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Disclosures
Gurpreet Gandhoke, MD, and R. Mark Richardson, MD, PhD, have reported no relationships with proprietary entities producing health care goods or services.

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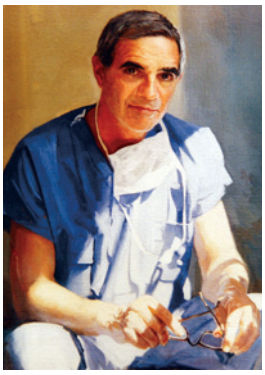
In Memoriam: **Peter Jannetta, MD, DSc**

by Raymond Sekula, MD



On April 11, 2016, former professor and the first department chair of the University of Pittsburgh Department of Neurological Surgery, **Peter Joseph Jannetta, MD, DSc**, died. Just days before his death, he gave a wonderful presentation, entitled "Remembering Walter Dandy," at a combined Grand Rounds for the departments of Neurological Surgery and Neurology concerning Walter Dandy, a pioneering neurosurgeon, along with Mary Ellen Dandy Marmaduke, daughter of Dr. Dandy.

An outstanding student athlete at William Penn High School, Dr. Jannetta matriculated to the University of Pennsylvania, where he participated in three sports: swimming, lacrosse, and football, and graduated from the University of Pennsylvania School of Medicine. He interned at the Hospital of the University of Pennsylvania, went on to a surgical residency at that institution, and was the first member of a National Institutes of Health Training Grant. On completion of his chief residency in general surgery at the University of Pennsylvania, Dr. Jannetta began a three and one-half year residency-training program in neurosurgery at the University of California, Los Angeles.

He then became associate professor and chief of the Division of Neurosurgery at Louisiana State University School of Medicine, New Orleans. In 1971, Dr. Jannetta was selected to be the chief of the Division of Neurosurgery at the University of Pittsburgh and then department chair in 1973. While at the University of Pittsburgh, the concepts of vascular compression of the cranial nerves and of microvascular decompression (MVD) developed rapidly under Dr. Jannetta's leadership, and a number of other contributions in cranial nerve pathophysiology were made.

Dr. Jannetta performed the first MVD procedure for trigeminal neuralgia in 1966. Although the procedure was initially rejected by senior colleagues, he persisted. And within a short period of time following the publication of his initial report, enthusiasm by younger neurosurgeons for the MVD procedure overwhelmed the detractors. Today, the microvascular decompression procedure is performed thousands of times each year throughout the world. Since Dr. Jannetta's original report, microvascular decompression has become the standard of care for patients with facial pain who can tolerate a general anesthetic.

In 1989, Dr. Jannetta received an honorary Doctor of Science degree from Washington and Jefferson College. In 1990, he was selected as Vectors/Pittsburgh Man of the Year in the Sciences. He is one of the recipients of the 1990 Horatio Alger Award. In 1983, he received the Herbert Olivecrona Award. In September of 2000, he was the recipient of the Fedor-Krause Medal of Honor, given to him by the German Neurosurgical Society. From 1976 to 1978, he was the Francis Sargent Cheever

(Continued on Page 5)

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

Chairman's Message

Big Shoes to Fill

As I reflect on the recent passing of the legendary neurosurgical icon Dr. Peter Jannetta, a number of words come to mind.

Respect. Most neurosurgeons — and physicians, for that matter — take care of one patient at a time, offering the best care they can to each. Dr. Jannetta did that and so much more. In addition to caring for thousands of patients from around the world, he also taught, and earned the unwavering respect from, his residents and fellows, as well as a multitude of surgeons from all over the globe who came to learn from him.

Charisma. Dr. Jannetta's smile was infectious. His presence would light up a room, a lecture hall, or a social event. People were drawn to him because of his personality and charisma.

Conviction. Although many colleagues doubted Dr. Jannetta's theories, he steadfastly pushed forward. Some of his theories he proved beyond any doubt; others remain in evolution. He was dedicated to finding solutions for some of medicine's most complex problems. His superior intellect allowed him to adeptly address any issue and astutely devise a strategy to gain an optimal outcome.

