



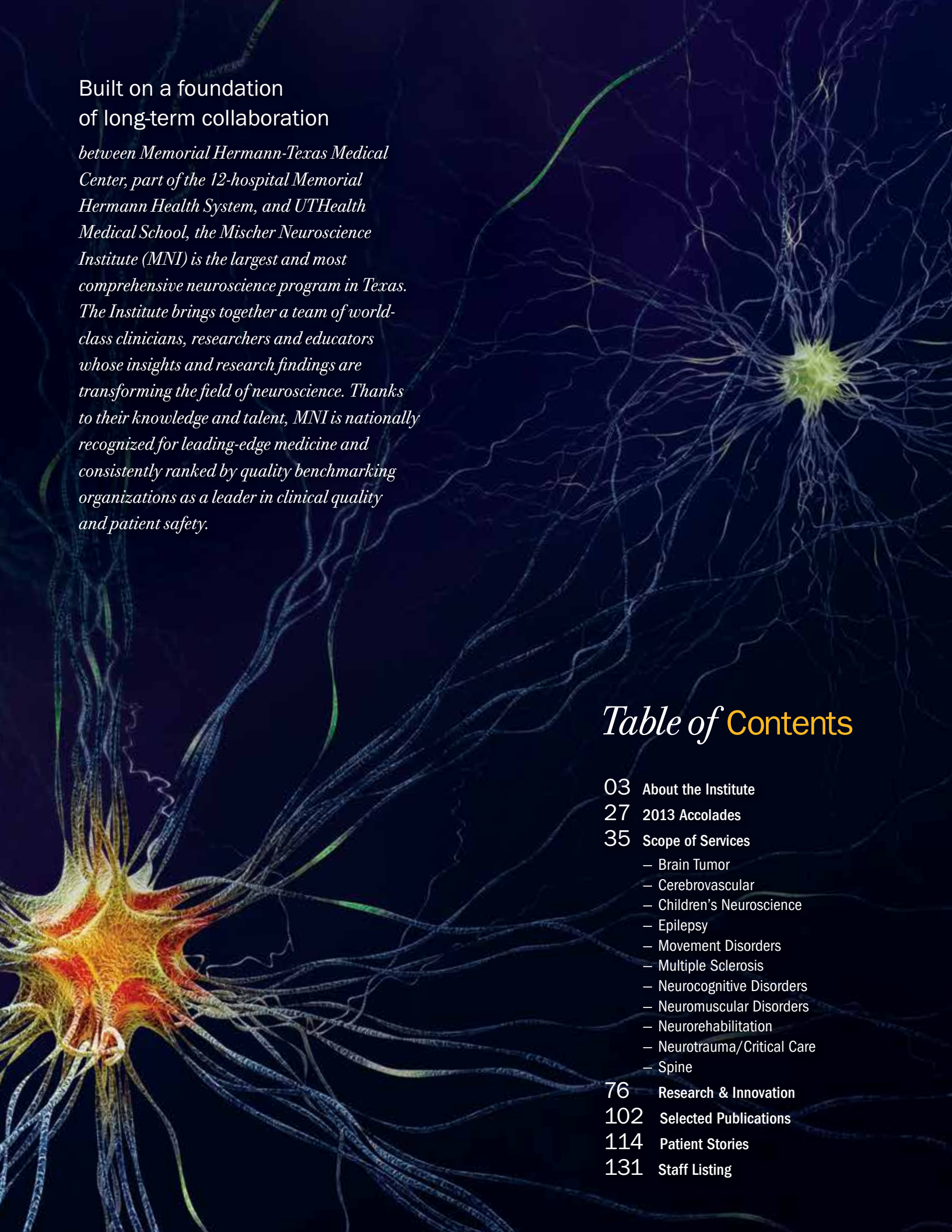
**MISCHER NEUROSCIENCE INSTITUTE REPORT 2013**

Mischer  
Neuroscience Institute

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**MEMORIAL<sup>®</sup>**  
**HERMANN**





## Built on a foundation of long-term collaboration

*between Memorial Hermann-Texas Medical Center, part of the 12-hospital Memorial Hermann Health System, and UTHealth Medical School, the Mischer Neuroscience Institute (MNI) is the largest and most comprehensive neuroscience program in Texas. The Institute brings together a team of world-class clinicians, researchers and educators whose insights and research findings are transforming the field of neuroscience. Thanks to their knowledge and talent, MNI is nationally recognized for leading-edge medicine and consistently ranked by quality benchmarking organizations as a leader in clinical quality and patient safety.*

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## Dear Esteemed Colleagues,

2013, our sixth anniversary, was a year of recognitions and strategic expansion at the Mischer Neuroscience Institute (MNI) at Memorial Hermann-Texas Medical Center and Mischer Neuroscience Associates (MNA), a citywide network of neurosurgeons and neurologists. Among those recognitions is the highly coveted Comprehensive Stroke Center certification awarded by The Joint Commission (TJC) and the American Heart Association/American Stroke Association. MNI is home to the first and only stroke program in Texas to meet TJC's rigorous standards.

While the neurosurgery program continues to grow, a major focus in 2013 was the expansion of neurology services across the city. Since 2008, MNI has worked to extend its neurosurgery program from the Texas Medical Center across the city. New additions to the MNA Neurology team work hand in glove with affiliated neurosurgeons in the community, reducing wait times for patients, and providing the full continuum of neuroscience care in outlying communities.

MNI's reach extends beyond Houston through the Telemedicine Program, which now includes 13 community hospitals in Southeast Texas. Through remote presence technology, patients at these hospitals benefit from neurology expertise, prompt diagnosis and a treatment plan based on the best available protocols, and opportunities to participate in clinical trials.

A focus on innovation, quality outcomes and physician education continues to attract physician faculty members to MNI, MNA and UTHealth Medical School. In this 12-month period, 15 new recruits, including



neurosurgeons, neurologists and neurointensivists were welcomed to MNI and UTHealth. These new team members ensure that patients across the city receive the highest quality services throughout the entire neuroscience continuum of care.

Ryan Kitagawa, M.D., has joined the Mischer Neuroscience Institute neurosurgery team as director of neurotrauma at Memorial Hermann-TMC. Baraa Al-Hafez, M.D., has also joined the neurosurgery team, providing exceptional care at two locations - Memorial Hermann Katy Hospital and Memorial Hermann Memorial City Medical Center. Among new neurology recruits are Reza Sadeghi, M.D., who sees inpatients and outpatients at Memorial Hermann Northwest Hospital and Memorial Hermann Southwest Hospital; Usha Aryal, M.D., who sees inpatients at Memorial Hermann Southwest and outpatients at Mischer Neuroscience Associates Northwest; and Jack Ownby, M.D., who treats inpatients at Memorial Hermann Southwest.

## DIRECTORS' LETTER

At Neurology Consultants of Houston, which is now affiliated with Mischer Neurosciences, Mary Ellen Vanderlick, M.D., William Irr, M.D., and Leanne Burnett, M.D., provide outpatient neurology services. Bob Fayle, M.D., has joined the outpatient neurology team at Houston Neurological Institute, which serves Pasadena and Pearland.

Three outpatient neurologists have joined UT Physicians and UTHealth Medical School. Rony Ninan, M.D., and Anjail Sharief, M.D., are affiliated with Memorial Hermann-TMC. Raja Mehanna, M.D., specializes in movement disorders at Memorial City Medical Center, Memorial Hermann-TMC and Memorial Hermann The Woodlands Hospital. Takijah T. Heard, M.D., is now director of pediatric neurophysiology at Children's Memorial Hermann Hospital. In addition, two neurointensivists have joined the inpatient neurology team at Memorial Hermann-TMC: Tiffany Chang, M.D., and Nancy Edwards, M.D.

At the same time we expanded our capability to treat neurological disease through new technology, including stereoelectroencephalography (SEEG), robotic SEEG and laser-assisted interstitial thermal therapy for epilepsy, and novel techniques to treat stroke, brain tumors in children, pediatric epilepsy, retinoblastoma and treatment-refractory depression.

We are proud of the accomplishments of our terrific team and pleased to share with you the Mischer Neuroscience Institute Clinical Achievements Report for fiscal year 2013, which highlights ongoing efforts in quality, safety, clinical care and research from July 2012 through June 2013. The report is a publication of MNI, part of the 12-hospital Memorial Hermann Health System, in collaboration with UTHealth Medical School. We hope you find the information helpful in making choices for the care of your patients with neurological disorders.

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

With best wishes,



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

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

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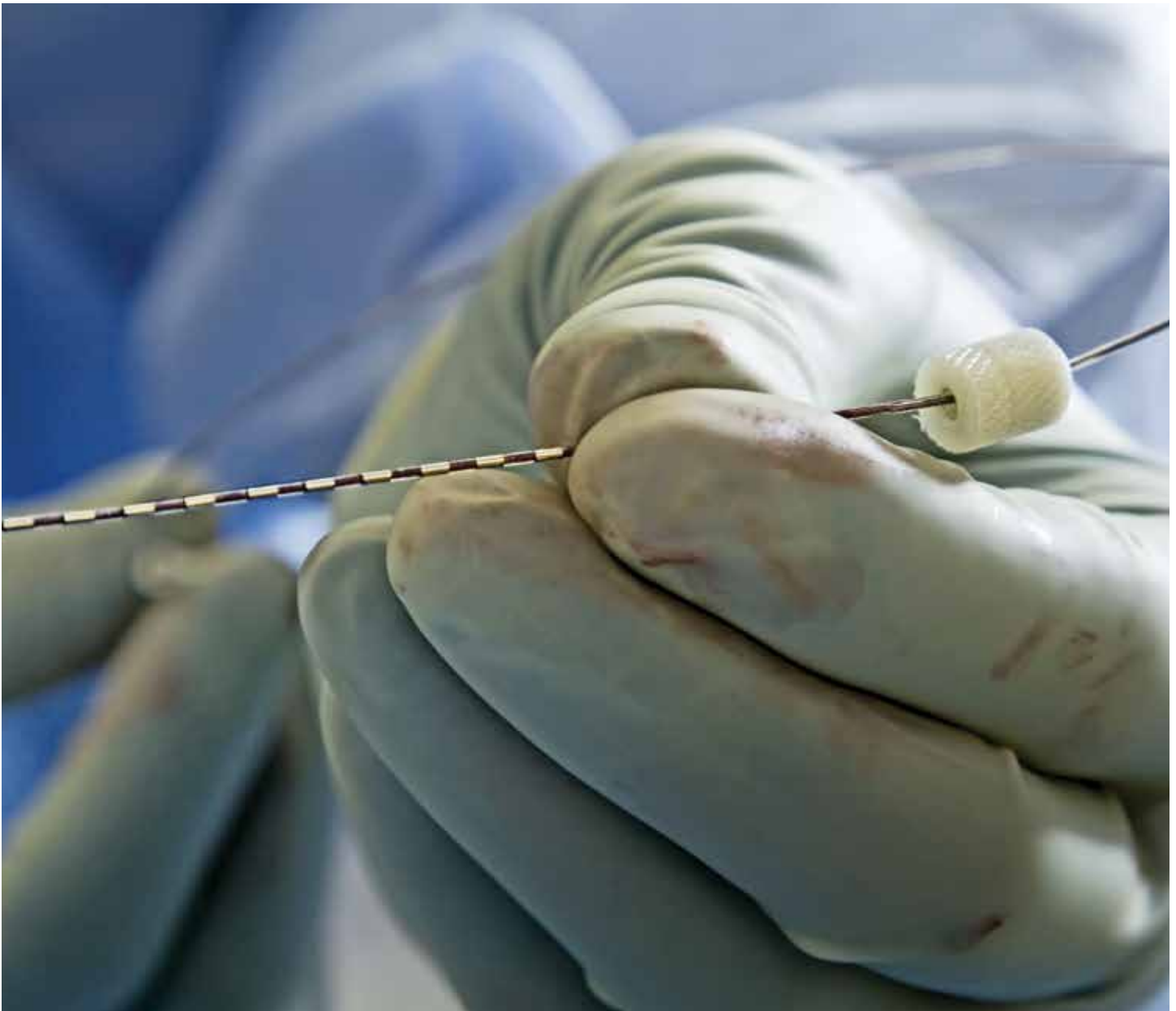


A handwritten signature in black ink, appearing to read 'James Grotta'.

**James C. Grotta, M.D.**  
CO-DIRECTOR  
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# *About the Institute*

The highest-quality care with the best outcomes, an impeccable patient safety record, the highest patient and referring physician satisfaction, the advancement of medicine – these are major goals at the Mischer Neuroscience Institute (MNI) at Memorial Hermann-Texas Medical Center. We're attaining them daily through a holistic focus on the needs of patients and a relentless dedication to quality improvement, research, teaching the next generation of healthcare professionals, innovation and growth.

As the only Joint Commission-certified Comprehensive Stroke Center in Texas – the highest level of stroke care certification – MNI has solidified its position among an elite group of providers focused on complex stroke care.



This comprehensive, integrated approach has led to the creation of Houston's leading epilepsy and neurotrauma programs, a cerebrovascular center where affiliated physicians treat more aneurysms and arteriovenous malformations than any other center in the region, an established pediatric neurosurgery program in collaboration with The University of Texas M. D. Anderson Cancer Center, an unmatched spinal neurosurgery and reconstructive peripheral nerve surgery program and a Brain Tumor Center that annually diagnoses and treats hundreds of new tumor patients. MNI is also proud of innovations in the treatment of multiple sclerosis, movement disorders, neurocognitive disorders, neuromuscular diseases and traumatic brain injury. MNI advances health every day.

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

That continuum of care is extended across the city through the strategic expansion of Mischer Neuroscience Associates, a citywide network of neurologists and neurosurgeons, and has reduced referral wait times by





building a new structure for the practice of neurology. Through a telemedicine program, MNI offers patients in outlying communities access to stroke and neurology expertise and opportunities to participate in clinical trials. Thirteen community hospitals in Southeast Texas are now linked to MNI through remote presence robotic technology. In addition, we are reaching larger numbers of people and engaging them in a powerful way through new patient access portals on our website and social media events.

In the last six years, we have seen strong growth in consumer preference for neuroscience care at Memorial Hermann. During that time, we have reported mortality

rates well below the national expected benchmark and seen a greater than 50 percent reduction in length of stay, despite the increased acuity of the patients we treat.

As physicians, seeing our patients do well is the main joy of our profession. As a team, we hold each other accountable for the care we deliver. Laboratory research and clinical studies allow us to take our work a step further, extending our expertise beyond our walls and communities to patients across the nation and around the world. MNI physicians and researchers make a personal and professional commitment to discovery and to bringing that new knowledge to the bedside quickly, which is why we remain at the forefront of neuroscience.

# At a Glance

## Physician Team

|                                |     |
|--------------------------------|-----|
| Staff Physicians               | 82  |
| Clinical Residents and Fellows | 51  |
| Medical Students on Rotation   | 301 |
| Research Fellows               | 15  |
| Advanced Practice Nurses       | 12  |
| Physician Assistants           | 3   |

## Inpatient Facilities

|                            |     |
|----------------------------|-----|
| Total Neuro Beds           | 136 |
| Neuro ICU Beds             | 32  |
| Neuro Step Down Beds (IMU) | 12  |
| Neuro Acute Care Beds      | 52  |
| Neuro Rehabilitation Beds  | 23  |
| Stroke Unit Beds           | 12  |
| Dedicated Operating Rooms  | 6   |
| EMU Beds – Pediatrics      | 6   |
| EMU Beds – Adult           | 6   |

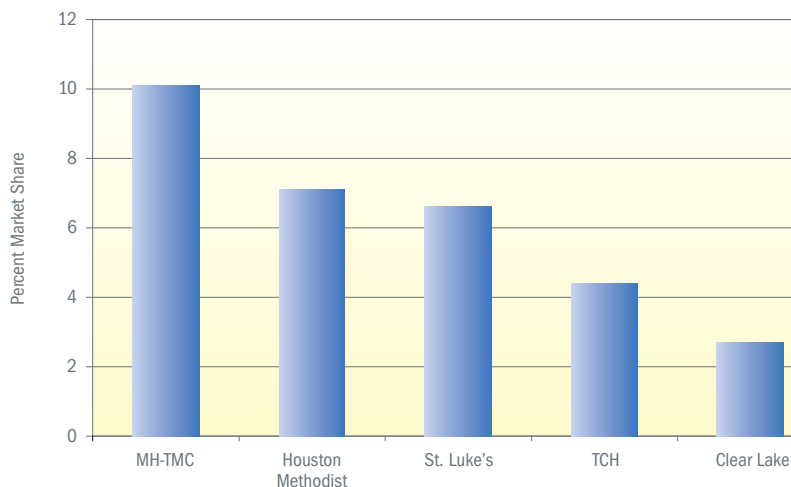
## Research

|                               |  |
|-------------------------------|--|
| Research Projects in Progress | More than 200                                  |
| Grants Awarded                | \$11.5 million<br>(Neurology and Neurosurgery) |

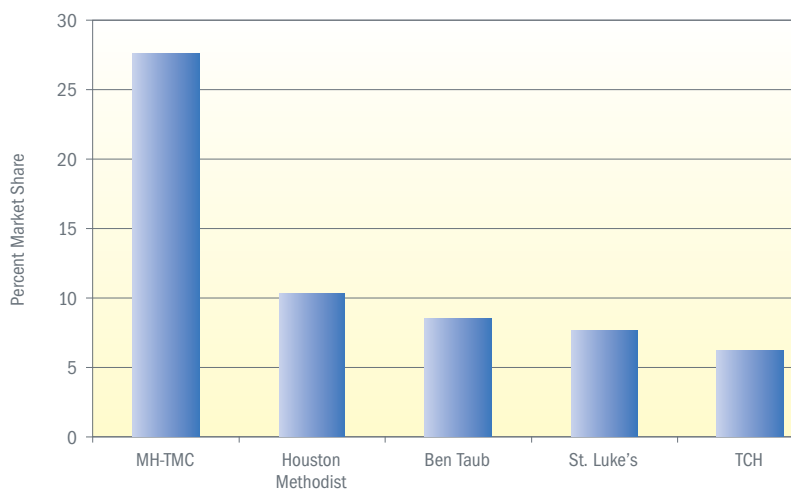
## Specialty Equipment includes:

- Leksell Gamma Knife® Perfexion™
- Varian Trilogy Linear Accelerator
- Siemens Artis™ zee (intra-operative angiography suite)
- Robotic SEEG
- RP-7™ Remote Presence System
- 3D C-Arm
- Philips Healthcare endovascular temperature modulation system
- Simultaneous electroencephalography and polysomnography
- Continuous EEG monitoring
- Magnetoencephalography imaging (Magnes 3600 WH)
- MRI capable of advanced spectroscopic and diffusion tensor imaging with tractotomy

## Neurology Market Share FY13



## Neurosurgery Market Share FY13

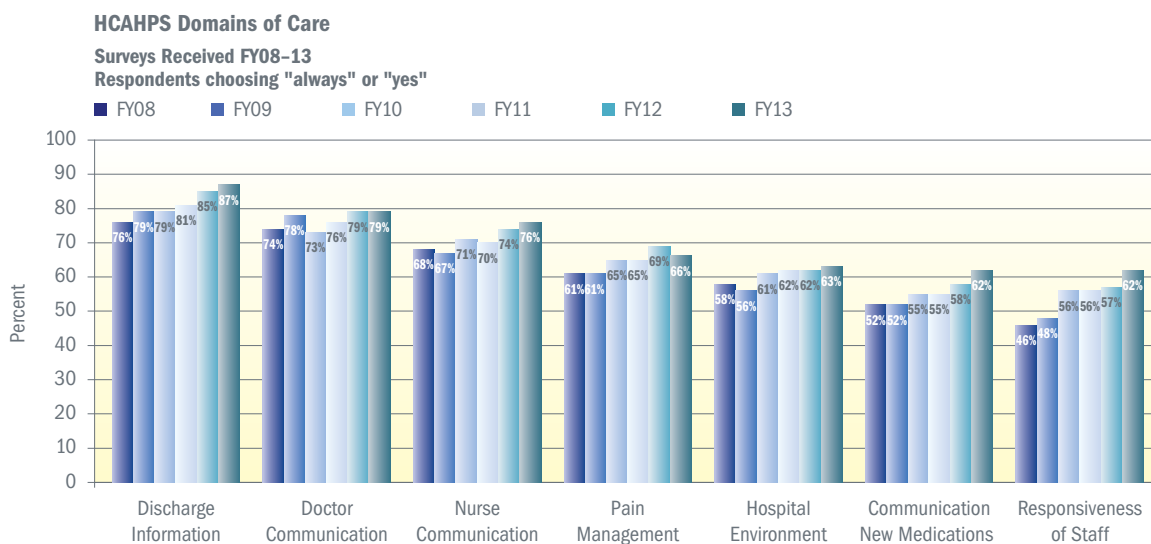
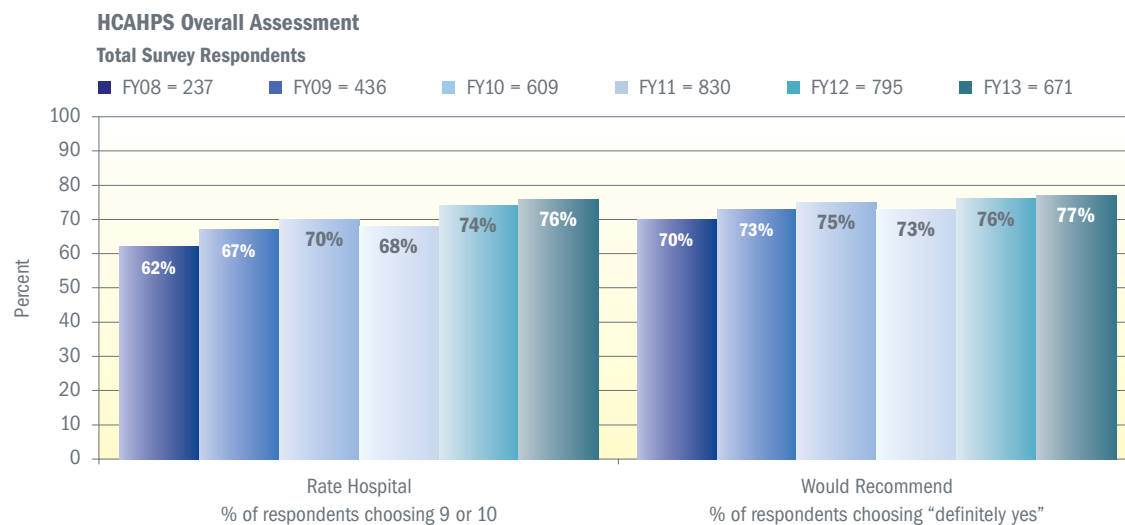


Source: Texas Hospital Association Patient Data System (FY2011Q1 – FY2013Q4) provided by Truven, formerly Thomson Reuters. Texas Hospital Inpatient Discharge Public Use Data File, [FY2007 Q1 – FY2013 Q1] provided by Texas Department of State Health Services, Center for Health Statistics; Q2FY2013 – Q4FY2013 discharges estimated by using historical data by hospital. Excludes Normal Newborns and SNF. Expanded Greater Houston consists of 12 counties: Austin, Brazoria, Chambers, Fort Bend, Galveston, Harris, Liberty, Montgomery, San Jacinto, Waller, Walker and Wharton.



# The Patient Experience

Patients from around the world come to the Mischer Neuroscience Institute for treatment based on our high-quality outcomes and reputation for providing the best possible healthcare experiences. The close cooperation of MNI team members, along with a redesigned administrative structure that allows nurses to spend more time coordinating patient care, has led to an upward trend in patient satisfaction over the last six years. Data gathered by the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey shows consistent improvement in domains considered critical to ensuring a high level of patient satisfaction.



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.







# 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 stroke program in Texas to meet The Joint Commission's rigorous standards for the highly coveted Comprehensive Stroke Center certification.
- Launching the first Mobile Stroke Unit in the United States to deliver clot-busting treatment onsite within the first hour of symptom onset.
- The first and only hospital in the south-central United States offering intra-arterial chemotherapy for retinoblastoma, the most modern treatment for the disease.
- Site of the first single-center clinical trial for recurrent medulloblastoma, ependymoma and atypical teratoid-rhabdoid tumors using the direct infusion of chemotherapy into the fourth ventricle.
- The first in Texas to use robotic stereoencephalography (SEEG) for 3-D mapping of epileptic seizures.
- The first in Houston to offer amyloid imaging, a new diagnostic tool that enables physicians to diagnose Alzheimer's disease and will give researchers insights into how they might one day prevent the disorder.
- The first center to conduct a national, multicenter trial for hypothermia in head injury.
- The first neurosurgery center to offer all advanced modalities of treatment – expert microsurgery, interventional neuroradiology/endovascular surgery and Gamma Knife® radiosurgery – for complex lesions.
- The North American leader in studies of primary progressive multiple sclerosis and the most active center in Texas in the conduct of organized clinical trials of new therapies for MS.
- The first facility in Houston and one of the first in the United States to test the clot-dissolving drug tPA for acute stroke.
- The first center in Houston to test and prove the efficacy of three disparate treatments for stroke prevention: carotid surgery; administration of antiplatelet drugs, including aspirin; and patent foramen ovale closure.
- The first facility in the region to do vagus nerve stimulation. MNI remains the No. 1 program in the United States in the number of vagal nerve stimulators implanted in epilepsy patients.
- MNI brought the first clinical magnetoencephalography (MEG) sensor to Houston and have updated the technology to the Magnes 3600 WH.
- The Institute houses 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 one of only 16 Traumatic Brain Injury (TBI) Model Systems funded by the National Institute on Disability and Rehabilitation Research. TBI Model Systems are national leaders in TBI-related care and research.
- TIRR Memorial Hermann is the only hospital in Houston – and one of only seven designated centers in the nation – in the Christopher and Dana Reeve Foundation NeuroRecovery Network.

# Group Practice Without Walls: Mischer Neuroscience Institute Expands Its Citywide Neuroscience Network

Before the 2012 arrival of neurologist Philip Blum, M.D., on the Memorial City Medical Center Campus, patients could expect a minimum three-month wait to see a neurologist after referral from a primary care physician. Today, thanks to Dr. Blum's fulltime practice, the addition of other specialists affiliated with Mischer Neuroscience Associates (MNA) and a new structure for the practice of neurology, the average wait time for patients in the highly populated Memorial City community is a matter of days rather than months.

"We faced a number of challenges related to the practice of neurology on our campus," says Keith Alexander, CEO. "We had an ample number of affiliated private-practice neurologists, but their practices were and continue to be

very busy. Because of the high caseload they carry, fewer and fewer were willing to provide the 24/7 emergency department call coverage we need to maintain our Joint Commission designation as a Primary Stroke Center. They also had less time to round on hospitalized patients."

The solution at Memorial City and other hospitals in the Memorial Hermann Health System is a more highly specialized neurology network that includes private-practice physicians, physician practices and community-based physicians who have signed lease agreements with Memorial Hermann, and neuro-hospitalists or intensivists who provide emergency coverage and care for inpatients. Under the new structure, neurologists are no longer caught between the demands of the office and hospital.

"The traditional model of the neurologist running back and forth between hospital and clinic, seeing patients in both settings, is no longer viable," says Dr. Blum, a general neurologist who sees outpatients at Memorial City under an agreement with Mischer Neuroscience Associates. "With healthcare reform and changes in Medicare reimbursement, there's just not enough time to run a busy neurology practice and see seriously ill inpatients. So we've split neurology into outpatient care and inpatient care using a hospitalist neurology model. My focus is on the outpatient side, relieving the overburdened private-practice neurologists and ensuring that patients gain access to the healthcare system quickly. Even the most common neurological diseases aren't good, and having







to wait months to see a specialist adds to the patient's emotional anxiety and stress.”

Working on the inpatient side at Memorial Hermann Southwest Hospital is neurointensivist John Ownby, M.D., who is triple boarded in internal medicine, neurology and critical care medicine. Dr. Ownby, who has expertise in ethics, end-of-life issues and palliative care, offers inpatients prompt access to a neurologist and also provides emergency coverage.

“Many discharged neuroscience patients are seriously ill and fragile, and unless they're seen quickly on the outpatient side, they'll bounce back into the hospital,” Dr. Ownby says. “Those transitions must be managed efficiently and rapidly. Squeezing patients who need a rapid transition of care into a busy neurologist's schedule creates chaos, and everyone suffers. The presence of our outpatient neurologists has relieved some of that pressure.”

MNA Neurology complements the citywide neurosurgery expansion begun in 2008 by Dong Kim, M.D., director of the Mischer Neuroscience Institute (MNI) and professor and chair of the Vivian L. Smith Department of Neurosurgery. “The neurology program at Memorial Hermann-Texas Medical Center has always been strong,” says Amanda Spielman, chief operating officer for neurosciences. “After Dr. Kim arrived, established MNI and strengthened the neurosurgical side, we began to build neurosurgery capabilities across the Memorial Hermann Health System, choosing outlying facilities based on demand and potential for growth. Once the neurosurgery capabilities were in place, we needed general neurologists to manage the care of their patients. We also knew that as an accountable care organization under healthcare reform we had to build our infrastructure to include the entire continuum of neuroscience in order to provide care for large employee populations.”

At the same time, Spielman and Dr. Kim began to hear from neurologists who refer to Memorial Hermann for neurosurgery that they felt pressured by changing reimbursement patterns. Some wondered if they could survive in private practice. “Many neurologists with long-term established practices wanted to maintain their own identity, so we worked with legal and financial experts at Memorial Hermann to create a model – other than outright acquisition – to integrate neurologists across the city,” Spielman says. “Our model has proved to be mutually beneficial: leased neurology practices benefit from Memorial Hermann's market leverage, and Mischer Neurosciences can offer employers, managed care providers and patients a larger network of affiliated physicians.”

Spielman met with CEOs across the Memorial Hermann system to identify high-quality physicians with whom they wanted to align. “This has been a year of identifying potential partners and investigating opportunities,” she says. “The goal is to have at least one anchor practice near each of Memorial Hermann's acute care hospitals to support the outpatient needs of neurology patients. We're growing but we're doing it cautiously, making sure that we have the right network of providers as the healthcare market changes. The practices we're adding are of the highest quality.”

