MISCHER NEUROSCIENCE INSTITUTE REPORT 2012

Mischer
Neuroscience Institute

MEMORIAL HERMANN

When physicians
and patients choose

the Mischer Neuroscience Institute located at Memorial Hermann-Texas Medical Center, part of the 12-hospital Memorial Hermann Health System, they're choosing the largest and most comprehensive neuroscience program in Texas. The renowned faculty at the Institute works together in a coordinated attack against neurological disease. Thanks to their knowledge and talent, the Mischer Neuroscience Institute is nationally recognized for leading-edge medicine and consistently ranked among quality benchmarking organizations as a leader in clinical quality and patient safety.

Table of Contents

Dear Esteemed Colleagues,

2012 marks the fifth anniversary of the Mischer Neuroscience Institute (MNI) at Memorial Hermann. Since 2007, when we organized Memorial Hermann-Texas Medical Center's neurology and neurosurgery services under the MNI umbrella, we have become the No. 1 neuroscience provider in Houston and the largest provider in the southern half of Texas.

We are pleased to share with you the Mischer Neuroscience Institute Clinical Achievements Report for fiscal year 2012, which highlights our efforts in quality, safety, clinical care and research from July 2011 through June 2012. The report is a publication of MNI, part of the 12-hospital Memorial Hermann system, in collaboration with The University of Texas Health Science Center at Houston (UTHealth) Medical School. We hope you find the information interesting and valuable.

Our focus on innovation, quality outcomes and physician education continues to attract physician faculty members to MNI and UTHealth Medical School. In this 12-month period, we welcomed 16 faculty members. At the same time we expanded our capability to treat neurological disease through the addition of advanced technology, including a new Varian Trilogy linear accelerator for stereotactic radiosurgery, which will allow for noninvasive, focused treatment of cranial and spinal lesions. We have also added a second Magnes 3600 WH MEG brain imager, expanding our use of the technology in diagnosing epilepsy, aneurysms, cortical brain lesions, arteriovenous malformations and brain tumors.

Through our telemedicine program, we offer patients in outlying communities access to our stroke and neurology expertise and opportunities to participate in clinical trials. Eleven community hospitals in Southeast Texas are now linked to MNI through remote presence robotic technology; nine went live in 2012. 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, including a live Twittercast of a brain tumor resection.

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

We are proud of the work of our terrific physicians, nurses, scientists, and staff. Our promise to provide exceptional patient care with the best possible outcomes remains front and center. Watch for new programs and services in 2013 and an expansion of our commitment to research and innovation.

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

With best wishes,

Dong H. Kim, M.D.
DIRECTOR
MISCHER NEUROSCIENCE INSTITUTE
AT MEMORIAL HERMANN

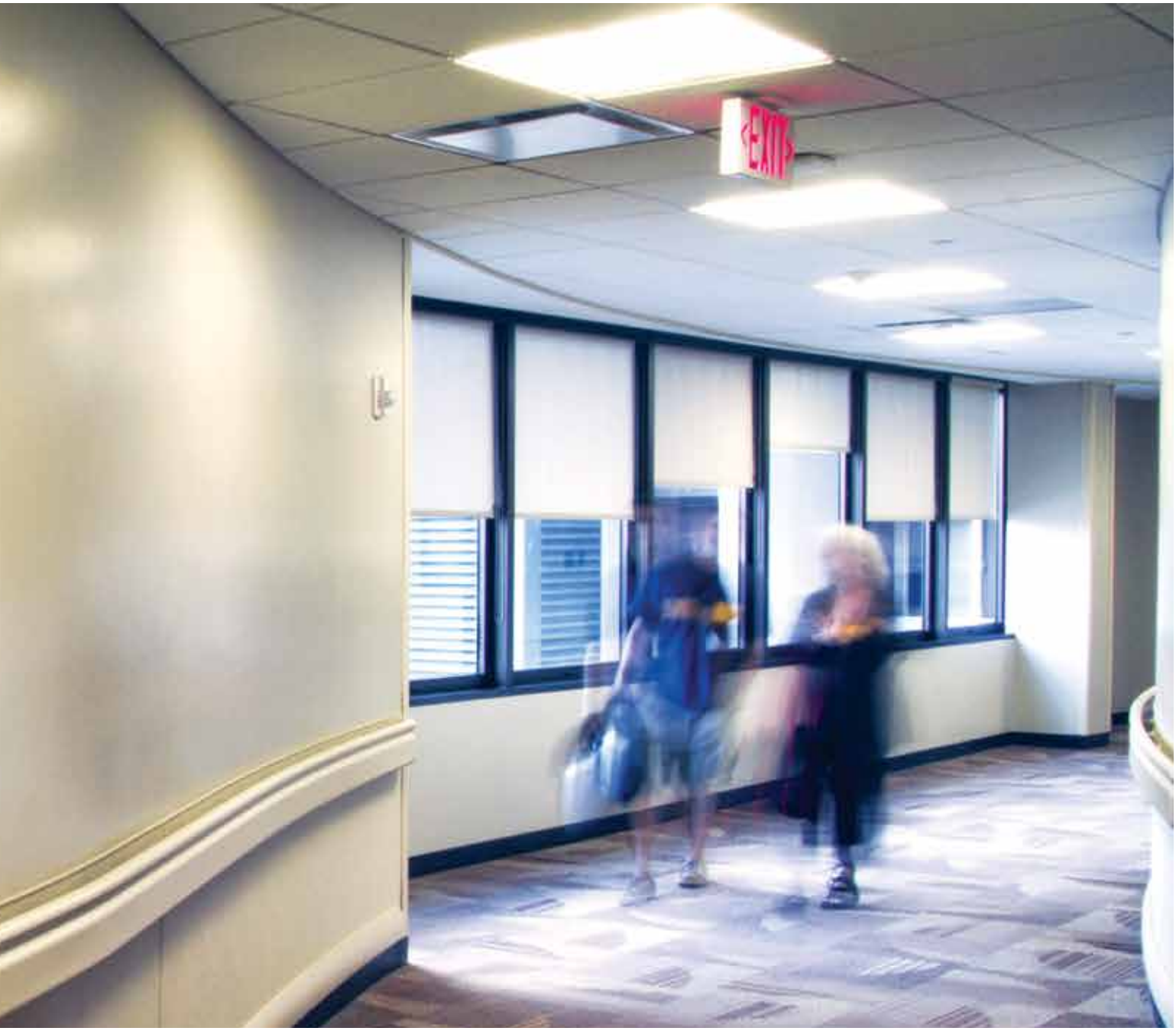
PROFESSOR AND CHAIR
VIVIAN L. SMITH DEPARTMENT OF NEUROSURGERY
UTHEALTH MEDICAL SCHOOL
713.500.6170

James C. Grotta, M.D.
CO-DIRECTOR
MISCHER NEUROSCIENCE INSTITUTE
AT MEMORIAL HERMANN

PROFESSOR AND CHAIR
DEPARTMENT OF NEUROLOGY
UTHEALTH MEDICAL SCHOOL
713.500.7088

About Our Institute

Shaping the future of neuroscience in a city known for medical excellence takes dedication – to quality, patient satisfaction, operational excellence, research, innovation and growth. To accomplish these goals, Memorial Hermann's Mischer Neuroscience Institute brings together a team of world-class clinicians, researchers and educators. A collaborative effort between Memorial Hermann-Texas Medical Center and The University of Texas Health Science Center at Houston (UTHealth) Medical School, we are the largest neuroscience provider in 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.