Responsibility. Dr. Jannetta not only put the University of Pittsburgh Department of Neurological Surgery on the map; he also transformed it into one of the most academically prolific departments in the nation. He created a culture of innovation and productivity. As his successor, I have the great pleasure and responsibility of continuing that legacy. With the contributions of our distinguished faculty and residents, we will take this department to the next level of prominence and success.

Department chairman Robert Friedlander, MD, (center) with Peter Jannetta, MD, (right) and Mary Ellen Dandy Marmaduke during Dr. Jannetta's April visit to the department to give a presentation on the life of Walter Dandy.

Serendipity. It is fortunate that only days prior to his passing, Dr. Jannetta gave his last public presentation in our department. He appeared here with Mary Ellen Dandy Marmaduke, daughter of the great neurosurgeon Walter Dandy, who spoke about her father's life. There were many similarities between these two great neurosurgical giants. This talk was Dr. Jannetta's last gift to the department.

Peter, it was an honor to have had the opportunity to know you. You will be missed.

Robert M. Friedlander, MD, MA
Chairman and Walter E. Dandy Professor of Neurological Surgery
Co-Director, UPMC Neurological Institute

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National Traumatic Brain Injury Biospecimens Repository Established in Pitt's Department of Neurosurgery

A national repository of biological samples from patients who have sustained traumatic brain injuries (TBIs) has been established in the Department of Neurological Surgery at the University of Pittsburgh. This biorepository supports the Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) study, a multi-center initiative funded by the National Institutes of Health (NIH) that is intended to revolutionize clinical care for brain-injured patients. A central goal of the TRACK-TBI biorepository is to identify blood-based biomarkers that can assist hospital-based clinicians in diagnosing TBIs and allow industry partners in the laboratory to identify new, effective treatments. Three thousand participants who have sustained a TBI are being recruited into the TRACK-TBI study, and a large, high-quality database of clinical, imaging, biomarker, and outcome data is being generated.

In collaboration with the TRACK-TBI coordinating center at the University of California San Francisco (led by Geoff Manley, MD) and our 11 U.S. partner sites, David Okonkwo, MD, PhD, and Ava Puccio, RN, PhD, at the University of Pittsburgh recently received a large supplemental award from the U.S. Department of Defense to establish the TRACK-TBI biorepository. Following laboratory renovations and certification in February 2016, the Department of Neurological Surgery at the University of Pittsburgh became the official new home of the TRACK-TBI biospecimens repository.

The TRACK-TBI biorepository is already the largest centralized collection of biological samples from TBI patients in the US. For a complex disorder like TBI, which has global incidence but lacks definitive clinical classification for diagnosis and therapy, multicenter collaboration is key for progress in research. Only with large numbers of patients and samples will researchers be able to address the many variations of TBIs. Similar to other disease processes, such as cardiovascular disease and cancer, diagnoses must be matched with a biomarker of injury and genetic markers for treatment directives.

"Front-runner" Biomarkers for Diagnoses

Our partnership with the TRACK-TBI effort has already borne fruit, with an early indication from the pilot work on a biomarker of interest, glial fibrillary acidic protein (GFAP), a brain-specific protein released into serum as a pathophysiological response to TBI. Based on the initial TRACK-TBI sample set (215 patients), the measurement of GFAP in blood has been shown to be effective in identifying patients with a high likelihood of having abnormal pathology seen on a CT scan. Other biomarkers of interest, now undergoing further study, include ubiquitin C-terminal hydrolase L1 (UCHL-1) and neuroinflammatory markers.

Through the support of the NIH and the Department of Defense, and in partnership with the national TRACK-TBI study, investigators at the University of Pittsburgh Department of Neurological Surgery are generating an international resource statistically powered to validate new, clinically relevant TBI biomarkers.

Trial to Test Gene Therapy for Parkinson's Disease *(Continued from Page 8)*

in a single surgical setting, using convection-enhanced delivery (CED) (see Figure 1 on page 8). In previous gene therapy and drug infusion trials for PD, the absence of CED and an inability to visualize progression of the infusion are thought to have been responsible for a lack of robust therapeutic efficacy.

