approximately 30 states have approved dry needling as a procedure within the scope of the physical therapy practice.

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Dr. Stepien is a physical therapist at The Virginia Therapy and Fitness Center. Her certifications and training includes: North American Institute of Orthopaedic Manual Training, Level I & II; Theraband Academy, Beyond Ball, Institute of Advanced Musculoskeletal Treatments, Trigger Point Dry Needling. Jessica's commitment to quality in patient care returns her patients back to physical excellence while achieving their goals and maximizing their quality of life. During her graduate studies, Jessica was awarded the K. Madison Smith Award for Clinical Excellence as voted on by her clinical internship instructors, the 2012 Outstanding Graduate Award as voted on by her Shenandoah University professors, and received the Best Performance on Physical Therapy Comprehensive Exam for her graduation class.

Advances in Bone Grafts and Fusion Augmentation

Marcus M. Martin, Ph.D., and Anne G. Copay, Ph.D.

One of the main sources of back pain is clinical spinal instability.[1] This pain often originates at the motion segments of the spine or intervertebral discs. The resultant back pain is often treated with the surgical stabilization of a painful spine segment. Instrumentation provides an immediate stabilization of the spine segment, while bone grafts facilitate a biologic response to promote the formation of new bone. The formation of new bone permanently fuses the spine segments. Once fusion occurs, mechanical loads are transferred from the instrumentation to the fused spine segment. If fusion does not occur, the instrumentation will remain subject to mechanical loads and may eventually fail due to metal fatigue.[2] Furthermore, continued motion in a painful spine segment is likely to remain a source of pain.

Bone grafts are utilized as either scaffolding for osteogenesis (bone formation) or stimulation of bone growth in a desired area. Recently, there has been an increased emphasis on incorporating biologic therapies in bone-forming grafts.

The **mechanisms of actions** of bone grafts fall into three general types:

- **Osteogenesis:** The bone graft contains bone-forming cells (osteoblasts). Bone harvested from a person's iliac crest is typically used and contains osteoblasts. Local bone removed at the surgical site is a convenient source of graft, but generally contains cortical bone with much fewer osteoblasts.
- **Osteoconduction:** The graft material acts as a scaffold onto which bone cells can attach, grow, divide, and migrate. Osteoblasts work much better when they have a scaffold or matrix for attachment.
- **Osteoinduction:** The bone graft contains chemicals that attract primitive stem cells and immature bone cells, then promote the proliferation and differentiation of these cells into bone-forming cells.

Grafts may be **classified** according to their composition and mechanism of actions.

- **Bone:** Grafts made of bone are osteoconductive and may be osteogenic if they contain bone-forming cells.
  - Autografts: patients's own bone (iliac crest or local bone)
  - Allografts: donor bone (cadavers or tissue bank)
    - Demineralized bone matrix (DBM): human-derived bone powder is demineralized, leaving only the organic bone matrix
    - Mineralized allograft: cortical/cancellous bone chips are chopped-up pieces of bone
      - Xenograft: mineralized cortical granules of bone derived from another species (most commonly cows and pigs).
- **Ceramics:** Ceramics are synthetic materials manufactured so that each ceramic granule mimics human cancellous bone. Ceramics are primarily osteoconductive. Common ceramic materials are:
  - Hydroxyapatite (HA)
  - Tricalcium Phosphate (TCP)
  - Biphasic Calcium Phosphate (HA:TCP)
  - Calcium Sulfate
- **Cell-signaling materials:** Cell-signaling materials are osteoinductive.
  - Bone Morphogenetic Proteins (BMPs) are proteins present in small quantities within bone. It would require hundreds of kilograms of bone to extract milligram quantities of BMP. Researchers were able to produce these proteins in large quantities through the use of recombinant DNA technology. BMPs promote the migration of primitive stem cells and immature bone cells, their proliferation, and their differentiation into bone-forming cells.
  - i-FACTOR Biologic Bone Graft combines a unique anorganic bone mineral (ABM) and small peptide (P-15) that acts as an attachment factor for specific integrins on osteogenic cells.

Historically, bone harvested from the iliac crest has been the graft of choice in spine surgery. However, its effectiveness depends on the patient's bone quality.

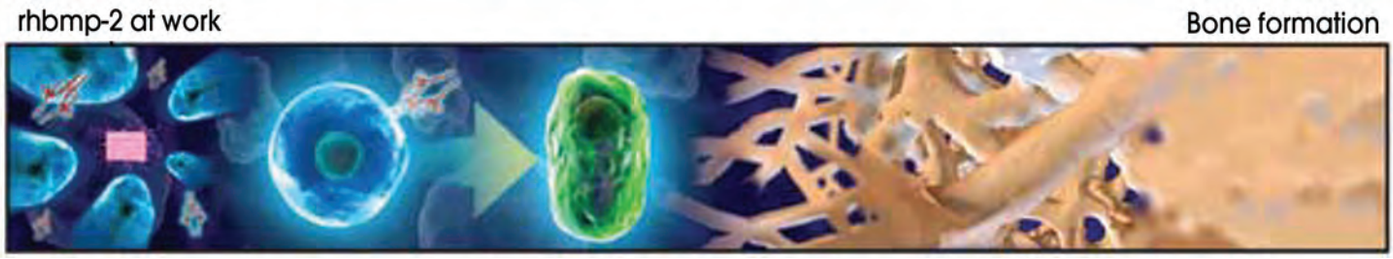

Figure 1. BMPs are osteoinductive proteins that promote cell migration of bone-forming cells such as osteoblasts (shown in green), osteoprogenitor cells, and undifferentiated mesenchymal stem. *Image courtesy of Medtronic, Inc.*

Furthermore, the added surgical procedure required to harvest bone from the iliac crest may lead to increased morbidity, blood loss, injury to local nerves, damage to blood and lymphatic vessels, infection, disturbances in gait, prolonged hospitalization, and protracted recuperative time.[3]

In 2006, the FDA approved the use of bone morphogenetic proteins (BMPs) in spinal fusion. BMPs are members of the TGF β superfamily of biological molecules. BMP molecules share a similar structure and amino acid sequence at the carboxyl terminal region. Different BMPs are not interchangeable, though some such as BMP-2 and BMP-4 show significant homology. Through signal transduction, BMP receptors effect the mobilization of members of the SMAD family of proteins which are associated with bone development.[4] BMPs interact with bone morphogenetic protein receptors (BMPRs) on the cell surface. This initiates a cascade of events that can facilitate bone formation. BMPs may be active at multiple points throughout this cascade. First, BMPs induce cell migration to the site of administration. Osteoprogenitor cells, osteoblasts, and mesenchymal stem cells respond to the chemotaxic signal. Mesenchymal stem cells are undifferentiated and can produce several connective tissue cells including cartilage-producing chondrocytes and bone-producing osteoblasts. The proliferative response may be enhanced by molecular signals released by cells at the injury site. BMPs affect undifferentiated cells but do not appear to have a cell-specific effect on mature differentiated cells.[5] (Figure 1)

Currently, a clinical trial has been launched investigating the use of P-15, an amino acid peptide, in cervical fusion. i-FACTOR™ (Cerapedics, Broomfield, CO) is a peptide-enhanced bone graft that utilizes a unique small peptide (P-15™) intended to stimulate the natural bone healing process. It combines anorganic bone mineral (ABM) and P-15 to act together as an attachment factor for specific integrins on osteogenic cells. (Figure 2)