Our comprehensive, integrated approach has led to the creation of Houston's first and largest stroke team, its leading epilepsy and neurotrauma programs, a cerebrovascular center that treats more aneurysms and arteriovenous malformations than any other center in the region, a rapidly expanding pediatric neurosurgery program and a brain tumor center that annually diagnoses and treats hundreds of new tumor patients. We are proud of our innovations in multiple sclerosis, brain injury, spine surgery and more. And we make more neuroscience breakthroughs every day.

As physicians, we find our personal interactions with patients and the care we provide each one of them enormously rewarding. 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. Through basic science research, clinical discovery and the development of new, breakthrough treatments, the Mischer Neuroscience Institute is leading the way.

At a Glance

Physician Team

Staff Physicians	63
Clinical Residents and Fellows	42
Medical Students on Rotation	310
Research Fellows	16
Advanced Practice Nurses	11
Physician Assistants	3

Inpatient Facilities

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

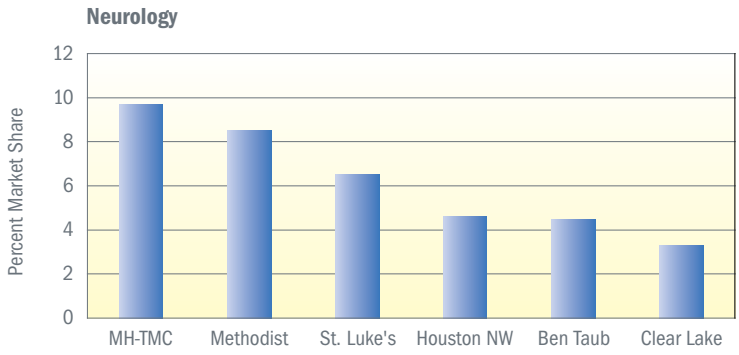
Research

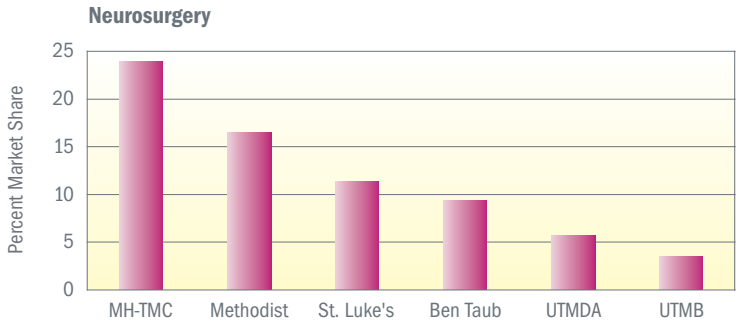
Research Projects in Progress	More than 200
Grants Awarded	$10.5 million (Neurology and Neurosurgery)

Specialty Equipment includes:

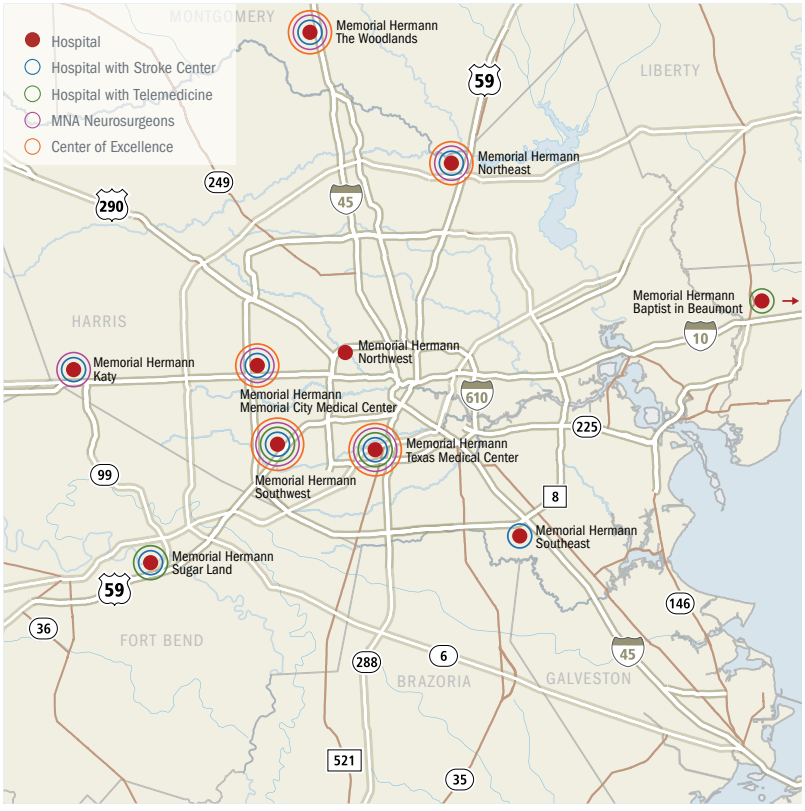
- Leksell Gamma Knife® Perfexion™
- Varian Trilogy Linear Accelerator
- Siemens Artis™ zee (intra-operative angiography suite)
- RP-7TM Remote Presence System
- 3D C-Arm
- Philips Healthcare endovascular temperature modulation system
- Simultaneous electroencephalography and polysomnography
- Continuous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

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





Source: Texas Hospital Association Patient Data System (FY2010 Q1 – FY2012 Q3) provided by Thomson Reuters. Texas Hospital Inpatient Discharge Public Use Data File, [FY2008 Q1 – FY2011 Q4] provided by Texas Department of State Health Services, Center for Health Statistics; Q1 FY2012 – Q3 FY2012 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.

