Over the last two decades, minimally invasive neuroendovascular techniques have transformed the practice of the treatment of intracranial aneurysms. Although at first only aneurysms with favorable anatomy and dome-to-neck ratio were considered for endovascular treatment, the widespread adoption of balloon remodeling and stent-assisted coiling has significantly expanded the range of treatable aneurysm geometries. These adjunctive techniques also, in many cases, facilitate a higher density of coil packing, which may reduce the rate of future aneurysm recurrence. The recent introduction of flow diverting devices, such as the Pipeline™ Embolization Device has enabled successful treatment of even larger and more complex aneurysms. Remarkably, there has yet to be a report of aneurysm recurrence following successful occlusion with the Pipeline device. This suggests that advances in endovascular technology may ultimately overcome the limitation of long-term treatment durability and minimize the need for repeated follow-up imaging studies.

Flow diversion strategies have been primarily used for aneurysms arising from the larger segments of the proximal internal carotid, and FDA approval for the Pipeline device only extends to the superior hypophyseal segment. The treatment of wide-necked aneurysms of the more distal anterior cerebral and the posterior circulations remains challenging. Particularly in the case of cerebral aneurysms arising at a vessel bifurcation, the use of a flow diverter remains less than ideal. For these distal aneurysms with wide necks, complex morphology, and small diameter parent vessel, stent-assisted coil embolization remains an important treatment technique.

Approved by the FDA in 2005, the Neuroform stent was the first in a line of self-expanding stents designed specifically for use in stent-assisted coil embolization in the cerebral vasculature. This device subsequently went through several design iterations in an effort to facilitate its intracranial delivery. The cells comprising the wall of this stent are easily crossed with a coiling microcatheter.
Chairman’s Message

Failure, Failure, Failure ... Success!

To perform a successful clinical trial — properly achieving the goals of the trial and successfully testing the initial hypothesis — is often an extremely difficult goal to achieve. A question as simple as: “Is it good to reestablish blood flow in a major occluded artery in the brain?” should be extremely simple to answer. However, except for the original tPA trial published in 1995 and PROACT II in 1999, no other intervention has demonstrated any efficacy in the treatment of ischemic stroke. This dismal record has finally changed.

The Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands (MR CLEAN), published in the New England Journal of Medicine in December of 2014, is the first trial demonstrating a positive effect of revascularizing major occluded cerebral arterial occlusions.

Why did this study succeed while many others failed? There are many critical reasons. First, this study carefully analyzed the causes for previous failures, and specifically made efforts to address them. Among the most important correction was making sure patients had the disease in question. This seems straightforward, but in the desire to treat occluded vessels expeditiously, some of the patients treated in previous studies did not have major arterial occlusions. Another important modification is the use of safer and more effective devices to remove the thrombus from the occluded vessels. Finally, the Dutch government decided not to reimburse for procedures required for revascularization outside of the trial, therefore minimizing and eliminating selection bias during the randomization process.

The MR CLEAN data was further validated by the recently released results of the SWIFT-PRIME, EXTEND-IA, and ESCAPE trials. The International Stroke Conference, held in Nashville, Tenn. on February 11-13, literally changed the landscape of stroke care forever by highlighting the importance of quickly opening occluded intracranial blood vessels to improve stroke outcomes. We are proud that our own UPMC Center for Neuroendovascular Therapy — led by Tudor Jovin, MD, Brian Jankowitz, MD, Andrew Ducruet, MD, and Ashu Jadhav, MD, PhD — was the #2 and #5 leading enroller of the only two North American studies. Our ability to aid a greater proportion of the acute stroke population is of landmark significance. It is critical to fully understand what has been done in previous trials in order to maximize our gains in proposed or current trials.

The MR CLEAN trial also underscores the importance of close collaboration between industry and academic centers to not only develop better devices, but to also design better trials.

It is likely that, in the not too distant future, we will see significant increases in the number of stroke victims treated with these advanced approaches. At UPMC, our stroke team is fully equipped and experienced to provide these advanced and exciting treatments.

Robert M. Friedlander, MD, MA
Chairman and Walter E. Dandy Professor of Neurosurgical Surgery
Intracranial Aneurysms
(Continued from Page 1)

to deliver coils into the aneurysm, or the coiling catheter can be positioned first within the aneurysm and subsequently “jailed” by stent deployment.