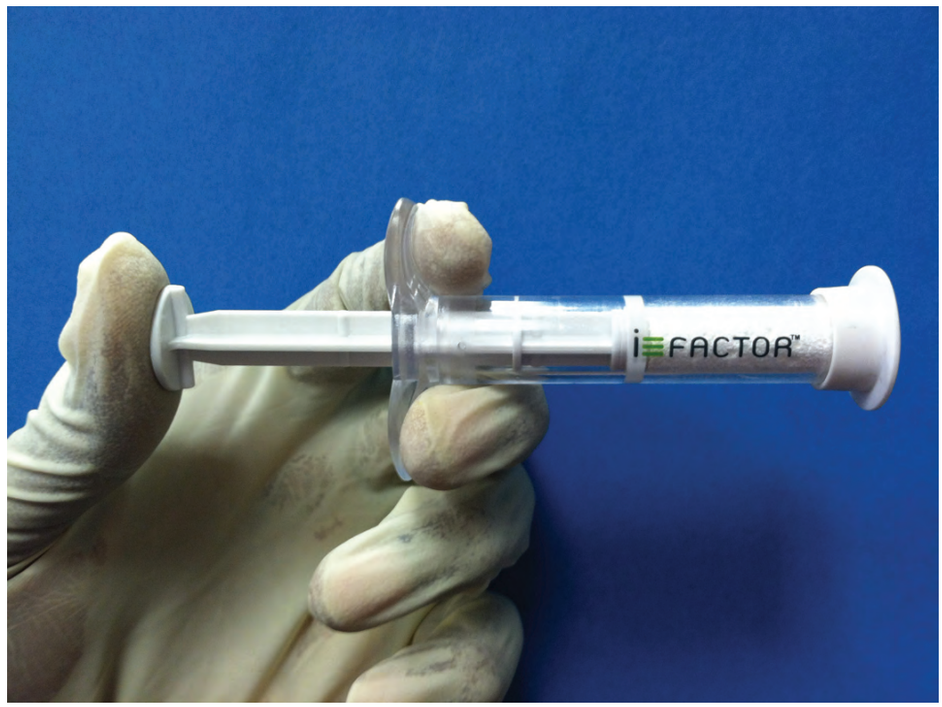

Figure 2. iFACTOR Bone Graft is injected during spinal fusion surgeries. *Image courtesy of Cerapedics, Inc.*

M.M. Martin and A.G. Copay/Journal of the Spinal Research Foundation 8 (2013) 41–44

The first step in the bone formation process is cell attachment. Osteogenic precursor cells bind to P-15 via their α2β1 integrins, which are signaling receptors. i-FACTOR bone graft is placed in a bony defect in the presence of bleeding bone, an environment rich with osteogenic cells. It is intended to increase the opportunity for cell binding in the fusion site by making an abundance of P-15 available to osteogenic precursor cells, potentially resulting in enhanced cell attachment. Osteogenic cells contain α2β1 integrins that act as signaling receptors, allowing cells to attach to P-15. Cell binding between P-15 and α2β1 integrins is intended to initiate natural signaling of mechanical and chemical information within the cell and the extracellular matrix, contributing to the production of specific growth factors, cytokines, and bone morphogenetic proteins (BMPs) and ultimately, leading to new bone formation. i-FACTOR is designed to stimulate a healing response only in the presence of bone-forming cells. This novel mechanism of action is intended to enhance the body's natural bone healing process.

P-15 Small Peptide- i-FACTOR technology is based on the biological activity resulting from a synthetically derived form of a 15-amino acid peptide found in type I human collagen. Type I human collagen is the primary organic component found in autograft bone. This 15-amino acid peptide is responsible for the attachment and proliferation of osteogenic cells. These cells attach to the synthetic P-15 part of i-FACTOR in a similar way they would attach to type I collagen.

- Anorganic Bone Mineral (ABM) provides the optimal surface for irreversible electrostatic binding of P-15. ABM is a naturally porous bone scaffold with a physiological rate of resorption, resulting in a substrate favorable to osteogenic cell growth and formation.

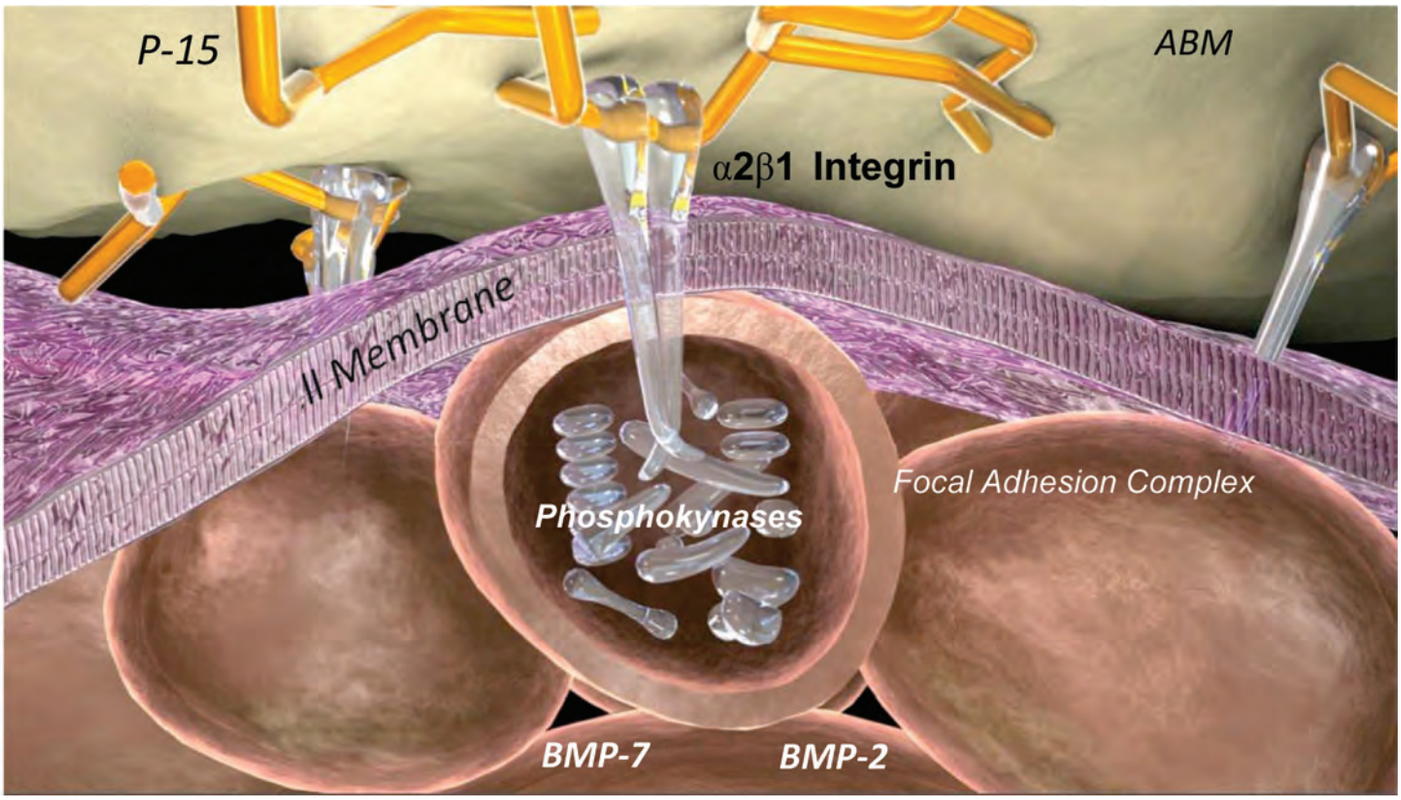

Figure 3. P-15: A synthetic fifteen amino acid polypeptide that mimics the cell-binding of Type 1 human collagen and is responsible for osteogenic cell attachment via α2-β1 integrins which activates the body's production of BMPs and growth factors. *Image courtesy of Cerapedics, Inc.*