R. Mark Richardson, MD, PhD, FAANS, who has extensive experience in the use of interventional MRI for neurosurgical procedures, will lead the trial at UPMC in collaboration with movement disorders colleagues in neurology. Paul Larson, MD, will lead the trial at the initiating site, the University of California San Francisco (UCSF), where Dr. Richardson contributed to the preclinical development of gene therapy delivery strategies employed in this trial. Based on preclinical work from the laboratory of Krystof Bankiewicz, MD, PhD, two previous AAV2-AADC Phase 1 trials were completed, without the use of interventional MRI (at UCSF[3] and Jichi Medical University, Japan), that did not reveal any unexpected safety issues. The current trial is sponsored by Voyager Therapeutics, a clinical gene therapy company based in Cambridge, Mass. Appropriate candidates are generally those who would qualify for DBS and who have not had problems with impulse control.

We are optimistic that this trial, which represents the leading edge of the neurosurgical delivery of gene therapy, will successfully establish a framework for achieving both therapeutic efficacy and future advances in the field.

For additional trial information, visit **clinicaltrials.gov/ct2/show/NCT01973543**.

AANS Annual Scientific Meeting Summaries of Abstract Awards

Gurpreet Gandhoke, MD, Christopher Deibert, MD, Ian Pollack, MD, and **Nathan Zwagerman, MD**, have each been selected to receive awards for abstracts submitted for the American Association of Neurological Surgeons (AANS) Annual Scientific Meeting, which was held in Chicago from April 30 – May 4. More than 1,500 abstracts were submitted.

Below is a summary of their abstracts.

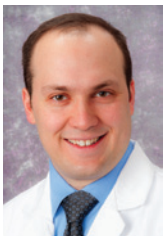
Dr. Gandhoke will receive the Sanford J. Larson Award for the abstract, "Incidence of Position Related Neuropraxia in 4,489 Consecutive Patients Undergoing Spine Surgery. Role of SSEP Monitoring?" The award is presented for the best spine research paper.

No large database study exists looking at the incidence of peripheral nerve injury from positioning during spine surgery.

Records of 4,489 consecutive patients undergoing spine surgery at a university hospital were reviewed. Incidence of peripheral nerve injury from positioning among these patients is reported. Intraoperative monitoring (IOM) changes related to arm and leg positioning and their sensitivity and specificity predicting the development of a new position-related peripheral nerve injury is calculated. Impact of length of surgery and of variables including age, sex, body mass index, diabetes mellitus, hypertension, coronary artery disease, cardiovascular disease, and history of smoking, on the development of a new peripheral nerve injury was defined.

Positions were: arms abducted and flexed at the elbow, n=2904 (64.7%); arms tucked at the side, n=1570 (35%); and the lateral position, n=15 (0.3%). Thirteen out of 4,489 (0.29%, CI95% 0.15-0.49%) patients developed a new position-related peripheral nerve deficit. Seven of those 13 (54%) developed meralgia paresthetica, and six (46%) developed ulnar neuropathy. Seventy-two of the 4,489 (1.6%) patients developed IOM changes from positioning, all of whom underwent a repositioning maneuver. One of these 72 (1.3%) developed a new position-related nerve deficit. Of the 4,417 (98.4%) patients who did not develop position-related IOM changes, 12 (0.3%) developed a new position-related nerve deficit. Sensitivity of IOM to detect a new position-related nerve deficit was 7.69%, and the specificity was 98.41%. The positive predictive value was 1.39% (CI95% 0.04-7.5%), and the negative predictive value was 99.73% (CI95% 99.53-99.86%). Neither the length of surgery nor any analyzed patient-related variable were shown to have a statistically significant impact on the development of a new neuropraxia.

The incidence of a new position-related nerve deficit in spine surgery was 0.29%. IOM has high specificity and poor sensitivity in detecting a position-related nerve deficit.



Dr. Deibert will receive the Ronald L. Bittner Award on Brain Tumor Research for the abstract, "IDH Mutant Gliomas Escape Natural Killer Cell Immune Surveillance Through Downregulation of NKG2D Ligands." The award is given for the best abstract paper submitted on brain tumor research by a resident or junior faculty member.

Glioblastoma multiforme, the most common primary brain tumor, carries a median survival of 15 months despite maximal resection followed by combined chemotherapy and radiation. One subtype of this disease is characterized by a mutation in the gene coding for isocitrate dehydrogenase (IDH), causing tumor cells to produce less protein than typical cells.

