



MISCHER NEUROSCIENCE INSTITUTE **REPORT 2011**

Mischer  
Neuroscience Institute

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MEMORIAL<sup>®</sup>  
HERMANN

## When physicians and patients choose

*the Mischer Neuroscience Institute located at Memorial Hermann-Texas Medical Center, part of the 11-hospital Memorial Hermann Healthcare System, they're choosing the largest and most comprehensive neuroscience program in Texas. The renowned faculty at the Mischer Neuroscience Institute works together in a coordinated attack against neurological disease. Thanks to their knowledge and talent, the Mischer Neuroscience Institute is nationally recognized for leading-edge medicine and consistently ranked among quality benchmarking organizations as a leader in clinical quality and patient safety.*

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**Dr. Kim**



**Dr. Grotta**

## Dear Esteemed Colleagues,

We are pleased to share with you the Mischer Neuroscience Institute (MNI) Clinical Achievements Report for fiscal year 2011, which highlights our clinical expertise and accomplishments in quality, safety, clinical care and research from July 2010 through June 2011. The report is a publication of MNI, part of the 11-hospital Memorial Hermann system, in collaboration with The University of Texas Health Science Center at Houston (UTHealth) Medical School. We hope you find the information on the pages that follow interesting, informative and valuable.

We had much to celebrate over the last year. Our quality outcomes and long history of innovation in the field of neuroscience continue to ensure that we attract accomplished physician faculty members who share our commitment to raising the bar with first-rate clinical programs, continued growth and breakthrough research applied daily in the operating room and at the bedside. In 2010, we welcomed eight talented faculty members to MNI: neurosurgeon Arthur L. Day, M.D.; neurologist and neuro-oncologist Jay-Jiguang Zhu, M.D., Ph.D.; neuropsychiatrist and behavioral neurologist Paul Schulz, M.D.; vascular neurologist Vivek Misra, M.D.; neurologists Anita Madan, M.D., and Holly Varner, M.D.; and researchers Min Li, Ph.D., and Ying Xia, M.D., Ph.D.

We also expanded our capability to treat neurological disease through the addition of new technology, including the most technologically advanced Gamma Knife model available – the new Leksell Gamma Knife® Perfexion™. We acquired a Siemens Artis™ zee biplane system in our vascular interventional suite, which allows for improved visualization and greater precision in the treatment of some of the most complex brain and spine vascular diseases. A new Varian Trilogy linear accelerator for stereotactic radiosurgery will allow noninvasive treatment of benign and malignant tumors, and the addition of a Magnes 3600 WH MEG brain imaging system will allow us to expand the technology’s use in diagnosing epilepsy, aneurysms, cortical brain lesions, arteriovenous malformations and brain tumors.

We are proud of these accomplishments and remain committed to quality and safety, the core strategies that underlie our promise to provide the best possible outcomes and exceptional patient care. We keep this promise top of mind as we continue to develop new programs and services, strengthen awareness of and preference for MNI and expand our support of research and innovation.

Please feel free to contact us directly if you would like additional information about our services and programs.

With best wishes,

**Dong H. Kim, M.D.**  
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# *About* Our Institute



Leading the way in neuroscience in a city known for medical excellence takes dedication. To accomplish this, Memorial Hermann's Mischer Neuroscience Institute brings together a team of world-class clinicians, researchers and educators. A collaborative effort between Memorial Hermann-Texas Medical Center and The University of Texas Health Science Center at Houston (UTHealth) Medical School, we are the largest neuroscience provider in South Texas and one of only a few institutions in the country to provide all aspects of neuroscience care, from neurology to neurosurgery to neurorehabilitation. This comprehensive approach has led to the creation of Houston's first and largest stroke team, its leading epilepsy and neurotrauma programs, a cerebrovascular center that treats the the most aneurysms and arteriovenous malformations in the region, and a brain tumor program that annually diagnoses and treats hundreds of new tumor patients. We are proud of our innovations in multiple sclerosis, brain injury, spine surgery and more. And we make more neuroscience breakthroughs every day.



# At-a-Glance

## Physician Team

Staff Physicians	40
Clinical Residents and Fellows	39
Medical Students on Rotation	252
Research Fellows	7
Advanced Practice Nurses	2
Physician Assistants	15

## Inpatient Facilities

Total Neuro Beds	136
Neuro ICU Beds	32
Neuro Step Down Beds (IMU)	12
Neuro Acute Care Beds	45
Neuro Rehabilitation Beds	23
Stroke Unit Beds	12
Dedicated Operating Rooms	6
EMU Beds – Pediatrics	6
EMU Beds – Adult	6

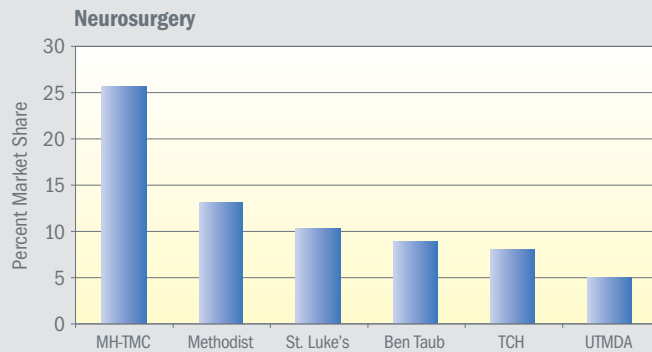
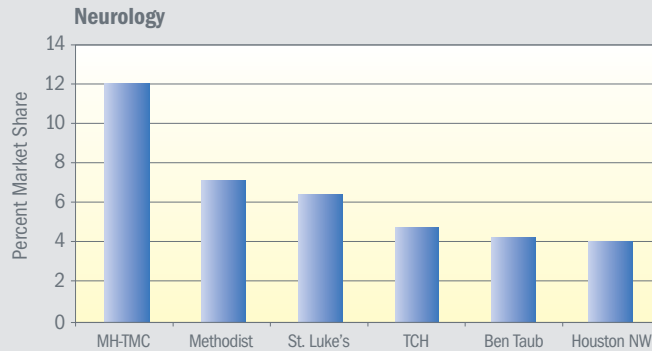
## Research

Research Projects in Progress	More than 200
Grants Awarded	\$17 million
	(Neurology and Neurosurgery)

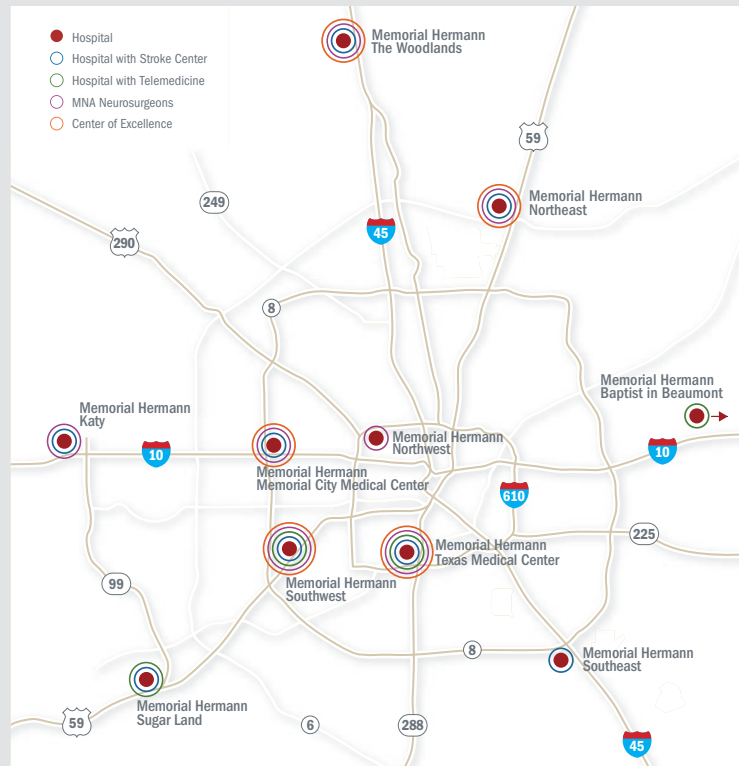
## Specialty Equipment

- Leksell Gamma Knife® Perfexion™
- Siemens Artis™ zee (intra-operative angiography suite)
- RP-7™ Remote Presence System
- Philips Healthcare Endovascular Temperature Modulation System
- Simultaneous electroencephalography and polysomnography
- Magnes 3600 WH Magnetoencephalography Brain Imaging System
- MRI capable of advanced spectroscopic and diffusion tensor imaging with tractotomy
- Varian Trilogy LINAC for Stereotactic Radiosurgery

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, creating five centers of excellence. 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.



Source: Texas Hospital Association Patient Data System (FY2009 Q1 - FY2011 Q4) provided by Thomson Reuters Texas Hospital Inpatient Discharge Public Use Data File, [FY2007 Q1 - FY2011 Q1] provided by Texas Department of State Health Services, Center for Health Statistics; Q2FY2011 - Q4 FY2011 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.



# A History of Firsts



- The first Stroke Center in Houston and one of the first dedicated stroke programs in the world.
- The first and only hospital in the Texas Medical Center to receive state of Texas designation as a primary stroke center.
- 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® – 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. We remain the No.1 program in the United States in the number of vagal nerve stimulators implanted in epilepsy patients.
- Brought the first clinical magneto-encephalography (MEG) sensor to Houston and recently updated the technology to the new Magnes 3600 WH. It remains the only MEG in clinical use throughout Texas, Louisiana, Arkansas and Oklahoma.
- One of only a few inpatient Epilepsy Monitoring Units in the country with the unique capability of simultaneously performing electroencephalography and polysomnography.
- TIRR Memorial Hermann is the only center in Houston – and one of only seven designated centers in the nation – in the Christopher and Dana Reeve Foundation NeuroRecovery Network.

# Achieving Excellence in Quality, Safety and Cost Effectiveness

Memorial Hermann has a longstanding commitment to quality, safety and cost effectiveness. These are also the three tenets of the University HealthSystem Consortium (UHC), an alliance of 113 academic medical centers and 254 of their affiliated hospitals, representing approximately 90 percent of the nation's nonprofit academic medical centers. In 2010, the organization ranked Memorial Hermann-Texas Medical Center as No. 20 on its list of top academic medical centers in the country. In an effort to continue to improve patient care, Memorial Hermann-TMC is committed to raising that ranking even higher.

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**UHC's Core Characteristics:**

- Execution
- Authenticity
- Sustainability
- Team collaboration
- Intentional actions
- Transparency
- Inspiration
- Professionalism
- Safety
- Community

"The UHC rankings are an objective measure of quality and demonstrate a high standard of patient care," notes Dong H. Kim, M.D., director of the Mischer Neuroscience Institute (MNI), chief of neurosurgery at Memorial Hermann-TMC and chair of the Vivian L. Smith Department of Neurosurgery at The University of Texas Health Science Center at Houston (UTHealth) Medical School. "At Memorial Hermann, quality and safety are core strategies that underlie our commitment to providing optimal clinical outcomes through patient-centered care. To deliver on that promise, physicians and staff at the Mischer Neuroscience Institute have embraced a culture of accountability and innovation, which has led to a relentless focus on continuous improvement."





Improvements made by MNI in 2010 include decreases in bloodstream infections, ventilator-associated pneumonias, urinary tract infections and surgical-site infections. All of these efforts have reduced costs and enhanced quality and patient safety.

According to UHC, the nation's top-performing academic medical centers consistently embody a core set of characteristics. These organizational traits include a shared sense of purpose; a distinctive, interactive leadership style; an accountability system for service, quality and safety; a focus on results; and collaboration among administrative leaders, clinical chairs and staff.

Memorial Hermann-TMC CEO Craig Cordola recently set a new goal of achieving and maintaining a UHC top-10 ranking. "To set the standard for quality patient care in the future, we created a set of attributes that we'll use to characterize the way work is done, how staff members treat one another and how care is delivered on our Campus," Cordola says. "Building on the Memorial Hermann system's core behaviors – accountable, innovative, collaborative, compassionate, competent and respectful – we're seeking to incorporate 10 more attributes: execution, authentic, sustainable, team, intentional, transparent, inspired, professionalism, safe and community. We're confident that this new vision will lead to new levels of quality, safety and cost effectiveness."

# Designing Our Future: Improving Efficiencies and Quality

The passage of two pieces of legislation, H.R. 3590, the Patient Protection and Affordable Health Care Act in December 2009, and H.R. 4872, the Reconciliation Act of 2010 in March 2010, constitutes the largest change in America's healthcare system since the 1965 passage of Medicare. It also marks the beginning of what will be a long process of rulemaking and implementation, with dozens of effective dates of major components of reform scheduled over the next 10 years. While the law will present challenges for healthcare providers across the country—requiring resources and capabilities that exceed those of most hospitals—Memorial Hermann is well prepared for changes that will support and improve quality care.

“As healthcare reform moves hospitals away from the current model's volume-driven, fee-for-service structure to a pay-for-performance structure tied to clinical outcomes, the Mischer Neuroscience Institute (MNI) is examining processes and investigating opportunities to improve efficiencies and quality,” says Dong H. Kim, M.D., director of MNI, chief of neurosurgery at Memorial Hermann-Texas Medical Center and chair of the Vivian L. Smith department of Neurosurgery at The University of Texas Health Science Center at Houston (UTHealth) Medical School. “In line with our focus on innovation and strategic planning, we're committed to Memorial

Hermann's 'Creating a New Healthcare Model' initiative, which is redefining our organizational structure and business model to ensure continued success in the post-reform healthcare environment.”

Recently, the Centers for Medicare & Medicaid Services (CMS) issued a proposed rule establishing a hospital value-based purchasing program for acute care hospitals for inpatient services provided to Medicare beneficiaries. Under the proposed rule, which was created to improve clinical outcomes and patient satisfaction, hospitals will receive value-based incentive payments beginning in fiscal year 2013, based on clinical outcomes and patient satisfaction with services provided.

“This change represents a dramatic shift in how Medicare will pay hospitals,” says Jeffrey Katz, M.D., chief medical officer of the Memorial Hermann-TMC Campus. “As part of the CMS Hospital Quality Initiative, hospitals will be scored on quality measures and patient satisfaction. CMS will designate hospitals in the top 50 percent as 'top performers' and they will receive no cuts in reimbursement. Hospitals with measures below the 50th percentile will face reductions in reimbursement of 1 percent to 3 percent.”

Closely related to the issue of value-based purchasing, the federal government is seeking to regulate the length of inpatient hospital stays. “We, and hospitals across the nation, face a delicate balancing act in the coming months and years as we seek to reduce the time our patients spend in our hospital while also effectively treating the whole person, which can include multiple diagnoses,” Dr. Katz says. “This issue is a key component of national healthcare reform, and therefore remains a priority in all our service lines, including Neuroscience.”

As with the potential for payment cuts related to patient satisfaction, hospitals also will face negative incentives for readmissions. Medicare has targeted acute myocardial infarction, pneumonia and congestive heart failure as areas in which to reduce readmissions. Beginning in 2013, any patient with one of these diagnoses who is readmitted within 30 days will trigger a reduction of 1 percent of all Medicare reimbursements to that hospital, which will increase to 2 percent in 2014 and 3 percent in 2015.

To thrive in the new post-reform environment and improve clinical outcomes, hospitals and affiliated physicians will need to be more closely aligned in healthcare delivery. Memorial Hermann is working with its physician network, MHMD, to create an Accountable Care Organization (ACO) in which caregivers are held responsible for the care they provide. ACOs reward hospitals and physicians for delivering more efficient, coordinated quality care founded on evidence-based medicine.

“Technology will be critical as we move toward more coordinated, efficient quality care with the best clinical outcomes,” Dr. Kim says. “Having our electronic medical records and clinical decision support integrated with computerized physician order entry, which uses order sets built on evidence-based medicine, will help

contribute to improved care delivery. We continue to improve our clinical documentation processes and reduce our length of stay, which will help us improve operations now and in the future.”

Quality and safety will continue to be important factors in healthcare delivery as hospitals are held accountable for hospital-acquired infections and complications that result from unsafe care. Memorial Hermann is active in a leadership role in the new Center for Transforming Healthcare launched by The Joint Commission to develop solutions that target patient safety and quality issues.



“We strive every day to increase efficiency of services and enhance quality of care,” Dr. Katz says. “We will continue to invest in the technology that enables our physicians to treat illness in novel and innovative ways and eliminates inefficient operational delays.”

As legislators continue to roll out new regulations as part of national healthcare reform, MNI and Memorial Hermann are prepared for the changes. “Our commitment to quality is an integral part of who we are as an institution,” Dr. Kim says. “We’re proud of the terrific work of our physicians and researchers, and of the impact they have on the lives of our patients, and we’re confident that we’ll continue to provide the highest level of care to our patients.”



# 2011 Accolades



We are proud to share *with you* highlights of our accomplishments in clinical care, research and academic endeavors as individuals and as an institution.

## 2011 Accolades



### The Vivian L. Smith Department of Neurosurgery Recognized for Academic Impact

The Vivian L. Smith Department of Neurosurgery at The University of Texas Health Science Center at Houston (UTHealth) Medical School was ranked 9th and 12th nationally in a study of academic productivity that appeared in the September 2010 issue of the *Journal of Neurosurgery*<sup>1</sup>.

The authors of the article used the h index, a measure of the number of citations received by a collection of work, to estimate the relative academic impact of 99 departments of neurosurgery with residency programs participating in the U.S. National Residency Matching Program, and 14 analogous Canadian programs. Two lists of rankings were created: the first

tracked impact based on publication in neurosurgery journals and the second tracked impact across all neuroscience journals.

Among institutions cited in neurosurgery journals, the UTHealth Medical School's Neurosurgery department ranked 12th nationally in a tie with the University of Pennsylvania and the Cleveland Clinic Foundation. In rankings tallied across all neuroscience journals, the department was ninth nationally. These rankings are the highest of any neurosurgery program in Texas.

"We're proud of the work of our physicians and researchers," says Dong H. Kim, M.D., director of the Mischer Neuroscience Institute and professor and chair of the Vivian L. Smith Department of Neurosurgery at the UTHealth Medical School. "These are terrific rankings – the result of our shared commitment to

advancing medical knowledge by reporting the results of our basic science studies and participation in clinical trials.”

Introduced in 2005 as a means of characterizing the scientific output of a researcher, the h index is defined as the number of papers, h, by an individual with citation counts of h or higher. The number of times an article has been cited by other works is often used as a measure of impact, note the article’s authors.

They also reported significant correlations between the citation indices and faculty size, number of publications, types of degrees held by the faculty and funding by the National Institutes of Health (NIH). The Neurosurgery department ranks seventh nationally in funded NIH grants.

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<sup>1</sup> Ponce FA, Lozano AM. Academic impact and rankings of American and Canadian neurosurgical departments as assessed using the h index. *Journal of Neurosurgery* 113:447-457, 2010.



## James Grotta, M.D., Honored with Academic Mentorship Award and Named Health Care Heroes Finalist

The American Heart Association presented one of its highest honors, the Eugene Braunwald Academic Mentorship Award, to James C. Grotta, M.D., chief of neurology at Memorial Hermann-Texas Medical Center, co-director of the Mischer Neuroscience Institute (MNI) and professor and chair of the Neurology department at The University of Texas Health Science Center at Houston (UTHealth) Medical School. He was recognized for exceptional achievement in guiding and inspiring young trainees throughout his career in research and administration.

Dr. Grotta received the award during opening ceremonies of the American Heart Association’s 2010 Scientific Sessions held last November in Chicago. “The award is a testament to your long and distinguished career – and a real compliment to your record of mentoring young researchers who will help push the scientific community toward neurological breakthroughs for many years to come,” wrote American Heart Association executive vice president Midge LaPorte Epstein in an announcement letter. “Your impact in the field will no doubt be felt long after your own time in the laboratory is finished.”

The Eugene Braunwald Academic Mentorship Award followed Dr. Grotta’s selection as a 2010 “Health Care Heroes” finalist by the Houston Business Journal. The Health Care Heroes Awards are presented annually to honor those who serve, innovate and save lives.

Dr. Grotta, who holds the Roy M. and Phyllis Gough Huffington Distinguished Chair, has played a leadership role in many clinical research studies of

## 2011 Accolades

both thrombolytic drugs and cytoprotective agents following stroke, and has been funded by the National Institutes of Health (NIH) for laboratory studies on the biology of brain injury and recovery in animal stroke models. He is currently funded by the NIH for a project to carry out a series of novel pilot studies aimed at amplifying the existing benefits of intravenous tPA and achieving clinically meaningful neuroprotection using hypothermia.

In 1988, Dr. Grotta was instrumental in founding MNI's Stroke Center, one of the first dedicated stroke programs in the world and the first Joint Commission-accredited primary stroke center in the region. Under his leadership, Memorial Hermann-TMC was the first

in Houston and one of the first in the United States to test tPA for acute stroke.

Dr. Grotta orchestrated the development of a highly successful collaborative network between the MNI Stroke Center, Memorial Hermann-TMC, Houston Fire Department Emergency Medical Services and other regional stroke centers to increase the delivery of appropriate therapy to a large number of acute stroke patients in Houston. As a result, the Stroke Center remains the American leader in number of acute stroke patients treated with tPA, with an administration track record of 10 times the national average. He has extended these efforts to rural areas through regional educational programs and, more recently, telemedicine.





Dr. Grotta also directs an NIH-funded and Accreditation Council for Graduate Medical Education-accredited stroke training program with a strong emphasis on basic and clinical research. He has assembled a multidisciplinary stroke faculty that has graduated more than 40 clinician-scientists specializing in stroke research.

He has been an editor of the *Annals of Neurology*, *Stroke* and many other peer-reviewed journals, and a member of several NIH and FDA review panels. He was a recipient of the Feinberg award for Excellence in Clinical Stroke from the American Heart Association in 1999, the AHA Physician of the Year Award for 2006 and awards for teaching excellence at the UTHealth Medical School for 14 years. He has authored or co-authored more than 200 articles in peer-reviewed journals.

### Neuromuscular Disorders Center Designated GBS/CIDP Center of Excellence

The GBS/CIDP Foundation International has designated the Neuromuscular Disorders Center at Mischer Neuroscience Institute (MNI) and The University of Texas Health Science Center at Houston (UTHealth) department of Neurology as a center of excellence for the diagnosis and treatment of Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP) and other inflammatory peripheral neuropathies. The designation was awarded in recognition of the high standards maintained and quality of patient care provided at the center, which is one of only six such centers of excellence in the United States.

The MNI neuromuscular disorders team includes Kazim Sheikh, M.D., professor of neurology at the UTHealth Medical School, director of the MNI Neuromuscular Disorders Center and director of the Muscle and

Nerve Laboratory at Memorial Hermann-Texas Medical Center; Parveen Athar, M.D., assistant professor of neurology and director of the MNI Electromyography Laboratory; and Suur Biliciler, M.D., assistant professor of neurology, all of whom provide adult care.

