neurosurgery news

UCSF Brain and Spinal Injury Center Redefines National Standards for Neurotrauma

Over the last two years, the UCSF Brain and Spinal Injury Center (BASIC) at San Francisco General Hospital has led one of the most ambitious infrastructure overhauls for clinical care in decades. Led by Chief of Neurosurgery Geoffrey Manley MD, PhD, investigators at BASIC have worked with neuroscientists at the National Institutes of Health (NIH) and the U.S. Department of Defense to develop the Common Data Elements (CDE) for Traumatic Brain Injury: new standards for reporting and defining brain injuries across studies to transform care for patients.[1]

According to the Centers for Disease Control and Prevention, approximately 1.7 million Americans sustain traumatic brain injuries each year. Despite decades of research and over two dozen clinical trials, there have been no new effective therapeutic developments for these patients. One major hindrance is that the diagnostic framework for traumatic brain injury has not changed in over 30 years, despite advances in our understanding of the disease process. Current classification schemes do not take into account pathophysiological mechanisms responsible for neurological deficits. The challenges for clinicians are further compounded by the heterogeneity of traumatic brain injury and the lack of validated outcome measures for informing patients of their prognoses for recovery. Patients who enter the emergency department with a head injury typically undergo a CT scan and a neurological exam to determine impairment to eye, verbal, and motor skills. Injuries are then rated on the Glasgow Coma Scale, which defines them as mild, moderate, or severe. A patient initially diagnosed with a "severe" brain injury may go on to have a normal recovery, while a patient with a "mild" injury may experience life-long social, cognitive, or behavioral impairments.

While technology has advanced to provide better imaging modalities and molecular profiling of tissue following injury, the implementation of those advances in the clinic has lagged behind, leaving physicians unable to appropriately stratify patients for clinical trials and predict outcomes. "For diseases like cancer, modern classification systems are a mixture of anatomy, physiology, metabolism, immunology, and genetics," said Dr. Manley. "For TBI we have mild, moderate, and severe. Within those categories there are no standardized definitions across treatment centers and neuroimaging is only adjunctive."

Recent studies of soldiers and athletes suffering repetitive head injury have also tied brain injury to some types of psychological disorders and even neurodegenerative disorders like dementia, adding to the complex constellation of symptoms seen with head injury and underscoring the need to take neurocognitive measures into account when making diagnoses and counseling patients.

The outstanding work in neurotrauma at San Francisco General Hospital has earned the hospital the first certification for traumatic brain injury by the Joint Commission. The hospital will now serve as a model for other hospitals that seek the new Joint Commission certification.

Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI)

To test and refine the CDE, UCSF has collaborated with the University of Pittsburgh Medical Center, the University Medical Center Breckenridge, and Mount Sinai Rehabilitation Center to perform a prospective, longitudinal study of traumatic brain injury.[2] This study established data repositories for clinical informatics, biospecimens, neuroimaging, and neurocognitive outcome assessments.

Patients enrolled in the TRACK-TBI study were selected from patients who underwent CT imaging as part of the regular standard of care in the emergency department. Blood draws were performed for genetic and proteomic analyses, and at two weeks patients returned for a 3T MRI scan. Preliminary data from patients with "mild" Glasgow Coma scores show that some of these patients had normal CT scans but abnormal MRI scans, indicating that CT is not sensitive enough to remain the clinical standard for assessing traumatic brain injury. At six months following enrollment, patients underwent neurocognitive assessments and were evaluated for symptoms of post-traumatic stress disorder (PTSD) using the civilian version of the PTSD Checklist from the National Center for PTSD. Of the 216 patients enrolled in the study with mild traumatic brain injury, 25% had symptoms of PTSD.

Dr. Manley and his colleagues are now in the process of implementing TRACK-TBI II, which will further the

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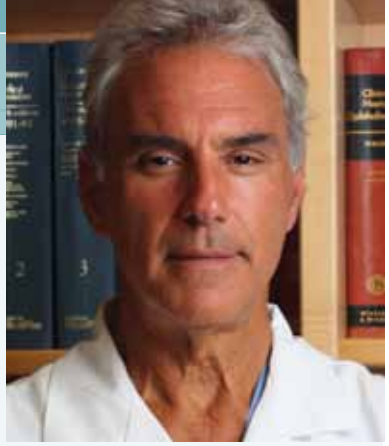

This year I am honored to be serving as the 81st President of the American Association of Neurological Surgeons, and one of the primary goals during my tenure will be to advance patient safety in neurosurgery. Patient safety has been a focus of mine since my neurosurgical residency and it is a personal accomplishment for me to be able to address it on a national scale through the AANS.