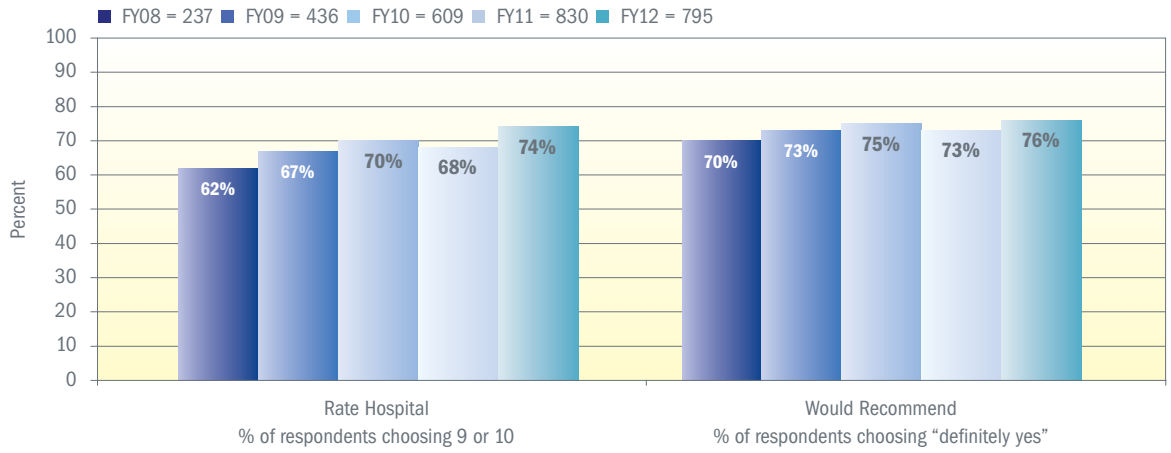


The Patient Experience

Patients from around the world come to the Mischer Neuroscience Institute for treatment, based on our high-quality outcomes and our 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 with patients, has led to an upward trend in patient satisfaction over the last five years. Data gathered by the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey shows consistent improvement in domains considered critical to ensuring a high level of patient satisfaction.

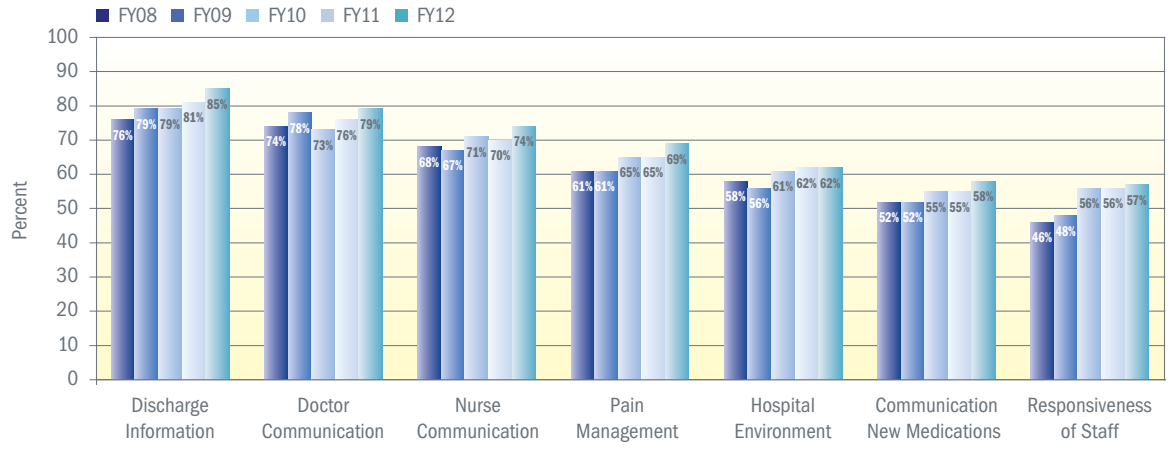
HCAHPS Overall Assessment

Total Survey Respondents



HCAHPS Domains of Care

Surveys Received FY08–12
Respondents choosing "always" or "yes"



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 hospital in the Texas Medical Center to receive state of Texas designation as a primary stroke center.
- 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. We remain the No. 1 program in the United States in the number of vagal nerve stimulators implanted in epilepsy patients.
- We brought the first clinical magnetoencephalography (MEG) sensor to Houston and recently updated the technology to the new Magnes 3600 WH.
- We house one of only a few inpatient Epilepsy Monitoring Units in the country with the unique capability of simultaneously performing electroencephalography and polysomnography.
- TIRR Memorial Hermann is the only hospital in Houston – and one of only seven designated centers in the nation – in the Christopher and Dana Reeve Foundation NeuroRecovery Network.
- 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.

Creating a Culture of Safety in an Era of Higher Patient Acuity

As healthcare reform moves hospitals away from the former volume-driven, fee-for-service structure to a pay-for-performance model tied to clinical outcomes, the Mischer Neuroscience Institute (MNI) continues to examine processes and investigate opportunities to improve efficiencies and quality, with special attention focused on patient outcomes, safety and satisfaction.

"Five years ago we faced enormous challenges in terms of our rates of bloodstream infections, surgical site infections and ventilator-associated pneumonias," says Imoigele Aisiku, M.D., director of neurocritical care at Memorial Hermann-Texas Medical Center and associate professor and vice chair of critical care in the Vivian L. Smith Department of Neurosurgery at The University of Texas Health Science Center at Houston (UTHealth) Medical School. "Thanks to careful attention and tracking using newly developed audit tools, we've had zero bloodstream infections (BSIs) for the last seven months."

Central line-associated bloodstream infections (CLABSIs) have a reported mortality of 15 to 25 percent nationally,

according to the Centers for Disease Control and Prevention. To reduce BSIs, quality teams at MNI looked at the necessity for central-line utilization.

"Through close daily monitoring done as part of a nurse- and physician-driven initiative, we assessed the need for central lines on an individual patient basis, using an array of audit tools piloted to evaluate their necessity," Dr. Aisiku says. "When we found that having central lines in place longer than five or six days was associated with a higher rate of infection, we became more aggressive about noting when and where they were in place. We reduced the number of central lines placed and the duration of use, and our infection rate went down." In 2011, MNI reported five BSIs. In fiscal year 2012, only two BSIs were logged in the first five months of the year, marking two consecutive years of BSI reduction. MNI also reduced the number of surgical site infections in 2010, 2011 and 2012, in spite of higher patient acuity and increased volumes. The Institute reported a 70 percent reduction in patient falls for the last four months of 2012, and reduced length of stay in the Neuroscience ICU. Since 2007, MNI has reduced observed-to-expected mortality, using University HealthSystem Consortium benchmarks, by 50 percent.

"This is a five-year story," says Miriam Morales, manager of quality and performance for MNI. "Over time, we have collected data and are building a data warehouse. Now, we're integrating those data with nursing and patient safety metrics to provide physicians with more than just patient outcomes. Physicians review dashboards that include mortality, length of stay, infections, patient satisfaction, nursing and patient safety metrics."

"Ventilator-associated pneumonia (VAP) is our current area of focus," Dr. Aisiku says. "In the last six months we've done a significant amount of education with nursing and respiratory therapy to improve our VAPs.

It's paying off. We reported zero VAPs in the last two months of fiscal year 2012."

The focus on patient safety is critical to MNI's continued leadership in the field of neuroscience. Beginning in 2013, the Centers for Medicare & Medicaid Services (CMS) will use a value-based purchasing program for acute care hospitals for inpatient services provided to Medicare beneficiaries. Under the new rule, which was created to improve clinical outcomes and patient satisfaction, hospitals will receive value-based incentive payments tied to clinical outcomes and patient satisfaction with services provided.