Despite the relative ease of deployment of these stents, a single stent placed into one parent vessel limb of a broad-based aneurysm at the middle cerebral artery bifurcation or basilar apex often does not adequately protect the origin of the second parent artery. Such aneurysms often require two stents deployed in a “Y-stent” configuration to effectively protect the parent arteries. An upcoming multi-center clinical trial will evaluate a new device that will expand our ability to specifically treat these challenging aneurysms with a single device.

The BARREL® Vascular Reconstruction Device is a barrel-shaped neck remodeling device (see Figure 1, Page 1). BARREL has been approved in Europe since December 2013. In April 2014, the Food and Drug Administration granted investigational device exemption, and a multi-center clinical trial is currently being planned. UPMC was chosen as one of the clinical sites for this trial. The BARREL device is specifically designed to treat wide-necked bifurcation aneurysms of the middle cerebral artery and basilar apex. The larger diameter of the central portion of the stent serves to bridge the aneurysm neck so that the device placed in a single arm may effectively protect both parent vessels without the need for a Y-stent construct.

Another limitation of the first generation of intracranial stent devices is the need for a relatively large delivery microcatheter. These catheters can be difficult to navigate into very distal vasculature or small parent vessel diameters, and a second, smaller microcatheter is often required to deliver coils. Another recent focus of investigation has therefore been the design of stents that can be deployed through a smaller microcatheter. The Low-Profile Visualized Intraluminal Support Device™ (LVIS) (Figure 2) is a self-expanding, braided nitinol stent that recently received FDA approval under a humanitarian device exemption for use in the treatment of wide-neck intracranial aneurysms. UPMC has participated in the pivotal clinical trial that ultimately led to the approval of this device. Importantly, a version of this device (LVIS Jr.) can be delivered through a standard sized coiling microcatheter, which offers a decided advantage in placing this device in the distal vasculature or small vessels.

Given our extensive experience in the endovascular treatment of patients with cerebral aneurysms, UPMC continues to be selected to participate in clinical trials of promising new devices. Through active participation in such trials, our center continues its tradition of embracing technological advances in the treatment of cerebrovascular disease. This ensures that we remain at the leading edge of neuroendovascular therapy and helps to position our center as a leader in shaping the future practice of cerebrovascular surgery. Most importantly, our involvement in the development of these devices and techniques allows us to offer our patients the latest minimally invasive technologies for the treatment of their disease.

Cerebrovascular Film Review

The UPMC Comprehensive Center for Cerebrovascular Neurosurgery is pleased to provide a complimentary review of patient imaging studies. This service is available for either a new diagnosis or as a second opinion. Please visit our website at neurosurgery.pitt.edu/cerebro-film-review, or call us at 412-647-3685 for more information.
Pituitary adenomas occur in the pituitary gland, and contemporary studies show that they are far more common than previously thought, with a prevalence of almost one per 1,000 individuals worldwide. Recent studies consistently document that the incidence of newly diagnosed, clinically active pituitary adenomas is between one and four per year in a population of 100,000.

Fortunately, most pituitary tumors have a benign behavior, but invasive and malignant types are found occasionally. The spectrum of the clinical presentation of pituitary adenomas is wide, including severe headaches, visual loss, and hormonal imbalance; the sequelae of hormonal and neurological impairment can severely alter quality of life and shorten lifespan. Given the high prevalence of pituitary tumors and the complexity of their diagnosis and management, there is a need to increase awareness within the medical community and public about the importance of evaluating and treating pituitary tumors at multidisciplinary centers with high volume and large experience.

The UPMC Pituitary Center is an integrated group of renowned experts in multiple fields, including: neurosurgery, endocrinology, otolaryngology, neuro-ophthalmology, endovascular neurosurgery, radiation oncology (including Gamma Knife® radiosurgery), neuroanesthesia, neuro-oncology, and neuropathology. As one of the leading centers for pituitary tumors worldwide, our triple mission is to provide comprehensive care and support to patients with pituitary disorders; to provide residency and fellowship training and continuing medical education in the management of pituitary and neuroendocrine disease; and to contribute to basic science and clinical research in pituitary disorders.