Among them is Houston Neurological Institute (HNI), led by Kim Monday, M.D., who is board certified in adult neurology, clinical neurophysiology (EMG/EEG and intraoperative monitoring) and sleep medicine. Dr. Monday has been repeatedly named a Texas Monthly Super Doctor and a Top Doctor by both H Magazine and The Consumer's Guide to Top Doctors. HNI, the first private group to join Mischer Neuroscience Associates, provides outpatient care to Houston and surrounding areas, including Pearland, Pasadena, Deer Park, Clear Lake and Dickinson.





“We’d been interested in the idea of a virtual group practice for some time,” Dr. Monday says. “Dr. Kim’s vision of a group of community neurologists and neurosurgeons located across the Houston area was in keeping with my own vision, and we are delighted to be working together to improve care for patients in the area.”

In the last year Memorial Hermann and UTHealth have also recruited 15 physicians to join MNA, MNI and UTHealth Medical School. “Our aim is to extend the exceptional care we provide in the Texas Medical Center to patients across Houston through Mischer Neurosciences, a citywide neuroscience network,” Dr. Kim says. “The presence of these new team members moves us closer to our goal of recruiting the highest-quality group of providers to deliver the full continuum of neuroscience care throughout the Greater Houston area. These new additions to the growing MNA Neurology team allow us to provide the full range of neurology services in the community, from stroke care to electromyography to deep brain stimulation.”

Dr. Blum believes the high-quality pipeline between neurology and neurosurgery brings great benefit to the city. “Dr. Kim has built a large group of first-class neurosurgeons,” he says. “That original MNA group and the patients they serve deserve a first-class group of neurologists to collaborate with them hand in glove. That is a tricky thing to accomplish. Hats off to Dr. Kim, who as a neurosurgeon had the skill to build this network by crossing the line from a surgical to a medical specialty. Neurology runs on a completely different model. Building a citywide network that includes both neurology and neurosurgery requires a lot of work from our side to help neurosurgeons better understand our specialty.”

Dr. Monday appreciates having the freedom to focus on improving patient care. “Dr. Kim is a good partner for us,” she says. “It’s been a joy to work with Dr. Kim and Amanda. We’ve been continually impressed by the support they’ve given us. When there are hiccups, as there are bound to be in building anything new, they haven’t abandoned ship. This is the model of the future.”

# Stroke Program Receives Joint Commission Advanced Certification as a Comprehensive Stroke Center

In 2013, The Joint Commission (TJC) and the American Heart Association/American Stroke Association awarded Mischer Neuroscience Institute (MNI) at Memorial Hermann-Texas Medical Center the highly coveted Comprehensive Stroke Center (CSC) certification. MNI is the first and only stroke program in Texas to meet TJC's rigorous standards, solidifying its position among an elite group of providers focused on complex stroke care.

Comprehensive Stroke Center certification recognizes hospitals with the infrastructure, staff and training to receive and treat patients with highly complex strokes. Between September 2012, when TJC released its new qualifications for CSC certification, and MNI's rigorous onsite review in March 2013, the stroke team geared up to meet the new standards.

"We had a great program as a Joint Commission-certified Primary Stroke Center, but we had some work to do to build a Comprehensive Stroke Center, which is many steps higher," says Nicole Harrison, RN, administrative director of neuroscience at MNI. "Close collaboration among neurologists and neurosurgeons was critical to

achieving the advanced certification, which goes beyond the Primary Stroke Center focus on ischemic stroke to encompass the surgical treatment of hemorrhagic stroke.

We had great roads in place, and during our six-month preparation for the review we built the overpasses."

"We met very particular and exacting requirements and in the process created new pathways to work as a team in providing care for all of our patients, including those admitted to other service lines. It speaks to the excellence of our stroke team and the outstanding treatment we provide."

A stroke leadership committee comprised of physicians and other caregivers from key departments at Memorial Hermann-Texas Medical Center was formed to guide the processes necessary to achieve the certification. The group held weekly meetings for six months to ensure that all standards of practice and protocols were integrated across every discipline.

"Collecting the data we needed for CSC certification allowed us to see evidence-based opportunities to make our stroke care even better," Harrison says. "We made significant improvements in the peer-review process, and we also implemented a cognitive screening and depression screening process for every patient prior to discharge and post discharge."

To ensure that the Stroke Program had the necessary support to achieve Comprehensive Stroke Center



certification, new team members were added, including additional stroke coordinators, data extractors and advanced nurse practitioners. Harrison credits Memorial Hermann-TMC administration and Sean I. Savitz, M.D., medical director of the Comprehensive Stroke Center, with ensuring MNI's success throughout the certification process.

"Our administrative leadership team was crucial in securing the resources we needed to make this certification happen," she says. "Without that support, MNI couldn't have achieved this milestone."

"It is a difficult certification to achieve, and the accomplishment is truly a multidisciplinary effort," says James Grotta, M.D., co-director of MNI and professor

and chair of the department of Neurology at UTHealth Medical School. "Only 59 centers across the country have achieved this goal, and no others in Texas.

We met very particular and exacting requirements and in the process created new pathways to work as a team in providing care for all of our patients, including those admitted to other service lines. It speaks to the excellence of our stroke team and the outstanding treatment we provide."

Harrison cites education as an integral piece of the certification. "We're already seeing benefits for patients," she says. "We have the infrastructure in place to sustain the two-year certification into the future and to continue to improve."



# Telemedicine Extends Stroke Expertise to Southeast Texas

Before Baptist Beaumont Hospital joined the Mischer Neuroscience Institute's (MNI) Telemedicine Program in 2002, there were no acute care hospitals equipped to treat ischemic stroke between Houston, Texas, and Lake Charles, Louisiana. The two cities lie 132 miles apart in the southwest tip of the Stroke Belt, an area of the southeastern United States with an unusually high

"The average age of our stroke patients is 62, which is very young," says Donna Biscamp, RN, CEN, an emergency department nurse who serves as the hospital's ED stroke champion. "Because of our telemedicine program and the physicians affiliated with the Mischer Neuroscience Institute, we've been able to deliver tPA at high rates. As a result, many of our former patients who would otherwise be in nursing homes are walking, talking and living active lives."

Biscamp, who began collecting data in 2007, is enthusiastic about the stroke program's growth. "In 2007, 202 patients presented with stroke, and we were able to administer tPA to 12 patients, or 6 percent," she says. "By 2012, our program had more than doubled in size. We saw 484 stroke patients, 55 of whom received tPA. Those numbers translate to lives and quality of life saved."

Among those who have benefited is 66-year-old Orange, Texas, resident Johnny Wilson, who, while helping dress his grandchildren in March 2012, became dizzy and began vomiting. His wife Trudy Wilson caught him as he fell and eased him to the ground.

"When I saw Johnny's mouth drawing to the right and his right arm going limp, I knew he was having a stroke," she recalls. "I'd heard good things about Baptist Beaumont Hospital – a friend's mother was treated for stroke there. An ambulance happened to be parked at the nursing home across the street from us, and I asked them to take



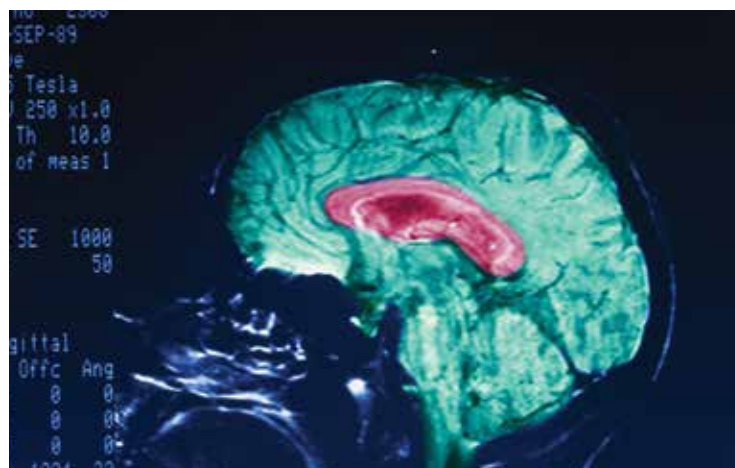
incidence of stroke and other forms of cardiovascular disease. With only a handful of neurologists available to provide on-call coverage for a 75- to 100-mile service area, the hospital was ill equipped to provide care for the area's older population. But thanks to telemedicine and its partnership with MNI, Baptist Beaumont Hospital has been accredited as a Primary Stroke Center since 2007 and has morphed into a powerhouse for the delivery of tPA.

Johnny to Baptist Beaumont. I followed in my car, and by the time I got to the emergency center, they'd done a CT scan and had Johnny in a room with computers and a lady on the screen. She was examining him remotely. It was amazing.”

The physician on the screen was Nicole R. Gonzales, M.D., an assistant professor of neurology at UTHealth Medical School, who was on call for telemedicine at MNI. From her laptop control screen, Dr. Gonzales logged on to Memorial Hermann-Texas Medical Center's RP-7™ Remote Presence Robotic System, a teleconferencing technology that links the MNI Stroke Center to 13 outlying hospitals. The system includes a robot that can be remotely maneuvered by the stroke team member on call. Equipped with two-way video capability, it allows physicians to consult with specialists, see patients and view monitors and other clinical data sources firsthand from remote locations.

When Dr. Gonzales activated her computer, the emergency staff in Beaumont directed their remote presence robot toward Wilson, allowing physician and patient to view each other on the screen and talk. Dr. Gonzales could see Wilson's facial droop, and he demonstrated right-side weakness. Based on his CT results, the physical exam conducted by emergency physician Loc Nguyen, M.D., and her observations via computer, Dr. Gonzales determined that he would be a good candidate for tPA. When the tPA had no effect, Wilson was transported by Memorial Hermann Life Flight® to MNI, where a CT angiogram of the brain showed a basilar artery occlusion.

At MNI, Wilson was treated by neurointerventionalist Roc Chen, M.D., an assistant professor in the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School, who used an endovascular technique



to open the artery. “We navigated a special catheter and device through the femoral artery in the groin to the aorta to the vertebral artery in the neck, which is the main trunk for the basilar artery,” Dr. Chen says. “We were able to remove the clot in time and completely open the artery and its occluded branches. Ultimately, he did quite well.”

Wilson was transferred to TIRR Memorial Hermann for inpatient rehabilitation at the end of March and discharged in late April. He continued his therapy at TIRR Memorial Hermann Outpatient Rehabilitation at Kirby Glen in southwest Houston.

“Telemedicine saved Johnny's life,” Trudy Wilson says. “Everyone calls him the Miracle Man because of the size and nature of his stroke. The doctors and nurses who treated him knew exactly what was happening to him and what needed to be done. I think telemedicine is the best technology ever designed.”

Baptist Beaumont Hospital and Memorial Hermann Southwest Hospital were early adopters of telemedicine. Eleven other hospitals in Southeast Texas are now live with the technology: Memorial City Medical Center, Memorial Hermann Northwest Hospital, Huntsville



Memorial Hospital, Bellville General Hospital, Matagorda Regional Medical Center, Baptist Orange Hospital, the Medical Center of Southeast Texas in Port Arthur, Citizens Medical Center in Victoria, St. Joseph Hospital-Downtown in Houston, DeTar Healthcare System in Victoria and Tomball Regional Medical Center in Tomball.

At Citizens Medical Center in Victoria, stroke center coordinator Katrin McDonough, RN, ACLS, TNCC, EMT-B, reports, “With only sporadic neurology coverage, we were hardly administering any tPA before joining the telemedicine network in December 2012.” In less than a year, the hospital has become one of the network’s busiest sites for stroke treatment after Baptist Beaumont Hospital.

“Emergency physicians are delighted to have neurology coverage through telemedicine,” McDonough says. “As a result, our tPA administration rate is now 17 percent. The relationship with MNI is a good resource for us all the

way around. They’re available when we have questions about a particular patient and are a great resource for physicians in general.”

McDonough and her team also work with the Victoria Fire Department to improve their stroke recognition and care and are working to raise community awareness about stroke. “We need to raise awareness of the signs and symptoms of stroke and the importance of seeking immediate medical care when stroke is suspected,” she says.

The MNI Telemedicine Program began at UTHealth Medical School more than a decade ago with a grant from the United States Department of Defense, and has morphed into its present form thanks to a gift from the Alexander Foundation. “Our ultimate goal is to build a collaborative network of hospitals working together to deliver comprehensive neurological and neurosurgical



care in the Southeast Texas region,” says Tzu-Ching (Teddy) Wu, M.D., medical director of the program. “As the Texas Medical Center hub, MNI provides 24/7 stroke consultations, as well as consults for other conditions, for our network hospitals. The program allows us to treat as many patients as possible at our partner hospitals, avoiding unnecessary patient transfers.” MNI’s stroke team provided more than 1,000 telemedicine consults in the last year.

In addition to access to physicians who are experts at neuroscience care for telemedicine consultation, benefits to hospitals in the telemedicine network include higher-quality care and decreased treatment delays as patients receive prompt diagnosis with a treatment plan based on the best available protocols. “More patients and families receive treatment where they live, in their community, rather than having to drive long distances to Houston,” Dr. Wu says. “Patients who require a higher level of care have a guaranteed transfer process that gives them access to the most advanced treatments and the best tertiary-care neuroscience partner in the region.”

Dr. Wu sees excitement among emergency department physicians and nurses as they collaborate with MNI on treatment protocols and plans, continue their education about stroke and expand their knowledge of evidence-based neurological care. “We work closely with the emergency department director and stroke coordinator at each hospital in the network to ensure that we’re delivering the highest quality acute neurological care,” he says. “Having specialists and subspecialists to

rely on helps build confidence in their practice environment. We also work with the local EMS providers to help extend access throughout the community.”

Dr. Wu believes telemedicine is part of an emerging trend in health care to bring doctors to their patients. “Telemedicine has taught us that you don’t need a major medical center to provide good stroke care,” he says.

“Telemedicine has taught us that you don’t need a major medical center to provide good stroke care. What you do need is community awareness, knowledgeable emergency physicians, an expert neurologist and a strong telemedicine program.”

“What you do need is community awareness, knowledgeable emergency physicians, an expert neurologist and a strong telemedicine program. MNI can now offer patients in outlying communities the opportunity to participate in clinical trials that would otherwise be unavailable to them, which helps the entire medical community by expanding knowledge.”

The stroke team at Baptist Beaumont Hospital recently used telemedicine to enroll a stroke patient in the CLOTBUST Hands-free Trial under way at the Mischer Neuroscience Institute. The trial is pioneering the use of a hands-free, operator-independent device to deliver external ultrasound to enhance the effects of tPA – a device that potentially could be used in any community hospital. A study led by Andrew Barreto, M.D., assistant professor of neurology at UTHealth Medical School, recently showed the safety of using the device in patients treated with tPA, and the MNI stroke team is now participating in a large international trial to test the efficacy of the combined approach in patients with acute stroke.

“In the future, we hope to move beyond stroke to offer multiple services from MNI’s telemedicine center,” Dr. Wu says. “We think the possibilities are limitless.”

# Advancing the Field of Neuroscience

Investigators at Mischer Neuroscience Institute (MNI), working together with UTHealth Medical School, are shaping the future of medicine through clinical discovery and the development of breakthrough treatments.



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

Traumatic brain injury (TBI) resulting in subdural hematoma occurs in more than 40,000 Americans annually, and up to 70 percent of these injuries result in death or severe disability. Standard treatment includes the surgical removal of the hematoma, but after evacuation, an ischemia-reperfusion injury occurs at the time of brain tissue reperfusion.

“Therapies to improve outcomes are desperately needed,” says principal investigator Dong Kim, M.D., director of MNI and professor and chair of the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School. “In the HOPES trial we aim to test whether rapid induction of early hypothermia before emergent craniotomy for traumatic subdural hematoma will produce better outcomes.”

Patients randomized to the trial are cooled to 35°C prior to opening the dura, followed by maintenance at 33°C for a minimum of 48 hours. Intravascular cooling catheters are used to induce hypothermia or to maintain normothermia. Outcomes of 20 participants will be

measured by the Glasgow Outcome Scale-Extended at six months.

Support for the HOPES study, which began enrolling subjects in the fall of 2013, is provided by the Vivian L. Smith Foundation for Neurologic Research and Zoll Medical.

### Methotrexate Infusion into the Fourth Ventricle in Children with Malignant Fourth Ventricular Brain Tumors: A Pilot Study

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

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



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

### CLOTBUST-Hands Free

The results of a Phase I/II study of a novel treatment for stroke – a device called CLOTBUST-Hands Free – were published Oct. 24, 2013, in *Stroke*. Led by neurologists James C. Grotta, M.D., and Andrew Barreto, M.D., the study was a first-of-its-kind, National Institutes of Health-sponsored pilot safety trial of tPA plus an operator-independent ultrasound device in patients with ischemic stroke due to proximal intracranial occlusion. James C. Grotta, M.D., co-director of MNI and professor and chair of the department of Neurology at UTHealth Medical School, was 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.



## RESEARCH UPDATE

Twenty participants at two American study sites – UTHealth Medical School and the University of Alabama at Birmingham – tolerated the two-hour treatment with the helmet-like device and none developed symptomatic intracerebral hemorrhage. “Sonothrombolysis using CLOTBUST-Hands Free in combination with tPA appears to be safe,” says Dr. Barreto, co-investigator of the study and an assistant professor of neurology at UTHealth Medical School. “Recanalization rates warrant more widespread use of operator-independent, ultrasound-enhanced thrombolysis and evaluation in a Phase III efficacy trial.”

The results of the original multicenter, randomized CLOTBUST trial, coordinated by UTHealth Medical School and published in the *New England Journal of Medicine* in 2004<sup>1</sup>, 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,” Dr. Barreto says. “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

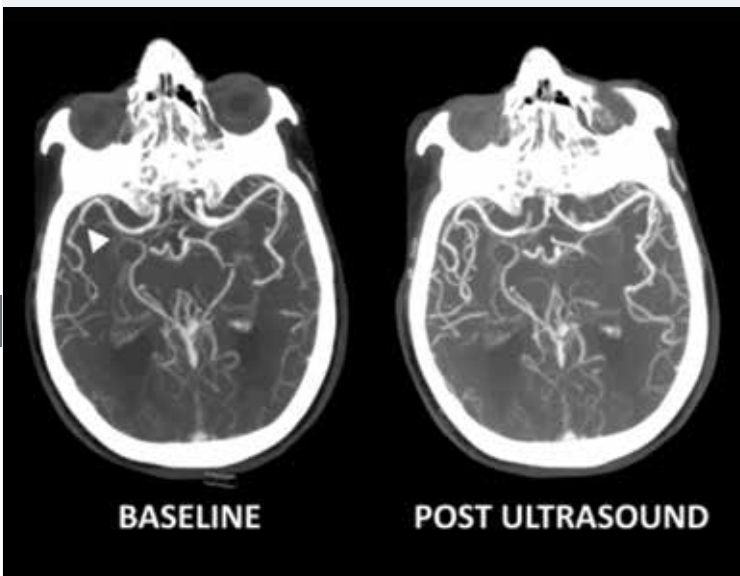
more efficient to develop a head frame for hands-free application of ultrasound than to train neurologists how to use the handheld device.” Study co-investigator Andrei Alexandrov, M.D., a former member of the MNI stroke team and current director of the Comprehensive Stroke Research Center at the University of Alabama at Birmingham, developed the helmet-like, hands-free device under study.

An international Phase III clinical trial of the CLOTBUST-Hands Free device began in the summer of 2013. The randomized, double-blind, placebo-controlled trial will recruit 830 patients in approximately 60 sites around the world. The UTHealth Medical School site was the first in the world to enroll a patient.

“We hope this will be the definitive trial to determine if the delivery of ultrasound in combination with tPA results in better outcomes than the use of tPA alone,” says Dr. Barreto, who is the North American principal investigator for the trial. “We will be assessing whether the treatment leads to less disability and more independence for stroke victims.”

The Phase III trial, called Combined Lysis of Thrombus with Ultrasound and Systemic tPA for Emergent Revascularization in Acute Ischemic Stroke (CLOTBUST-ER), will enroll patients at Memorial Hermann-Texas Medical Center and Memorial Hermann Southwest Hospital in Houston and Baptist Beaumont Hospital in Beaumont, Texas.

<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.



## Intra-arterial Delivery of Chemotherapy for Retinoblastoma

Children’s Memorial Hermann Hospital is the only hospital in the south-central United States offering intra-arterial chemotherapy for the treatment of retinoblastoma, a rare pediatric eye malignancy that affects only 250 to 350 new patients each year. The treatment requires a large multispecialty team that involves close collaboration between endovascular neurosurgery, ocular oncology and medical neuro-oncology.

“Having the capability to inject chemotherapy directly into the arteries that feed the eye eliminates the side effects of systemic chemotherapy and maximizes the therapeutic dose to the eye,” says endovascular neurosurgeon Mark Dannenbaum, M.D., an expert on cerebrovascular surgery and neurointerventional techniques and an assistant professor of neurosurgery at UTHealth Medical School. “The technique is very new and a paradigm shift in the treatment of retinoblastoma. Before its development, removal of the eye was the standard-of-care treatment for retinoblastoma that had not metastasized.”

To initiate the procedure, Dr. Dannenbaum places a microcatheter into the ophthalmic artery using a neuroendovascular technique. He collaborates with Amy Scheffler, M.D., an ocular oncologist and retina specialist affiliated with Children’s Memorial Hermann Hospital, who infuses a high concentration of chemotherapy directly into the tumor bed.

“This is exciting and groundbreaking clinical work,” Dr. Dannenbaum says. “We’re saving eyes and providing a cure for this treatable type of cancer.”



Physicians at Mischer Neuroscience Institute and Children’s Memorial Hermann Hospital are also engaged in research investigating other new ways to save eyes that have failed conventional therapies.

## Deep Brain Stimulation Therapy for Treatment-Refractory Depression

A pilot clinical study under way at Mischer Neuroscience Institute and UTHealth Medical School aims to assess the safety and efficacy of medial forebrain bundle deep brain stimulation (DBS) as a treatment for major depressive disorder (MDD).

“Depression affects up to 10 percent of the U.S. population and of those at least 10 to 15 percent do not benefit from existing therapies, giving us a rationale for exploring potentially effective new treatments,” says Albert J. Fenoy, M.D., an assistant professor in the Vivian L. Smith Department of Neurosurgery who is principal investigator of the study. “The median forebrain bundle seems to be intricately involved in the reward pathway, and data from the University of Bonn suggest that

## RESEARCH UPDATE

DBS at this site may reduce symptoms in patients with treatment refractory depression.”

A collaboration between the department of Neurosurgery and the department of Psychiatry and Behavioral Sciences, the study is supported by UTHealth Medical School and the Dunn Foundation. Study participants will include 10 patients between the ages of 22 and 65 with treatment-refractory MDD identified using the Structured Clinical Interview for DSM-IV, who manifest a current major depressive episode of disabling severity and are refractory to prolonged treatment trials with

conventional medication, electro-convulsive therapy and psychotherapy. They must show a marked impact of depression on their health and functional status as evidenced by major impairment in functioning, repeated hospitalizations or serious suicidal or other self-injurious behavior. Standardized neuropsychological tests will be used before and after DBS to assess learning and memory, executive function, psychomotor function, visuospatial processing and language.

“Our DBS program at Mischer Neuroscience Institute is robust – we typically do one case a week as a treatment for Parkinson’s disease, essential tremors and dystonia,” Dr. Fenoy says. “Our patients respond beautifully. Over the years we have refined our techniques in implantation, targeting and programming. These patients experience dramatic improvements in their quality of life. We hope to be able to offer the same outcomes to patients with treatment-refractory depression.”

### Conversion of Skin Fibroblasts into Neural Stem Cells

In the laboratory, investigator Qilin Cao, M.D., and his team have developed a novel approach to stem cell therapy for the treatment of spinal cord injury (SCI) and stroke: converting human skin fibroblasts into neural stem cells.

“Transplantation of neural stem cells has great therapeutic potential for the treatment of neurological diseases, including spinal cord injury,” says Dr. Cao, an associate professor in the Vivian L. Smith Department of Neurosurgery and an international leader in the use of stem cells to treat SCI. “However, the current sources of neural stem cells are associated with ethical controversies and the risk of tumor formation and





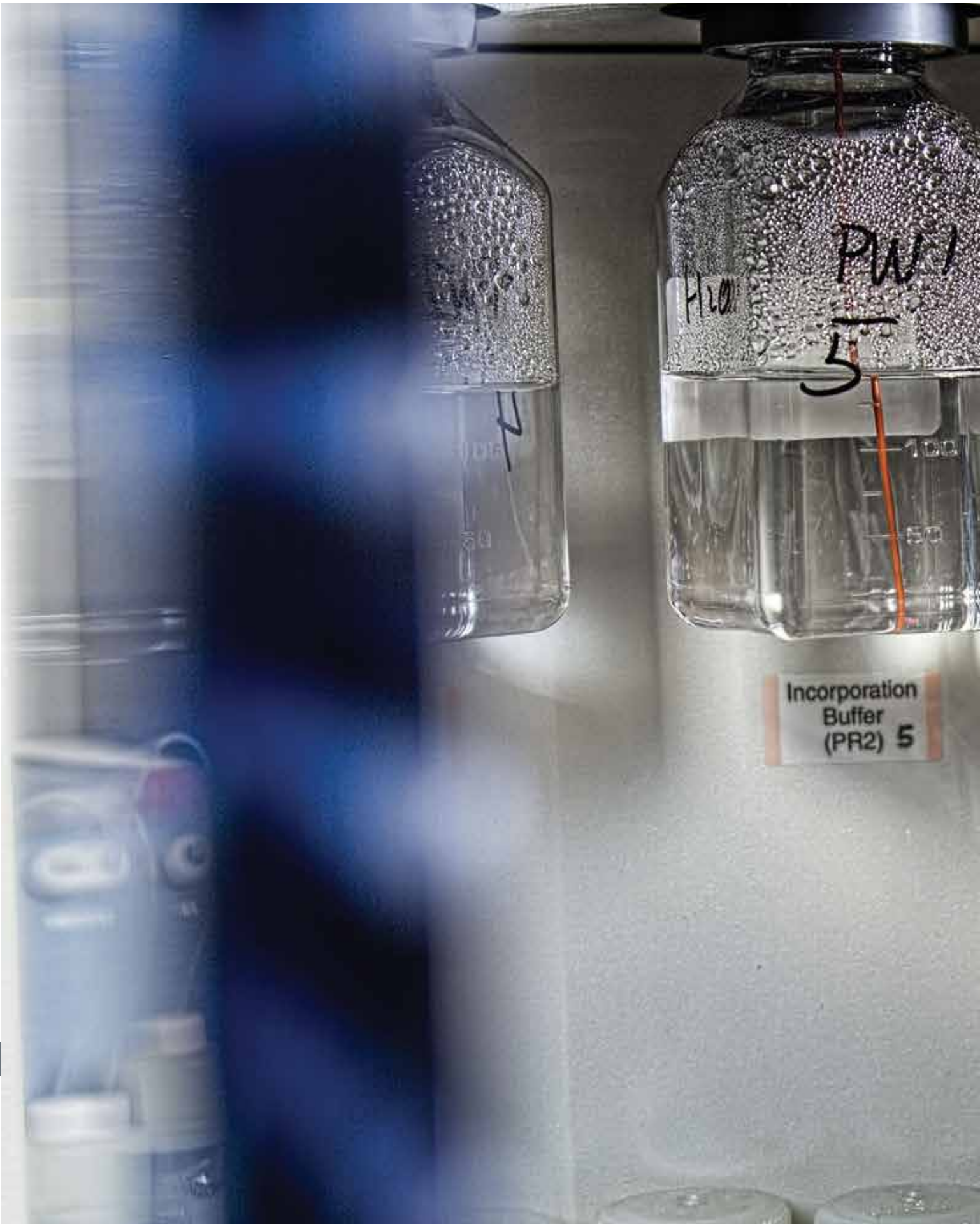


immune system rejection. Because these directly induced neural stem cells are derived from patients' own skin fibroblasts, we can circumvent these issues."

The direct conversion of patients' fibroblasts into neural stem cells is done without passing through the pluripotent stem cell stages, which have the potential to become tumors after transplantation. "We believe the cells can be transplanted back to the patients from whom they came as isografts, without immunosuppression or the risk of tumor formation,"

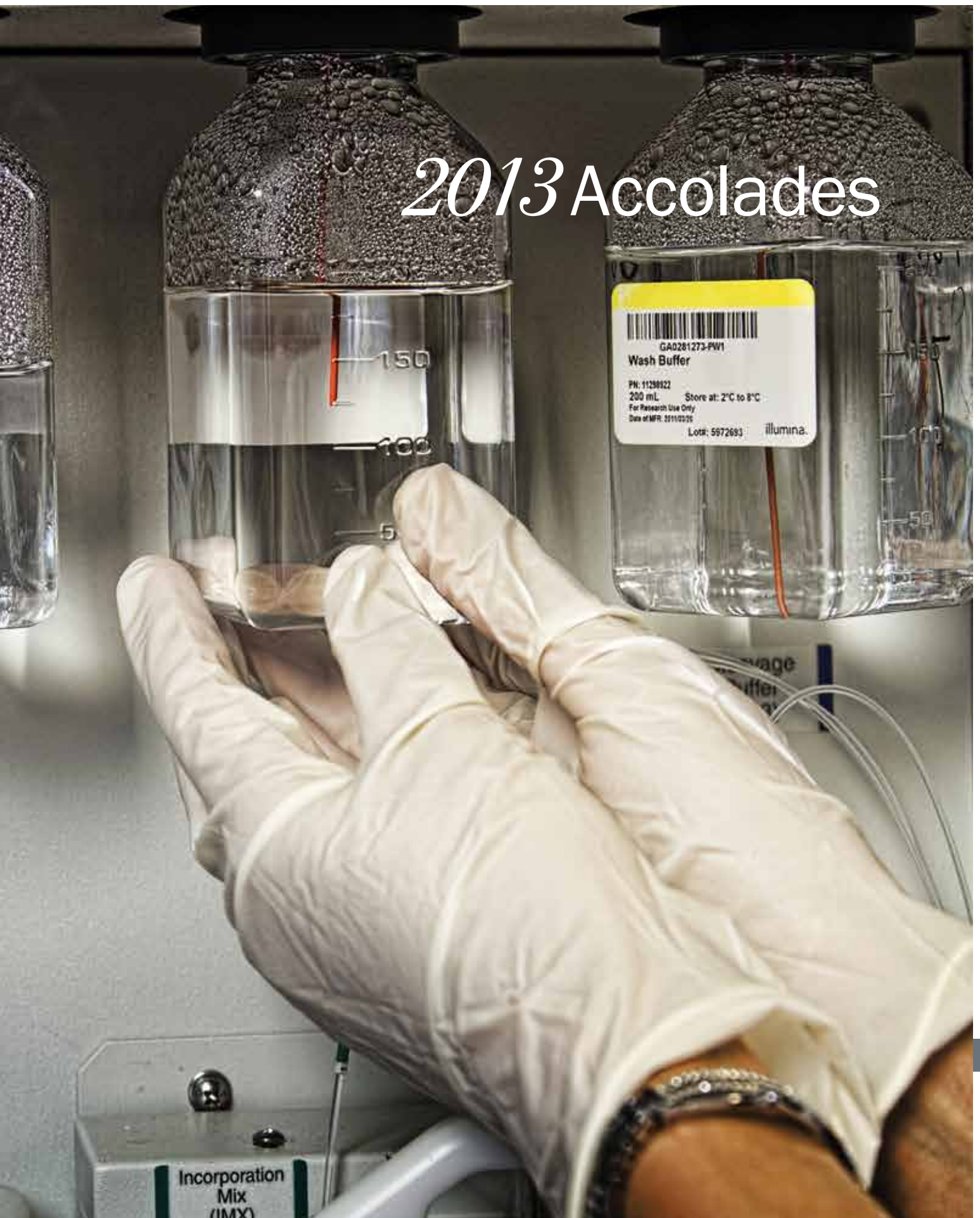
he says. "They have the capability to differentiate into functional neurons and glial cells to promote function recovery by replacing the lost neural cells after spinal cord injury, stroke or other neurological diseases."

