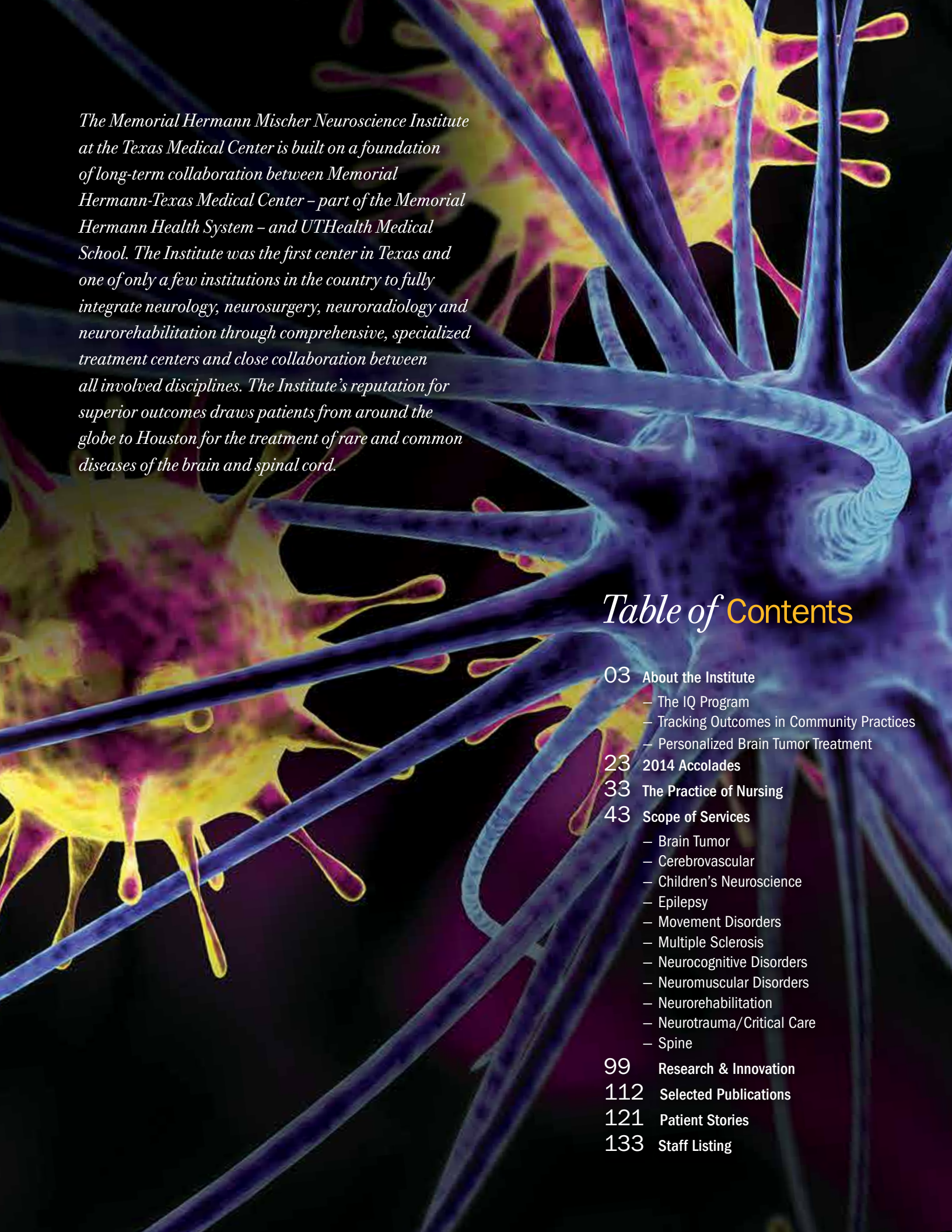


MISCHER NEUROSCIENCE INSTITUTE **REPORT 2014**



Mischer
Neuroscience Institute

MEMORIAL
HERMANN



The Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center is built on a foundation of long-term collaboration between Memorial Hermann-Texas Medical Center – part of the Memorial Hermann Health System – and UTHealth Medical School. The Institute was the first center in Texas and one of only a few institutions in the country to fully integrate neurology, neurosurgery, neuroradiology and neurorehabilitation through comprehensive, specialized treatment centers and close collaboration between all involved disciplines. The Institute’s reputation for superior outcomes draws patients from around the globe to Houston for the treatment of rare and common diseases of the brain and spinal cord.

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Dear Esteemed Colleagues,

At the Memorial Hermann Mischer Neuroscience Institute and UTHealth Medical School, affiliated physicians endeavor to take a multidisciplinary approach to neuroscience care and research. This involves clinicians of different specialties working together and ever-increasing efforts to integrate innovation with clinical management, and embrace and embed research processes into daily clinical practice.

In 2014, the neurosurgery program moved to the top 10 nationally in neurosurgery mortality rankings as measured by the University HealthSystem Consortium (UHC). In average length of stay, neurosurgery moved up to No. 6 nationally. Neurology also has climbed steadily in both categories to be among the top 20 percent nationally. To generate the UHC rankings, the consortium assesses quality and safety performance using an acuity-adjusted outcomes-based approach across six domains of care: mortality, effectiveness, safety, equity, patient centeredness and efficiency. UHC also takes into account Agency for Healthcare Research and Quality (AHRQ) patient safety measures, Joint Commission core measures and publicly reported patient satisfaction rankings from the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey. The data are provided by 122 participating hospitals and analyzed by UHC.

At the Brain Tumor Center, neurosurgeons, neuro-oncologists, neuroradiologists and radiation oncologists see patients together in clinic, rather than shuttling them from one specialist to another at a particularly difficult and stressful time for patients and their loved ones. Designed for patient convenience, this approach to practice also allows for quicker and better clinical decision-making with



input from two or three specialists. A similar approach is also in place at the Texas Comprehensive Epilepsy Program, where the team works together to treat more than 500 adults and children with seizure disorders annually.

The Telemedicine Program overcomes the distance barrier by extending stroke and neurology expertise far beyond the Institute's walls, helping emergency physicians in community hospitals throughout Southeast Texas make accurate diagnoses and save lives. Through remote presence technology, patients at 13 community hospitals benefit from neurology expertise, prompt diagnosis and a treatment plan based on the best available protocols, as well as opportunities to participate in clinical trials.

During the past year the Mischer Neuroscience Institute and UTHealth Medical School welcomed many new recruits. Neurosurgeons Baraa Al-Hafez, M.D., and George Al Shamy, M.D.; interventional pain management specialist Nadya Dhanani, M.D., and pediatric neurosurgeon Manish

DIRECTORS' LETTER

Shah, M.D., joined the team. Dr. Al-Hafez focuses on neurosurgery at Memorial Hermann Memorial City Medical Center, Memorial Hermann Katy Hospital and Memorial Hermann Sugar Land Hospital. Dr. Al Shamy is affiliated with Memorial Hermann The Woodlands Hospital. Dr. Dhanani is affiliated with the Memorial Hermann Spine Center at the Mischer Neuroscience Institute, and Dr. Shah is a member of the medical staff at Children's Memorial Hermann Hospital.

Neurologists Allison Boyle, M.D., and Stephen A. Thompson, M.D., FRCPC, have joined the UTHealth Medical School faculty as assistant professors. Dr. Boyle brings diagnostic, treatment and rehabilitative expertise in post-traumatic brain injuries and movement disorders to Memorial Hermann-Texas Medical Center and Memorial Hermann The Woodlands, joining the UT MOVE team in collaboration with the Halle Center. Dr. Thompson adds experience in epilepsy and special skills in stereoelectroencephalography to further the dynamic work of the Texas Comprehensive Epilepsy Program.

Neurology recruits joining Mischer Neuroscience Associates (MNA) are Fatima Ibrahim, M.D., at MNA North Houston and MNA The Woodlands; Priti Palvadi, M.D., and Robert Fayle, M.D., at Houston Neurological Institute; José Diaz, M.D., and Ankit Patel, M.D., at Katy Neurology; Courtney Preston, M.D., at Patient Centered Neurology; and neurohospitalist Shirish Satpute, M.D., who is affiliated with Memorial Hermann Southwest Hospital. Genetic counselor Krista Qualmann now provides adult neurogenetic counseling services.

We are pleased to share with you the Mischer Neuroscience Institute Clinical Achievements Report for fiscal year 2014, which highlights ongoing efforts in quality, safety, clinical care and research from July 2013 through June 2014. This year's report includes something new: a section that recognizes the accomplishments of our nurses, who take

an active role in leading improvement by driving quality initiatives. More than 175 registered nurses – and a total of 236 employees – have been recruited in the past three years to keep pace with the Institute's rapid expansion.

As physicians, seeing our patients do well is the main joy of our profession. As a team, we hold each other accountable for the quality of care we deliver, the experience of our patients and the outcomes we produce. Laboratory research and clinical studies are finding new treatments that do not exist today.

Last but not least, the education of future neuroscience providers is also a top priority, as we aggressively incorporate new concepts into our neurology and neurosurgery postgraduate educational programs.

We hope you find our 2014 report of interest. Please feel free to contact us directly if you would like additional information about our services and programs.

With best wishes,



A handwritten signature in black ink, appearing to read 'D. Kim'.

Dong H. Kim, M.D.
DIRECTOR, MEMORIAL HERMANN MISCHER NEUROSCIENCE
INSTITUTE AT THE TEXAS MEDICAL CENTER

PROFESSOR AND CHAIR, VIVIAN L. SMITH DEPARTMENT OF
NEUROSURGERY, UTHealth MEDICAL SCHOOL
713.500.6170



A handwritten signature in black ink, appearing to read 'Jerry Wolinsky'.

Jerry S. Wolinsky, M.D.
CO-DIRECTOR, MEMORIAL HERMANN MISCHER NEUROSCIENCE
INSTITUTE AT THE TEXAS MEDICAL CENTER

INTERIM CHAIR, DEPARTMENT OF NEUROLOGY, BARTELS FAMILY
AND OPAL C. RANKIN PROFESSOR OF NEUROLOGY
DIRECTOR, MULTIPLE SCLEROSIS RESEARCH GROUP AND
MRI ANALYSIS CENTER, UTHealth MEDICAL SCHOOL
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About the Institute

Innovation and quality, an impeccable patient safety record, the best outcomes, the highest patient and referring physician satisfaction – these are the goals of physicians affiliated with the Memorial Hermann Neuroscience Institute at the Texas Medical Center. They are attaining them daily through a holistic focus on the needs of patients and a relentless dedication to continuous improvement, a coordinated research effort and preparing the next generation of healthcare professionals to advance medicine.

The Mischer Neuroscience Institute is Houston's undisputed leader in neuroscience care. As the first stroke program in Texas and the only one in the region to meet The Joint Commission's rigorous standards for Comprehensive Stroke Center certification, and one of the few hospitals in the country recognized with the American Heart Association's



Get With The Guidelines®—Stroke Gold Plus Achievement Award, the Institute stands among an elite group of providers focused on complex stroke care. This same comprehensive, integrated approach has led to the creation of the Southwest's leading epilepsy program, a highly ranked neurotrauma program, a cerebrovascular center where affiliated physicians treat more aneurysms and arteriovenous malformations than any other center in the region, an established pediatric neurosurgery program in collaboration with The University of Texas MD Anderson Cancer Center, an unmatched spinal neurosurgery and reconstructive peripheral nerve surgery program and a Brain Tumor Center that diagnoses

and treats hundreds of new tumor patients each year. Affiliated physicians are proud of their innovations in the treatment of multiple sclerosis, movement disorders, neurocognitive disorders, neuromuscular diseases and traumatic brain injury.

To attain these achievements, Mischer Neuroscience Institute brings together a team of world-class clinicians, researchers and educators. A collaborative effort between Memorial Hermann-Texas Medical Center and UTHealth Medical School, the Institute is the foremost neuroscience provider in the southern half of Texas and one of only a few institutions in the country to provide the



full continuum of neuroscience care, from neurology and neurosurgery to neuroradiology and neurorehabilitation.

The Institute has extended that continuum of care across the city through the strategic expansion of Mischer Neuroscience Associates, a citywide network of neurologists and neurosurgeons, and reduced referral wait times by building a new structure for the practice of neurology in the community. Through its telemedicine program, the Institute offers patients in outlying communities access to stroke and neurology expertise and opportunities to participate in clinical trials. Thirteen community hospitals in Southeast Texas are now linked

to the Institute through remote presence robotic technology. In addition, affiliated physicians are reaching larger numbers of people and engaging them in a powerful way through new patient access portals on its website, neuro.memorialhermann.org, and social media events.

In the last seven years, the Institute has seen strong growth in consumer preference for neuroscience care at Memorial Hermann. During that time, affiliated physicians have reported mortality rates well below the national expected benchmark and seen a greater than 50 percent reduction in length of stay, despite the increased acuity of the patients they treat.

At a Glance

Physician Team

Staff Physicians	97
Clinical Residents and Fellows	39
Medical Students on Rotation	285
Research Fellows	30
Advanced Practice Providers	22

Inpatient Facilities

Total Neuro Beds	172
Neuro ICU Beds	38
Neuro IMU Beds	12
Neuro Acute Care Beds	74
Neuro Rehabilitation Beds	23
Stroke Unit Beds	12
Dedicated Operating Rooms	8
EMU Beds – Pediatrics	6
EMU Beds – Adult	7

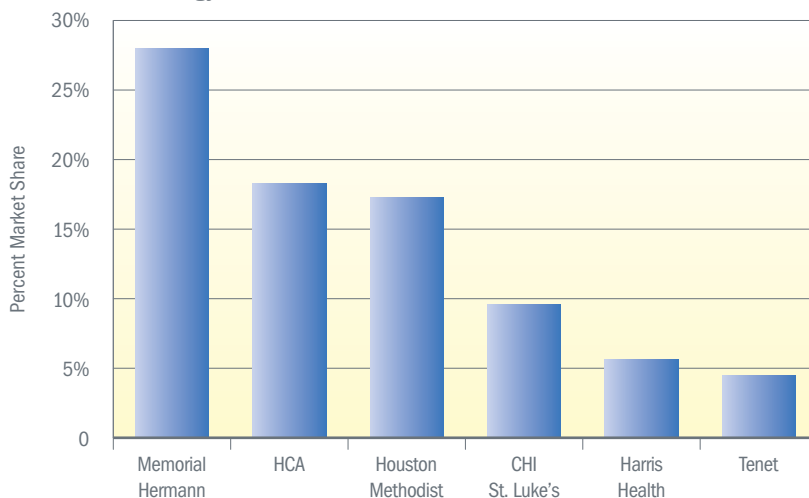
Research

Research Projects in Progress	More than 200
Grants Awarded	\$10.7 million (Neurology and Neurosurgery)

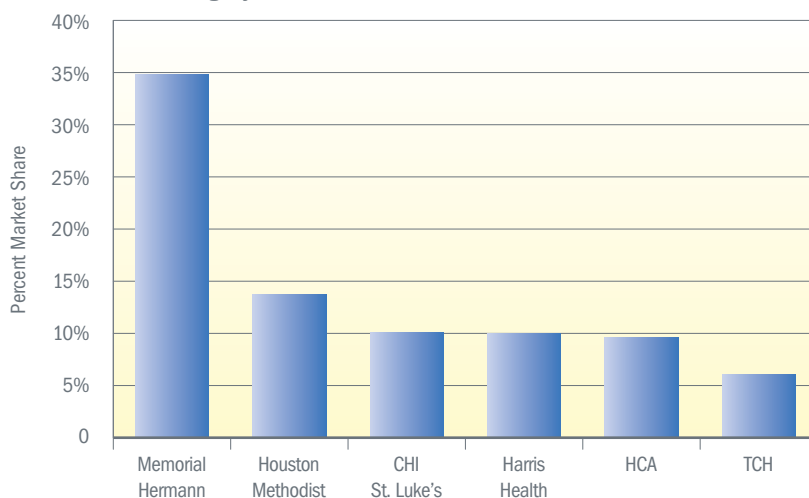
Specialty Equipment includes:

- Leksell Gamma Knife® Perfexion™
- Varian Trilogy Linear Accelerator
- Siemens Artis™ zee (intra-operative angiography suite)
- Robotic SEEG (ROSA)
- RP-7™ Remote Presence System
- 3D C-Arm
- Philips Healthcare endovascular temperature modulation system
- Simultaneous electroencephalography and polysomnography
- Continuous EEG monitoring
- Magnetoencephalography imaging (Magneis Elekta® Neuromag TRIUX)
- MRI capable of advanced spectroscopic and diffusion tensor imaging with tractotomy
- Portable CT machine

Neurology Market Share FY14



Neurosurgery Market Share FY14



Source: Texas Hospital Association Patient Data System (FY2012Q1 – FY2014Q4) provided by Truven Health, formerly Thomson Reuters. Texas Hospital Inpatient Discharge Public Use Data File, [FY2007 Q1– FY2014 Q1] provided by Texas Department of State Health Services, Center for Health Statistics; Q2FY2014 – Q4FY2014 discharges estimated by using historical data by hospital. Excludes Normal Newborns and SNF. Expanded Greater Houston consists of 12 counties: Austin, Brazoria, Chambers, Fort Bend, Galveston, Harris, Liberty, Montgomery, San Jacinto, Waller, Walker and Wharton.

The Patient Experience

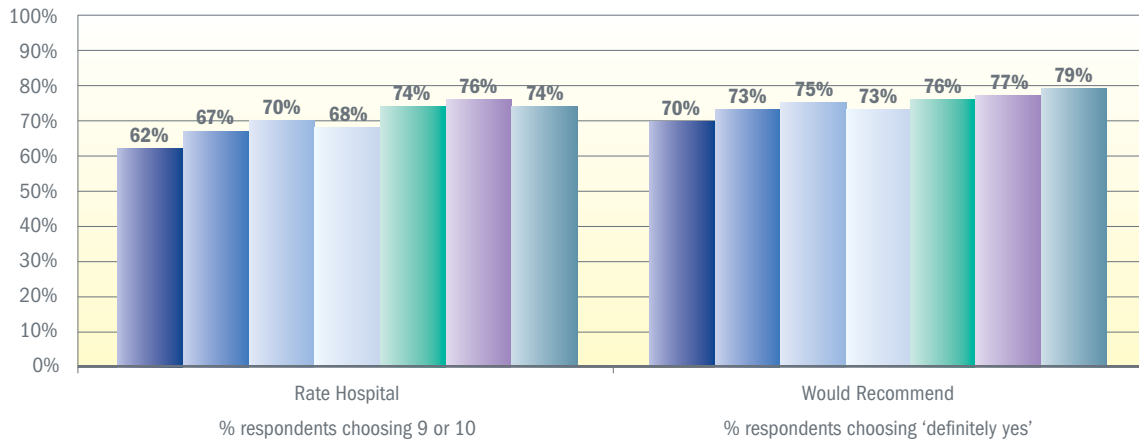
The Mischer Neuroscience Institute's reputation for high-quality outcomes and the best possible healthcare experiences draws patients from around the world. The close cooperation of affiliated physicians and an innovative administrative structure that allows nurses to spend more time coordinating patient care has led to an upward trend in patient satisfaction over the last seven years. Data gathered by the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey shows consistent improvement in domains considered critical to ensuring a high level of patient satisfaction.

HCAHPS Overall Assessment

Surveys Received FY08-14

Total Survey Respondents per Year:

FY08 = 237 FY09 = 436 FY10 = 609 FY11 = 830 FY12 = 795 FY13 = 671 FY14 = 792

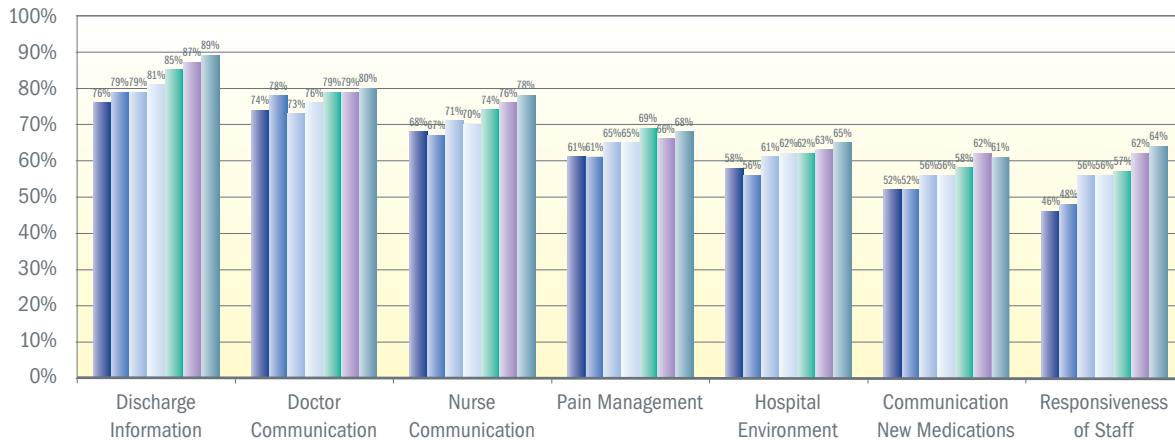


HCAHPS Domains of Care

Surveys Received FY08-14

Respondents choosing "always" or "yes"

FY08 FY09 FY10 FY11 FY12 FY13 FY14



Source: Press Ganey, national hospital survey vendor, for all surveys received from patients discharged from 5 Jones, 7 Jones/NSICU, NIMU, Stroke, Spine and EMU. HCAHPS scores have not been adjusted to account for a survey mode administration change.

A History of Firsts

- The first stroke center in Houston and one of the first dedicated stroke programs in the world.
- The first stroke program in Texas and the only one in the region to meet The Joint Commission's rigorous standards for the highly coveted Comprehensive Stroke Center certification.
- One of the few hospitals in the country recognized with the American Heart Association's Get With The Guidelines®—Stroke Gold Plus Achievement Award.
- Launched the first Mobile Stroke Unit in the United States to deliver clot-busting treatment onsite within the first hour of symptom onset.
- The first and only hospital in the south-central United States offering intra-arterial chemotherapy for retinoblastoma, the most modern treatment for the disease.
- Site of the first single-center clinical trial for recurrent medulloblastoma, ependymoma and atypical teratoid-rhabdoid tumors using the direct infusion of chemotherapy into the fourth ventricle.
- The first in Texas to use robotic stereoecephalography (SEEG) for 3-D mapping of epileptic seizures.
- The first in Houston to offer amyloid imaging, a new diagnostic tool that enables physicians to diagnose Alzheimer's disease and will give researchers insights into how they might one day prevent the disorder.
- The first center to conduct a national, multicenter trial for hypothermia in head injury.
- The first neurosurgery center to offer all advanced modalities of treatment – expert microsurgery, interventional neuroradiology/endovascular surgery and Gamma Knife® radiosurgery – for complex lesions.
- The North American leader in studies of primary progressive multiple sclerosis and the most active center in Texas in the conduct of organized clinical trials of new therapies for MS.
- The first facility in Houston and one of the first in the United States to test the clot-dissolving drug tPA for acute stroke.
- The first center in Houston to test and prove the efficacy of three disparate treatments for stroke prevention: carotid surgery; administration of antiplatelet drugs, including aspirin; and patent foramen ovale closure.
- The first facility in the region to do vagus nerve stimulation. The Institute remains the No. 1 program in the United States in the number of vagus nerve stimulators implanted in epilepsy patients.
- The Mischer Neuroscience Institute brought the first clinical magnetoencephalography (MEG) sensor to Houston and has updated the technology to the Elekta Neuromag® TRIUX.
- The Institute houses one of only a few adult and pediatric inpatient Epilepsy Monitoring Units in the country with the unique capability of simultaneously performing electroencephalography and polysomnography.
- TIRR Memorial Hermann is one of only 16 Traumatic Brain Injury (TBI) Model Systems funded by the National Institute on Disability and Rehabilitation Research. TBI Model Systems are national leaders in TBI-related care and research.
- TIRR Memorial Hermann is the only hospital in Houston – and one of only seven designated centers in the nation – in the Christopher and Dana Reeve Foundation NeuroRecovery Network.





The IQ Program: A Search for New Ways to Improve Quality and Expand Research

A new program at the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center is organizing data to improve physician and service performance, fostering innovative ways to measure quality and track long-term outcomes, and increasing infrastructure support to enable faculty to conduct a range of clinical trials and patient-centered research.

H. Kim, M.D., director of the Mischer Neuroscience Institute and professor and chair of the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School. “Physicians receive feedback about their performance using metrics they defined and data they validated. Because the data is credible to them, they respond to it quickly with ideas for improvement.”



The Innovation and Quality (IQ) Program uses data to help physicians improve their compliance with proven, evidence-based guidelines, and create new measures that will lead to better care and improved patient outcomes. “When providers receive detailed feedback about their performance, it helps them identify areas in which they can improve. The simple act of raising awareness can lead to rapid improvement,” says Dong

One goal of the IQ Program is the creation of datasets for neurosurgical conditions that will be used to monitor overall physician performance. “For instance, in cases of traumatic brain injury we monitor our performance by adding our own metrics to specific measures recommended by the National Institute of Neurological Disorders and Stroke,” says Georgene Hergenroeder, M.H.A., RN, CCRC, assistant professor of neurosurgery and IQ Program director. “Each of our patients will be assessed using standardized neurological outcomes measures at specified intervals so that we can determine how they are progressing compared to baseline and to group norms for their neurological condition. These metrics will also be incorporated into our clinical trials to determine if the study drug or device is having the desired impact.

“We measure our performance by our patients – their outcomes and their satisfaction. By analyzing the combined metrics, we can determine where we can improve our performance,” Hergenroeder says.



“For instance, American Diabetes Association Guidelines for critically ill patients and American Heart Association/American Stroke Association Guidelines recommend that patients’ blood glucose levels be maintained to avoid extremes. We are monitoring blood glucose levels by disease type as well as by provider. Physicians are notified routinely of the percentage of their patients and patient days that fell either inside or outside of the acceptable range.”

Physicians and nurses at the Mischer Neuroscience Institute have successfully tracked standard quality metrics for the past few years, says Miriam Morales, director of strategic analytics. Now, they’re looking at physician performance and interventions in meaningful ways that tie these and other metrics directly to outcomes.

“Dr. Kim has assembled a team of more than 30 physicians, researchers, quality improvement and IT specialists, biostatisticians, department chairs,

directors, research nurses, fellows and operations staff, and charged them with the creation of an infrastructure that will help us conduct innovative studies, promote our quality efforts and find innovative ways to improve quality,” Morales says. “By integrating all of our data, we can see in real time how patients

are doing on neuro-critical lab values such as oxygen saturation, intracranial pressure and potassium management. This takes us beyond the information available in the electronic health record for a look at individual physician performance.

“We are constantly asking questions and modifying our IQ tools,” Morales says. “The infrastructure we’re creating will track a range of outcomes – pain, neurological worsening, functionality,

cognition, quality of life and others – across various subsets of our patient population. We can track how well our doctors are adhering to a protocol. We can find better ways to track outcomes. Once we have the infrastructure in place, we’ll have access to a rich data source that includes long-term outcomes and enables us to identify the best interventions for a particular condition. We can then tie that data to decisions about future research, enabling us to positively impact patient outcomes throughout the timeline of patient care.”

Clinical research is crucial to optimizing care and providing patients with state-of-the-art treatment options. Physicians affiliated with the Mischer Neuroscience Institute are melding research and clinical practice. Patients are evaluated, and those who meet qualifying criteria are invited to participate in

“We measure our performance by our patients – their outcomes and their satisfaction. By analyzing the combined metrics, we can determine where we can improve our performance.”

– **Georgene Hergenroeder, M.H.A., RN, CCRC**



innovative research studies. In addition, neuroscience patients are offered the opportunity to participate in research by consenting to allow their tissue samples to be banked in the Neuroscience Research Repository (NRR) for current and future research. As an example, Dr. Kim and Teresa Santiago-Sim, Ph.D., have used the NRR to collect samples and detailed genetic data on intracranial aneurysm patients and their family members. Through this important effort, a gene mutation present in a subset of patients who develop intracranial aneurysms has been identified.

The gene mutation was evaluated in animal models to confirm its contribution to the disease process. The finding is clinically useful and is a guide for close monitoring of patients with a family history of aneurysm who have the mutation. Future study of this gene is expected to uncover underlying genetic mechanisms. Clinical trials, which test novel treatments to advance cures, are only available at select centers for patients who meet very specific study criteria. Prior to offering a study to patients, the study design and the test treatment undergo rigorous testing as well as scientific and ethical reviews of risk and benefits.

“Through clinical trials patients collaborate with us to improve the care of future patients as well as their own care,” Dr. Kim says. “The IQ program relies on experienced researchers testing novel treatments in clinical trials and transitioning the results of that research to clinical practice. The IQ staff will help faculty by providing administrative and regulatory support, with a 24/7 on-call system of clinical nurses to monitor and enroll patients into trials, and a team to provide statistical analyses.”

For example, a trial currently under way is based on what researchers have learned about brain



trauma from previous trials conducted at Memorial Hermann-Texas Medical Center, UTHealth Medical School and collaborating centers across the country. Clinician researchers cool patients with brain trauma-associated subdural hematoma prior to surgical evacuation of the blood clot. Preliminary studies indicated that cooled subdural hematoma patients had better cognitive function at six months after injury than patients treated with standard care at normal temperature. The new trial, offered at Memorial Hermann-TMC and a few other centers, will definitively determine if cooling subdural hematoma patients prior to clot evacuation improves outcome. If the treatment results in superior outcomes, it will be incorporated into standard care. As the IQ program expands, researchers will design new trials to help neuroscience patients reach their desired functional potential.

Tracking Outcomes in Community Practices: Mischer Neuroscience Associates Extends Accountability for Quality Across the City

Most people would agree that it's one thing to say you're the best, but something entirely different to prove it. That's exactly what leadership at the Memorial

Hermann Mischer Neuroscience Institute at the Texas Medical Center has been doing for the past five years by monitoring patient care, tracking outcomes and holding affiliated physicians and nurses accountable for the care they provide. At the same time, the Institute's arm in the community, Mischer Neuroscience Associates (MNA), is creating an innovative roadmap for tracking quality in its physician practices across the city.

"After many years of looking at quality metrics for our programs and physicians at the Texas Medical Center, we decided it was time to extend our performance improvement initiatives across the Memorial Hermann Health System," says Amanda Spielman, chief operating officer for neurosciences. "During that time we also built a neurology network to partner with our neurosurgeons in the community. Once we had a high-performance team with the full range of neuroscience providers in place, we wanted to know

if we were looking at the right benchmarks for quality, safety and performance improvement based on the types of cases done in the community. We asked ourselves,

how do you take a successful quality effort and move it from an academic medical center into the community? There's no roadmap in existence for an effort like that, so we set out to create one."

MNA neurosurgeon Paul D. Boone, M.D., practices at Memorial Hermann Memorial City Medical Center and has been very involved in the initiative to track quality outcomes in the community. "MNA is a collaborative effort between neurosurgeons, neurologists and pain management specialists who have made a commitment to excellence," says Dr. Boone, who served on the

faculty at Vanderbilt University Medical Center for eight years before relocating to Houston and joining Mischer Neuroscience Associates. "As part of that commitment, we needed to have a surveillance program in place that would allow us to look at quality data and track our outcomes. Our goal was to apply the same standards we use at the Texas Medical Center to our community



"Our goal was to apply the same standards we use at the Texas Medical Center to our community practices. Today, we're tracking mortality, surgical site infections, length of stay, patient satisfaction and other data as a group, and using it to modify our clinical practice to ensure that we deliver best-practices care."

- Paul D. Boone, M.D.





practices. Today, we're tracking mortality, surgical site infections, length of stay, patient satisfaction and other data as a group, and using it to modify our clinical practice to ensure that we deliver best-practices care."

Traditionally, community practices have been more focused on the business of medicine than academic medical centers – scheduling patients, filing insurance forms, reviewing test results and following up. "It's very unusual for community practices to engage in this kind of self-assessment," Dr. Boone says. "Physicians in the community run busy practices and in general don't track their quality metrics. With healthcare reform, government agencies and others are collecting data and making it available on the Internet. What we're trying to do is put more focus on the quality of medicine we deliver, not just the business. We all believe we're providing superior care, but if we rely on our own self-assessments, there may be surprises when we see the actual data. By proactively looking at our own data and continuously improving our practice, we stay ahead of the curve."

MNA practices are now holding regular Morbidity and Mortality (M&M) Conferences in which cases with complications or unexpected outcomes are reviewed. "This is just one example of moving initiatives typically done at academic medical centers to the community," he says. "M&M Conferences allow us to sit down as partners and have cases presented to us. If an outcome was unexpected, we look at it analytically and discuss what could have been done differently. In this way we identify small problems before they become larger and implement practices to prevent future occurrences."

As healthcare reform moves the focus of medicine toward keeping patients healthy, Dr. Boone expects the MNA quality and accountability effort to expand. "As demographics change and new technology emerges, health care is transforming before our eyes," he says. "As a group we're working hard to make sure we're not only prepared for those changes, but leading them."

Neuro-oncology Personalizes Brain Tumor Treatment and Extends Patient-specific Care Across Houston

The traditional goal of neuro-oncology has been to ensure that patients live as long as possible with enhanced quality of life. Physicians affiliated with the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center and UTHealth Medical School have added to that three broader goals: to maximize function through personalized brain tumor treatment, to help patients maintain meaningful life roles insofar as possible at every stage of treatment and recovery, and to provide collaborative care that brings multidisciplinary medical resources to patients at clinic locations across Houston.

“Personalized brain tumor treatment has been made possible by the capability to identify specific cancer genetic signatures, which allows neuro-oncologists to choose one chemotherapeutic drug over another, a dramatic change in the way we treat primary and metastatic brain tumors,” says fellowship-trained neuro-oncologist Sigmund Hsu, M.D., an assistant professor in the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School. “Before the discovery of these signatures, we made decisions about treatment based on the location of the tumor in the body and how it looked under the microscope during pathological examination. Advancements made through cancer research have allowed us to move away from the shotgun approach to treatment and moved us a step closer to finding the silver bullet.”

Dr. Hsu leads the new Mischer Neuroscience Institute Cancer Neurology Clinic for the treatment of patients

with neurological issues resulting from chemotherapy, and the Brain Metastases Clinic, whose staff of affiliated neuro-oncologists, neuroradiologists, neuropathologists, oncologists and neurosurgeons works closely with oncologists to provide personalized and innovative care to patients with brain tumors.