As is the case in many areas of surgery, numerous studies show better outcomes and lower complication rates at centers with more experienced pituitary surgeons. In a study involving 958 neurosurgeons, 87 percent reported having performed fewer than 200 pituitary operations; 9.7 percent reported 200 to 500 pituitary operations; and only 3 percent reported more than 500 operations. The incidence of complications was higher with less experienced surgeons; there was a significant decrease in morbidity and mortality after 200 and 500 operations. In another study, patients treated at high-volume hospitals by high-volume surgeons had lower mortality rates, better hospital discharge dispositions, and fewer complications. These multiple studies indicate that a high surgical volume allows surgeons to learn from past experience and to apply accumulated knowledge to patient selection, surgical goals, and operative techniques to achieve optimal outcomes and avoid complications. This experience-outcome effect is likely more pronounced in complex cases such as invasive adenomas, reoperations for recurrent adenomas, giant pituitary adenomas, Cushing’s disease, and acromegaly.

The impact of accumulating volume and experience was also confirmed in our own experience. Since the introduction of the endoscopic endonasal approach, more than 1,000 pituitary surgeries have been performed at UPMC. Our surgical team, consisting of Dr. Fernandez-Miranda and Dr. Paul Gardner from Neurosurgery, and Dr. Carl Snyderman and Dr. Eric Wang from otolaryngology, currently performs close to 100 operations for pituitary tumors every year (more than 500 since 2009). We have recently reported our outcomes for the first 555 cases performed with a purely endoscopic endonasal approach, showing better preservation of pituitary function and excellent visual outcomes when compared to other series. Remarkably, only one patient (0.2 percent) suffered a major vascular injury and stroke in comparison to a risk of stroke of 1 percent (five times higher) at lower-volume centers. Even within our series, there has been a dramatic decrease in complications such as cerebrospinal fluid leak rates over time, from 11.5 to 2.9 percent.

In the era of quality-based, cost-effective care, the referral of pituitary patients to high-volume centers such as the UPMC Pituitary Center is an opportunity to improve quality of care and patient satisfaction. Health care costs are also decreased secondary to improved clinical outcomes, reduced hospital stay, and exceedingly low risk of adverse sequelae such as hypopituitarism and other complications, or ineffective surgery that can result in long-term, expensive medical treatments.
Dynamic Stabilization of the Lumbar Spine: A Decade of Experience

by Erin Paschel, MPAS, PA-C, and Peter C. Gerszten, MD, MPH

The surgical management of low back and/or lower extremity pain due to degenerative disc disease, lumbar stenosis, or acute disc herniation may be considered when conservative measures of treatment have failed. Lumbar decompression with implantation of pedicle screws and rigid fixation using titanium rods has long been considered the standard of treatment for some cases of degenerative disc disease, spondyloolisthesis, and facet-mediated pain syndromes. However, lumbar fusion may not be the best surgical option for all patients. For this reason an alternative to rigid fixation was adopted at our institution for patients who otherwise were felt to be candidates for rigid fixation and subsequent arthrodesis with a goal of avoiding segmental fusion. To date, over 200 patients have undergone implantation with the Dynesys® (Zimmer Spine) lumbar posterior dynamic stabilization system using flexible rods at UPMC. This procedure was initially implemented in 2005 for the treatment of symptomatic single-level Grade I lumbar spondyloolisthesis. However, the indications have expanded to include degenerative lumbar stenosis, recurrent and acute disc herniation, intractable mechanical low back pain from discogenic origin, and facet cysts causing stenosis and instability.

The Dynesys® dynamic stabilization system is a non-rigid system that was developed to stabilize the lumbar spine. It was first introduced in 1994 by Dr. Gilles Dubois in St. Jean, France and has been implanted in more than 60,000 patients worldwide. The goal is to hold lumbar segments in a more natural anatomic position while preserving natural anatomical structures and constraining spinal motion with a less-invasive paraspinal approach. The system is intended to be used without bone graft in skeletally mature patients in up to five contiguous levels from L1-S1. Three proprietary components are used to stabilize the spine with this system, which is tensioned to create dynamic interaction between the components. Low-profile titanium-alloy screws with mono-axial heads are placed laterally through the pedicles to anchor the system, sparing the facet joints. A polycarbonate-urethane spacer runs over the cord and between the screw heads to limit spinal extension. The spacer is custom cut to accommodate individual patient anatomy at different segments. A polyethylene-terephthalate cord runs through the spacer to connect the screws and limit spinal flexion while maintaining the spine segments in a more natural anatomic position. The interaction between the cord and spacer creates dynamic stability by absorbing and releasing energy to share the load of the spine with the patient’s natural spinal anatomy.