The researchers are currently testing the long-term safety and therapeutic efficacy of these induced neural cells in the hope of beginning clinical trials in the near future.

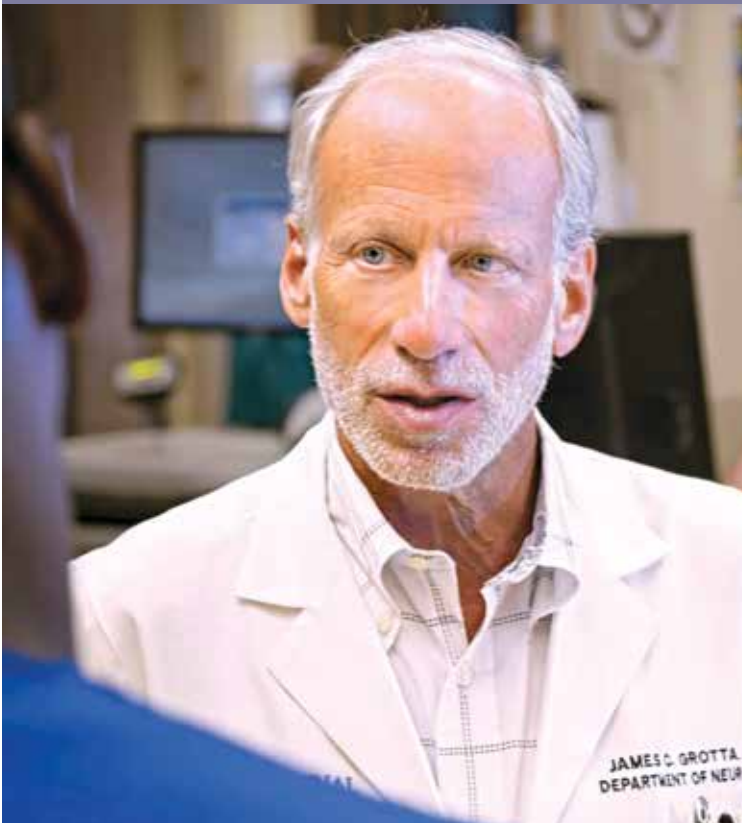




# 2013 Accolades







### James Grotta, M.D., Led Research in Houston for Top 9 NEJM Paper

The 1995 paper announcing results of the first major trial showing the benefits of the then-new clot-busting drug tPA as a treatment for stroke was voted one of the top nine papers in the 200-year history of the *New England Journal of Medicine*. James C. Grotta, M.D., chair of the department of Neurology and the Roy M. and Phyllis Gough Huffington Distinguished Professor of Neurology at UTHealth Medical School, was principal investigator in Houston, one of six clinical sites that enrolled patients in the trial. The groundbreaking research took place at Memorial Hermann-Texas Medical Center.

The paper, “Tissue Plasminogen Activator for Acute Ischemic Stroke,” published in the Dec. 14, 1995, issue, revealed the first promising treatment for stroke and ultimately changed the way neurologists manage the disease. Administered within three hours of the onset of symptoms, tPA can reduce the effects of stroke and permanent disability.

“At the time we were doing this study, there was no existing treatment for stroke patients,” says Dr. Grotta, who is co-director of the Mischer Neuroscience Institute, a collaboration between Memorial Hermann-Texas Medical Center and UTHealth Medical School. “I think we were aware of the potential significance of our research for a number of reasons. The treatment we were testing and the timeframe for administering it were far more aggressive than anything done before. And we had a great group of gung-ho investigators and leadership. But given past disappointments, it was still a surprise when we first saw the positive results. Once we saw the results, we knew it was important and would have a big impact.” Dr. Grotta was quoted in a *New York Times* article announcing the research results, saying, “Until today, stroke was an untreatable disease.”

Barbara Tilley, Ph.D., director of the division of Biostatistics and Lorne C. Bain Distinguished Professor at The University of Texas School of Public Health, part of UTHealth, was principal investigator for the Coordinating Center for the National Institute of Neurological Disorders and Stroke tPA Stroke Study Group. At the time of the study, she was on the faculty at Henry Ford Health Sciences Center in Detroit and helped design, manage and analyze data for the trial. “It’s still the only treatment to date shown to be effective in reducing the effects of stroke for those who have stroke caused by a blood clot in the brain,” Dr. Tilley says. “The longer the time to treatment in stroke cases, the lower the effect of the treatment.”

UTHealth Medical School researchers continue to push the boundaries of stroke treatment. “The battle to reduce the effects of stroke is won or lost in the first hour after the onset of symptoms,” Dr. Grotta says. “We continue to develop new treatments that build on tPA and new systems to get these treatments to patients faster. The other revolution in stroke treatment is learning how to stimulate the brain’s intrinsic recovery process.”

That revolutionary work includes research led by Sean I. Savitz, M.D., professor of neurology, director of the Stroke Program and director of the Vascular Neurology Program at UTHealth Medical School, whose team is testing stem cell therapies to see if they can assist the brain in recovering from stroke.

In addition to voting the article among the top nine stories, readers also selected the paper as the most important study published in the journal in the 1990s.

## Ten Physicians Affiliated with MNI Named to U.S. News Top Doctors List

Three neurosurgeons, four neurologists and three pediatric neurologists affiliated with the Mischer Neuroscience Institute (MNI) have been recognized among the *U.S. News & World Report* Top Doctors for 2012. Physicians named to the list are selected based on a peer nomination process that complements the longstanding medical tradition of seeking physician recommendations from trusted colleagues.

Neurosurgeons named to the list are Dong Kim, M.D., director of MNI, chief of neurosurgery at Memorial Hermann-Texas Medical Center and professor and chair of the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School; Daniel H. Kim, M.D., FACS, FAANS, director of reconstructive spinal and peripheral nerve surgery at MNI and professor of neurosurgery at UTHealth Medical School; and David I. Sandberg, M.D., FAANS, FACS, FAAP, director of pediatric neurosurgery at MNI, associate professor in the departments of Neurosurgery and Pediatric Surgery at UTHealth Medical School, and associate professor of neurosurgery at The University of Texas M. D. Anderson Cancer Center.

MNI-affiliated neurologists recognized among the nation's best are James Ferrendelli, M.D., professor in the department of Neurology; James C. Grotta, M.D., co-director of MNI, chief of neurology and director of the Stroke Center at Memorial Hermann-TMC, Roy M. and Phyllis Gough Huffington Distinguished Chair in Neurology and professor and chair of the department of Neurology; Kazim Sheikh, M.D., professor of neurology and director of the Neuromuscular Program at UTHealth Medical School; and Jerry S. Wolinsky, M.D., Bartels Family and Opal C. Rankin Professor in the department of Neurology, director of the Multiple Sclerosis Research Group and director of the Magnetic Resonance Imaging Analysis Center at UTHealth Medical School.

Pediatric neurologists included on the list are Ian Butler, M.D., professor and director of the division of Child & Adolescent Neurology in the department of Pediatric Surgery; Pauline Filipek, M.D., professor in the department of Pediatrics and the Children's Learning Institute; and Pedro Mancias, M.D., associate professor in the division of Child & Adolescent Neurology.

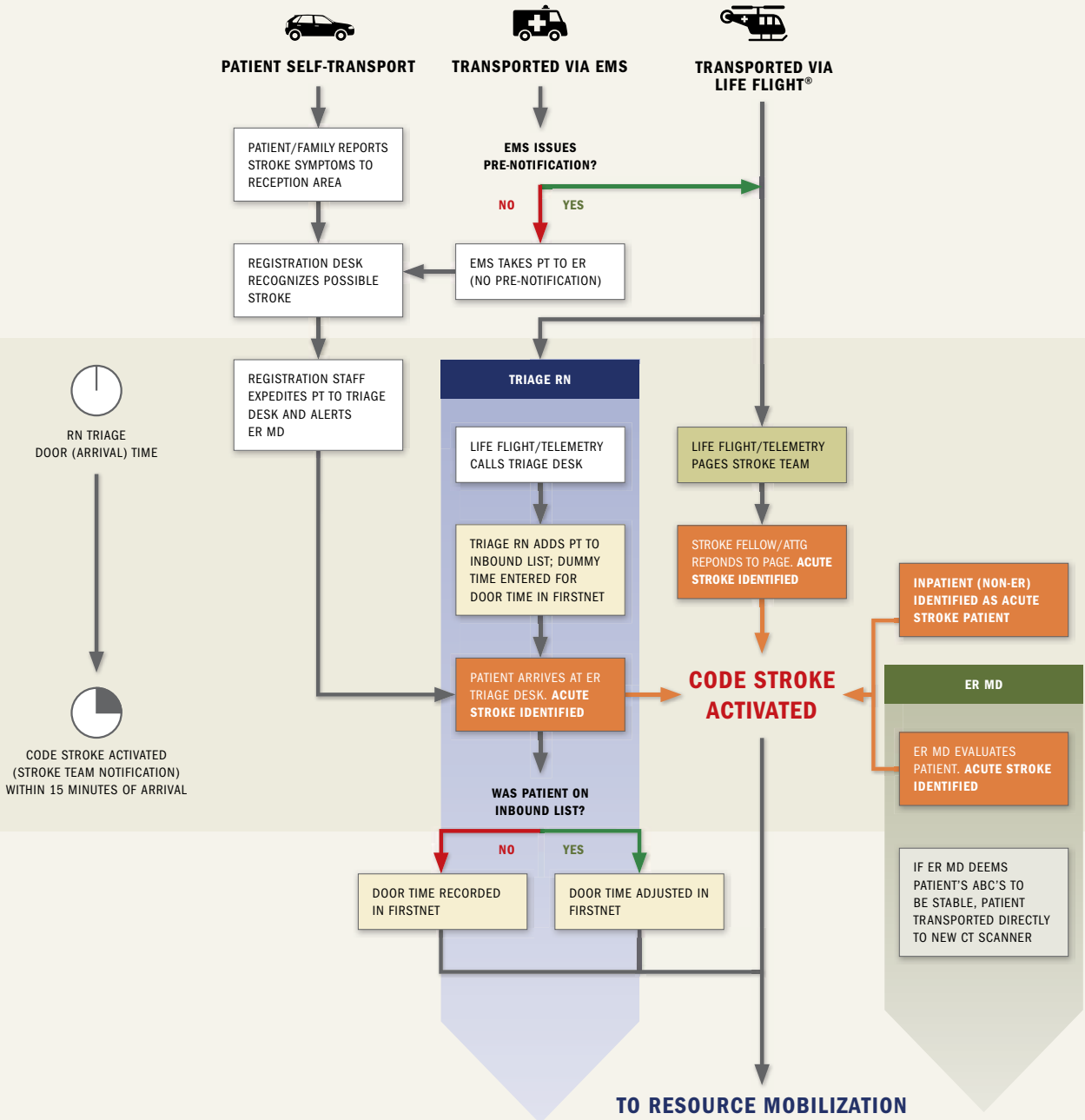
"We are honored to be recognized by our peers for the quality of care we provide to our patients and their families every day," says Dr. Kim.

*U.S. News* determines the physicians who qualify as Top Doctors by teaming up with Castle Connolly, a New York City-based company that has worked for nearly two decades to identify the nation's top doctors. Castle Connolly bases its selections on nominations submitted by other doctors and reviewed by its physician-led research team.

## MNI STROKE CENTER: DOOR-TO-NEEDLE FLOWCHART

### Acute Cerebrovascular Symptoms with Onset < 12 Hours of:

- Altered mental status w/o trauma
- Hearing loss
- Unilateral weakness
- Headache
- Facial weakness
- Dizziness
- Vision loss/changes
- Aphasia or dysarthria
- Ataxia





## Stroke Team Reduces Door-to-Needle Time

With the implementation of new processes, the Mischer Neuroscience Institute Stroke Team has reduced the median door-to-needle (DTN) time for delivery of intravenous tissue plasminogen activator (tPA) by 15 minutes at Memorial Herman-Texas Medical Center. Data from the quality improvement project were presented by members of the team at the 8th World Stroke Congress, held in 2012 in Brasilia, Brazil.

“We all know that the benefit of intravenous tPA in acute ischemic stroke patients is greatest when given early,” says Claude Nguyen, M.D., a research collaborator at UTHealth Medical School who led the quality improvement project. “Guidelines for hospitals in the United States recommend treatment within 60 minutes of arrival in the emergency department. In late 2011, we began to see increasing door-to-needle times without any obvious explanation, and we set out to identify the causes and implement new processes to expedite treatment.”

A committee of physicians, nurses and administrative and ancillary staff from the emergency department, neurology service and radiology reviewed times for patients treated with tPA based on data retrospectively collected from standardized time points in the hospital’s electronic medical record. They then compared them with prospective data collected by the treating physician.

“Using the Total Quality Improvement method, we created a detailed flowchart starting from pre-notification by paramedics through thrombolytic administration,” Dr. Nguyen says. “Next, we identified steps of the process that could be improved and implemented changes designed to decrease time.”

The review of process impediments revealed some surprises involving technologies implemented to promote patient safety and operational efficiency. “We found discrepancies between patient arrival times documented in the electronic medical record compared to those recorded by the treating physician, which were caused by a new computer system designed to assist patient triage,” he says. “Other sources of delay included the complexity of the communication plan used to alert stroke neurologists, triaging between multiple CT scanners and obtaining medication from a computerized system designed to improve patient safety.”

A new paging plan reduced the amount of redundancy in cross-communication, and CT technicians were added to the paging pathway to help triage acute stroke patients to an available scanner quickly. Access to the computerized medication system was extended to include research nurses, and tPA was made more widely available at the CT scanning site itself.

“Our project highlights the importance of regular review of treatment processes to ensure that we operate as a well-oiled machine, especially in the face of technology changes and patient volume increases,” Dr. Nguyen says. “On average, only about 5 percent of patients with ischemic stroke arrive at the hospital early enough to be treated with tPA, but we’ve found that we’re treating about 25 percent of patients with symptoms within three hours. Despite our high volumes, our complication rate is low when compared to the literature, and we’ve been able to safely produce a decrease in mortality associated with ischemic stroke over the last two years. With our lower door-to-needle times, we’ll be able to treat an even higher percentage of patients safely.”

### A New Textbook by Kiwon Lee, M.D., Presents Current Perspectives in Neurocritical Care

Neurointensivist Kiwon Lee, M.D., an experienced critical care specialist with a strong interest in driving quality initiatives, has written the first practical, protocol-based guide to the emerging field of neurocritical care. Published by McGraw Hill Medical, *The NeuroICU Book* combines the latest evidence-based clinical perspectives in critical care medicine, neurology and neurosurgery.

Using detailed case studies and a question-and-answer format, the book helps build competency in recognizing acute changes in neurologic function and addresses organ insufficiencies and failures, exposing readers to the real-life challenges of the modern neuroscience ICU.

In addition to providing an indispensable primer for daily clinical work, the book's balanced coverage of neurological and critical care provides outstanding preparation for the neurocritical care board certification exam.

In his foreword, George C. Newman, M.D., Ph.D., chair of the department of Neurosensory Sciences at Albert Einstein Medical Center in Philadelphia, writes, "This work is a dialogue. It could be between two colleagues from different disciplines, between a resident or fellow with a mentor, or between two neurointensivists trying to work through a challenging patient care dilemma. Each chapter considers a case vignette or a small number of vignettes. The patients presented illustrate the typical, common problems encountered in a Neuro ICU. This book is sure to be a favorite for many years to come. It is not a volume that will sit on an office shelf; it will live out in the ICU or the ED. One can only hope that the binding and pages are sturdy enough to handle the usage."

Dr. Lee joined the staff of Mischer Neuroscience Institute in 2012 as director of neurocritical care.

### Improved Online Access for Patients and Physicians

More than a year has passed since leadership at Memorial Hermann-Texas Medical Center made the decision to create a distinct domain and new design for the Mischer Neuroscience Institute (MNI) website. Since then, they've tracked a dramatic increase in visits to the site.

"Dr. Kim's overall goal was to give MNI a greater presence on the Internet and make the website more useful to consumers and referring physicians," says Will Radcliffe, Web producer for Memorial Hermann-TMC. "Early on, we made the decision to make the process of contacting us online very easy. We're mindful of the



fact that medical information and health care itself can be hard to access, and that our environment can be intimidating to consumers.” Neurosurgeon Dong Kim, M.D., is director of the Mischer Neuroscience Institute (MNI) and professor and chair of the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School.

To break down barriers between MNI and consumers, the design team added two portals that provide immediate access. “Get a second opinion” and “Contact us” are quick links in the upper right-hand side of the site’s first page. Consumers who enter their names, phone numbers, email addresses and a brief description of their condition get a quick response. A new “Refer a patient” link provides physicians with fields to enter their names, phone numbers, email addresses and the name of a preferred MNI-affiliated physician.

“We hoped that making contact information easily accessible would help bridge the gap between visitors to our site and the Institute,” Radcliffe says. “Since adding those three access portals, we’ve seen our volume of inquiries go through the roof.”

To ensure transparency of healthcare information, “Quality and Outcome Measures” appears as a heading on page one of the site, which also includes extensive, easy-to-understand information about a range of neurological conditions, from stroke and epilepsy to multiple sclerosis and brain tumors, as well as the treatments and technology available at the Institute. Physicians and patients have access to hour-long webinars on a variety of topics.

Memorial Hermann search engine optimization (SEO) specialist Kelly McCormick works with Radcliffe to ensure that website content is accessible to Web search engines. “The design team created a very comprehensive

and authoritative website,” McCormick says. “MNI’s capabilities speak for themselves. My job is to make sure that the Institute is in the conversations. We find it very easy to guide consumers to the website because MNI is recognized as a neuroscience authority locally and nationally.”

Any media coverage MNI gets also helps drive consumers to the site. For instance, a nationally televised ABC World News segment on trigeminal neuralgia featuring Dr. Kim led to an increase in traffic and prompted a Facebook campaign targeting people who mention the disorder in their profiles. Dr. Kim’s trigeminal neuralgia webinar is also available on YouTube and had been viewed more than 16,000 times by the fall of 2013.

Radcliffe says the best measure of MNI’s success on the Web is the continued increase in visits to the site. “We’re showing record numbers every month, which means we’re helping more patients and families gain access to the high-quality care available at the Mischer Neuroscience Institute.”









# Brain Tumor

Fellowship-trained neurologist and neuro-oncologist Jay-Jiguang Zhu, M.D., Ph.D., and fellowship-trained neuro-oncologist Sigmund H. Hsu, M.D., have added strength to the Mischer Neuroscience Institute's Brain Tumor Center. Dr. Zhu 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. Dr. Hsu's

clinical and research interests include discovery of new and more effective therapies for patients with primary brain tumors, treatment of metastatic cancer to the brain and spinal fluid, and the evaluation and treatment of neurological problems in cancer patients.

Dr. Zhu 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 TTF-100A for newly diagnosed glioblastoma multiforme (GBM) patients in combination with temozolomide, compared to temozolomide alone. The device, which patients wear on the scalp, provides a constant, safe, low-voltage electric field that has been shown to reduce tumor cell survival and division capacity. Dr. Zhu is also principal investigator of a randomized, double-blind, controlled Phase IIB clinical trial testing the safety and efficacy of the vaccine ICT-107 for newly diagnosed GBM patients following resection and chemoradiation, which began enrollment in August 2011. The third trial, an open-label Phase I/II (Safety Lead-In) study of trans sodium crocetinate (TSC) with concomitant treatment of fractionated radiation therapy and temozolomide in newly diagnosed GBM, examines the safety and efficacy of radiation sensitizing effect of TSC in combination with fractionated radiation.

In addition to routine multidisciplinary brain tumor clinics, MNI offers patients specialized care through three clinics. The Pituitary Tumor and Vision Change





## Prospective Multicenter Trial of NovoTTF-100A Together with Temozolomide Compared to Temozolomide Alone in Patients with Newly Diagnosed Glioblastoma Multiforme

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

*Associate Professor*

Vivian L. Smith Department of Neurosurgery

UTHealth Medical School

The purpose of this prospective, randomized, controlled study is to collect data on the clinical results of an experimental device, the NovoTTF-100A, for the treatment of newly diagnosed glioblastoma multiforme (GBM). The NovoCure device generates an electric field, which is applied to the human scalp through electrodes. It has been shown that when properly tuned, very low-intensity, intermediate-frequency electric fields (TTFields) stunt the growth of tumor cells.

Consented subjects will be randomized at a 2:1 ratio of NovoTTF-100A with temozolomide compared to temozolomide alone, starting 4 to 7 weeks from the last day of radiation therapy. Subjects are expected to wear the device 23 hours per day for up to 24 months, or progression of the tumor. The standard of care for newly diagnosed GBM is surgical resection or biopsy if the tumor is not resectable, followed by concurrent radiotherapy and chemotherapy with the oral alkylating agent temozolomide (Temodar®). Subsequently patients receive maintenance temozolomide 5 days out of 28 days (1 cycle) for 6 months.

Clinic ensures early and precise diagnosis of patients with pituitary and other parasellar tumors, which may cause a broad range of disorders and present with a variety of symptoms, including hormonal changes, vision loss and infertility. In 2013, MNI added a Brain Metastases Clinic, whose staff of affiliated neuro-oncologists, neuroradiologists, radiation oncologists, neuropathologists, oncologists and neurosurgeons works closely with oncologists to provide personalized and innovative care to patients with brain tumors. In addition, a Cancer Neurology Clinic for the treatment of patients with neurological issues resulting from chemotherapy was opened.

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

## QUALITY & OUTCOMES MEASURES

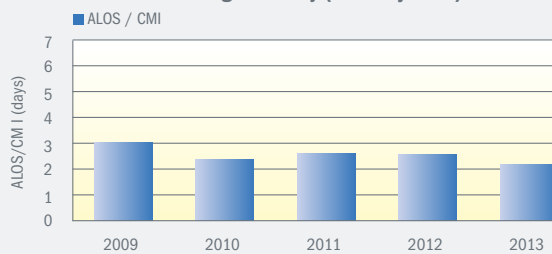
### BRAIN TUMOR • SCOPE OF SERVICES

#### Brain Tumor Volumes



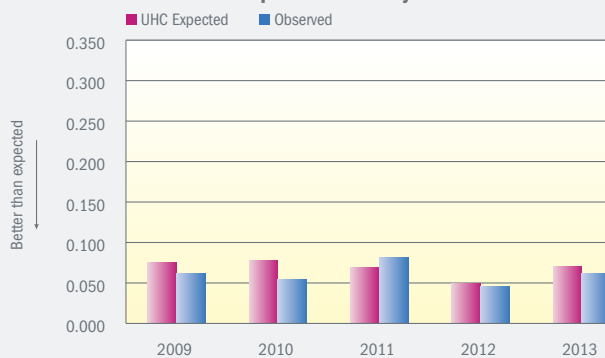
Source: Chart data based on DRG per fiscal year

#### Brain Tumor: Length of Stay (CMI Adjusted)



Source: Chart data from the University HealthSystem Consortium

#### Brain Tumor: Inpatient Mortality



Source: Chart data from the University HealthSystem Consortium

MNI acquired the region's first Leksell Gamma Knife® in 1993, and is now using the more advanced Leksell Gamma Knife Perfexion™. Patients who benefit from the Perfexion's sophisticated software with dose-to-target conformation include those with meningiomas and vestibular schwannomas; arteriovenous malformations; medically refractory trigeminal neuralgia; and metastases. Multiple intracranial metastases can usually be treated in a single outpatient procedure.

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

The Brain Tumor Center's clinical team works closely with referring physicians throughout the radiosurgical treatment process. A neurosurgeon and a radiation oncologist assess each candidate to determine whether radiosurgical treatment is the best option. Nurse navigators work directly with patients on scheduling and pretreatment education, and provide support and care on the day of treatment.

Breakthrough approaches to treatment at MNI are allowing the Institute to grow the number of patients treated for brain tumors. Since 2009, our volumes have increased by nearly 50 percent.

# Cerebrovascular

In 2013, the Mischer Neuroscience Institute received the highly coveted Comprehensive Stroke Center certification from The Joint Commission (TJC) and the American Heart Association/American Stroke Association. Under the direction of Sean Savitz, M.D., the Stroke Center at MNI is the only stroke program in the state of Texas to meet TJC's rigorous standards, solidifying its position among an elite group of providers focused on complex stroke care.

Opened in 1988 by James C. Grotta, M.D., as one of the first dedicated stroke programs in the world, Mischer Neuroscience Institute's Stroke Center is home to the 10-county Greater Houston area's largest onsite stroke

team. Neurologists affiliated with the Center use leading-edge technology to diagnose and treat more than 1,700 patients annually, ensuring that each patient gets the appropriate treatment as quickly as possible. By working closely with the Houston Fire Department and local EMS services, the MNI stroke team has logged an impressive record of success in the administration of tPA – more than 10 times the national average of 2 to 3 percent. With the implementation of new processes, the stroke team has reduced the median door-to-needle time for the delivery of tPA by 15 minutes at Memorial Hermann-Texas Medical Center. Data from the quality improvement project were presented by members of the team at the 8th World Stroke Congress in Brasilia, Brazil.





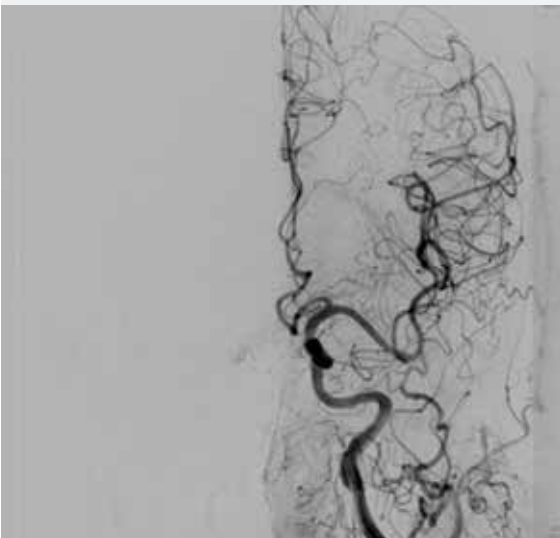
*Stroke*. 2013 Dec;44(12):3376-81.

## **CLOTBUST-Hands Free: Pilot Safety Study of a Novel Operator-Independent Ultrasound Device in Patients With Acute Ischemic Stroke**

Barreto AD, Alexandrov AV, Shen L, Sisson A, Bursaw AW, Sahota P, Peng H, Ardjomand-Hessabi M, Pandurengan R, Rahbar MH, Barlinn K, Indupuru H, Gonzales NR, Savitz SI, Grotta JC

**Background and Purpose:** The Combined Lysis of Thrombus in Brain Ischemic with Transcranial Ultrasound and Systemic tPA-Hands-Free (CLOTBUST-HF) study is a first-of-its-kind, NIH-sponsored, multicenter, open-label, pilot safety trial of tPA plus a novel operator-independent ultrasound device in patients with ischemic stroke due to proximal intracranial occlusion.

**Methods:** All patients received standard dose IV tPA, and shortly after tPA bolus, the CLOTBUST-HF device delivered 2 hours therapeutic exposure of 2MHz pulsed wave ultrasound. Primary outcome was occurrence of symptomatic intracerebral hemorrhage (sICH). All patients underwent pre- and post-treatment transcranial Doppler ultrasound or CT angiography. NIHSS scores were collected at 2 hours and mRS at 90 days.



**Results:** Summary characteristics of all 20 enrolled patients were 60% male, mean age of 63 (SD=14) years, and median NIHSS of 15. Sites of pre-treatment arterial occlusion were: 14/20 (70%) MCA, 3/20 (15%) terminal ICA and 3/20 (15%) vertebral. The median (IQR) time tPA to beginning of sonothrombolysis was 22 (13.5, 29.0) minutes. All patients tolerated the entire 2 hours of insonation and none developed sICH. No serious adverse events were related to the study device. Rates of 2-hour recanalization were: 8/20 (40%; 95% CI: 19-64) complete and 2/20 (10%; 95% CI: 1-32) partial. MCA occlusions demonstrated the greatest complete recanalization rate: 8/14 (57%; 95% CI: 29-82). At 90 days, 5/20 (25%, 95% CI: 7-49) patients had a mRS 0-1.

**Conclusions:** Sonothrombolysis using a novel, operator-independent device in combination with systemic tPA appears safe and recanalization rates warrant evaluation in a Phase III efficacy trial.