- Hydrogel Carrier- i-FACTOR Putty uses carboxymethylcellulose (CMC), an inert and biocompatible hydrogel, to aid in the handling and placement of the ABM/P-15 particles at the graft site.

i-FACTOR bone graft received the CE Mark, a regulatory conformity marking for products on the European market, in late 2008. It has been utilized clinically in over 10,000 spine, trauma, and orthopedic surgeries worldwide. Currently, i-FACTOR bone graft is commercially available in both a Putty and Flex (flexible strip) form in more than 20 countries outside the United States. i-FACTOR bone graft is currently being evaluated in the United States (FDA) as part of an Investigational Device Exemption (IDE) clinical study in the cervical spine and is not available for sale in the US.

A study of the early fusion rates and the rate of graft-related complications during an ALIF was performed comparing autograft, i-FACTOR (P-15) and Infuse (rhBMP). Over 24 months, data was collected from 95 consecutive ALIF implants in 75 patients (57 single level, 16 double level and 2 three level surgeries). Of these, 10 were Infuse (rh-BMP), 10 were autograft (iliac crest bone) and 75 were i-FACTOR (P-15). Outcomes were assessed based on standard cut coronal CT scans and graft-associated complications. Based upon 3 month data, all groups demonstrated excellent early fusion rates with bony bridging occurring faster in Infuse and i-FACTOR patients. At the 3 month point, 3 out of 10 autograft patients suffered from significant graft site pain; 1 out of 10 BMP patients had a clinical complication; none of the 45 iFACTOR patients had a clinical complication, though graft migration was noted. The study data will have to be analyzed after longer term follow-up to draw clinically relevant conclusions from the study; however, the three month data is very promising.

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Marcus M. Martin, Ph.D.

Dr. Martin's research interests include neuroimmunology, virology and immunology. He is engaged in collaborative research through SRF, with the Medical University of South Carolina Children's Hospital, geared toward the development of neuroprotective and neuroregenerative compounds for the treatment of nerve pathology. Dr. Martin's current research collaborations include research initiatives to apply stem cell therapy for tissue preservation, the development of regenerative therapies for intervertebral discs, and the development of novel methods of enhancing bone fusion.

Anne G. Copay, Ph.D.

Dr. Copay studies the outcomes of surgical and non-surgical spine treatments. She published several articles on the outcomes of spine fusion. She has ongoing research projects concerning the effectiveness of new spine technologies and the long-term outcomes of surgical treatments.

4WEB Spinal Truss System™

Timothy Gainey, Ph.D.

The Annual Meeting of the North American Spine Society has always provided the perfect backdrop for original ideas and novel products, and supported a forum for creative exchange. This past year's NASS meeting in Dallas, TX did not disappoint those looking for innovation. One product in particular that garnered a lot of attention was the 4WEB Spinal Truss System. The cage was conceived by Jessee Hunt and initially developed as a device that would provide structural support for interbody fusion. Its open configuration was designed to sustain strength without impeding or restricting the potential for bone to grow into and through the implant. It is believed that by doing so, this new device would enable greater bone formation and fusion without compromising initial healing or mechanical support (Figure 1). Modeled from a truss structure, the inherent design goal was to extend the strain to the margins of the construct and reduce the concentration of forces at the surface of the implant in contact with the bony endplates—, essentially dissipating load broadly across the entire surface (Figure 2).

It has been known for some time that distribution and dissipation of stress are the hallmarks of bone remodeling. In that light, this device represents a unique foray into applied design that integrates the strength inherent to truss geometry, the architecture of static distribution force, and the dynamics of bone remodeling as a fresh therapeutic approach to spine surgery. Recent advances in engineering technology (additive fabrication in particular) have aligned, and a new potential for complex and intricate designs and structures previously unavailable to medical manufacturing has emerged. The 4WEB Truss Implant Technology represents a first opportunity to view that technology in a clinical application. A final design was evaluated and optimized by Lisa Ferrara, Ph.D. (OrthoKinetic Technologies, LLC, Southport, NC) that would effectively minimize the material and maximize the distribution of strain—her guidance defining lateralization of force and reduction of subsidence risk as an integrated facet of the process. The 4WEB truss was fabricated from medical grade titanium alloy using Electron Beam Welding, conferring a rigid truss structure that was subsequently validated for strength, stress, and strain distribution.

The 4WEB Spinal Truss System was subjected to a number of rigorous tests including finite element analysis, subsidence and mechanical performance evaluation, as well as a 12-month large animal study. Even with the greatest confidence in product design, sometimes it is not possible to anticipate the serendip-

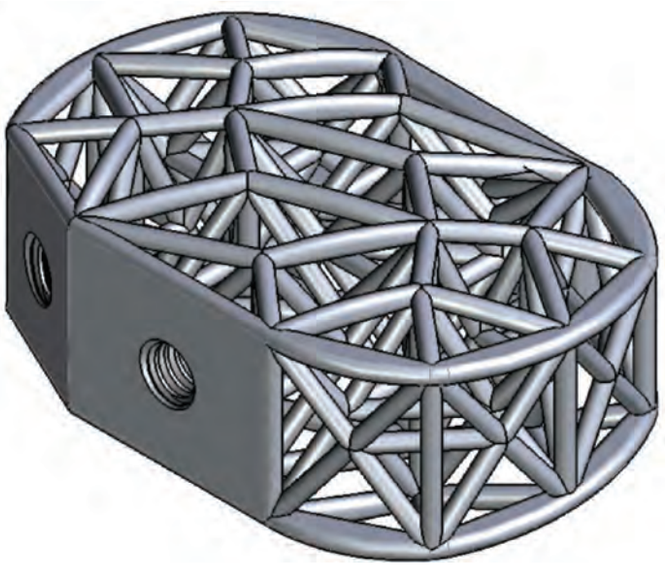

Figure 1. The 4WEB Spinal Truss System was designed to promote greater bone formation and fusion. *Image courtesy of 4WEB Inc.*

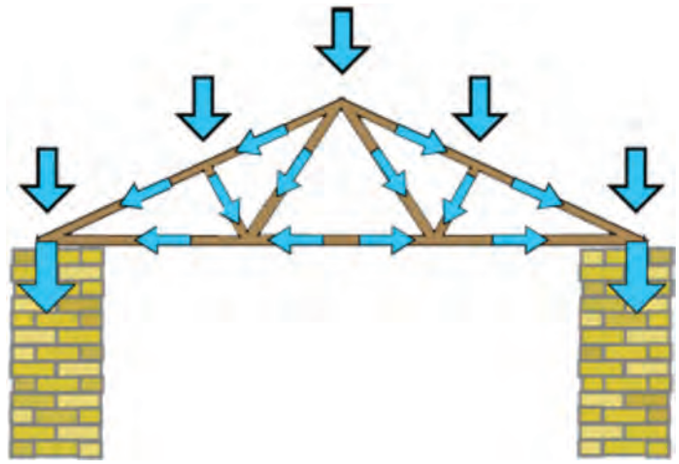

Figure 2. The 4WEB design is based upon truss geometry in order to disperse the load force across the structure's surface. *Image courtesy of 4WEB, Inc.*

ity of biologic translation. Working with Peggy Lalor, Ph.D. (Histion, Inc., Everett, WA), a respected authority of bone pathology, Jessee was on pins and needles waiting for the histology results. Her remark of never having seen such profuse filling of an interbody spine fusion device filled with autograft at 3-months increased the excitement surrounding this technology. Several additional independent reviews and positive clinical reception from all physicians who have had the chance to interpret the histology, and an expedited review and clearance by FDA of the devices for clinical use as an ALIF for lumbar spine fusion, and more recently as a cervical fusion device validate the animal study results.