When the patient bends forward, the cord engages and acts as a tension band, limiting flexion. When the patient bends backward, the screw heads interact with the spacer which resists the compressive load and limits overall extension.

This device can also function as a hybrid, called Zimmer DTO® or dynamic transition option, where rigid fixation of one or multiple segments is coupled with dynamic stabilization by inserting a rod attached to a universal bumper to maintain mobility while still decompressing the diseased segment. This is useful in patients with a previously fused segment presenting with adjacent level disease requiring decompression and stabilization alone, as well as for patients with varying degrees of disease at consecutive lumbar segments.

Given our decade-long experience with this technology, we analyzed patient data following dynamic stabilization with both the Dynesys dynamic stabilization system and the DTO. Favorable outcomes were demonstrated in the carefully selected patients. The procedure is reserved for young men and women with primarily radicular complaints due to acute or recurrent disc herniation or lumbar stenosis with mechanical low back pain, where a wide decompression is necessary to adequately decompress the nerve roots, rendering the facet joints unstable. Patients with mechanical back pain due to facet disease with mild or no associated stenosis also are potential candidates for dynamic stabilization without decompression, as the spacers provide distraction of the neural foramen and adequately decompress the nerve roots at the treated level.

Dynamic stabilization is ideal for younger patients with multi-level disease in order to avoid performing a multi-level fusion. Nearly half of the patient undergoing implantation of the Dynesys system required two, three, or four levels of stabilization. Single-level dynamic stabilization was more prevalent with the additional use of the DTO system, as this is a good option for patients with a previous lumbar fusion who have adjacent disease, and helps to avoid a multi-level fusion. The overall infection rate for our series is comparable to that of conventional rod and screw fusion.

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Functional Neurosurgery: It’s About Quality of Life

by R. Mark Richardson, MD, PhD

(This article is reprinted with permission from an article that appeared in the September 2014 issue of the Allegheny County Medical Society Bulletin.)

Functional neurosurgery describes a field of elective procedures whose goal is to improve a patient’s quality of life. Two related specialties within functional neurosurgery include surgery for epilepsy and surgery for movement disorders. Not considered life-saving, these surgeries unfortunately often are considered a last resort, only to be used after years, and sometimes decades, of exhaustive medical therapy. This outdated way of thinking is a barrier for many patients to learn about the potential role of brain surgery in the treatment of their epilepsy, Parkinson’s disease (PD), essential tremor, or dystonia.

Surgical removal of the seizure focus is the only potential cure for focal epilepsy. While approximately 15 percent of patients with epilepsy may benefit from a diagnostic or therapeutic surgical intervention, patients continue to be referred for surgical treatment an average of two decades after onset of seizures, which is much too late to avoid many irreversible disabilities. This occurs despite publication of a landmark randomized controlled trial nearly 15 years ago that demonstrated the superiority of surgery for drug-resistant temporal lobe epilepsy over the continuation of medical treatment alone. The underutilization of surgical treatment is alarming, especially given that seizure surgery is safe; significant morbidity following surgery occurs in only 3 percent of patients, while most patients experience major improvement in their quality of life. Both the American Academy of Neurology and the International League Against Epilepsy recommend that patients with epilepsy who have failed to achieve seizure freedom after adequate trials of two antiepileptic medications should be referred to an epilepsy surgery center.

Surgery for movement disorders primarily involves the implantation of deep brain stimulating (DBS) electrodes in patients who are not adequately treated by medication and who meet other qualifying criteria. Randomized, double-blinded studies have provided Class 1 evidence that deep brain stimulation is better than high-level medical management for patients with both advanced Parkinson’s disease (PD) and PD with early motor complications. Nonetheless, many patients with PD have never heard of DBS, despite the fact that symptoms can improve in appropriately selected patients by 40 to 60 percent and that the risk of permanent neurological deficit from DBS surgery is only 1 percent. DBS is even more efficacious in the treatment of essential tremor. With regard to dystonia, multicenter, double-blinded studies have also shown that DBS produces an average improvement in symptoms of >50 percent in generalized dystonia, with smaller studies demonstrating efficacy in focal and segmental dystonias. Yet dystonia patients often undergo many years of unsatisfactory response to medication and botulinum toxin without ever knowing about DBS.