Directed by Teddy Wu, M.D., the MNI/UTHealth 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-affiliated neurologists to review CT scans and advise local physicians on treatment outcomes. Through telemedicine, MNI can now offer patients in outlying communities an opportunity to participate in clinical trials that would otherwise be unavailable to them, which expands medical knowledge as it saves lives. Baptist Beaumont Hospital and Memorial Hermann Southwest Hospital were early adopters of telemedicine. Since then, 11 more sites in Southeast Texas have gone live with the technology: Memorial City Medical Center, Memorial Hermann Northwest Hospital, Huntsville Memorial Hospital, Bellville General Hospital, Matagorda Regional Medical Center, Baptist Orange Hospital, the Medical Center of Southeast Texas in Port Arthur, Citizens Medical Center in Victoria, St. Joseph Hospital-Downtown in Houston, DeTar Healthcare System in Victoria and Tomball Regional Medical Center in Tomball.

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

new type of endovascular flow-diverting stent, called a pipeline embolization device, that reconstructs the lumen of the aneurysm's parent artery in areas that are difficult to reach surgically, as an alternative to clipping or endovascular coiling.

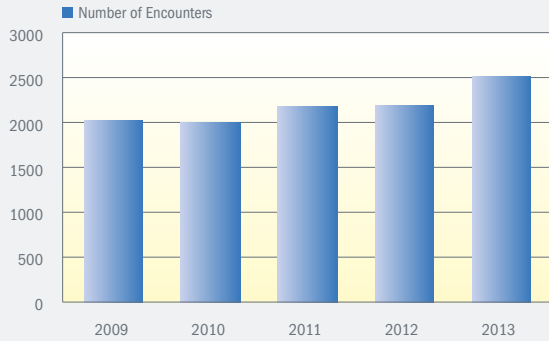
MNI and UTHealth Medical School conduct more research than any other Stroke Center in the south or southwestern United States, participating in multicenter and single-center clinical trials that improve treatments for patients who cannot be treated elsewhere. Research under way includes thrombolytic treatment for wake-up stroke, the safety of pioglitazone for hematoma resolution in intracerebral hemorrhage, and autologous bone marrow stem cell treatment for acute ischemic stroke. Investigators are also seeking to increase the effect of standard-of-care treatment by combining tPA with ultrasound, anticoagulants and hypothermia, as well as exploring new methods of stroke prevention.

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

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

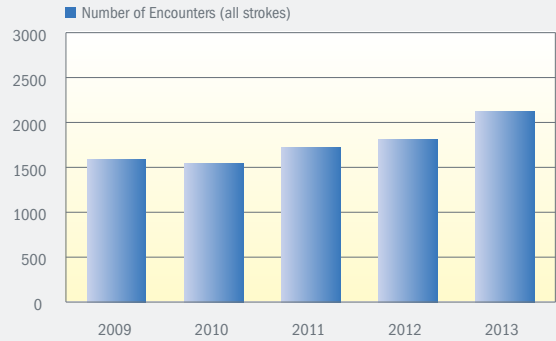
# QUALITY & OUTCOMES MEASURES

## Cerebrovascular Volumes



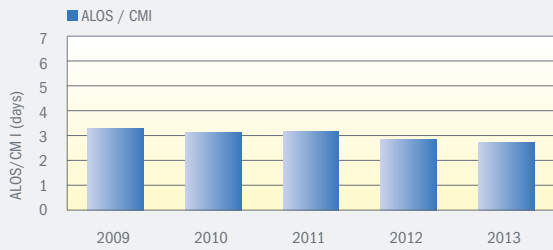
Source: Chart data based on DRG per fiscal year

## Stroke Volumes



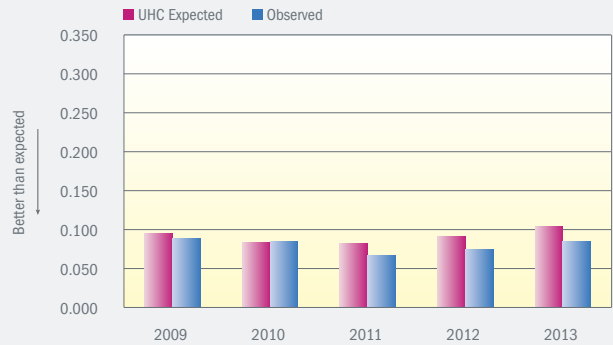
Source: Chart data based on DRG per fiscal year

## AIS: Length of Stay (CMI Adjusted)



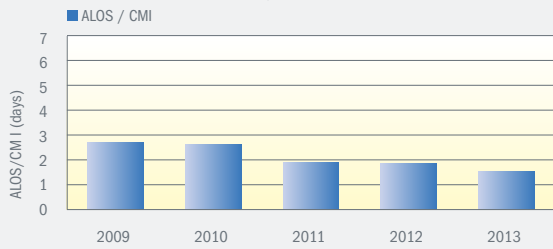
Source: Chart data from the University HealthSystem Consortium

## AIS: Inpatient Mortality



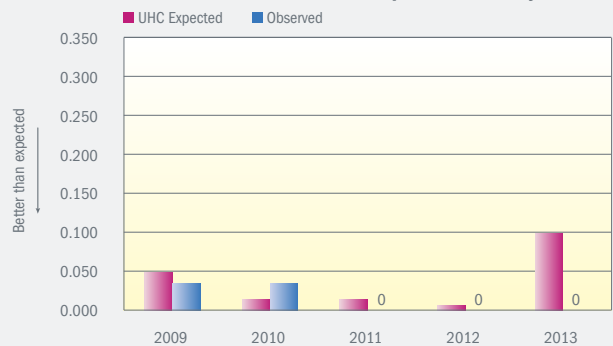
Source: Chart data from the University HealthSystem Consortium

## Arteriovenous Malformation: Length of Stay (CMI Adjusted)



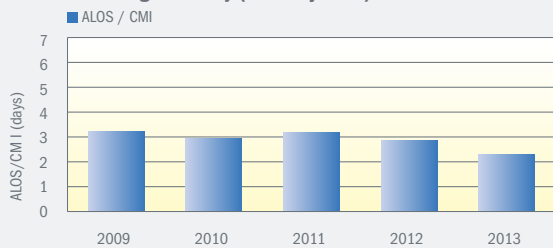
Source: Chart data from the University HealthSystem Consortium

## Arteriovenous Malformation: Inpatient Mortality



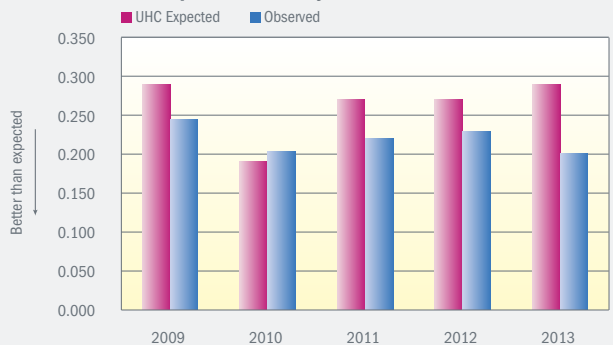
Source: Chart data from the University HealthSystem Consortium

## ICH: Length of Stay (CMI Adjusted)



Source: Chart data from the University HealthSystem Consortium

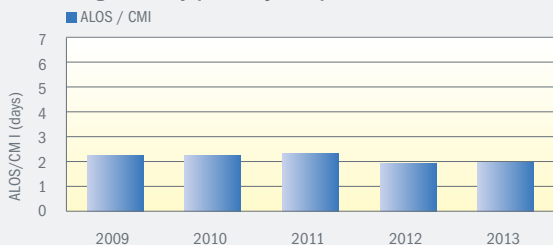
## ICH: Inpatient Mortality



Source: Chart data from the University HealthSystem Consortium

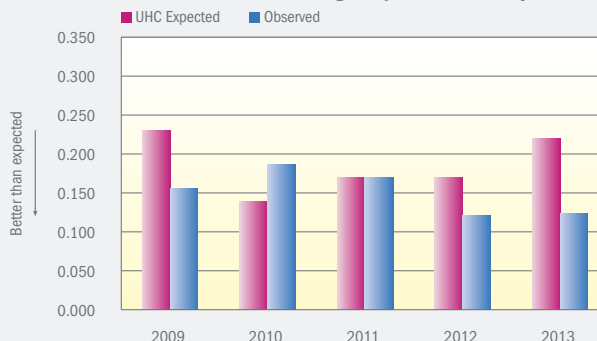


**Sub-arachnoid Hemorrhage: Length of Stay (CMI Adjusted)**



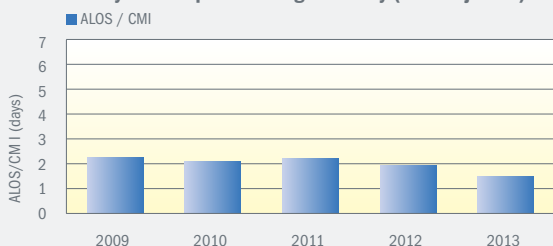
Source: Chart data from the University HealthSystem Consortium

**Sub-arachnoid Hemorrhage: Inpatient Mortality**



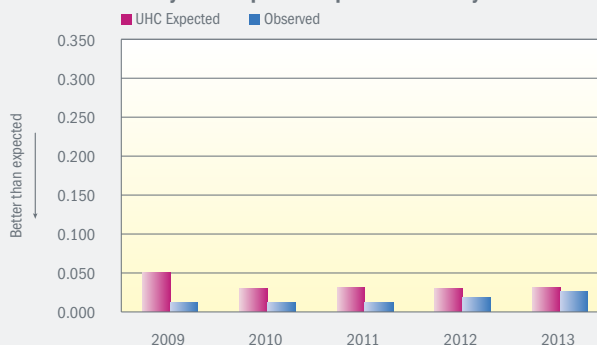
Source: Chart data from the University HealthSystem Consortium

**Aneurysm Unruptured: Length of Stay (CMI Adjusted)**



Source: Chart data from the University HealthSystem Consortium

**Aneurysm Unruptured: Inpatient Mortality**



Source: Chart data from the University HealthSystem Consortium

**Stroke Core Measures**

| CLINICAL MEASURE                               | MEASURE DESCRIPTION  | GWTG STROKE PERFORMANCE MEASURE GOAL | MEMORIAL HERMANN |       |       |       |       |       |
|--|--|--------------------------------------|------------------|-------|-------|-------|-------|-------|
|  |  |                                      | 2007             | 2008  | 2009  | 2010  | 2011  | 2012  |
| <b>VTE Prophylaxis (End of Day 2)</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.                       | 85.0%                                | 93.3%            | 98.3% | 100%  | 98.8% | 97.7% | 99.3% |
| <b>Antithrombotics at discharge</b>            | Ischemic stroke patients prescribed antithrombotic therapy at hospital discharge.  | 85.0%                                | 97.5%            | 98.0% | 96.9% | 96.9% | 100%  | 99.4% |
| <b>Anticoagulation for Atrial Fibrillation</b> | Ischemic stroke patients with atrial fibrillation/flutter who are prescribed anticoagulation therapy at hospital discharge.  | 85.0%                                | 100%             | 96.9% | 100%  | 100%  | 100%  | 99.0% |
| <b>Thrombolytic Therapy</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.       | 85.0%                                | 100%             | 100%  | 100%  | 99.2% | 95.4% | 97.9% |
| <b>Antithrombotic (End of Day 2)</b>           | Ischemic stroke patients administered anti-thrombotic therapy by the end of hospital day 2.  | 85.0%                                | 96.5%            | 100%  | 99.0% | 100%  | 97.3% | 94.9% |
| <b>Statin at discharge</b>                     | Ischemic stroke patients with LDL >= 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. | 85.0%                                | 88.7%            | 88.1% | 87.1% | 87.8% | 94.5% | 98.2% |

Source: Chart data based on calendar year



# Children's Neuroscience

With the arrival of David Sandberg, M.D., FACS, FAAP, in 2012, the Mischer Neuroscience Institute added significant strength to its Children's Neuroscience Center. Dr. Sandberg is a national leader in developing novel techniques to treat malignant brain tumors in children. Prior to his arrival to Houston, he performed translational studies that demonstrated the safety of infusing chemotherapeutic agents directly into the fourth ventricle to treat children with malignant brain tumors in this location. The promising results of these studies have led to a pilot clinical trial in collaboration with The University of Texas M. D. Anderson Cancer Center, which Dr. Sandberg is leading as principal investigator.

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

Pediatric neurosurgeons at the Mischer Neuroscience Institute are important members of the Texas Fetal Center, a national leader in providing diagnosis, treatment and complete care for mothers with high-risk



pregnancies and infants with congenital anomalies or genetic conditions. The multidisciplinary team performed the first fetal spina bifida repair in the region, and patients are now being referred to the center for fetal myelomeningocele repair from throughout Texas and a number of surrounding states.

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



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

Children's Memorial Hermann Hospital is a leading-edge center for the treatment of retinoblastoma, a rare pediatric eye malignancy that affects only 250 to 350 new patients each year. It is the only hospital in the south-central United States offering intra-arterial chemotherapy, the most modern treatment for the disease, which enables children to have chemotherapy injected into the arteries that feed the eye, eliminating the side effects of systemic chemotherapy and maximizing the dose to the eye. Treatment of retinoblastoma requires a large multispecialty team that combines endovascular neurosurgery, ocular oncology and medical neuro-oncology working closely together.

Physicians affiliated with Mischer Neuroscience Institute and Children's Memorial Hermann Hospital are also engaged in research investigating new ways to save eyes that have failed conventional therapies.

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

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

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

Sandberg DI, Khatua S, Rytting M, Zaky W, Kerr M, Tomaras M, Butler T, Ketonen L, Kundu U, Moore BD, Yang G

**Introduction:** Under an IRB-approved protocol, methotrexate was infused into the fourth ventricle in patients with recurrent malignant fourth ventricular tumors. We present preliminary results of this study, which marks the first report in humans of direct chemotherapy administration into the fourth ventricle.

**Methods:** Patients with recurrent, malignant tumors originating within the fourth ventricle underwent tumor resection and catheter placement into the fourth ventricle. The catheter was attached to an Ommaya reservoir. After confirmation of cerebrospinal fluid flow by CINE MRI, methotrexate was infused over 3 cycles, each consisting of 4 consecutive daily infusions (2 mg). Serum and cerebrospinal fluid (CSF) methotrexate levels and CSF cytology studies were obtained daily, and MRI scans of the brain and total spine were obtained after the first and third cycle. Neuropsychological evaluation was performed before and after intraventricular chemotherapy.

**Results:** To date, 2 patients have each completed 3 cycles of therapy. Maximum serum methotrexate level was 0.08 micromoles/liter, and median trough CSF level was 22.27 micromoles/liter (range 0.53-212.36). Neither patient had any adverse events or even minor side effects. The first patient, a 19-year-old boy with recurrent medulloblastoma, had a partial response to therapy, with decreased tumor in the fourth ventricle and spine and fewer malignant cells on cytology analysis. The second patient, an 8-year-old boy with recurrent ependymoma, had stable disease. Neither patient had leukoencephalopathy on MRI scans.

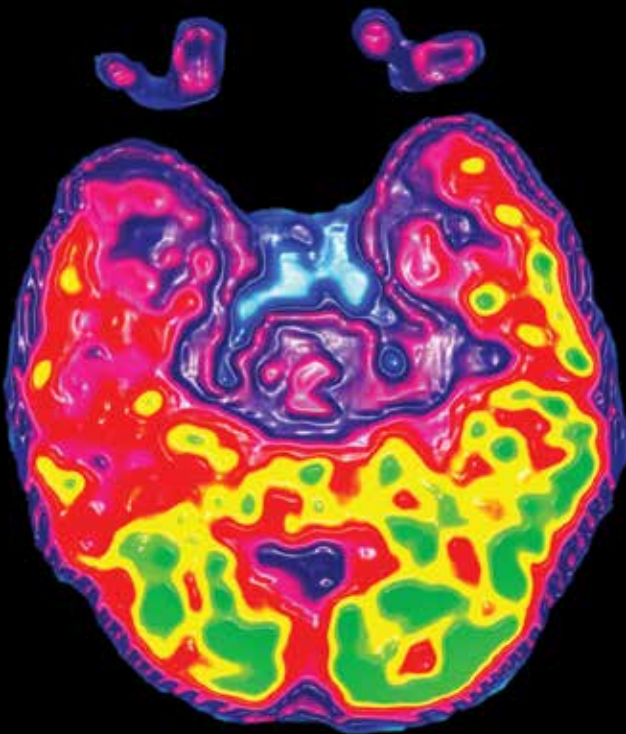
**Conclusions:** Direct infusion of methotrexate into the fourth ventricle is safe and may represent a promising new means of treating recurrent malignant fourth ventricular brain tumors.

# Epilepsy

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

At the heart of the program is a state-of-the-art 12-bed Epilepsy Monitoring Unit (EMU), the largest and most comprehensive unit of its kind in the region. Affiliated physicians deploy a complete set of established and emerging diagnostic technologies that provide us with comprehensive datasets to help define and localize the seizure network in the brain. The full suite of diagnostic tools includes magnetoencephalography (MEG) to map both seizure networks and neurological function, video EEG, 3-Tesla structural MRI, functional MRI and diffusion tensor tractography, positron emission tomography (PET), single photon emission computed tomography (SPECT), memory and intracarotid amyltal (Wada) testing and in-depth neuropsychological testing. The program is a national leader in combining the use of MEG and functional MRI to map the brain and record brain activity. It is also one of only a few inpatient units in the country with the capability to perform electroencephalography and polysomnography simultaneously.

The number of patients affiliated physicians treat annually continues to grow. Our affiliated board-certified neurologists and neurosurgeons diagnose and treat more than 500 pediatric and adult patients each year for seizure disorders. Genetic anomalies, brain trauma, structural abnormalities, stroke and brain tumor rank among the top underlying causes of epilepsy, but because seizures manifest differently among individuals, specific determination of the origin of seizures is crucial to planning the most effective treatment for individual patients.





*Epilepsia*. 2013 Dec;54(s9):72-8

## Resection Strategies in Tumoral Epilepsy: Is a Lesionectomy Enough?

Esquenazi Y, Tandon N

**Purpose:** Resection strategies in patients with tumor-related epilepsy vary from lesionectomy to epilepsy operations, with no clear consensus on optimal approaches. The objective of this study is to use our prior experience in the management of these patients to derive optimal strategies for the surgical management of epilepsy related to brain tumors.

**Methods:** A prospectively compiled database of epilepsy and tumor patients was used to identify patients who underwent a surgical resection of a neoplasm but then developed epilepsy, or those who presented with epilepsy and were found to harbor a brain tumor. Data regarding demographics, seizure frequency, histopathology, details of the surgical resection and seizure outcomes were compiled.

**Key Findings:** Over a period of 8 years, of the 235 consecutive patients that underwent cranial procedures for epilepsy and the 75 patients that underwent resection of low/intermediate grade gliomas, 13 (5.5%) and 21 (28%) patients respectively had tumoral epilepsy. Median patient age was 37 years, 22 patients were male and 18 tumors were in the left hemisphere. Tumoral epilepsy had a propensity for temporal (50%) and peri-rolandic (26.5%) locations. The etiology was WHO grade I tumors in 29%, grade II in 35% and grade III in 33%. A major difference in these two groups was the latency between the diagnosis of epilepsy and surgery – this was four years in the epilepsy group and two weeks in the tumor group. In the epilepsy group, following lesionectomy in three and tailored resections in the majority, seizure outcomes were Engel class 1 in all except one case (who had a class 3 outcome). One patient in this group underwent a second intervention due to seizure recurrence. In the tumor group, after the initial operation seven additional resections were performed due to seizure recurrence – all re-resections were related to residual or recurrent tumors after initial surgery. Outcomes in this group were Engel class 1A in 18 patients and 1B, 1C and 2A in 1 patient each. Drawing upon these data, we propose a classification of the likely etiology of failure in seizure control, in patients with tumoral epilepsy.

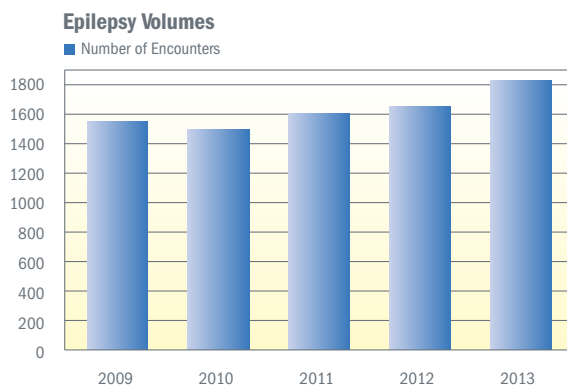
**Significance:** The major distinction between epilepsy resulting from neoplasms and neoplasms presenting with multiple seizures is the timeline between diagnosis and therapy. This retrospective review reiterates the concept that a complete resection of the lesion is the best approach for dealing with tumors presenting with epilepsy. In cases where seizures recur after tumor resection, the reason is most likely to be residual or recurrent tumor. In cases where tumor infiltrated the mesial temporal structures (amygdala-hippocampus), a typical antero-mesial temporal lobectomy was also performed. Overall excellent outcomes (Engel class I in 94%) can be accomplished following aggressive initial tumor resection, re-resection in the context of recurrence and epilepsy style operations in selected patients with a longer history of seizures.

Once a diagnosis is made, affiliated physicians 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. The program’s surgical complication rates have remained extremely low over the past nine years. To date, our affiliated epilepsy surgeon has performed more than 400 craniotomies for the treatment of epilepsy, with a zero percent mortality rate and a very low rate of permanent morbidity. Additionally, we go beyond the medical and surgical treatment of epilepsy by offering counseling to patients to help them cope with their diagnosis. Specialized counselors ensure that recently diagnosed patients have the emotional support they need.

We are also leaders in innovative surgical approaches for epilepsy, with new surgical approaches and technologies implemented in the past year, including stereoelectroencephalography (SEEG), robotic SEEG and laser-assisted interstitial thermal therapy (Visualase). MNI is a pioneering site for the latter technique – the application of laser surgery for well-delineated focal epilepsies – with carefully selected patients treated in

a highly advanced, minimally invasive fashion that ablates the seizure focus. In addition to using the Visualase technique for the treatment of temporal lobe epilepsy associated with hippocampal sclerosis, affiliated physicians use it in novel ways, including the ablation of deep-seated periventricular nodular heterotopias. The program is the second in the country to perform robotic SEEG, a technique that helps localize the seizure focus with precision and in a minimally invasive fashion. Our safety and efficacy data following all types of surgical intervention for epilepsy are excellent.

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



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





# 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. In 2013, the Willis-Ekbom Disease Foundation recognized the program for highly developed expertise in the diagnosis and management of Willis-Ekbom disease/restless legs syndrome and certified it as a WED-RLS Quality Care Center.

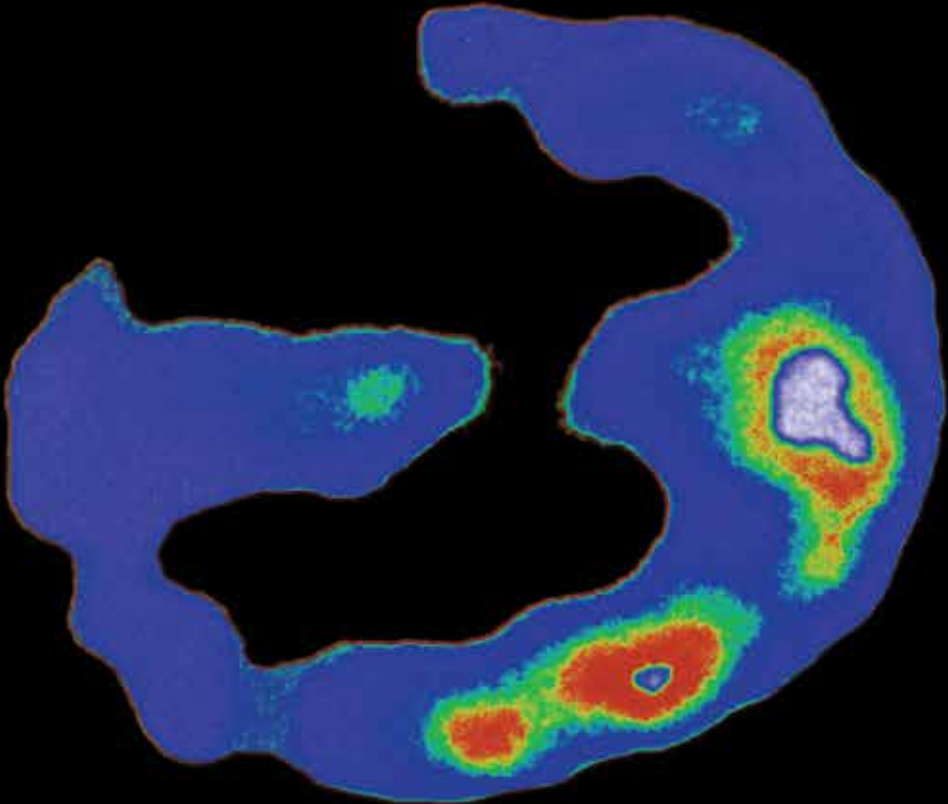
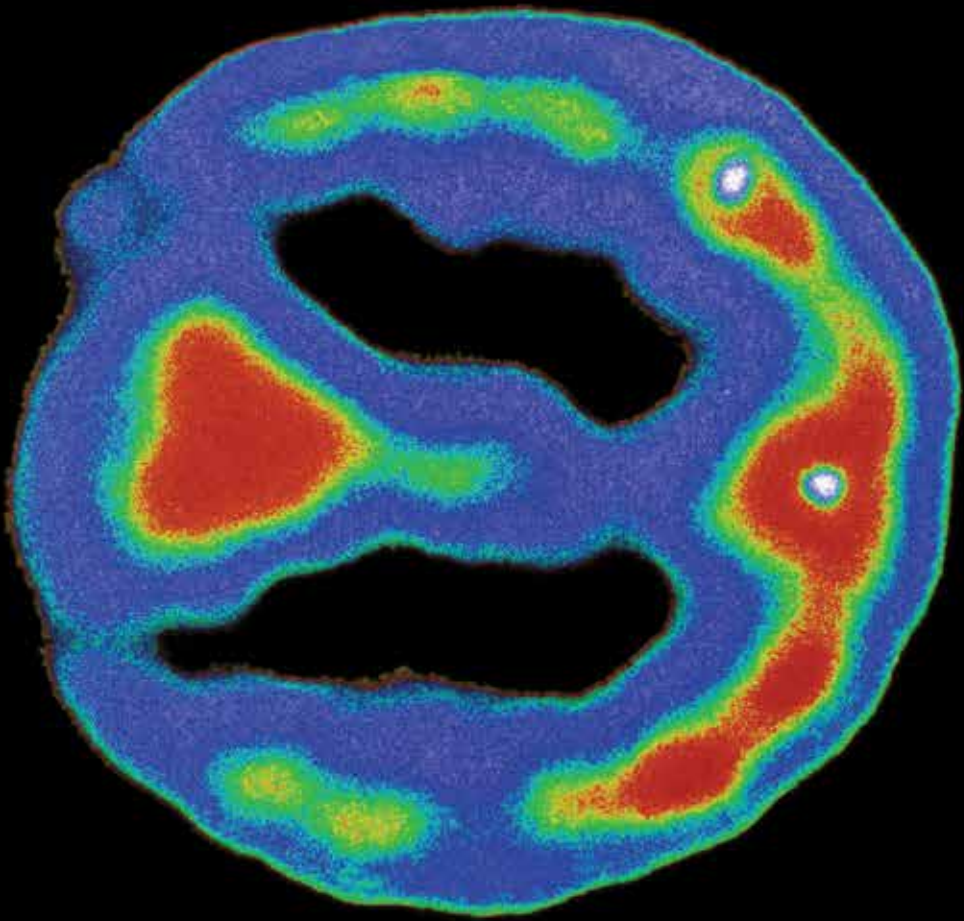
The Movement Disorders and Neurodegenerative Diseases Program is a collaborative effort of the Mischer Neuroscience Institute and UT MOVE, with specialty clinics that include Spasticity Management, DBS Selection and Programming, Botox® Injection and Intrathecal Baclofen Pump Therapy. Because rehabilitation is integral to good outcomes, affiliated physicians work closely with the physical and occupational therapists and speech-language pathologists in the program's inpatient and outpatient clinics and at TIRR Memorial Hermann to research new approaches to improving treatment. In 2013, patient visits dramatically increased, and new UT MOVE clinics were established at Memorial City Medical Center and Memorial Hermann The Woodlands Hospital.

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

methods to manage Parkinson's disease, Parkinsonian disorders, generalized and focal dystonia, essential tremor, Huntington's chorea, 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. Affiliated physicians maintain patients at the highest level of function possible, based on symptom-driven therapeutic goals set by the physician and patient. In developing and adjusting our treatment plans, 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. In 2013, the program partnered with TIRR Memorial Hermann to develop a comprehensive UT MOVE/Neurorehabilitation Program that will incorporate neurological-driven rehabilitation as part of the treatment approach.

Our deep brain stimulation (DBS) program for Parkinson's tremor, dystonia and essential tremor is known for low complication rates and outstanding outcomes. Based



## Enroll-HD: A Prospective Registry Study in a Global Huntington's Disease Cohort, a CHDI Foundation Project

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

*Assistant Professor*

Department of Neurology, UTHealth Medical School

Enroll-HD is an observational, prospective, multicenter study with sites in North America, Latin America, Europe, Asia, Australia and New Zealand. The study has three aims: to improve the understanding of the dynamic phenotypic spectrum and the disease mechanisms of Huntington's disease (HD) by collecting natural history data covering the cognitive, behavioral and motor domains that allow insights into the neurobiology of HD, collecting data and biologic samples to identify genetic and environmental factors influencing and/or modifying the HD phenotype and disease progression, and promoting studies that may provide clues to the pathogenesis of HD; to promote the development of evidence-based guidelines to inform clinical decision-making and improve health outcomes for participants and their family units; and to provide a platform to support the design and conduct of clinical trials.