Assessments of the bone histology from the preclinical model offered insight into bone remodeling that under-anticipated the implications of the design. In an effort to lessen stress shielding, the 4WEB Spinal Truss System accentuated load sharing while hastening structural bone constructs that interfaced and accepted the truss load. Unprecedented amounts of bone were deposited throughout the cage that resulted in an integrated fusion mass throughout the cage.

The 4WEB Spinal Truss System— Load Transfer Design

The open web design increases volume for bone deposition, and at the same time, provides tensile struts that facilitate apposition. These effects were collaterally efficient, assuring biomechanical support analogous to rebar in cement and stimulating an osteogenic response via a load transfer mechanism. Wolf's Law describes the nature in which bone remodels, stating that bone in a healthy person or animal will adapt to the loads it is placed under to reduce strain. If loading on a particular bone increases, the bone will remodel over time to resist strain associated with loading and translate the force in tension.

Recent advances in applied bone biomechanics define optimal structural cues that encourage or escort bone remodeling. Insight emerging from this field addresses the eventuality of material evolution and the appearance of structural synergy with load bearing, strain energy density, and resultant bone formation. The innovation of the 4WEB geometric design incorporates unique engineering concepts that integrate truss resolution from global loading potentials resulting in augmented bone formation with unique reciprocity and reliance on trajectory driven loading (Figure 3). Impressive about bone formation around the construct is that bone that formed both inside and outside the 4WEB Spinal Truss System is matched (Figures 4a and 4b). The bone image inside the cage has been rendered at higher magnification to demonstrate the lamellar bone structure on both sides of the truss.

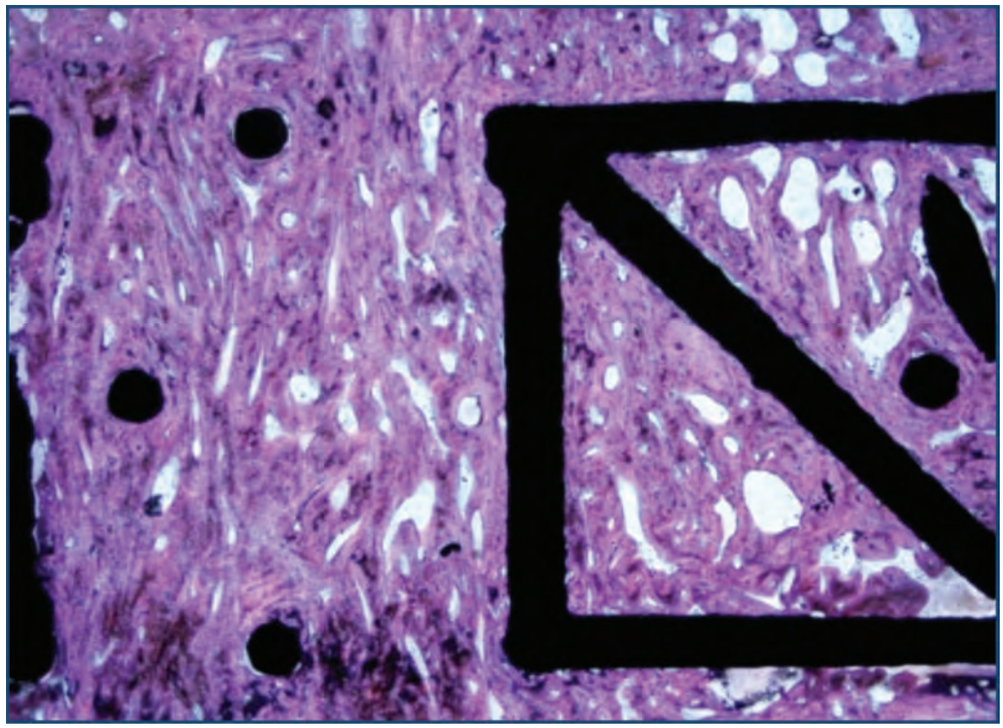

Figure 3. Bone formation utilizing the 4WEB Spinal Truss System. *Image courtesy of 4WEB, Inc.*

T. Gainey/Journal of the Spinal Research Foundation 8 (2013) 45–48

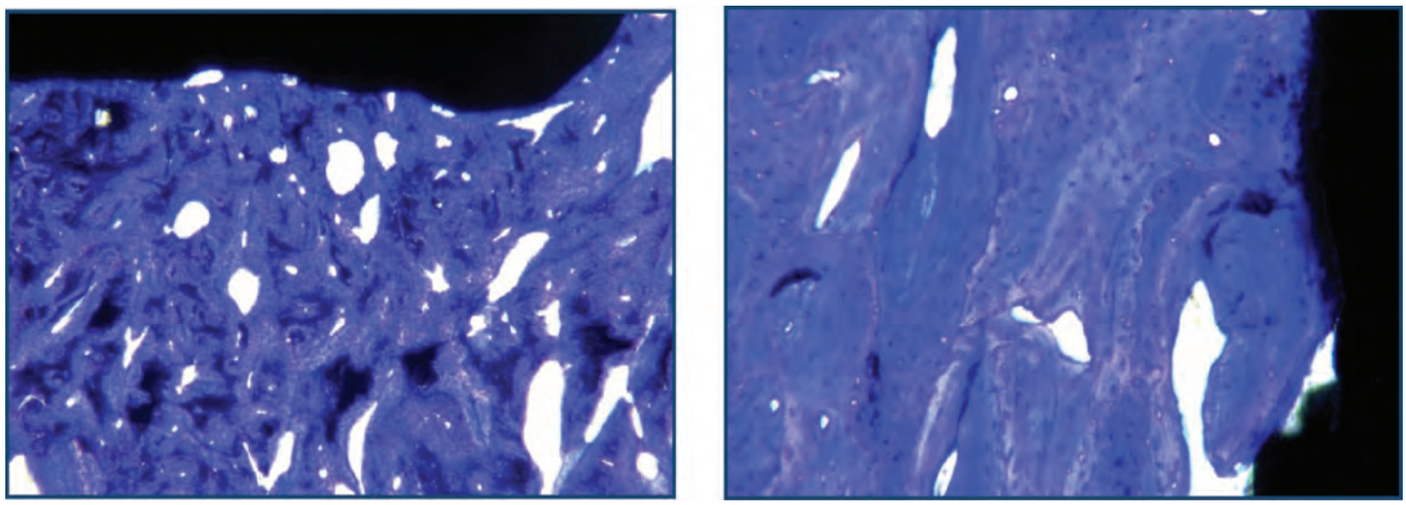

Figure 4. Left: bone formation outside of the 4WEB cage. Right: bone formation inside the 4WEB cage. *Images courtesy of 4WEB, Inc.*

The 4WEB Spinal Truss System—Surface Topology

The additive fabrication process used to manufacture the intricate 4WEB design results in a fully fused solid that has a micro texture surface topology/energy that has been shown to guide mesenchymal stem cells toward an osteogenic lineage. Presented at the AAOS, and later published in *The Spine Journal*, an evaluation of acid-etched titanium alloy surfaces was reported to guide stem cell osteogenic differentiation.[1] While the concept of surface topology triggering cell recognition and tissue differentiation is not a new concept, the 4WEB design maximizes this mechanical asset by providing the microstructure to all of the struts that run throughout the bone implant construct rather than restricting the surface topology to select contact surfaces seen in predicate devices.