The immune system is a key component of our bodies' ability to fight developing cancer. For cancer to survive, it must develop strategies to avoid the immune response. Natural killer (NK) cells represent an early line of defense against cancer by killing tumor cells through direct contact. We postulated that the decreased protein created by IDH mutant (IDHmut) gliomas provides an avenue of immune escape by prohibiting communication between NK and tumor cells.

Searching a national registry of genetically sequenced gliomas, we identified a group of proteins termed NKG2D ligands that are expressed at a lower level in IDHmut gliomas. These proteins are known to promote NK cell killing. In our initial series of experiments, we verified a lower level of expression of NKG2D ligands in IDHmut gliomas. This corresponded with a decreased immune response by NK cells.

Building on this information, we sought a strategy to reverse the effects of IDH mutations and restore the immune response. Decitabine is a known chemotherapeutic used in the treatment of myelodysplastic disorders with similar genetic alterations. Subsequently, we treated IDHmut glioma cells with decitabine and observed an increase of NKG2D ligands. Furthermore, IDHmut gliomas showed an increase in recognition and destruction by NK cells following treatment with decitabine. Our work demonstrates the ability to target a specific genetic alteration in a subtype of glioma to stimulate a basic immune response. While these results are promising, they need to be translated to patient trials and evaluated for both effectiveness and safety.

Dr. Pollack will receive the Columbia Charity Softball Award for the abstract, "Immune Responses and Clinical Outcome after Glioma-Associated Antigen Vaccination in Children with Recurrent Low-Grade Gliomas." The award is given for the best pediatric tumor abstract.

A pilot study focused on children with tumors that progressed after at least two prior treatment regimens involved the testing of a novel vaccine that incorporates peptides derived from proteins that were shown to be overexpressed in childhood low-grade gliomas, as well as an immunoadjuvant. This study was designed to test safety and immunological efficacy and demonstrated that the vaccine was well tolerated and generated strong immunoreactivity against one or more of the targeted antigens in all of the evaluable vaccine recipients. An encouraging frequency of objective radiological responses was obtained, and several children have completed the vaccine course and have remained progression-free for more than two years after completing the treatment regimen.

This study was supported by National Institutes of Health (NIH) grants R21CA149872 and P01NS40923; the UPCI Immunologic Monitoring and Cellular Products Laboratory, which is supported in part by NIH award P30CA47904; and the Pediatric Clinical and Translational Research Center, which is supported by NIH grants UL1RR024153 and UL1TR000005. Support was also provided by grants from the Pediatric Low-Grade Glioma Initiative via the National Brain Tumor Society, as well as the Ellie Kavalieros DIPG Research Fund, the Connor's Cure Fund, the Ian's Friends Foundation, and the Translational Brain Tumor Fund of the Children's Hospital of Pittsburgh Foundation.

Building upon the pilot study data, a five-year $1.8 million phase II trial was awarded R01 funding from the National Cancer Institute (NIH-1R01CA187219-01) to further evaluate this vaccine regimen, with an emphasis on assessing clinical efficacy in a larger patient cohort in conjunction with correlative immunological parameter.

Dr. Zwagerman will receive the Synthes Skull Base Award for the abstract, "A Prospective, Randomized Control Trial for Lumbar Drain Placement after Endoscopic Endonasal Skull Base Surgery." The award is given for the best abstract related to skull base surgery.

Cerebral spinal fluid (CSF) leaks may occur after complex skull base surgery and seem especially common during the Endoscopic Endonasal Approach (EEA). Lumbar drain placement after complex EEA surgery is thought to reduce the occurrence of CSF leaks, but this is inconsistent among providers. In this study, subjects were randomized to either receive or forego an immediate postoperative lumbar drain with a comparison of the primary endpoint of postoperative CSF leak. The inclusion criteria included: 1) extensive arachnoid dissection; 2) dissection into a ventricle or cistern; or 3) dural defect greater than 1 cm^2. Demographic data, tumor location, defect size, complications, and leak rates were collected.