Pedro Mancias, M.D., a member of the medical staff at Children's Memorial Hermann Hospital and an associate professor of pediatric neurology, provides pediatric care.

### Andrew Barreto, M.D., Graduates from Physician Quality & Safety Leadership Academy

Andrew Barreto, M.D., assistant professor of neurology at The University of Texas Health Science Center at Houston (UTHealth) Medical School, was among seven graduates in the second class of the Physician Quality & Safety Leadership Academy, a collaborative effort of Memorial Hermann-Texas Medical Center and the UTHealth Medical School. The Academy was created in 2008 to build a core group of physician leaders considered experts in this arena.

Dr. Barreto was nominated for the Academy by Neurology department chair James C. Grotta, M.D., co-director of the Mischer Neuroscience Institute. Highlights of the nine-month course included immersion in Six Sigma methodology and LEAN process, and the opportunity to interact with nationally renowned physician quality advocates, including Brent James, M.D., and Jim Reinertsen, M.D.

Projects were selected in conjunction with Academy leaders, and the results of the physicians' work were presented at the Academy's graduation ceremony. Dr. Barreto's project was titled "Time to Intra-arterial Therapies for Stroke Patients."

## 2011 Accolades

### Nicole Gonzales, M.D., Receives Young Investigator's Award

Nicole R. Gonzales, M.D., was honored at the 5th Annual Young Investigator's Appreciation Luncheon to recognize the research achievements of junior faculty at The University of Texas Health Science Center at Houston (UTHealth) Medical School. Her work was recognized by Larry R. Kaiser, M.D., F.A.C.S., former president of UTHealth Medical School.

Dr. Gonzales is principal investigator of "The Safety of Pioglitazone for Hematoma Resolution in Intracerebral Hemorrhage (SHRINC) and MRI Evaluation of Hematoma Resolution as a Surrogate Marker of Clinical Outcome in Intracerebral Hemorrhage." The study compares the safety of pioglitazone with standard of care for patients with spontaneous intracerebral hemorrhage. The hope is that the drug can stimulate the body's own cells to absorb the hematoma faster and, as a result, lead to more rapid recovery.

### Neurosurgery Chief Resident Recognized by the Gold Foundation

Neurosurgery chief resident Bart MacDonald, M.D., is among six residents at The University of Texas Health Science Center at Houston (UTHealth) Medical School to receive the Arnold P. Gold Foundation's Humanism and Excellence in Teaching Award. Nominated by fourth-year medical students, he was recognized for his compassion and empathy in the delivery of care to patients and for illustrating professional behavior.

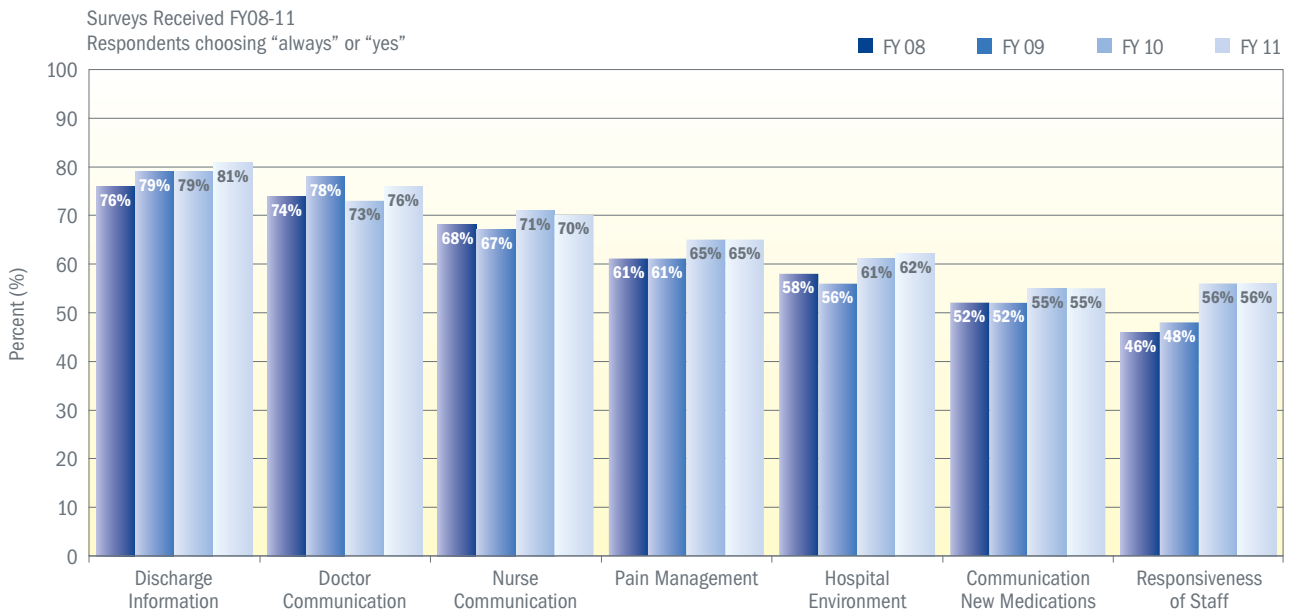
Dr. MacDonald received his medical degree from the Medical College of Georgia in Augusta in 2000, followed by an internship in general surgery at the University of Florida in Gainesville. He completed his first year of neurosurgical residency at the University of North Carolina in Chapel Hill in 2001, followed by four years at Brigham and Women's Hospital and Children's Hospital in Boston, where he also conducted research in hydrocephalus. His clinical and research interests include complex spine and vascular neurosurgery.

The Arnold P. Gold Foundation advances humanism in medicine, perpetuating the tradition of the caring doctor.

# Patient Experience

Patients from around the world choose to receive treatment at the Mischer Neuroscience Institute based on our high-quality outcomes and our reputation for providing the best possible healthcare experiences, both of which are supported by our commitment to communication and responsiveness. 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 Domains of Care



Source: Press Ganey, national hospital survey vendor, for all surveys received from patients discharged from 3 Jones, 7 Jones/ NSICU, 4 Jones/NIMU/Stroke and EMU  
HCAHPS scores have not been adjusted to account for a survey mode administration change

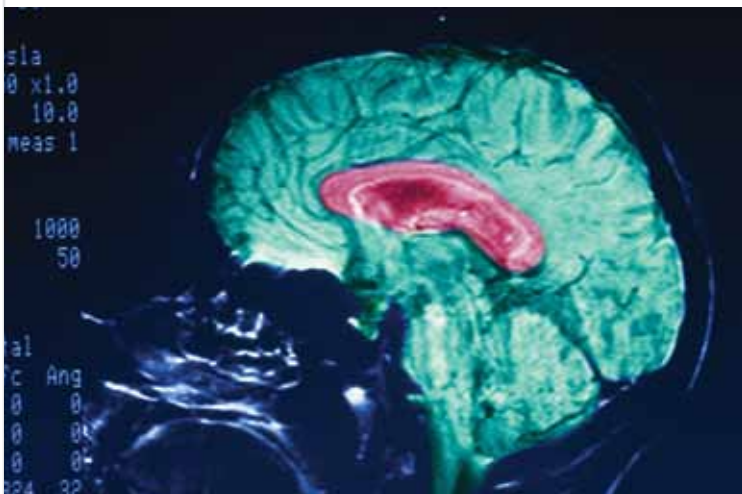




*Scope of Services*

# Brain Tumor

With the arrival of fellowship-trained neurologist and neuro-oncologist Jay-Jiguang Zhu, M.D., Ph.D., in September 2010, the Mischer Neuroscience Institute (MNI) added significant strength to its Brain Tumor Center. Dr. Zhu joined MNI from Boston, where he trained at Massachusetts General Hospital and served on the faculty of Tufts University. He 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 metastasis. He currently serves as 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 medical device called Novo TFF-100A for newly diagnosed glioblastoma multiforme (GBM) patients in combination with temozolomide, compared to temozolomide alone. The device, which patients wear on their scalp, emits a constant, safe, low-voltage signal that has been shown to reduce tumor cell survival and division capacity. The Novo TFF-100A was recently approved by the FDA for the treatment of progressive GBM; the trial is open to newly diagnosed GBM patients. Dr. Zhu is also principal investigator in a trial of Azixa™ (verubulin), an investigational cancer drug being developed for the treatment of newly diagnosed GBM patients. A randomized, double-blind, controlled Phase IIB clinical trial of the safety and efficacy of the vaccine ICT-107 for newly diagnosed GBM patients following resection and chemoradiation has been approved, and began enrollment in August 2011.

Our team focuses on providing the best state-of-the-art treatment and access to investigational trials as appropriate. We use innovative and advanced technologies, including motor and language mapping, functional neuroimaging, frameless stereotactic navigation in surgery, and awake craniotomies performed under local anesthesia. We also perform minimally invasive procedures, including neuroendoscopy and stereotactic radiosurgery.

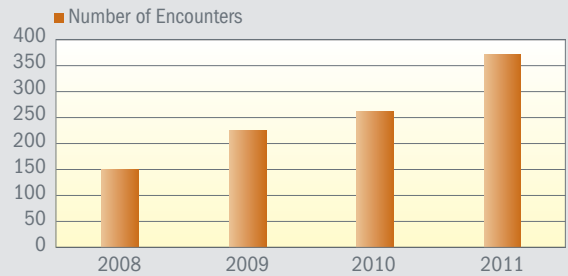
## QUALITY & OUTCOMES MEASURES

After acquiring the region's first Leksell Gamma Knife® in 1993, we recently acquired the most 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.

Our clinical team works closely with referring physicians throughout the Gamma Knife treatment process. A neurosurgeon and a radiation oncologist assess each candidate to determine whether radiosurgical treatment is the best option. Our Gamma Knife nurse navigators work directly with patients on scheduling and pretreatment education, and provide support and care on the day of treatment.

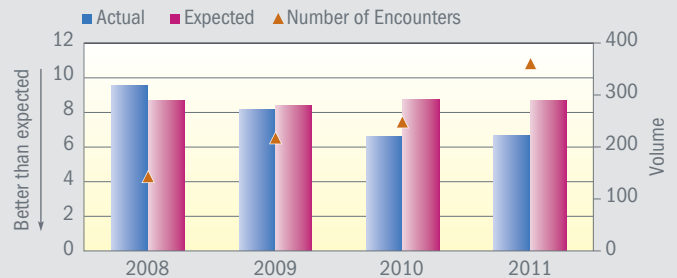
Breakthrough approaches to treatment at MNI are allowing us to grow the number of patients treated for brain tumors. At the same time, our mortality rate and average length of stay are well below the national benchmark established by the University HealthSystem Consortium.

### Brain Tumor Volume



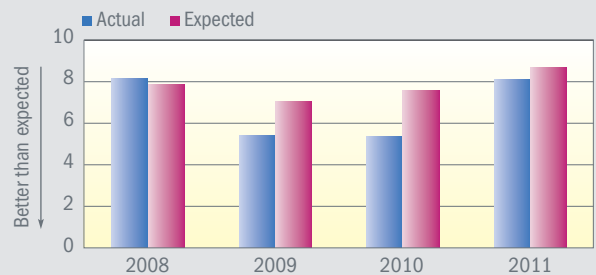
Source: chart data based on ICD9 codes, per fiscal year

### Brain Tumor (all types): Length of Stay



Source: chart data based on ICD9 codes, per fiscal year

### Brain Tumor (all types): Inpatient Mortality



Source: chart data based on ICD9 codes, per fiscal year

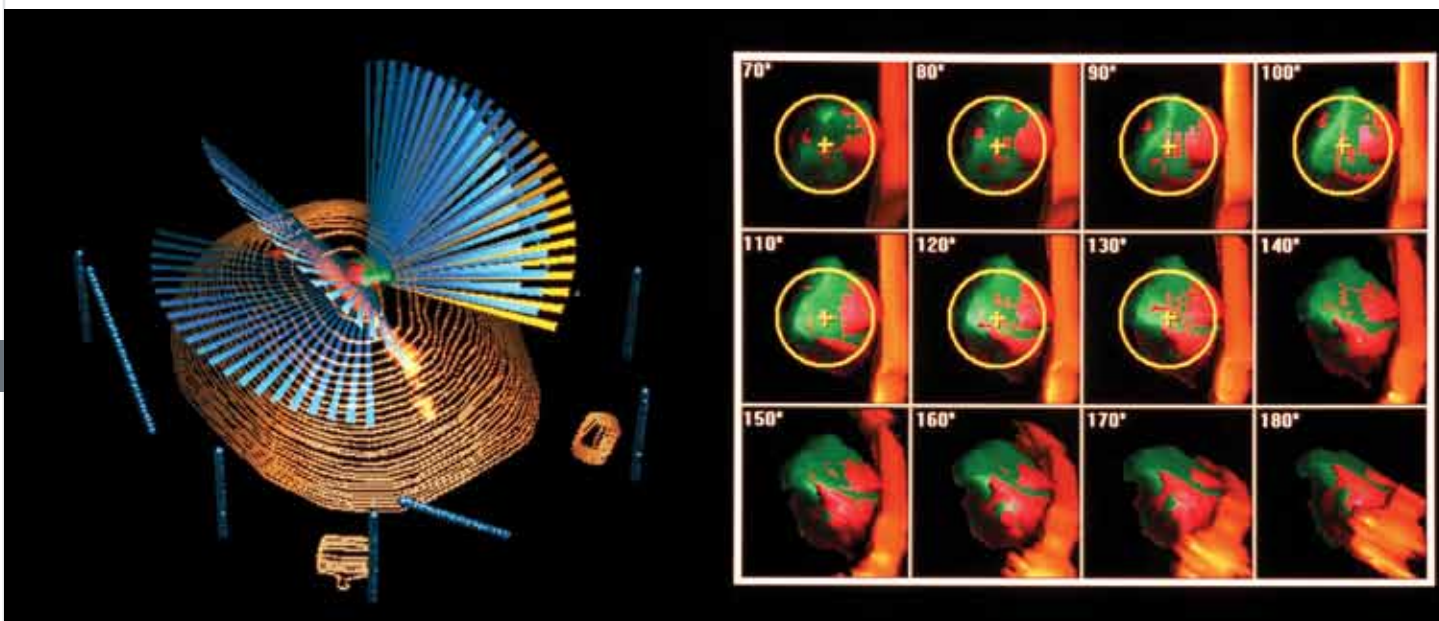
# Cerebrovascular

Opened in 1988 as one of the first dedicated stroke programs in the world, Mischer Neuroscience Institute's Stroke Center is home to the 10-county Greater Houston area's largest onsite stroke team. Neurologists at the Center use leading-edge technology to diagnose and treat more than 1,000 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, our stroke team has logged an impressive record of success in the administration of tPA – more than 10 times the national average of 2 percent.

In 2010, The Joint Commission re-credentialed Memorial Hermann-Texas Medical Center as a comprehensive stroke center, the highest designation offered by the organization. Two Memorial Hermann hospitals earned The Joint Commission's Gold Seal of Approval™ for

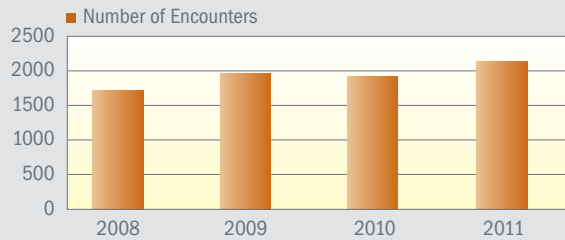
Primary Stroke Centers, and three facilities were named Community Stroke Support Facilities. In addition, the state of Texas designated Memorial Hermann-TMC as a primary stroke center, making us the first hospital in the Texas Medical Center to receive this designation.

Our Telemedicine Program extends our stroke and neurology expertise far beyond our walls, helping emergency physicians in community hospitals throughout southeast Texas make accurate diagnoses and save lives. Remote presence robotic technology has enhanced MNI's telemedicine program by linking outlying hospitals electronically to the Neurology department, providing real-time visual interaction between neurologists and patients, and allowing MNI neurologists to review CT scans and advise local physicians on treatment outcomes. Through telemedicine, we can now offer patients in outlying



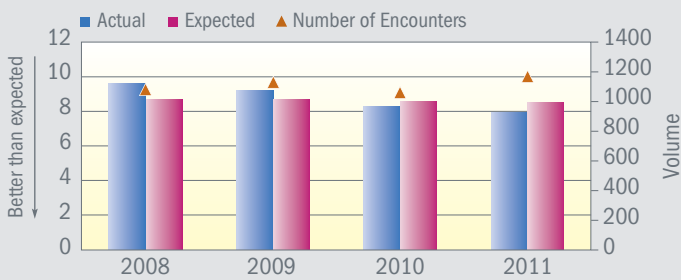


**Cerebrovascular Volume**



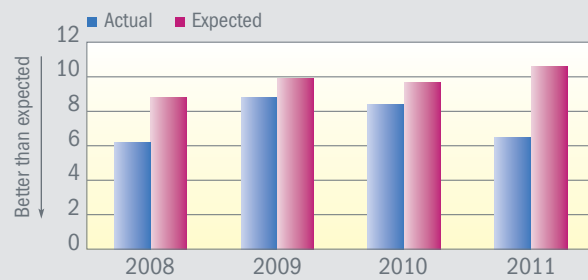
Source: chart data based on DRGs and ICD9 codes, per fiscal year

**Acute Ischemic Stroke: Length of Stay**



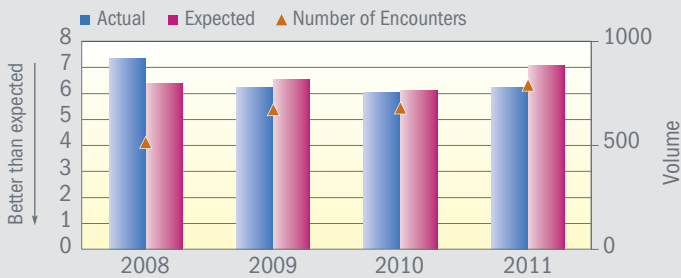
Source: chart data based on ICD9 codes, per fiscal year

**Acute Ischemic Stroke: Inpatient Mortality**



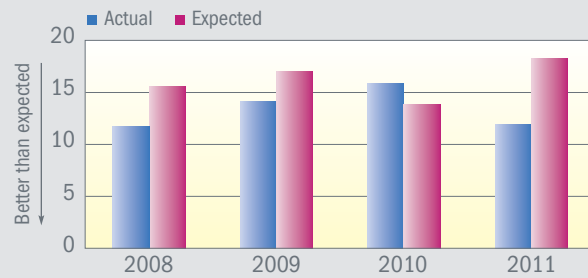
Source: chart data based on ICD9 codes, per fiscal year

**Intracranial Hemorrhage: Length of Stay**



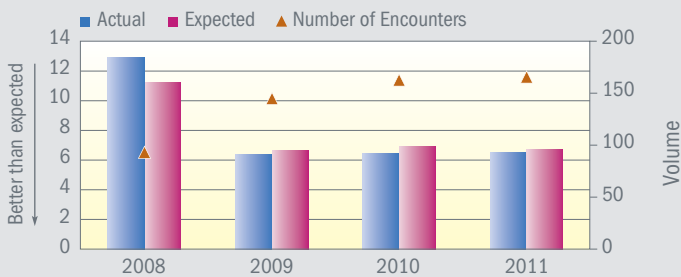
Source: chart data based on DRGs, per fiscal year

**Acute Ischemic Stroke: Inpatient Mortality**



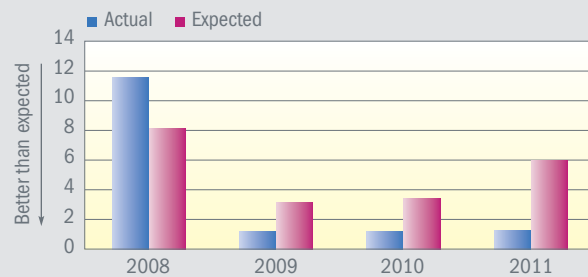
Source: chart data based on DRGs, per fiscal year

**Aneurysm Unruptured: Length of Stay**



Source: chart data based on ICD9 codes, per fiscal year

**Aneurysm Unruptured: Inpatient Mortality**



Source: chart data based on ICD9 codes, per fiscal year

**Stroke Core Measures**

Clinical Measure	Measure Description	2010 National Average	GWTG Stroke Performance Measure Goal	2007	2008	2009	2010
<b>DVT prophylaxis</b>	Ischemic and hemorrhagic stroke patients who received VTE prophylaxis or have documentation why no VTE prophylaxis was given the day of or the day after hospital admission.	88.1%	85.0%	93.3%	98.3%	100%	98.8%
<b>Antithrombotics at discharge</b>	Ischemic stroke patients prescribed antithrombotic therapy at hospital discharge.	98.7%	85.0%	97.5%	98.0%	96.9%	96.9%
<b>Anticoagulation for atrial fibrillation</b>	Ischemic stroke patients with atrial fibrillation/flutter who are prescribed anticoagulation therapy at hospital discharge.	95.4%	85.0%	100%	96.9%	100%	100%
<b>IV tPA use (eligible &lt; 2 hour arrival)</b>	Acute ischemic stroke patients who arrive at this hospital within 2 hours of time last known well and for whom IV tPA was initiated at this hospital within 3 hours of time last known well.	71.5%	85.0%	100%	100%	100%	99.2%
<b>Early antithrombotics (&lt;48 hour arrival)</b>	Ischemic stroke patients administered anti-thrombotic therapy by the end of hospital day 2.	97.3%	85.0%	96.5%	100%	99.0%	100%
<b>Lipids measure (statin at discharge)</b>	Ischemic stroke patients with LDL $\geq$ 100 mg/dL, or LDL not measured, or who were on a lipid-lowering medication prior to hospital arrival, are prescribed statin medication at hospital discharge.	92.5%	85.0%	88.7%	88.1%	87.1%	87.8%

Source: chart data based on calendar year

communities an opportunity to participate in clinical trials that would otherwise be unavailable to them, which expands medical knowledge as it saves lives.

In addition to breakthrough treatment for stroke, our cerebrovascular team provides coordinated care for patients with aneurysms, carotid occlusive disease and intracranial vascular malformations, including endovascular treatment. Procedures include angioplasty, stenting and embolization. Radiosurgery is also available for vascular malformations. Our neurosurgeons are skilled at clot retrieval, hemicraniectomy for severe strokes, microvascular clipping of aneurysms, endovascular embolization, extracranial-intracranial bypass and carotid endarterectomy.

We conduct more research than any other center in the south or southwestern United States, participating in multicenter and single-center clinical trials that

improve treatments for patients who cannot be treated elsewhere. Research under way includes thrombolytic treatment for wake-up stroke, the safety of pioglitazone for hematoma resolution in intracerebral hemorrhage and the safety of autologous bone marrow 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 that include carotid artery stenting and patent foramen ovale closure.