“Our goal with both clinics is to provide a much-needed niche service to the general oncologic community,” says Dr. Hsu, who provides consultation at Memorial Hermann-Texas Medical Center, Memorial Hermann Memorial City Medical Center and Memorial Hermann The Woodlands Hospital. “Cancer patients present with a complex mix of health issues. The problem itself may be easy to identify but the cause can be more difficult to determine. Is the problem with a breast cancer patient’s leg related to a herniated disk – completely unrelated to the breast cancer – or is it related to radiation or chemotherapy toxicity or to the malignancy itself? As a neurologist I can look at the big picture from a comprehensive perspective.”

With the addition of genetic counselor Krista Qualmann, M.S., the Mischer Neuroscience Institute now operates a Neurogenetics Clinic offering adult genetic counseling services based on an evaluation of personal and family medical history. Qualmann identifies genetic risk and explains inheritance patterns, provides education on the natural history of disease and discusses the risks, benefits and limitations of available genetic

testing options. She also makes recommendations for screening, treatment and management and provides supportive counseling.

The three new clinics extend the range of services for brain tumor patients begun in 2011 with the opening of the Institute's Pituitary and Vision Change Clinic, which brings together a diverse range of subspecialists to diagnose, evaluate and treat specific disorders. Led by Arthur L. Day, M.D., program director and director of clinical education in neurosurgery at the Mischer Neuroscience Institute and a professor and vice chair in the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School, the clinic uses the same integrative approach that has brought national acclaim to the Institute. Physicians at the clinic incorporate neurology, endocrinology, neuro-ophthalmology, stereotactic radiosurgery with Gamma Knife® technology, diagnostic radiology, interventional neuroradiology, radiation oncology and neuropathology for a comprehensive diagnosis and treatment plan. The team's combined expertise includes pituitary-region tumors, including non-secretory tumors, TSH-secreting tumors, growth hormone-secreting tumors (acromegaly), corticotrophin-secreting tumors (Cushing's disease), prolactin-secreting tumors, craniopharyngiomas, Rathke's cleft cysts and pituitary cysts. Parasellar tumors treated include meningiomas arising from the orbit or skull base near the pituitary gland and optic nerves, craniopharyngiomas, germ cell tumors, epidermoid cysts, gliomas and metastatic tumors.

Physicians affiliated with the Institute are also investigating ways to reduce cytotoxicity in the treatment of brain tumors. The ReACT trial is a significant step forward in using next-generation sequencing (NGS) for the treatment of GBM.



“Mutations that lead to epidermal growth factor receptor (EGFR) overexpression or overactivity have been associated with a number of cancers including GBM, in which a specific mutation called EGFRvIII is often observed,” says Dr. Hsu, whose clinical and research interests include the discovery of new and more effective therapies for patients with primary brain tumors, treatment of metastatic cancer to the brain and spinal fluid and the evaluation and treatment of neurological problems in cancer patients. “While we’ve used NGS and genetic-based treatment for brain metastases of melanoma, lung cancer and breast cancer, we’re still in the infancy of using genomics for primary brain tumors such as GBM.”

Last year, the Mischer Neuroscience Institute was chosen as a site for the FoundationOne™ Registry, to which physician researchers report data gathered using proprietary genomic profiling technology to expand patients' treatment options. FoundationOne's next-generation sequencing interrogates the entire coding sequence of 236 cancer-related genes plus 47 introns from 19 genes that are often rearranged or altered in solid tumor cancers. By identifying mutations in these genes, the technology gives physicians more information about which unique tumor types are more likely to respond to certain chemotherapeutic drugs or may be a good match for a clinical trial.

Dr. Hsu was recruited to the Institute by fellowship-trained neurologist and neuro-oncologist Jay-Jiguang Zhu, M.D., Ph.D., who is director of the Clinical Cancer Program and an associate professor in the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School. "Thanks to next-generation sequencing, we understand more about the underlying DNA mutations that drive cancer growth, which has allowed us to adapt treatment to the specific genetics of the tumor," says Dr. Zhu, who focuses his practice on primary brain tumors and primary central nervous system (CNS) lymphomas as well as brain metastases and leptomeningeal spread of systemic malignancies. "As we learn more, we're replacing traditional cytotoxic treatments with less toxic, potentially more effective therapies that target changes in a patient's unique DNA that promote the survival of cancer cells. These breakthrough approaches to treatment with more clinical trials available at MNI have allowed us to



"Developing biological agents with improved efficacy and reduced toxicity is only half the battle. Every patient we treat deserves the opportunity to continue to live life in meaningful ways."
- Jay-Jiguang Zhu, M.D., Ph.D.

increase our volumes by nearly 50 percent since 2009."

Dr. Zhu is principal investigator of three clinical trials that give eligible study participants access to new and advanced treatments. The first is a Phase III multicenter, randomized, controlled trial designed to test the efficacy and safety of an experimental, portable, battery-

operated medical device called the NovoTTF-100A for newly diagnosed GBM patients in combination with temozolomide, compared to temozolomide alone. The device, which patients wear on their scalp, provides a constant, safe, low-voltage electric field that has been shown to reduce tumor cell survival and division capacity.

Dr. Zhu is also principal investigator of a randomized, double-blind, controlled Phase IIB clinical trial testing the efficacy of the vaccine

ICT-107 for newly diagnosed GBM patients following resection and chemoradiation. ICT-107 is an autologous vaccine consisting of dendritic cells from the patient's own immune system, which are isolated from blood by apheresis and pulsed with synthetic peptides from six GBM-specific stem cell-associated antigens - MAGE-1, HER2, AIM2, TRIP-2, GP100 and interleukin 13 receptor alpha. The sensitized dendritic cells are then returned to the patient by subcutaneous injection as an immunotherapy to attack the tumor.

The third trial, an open-label Phase I/II (Safety Lead-in) study of trans sodium crocetinate (TSC) with concomitant radiation therapy and temozolomide in newly diagnosed GBM, examines the safety and efficacy of the radiation sensitizing effect of TSC in combination with fractionated radiation.



Dr. Zhu works with the Institute's Cancer Research Program as part of a new Brain Tumor Research Program. "Our objective is to gain understanding of the molecular changes in patient tumor specimens," Dr. Zhu says. "Understanding those changes will give us prognostic factors that enable us to determine which patients will respond well to a given drug or treatment with multiple drugs. Some genes have already been identified, and we're looking for others with prognostic value. Knowledge of the molecular changes that take place in cancer cells will help us define treatment targets for specific patients, and aid in choosing chemotherapies or specific molecular-based treatments. Our ultimate goal is to provide personalized cancer care, maximize efficacy and minimize toxicity for each patient."

In the pediatric arena, the promising results of translational studies conducted by David Sandberg, M.D., FAANS, FACS, FAAP, director of pediatric neurosurgery at Children's Memorial Hermann Hospital in the Texas Medical Center, have demonstrated the safety of infusing chemotherapeutic agents directly into the fourth ventricle of the brain. These studies led to a pilot clinical trial, available only at Children's Memorial Hermann Hospital and The University of Texas MD Anderson Cancer Center, for children with recurrent tumors in this area of the brain. This radically new approach to chemotherapy allows Dr. Sandberg and team members to circumvent the blood-brain barrier and deliver agents directly to the site of disease, minimizing side effects by decreasing systemic drug exposure.

“The collaboration with MD Anderson is good news for children and adolescents with brain tumors,” says Dr. Sandberg, who holds joint appointments as associate professor in the Vivian L. Smith Department of Neurosurgery and the department of Pediatric Neurosurgery at UTHealth Medical School, and is also an associate professor in the department of Neurosurgery at MD Anderson Cancer Center. “Using novel approaches to surgery and chemotherapy, we have the potential to minimize side effects from treatment and achieve better long-term survival rates.”

In addition to the single-center clinical trial for recurrent medulloblastoma, ependymoma and atypical teratoid-rhabdoid tumors using direct infusion of chemotherapy into the fourth ventricle, other novel approaches are being investigated by the combined research team, including administration of natural killer cells into the fourth ventricle to attack tumor cells via cell-directed therapy.

As the Institute continues the expansion of services across the city, neuro-oncology services once available only at Memorial Hermann-Texas Medical Center, Memorial Hermann Memorial City Medical Center and Memorial Hermann The Woodlands Hospital are now provided at Memorial Hermann Southwest Hospital and TIRR Memorial Hermann. “The Mischer Neuroscience Institute’s infrastructure expansion and Memorial Hermann’s presence across Houston have allowed for the extension of neuro-oncology expertise and capabilities outside the Texas Medical Center,” says Dr. Zhu, who also consults on patients with brain tumors at TIRR Memorial Hermann, the top rehabilitation hospital in the southern half of the United States.

In 2013, TIRR Memorial Hermann extended its cancer rehabilitation programs throughout the Greater Houston community and added survivorship wellness programs at key locations. “Many people return to normal life after cancer treatment but a growing number, as a result of their diagnoses, are learning to cope with a decline in function related either to the disease or to the effects of chemotherapy and radiation therapy, which have complications of their own,” says Jacob Joseph, M.D., clinical chief of Specialty Rehabilitation Programs at TIRR Memorial Hermann and an assistant professor of physical medicine and rehabilitation at UTHealth Medical School. “We see a lot of people who are excited to be alive after their cancer treatment, but then they discover they’re living with issues that affect their quality of life. These patients have led us to collaborate with the Mischer Neuroscience Institute and make a concerted effort to address survivorship issues in greater depth.”

Dr. Zhu considers the collaboration with TIRR Memorial Hermann an important part of the comprehensive continuum of care offered by physicians affiliated with the Institute. “Developing biological agents with improved efficacy and reduced toxicity is only half the battle,” he says. “Every patient we treat deserves the opportunity to continue to live life in meaningful ways.”







The Mischer Neuroscience Institute Moves to the Top 10 Nationally in Neurosurgery Mortality Rankings

The University HealthSystem Consortium (UHC) has ranked the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center and UTHealth Medical School’s neurosurgery program among the top 10 in the nation in mortality. In average length of stay, neurosurgery moved up to No. 6 nationally.

UHC represents and ranks the top academic medical centers in the nation, fostering collaboration among its 120 medical centers and 300 affiliated member hospitals, and helping them achieve excellence in quality, safety and cost effectiveness. To generate the listing, the consortium assesses quality and safety performance using an acuity-adjusted outcomes-based approach across six domains of care: mortality, effectiveness, safety, equity, patient centeredness and efficiency.

The organization also takes into account Agency for Healthcare Research and Quality (AHRQ) patient safety measures, Joint Commission core measures and publicly reported patient satisfaction rankings from the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey.

“Competition continues to grow among academic medical centers, and hospitals across the country are successfully raising the bar in terms of quality and patient safety,” says Amanda Spielman, chief operating officer for neurosciences at Memorial Hermann Health System.

The success of the Mischer Neuroscience Institute and Memorial Hermann-Texas Medical Center, which was once again ranked among the 25 top-performing academic medical centers in the nation, is driven by affiliated physicians and a strong collaboration between the hospital and UTHealth Medical School. “The Mischer



Neuroscience Institute and UTHealth have collaborated to develop a culture of patient safety, which has resulted in significantly improved outcomes,” says Dong H. Kim, M.D., director of the Institute and professor and chair of the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School. “Five years ago the Institute was ranked 110th in mortality among neurosurgery programs at academic medical centers. We’re proud of the gains we’ve made in neurosurgery and hope to improve further going forward.”

Memorial Hermann and UTHealth Unveil the Nation’s First Mobile Stroke Unit

A team at Memorial Hermann-Texas Medical Center and UTHealth Medical School has unveiled the country’s first Mobile Stroke Unit, made possible by a consortium of partners from the Texas Medical Center, the Houston Fire Department and generous donors. The mobile unit is equipped with a CT scanner that allows the onboard team of a doctor, nurse, CT technician and paramedic to quickly assess whether a patient is having an ischemic stroke, allowing for the administration of the clot-busting drug tPA. “It requires a CT scan to make this determination, but with current practice it takes more than an hour once a stroke patient is brought to the emergency room to have the test and receive treatment. So if we can put the emergency room in the ambulance and take the CT scanner to the patient, we can treat the patient at the scene and save over an hour,” says neurologist James C. Grotta, M.D., who is principal investigator of a trial that will measure cost savings and outcomes. “That hour could mean saving 120 million brain cells.”

Shortly after observing a similar mobile stroke unit in Germany, Dr. Grotta had the opportunity to present his idea to UTHealth Development Board members. He was surprised when a couple approached him and offered to

donate a used ambulance. That couple, John and Janice Griffin, are owners of Frazer Ltd., a third-generation, family-run Houston company that builds emergency vehicles. After looking at the needs of a mobile stroke unit, the Frazer team felt it would need to be engineered from the ground up.



“We really liked the possibilities of moving medicine forward,” says Laura Griffin Richardson, CEO and president of Frazer. “Our company likes to push the limits and this has never been done before. We’re excited to be located in Houston, the forefront of the medical community. Once everyone sees the possibility of putting a CT scanner in an emergency vehicle, the question is: what else can we do?”

Local businesses also generously supported the stroke unit, giving \$1.1 million to UTHealth Medical School and the Memorial Hermann Foundation. Operated in conjunction with the Houston Fire Department, Bellaire Fire Department and West University Fire Department, the mobile unit responds to calls within a 5-mile radius, transporting patients to stroke centers including Memorial Hermann-TMC, Houston Methodist Hospital and St. Luke’s Medical Center.

“We know we can speed up treatment, but we don’t know how much that speed will affect recovery,” Dr. Grotta says. “We really don’t have data on how receiving tPA within an hour to 80 minutes affects patient outcomes, including the amount of disability. This study will help us determine how much more helpful receiving tPA so early is. However, it depends entirely on the stroke victims, family and bystanders calling 911 immediately if stroke symptoms are suspected. For now, the Mobile Stroke Unit depends on the onboard expertise of Dr. Grotta to determine if the patient is having a stroke and may benefit from treatment. The clinical trial includes determining if telemedicine connectivity to the ambulance, which physicians across the state use to consult stroke experts affiliated with the Mischer Neuroscience Institute at the Texas Medical Center and UTHealth Medical School, can be applied to the Mobile Stroke Unit. If so, in the future the unit potentially could respond to calls using telemedicine, increasing cost effectiveness.

Co-investigators of the clinical trial are Elizabeth Noser, M.D., clinical assistant professor; Tzu-Ching “Teddy” Wu, M.D., medical director of the Mischer Neuroscience Institute Telemedicine Program; Mary Sarah Baraniuk, Ph.D., assistant professor in the School of Public Health; Suja Rajan, Ph.D., assistant professor in the School of Public Health; and Barbara Tilley, Ph.D., Lorne Bain Distinguished Professor in Public Health and Medicine and director of the division of Biostatistics at UTHealth Medical School.

The Mobile Stroke Unit was completed in early February 2014, and the first patients were treated in May. The study, which will require three to five years to complete, began on July 1, 2014.

Fifteen Physicians Named Among Houston’s Top Doctors for 2014

Fifteen physicians affiliated with the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center and UTHealth Medical School have been named to Houstonia magazine’s 2014 listing of Top Doctors in Houston. They include neurosurgeons Dong H. Kim, M.D., Peng Roc Chen, M.D., Arthur Day, M.D., Albert Fenoy, M.D., Joseph Hsieh, M.D., Daniel H. Kim, M.D., David I. Sandberg, M.D., and Nitin Tandon, M.D. Neurologists named to the list are Suur Biliciler, M.D., Giridhar Kalamangalam, M.D., Sean I. Savitz, M.D., Mya Schiess, M.D., Paul Schulz, M.D., Jeremy Slater, M.D., and Jerry Wolinsky, M.D. Physicians named to the 2014 list were selected based on nominations solicited from nearly 16,000 medical professionals practicing in eight counties in the Greater Houston area.

Dr. Dong Kim is director of Mischer Neuroscience Institute and professor and chair of the Vivian L. Smith Department of Neurosurgery at UTHealth Medical



School. As director of the Institute, he leads the clinical neuroscience efforts for the Memorial Hermann Health System as well as UTHealth Medical School. Dr. Kim is noted for his experience with brain tumors and cysts of all types, and also leads ongoing investigations into the origin, development and treatment of brain aneurysms, genetic changes in brain tumors and the use of stem cells to treat spinal cord injuries.

Dr. Roc Chen is an assistant professor of neurosurgery at UTHealth Medical School. Prior to joining the medical school and Mischer Neuroscience Institute, he was an assistant professor of neurosurgery, director of the Cerebrovascular and Neuroendovascular Program and director of the Skull Base Program at Baylor College of Medicine. Dr. Chen specializes in carotid and vertebral occlusive diseases; intracranial aneurysms and subarachnoid hemorrhages; intracranial occlusive diseases that require endarterectomy, bypass or stenting; brain arteriovenous malformations; and brainstem and cerebral cavernous malformations.

Dr. Art Day specializes in cerebrovascular and skull base neurosurgery and in microsurgical treatments of brain tumors and minimally invasive spinal surgery. A professor of neurosurgery and vice chair and director of clinical education in the Vivian L. Smith Department of Neurosurgery, Dr. Day practiced at the University of Florida for 25 years, ultimately rising to the positions of professor, co-chair and program director of the department of Neurosurgery. In 2002, prior to joining Mischer Neuroscience Institute, he moved to Boston as a professor of surgery at Harvard Medical School with a clinical practice at Brigham and Women's Hospital. He is past president of the Society of Neurological Surgeons and has held leadership positions in many other medical professional societies, and has received numerous awards and honors.

Dr. Albert Fenoy specializes in surgery for neck and back pain using minimally invasive techniques as well as complex instrumentation. He also specializes in cranial neurosurgery and deep brain stimulation for movement disorders such as Parkinson's disease and essential tremor. His research has focused on the electrophysiology and clinical manifestations of basal ganglia disease and electrophysiology of the human auditory cortex, as well as craniocervical junction abnormalities. He is an assistant professor of neurosurgery at UTHealth Medical School.

A graduate of Harvard Medical School, Dr. Joseph Hsieh holds both an M.B.A. and an M.P.H. from The Anderson School of Management and the School of Public Health at the University of California, Los Angeles. He specializes in complex spinal reconstruction as well as minimally invasive approaches to the treatment of deformity, fracture, myelopathy, spinal arteriovenous malformations, spondylolisthesis, disc herniation, spinal stenosis and spondylosis. He has presented his work on policy in neurosurgery and spine both nationally and internationally, and continues research on quality initiated during time he spent in Washington, D.C., as the Plante Policy fellow for the Congress of Neurological Surgeons.

Daniel H. Kim, M.D., FAANS, FACS, is director of reconstructive and peripheral nerve surgery at the Institute and professor of neurosurgery at UTHealth Medical School. An expert in minimally invasive spinal surgery – both endoscopic and robotic – peripheral nerve surgery and complex spinal reconstruction, Dr. Kim has won numerous awards and honors, authored hundreds of papers published in peer-reviewed journals and is the author of 17 surgical textbooks. He is a preeminent researcher in peripheral nerve repair through nerve transfer and nerve graft, and is also recognized for his work in neurorehabilitation through robotics and cortical stimulation, spinal biomechanics and innovative neuromodulation treatments for chronic pain.

David Sandberg, M.D., FAANS, FACS, FAAP, holds joint appointments as an associate professor in the departments of Neurosurgery and Pediatric Surgery at UTHealth Medical School, and is co-director of the combined pediatric brain tumor program based at The University of Texas MD Anderson Cancer Center and Children's Memorial Hermann Hospital. Dr. Sandberg's major clinical interests include pediatric brain tumors, minimally invasive endoscopic approaches to brain tumors and hydrocephalus, congenital spinal anomalies, vascular malformations of the brain, spasticity and craniofacial disorders in children. His research interests focus on novel means of delivering therapeutic agents into the brain for the treatment of childhood brain tumors, and he is principal investigator of a clinical trial investigating, for the first time in humans, chemotherapy administration into the fourth ventricle of the brain. Dr. Sandberg is a member of the board of directors of the Foundation for International Education in Neurological Surgery.

Dr. Nitin Tandon is an associate professor in the Vivian L. Smith Department of Neurosurgery. His clinical interests focus on epilepsy surgery, including placement of subdural grid electrodes, amygdalo-hippocampectomy, anterior temporal lobectomy and neo-cortical resections; brain mapping and awake craniotomies; brain tumor surgery, including tumors in speech and motor cortex, insular tumors, intra-ventricular tumors, pineal tumors, pituitary and parasellar tumors; cavernous malformation surgery; and microvascular decompression for trigeminal neuralgia. Dr. Tandon's research interests include brain mapping with functional MRI, electrical stimulation and diffusion tractography, and intracranial electrophysiology. His research has been published widely in peer-reviewed journals.

Dr. Suur Biliciler is an assistant professor in the department of Neurology at UTHealth Medical School. Her clinical interests include nerve and muscle biopsies,



as well as the diagnosis, treatment and management of all types of neuromuscular disorders. Her research focuses on muscular dystrophies and myopathies.

Giridhar Kalamangalam, M.D., D.Phil., specializes in epilepsy clinical neurophysiology. An associate professor of neurology at UTHealth Medical School, he has a special interest in diagnosis of paroxysmal disorders and management of refractory epilepsy, including pre-surgical evaluation.

Dr. Sean Savitz, a professor of neurology, holds the Frank M. Yatsu Chair in Neurology and is director of the Vascular Neurology Program and Fellowship at UTHealth Medical School. He is director of the Stroke Program at Mischer Neuroscience Institute and has a special interest in the use of stem cell therapy for stroke.

Dr. Mya Schiess is director of UT MOVE, a collaborative effort of Mischer Neuroscience Institute and UTHealth Medical School, with specialty clinics that include Spasticity Management, DBS Selection and Programming, Botox® and Intrathecal Baclofen Pump Therapy. She is a professor of neurology with clinical interests in the medical and surgical management of Parkinson's disease and Parkinsonian syndromes, tremor states, dystonia, ataxia and other neurodegenerative diseases.

Dr. Paul Schulz is professor and vice chair of the department of Neurology, and director of the Memory Disorders and Dementia Clinic at UTHealth Medical School. In 2010, he moved from Baylor College of Medicine to Mischer Neuroscience Institute, where he sees patients who have cognitive, behavioral or mood disorders. His group is investigating environmental and genetic risk factors for dementia in order to understand why it develops.

Dr. Jeremy Slater is director of the Texas Comprehensive Epilepsy Program and medical director of the Epilepsy Monitoring Unit at Memorial Hermann-

Texas Medical Center, where he is also medical director of neurophysiology. An associate professor in the department of Neurology, Dr. Slater holds clinical interests in adult epilepsy and sleep disorders.

Dr. Jerry Wolinsky is co-director of Mischer Neuroscience Institute and interim chair of the department of Neurology at UTHealth Medical School, where he is also on the faculty of the Graduate School of Biomedical Sciences. He also serves as director of the Multiple Sclerosis Research Group and the Magnetic Resonance Imaging Analysis Center at UTHealth. He is recognized among The Best Doctors in America and America's Top Doctors, and has authored more than 300 publications.

The Mischer Neuroscience Institute Named a Willis-Ekbom Disease Foundation Quality Care Center

The Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center was recently named a Willis-Ekbom Disease (WED) Foundation Quality Care Center - the third neuroscience program in the country to receive the prestigious designation. The WED Foundation, formerly known as the Restless Legs Syndrome (RLS) Foundation, launched the program in 2013 to improve diagnosis and treatment for individuals living with Willis-Ekbom disease.

Willis-Ekbom Foundation Quality Care Centers are recognized leaders in providing comprehensive care for the WED/RLS community and serve as liaisons to patients' primary care providers. Institutions granted the three-year certification are selected because they adhere to the WED Foundation's high standards of care, track and report patient outcomes and share findings through presentations at professional meetings and publications.

"We're honored to be named a Willis-Ekbom Disease Foundation Quality Care Center, and look forward to

helping advance understanding of this common disease to improve patient outcomes,” says William Ondo, M.D., professor of neurology at UTHealth Medical School. Dr. Ondo, a diplomate of the American Board of Psychiatry and Neurology who is also certified by the American Board of Sleep Medicine, has clinical interests that include Parkinson’s disease, generalized and focal dystonias, tremor, Huntington’s chorea and other choreas, ataxic disorders, and drug-induced movement abnormalities and gait disorders.

Arthur Day, M.D., Honored by Neurosurgical Association



Arthur L. Day, M.D., professor of neurosurgery at UTHealth Medical School and a neurosurgeon affiliated with the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center, has received one

of the top honors awarded by the Congress of Neurological Surgeons.

At the association’s annual meeting in San Francisco Oct. 19-23, 2013, Dr. Day was presented the Founders’ Laurel Award in recognition of his exceptional service, lifelong dedication and meritorious accomplishments in the field of medical education.

Dr. Day is recognized internationally for his expertise in cerebrovascular and skull base neurosurgery and directs the neurosurgery residency training program at UTHealth Medical School. He is a past president of the association, which is dedicated to advancing neurosurgery by providing members with educational and career development opportunities. He has also served as chair of the American Board of Neurological Surgery and recently concluded his presidency of the Society of Neurological Surgeons.

Dr. Day received his medical degree from Louisiana University School of Medicine in New Orleans and completed a neurosurgery residency and a brain tumor immunology/neuropathology fellowship at the University of Florida at Gainesville.

Dr. Day leads the Pituitary Tumor and Vision Change Clinic at the Institute.

Nneka Ifejika, M.D., Selected for AAPMR Academy Leadership Program



Nneka Ifejika, M.D., assistant professor in the department of Neurology at UTHealth Medical School, was selected for the inaugural class of the American Academy of Physical Medicine and Rehabilitation (AAPMR)

Academy Leadership Program.

Dr. Ifejika-Jones is one of only 10 academy members selected from a national pool to participate in the two-year program, which is designed to identify and train early-career physical medicine and rehabilitation physicians to assume future leadership positions. A member of the Memorial Hermann Stroke Center at the Mischer Neuroscience Institute, she has served as director of the Institute’s Neurorehabilitation Program since 2007.

Dr. Ifejika received her medical degree and master’s in public health, with honors, at the University of North Carolina in Chapel Hill. She completed her residency in physical medicine and rehabilitation at Baylor College of Medicine in Houston and is certified by the American Board of Physical Medical and Rehabilitation.

As director of neurorehabilitation, Dr. Ifejika has established a research program in stroke outcomes and health disparities. In 2010, she received a grant from

the National Institute of Neurological Disorders and Stroke (NINDS) to study the impact of intravenous thrombolysis and healthcare-associated infections on rehabilitation care. Within a two-year period, she published five articles as first author in peer-reviewed journals and received the AAPMR's Best Neurological Rehabilitation Research Award.

Dr. Ifejika's primary focus is to advance the field of neurorehabilitation through clinical research that addresses age- and ethnicity-related disparities in stroke care, from acute onset of symptoms through the post-stroke continuum. Her work focuses on the disability gap between minorities and non-minorities in stroke outcomes. She subspecializes in stroke and multiple sclerosis rehabilitation and has received training in measurements of disease severity and disability in both conditions. Her interests include treatment of neurologic disease-related complications, including musculoskeletal, behavioral, spasticity and gait abnormalities.

Karl Schmitt, M.D., and Scott Shepard, M.D., Named TIRR Memorial Hermann Consultants of the Year



Neurosurgeons Karl Schmitt, M.D., and Scott Shepard, M.D., were selected as Consultants of the Year, an annual recognition granted by TIRR Memorial Hermann. In keeping with the rehabilitation hospital's tradition, the

Consultant of the Year award recognizes and celebrates outstanding healthcare providers who embody TIRR Memorial Hermann's model of patient-centric care.

"Our consultants contribute daily to our successes as the healthcare provider of choice for rehabilitation in our community," says Gerard E. Francisco, M.D., chief medical officer at TIRR Memorial Hermann and professor and chair of the department of Physical Medicine and

Rehabilitation at UTHealth Medical School. "Dr. Schmitt and Dr. Shepard provide outstanding service to our patients and families through a neurosurgery clinic at TIRR Memorial Hermann that brings surgical care to our patients. The clinic is part of our medical home model, a rarity among freestanding rehabilitation hospitals."

Dr. Schmitt, who is certified by the American Board of Neurological Surgery, specializes in complex spinal surgery, minimally invasive spine surgery, spinal cord and spinal column tumors, spinal and cranial trauma and general neurosurgery. He received his medical degree and completed his neurosurgery residency at The University of Texas Medical Branch at Galveston, followed by the Yale Comprehensive Spinal Fellowship at Yale University Medical School in New Haven, Connecticut. Dr. Schmitt is an assistant professor in the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School.

A board-certified neurosurgeon with expertise in brain and spinal cord tumors as well as spinal and pituitary surgery, Dr. Shepard is an assistant professor in the Vivian L. Smith Department of Neurosurgery. He received his medical degree at Weill Cornell Medical College in New York City, where he received several prestigious honors recognizing his outstanding scholastic performance. He completed his residency at the University of California, San Francisco, where he served as chief resident in neurosurgery. He was also a research fellow at CNS Injury and Edema Center and Brain Tumor Research Center at the University of California, San Francisco, and he completed a fellowship in surgical neuro-oncology at Memorial Sloan Kettering Hospital in New York City. Prior to joining the Mischer Neuroscience Institute, Dr. Shepard was on the faculty at Robert Wood Johnson Medical School in New Brunswick, N.J., where he served as an assistant professor of neurosurgery.

TIRR Memorial Hermann Consultants of the Year are nominated by TIRR Memorial Hermann attending physicians and selected by the hospital's Medical Executive Committee.





The Practice of Nursing

Building a Self-driven Quality Process Through Transparency, Education and Support

Empowering nurses at the bedside to implement quality initiatives has led to dramatic improvements in quality metrics across the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center, particularly in the Neuroscience Intensive Care Unit where patients are most at risk.

“We set a goal of reducing our catheter-associated urinary tract infection (CAUTI) rate by 25 percent during fiscal year 2014,” says Allison Murphy, RN, B.S.N., CNRN, quality improvement coordinator in the Neuroscience ICU (NSICU). “A literature review showed that the two populations at highest risk for CAUTIs are neuroscience and burn patients, but there’s not much data specific to the prevention of CAUTIs in neuro patients. Basically, there’s one way to lower the CAUTI rate – if the patient doesn’t need the Foley catheter, it should come out.”

As part of a multidisciplinary quality initiative, rounds were instituted twice a day – including an attending physician, quality improvement nurse, infection prevention, nurse manager and the bedside nurse. The goal was to remove invasive lines from patients as soon as they became unnecessary. To raise awareness, nurses involved in the care of a patient who developed a CAUTI were asked to submit a short overview of their thoughts on the care of the patient and what the nursing staff could have done to prevent the infection.

At the same time, nurses began meticulous screening of patients for urinary tract infections during the first two calendar days after admission, as recommended by the Centers for Disease Control and Prevention, which resulted in the discovery over a three-month period of more than 40 patients out of 470 who were admitted with a UTI.

“By making this a joint effort between nursing and physicians, we exceeded our 25 percent goal during fiscal year 2014,” Murphy says. “By looking at catheter necessity twice a day, we discovered that many of them weren’t needed. In the NSICU, nurses now have the permission of the medical director to make the decision to remove a Foley catheter if the patient does not meet the guidelines describing the need for the catheter. Over the past fiscal year, we’ve reduced our CAUTI rates in the NSICU by 35 percent.”

One factor leading to the success of this initiative and others was a move to improve nurse performance through metrics transparency. Murphy developed a dashboard, which is posted monthly, showing the individual nurses’ names and their performance metrics.

“The culture here is to own the work you do and be proud of it,” she says. “I love working in a unit like that. We allow nurses to do exceptional work without interference and applaud the ones who do. For nurses who need to improve their metrics in specific areas, we’re here to



provide education, coaching and support. Nurses know exactly where they stand from month to month so there are no surprises. It's a very self-driven quality process."

Transparency, awareness and education have led to a 58 percent reduction in mislabeled specimens, a 42 percent reduction in blood culture contamination, a 75 percent reduction in falls and a 35 percent reduction in CAUTIs during the past fiscal year. "The improvements we've made in quality in the Neuroscience ICU are not just because of one or two people, but because of the work everyone on the unit has done," Murphy says. "The dashboards are great in showing where each individual nurse stands. We give them the tools, and they run with it. That sense of engagement and empowerment has made a huge difference."

Leadership at the Mischer Neuroscience Institute helps nurses improve quality in other ways. "We encourage and support nurses in getting certifications," says Nicole Harrison, RN, B.S.N., M.B.A., administrative director of the Institute. "When they pass their test, they're reimbursed for costs incurred for certification. Ultimately, certifications help them move up the career ladder and translate to salary increases when they reach that next level in their nursing career."

Memorial Hermann-Texas Medical Center also pays for airfare and conference fees to expand opportunities for education and support nurses in learning more about their discipline. Colleen Zuckero, RN, B.S.N., CNRN, clinical education specialist and manager of the Neuroscience ICU, attended the American Association for

Neuroscience Nursing Annual Education Meeting, held in Anaheim, California, in March 2014. “There were at least 200 different sessions to choose from, so we had the opportunity to tailor the curriculum to our particular interests and educational needs,” Zuckero says. “The benefit is huge. You improve your evidence-based practice and come back to the hospital and present new knowledge in ways that motivate nurses to improve their own practice. It sparks initiative and inspires them to begin research projects to be presented at future conferences. I think of everyone on this unit as a potential educator. We’re all learning, teaching and working to improve quality. When I hear nurses say that what they do at the bedside isn’t really leadership, I tell them, ‘No! You’re leading the country by setting national benchmarks.’”

Paul Gordon, RN, B.S.N., SCRNP, CNRN, attended the 2014 International Stroke Conference held in San Diego in February 2014 and describes the experience as very enlightening. “It gave me a new view of my practice and also made me aware that we could improve the quality of research if more nurses were involved,” he says. “My goal is to attend every national stroke conference and encourage my colleagues to do so as well.”

Gordon, a staff nurse on the Stroke Unit and chair of the Unit Practice Council, shared what he learned at the council’s monthly meeting. “Everything we learn and share helps our practice,” he says. “New nurses here will find people who open their arms and help. They’ll find proper compensation in a welcoming environment,

as well as support for achieving certifications and an emphasis on conducting and publishing research to be presented nationally.”