"Quality and safety will continue to be the important factors in healthcare delivery as hospitals are held accountable for hospital-acquired conditions and complications that result from unsafe care," says Dong Kim, M.D., director of MNI and professor and chair of the Vivian L. Smith Department of Neurosurgery at the UTHealth Medical School. "We strive every day to increase efficiency of services and enhance quality of care. We're proud of the advances we've made and will continue to provide the highest level of care to our patients."

Driving Quality Improvements with Data: From Nursing Quality Initiatives to Physician Scorecards

Empowering nurses at the bedside to provide good customer service and implement quality improvement initiatives led to a dramatic upswing in patient satisfaction scores at the Mischer Neuroscience Institute (MNI) in 2012.

"Over the years, patient acuity and the demands on nursing have increased. At the same time, nurses are working 12-hour shifts two to three days a week, which means patients have multiple nurses during their hospitalization," says Nicole Harrison, R.N., administrative director of nursing at MNI. "When a nurse comes to work and assumes care of a patient for the first time, there's much to learn. Patients have more complex medical histories to review and understand, so nurses have to hit the ground running. We wanted to provide greater consistency for our patients so we restructured the neuroscience nursing team to focus more strongly on quality and customer service. By doing so, we've improved the overall patient experience."

That improvement is reflected in MNI's HCAHPS scores, which improved in seven of the eight areas tracked, including overall rating, communication about new medication, discharge information, pain management, nurse communication, responsiveness of hospital staff and communication with physicians. HCAHPS (Hospital Consumer Assessment of Healthcare Providers and Systems), a standardized survey instrument and data collection methodology that allows valid comparisons to be made of hospitals across the country, is the first national, publicly reported survey for measuring patients' perceptions of their hospital experience.

Harrison has led the nursing initiative to improve the patient experience since joining MNI at the end of October 2011. "We redesigned our structure to give our nurses more support at the bedside and in doing so, we created a solid platform for the launch of our quality and customer service initiatives," she says. "Our nurses are in charge, and they drive the unit. They're involved in decision-making through committees and one-on-one meetings with directors. We've made it clear – from the top down – that nurses are valued and equal members of the patient care team. As the people who care for our patients day in and day out, they're aware of patient and family concerns, and they notice the smallest changes in the patient's condition, which is especially important after a neurological event. They make a vital contribution to the physicians' knowledge of their patients' status by participating in daily rounds."

Harrison and her team have moved away from the traditional nursing model that gives one charge nurse responsibility for the flow of an entire unit, including bed assignment, patient throughput, staffing issues, quality and peer-to-peer support at the bedside. "With the multitude of important, necessary functions of the traditional charge nurse role, it was evident that our charge nurses didn't have the time to devote to each of these details," she says. "We started by taking a hard look at where we were focusing our energy. We have

39 beds on the neuroscience unit. On a typical day, between 11 and 15 patients are discharged or admitted – a high number. We knew we were busy, but we started wondering if the energy we were expending was really making a difference in quality and patient satisfaction. So rather than adding staff, we restructured for more efficiency."

The new structure includes an operational leader responsible for bed assignment, timely discharge and admission, staffing, patient flow and work flow – and two team leaders, who split the unit in half and focus on the quality and customer service portion of patient care, allowing the team to provide very personalized service. They share responsibility for rounding on each patient and looking at specific patient satisfaction measures using an audit tool designed by the nursing team and based on HCAHPS survey questions. In addition to those measures, they ascertain patient-specific goals as identified by the patient and work to implement a plan to meet those goals.

Harrison says the quality customer service initiatives create a better experience for patients and families. "This is about getting back to the basics of courtesy and real caring. We have a great unit and a lot of really dedicated nurses who want to do what's best for the patient. And our patients love it."

Dong Kim, M.D., director of MNI and professor and chair of the Vivian L. Smith Department of Neurosurgery at The University of Texas Health Science Center at Houston (UTHealth) Medical School, believes in forging a strong physician partnership with nurses. "Part of empowering nurses is encouraging them to think about what's not working well," Dr. Kim says. "We want them to share their ideas about transforming care at the bedside with us. How can we improve the flow in the work environment? No one knows our patients better than the people working at the bedside. We also encourage them to be engaged in evidence-based research and to achieve certification in their discipline. We want them to help us continue to improve."

To ensure that new recruits have a solid foundation in neuroscience and are well equipped to work independently, Nicole Harrison and her team have created a new nurse education structure. Rather than reporting through the hospital's Education department, three neuroscience educators report to her. Open positions are filled through the MNI Nursing Academy using a model similar to a residency or internship with the exception that the speed at which nurses advance through the academy is personalized to the individual. "Changing a culture takes time," says James Grotta, M.D., co-director of MNI and professor and chair of the department of Neurology at the UTHealth Medical School. "In a short time, we've done a good job of

getting the right people in the right roles. Leadership is so important to drive the ship to quality outcomes. We want leaders who empower our bedside nurses and help us grow professional nursing within our service line. Building a good foundation of nurses with expertise in neuroscience and retaining them is one of our critical success factors. It's a work in progress."