We extend our cerebrovascular continuum of care through inpatient and outpatient neurorehabilitation in Memorial Hermann-TMC's 23-bed rehabilitation unit and at TIRR Memorial Hermann, a top-tier, 119-bed rehabilitation hospital. Patients benefit from comprehensive inpatient and outpatient services, state-of-the-art technology and innovative therapies and techniques.

# Epilepsy

The Texas Comprehensive Epilepsy Program is the only Level IV National Association of Epilepsy Centers-certified program in Houston. A collaborative effort between Memorial Hermann-Texas Medical Center, Children's Memorial Hermann Hospital and The University of Texas Health Science Center at Houston (UTHealth) Medical School, we are the leading program in the southwestern United States for the diagnosis and treatment of epilepsy in patients of all ages.

The number of patients we treat annually continues to grow. Today, our board-certified neurologists and neurosurgeons diagnose and treat more than 350 pediatric and adult patients each year for seizures and epilepsy. Genetics, brain trauma, structural abnormalities, stroke and brain tumor rank among the top underlying causes, but because epilepsy and other types of seizures manifest differently among individuals, determination of the origin of seizures is crucial to planning the most effective treatment.

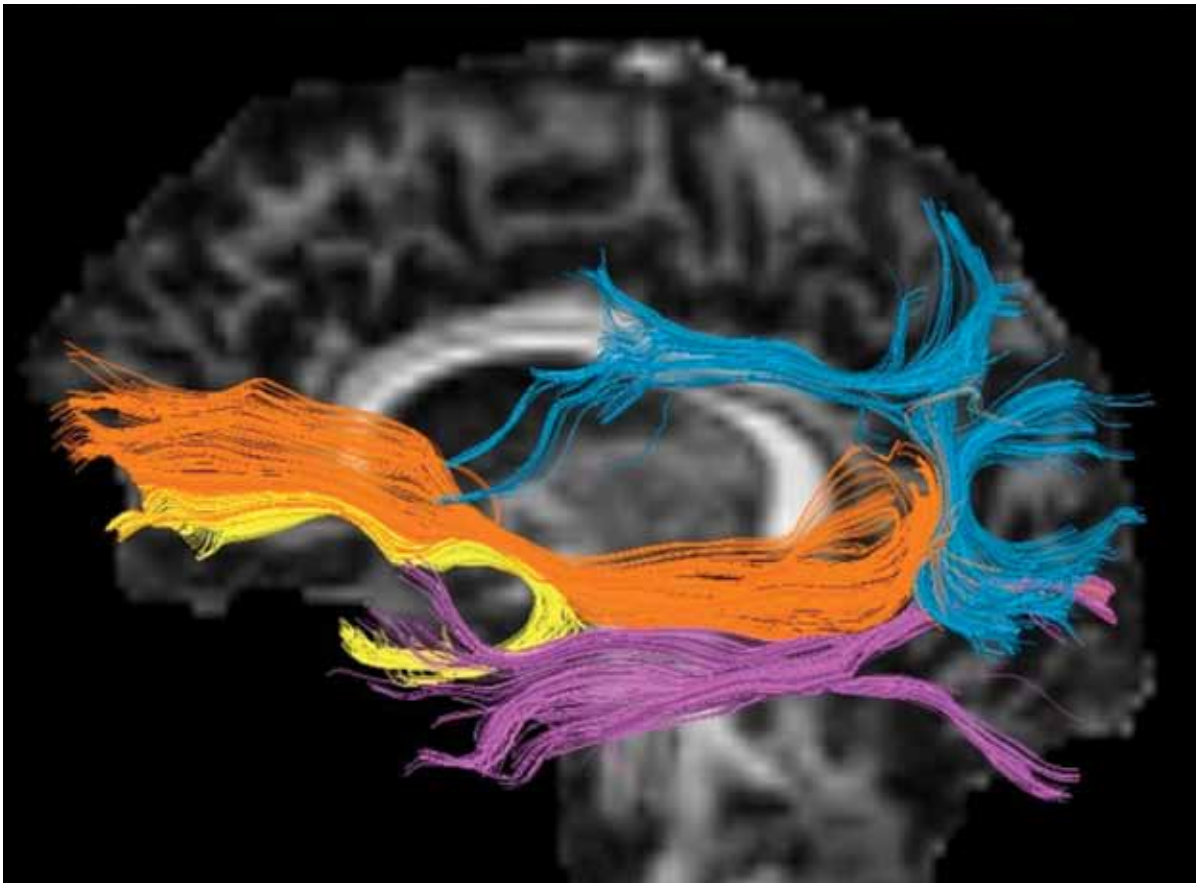
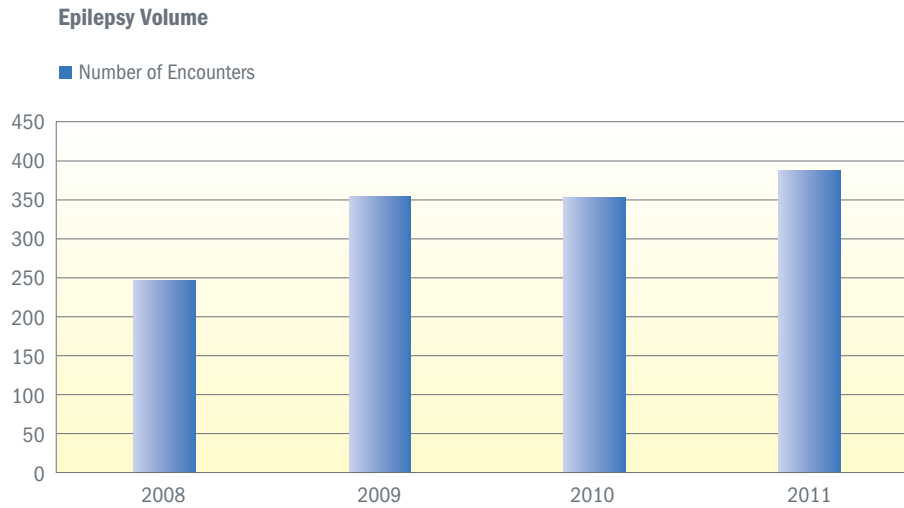


Photo Courtesy of Nitin Tandon, M.D.



Source: chart data based on DRG codes, per fiscal year

The Texas Comprehensive Epilepsy Program diagnoses and treats more than 350 pediatric and adult patients annually for seizures and epilepsy. Thanks to advanced diagnostic tools that allow us to localize the origin of seizures and map brain function, the number of MNI patients who benefited from successful resective surgeries increased in fiscal year 2011.

Our full suite of diagnostic tools includes magnetoencephalography (MEG) to map neurological function, video EEG, 3-Tesla structural MRI, functional MRI and tractography, PET and SPECT, memory and speech (Wada) testing and neuropsychological testing. We are a national leader in combining the use of MEG and functional MRI to map the brain and record brain activity, and we remain the only center in Texas, Louisiana, Arkansas and Oklahoma to offer this service since bringing the first MEG imager to Houston in 1997. Each year, we perform more than 150 noninvasive MEG procedures on pediatric and adult patients. We are also one of only a few inpatient units in the country with the capability to perform electroencephalography and polysomnography simultaneously.

Once a diagnosis is made, we offer the most advanced treatment options available, including drug therapy, the ketogenic diet, vagus nerve stimulation (VNS), focal cortical resection, lobectomy, hemispherectomy and corpus callosotomy. We also go beyond diagnosis and treatment of epilepsy by counseling patients in ways to cope with their diagnosis. Specialized counselors ensure that recently diagnosed patients have the emotional support they need.

Our team has been involved in research related to most epilepsy treatments approved in the United States in the last 15 years, including a number of drug and intravenous therapies and VNS therapy. Current research includes lacosamide monotherapy and adjunctive therapy for partial-onset seizures, the epilepsy phenome/genome project, oxygen-enhanced magnetic resonance imaging in non-lesional focal epilepsy and a quantitative analysis of the electroencephalogram in epilepsy.

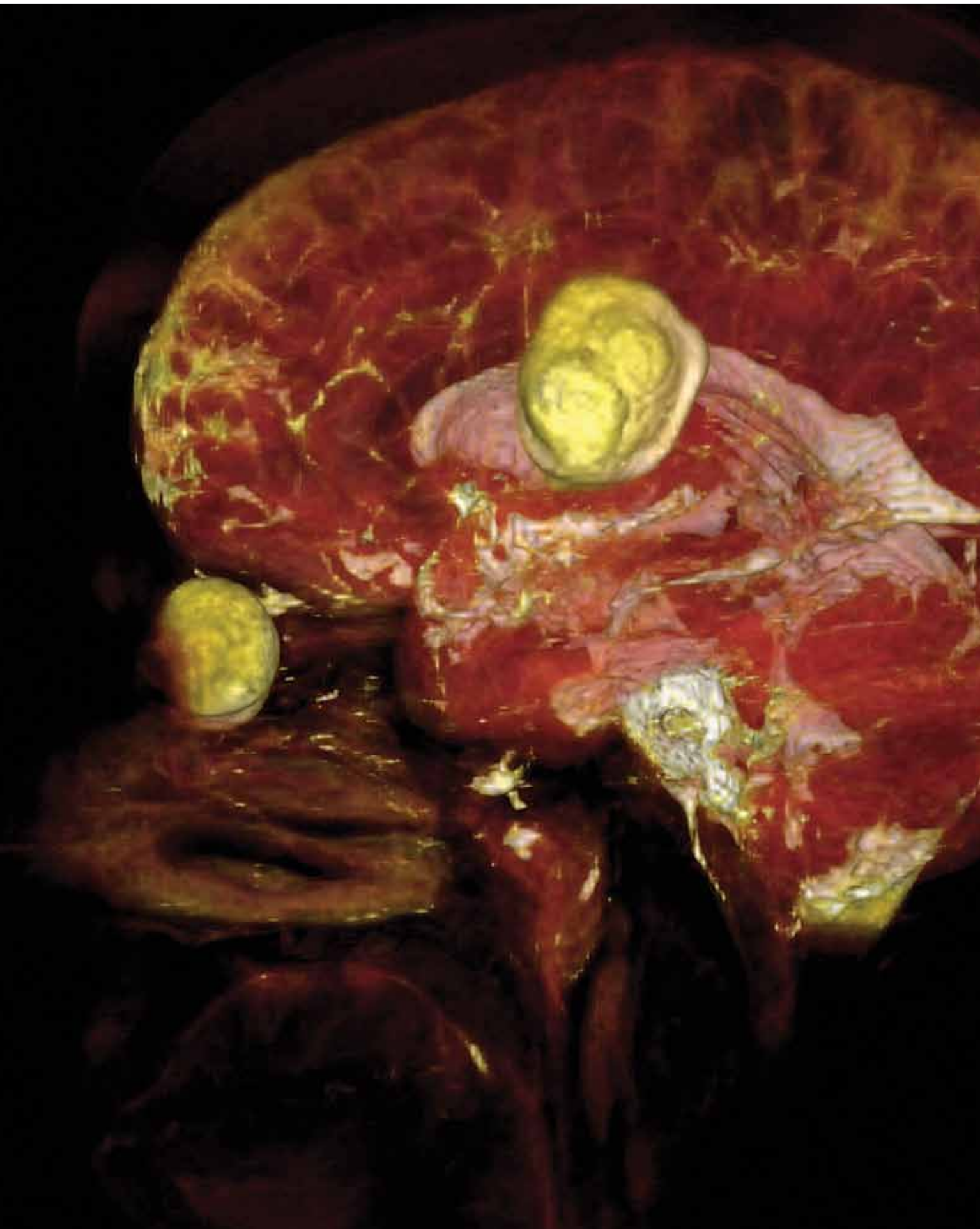


Photo Courtesy of Nitin Tandon, M.D.

# Memory Disorders and Dementia

Physicians in the Memory Disorders and Dementia Program at the Mischer Neuroscience Institute are dedicated to evaluating and treating persons with cognitive and behavioral changes, and performing cutting-edge research into the diseases that produce these disorders.

Dementias are a group of disorders that impair thinking or behavior in more than two spheres, such as memory, language, finding one's way around, a change in personality or a change in behavior. For a diagnosis of dementia, these changes must have a significant impact on a person's daily life, such as impairing the ability to work. We treat all the known causes of dementia, including infections, trauma, medications, vitamin or hormone deficiencies, vascular disease and strokes. The condition can also be caused by neurodegenerative disorders in which brain cells die without an obvious cause, such as Alzheimer's disease (AD), frontotemporal dementia (FTD) and Parkinson's disease. The number of persons affected by dementia is enormous: AD alone affects more than 5.3 million Americans.

Physicians in the MNI Dementia Program perform advanced research focused on developing ways to provide early diagnosis and treatment for these devastating illnesses. Our investigations are directed at determining which individuals will develop dementia, finding accurate tools to diagnose dementia and

determine the type of dementia from which a person suffers, and finding ways to stop the progression of dementing illnesses.

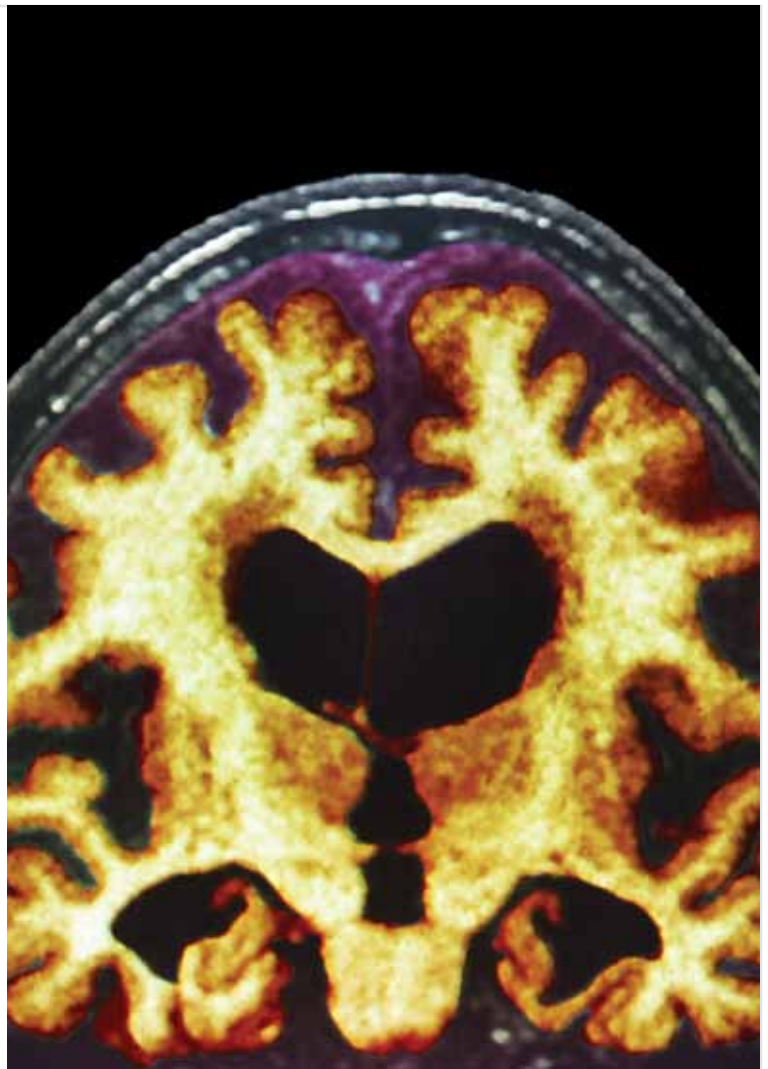
Our Presymptomatic Diagnosis and Treatment of Dementia Clinic is dedicated to reducing the risk of developing dementia and to developing new diagnostic and treatment tools. Our team has identified multiple risk factors for dementia, including family history, head trauma that produces a loss of consciousness, high blood pressure, high cholesterol or triglycerides, diabetes, obesity, smoking, post-traumatic stress disorder and many others. At the clinic, physicians evaluate individuals at risk for dementia who are asymptomatic, and treat their risk factors. We have shown that risk factor reduction is associated with a dramatic decrease in a person's risk for developing dementia. We are also investigating new treatments to delay or ameliorate the development of dementia. We believe that treatment interventions will be much more effective if introduced early in the molecular cascade of events that lead to these diseases. Because early diagnosis is critical, we are investigating tools to accomplish that. Currently there are no diagnostic tests for dementia, much less before symptoms develop.

Our laboratory partner in developing new treatments is the George P. and Cynthia W. Mitchell Center for Research in Alzheimer's Disease and Related Brain Disorders.

Investigators take findings from our clinical studies to their laboratory and use animal models to investigate how risk factors dramatically increase the probability of developing these diseases. They are identifying additional biomarker changes in animals that can be studied in humans and testing for medications that are effective against these diseases. They also recently identified a potential infection basis to Alzheimer disease in mice that we are now investigating clinically. Our other goal is to translate medication discoveries in animals to human trials to establish new preventive treatments.

The second most common neurodegenerative disorder is frontotemporal dementia. It is intimately associated with amyotrophic lateral sclerosis (ALS), a devastating disorder that produces progressive weakness to the point of death. Our Frontotemporal Dementia Clinic is dedicated to determining the environmental and genetic causes of these disorders, and developing treatments for them.

Over the last two decades, researchers have discovered that several psychiatric syndromes have a neurologic basis, including bipolar disorder, schizophrenia, major depressive disorder and post-traumatic stress disorder (PTSD). It has also become apparent that neurologic disorders can produce symptoms that are identical to those associated with those psychiatric disorders. In our Neuropsychiatry and Behavioral Neurology



Clinic, we evaluate patients to determine whether their neuropsychiatric symptoms are due to neurologic or psychiatric disorders, and treat their disorders or make appropriate referrals. A major focus of the research component of this clinic is traumatic brain injury (TBI) and PTSD. Together with the Center for Translational Injury Research, we are investigating treatments for TBI and the causes, treatments, and prevention of PTSD.

By using sophisticated new technologies to study these disorders at the cellular and clinical levels, we hope to realize our goal of diagnosis before patients become symptomatic with dementia and to find new treatments to prevent dementia.

## Medical and Environmental Risk Factors Associated with Frontotemporal Dementia: A Case-Control Study in a Veteran Population

**PRINCIPAL INVESTIGATOR:** Paul Schulz, M.D., Associate Professor, Department of Neurology, and Director of the Memory Disorders and Dementia Clinics, The University of Texas Health Science Center at Houston (UTHealth) Medical School

Very little is known about the medical and environmental risk factors associated with frontotemporal dementia (FTD). In this study, researchers evaluated medical and environmental disorders associated with FTD in a population of 845 veterans seen over a five-year period. They concluded that there is a significant increase in the risk of developing FTD in patients with traumatic brain injury. FTD also appears to be associated with a decrease in heart disease, suggesting an underlying metabolic change.

### Adjusted odds ratios and 95% confidence intervals for association of medical and environmental factors with FTD

	Model 1		Model 2	
	All dementias		All dementias except Vascular Dementia (VaD)	
	OR (95%CI)	<i>p</i>	OR (95%CI)	<i>p</i>
<b>Heart disease</b>	0.4 (0.3-0.96)	<b>0.040</b>	0.4 (0.2-0.98)	<b>0.047</b>
<b>Cerebrovascular diseases</b>	0.5(0.2-1.1)	0.095		
<b>Traumatic brain injury</b>	4.4 (1.6-11.8)	<b>0.003</b>	3.8 (1.4-10.2)	<b>0.008</b>

**Model 1:** included all patients with dementias. The covariates were age, TBI, heart disease, cerebrovascular disease and anemia.

**Model 2:** included all patients with dementias except VaD. The covariates included those in model 1 except cerebrovascular disease.



# 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 has established a track record of providing outstanding care with excellent outcomes. Our 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, 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.

Our treatment philosophy is grounded in the early identification of disease and early use of neuromodulating or neuroprotective approaches. We maintain patients at the highest level of function possible, based on symptom-driven therapeutic goals set by physician and patient. In developing and adjusting our treatment plans, we consider the whole person, as well as the patient's environment and support groups. We also emphasize education, and encourage patients to stay mentally and physically active and to have fun.

Our deep brain stimulation (DBS) program for Parkinson's tremor, dystonia and essential tremor is known for low complication rates and outstanding outcomes. Based on the skill of our neurological and neurosurgical teams and our expertise in DBS programming, we advocate for early use of deep brain stimulation in appropriate patients.

The Movement Disorders and Neurodegenerative Diseases Program is a collaborative effort of the Mischer Neuroscience Institute and UT MOVE, with specialty clinics that include Spasticity Management, DBS Selection and Programming, Botox® Injection and Intrathecal Baclofen Pump Therapy. Because rehabilitation is integral to our outcomes, we work closely with the physical and occupational therapists and speech-language pathologists in our inpatient and outpatient clinics and at TIRR Memorial Hermann to research new approaches to improving treatment.