Participants include individuals 18 years of age or older who are HD gene expansion mutation carriers independent of the phenotypical manifestation or stage of HD, and controls who do not carry the mutation. The study, which is sponsored by the CHDI Foundation in New York City, aims to recruit all subjects who are eligible and willing to participate, with a goal of enrolling approximately one-third of the HD-affected population in each study region. For more information about the trial, contact Chad Tremont at 713.500.6624.

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. In 2013, we recorded record growth in our DBS program. UT MOVE initiated a referral program to serve community neurologists who select patients for deep brain stimulation. We provide intraoperative micro-electrode recording and electrode stimulation testing to determine and confirm the best DBS placement to reduce disease symptoms, and share the results with referring neurologists. Following DBS placement, patients are returned to the referring physician.

Recent research includes a longitudinal prospective study on biomarkers and presymptomatic biomarkers for Parkinsonian syndromes, onabotulinum toxin-A injections for nocturnal bruxism, deep brain stimulation in the treatment of medication-refractory tremors in patients with co-morbid peripheral neuropathy, evaluation of a novel scale to assess psychosis in patients with idiopathic Parkinson's disease, medications for patients with restless legs syndrome, managing sleep problems in Parkinson's patients and DBS for orthostatic tremor. The program regularly takes part in clinical trials of devices for deep brain stimulation and is unique in its participation in worldwide registry databases for both DBS stimulation implants and intrathecal baclofen pumps.



# Multiple Sclerosis

The Mischer Neuroscience Institute's Multiple Sclerosis Program has established a track record of leading-edge care using groundbreaking techniques to diagnose, evaluate, manage and treat adult patients with MS and other demyelinating disorders. The scope of expertise of our affiliated physicians 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. Recently completed research includes a National Institutes of Health-sponsored trial of combined therapy with interferon beta-1a and glatiramer acetate in patients with early relapsing MS (the CombiRx Trial), the safety and efficacy of oral fampridine-SR, detection of MS-related cognitive impairment, Epstein-Barr virus and MS, and serial magnetic resonance spectroscopy in MS, among others. Investigators in the MSRG and the department of Diagnostic and Interventional Imaging also recently completed a National MS Society-sponsored study of chronic cerebrospinal vascular insufficiency (CCSVI).

The program was the first in the world to conduct preclinical studies on the effects of combined therapy with immunomodulating drugs and to explore the effects

of oral cytokines in modulating MS and Type 1 diabetes. 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 affiliated physicians are at the forefront of investigator-initiated research in immune regulation in MS, infection as a cause of MS, MS-related cognitive impairment and MS-related MRI findings.



In the department of Neurology's state-of-the-art Magnetic Resonance Imaging Analysis Center, physicians use spectroscopic and diffusion tensor imaging with tractotomy, as well as other advanced diagnostic tools. Following diagnosis, patients benefit from breakthrough treatment options that include injectable immunomodulators, immunosuppressives and other agents designed to treat the debilitating symptoms of MS. Investigators also use the MRI

*Multiple Sclerosis Journal. Published online 4 July 2013. DOI: 10.1177/1352458513494493*

## **Chronic Cerebrospinal Venous Insufficiency: Masked Multimodal Imaging Assessment**

Brod SA, Kramer LA, Cohen AM, Barreto AD, Bui T-T, Jemelka JR, Ton K, Lindsey JW, Nelson F, Narayana PA, Wolinsky JS

**Background:** Chronic cerebrospinal venous insufficiency (CCSVI) was implicated in the pathophysiology of multiple sclerosis (MS).

**Objective:** We evaluated neurosonography (NS), magnetic resonance venography (MRV), and transluminal venography (TLV) in subsets of MS patients drawn from a single-center, prospective, case-control study of 206 MS and 70 non-MS volunteers.

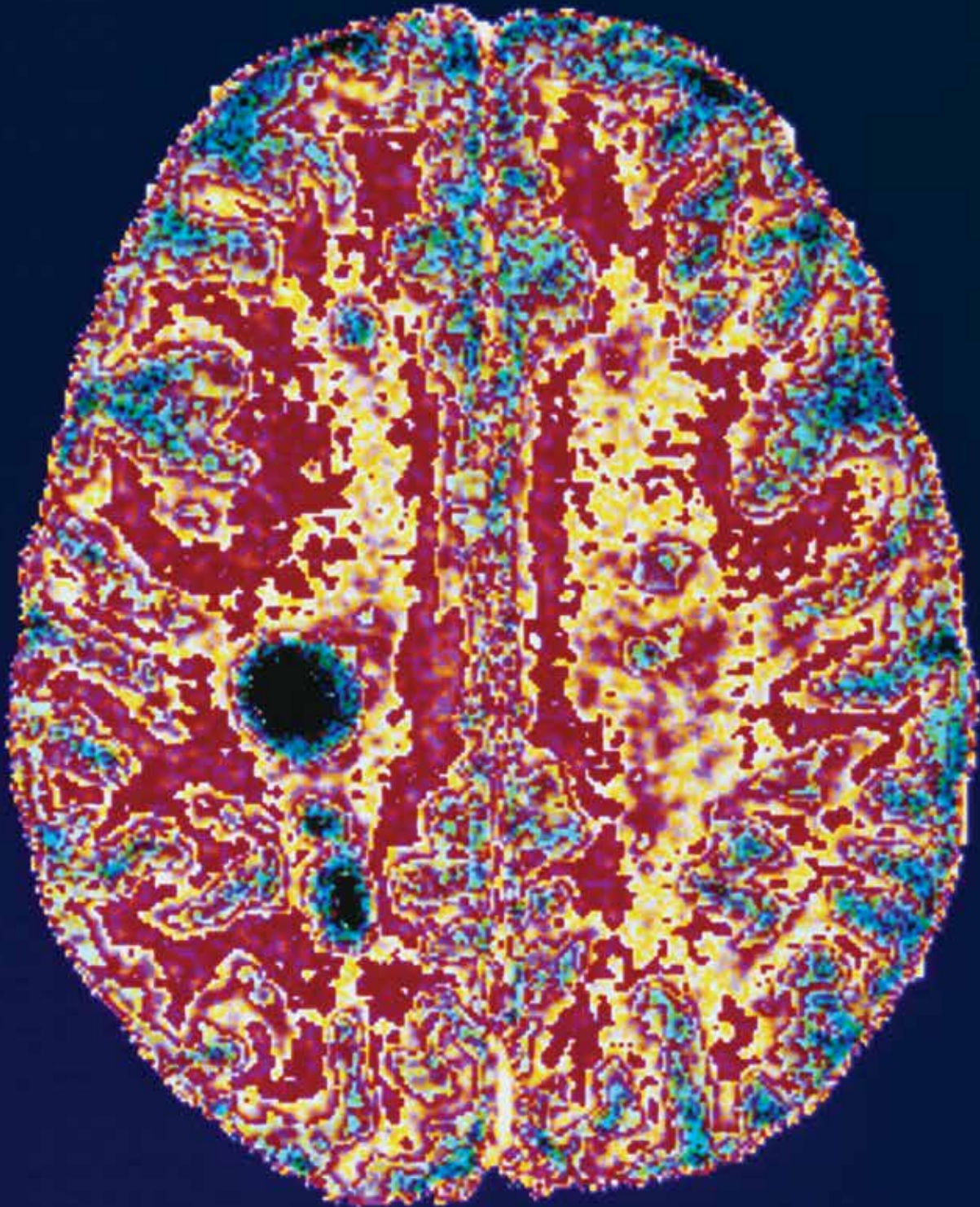
**Methods:** As previously reported, findings on high-resolution B-mode NS imaging with color and spectral Doppler of the extracranial and intracranial venous drainage consistent with CCSVI were similar among MS and non-MS volunteers (3.88% versus 7.14%;  $p = 0.266$ ). Ninety-nine MS participants consented to intravascular contrast-enhanced 3D MRV to assess their major systemic and intracranial venous circulation, and 40 advanced to TLV that included pressure measurements of the superior vena cava, internal jugular, brachiocephalic and azygous veins.

**Results:** NS findings and MRV patterns were discrepant for 26/98 evaluable subjects, including four with abnormal findings on NS that had normal venous anatomy by MRV. In no instance were TLV pressure gradients indicative of clinically significant functional stenosis encountered. The three imaging approaches provided generally consistent data with discrepancies referable to inherent technique properties.

**Conclusions:** Our findings lend no support for altered venous outflow dynamics as common among MS patients, nor do they likely contribute to the disease process.

Analysis Center to monitor the effects of promising oral drugs in pivotal efficacy trials. The Center was pivotal in providing quantitative imaging data that supported the recent regulatory approval of the oral agent teriflunomide for use in relapsing forms of MS in the United States, Europe and a growing number of countries worldwide, determining the optimal drug dose and extending the results of its benefits when used in first symptom-onset disease.

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



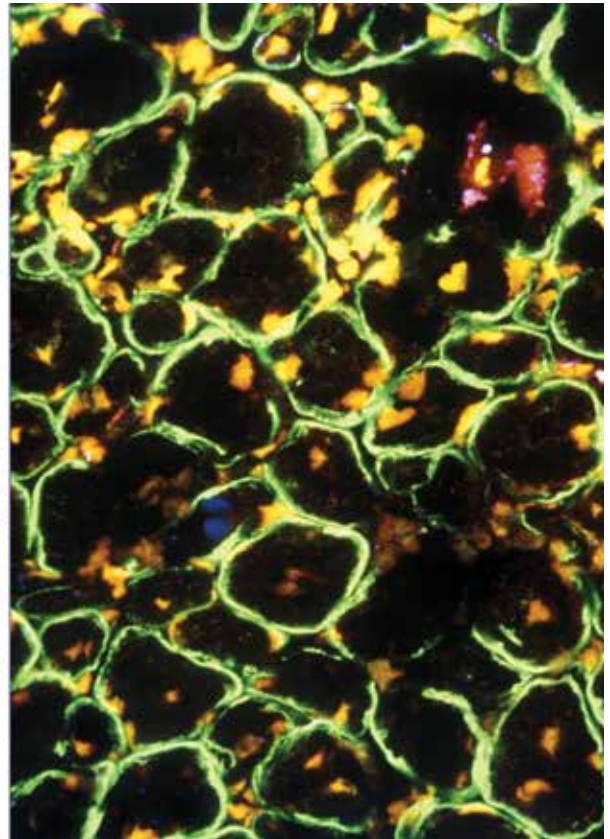
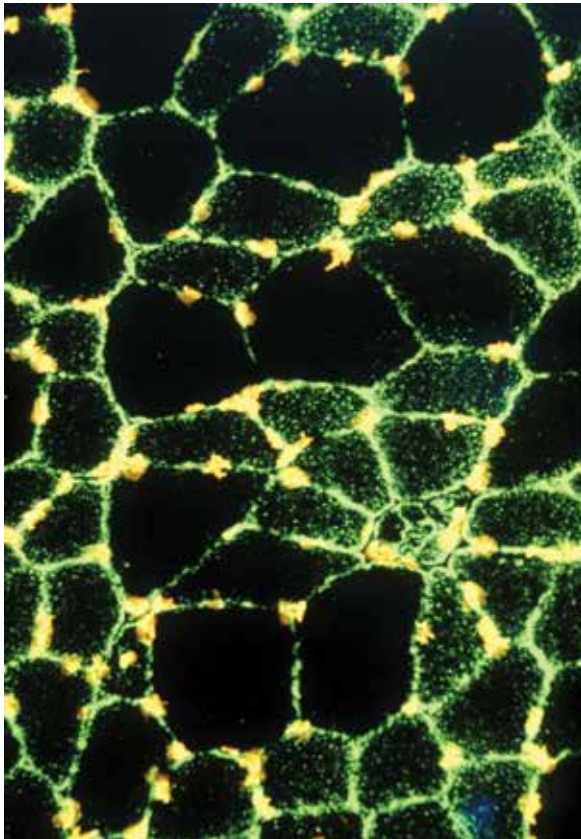


# Neuromuscular Disorders

Physicians affiliated with the Neuromuscular Diseases Program are subspecialized in complex neuromuscular disorders that are difficult to diagnose and treat, including neurodegenerative disorders, inflammatory nerve and muscle disorders, autoimmune neuromuscular junction disorders, traumatic nerve injuries and toxic metabolic disorders of the peripheral nerves and muscles. The program is a designated center of excellence for Guillain-Barré syndrome (GBS) and chronic inflammatory demyelinating polyneuropathy

(CIDP) and records more than 2,000 patient visits annually, primarily adults age 18 and older. About two-thirds of our patients are over the age of 50.

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





*Journal of the Peripheral Nervous System, June 2013; Volume 18, Supplement 2, p. 69*

## **Sialic acid-enriched IVIG fractions are efficacious in an antibody induced preclinical model of GBS**

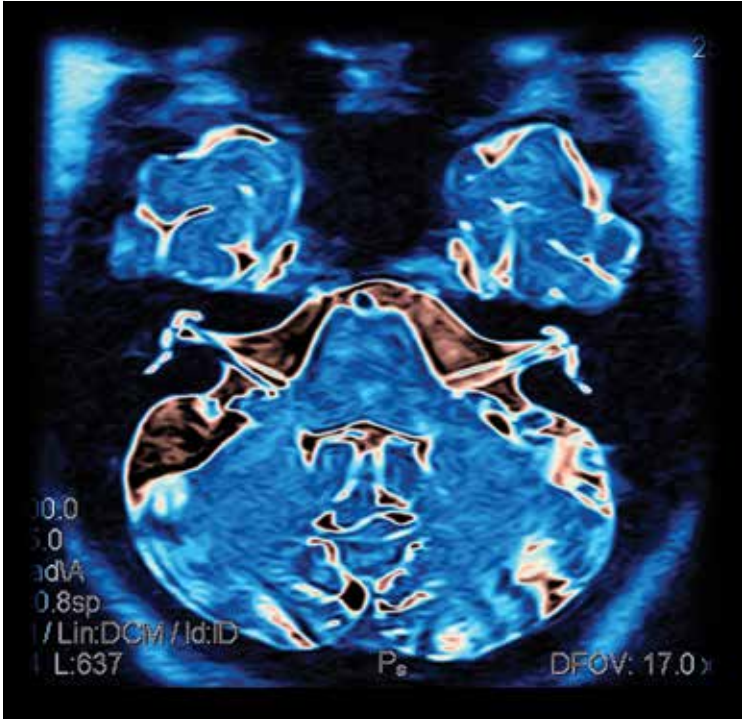
Massaad CA, Pillai L, Liu W, Sheikh KA

High doses of Intravenous immunoglobulin (IVIG), requiring infusion over several days, are widely used for the treatment of Guillain-Barré syndrome (GBS) and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Recent studies indicate that autoantibody- and Fc receptor-mediated inflammatory cascade is abrogated by sialic acid-enriched minor populations present in commercial IVIG preparations. We have recently established that Fc-receptor activation is critically involved in neural injury in a mouse model of GBS. In this study, we investigated the effects of sialic acid-enriched IVIG (seIVIG) and compared them with whole/native IVIG (nIVIG) and sialic acid-deficient IVIG (sdIVIG) in an established model of nerve repair in which anti-ganglioside antibodies significantly inhibit axon regeneration. We used lectin affinity-chromatography to generate various IVIG fractions and used them in a passive transfer model of anti-ganglioside antibody-mediated inhibition of axon regeneration.

Behavioral, electrophysiological and morphological studies showed beneficial effects of nIVIG and seIVIG on abrogating the adverse effects of anti-ganglioside antibodies on nerve repair. Notably, seIVIG was equally efficacious at a dose tenfold lower than the nIVIG. sdIVIG was ineffective in modulating anti-glycan antibody-mediated inhibition of nerve repair. Further, our lectin chromatographic studies indicate that various commercial IVIG preparations have up to twofold variation in seIVIG content.

Our findings have translational implications as smaller amounts of IVIG and shorter infusion times are preferable because common side effects of IVIG relate with rate of infusion and amount administered. Shorter infusion times are likely to increase patient acceptance of repeated IVIG infusions necessary for the treatment of chronic immune neuropathies such as CIDP.

**Acknowledgements:** Supported by the GBS/CIDP Foundation International and NIH/NINDS (NS42888 and NS54962).



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

The 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. Their preferred technique is open biopsy under local anesthesia, which reduces the likelihood of missing abnormalities in cases of patchy involvement, such as in inflammatory myopathies. The lab also performs skin biopsies for the diagnosis of small-fiber neuropathy and is the only center in Houston that processes skin biopsy specimens for the diagnosis of small-fiber neuropathies.

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

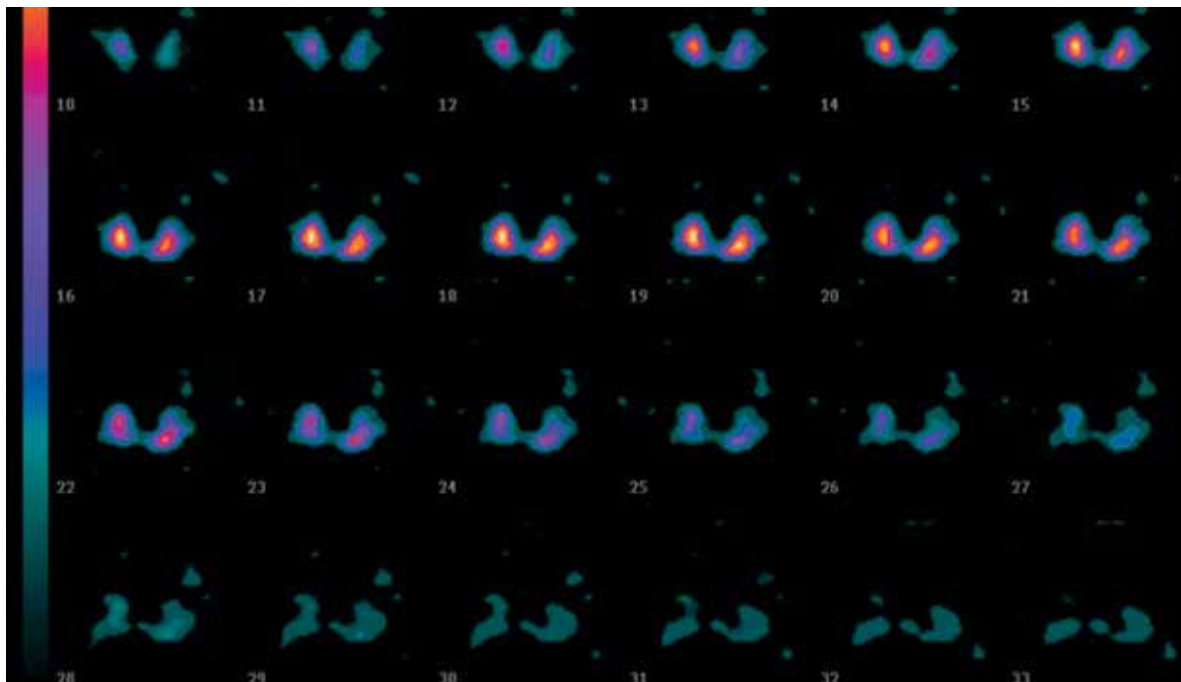
# Neurocognitive Disorders

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

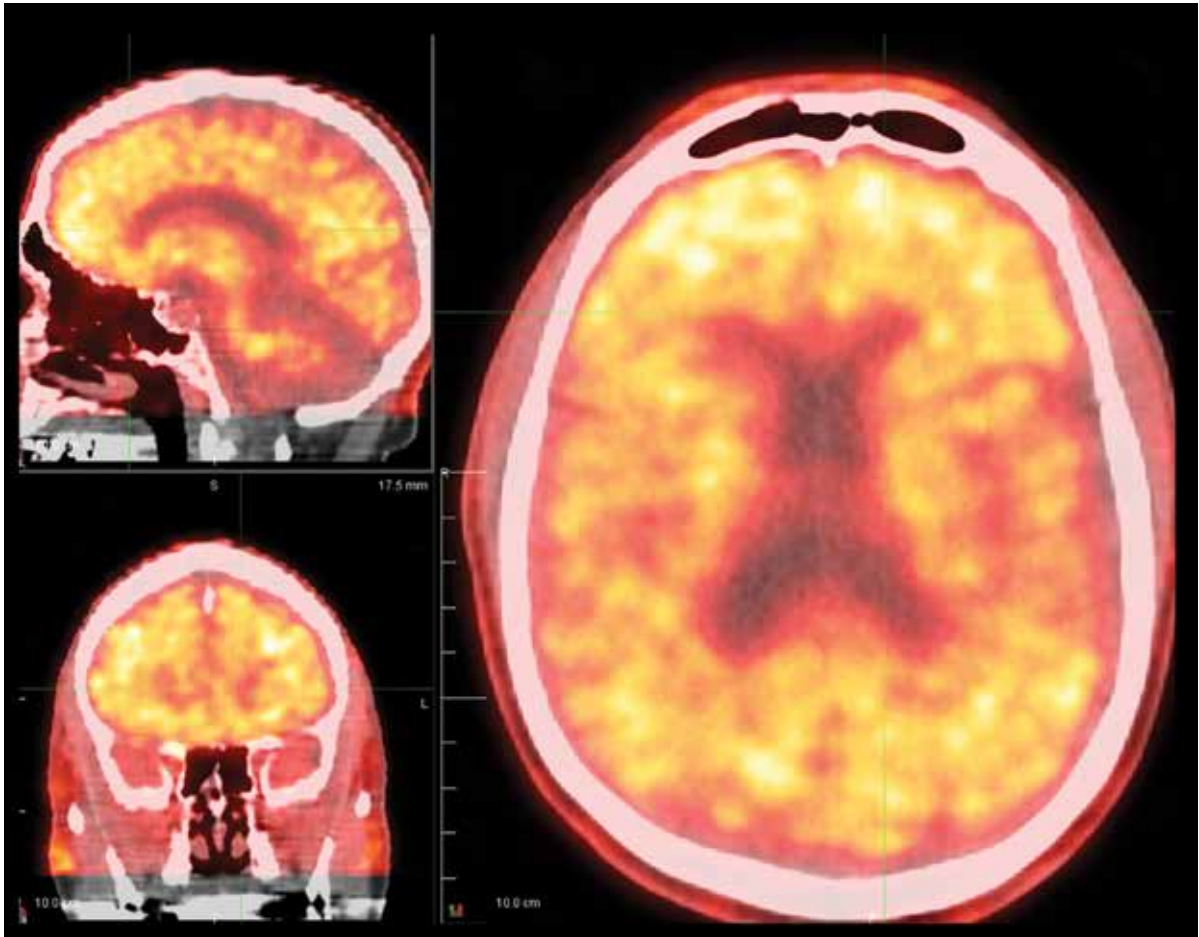
MNI was the first in Houston to offer a new diagnostic tool that tests for Alzheimer's disease with high reliability using a florbetapir (Amyvid™) scan to rule out the disorder. Affiliated physicians are also developing new PET agents to distinguish Alzheimer's disease from frontotemporal dementia, the second most common neurodegenerative dementia. In addition, they are

developing tests for Alzheimer's disease that may lead to earlier and more cost-efficient diagnosis. In 2013, the Center recruited three neuropsychologists to expand its diagnostic program and moved to a new location to accommodate further expansion.

Neurodegenerative diseases affect millions of Americans, but their causes remain unclear. Researchers at MNI are currently investigating genetic contributions to neurodegenerative diseases by comparing healthy patients to those with disease and by testing for a transmissible component to the disorders. Using sophisticated new technologies, physicians at the Neurocognitive Disorders Center are studying Alzheimer's disease and its risk factors at the clinical and cellular







levels. Their goal is to diagnose dementia before patients become symptomatic and to find new treatments to delay or prevent development of the disorder.

Traumatic brain injury is known to increase the risk of Alzheimer's disease. Recently, researchers at the Center found that even minor traumatic brain injury leads to a fourfold increase in the risk for frontotemporal dementia. They have also found that post-traumatic stress disorder may contribute to dementia, increasing the risk of stroke and substance abuse and resulting in permanent changes in the brain. Researchers at the Center are investigating other risk factors for dementia, including

family history, high blood pressure, high cholesterol or triglycerides, diabetes, obesity and smoking, with the aim of reducing risk.

MNI's new Stroke and Dementia Prevention Program, made possible by a gift from Bruce and Diane Halle, builds on the recognition that there are multiple, modifiable risk factors for dementia. Physicians at the clinic evaluate patients with symptoms and also those without symptoms who are at risk based on family history.

*Alzheimer's and Dementia, 2012, 8:204-210*

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

Kalkonde YV, Jawaid A, Qureshi SU, Shirani P, Wheaton M, Pinto-Patarroyo GP, Schulz PE

Countless Americans suffer from frontotemporal dementia (FTD), the second most common neurodegenerative dementia, causing untold suffering among loved ones. The average age of onset is in the 50s, robbing families of loved ones when children are in high school and careers are flourishing.

About 40 percent of patients with FTD have a family member with the disorder, suggesting that changes in the genetic code may contribute to the risk of developing FTD; however, in 60 percent of patients, the cause is unknown. After investigating the potential role for 20 genetic factors, researchers at MNI found that in patients who have been rendered unconscious by injury once, even briefly, FTD is four times more common than in all other dementias combined. They also found that patients with FTD are less than half as likely to have heart disease, suggesting that FTD is systemic; moreover, it may be associated with changes in fat and cholesterol metabolism that lead to less heart disease.

The research team has taken these findings to the laboratory to understand how trauma increases the risk for FTD. We hope that investigations into factors that modify the risk for FTD will lead to an understanding of the processes underlying the disorder.

FTD cannot currently be diagnosed during life, making it difficult to design treatment trials for the disorder. We know that the molecular basis for FTD in 50 percent of patients involves deposition of a cellular protein called tau and are currently developing new PET agents to visualize tau proteins in the brain. Our hope is that these agents will provide the capability to diagnose FTD and reveal those at risk for FTD before it develops, allowing us to test treatments designed to prevent the disorder.

# Neurorehabilitation

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

## MISCHER NEUROREHABILITATION

Memorial Hermann-Texas Medical Center's 23-bed inpatient neurorehabilitation unit provides comprehensive rehabilitation care, consisting of an intensive program of physical therapy, occupational therapy and speech-language pathology. Patients and families are an integral part of MNI's Neurorehabilitation Program. Upon admission, they discuss their goals with an 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.

Affiliated physicians provide outstanding patient care and conduct award-winning research on the underlying conditions that impact rehabilitation progress, applying their advanced knowledge directly to the care of each patient they serve. This level of advanced training is a critical component of the rehabilitation process, particularly as Mischer Neurorehabilitation serves as an extension of MNI's world-renowned vascular neurology and neurosurgical programs. Because they are trained in the administration of the National Institutes of Health Stroke Scale and the modified Rankin Scale, used by vascular neurologists to assess stroke deficits and post-stroke disability, they can directly interpret acute neurologic changes and communicate across disciplines without the need for outside consultation. This combination of clinical excellence and research









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

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

*Director, Brain Injury Research Center (BIRC), TIRR Memorial Hermann*

*Associate Professor, Baylor College of Medicine Department of Physical Medicine and Rehabilitation*

*Adjunct Clinical Professor, University of Houston Department of Psychology*

CO-INVESTIGATORS:

**Mark Sherer, Ph.D., ABPP, FACRM**, senior scientist and director of research at TIRR Memorial Hermann and a clinical professor in the department of Physical Medicine and Rehabilitation at Baylor College of Medicine;

**David B. Arciniegas, M.D.**, senior scientist and medical director for brain injury research at TIRR Memorial Hermann, executive director of the Beth K. and Stuart C. Yudofsky Division of Neuropsychiatry at Baylor College of Medicine (BCM), and professor in the BCM Menninger Department of Psychiatry and Behavioral Sciences;

and **Kacey Maestas, Ph.D.**, and **Alison Clark, Ph.D.**, investigators at TIRR Memorial Hermann's Brain Injury Research Center.

This study is a novel, innovative, preliminary investigation of the effectiveness of Acceptance and Commitment Therapy (ACT) for reducing emotional distress, improving health-related quality of life and increasing participation for persons with traumatic brain injury (TBI). The study is also investigating the importance of the ACT process components (acceptance of thoughts/feelings and commitment to valued activities) for determining outcomes. As a preliminary trial, the study is anticipated to provide a foundation for future multicenter comparative effectiveness trials in which ACT can be evaluated in comparison to traditional cognitive-behavioral therapy and to psychotropic medications. This stages-of-research approach is consistent with the National Institute on Disability and Rehabilitation Research (NIDRR) long-range plan, which went into effect in 2013. In anticipation of future trials, the current study will also pilot an innovative method of assessing a physiological correlate of emotional distress, through sampling of cortisol levels obtained from hair samples (hair CORT). A consistent and replicable correlation between hair CORT levels and measures of emotional distress would yield a biomarker of emotional distress among persons with TBI. Potential biological treatment targets (e.g., HPA axis dysfunction) also may be revealed by such a relationship. The effectiveness of treatments of emotional distress – whether those treatments are psychological, environmental and/or pharmacologic – would be evaluable both symptomatically and physiologically. Finally, identifying a relationship between hair CORT levels and sustained emotional distress in the late post-injury period also may reveal an important and potentially modifiable contributor to adverse long-term health outcomes in this population.

**\* When TIRR Memorial Hermann's Brain Injury and Stroke Program was re-designated a Traumatic Brain Injury Model System in 2012 by the National Institute on Disability and Rehabilitation Research, the program received a \$2.2 million federal grant, a portion of which is funding this clinical trial.**



innovation makes the Mischer Neurorehabilitation team a leader in the post-acute treatment of neurologic conditions.

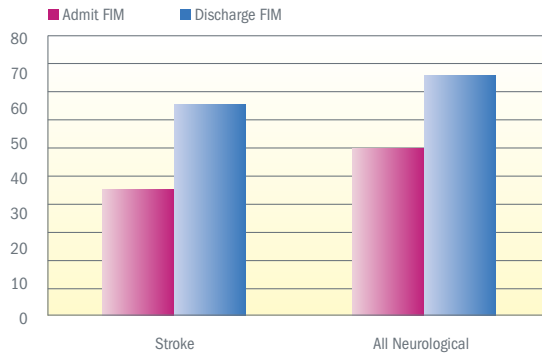
#### **TIRR MEMORIAL HERMANN**

An international leader in medical rehabilitation and research for more than 50 years, TIRR Memorial Hermann is a model for interdisciplinary rehabilitation services, patient care, education and research. The hospital's Brain Injury and Stroke Program has been designated a Traumatic Brain Injury Model System (TBIMS) with funding from the National Institute on Disability and Rehabilitation Research (NIDRR) since 1987, and is one of only 16 in the nation. For 24 consecutive years, *U.S. News & World Report* has named the hospital to its list of "America's Best Hospitals." In 2013, TIRR Memorial Hermann was ranked third in the nation.