The Neuroscience Research Repository and Neurocore

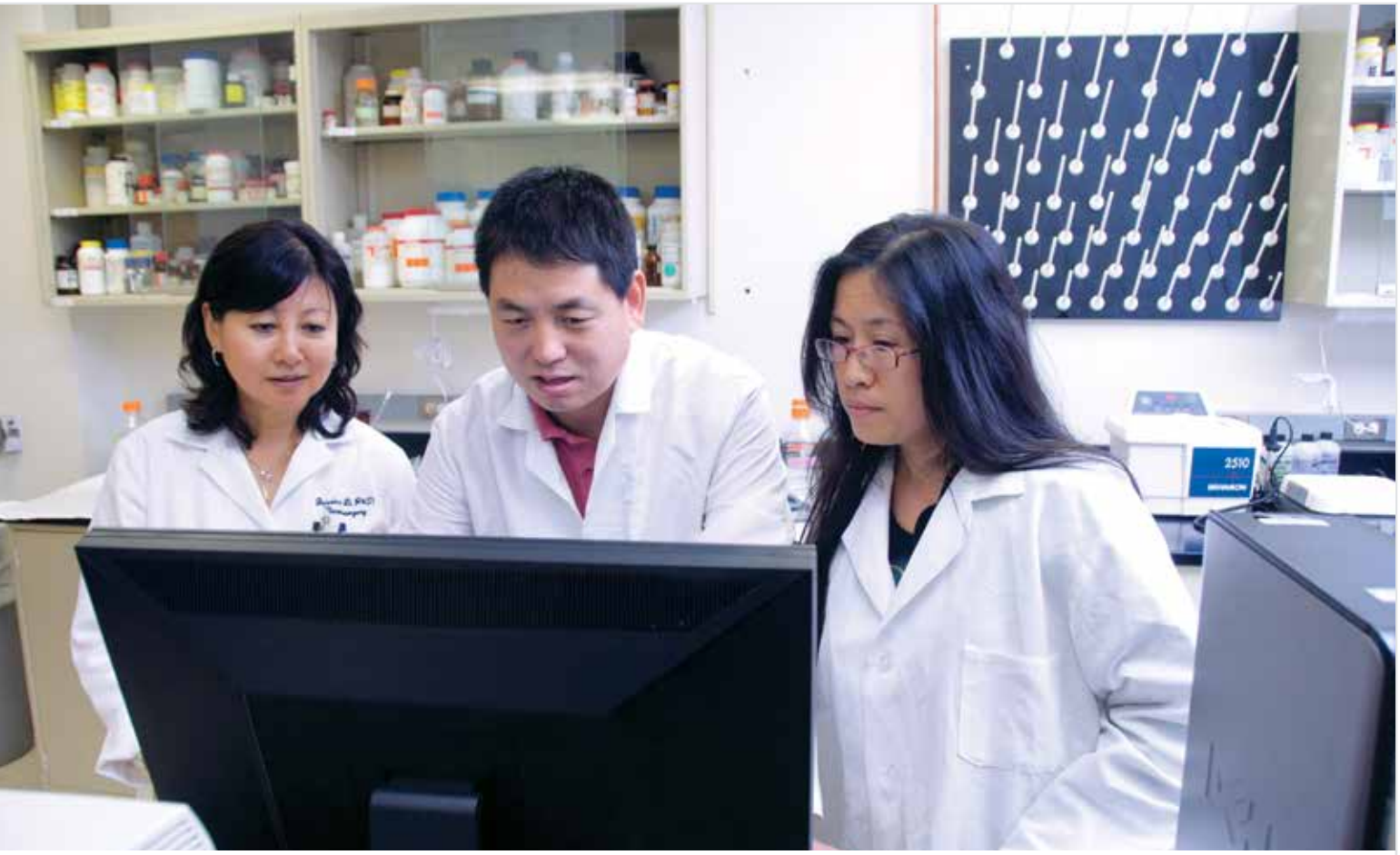
The nursing quality initiatives are part of a larger focus at MNI on collecting data and creating the capability to use it to improve care, which includes the Neuroscience Research Repository (NRR). A collaborative project of Memorial Hermann and the Vivian L. Smith Center for Neurologic Research at the UTHealth Medical School, researchers at the NRR collect samples from consenting patients for clinical, genomic and proteomic analysis. These samples serve as the foundation for basic and clinical studies, and are changing the way care is delivered.

"Advances in biomedical research technology like the NRR present a range of new opportunities for a greater understanding of neurological illness and injury and the development of novel therapies," Dr. Kim says. "The beauty of the NRR is that it integrates reliable clinical data with biologic information from patient tissue specimens, providing us with insight into a broad spectrum of health issues related to injury and disease of the brain, spine and central nervous system." Patient data for the NRR is gathered through a clinical documentation and communication program called Neurocore and electronically transferred to the NRR database for analysis.

"Healthcare providers across the country are transitioning as quickly as possible to electronic medical records. We aim to maximize the potential of electronic systems," says Gigi Hergenroeder, M.H.A., R.N., director of the NRR and an assistant professor in the Vivian L. Smith Department of Neurosurgery. "Dr. Kim has worked with Memorial Hermann-Texas Medical Center to put the main source of the patient data for the NRR into place through the development of Neurocore. Because of his vision and the support of the Vivian L. Smith Foundation, we now have a priceless resource combining clinical data, which provides an overall picture of the patient's condition, with tissue samples for scientific analysis. The result is a much more complete picture of the injury or disease process."

The system also offers clinical decision support through embedded protocols for the treatment of specific conditions. "Neurocore has the capability to analyze information with a narrow and deep focus, making it particularly useful in specialties like neuroscience," Dr. Kim says. "It facilitates research and evidence-based medicine and supports our mission as a medical school and teaching hospital to educate future leaders in neuroscience by helping our residents advance their knowledge and practice. It also offers us the opportunity to monitor adherence to and departure from protocols, as well as to change existing protocols and introduce new ones."

Researchers began enrolling patients in the NRR at Memorial Hermann-TMC in the spring of 2009. As the repository's inventory expands, the availability of tissue samples is quickening the pace of research. "If our researchers want to study, for example, a brain tumor population or an aneurysm population, our tissue and serum stores catapult their research by eliminating the time spent collecting data and samples," Hergenroeder says. "By speeding the creation of new knowledge, the Vivian L. Smith Center is making a huge contribution to neurological science and practice."



"Neurocore builds on the existing clinical electronic record of the hospital by bringing us closer to a larger and more integrated data warehouse," Dr. Kim says. "That datamart, along with other technology improvements on the horizon, will help us create an environment that promotes the best delivery of care."

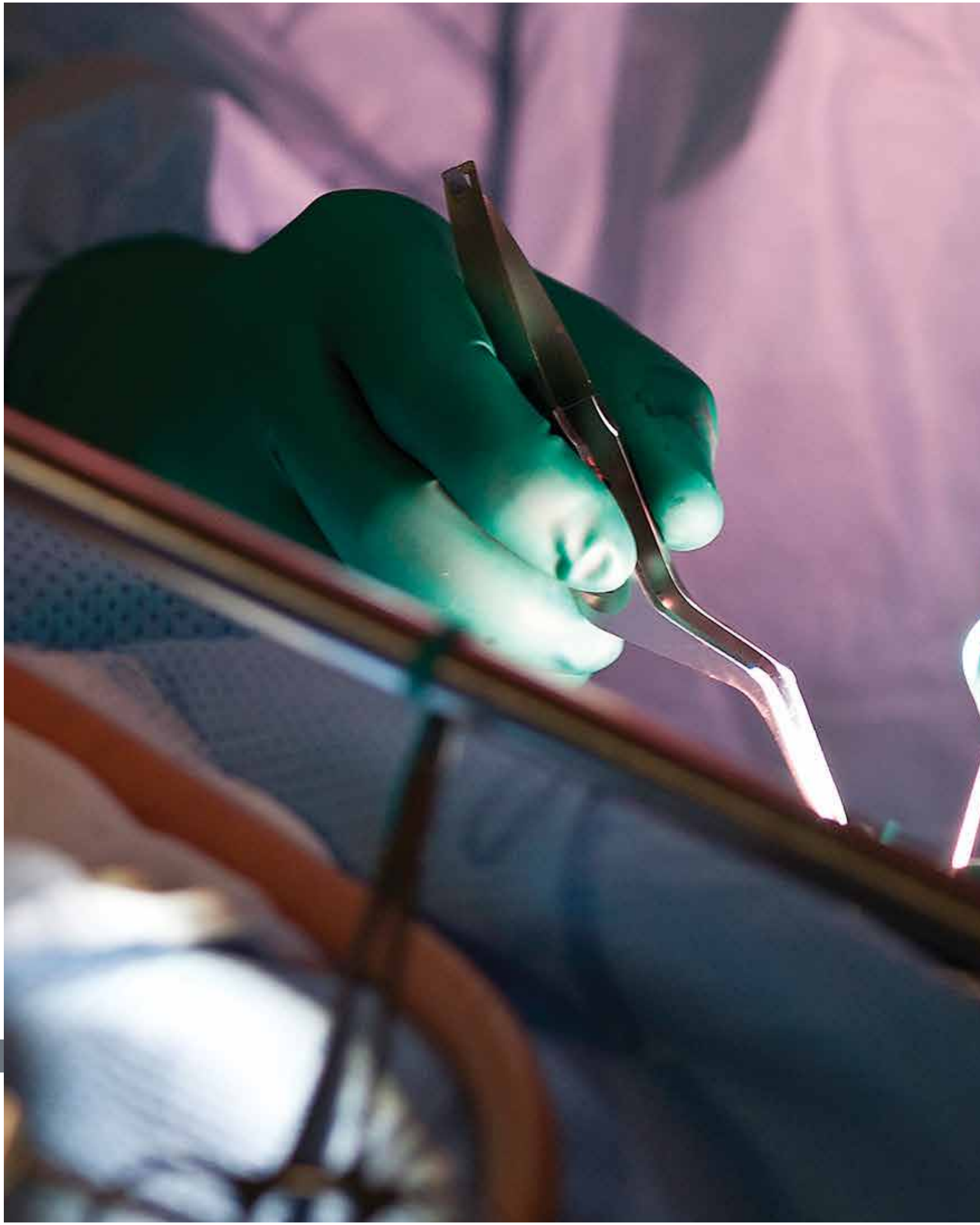
Using the Datamart to Provide Feedback on Quality and Outcomes