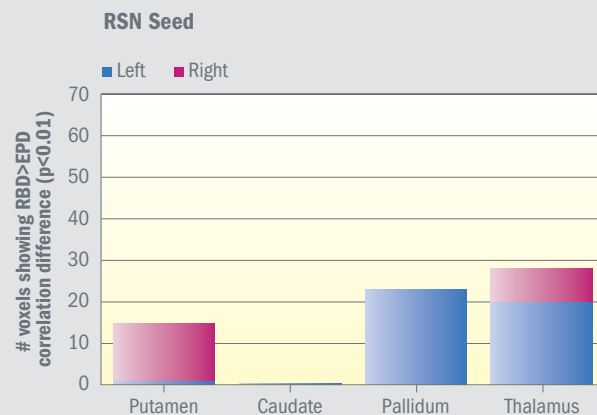
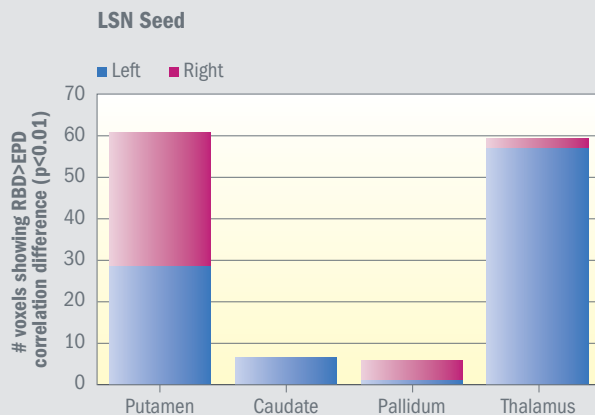
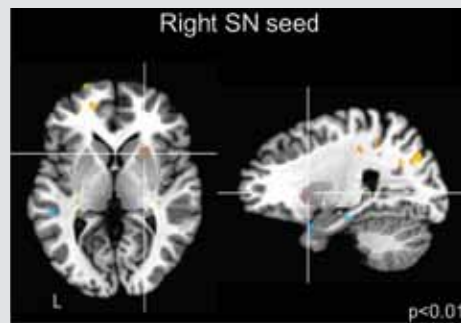
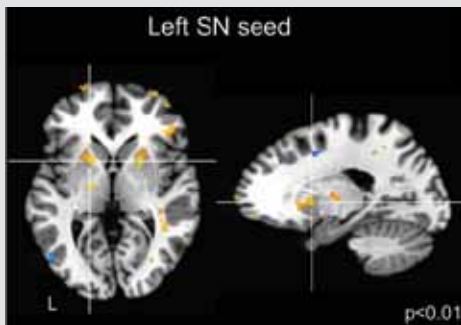
## Substantia Nigra Rest State fMRI Correlation Differences Between REM Sleep Behavior and Early PD Patients

**PRINCIPAL INVESTIGATOR:** Mya Schiess, M.D., Professor and Adriana Blood Chair in Neurology, Director of the Movement Disorders Clinic and Director of UT MOVE at The University of Texas Health Science Center at Houston (UTHealth) Medical School

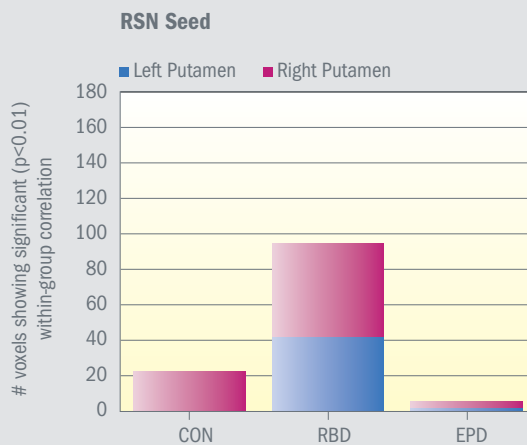
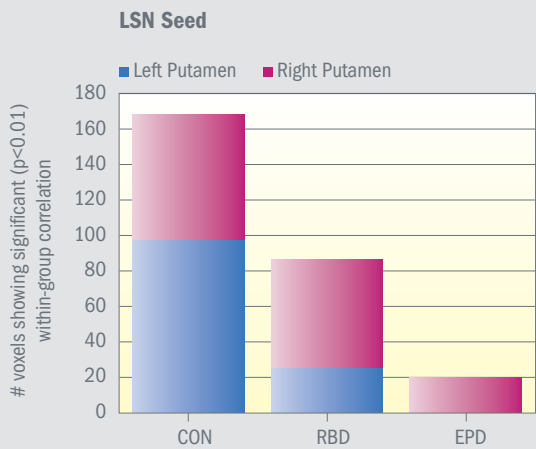
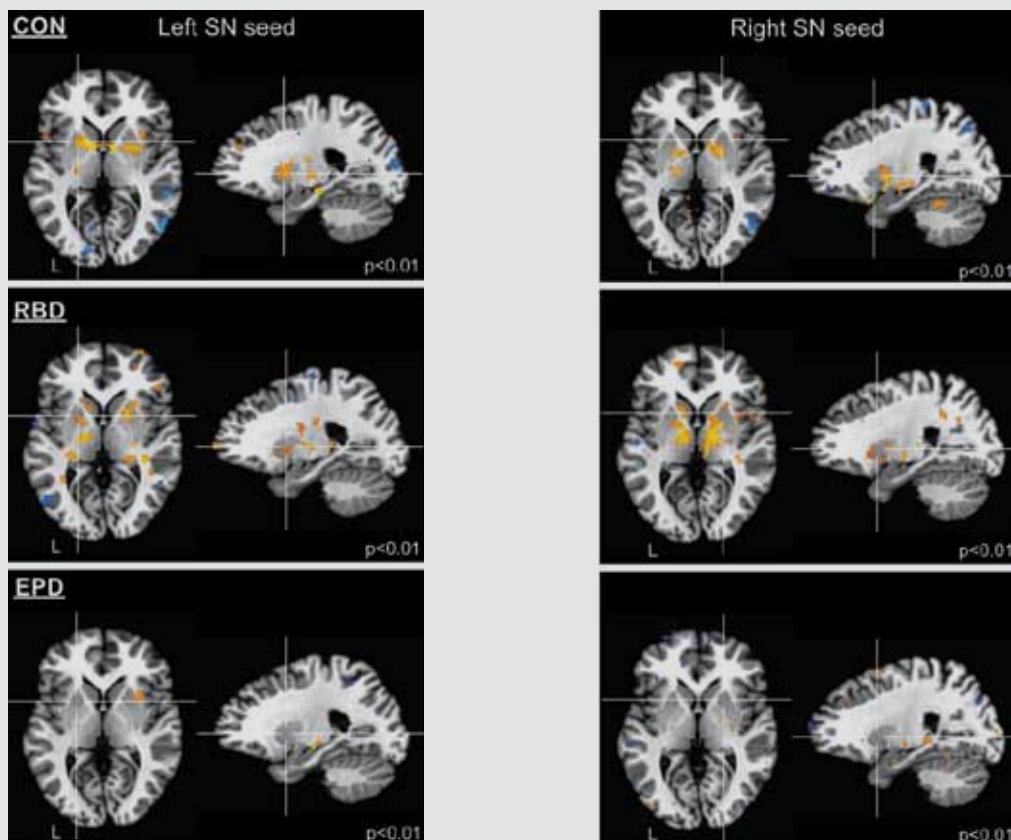
**CO-PRINCIPAL INVESTIGATOR:** Timothy Ellmore, Ph.D., Assistant Professor, Vivian L. Smith Department of Neurosurgery, The University of Texas Health Science Center at Houston (UTHealth) Medical School.

Dr. Schiess and her research team sought to determine whether resting-state functional MRI (fMRI) connectivity of the substantia nigra (SN) distinguishes REM sleep behavior disorder patients from patients diagnosed with early Parkinson’s disease. Data from the clinical trial show that SN-putamen temporal coherence, as measured by resting-state fMRI, decreases from control to REM sleep behavior disorder to early Parkinson’s disease groups. The researchers concluded that this functional connectivity metric may be useful for tracking disease progression and/or predicting Parkinson’s onset.

### RBD vs. EPD Correlation Comparison



Significant Within-Group Correlation

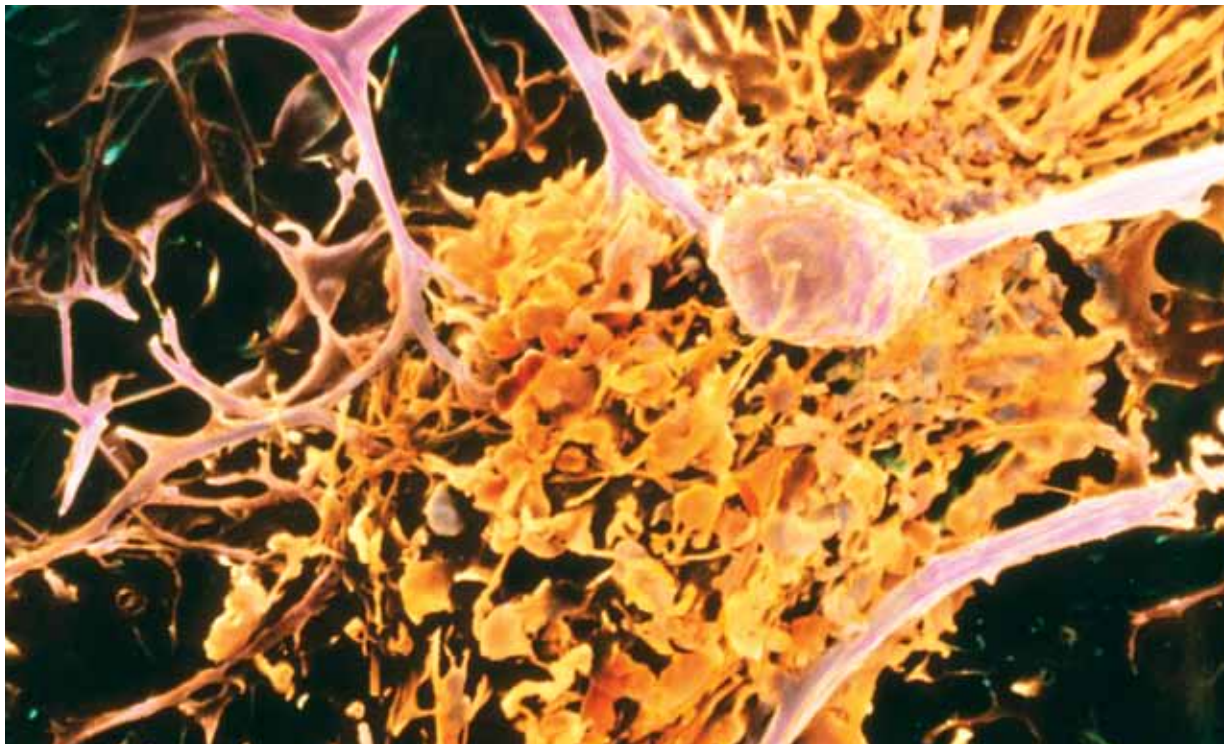


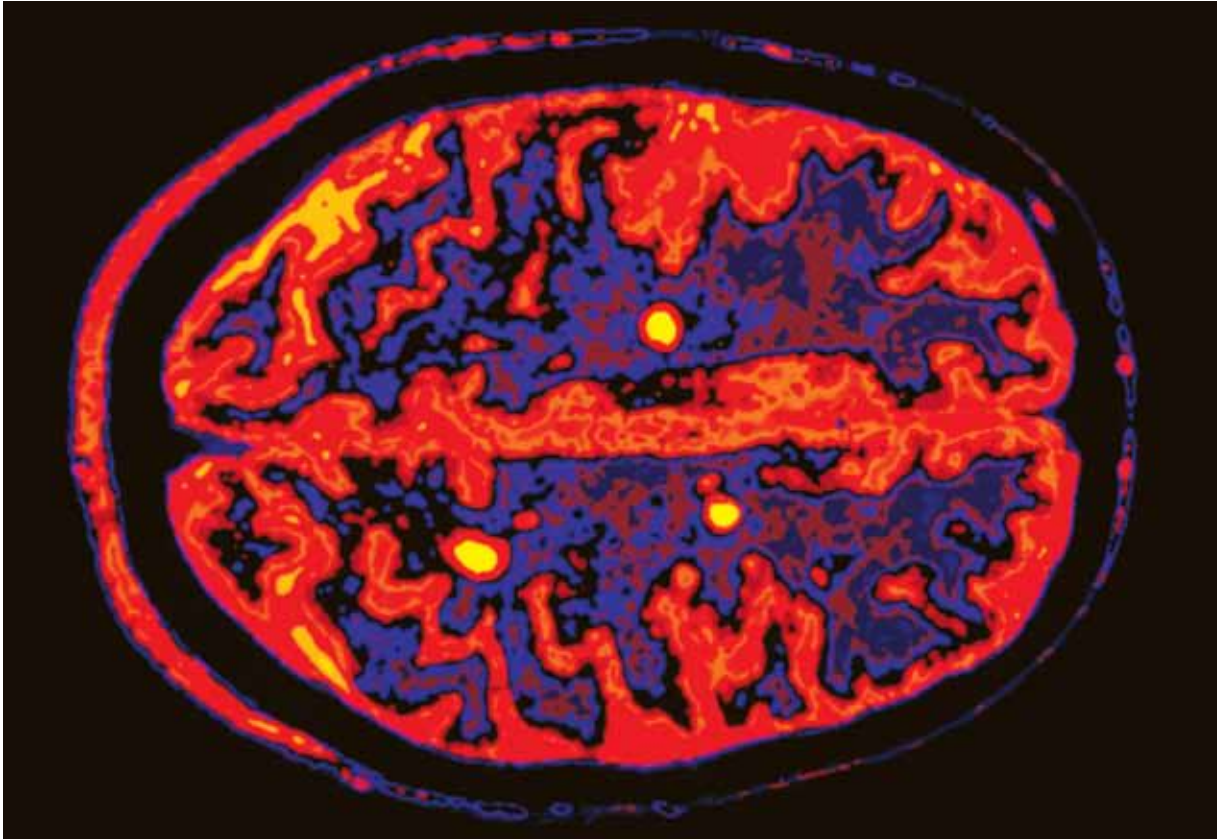
# Multiple Sclerosis

The Mischer Neuroscience Institute's Multiple Sclerosis Program has established a track record of cutting-edge care using groundbreaking techniques to diagnose, evaluate, manage and treat adult patients with MS and other demyelinating disorders. Our scope of expertise is broad and includes patients in all stages of MS, as well as those with neuromyelitis optica, transverse myelitis and optic neuritis. We 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 numerous international studies, several of which were pivotal in gaining FDA approval of currently available treatments for MS. Recent research includes participation in two clinical trials of the new drug fingolimod as the first oral agent approved by the FDA for the treatment of MS, an important addition to available therapies for the management of relapsing forms of multiple sclerosis. Investigators in the MSRG are also engaged in a National Institutes of Health-sponsored trial of combined therapy in early relapsing MS and a National MS Society-sponsored study of chronic cerebrospinal vascular insufficiency (CCSVI).





We were the first center 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. We are the first and only center in Houston to direct national and international clinical trials in MS, and we remain 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. Our 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 our state-of-the-art Magnetic Resonance Imaging Analysis Center, we use spectroscopic and diffusion

tensor imaging with tractotomy, as well as other advanced diagnostic tools. Following diagnosis, patients benefit from 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.

Our goal is to maintain our 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, we work closely with the physical medicine and rehabilitation specialists and therapists at TIRR Memorial Hermann, as well as the neurorehabilitation team at MNI.

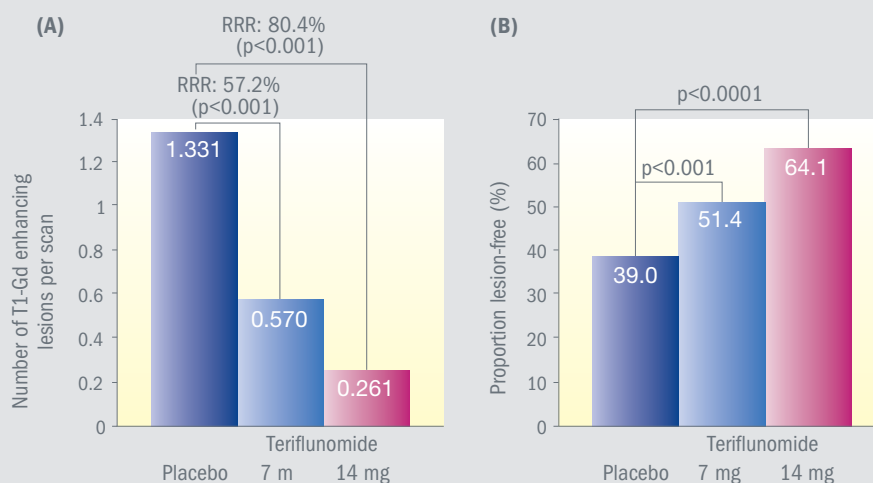
## A Phase III, Placebo-controlled Trial (TEMSO) of Oral Teriflunomide in Multiple Sclerosis with Relapses: Additional Magnetic Resonance Imaging Outcomes

**PRINCIPAL INVESTIGATOR:** Jerry Wolinsky, M.D., Bartels Family and Opal C. Rankin Professor of Neurology, Director of the Multiple Sclerosis Research Group (MSRG) and Director of the Magnetic Resonance Imaging Analysis Center at The University of Texas Health Science Center at Houston (UTHealth) Medical School

In this international clinical trial, researchers reported additional MRI outcomes from TEMSO, a randomized, double-blind, placebo-controlled, parallel-group study of 1,088 subjects. Patients were randomized to placebo or teriflunomide, a novel oral disease-modifier in development for multiple sclerosis with relapses, once daily for 108 weeks. MRI scans were performed at baseline and at weeks 24, 48, 72 and 108. As was previously reported in the TEMSO trial, teriflunomide was superior to placebo across a range of MRI parameters over the 108-week study, with evidence of significantly reduced disease activity and severity. The researchers concluded that significant reductions in relapse rate and disease progression, as well as a favorable safety profile, support a role for teriflunomide as an effective potential first-line oral monotherapy for MS with relapses.

Wolinsky JS, O'Connor P, Confavreux C, Comi G, Kappos L, Olsson TP, Truffinet P, Wang L, Miller A, Freedman M (2011) A placebo-controlled phase III trial (TEMSO) of oral teriflunomide in multiple sclerosis with relapses: Additional magnetic resonance imaging (MRI) outcomes. *Neurology* 76(S4):A545-6.

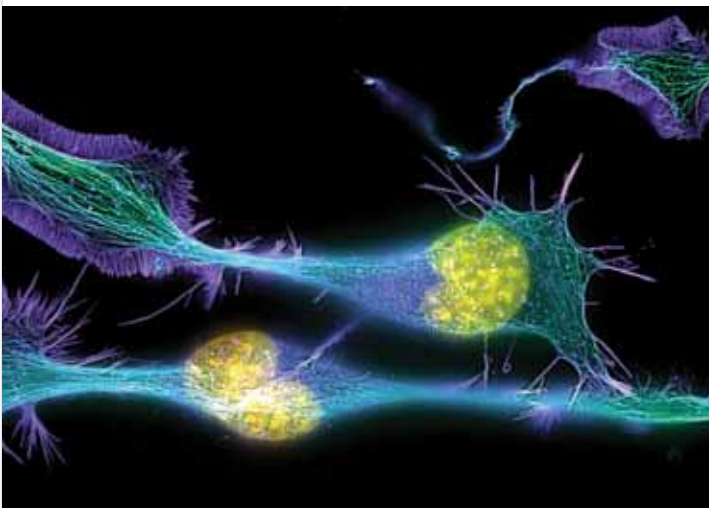
### Number of gadolinium(Gd)-enhancing T1 lesions per scan(A) and proportion of patients free from Gd-enhancing T1 lesions(B).



RRR: relative risk reduction

O'Connor, P, JS Wolinsky, et al. (2011). "Randomized Trial of Oral Teriflunomide for Relapsing Multiple Sclerosis." *New England Journal of Medicine* 365(14): 1293-1303.

# Neuromuscular Disorders



Physicians affiliated with the Mischer Neuroscience Institute's Neuromuscular Disorders 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 records more than 2,000 patient visits annually, primarily adults age 18 and older. About two-thirds of our patients are over the age of 50.

Our advanced 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.

Our Muscle and Nerve Laboratory helps 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. Our 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.





The GBS/CIDP Foundation International has designated our Neuromuscular Disorders Program as a center of excellence for the diagnosis and treatment of Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP) and other inflammatory peripheral neuropathies. The designation was awarded in recognition of the high standards maintained and quality of patient care provided at the program, which is one of only six such centers of excellence in the United States.

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, our investigators are studying the pathogenesis of autoimmune neuropathies, immune effectors and nerve repair, novel strategies to enhance axon regeneration and nerve repair, and the development of MRI technology to assess neuromuscular disorders in preclinical and clinical studies.



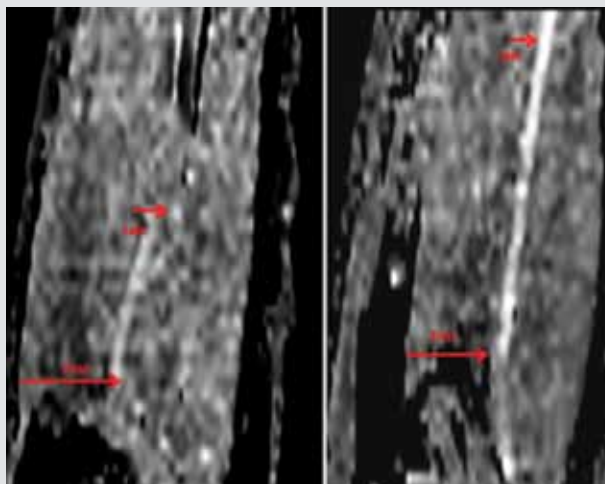
## Non-Invasive Imaging to Quantify Peripheral Nerve Injury and Repair in Clinic

**PRINCIPAL INVESTIGATOR:** Kazim Sheikh, M.D., Professor, Department of Neurology, The University of Texas Health Science Center at Houston (UTHealth) Medical School, and Director of the Neuromuscular Disorders Center at Mischer Neuroscience Institute

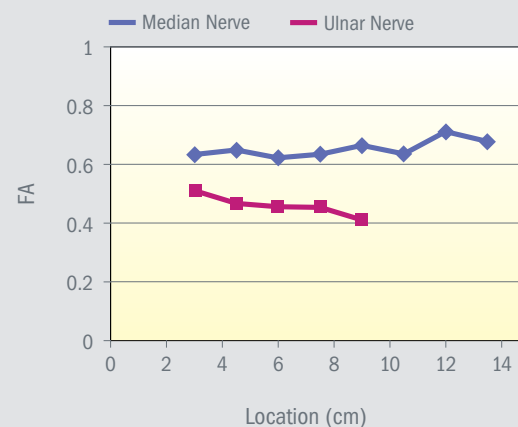
**CO-INVESTIGATORS:** Ponnada Narayana, Ph.D., M.Sc., Professor, Department of Radiology, and Director of Magnetic Resonance Research, The University of Texas Health Science Center at Houston (UTHealth) Medical School.  
Milan Sen, M.D., Assistant Professor, Department of Orthopedic Surgery, The University of Texas Health Science Center at Houston (UTHealth) Medical School

Traumatic neuropathies form an important subgroup among peripheral disorders because they commonly affect young adults with a higher probability of nerve regeneration and recovery, assuming optimal case management. Despite substantial evidence of the higher regenerative capacity of injured nerves in young patients, short- and long-term outcomes following peripheral nerve injury are unsatisfactory.

Our previous experimental work with quantitative diffusion tensor imaging (DTI) shows that the noninvasive modality is sensitive and specific in determining nerve integrity, Wallerian-like degeneration and regenerative response. With funding from the National Institutes of Health, our investigators are studying the feasibility and effectiveness of DTI in imaging normal human nerves and patients with traumatic nerve injury.



**Right Forearm Spatial Variation of FA**



The DTI image in the left panel show an injured nerve; the image on the right depicts an uninjured nerve. The nerve signal can be quantified along the length of the nerve as shown in the graph.

# Neurorehabilitation

Patients recovering from neurological illness or injury benefit from innovative neurorehabilitative technology and integrated care at the Mischer Neuroscience Institute (MNI) and TIRR Memorial Hermann. Subspecialists affiliated with both facilities are expert in the treatment of hemorrhagic and ischemic stroke; neurological disorders such as multiple sclerosis, Parkinson's disease and Guillain-Barré syndrome; traumatic brain injury; spinal cord injury; neurodegenerative disorders; and general neurorehabilitation.