How can these discrepancies between surgical efficacy and utilization be explained? Several factors play prominent roles in prohibiting patients from accessing neurosurgical consultation. First is the concept of whether or not symptoms of these neurological diseases are “controlled.” Technical definitions aside, it is most important to listen to the patient. The extent to which a patient can maintain a normal quality of life is the best indicator of whether medications are adequately controlling symptoms. A second set of factors includes misunderstanding both the appropriate time for referral and the associated surgical risks. Identifying the appropriate time to refer patients is best framed by assessing quality of life. When disease symptoms or medication side effects prevent patients from doing the things in life they most enjoy, it’s time for neurosurgical consultation. The risks of functional neurosurgical procedures are quite low in experienced centers; in fact, this is a basic tenant of the subspecialty. A third factor is the assumption that anyone referred to a neurosurgeon is going to have an operation. Surgery for epilepsy and movement disorders is an interdisciplinary process, requiring not just the surgeon, but also neurologists, neuropsychologists, and the patient’s general practitioner. A multidisciplinary board often makes the formal recommendation, so the most important role the surgeon plays initially is to provide the patient with objective information about the potential role of surgery. Empowering patients with this information is an important way to allow them to regain some control over their disease.
News & Notes

Pollack, Gardner, Snyderman Co-Author Books

Ian Pollack, MD, is co-author of the newly released Principles and Practice of Pediatric Neurosurgery, a completely revised third edition of the most authoritative guide to the management of pediatric neurosurgical disorders encountered in clinical practice.

According to the book’s publisher, Thieme Publishers, this full-color book “provides pediatric neurosurgeons with a clear understanding of the current evidence base of practice and treatment in the subspecialty. This book is an essential reference for all residents and practitioners in neurosurgery and neurology who treat pediatric patients.”

Paul Gardner, MD, and Carl Snyderman, MD, MBA, are co-authors of the new book Skull Base Surgery, part of the Master Techniques in Otolaryngology - Head and Neck Surgery series published by Wolters Kluwer.

The book offers step-by-step expert instruction on more than 45 procedures, covering both open and minimally invasive approaches to the skull base. The publisher calls it a “vital resource for students, generalist surgeons, and skull base specialists in otolaryngology and neurosurgery.”

Spinal Cord Injury Clinical Trial Announced

InVivo Therapeutics announced that UPMC Presbyterian will serve as a clinical trial site in the company’s ongoing Investigational Device Exemption (IDE) pilot study of its Neuro-Spinal Scaffold in patients with acute spinal cord injury (SCI). David O. Okonkwo, MD, PhD, is the study’s principal investigator here.

Maroon to Co-Chair The Crucible Hike

Joseph Maroon, MD, will serve as honorary co-chairman of The Crucible, a three-day, 70-mile, extreme hike through western Pennsylvania’s Laurel Highlands. The hike, scheduled for May 15-17, is intended to help raise awareness and money for area veterans and military families. Dr. Maroon will co-chair the event with former Pittsburgh Steeler Rocky Bleier, a U.S. Army veteran and recipient of the Purple Heart and Bronze Star.

Special Lectures and Appearances

Partha Thirumala, MD, was a visiting professor at the Park Clinic in Calcutta, India, on October 9. He was also a special guest lecturer at the Annual Conference of the Skull Base Surgery Society of India in Pondicherry, India, on October 12.

Paul Gardner, MD, was co-director of the Endoscopic Skull Base Hands-On Cadaver Workshop at the Pondicherry conference.

Juan Fernandez-Miranda, MD, was director of the European Association of Neurosurgical Societies/World Federation of Neurosurgical Societies (EANS-WFNS) 3D Surgical Neuroanatomy pre-congress course at the EANS Congress in Prague, Czech Republic, on October 12.

Paul Gardner, MD, was director of the Endoscopic Endonasal Skull Base Surgery pre-congress course at the Prague congress.