The trial, which included 170 patients, was stopped early due to a significant difference in CSF leak rate between the intervention (drain) and control (no drain) groups. The most significant variable associated with postoperative leak was no drain ($p<0.011$). A difference in leak rate ($p<0.021$) was found based upon the tumor location (anterior, posterior, suprasellar). However, when a drain was employed, tumor location was not a significant factor in post-op leak ($p<0.507$). Defect size was noted to be larger in the group with leaks compared to the control group (6.86 cm^2 versus 2.78 cm^2, $p < 0.076$). Thirty-six patients had anterior fossa pathology (olfactory groove or planum). The leak rate was 10% with and 35% without a drain ($p<0.11$). Fifty patients had posterior fossa pathology (clival). The leak rate was 13% with and 30% without a drain ($p<0.12$). Finally, 85 patients had suprasellar lesions. The leak rate was 4.7% with and 9.5% without a drain ($p<0.43$).

For patients undergoing endoscopic endonasal skull base surgery, lumbar drain placement lowers the rate of postoperative CSF leak. The impact seems to be greatest in patients with large anterior or posterior cranial base defects.

In Memoriam: **Peter Jannetta, MD, DSc** *(Continued from Page 1)*

Distinguished Professor at the University of Pittsburgh School of Medicine. He was the Walter E. Dandy Professor of Neurosurgery at the University of Pittsburgh School of Medicine from 1992 to 2000. In 1992, the university also established the Peter J. Jannetta Chair in Neurological Surgery.

Dr. Jannetta is survived by his wife, Diana Jannetta; his first wife, Ann Jannetta; four daughters, Susan Jannetta of New York City, Joanne Lenert of Dunn Loring, Va., Carol Jannetta of Dover, Mass., and Elizabeth Jannetta of New York City; two sons, Peter T. Jannetta of Oakland and Michael Jannetta of Putnam Valley, N.Y.; one stepson, Robert Davant III of Washington's Landing; and one stepdaughter, Hilary Rose of Ross; eight grandchildren and two step-grandchildren.

Within neurosurgery, Dr. Jannetta is known as an innovator and luminary. Throughout the years, Dr. Jannetta's significant contributions on neurological surgery have been recognized by institutions throughout the world.

A Two-Year Cost-Effectiveness Comparison Between Open Transforaminal and Minimally Invasive Lateral Lumbar Interbody Fusions

by Gurpreet Gandhoke, MD

In people under the age of 45 years, lower back pain is the most expensive cause of work-related disability. Minimally invasive spine surgeries (MISS) that minimize tissue injury and accelerate overall recovery, such as lateral lumbar interbody fusion (LLIF), face the challenge of demonstrating their cost-effectiveness when compared to traditional open approaches, such as trans-lumbar interbody fusion (TLIF). A comprehensive study comparing the cost-effectiveness between these two procedures was performed.

Seventy-four patients (45 one level open TLIF; 29 one level stand-alone LLIF) were evaluated after meeting the inclusion criteria (see Table 1) and underwent surgery at UPMC with a follow-up after two years. Pre-operative and two-year post-operative pain, disability, health state and quality-of-life were assessed using the following self-reported outcomes instruments: VAS BP-LP, SF36 PCS, SF36 MCS, ODI, and EQ-5D. The direct medical care costs were calculated using the University of Pittsburgh's health care system database of all charges incurred from the diagnosis to final follow-up. The total US dollar amount paid by the insurance company was divided into physician and hospital services. The primary aim of the study was to determine if LLIF or TLIF is more cost-effective in the treatment of lumbar spondylosis using the ICER calculation: (Cost LLIF – Cost TLIF)/(QALY LLIF–QALY TLIF), MCID and MCED. Indirect costs were estimated using the SHCA by multiplying the change in hours worked by the national gross wage ($50,000) reported by the World Bank. Paired t-tests and Wilcoxon rank sum tests were used for statistical analyses. Significant improvements were observed at the two-year follow-up for both procedures utilizing SF36PCS, ODI, VAS BP, VAS LP and EQ5D. ICER calculations revealed similar mean cumulative QALYs-gained at the two-year interval (0.67 for TLIF and 0.60 for LLIF; p=0.331). Median total cost of care following TLIF and LLIF were $44,068 and $45,574, respectively; (p=0.960). MCED thresholds with an anchor of less than $50,000/QALY were higher than MCID thresholds for all patient-reported outcome measures. The total mean cost and EQ5D were statistically equivalent between both groups.