## **Mischer Neurorehabilitation**

Memorial Hermann-Texas Medical Center's 23-bed inpatient neurorehabilitation unit provides comprehensive care and an aggressive program of physical therapy, occupational therapy and speech-language pathology. Patients and families are an integral part of our Neurorehabilitation Program. Upon admission, they discuss their goals with our interdisciplinary team and together, we develop a treatment plan designed to help them reach their highest level of function. Mischer Neurorehabilitation provides innovative and evidence-driven rehabilitation by blending manual and technologic therapies, including Korebalance™, Bioness® and IREX® Virtual Reality.

## **TIRR Memorial Hermann**

A national leader in medical rehabilitation and research, TIRR Memorial Hermann is a model for interdisciplinary rehabilitation services, patient care, education and research. The hospital is one of only six in the nation designated as model systems by the National Institute on Disability and Rehabilitation Research (NIDRR) for both its spinal cord injury and traumatic brain injury programs. For 22 consecutive years, *U.S. News & World Report*

has named the hospital to its list of "America's Best Hospitals." In 2011, TIRR Memorial Hermann was ranked fourth in the nation.

Research done at the hospital is conducted by physicians and scientists, and also by our therapists, nurses, chaplain and the residents who rely on us to advance their knowledge in specialized areas of rehabilitation medicine. Our Brain Injury Research Center (BIRC) brings together world-renowned researchers to study the many complicated facets of recovery from brain injury, leveraging resources from NIDRR and from the National Institutes of Health to conduct research identifying effective treatments.

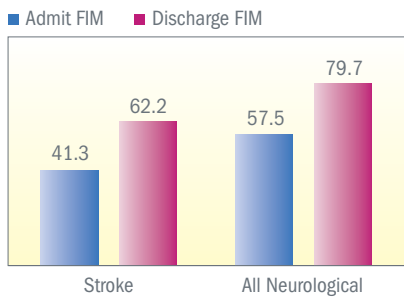
TIRR Memorial Hermann's Physician and Specialty Clinic is a physician-based clinic designed to meet the needs of individuals with disabilities age 13 and older who require initial or continuing care by a physician. The clinic is redefining the hospital's outpatient rehabilitation care model by providing a patient-centered medical home for people with disabilities. Seventeen specialty medical clinics include brain injury, stroke, spasticity management, neurosurgery, neurology, neuropsychology, psychiatry and more.

TIRR Memorial Hermann Adult and Pediatric Outpatient Rehabilitation logged more than 50,000 outpatient therapy visits in 2010. Innovative technology in use at the center includes Bioness equipment and the Lokomat®, the world's first driven-gait orthosis. We are the only facility in Texas with pediatric legs for the Lokomat. The outpatient center provides comprehensive physical, occupational and speech therapy as well as support groups, counseling and individualized training to prepare families and caregivers

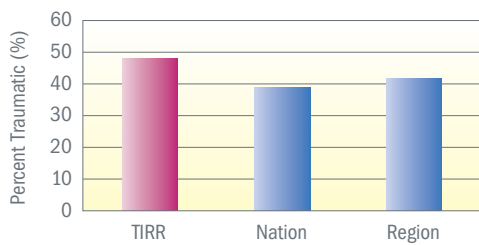
for taking on the additional responsibilities of caring for patients after inpatient discharge.

Although our patients are much higher acuity than most rehabilitation facilities nationwide, TIRR Memorial Hermann consistently has significant, positive functional independence measure (FIM) change scores.

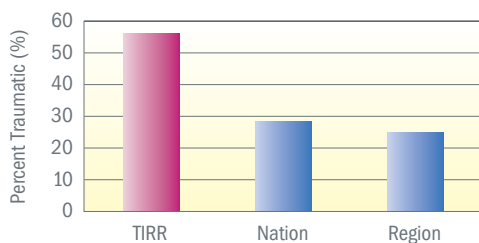
**Neurorehabilitation: Functional Independence Measure Change**



**Brain Injuries Treated**



**Spinal Cord Injuries Treated**



Source: chart data based on calendar year 2010

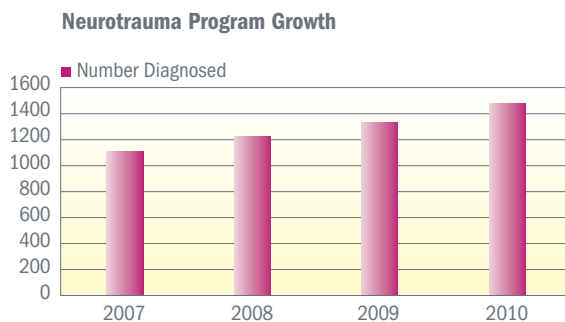


# Neurotrauma/Critical Care

The Mischer Neuroscience Institute's Neurotrauma/Critical Care Program is internationally recognized for the treatment of high-acuity brain and spinal cord injuries. Our program continues to grow, with more than 1,400 patients diagnosed in 2010.

Patients with acute neurological injuries benefit from Memorial Hermann-Texas Medical Center's Level I Trauma Center – one of only two in the area and 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.

Accredited by the Commission on Accreditation of Medical Transport Services, Memorial Hermann Life Flight provides high-quality care and safe air transport for critically ill and injured patients via helicopter and fixed-wing aircraft. Our helicopter service responds within a 150-mile radius of Memorial Hermann-TMC.



Our Neurotrauma Program continues to grow. In calendar year 2010, more than 1,400 patients with acute neurological injuries benefited from Memorial Hermann-Texas Medical Center's Level I Trauma Center and care provided at the Mischer Neuroscience Institute.

Fixed-wing service is available beyond 150 miles with world operating authority. Memorial Hermann Life Flight, the only hospital-based air ambulance service in Houston, operates 24 hours a day, 365 days a year, weather permitting. Since its inaugural flight, the medical transport service has flown more than 130,000 missions.

The Mischer Neuroscience Institute houses the largest and busiest neurointensive care unit of its kind in the region. Neurointensivists and experienced mid-level practitioners staff our dedicated Neuro ICU around the clock to provide ongoing intensive care to critically ill patients.

We are an international leader in research conducted on innovative treatments following neurotrauma, including participation in several multicenter trials. Investigators at MNI and TIRR Memorial Hermann are studying biomarkers for pain in spinal cord injury, cranioplasty outcome following decompressive craniectomy, the effects of erythropoietin on cerebrovascular dysfunction and anemia in traumatic brain injury (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.



# Spine

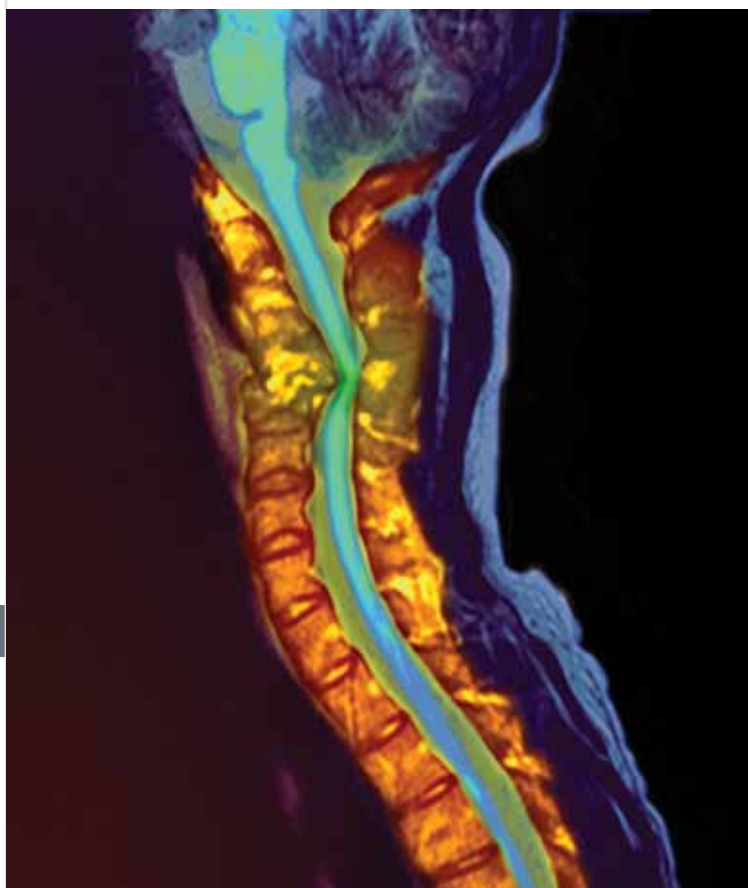
The highly skilled spine surgeons at the Mischer Neuroscience Institute are known for their expertise and innovative treatment options for patients with back pain resulting from trauma, degenerative disc disease, osteoporosis and related stress fractures, and deformity, including kyphosis and scoliosis.

We perform more than 1,000 surgeries each year in new, state-of-the-art facilities equipped with advanced instruments and dynamic imaging systems. Our clinicians provide exceptional care for patients with traumatic spine injury, including the 10 to 20 percent of admissions through our Level I Trauma Center 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 four years.

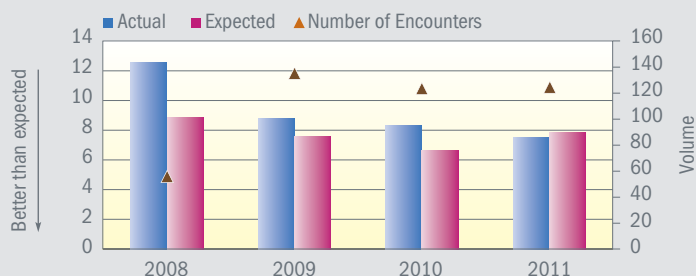
We are skilled at innovative procedures for the relief of neck and back pain, including minimally invasive approaches. Specialties include lumbar fusion, lumbar microdiscectomy, anterior cervical spine fusion, scoliosis surgery, spine osteotomies, kyphoplasty, thermal nucleoplasty, micro-endoscopic discectomy, transforaminal lumbar interbody fusion (TLIF) and disc replacement surgery.

Research under way at the MNI 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 evaluating the safety and preliminary efficacy of the anticonvulsant drug riluzole in patients with acute SCI.



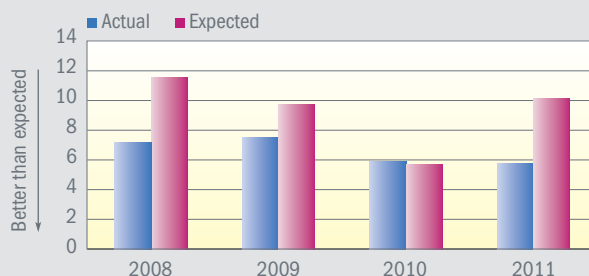


**Spinal Tumor: Length of Stay**



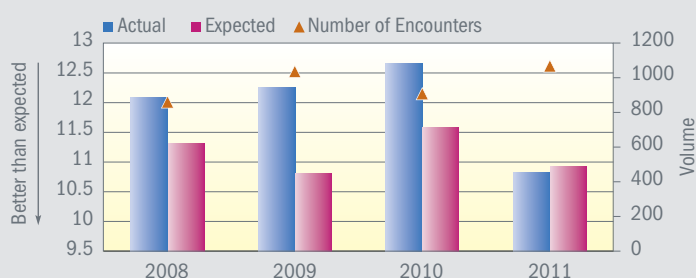
Source: chart data based on ICD9 codes, per fiscal year

**Spinal Tumor: Inpatient Mortality**



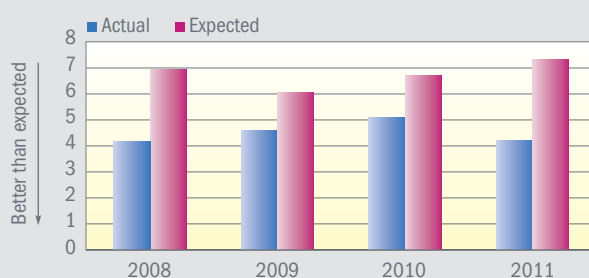
Source: chart data based on ICD9 codes, per fiscal year

**Spine Trauma: Length of Stay**



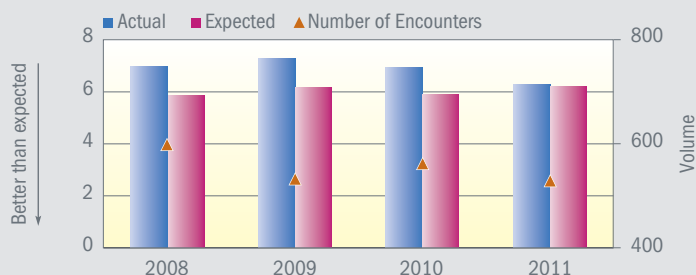
Source: chart data based on ICD9 codes, per fiscal year

**Spine Trauma: Inpatient Mortality**



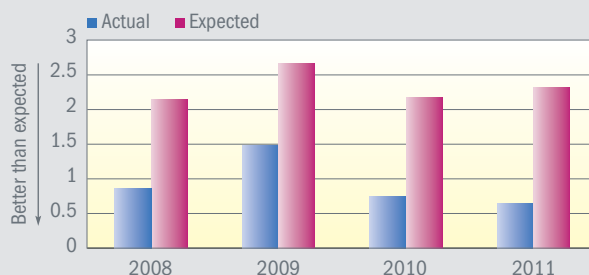
Source: chart data based on ICD9 codes, per fiscal year

**Spine Degenerative or Elective: Length of Stay**



Source: chart data based on ICD9 codes, per fiscal year

**Spine Degenerative or Elective: Inpatient Mortality**



Source: chart data based on ICD9 codes, per fiscal year

# Research & Innovation

Physicians at the Mischer Neuroscience Institute and The University of Texas Health Science Center at Houston (UTHealth) Medical School are engaged in a broad and intensive research program focused on the mechanisms, treatment and cure of neurological disease and injury. We use diverse approaches – molecular, transgenic and electrophysiological techniques – in biomedical studies, translational research, clinical trials and technology development and assessment.

Our projects are supported by the National Institutes of Health, the Vivian L. Smith Foundation for Neurologic Disease, the American Stroke Association and other granting agencies. They 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 2010 calendar year, researchers at the Institute and the UTHealth Medical School received more than \$11.7 million in 41 grants and contracts – over \$7.5 million for neurology and \$4.2 million for neurosurgery. The following listing is a sample of ongoing or recently completed research projects.

## **CEREBROVASCULAR**

### **A Randomized, Double-Blind, Placebo-Controlled Ascending Single-Dose Study of the Intravenous Infusion of CNTO 0007 in Subjects Who Have Experienced Ischemic Cerebral Infarction.**

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

A safety and tolerability study of a single intravenous (IV) infusion of CNTO 0007, human stem cell product obtained from the umbilical cord of a single healthy donor, compared with placebo when administered subacutely following an ischemic stroke.

### **A Randomized Multicenter Clinical Trial of Unruptured Brain AVMs (ARUBA)**

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

ARUBA is an FDA and institutional IRB approved randomized multicenter international clinical trial designed to determine whether medical management improves long-term outcomes of patients with unruptured brain AVMs, compared to interventional therapy (with endovascular procedures, neurosurgery, or radiotherapy, alone or in combination). This trial tests whether medical management or interventional therapy will reduce the risk of death or

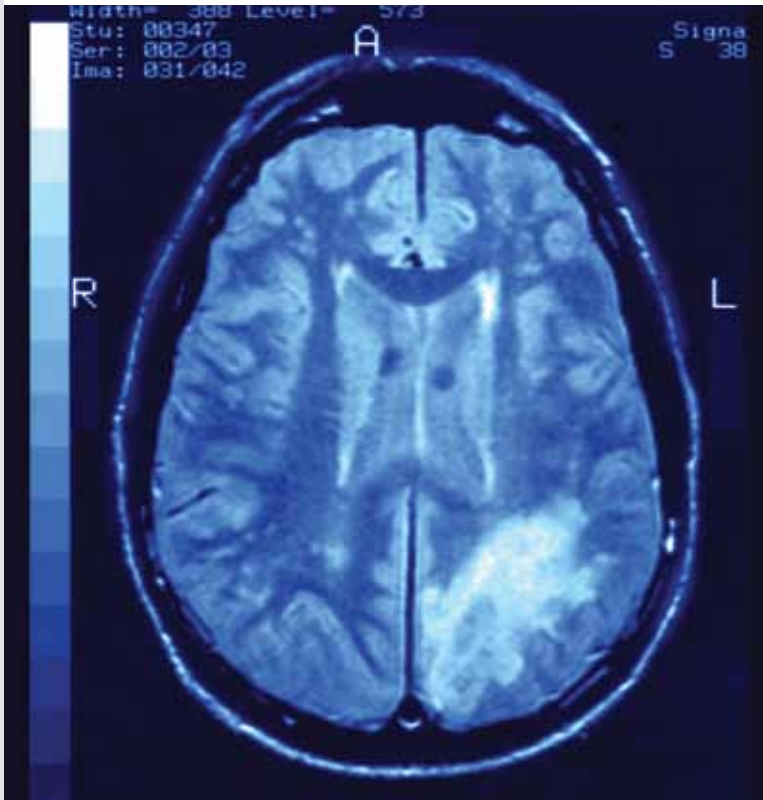
stroke (due to hemorrhage or infarction) by at least 46 percent (an absolute magnitude of about 9.5 percent over five years). A total of 400 patients will be enrolled in order to detect the hypothesized 46 percent reduction in event rate, analyzed using the intention-to-treat principal. This sample size supports a test of non-inferiority if medical management is not superior to interventional therapy. Patients are followed for a minimum of five years and a maximum of 10 years from randomization.

### **Albumin in Acute Stroke Trial – ALIAS: A Phase III Randomized Multicenter Clinical Trial of High-Dose Human Albumin Therapy for Neuroprotection in Acute Ischemic Stroke**

PRINCIPAL INVESTIGATOR: **Elizabeth Jones, M.D.**

An efficacy study to determine whether IV high-dose albumin reduces stroke severity compared to standard care (with or without tPA) in patients within five hours of stroke onset. This study is the first to be organized and run by Emergency Physicians, and is the final pivotal step in determining if albumin is an effective stroke treatment.





#### **Assessment of Spleen Size Reduction and Inflammatory Markers in Acute Stroke over Time (ASSIST)**

PRINCIPAL INVESTIGATOR: **Preeti Sahota, M.D.**

An observational study to evaluate the 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 targeting the immune processes in the spleen.

#### **Blood-Brain Barrier Permeability Changes as a Predictor of Complications in tPA-treated Patients**

PRINCIPAL INVESTIGATOR: **Tzu-Ching Wu, M.D.**

Hemorrhagic transformation and cerebral edema can be devastating complications of stroke. This retrospective study is investigating the relationship between permeability of the blood-brain barrier and stroke complications.

#### **Bugher Foundation Center for Stroke Prevention**

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

This project is focused on identifying gene mutations associated with cerebral aneurysm formation and understanding molecular mechanisms that lead to the disease.

#### **Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST)**

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

In an effort to find better ways to prevent strokes in people with carotid stenosis, this national, multi-center research study is comparing carotid endarterectomy to the study procedure, carotid artery stenting. Researchers are evaluating the relative effectiveness of both treatments in preventing stroke, myocardial infarction and death in the 30-day period immediately following the procedure.

#### **Clinical Outcome and Patient Factors in Refusal to Intravenous Tissue Plasminogen Activator Therapy for Management of Acute Ischemic Stroke – Perspectives from a Comprehensive Stroke Treatment**

PRINCIPAL INVESTIGATOR: **Farhaan S. Vahidy, Ph.D.**

This is a retrospective chart review study to compare the clinical outcome in patients who are eligible to receive tPA treatment, yet refuse it, as compared to patients who received the treatment. In addition, researchers are seeking to highlight some predictors in patient characteristics for tPA refusal.

#### **CLOTBUST-HF Combined Lysis of Thrombus in Brain Ischemia with Transcranial Ultrasound and Systemic tPA-Hands-Free: A Phase I/II Pilot Safety Trial**

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

The safety of a novel, external hands-free transcranial Doppler ultrasound system is being tested in two study groups: healthy subjects and people with ischemic stroke.

### **Combination Treatment of rtPA and Apyrase for Stroke**

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

This pre-clinical study is designed to evaluate the role of apyrase, an endogenous vascular ATPase, as a mechanism to prevent thrombosis after ischemic stroke when used in combination with rtPA.

### **Combination Therapy of Aspirin and Apyrase for Stroke**

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

This pre-clinical proposal is designed to evaluate the role of apyrase, an endogenous vascular ATPase, in combination with aspirin to prevent thrombosis after ischemic stroke.

### **DIAS 4 – Desmoteplase in Acute Stroke**

PRINCIPAL INVESTIGATOR: **George Lopez, M.D., Ph.D.**

An efficacy study to determine whether the potent IV clot busting drug desmoteplase improves outcome in patients who arrive too late for IV tPA but within nine hours of stroke onset. Desmoteplase is derived from vampire bat saliva and previous studies suggest benefit in patients with normal CT scans and persisting arterial occlusion beyond three hours.

### **Defining Genetic and Environmental Modifiers of Vascular Disease**

PRINCIPAL INVESTIGATOR: **Hariyadarshi Pannu, Ph.D.**

This research focuses on defining molecular differences between vascular beds, the role these differences play in conferring differential susceptibility to vascular diseases and the identification of factors that lead to variable gender-specific vascular disease susceptibility.

### **Ethnic/Racial Variation in Intracerebral Hemorrhage (ERICH)**

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

A genetic study aimed at determining the significant medical, environmental, and genetic risk factors and causes of stroke and how they may 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.**

A multi-site registry 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 principled by Micrus Endovascular Corporation, out of San Jose, California.

### **Genetic Analysis of Cerebral Aneurysms**

PRINCIPAL INVESTIGATOR: **Teresa Santiago-Sim, Ph.D.**

Researchers are identifying genetic alterations that predispose individuals to cerebral aneurysms as well as potential cerebral aneurysm biomarkers that can aid in the diagnosis of individuals at an increased risk of developing the disease.



### **Influence of Changes in Corticospinal Tract Integrity over Time on Clinical Outcome in Acute Ischemic Stroke (ICT-AIS)**

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

This is a prospective pilot study to evaluate the influences of changes in corticospinal tract integrity over time on motor and cognitive outcomes in patients with acute ischemic stroke in the middle cerebral artery territory within 48 hours of stroke onset. Patients will undergo detailed cognitive and fine-motor testing as well as advanced neuroimaging.

### **Intra-Arterial Treatment (IAT) in Patients with Unknown Stroke Onset Time**

PRINCIPAL INVESTIGATOR: **Ramy El Khoury, M.D.**

Patients who wake up with stroke symptoms or patients with unknown stroke symptom onset time are typically outside the conventional three-hour window for intravenous tPA. This is a retrospective study looking at safety of IAT in patients presenting with unknown stroke onset times.

### **Is the Drip-and-Ship Approach to Delivering Intra-Arterial Therapy after IV tPA Safe for Acute Ischemic Stroke?**

PRINCIPAL INVESTIGATOR: **Ramy El Khoury, M.D.**

Intra-arterial therapy is an investigational therapy for stroke. We are looking at the safety of treating patients at outside facilities with intravenous tPA and then transferring them for clot removal via intra-arterial procedures at our institution.