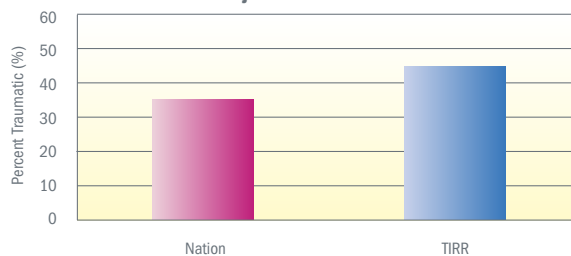
Research done at the hospital is conducted by physicians and scientists, and also by therapists,

nurses, the chaplain and residents as they advance their knowledge in subspecialty areas of rehabilitation medicine. The Brain Injury Research Center (BIRC) brings together world-renowned researchers to study the complicated facets of recovery from brain injury, leveraging resources from NIDRR to conduct research identifying effective treatments. Last year, the Spinal Cord Research Program broadened its team with the addition of experts in cognitive and psychosocial research. These new faculty use a holistic approach to studying various aspects of recovery for people with spinal cord injury and disorders across the lifespan, and identify new ways to improve function and quality of life. The Independent Living Research Utilization (ILRU) program is a national center for information, training, research and technical assistance in independent living. Ongoing research at the UTHealth Motor Recovery Lab at TIRR Memorial Hermann revolves around spasticity management, robotic therapy, neural interface and noninvasive brain stimulation.

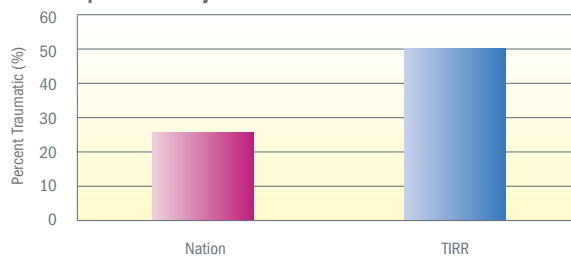
**Neurorehabilitation:  
Functional Independence Measure Change**



**Traumatic Brain Injuries Treated**



**Spinal Cord Injuries Treated**



Source: Chart data based on calendar year 2012

In 2013, with the completion of the TIRR Memorial Hermann Research Center, all of the hospital's research programs came together under one roof for the first time in the institution's history. The proximity of researchers fosters discussion, exchange of ideas and cross-pollination between research projects and clinical care, and ensures continuous two-way communication between clinicians and researchers throughout the entire investigation process. It also allows clinicians to put new knowledge to work more quickly and effectively to advance the care of patients.

Although the medical acuity of patients is much higher than in most rehabilitation facilities nationwide, TIRR Memorial Hermann consistently has significant, positive functional independence measure (FIM) change scores due to innovations in therapy and equipment. In addition to two Restorative Therapies FES (functional electronic stimulator) bikes, Bioness® hand rehabilitation and foot drop systems, the VitalStim Experia™ clinical unit and IOPI Medical's Iowa Oral Performance Instrument, the hospital has have added a closed-loop body weight support system by Bioness, called the Vector Elite, in its main therapy gym. The system offers patients a supported environment for training in balance, gait, transitional movement, up and down stairs, and prone activities or floor-to-standing support. The closed-loop system allows the patient to walk continuously in the gym environment for more than 100 feet of track.

We have acquired and trained with two robotic exoskeleton devices for future research or clinical use – Ekso™ and ReWalk™. Our physical therapy team has collaborated with physician leaders in the Spinal Cord Injury Program and received a TIRR Memorial Hermann Innovations grant to support a pilot study with the devices.

In addition, our weekend therapy program and “seven meaningful days” philosophy has allowed our teams to improve efficiency of care delivery, resulting in greater functional progress for patients. We began a late-shift therapy program in 2013, with six therapists working an alternative schedule from noon to 8:30 p.m. to better address functional therapies on the unit. Our speech-language pathologists completed skill training in fiber-optic endoscopic evaluation of swallowing (FEES) and have implemented these effective assessments and treatments fully into care.

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

TIRR Memorial Hermann Adult and Pediatric Outpatient Rehabilitation logged more than 85,000 outpatient therapy visits during the fiscal year in four locations: Kirby Glen, Memorial City Medical Center, Memorial Hermann Northwest Hospital and Memorial Hermann The Woodlands Hospital. Staff members provide comprehensive physical, occupational and speech therapy as well as neuropsychology, support groups, counseling and individualized training to prepare families and caregivers for taking on the additional responsibilities of caring for patients after inpatient discharge.

Innovative technology in use at the Kirby Glen center includes Bioness equipment and the Lokomat®, the world’s first driven-gait orthosis. The center is one of only two facilities in Texas with pediatric legs for the Lokomat.

Considered one of the nation’s premier brain injury rehabilitation programs, the Challenge Program at TIRR Memorial Hermann Adult and Pediatric Outpatient Rehabilitation at Kirby Glen and TIRR Memorial Hermann-The Woodlands is one of only a few programs in the country offering a holistic, community reintegration model using interdisciplinary teams of professionals to manage the rehabilitative care of brain-injured patients. The program provides support for return to work, return to academics and return to independence with a specialized team of physical, occupational, speech and vocational therapists, as well as licensed clinical social workers and neuropsychologists.

In 2013, TIRR Memorial Hermann expanded its reach across Houston through a comprehensive, integrated rehabilitation network that reaches beyond the Texas Medical Center to outlying communities where people live and work. During the year, the rehabilitation hospital opened new outpatient clinics at Memorial City Medical Center, Memorial Hermann Northwest Hospital and Memorial Hermann The Woodlands Hospital. All Memorial Hermann inpatient and outpatient rehabilitation services are now organized under the leadership of TIRR Memorial Hermann, ensuring the availability of expert rehabilitative care throughout Houston. Inpatient units serve the community at Memorial Hermann Northwest Hospital, Memorial Hermann Rehabilitation Hospital-Katy, Memorial Hermann Southeast Hospital, Memorial Hermann Southwest Hospital, Memorial Hermann-Texas Medical Center and TIRR Memorial Hermann-The Woodlands.



# Neurotrauma and Neuroscience Critical Care



The Mischer Neuroscience Institute's Neurotrauma and Neuroscience Critical Care Program is internationally recognized for the treatment of high-acuity brain and spinal cord injuries. Affiliated physicians manage more neurotrauma cases than any other center in the southwestern United States, with neurointensivists and experienced mid-level practitioners staffing a dedicated Neurotrauma ICU around the clock to provide ongoing intensive care to critically ill patients. Our faculty and program continues to grow, with more than 3,400 brain and spine trauma patients treated in the first nine months of 2013.

MNI's Neurotrauma and Neuroscience Critical Care Program is an international leader in research conducted

on innovative treatments following neurotrauma, including participation in several multicenter trials. Investigators at MNI and TIRR Memorial Hermann are studying biomarkers for pain in spinal cord injury, cranioplasty outcome following decompressive craniectomy, adult stem cell therapy in severe traumatic brain injury (TBI) and acute stroke patients, the effects of erythropoietin on cerebrovascular dysfunction and anemia in TBI, neural and behavioral sequelae of blast-related TBI, progesterone for the treatment of TBI, the safety and pharmacokinetics of riluzole in patients with traumatic acute spinal cord injury and other basic science research and clinical trials.

In 2013, the Mischer Neuroscience Institute became the first in Texas to receive the highly coveted Comprehensive Stroke Center certification from The Joint Commission (TJC) and the American Heart Association/American Stroke Association. MNI's Neurotrauma ICU team provides comprehensive high-level care for all neurological and neurosurgical vascular emergencies and illnesses, with more than 3,800 vascular cases treated annually. With a dedicated ICU team in a closed-unit model, we are the primary care team for surgical vascular patients, providing leading-edge care 24/7.

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

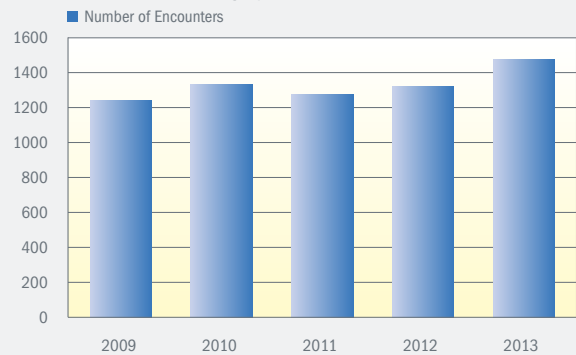
## QUALITY & OUTCOMES MEASURES

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

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

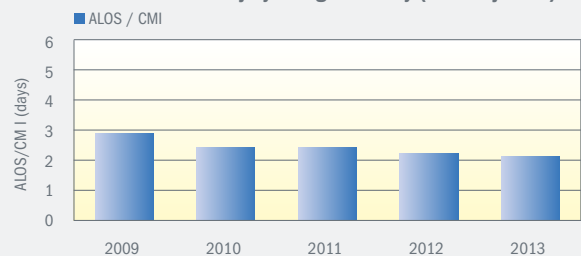
Memorial Hermann Life Flight, which is accredited by the Commission on Accreditation of Medical Transport Services, provides high-quality care and safe air transport for critically ill and injured patients. Our Adult and Children's Transport Teams operate within a 300-mile radius of Houston using ground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

### Traumatic Brain Injury Volumes



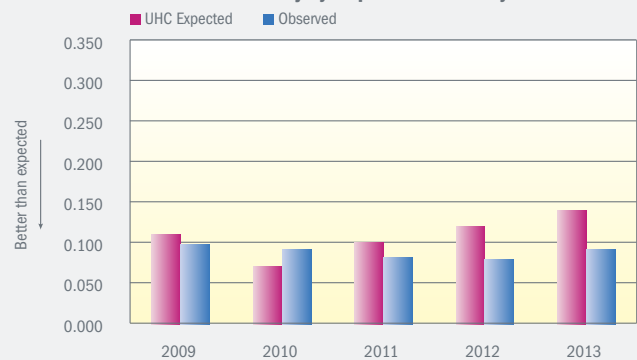
Source: Chart data based on DRG per fiscal year

### Traumatic Brain Injury: Length of Stay (CMI Adjusted)



Source: Chart data from the University HealthSystem Consortium

### Traumatic Brain Injury: Inpatient Mortality



Source: Chart data from the University HealthSystem Consortium

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

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

*Director, Mischer Neuroscience Institute*

*Professor and Chair, Vivian L. Smith Department of Neurosurgery*

UTHealth Medical School

**Background:** Traumatic brain injury (TBI) resulting in subdural hematoma occurs in more than 40,000 Americans annually with up to 70 percent of these injuries resulting in death or severe disability. Therapies to improve outcome are desperately needed. Standard treatment includes the surgical removal of the hematoma; however, after evacuation, an ischemia-reperfusion injury occurs at the time of brain tissue reperfusion. Hypothermia is proposed to reduce the effects of this ischemia-reperfusion injury. In fact, retrospective subgroup analysis of NABIS:H I and NABIS:H II hypothermia trials revealed that TBI patients undergoing surgical evacuation of intracranial hematomas who were treated with hypothermia had significantly improved neurologic outcomes compared to patients treated with normothermia. The HOPES Trial aims to test whether treatment with early hypothermia prior to surgical evacuation of a subdural hematoma improves patients' outcomes.

**Primary Objective:** The primary objective is to determine if rapid induction of hypothermia prior to emergent craniotomy for traumatic subdural hematoma (SDH) will improve outcome as measured by Glasgow Outcome Scale-Extended (GOSE) at 6 months.

**Methods:** This randomized, prospective trial will study the effect of very early cooling in patients undergoing surgical evacuation of acute subdural hematomas (35°C prior to opening the dura followed by maintenance at 33°C for a minimum of 48 hours). Intravascular cooling catheters (Thermogard XP Device, Zoll) will be utilized to induce hypothermia or to maintain normothermia.

**Sites/Collaborators:** UTHealth Medical School and Memorial Hermann-Texas Medical Center; The University of Pittsburgh Medical Center and UPMC Presbyterian; The University of Miami and Ryder Trauma Center, Jackson Memorial Hospital; Berry Consultants; and Baylor College of Medicine.

# Spine Disorders

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

With the addition of nationally and internationally renowned neurosurgeon Daniel H. Kim, M.D., FAANS, FACS, to the MNI team, we significantly expanded our spinal neurosurgery program and added expertise in reconstructive peripheral nerve surgery. Dr. Kim is a fellowship-trained, board-certified neurosurgeon with

expertise in minimally invasive spinal surgery, both endoscopic and robotic; peripheral nerve surgery; and complex spinal reconstruction. A clinical and educational leader in his field, Dr. Kim has been recognized with numerous awards and honors, authored hundreds of papers and published 16 surgical textbooks, many of which are used at leading medical schools to teach standard-of-care techniques for neurosurgery. Two new textbooks were published in 2013: *Surgical Anatomy and Techniques to the Spine* and *Lumbosacral and Pelvic Procedures*. He is a preeminent researcher in peripheral nerve repair through nerve transfer and nerve graft, and is also recognized for his work in neurorehabilitation through robotics and cortical stimulation, spinal biomechanics and innovative neuromodulation treatments for chronic pain.







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

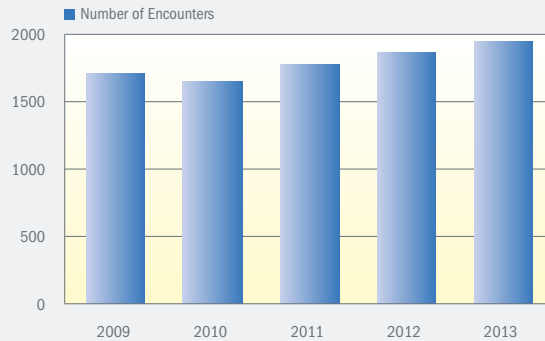
The Center's clinicians provide exceptional care for patients with traumatic spine injury, including the 10 to 20 percent of admissions through the Level I Texas Trauma Institute that involve neurological damage.

Based on benchmark University HealthSystem Consortium data, the Spine Center's inpatient mortality for spine trauma, degenerative spine disease and elective spine surgery has been consistently lower than expected for the past six years. As faculty at UTHealth Medical School, surgeons at the Center educate the next generation of spine experts and shape the future of medicine through basic science research, clinical discovery and the development of new, breakthrough treatments.

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

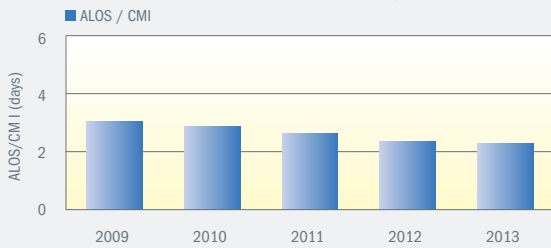
Research under way at the MNI Spine Center is focused on bringing promising therapies for spinal cord injury (SCI) patients from the laboratory to clinical trials in a manner that will provide evidence of effectiveness, with maximum safety, to patients undergoing treatment. Investigators are currently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

### Spine Volumes



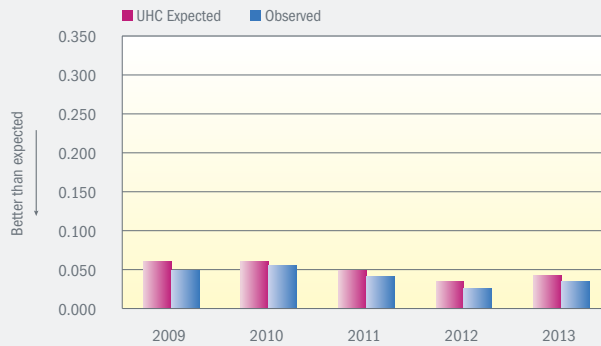
Source: Chart data based on DRG per fiscal year; adult populations

### Spine Trauma: Length of Stay (CMI Adjusted)



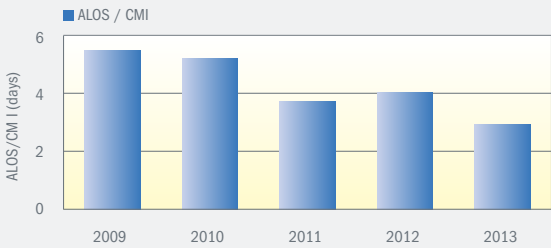
Source: Chart data from the University HealthSystem Consortium

### Spine Trauma: Inpatient Mortality



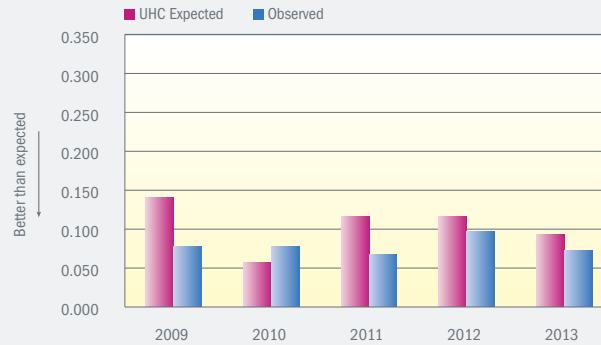
Source: Chart data from the University HealthSystem Consortium

### Spine Tumors: Length of Stay (CMI Adjusted)



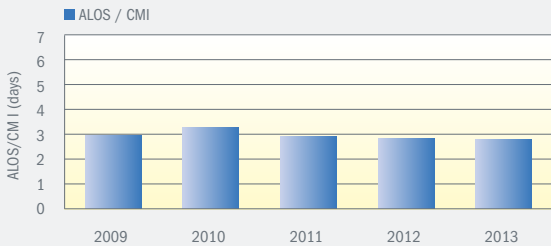
Source: Chart data from the University HealthSystem Consortium

### Spine Tumors: Inpatient Mortality



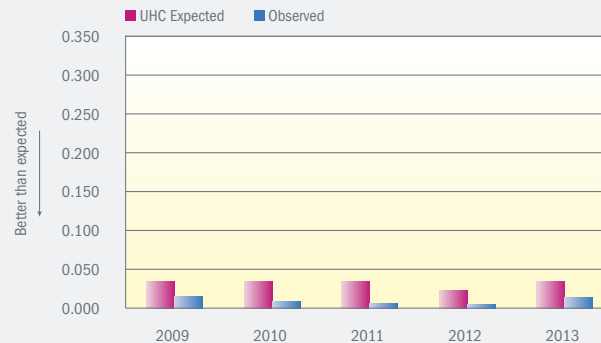
Source: Chart data from the University HealthSystem Consortium

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



Source: Chart data from the University HealthSystem Consortium

### Spine Degenerative or Elective: Inpatient Mortality



Source: Chart data from the University HealthSystem Consortium



*Research  
and Innovation*







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

These 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 2012-2013 fiscal year, researchers at the Institute and UTHealth Medical School received more than \$11.5 million in 67 grants and contracts. The following listing is a sample of ongoing or recently completed research projects.

## **CEREBROVASCULAR**

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

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

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

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

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

All study participants in this randomized multicenter trial will be treated with rt-PA (0-3 hours or 0-4.5 hours) and randomized to one of three study arms: intravenous tPA

along with low-dose Argatroban, high-dose of Argatroban or standard IV tPA alone. This trial is designed to estimate overall treatment benefit among stroke patients randomized to receive one of the three treatments. The study will also verify the safety of a low-dose combination of Argatroban and rt-PA, test the safety of a high-dose combination treatment and assess the rates of early recanalization to determine treatment effect and assess reliability in predicting outcomes of the drug combination.

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

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

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



**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 the molecular mechanisms that lead to disease.

**Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST)**PRINCIPAL INVESTIGATOR: **Nicole Gonzales, M.D.**

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

**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.

**Delay in Evaluation and Treatment of Posterior Circulation Stroke Compared with Anterior Circulation Stroke**PRINCIPAL INVESTIGATOR: **Amrou Sarraj, M.D.**

Failure to recognize early symptoms of acute posterior circulation cerebral ischemia may delay timely diagnosis and treatment. In this study, researchers are investigating whether there were differences in symptom onset in arrival at our Emergency department (ED), arrival to neurology evaluation, and ED arrival to treatment between patients with posterior circulation ischemia (PCI) versus anterior circulation ischemia (ACI). We are also assessing whether various symptoms are associated with differences in time to evaluation or time to treatment between ACI and PCI.

**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.

**Ethnic/Racial Variation in Intracerebral Hemorrhage (ERICH)**PRINCIPAL INVESTIGATOR: **Nicole Gonzales, M.D.**

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

### **Evaluation of Presidio and Cerecyte Coils in Large and Giant Aneurysms**

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

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

### **Genetic 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 increased risk of developing disease.

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

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

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



### **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.

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

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

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





### **Intra-arterial Vasospasm Trial (IVT)**

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

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

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

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

### **Mobile Stroke Unit**

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

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

### **Optimizing Prediction Scores for Poor Outcome After Intra-arterial Therapy for Anterior Circulation Acute Ischemic Stroke**

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

Intra-arterial therapy (IAT) is an approach to promote recanalization of large artery occlusions (LAO) in acute ischemic stroke (AIS) but is resource intensive. Previous studies evaluated different variables that affect clinical

outcome after IAT. To better identify patients who have poor outcomes despite IAT, we compared the performance of previous predictive scoring systems that relied either on clinical or imaging variables in patients undergoing IAT. We then combined imaging and clinical variables to optimize a score that would better predict poor outcome after IAT for AIS.

### **Pleiotropic Transcription Factors as a Target for Intracerebral Hemorrhage Treatment**

PRINCIPAL INVESTIGATOR: **Jaroslawn 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.

### **PURSUIT: Pre-hospital Utility of Rapid Stroke Evaluation Using In-ambulance Telemedicine**

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

This trial is studying the feasibility of using telemedicine to evaluate patients with acute stroke in the ambulance.

### **Refining Prediction Scores for Poor Outcome After Intra-arterial Therapy for Anterior Circulation Acute Ischemic Stroke: Adding Collateral Status Improves Prediction Scores**

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

Intra-arterial therapy (IAT) is widely practiced, but is of unproven benefit. To improve patient selection for IAT, we sought to refine the HIAT2 (Houston Intra-Arterial Therapy 2) score to include the presence of collateral circulation to devise a HIAT3.

### **Risk of Hemorrhage in Patients on Warfarin Who Are Treated with Tissue Plasminogen Activator for Acute Ischemic Stroke**

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

Tissue plasminogen activator (tPA) remains the only proven treatment for ischemic stroke but concurrent use of warfarin at the time of stroke poses a potential risk for symptomatic intracerebral hemorrhage (sICH). Few studies have addressed this risk. We studied all patients admitted to our service who were on warfarin at the time of their acute ischemic stroke and were treated with IV tPA in order to define incidence and risk factors of sICH.

### **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.



#### **Study of ALD-401 Derived from Autologous Bone Marrow Delivered via Intracarotid Infusion in Ischemic Stroke Patients**

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

This Phase I trial involves administering bone marrow-derived purified stem cells by intra-arterial infusion 13 to 19 days after an ischemic stroke. This study is the first ever to harvest an acute stroke patient's own stem cells from the iliac crest of the leg, separate them and inject them back into the patient intravenously as a potential new treatment for stroke.

#### **Study to Examine the Effects of MultiStem in Ischemic Stroke**

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

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

#### **Thrombolysis in Pediatric Stroke Study (TIPS)**

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

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

#### **Tissue Plasminogen Activator for Acute Cerebellar Strokes**

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

Cerebellar infarction is an important subcategory of ischemic stroke. Tissue plasminogen activator (tPA) remains the only proven treatment for ischemic stroke. We hypothesized that pure cerebellar strokes are less often treated with tPA. We aimed to determine the percentage of cerebellar strokes treated with tPA and the main reasons why patients with cerebellar strokes are not treated with tPA.

#### **Using Propensity Scores to Simulate a Randomized Controlled Trial to Assess the Added Benefit of Combining Intra-arterial Therapy with IV tPA**

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

In light of recent studies, the superiority of combining intra-arterial therapy (IAT) with IV tPA compared with IV tPA alone is yet to be established. To test the additive value of treating patients with IAT, we compared outcomes in patients treated with IV tPA with those who received IV tPA followed by intra-arterial intervention in a novel study design.

## **EPILEPSY**

### **Analysis of the Role of Sv2a Phosphorylation in Epilepsy**

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

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

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

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

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

### **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.

### **PECA Visiting Professorship to Central America**

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

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

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

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

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

### **Quantitative Analysis of Electroencephalogram in Epilepsy**

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

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

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

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

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

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

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

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



## **MOVEMENT DISORDERS AND NEURODEGENERATIVE DISEASES**

### **Amyloid-beta Oligomers and Alzheimer's Diagnosis**

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

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

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

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

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

Prospective, open-label, 1:1 randomized trial evaluating two dosing schedules of Xeomin [Short Flex and Long Flex] in subjects who report that they receive therapeutic benefit from onabotulinumtoxinA (Botox®) treatment for less than 10 weeks.

### **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.

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

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

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

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

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

Enroll-HD is an observational, prospective, multicenter study with sites in North America, Latin America, Europe, Asia, Australia and New Zealand. The study has three aims: to improve the understanding of the dynamic phenotypic spectrum and the disease mechanisms of Huntington's disease (HD) by collecting natural history data covering the cognitive, behavioral and motor domains that allow insights into the neurobiology of HD, collecting data and biologic samples to identify genetic and environmental factors influencing and/or modifying the HD phenotype and disease progression, and promoting studies that may provide clues to the pathogenesis of HD; to promote the development of evidence-based guidelines to inform clinical decision-making and improve health outcomes for participants and their family units; and to provide a platform to support the design and conduct of clinical trials.

### **Epigenetic Changes in Alzheimer Disease**

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

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

### **Identifying Risk Factors for PTSD and Testing Preventions**

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

A study of patients coming to the Memorial Hermann-Texas Medical Center Emergency Department after a traumatic event to discover the risk factors for developing post-traumatic stress disorder (PTSD) and to test treatments to prevent its development.

### **Measuring the Amyloid of Alzheimer Disease in Blood**

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

The amyloid deposited in the brains of patients with AD can also be found in their blood in minute quantities. Dr. Soto is developing a very sensitive assay to determine whether blood amyloid levels can be used to diagnose AD or to test whether treatments for AD are effective.

### **Pathogenesis, Transmission and Detection of Zoonotic Prion Diseases**

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

Researchers are studying the pathogenesis and routes of propagation of bovine spongiform encephalopathy and



chronic wasting disease, and developing novel strategies for the detection of infected animals.

### **Pathogenic Mechanism of Prion Disease**

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

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

### **PET Imaging for Alzheimer Dementia**

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

It can be difficult to diagnose Alzheimer disease during life. This study is testing whether PET imaging can be used to identify persons depositing the amyloid of AD in their brains before they have AD, i.e., when they have just memory loss.

### **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.

### **Phase 3, Multicenter, Double-Blind, Placebo-Controlled, Single-Treatment Efficacy and Safety Study of MYOBLOC® (Part A) Followed by Open-Label, Multiple-Treatment With MYOBLOC (Part B) in the Treatment of Troublesome Sialorrhea in Adult Subjects.**

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

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

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

### **Phase 3b, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of DYSPORT Using 2mL Dilution in Adults With Cervical Dystonia.**

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

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

### **Phase 3b, Prospective, Multicenter, Open-Label Extension Study To Assess Long Term Safety and Effectiveness of DYSPORT Using 2 mL Dilution In Adults With Cervical Dystonia**

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

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

(The two above are part of the same study; first listing is a placebo-controlled study and the second is an open-label extension.)

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

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

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

### **Potential Biomarkers for Parkinson's Disease**

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

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

### **Transmissible Component to Alzheimer Dementia**

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

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

### **MULTIPLE SCLEROSIS**

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

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

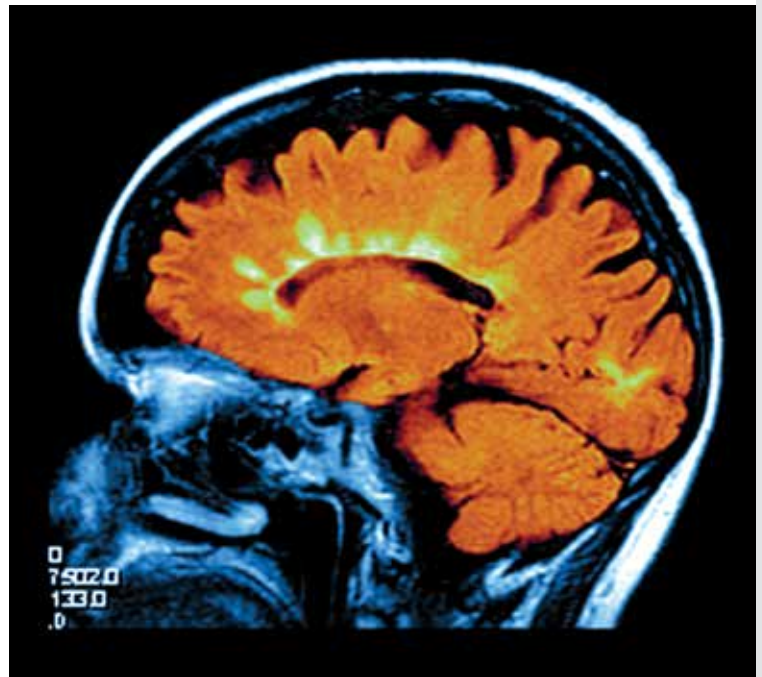
This study aims to develop and apply a multimodal MRI approach to the evaluation of cognitive impairment in patients with multiple sclerosis.

#### **Phase IV Randomized, Double-blind, Multicenter, Parallel-group Study, Comparing the Efficacy and Safety of FTY-720 0.5 mg Administered Orally Once Daily versus 0.25 mg versus Glatiramer Acetate 20 mg sc qd in Patients with Relapsing Remitting Multiple Sclerosis**

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

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

The above trials are evaluating the first oral drug FDA approved for treatment of relapsing forms of multiple sclerosis. The aims of the phase IV trials are to evaluate



a lower dose of the drug to decrease currently seen side effects and to evaluate the drug in the progressive type of multiple sclerosis for which there is no FDA-approved treatment.