Peter Gerszten, MD, gave the keynote address at the Annual International Symposium on Long-Term Control of Metastases to the Brain and Spine in Las Vegas, Nev., on November 8.

L. Dade Lunsford, MD, was a special lecturer at the Third Annual Miami Neuro Symposium held at Baptist Health South Florida on December 4.

In the News

Robert Friedlander, MD, was featured in an October 7, WTAE-TV Action News story that discussed the surgery and recovery of a young woman suffering from a deep-seated brain lesion.

David O. Okonkwo, MD, PhD, was noted in an October 25 Pittsburgh Tribune Review article that took a look at a trauma patient whose book, Eight Twenty Eight: When Love Didn’t Give Up, chronicles recovery from a car crash.

Congratulations

Chief resident Kimberly A. Foster, MD, received the best presentation award at the 10th Annual Department of Neurological Surgery Stuart Rowe Society Lectureship and Research Day held in November. Residents Christopher Newman, MD, and Zachary Tempel, MD, shared this year’s runner-up award.

Matt El-Kadi, MD, PhD, was the recipient of the UPMC Passavant Hospital Foundation Legacy of Caring Award in October for his contribution to the growth and development of UPMC Passavant.

A Huntington’s disease research paper authored by Robert Friedlander, MD, “Inhibition of Mitochondrial Protein Import by Mutant Huntington,” was recommended by the peer-review website F1000Prime.com as being of special significance in its field. Dr. Friedlander was also named to the Brain Aneurysm Foundation’s medical advisory board.

Paul Gardner, MD, was board-certified by the American Board of Neurological Surgeons.

Gurpreet S. Gandhoke, MD, was recently named the Mayfield Clinical Science Award winner by the CNS/AANS Section on Disorders of the Spine and Peripheral Nerves for his paper reporting on the cost-effectiveness of lumbar fusion surgery.

Diane Carlisle, PhD, was invited to serve on the NIH Tobacco Control and Regulatory Research special emphasis panel.

Hideyuki Kano, MD, PhD, has been selected for inclusion in the 2015 edition of Marquis’ Who’s Who in America.
Dynamic Stabilization of the Lumbar Spine: A Decade of Experience (Continued from Page 5)

constructs. There is no additional risk incurred while undergoing dynamic stabilization versus traditional lumbar fusion.

A prospective, randomized, multi-institutional Investigational Device Exemption (IDE) study of the Dynesys dynamic stabilization system found similar results to our own experience. In the study, 367 patients at 28 centers were randomized to dynamic stabilization versus a standard spinal fusion surgery.

Patients treated with this system reported significant clinical improvement at three-year follow-up. Self-reported outcomes were significantly better for patients undergoing Dynesys dynamic stabilization compared to standard pedicle fusion at all time points. Treatment with the Dynesys system was significantly better for Visual Analog Scale (VAS) Back Pain, VAS Patient Satisfaction, and VAS Likelihood to Recommend scores after three years. The overall major complication rate was only 0.4 percent compared to 0.9 percent in the fusion group. With favorable published data and UPMC’s large, positive clinical experience, we continue to utilize the Dynesys and DTO systems for select patients in order to avoid spinal fusion surgery.

Lateral view of single level Dynesys implant.

Used with permission from Zimmer Spine.

Free Online CME
To take the CME evaluation for this issue, visit our education website: UPMCPhysicianResources.com/Neurosurgery.

A world-renowned health care provider and insurer, Pittsburgh-based UPMC is inventing new models of accountable, cost-effective, patient-centered care. It provides more than $887 million a year in benefits to its communities, including more care to the region’s most vulnerable citizens than any other health care institution. The largest nongovernmental employer in Pennsylvania, UPMC integrates more than 60,000 employees, more than 20 hospitals, more than 500 doctors’ offices and outpatient sites, a more than 2.5-million-member health insurance division, and international and commercial operations. Affiliated with the University of Pittsburgh Schools of the Health Sciences, UPMC ranks No. 12 in the prestigious U.S. News & World Report annual Honor Roll of America’s Best Hospitals — and No. 1 in Pennsylvania. For more information about our programs, continuing medical education, Video Rounds, news, and events, please visit UPMCPhysicianResources.com/Neurosurgery.