### **Minimally Invasive Surgery Plus tPA for Intracerebral Hemorrhage Evacuation (MISTIE)**

PRINCIPAL INVESTIGATOR: **George Lopez, M.D.**

This study was designed to produce data regarding the capability of minimally invasive surgery with recombinant tissue plasminogen activator (rt-PA) to remove blood clots from intra-cerebral hemorrhage patients.

### **MR and Recanalization of Stroke Clots Using Embolectomy (MR RESCUE)**

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

A comparison of intra-arterial (IA) catheter-based mechanical clot removal to standard care in patients up to eight hours after stroke onset who are ineligible for or have failed treatment with IV tPA. This study is testing whether we can use an MRI in order to select patients who may benefit in this extended time window.

### **Neurofluctuations in Patients with Subcortical Ischemic Stroke (NISS)**

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

The purpose of this prospective observational study is to capture and report the incidence of neurological exam fluctuations and their outcome in subcortical (lacunar) stroke patients receiving standard care. The results may be used to evaluate the results of new treatments for this disorder.

### **Neuroimaging of Cerebrovascular Function**

PRINCIPAL INVESTIGATOR: **Timothy Ellmore, Ph.D.**

Researchers are studying the use of high-resolution structural and functional neuroimaging to measure aspects of brain anatomy and function in humans at risk for cerebrovascular disease. The team is also studying patients who have had hemorrhagic strokes in order to assess the extent of damage, impact on cognitive function, and risk for additional cerebrovascular incidents.

### **Phase 2/3 Study of Intravenous Thrombolysis and Hypothermia for Acute Treatment in Ischemic Stroke. The Intravascular Cooling in the Treatment of Stroke 2/3 (ICTUS 2/3) Trial**

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

Brain cooling has been shown to decrease brain swelling and reduce loss of neurologic function after

an acute stroke. It has also been proven to be highly effective in saving lives and preventing neurological damage after cardiac arrest and after oxygen deprivation in newborns. This trial will look specifically at whether hypothermia can be used safely in elderly 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.

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

PRINCIPAL INVESTIGATOR: **James Grotta, 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 at increased risk of bleeding.

### **Relation of Coagulability and Iodine Exposure to Outcome of Patients with Ischemic Strokes Treated with Intra-Arterial Therapy**

PRINCIPAL INVESTIGATOR: **Ramy El Khoury, M.D.**

Coagulation disorders and excess iodine exposure could worsen patient outcome. We are studying the relation between these two factors in patients treated with intra-arterial therapy.

### **Retrospective Comparison of Pediatric Stroke Patients Treated With or Without Intravenous tPA and Descriptive Analysis**

PRINCIPAL INVESTIGATOR: **Ramy El Khoury, M.D.**

More commonly than previously thought, children can have strokes. We are aiming to describe our single-center experience in treating pediatric patients with intravenous tPA.

### **Safety/Feasibility of Autologous Mononuclear Bone Marrow Cell Treatment for Acute Ischemic Stroke**

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

Cell-based therapy has emerged as a novel investigational approach to enhance recovery after ischemic stroke. Numerous studies have shown that the administration of cells is safe and improves outcome in animal models. Our researchers will enroll 30 patients who have suffered an ischemic stroke in a safety study of an IV infusion of the patient's own cells within 24 to 72 hours after the onset of symptoms.

### **Safety of Autologous Bone Marrow Cell Treatment for Acute Ischemic Stroke Trial – Reasons for Poor Enrollment**

PRINCIPAL INVESTIGATOR: **Preeti Sahota, M.D.**

This retrospective study is to assess and understand the reasons for poor patient enrollment in the Safety of Autologous Bone Marrow Cell Treatment for Acute Ischemic Stroke Trial. The study is closed and in the data analysis stage seeking to better understand why people are reluctant to enroll in research trials.

### **Safety of Intravenous Thrombolysis for Wake-Up Stroke**

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

This is a safety study of acute treatment with IV tPA in ischemic stroke patients who wake up with their stroke

symptoms. The administration of tPA must occur within three hours of awakening from sleep. The primary aim of this study is to demonstrate the safety of IV tPA in ischemic stroke patients who present to the emergency department after awakening.

### **Safety of Pioglitazone for Hematoma Resolution in Intracerebral Hemorrhage (SHRINC) and MRI Evaluation of Hematoma Resolution as a Surrogate Marker of Clinical Outcome in Intracerebral Hemorrhage**

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

This study compares the safety of pioglitazone with standard of care for patients with spontaneous cerebral hemorrhage. The drug is administered in increasing doses from 0.1 to 2 mg/kg/d for three days, followed by a lower maintenance dose, within 24 hours of the start of symptoms.

### **SPOTRIAS Project 2: A Pilot Study to Determine the Safety of Argatroban Injection in Combination with rtPA in Patients with Acute Ischemic Stroke**

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

This clinical trial is assessing the safety of combining the anticoagulant argatroban and recombinant tPA to treat patients who have had acute ischemic stroke.

### **Stem Cells in Stroke Patients (STEM)**

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

This is a safety study of bone marrow cell harvest and IV administration of the patient's own mononuclear stem cells in patients within 72 hours of stroke onset. This is the first human study of stem cells in stroke patients, the only one in Houston, and an approach that reduces injury and promotes recovery in animal models.



### **Surgical Treatment Modalities for Intracerebral Hemorrhage (ICH) Management**

PRINCIPAL INVESTIGATOR: **Ramy El Khoury, M.D.**

Intracerebral hemorrhage represents about 15 percent of all strokes. We are comparing outcomes for two different surgical techniques – hemicraniotomy and hemicraniectomy – in cerebral hemorrhage patients.

### **The Interventional Management of Stroke Trial – IMS III**

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

An efficacy study adding an intra-arterial (IA) catheter-based mechanical clot removal to IV tPA compared to standard IV tPA treatment alone in patients within three hours of stroke onset. This is the final pivotal step in determining if the combined IV + IA approach is effective in improving clinical outcome.

### **The Weekend Effect on Intra-arterial Therapy**

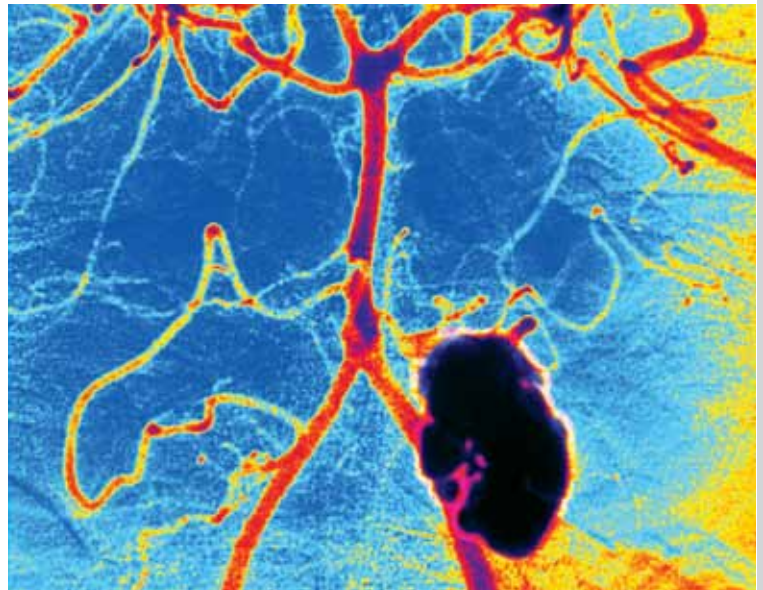
PRINCIPAL INVESTIGATOR: **Ramy El Khoury, M.D.**

Intra-arterial therapy for acute stroke is an emergency procedure. Previous cardiac studies showed a possible ‘weekend effect’ where patients treated on the weekend have worse outcomes. We are studying whether the ‘weekend effect’ exists for intra-arterial therapy in comprehensive stroke centers.

### **To Retrospectively Study Predictors of Outcome in Sub-Acute Ischemic Stroke in Middle Cerebral Artery (MCA) Territory During Hospitalization**

PRINCIPAL INVESTIGATOR: **Preeti Sahota, M.D.**

The purpose of this retrospective study is to identify the predictors of outcome in patients with ischemic stroke in middle cerebral artery (MCA) territory during the sub-acute stage (day two to day seven, or discharge time, whichever is earlier), irrespective of whether they



undergo thrombolytic or interventional therapies during the acute stage (day one). The rationale behind this study is that the outcome during the sub-acute phase is likely to have a bearing on the kind of patients we select for our interventional clinical trials during this period, such as stem cell therapy.

### **Treatment of Central Retinal Artery Occlusion with Intra-arterial Thrombolysis**

PRINCIPAL INVESTIGATOR: **Ramy El Khoury, M.D.**

Central retinal artery occlusion can cause complete vision loss. We are looking at outcomes of patients treated with endovascular therapy.

### **Utilization of Intensive Care Resources in Severe Intracranial Hemorrhage**

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

Researchers are identifying all patients with intracranial hemorrhage treated by the Mischer Neuroscience Institute stroke team from 2004 to January 2009. This review of medical charts is capturing information that predicts whether patients should receive prolonged care or hospice care.

**EPILEPSY****A Multicenter, Open-label Extension Trial to Assess the Long-Term Use of Lacosamide Monotherapy and Safety of Lacosamide Monotherapy and Adjunctive Therapy in Subjects with Partial-Onset Seizures**PRINCIPAL INVESTIGATOR: **Jeremy Slater, M.D.**

This study is demonstrating the effectiveness and safety of administering lacosamide, an investigational anticonvulsant, to patients with partial-onset seizures who are withdrawn from one to two established antiepileptic drugs.

**Correlation of Waking Background Alpha Frequency with Measures of Attention and Reaction**PRINCIPAL INVESTIGATOR: **Jeremy Slater, M.D.**

Researchers are studying alpha brainwave frequency and its relationship to varying levels of alertness.

**Diffusion Imaging for Seizure Focus Localization**PRINCIPAL INVESTIGATOR: **Timothy Ellmore, Ph.D.**

This project is evaluating the feasibility of using diffusion-weighted MRI (DW-MRI) to localize the seizure onset zone in epilepsy patients.

**Initial Treatment of Status Epilepticus (ITSE): A Preliminary Study for FIRST: Comparison of Fosphenytoin and Levetiracetam**PRINCIPAL INVESTIGATOR: **Omotola Hope, M.D.**

This retrospective review of charts is being undertaken in preparation of a pilot study comparing two drugs, fosphenytoin and levetiracetam, for the control of status epilepticus unresponsive to lorazepam.

**Lateralizing Memory Function in Epilepsy Patients with Oxygen-Enhanced fMRI**PRINCIPAL INVESTIGATOR: **Timothy Ellmore, Ph.D.**

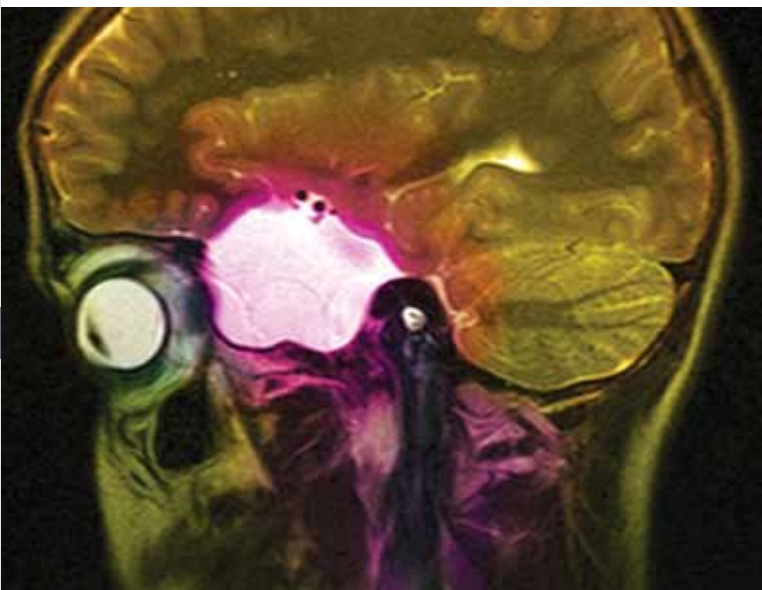
This ongoing study is evaluating the effectiveness of oxygen-enhanced functional magnetic resonance imaging for increasing memory task-related blood oxygen level-dependent signals in the hippocampus and neocortex of epilepsy patients and control subjects.

**Oxygen-Enhanced Magnetic Resonance Imaging in Non-lesional Focal Epilepsy**PRINCIPAL INVESTIGATOR: **Giridhar 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.

**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.



**SP902: A Historical-Controlled, Multicenter, Double-Blind, Randomized Trial to Assess the Efficacy and Safety of Conversion to Lacosamide 400mg/day Monotherapy in Subjects with Partial-Onset Seizures**

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

Lacosamide is an investigational anticonvulsant drug. This study is demonstrating the effectiveness and safety of administering lacosamide to patients with partial-onset seizures who are withdrawn from one to two established antiepileptic drugs.

**MULTIPLE SCLEROSIS**

**A Multicenter, Double-Blind, Randomized Study Comparing the Combined Use of Interferon Beta-1a and Glatiramer Acetate to Either Agent Alone in Patients with Relapsing-Remitting Multiple Sclerosis**

PRINCIPAL INVESTIGATOR: **John William Lindsey, M.D.**

This Phase III study is investigating whether combined treatment with the drugs interferon beta-1a intramuscular given once weekly and glatiramer acetate subcutaneous given daily is more effective than either drug alone in treating relapsing-remitting multiple sclerosis.

**Acorda Protocol MS F203: Double-Blind, Placebo-Controlled, 21-week, Parallel-Group Study to Evaluate the Safety and Efficacy of Oral Fampridine-SR (10 mg BID) in Subjects with Multiple Sclerosis and Acorda F203 Extension: An Open Label Extension Study to Evaluate the Safety, Tolerability and Activity of Oral Fampridine-SR in Subjects with Multiple Sclerosis who Participated in the MS f203 Trial.**

PRINCIPAL INVESTIGATOR: **John William Lindsey, M.D.**

In this placebo-controlled study, researchers are assessing the safety and efficacy of fampridine-SR in patients diagnosed with multiple sclerosis.

**Automated MR Image Analysis in MS: Identification of a Surrogate**

PRINCIPAL INVESTIGATOR: **Ponnada A. Narayana, Ph.D.**

Researchers are developing a general, PC-based automated image analysis system and applying it to determine those MRI metrics that best predict near-term clinical change in 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 is the first to use fMRI, DTI and other advanced imaging techniques to evaluate the effect of cortical lesions and white matter tract damage on cognitive function in multiple sclerosis patients.

**Double-Blind, Placebo-Controlled, 20-Week, Parallel-Group Study to Evaluate Safety, Tolerability and Activity of Oral Fampridine-SR in Subjects with Multiple Sclerosis and Open Label Extension Study to Evaluate Safety, Tolerability and Activity of Oral Fampridine-SR in Subjects with Multiple Sclerosis**

PRINCIPAL INVESTIGATOR: **John William Lindsey, M.D.**

Researchers are investigating the safety and efficacy of three dose levels of fampridine-SR – 20 mg, 30 mg and 40 mg – in patients diagnosed with multiple sclerosis.



#### **Epstein-Barr Virus and Multiple Sclerosis: Correlation of Activity**

PRINCIPAL INVESTIGATOR: **John William Lindsey, M.D.**

Epstein-Barr virus is a common infection linked to MS, but it is not known if the virus actually causes the disease. This study will investigate the correlation between reactivation of Epstein-Barr virus and disease activity in multiple sclerosis. The results of this will be important in determining whether this virus may be the cause of multiple sclerosis.

#### **Evaluation of Oral Administration of ACTH (corticotrophin) in Normal Volunteers – A Pilot Study**

PRINCIPAL INVESTIGATOR: **Staley Brod, M.D.**

This study was designed as a prospective cohort study to determine whether oral administration of ACTH has immunological and endocrinological effects.

#### **MRI Analysis Center for Protocol EFC6058 - A Multi-Center 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, Multi-Center, 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.

#### **MRI Analysis Center for Protocol LTS6050 – A Long- term Extension of the Multinational, Double-Blind, Placebo Controlled Study EFC6049 (HMR1726DI3001) to Document the Safety of Two Doses of Teriflunomide (7 and 14 mg) in Patients with Multiple Sclerosis with Relapses**

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

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

#### **National Multiple Sclerosis Society (NMSS): Chronic Cerebrospinal Venous Insufficiency and its relationship to MS**

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

This NMSS-funded study is an ongoing interdisciplinary project to determine if punitive alterations in cerebral venous outflow can be reliably measured and if any abnormalities can be specifically associated with multiple sclerosis.

#### **Open Label Study to Evaluate the Safety of Copaxone® and to Monitor the Neurologic Course of the Disease in Multiple Sclerosis Patients Treated with Copaxone**

PRINCIPAL INVESTIGATOR: **John William Lindsey, M.D.**

Researchers are seeking to better understand the long-term efficacy and side effects of the drug Copaxone (glatiramer acetate) therapy in multiple sclerosis patients.

### **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.

### **MOVEMENT DISORDERS AND NEURODEGENERATIVE DISEASES**

#### **A Natural History of Rapid Eye Movement (REM) Sleep Behavior Disorder as Prognostic for Parkinson's Disease**

PRINCIPAL INVESTIGATOR: **Mya Schiess, M.D.**

Researchers are validating a combination of biological and clinical markers in people with REM sleep behavior disorder as an indicator of the state of idiopathic Parkinson's disease before symptoms appear.

#### **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 $\beta$  oligomers in human biological fluids. Investigators are optimizing the experimental conditions of cyclic amplification of A $\beta$  misfolding, identifying A $\beta$  misfolded oligomers in AD biological fluids, and evaluating the sensitivity and specificity and the earliest time during the pre-symptomatic phase in which A $\beta$  oligomers can be detected in biological fluids.

### **Cross-sectional Cohort Study of Laboratory and Clinical Patterns in Early Parkinson's Disease**

PRINCIPAL INVESTIGATOR: **Mya Schiess, M.D.**

This study is designed to characterize and define serum and cerebrospinal fluid values for inflammatory cytokines and early idiopathic Parkinson's disease (IPD). Researchers are also looking for patterns in early IPD, hoping that they may lead to early diagnosis before symptoms occur.

#### **Cyclic Amplification of Prion Protein Misfolding**

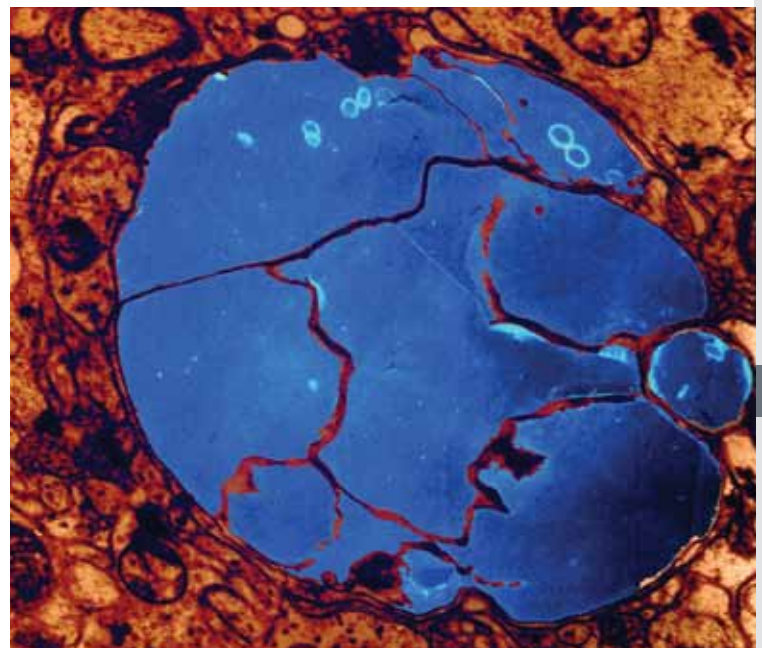
PRINCIPAL INVESTIGATOR: **Claudio Soto, Ph.D.**

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.

#### **Neurodegeneration in Prion Diseases**

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

This study is investigating the mechanism of brain degeneration in prion diseases and, in particular, the role of the endoplasmic reticulum chaperone protein Grp58.



### **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.

### **Peripheral and Central Protein Biomarkers of Brain MR Activity in Demyelinating Disease**

PRINCIPAL INVESTIGATOR: **Staley Brod, M.D.**

By studying patients with new or disappearing brain lesions, it may be possible to identify protein markers that repair damage to the brain and can be used as future therapies. This sub-study is investigating whether specific proteins in the blood and spinal fluid change in the presence of new brain lesions.

### **Small-Molecule Beta-sheet Breaker Peptidomimetics for Alzheimer's Therapy**

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

This project seeks to identify small chemical molecules mimicking the structure and activity of  $\beta$ -sheet breaker peptides previously demonstrated to be active in inhibiting and disassembling amyloid fibrils.

### **NEUROMUSCULAR DISORDERS**

#### **Baxter-PNS 2010-2011 Fellowship Award**

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

The purpose of this project is to evaluate whether neuron-specific inhibition of RhoA leads to enhanced regeneration and repair in injured nerves.

#### **Biologic Effects of Anti-Ganglioside Antibodies**

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

Examine the biologic effects of anti-ganglioside antibodies on nerve regeneration.

#### **GBS/CIDP Foundation Grant**

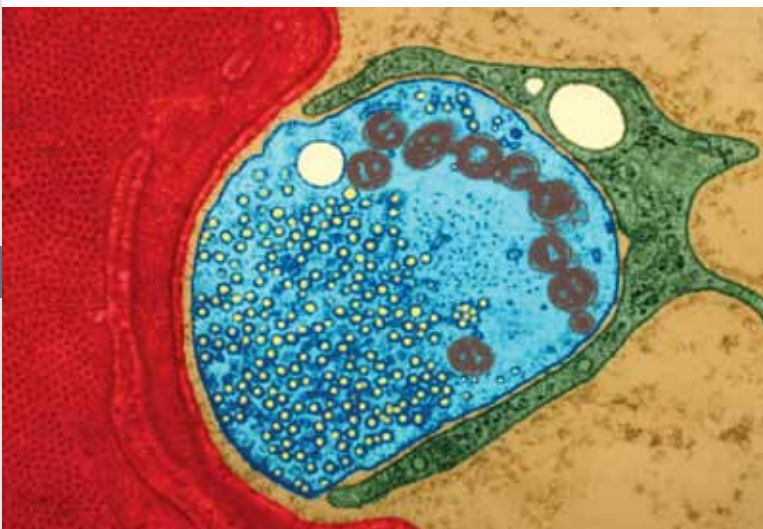
PRINCIPAL INVESTIGATOR: **Kazim Sheikh, M.D.**

Researchers are engineering chimeric proteins to enhance nerve repair in antibody-mediated preclinical models of autoimmune neuropathy.