Summary

The 4WEB Spinal Truss System utilizes the geometric distribution provided in a truss design to redistribute axial loading vectors and exploit the generation of shear forces that accentuate bone formation. This bone formation is highly organized, stabile, and hastens the deposition of structural lamellar bone in a very short time. Histopathological assessment did not reveal any evidence of hypertrophic cartilage formation, suggest instability, or provide any evidence of inflammatory changes in the marrow that might resonate with chronic reactive bone.

Finite element analysis shored up a basis for stress distribution that would minimize the likelihood of subsidence while accentuating the open structure that would allow bone to pass throughout the construct and integrate with the two adjacent cranial and caudal vertebral bodies. Topologic surface features of titanium struts mirrored roughness assessments that have been shown to actively promote osteoblast phenotype and reduce surface proliferation. The added enhancement of the additive fabrication technology contributed and correlated with the impressive quality and substantial quantity of bone that was seen within the devices tested in the large animal model.

Although the 4WEB Spinal Truss System has only recently received FDA clearance for ALIF and ACDF procedures, available clinical data suggests that reduced pain, accelerated return to function, and demonstrated bone production are hallmarks of the success of the device. The robust response demonstrated radiographically at 4 months provides confidence that fusion is accelerated and that the open structure of the system does not hamper clinical evaluation (Figure 5). Given the accelerated forma-

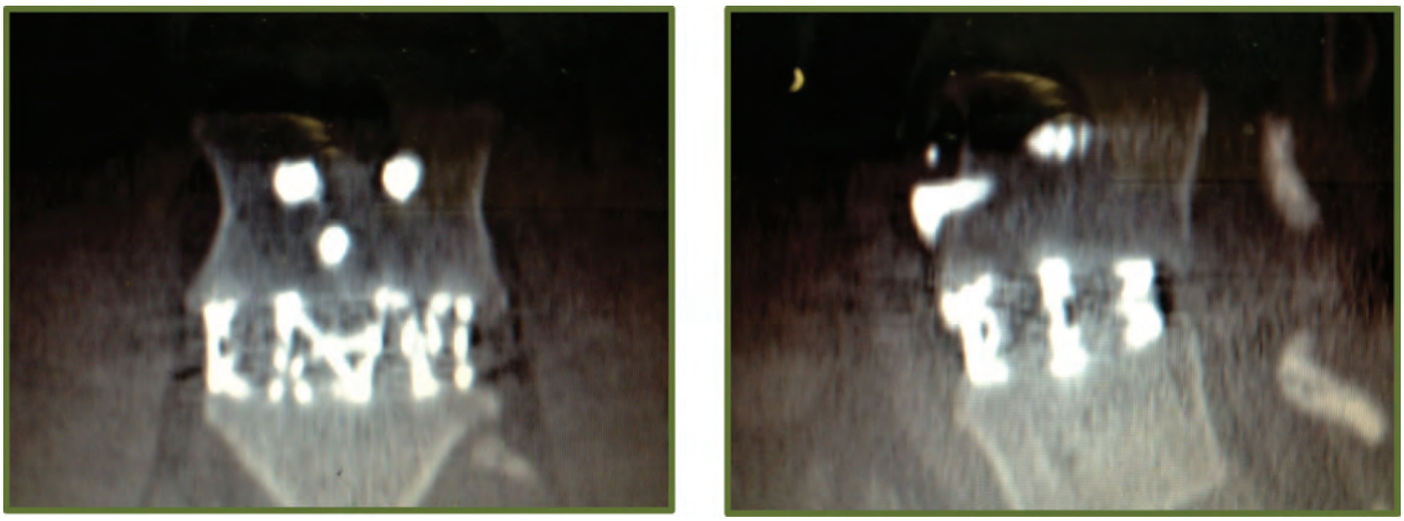

Figure 5. Radiographic evidence of fusion at 4 months after the cage was implanted. *Images courtesy of 4WEB, Inc.*

tion of bone and reduction of pain attendant to use of the 4Web geometry, perhaps the next consideration is then furthered by optimization of intent to achieve better clinical outcome, lessened patient morbidity, and demonstrated improvement in quality of life. Offering relief of pain, enhanced bone formation, and return to function, the 4WEB Spinal Truss System represents a tool affording a unique strategy for securing a stable fusion in treating degenerative disc disease.

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Minimally Invasive Approaches for Spine Surgery

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Florence C. Paillard, Ph.D., and Casey C. Roberts

History and Rationale of Minimally Invasive Spine Surgery

It is estimated that 80% of the US population will experience some form of back pain in their lifetimes.[1] In many instances these symptoms are secondary degenerative spinal conditions broadly referred to as degenerative disc disease. Diagnoses include spinal stenosis, disc herniations, spondylolisthesis, and other degenerative conditions. The first attempt at care for most spinal conditions includes nonsurgical care such as physical therapy and corticosteroid injections in the spine. When those nonsurgical procedures fail, surgery may be considered.

Traditional open surgery techniques for posterior lumbar fusion procedures are widely accepted as the basis of surgery in patients with prolonged or severe pain, loss of function, and/or instability. However, these open procedures, which involve large 5- to 6-inch incisions, are associated with lengthy hospital stays, long-term use of narcotic pain medication, and sizeable direct (hospital bills) and indirect (loss of patient productivity) costs.[2,3,4] Additionally, complications related to open surgical procedures have become a concern. All of these open procedures can be associated with incision-related pain and increased post-operative infections.[3,5] There are also specific complications associated with particular surgeries. For instance, posterior lumbar interbody fusion (PLIF), the fusion of vertebrae accessed through an incision in the back, involves significant dissection of the spine muscles. This potentially leads to permanent muscle denervation and loss of function of the erector spinae, a large back muscle that runs up on each side of the spine and helps support the torso.[6,7] Anterior lumbar interbody fusion (ALIF), the fusion of vertebrae accessed through the abdomen, may result in injury to the ureters, which carry urine from the kidneys to the bladder, large blood vessels, and the sympathetic plexus, a nerve complex which resides in the abdomen and are all in close proximity to the surgical site.[8] In an open ALIF, the large incision through the abdominal muscles may also result in delayed recovery of abdominal muscle strength and function.