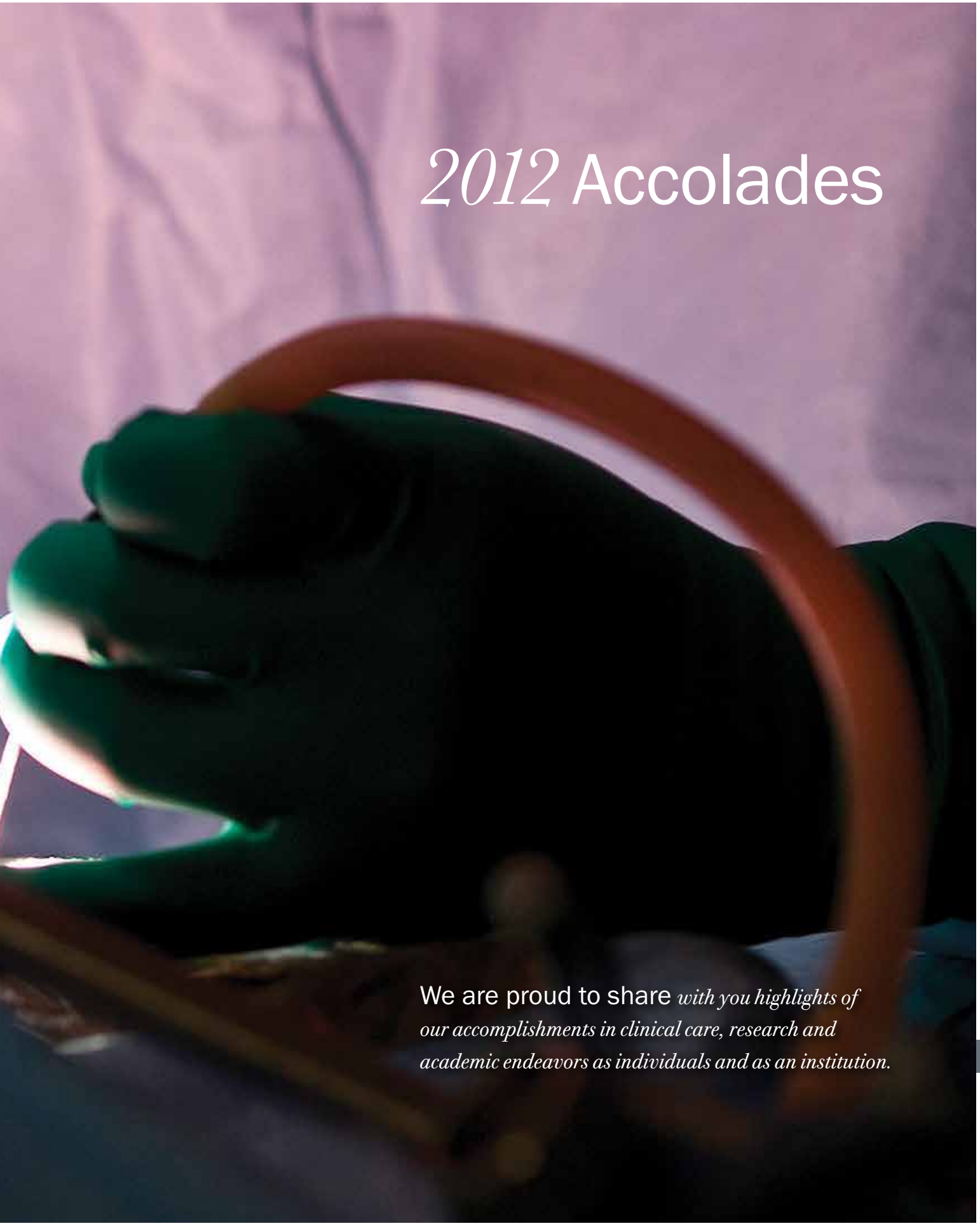
To effect change and improve quality, MNI's datamart facilitates quality data analyses, generates service-line dashboards and develops physician scorecards.

"Neurocore improves physician documentation, communication, protocol adherence and patient care," says Miriam Morales, manager of quality and performance for MNI. Morales uses information generated by Neurocore, integrated with nursing and patient safety metrics, to provide MNI physicians with data on discharges, length of stay, mortality and infections. "Ultimately, we plan to integrate hospital financial data, patient satisfaction and physician outcomes," she says.

Each month at neuroscience service-line meetings performance is reviewed, action plans are developed or updated and leaders are identified to address quality concerns. These combined efforts have improved physician documentation, improved clinical practice, reduced observed-to-expected mortality ratios and improved patient safety.

"While we've made excellent progress toward improvement, there remains the goal of fully integrating all our data across the neuroscience service line," Dr. Kim says. "We believe that current clinical data is fundamental to performance improvement. Future initiatives will include automation of dashboards and physician-specific drill-down features. Once completed, the datamart will integrate all financial and clinical information and facilitate continued improvement."





2012 Accolades

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

Mischer Neuroscience Institute Celebrates Five Years

The Mischer Neuroscience Institute (MNI) at Memorial Hermann marked its fifth anniversary by renewing its commitment to be the best locally, nationally and internationally, and to lead the world in advancing the art and science of neurology and neurosurgery. Since its founding, MNI has reported strong growth in consumer preference for neuroscience care at Memorial Hermann – a 9.4 percentage point increase in preference scores in just four years. Length of stay has been reduced by more than half, and mortality is well below the national expected benchmark. Neurosurgery volume has grown from 7,500 cases in 2008 to nearly 9,000 in 2012, and funded research for the combined Neurology and Neurosurgery departments now exceeds $10.5 million.