Nurses interested in leadership roles can apply for the Nursing Leadership Development Academy, which was established by Memorial Hermann-TMC chief nursing officer Victoria King, M.H.A., M.S.N., RN, CNOR, NEA-BC.

“We’ve graduated one class and are finishing up our second,” she says. “The academy is closely linked to quality improvement because of our focus on evidence-based best practices. Nurses begin to understand how we’re driving quality at the uppermost part of the organization. The grand thing is that eight of them from the first class of 30 have been promoted to leadership roles.

“Nursing has a voice at our hospital, and nurses play an important role in creating our processes,” King

adds. “We support them through incentive programs for critical staffing, preceptor bonuses, certification reimbursement, service awards, nomination of nurses for local and national awards, handwritten letters from senior leaders for outstanding performance, continuing education opportunities and paid travel and attendance at conferences, to name just a few things we do to encourage quality. Our nurse retention rates are proof of our success. In the future nurses will have even more responsibility and autonomy. As the focus of healthcare reform moves toward keeping people healthy, nursing will become even more important. As nurses, we teach health. Opportunities will abound for us to lead the way.”

“The culture here is to own the work you do and be proud of it. I love working in a unit like that. We allow nurses to do exceptional work without interference and applaud the ones who do.”

– Allison Murphy, RN, B.S.N., CNRN

Leaders in Neuroscience Nursing

More than 175 registered nurses – and a total of 236 employees – have been recruited in the past three years to keep pace with the rapid expansion of the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center. Many of the nurses started at the bedside and quickly moved into leadership positions. Their management style is based on an understanding of the needs of bedside nurses, and they work together across units to provide support and encourage creativity, autonomy and teamwork.

Among them is Odun Atunrase, RN, B.S.N., clinical manager of the Spine Unit, who started as a floor nurse in 2009 and moved up to charge nurse shortly afterward. By 2012 he was a team leader in a pilot project designed to improve the customer experience by rounding on patients and families to ensure that their needs and expectations were met. In February 2014, he was promoted to manager of the Spine Unit, which had opened a few months earlier as a specialized unit in a renovated space. He had a plan in mind.

Atunrase describes himself as a “big believer” in Maslow’s hierarchy of needs, a pyramid with the largest, most fundamental levels of human needs at the bottom and the need for self-actualization forming the peak. “I took the hierarchy beyond the level of the individual and began to apply the principles to my unit,” he says. “To get to a place of self-actualization as a unit, we had to work our way up the pyramid from physiological needs, to safety, then belonging and self-esteem.”

After making sure his unit was adequately staffed and supplied – the physiological needs – he moved on to



Maslow's Hierarchy of Needs

safety, which he defined as staff education, orientation to the unit and role, and understanding hospital policies and the fundamentals of customer service. “Safety is also linked to accountability, effective performance and meeting outcome metrics,” Atunrase says. “Then we moved on to the higher-level need to belong. I wanted to make sure our team had a cultural identity. We knew our strengths were proactiveness and teamwork. We reviewed and reinforced that in one-on-one meetings so that everyone felt engaged. We also had weekly staff huddles and made sure every staff member had input, paying special attention to our new nurses.”

At the same time, Atunrase’s unit started to lead the neuroscience service line in HCAHPS scores and has placed either first or second among all service lines

at Memorial Hermann-TMC, since December 2013. In March 2014, his unit received the hospital's quality award for outstanding customer satisfaction. By that time, seven Spine Unit staff members had received standing ovations at weekly patient experience meetings attended by hospital executives. "We had great scores and knew we had built a team, which met our need for self-esteem," he says. "Then we moved to the self-actualization part – philanthropy, creativity and fulfillment. We really wanted to set an example as a group and find the meaning in what we're doing. Managers from units outside the Mischer Neuroscience Institute now ask us if their staff can orient with us. We're acting from the heart and touching others in the process."

Shanequa Sostand, RN, B.S.N., worked as staff nurse for five years before starting at the Institute in 2008, where she spent her first four months at the bedside in the Stroke Unit. She was promoted to charge nurse and in January 2014, to manager of the Stroke Unit.

Sostand describes her management style as a mix of engagement, empowerment and teambuilding. "I truly have an open door policy," she says. "We support our staff members and at the same time are supported by the entire leadership team. If we let them know what we need, they will help us get it. That support from leadership has made a huge difference in the growth of the neuroscience service line."

Transparency on the units has encouraged accountability and empowerment. "When it comes to performance evaluations, there are no surprises here," Sostand says. "Our quality metrics and each nurse's success at meeting them are posted monthly. We're here to help those who aren't meeting the metrics improve their performance."



"We support our staff members and at the same time are supported by the entire leadership team. If we let them know what we need, they will help us get it. That support from leadership has made a huge difference in the growth of the neuroscience service line."

– **Shanequa Sostand, RN, B.S.N.**



Daily rounding with attending physicians empowers nurses by allowing them to make decisions about patient care with the doctors, who consider nurses' input on patient condition invaluable. "We're at the bedside 24/7," she says. "When nurses round with physicians, they help develop the plan for the day. If patients or family members have questions about the plan, we can answer them because we're all on the same page."

Clinical director of patient care Enedra Allen-McBride, RN, M.S.N., started at the bedside at Memorial Hermann-TMC in 2003, and worked there for a year and a half before moving to The University of Texas MD Anderson Cancer Center, where she climbed the career ladder to associate director, working under Nicole Harrison's leadership. Harrison recruited her back to the Mischer Neuroscience Institute in 2011.

As clinical director of the neuroscience service line, Allen-McBride is responsible for providing leadership, direction and support to patient care areas. She is heavily involved in the day-to-day operations of the seven units that report to her – mentoring managers and quality coordinators on budgeting, management, quality and leadership skills.

“I meet with each manager once a week to discuss what’s going well and the concerns and challenges they face,” she says. “I round on the units, which gives me the opportunity to get to know our staff. We have over 300 employees and I take pride in being able to recognize each one of them and have conversations with them. I want them to know me, and put a face to a name. Leadership is not just about what we do at work but getting to know them personally. My relationships with my managers keep me connected to the staff and unit.

“It’s especially important to me to know my managers,” Allen-McBride adds. “They’re on the front line and have the hardest job. My door is always open and if they need me after hours, they know I’m always available. The opportunity and support Nicole has given me trickles down. I pay it forward to my managers. It’s exciting to work in an environment that fosters growth among

all our colleagues, and it’s just going to get better. We’re dedicated to our patients, our people and the extraordinary work we do each and every day.”

Dong Kim, M.D., director of the Institute and professor and chair of the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School, recognizes the important role nurses play as advocates for neuroscience patients. “Because they’re at the bedside the majority of the day, they ensure that the medical plan stays on course and keep affiliated physicians informed of even the smallest change in patient status,” he says. “Having well-trained, dedicated neuroscience nurses is essential to producing superior outcomes and to realizing our vision for the future at MNI. We want our nurses – whether they’re at the bedside or in management – to participate fully in creating that vision by sharing their ideas as equal members of the team.”



Hardwiring Cultural Change Through Nurse-Physician Committees

When neuro-intensivist Kiwon Lee, M.D., FACP, FAHA, FCCM, accepted the position of director of neurocritical care at the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center in 2012, he came with a plan – to build strong collegial relationships between physicians and nurses, particularly in the Neuroscience Intensive Care Unit.

“When I started here, doctors were rounding on patients and writing orders for nurses to carry out later. We consider that outdated medicine,” says Dr. Lee, an associate professor in the department of Neurology and the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School. “We want to be proactive in providing care rather than reactive, and quick administration of critical medical treatment can occur only when communication is seamless. Nurses have to be part of the discussion, which is why they round with us. When they give their input and make decisions with us, there’s no lag between the decision-making process and the execution.”

Dr. Lee is also a strong proponent of education. “When nurses and doctors are on the same page, communication is efficient,” he says. “We consider nurses our partners and want them to be as knowledgeable as we are about the patient.

This is the only way to provide excellent critical care service and produce better outcomes.”

Cultural change at the Mischer Neuroscience Institute has been formalized through eight committees, each co-chaired by a nurse and a doctor. Tiffany Chang, M.D., co-chairs the Clinical Practice Committee with Colleen Zuckero, RN, B.S.N., CNRN, clinical education

specialist and manager of the Neuroscience ICU. “Collaboration is critical to the care of neuroscience patients. It’s no longer a culture of doctors giving orders and nurses following them,” says Dr. Chang, an assistant professor in the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School. “The nurse is an active member of the treatment team, rounding with us in the morning and advocating for the needs of patients. They know the patient best because they’re at the bedside 24/7. We respect their input as an important member of the team.”

The new committee structure plays a vital role in continuous quality improvement. “For example, data collected by the Quality and Safety Committee provides information that aids the Clinical Practice Committee with process improvement initiatives,” says Nicole Harrison, RN, B.S.N., M.B.A., administrative director of the Institute. “If we discover a need to reeducate

“We consider nurses our partners and want them to be as knowledgeable as we are about the patient. This is the only way to provide excellent critical care service and produce better outcomes.”

– **Kiwon Lee, M.D.,
FACP, FAHA, FCCM**

nurses based on the data, the Staff/Nursing Education Committee puts together a plan and disseminates the information. The new structure ensures that nurses and doctors alike are aware of everything that goes on in the Neuroscience ICU. It also positions us as equal partners on the patient care team. Nurses can agree or disagree. It's complete equality."

H. Alex Choi, M.D., chairs the Critical Care Research and Evidence-based Practice Committee with Christina Luther, RN, and the Cerebrovascular Committee with Christine Glendening, RN. "The challenges nurses face are different than the challenges doctors face," says

Dr. Choi, an assistant professor in the department of Neurology and the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School. "Nurses are on the front lines around the clock. When we work together cohesively and creatively, our patients benefit. We understand that it's the nurses who take care of patients. If physicians and nurses are not on the same page and moving in the same direction, treatment becomes fragmented. Families don't understand what's happening to their loved one and our patients suffer. With good communication and teamwork, everyone excels in patient care and academic development."





*Scope of Services
and Quality Outcomes*



Brain Tumor

Neuro-oncologists Jay-Jiguang Zhu, M.D., Ph.D., and Sigmund H. Hsu, M.D., continue to expand the capabilities of the Brain Tumor Center at the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center. Dr. Zhu, fellowship trained at Massachusetts General Hospital, focuses his practice on primary brain tumors – gliomas, meningiomas and pituitary adenomas – and primary CNS lymphomas, as well as brain metastases and leptomeningeal spread of systemic malignancies. He is also interested in quality of life, including cognitive function during and after radiotherapy and chemotherapy; neurological complications of systemic chemotherapies; and clinical trials focused on developing new treatment

options for primary brain tumors and CNS metastases. Dr. Hsu, fellowship trained at The University of Texas MD Anderson Cancer Center, has clinical and research interests in the discovery of new and more effective therapies for patients with primary brain tumors, treatment of metastatic cancer to the brain and spinal fluid, and the evaluation and treatment of neurological problems in cancer patients.

Dr. Zhu is principal investigator in three trials that give eligible study participants access to new and advanced treatments. The first is a Phase III multicenter, randomized, controlled trial designed to test the efficacy and safety of a

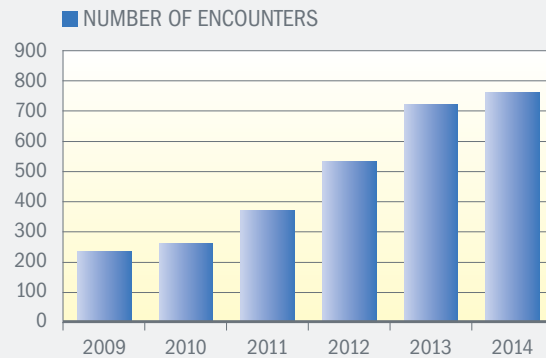


QUALITY & OUTCOMES MEASURES

medical device called Novo TTF-100A for newly diagnosed glioblastoma multiforme (GBM) patients in combination with temozolomide, compared to temozolomide alone. The device, which patients wear on their scalp, provides a constant, safe, low-voltage electric field that has been shown to reduce tumor cell survival and division capacity. Dr. Zhu is also principal investigator of a randomized, double-blind, controlled Phase I/II (Safety Lead-In) study of trans sodium crocetinate (TSC) with concomitant treatment of fractionated radiation therapy and temozolomide in newly diagnosed GBM, examines the safety and efficacy of radiation sensitizer of TSC in combination with fractionated radiation.

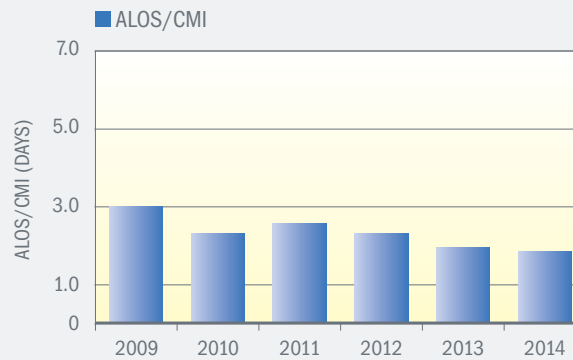
Dr. Hsu is principal investigator of one of the first clinical trials to use immunotherapy in combination with standard anti-angiogenic therapy for cancer. Called “ReACT: A Phase II Clinical Trial Targeting the EGFRvIII Mutation in Glioblastoma Patients with Relapsing Disease,” the study is investigating whether adding an experimental vaccine called rindopepimut, also known as CDX-110, to the commonly used chemotherapeutic drug bevacizumab can improve progression-free survival of patients with relapsed EGFRvIII-positive GBM. Dr. Hsu is also principal investigator in the trial of a novel taxol chemotherapy compound, TPI-287, which crosses the blood-brain barrier and will be administered in combination with bevacizumab for patients with glioblastoma.

Brain Tumor Volumes



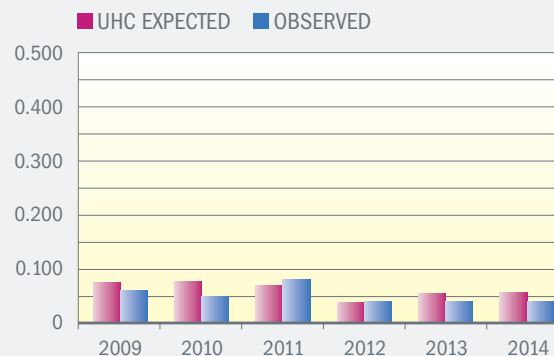
Source: Chart data based on DRG per fiscal year

Brain Tumor: Length of Stay (CMI Adjusted)



Source: Chart data from the University HealthSystem Consortium

Brain Tumor: Inpatient Mortality



Source: Chart data from the University HealthSystem Consortium

RESEARCH HIGHLIGHT

Phase I/II Dose-Escalation Study of TPI 287 in Combination with Bevacizumab Followed by Randomized Study of the Maximum Tolerated Dose of TPI 287 in Combination with Bevacizumab versus Bevacizumab Alone in Adults with Recurrent Glioblastoma

PRINCIPAL INVESTIGATOR: **Sigmund Hsu, M.D.**

Associate Professor

Vivian L. Smith Department of Neurosurgery

UTHealth Medical School

The treatment of patients with bevacizumab-resistant glioblastoma is a significant challenge. Researchers affiliated with the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center are participating in a two-part trial of a novel taxane drug, TPI 287, in combination with bevacizumab for patients with recurrent glioblastoma. Unlike other anti-microtubule chemotherapy agents, TPI 287 readily crosses the blood-brain barrier.

The trial is divided into two parts. Phase I is a dose-escalation study designed to determine the safety, maximum tolerated dose and efficacy of TPI 287 in combination with bevacizumab in subjects who have glioblastoma multiforme (GBM) that has progressed following prior radiation therapy and temozolomide. Phase II is a randomized study that will determine the safety and efficacy of the Phase I maximum tolerated dose of TPI 287 in combination with bevacizumab versus bevacizumab alone in subjects who have GBM that has progressed following prior radiation therapy and temozolomide.

In addition to routine multidisciplinary brain tumor clinics, physicians affiliated with the Mischer Neuroscience Institute offer patients specialized care through three clinics. The Pituitary Tumor and Vision Change Clinic ensures early and precise diagnosis of patients with pituitary and other parasellar tumors, which may cause a broad range of disorders and present with a variety of symptoms, including hormonal changes, vision loss and infertility. At the Brain Metastases Clinic, a team of affiliated neuro-oncologists, neuroradiologists, radiation oncologists, neuropathologists, oncologists and neurosurgeons works closely with oncologists to provide personalized and innovative care to patients with brain tumors. Specialists at the Cancer Neurology Clinic treat patients with neurological issues resulting from chemotherapy. At the Neurogenetics Clinic, a genetic counselor identifies genetic risk and explains inheritance patterns, provides education on the natural history of disease and discusses the risks, benefits and limitations of available genetic testing options.

The brain tumor team focuses on providing the best state-of-the-art treatment and access to investigational trials as appropriate. The Brain Tumor Center was chosen as a site for the FoundationOne™ Registry study. The FoundationOne tumor genomic analysis test is the leading next-generation sequencing technology, enabling physicians affiliated with the Institute to recommend optimal personalized treatment for patients with cancer. Patients benefit from other innovative and advanced technologies, including motor and language mapping, functional neuroimaging, frameless stereotactic navigation in surgery, and awake craniotomies performed under local anesthesia, as well as minimally invasive procedures, including neuroendoscopy and stereotactic radiosurgery.

The Mischer Neuroscience Institute acquired the region's first Leksell Gamma Knife® in 1993, and is now using

the more advanced Leksell Gamma Knife Perfexion™. Patients who benefit from the Perfexion's sophisticated software with dose-to-target conformation include those with meningiomas and vestibular schwannomas; arteriovenous malformations; medically refractory trigeminal neuralgia; and metastases. Multiple intracranial metastases can usually be treated in a single outpatient procedure.

The Varian Trilogy linear accelerator is the first in a powerful new generation of cancer-fighting technologies, offering highest dose rates for shorter sessions. The system delivers 3-D conformal radiotherapy, IMRT, extracranial and intracranial stereotactic radiosurgery, fractionated stereotactic radiation therapy, stereotactic body radiosurgery (SBRT) and intensity-modulated radiosurgery for cancer and neurosurgical treatment.

The clinical team affiliated with the Brain Tumor Center works closely with referring physicians throughout the radiosurgical treatment process. A neurosurgeon and a radiation oncologist assess each candidate to determine whether radiosurgical treatment is the best option. Nurse navigators work directly with patients on scheduling and pretreatment education, and provide support and care on the day of treatment. The Center also sponsors a well-attended brain tumor support group that meets the second Wednesday of every month.

Breakthrough approaches to treatment provided by specialists affiliated with the Mischer Neuroscience Institute have led to an increase in the number of patients treated for brain tumors. Since 2009, volumes have increased by more than 250 percent.





Cerebrovascular

In 2013, the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center received the highly coveted Comprehensive Stroke Center certification from The Joint Commission (TJC) and the American Heart Association/American Stroke Association (AHA/ASA). Less than a year later, on Jan. 1, 2014, the AHA recognized Memorial Hermann-Texas Medical Center with the Get With The Guidelines®—Stroke Gold Plus Achievement Award. Under the direction of Sean Savitz, M.D., the Memorial Hermann Stroke Center at the Mischer Neuroscience Institute was the first stroke program in the state of Texas to meet TJC's rigorous standards, solidifying its position among an elite group of providers in the country focused on complex stroke care.

Opened in 1988 by James C. Grotta, M.D., as one of the first dedicated stroke programs in the world, the Stroke Center is home to the 10-county Greater Houston area's largest onsite stroke team. Neurologists affiliated with the Center use leading-edge technology to diagnose and treat more than 2,000 stroke and aneurysm patients annually, ensuring that each patient gets the appropriate treatment as quickly as possible. By working closely with the Houston Fire Department and local EMS services, the stroke team has logged an impressive record of success in the administration of tPA – more than 10 times the national average of 2 to 3 percent.

In addition to breakthrough treatment for stroke, the cerebrovascular team provides coordinated care for patients with aneurysms, carotid occlusive disease and intracranial vascular malformations, including



open surgical and endovascular treatments such as angioplasty, stenting and embolization. Also available is the relatively new Pipeline™ endovascular flow-diverting stent, a device that reconstructs the parent vessel lumen of difficult-to-reach aneurysms as an alternative to clipping or endovascular coiling. Affiliated neurosurgeons are skilled at microvascular clipping of aneurysms using the best skull base approaches to minimize brain manipulation, extracranial-intracranial bypass procedures, carotid endarterectomy and hemicraniectomy for severe strokes. State-of-the-art radiosurgery using the Leksell Gamma Knife® Perfexion™ is regularly used for vascular malformations best treated nonsurgically.

The Mischer Neuroscience Institute/UTHealth Telemedicine Program, directed by Teddy Wu, M.D.,

RESEARCH HIGHLIGHT

ARTSS-2: A Pilot, Phase IIb, Randomized, Multicenter Trial of Argatroban in Combination with Recombinant Tissue Plasminogen Activator for Acute Stroke

PRINCIPAL INVESTIGATOR: **Andrew Barreto, M.D.**
Associate Professor, Department of Neurology,
UTHealth Medical School

In this safety and efficacy study of argatroban, a synthetic direct thrombin inhibitor, researchers are investigating the overall treatment benefit, i.e., improvement in disability, among ischemic stroke patients treated with recombinant tissue plasminogen activator (rt-PA), the only proven treatment for acute ischemic stroke, in combination with argatroban. Rt-PA fails to reperfuse brain tissue in most patients with large thrombi. In a Phase IIa low-dose safety study with 65 participants, the two drugs appeared safe when delivered concomitantly, and recanalization rates were greater than historical controls. This Phase IIb study will provide evidence-based hypotheses and data needed to design a larger definitive trial.

Estimated enrollment is 105 participants who will be randomized to one of three arms: low-dose argatroban, a high dose of the agent, or neither. Researchers at UTHealth Medical School are running every facet of this 13-center international trial under way in the United States and the United Kingdom. The estimated study completion date is mid-2015.

extends stroke and neurology expertise far beyond the Institute's walls, helping emergency physicians in community hospitals throughout Southeast Texas make accurate diagnoses and save lives. Remote presence robotic technology has enhanced the telemedicine program by linking outlying hospitals electronically to the Neurology department, providing real-time visual interaction between neurologists and patients, and allowing affiliated neurologists to review CT scans and advise local physicians on treatment outcomes. Through telemedicine, physicians can now offer patients in outlying communities an opportunity to participate in clinical trials that would otherwise be unavailable to them, which expands medical knowledge as it saves lives. Baptist Beaumont Hospital and Memorial Hermann Southwest Hospital were early adopters of telemedicine. Since then, 11 more sites in Southeast Texas have gone live with the technology: Memorial Hermann Memorial City Medical Center, Memorial Hermann Northwest Hospital, Memorial Hermann The Woodlands Hospital, Huntsville Memorial Hospital, Matagorda Regional Medical Center, Baptist Orange Hospital, the Medical Center of Southeast Texas in Port Arthur, Citizens Medical Center in Victoria, St. Joseph Hospital-Downtown in Houston, DeTar Healthcare System in Victoria and Tomball Regional Medical Center in Tomball.

Physicians at the Mischer Neuroscience Institute and UTHealth Medical School conduct more research than any other stroke program in the southern or southwestern United States, participating in multicenter and single-center clinical trials testing new treatments for patients who cannot be treated elsewhere. Research has included thrombolytic treatment for wake-up stroke, the safety of pioglitazone for hematoma resolution in intracerebral hemorrhage, and autologous bone marrow stem cell treatment for acute ischemic stroke. Investigators are also seeking to increase the effect of standard-



of-care treatment by combining tPA with ultrasound, anticoagulants and hypothermia, as well as exploring new methods of stroke prevention.

The Stroke Center is also pioneering the use of a hands-free, operator-independent device to deliver external ultrasound to enhance the effects of tPA – a device that potentially could be used in any community hospital. A study led by Andrew Barreto, M.D., has shown the safety of using this device in patients treated with tPA, and the stroke team is now participating in a large international trial to test the efficacy of the combined approach in patients with acute stroke.

A team led by James Grotta, M.D., at Memorial Hermann-Texas Medical Center and UTHealth Medical School unveiled the country's first mobile stroke unit, made possible by a consortium of partners from the Texas

Medical Center, the Houston Fire Department and generous donors. The mobile unit is equipped with a CT scanner that allows the onboard team of a doctor, nurse, CT technician and paramedic to quickly assess whether a patient is having an ischemic stroke, allowing for early administration of the clot-busting drug tPA. The mobile stroke unit was completed in February 2014, and the first patients were treated in May. The study, which will require three to five years to complete, began on July 1, 2014.

The Stroke Center's cerebrovascular continuum of care is extended through inpatient and outpatient neurorehabilitation in Memorial Hermann-TMC's 23-bed rehabilitation unit and at TIRR Memorial Hermann, an international leader in medical rehabilitation and research. Patients benefit from comprehensive inpatient and outpatient services, state-of-the-art technology and innovative therapies and techniques.

The Intra-arterial Vasospasm Trial: A Multicenter Randomized Study

PRINCIPAL INVESTIGATOR: **Peng Roc Chen, M.D.**

Director, Cerebrovascular/Endovascular Program

Assistant Professor, Vivian L. Smith Department of Neurosurgery, UTHealth Medical School

Cerebral vasospasm is a devastating health problem and a major contributor to poor outcome following subarachnoid hemorrhage (SAH). The estimated case fatality following an SAH is 25 to 50 percent with a large proportion of these being secondary to the deleterious consequences of cerebral vasospasm. Up to 70 percent of patients who survive the initial SAH develop signs of vasospasm, which if untreated can lead to devastating strokes. To date, the armamentarium in predicting, preventing and optimizing outcome following severe vasospasm remains limited, primarily because the underlying pathogenesis is not fully understood.

Despite improvements in microsurgical and endovascular techniques to treat aneurysms, neurosurgeons have not made significant strides in the treatment of cerebral vasospasm. Traditional therapy of hypertensive, hypervolemic and hemodilution, which has been adopted in clinical practice, carries considerable cardiopulmonary risks. Endovascular treatments such as angioplasty and administration of intra-arterial drugs, particularly calcium-channel blockers, have been considered a quintessential treatment to minimize potential devastating ischemic stroke from the delayed cerebral vasospasm.

Based on the results of a recent national survey conducted by the PI through the joint AANS/CNS cerebrovascular section, there is considerable variability in the intra-arterial treatment of cerebral vasospasm, leading to variable outcomes. The commonly used intra-arterial drugs for treating vasospasm are single agents: verapamil, nicardipine, milrinone and nitroglycerin. There is no conclusive literature suggesting the best trans-arterial infusion agent or combination agents, and the treatment result is, in general, unsatisfactory.

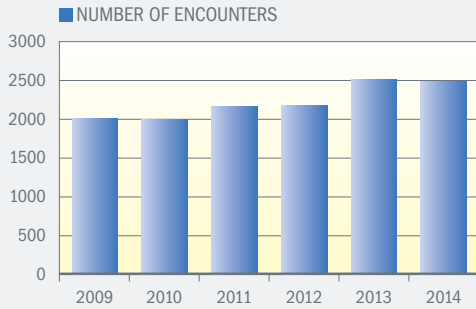
A retrospective review was conducted recently of consecutive patients treated for cerebral vasospasm at UTHealth Medical School and Memorial Hermann-Texas Medical Center. The researchers concluded that treatment of cerebral vasospasm with an intra-arterial (IA) cocktail of nitroglycerine, verapamil and nicardipine provides significantly better angiographic improvement of vasospasm than single-agent therapy. The results were presented at the International Stroke Conference 2014, held in San Diego, California.

Based on these results, the researchers pursued this prospective evaluation of the efficacy of multi-agent vasodilator infusion therapy versus current typical single-agent therapy. The goal of this study is to determine the optimal intra-arterial drugs and the most effective regimen for treating cerebral vasospasm. Given that each of the four commonly used IA vasodilators has its own acting mechanisms, combining these medications for IA infusion will potentially provide the synergistic effects of cerebral vasodilation and minimize cardiovascular instability induced by a high dose of single-agent treatment.



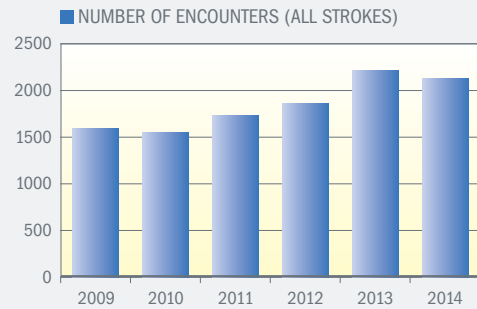
QUALITY & OUTCOMES MEASURES

Cerebrovascular Volumes



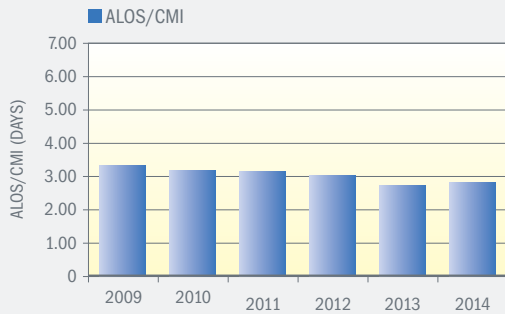
Source: Chart data based on DRG per fiscal year

Stroke Volumes



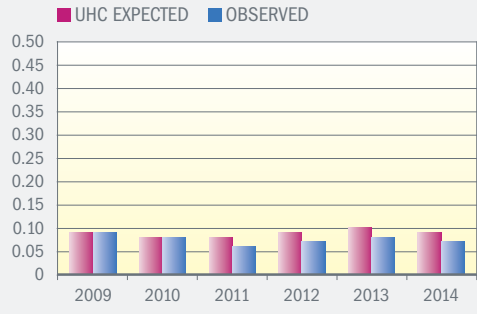
Source: Chart data from the University HealthSystem Consortium

Acute Ischemic Stroke: Length of Stay (CMI Adjusted)



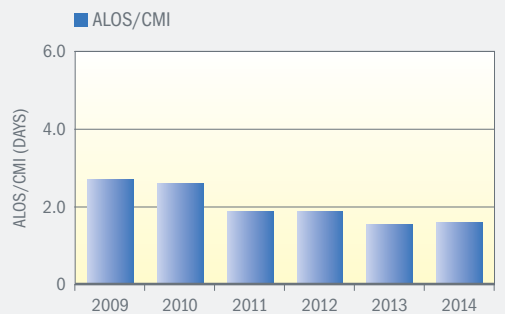
Source: Chart data from the University HealthSystem Consortium

Acute Ischemic Stroke: Inpatient Mortality



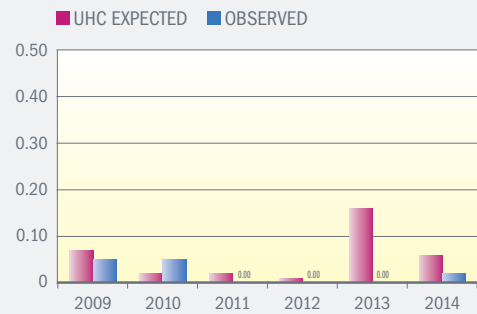
Source: Chart data from the University HealthSystem Consortium

Arteriovenous Malformation: Length of Stay (CMI Adjusted)



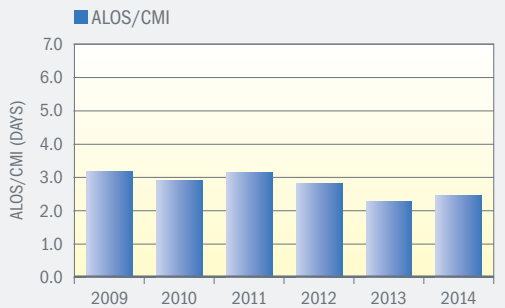
Source: Chart data from the University HealthSystem Consortium

Arteriovenous Malformation: Inpatient Mortality



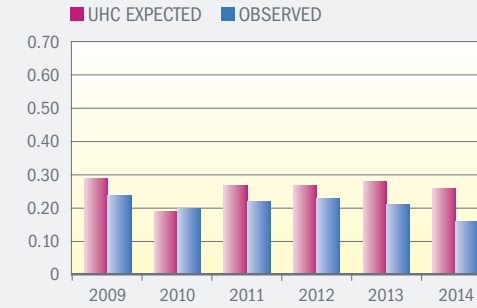
Source: Chart data from the University HealthSystem Consortium

Intracerebral Hemorrhage: Length of Stay (CMI Adjusted)



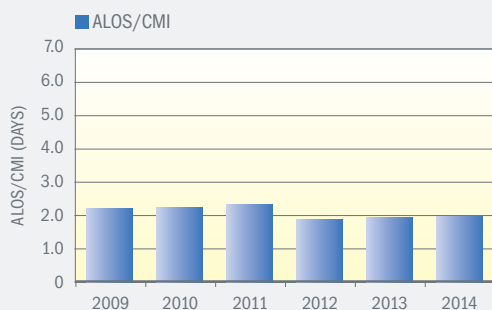
Source: Chart data from the University HealthSystem Consortium

Intracerebral Hemorrhage: Inpatient Mortality



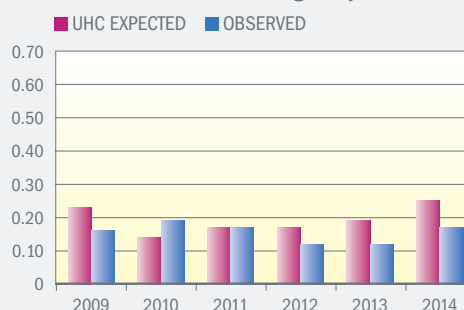
Source: Chart data from the University HealthSystem Consortium

**Sub-arachnoid Hemorrhage:
Length of Stay (CMI Adjusted)**



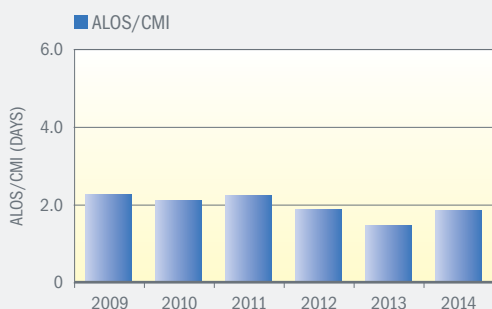
Source: Chart data from the University HealthSystem Consortium

Sub-arachnoid Hemorrhage: Inpatient Mortality



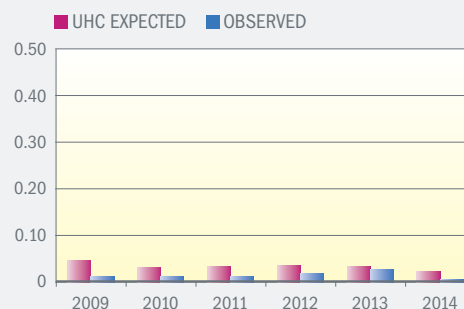
Source: Chart data from the University HealthSystem Consortium

Aneurysm Unruptured: Length of Stay (CMI Adjusted)



Source: Chart data from the University HealthSystem Consortium

Aneurysm Unruptured: Inpatient Mortality



Source: Chart data from the University HealthSystem Consortium

Stroke Core Measures

Fiscal Year	GWTC Measure Goal	2011	2012	2013	2014
STK-1 - VTE Prophylaxis	85%	97.7%	99.3%	99.11%	99.92%
STK-2 - Discharged on Antithrombotic Therapy	85%	100%	99.4%	98.83%	99.59%
STK-3 - Anticoagulation Therapy for atrial Fib.	85%	100%	99%	97.93%	98.09%
STK-4 - Thrombolytic Therapy	85%	95.4%	97.9%	97%	94.62%
STK-5 - Antithrombotic Therapy by End of Hospital Day 2	85%	97.3%	94.9%	92.88%	97.92%
STK-6 - Discharged on Statin Medication	85%	94.5%	98.2%	98.22%	99.22%
STK-8 - Stroke Education	85%	92.96%	94.91%	96.2%	97.36%
STK-9 - Assessed for Rehab	85%	97.36%	99.41%	99.29%	99.91%

Source: Chart data based on fiscal year



Children's Neuroscience

With the arrival of David Sandberg, M.D., FAANS, FACS, FAAP, the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center added significant strength to its Children's Neuroscience Center.