In the last two decades, spine surgery has greatly benefited from innovations in surgical techniques which have made it possible to use less invasive surgical approaches. These minimally invasive techniques allow the surgeon to access the spine via smaller incisions (typically 1–2 inches instead of 5–6 inches), resulting in less dissection and less tissue trauma than classic open surgeries. Reducing tissue trauma during surgery has an important impact on patient outcomes because it decreases blood loss and scarring. This reduces the incidence of complications, such as infections, shortens the length of hospital stay, and speeds recovery.[3,5] Minimally invasive procedures can be performed as an outpatient surgery, where the patient can return home that same day. Patients also tend to be ambulatory right away.

Although many benefits can be obtained by using a minimally invasive surgical technique, some of the disadvantages must be considered; in some cases, the disadvantages of the minimally invasive approach may negate its advantages. The minimally invasive technique has a steep learning curve, and in the hands of an inexperienced surgeon, operative times may be prolonged, decreasing the advantages of the technique.[9] Moreover, during minimally invasive surgeries, x-rays (fluoroscopy) are used to visualize the anatomy and guide the surgeon; thus, the exposure of the patient and the surgeon to increased radiation doses must also be considered. The issue of reduced visibility has been one of the greatest barriers to the widespread adoption of minimally invasive spine surgery.[10] To be competent in minimally invasive techniques, the surgeon must have an exact knowledge of the spinal anatomy and all associated anatomical structures since the traditional visual and tactile landmarks may or may not be present to guide the surgeon during the surgery. Without these visual and tactile cues, there is risk for misplacing spinal instrumentation or causing inadvertent neurological damage.[11,12]

Techniques Used in Minimally Invasive Spine Surgery

Advances in minimally invasive surgical technologies in the last several decades were first made for joint

surgeries (such as knee and shoulder) by introducing arthroscopic surgery and gynecologic surgeries with the advent of laparoscopy. In these techniques, the joint space or abdominal cavity is expanded, and a camera is inserted to visualize the tissues. However, these techniques are rarely used in spine surgery because there is no joint space or cavity to expand, rendering the introduction of a camera impossible. Thus, the field of spine surgery had to develop specific tools to enable spine surgeons to perform minimally invasive surgeries. Herein we describe some of the innovative techniques that have made minimally invasive spine surgery possible.

Retractors and Dilators

Typically when a physician performs a traditional open spine surgery, a large incision (5 to 6 inches) is made, and large retractors are used to hold the skin and muscles back to provide visualization of the levels of the spine under operation. When a physician performs a less invasive surgery, a 1-inch incision is made, and small tubular dilators (about ½ inch) are used to reach the area of the spine to be operated on. The dilator splits the muscles of the back creating a channel to the surgical site. This is often accomplished through native avascular muscle planes, thus reducing the amount of bleeding, tissue retraction, and trauma to the spine musculature. This method is less damaging than an open surgery where back muscles are dissected to access the spine. The dilators progressively get larger until the physician feels that he or she has a big enough window to perform the procedure. A small retractor is then placed over the dilator to hold the viewing space open. A light source can then be placed within the retractor for better visualization. These small, minimally invasive retractor systems allow for the same direct visualization of the spine as open surgery, but do so with a much smaller footprint.

Devices

Spine fusion surgeries sometimes require placement of hardware such as cages, screws, plates, and rods. Cages are hardware that acts like a spacer and may be made of metal, carbon fiber, ceramic, bone, or other materials. These devices, some of which were typically large, have been redesigned by manufacturers to be smaller so they would fit through small incisions, allowing fusion surgeries to be performed in a minimally invasive fashion.

Intraoperative X-ray (Fluoroscopy)

A minimally invasive spine surgery significantly reduces tissue trauma, but in doing so, the ability to visualize the spine is also greatly diminished. For this, the physician must heavily rely on specialized image guidance during surgery. Radiographic imaging for these surgeries is usually achieved with a C-arm x-ray machine, which gives the surgeon a 360 degree view of the spine while performing different parts of the procedure (Figure 1).

Intraoperative Neuromonitoring

When performing a minimally invasive spine surgery, the spine surgeon may not be able to see the specific

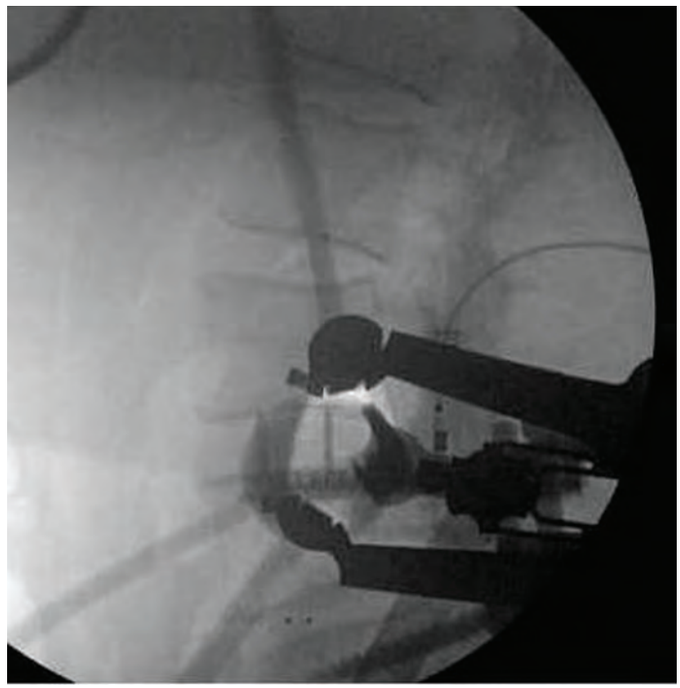

Figure 1. Fluoroscopic (x-ray) image taken during a procedure. This imaging technique allows the surgeon to visualize the structures on a screen to accurately perform the minimally invasive surgery procedures. Here, the hardware seen on the right side of the image are the retractors.

D.G. Orndorff et al./Journal of the Spinal Research Foundation 8 (2013) 49–55

nerve anatomy below the surface of the skin. To protect the nerves from damage during the surgery, the surgeon uses a technique called neuromonitoring, which records the activity of the nerves that activate the spine muscles. One of these techniques, called electromyogram (EMG) monitoring, assesses nerve root function by recording muscle activity during the surgical procedure. This gives the physician the ability to track the nerve function and ensure the nerves are intact and protected.

Bone Graft Substitute

An important technological advance that has reduced the invasiveness of spine surgery is the development of bone graft substitutes. Examples of these grafts include recombinant human bone morphogenic protein (BMP), which is loaded onto a sponge; demineralized bone matrix; synthetic bone graft, often made of ceramic; and allograft, bone from donors or cadavers.[13] The bone graft substitute is placed into the disc space, generally with a cage, to promote vertebral fusion. The use of bone graft substitute avoids harvesting bone from the patient's hip to use as a bone graft during the spine fusion procedure. Harvesting bone from the patient's hip requires an additional incision in the hip and removal of a piece of the hip bone. Ultimately, this leads to complications and often leaves patients with persistent pain lasting at least 2 years.[14] By eliminating the need to harvest bone from the patient's hip, bone graft substitutes have reduced the overall invasiveness of the spine fusion surgeries.