TLIF and LLIF produced equivalent two-year patient outcomes at an equivalent cost-effectiveness profile. This was the first study of its kind that

both followed a standardized method of reporting and analyzed cost data for evaluating a MISS procedure. The anchor-based modality using the HTI anchor was used to calculate the MCID values. The AUC of the ROC graphs supported the accuracy and reliability of the thresholds thus defined, compared with previous studies. Currently, the commonly accepted cost-effectiveness threshold for most surgical interventions is approximately $100,000. TLIF ($65,179/QALY-gain) and LLIF ($72,260/QALY-gain) fell within the currently accepted cost-effectiveness threshold.

Cost-effectiveness is an important aspect of health care delivery, especially with spine surgery. A p-value of less than 0.05 may not be sufficient to recommend a particular surgical approach, as surgery must provide an economic benefit in addition to adding quality life years to the patient. This study demonstrated that when studying direct and indirect costs, TLIF and LLIF reveal no statistically significant difference in cost or QALY at a two-year follow-up.

Table 1.

Inclusion Criteria	Exclusion Criteria
MRI evidence of lumbar spondylosis	Evidence of non-spinal cause for back pain or radiculopathy
Exhausted 6 weeks of conservative therapy without symptomatic response	Active lawsuit or workman's compensation
	No follow-up available
	Musculoskeletal systemic disease including metabolic bone disease and inflammatory arthritis
	Surgical site infection requiring return to OR for incision and debridement
	Symptomatic pseudoarthrosis requiring surgical correction

News & Notes

Congratulations

Adam S. Kanter, MD, received the Early Achievement Award from the University of Vermont School of Medicine on March 11. The award is presented to an alumnus who has graduated within the past 15 years and has demonstrated outstanding community, scientific, or academic achievement

Nitin Agarwal, MD, Gurpreet Gandhoke, MD, Ezequiel Goldschmidt, MD, Michael McDowell, MD, Alp Ozpinar, MD, David J. Salvetti, MD, and **Zachary Tempel, MD**, were each selected as Charles Kuntz Scholars at Spine Summit 2016, the 32nd annual meeting of the AANS/Congress of Neurological Surgeons (CNS) Joint Section on Disorders of the Spine and Peripheral Nerves, held in Orlando, Fla., March 16-19. The scholarship is presented to authors of outstanding abstracts detailing a laboratory or clinical investigation in the area of spinal disorders.

Dr. Tempel was also awarded the Young Investigator Award at the 2016 Society for Lateral Access Surgery (SOLAS) annual meeting held in Carlsbad, Calif., March 10-12. Dr. Tempel received the award for the abstract, "Does Concave Versus Convex Approach Matter When Using Lateral Lumbar Interbody Fusion For Adult Scoliosis?"

Dr. Goldschmidt was also awarded the best abstract award at the North American Skull Base Society annual meeting held in Scottsdale, Ariz., on February 12-14. Dr. Goldschmidt received the award for the abstract, "Effect of In Vivo Oxidized Cellulose on In Vitro Growth of Human Respiratory Mucosa and Sub-Mucosa During Endoscopic Skull Base Approaches."

Nduka Amankulor, MD, was awarded one of the four best oral poster presentation awards during the Society for Neuro-Oncology annual meeting held in San Antonio, Tex., November 19-22.

Amir Faraji, MD, was selected as the winner of the Society of Neurological Surgeons/Research Update in Neuroscience for Neurosurgeons (RUNN) course resident award for his submission, "Antioxidant Nanoparticles for Use in Traumatic Brain Injury."

Ian Pollack, MD, will receive the Children's Brain Tumor Foundation's Award for Scientific Excellence at the group's 14th Annual Dream and Promise Gala, June 1, in New York.

Special Lectures and Appearances

Joseph Maroon, MD, was a distinguished visiting professor at the Inova Neuroscience and Spine Institute, on January 19 in Falls Church, Va.

Paul Gardner, MD, was co-director of the V Brain Tumor & Minimally Invasive Spine Symposium, held March 17-20 in Hollywood, Fla.

Elizabeth Tyler-Kabara, MD, PhD, was chair of Medical Bionics Summit 2016, held April 6-7 in Washington, D.C.

Adam S. Kanter, MD, was scientific program chair of Spine Summit 2016, the 32nd annual meeting of the AANS/CNS Joint Section on Disorders of the Spine and Peripheral Nerves, held March 16-19 in Orlando, Fla.