Dr. Sandberg is a national leader in developing novel techniques to treat malignant brain tumors in children. Prior to his arrival to Houston, he performed translational studies that demonstrated the safety of infusing chemotherapeutic agents directly into the fourth ventricle to treat children with malignant brain tumors in this location. The promising results of these studies have led to a pilot clinical trial, which Dr. Sandberg leads as principle investigator, in collaboration with The University of Texas MD Anderson Cancer Center.

To avoid the many complications of ventriculoperitoneal shunting for children with hydrocephalus, pediatric neurosurgeons affiliated with the Institute frequently perform minimally invasive endoscopic techniques such as third ventriculostomy, septostomy, choroid plexus coagulation and fenestration of arachnoid cysts. Selected brain tumors can be biopsied or removed completely via endoscopic techniques. All of these procedures are performed via very small incisions with minimal hair shaving. In collaboration with otolaryngologists affiliated with Memorial Hermann-Texas Medical Center, neurosurgeons remove some tumors via endoscopic transnasal approaches without an external incision.

Pediatric neurosurgeons at the Mischer Neuroscience Institute are important members of The Fetal Center at Children's Memorial Hermann Hospital, a national leader in providing diagnosis, treatment and complete

care for mothers with high-risk pregnancies and infants with congenital anomalies or genetic conditions. The multidisciplinary team performed the first fetal spina bifida repair in the region, and patients throughout Texas and a number of surrounding states are now being referred to the Center for fetal myelomeningocele repair. Stephen Fletcher, D.O., leads fetal pediatric neurosurgery efforts.

In collaboration with nationally recognized craniofacial plastic surgeons, pediatric neurosurgeons affiliated with Children's Memorial Hermann Hospital perform both conventional and minimally invasive endoscopic surgeries to repair craniosynostosis and other complex craniofacial anomalies. The multidisciplinary Texas Cleft-Craniofacial Team was established in 1952 and has been a regional leader for pediatric craniofacial surgery for decades.

The Mischer Neuroscience Institute is also a center of excellence for pediatric epilepsy surgery and comprehensive specialized care for children with intractable epilepsy. The pediatric Epilepsy Monitoring Unit is the largest and most comprehensive of its kind in the southwestern United States. In addition to MRI and CT with low radiation dose protocols for pediatric patients, affiliated physicians use noninvasive magnetoencephalography (MEG) to map brain activity to locate the source of epileptic seizures and minimize risk for children undergoing resective surgery for refractory epilepsy. For the most accurate diagnosis they also use stereo EEG, video EEG, PET, SPECT, memory and speech (Wada) testing and neuropsychological testing. Interventions include medical management and the ketogenic diet as well as surgery, including vagus nerve

stimulation and laser ablation procedures. Nitin Tandon, M.D., directs the adult and pediatric epilepsy surgery program. Pediatric neurosurgeon Manish Shah, M.D., who has special expertise in pediatric epilepsy surgery, was recruited from Washington University in St. Louis in August 2014. Dr. Shah is also an expert in functional neurosurgery and surgical management of spasticity in children and performs selective dorsal rhizotomies, baclofen pump placements and advanced deep brain stimulation techniques.

Three other centers of excellence focus on West syndrome, dysautonomia, and neurometabolic and mitochondrial disorders. The West Syndrome Center of Excellence opened in the spring of 2014, with a generous philanthropic gift from the West Syndrome Foundation. The Center attracts patients from around the world for treatment of West syndrome. Investigators will conduct research on the causes of the syndrome and related pediatric epilepsy disorders as well as increase awareness of the disease.

Pediatric neurologist Ian J. Butler, M.D., and pediatric cardiologist Mohammed Numan, M.D., are co-directors of the Dysautonomia Center of Excellence. The two physicians work together to create individualized treatment plans for each patient based on the most advanced modalities. Mary Kay Koenig, M.D., directs the Mitochondrial Center of Excellence, where affiliated physicians provide comprehensive services to aid in the diagnosis and management of neurometabolic and mitochondrial disorders.

Children's Memorial Hermann Hospital is a leading-edge center for the treatment of retinoblastoma, a rare pediatric eye malignancy that affects only 250 to 350 new patients each year. It is one of just a handful of hospitals in United States at which physicians

offer intra-arterial chemotherapy, the most modern treatment for the disease, which enables children to have chemotherapy injected into the arteries that feed the eye, eliminating the side effects of systemic chemotherapy and maximizing the dose to the eye. Treatment of retinoblastoma requires a large multispecialty team that combines endovascular neurosurgery, ocular oncology and medical neuro-oncology working closely together. Physicians affiliated with the Mischer Neuroscience Institute and Children's Memorial Hermann Hospital are also engaged in research investigating new ways to save eyes that have failed conventional therapies.

The Children's Neuroscience Center provides a broad range of diagnostic and treatment services for children with complex neurological problems, including autism, brachial plexus disorders, brain tumors and malformations, cerebral palsy, congenital hydrocephalus, craniofacial disorders, developmental disorders, epilepsy, chronic headache and migraine, head trauma, learning disabilities, movement disorders, myopathy, neurofibromatosis, neurometabolic disorders, neuromuscular disorders, pediatric stroke, peripheral nerve disorders, sleep disorders, spina bifida, Tourette syndrome and tuberous sclerosis complex. Physicians affiliated with the Center have specialized pediatric neurosurgical expertise in congenital malformations, including Chiari malformation, endoscopic neurosurgery, and treatment for pediatric stroke, spinal deformities and traumatic brain and spine injury.

Care at Children's Memorial Hermann Hospital is delivered in a child-friendly, reassuring environment to promote wellbeing and the best possible outcomes. When surgery is required, affiliated physicians use advanced imaging techniques and minimally invasive procedures that lower patient risk. Onsite sedation is available for imaging studies with care provided by specially trained pediatric anesthesiologists and pediatric nurses.

Methotrexate Infusion Directly into the Fourth Ventricle in Children with Malignant Fourth Ventricular Brain Tumors: A Pilot Clinical Trial

PRINCIPAL INVESTIGATOR: **David I. Sandberg, M.D.**

Director, Pediatric Neurosurgery, Mischer Neuroscience Institute

Professor, The Vivian L. Smith Department of Neurosurgery

Associate Professor, Department of Pediatric Surgery, UTHealth Medical School

Under an IRB-approved protocol, methotrexate was infused into the fourth ventricle in patients with recurrent malignant fourth ventricular tumors. Preliminary results of this study are the first report in humans of direct chemotherapy administration into the fourth ventricle.

Patients with recurrent, malignant tumors originating within the fourth ventricle underwent tumor resection and catheter placement into the fourth ventricle. The catheter was attached to an Ommaya reservoir. After confirmation of cerebrospinal fluid flow by CINE MRI, methotrexate infusions were initiated. Each cycle consisted of four consecutive daily infusions (2 mg). Serum and cerebrospinal fluid (CSF) methotrexate levels and CSF cytology studies were obtained daily, and MRI scans of the brain and total spine were obtained after every three cycles. Neuropsychological evaluation was performed before and after intraventricular chemotherapy.

Five patients have received treatment to date; two had ependymoma and three had medulloblastoma. Both patients with ependymoma progressed despite therapy, but all three patients with metastatic medulloblastoma had a reduction in tumor burden. None of the patients have shown any treatment-related toxicity. We conclude that chemotherapy infusions directly into the fourth ventricle are safe and may benefit patients with recurrent malignant tumors. This trial will form the basis for additional trials investigating novel agents that will be administered into the fourth ventricle.

Epilepsy

Over the past two years, the Texas Comprehensive Epilepsy Program, the leading program in the southwestern United States for the diagnosis and treatment of epilepsy in patients of all ages, has seen phenomenal growth both in volumes of medically and surgically treated patients and in numbers of faculty. Affiliated physicians now include six fulltime adult and three fulltime pediatric epileptologists. A collaborative effort between Memorial Hermann-Texas Medical Center, Children's Memorial Hermann Hospital and UTHealth Medical School, the program is the premier Level IV National Association of Epilepsy Centers-certified program in Houston.

At the heart of the program is a state-of-the-art 12-bed Epilepsy Monitoring Unit (EMU), the largest and most comprehensive unit of its kind in the region. Affiliated physicians deploy a complete set of established and emerging diagnostic technologies that provide

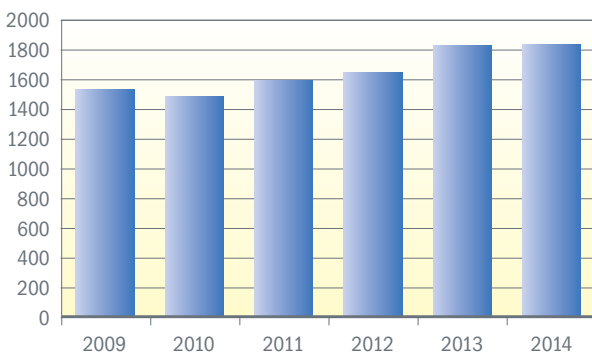
comprehensive datasets to help define and localize the seizure network in the brain. The full suite of diagnostic tools includes magnetoencephalography (MEG) to map both seizure networks and neurological function, video EEG, 3-Tesla structural MRI, functional MRI and diffusion tensor tractography, positron emission tomography (PET), single-photon emission computed tomography (SPECT), memory and intra-carotid amygdala (Wada) testing and in-depth neuropsychological testing. The Texas Comprehensive Epilepsy Program is a national leader in combining the use of MEG and functional MRI to map the brain and record brain activity. It operates one of only a few inpatient units in the country with the capability to perform electroencephalography and polysomnography simultaneously.

The number of patients affiliated physicians treat annually continues to grow. Board-certified neurologists and neurosurgeons diagnose and treat more than 1,800 pediatric and adult patients each year for seizure disorders. Genetic anomalies, brain trauma, structural abnormalities, stroke and brain tumor rank among the top underlying causes of epilepsy, but because seizures manifest differently among individuals, specific determination of the origin of seizures is crucial to planning the most effective treatment for individual patients.

Once a diagnosis is made, physicians offer the most advanced treatment options available, including drug therapy, the ketogenic diet, vagus nerve stimulation (VNS), focal cortical resection, lobectomy,

Epilepsy Volumes

■ NUMBER OF ENCOUNTERS



Source: Chart data based on DRG&/or ICD9 primary or secondary diagnosis, per fiscal year



hemispherectomy and corpus callosotomy. The program's surgical complication rates have remained extremely low over the past nine years. At the current time, the Institute's affiliated epilepsy surgeon has performed more than 500 craniotomies for the treatment of epilepsy, with a zero percent mortality rate and a very low rate of permanent morbidity. Additionally, the program goes beyond the medical and surgical treatment of epilepsy by offering counseling to patients to help them cope with their diagnosis. Specialized counselors ensure that recently diagnosed patients have the emotional support they need.

Affiliated physicians are also leaders in innovative surgical approaches for epilepsy, with new surgical approaches and technologies implemented in the

past two years, including stereoelectroencephalography (SEEG), robotic SEEG and MR-guided laser interstitial thermal therapy (Visualase®). The Mischer Neuroscience Institute is a pioneering site for the latter technique – the application of laser surgery for well-delineated focal epilepsies – with carefully selected patients treated in a highly advanced, minimally invasive fashion that ablates the seizure focus. In addition to using the Visualase technique for the treatment of temporal lobe epilepsy associated with hippocampal sclerosis, physicians use it in novel ways, including the ablation of deep-seated periventricular nodular heterotopias. The program is the second epilepsy program in the country to perform robotic SEEG, a technique that helps localize the seizure focus with precision and in a minimally invasive fashion. The safety and efficacy



data reported by affiliated physicians following all types of surgical intervention for epilepsy are excellent. They will also be initiating treatment with a newly FDA-approved technique for responsive neuromodulation (NeuroPace®).

The epilepsy team has been involved in cutting-edge research related to most epilepsy treatments approved in the United States in the last 15 years, including a number of pharmacological therapies and VNS therapy. Current drug trial research includes lacosamide monotherapy and adjunctive therapy for partial-onset seizures; an open-label extension study of rufinamide as an adjunctive therapy in patients with refractory partial-onset seizures; and vigabatrin therapy for refractory focal epilepsy. Faculty at UTHealth Medical School pursue several other lines of clinical and scientific research, such as the use of tractography to lateralize temporal lobe epilepsy and to delineate the epileptogenic network; oxygen-enhanced magnetic resonance imaging in non-lesional focal epilepsy; correlation of waking background alpha frequency with measures of attention and reaction; and the use of intracranial electrocorticography to study a variety of cognitive and language processes. Research funding for faculty comes from a variety of sources including major National Institutes of Health and National Science Foundation grants; in addition, they pursue collaborative interdisciplinary research with a number of other local institutions. The program is also a member of the National Critical Care EEG Monitoring Research Consortium (CCEMRC) and has contributed patient data to national projects.

RESEARCH HIGHLIGHT

Epilepsy Research, 2014 March;108(3):547-54
[Published online 8 Feb 2014]

Stereotactic Laser Ablation of Epileptogenic periventricular Nodular Heterotopia

Esquenazi Y, Kalamangalam GP, Slater JD, Knowlton RC, Friedman E, Morris S-A, Shetty A, Gowda A, Tandon N

Periventricular nodular heterotopia (PVNH) is a brain malformation caused by abnormal neuronal migration in which a subset of neurons fails to migrate into the developing cerebral cortex, remaining as nodules lining the ventricular surface. PVNH is frequently associated with pharmaco-resistant epilepsy, and its deep location has limited treatment by resective surgery.

In this article, researchers describe the novel application of MR-guided laser interstitial thermal therapy (MRgLITT) for the treatment of PVNH epilepsy in two patients. In the first case, laser ablation of the epileptogenic PVNH allowed for a favorable adjustment of anticonvulsant medication. In the second case, PVNH ablation and temporal lobectomy left the patient seizure free. They concluded that MRgLITT shows promise as a minimally invasive technique for the ablation of epileptogenic PVNH and that the use and long-term efficacy of the technique require further investigation.

Movement Disorders and Neurodegenerative Diseases

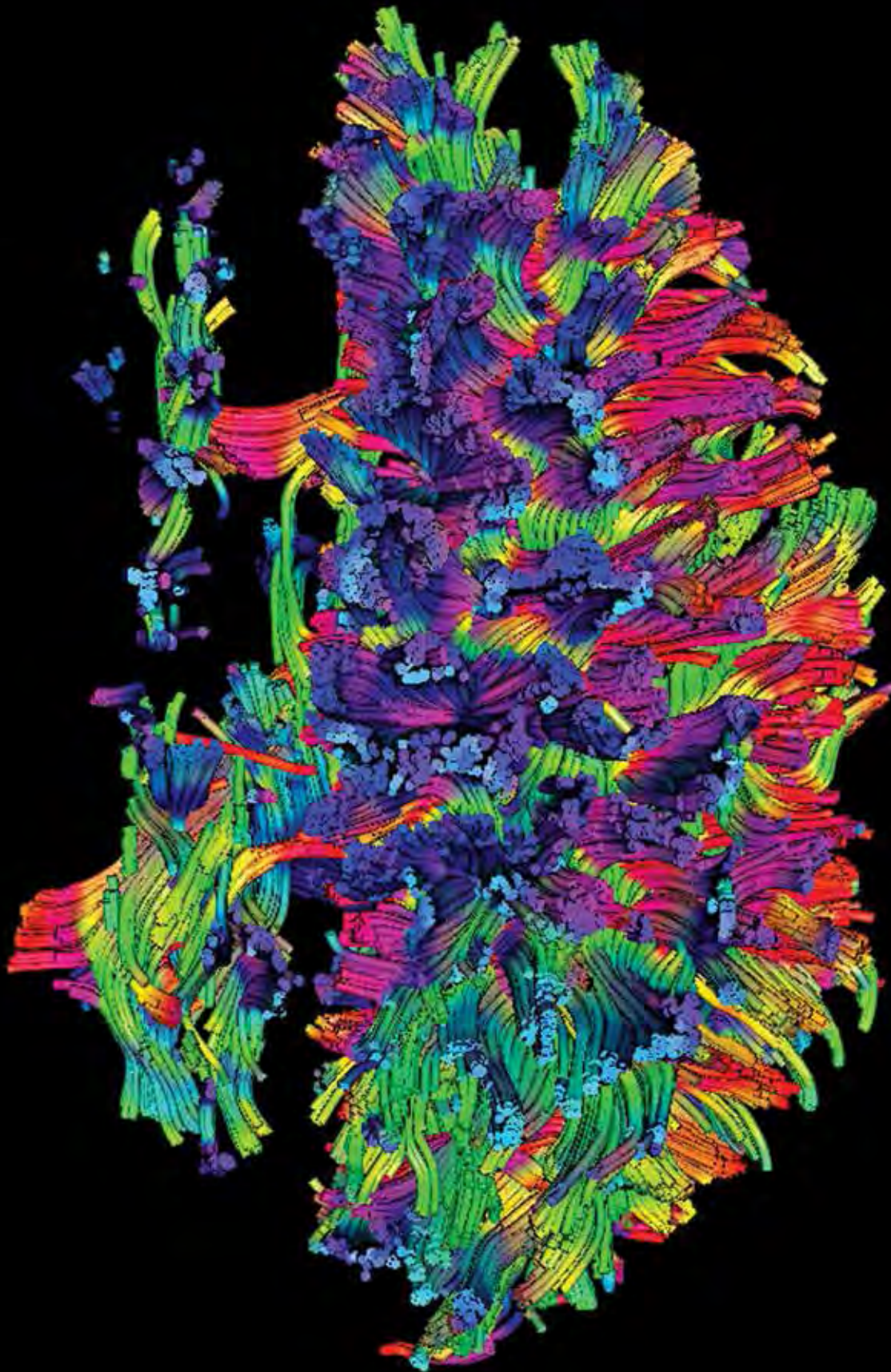
Using pioneering techniques to diagnose, evaluate, manage and treat adult and geriatric patients, the Movement Disorders and Neurodegenerative Diseases Program, called UT MOVE, has established a track record of providing outstanding care with excellent outcomes. In 2013, the Willis-Ekbom Disease Foundation recognized the program for highly developed expertise in the diagnosis and management of Willis-Ekbom disease/restless legs syndrome and certified it as a WED-RLS Quality Care Center.

The UT MOVE Program is a collaborative effort of the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center and UTHealth Medical School, with specialty clinics that include Spasticity Management, DBS Selection and Programming, Botox® Injection and Intrathecal Baclofen Pump Therapy. Because rehabilitation is integral to good outcomes, we work closely with the physical and occupational therapists and speech-language pathologists in inpatient and outpatient clinics and at TIRR Memorial Hermann to research new approaches to improving treatment. In 2013, patient visits continued to increase, and a new UT MOVE clinic was established at Memorial Hermann The Woodlands Hospital.

The movement disorders medical team uses proven and investigational medications and interventional

methods to manage Parkinson's disease, Parkinsonian disorders, generalized and focal dystonia, essential tremor, Huntington's chorea, restless legs syndrome, Alzheimer's disease, cortical and subcortical dementias, cerebral palsy, spasticity, ataxias, gait disorders, spinal and brain trauma-related movement abnormalities, multiple sclerosis-related movement abnormalities and other inherited and acquired neurodegenerative diseases. The team's treatment philosophy is grounded in the early identification of disease and early use of neuromodulating or neuroprotective approaches. Affiliated physicians maintain patients at the highest level of function possible, based on symptom-driven therapeutic goals set by the physician and patient. In developing and adjusting our treatment plans, they consider the whole person, as well as the patient's environment and support groups. They also emphasize education, and encourage patients to stay mentally and physically active and to have fun. The program partners with TIRR Memorial Hermann in a comprehensive UT MOVE/Neurorehabilitation Program that incorporates neurologically driven rehabilitation as part of our treatment approach.

The deep brain stimulation (DBS) program for Parkinson's tremor, dystonia and essential tremor, offered at the Mischer Neuroscience Institute at the Texas Medical





Center and through Mischer Neuroscience Associates in the community, is known for low complication rates and outstanding outcomes. Based on the skill of neurological and neurosurgical teams and their expertise in DBS programming, we advocate for early use of deep brain stimulation in appropriate patients. In 2014, the DBS program experienced record growth, and the director was the only representative from the United States participating in the international Consensus Panel to formulate Criteria for the Selection of Parkinson's Disease patients for DBS therapy.

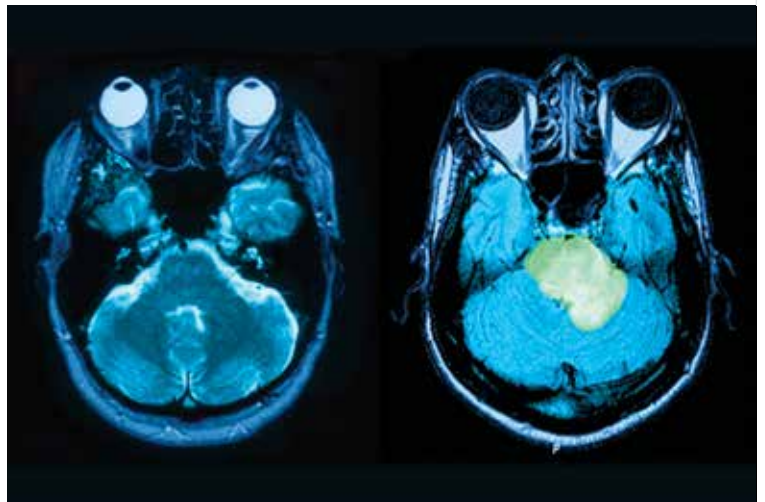
In addition, UT MOVE operates a referral program to serve community neurologists who select patients for deep brain stimulation. UT MOVE physicians provide intraoperative micro-electrode recording and electrode stimulation testing to determine and confirm the best DBS placement to reduce disease symptoms. The results are shared with referring neurologists, allowing them to benefit from this information and improving subsequent programming. Following DBS placement, patients are returned to the referring physician.

Research within the division of Movement Disorders at UTHealth Medical School has increased dramatically in recent years. The program is part of the Parkinson's Study Group, Huntington's Study Group, Tremor Research Group, Dystonia Coalition and Restless Legs Syndrome Study Group. Recent research includes a longitudinal prospective study on biomarkers and pre-symptomatic biomarkers for Parkinsonian syndromes, which led in 2013 to finding immune-mediated markers of disease activity and proposed cell therapy intervention for Parkinsonism. Additional research includes deep brain stimulation in the treatment of medication-refractory tremors in patients with co-morbid peripheral neuropathy, evaluation of a novel scale to assess psychosis in patients with idiopathic Parkinson's disease, managing sleep problems in Parkinson's patients, a novel medication for Huntington's disease and a Huntington's disease bio repository study. Other endeavors include a dystonia bio repository trial, novel medications for Parkinson's disease and Parkinson's dyskinesia, a novel medication for tardive dyskinesia, a botulinum toxin B trial for sialorrhea and two different botulinum toxin trials for cervical dystonia. The program is also the coordination center for the focused ultrasound brain surgery for essential tremor trial.

Multiple Sclerosis

The Multiple Sclerosis Program at the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center has established a track record of leading-edge care using groundbreaking techniques to diagnose, evaluate, manage and treat adult patients with MS and other demyelinating disorders. The scope of expertise of affiliated physicians is broad and includes patients in all stages of MS, as well as those with neuromyelitis optica, transverse myelitis and optic neuritis. The physicians are experienced in the appropriate use of aggressive therapies in severe cases.

Organized in 1983, the Multiple Sclerosis Research Group (MSRG) has participated in numerous clinical trials of novel disease-modifying therapies, serving as the lead center for international studies, several of which were pivotal in gaining FDA approval of currently available treatments for MS. Recently completed research includes a National Institutes of Health-sponsored trial of combined therapy with interferon beta-1a and glatiramer acetate in patients with early relapsing MS (the CombiRx Trial); the safety and efficacy of oral fampridine-SR; detection of MS-related cognitive impairment; the relationship of Epstein-Barr virus and MS; and serial magnetic resonance spectroscopy in MS, among others. Investigators in the MSRG and the department of Diagnostic and Interventional Imaging at UTHealth Medical School also recently completed a National MS Society-sponsored study of chronic cerebrospinal vascular insufficiency (CCSVI) and have embarked on a study designed to determine if pharmacological manipulation of cerebral perfusion pressure can protect brain tissue in MS patients.



The program was the first in the world to conduct preclinical studies on the effects of combined therapy with immunomodulating drugs and to explore the effects of oral cytokines in modulating MS and Type 1 diabetes. It is the first and only center in Houston to direct national and international clinical trials in MS, and remains the North American leader in studies of primary progressive multiple sclerosis, as well as the most active center in Texas in the conduct of organized clinical trials of new therapies for MS. Affiliated physicians are at the forefront of investigator-initiated research in immune regulation in MS, infection as a cause of MS, MS-related cognitive impairment and MS-related MRI findings.

In the department of Neurology's state-of-the-art Magnetic Resonance Imaging Analysis Center, physicians use spectroscopic and diffusion tensor imaging with tractotomy, as well as other advanced diagnostic tools. Following diagnosis, patients benefit from

Multiple Sclerosis Journal, 2014, Vol. 20(3), 365-73

Hypoperfusion and T1-hypointense Lesions in White Matter in Multiple Sclerosis

Narayana PA, Zhou Y, Hasan KM, Datta S, Sun X, Wolinsky JS

Background: Longitudinal magnetic resonance imaging (MRI) studies show that a fraction of the multiple sclerosis (MS) T2-lesions contain T1-hypointense components that may persist to represent severe, irreversible tissue damage. It is not known why certain lesions convert to persistent T1-hypointense lesions.

Objective: We hypothesized that the T1-hypointense lesions disproportionately distribute in the more hypoperfused areas of the brain. Here we investigated the association between hypoperfusion and T1-hypointense lesion distributions.

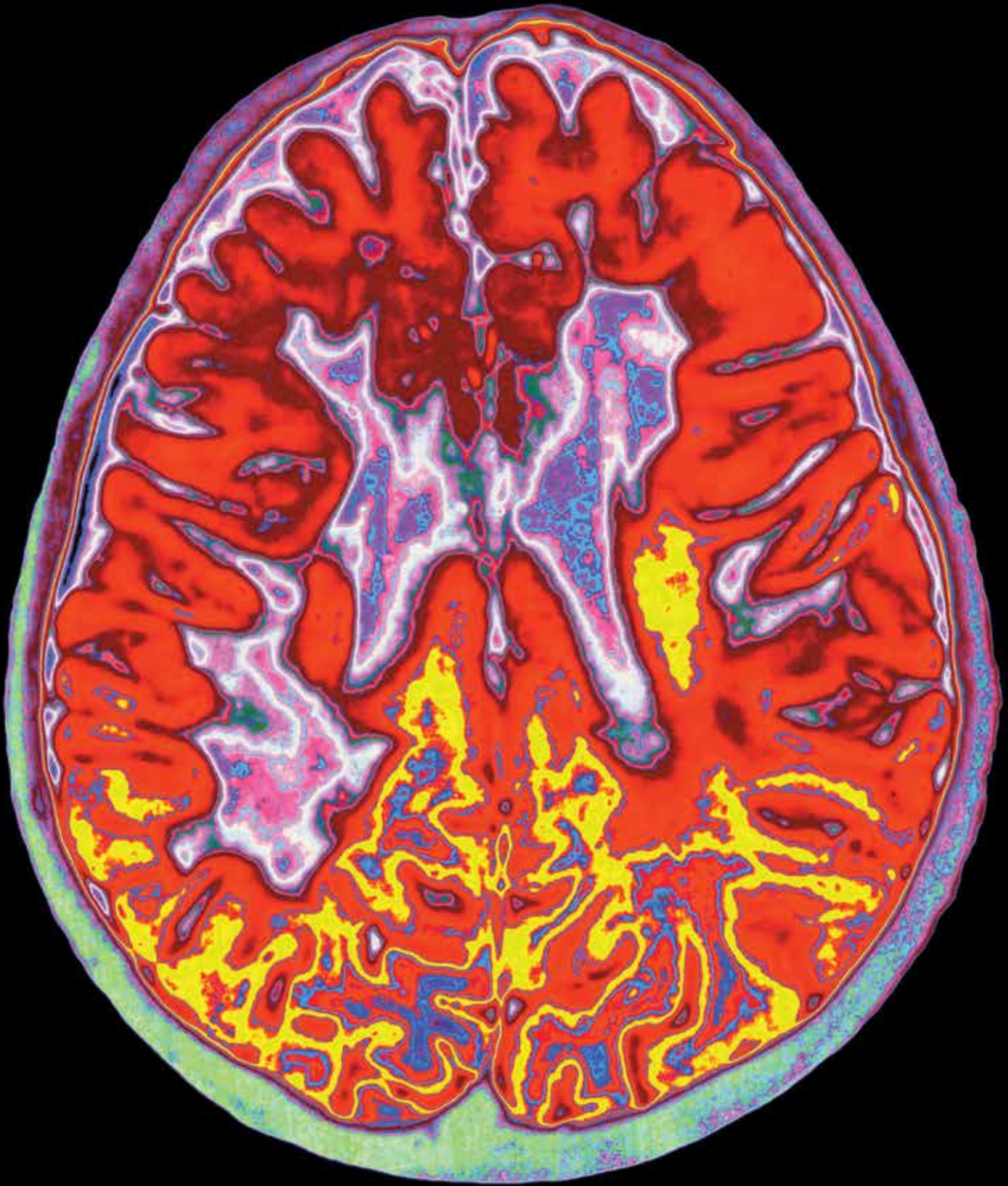
Methods: MRI and cerebral blood flow (CBF) data were acquired on 45 multiple sclerosis (MS) patients and 20 healthy controls. CBF maps were generated using pseudo-continuous arterial spin labeling technique. The lesion probability distribution maps were superimposed on the CBF maps.

Results: Two distinct CBF clusters were observed in the white matter (WM) both in healthy controls and MS patients. An overall reduction in CBF was observed in MS patients compared to healthy controls. The majority of the T1-hypointense lesions were concentrated almost exclusively in the WM regions with lower CBF. The T2-hyperintense lesions were more generally distributed in both higher and lower perfused WM.

Conclusion: This study suggests an association between hypoperfusion and T1-hypointense lesions.

breakthrough treatment options that include injectable immunomodulators, immunosuppressives and other agents designed to treat the debilitating symptoms of MS. Investigators also use the MRI Analysis Center to monitor the effects of promising oral drugs in pivotal efficacy trials. The Center was pivotal in providing quantitative imaging data that supported the regulatory approval of the oral agent teriflunomide for use in relapsing forms of MS in the United States, Europe and a growing number of countries worldwide, determining the optimal drug dose and extending the results of its benefits when used in first symptom-onset disease.

The Multiple Sclerosis Program's goal is to maintain patients at the highest level of function possible, with early use of immunoactive agents to prevent disease progression. Because rehabilitation is integral to each patient's treatment plan, affiliated physicians work closely with the physical medicine and rehabilitation specialists and therapists at TIRR Memorial Hermann, a national leader in medical rehabilitation and research, as well as the inpatient neurorehabilitation team at the Mischer Neuroscience Institute.



Neurocognitive Disorders

Physicians affiliated with the Neurocognitive Disorders Center evaluate and treat patients who present with changes in thinking, behavior and mood, and investigate the disorders underlying these changes. Because many neurological and psychiatric disorders present with similar symptoms, early and accurate diagnosis is critical to timely treatment.

The Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center was the first in Houston to use a PET imaging agent that binds to amyloid in the brain, allowing physicians to test for Alzheimer's disease (AD) with greater specificity. By using a florbetapir scan to rule out the disorder, physicians affiliated with the Center have been able to provide patients with the assurance that they do not have AD. Using this and other sophisticated new technologies, they are studying Alzheimer's disease and its risk factors at the clinical and cellular levels. Their goal is to diagnose AD and other dementias earlier and more cost effectively, before patients become symptomatic, and to find new treatments to delay or prevent development of the disorder. Another continued focus is the investigation of a transmissible component to AD in blood, and the development of a blood test for AD.