Various Minimally Invasive Spine Surgery Procedures

Lumbar Microdiscectomy

This surgery is performed on patients with herniations (bulging) of the intervertebral discs of the spine (see Figure 2 for anatomy). The chief complaint from these patients is usually pain (called sciatic pain or sciatica) that originates in the spine and may radiate into the buttock(s) and down the leg(s) (see Figure 2 for anatomy). Physical examinations performed by physicians provide information that links the cause of the pain to a specific level of the spine. Imaging of the lumbar spine using fluoroscopy usually reveals a nerve root compression (pinched nerve) by a herniated disc (Figure 3, left panel). Nonsurgical

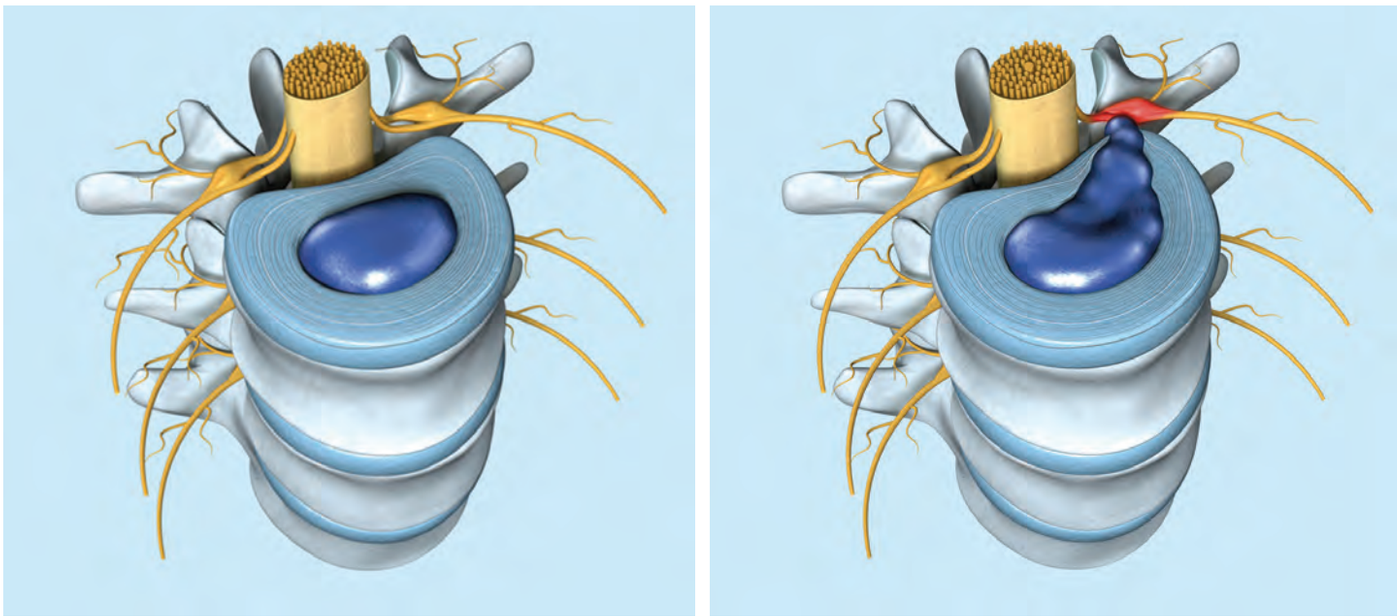

Figure 2. Nerve root compression. Left: axial view of an intervertebral disc without nerve (shown in yellow) compression. Right: nerve root compression due to a herniated/damaged disk.

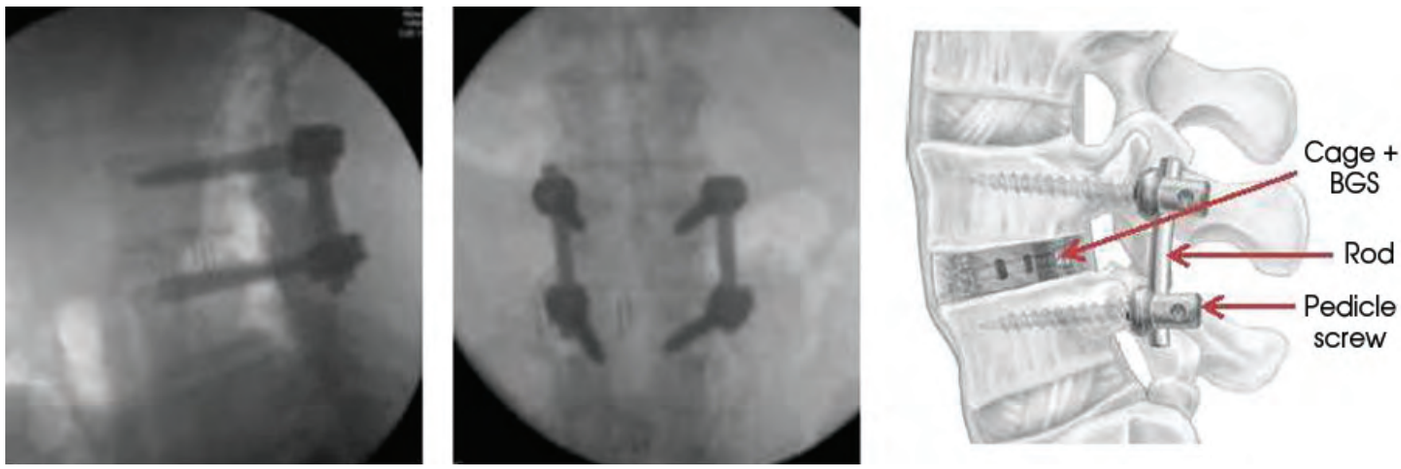

Figure 3. Spine fusion. This shows how two vertebrae are fused. A cage plus a bone graft substitute (BGS) is inserted in the disc space after removal of the disc. In this case, the two vertebrae have been secured with 2 pedicle screws linked by a rod. Left: Fluoroscopic image of the completed surgery (side view); the 2 screws and rod are easily spotted; note the cage in the disc space (faint vertical lines). Center: Back view of completed surgery. Right: Explanatory diagram of what is shown in the left panel. *Image modified and adapted from Mummaneni PV, Rodts GE Jr. The mini-open transforaminal lumbar interbody fusion.* Neurosurgery. *2005;57:256–61.*

approaches are almost always prescribed for patients with disc herniations; these treatments include physical therapy, pharmacological pain management, and spinal injections with corticosteroids. If the patient's symptoms do not resolve through nonsurgical care, a microdiscectomy (also called microdecompression) is performed microscopically to relieve pressure on the spinal nerves. During microdiscectomy, the surgeon performs a 1-inch incision posteriorly at the level of the herniated disc and uses a microscope to access the spine. First, the surgeon removes a small piece of bone from the lamina (the bones in the back of the spine) (Figure 3, center panel); this reduces pressure on the sciatic nerve and provides access to the damaged disc below. The surgeon then removes the herniated/damaged part of the disc to relieve pressure on the nerve root (Figure 3, right panel).

Lumbar Fusion

Lumbar fusion surgeries are indicated when there is radiographic evidence of instability or deformity. Fusion procedures are necessary when nonsurgical approaches have failed and patients are in significant pain from conditions such as degenerative disc disease or recurrent disc herniations. The goal of lumbar fusion surgery is to create solid bone between two adjoining vertebrae by removing the disc and fusing the two vertebrae; this eliminates any movement between the bones and reduces pain and nerve irritation. Generally, the damaged disc is eliminated, and the bone surfaces of adjacent vertebrae are prepared for fusion. Bone graft substitute, such as autograft, and usually a cage is inserted into the disc space. The cage acts like a spacer, and the bone graft substitute enhances fusion between the two adjacent vertebrae. Rods and screws are often placed between the two vertebrae to provide additional support while the two vertebrae are becoming fused, a process that usually takes 6 to 12 months. All these procedures are performed using x-ray (fluoroscopic) imaging to visualize the procedure.