A report by the Institute of Medicine ("To Err is Human: Building a Safer Health System") published in 1999 estimated that the number of deaths due to medical errors may be as high as 98,000 per year. Many of these errors are due to an inadequate network of safeguards – as the IOM noted in their report, healthcare agencies can best improve safety through a systems approach to ensure that the multiple gaps that converge to bring about catastrophic mistakes are closed. In the last decade surgical checklists have reduced many avoidable hospital errors and more of these need to be implemented in everyday clinical practice across disciplines.

But plugging holes in the system and creating checklists are not enough. We must change our culture so that safety concerns are of the utmost importance and that each member of the care team has a personal sense of accountability. At large institutions in particular, where patients are cared for by many employees from a variety of departments, blame is easily laid on others. For surgical patients, the attending surgeon must assume responsibility for the welfare of their patients. In the surgical community that means improving communication in the OR and with nursing staff on the wards and moving beyond the mindset of "but this is how it has always been done here."

So the main challenge for the future will be answering the question "How do we get everyone to feel accountable?" At the Department of Neurological Surgery at UCSF, we have recently created an online video, "Creating a Culture of Safety Within Operative Neurosurgery," based on the World Health Organization surgical safety guidelines and highlighting the crucial steps to establish an environment in which communication between members of the surgical team is valued, thus minimizing errors and improving patient safety. It also stresses the importance of verifying checklists for items such as patient consent, history, and site marking; as well as communicating effectively with the postoperative team. Within our Department at UCSF, the video will be mandatory viewing for members of the surgical team and will include a quiz to ensure viewing compliance. You can find the video at: http://neurosurgery.ucsf.edu/index.php/education_safety.html

At the AANS, our goal is to influence neurosurgeons nationally. In January of this year, the NeuroPoint Alliance kicked off the pilot program for the National Neurosurgery Quality and Outcomes Database (N^2QOD) Project – a comprehensive national outcomes registry to collect clinical, demographic, and quality-of-life data on neurosurgical patients. The registry will allow for the systematic, prospective data collection and self-assessment that will define the future of clinical care in all specialties. As stated in the N^2QOD Objectives and Data Collection Guidelines, the system will also give neurosurgeons "the means to assess risk-adjusted measures of the value and durability of treatment responses, understand their patient's perspectives with respect to clinical outcomes, and compare the relative effectiveness of therapeutic interventions."

The AANS is also advancing comparative effectiveness research through our Neurosurgery Research and Education Foundation (NREF). As an independent source of support for residents and young faculty engaged in neurosurgical research, it is critical for NREF to encourage neurosurgeons at the beginning of their careers to focus on enhancing quality through robust data collection grounded in outcomes science theory. Another important goal for NREF will be to partner with industry to increase support for these types of initiatives and for clinical trials that focus not only on survival endpoints but also on quality of life after treatment.

This is a call to all in the medical community to take part in the movement to improve patient safety. By changing our culture, we can save the lives of thousands of our patients.

Mitchel S. Berger MD

Kathleen M. Plant
Distinguished Professor and Chair

Director,
Brain Tumor Research Center

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work of the first study by extending the data collection to 10 sites across the United States. The goals are to provide clinicians and researchers with current information that links genomic data, imaging characteristics, neurocognitive outcomes, quality-of-life measures, and patient-specific demographic information.

International Traumatic Brain Injury Research Initiative

The shift in traumatic brain injury research and classification is also taking place abroad and the first cooperative international group to perform prospective studies of head injury was established in October 2011. Led in the United States by Dr. Manley, the International Traumatic Brain Injury Research Initiative will bring together the NIH, the Canadian Institute of Health Research, and the European Commission.

Better Pre-Clinical Outcome Measures for Spinal Cord Injury

Standards for neurotrauma research are not only due for an update at the clinical level. As Dr. Manley and his collaborators work to re-invent guidelines for classifying traumatic brain injury, BASIC principal investigator and bioinformatics expert Adam Ferguson PhD is looking to do the same for preclinical models of spinal cord injury.