With support from a generous donor, the researchers are developing new PET agents to image inflammation and another important brain protein called tau. They expect these new agents to be useful in investigations of the pathologic mechanisms underlying AD, traumatic brain injury and other neurocognitive disorders, resulting in new treatment approaches.

Affiliated physicians are also developing new PET imaging agents to distinguish Alzheimer's disease from frontotemporal dementia, the second most common neurodegenerative dementia. In 2014, the Center expanded its diagnostic program with the addition of a third neuropsychologist.



RESEARCH HIGHLIGHT

Neurodegenerative diseases affect millions of Americans, but their causes remain unclear. Researchers affiliated with Center are investigating genetic contributions to neurodegenerative diseases by comparing healthy patients to those with disease and by testing for a transmissible component to the disorders. They are also studying the potential use of stem cells in the treatment of neurodegenerative disorders.

Traumatic brain injury is known to increase the risk of Alzheimer's disease. Researchers affiliated with the Center have found that even minor traumatic brain injury leads to a fourfold increase in the risk for frontotemporal dementia. They have also found that post-traumatic stress disorder (PTSD) may contribute to dementia, increasing the risk of stroke and substance abuse and resulting in permanent changes in the brain. They are investigating other risk factors for dementia, including family history, high blood pressure, high cholesterol or triglycerides, diabetes, obesity and smoking, with the aim of reducing risk. These investigations in a treatment trial aimed at preventing the development of PTSD allow them to target patients at the highest risk.

The Stroke-Dementia Prevention Clinic builds on the recognition that there are multiple, modifiable risk factors for dementia. Physicians at the clinic evaluate patients with symptoms and also those without symptoms who are at risk based on family history.

Cell Reports, 10 April 2014, 7:261-68

Detection of Misfolded A β Oligomers for Sensitive Biochemical Diagnosis of Alzheimer's Disease

Salvadores N, Shahnawaz M, Scarpini E, Tagliavini F, Soto C

Alzheimer's disease (AD) diagnosis is hampered by the lack of early, sensitive and objective laboratory tests. In this article we describe a sensitive method for biochemical diagnosis of AD based on specific detection of misfolded A β oligomers, which play a central role in AD pathogenesis.

The protein misfolding cyclic amplification assay (A β -PMCA) exploits the functional property of A β oligomers to seed the polymerization of monomeric A β . A β -PMCA allowed detection of as little as 3 fmol of A β oligomers. Most importantly, using cerebrospinal fluid, we were able to distinguish AD patients from control individuals affected by a variety of other neurodegenerative disorders or nondegenerative neurological diseases with overall sensitivity of 90 percent and specificity of 92 percent. These findings provide the proof-of-principle basis for developing a highly sensitive and specific biochemical test for AD diagnosis.

Neuromuscular Disorders



Physicians affiliated with the Neuromuscular Diseases Program are subspecialized in complex neuromuscular disorders that are difficult to diagnose and treat, including neurodegenerative disorders, inflammatory nerve and muscle disorders, autoimmune neuromuscular junction disorders, traumatic nerve injuries and toxic metabolic disorders of the peripheral nerves and muscles. The program is a designated center of excellence for Guillain-Barré syndrome (GBS) and chronic inflammatory demyelinating polyneuropathy (CIDP) and records more than 4,000 patient visits annually, primarily adults age 18 and older. About two-thirds of patients seen by affiliated physicians are over the age of 50.

Neurodiagnostic facilities include a state-of-the-art Electromyography (EMG) Laboratory and a Muscle and Nerve Laboratory. The EMG Lab provides comprehensive nerve conduction studies and EMG evaluations performed by expert staff.

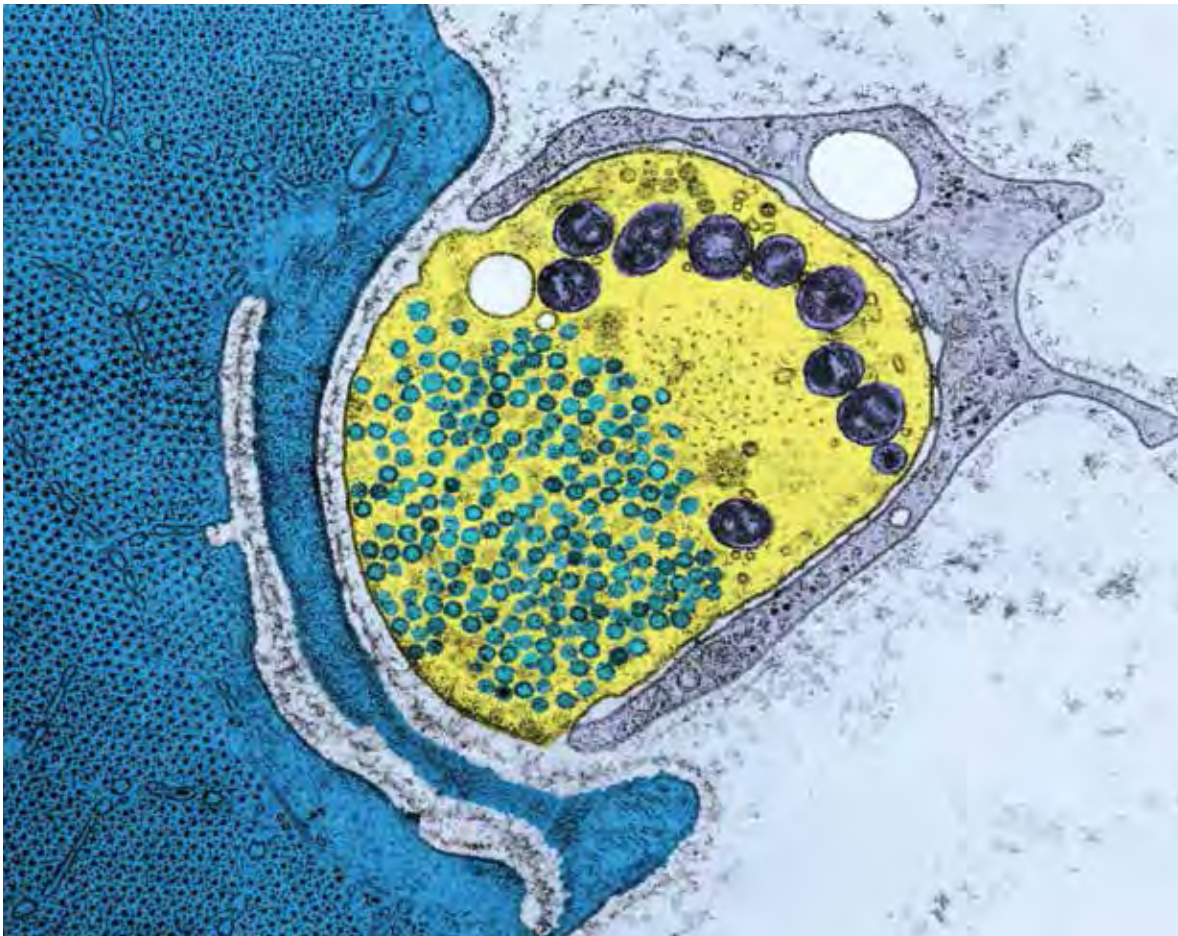
Because electrodiagnostic evaluation is an extension of clinical findings, our medical specialists perform a focused neuromuscular examination, including history and physical, before conducting the electrical test. In addition to nerve conduction and EMG, electrodiagnostic studies available at the lab include repetitive nerve stimulation, blink reflexes, cranial nerve studies, single-fiber electromyography and facial/trigeminal neuropathy. An invaluable diagnostic test, EMG provides evidence in support of diagnoses of peripheral neuropathies; motor neuron diseases such as amyotrophic lateral sclerosis and spinal muscular atrophy; muscle disorders such as myopathy and muscular dystrophy; neuromuscular junction disorders such as myasthenia gravis; entrapment neuropathies such as carpal tunnel syndrome, ulnar and peroneal neuropathies; and traumatic nerve injury, including evaluation of the brachial plexus and facial neuropathy. The Neuromuscular Disorders Program is the only program in Houston that provides single-fiber EMG.

Studies conducted in the Muscle and Nerve Laboratory help improve diagnosis in cases with limited neuromuscular findings by locating abnormalities at a pathologic/microscopic level. Affiliated subspecialists perform muscle, nerve and skin biopsies, which are further processed by highly experienced staff. Their preferred technique is open biopsy under local anesthesia, which reduces the likelihood of missing abnormalities in cases of patchy involvement, such as in inflammatory myopathies. They also perform skin

biopsies for the diagnosis of small-fiber neuropathy, and the lab is the only center in Houston that processes skin biopsy specimens for the diagnosis of small-fiber neuropathies.

Current research is focused on developing new strategies to treat neuropathic disorders and enhance nerve repair. With funding from the National Institutes of Health and the GBS/CIDP Foundation International,

affiliated investigators are evaluating the role and pathogenic mechanisms of anti-ganglioside antibodies in autoimmune neuropathy; using diffusion tensor imaging to assess and quantify nerve degeneration and regeneration in patients with traumatic nerve injuries; investigating modulation of FcRn as a strategy to prevent autoantibody-mediated nerve injury; and examining the pathobiologic effects of anti-ganglioside antibodies on nerve regeneration.



Neurorehabilitation

Patients recovering from neurological illness or injury benefit from innovative neurorehabilitative technology and integrated care at the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center and TIRR Memorial Hermann. Subspecialists affiliated with both facilities are expert in the treatment of traumatic brain injury, spinal cord injury, stroke, brain and spinal tumors and other neurological disorders such as multiple sclerosis, Parkinson's disease and Guillain-Barré syndrome.



MISCHER NEUROREHABILITATION

Mischer Neurorehabilitation's clinical, research and education programs are led by neurorehabilitation specialist Nneka Ifejika, M.D., an award-winning author, mentor and reviewer in the fields of neurology and physiatry. In 2010, Dr. Ifejika received a grant from the National Institute of Neurological Disorders

and Stroke (NINDS) to study the impact of intravenous thrombolysis and healthcare-associated infections on rehabilitation care. Within a two-year period, she published five articles in peer-reviewed journals and received the American Academy of Physical Medicine and Rehabilitation Best Neurological Research Award.

Under Dr. Ifejika's direction, Memorial Hermann-Texas Medical Center's 23-bed inpatient neurorehabilitation unit provides comprehensive rehabilitation care, consisting of an intensive program of physical therapy, occupational therapy and speech-language pathology. The program is distinguished from others by its focus on incorporating clinical research in stroke prevention and health disparities in the rehabilitation setting.

Patients and families are an integral part of the Neurorehabilitation Program. Upon admission, they discuss their goals with an interdisciplinary team and together, they develop a treatment plan designed to help the patient reach the highest possible level of function. Mischer Neurorehabilitation provides innovative and evidence-driven rehabilitation by blending manual and technologic therapies, including Korebalance™, Bioness® and IREX® Virtual Reality.

Affiliated physicians provide outstanding patient care and conduct award-winning research on the underlying conditions that impact rehabilitation progress, applying their advanced knowledge directly to the care of each patient they serve. This level of advanced training is a critical component of the rehabilitation



Swipe Out Stroke (SOS): Feasibility of Using a Consumer-based Electronic Application to Improve Compliance with Weight Loss in Obese Minority Stroke Patients

PRINCIPAL INVESTIGATOR: **Nneka L. Ifejika, M.D.**

Director of Neurorehabilitation, Mischer Neuroscience Institute

Assistant Professor, Department of Neurology, UTHealth Medical School

Background: Minority compliance with obesity management has been a long-standing concern in the stroke community. Unfortunately, structured weight loss programs are expensive, and compliance significantly decreases upon program completion. Information technology is an innovative, cost-effective way to bridge this gap. Minorities spend more than 4.5 billion dollars annually on consumer electronics, making studies that utilize media consumption ideal for health outreach and health promotion efforts in minority communities. Many patients would benefit from an electronic application that facilitates personal contact, provides positive reinforcement and gives support using a low-cost, Smartphone-based platform.

To date, there are no studies evaluating the feasibility of using a consumer-based electronic application (CBEA) to improve compliance with weight loss in high-risk, obese minority stroke patients. This proposal will address this critical gap by examining whether such an intervention will improve adherence with weight loss measures, thereby improving related vascular risk factors, such as hypertension, in patients within the critical first six months post stroke.

Objectives: The study will evaluate the feasibility (dropout rate and adherence) of using a physician-monitored CBEA to improve weight loss in obese minority stroke patients compared to usual care. The investigators hypothesize that participants who are randomized to the CBEA group will have a lower dropout rate and higher adherence to the weight loss intervention compared to usual care. The second aim of the study is to examine percentage weight loss in the CBEA group and the usual care group, based on the hypothesis that patients who use the physician-managed CBEA will have a larger percent weight loss at six months compared to usual care. Results from this study will have broader implications for translation to other conditions correlated with obesity that have increased incidence in the minority community, e.g., myocardial infarction. The National Institute of Neurological Disorders and Stroke (NINDS) has developed a health disparities division, which has a paucity of Phase I minority-initiated trials. This pilot study will provide critical information with the potential to inform an efficacy study.



process, particularly as Mischer Neurorehabilitation serves as an extension of the Mischer Neuroscience Institute's world-renowned vascular neurology and neurosurgical programs. Because they are trained in the administration of the National Institutes of Health Stroke Scale and the modified Rankin Scale, used by vascular neurologists to assess stroke deficits and post-stroke disability, they can directly interpret acute neurologic changes and communicate across disciplines without the need for outside consultation. This combination of clinical excellence and research innovation makes the Mischer Neurorehabilitation team a leader in the post-acute treatment of neurologic conditions.

TIRR MEMORIAL HERMANN

An international leader in medical rehabilitation and research for 55 years, TIRR Memorial Hermann is a

model for interdisciplinary rehabilitation services, patient care, education and research. The hospital's Brain Injury and Stroke Program has been designated a Traumatic Brain Injury Model System (TBIMS) with funding from the National Institute on Disability and Rehabilitation Research (NIDRR) since 1987, and is one of only 16 in the nation. For 25 consecutive years, *U.S. News & World Report* has named the hospital to its list of "America's Best Hospitals." In 2014, TIRR Memorial Hermann was ranked third in the nation.

Research at the hospital is conducted by affiliated physicians and scientists, and also by therapists, nurses, the chaplain and residents as they advance their knowledge in subspecialty areas of rehabilitation medicine. The Brain Injury Research Center (BIRC) brings together world-renowned researchers to study the complicated facets of recovery from brain injury,



leveraging resources from NIDRR to conduct research identifying effective treatments. The Spinal Cord Injury and Disability Research Center has broadened its team with the addition of experts in cognitive and psychosocial research. These new faculty use a holistic approach to studying various aspects of recovery for people with spinal cord injury and disorders across the lifespan, and identify new ways to improve function and quality of life. The Independent Living Research Utilization (ILRU) program is a national center for information, training, research and technical assistance in independent living. The NeuroRecovery Research Center has been expanded to include Robotics, the UHealth Motor Recovery Laboratory at TIRR Memorial Hermann, the Neuromodulation and Neural Interfaces Lab, NeuroMyoelectric Engineering for Rehabilitation and the Neurorehabilitation Research Laboratory.

With the completion of the TIRR Memorial Hermann Research Center, all of the hospital's research programs are now together under one roof for the first time in the institution's history. The proximity of researchers fosters discussion, exchange of ideas and cross-pollination between research projects and clinical care, and ensures continuous two-way communication between clinicians and researchers throughout the entire investigation process. It also allows clinicians to put new knowledge to work more quickly and effectively to advance the care of patients.

Although the medical acuity of patients is much higher than in most rehabilitation facilities nationwide, TIRR Memorial Hermann consistently has significant, positive functional independence measure (FIM) change scores due to innovations in therapy and

QUALITY & OUTCOMES MEASURES

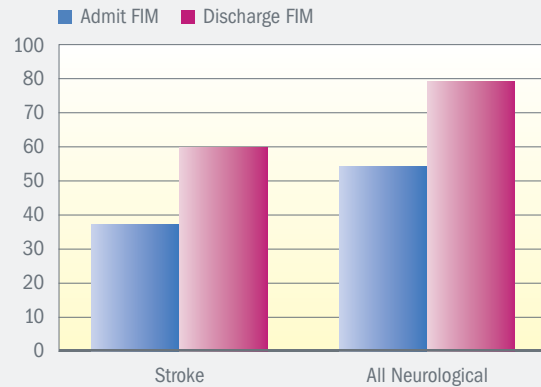
equipment. In addition to two Restorative Therapies FES (functional electronic stimulator) bikes, Bioness® hand rehabilitation and foot drop systems, the VitalStim Experia™ clinical unit and IOPI Medical's Iowa Oral Performance Instrument, the hospital has a closed-loop body weight support system by Bioness, called the Vector Elite, in its main therapy gym. The Vector allows patients to walk continuously in the gym environment over more than 100 feet of track.

The hospital has acquired and trained with two robotic exoskeleton devices for research and future clinical use – Ekso™ and ReWalk™. The physical therapy team has collaborated with physician leaders in the Spinal Cord Injury and Disability Research Center and received a TIRR Memorial Hermann Innovations grant to support a pilot study with the devices. In addition, the hospital's weekend therapy program and “seven meaningful days” philosophy has allowed our teams to improve efficiency of care delivery, resulting in greater functional progress for patients. Our speech-language pathologists have implemented fiber-optic endoscopic evaluation of swallowing (FEES) fully into care.

The TIRR Memorial Hermann Outpatient Medical Clinic is a physician-based clinic designed to meet the needs of individuals with disabilities who require initial or continuing care by a physician. The clinic is redefining the hospital's outpatient rehabilitation care model by providing a patient-centered medical home for people with disabilities. Thirty-three specialty medical clinics include brain injury, stroke, spasticity management, neurosurgery, neurology, neuropsychology, psychiatry, urology, gynecology, cardiology, gastroenterology, cognitive behavioral therapy and more, in addition to pharmacist-run wellness clinics for anticoagulation, diabetes and hypertension management.

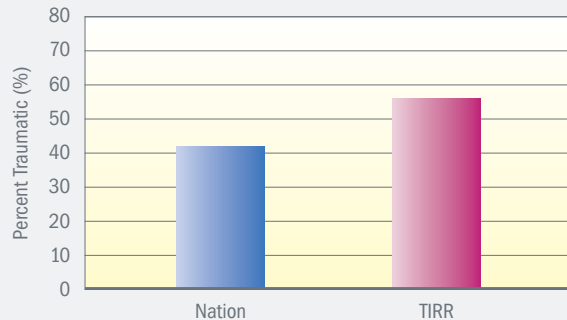
TIRR is a registered trademark of TIRR Foundation.

Neurorehabilitation: Functional Independence Measure Change



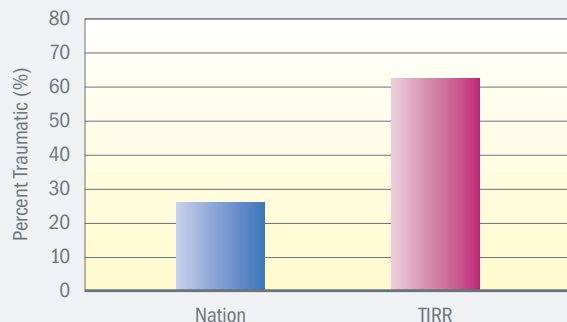
Source: chart data based on calendar year 2013

Traumatic Brain Injuries Treated



Source: chart data based on calendar year 2013

Spinal Cord Injuries Treated



Source: chart data based on calendar year 2013

Neurotrauma and Neuroscience Critical Care

The Neurotrauma and Neuroscience Critical Care Program at the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center is internationally recognized for the treatment of high-acuity brain and spinal cord injuries. Affiliated physicians manage more neurotrauma cases than any other center in the southwestern United States, with neurointensivists and experienced mid-level practitioners staffing the dedicated Neuroscience ICU around the clock to provide ongoing intensive care to critically ill patients. The number of faculty

and size of the program continue to grow, with nearly 2,400 brain and spine trauma patients treated in calendar year 2013.

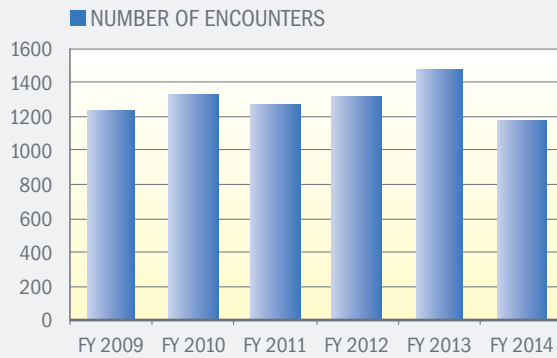
The Neurotrauma and Neuroscience Critical Care Program is an international leader in research conducted on innovative treatments following neurotrauma, including participation in several multicenter trials. Investigators at the Mischer Neuroscience Institute, UTHealth Medical School and TIRR Memorial Hermann are studying biomarkers for pain in spinal cord injury; cranioplasty





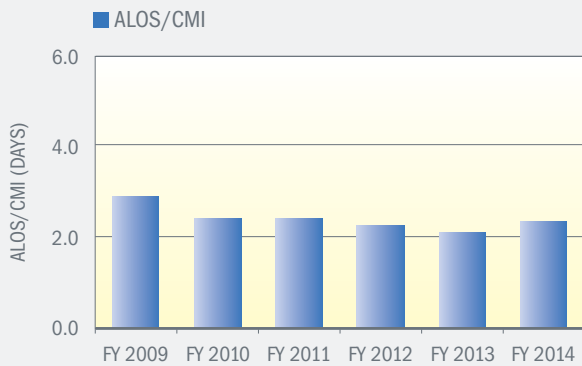
QUALITY & OUTCOMES MEASURES

Traumatic Brain Injury Volumes



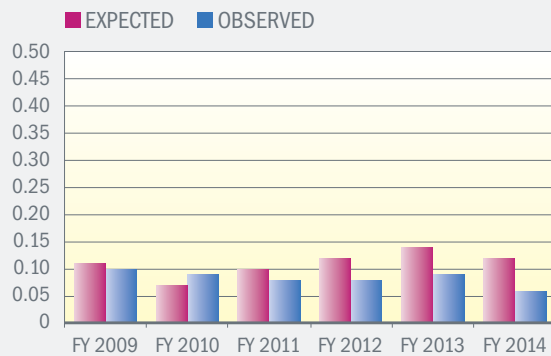
Source: Chart data based on DRG per fiscal year

Traumatic Brain Injury: Length of Stay (CMI Adjusted)



Source: Chart data from the University HealthSystem Consortium

Traumatic Brain Injury: Inpatient Mortality



Source: Chart data from the University HealthSystem Consortium

outcome following decompressive craniectomy; adult stem cell therapy in severe traumatic brain injury (TBI) and acute stroke patients; the effects of erythropoietin on cerebrovascular dysfunction and anemia in TBI; neural and behavioral sequelae of blast-related TBI; progesterone for the treatment of TBI; the safety and pharmacokinetics of riluzole in patients with traumatic acute spinal cord injury; and other basic science research and clinical trials. The Neuroscience Critical Care Program, which is led by Kiwon Lee, M.D., FACP, FAHA, FCCM, associate professor and vice chair of neurosurgery and neurology for critical care, utilizes the most advanced medical technologies and devices, including a multimodal monitoring system.

The Mischer Neuroscience Institute was the first in Texas and the only center in the region to receive the highly coveted Comprehensive Stroke Center certification from The Joint Commission and the American Heart Association/American Stroke Association. The Neuroscience ICU team provides comprehensive high-level care for all neurological and neurosurgical vascular emergencies and illnesses, with more than 2,500 vascular cases treated annually. The dedicated ICU team operates in a closed-unit model and is the primary care team for surgical vascular patients, providing leading-edge care 24/7.

Patients with acute neurological injuries benefit from the Texas Trauma Institute at Memorial Hermann-Texas Medical Center – one of only two Level I trauma centers in the area and one of the busiest in the nation – and from Memorial Hermann Life Flight®, the first air medical transport service established in Texas and the second in the nation. Built on the

RESEARCH HIGHLIGHT

hospital's long-term collaboration with UTHealth Medical School, the 200-bed Texas Trauma Institute provides high-quality care to both adult and pediatric trauma patients and offers a full spectrum of service including access to Houston's only verified burn center. Physicians affiliated with the Institute drive innovations in trauma care by moving research quickly from the laboratory to the bedside.

Patients at the Texas Trauma Institute also have access to additional services essential to trauma care: trauma and neurocritical care; trauma surgery; orthopedic surgery; emergency general surgery; emergency medicine; neurology and neurosurgery; oral maxillofacial, plastic and ENT surgery; hand surgery and plastic reconstructive surgery; transfusion medicine; physical medicine and rehabilitation; obstetrics and gynecology; urology; ophthalmology; heart and vascular; anesthesia; radiology; and hospitalists.

Memorial Hermann Life Flight, which is accredited by the Commission on Accreditation of Medical Transport Services, provides high-quality care and safe air transport for critically ill and injured patients. The Adult and Children's Transport Teams operate within a 300-mile radius of Houston using ground ambulance, a 150-mile radius using 24/7 air ambulance and far beyond using private jet services. Memorial Hermann-TMC was the first hospital to give blood transfusions during transport. For staff members, every second counts.

Stroke, 2013 Jul;44(7):1825-9

Impact of Acute Cocaine Use on Aneurysmal Subarachnoid Hemorrhage

Chang TR, Kowalski RG, Caserta F, Carhuapoma JR, Tamargo RJ, Naval NS

In this retrospective study, researchers analyzed the impact of acute cocaine use, which has been temporally associated with aneurysmal subarachnoid hemorrhage (aSAH), on patient presentation, complications and outcomes. They reviewed data of patients admitted with aSAH between 1991 and 2009, and compared it with aSAH patients who had not had recent exposure to cocaine. Complications included aneurysm re-rupture and delayed cerebral ischemia, and outcome measures included hospital mortality and functional outcome.

Data for 1,134 aSAH patients, 142 of which had associated cocaine use, were reviewed. The researchers found that cocaine users were more likely to be younger and had higher rates of aneurysm re-rupture. Cocaine users were also less likely to survive hospitalization than nonusers. After controlling for other factors impacting aSAH outcome, there were no differences in delayed cerebral ischemia or functional outcomes between the two groups.

PerihematOmal Response to Tissue Injury and Clinical Outcomes (PORTICO)

PRINCIPAL INVESTIGATOR: **Nancy J. Edwards, M.D.**

Assistant Professor, Vivian L. Smith Department of Neurosurgery

UTHealth Medical School

Intracranial hemorrhage (ICH) accounts for 10 to 15 percent of all strokes in the United States (approximately 2 million cases annually worldwide) and has been associated with high mortality and morbidity. Patients who do survive are often left with significant neurological disability due to 1) primary brain injury from the hemorrhage itself along with 2) a series of secondary brain injuries that occur hours to weeks from hemorrhage ictus. One manifestation of this type of secondary brain injury is radiographically observable perihematomal edema (PHE). PHE often contributes to in-hospital neurologic deterioration and may even affect long-term clinical outcomes.

PORTICO is a prospective observational study whose goal is to identify biomarkers of inflammation and hemoglobin degradation that correlate with clinical and radiologic outcomes, including the degree of PHE and the functional neurologic status of our ICH patients in the long-term. The researchers will examine several target biomarkers in serum and CSF in a longitudinal fashion; for those patients who require intracranial hematoma evacuation, they will also analyze cross-sectional data from perihematomal neuronal tissue obtained during the evacuation. Biologic samples of consenting patients will be banked in the Neuroscience Research Repository according to protocol. The medical records of enrolled patients will be reviewed for relevant clinical information – baseline demographic variables, etiology of ICH, severity of ICH, placement of a ventricular drain, need for intubation/mechanical ventilation, medical/surgical complications that develop through the patient’s hospital course and disposition. Neuroradiologic images obtained during the routine clinical care of the patient will be volumetrically analyzed.

The neurologic status and functional independence of enrolled ICH patients will be measured at discharge and 90 days. Outcome scoring systems such as the modified Rankin Scale, Barthel Index, and Euro-qol will be used; these are all widely accepted and experimentally validated as measures of neurologic outcome following brain injury. As no changes will be made to patient care and there is no study intervention, there is minimal risk to the patient and no adverse events are expected.

Spine Disorders

The renowned spine surgeons affiliated with the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center offer the most advanced treatments available today, both surgical and nonsurgical. They perform more than 2,000 procedures annually, making the spine program the largest in the region. Thanks to their knowledge and talent, the Institute is nationally recognized for leading-edge medicine and consistently ranked among quality benchmarking organizations as a leader in clinical quality and patient safety.

Nationally and internationally renowned neurosurgeon Daniel H. Kim, M.D., FAANS, FACS, has expanded the spinal neurosurgery program and added expertise in

reconstructive peripheral nerve surgery. Dr. Kim is a fellowship-trained, board-certified neurosurgeon with expertise in minimally invasive spinal surgery, both endoscopic and robotic; peripheral nerve surgery; and complex spinal reconstruction. A clinical and educational leader in his field, Dr. Kim has authored hundreds of papers and published 16 surgical textbooks, many of which are used at leading medical schools to teach standard-of-care techniques for neurosurgery. Two new textbooks were published in 2013: *Surgical Anatomy and Techniques to the Spine and Lumbosacral and Pelvic Procedures*. He is a preeminent researcher in peripheral nerve repair through nerve transfer and nerve graft, and is also recognized for his work



in neurorehabilitation through robotics and cortical stimulation, spinal biomechanics and innovative neuromodulation treatments for chronic pain.

At the Spine Center a multidisciplinary team works in new, state-of-the-art facilities equipped with advanced instrumentation and dynamic imaging systems. They are skilled in minimally invasive spine procedures and innovative treatment options for patients with back pain resulting from trauma, degenerative disc disease, osteoporosis and related stress fractures, and deformity. Rehabilitation begins in the hospital following surgery.

The Center's clinicians provide exceptional care for patients with traumatic spine injury, including the 10 to 20 percent of admissions through the Level I Texas Trauma Institute that involve neurological damage. Based on benchmark University HealthSystem Consortium data, the Spine Center's inpatient mortality for spine trauma, degenerative spine disease and elective spine surgery has been consistently lower than expected for the past six years. As faculty at UTHealth Medical School, surgeons at the Center educate the next generation of spine experts and shape the future of medicine through basic science research, clinical discovery and the development of new, breakthrough treatments.

Pain management is a critical part of the Institute's spine program. Gunjan S. Patel, M.D., who is fellowship trained and board certified in physical medicine and rehabilitation, specializes in non-surgical interventional spine, musculoskeletal and electrodiagnostic medicine. Her primary focus is on nonsurgical musculoskeletal and spine care, such as physical therapy, epidural injections and electrodiagnosis of nerve and muscle conditions that cause pain, numbness, tingling or weakness.

Anesthesiologist and Interventional pain management specialist Nadya M. Dhanani, M.D., joined the Spine Center team in 2014 after completing her fellowship in pain medicine at The University of Texas MD Anderson Cancer Center.

Physicians affiliated with the Mischer Neuroscience Institute are committed to providing exceptional clinical care with a strong focus on patient safety and the highest quality outcomes for patients. They specialize in artificial disk replacement, birth palsies, brachial plexus injuries, carpal tunnel syndrome, congenital spine disorders, median nerve injuries, nerve sheath tumors, neurofibromatosis, neuromodulation for nerve injuries, neuromodulation for chronic headache, pelvic plexus injuries, peripheral nerve injuries, peroneal nerve injuries, pudendal nerve entrapment, piriformis syndrome, radial nerve injuries, sciatic nerve injuries, spinal AVMs, spinal stenosis, spine and spinal cord tumors, spine deformity, spine disk herniation, spine fractures, spine infection, tibial nerve injuries and ulnar nerve entrapment.

Research under way at the Spine Center is focused on bringing promising therapies for spinal cord injury (SCI) patients from the laboratory to clinical trials in a manner that will provide evidence of effectiveness, with maximum safety, to patients undergoing treatment. Investigators are currently engaged in a Phase II trial of the anticonvulsant drug riluzole in patients with acute SCI, and a new stem cell trial for degenerative spine and trauma spine fusions.

A Randomized Trial Comparing Manual Physical Therapy to Therapeutic Exercises, to a Combination of Therapies, for the Treatment of Cervical Radiculopathy

PRINCIPAL INVESTIGATOR: **Gunjan S. Patel, M.D.**

Clinical Assistant Professor, Vivian L. Smith Department of Neurosurgery, UTHealth Medical School

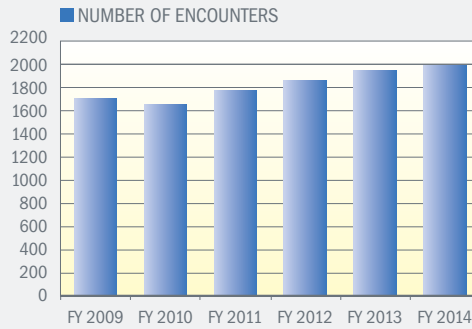
Objective: To determine which treatment method will produce superior outcomes for patients with cervical radiculopathy: manual physical therapy, therapeutic exercises or a combination of manual physical therapy and therapeutic exercises.

Design: Thirty patients with cervical radiculopathy were randomized into three treatment groups, one group receiving only manual physical therapy interventions, a second receiving only therapeutic exercises and the third receiving both manual physical therapy techniques and therapeutic exercises. Each patient was seen in three sessions per week for three weeks. The patients were then reevaluated by a therapist who was blinded as to which treatment group each patient received. Self-report measures of pain and function using a numeric pain rating scale (NPRS) and the Neck Disability Index (NDI), along with goniometric measurements of active cervical rotation were used as outcome measures. Results were analyzed using independent groups ANOVA.

Results: Each patient completed the Numeric Pain Rating Scale, in which they rated their current pain on a scale between 0 and 10, with 0 being the rating for no pain and 10 being the worst pain imaginable. This form was completed at the initial visit, once per week and at the final reassessment. The results showed that all three groups demonstrated significant improvements in pain, with the combination group showing significantly greater results when compared to the other two groups as determined by ANOVA. There was also no significant difference found between the severity of initial pain and the amount of improvement. The results of this study support the notion that even patients suffering from severe pain due to cervical radiculopathy may benefit from physical therapy interventions. The NDI contains 10 items, seven related to activities of daily living, two related to pain and one related to concentration. Each item is scored from 0 to 5 and the total score is expressed as a percentage, with the higher scores corresponding to greater disability. This form was completed at the initial visit, once per week, and at the final reassessment. The statistical results from the ANOVA showed that all three groups demonstrated significant improvements in function, with the combination group again showing the greatest results compared to the other two groups.