#### **Combination Therapy in Multiple Sclerosis**

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

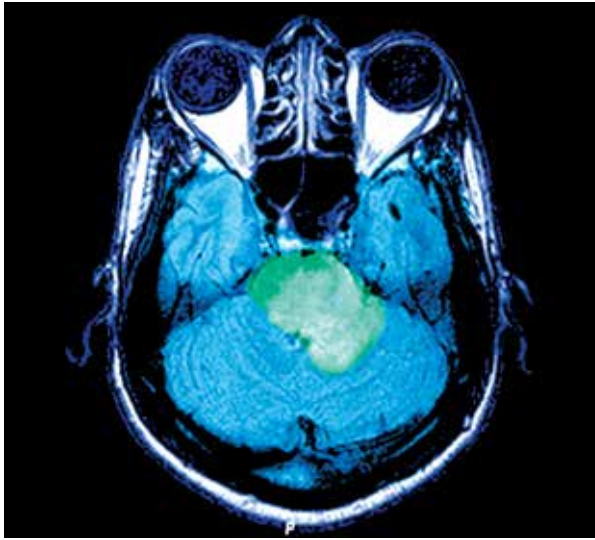
This study is determining if the combination of interferon beta-1a and glatiramer acetate is superior to either drug as monotherapy in relapsing-remitting multiple sclerosis.

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

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

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





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

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

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

**Pilot Clinical Trial of ACTHarGel 14 days Subcutaneous (SQ) versus ACTHarGel Five Days SQ for the Treatment of MS Exacerbations**

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

We will determine if ACTH injections given for 14 days are superior to injections given for five days for recovery from MS attacks. ACTH injections are an FDA-approved treatment for MS attacks but it is not known if treatment for more than five days improves recovery. We will examine MR brain scans and immune function periodically for 90 days after MS attack to determine if ACTH improves MR brain scans and immune function.

**Serial Magnetic Resonance Spectroscopy in Multiple Sclerosis**

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

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

**NEUROMUSCULAR DISORDERS**

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

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

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

**International GBS Outcome Study (IGOS)**

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

Researchers will learn more about clinical and biological factors that influence the course of the disease Guillain-Barré syndrome (GBS), the outcome of patients with GBS and find factors that could help diagnose GBS sooner. The purpose is to create new knowledge for the benefit of future patients and society in general.

## NEURO-ONCOLOGY

### **NovoTTF™-100A Device for Patients with Newly Diagnosed Glioblastomas**

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

The study is a pivotal (analogous to drug Phase III), randomized, controlled trial designed to test the efficacy and safety of a new medical device, the NovoTTF-100A, for newly diagnosed GBM patients when used in combination with temozolomide as compared to temozolomide alone. Enrollment for this study will be 4 to 7 weeks following radiation and temozolomide treatment. Treatment will continue until second progression or 24 months. Eligible participants must be >18 years old and screened for co-morbidities with labs. Some exclusion criteria are implanted pacemaker, defibrillator or DBS or clinically significant arrhythmias. There are other criteria that must be present to be considered eligible for this trial.

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

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

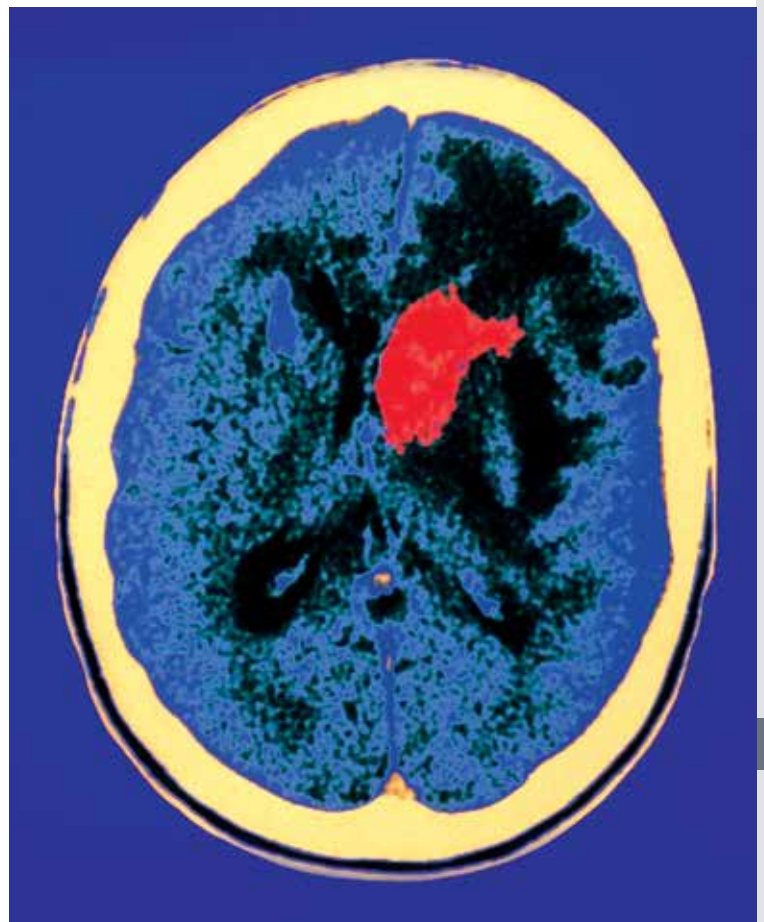
This is a randomized, double-blind Phase IIB multicenter study of the safety and efficacy of the ICT-107 vaccine in newly diagnosed patients with glioblastoma multiforme (GBM) following tumor resection. ICT-107 is an immunotherapy in which the patient's immune response will be stimulated to kill the tumor cells. Some of the patient's white blood cells (WBC) will be removed and cultured in a laboratory with purified antigens, similar to those on GBM cells. The patient's own WBC/dendritic cells (DCs) that have been exposed to the tumor antigens will then be given back to the patient as a vaccine over several months. The goal is for the ICT-107 vaccine to stimulate the patient's immune response to kill the remaining GBM tumor cells after surgery and chemotherapy. Eligible

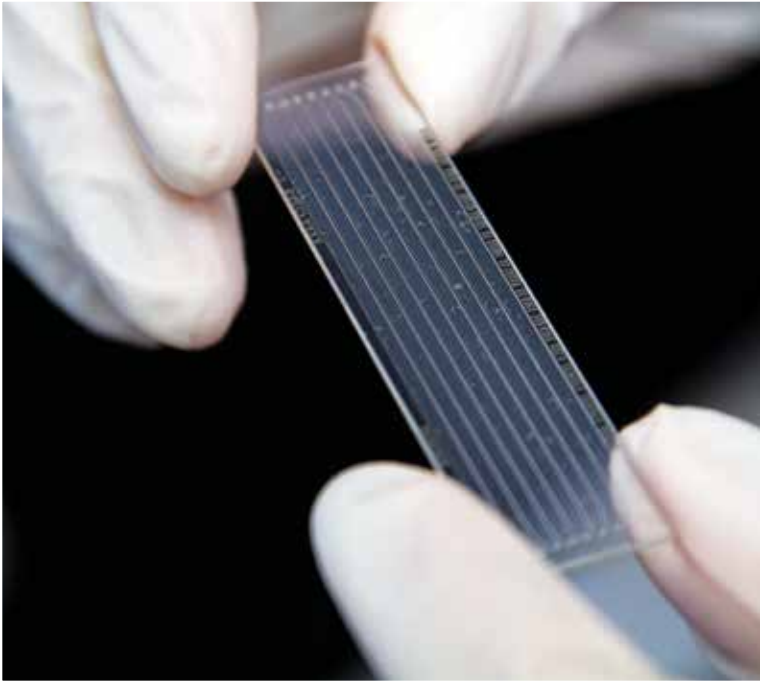
participants must be 18+ years old, with newly diagnosed glioblastoma multiforme (GBM). Patients must be consented after full tumor resection surgery and prior to starting chemo-radiation therapy. Initial screening procedures include HLA typing and apheresis to isolate peripheral blood mononuclear cells (PBMCs) to be used for the preparation of study treatment (ICT-107 and control). Patients will be randomized by age in a 2:1 ratio to ICT-107 or control.

### **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.





### **Identify New Markers and Therapeutic Targets in Brain Tumor Using Molecular and Genetic Approaches**

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

Gene profiling, microRNA profiling and proteomics will be used to identify new target molecules that can be used to develop personalized medicine.

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

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

This Phase II study will enroll patients into three groups. Group 1 are patients who have never been treated with bevacizumab. These patients will be randomly assigned to receive either rindopepimut/GM-CSF or KLH, each along with bevacizumab. Treatment assignment for Group 1 will be blinded. Group 2 and Group 2C patients are those who are refractory to bevacizumab (experienced recurrence or progression of glioblastoma while on bevacizumab or within 2 months of discontinuing bevacizumab). These

patients will all receive rindopepimut/GM-CSF along with bevacizumab. Patients will be treated until disease progression or intolerance and all patients will be followed for survival. Patients may be treated with other therapies that are not part of the study after discontinuing treatment with the study vaccine.

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

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

This open-label study will evaluate the safety and efficacy of TSC when dosed concomitantly with the standard of care (radiation therapy and temozolomide) for newly diagnosed glioblastoma in adults. All patients will receive TSC in the study. The overall objectives of this Phase 1/2 clinical study in newly diagnosed GBM patients are to evaluate the safety and tolerability, efficacy, PK profile, PFS/time to disease progression, quality of life, and overall survival in adults. The primary objective of the Phase 1 portion of the study is to evaluate the safety (DLT rate) and to define the dosing regimen of TSC for the larger Phase 2 study. The primary clinical endpoint is overall survival at 24 months and patients will be followed for up to 3 years.

### **Study Function of Zinc Transporter (ZIP4) in Brain Tumor Progression, Develop Novel ZIP4 Based Therapy for Brain Tumor**

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

Our previous studies indicate that ZIP4 plays a critical role in tumor growth and metastasis. This project will further characterize the molecular mechanism of ZIP4-induced tumor progression.

### **Study of the Role of MicroRNAs in Brain Tumor Pathogenesis**

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

The function of oncogenic and tumor suppressor microRNAs will be evaluated in brain tumor cells and tissues, and targeted therapy will be designed based on the expression profile and the function of those microRNAs.

### **NEUROREHABILITATION**

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

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

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

#### **The Use of Ventriculostomy or Hemicraniectomy as a Predictor of Rehabilitation Level of Care in Patients with Intracerebral Hemorrhage**

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

The purpose of this research project is to determine whether patients with intracerebral hemorrhage who underwent surgical intervention for increased intracranial pressure are more likely to receive post-stroke care at an inpatient rehabilitation facility, a skilled nursing facility or a long-term acute care facility.

### **NEUROTRAUMA/CRITICAL CARE**

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

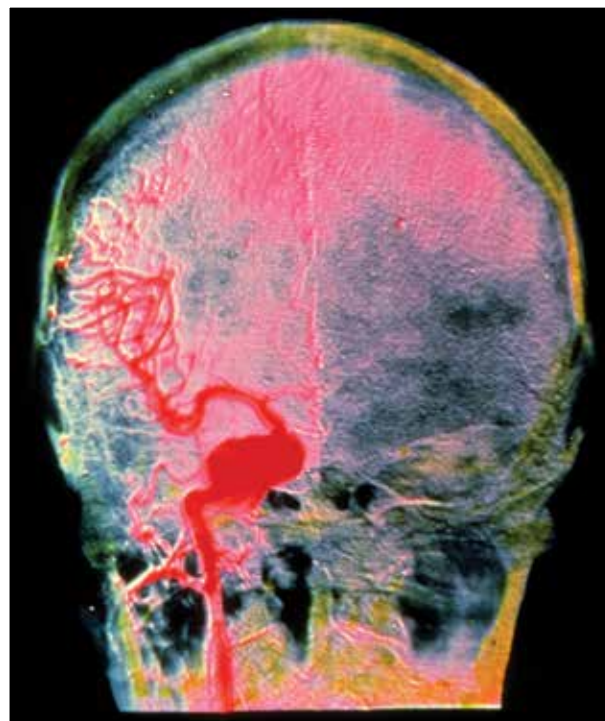
PRINCIPAL INVESTIGATOR: **H. Alex Choi, M.D.**

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

#### **A Pilot Study to Identify Biomarkers Associated with Chronic TBI**

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

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





### **Biomarkers for Pain in Spinal Cord Injury**

PRINCIPAL INVESTIGATOR: **Gigi Hergenroeder, RN**

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

### **Biomarkers Prognostic for Elevated Intracranial Pressure**

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

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

### **Combinatory Strategies to Functional Remyelination After Spinal Cord Injury**

PRINCIPAL INVESTIGATOR: **Qi Lin 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 (SCI).

### **CSF Diversion Assessment and Ventriculoperitoneal Shunt Dependence Study**

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

This study aims to analyze the relationship between the total amount of CSF diversion and long-term ventriculoperitoneal shunt dependence. The important variables for investigation are red blood cell clearance and the ventriculoperitoneal shunt dependence.

Evaluation of predictors of VP shunt dependence is done particularly for patients with high-grade aneurysmal subarachnoid hemorrhage.

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

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

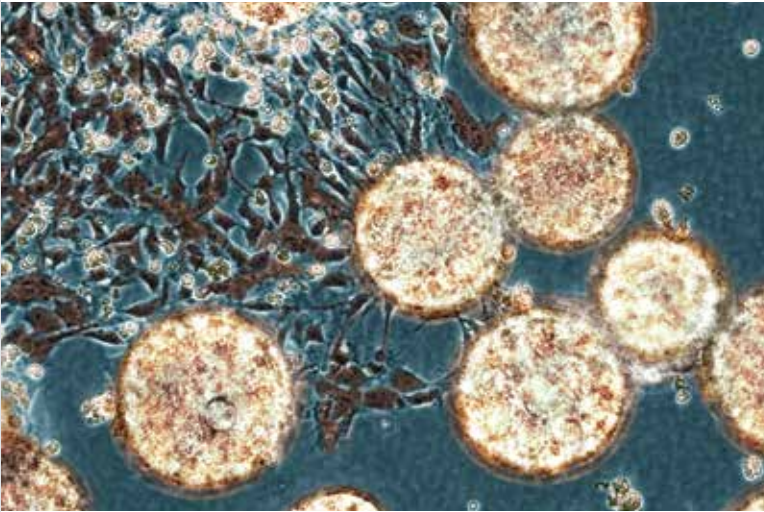
The advancement of critical care has brought to the forefront ethical issues regarding continuation of aggressive medical measures to prolong life in the severely brain-injured patient. Studies have shown minorities, especially black or Hispanic individuals, seek more care at the end of life. We are studying this disparity in the acutely brain-injured patients and their families and exploring the possible social/cultural/religious reasons for these differences.

### **Gene Transcription and Regulation of Stem Cell Differentiation**

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

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





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

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

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

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

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

This randomized, prospective trial will study the effect of very early cooling in patients undergoing surgical evacuation of acute subdural hematomas (35°C prior to opening the dura followed by maintenance at 33°C for a minimum of 48 hours). Intravascular cooling catheters (Thermogard XP Device, Zoll) will be utilized to induce hypothermia or to maintain normothermia. The primary objective is to determine if rapid induction of hypothermia prior to emergent craniotomy for traumatic subdural hematoma (SDH) will improve outcome as measured by Glasgow Outcome Scale-Extended (GOSE) at 6 months.

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

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

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

### **Hyperoxia and Delayed Cerebral Infarction in Subarachnoid Hemorrhage**

PRINCIPAL INVESTIGATOR: **Sang-Beom Jeon, M.D., H. Alex Choi, M.D., and Kiwon Lee, M.D.**

Hyperoxia has been proposed as a potential therapeutic option for brain injury and has been correlated with worse outcomes after brain injury. We are studying the effects of hyperoxia on brain physiology and clinical outcome after subarachnoid hemorrhage.

### **Intrathecal Nicardipine Injection via External Ventricular Drain in Aneurysmal Subarachnoid Hemorrhage**

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

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



**Norepinephrine and TBI-associated Prefrontal Dysfunction: Research Supplement to Promote Diversity in Health-related Research**

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 National Institutes of Health grant is particularly focused on the investigation of the dysregulated neurotransmitter signaling (norepinephrine and serotonin) in the prefrontal cortex.

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

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

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







### **Novel Neuroprotection Therapeutic Approaches for Spinal Cord Injury**

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

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

### **Novel Restorative Therapy for Spinal Injury**

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

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

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

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

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

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

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

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

## **OTHER**

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

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

This investigation involves an integrated application of functional MRI, diffusion tensor imaging tractography and intra-cranial electrophysiology to understand the mechanisms of language production.

### **Acupuncture Therapy for Neurological Disorders**

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

In collaboration with Chinese scientists, this study tests the effects of electroacupuncture (EA) on several neurological disorders including stroke, epilepsy and Parkinson's disease. EA is a relevant analogy of deep brain stimulation (DBS). The major difference between these two modalities is the area of stimulus, i.e., brain (DBS) versus body (acupuncture).



### **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, RN**

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 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.

### **Fronto-Basal-Ganglia Circuits for Self-Control**

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

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

### **Hypoxic Dysfunction of Cortical Neurons**

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

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

### **Intracranial Electrophysiology and Connectivity of Language Regions in Humans**

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

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



### **Nano-engineered, Multichannel Scaffolds for Axon Regeneration**

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

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

### **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, so called “tip-of-tongue” phenomena.

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

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

This National Institutes of Health-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-Texas Medical Center in the spring of 2009.



### **Representation and Binding of Spatial and Temporal Episodic Memories in Human Hippocampus**

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

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



# Selected Publications

## **BROD, STALEY**

Barreto AD, Brod SA, Bui T, Jemalka J, Kramer LA, Ton K, Cohen AM, Lindsey JW, Nelson F, Narayana PA, Wolinsky JS. Chronic Cerebrospinal Venous Insufficiency: Case-Control Neurosonography Results. *Ann Neurol*. 2013 Jun;73(6):721-8.

Brod SA, Barreto AD, Kramer L, Cohen A, Bui T-T, Jemelka J, Ton K, Lindsey J, Nelson F, Narayana P, Wolinsky J. Chronic cerebrospinal venous insufficiency: masked multimodal imaging assessment. *Mult Scler*. 2013 Oct 19(11):1499-1507.

Brod SA, Bauer V. Ingested (oral) Neuropeptide Y Inhibit Acute EAE. *J Neuroimmunol*. 2012 Sep 15;250(1-2): 44-49.

Brod SA, Bauer V. Ingested (oral) thyrotropin releasing factor (TRH) Inhibits EAE. *Cytokine*. 2013 Jan;61: 323-328.

## **CHOI, H. ALEX**

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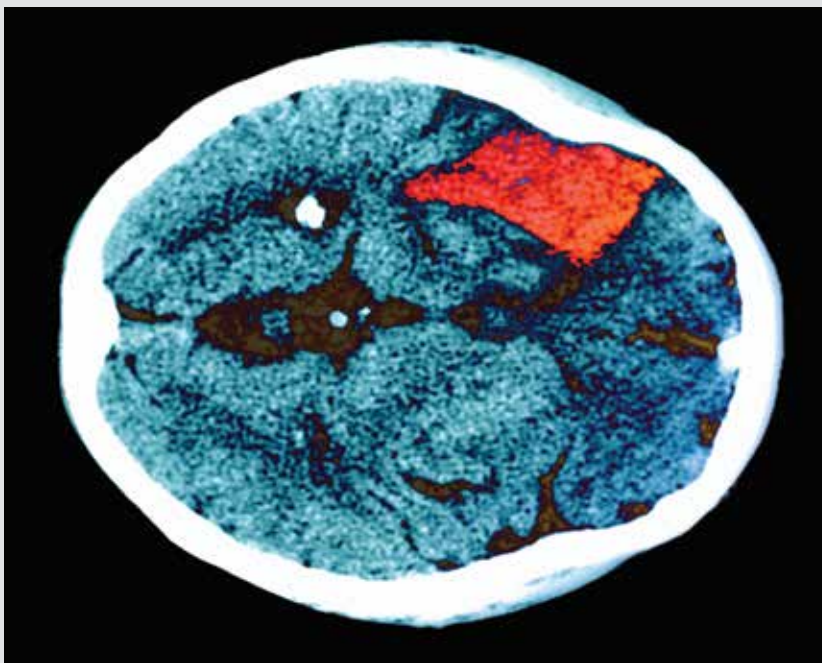
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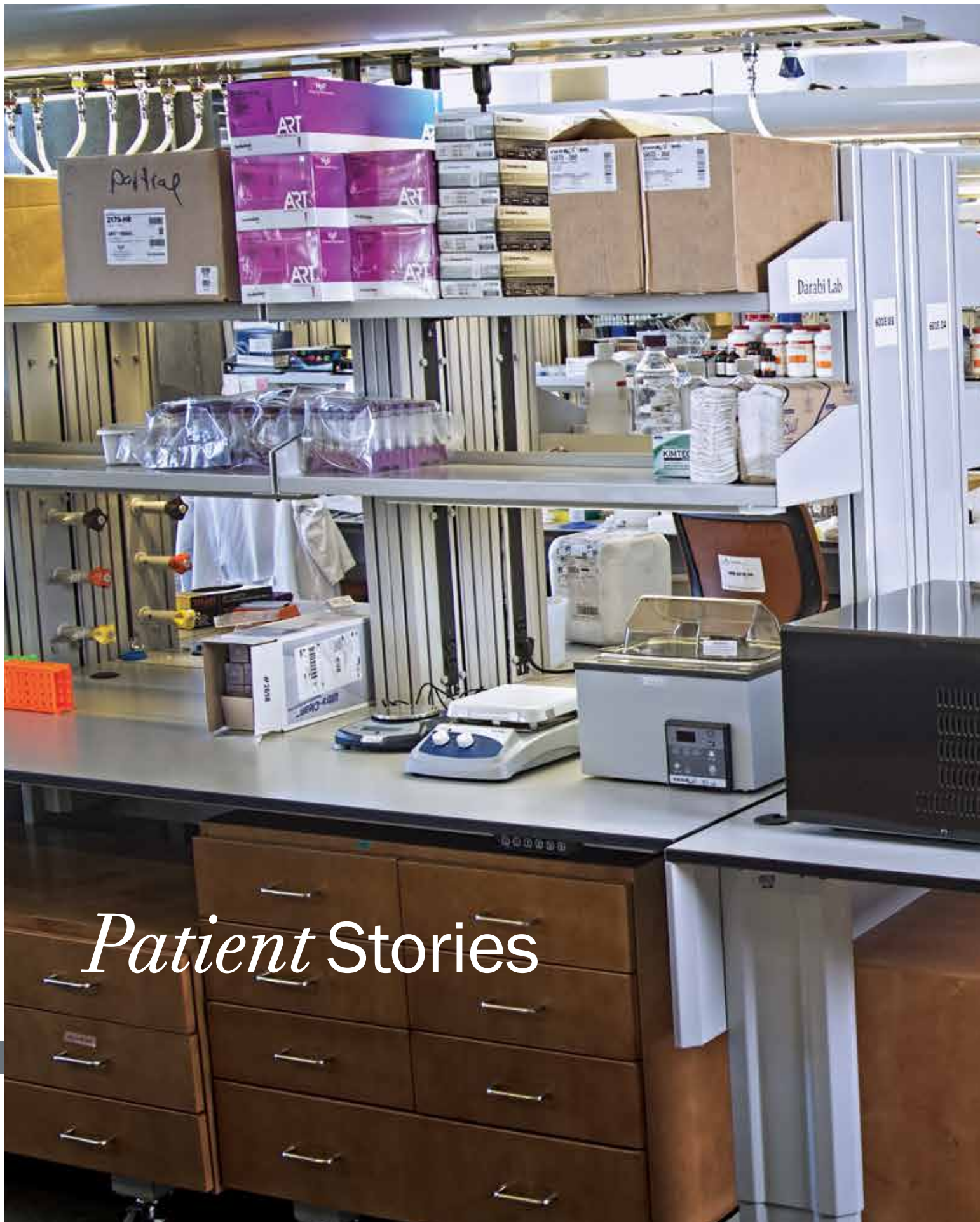
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# *Patient Stories*





## Lindsay Holstead: Back in the Saddle

Equestrian Lindsay Holstead was leading her warmblood to the pasture on an unseasonably cold day in April 2013, when he became rambunctious and began to buck. “He’d torn a ligament eight months earlier and had been exercised daily on a treadmill, but hadn’t been turned out for all that time,” Holstead says. “So he was especially frisky. He bucked and bumped into me. I lost my balance and fell, and his hoof hit me in the right side of the forehead where it curves toward the temple, shattering my skull.”

Holstead was unconscious when the stable in Magnolia, Texas, called 911. Paramedics with the Montgomery County Fire and Rescue Service arrived on the scene, saw the skull fracture, splintered bone and scalp and facial lacerations and called Memorial Hermann Life Flight® for transport to Memorial Hermann-Texas Medical Center’s Level I Texas Trauma Institute.

At the Institute, a CT scan showed a right frontal depressed skull fracture, subarachnoid hemorrhage, subdural hematoma and fractures of the right maxillary sinus, inferior orbit wall and greater sphenoid wing. Neurosurgeon Karl M. Schmitt, M.D., an assistant professor of neurosurgery at UTHealth Medical School, performed a craniotomy. In a four-hour surgery, he debrided the facial laceration and skull fracture and repaired a tear in the dura, the tough fibrous membrane that surrounds the brain and spinal cord.

Holstead was taken to Mischer Neuroscience Institute’s Neurotrauma ICU in serious but stable condition. After two days in intensive care, she was transferred to Memorial Hermann-TMC’s Signature Suites. Two days later she was released to home.

“Dr. Schmitt saved my life,” she says. “Everyone did an outstanding job. I bounced back very well and quickly. I’m glad to be here, period.”

Two weeks after her surgery she followed up with neurosurgeon Scott Shepard, M.D., a member of the MNI team and an assistant professor of neurosurgery at UTHealth Medical School. In November, Dr. Shepard placed an artificial prosthetic implant to repair a skull defect where a portion of Holstead’s bone was destroyed.

“I want to say how truly amazing everyone was at the hospital during my time of need. The Memorial Hermann team was steadfast, professional, attentive and did everything the right way,” she says. “The doctors were fantastic and saved my life. I had never had the need to be admitted to Memorial Hermann-TMC for trauma before, and my family and I were highly impressed. I often question where I might be today if it weren’t for the Memorial Hermann team.”





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“The Memorial Hermann team was steadfast, professional, attentive and did everything the right way. The doctors were fantastic and saved my life.”

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## Thomas Campbell: Reversing Dementia

Houston resident Thomas Campbell\* was working on contract with a civil engineering group when he noticed he was tripping frequently when he walked.

“My walking speed had slowed over time,” the 66-year-old recalls. “I had minor spells when I felt a little dizzy or off balance, and they got progressively worse. I also noticed I had less agility. It seemed like there was less connection between what I wanted to do with my feet and legs and what was actually happening. I wrote it off to old age.” His wife Julia Campbell believed his symptoms were caused by something else.

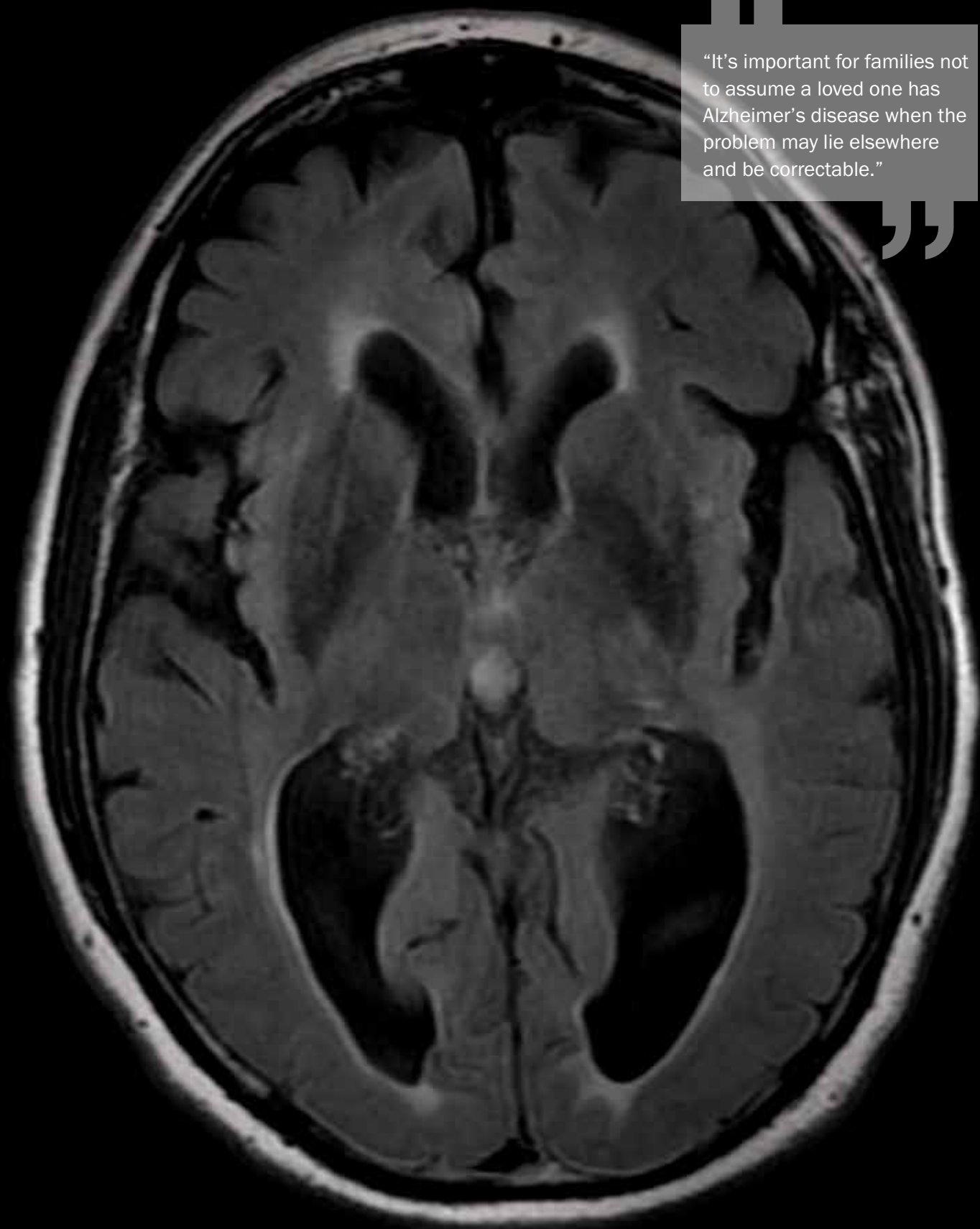
“We’d been traveling back and forth between Houston and California, and when we came home permanently, it really hit me that Thomas had changed,” says Campbell, who describes herself as a relentless researcher. “When you’ve been married for a long time, you get to know your husband really well. I noticed physical and behavioral changes that were part of the progression of symptoms, and told him that this was just not normal for people our age. I started researching his symptoms online and one by one, I eliminated the neurological disorders.” She was left with normal pressure hydrocephalus (NPH), a rise in cerebrospinal fluid (CSF) in the brain that causes the ventricles to swell, putting pressure on brain tissue that can result in temporary or permanent damage. She believed her husband’s symptoms were consistent with what she had read.