"When I read clinical reports of brain and spinal cord injury in humans, I noticed that the outcome measures being reported were very different from the outcome measures being reported in the preclinical literature," said Dr. Ferguson. While some clinical variables such as motor function or cognitive impairment had counterparts in preclinical data, others, like body temperature under anesthesia or bladder recovery following injury, did not. Many of those neurocritical variables are generally not seen as primary outcomes in basic science. But while left out of published manuscripts, these types of data are often still recorded during experiments and reside in the notebooks and cabinets of spinal cord injury scientists all over the world.

This disconnect in reported outcomes is a hurdle to translating laboratory findings into useful clinical therapies and has prompted Dr. Ferguson and his colleagues to develop a preclinical set of CDE that mirror the clinical CDE for spinal cord injury that are currently under development by the NIH. They have reached out to several centers around the world that work with models of spinal cord injury to build a large database that can be mined for more clinically relevant outcome measures and increase the statistical significance of the collective findings. "If the clinical CDE has revealed an important outcome measure, we need to make sure we have something analogous," says Dr. Ferguson. "If not, we should build it." The goal will be to standardize outcome measures in rodents and monkeys and analyze them across species, eventually comparing them to human outcomes.

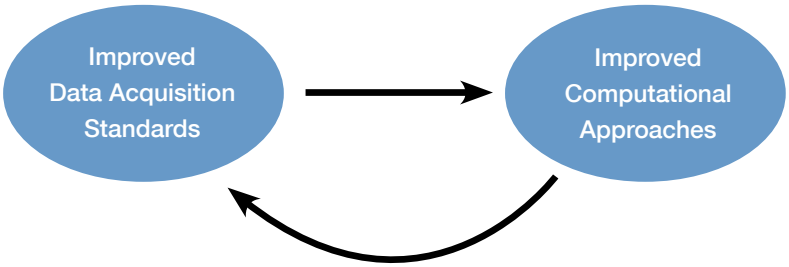
Using Bioinformatics to Enlarge the Picture of Spinal Cord Injury

Two years into the development of the preclinical CDE, BASIC's database includes data from approximately 3,000 rodents and 40 primates from the California Primate Consortium. So far they have been able to map the preclinical raw data onto some of the clinical CDE literature – measures conserved across laboratories and species with clinical counterparts – providing the first outcome targets to expedite translational testing.

Dr. Ferguson expects that in applying multivariate analysis to the new database, new patterns will emerge to help characterize the "syndrome" of spinal cord injury.[3] The power of combining sophisticated computer and statistical methods to sort through and organize vast quantities of information will allow scientists to build a larger picture of the epidemiology of spinal cord injury – not only a single result following an isolated insult, but a mosaic created from integrating the results of multiple functional and biological assays from many laboratories.

Ultimately, aligning preclinical and clinical standards on large scale has the potential to greatly impact the lives of patients waiting for new treatments for brain and spinal cord injury. "USCF BASIC is a special environment where you have crosstalk between clinicians and basic scientists who are working to bridge the gaps across species and make translational therapeutic testing a reality," said Dr. Ferguson.

Targets for Improved Information Processing in Translational Neurotrauma



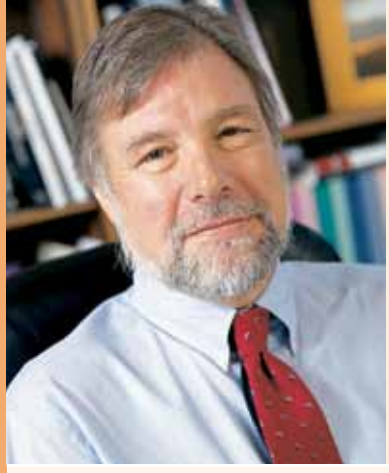
Adapted from: Ferguson AR, Stuck ED, Nielson JL. Syndromics: A Bioinformatics Approach for Neurotrauma Research. **Transl Stroke Res** 2011;2(4):438-54.

Further Information:

1. To view the Common Data Elements for traumatic brain injury, visit: http://www.commondataelements.ninds.nih.gov/TBI.aspx

2. For more about the TRACK-TBI study, visit: http://www.brainandspinalinjury.org/research.php?id=189

3. Ferguson AR, Stuck ED, Nielson JL. Syndromics: A Bioinformatics Approach for Neurotrauma Research. **Transl Stroke Res** 2011;2(4):438-54.