#### **Neuroprotection and Enhancement of Nerve Repair with Erythropoietin (EPO) in Experimental Allergic Neuritis (EAN)**

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

The purpose of this study is to examine the neuroprotective properties of EPO in EAN.



### **Noninvasive Imaging to Quantify Peripheral Nerve Injury and Repair in Clinic**

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

Researchers are studying diffusion tensor imaging to assess and quantify nerve degeneration and regeneration in patients with traumatic nerve injuries.

### **Pathogenesis of Anti-Ganglioside Anti-Mediated Neuropathies**

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

Researchers are evaluating the role of pathogenic mechanisms of anti-ganglioside antibodies in autoimmune neuropathy.

### **Phenotype Differences in Motor and Sensory Neuron Regeneration in Inbred Mice**

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

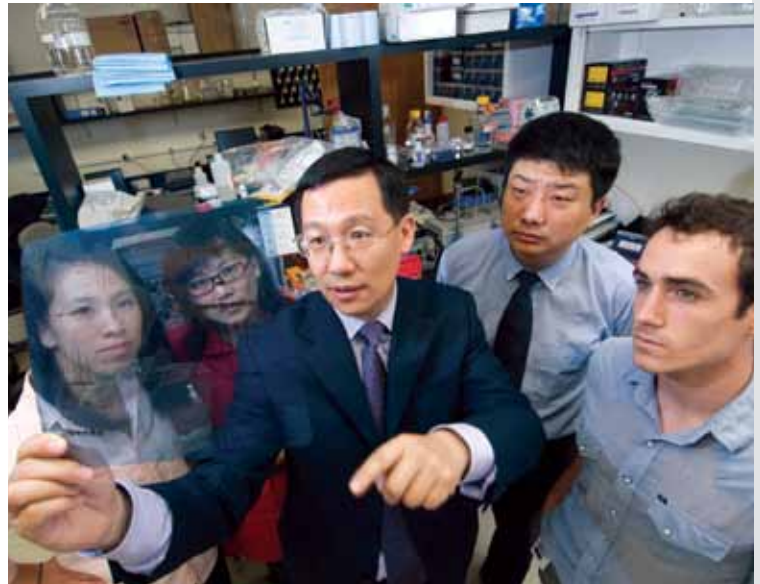
This study is determining the genetic drivers of phenotypic differences in nerve regeneration in inbred mice.

## **NEURO-ONCOLOGY**

### **Identification of New Markers and Therapeutic Targets in Glioblastoma Multiforme (GBM)**

PRINCIPAL INVESTIGATOR: **Min Li, Ph.D.**

This study is to identify new markers for diagnosis and novel therapeutic targets for molecular-targeted therapy in GBM using genetic and molecular approaches.



## **NEUROREHABILITATION**

### **Deep Venous Thrombosis in Post-Stroke Hemiplegia: Associated Risk Factors Placing Patients at Risk**

PRINCIPAL INVESTIGATOR: **Nneka Ifejika-Jones, M.D.**

Researchers are gathering preliminary data on acute stroke patients who have developed a deep venous thrombosis (DVT) during hospitalization for inpatient neurorehabilitation, despite having received preventive medication.

### **Functional Brain Reorganization in Stroke Recovery**

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

Investigators are using MEG to assess how the brain reorganizes itself during spontaneous recovery from stroke. They are also studying the effects of constraint induced therapy in the recovery process of language, sensory and movement functions.



### Improving Ambulation Post-Stroke with Robotic Training

PRINCIPAL INVESTIGATOR: **Elizabeth Noser, M.D.**

The goal of this research is to look at a new rehabilitation technique for people who have suffered a stroke causing difficulty walking. The present study is a research study designed to compare robotic-assisted rehabilitation therapy using the Lokomat<sup>®</sup> with standard physician therapy to improve walking after stroke.

### NEUROTRAUMA/CRITICAL CARE

#### Biomarkers for Pain in Spinal Cord Injury

PRINCIPAL INVESTIGATOR: **Gigi Hergenroeder, R.N.**

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. Acute patients, and 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 ultimate 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: **Qilin Cao, Ph.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.

#### 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.

### **Norepinephrine and TBI-Associated Prefrontal Dysfunction**

PRINCIPAL INVESTIGATOR: **Nobuhide Kobori, M.D.**

The overall goal of the project is to identify the biochemical and cellular mechanisms underlying cognitive function deficits due to traumatic brain injury. The NIH grant is particularly focused on the investigation of the dysregulated neurotransmitter signaling (norepinephrine and serotonin) in the prefrontal cortex.

### **Novel Neuroprotection Therapeutic Approaches for Spinal Cord Injury (SCI)**

PRINCIPAL INVESTIGATOR: **Qilin Cao, Ph.D.**

The goal of this grant is to study the molecular mechanism to regulate the blood-brain barrier of the normal adult central nervous system 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: **Qilin Cao, Ph.D.**

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

### **Project 2-Effects of Erythropoietin on Anemia and Need for Transfusion (a component of the Program Project “Vascular Mechanisms of Secondary Injury after Traumatic Brain Injury (TBI)”)**

PRINCIPAL INVESTIGATOR: **Imoigele Aisiku, M.D.**

This study examines the effects of TBI on cerebral blood flow (CBF) and the effect of erythropoietin in CBF.

### **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 II b - Phase III randomized study of the efficiency of riluzole for the treatment of acute spinal cord injury.



### **OTHER**

#### **A Cross-model Synthetic Approach to Eloquent Cortical Regions**

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

The purpose of this study is to understand the mechanisms of language production through an integrated application of functional MRI, diffusion tensor imaging tractography and intra-cranial electrophysiology.



### **Brain Mapping with MEG**

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

This study is using noninvasive MEG imaging to compare the structure and function of the nervous system of subjects who have developed normally and people with learning disabilities or neurological diseases such as epilepsy, stroke, autism and other disorders.

### **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.

### **Clinical Interventions to Increase Organ Procurement, Nutritional Status and Enteral Absorption Capability after Brain Death**

PRINCIPAL INVESTIGATOR: **Gigi Hergenroeder, R.N.**

This study is gathering preliminary data evaluating the effect on donor organ outcome of enteral feeding with immunomodulating nutrition containing omega-3 and omega-6 fatty acids, antioxidants and glutamine.

### **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 as used in standard medical care, to closely study the areas of the brain involved in language, movement and vision.

### **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.

### **Hemicraniectomies for Malignant Middle Cerebral Artery Syndrome—Variability in Surgical Technique and Prognosticating Factors**

PRINCIPAL INVESTIGATOR: **Tzu-Ching Wu, M.D.**

This retrospective study is to review hemicraniectomies performed for malignant middle cerebral artery syndrome and grade the adequacy of the decompression based on predefined radiological aspects. The study assessed whether there is indeed variability in hemicraniectomy/decompression techniques and it compared clinical outcomes in two groups: optimal vs. suboptimal decompression.

### **Nano-Engineered, Multi-Channel Scaffolds for Axon Regeneration**

PRINCIPAL INVESTIGATOR: **Qilin Cao, Ph.D.**

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

### **Neuroprotection Against Hypoxic/Ischemic Injury and Other Neurological Disorders**

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

This NIH-funded study is investigating brain protection against ischemia, hypoxic dysfunction and epileptic hyper-excitability, and exploring the effects of acupuncture on neurological disorders.

### **Neuroscience Research Repository (NRR)**

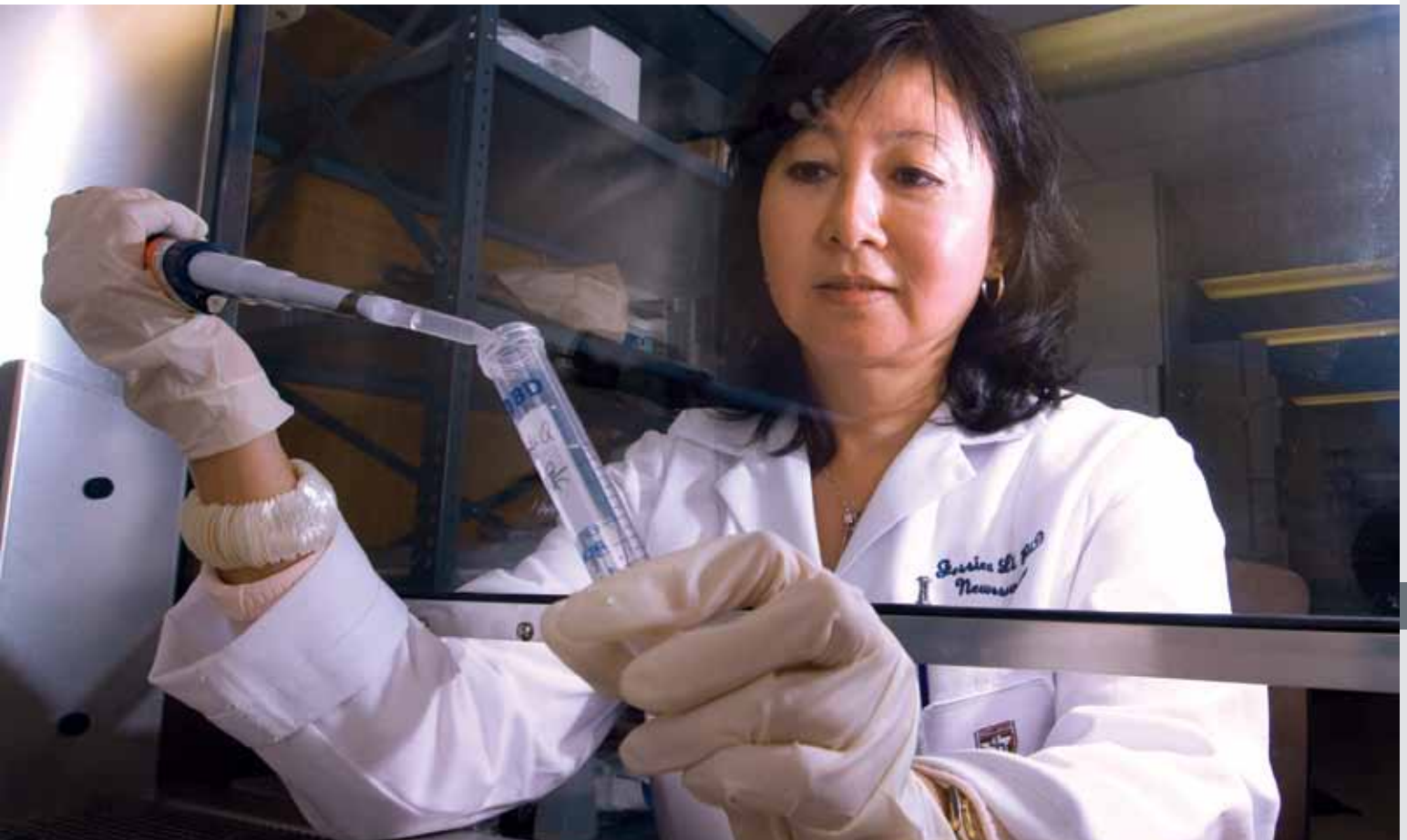
PRINCIPAL INVESTIGATOR: **Dong H. Kim, M.D.**

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-TMC in the spring of 2009.

### **The Neural Substrates of Common and Proper Naming**

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

This project uses intra-cranial brain recordings to understand the location and interaction between the substrates involved in fluent generation of nouns and verbs, and in their failure to do so, called the “tip-of-tongue” phenomenon.



# Selected Publications

## **ARONOWSKI, JAROSLAW**

Britton GL, Kim H, Kee PH, Aronowski J, Holland CK, McPherson DD, Huang SL. In vivo therapeutic gas delivery for neuroprotection with echogenic liposomes. *Circulation*. 19 Oct 2010; 122(16):1578-87. [E-pub 4 Oct 2010]

Sharma S, Yang B, Strong R, Xi X, Brenneman M, Grotta JC, Aronowski J, Savitz SI. Bone marrow mononuclear cells protect neurons and modulate microglia in cell culture models of ischemic stroke. *Journal of Neuroscience Research* Oct 2010; 88(13):2869-76.

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## **BARRETO, ANDREW**

Martin-Schild S, Albright KC, Halleivi H, Barreto AD, Philip M, Misra V, Grotta JC, Savitz SI. Intracerebral hemorrhage in cocaine users. *Stroke* Apr 2010; 41(4):680-4. [E-pub 25 Feb 2010]

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Brod SA, Hood ZM. 2010. Ingested (oral) SST (somatostatin) Inhibits EAE. *Neurology* 74 Suppl 2, A560.

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Cai J, Zhu Q, Zheng K, Li H, Qi Y, Cao QL, Qiu M (2010) Co-localization of Nkx6.2 and Nkx2.2 homeodomain proteins in differentiated myelinating oligodendrocytes. *Glia* 2010; 58: 458-468.

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Ellmore, T.M., Hood A.J., Castriotta R., Stimming E.F., Bick R.J., Schiess M.C. Reduced volume of the putamen in REM Sleep Behavior Disorder patients. (2010) *Parkinsonism and Related Disorders*, 16(10): 645-649.

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Ellmore, T.M., Beauchamp, M.S., Breier, J.I., Slater, J.D., Kalamangalam, G.P., O'Neill, T., Disano M.A., Tandon, N. Temporal lobe white matter asymmetry and language laterality in epilepsy patients. *Neuroimage* 2010; 49(3) 2033-2044.

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Sharma S, Yang B, Xi X, Grotta JC, Aronowski J, Savitz SI. IL-10 directly protects cortical neurons by activating PI-3 kinase and STAT-3 pathways. *Brain Research* 10 Feb 2011; 1373: 189-94. [E-pub 4 Dec 2010]

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# *Patient* Stories



## Christine Smid: Relief from the Suicide Disease

Twenty-five-year-old Christine Smid was in good health until 2007, when she began to notice a sharp pain in her face that began just below the eyelid and extended down to her upper teeth and lip. “It came out of nowhere, a burning, shocking pain that ran from my left cheek to my two front teeth,” Smid says. “It started one morning while I was making my bed. After that, I had pain several times a week, varying from a second to five minutes.”

Because the pain involved her front teeth, she sought help from a dentist in Austin, where she was working on an undergraduate degree in biomedical engineering at The University of Texas. Following root canals on her two front teeth, the pain subsided – but only temporarily. The dentist performed two more root canals on the same teeth, thinking he’d left an exposed root.

While visiting family in Lake Jackson, Texas, she saw her hometown dentist, who recognized the symptoms of trigeminal neuralgia (TN) and referred her to a neurologist in Houston. Often referred to as the “suicide disease,” TN has been described as one of the most painful conditions known.

“I tried two different medications normally prescribed for seizures – Carbatrol® and Tegretol®. They helped but they also affected me cognitively,” Smid says. “By then I was a graduate student and couldn’t afford to have anything interfering with my cognitive abilities, so I stopped the medication and just dealt with the pain. I kept hoping it would leave as spontaneously as it came.”

Smid lived with the pain for four years before she was referred to Dong Kim, M.D., director of the Mischer Neuroscience Institute and professor and chair of the Vivian L. Smith Department of Neurosurgery at The University of Texas Health Science Center at Houston (UTHealth) Medical School. Dr. Kim discussed her treatment options, including stereotactic radiosurgery with the Leksell Gamma Knife® Perfexion™ and microvascular decompression. After reviewing the results of a CT angiogram, physician and patient opted for microvascular decompression of the trigeminal nerve.

Smid went to surgery on January 19, 2011. “As with most cases of trigeminal neuralgia, the pain was caused by a normal artery contacting the nerve,” Dr. Kim says. “Arteries pulsate with blood flow, and the rhythm of the pulsations triggers the trigeminal nerve to fire, which the brain interprets as face pain. As we grow older, arteries that are normal and initially straight can become longer and curve so that they touch the nerve.”

The decompression was successful, and after struggling with the pain of TN for four years, she is now pain free. “I would recommend the surgery to anyone suffering from trigeminal neuralgia,” says Smid, who is now in the third year of her doctoral program in biomedical engineering. “Working with Dr. Kim was wonderful. I had no complications and recovered well. Everything was done through a quarter-size hole behind my left ear. They shaved my head in that area but the rest of my hair covered it up. People couldn’t believe I had brain surgery. It was so easy.”

“ I had no complications and recovered well. People couldn't believe I had brain surgery. It was so easy. ”



## Gary McGehee: Home on the Range

When 63-year-old West Texas rancher Gary McGehee began experiencing episodes of tingling in his left shoulder and arm in 2010, he was treated for heart disease in San Angelo, the town located nearest the ranch he and his wife Carolyn own in Irion County. His cardiologist diagnosed stress-related angina and prescribed medication that McGehee took for nearly a year. But his condition continued to worsen, and the episodes became more frequent and more severe.

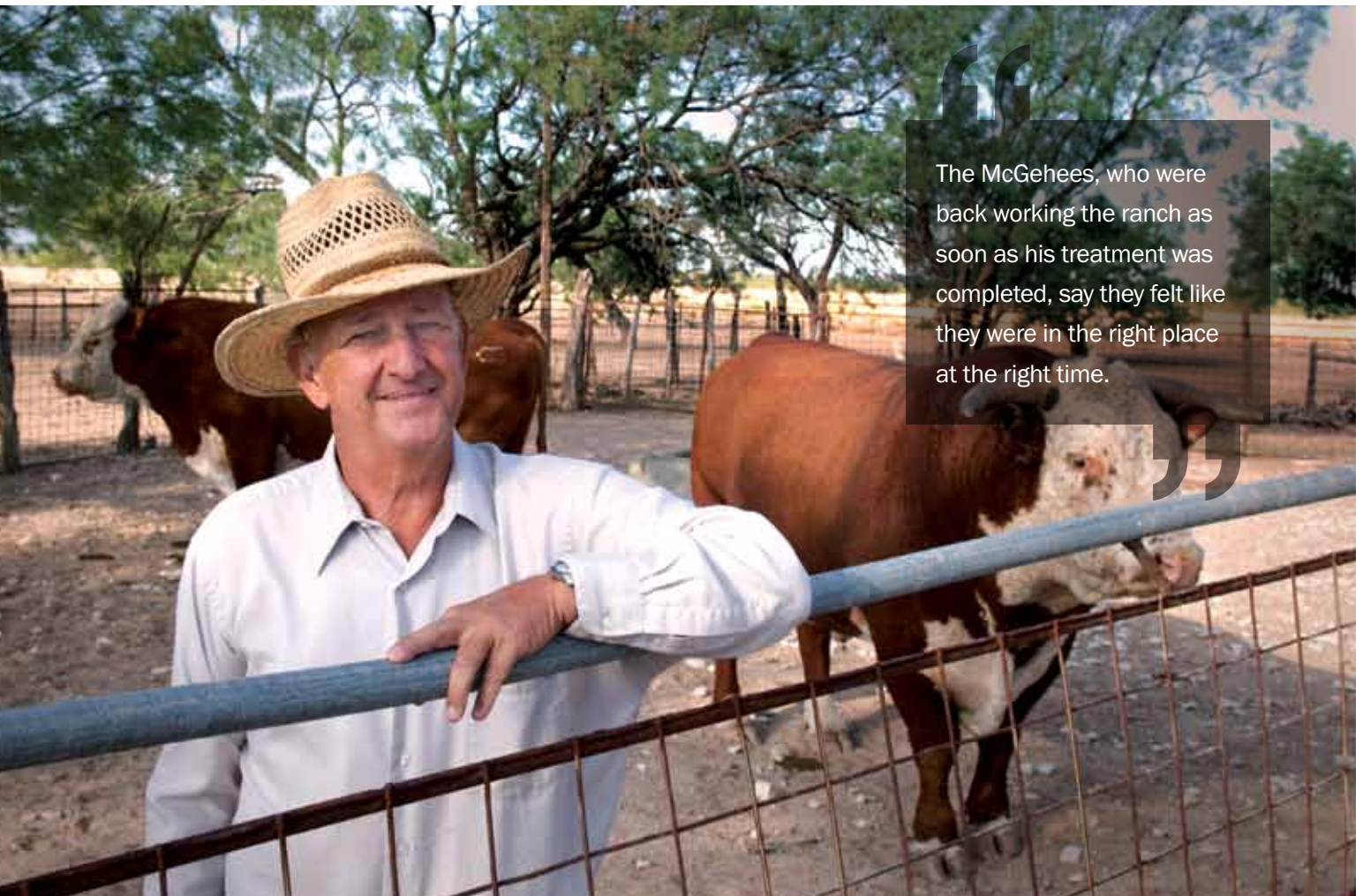
“Gary began having symptoms about a year before he came to see me,” says Nitin Tandon, M.D., a neurosurgeon at the Mischer Neuroscience Institute (MNI) and an associate professor in the Vivian L. Smith Department of Neurosurgery at The University of Texas Health Science Center at Houston (UTHealth) Medical School. “In addition to the left arm and shoulder numbness, he was blanking out frequently, which suggested he was having complex partial seizures.”

In December 2010, McGehee suffered a tonic-clonic seizure that triggered a visit to an emergency center in San Angelo, where an MRI study revealed an extensive brain mass involving the right temporal lobe, the hippocampus and the right insular cortex – and extending partly into the inferior portion of the frontal lobe. His son Michael McGehee, M.D., a third-year resident at the Baylor/UTHealth Alliance for Physical Medicine and Rehabilitation in Houston, arranged for him to be seen by Dr. Tandon at MNI.

“By the time I saw Gary, he was having five or six uncontrolled seizures daily despite the multiple anticonvulsant medications he was taking,” Dr. Tandon says. An MRI confirmed the location and extent of the tumor, and using Wada testing, Dr. Tandon and his team confirmed their suspicion that the side of the brain opposite the tumor was his dominant hemisphere for language and memory. They took McGehee to the OR on January 17, 2011.

The tumor Dr. Tandon removed measured 8 x 7 centimeters, about the size of a peach. “Despite its large size and intrusion into several important structures in the brain, we were able to resect the entire visible tumor,” the neurosurgeon says. The pathology report confirmed a grade 2 astrocytoma, and McGehee’s case was discussed at MNI’s weekly multidisciplinary Brain Tumor Board.

“Balancing the benefits and risks of treatment versus observation based on Mr. McGehee’s physical health, tumor size and location before surgery, age and seizure frequency, we recommended the standard-of-care treatment for tumors of this type to kill any cancer cells undetectable by standard imaging techniques,” says fellowship-trained neurologist and neuro-oncologist Jay-Jiguang Zhu, M.D., Ph.D., who is an associate professor in the department of Neurosurgery and the department of Neurology at the UTHealth Medical School. “He underwent six weeks of radiation and daily oral chemotherapy with temozolomide, followed by temozolomide only at five days out of 28 days.”