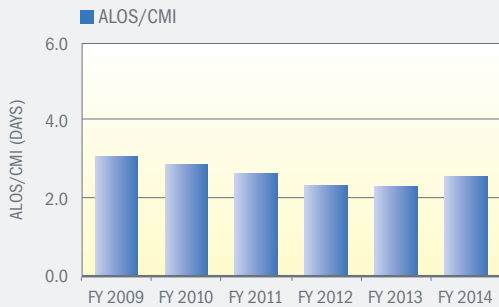
Conclusions: There has been research supporting the effectiveness of various physical therapy interventions for the treatment of cervical radiculopathy. There have been few randomized and blinded studies that have compared the effectiveness of one of these interventions over another. This study suggests that a multimodal treatment approach using a combination of manual therapy and strengthening exercises is superior to either intervention alone. Furthermore, patients with increased severity of symptoms at baseline, increased age, and lower initial functional scores may also benefit from physical therapy interventions and may result in near equal outcomes for those patients who have less severe initial symptoms/signs.

Spine Volumes



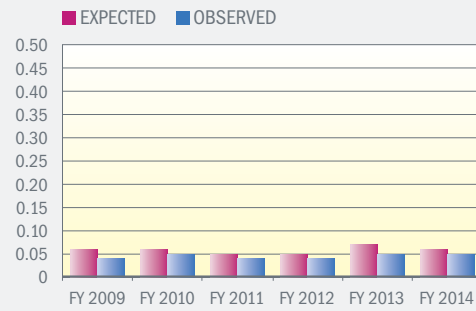
Source: Chart data based on DRG per fiscal year; adult populations

Spine Trauma: Length of Stay (CMI Adjusted)



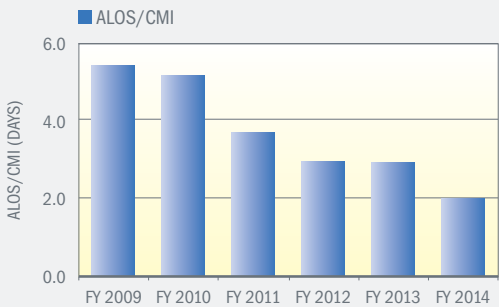
Source: Chart data from the University HealthSystem Consortium

Spine Trauma: Inpatient Mortality



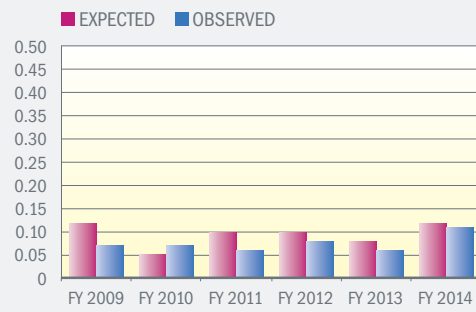
Source: Chart data from the University HealthSystem Consortium

Spine Tumors: Length of Stay (CMI Adjusted)



Source: Chart data from the University HealthSystem Consortium

Spine Tumors: Inpatient Mortality



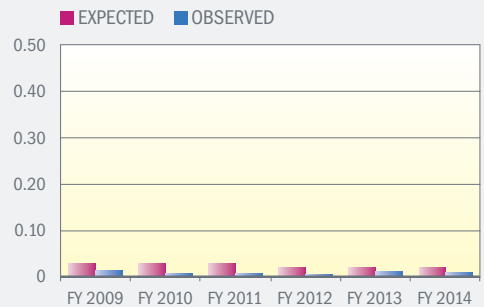
Source: Chart data from the University HealthSystem Consortium

Spine Degenerative or Elective: Length of Stay (CMI Adjusted)

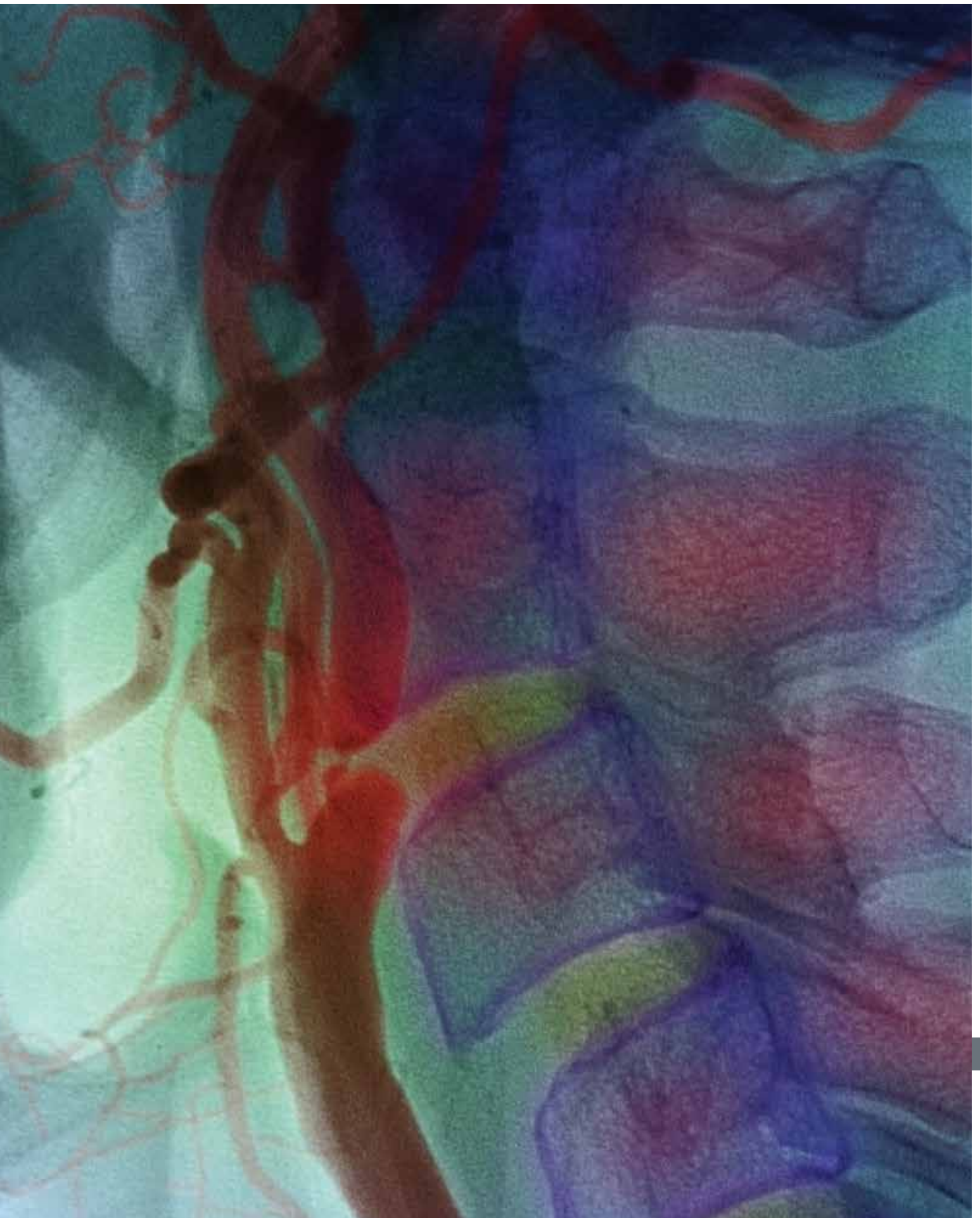


Source: Chart data from the University HealthSystem Consortium

Spine Degenerative or Elective: Inpatient Mortality



Source: Chart data from the University HealthSystem Consortium



A close-up photograph of a laboratory setting. A person wearing blue nitrile gloves is using a pipette to transfer liquid into a multi-well plate. The plate is placed in a centrifuge rotor, which is visible in the background. The rotor has several numbered slots (1-8) and a central hub. The pipette is held at an angle, and the liquid is being dispensed into one of the wells. The scene is brightly lit, and the focus is on the hands and the pipette.

Research
and Innovation

Physicians affiliated with the Memorial Hermann Mischer Neuroscience Institute and UTHealth Medical School are engaged in a broad and intensive research program focused on the mechanisms, treatment and cure of neurological disease and injury. They use diverse approaches – molecular, transgenic and electrophysiological techniques – in biomedical studies, translational research, clinical trials and technology development and assessment.

Research is supported by the National Institutes of Health, the Vivian L. Smith Foundation for Neurologic Disease, the American Stroke Association and other granting agencies. Research projects cover major areas of neurological disease, including stroke, aneurysm, spinal cord injury, brain tumor, stem cell therapies, neuroprotection, hypoxic encephalopathy, epilepsy, traumatic brain injury and Parkinson's disease. During the 2013-2014 fiscal year, researchers at the Institute and UTHealth Medical School received more than \$10.7 million in 76 grants and contracts. The following listing is a sample of ongoing or recently completed research projects.

CEREBROVASCULAR

A Phase III, Randomized, Placebo-controlled, Double-blind Study of the Combined Lysis of Thrombus with Ultrasound and Systemic Tissue Plasminogen Activator (tPA) for Emergent Revascularization (CLOBUST-ER) in Acute Ischemic Stroke

PRINCIPAL INVESTIGATOR: **Andrew D. Barreto, M.D.**

A randomized, placebo-controlled, double-blind Phase III clinical study to evaluate the efficacy and safety of ultrasound (US) using the SonoLysis headframe as an adjunctive therapy to tissue plasminogen activator (tPA) treatment in subjects with acute ischemic stroke.

Advanced Artificial Extracellular Matrix for Treatment of Chronic Stroke

PRINCIPAL INVESTIGATOR: **Laura Smith Callahan, Ph.D.**

The study aims to develop a di-functionalized hyaluronic acid matrix containing optimized neuroigin and laminin concentration for axon extension and restoration of neurological function in rat models of stroke.

ARTSS-2: A Pilot, Phase IIB, Randomized, Multicenter Trial of Argatroban in Combination with Recombinant Tissue Plasminogen Activator for Acute Stroke

PRINCIPAL INVESTIGATOR: **Andrew D. Barreto, M.D.**

All study participants in this randomized multicenter trial will be treated with rt-PA (0-3 hours or 0-4.5 hours) and randomized to one of three study arms: intravenous tPA along with low-dose argatroban, high-dose of argatroban or standard IV tPA alone. This trial is designed to estimate overall treatment benefit among stroke patients randomized to receive one of the three treatments. The study will also verify the safety of a low-dose combination of argatroban and rt-PA, test the safety of a high-dose combination treatment and assess the rates of early recanalization to determine treatment effect and assess reliability in predicting outcomes of the drug combination.

Assessment of Spleen Size Reduction and Inflammatory Markers in Acute Stroke Over Time (ASSIST)

PRINCIPAL INVESTIGATOR: **Sean Savitz, M.D.**

An observational study to evaluate changes in spleen size and blood flow over time using ultrasound and corresponding changes in inflammatory cytokines in acute stroke patients presenting within six hours of symptom onset. The results of the study may provide insight into potential future therapies for acute stroke by targeting immune processes in the spleen.

Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST)

PRINCIPAL INVESTIGATOR: **Nicole Gonzales, M.D.**

To find better ways to prevent stroke in subjects with carotid stenosis, this national, multicenter research study is comparing carotid endarterectomy to the study procedure – carotid artery stenting. Researchers are evaluating the long-term relative effectiveness of both treatments in preventing stroke, myocardial infarction and death.

Ethnic/Racial Variation in Intracerebral Hemorrhage (ERICH)

PRINCIPAL INVESTIGATOR: **Nicole Gonzales, M.D.**

This genetic study is aimed at determining the significant medical, environmental and genetic risk factors and causes of stroke – and how they vary by race and ethnicity. Genes influencing blood pressure, blood vessel walls, clotting and other factors may increase the risk of developing a hemorrhagic stroke. New treatments that affect these factors may be developed to prevent stroke.

Evaluation of Presidio and Cerecyte Coils in Large and Giant Aneurysms

PRINCIPAL INVESTIGATOR: **P. Roc Chen, M.D.**

This multisite registry is designed to assess the angiographic outcomes and morbidity/mortality of endovascular treatment of large and giant aneurysms using at least one Presidio™ framing coil in conjunction with other Cerecyte® coils. Data is collected on immediate and 12-month post-treatment angiographic occlusion rates, morbidity and mortality rates, retreatment rates, packing density and recurrence rates. This study is sponsored by Micrus Endovascular Corporation in San Jose, California.

Genetic Basis of Vascular Disease

PRINCIPAL INVESTIGATOR: **Dianna Milewicz, M.D., Ph.D.**

This study aims to obtain samples from patients with a variety of vascular diseases in order to perform genetic analyses. When a new gene is associated with vascular disease, patients with mutations will be followed to characterize the disease phenotype.

Genetic Basis of Cerebral Aneurysms

PRINCIPAL INVESTIGATORS: **Teresa Santiago-Sim, Ph.D., and Dong H. Kim, M.D.**

This study aims to identify the genetic basis of cerebral aneurysms using genetic linkage analysis on families with multiple affected members.

HASTIER

PRINCIPAL INVESTIGATOR: **Nancy Edwards, M.D.**

Researchers are conducting an imaging study of the neurovascular impact of reperfusion with hypothermia and tPA, including blood-brain barrier changes/permeability, hemorrhagic transformation, and infarct growth.

High Dose Deferoxamine in Intracerebral Hemorrhage (Hi-Def In Ich)

PRINCIPAL INVESTIGATOR: **Nicole Gonzales, M.D.**

This study is evaluating deferoxamine as a potential treatment for intracerebral hemorrhage. The drug is administered intravenously for five days. The primary aim is to determine whether DFO is a promising new treatment to evaluate in a larger efficacy trial.

ICTuS 2/3

PRINCIPAL INVESTIGATOR: **Nancy Edwards, M.D.**

This Phase 2/3 randomized controlled trial will determine whether the combination of thrombolysis and hypothermia is superior to thrombolysis alone for the treatment of acute ischemic stroke.

Imaging Variables as Predictors of Outcome after Intra-Arterial Therapy: The Superiority of Collateral Circulation

PRINCIPAL INVESTIGATOR: **Amrou Sarraj, M.D.**

Early ischemic changes on CT, collateral circulation, clot location and extension are important determinants of outcomes in patients with large artery occlusion (LAO). The study compared these variables as predictors of outcomes in patients treated with intra-arterial therapy (IAT).

Intra-arterial Vasospasm Trial (IVT)

PRINCIPAL INVESTIGATOR: **P. Roc Chen, M.D.**

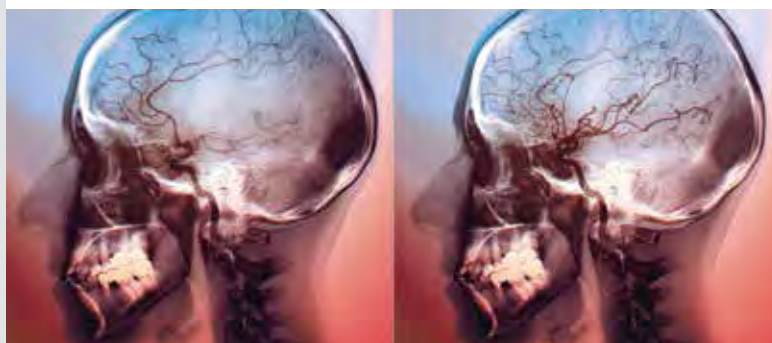
The primary objective of the study is to determine the optimal intra-arterial drug therapy and most effective treatment regimen for treating cerebral vasospasm following aneurysmal subarachnoid hemorrhage. This trial tests whether a combination of multiple drug agent infusion is likely to improve the treatment efficacy compared to single agents.



Intrathecal Nicardipine Injection via External Ventricular Drain in Aneurysmal Subarachnoid Hemorrhage

PRINCIPAL INVESTIGATOR: **Kiwon Lee, M.D.**

For patients suffering from angiographic and symptomatic vasospasm, the treatment with calcium channel blocker by injection via EVD has been anecdotally studied and reported but the exact mechanisms remain elusive. It is not clear whether the effect is on proximal vessels versus distal vessels. The effect of the treatment has not been studied systematically by angiogram before and after the treatment. This prospective clinical trial investigates the effect of intrathecal injection of L-type dihydropyridine calcium channel blocker on angiographic and clinical results for vasospasm. The endpoints will be digital subtraction angiography performed on bleed day 0-1 and 7 compared with the placebo arm.



Mobile Stroke Unit

PRINCIPAL INVESTIGATOR: **James Grotta, M.D.**

This study is investigating whether a pre-hospital stroke treatment based on an ambulance that includes all diagnostic tools required for pre-hospital thrombolysis can significantly decrease the delay between alarm (911 call), therapy decision and administration of thrombolysis in eligible acute ischemic stroke patients.

Pleiotropic Transcription Factors as a Target for Intracerebral Hemorrhage Treatment

PRINCIPAL INVESTIGATOR: **Jaroslav Aronowski, Ph.D.**

Researchers are evaluating the role of transcription factor Nrf2 in regulating cytoprotection, antioxidative defense and detoxification of brains injured by intracerebral hemorrhage.

PORTICO

PRINCIPAL INVESTIGATOR: **Nancy Edwards, M.D.**

In this observational study researchers are attempting to identify biomarkers of inflammation and hemoglobin degradation that correlate with clinical and radiologic outcomes.

Prospective Analysis of the Use of Thrombelastography (TEG) in Prediction of Hemorrhage in Stroke Patients

PRINCIPAL INVESTIGATOR: **Tiffany Chang, M.D.**

This is an observational study to evaluate the use of thrombelastography (TEG) analysis to assess the

coagulation status of patients with acute stroke presenting within three hours of symptom onset. The purpose of the study is to evaluate the efficacy of TEG as means of identifying those ischemic and hemorrhagic stroke patients who are at increased risk of bleeding.

Retrospective Vasospasm Registry

PRINCIPAL INVESTIGATOR: **P. Roc Chen, M.D.**

The registry compares single-agent versus multiple-agent drug infusion to treat cerebral vasospasm post-SAH.

Skull Film Validation Registry

PRINCIPAL INVESTIGATOR: **P. Roc Chen, M.D.**

This registry validates skull X-rays as a safe, effective and low-cost tool to identify potential aneurysm recurrence or coil compaction.

Study to Examine the Effects of MultiStem in Ischemic Stroke

PRINCIPAL INVESTIGATOR: **Sean Savitz, M.D.**

This randomized, double-blind placebo-controlled study is testing the effectiveness of allogeneic bone marrow-derived stem cells (called Multistem) in patients with acute ischemic stroke.

Thrombolysis in Pediatric Stroke Study (TIPS)

PRINCIPAL INVESTIGATOR: **James Grotta, M.D.**

The first trial in the world for children with acute ischemic stroke, this randomized multicenter study is evaluating the safety, optimal dose, and efficacy of tPA for acute ischemic stroke in children.

EPILEPSY

Analysis of the Role of Sv2a Phosphorylation in Epilepsy

PRINCIPAL INVESTIGATOR: **Roger Janz, Ph.D.**
SUB-INVESTIGATORS: **Nitin Tandon, M.D., and**
Georgene W. Hergenroeder, M.H.A., B.S.N., RN

The major goals of this project are to investigate the mechanism of action of levetiracetam and the role of SV2A in human epilepsy. This experiment will test the hypothesis that epilepsy in human tissue leads to changes in the phosphorylation of SV2A and if levetiracetam treatment affects these changes.

Analysis of the Role of SV2A Phosphorylation in Epilepsy and Role of Synaptic Proteins in Human Epilepsy

PRINCIPAL INVESTIGATOR: **Roger Janz, Ph.D.**

This study is analyzing the phosphorylation sites of SV2A in human epilepsy brain tissue.

Bio-Nano-Chip for Anticonvulsant Drug Assay in Epilepsy Patients

PRINCIPAL INVESTIGATOR: **Girdhar Kalamangalam, M.D., D.Phil.**

The goal of the study is to test a novel portable “lab-on-a-chip” device for assaying common anticonvulsant drugs in patients with epilepsy.

Chart Review of Patients Who Underwent Craniotomies for Tumor Resection and Epilepsy Surgery

PRINCIPAL INVESTIGATOR: **Nitin Tandon, M.D.**

This retrospective review of patients who have undergone craniotomies will be used to create a database of patients who have previously undergone surgery by the principal investigator for central nervous system tumors or epilepsy.

Fronto-Basal-Ganglia Circuits for Selective Stopping and Braking

PRINCIPAL INVESTIGATOR: **Nitin Tandon, M.D.**

This project uses intra-cranial brain recordings and fMRI to understand the dynamics of the brain substrates involved in cognitive control.

Intracranial Electrophysiology and Connectivity of Language Regions in Humans

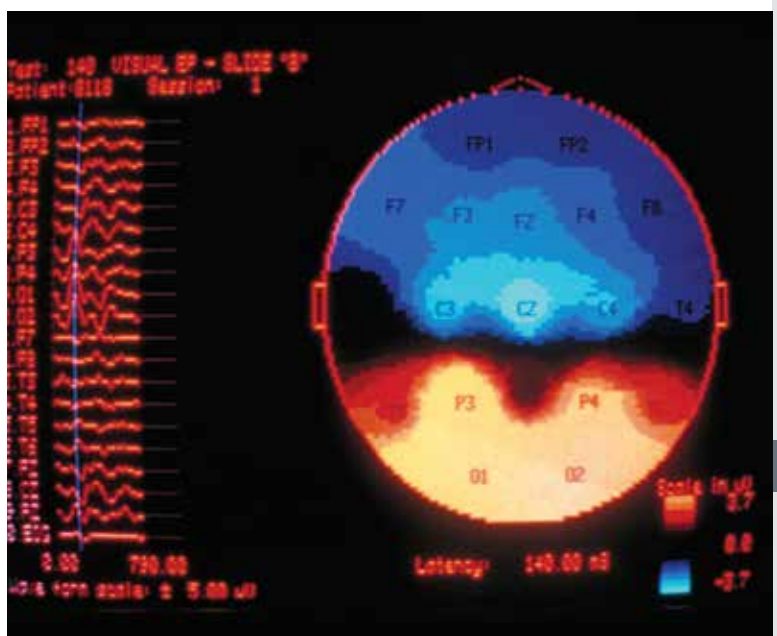
PRINCIPAL INVESTIGATOR: **Nitin Tandon, M.D.**

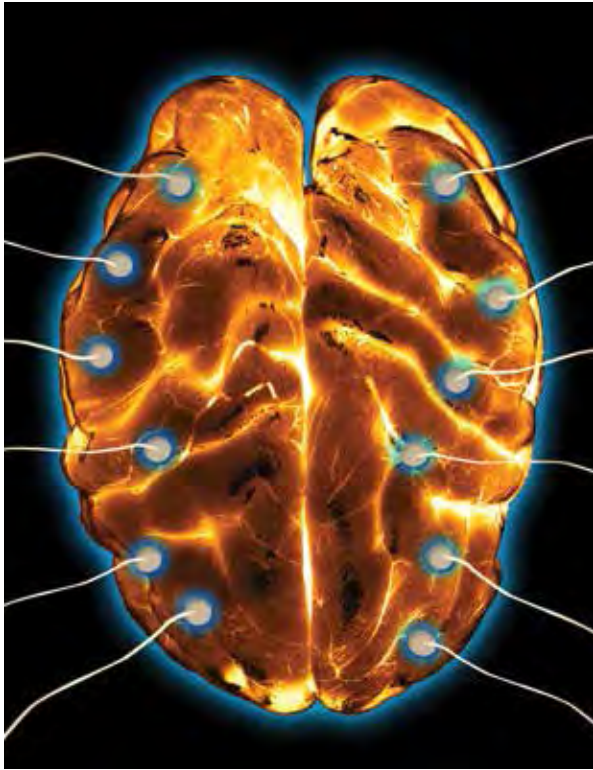
This study is designed to make accurate intermodal comparisons of intracranial EEG, fMRI, DTI tractography and electrical cortical stimulation mapping.

Oxygen-enhanced Magnetic Resonance Imaging in Non-lesional Focal Epilepsy

PRINCIPAL INVESTIGATOR: **Girdhar Kalamangalam, M.D., D.Phil.**

This ongoing study is evaluating how effective oxygen-enhanced MRI scans are at identifying subtle brain lesions in patients with refractory focal epilepsy.





PECA Visiting Professorship to Central America

PRINCIPAL INVESTIGATOR: **Giridhar Kalamangalam, M.D., D.Phil.**

The goal of the opportunity is to develop collaborative educational and clinical links to advance basic and advanced epilepsy care in Central Panama, based at Hospital Luis “Chicho” Fábrega in Santiago de Veraguas, Panama.

Prospective, Open-label Study of the Structure and Function of the Retina in Adult Patients with Refractory Complex Partial Seizures Treated with Vigabatrin (Sabril®)

PRINCIPAL INVESTIGATOR: **Jeremy Slater, M.D.**

This study examines the efficacy of ocular computerized tomography (OCT) in predicting the onset of retinal dysfunction occurring in patients treated with the antiepileptic drug vigabatrin.

Quantitative Analysis of Electroencephalogram in Epilepsy

PRINCIPAL INVESTIGATOR: **Giridhar Kalamangalam, M.D., D.Phil.**

By analyzing EEG and video EEG data already collected for clinical purposes, this study seeks new ways of understanding brain function in normal subjects and in people with neurological problems such as seizures.

Representation and Binding of Spatial and Temporal Episodic Memories in the Human Hippocampus

PRINCIPAL INVESTIGATOR: **Nitin Tandon, M.D.**

The goal of this project is to determine the neural basis of human episodic memory using an innovative combination of high-resolution functional magnetic resonance imaging and intracranial EEG (iEEG).

Study of Changes in Human Electroencephalography and Electrocorticography Related to Sensory System Plasticity

PRINCIPAL INVESTIGATOR: **Jeremy Slater, M.D.**

This study is examining changes that occur in the scalp-recorded electroencephalogram and electrocorticography correlating with specific changes in sensory processing, such as those which occur with multisensory integration of vision and hearing, to gain a better understanding of how the brain interprets the outside world.

VNS Therapy Automatic Magnet Mode Outcomes Study in Epilepsy Patients Exhibiting Ictal Tachycardia

PRINCIPAL INVESTIGATOR: **Jeremy Slater, M.D.**

The goal of this study is to obtain baseline clinical outcome data (Stage 1) upon which to base a subsequent study (Stage 2) of the Model 106 VNS implantable pulse generator.

MOVEMENT DISORDERS AND NEURODEGENERATIVE DISEASES

Absorption, Metabolism and Biodistribution of Prions after Oral Ingestion

PRINCIPAL INVESTIGATOR: **Claudio Soto, Ph.D.**

This project aims to study the fate of the PrPSc infectious agent when administered orally into experimental animals as well as natural hosts, how this varies in distinct strains/species of the agent and provides a detailed characterization of the various processes controlling PrPSc fate.

Amyloid-beta Oligomers and Alzheimer's Diagnosis

PRINCIPAL INVESTIGATOR: **Claudio Soto, Ph.D.**

The major goal of this project is to adapt the protein misfolding cyclic amplification (PMCA) technology for the specific and highly sensitive detection of misfolded A oligomers in human biological fluids. Investigators are optimizing the experimental conditions of cyclic amplification of A misfolding, identifying A misfolded oligomers in AD biological fluids, and evaluating the sensitivity and specificity and the earliest time during the pre-symptomatic phase in which A oligomers can be detected in biological fluids.

CD FLEX: An Open-label, Non-inferiority Study Evaluating the Efficacy and Safety of Two Injection Schedules of Xeomin® (incobotulinumtoxinA) [Short Flex versus Long Flex] in Subjects with Cervical Dystonia with < 10 Weeks of Benefit from OnabotulinumtoxinA Treatment

PRINCIPAL INVESTIGATOR: **Erin Furr-Stimming, M.D.**

SUB-INVESTIGATORS: **William Ondo, M.D., and Raja Mehanna, M.D.**

This prospective, open-label, 1:1 randomized trial is evaluating two dosing schedules of Xeomin [Short Flex

and Long Flex] in subjects who report that they receive therapeutic benefit from onabotulinumtoxinA (Botox®) treatment for less than 10 weeks.

Cross-seeding of Protein Misfolding as a Disease Mechanism

PRINCIPAL INVESTIGATOR: **Claudio Soto, Ph.D.**

This project proposes to analyze the molecular cross-talk between various protein misfolding disorders using several in vivo and in vitro models.

Cyclic Amplification of Prion Protein Misfolding

PRINCIPAL INVESTIGATOR: **Claudio Soto, Ph.D.**

The major goals of this project are to understand the mechanism of prion replication and the nature of the infectious agent, and to develop novel strategies for diagnosis of prion diseases.

Detection of Alpha-Synuclein Oligomers for the Diagnosis of Parkinson's Disease

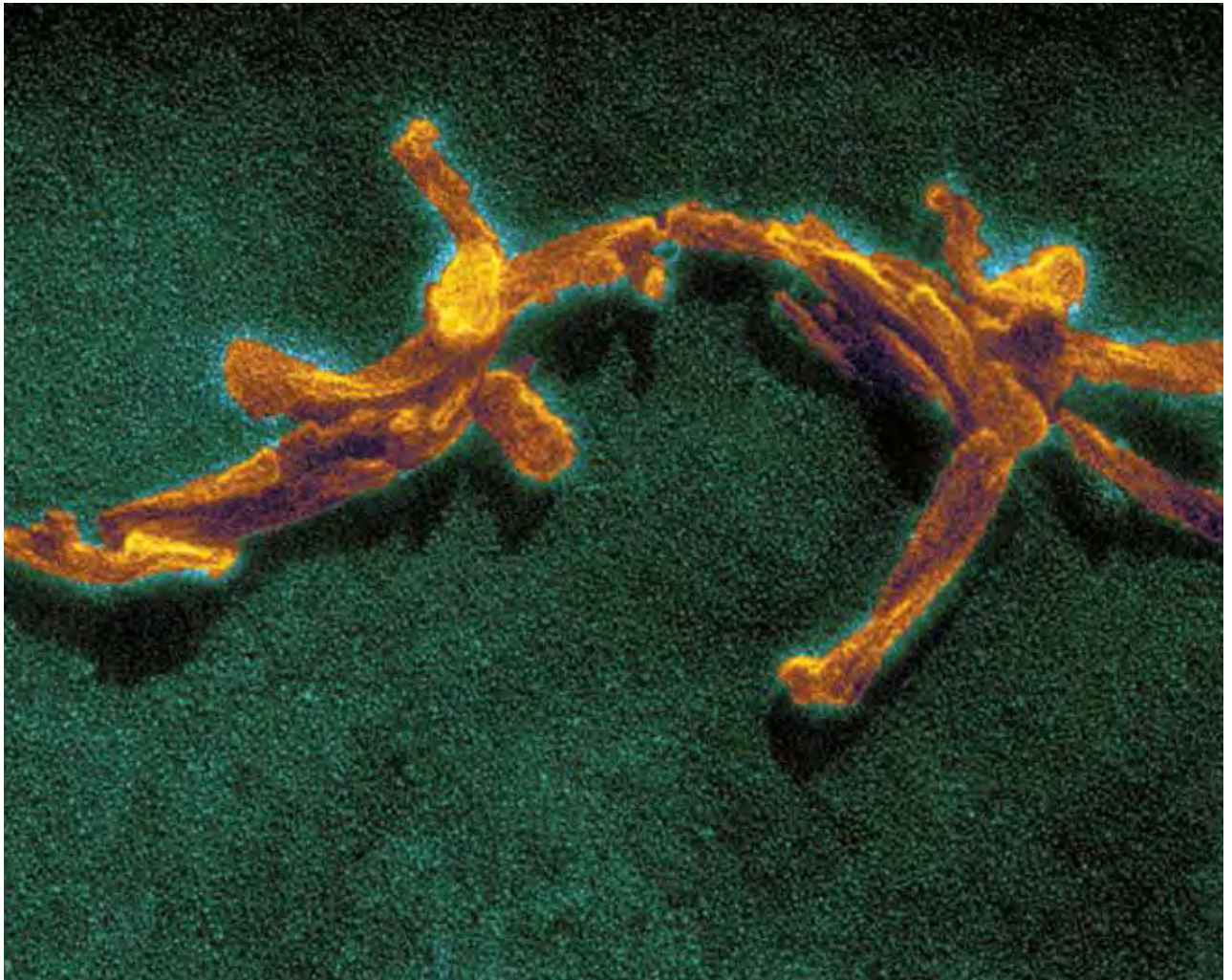
PRINCIPAL INVESTIGATOR: **Claudio Soto, Ph.D.**

This project aims to adapt and develop the PMCA technology to detect alpha-synuclein oligomers in the cerebrospinal fluid of patients affected by Parkinson's disease

Development of a Biochemical Diagnosis for Creutzfeldt-Jakob Disease

PRINCIPAL INVESTIGATOR: **Claudio Soto, Ph.D.**

This is a partnership between Amprion, Inc. and the UTHealth Medical School to develop and validate a novel diagnosis for Creutzfeldt-Jakob disease.



Dystonia Coalition Projects: Natural History and Biospecimen Repository for Dystonia; Comprehensive Rating Tools for Cervical Dystonia; Validity and Reliability of Diagnostic Methods and Measures of Spasmodic Dysphonia

PRINCIPAL INVESTIGATOR: **William Ondo, M.D.**

This collaborative, international effort has two primary goals. The first is to create a biospecimen repository and associated clinical database to be used as a resource for dystonia and related disease research. The second goal is to create and validate various rating scales for focal dystonias to be used during a typical clinical examination.

Enroll-HD: A Prospective Registry Study in a Global Huntington's Disease Cohort

PRINCIPAL INVESTIGATOR: **Erin Furr-Stimming, M.D.**

Enroll-HD is an observational, prospective, multicenter study with sites in North America, Latin America, Europe, Asia, Australia and New Zealand. The study has three aims: to improve the understanding of the dynamic phenotypic spectrum and the disease mechanisms of Huntington's disease (HD) by collecting natural history data covering the cognitive, behavioral and motor domains that allow insights into the neurobiology of HD, collecting data and biologic

samples to identify genetic and environmental factors influencing and/or modifying the HD phenotype and disease progression, and promoting studies that may provide clues to the pathogenesis of HD; to promote the development of evidence-based guidelines to inform clinical decision-making and improve health outcomes for participants and their family units; and to provide a platform to support the design and conduct of clinical trials.