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Michael S. Beattie PhD is a professor of neurological surgery and co-director of the UCSF Brain and Spinal Injury Center (BASIC). Dr. Beattie has been interested in the neural mechanisms of recovery after brain and spinal cord injury for many years. He and his wife and collaborator, Dr. Jacqueline Bresnahan (also a member of the Neurosurgery faculty), moved their laboratory to BASIC from Ohio State University, where Dr. Beattie was the founding chair of the Department of Neuroscience, in 2006. Their group is known for developing preclinical models to study recovery of function after spinal cord injury, and for studies of the biology of neural injury and repair. Current projects include analyses of the interrelationship of post-injury inflammatory events and excitotoxic cell death, the roles of oligodendrocyte death and replacement in recovery after injury, and the development of stem and progenitor cell transplantation strategies for promoting recovery after spinal cord injury. BASIC's location at San Francisco General Hospital (SFGH) along with the physician-scientists of the UCSF Neurotrauma program promotes basic and clinical science interactions, and Dr. Beattie's goal is to help translate the laboratory's expertise in the biology of injury and recovery to treatments that can be implemented and tested in neurotrauma patients at SFGH and other centers.

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Wan JJ, Cohen MJ, Rosenthal G, Haitsma IK, Morabito DJ, Derugin N, Knudson MM, **Manley GT.** Refining resuscitation strategies using tissue oxygen and perfusion monitoring in critical organ beds. J Trauma 2009;66(2):353-7.

Geoffrey T. Manley MD, PhD is the chief of neurosurgery at San Francisco General Hospital and professor and vice chairman of neurological surgery at UCSF. He also co-directs the UCSF Brain and Spinal Injury Center. He is a trauma neurosurgeon with clinical interests in brain injury, spinal cord injury, and neurocritical care. His translational research interests span from the laboratory to the bedside. Dr. Manley is a graduate of the Medical Scientist Training Program at Cornell University Medical College, where he earned his medical degree as well as his doctorate degree in neuroscience. He completed his residency in neurosurgery at UCSF and a postdoctoral fellowship in molecular biophysics. Dr. Manley is also a faculty member of the California Institute for Quantitative Biosciences and the UCSF Center for Clinical and Translational Informatics.

Dr. Manley is an internationally recognized expert in neurotrauma. He has published over 150 manuscripts that reflect a wide range of research interests from molecular aspects of brain injury to the clinical care of traumatic brain injury (TBI) patients. He has helped to define new molecular mechanisms and develop advanced neuromonitoring and informatics tools for TBI. He is currently leading national and international efforts to create a modern knowledge warehouse that integrates clinical, imaging, proteomic, genomic, and outcome biomarkers of TBI to drive the development of a new TBI classification system. As demonstrated in other diseases, a more precise classification of TBI could revolutionize diagnosis, direct patient-specific treatment, and improve outcome. His many honors include the General Motors Trauma Research Award and the Trauma Research Award from the American College of Surgeons. He has served as a consultant for the Prehospital Guidelines Committee for the World Health Organization and on a number of committees for the National Institutes of Health and the U.S. Department of Defense.

Orin Bloch MD received his undergraduate degree from the University of Pennsylvania in Philadelphia, PA and attended medical school at UCSF where he graduated Alpha Omega Alpha. During medical school he developed an interest in cerebral water physiology and spent a year working in the laboratory of Alan Verkman MD, PhD supported by a research fellowship from the Howard Hughes Medical Institute.

Dr. Bloch became a resident in the Department of Neurological Surgery in 2007, with a primary focus in surgical neuro-oncology and skull base tumors. As resident, he has published numerous manuscripts in peer-reviewed journals on the clinical management of primary brain and skull base tumors, and served as a guest editor for an issue of *Neurosurgery Clinics of North America.* In 2010, he received an NIH National Research Service Award to study mechanisms of immunoresistance in gliomas in the laboratory of Andrew Parsa, MD, PhD. Dr. Bloch received the Stryker Neuro-Oncology award at the 2011 annual meeting of the Congress of Neurological Surgeons for his work on the role of tumor-associated macrophages in promoting immunosuppression in gliomas. He has also been awarded a K99/R00 Pathway to Independence Award from the NIH to continue his work in glioma immunology over the next 5 years.