“The McGehees, who were back working the ranch as soon as his treatment was completed, say they felt like they were in the right place at the right time.”

McGehee tolerated the treatment well, with only mild fatigue, and is now followed by blood work every four weeks and MRI studies every two to three months. Since undergoing treatment, he has had no seizures and no tingling in his arm. His MRI on June 16, 2011, showed no evidence of tumor recurrence. “His prognosis is excellent,” Dr. Tandon says.

McGehee’s case stands out to Dr. Tandon for three reasons. “First, he suffered for nearly a year without a correct assessment of the etiology of his symptoms. Second, it was an uncommon tumor – an extensive paralimbic-insular glioma that had grown to this size without major disruption of essential functions. In a surgery of this type, it’s of great importance to preserve the subcortical pathways as well as the vessels supplying the blood to the tumor. The surgery can be complex and long – Gary’s took nine hours – so many surgeons prefer

to do subtotal resections or biopsies of gliomas like these, because they’re unwilling to take the risk of pushing the surgery to the point of accomplishing a complete resection. As has been shown multiple times, the extent of resection correlates strongly with the long-term outcome. And lastly, for me it was a great privilege to take care of a family member of one of our colleagues.”

The McGehees, who were back working the ranch as soon as his treatment was completed, say they felt like they were in the right place at the right time. “From my perspective, it was a miracle that we got Gary through this and that miracle came through Dr. Tandon,” Carolyn McGehee says. “He rearranged his schedule to get Gary into surgery as quickly as possible. We were fortunate that our son in Houston got us to the right people, and that everything went smoothly. We’re still amazed.”

## Janie Totten: Against All Odds

As a three-year survivor of glioblastoma multiforme (GBM), Janie Totten has defied the odds. “I was determined that I wasn’t going to let this cancer beat me,” says the 60-year-old Houston resident. After my surgery, I did exercises at home with my arms and fingers and got stronger and stronger. I decided I was going to walk and do everything I did before I was diagnosed with brain cancer, but at a slower pace. I always kept a positive attitude, and I had a lot of support from my husband, my son Christopher and my daughter Caroline – and lots of prayers. I knew everyone cared.”

Totten’s positive attitude and strong will to live are just two of the many factors contributing to her long-term survival, says fellowship-trained neurologist and neuro-oncologist Jay-Jiguang Zhu, M.D., Ph.D., who has managed Totten’s care since he joined the Mischer Neuroscience Institute (MNI) in September 2010. “The median survival for patients with GBM is 14.6 months after diagnosis,” Dr. Zhu says. “Mrs. Totten has done well because she has many things going for her – her age, the type of tumor resection and the skill with which it was performed, as well as her physical and emotional strength. She had no significant disability following removal of the tumor. She tolerated radiation and chemotherapy well, and she had a good support system at home. Because she was treated at MNI, she had the benefit of the multidisciplinary resources of our weekly Neuro-Oncology Tumor Board at which neurosurgeons, radiation oncologists, neuroradiologists and neuropathologists discuss cases to ensure the best treatment.”

Totten presented at the Emergency department of Memorial Hermann Northeast Hospital in September 2008, with numbness in her legs following a seizure. When a CT scan revealed a brain mass, she was referred to Dong Kim, M.D., director of the Mischer Neuroscience Institute and professor and chair of the Vivian L. Smith Department of Neurosurgery at The University of Texas Health Science Center at Houston (UTHealth) Medical School. Dr. Kim performed a total resection of the GBM, following motor function mapping done by MNI neurosurgeon Nitin Tandon, M.D., to maximize tumor removal while minimizing the possibility of motor deficit after surgery.

In late October 2008, Totten started a six-week course of radiation therapy and chemotherapy with oral temozolomide. By January 2009, she was receiving a maintenance dose of temozolomide five days out of every 28. She continued chemotherapy until mid-October 2010, during which time she was followed regularly with blood work and MRI studies.

“The standard for administration of temozolomide in GBM patients is six months,” says Dr. Zhu, who is an associate professor in the department of Neurosurgery and the department of Neurology at the UTHealth Medical School. “Mrs. Totten was able to tolerate her chemotherapy regimen for a year and a half without significant side effects, which contributed to her outcome. She was doing well, with the exception of episodic seizures about once every two months. Balancing the benefit and potential side effects of long-term use of temozolomide, we discussed stopping chemotherapy.”



“ I was determined that I wasn't going to let this cancer beat me. ”

After discontinuing the temozolomide, Dr. Zhu followed Totten every two months with MRI and physical examination; her MRI results were reviewed at the weekly meetings of the MNI Brain Tumor Board. When a lesion was discovered on an MRI study done in May 2011, she underwent stereotactic radiosurgery at Memorial Hermann-Texas Medical Center. The procedure was performed by Dr. Kim and radiation oncologist Clive Shkedy, M.D., using MNI's Leksell Gamma Knife® Perfexion™. As the most technologically advanced Gamma Knife model available, the Perfexion allows for the treatment of a broader range of anatomical structures than earlier Gamma Knife models. It also improves treatment planning and patient comfort, and reduces treatment time.

“By using the Gamma Knife, we can destroy most of the tumor,” says Dr. Zhu. “Moving forward, we'll follow her closely and plan to use the angiogenesis inhibitor bevacizumab if there's any evidence of tumor growth.”

Totten and her husband, George, have kept a journal since she began treatment in 2008. “Writing things down has helped us keep track of doctors' appointments, treatments and progress,” she says. “When you have the kind of surgery I had and undergo chemotherapy for as long as I did, it's hard to remember things, so the journal has been very useful. But the most important thing is to keep a positive attitude. Always stay strong, and never give up.”

## Christine Portillo: A Matter of Genetics

Christine Portillo's story has the power to save lives. It begins in 1998, the year her mother suffered a stroke as the result of two ruptured intracranial aneurysms.

"She recovered quickly and went back to work two weeks later, but we don't remember anyone telling the family that aneurysms can be hereditary," Portillo says. "And no one told her that she should be checked annually for a recurrence."

Twelve years later, near the end of 2010, Portillo's mother was diagnosed with normal pressure hydrocephalus (NPH), an abnormal increase of cerebrospinal fluid (CSF) in the brain's ventricles that occurs when the normal flow of CSF is in some way blocked. As the ventricles enlarge, pressure on the brain increases. She was admitted to Memorial Hermann-Texas Medical Center under the care of Dong H. Kim, M.D., director of the Mischer Neuroscience Institute and professor and chair of the Vivian L. Smith Department of Neurosurgery at The University of Texas Health Science Center at Houston (UTHealth) Medical School. He placed a ventricular shunt in the fluid-filled chamber to relieve pressure on the brain.

"Our entire family was by her side to help her through the surgery," Portillo says. "We came in for a follow-up with Dr. Kim about her progress and near the end of the consultation, he said, 'I'd really like you to see our geneticist.' So we sat around the table with the geneticist - my mom and dad, my sister and I.

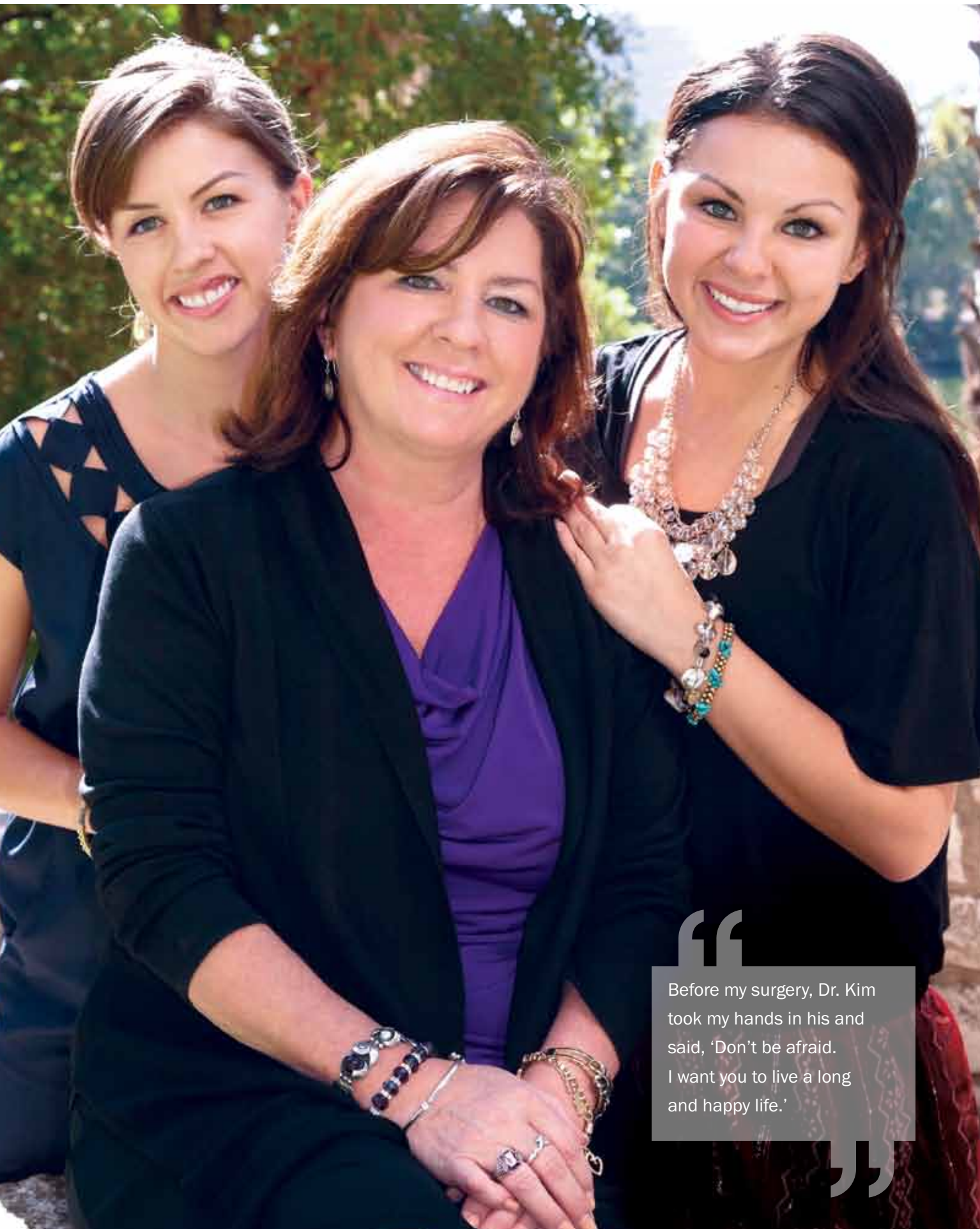
My two brothers weren't with us at the time. They told us we should be checked for aneurysm, and they gave us a letter to give to our family members recommending that they be screened as well."

Portillo, who is 51, was the first of her family members to undergo screening. The results of a magnetic resonance arteriogram (MRA) and subsequent cerebral arteriogram revealed the presence of five aneurysms, four of which were around the brain and could have caused serious hemorrhage. "Based on her family history and the fact that she presented with multiple aneurysms, she was at higher risk of rupture than patients in the general population, so I recommended surgery," Dr. Kim says.

Portillo underwent two procedures. On March 21, 2011, Dr. Kim performed a left frontal craniotomy and clipped the aneurysms in the left ophthalmic segment and left posterior communicating artery. At a two-week follow-up visit he noted that she was healing well, with no neurological deficits as a result of the surgery.

"My recovery was actually surprisingly rapid," she recalls. "Three weeks to the day after the surgery, I was back on my regular workout schedule at the Y." Between the two surgeries, she helped nurse her husband through a prostatectomy, helped plan her eldest daughter's wedding, continued her job search online and accepted a position at a Houston-based design and marketing communications firm.





“  
Before my surgery, Dr. Kim took my hands in his and said, ‘Don’t be afraid. I want you to live a long and happy life.’  
”

Portillo's second surgery took place on May 2, 2011. Dr. Kim performed a right frontal craniotomy and successfully clipped two additional intracranial aneurysms – in the right posterior communicating artery and the right anterior choroidal artery.

“During these months of interacting with Dr. Kim and MNI staff, I learned about my risk factors, particularly genetics and smoking,” she says. “I was a light smoker in the past – off and on – and I'm so proud of myself for quitting for good. I'm borderline high blood pressure. Other than that, I think my case was mostly a matter of genetics. I want people to know that if someone in their family was diagnosed with either a ruptured or unruptured aneurysm – whether they're a child, a sibling or a grandchild – they should be screened. I consider myself so fortunate that mine were discovered, and so grateful to have been operated on by someone of Dr. Kim's caliber.”

In follow-up, Portillo will be screened every year. She has also encouraged her two daughters to be screened according to the current guidelines – every five years, starting at age 30. Twenty-one-year-old Veronica Portillo is a recent graduate of The University of Texas at Austin, and 24-year-old Elyse Portillo is pursuing a medical degree at Baylor College of Medicine. Portillo's older sister, who was screened in early 2011, is free of aneurysm.

After consenting to participate, Portillo and her family became part of the more than 500 families affected by intracranial aneurysms that have been described to date in research conducted by Dr. Kim and Teresa Santiago-Sim, Ph.D., an assistant professor in the Vivian L. Smith Department of Neurosurgery. The study was funded by the National Institutes of Health and by the American Heart Association/Burgher Foundation.

“Our long-term goals are to identify causative mutations in intracranial aneurysms and altered molecular pathways that lead to disease,” Dr. Kim says.

Working with DNA samples stored in the department's Neuroscience Research Repository, Dr. Santiago-Sim has used linkage analysis of a large family with a history of hereditary intracranial aneurysms to identify a novel region in the genome. “In the process of characterizing the gene, we think we've identified a possible mutation,” she says.

“Standardized electronic health data and samples are collected in a uniform manner, which makes the information in the database very consistent,” she adds. “It's also very extensive, describing the type and shape of the aneurysm, whether it was ruptured or remained intact at the time of diagnosis, whether the patient has a positive or negative family history for aneurysms and other possible related inherited diseases such as polycystic kidney disease or stroke. This information will help us identify genotype-phenotype correlations that will ultimately improve the way we manage patient care.”

Portillo's strongest impression of her experience at MNI is the care she received. “It was phenomenal. We can't believe how lucky we are to live in a city with such amazing medical resources,” she says. “We felt like we've made friends. Because of the compassion of my caregivers, being a brain surgery patient seemed less frightening. Before my surgery, Dr. Kim took my hands in his and said, ‘Don't be afraid. I want you to live a long and happy life.’ He calmed and reassured me, and I remember being fascinated with his hands. Those are the hands that cured me.”

## Martha Mazzola: A Day Unlike Any Other

Martha Mazzola recalls very little of the evening she suffered an acute ischemic stroke. “It started out as a day just like any other, and along toward evening I found myself sitting on a chair at our kitchen table with my husband on his knees beside me saying he was going to call 911,” the 84-year-old Houston resident says. “I said, ‘Why? I’m fine.’ He told me that he couldn’t understand me, that my speech was totally garbled.”

Mazzola remembers that the ambulance passed nearby hospitals as it sped toward the Mischer Neuroscience Institute (MNI) at Memorial Hermann-Texas Medical Center, which houses the largest and most comprehensive neuroscience program in Texas and is home to the 10-county Greater Houston area’s largest onsite stroke team. By working closely with the Houston Fire Department and local EMS services, MNI’s stroke team has logged an impressive record of success in the administration of tissue plasminogen activator (tPA) – more than 10 times the national average of 2 percent.

When Mazzola arrived at the Emergency Center, neurologist Andrew Barreto, M.D., a member of MNI’s stroke team, administered tPA. He also determined that she was a good candidate for an additional investigational therapy that applies ultrasound energy to help dissolve the blood clots that cause ischemic stroke.

When her family consented, Mazzola became one of more than 35 people at two American study sites to benefit from participation in a Phase I/II study to determine the safety of a novel, external hands-free transcranial Doppler

ultrasound system in healthy volunteers and ischemic stroke patients. James C. Grotta, M.D., co-director of MNI and professor and chair of the department of Neurology at The University of Texas Health Science Center at Houston (UTHealth) Medical School, is principal investigator of the study, the formal name of which is “CLOTBUST-Hands Free: Combined Lysis of Thrombus in Brain Ischemia with Transcranial Ultrasound and Systemic tPA.” The device is under study at the UTHealth Medical School and the University of Alabama at Birmingham; if found to be



safe, it will enable the more widespread use of operator-independent, ultrasound-enhanced thrombolysis and the planning of a large Phase III efficacy trial.

The results of the original multicenter, randomized CLOTBUST trial, coordinated by the UTHealth Medical School and published in the *New England Journal of Medicine* in 2004, found that continuous transcranial Doppler ultrasound improved tPA-induced arterial recanalization. “In the original study, Dr. Grotta and the CLOTBUST investigators combined tPA with a handheld ultrasound probe,” says Dr. Barreto, who is co-principal investigator of CLOTBUST-Hands Free and an assistant professor at the UTHealth Medical School. “Half of the 126 patients enrolled received tPA alone and half were treated using tPA and the handheld device. When the results justified a larger study, the investigators decided it would be more efficient to develop a head frame for hands-free application of ultrasound than to train neurologists how to use the handheld device.” Andrei Alexandrov, M.D., also a co-principal investigator of the study and current director of the Comprehensive Stroke Research Center at the University of Alabama at Birmingham, developed the helmet-like, hands-free device currently under study. Dr. Alexandrov was previously a member of the MNI stroke team.

The CLOTBUST-HF study population includes 15 healthy volunteers who assessed the safety of the device in Phase I of the trial by tolerating two hours of transcranial ultrasound delivered through the head frame. All Phase I participants had normal brain MRIs before and after ultrasound. A detailed physical examination of skin integrity post-insonation determined that there also were no adverse dermatological effects.

Participants in Phase IIa and IIb received intravenous (IV) tPA according to American Heart Association/American Stroke Association treatment guidelines. Phase IIa of the study included 20 patients with ischemic stroke treated with IV tPA within 4.5 hours of the event; they will be followed for three years. Phase IIb, currently under way, will include 40 patients with ischemic stroke treated with IV tPA and randomized to receive either ultrasound therapy or sham therapy. All patients will be evaluated for arterial recanalization two hours after treatment to determine if the clot has dissolved. Patients will be followed for three months and have their stroke deficits measured using the National Institutes of Health Stroke Scale, and any remaining disability scored using modified Rankin Scale.

“Mrs. Mazzola’s clot had completely dissolved after the tPA plus hands-free ultrasound treatment was completed,” Dr. Barreto says. “Because we were able to open the artery so quickly, we averted a large, life-threatening stroke.”

Martha Mazzola says she’s amazed she survived the stroke with so little damage. “The EMS folks took me to the right hospital, and I’m glad I had the opportunity to participate in the study,” she says. “You can’t offer new treatments without people who are willing to be pioneers and test them. People have been surprised by the speed of my recovery, and I’m pleased with my results. I saw the scans of my brain before and after. Such a dramatic difference between the two!”

<sup>1</sup> Alexandrov AV, Molina CA, Grotta JC, Garami Z, Ford SR, Alvarez-Sabin, J, Montaner J, Saqqur M, Demchuk AM, Moyé LA, Hill MD, Wojner AW for the CLOTBUST Investigators. Ultrasound-Enhanced Systemic Thrombolysis for Acute Ischemic Stroke. *New England Journal of Medicine* 2004; 351:2170-2178.

## Rep. Gabrielle Giffords: On the Road to Recovery

The Mischer Neuroscience Institute (MNI) and TIRR Memorial Hermann took the national stage when U.S. Rep. Gabrielle Giffords was transferred to Memorial Hermann-Texas Medical Center's Neuroscience Intensive Care Unit on Friday, Jan. 21, 2011. The Arizona congresswoman was

shot in the head at pointblank range on Jan. 8 when an assailant opened fire outside a grocery store in Tucson, killing six people and wounding 13 others. She was transported to University Medical Center in critical condition, and a portion of her skull was removed to relieve brain swelling.



“

Gabby looked terrific when she returned to Congress. She has a strong will to recover, and we look forward to seeing the next milestone in her journey.

”

In a press conference immediately following Rep. Giffords' transition to Memorial Hermann-TMC, medical teams from both hospitals described her transfer of care as "seamless."

"It was a very smooth transfer, thanks to the collaborative efforts of both hospitals and the help of the U.S. Capitol Police and the Navy," says Imoigele Aisiku, M.D., medical director of the Neuroscience ICU and Neurosurgery Intermediate Care Unit at MNI. "She was medically stable when she arrived and began rehabilitation the following day. From medical data and our own experience, we know that the earlier we begin the rehabilitation process, the faster a patient will regain function down the road."

Rep. Giffords' physician team upgraded her condition from serious to good four days after her admission to MNI, and she was transferred to TIRR Memorial Hermann to begin inpatient rehabilitation. At the rehabilitation hospital, a multidisciplinary team of physicians, nurses and therapists who specialize in head trauma worked closely with Rep. Giffords to develop the best combination of therapies for a return to function.

"We're like an orchestra," says Gerard Francisco, M.D., chief medical officer of TIRR Memorial Hermann and professor and chair of the department of Physical Medicine and Rehabilitation at The University of Texas Health Science Center at Houston (UTHealth) Medical School, who was in charge of Rep. Giffords' care during her stay at the rehabilitation hospital. "The comprehensive rehabilitation services we provide treat the whole person and expedite recovery."

"Because TIRR Memorial Hermann is on our Campus, she had the same physician team in two locations from day one," says Dr. Aisiku, who is also vice chair of the division of Critical Care and an associate professor in the Vivian L. Smith Department of Neurosurgery at the UTHealth Medical School. "I continued to see her during her stay at TIRR Memorial Hermann, and when she was readmitted to the acute care hospital for cranioplasty, her physical medicine and rehabilitation team saw her here. There were no walls between us."

On May 18, neurosurgeon Dong Kim, M.D., performed a successful cranioplasty to replace the piece of Rep. Giffords' skull that was removed on Jan. 8. He attached a plastic computer-generated implant to her skull, along with a shunt to drain fluid, eliminating the need for a protective helmet.

On June 8, she celebrated another milestone – her 41st birthday. "Since Gabby arrived in Houston and at Memorial Hermann, we have been consistently pleased with the strides she has made," says Dr. Kim, who is director of the Mischer Neuroscience Institute and professor and chair of the Vivian L. Smith Department of Neurosurgery at the UTHealth Medical School. "I could not be more proud of how far she has come. She looked terrific when she returned to Congress on Aug. 1, and her presence there offers clear signs of cognitive improvement, physical strength and personal confidence. She has a strong will to recover, and we look forward to seeing the next milestone in her journey."

“

I continued to see her during her stay at TIRR Memorial Hermann, and when she was readmitted to the acute care hospital for cranioplasty, her physical medicine and rehabilitation team saw her here. There were no walls between us.

”



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