In July 2012, the couple discussed a possible diagnosis of NPH with Raymond Martin, M.D., a professor of neurology at UTHealth Medical School and medical director of outpatient neurology at Mischer Neuroscience Institute (MNI). After evaluating Campbell, Dr. Martin referred him to neurocognitive disorders expert Paul E. Schulz, M.D., whose clinical interests include dementias, such as Alzheimer’s disease and frontotemporal dementia, and disorders of memory, mood and behavior.

“The question of normal pressure hydrocephalus is not straightforward and requires thorough neuropsychological testing and evaluation of imaging studies to help us differentiate it from Alzheimer’s disease,” says Dr. Schulz, a professor of neurology at UTHealth Medical School. “Here was a man who had been charming, warm and outgoing, whose personality had progressively changed. As physicians dealing with the range of possible neurocognitive disorders, it’s our job to look for clues that help us piece together the total picture for each of our patients.”

On a series of basic cognitive tests, Campbell lost only 4 points out of a possible 30, but the pattern did not clearly point to a single disorder. “His initial MRI showed some small-vessel ischemic changes – small strokes,” Dr. Schulz says. “But were those ischemic changes enough to produce the results we saw on the cognition tests, or was something else going on?”

\*The patient’s name has been changed at the family’s request.



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“It’s important for families not to assume a loved one has Alzheimer’s disease when the problem may lie elsewhere and be correctable.”

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His MRI revealed enlarged ventricles, and his pattern of changes in attention and speed of thinking was consistent with increased pressure in the ventricles. All these clues made his condition look more like NPH than Alzheimer's disease."

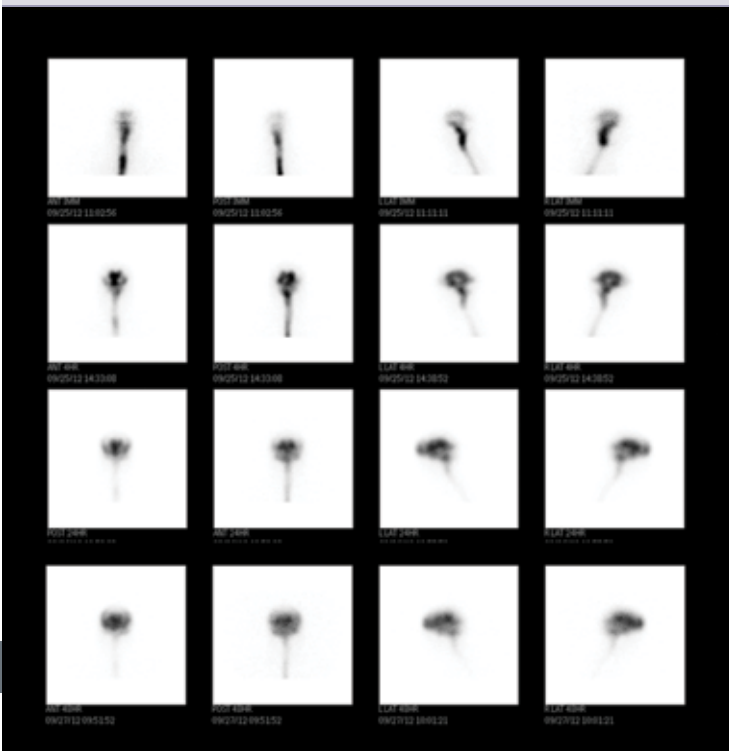
To gain more evidence, Dr. Schulz ordered a lumbar puncture and timed how long it took Campbell to walk 50 feet before and after the procedure. His speed in covering the distance dropped from 19 seconds to 15 seconds after the spinal tap. Dr. Schulz also tested his cognitive function. "When we withdrew some cerebrospinal fluid and noticed that the lowering of pressure led to improvement, we had another clue," he says. "Both his gait and personality improved after the lumbar puncture."

Dr. Schulz ordered another test to help support the diagnosis of NPH – a radionuclide cisternogram, a nuclear scan used to diagnose spinal fluid circulation problems and CSF leaks. After a lumbar puncture, small amounts of a radioisotope are injected into the fluid in the lower spine.

"On the cisternogram, we can observe how long it takes the contrast material to travel to the brain and exit into the blood, from which it is excreted," he says. "Normally, CSF goes through this cycle about every 300 minutes. At 24 hours, the dye was still visible in Thomas's brain and spine, and at 48 hours, we could still see it. Clearly, the spinal fluid was not being turned over at the normal rate."

The cisternogram results showing delayed CSF outflow, MRI findings of enlarged ventricles, the pattern of change on cognitive testing, and the slowed walking and improvement following lumbar puncture provided strong evidence of normal pressure hydrocephalus, as Julia Campbell suspected. The treatment for NPH is ventriculoperitoneal shunting, in which a burr hole is drilled in the skull and a small, thin catheter is passed into a ventricle of the brain. Another catheter is placed under the skin behind the ear and moved down the neck to the chest or abdomen. A valve connected to the two catheters is placed under the skin behind the ear. When pressure builds up in the ventricles, the valve opens and excess fluid drains into the chest or abdomen, decreasing intracranial pressure.

To add to the complexity of diagnosis, NPH is accompanied by Alzheimer's disease (AD) in about 50 percent of cases. "In these cases, a shunt for NPH may improve walking and incontinence, but not cognition," Dr. Schulz says. "However, new diagnostic tools give



us the capability to determine in advance which patients are likely to have AD and therefore are less likely to improve cognitively after placement of a shunt. In the past, before we could rule out Alzheimer's contributing to dementia, we had to tell our patients there was a 50-50 chance they'd improve with the shunt. You can imagine how you would feel as a physician if you recommended the surgery and your patient didn't improve. We can feel more confident about sending a patient to surgery and expecting a positive outcome by performing a florbetapir PET scan to rule out a contribution to altered cognition by Alzheimer's disease."

Florbetapir (Amyvid™) is a radioactive agent that binds to amyloid proteins in the brain, a hallmark of Alzheimer's disease, and allows them to be visualized on a PET scan. A negative scan reduces the likelihood that cognitive impairment is due to Alzheimer's disease. MNI was the first in Houston to offer this new diagnostic tool. In December 2012, when Campbell's diagnosis was more certain, Dong Kim, M.D., director of MNI and chair of the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School, placed the shunt. Campbell describes his response as "immediate and very positive."

When Dr. Schulz saw his patient in January after the surgery, he immediately recognized a dramatic change. "I could tell the moment he walked in that he was a different guy, but after normal pressure hydrocephalus, which causes a reversible dementia, it takes some time for the entire personality to return to normal. When I first saw him in January, he wasn't like the funny, charming man he is now."

Campbell describes Dr. Schulz as "excellent and very helpful in trying to figure out what was wrong with me. He determined with testing that I was suffering from some dementia. As I remember it, when I took the cognitive tests, I was not feeling as peppy as I normally am. I also wasn't very interested in taking the tests, I was there to get my brain shunt," he says, with characteristic wit. "My wife and I were both convinced I had NPH. The doctors said they had to do some tests first to be sure. After a while, they agreed with us."

Normal pressure hydrocephalus usually occurs in adults over the age of 60, and in most cases the cause remains unknown. If caught early and correctly diagnosed and treated, the resulting dementia can be reversed, as in Campbell's case.

He says he noticed more physical and intellectual energy after placement of the shunt. "I've received a tremendous benefit from it - no problems at all."

Julia Campbell adds, "It's important for families not to assume a loved one has Alzheimer's disease when the problem may lie elsewhere and be correctable. A little research of symptoms and the order in which they appeared really does help you get to the right medical specialist more quickly, speeding up the process leading to effective treatment.

"It's hard to find doctors who have good bedside manner," she says. "All the doctors who treated Thomas were great. Dr. Schulz is a good listener and was very attentive to my particular needs. It's really stressful when a family member undergoes physical and behavioral changes and you're trying to get him back to normal. Everything worked out really well."



## Tonya Daniel: Relief from 24/7 Headaches

Forty-two-year-old Tonya Daniel began suffering severe headaches when she was a teenager. Then they stopped, recurring only on occasion. Two years ago, the pain returned, and by 2012 she was living with a headache 24 hours a day.

After reviewing the results of her MRI, her primary care physician in Lawton, Oklahoma, diagnosed Chiari malformation and recommended that she see a neurologist. Like many modern, informed patients, she took charge of her health care and self-referred to a neurosurgeon.

“I started with a neurosurgeon in Oklahoma City – about an hour and a half away,” she says. “I wasn’t pleased so I saw another one in Colorado but didn’t feel comfortable with him either. On MedHelp’s online Chiari health forum I met a woman who had been treated by a neurosurgeon in Houston and was very pleased with her experience. So I scheduled an appointment.”

Daniel made the eight-hour trip to Houston and was seen at Mischer Neuroscience Institute’s Face Pain, Trigeminal Neuralgia and Chiari I Clinic by Dong Kim, M.D., director of MNI and professor and chair of the Vivian L. Smith Department of Neurosurgery. “Chiari I is a very specific syndrome that occurs in people whose posterior fossa is more shallow than normal or is situated lower in the brain,” Dr. Kim says. “A portion of the cerebellum starts herniating downward, causing pressure on the spinal cord, which in turn causes symptoms.”

Type I Chiari can be asymptomatic, but patients may also experience numbness and tingling of the hands, balance problems, and blurry vision in addition to headaches. When symptoms become severe, they can lead to hand weakness and fainting, or near fainting.

During the initial office visit, they discussed surgical options and what to expect during her recovery. When working with his patients, Dr. Kim listens carefully to the descriptions of their symptoms. “It’s most important to correlate the clinical picture and what the patient is feeling with what we’re seeing on MRI,” he says. “There’s no effective long-term treatment for Chiari malformation other than surgery. Medications may help at the beginning but eventually, as the symptoms worsen, they begin to fail.”

Dr. Kim, who performs more than 50 Chiari I malformation repairs annually, took Daniel to surgery on May 22, 2013. “It’s a straightforward procedure,” he says. “The goal of surgery is to provide more space in the foramen magnum without affecting the brain. We open the skull and widen the dura, the outermost of the three layers of meninges surrounding the brain and spinal cord. We remove the herniated tonsils, which has no effect on the patient.”

Hospitalized for three days, Daniel returned to Oklahoma after spending an extra night at a hotel in Houston before making the long trip home. She returned to work six weeks later.



“When I first met Dr. Kim, he said, ‘I can help you and you will be better,’ But I never dreamed I’d feel this much better.”

“When I first met Dr. Kim, he said, ‘I can help you and you will be better,’” she recalls. “But I never dreamed I’d feel this much better. I was caught in a very bad cycle. The headaches were keeping me awake at night and I would go to work exhausted, come home, take a shower and go to bed. Now my energy level is back, and I’m going strong.”

Daniel describes her experience at Mischer Neuroscience Institute as “phenomenal, from the lady who checked me in to the patient care tech who wheeled me out. Dr. Kim and his team are out of this world. I’ve never met so many healthcare professionals who so genuinely care.”

## Tommy Smith: A Walking Miracle

In the nine months that passed before 63-year-old Tommy Smith found his way to the office of Daniel H. Kim, M.D., FACS, FAANS, he gradually lost muscle function to the point of paralysis. By November 2012, he could no longer walk, feed himself or move his right hand.

“I could see myself deteriorating daily,” says Smith, who lives in Groveton, Texas. “During those months I was referred to one doctor after another, none of whom could help me.”

Earlier that year – in May – his family practitioner ordered an MRI that revealed severe ossification in the cervical spine, and referred him to neurosurgeon Stig Peitersen, M.D., in nearby Lufkin. Smith made an appointment, but the wait time was nearly four months. Concerned that her patient was rapidly losing function, the family physician referred him to another neurosurgeon, who told Smith he didn’t feel comfortable operating on him. A physician in Dallas didn’t accept his insurance, and another in Tyler said he didn’t have the tools to do the surgery. During these months Smith also saw a neurosurgeon in Houston who didn’t inspire his confidence.

“By then it was September and time for my appointment with Dr. Peitersen,” Smith says. “He was a very kind gentleman. He ordered an MRI and a CT, and told me he had done the surgery I needed, but that he does it only once every eight or 10 years. He knew of a neurosurgeon in Houston – they’d gone to medical school together – who does it regularly. ‘If I were sitting where you are,’ he said, ‘he’d be the man I’d choose to do the procedure.’”







“Dr. Kim was my last hope. I was standing face to face with death. He’s at the very top of my list as a doctor and as a person.”



Smith remembers his first meeting with Dr. Kim, who is internationally renowned for his expertise in spinal neurosurgery and reconstructive peripheral nerve surgery and directs the program at the Mischer Neuroscience Institute. “It was the first time anyone gave me hope,” he says. “Dr. Kim confirmed that I had a unique situation and said that his group specializes in this type of surgery. I was struck by his confidence and sense of humor when he told me there were three options to consider if I chose surgery. ‘Option 1: We operate on you and you stay the same. Option 2: We operate on you and you may potentially become paralyzed from the neck down. Option 3: We operate on you and you get better. Let’s choose option 3,’ he said. He looked me in the eye and spoke with great conviction. I trusted him completely.”

A clinical and educational leader in his field, Dr. Kim is the primary author of 16 textbooks on outpatient spinal procedures and surgeries, minimally invasive endoscopic spinal surgery, percutaneous endoscopic spine surgery, complex spinal reconstruction, spinal motion preservation surgery, spinal tumor surgery, adult and pediatric traumatic spinal injuries, image-guided spinal fusions, peripheral nerve surgery and reconstructive peripheral nerve surgery. He is a professor in the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School and an adjunct professor in the department of Bioengineering and Electrical Engineering Computer Science at Rice University. Dr. Kim is renowned for his research in radiographic nerve imaging, minimally invasive spine surgery, endoscopic spinal surgery, computer modeling of a spinal motion segment and reconstruction of peripheral nerve injuries.

“Mr. Smith was a fully functioning individual who was progressively losing strength in his arms, hands and legs,” he says. “Neurologically, he deteriorated very rapidly and by the time he came to my clinic he was using a wheelchair and walker. He had C1, C2 and C3

ossification of the posterior longitudinal ligament with very severe cervical stenosis causing neurogenic bladder and quadriparesis. He was at high risk of quadriplegia, and with the very high spinal cord compression and exuberant growth of bone spur pushing against his airway, he was losing the ability to breathe.”

Smith was scheduled for two surgeries during the first week in December: a posterior cranial cervical decompression and stabilization, followed three days later by an anterior decompression and stabilization. “When Dr. Kim saw me in the ICU after the first surgery, he told me he was pleased with the results and was considering not doing the second procedure. The next day a resident checked on me and told me I didn’t need the second surgery.”

“Many surgeons shy away from this type of very complex case because of the risk of paralysis,” Dr. Kim says. “Because we’re an academic center, challenging cases are referred to us, and we proceed when the patient understands the risk.”

Smith vividly remembers the three neurosurgeons who didn’t feel comfortable taking his case. “Dr. Kim was my last hope. I was standing face to face with death. Had he not done the surgery, I know I would be dead today. I can’t even find words for my feelings about the experience. With God’s mercy and grace and Dr. Kim’s abilities as a surgeon, I’m here talking, breathing and doing what I should be doing – a walking miracle. He’s at the very top of my list as a doctor and as a person.”

Dr. Kim recalls Smith skipping and hopping down the office hallway at a recent follow-up visit. “It’s very rewarding to me as a neurosurgeon to be able to save a patient from disability and watch him turn his life around,” he says. “That’s as dramatic and good as it gets.”

## Jim Hyndman: No Guts, No Glory

By the time Jim Hyndman was diagnosed with secondary progressive multiple sclerosis (MS) in 2009, he was unable to walk and suffering intense, painful lower-extremity muscle spasms. Today, he stands upright using a walking stick decorated with medallions from his travels. He credits the transformation to three subspecialists affiliated with the Mischer Neuroscience Institute (MNI) and a doctor of physical therapy at TIRR Memorial Hermann.

In August 2009, Hyndman was referred by a neurologist affiliated with Memorial Hermann The Woodlands Hospital to Staley Brod, M.D., professor of neurology and a member of the Multiple Sclerosis Research Group Clinic at UTHealth Medical School. Dr. Brod, who is board certified in internal medicine and neurology, started his patient on a regimen of pain medications, intravenous and oral chemotherapy, and oral baclofen, which acts on spinal cord nerves to decrease the number and severity of muscle spasms, relieve pain and improve muscle movement.

“When I first started on baclofen, I was taking half a pill a day,” Hyndman recalls. “A year later, I was up to 11 pills a day and still having muscle spasms that were strong enough to throw me out of bed at night.” When Dr. Brod saw that the high dose of oral baclofen was not improving Hyndman’s spasticity, he referred him to neurologist Erin Furr-Stimming, M.D., for evaluation for intrathecal baclofen pump implantation. The implantable pump delivers baclofen directly into the cerebrospinal fluid in the space between the spinal cord and the protective sheath surrounding the cord, minimizing the

side effects often associated with higher-dose oral or intravenous delivery of the drug.

Certified by the American Board of Psychiatry and Neurology, Dr. Furr-Stimming is a movement disorders specialist who focuses on the treatment of spasticity, Parkinson’s disease, dystonia and other neurodegenerative diseases. “Jim was actually tolerating the high dose of oral baclofen, however, he continued to experience significant lower-extremity spasms that were negatively affecting his quality of life,” she says. “We thought he would likely be a good candidate for intrathecal baclofen pump implantation.”

In May 2010 Dr. Furr-Stimming performed a neurological exam and talked with Hyndman about placement of a pump, which involves a surgical procedure. He agreed to undergo testing to determine if intrathecal baclofen would improve the spasms.

“When we perform an intrathecal baclofen trial, we’re looking for at least a 50 percent improvement in spasticity using the Modified Ashworth Scale,” she says. “We inject baclofen into the intrathecal space and evaluate its effectiveness at two hours and four hours post injection.”

“They videotaped me walking and recorded my range of motion, then injected the baclofen, waited two hours and evaluated me again,” Hyndman says. “There was quite a big difference. We waited two more hours and did the test again, and the results almost doubled in terms of my range of motion and ability to move.”

On June 30, 2010, MNI neurosurgeon Albert Fenoy, M.D., an assistant professor at UTHealth Medical School, surgically implanted a programmable pump under the skin of Hyndman's abdomen near the waistline. The pump, which releases prescribed amounts of baclofen, is a round metal disc about an inch thick and three inches in diameter attached to a catheter leading to the spinal canal. An external programmer allows Dr. Furr-Stimming to make adjustments in the dose, rate and timing of the medication.

During the months of programming medication delivery based on his body's response to baclofen, Hyndman underwent outpatient physical therapy near his home in The Woodlands. "My response to the pump was immediate," he says. "The spasms were gone but I still had tingling and my right foot would move on its own. After Dr. Furr-Stimming fine-tuned the settings to eliminate these movements and sync the pump with my needs, many, many months have passed without the need for further adjustment."

In February 2012, Dr. Furr-Stimming referred Hyndman to TIRR Memorial Hermann Adult and Pediatric Outpatient Rehabilitation at the Kirby Glen Center for specialized therapy. "That's when I met the person who pushed me over my next hurdle," he says. During the next four months, Jessica De La Rosa, PT, D.P.T., NCS, then physical therapy clinical coordinator and recently named director of outpatient rehabilitation, worked with Hyndman to improve his balance and mobility.

"Jessica worked wonders for me," he says. "I arrived with my walker and after we started therapy, she told me not to bring it back, that she was going to work with me until I could walk upright with a walking stick. I'd been through physical therapy off and on since 2009 and was really surprised at the quality and professionalism of the therapists at TIRR Memorial Hermann. Over the next few

months, Jessica had me walking backwards, walking unaided, walking in the grass instead of on a flat surface, walking without visual cues for balance, walking on a moving floor. I got to where I could keep my balance with the floor moving.

"I learned that some people in therapy don't take it seriously and give it their all, and as a result, they don't see the same results. No guts, no glory," he says. "Between Dr. Furr-Stimming and Jessica my life has changed dramatically in terms of how I get from one point to another. I'm in debt to both of those women."

At home, Hyndman walks unaided. "The issue for me is uneven ground or stepping up on a curb," he says. "The walking stick allows me to compensate for my balance issues. When my wife and I travel, I reserve a van with a lift and take my electric scooter with me. If I'm just going out to eat, I'll take my walking stick. If I don't know how far I'll have to walk to get from point A to point B, I have my scooter as back up. But my primary mode of mobility is my walking stick."

A trip to Switzerland before he was diagnosed with MS gave him the inspiration to start collecting metal medallions to nail to his walking stick. "In Switzerland I saw a lot of people hiking with walking sticks covered with medallions. I started collecting them, and now people stop me and ask me about them – my walking stick is a real conversation starter.

"I'm fortunate to have a really good medical team," says Hyndman, who just returned from vacation in California. "I can't say enough about the difference Dr. Brod, Dr. Furr-Stimming and Jessica have made in my life. When I started this journey, my challenge was learning to get around in a wheelchair. Now I'm walking around at home, and when I come in to see Dr. Furr-Stimming to have my pump refilled, I have my walking stick, period."



“I learned that some people in therapy don’t take it seriously and give it their all, and as a result, they don’t see the same results. No guts, no glory.”





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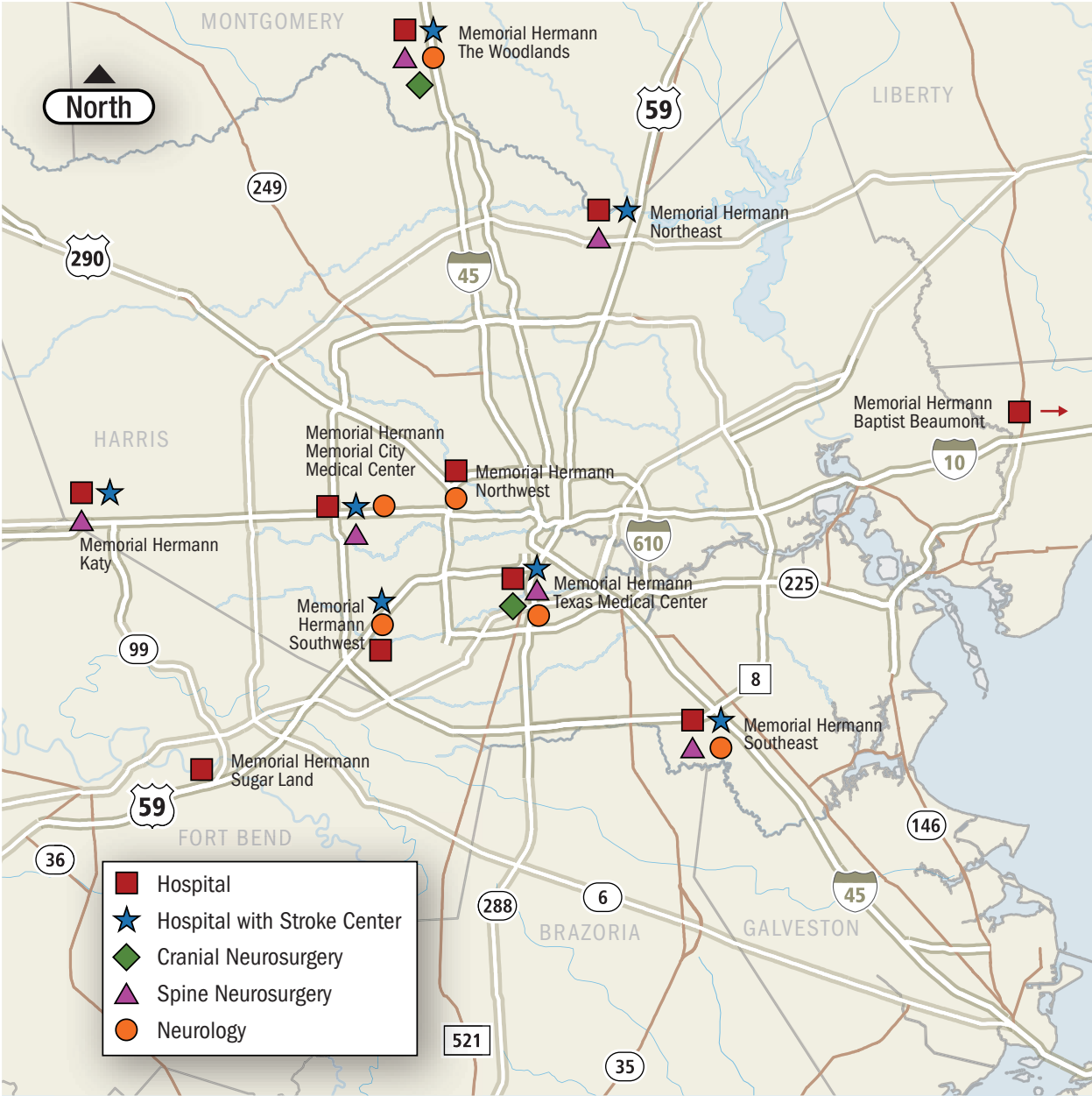
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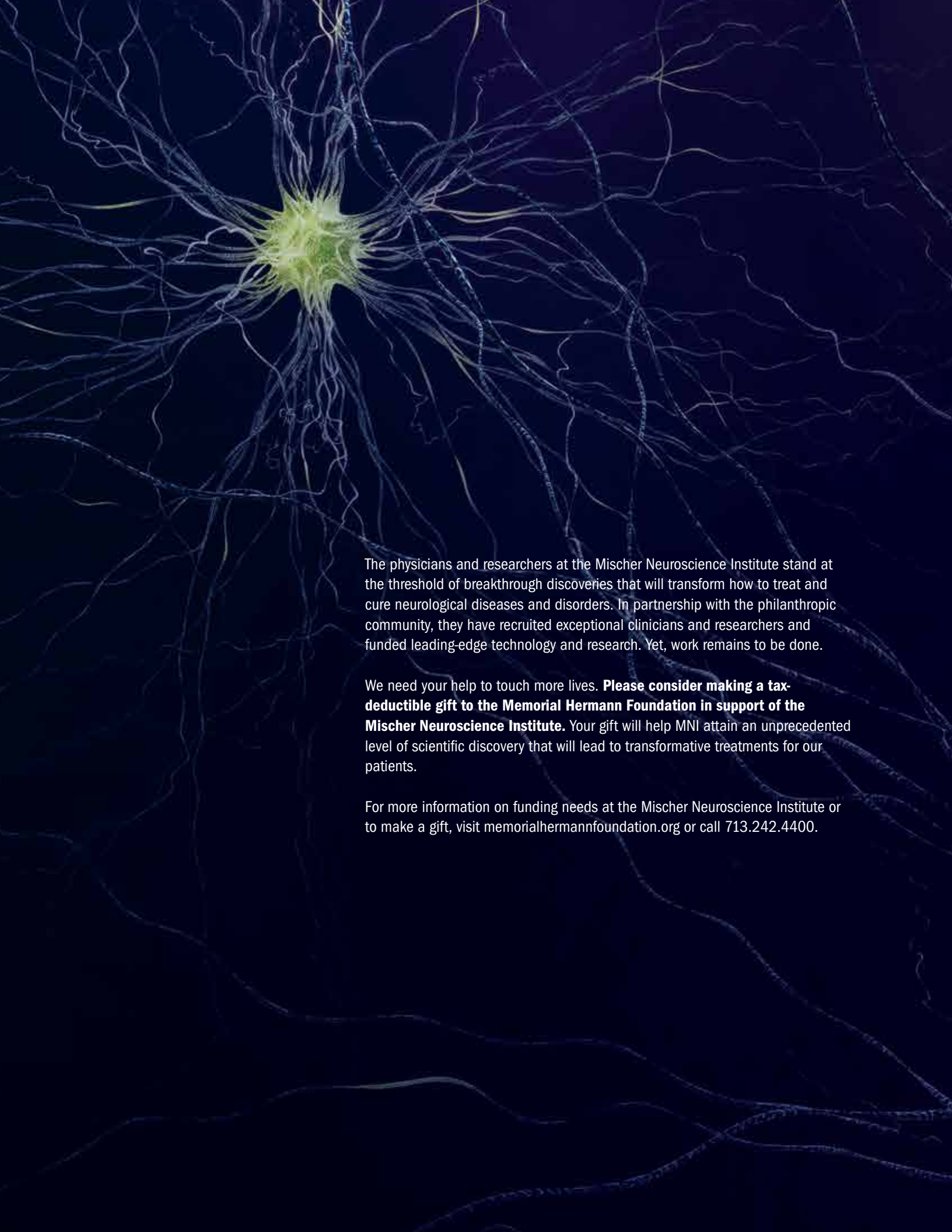
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# MISCHER NEUROSCIENCES LOCATIONS



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



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

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

For more information on funding needs at the Mischer Neuroscience Institute or to make a gift, visit [memorialhermannfoundation.org](http://memorialhermannfoundation.org) or call 713.242.4400.





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