Upon graduating from residency, Dr. Bloch will remain at UCSF as a clinical instructor in the Department of Neurological Surgery and complete a fellowship in skull base tumor surgery. He will also continue his post-doctoral research fellowship in the laboratory of Dr. Parsa, supported by his K99 award.

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Bloch O, Sughrue ME, Mills SA, Parsa AT. Signaling pathways in cranial chondrosarcoma: potential molecular targets for directed chemotherapy. J Clin Neurosci 2011;18(7):881-5.

Brian J. Jian MD, PhD completed undergraduate studies at the University of Pittsburgh, graduating with Honors in both neuroscience (BS) and the history and philosophy of science (BA). He then entered the MD/PhD program at the University of Pittsburgh, where he continued his interest in neurophysiology and extracellular recordings in the awake animal. Dr. Jian's work as an undergraduate and early medical student led him to NASA Ames' Research Center, where he evaluated the feasibility of humans' ability to live in high-gravitational fields, during his graduate years. He continued his PhD work identifying the vestibular nuclei as a multisensory integrative center capable of central nervous system plasticity.

Dr. Jian's arrival at UCSF in 2006 led him to develop new interests in the field of neuro-oncology. He has worked closely with Andrew Parsa MD, PhD to further the understanding of the immune system and its potential impact on primary brain tumors, specifically glioblastoma multiforme (GBM). In 2010, Dr Jian received a postdoctoral NIH National Research Service Award to gain experience with understanding the immunoevasive mechanisms of GBM. During a year in the laboratory of Dr. Parsa, he gained valuable insights into immunotherapy and current techniques of immunology and immune monitoring. He plans to continue this work with interests in participating and expanding current experimental vaccine therapy for GBM. After completing residency in 2012, Dr. Jian plans to stay in the San Francisco Bay Area.

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Neuro-Oncology Service Wins Patient Satisfaction Award for the Fifth Consecutive Year

The Neuro-Oncology Service was awarded the UCSF Medical Center Pinnacle Award for an unprecedented fifth year in a row. This award recognizes the UCSF medical service with the best patient satisfaction scores for outpatient care.

Above: Grace and Michael Farris

Right: Randi Murray, Marritje Greene, Ira Glass, and Cathy Podell

Celebrated Radio Host Ira Glass Headlines Benefit for UCSF Brain Tumor Center

On April 21, Ira Glass, host and producer of public radio's "This American Life," talked to supporters of the UCSF Brain Tumor Center about the loss of his brother-in-law Gordon Murray to brain cancer at a benefit at the St. Regis Hotel that raised $1.2 million for brain tumor research and caregiver support. "I know how lucky we were that he was able to receive the outstanding care he did at UCSF," said Mr. Glass. "It really is an extraordinary institution." Mr. Glass was joined by nine-year-old brain tumor survivor Grace Farris and her father Michael Farris, who credited the care Grace received at UCSF for saving her life. The funds from the benefit will support an initiative established by Mr. Glass' sister Randi Murray, Cathy and Mike Podell, and Marritje and Jamie Greene. The Brain Tumor Initiative aims to build better support for families and caregivers into the standard care for brain tumors, as well as fund a new intraoperative imaging suite and space for new research laboratories.

New Faculty

The Department of Neurological Surgery is pleased to announce the appointment of three new faculty members. Keith Quattrocchi MD, PhD, FACS has been appointed clinical associate professor of neurological surgery and will be working full time at Marin General Hospital as part of the UCSF Neurological Surgery community extension program. Arun Benet MD, assistant adjunct professor of neurological surgery, has joined the cerebrovascular research faculty. Orin Bloch MD has graduated from the Department's residency program and will remain at UCSF as a clinical instructor of neurological surgery in addition to completing a fellowship in skull base tumor surgery.

Aneurysm Text Wins Illustration Prize and is a Finalist for Independent Publishing Award

Seven Aneurysms: Tenets and Techniques for Clipping, written by Chief of Vascular Neurosurgery Michael Lawton MD, is a finalist for the 2012 Ben Franklin Award in Professional/Technical Writing. It summarizes techniques and strategies for common aneurysms that neurosurgeons will be treating in the future. The reference book contains 450 illustrations by biomedical illustrator Kenneth Xavier Probst who received an Award of Merit from the Association of Medical Illustrators for this work.

Lawton MT. Seven Aneurysms: Tenets and Techniques for Clipping. New York, NY: Thieme; 2010.