Peter C. Gerszten, MD, MPH, was an invited speaker at the 6th annual meeting of the Novalis Circle Society in Munich, Germany on February 20.

In the News

L. Dade Lunsford, MD, was a guest on the KDKA Radio Morning News Show with Larry Richert and John Shumway on February 29, where he discussed the Gamma Knife®.

Juan C. Fernandez-Miranda, MD, was featured in a spotlight article in the Pituitary Network Association's *Highlights* newsletter discussing his work and research in minimally invasive approaches in skull base surgery.

An article discussing a novel approach to find aberrant connections in certain hippocampal structures in temporal lobe epilepsy, coauthored by **R. Mark Richardson, MD, PhD, FAANS**, was featured on the February cover of the journal *Human Brain Mapping.*

Dr. Richardson was also quoted in a January 2016 Dell.com article that focused on how the new wave of neurotechnology is changing the way we study the brain and treat neurological diseases.

Additionally, Dr. Richardson was featured on *KDKA-TV 2 Evening News* on February 18 and the *Pittsburgh Tribune Review* on February 29 regarding his work in a new gene therapy enzyme study under way to aid in treatment of Parkinson's disease patients. (See related article on Page 8.)

Joseph Maroon, MD, was featured in a todayspigskin.com article, published on February 10, that addressed his stance on concussion and CTE through his treatment of WWE star wrestler Daniel Bryan.

Pittsburgh's Neurosurgery Interest Group (NSIG), led by **Raymond Sekula, MD**, and **Nitin Agarwal, MD**, was profiled in the Winter 2016 edition of the AANS *Young Neurosurgeons News* newsletter.

UPMC LIFE CHANGING MEDICINE

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Trial to Test Gene Therapy for Parkinson's Disease

UPMC is one of two medical centers conducting a Phase 1b gene therapy study for individuals who have been living with a Parkinson's disease (PD) diagnosis for at least five years and who have had varying responses to their current medication. The purpose of this gene therapy study is to test the safety and tolerability of AAV2-hAADC (adeno-associated viral vector serotype 2 encoding human aromatic L-amino acid decarboxylase) for the treatment of advanced PD with motor fluctuations. AAV2-hAADC is a recombinant gene transfer vector consisting of recombinant adeno-associated viral particles serotype 2 (AAV2) carrying the complementary deoxyribonucleic acid (cDNA) of the human AADC gene. When expressed, the AADC protein functions to convert levodopa to dopamine. In PD, levels of endogenous AADC decrease with increasing disease severity. This clinical trial employs a pro-drug approach, in that patients continue to take oral levodopa, which is converted to dopamine to a much greater extent in brain regions where AADC is over-expressed via gene transfer.

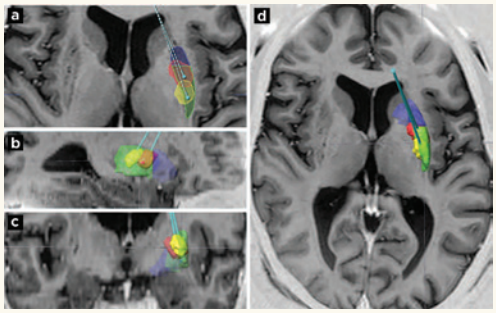

Figure 1. Modeling of three-dimensional infusion volumes in the human putamen.

Levodopa, the biosynthetic precursor of dopamine, is the most commonly used and effective medical treatment for PD. The long-term efficacy of levodopa, however, is limited by ongoing degeneration of the nigral cells that produce AADC, requiring increasing doses of levodopa for maintenance of the clinical response. These dose escalations become limited by the development of dyskinesias and other adverse effects, including severe motor fluctuations ("on" and "off" symptoms). In this trial, AADC will be over-expressed in the putamen, an area to which dopamine is normally transported by cells that degenerate in PD. Cells in the putamen, however, do not degenerate in PD and are capable of long-term expression of the transgene.

The ClearPoint® Neuro Navigation System, in place at UPMC since 2012 for deep brain stimulation (DBS) surgery, will be used to co-administer the viral vector along with a gadolinium-based contrast agent to visualize the infusion in near-real-time. The AAV2-hAADC vector is delivered bilaterally into the putamen

(Continued on Page 3)

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