Epigenetic Changes in Alzheimer's Disease

PRINCIPAL INVESTIGATOR: **Paul Schulz, M.D.**

DNA contains the genetic code from which all our cellular proteins are made. Mutations in DNA can rarely cause familial Alzheimer's disease (AD). However, there can be changes to the probability of DNA being made into proteins that are not due to genetic mutations. Rather, they can be due to chemical changes. This study is investigating whether epigenetic changes to the DNA code contribute to AD and whether these changes can be used as a diagnostic test for AD.

Identifying Risk Factors for PTSD and Testing Preventions

PRINCIPAL INVESTIGATOR: **Paul Schulz, M.D.**

This study of patients who present at the Memorial Hermann-Texas Medical Center Emergency department after a traumatic event aims to discover the risk factors for developing post-traumatic stress disorder (PTSD) and to test treatments to prevent its development.

Measuring the Amyloid of Alzheimer's Disease in Blood

PRINCIPAL INVESTIGATORS: **Claudio Soto, Ph.D., and Paul Schulz, M.D.**

The amyloid deposited in the brains of patients with Alzheimer's disease (AD) can also be found in their

blood in minute quantities. Dr. Soto is developing a sensitive assay to determine whether blood amyloid levels can be used to diagnose AD or to test whether treatments for AD are effective.

Mechanisms of Transmissibility in Prion Diseases

PRINCIPAL INVESTIGATOR: **Claudio Soto, Ph.D.**

The major goal of this project is to study the mechanism implicated in the transmission of prion disease with particular emphasis on the study of human prion diseases.

Pathogenesis, Transmission and Detection of Zoonotic Prion Diseases

PRINCIPAL INVESTIGATOR: **Claudio Soto, Ph.D.**

Researchers are studying the pathogenesis and routes of propagation of bovine spongiform encephalopathy and chronic wasting disease, and developing novel strategies for the detection of infected animals.

Pathogenic Mechanism of Prion Disease

PRINCIPAL INVESTIGATOR: **Claudio Soto, Ph.D.**

This Program Project grant involves several groups. Our major goal is to understand the molecular basis of human prion replication and to develop novel strategies for diagnosis.

PET Imaging for Alzheimer's Dementia

PRINCIPAL INVESTIGATOR: **Paul Schulz, M.D.**
(site PI for this multicenter study)

This study is testing whether PET imaging can be used to identify the amyloid of Alzheimer's disease (AD) in the brain in patients with memory loss, before they have AD.

Phase 3, Multicenter, Double-blind, Placebo-controlled, Single-treatment Efficacy and Safety Study of MYOBLOC® (Part A) Followed by Open-Label, Multiple-Treatment with MYOBLOC (Part B) in the Treatment of Troublesome Sialorrhea in Adult Subjects

PRINCIPAL INVESTIGATOR: **William Ondo, M.D.**

SUB-INVESTIGATORS: **Erin Furr-Stimming, M.D., and Raja Mehanna, M.D.**

This study will evaluate the efficacy and safety of MYOBLOC in the treatment of sialorrhea (drooling), which can be a symptom of many disease conditions. MYOBLOC will be injected directly into the salivary glands. MYOBLOC has been shown in previous trials to safely decrease saliva production, thereby demonstrating its potential as a safe and effective treatment for troublesome sialorrhea.

Phase 3b, Multicenter, Randomized, Double-blind, Placebo-controlled Study Evaluating the Efficacy and Safety of DYSPORT Using 2mL Dilution in Adults with Cervical Dystonia

PRINCIPAL INVESTIGATOR: **William Ondo, M.D.**

The purpose of the protocol is to evaluate the efficacy of Dysport using 2 mL dilution compared with placebo for the treatment of cervical dystonia.

Phase 3b, Prospective, Multicenter, Open-label Extension Study To Assess Long-term Safety and Effectiveness of DYSPORT Using 2 mL Dilution in Adults with Cervical Dystonia

PRINCIPAL INVESTIGATOR: **William Ondo, M.D.**

The purpose of the protocol is to assess the long-term safety of repeat treatment cycles of DYSPORT 500 U using a 2 mL dilution scheme for the treatment of cervical dystonia.

Phase 4, Open-Label, Efficacy and Safety Study of APOKYN® for Rapid and Reliable Improvement of Motor Symptoms in Parkinson's Disease Subjects with Delayed Onset of L-Dopa Action

PRINCIPAL INVESTIGATOR: **William Ondo, M.D.**

This study is designed to assess the effect of APOKYN treatment in rapid and reliable improvement of motor symptoms in Parkinson's disease (PD) subjects suffering from delayed or unreliable onset of levodopa (L-dopa) action.

Potential Biomarkers for Parkinson's Disease

PRINCIPAL INVESTIGATOR: **Ying Xia, M.D., Ph.D.**

Designed to explore, through both clinical and laboratory approaches, a potential biomarker for predicting the development/severity of Parkinson's disease, this project is a collaboration with Chinese clinicians and scientists with a grant application submitted to the U.S.-China Program for Biomedical Collaborative of the National Institutes of Health in September 2013.

Transmissible Component to Alzheimer's Dementia

PRINCIPAL INVESTIGATORS: **Claudio Soto, Ph.D., and Paul Schulz, M.D.**

The cause of Alzheimer's disease (AD) in 95% of individuals is unknown. Dr. Soto has shown that blood from a mouse with a gene that will cause it to develop an AD-like illness can greatly accelerate the development of amyloid deposition in the brains of other mice. The researchers are now testing whether there is a transmissible component to AD between humans or between humans and mice.

MULTIPLE SCLEROSIS

Combination Therapy in Multiple Sclerosis

PRINCIPAL INVESTIGATOR: **Jerry Wolinsky, M.D.**

This study is determining if the combination of interferon beta-1a and glatiramer acetate is superior to either drug as monotherapy in relapsing-remitting multiple sclerosis.

Detection of MS-related Cognitive Impairment: In Search of MRI Surrogate Markers

PRINCIPAL INVESTIGATOR: **Flavia Nelson, M.D.**

This study aims to develop and apply a multimodal MRI approach to the evaluation of cognitive impairment in patients with multiple sclerosis.

MRI Analysis Center for Protocol EFC6058 – A Multicenter, Double-blind, Parallel-group, Placebo-controlled Study of the Efficacy and Safety of Teriflunomide in Patients with Relapsing Multiple Sclerosis Who Are Treated with Interferon-Beta

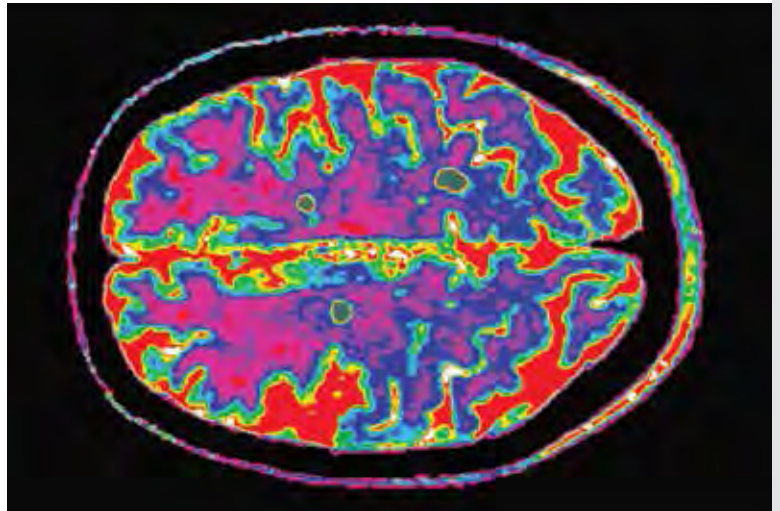
PRINCIPAL INVESTIGATOR: **Jerry Wolinsky, M.D.**

This study provides quantitative image analysis measures as supportive outcome measures.

MRI Analysis Center for Protocol EFC6260 – An International, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy and Safety of Two-Year Treatment with 7 mg Once Daily and 14 mg Once Daily versus Placebo in Patients with a First Clinical Episode Suggestive of Multiple Sclerosis

PRINCIPAL INVESTIGATOR: **Jerry Wolinsky, M.D.**

This pivotal clinical trial provides quantitative image analysis measures as supportive outcome measures.



Phase III Randomized, Double-blind, Multicenter, Placebo-controlled, Parallel-group Study, Comparing the Efficacy and Safety of FTY-720 0.5 Administered Orally Once Daily versus Placebo in Patients with Primary Progressive Multiple Sclerosis

PRINCIPAL INVESTIGATOR: **Flavia Nelson, M.D.**

The above trials are evaluating the first oral drug FDA approved for treatment of relapsing forms of multiple sclerosis. The aims of the Phase IV trials are to evaluate a lower dose of the drug to decrease currently seen side effects and to evaluate the drug in the progressive type of multiple sclerosis for which there is no FDA-approved treatment.

Phase IV Randomized, Double-blind, Multicenter, Parallel-group Study Comparing the Efficacy and Safety of FTY-720 0.5 mg Administered Orally Once Daily versus 0.25 mg versus Glatiramer Acetate in Patients with Relapsing Remitting Multiple Sclerosis

PRINCIPAL INVESTIGATOR: **Flavia Nelson, M.D.**

The goal of this Phase IV study is to evaluate a low dose of an oral drug called fingolimod (Gilenya®) for similar efficacy and fewer side effects compared to the current FDA-approved dose and to an injectable drug.

Serial Magnetic Resonance Spectroscopy in Multiple Sclerosis

PRINCIPAL INVESTIGATOR: **Jerry Wolinsky, M.D.**

Researchers are using serial magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) to gather data to better understand disease processes in patients with multiple sclerosis.

NEUROMUSCULAR DISORDERS

Noninvasive Imaging to Quantify Peripheral Nerve Injury and Repair in Clinic

PRINCIPAL INVESTIGATOR: **Kazim Sheikh, M.D.**

Researchers will be using DTI/MRI to assess nerve injury and/or repair in patients with traumatic and mechanical nerve injury (Sunderland grade II-V) with or without repair of median, ulnar or radial nerves or their major branches localized to upper extremity, within three years of nerve injury/repair. The purpose of this study is to determine the best method to use to create the clearest images in the shortest amount of time of intact and injured nerves with or without treatment/repair to quantify nerve injury particularly to the axons and measure repair overtime.

NEURO-ONCOLOGY

Celldex, NCT01498328

PRINCIPAL INVESTIGATOR: **Sigmund Hsu, M.D.**

This Phase II study of rindopepimut/GM-CSF examines the experimental cancer vaccine's efficacy in patients with relapsed EGFRVIII positive glioblastoma.

Cortice 17, NCT01933815

PRINCIPAL INVESTIGATOR: **Sigmund Hsu, M.D.**

This Phase 1/2 dose-escalation study of TPI 287 examines its efficacy in combination with bevacizumab followed

by randomized study of the maximum tolerated dose of TPI 287 in combination with bevacizumab versus bevacizumab alone in adults with recurrent glioblastoma.

Cortice 18, NCT02047214

PRINCIPAL INVESTIGATOR: **Sigmund Hsu, M.D.**

Researchers are conducting this Phase 2 dose-escalation study of TPI 287 in combination with bevacizumab in adults who have recurrent or progressive glioblastoma following a bevacizumab containing regimen.

Diffusion, NCT01465347

PRINCIPAL INVESTIGATOR: **Jay-Jiguang Zhu, M.D. Ph.D.**

In this open-label Phase 1/2 safety lead-in study, the safety and efficacy of trans sodium crocetinolate with concomitant treatment of fractionated radiation therapy and temozolomide is being evaluated in newly diagnosed glioblastoma patients.

Foundation One, NCT01851213

PRINCIPAL INVESTIGATOR: **Sigmund Hsu, M.D.**

In this prospective observational study, researchers are examining routine clinical practice patterns and the impact on clinical decision-making associated with the FoundationOne™ Next Generation Sequencing Test.

ICT- 107 Brain Tumor Vaccine for Patients with Newly Diagnosed Glioblastomas

PRINCIPAL INVESTIGATOR: **Jay-Jiguang Zhu, M.D., Ph.D.**

This is a randomized, double-blind Phase IIB multicenter study of the safety and efficacy of the ICT-107 vaccine in newly diagnosed patients with glioblastoma multiforme (GBM) following tumor resection. ICT-107 is an immunotherapy in which the patient's immune response will be stimulated to kill the tumor cells. Some of the patient's white blood cells (WBC) will be removed

and cultured in a laboratory with purified antigens, similar to those on GBM cells. The patient's own WBC/dendritic cells (DCs) that have been exposed to the tumor antigens will then be given back to the patient as a vaccine over several months. Researchers are investigating whether the ICT-107 vaccine will stimulate the patient's immune response to kill the remaining GBM tumor cells after surgery and chemotherapy.

Methotrexate Infusion Directly into the Fourth Ventricle in Children with Malignant Fourth Ventricular Brain Tumors: A Pilot Clinical Trial

PRINCIPAL INVESTIGATOR: **David I. Sandberg, M.D.**

Under an IRB-approved protocol, for the first time in humans, methotrexate was infused into the fourth ventricle in patients with recurrent malignant fourth ventricular tumors. Preliminary results of this study are extremely promising, as no patients suffered any new neurological problems and all patients with medulloblastoma responded to treatment.

NovoCure EF-14, NCT00916409

PRINCIPAL INVESTIGATOR: **Jay-Jiguang Zhu, M.D. Ph.D.**

In this prospective multicenter trial, researchers are examining the efficacy of the NovoTTF-100A device together with temozolomide in newly diagnosed glioblastoma multiforme patients, compared to treatment with temozolomide alone.

ReACT: A Phase II Clinical Trial Targeting the EGFRvIII Mutation in Glioblastoma Patients with Relapsing Disease

PRINCIPAL INVESTIGATOR: **Sigmund H. Hsu, M.D.**

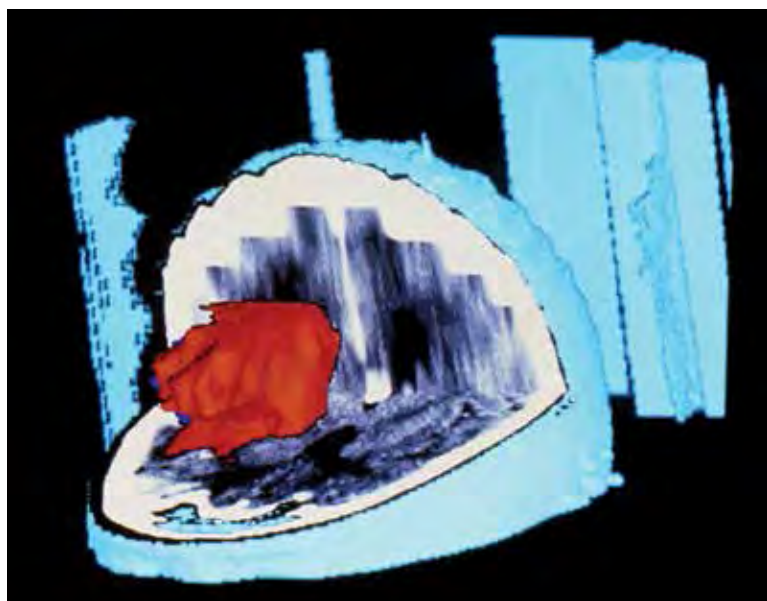
This Phase II study will enroll patients into three groups. Group 1 are patients who have never been treated with bevacizumab. These patients will be randomly assigned

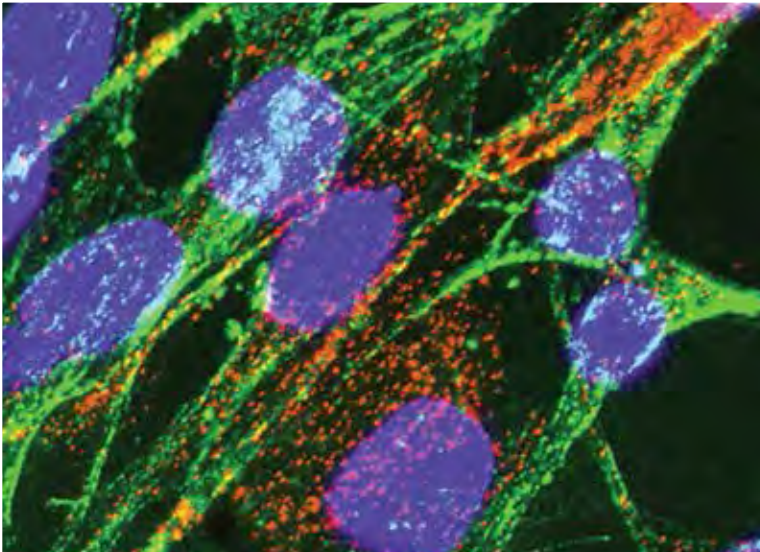
to receive either rindopepimut/GM-CSF or KLH, each along with bevacizumab. Treatment assignment for Group 1 will be blinded. Group 2 and Group 2C includes patients who are refractory to bevacizumab (who have experienced recurrence or progression of glioblastoma while on bevacizumab or within two months of discontinuing bevacizumab). These patients will all receive rindopepimut/GM-CSF along with bevacizumab. Patients will be treated until their disease progresses or they can no longer tolerate the treatment, and all patients will be followed for survival.

Safety and Efficacy Study of Trans Sodium Crocetin (TSC) With Concomitant Radiation Therapy and Temozolomide in Newly Diagnosed Glioblastoma (GBM)

PRINCIPAL INVESTIGATOR: **Jay-Jiguang Zhu, M.D., Ph.D.**

This open-label study will evaluate the safety and efficacy of TSC when dosed concomitantly with the standard of care (radiation therapy and temozolomide) for newly diagnosed glioblastoma in adults. All patients will receive TSC in the study. The overall objectives of this Phase 1/2 clinical study in newly diagnosed GBM patients are to evaluate the safety and tolerability, efficacy, PK profile, PFS/time to disease progression, quality of life, and overall





survival in adults. The primary objective of the Phase 1 portion of the study is to evaluate the safety (DLT rate) and to define the dosing regimen of TSC for the larger Phase 2 study. The primary clinical endpoint is overall survival at 24 months, and patients will be followed for up to three years.

Vaccine, NCT01280552

PRINCIPAL INVESTIGATOR: **Jay-Jiguang Zhu, M.D., Ph.D.**

In this randomized, double-blind, controlled Phase IIb study, researchers are testing the safety and efficacy of the ICT-107 vaccine in newly diagnosed patients with glioblastoma multiforme following resection and chemoradiation.

NEUROREHABILITATION

A Pilot Safety Study of Minocycline for the Treatment of Neuropathic Pain in Traumatic Spinal Cord Injury

PRINCIPAL INVESTIGATOR: **Gerard Francisco, M.D.**

This study is evaluating the safety of minocycline for the treatment of neuropathic pain in traumatic spinal cord injury.

Effectiveness of Acceptance and Commitment Therapy for Reducing Emotional Distress and Improving Participation Outcomes after Traumatic Brain Injury

PRINCIPAL INVESTIGATOR: **Angelle Sander, Ph.D.**

This study is a novel, innovative, preliminary investigation of the effectiveness of Acceptance and Commitment Therapy (ACT) for reducing emotional distress, improving health-related quality of life and increasing participation for persons with traumatic brain injury (TBI). The study is also investigating the importance of the ACT process components (acceptance of thoughts/feelings and commitment to valued activities) for determining outcomes.

NEUROTRAUMA/CRITICAL CARE

A Mechanism for Global Cerebral Edema after Subarachnoid Hemorrhage: Pathophysiology of Early Brain Injury

PRINCIPAL INVESTIGATOR: **H. Alex Choi, M.D.**

Early brain injury after subarachnoid hemorrhage is the most important determinant of outcome. Using cerebrospinal fluid and serum markers of inflammation, the researchers are exploring the mechanisms of early brain injury and global cerebral edema after subarachnoid hemorrhage.

A Pilot Study to Identify Biomarkers Associated with Chronic TBI

PRINCIPAL INVESTIGATOR: **Pramod Dash, Ph.D.**

The specific aim of this research is to determine if the biological fluids (blood/saliva) from chronic brain-injured patients (both blast and non-penetrating TBI) contain reproducible protein markers.

Biomarkers Prognostic for Elevated Intracranial Pressure

PRINCIPAL INVESTIGATOR: **Pramod Dash, Ph.D.**

This study is determining the cutoff values of ceruloplasmin and copper for patient classification and testing the diagnostic accuracy of these markers in blinded samples, and also determining if a temperature correction factor is required for the use of these assays in future scenarios.

Classification and Treatment of Blunt Cerebrovascular Injury

PRINCIPAL INVESTIGATOR: **Ryan Kitagawa, M.D.**

This is a retrospective review of all patients who were diagnosed with blunt cerebrovascular injury from 2010-2012 including a novel classification system.

Clinical Interventions to Increase Organ Procurement, Nutritional Status and Enteral Absorption Capability after Brain Death (R380T10585)

PRINCIPAL INVESTIGATOR: **Georgene W. Hergenroeder, M.H.A., B.S.N., RN**

This study evaluates the ability of a nutritional intervention to affect the inflammatory response.

Coagulation and Outcome from Acute Neurologic Injury Using Thrombelastography

PRINCIPAL INVESTIGATOR: **Tiffany Chang, M.D.**

This study examines the natural history of coagulation and platelet function in the setting of ICH, SAH, and TBI.

CSF Diversion Assessment and Ventriculoperitoneal Shunt Dependence Study

PRINCIPAL INVESTIGATOR: **Kiwon Lee, M.D.**

This study aims to analyze the relationship between the total amount of CSF diversion and long-term ventriculoperitoneal shunt dependence. The important variables for investigation are red blood cell clearance and the ventriculoperitoneal shunt dependence. Evaluation of predictors of VP shunt dependence is done particularly for patients with high-grade aneurysmal subarachnoid hemorrhage.

Ethnic Disparities in End-of-life Care in Brain-injured Patients

PRINCIPAL INVESTIGATOR: **H. Alex Choi, M.D.**

The advancement of critical care has brought to the forefront ethical issues regarding continuation of aggressive medical measures to prolong life in the severely brain-injured patient. Studies have shown minorities, especially black or Hispanic



individuals, seek more care at the end of life. Researchers are studying this disparity in acutely brain-injured patients and their families and exploring the possible social/cultural/religious reasons for these differences.

Gene Transcription and Regulation of Stem Cell Differentiation

PRINCIPAL INVESTIGATOR: **Jiaqian Wu, Ph.D.**

This research combines stem cell biology and systems-based approaches involving genomics, proteomics, bioinformatics and functional assays to unravel gene transcription and regulatory mechanisms governing stem cell differentiation. One major focus is investigating stem cell neural differentiation and developing effective and safe treatment for spinal cord injury and neurological diseases such as stroke. The other area lies in the study of regulatory networks of hematopoietic precursor cell self-renewal and differentiation using multipotent EML (erythroid, myeloid and lymphocytic) cells as a model system.

Hemodynamic Optimization for Early Goal-directed Therapy in Severe Brain Injury

PRINCIPAL INVESTIGATOR: **Kiwon Lee, M.D.**

This clinical study investigates the different dynamic variables in the intravascular volume status (including stroke volume variation, pulse pressure variation, cardiac indices and other pressure and volume related variables) and their effects on the injured brain.

Hypothermia for Patients Requiring Evacuation of Subdural Hematoma: A Multicenter Randomized Clinical Trial (HOPES)

PRINCIPAL INVESTIGATOR: **Dong H. Kim, M.D.**

This randomized, prospective trial will study the effect of very early cooling in patients undergoing surgical evacuation of

acute subdural hematomas (35°C prior to opening the dura followed by maintenance at 33°C for a minimum of 48 hours). Intravascular cooling catheters (Thermogard XP™ Device, Zoll) will be utilized to induce hypothermia or to maintain normothermia. The primary objective is to determine if rapid induction of hypothermia prior to emergent craniotomy for traumatic subdural hematoma (SDH) will improve outcome as measured by Glasgow Outcome Scale-Extended (GOSE) at six months.

The Use of Antiplatelet Agents after Cranial Surgery

PRINCIPAL INVESTIGATOR: **Ryan Kitagawa, M.D.**

Researchers are conducting a retrospective review of all patients who received antiplatelet agents after cranial surgery from 2010-2014.

The Use of Antiplatelet Agents after Traumatic Brain Injury

PRINCIPAL INVESTIGATOR: **Ryan Kitagawa, M.D.**

This study is a retrospective review of all patients who received antiplatelet agents after TBI from 2010-2012.

The Use of Antiplatelet and Anticoagulant Agents with Chronic, Subacute, and Acute on Chronic Subdural Hematoma

PRINCIPAL INVESTIGATOR: **Ryan Kitagawa, M.D.**

Investigators are conducting a retrospective review of all patients who received antiplatelet or anticoagulation agents after diagnosis of chronic, subacute, and acute on chronic subdural hematoma from 2010-2012.



Treatment of Acute Myocardial Infarction after Traumatic Brain Injury

PRINCIPAL INVESTIGATOR: **Ryan Kitagawa, M.D.**

This study is a retrospective review of all patients who suffered an acute myocardial infarction after TBI at Memorial Hermann-Texas Medical Center from 2010 to 2012.

Use of Vasopressors and Inotropes in Optimizing Cardiac Output for Resuscitating Severe Brain Injury Patients Using Multimodality Monitoring

PRINCIPAL INVESTIGATOR: **Kiwon Lee, M.D.**

This clinical study investigates the use of different vasoactive and inotropic agents for optimizing cardiac output and assessing its relationship with the brain oxygenation and cerebral energy metabolism using multimodality monitoring.

SPINE

Biomarkers for Pain in Spinal Cord Injury

PRINCIPAL INVESTIGATOR: **Georgene W. Hergenroeder, M.H.A., B.S.N., RN**

Investigators in this clinical trial believe that spinal cord injury (SCI) patients who develop chronic pain have biomarkers in their blood that can predict their condition. Patients two or more years post injury, who have been identified as having neuropathic pain or no pain, will be asked to donate blood samples that will be evaluated for biomarkers. The goal of the research is early intervention to prevent the onset of chronic pain.

Combinatory Strategies to Functional Remyelination after Spinal Cord Injury

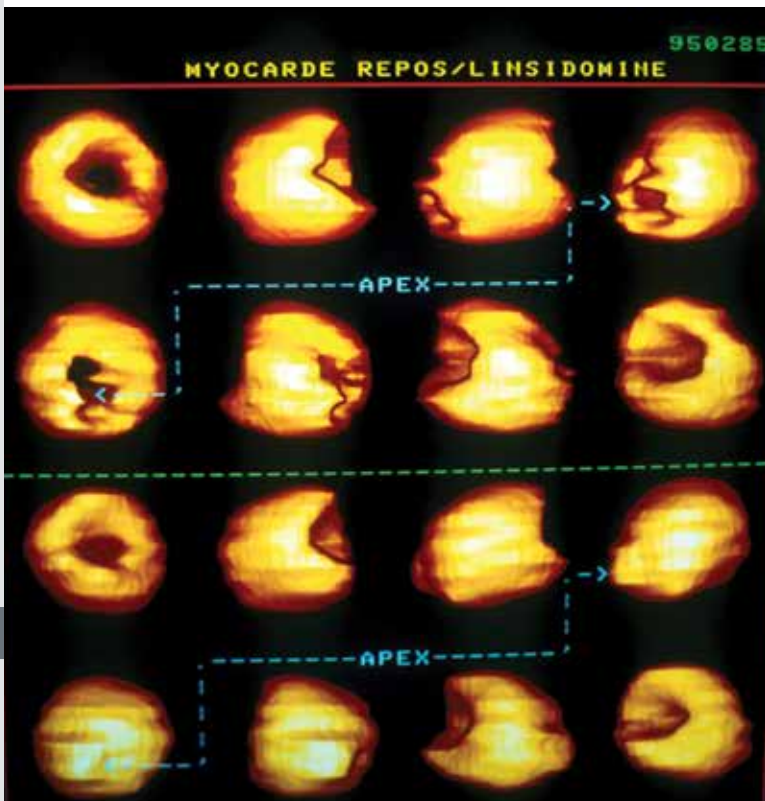
PRINCIPAL INVESTIGATOR: **Qi Lin Cao, M.D.**

Researchers are identifying optimal strategies to genetically modify oligodendrocyte precursor cells prior to transportation to promote remyelination and functional recovery after spinal cord injury.

Human Pluripotent Stem Cells in Cell-based Therapy for CNS Injury

PRINCIPAL INVESTIGATOR: **Ying Liu, Ph.D.**

This study focuses on dissecting the neural developmental pathways and the corresponding pathogenesis in spinal cord injury and stroke. Our long-term goal is to identify therapeutic targets for the treatment of CNS injury and neurodegenerative diseases.



Mischer Neuroscience Associates Quality and Outcomes Database

PRINCIPAL INVESTIGATOR: **Joseph Hsieh, M.D.**

The MNA Spine Surgery Quality and Outcomes Database is a non-IRB managed prospective registry for quality reporting.

Nano-engineered, Multichannel Scaffolds for Axon Regeneration

PRINCIPAL INVESTIGATOR: **Qi Lin Cao, Ph.D.**

Researchers are identifying optimal nano-scaffolds for axonal growth in vitro.

North American Clinical Trials Network for the Treatment of Spinal Cord Injury: Spinal Cord Injury Registry

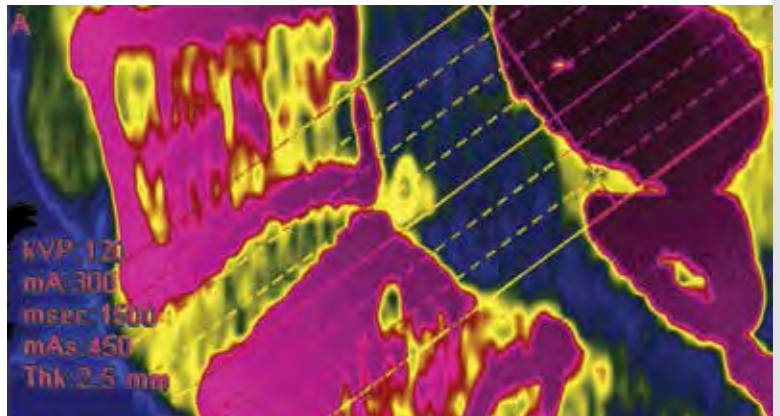
PRINCIPAL INVESTIGATOR: **Michele Johnson, M.D.**

Researchers hope to bring promising therapies for spinal cord injury (SCI) patients from the laboratory to clinical trials in a manner that will provide evidence of effectiveness, with maximum safety, to patients undergoing treatment. This is an observational study charting the natural course of SCI.

Novel Neuroprotection Therapeutic Approaches for Spinal Cord Injury

PRINCIPAL INVESTIGATOR: **Qi Lin Cao, M.D.**

The goal of this project is to study the molecular mechanism that regulates the blood-brain barrier of the normal adult CNS or after SCI, and to identify new therapeutic targets for SCI and other neurological diseases by protecting the blood-brain barrier.



Novel Restorative Therapy for Spinal Injury

PRINCIPAL INVESTIGATOR: **Qi Lin Cao, M.D.**

This study is examining the therapeutic potential of ApoE peptides for spinal cord injury.

Optimization of Tissue Engineering Matrices for SCI Treatment

PRINCIPAL INVESTIGATOR: **Laura Smith Callahan, Ph.D.**

The study aims to determine the optimal Young's Modulus and concentration of laminin (IKVAV) and n-cadherin (HAVDI) peptides on maturation of human induced pluripotent stem cell derived neural stem cells toward mature neurons in 2-D culture on continuous gradient polyethylene glycol hydrogels.

Safety and Pharmacokinetics of Riluzole in Patients with Traumatic Acute Spinal Cord Injury

PRINCIPAL INVESTIGATOR: **Michele Johnson, M.D.**

The purpose of this study is to develop acute care safety and pharmacokinetic profiles of riluzole in patients who have sustained a traumatic spinal cord injury. Researchers are also conducting exploratory analyses of functional outcomes for purposes of planning a subsequent Phase IIB – Phase III randomized study of the efficiency of riluzole for the treatment of acute spinal cord injury.

OTHER**A Microsurgical Robotic System**

PRINCIPAL INVESTIGATORS: **Daniel H. Kim, M.D., Mark Dannenbaum, M.D., Dongsuk Shin, Ph.D.**

In this study, researchers are developing a surgical robotic system capable of performing microsurgery in the brain.

A Robot-assisted, Image-guided Surgery System

PRINCIPAL INVESTIGATORS: **Daniel H. Kim, M.D., Mark Dannenbaum, M.D., Dongsuk Shin, Ph.D.**

The investigators are developing a robot-assisted, image-guided surgery system using a novel registration method, which includes a patient-specific registration guide. The patient-specific guide for registration is built based on the patient's CT data using a 3-D printer prior to surgery.

A Steerable Robotic Microcatheter Using an Electroactive Polymer

PRINCIPAL INVESTIGATORS: **Daniel Kim, M.D., Mark Dannenbaum, M.D., Dongsuk Shin, Ph.D.**

The researchers are developing a steerable robotic catheter system capable of navigating narrow blood vessels in the brain. The ElectroActive Polymer (EAP)-based catheter system represents a new tool for catheter-based cerebral intervention, and will improve the treatment of cerebral vascular disease.

Acupuncture Therapy for Neurological Disorders

PRINCIPAL INVESTIGATOR: **Ying Xia, M.D., Ph.D.**

In collaboration with Chinese scientists, this study tests the effects of electroacupuncture (EA) on several neurological disorders including stroke, epilepsy and

Parkinson's disease. EA is a relevant analogy of deep brain stimulation (DBS). The major difference between these two modalities is the area of stimulus, i.e., brain (DBS) versus body (acupuncture).