UCSF Study Shows Hospital Readmission Rates for Spine Surgery are Misleading

Neurological and orthopedic surgeons at UCSF recently reviewed thousands of hospital admissions for spine problems between 2007-2011 and analyzed "all cause" readmissions, the basis for the Centers for Medicare and Medicaid metric. Readmission rates can be used to determine a hospital's quality of care, as they can often reflect hospital-acquired infections or surgical complications. The UCSF investigators found that readmissions were being overestimated by up to 25% because "all cause" readmissions do not distinguish between planned, scheduled, and staged surgeries and unplanned surgeries for complications. Many complex spinal surgeries are scheduled to be performed in two or more stages spaced out during several weeks, and the subsequent surgeries are currently tagged as readmissions. Praveen Mummaneni MD, Christopher Ames MD, and Dean Chou MD, associate professors of neurological surgery, contributed to the report.

Matthew Tate MD, PhD winner of the 2012 William P. Van Wagenen Fellowship

Scott Baraban PhD, professor of neurological surgery and William K. Bowes Jr. Endowed Chair in Neuroscience Research, has been awarded a EUREKA grant from the NIH for the project "Using Zebrafish to Advance Our Understanding and Treatment of Epilepsy." Dr. Baraban and his team are using zebrafish mutants featuring a loss-of-function sodium channel mutation to identify molecular targets for therapeutic treatment and screen drug candidates. The epileptic zebrafish display a phenotype similar to monogenic epilepsy disorders primarily seen in children (e.g., Severe Myoclonic Epilepsy of Infancy and Dravet syndrome).

Mitchel S. Berger MD, Kathleen M. Plant Distinguished Professor and Chair of Neurological Surgery, has been appointed the 81st President of the American Association of Neurological Surgeons.

Adam Ferguson PhD, assistant professor of neurological surgery, has been given a $300,000 award by the Craig H. Neilsen Foundation for his project "Visualizing Translational Spinal Cord Research." The Ferguson laboratory has also been awarded 140,000 € for the project "Datasharing and Bioinformatics for Previously Funded Projects," led by postdoctoral researcher **Jessica Neilsen PhD.**

Neurosurgery resident **Seunggu Han MD** was nominated for a Kaiser Award for Excellence in Teaching for teaching medical students in the UCSF Brain Mind Behavior Course. He also served as guest editor for two volumes of *Neurosurgery Clinics of North America* and on the Neurosurgery Perioperative Safety Video Committee.

Annette Molinaro PhD, associate professor of neurological surgery and epidemiology and biostatistics, has been granted an R01 award from the NIH for the project "Novel Tree-based Statistical Methods for Cancer Risk Prediction."

Claudia Petritsch PhD, assistant professor of neurological surgery, and Noemi Andor MSc, assistant specialist in the Petritsch laboratory, were awarded a core exploratory grant from the Research Allocation Program at UCSF for the project "Interrogation of the Glioblastoma Exome to Identify Genetic Causes for Cellular Heterogeneity and Therapy Resistance." Ms. Andor was also awarded a one-year fellowship from the German Academic Exchange Service for her project entitled "Functional Mutations in Recurrent Gliomas."

Neurosurgery resident **Nathan Rowland MD, PhD** was given the 2012 Allen Nakagawa Neurosurgery Resident Publications Fund award.

Philip Starr MD, PhD, professor and Dolores Cakebread Endowed Chair of Neurological Surgery, delivered the Hunt-Wilson Lecture on "The Amazing World of Functional Neurosurgery" at the 2012 Annual Meeting of the American Association of Neurological Surgeons.

Matthew Tate MD, PhD graduating chief resident, was the recipient of the 2012 William P. Van Wagenen Fellowship from the American Association of Neurological Surgeons. Dr. Tate began his fellowship on July 1, 2012 at the Department of Neurosurgery at the Institute of Neuroscience of Montepellier, France. Under the mentorship of Dr. Hugues Duffau, Dr. Tate plans to utilize direct cortical stimulation in awake human patients to both establish a standardized functional atlas of human brain function and to investigate the functional consequence of brain plasticity following injury.

residents' publications

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Tarapore PE, Mukherjee P, Mummaneni PV, Ames CP. The appearance of dural sealants under MR imaging. AJNR Am J Neuroradiol. 2012 Mar 29. [Epub ahead of print].

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selected recent publications from the department of neurological surgery

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