There are a number of minimally invasive spine surgery procedures that can be used to achieve the fusion of the spinal vertebrae. These techniques, described below, mainly differ in the way the spine is accessed by the surgeon: through the front (lower abdomen), the back, or from the side. Consequently, these approaches mainly differ by the types of tissues or structures that are being penetrated, resected (cut), or retracted by the surgeon to access the spine. The characteristics of these techniques are summarized in Table 1.

D.G. Orndorff et al./Journal of the Spinal Research Foundation 8 (2013) 49–55

Table 1. Characteristics of the different minimally invasive surgeries for spine fusion.

Type of Fusion Surgery	Access	Duration of Surgery (hours)	Potential Complications	Comments and Contraindications
ALIF	Front (lower abdomen)	3.5	Damage to large vessels, organs, and nerves in the abdomen	Only option for patients with high iliac crests
PLIF	Back (midline)	3 to 6	Damage to spine muscles and their nerves; damage to dura	
TLIF	Back (to the side of the midline)	2.5	Damage to dura	• May not be possible in patients with high iliac crests; • Not indicated to fuse >3 vertebrae
XLIF	Side (above hip)	1 to 1.5	Transient leg pain due to retraction of the psoas	• Offers only limited access to spine (L5-S1 cannot be accessed); • Cannot be done in patients with high iliac crests

Mini-open ALIF (Anterior Lumbar Interbody Fusion). Because the intervertebral discs are on the front side of the spine (Figure 2, left panel for anatomy), spinal fusions can be obviously achieved via an anterior (front) approach. Anterior fusions require making an incision in the lower abdomen, often cutting through or splitting the abdominal muscles, and dissecting behind the abdomen to gain access to the lumbar spine. This procedure is best used when targeting the L4-L5 or L5-S1 level. The XLIF technique (describe below) is usually recommended for fusion of the levels above L5-S1. The advantage of this procedure is that it spares the patient's back muscles. However, the ALIF approach can result in damage to abdominal organs and structures because the surgeon has to dissect through the abdomen and retract these abdominal structures to reach the spine. These complications may include damage to the large blood vessels, leading to excessive blood loss); injury to the sympathetic plexus, causing retrograde ejaculation in men; injury to the ureters, the canals that bring urine from the kidneys to the bladder; or damage to the intestines.

Mini-open PLIF (Posterior Lumbar Interbody Fusion). In the PLIF, the surgeon accesses the spine posteriorly. A small incision is made in the middle of the back at the indicated level, and the back muscles are split or retracted to access the spine. The lamina, which blocks access from the back, needs to be removed on both sides to allow access to the disc, and the facet joints on both sides may also need to be trimmed (See Figure 2 for anatomy). The thecal sac is then retracted. The surgeon removes the damaged disc and inserts a cage with bone graft substitute into the disc space. Rods and screws are usually placed to further stabilize the spine. The main disadvantages of the PLIF is that it may result in damage to back muscles and/or their nerves, and create tears in the dura (the material that protects the spinal nerves), which is forcefully retracted. The advantage of PLIF over ALIF is that it does not damage the abdominal organs and structures.

Minimally Invasive TLIF (Transforaminal Lumbar Interbody Fusion). The TLIF is a modification of the PLIF that has become popular. In the TLIF, the

surgeon approaches the spine from the back, but a little more to the side (about 2 inches right or left of the midline), through a small incision. The back muscles are split using a series of dilators, and the facet joint on one side only is removed.[16] The rest of the procedure is similar to the PLIF; in comparison, the lateral (side) entry used in the TLIF minimizes the retraction of the nerve root and the dura, reducing the risk of nerve injury. The TLIF also reduces the amount of trauma to the back muscles. However, there is still a risk for damaging the dura.

XLIF (Extreme Lateral Interbody Fusion). This relatively new procedure uses a lateral (side) approach to access the lumbar spine above the L5-S1 level.[18] A small incision is made on the flank of the patient (just above the hip), and sometimes another small incision (1-inch long) is made just behind the first incision. The dilators are passed behind the abdominal contents (retroperitoneal) and through the hip flexor muscle (psoas) to gain access of the spine. The rest of the procedure is typical of a fusion surgery. The lateral approach avoids the vascular, visceral, and sexual dysfunction complications that may be associated with anterior approaches (ALIF), as well as the possible nerve damage and dural tear that may occur with posterior approaches (PLIF).[7] One potential, yet minor complication of the XLIF is transient leg pain or weakness due to retraction of the psoas muscle to access the spine.[7] Nevertheless, the lateral approach has an important limitation: the L5-S1 disc, a very common level of surgery, is situated too low to be safely accessed using the lateral approach due to the obstruction of the pelvis and the vasculature.

The reasons for performing one approach versus another include particular patient anatomy and surgeon expertise and preference. Regarding patient anatomy, the lateral approach may not be possible in patients with a "low riding" L4-L5 level and is contraindicated at L5-S1. The XLIF, and sometimes TLIF, may not be good options in patients whose iliac crest is high and blocks the passage from a lateral approach; in those patients the only method for accessing the spine is from the front (ALIF).

Conclusion

Minimally invasive techniques for spine surgery were initiated in the 1980's and have evolved and improved in the past 3 decades thanks to technical innovations. Such advances include better imaging techniques (such as fluoroscopy), dilators, smaller retractors, neuromonitoring, and bone graft substitutes. Today, minimally invasive surgery techniques are considered as effective as open surgery techniques to repair the spine. The main reason for using minimally invasive techniques is to minimize the trauma to tissues during surgery, which typically results in fewer complications, less pain, less time spent in the hospital, and faster recovery, all of which are very important outcomes for patients. Therefore, minimally invasive techniques have become the state of the art in back surgery and have replaced open surgeries, whenever it is feasible.

Now, virtually all levels of the spine can be accessed through minimally invasive approaches, making it amenable for use in an increasing number of patients and an increasing number of back problems. Skilled surgeons are now able to use minimally invasive approaches to treat complex disorders, including tumors, deformity, infection, and trauma.[11] Nevertheless, not all types of surgeries can be performed through minimally invasive techniques, and some patients may not be good candidates for minimally invasive spine surgery. Moreover, in some cases, the disadvantages of the minimally invasive approach may counteract its advantages, making open surgery a better option.

Several types of minimally invasive approaches are available for spinal fusion surgery. These various approaches mainly differ by the way the surgeon accesses the spine to perform the surgery. The choice of the appropriate approach for surgery mainly depends on the patient's anatomy and the surgeon's expertise and preference. Regardless of the approach chosen to manage a patient with a spine injury or disorder, the goal of the treatment is always to prevent the development of a neurologic deficit, enhance neurologic recovery, achieve a stable spine that will allow for appropriate rehabilitation, and prevent post-surgical deformity and pain.

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Spinal Research Foundation Research Partners

The Spinal Research Foundation has named 25 Research Partners across the country that share one core mission: improving spinal health care through research, education, and patient advocacy. These centers offer the best quality spinal health care while focusing on research programs designed to advance spinal treatments and techniques.

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