Comparative Analysis of Structural and Functional Characteristics of Language Regions as Measured by Functional Imaging and Invasive Electrophysiology

PRINCIPAL INVESTIGATOR: **Nitin Tandon, M.D.**

Researchers are working to accurately locate regions of the brain involved in the making of language. Functional MRI (fMRI) will be used to detect activity in various regions of the brain during tasks performed by patients with brain tumors or epilepsy, as well as normal subjects. The second part of the study is focused on patients being evaluated for epilepsy surgery. As part of the evaluation, they will undergo electrical brain stimulation using the same safety guidelines used in standard medical care, to closely study the areas of the brain involved in language, movement and vision.

Effects of Acupuncture on Neurological Disorders

PRINCIPAL INVESTIGATOR: **Ying Xia, M.D., Ph.D.**

This project uses current techniques to explore the effects of acupuncture on neurological disorders such as stroke and epilepsy and investigate the underlying mechanisms.

Fronto-Basal-Ganglia Circuits for Self-Control

PRINCIPAL INVESTIGATOR: **Nitin Tandon, M.D.**

This study addresses the neural architecture underlying how people use their goals to control inappropriate urges. Functional MRI and electrocorticography are used to understand the substrates and timing in the network involved in modulating and stopping action.

Hypoxic Dysfunction of Cortical Neurons

PRINCIPAL INVESTIGATOR: **Ying Xia, M.D., Ph.D.**

The study aims to investigate hypoxia-induced dysfunction of cortical neurons that form the pathophysiological basis of hypoxic encephalopathy. This project is partially supported by the National Institutes of Health.

Neuroprotection against Stroke and Parkinson's Disease

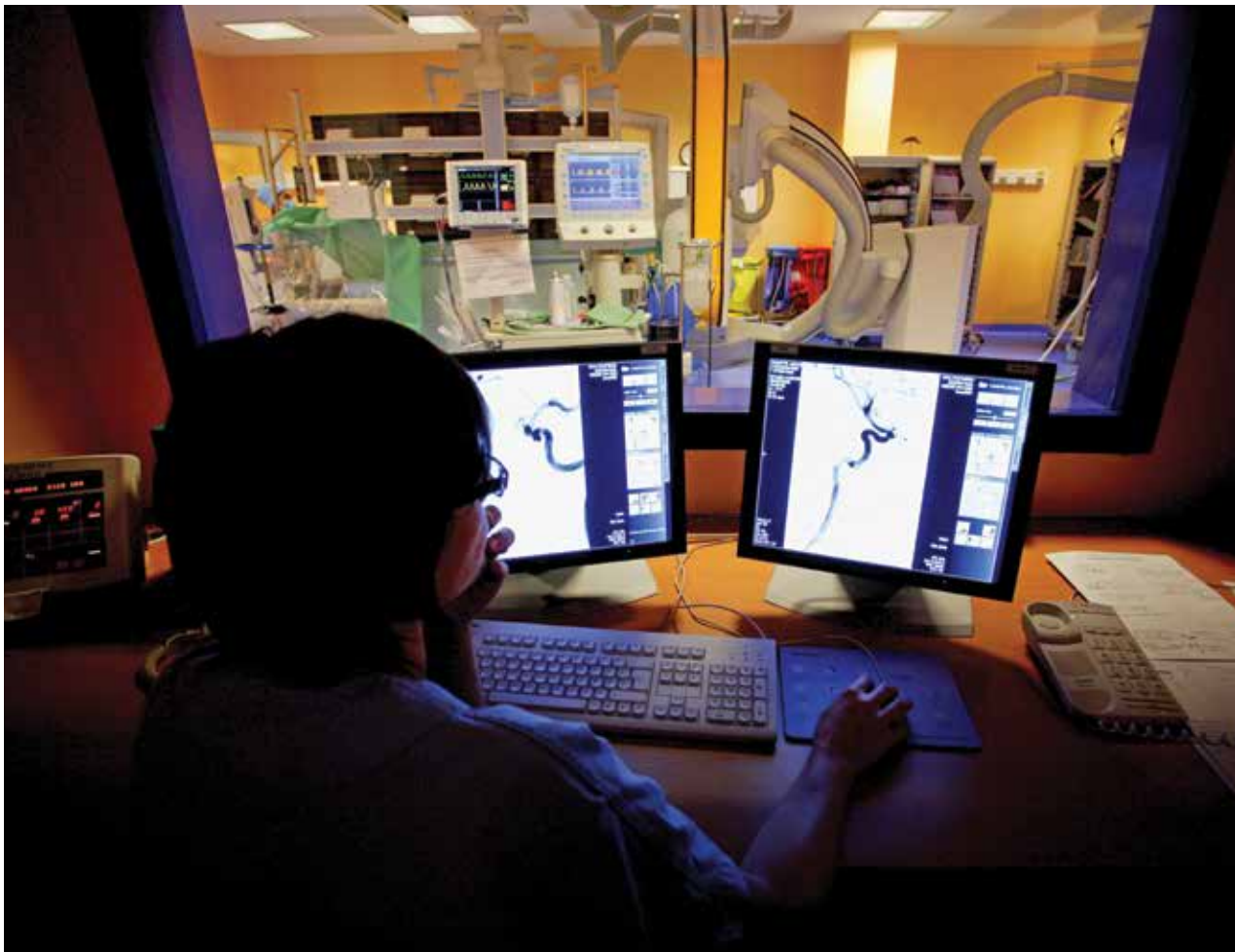
PRINCIPAL INVESTIGATOR: **Ying Xia, M.D., Ph.D.**

This National Institutes of Health-funded study is investigating brain protection against ischemia/hypoxia injury.

Neuroscience Research Repository (NRR)

PRINCIPAL INVESTIGATOR: **Dong H. Kim, M.D.**

The NRR is a prospective database and tissue sample bank that will improve knowledge of neurological illness and injury, and ultimately change the way patient care is delivered. The NRR collects samples from consenting patients for clinical, genomic and proteomic analysis. Researchers began enrolling patients in the NRR at Memorial Hermann-Texas Medical Center in the spring of 2009.



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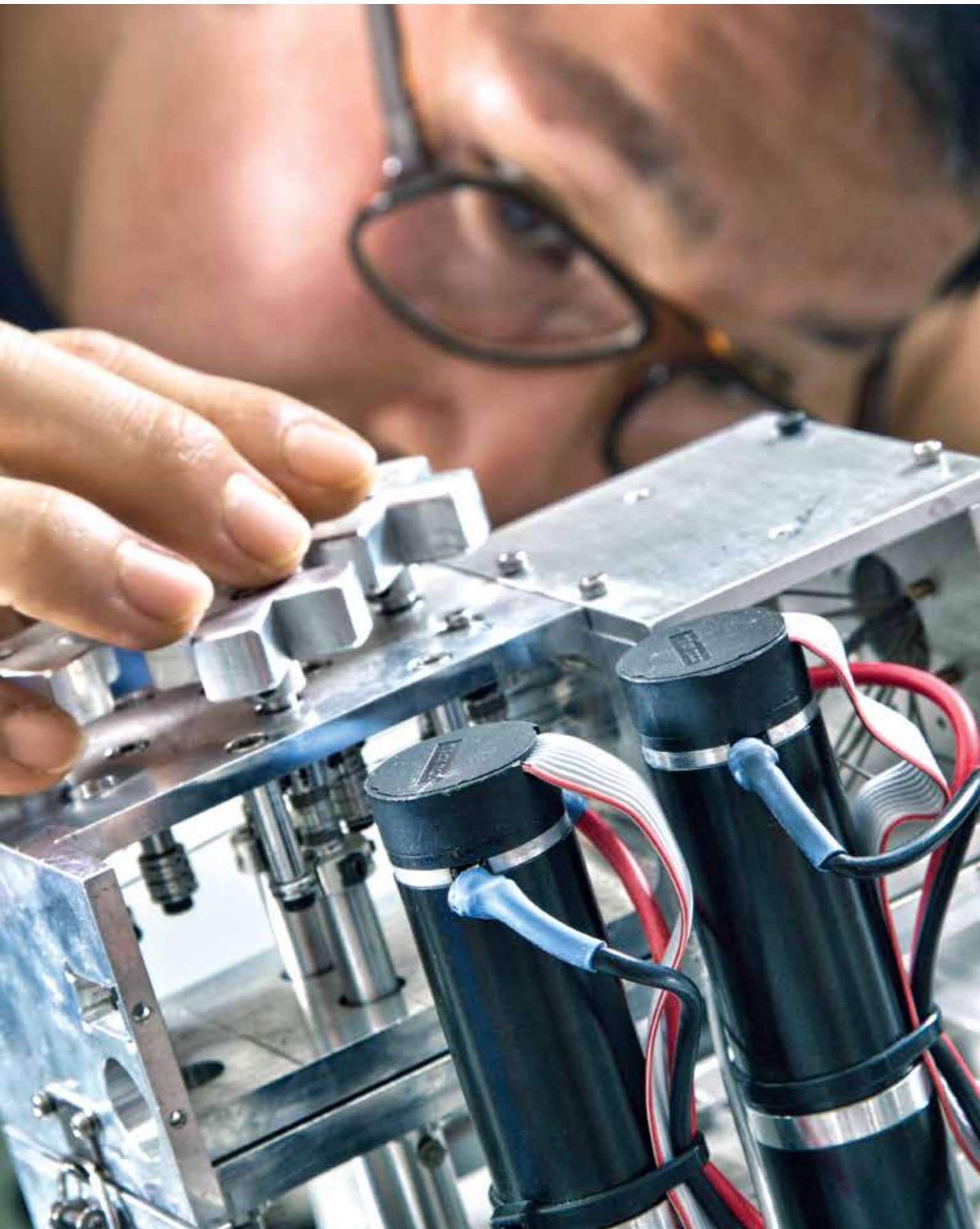
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Patient Stories

Isabella Colacchio: **Out of the Shadow**

As an infant, Isabella Colacchio was always fussy. “It seemed like she rarely slept,” says her mother Cara Colacchio, a resident of Langhorne, Pennsylvania, situated between Philadelphia and Trenton, New Jersey. “Bella would go through periods when it was worse and then better. She had headaches, stomachaches, extreme sensitivity to light and blurry vision. She struggled through kindergarten and had just gotten through the first grade when she told us, ‘By the way, I can’t see.’”

At the age of 9, when Bella’s symptoms worsened to the point that she could no longer attend school, her parents enrolled her in cyberschool. The following year – 2012 – she suffered heart palpitations and fainting spells, and was admitted to Children’s Hospital of Philadelphia. “We were just starting to figure out that she had dysautonomia and Ehlers-Danlos syndrome, when a neurologist saw her as an inpatient and found a pineal cyst,” Colacchio says.

The Colacchios saw several East Coast neurosurgeons who viewed the cyst as an incidental, asymptomatic finding and recommended against surgery. Unwilling to accept these opinions, they took Bella to a neurosurgeon in Los Angeles who agreed to operate but wanted to wait until she was older.

In the interim, Cara Colacchio discovered the Pineal Cyst Research page on Facebook, which ultimately led to an online conversation with Orlando, Florida, resident Nikki Tanner. Tanner had spent nearly 10 years and thousands of dollars seeing one specialist after another with no conclusive diagnosis and no relief from headaches before she met neurosurgeon Dong Kim, M.D., director of the Memorial Hermann Mischer Neuroscience Institute at the Texas

Medical Center. In 2013, Dr. Kim diagnosed a benign pineal cyst and resected it, ending a decade of pain for Tanner.

After a phone conversation with Dr. Kim, the Colacchios flew to Houston in January 2014 for a consultation. “Dr. Kim was very thorough and cautious, which we appreciated,” Cara Colacchio says. “He has an amazing presence – so kind and warm, which is rare in a surgeon. The entire staff went out of their way to make us feel comfortable. It was easy for us to make the decision to move forward with surgery, fly home and prepare for a return trip to Houston.”

On March 5, 2014, Dr. Kim performed a bilateral suboccipital craniectomy and resected Bella’s benign pineal cyst, a technically challenging procedure because of its deep location and the involvement of the brain stem and deep venous system. She was discharged three days later.

“Bella did very well. When I saw her two weeks after the surgery to remove the stitches, she no longer had double vision and her headaches were controllable with an over-the-counter medication,” says Dr. Kim, who is professor and chair of the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School. “Helping a young girl regain her vibrancy and energy is an incredibly rewarding experience for a neurosurgeon.”

Colacchio reports an added benefit of the surgery. “For the last three years Bella has been almost a shadow of herself. Now her stamina has increased and she no longer has fainting spells. She finished cyberschool with As and Bs, and has gone back to her music lessons – guitar, keyboards and voice – and to writing her own music. These are things she hasn’t done in three long years. To us, this is a miracle.”



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“The entire staff went out of their way to make us feel comfortable. It was easy for us to make the decision to move forward with surgery, fly home and prepare for a return trip to Houston.”

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Erick Sandoval: A Successful Brain Surgery Changes a Young Boy's Career Choice

At first Debra Johnson didn't associate her 11-year-old son's unusual behavior with seizure activity. "Erick would go through periods in which he seemed very spacey, and I couldn't figure out what was wrong," says Johnson, a resident of South Houston.

She was concerned enough to schedule an appointment with an epileptologist. When Erick had a seizure in the office while undergoing an electroencephalogram, the epileptologist prescribed an anticonvulsant and recommended an MRI.

Formerly sporadic, Erick's seizures became more intense. When results of the MRI revealed a small tumor in the right temporal lobe, Erick was referred to David Sandberg, M.D., FAANS, FACS, FAAP, who is director of pediatric neurosurgery at the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center and holds dual appointments as an associate professor in the Vivian L. Smith Department of Neurosurgery and the department of Pediatric Surgery at UTHealth Medical School. After reviewing the results with Johnson, the two physicians recommended immediate resection of the tumor.

"Initially, I was very nervous about the surgery," Johnson says. "But Dr. Sandberg assured us that the risks were minimal. He paid a lot of attention to Erick and was very good at making sure he understood exactly what was wrong and what would happen during the surgery. He made our family feel really comfortable."

On October 7, 2013, the two physicians accompanied Erick to the OR. After they determined through intraoperative electrocorticography that a small area adjacent to the tumor was the source of the seizures, Dr. Sandberg performed a craniotomy and placed grids of electrodes on the cortex of the brain, which allowed them to determine the exact source of the seizures and identify critical regions of the cortex to be avoided during surgery. He performed a gross total resection of the small tumor and removed a tiny area of the brain determined to be the epileptogenic focus.

On biopsy, pathology revealed a low-grade ependymoma, a tumor formed from ependymal cells that line the ventricles and passageways in the brain and spinal cord. "After the surgery, Erick was neurologically intact, and a postoperative MRI scan showed no evidence of the tumor," Dr. Sandberg says. "We'll need periodic MRIs but with gross total resection, there's a very good chance the tumor won't recur. Neurosurgeons at many institutions would have removed the tumor without removing the tissue that was the source of the seizures. By adding intraoperative electrocorticography, we were able to eliminate Erick's seizures and produce an excellent outcome."

Erick was discharged two days after surgery with no pain and no complications. In August 2014 he started sixth grade at Baylor College of Medicine Academy at Ryan Middle School, a health professions magnet school in Houston. "Getting a brain tumor diagnosis is really frightening, but Erick came back really fast and has had no seizures since the surgery," his mother says. "In addition to ending his seizures, the experience has had another long-term effect - he's decided he wants to be a doctor."



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Lisa Mosely: A Blessing in Disguise

Sean Michael Mosely II was born on May 6, 2014. A year earlier, on May 8, his mother, Lisa Mosely, was in the operating room with a neurosurgical team led by Dong Kim, M.D., director of the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center. The surgical plan: to remove a large pituitary adenoma that was pressing on her optic nerve.

Mosely's path to the OR was marked by a series of fortuitous twists and turns. "My husband and I decided we wanted to have kids," says the 30-year-old Kingwood, Texas, resident. "We had everything in place – good jobs and a nice house. We wanted to get a not-too-late start with our first child."

Mosely stopped taking birth control pills, but her period never returned and she started lactating – symptoms that continued for three months. When blood work done by her OB/GYN showed highly elevated prolactin levels, he referred her to a reproductive endocrinologist. "My prolactin levels were as high as a woman who was pregnant," Mosely says. "I couldn't get pregnant because my body believed it already was pregnant."

The endocrinologist prescribed cabergoline, an oral medication used to treat high prolactin levels. When Mosely's prolactin levels remained high on medication, the specialist suspected a pituitary tumor and ordered an MRI.

"My endocrinologist was very concerned about the radiologist's report," she says. "When it revealed a large tumor that contained a significant amount of blood, she

referred me to Dr. Kim. I was really nervous, but he put me at ease and I liked him immediately. 'Don't worry,' he told me. 'You'll be having kids in no time.'"

Dr. Kim scheduled surgery within two weeks of Mosely's office visit. He used a minimally invasive transnasal approach, and the complex procedure progressed like clockwork.

"It was a really easy surgery for me," she says. "I had a lot of energy and was back at work eight days later. Three months after my surgery, I found out I was pregnant. Along the way, I was told that normally you wouldn't find a tumor like mine unless you had symptoms. I believe that having a baby saved my vision. Had I stayed on birth control pills, we might not have found the tumor until it damaged my optic nerve."

"Finding the tumor and having it treated so quickly – and then getting pregnant – was a very neat experience," she adds. "I've had other medical issues in the past but have never experienced this level of attention, care and concern. Dr. Kim makes you feel like you're the most important patient he has."

"Seeing our patients do well is very special to us as physicians," says Dr. Kim, who is professor and chair of the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School. "Patients remind me every day why I became a doctor in the first place."



“I’ve had other medical issues in the past but have never experienced this level of attention, care and concern. Dr. Kim makes you feel like you’re the most important patient he has.”

William Hartman: The Rocket Scientist Meets the Brain Surgeon

For 33-year-old physicist William Hartman, undergoing any type of brain surgery to treat his epilepsy – even a minimally invasive procedure – required an enormous leap of faith. As part of the team responsible for analyzing how the International Space Station and its experiments interact with the space environment, any cognitive loss might have meant the end of his career. Hartman made that leap of faith last October, when he underwent an innovative procedure called MR-guided laser interstitial thermal therapy (MRgLITT) using the Visualase™ system at the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center.

Hartman traces his seizures to an accidental fall from a balcony when he was 3 years old. Airlifted to an Oklahoma hospital, he was comatose for four days. Almost a year to the day after the accident, he experienced a tonic-clonic seizure and was diagnosed with temporal lobe epilepsy. He began what he thought would be a lifelong regimen of drug therapies with only moderate success at alleviating his seizures.

“I changed medications often over the years, but none of them made a tremendous difference – I would have five seizures a month instead of 10,” he says. “And I had constant migraines.” Remarkably, he managed to live as normal a life as possible and earned his Ph.D. in physics in 2007. Legally unable to drive because of his seizures, he bought a home less than a mile from his job and within walking distance of a pharmacy and grocery store.

Hartman’s seizures continued, and in 2010, he was evaluated by physicians affiliated with the Texas

Comprehensive Epilepsy Program, the leading program in the southwestern United States for the diagnosis and treatment of epilepsy in patients of all ages. A collaborative effort between Memorial Hermann-Texas Medical Center, Children’s Memorial Hermann Hospital and UTHealth Medical School, the program is the premier Level IV National Association of Epilepsy Centers-certified program in Houston.

Program director Jeremy Slater, M.D., an associate professor of neurology at UTHealth Medical School, diagnosed Hartman with focal left temporal lobe epilepsy with left-sided hippocampal sclerosis. Given Hartman’s high functional state, his team of physicians agreed that the option of traditional open surgery carried a small but real risk of cognitive loss. Unwilling to take that risk, he underwent surgery to implant a vagal nerve stimulator (VNS), which uses electrical impulses to control seizures. The device is an effective treatment for some epilepsy patients whose condition is not improved by medications.

“The VNS helped and the seizures were less frequent,” Hartman says. “But I still had several seizures each weekend and up to 20 auras a day. I was able to hold them at bay somewhat during the week but when I relaxed, they piled up.”

When Hartman and his wife welcomed a baby boy in 2013, he was uncomfortable being left alone with his new baby and cautious when holding him for any length of time. “It was time to replace the battery in my VNS, and that’s when Dr. Tandon suggested MR-guided laser interstitial thermal therapy.”

Nitin Tandon, M.D., an associate professor in the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School, believed that Hartman was an ideal candidate for the procedure. “The area of his brain that was causing the seizures was evident,” Dr. Tandon says. “This new technology allows for laser precision to a degree that’s impossible to achieve with traditional open surgery.”

Knowing that Hartman was concerned about the risks, Dr. Tandon connected him with a chemist who had undergone the same procedure. “It was very helpful for me to talk to another scientist who was on the other side of what I was facing, and who had experienced great success with the procedure,” Hartman says. “My wife and I decided it was worth the risk.”

On Oct. 23, 2013, Dr. Tandon and the surgical team made a 4-millimeter incision and a 3.2-millimeter drill hole using a stereotactic head frame. “The drill hole is used for the insertion of the laser applicator,” Dr. Tandon says. “After the applicator was positioned in the target area, we placed him in the MRI scanner and turned on the laser fiber. We can measure the precise amount of heat produced by the laser and can see in real-time images the structures of the brain being heated by the fiber, minimizing the risk of potential damage to surrounding healthy tissue.”

The surgery lasted almost five hours, although the actual ablation took only a few minutes. Real-time MR imaging allowed Dr. Tandon to confirm the surgical results immediately. Like most patients who undergo MRgLITT, Hartman was discharged the following day.



“The effects were immediate,” he says. “Before the surgery, the auras I had experienced almost my entire life were a constant, almost like a sixth sense. They became stronger any time a seizure was coming on. I woke up from the surgery, and the sixth sense was completely gone. I knew immediately the procedure was a success.”

Hartman returned to work just 10 days after the surgery and has not suffered a seizure or aura since. “I used to wake up several times a night to swipe the magnet across my VNS to be able to go back to sleep,” he says. “The difference has been life changing. I can play with my son, sleep normally and drive a car.”

Dr. Slater, Hartman’s neurologist, is optimistic about his long-term prognosis. “His exercise tolerance has improved, his overall level of anxiety has dropped and he handles stress much more easily. As he continues to show progress and has no signs of seizures or auras, we will slowly wean him from his anticonvulsant medication and then turn off his VNS,” he says. “He’s doing incredibly well. We couldn’t be more pleased with his outcome.”

Maria Trevino: **Back at Work After DBS for Parkinson's Disease**

Diagnosed in 2007 with Parkinson's disease, Maria Trevino describes herself today as "a new person" thanks to the skill of the deep brain stimulation (DBS) team at the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center.

When Trevino learned about movement disorders specialist Mya Schiess, M.D., in 2010, after treatment at another institution, she scheduled an appointment. "Ms. Trevino had tremor, rigidity and slow movement especially on her right side," says Dr. Schiess, who is professor and vice chair of the department of Neurology and holds the Adriana Blood Endowed Chair at UTHealth Medical School. "When we first knew her as a patient and even early in follow-up, she had unilateral symptoms and could not normalize her motor function. But a trained eye could see she was having difficulty."

Parkinson's symptoms are caused by a lack of dopamine, a natural substance usually found in the brain. As the disease progressed, Dr. Schiess switched Trevino from a dopamine agonist regimen - often the first medication prescribed to treat Parkinson's disease - to carbidopa/levodopa, which works by being converted to dopamine in the brain. Her stiffness and slow movement improved.

"Early on in the relationship, we educate our patients about Parkinson's disease and all the treatment options," says Dr. Schiess, who is director of UT MOVE, a program focused on clinical care, education and basic science research on the neurological conditions

of motor systems disruption, including movement disorders, cerebral palsy, spasticity, neurodegenerative diseases and dementias. "When we talked about deep brain stimulation, she was quite interested."

Approved by the FDA for the treatment of Parkinson's disease in 2002, DBS uses a surgically implanted, battery-operated medical device called a neurostimulator - about the size of a stopwatch - to deliver electrical stimulation to targeted areas in the brain that control movement, blocking the abnormal nerve signals that cause symptoms.

When her symptoms progressed, Trevino, a human resources executive with a long and successful career in the hotel industry, made the decision to retire. Ten months later, after DBS surgery, she returned to work.

In July 2013, Dr. Schiess, her movement disorders fellow Michael Soileau, M.D., and neurosurgeon Albert Fenoy, M.D., took Trevino to the OR, where Dr. Fenoy placed a DBS electrode into Trevino's subthalamic nucleus. "We placed a stereotactic frame on her head and using MRI visualization, we made two burr holes in the skull while she was awake, and descended microelectrodes into the brain to verify neuronal activity and confirm that we'd reached the target areas," says Dr. Fenoy, a deep brain stimulation specialist affiliated with the Mischer Neuroscience Institute and an assistant professor in the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School. "Then we placed the actual DBS leads and test stimulated to



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“I decided to do DBS because I wanted to be normal, and that decision has made a huge difference in my life. When I see people now, they don't know there's anything wrong with me.”

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see what kind of response she had and whether she had any side effects. The surgery went extremely well.” Two weeks later, with Trevino under general anesthesia, they placed extensions from the electrodes to the neurostimulator and implanted it in her chest under the clavicle.

“I decided to do DBS because I wanted to be normal, and that decision has made a huge difference in my life,” Trevino says. “When I see people now, they don’t know there’s anything wrong with me.

“Dr. Schiess and I clicked from day one,” she adds. “She’s a beautiful, caring person, and I love her dearly. Dr. Schiess, Dr. Fenoy, and Dr. Soileau are my guardian angels. They’re the best in town. That lady is amazing. She treats you like family. She’s 100 percent my idol.”

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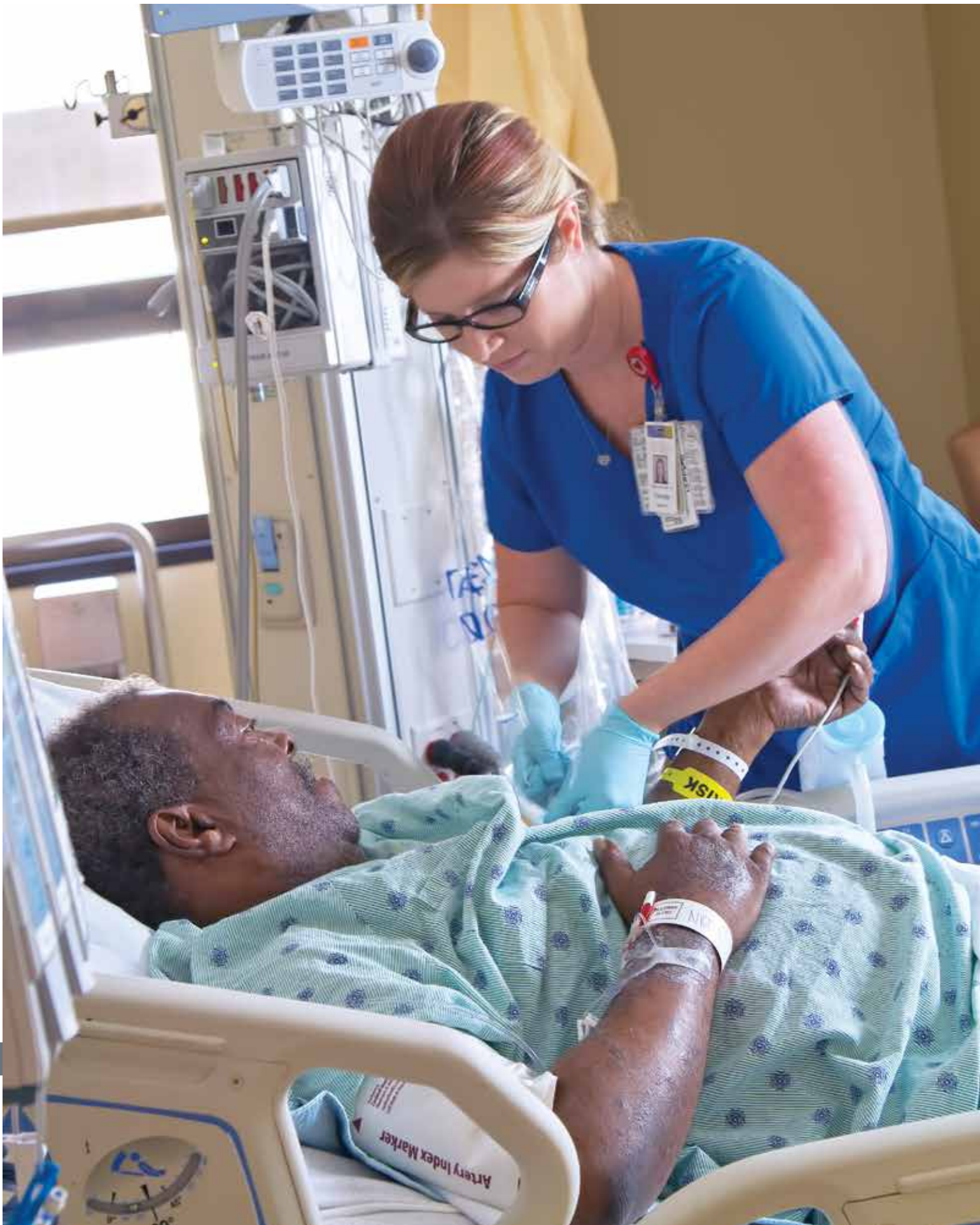
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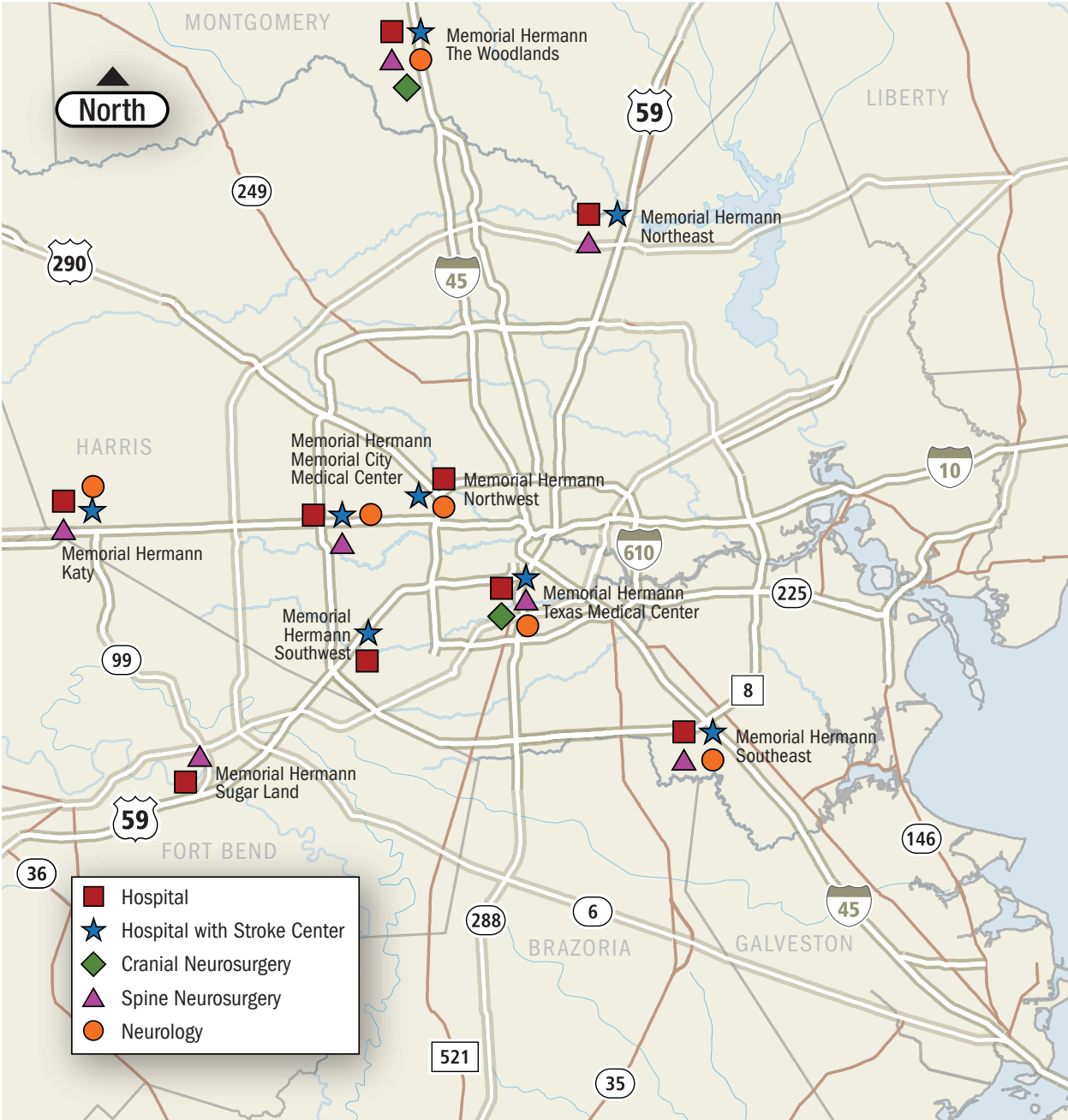
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MISCHER NEUROSCIENCES LOCATIONS



MNI's infrastructure expansion has allowed the Institute to extend its neuroscience expertise and capabilities outside the Texas Medical Center and into the community through the development of neuroscience centers at Memorial Hermann community hospitals and beyond. Together, the centers bring distinctive subspecialty services to the community, and when combined with the specialized skills of neurosurgeons and neurologists at MNI, they offer suburban patients comprehensive consultation, evaluation and treatment for a range of disorders.

A microscopic image of neurons. The cell bodies and dendrites are highlighted in a vibrant yellow and orange glow, while the long, thin axons are shown in a deep blue. The background is dark, making the glowing structures stand out prominently.

The physicians and researchers at the Mischer Neuroscience Institute stand at the threshold of breakthrough discoveries that will transform how to treat and cure neurological diseases and disorders. In partnership with the philanthropic community, they have recruited exceptional clinicians and researchers and funded leading-edge technology and research. Yet, work remains to be done.

We need your help to touch more lives. **Please consider making a tax-deductible gift to the Memorial Hermann Foundation in support of the Mischer Neuroscience Institute.** Your gift will help MNI attain an unprecedented level of scientific discovery that will lead to transformative treatments for our patients.

For more information on funding needs at the Mischer Neuroscience Institute or to make a gift, visit memorialhermannfoundation.org or call 713.242.4400.



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