From Gamma Knife® radiosurgery and brain mapping with MEG technology to advanced care for neurovascular diseases, epilepsy, stroke, multiple sclerosis and movement disorders, Memorial Hermann-Texas Medical Center was the first hospital in Houston to offer a comprehensive neuroscience program, with many of its specialty centers in place for decades. In 2006, a gift from Houston businessman and philanthropist Walt Mischer and his family paved the way for the recruitment of internationally known Harvard neurosurgeon Dong H. Kim, M.D., as director of MNI and professor and chair of the Vivian L. Smith Department of Neurosurgery at The University of Texas Health Science Center at Houston (UTHealth) Medical School. Under the direction of Dr. Kim and renowned neurologist and MNI co-director James C. Grotta, M.D., professor and chair of the department of Neurology, these specialty centers came together within the new Mischer Neuroscience Institute at Memorial Hermann.

Over the next five years, with the support of Memorial Hermann and UTHealth, the two physician leaders established new clinical and academic programs and recruited more than more than 90 nationally recognized clinicians, researchers and educators whose insights and research findings are transforming the field of neuroscience. MNI now encompasses centers of excellence in brain tumor, cerebrovascular disease, epilepsy, memory disorders and dementia, movement disorders and neurodegenerative diseases, multiple sclerosis, neuromuscular disorders, neurorehabilitation, neurotrauma/critical care, spine and the Children's

Neuroscience Center. These centers are supported by the Institute's $13.5 million neuroscience intensive care unit, which opened in 2009 and was designed with input from physicians, nurses, patients and family members.

The MNI neurosurgery program is complemented by an equally strong neurology program, which boasts the first stroke center in Houston, one of the first dedicated stroke programs in the world and the first Joint Commission-accredited primary stroke center in the region. In 2009, MNI's track record in the treatment of stroke helped lead to the designation of five Memorial Hermann hospitals as primary stroke centers by the Texas Department of State Health Services: Memorial Hermann-Texas Medical Center, Memorial Hermann Memorial City Medical Center, Memorial Hermann Southwest Hospital, Memorial Hermann Katy Hospital and Memorial Hermann The Woodlands Hospital.

Telemedicine links were established between those centers and MNI neurologists to ensure 24/7 emergency consultation. Today, MNI's remote-presence robotic system, an advanced teleconferencing technology equipped with two-way video capability, links neurologists at the MNI Stroke Center to 11 outlying facilities, including Baptist Beaumont Hospital, Baptist Orange Hospital, Huntsville Memorial Hospital, Bellville General Hospital, Matagorda Regional Medical Center, Memorial Livingston Hospital, Citizens Medical Center in Victoria, Texas, Cleveland Regional Medical Center, Memorial Hermann Southwest Hospital, Medical Center of Southeast Texas and St. Joseph Medical Center in Houston. The technology allows emergency physicians in community hospitals to consult with MNI neurologists, who can see patients and view monitors and other clinical data sources firsthand from remote locations.

"Our ultimate goal is to build a collaborative network of hospitals working together to deliver comprehensive neurological and neurosurgical care in the southern half of Texas," Dr. Grotta says. "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."

In 2008, under Dr. Kim's leadership, the Institute broadened its commitment to teaching with the launch of the UTHealth Medical School's Neurosurgery Residency Program. From 2011 to 2012, the number of neurosurgery residents nearly doubled, and 16 research fellows are now in training at MNI. "There's a dire shortage of neurosurgeons throughout the country," Dr. Kim says. "We have the expert faculty in place to support a residency, and we're the market leader in Houston in cranial neurosurgery. The neurosurgery residency reinforces the strength of our program at the Mischer Neuroscience Institute and will lead to even more research. With its addition, the medical school now has a residency in every field." During that same time period the number of neurology residents jumped from 227 to 264.

MNI has also added new equipment to its arsenal against neurological disease, including the state-of-the-art Leksell Gamma Knife® Perfexion™ and a Siemens Artis™ zee biplane system. Both expand the Institute's treatment capability and allow physicians to accommodate increases in patient volume. In 2011, MNI opened two new specialized clinics: the Face Pain, Trigeminal Neuralgia and Chiari I Clinic, which gives patients suffering from difficult-to-diagnose face pain new treatment options, and the Pituitary Tumor and Vision Change Clinic, which brings together an interdisciplinary team to provide comprehensive diagnosis and treatment plans for patients with pituitary-region tumors.

Dr. Kim's vision to establish a tissue repository for research into neurological injury, similar to the large tumor repositories that support cancer research, led to the development of the Neuroscience Research Repository (NRR). "There was no such bio-bank of human samples from patients suffering brain injuries from trauma, stroke or hemorrhage," Dr. Kim says. "We envisioned the NRR as a resource for investigators already in the field and a tool that would stimulate others to enter the field." A collaborative project of Memorial Hermann and the Vivian L. Smith Center for Neurologic Research at the UTHealth Medical School, the NRR collects samples from consenting patients for clinical, genomic and proteomic analysis to serve as the foundation for basic science and clinical studies, which ultimately will change the way care is delivered.

Future projects include a second Neuroscience ICU and new subspecialty clinics. "We've set our sights high," Dr. Kim says. "We put together our neuroscience strategy five years ago. Since then we've worked it aggressively and are seeing tremendous results. Our aim is to push the envelope in neurological and neurosurgical care in ways that are appropriate for the patients we treat and that advance the field of neuroscience."

Arthur L. Day, M.D., Named President of the "Senior Society"

Arthur L. Day, M.D., vice chair, program director and director of clinical education in neurosurgery at the Mischer Neuroscience Institute at Memorial Hermann, assumed the prestigious position of president of the Society of Neurological Surgeons in May 2011.

The oldest neurosurgical society in the world, the Society of Neurological Surgeons, also known as the "Senior Society," counts among its members academic department chairmen, residency program directors and other neurosurgical leaders.

"Becoming the president of this esteemed group is perhaps the pinnacle to which an academic neurosurgeon can aspire," says Dr. Day, who is a professor in the Vivian L. Smith Department of Neurosurgery at The University of Texas Health Science Center at Houston (UTHealth) Medical School. "I am honored and humbled by this appointment and opportunity to serve our specialty."

An accomplished clinician and researcher, Dr. Day came to MNI from the department of Neurosurgery at Harvard Medical School and Brigham and Women's Hospital in Boston, where he served as a professor and program director of neurosurgery from 2002 to 2009, and chair of the department from 2007 to 2009. He received his medical degree at Louisiana State University in New Orleans in 1972, followed by a neurological residency and a neuropathology fellowship in brain tumor immunology at the University of Florida (UF) at Gainesville. After completing his training, he joined the UF faculty and rose to the rank of professor, program director and co-chair of the department.

Dr. Day's clinical interests include stroke and carotid artery disease, brain aneurysms, vascular malformations of the brain and spinal cord, skull base and orbital tumors, microsurgical treatment of all types of brain tumors, trigeminal neuralgia and hemifacial spasm, minimally invasive spinal surgery and sports-related neurological injuries. His clinical research has focused on new and safer surgical approaches to complex tumors and vascular lesions of the skull base, especially those affecting the visual system. His research interests have included neuroprotection with estrogens in ischemic and hemorrhagic stroke and biomarkers of neural injury.

A fellow of the American Surgical Association and former governor of the American College of Surgeons, Dr. Day served as vice president of the World Congress of Neurological Surgery in 2009. He is a past president of the Congress of Neurological Surgeons, past chair of the American Board of Neurological Surgery, and recently completed a six-year term as a member of the Residency Review Committee for Neurosurgery. He has served on the editorial board of numerous journals and has been consistently named among the Best Doctors in America, America's Top Doctors, Best Doctors and America's Top Doctors for Cancer. He has published widely, including authoring or coauthoring nearly 170 original articles and book chapters, as well as co-editing a book about neurological sports injuries. He has been invited as a visiting professor at many prominent universities throughout the United States and the world.

James Grotta, M.D., Named UTHealth President's Scholar

In May 2011, The University of Texas Health Science Center at Houston (UTHealth) Medical School presented its highest academic honor, the President's Scholar Award for Research, to James C. Grotta, M.D., for his achievements in the field of stroke research and treatment.

Dr. Grotta, who is co-director of the Mischer Neuroscience Institute (MNI), joined the UTHealth Medical School faculty in 1979. He is professor and chair of the department of Neurology and the Roy M. and Phyllis Gough Huffington Distinguished Chair at the Medical School, as well as the director of the Vascular Neurology Program.

From the early days in the late 1970s when Dr. Grotta published his seminal articles on calcium's role in focal ischemic stroke and global cerebral ischemia, to his groundbreaking research into the effectiveness of tissue plasminogen activator (tPA), Dr. Grotta has positioned UTHealth Medical School as a pioneer institution in the field of stroke research and treatment.

Dr. Grotta has "devoted his entire career to creating an internationally known clinical laboratory research and clinical program in cerebrovascular disease," noted Giuseppe N. Colasurdo, M.D., president ad interim of UTHealth and dean of the UTHealth Medical School, and John H. Byrne, Ph.D., chairman of the department of Neurobiology and Anatomy and assistant dean for research at the Medical School, in their letter of nomination.

To participate in the landmark 1995 clinical trial investigating the use of tPA within three hours of the onset of stroke symptoms, Dr. Grotta organized a consortium of Houston Fire Department paramedics and other Houston stroke centers equipped to rapidly assess, triage and randomize patients within the three-hour treatment window. “No such trial in stroke had ever been conducted in the world,” Drs. Colasurdo and Byrne wrote, and this success sent a “signal to the National Institutes of Health that UTHealth was one of only a handful of centers” in the country capable of conducting hyperacute stroke trials.

Through his work with imaging, Dr. Grotta and his fellows discovered that continuous transcranial Doppler ultrasound monitoring with tPA produced better outcomes than the use of tPA alone, leading to a Phase IIb study, the results of which were published in the New England Journal of Medicine in 2004.

As tPA has remained the only proven therapy for acute stroke, the National Institute of Neurological Disorders and Stroke (NINDS) created a program grant called SPOTRIAS in the early 2000s that funds centers to test new therapeutic approaches. The UTHealth Medical School was selected to be one of the four original centers in the United States to receive SPOTRIAS funding. All of the original projects in the program grant were based on research from the MNI stroke program under Dr. Grotta’s direction.

UTHealth became “a beacon for highly talented neurologists to train and complete a stroke fellowship” with Dr. Grotta, his nominators wrote. His success as a mentor garnered him a T32 training award from the National Institutes of Health over the past 15 years to develop academic leaders in stroke.

He has published extensively in both clinical and basic research, and has nearly 300 peer-reviewed publications to his name. He also has written 70 book chapters and edited seven books. His 1995 New England Journal of Medicine article on tPA use was recently named one of the publication’s top nine articles of its 200-year history.

“Over two decades, Jim has epitomized the consummate academic physician,” says Dong H. Kim, M.D., director of MNI and chair of the Vivian L. Smith Department of Neurosurgery at the UTHealth Medical School. “He has built an internationally recognized stroke program that is one of the best in the world, he has trained residents and fellows who have also become leaders in the stroke field and he has both performed and fostered groundbreaking research that has increased our understanding of the mechanisms of injury following stroke, and offered new possibilities for treatment. We are all extremely fortunate to have Jim lead us.”

Sean Savitz, M.D., Named Stroke Program Director

Sean Savitz, M.D., has been named director of the Stroke Program at the Mischer Neuroscience Institute (MNI) at Memorial Hermann. He has been co-director of the Vascular Neurology Program, director of translational stroke research and director of the Vascular Neurology (Stroke) Fellowship Program at The University of Texas Health Science Center at Houston (UTHealth) Medical School since 2007.

“Sean brings great new ideas and leadership to the program, while at the same time continuing its tradition of excellent clinical research and education,” says James Grotta, M.D., co-director of MNI, professor and head of the department of Neurology at the UTHealth Medical School and founder of the Stroke Program.

"Under Sean's direction, the Vascular Neurology Fellowship Program has doubled in size and productivity. At the same time, he has developed and funded the world's leading translational research program in stem cell therapy for stroke."

Dr. Savitz graduated from Harvard University and received his medical degree from the Albert Einstein College of Medicine. He completed his residency and fellowship in the Harvard Medical School Neurology Program at Beth Israel Deaconess Medical Center and Children's Hospital in Boston.

UTHealth Fellow Honored with New Investigator Award

Amrou Sarraj, M.D., a vascular neurology fellow at The University of Texas Health Science Center at Houston (UTHealth) Medical School, received the Mordecai Y. T. Globus New Investigator Award, presented by the American Stroke Association at the International Stroke Conference 2012.

Dr. Sarraj's work "Optimizing Prediction Scores for Poor Outcome After Intra-arterial Therapy for Anterior Circulation Acute Ischemic Stroke" was presented on February 2 in New Orleans. The study suggests that combining critical and radiographic variables can better predict poor outcome after patients undergo intra-arterial thrombolysis.

The Globus Award is named for the late renowned cerebrovascular researcher, Dr. Mordecai Y. T. Globus, and is given to a researcher who is still in training. "It's a great honor for me and a significant achievement for Mischer Neuroscience Institute's Stroke Center and the UTHealth Medical School," Dr. Sarraj says.

In Memoriam: Frank Yatsu, M.D.

Frank Yatsu, M.D., professor emeritus of neurology, died March 9, 2012. He was 79.

Dr. Yatsu joined The University of Texas Health Science Center at Houston (UTHealth) Medical School in 1982 as the second chair of the department of Neurology and was celebrated at a retirement ceremony on January 14, 2011.

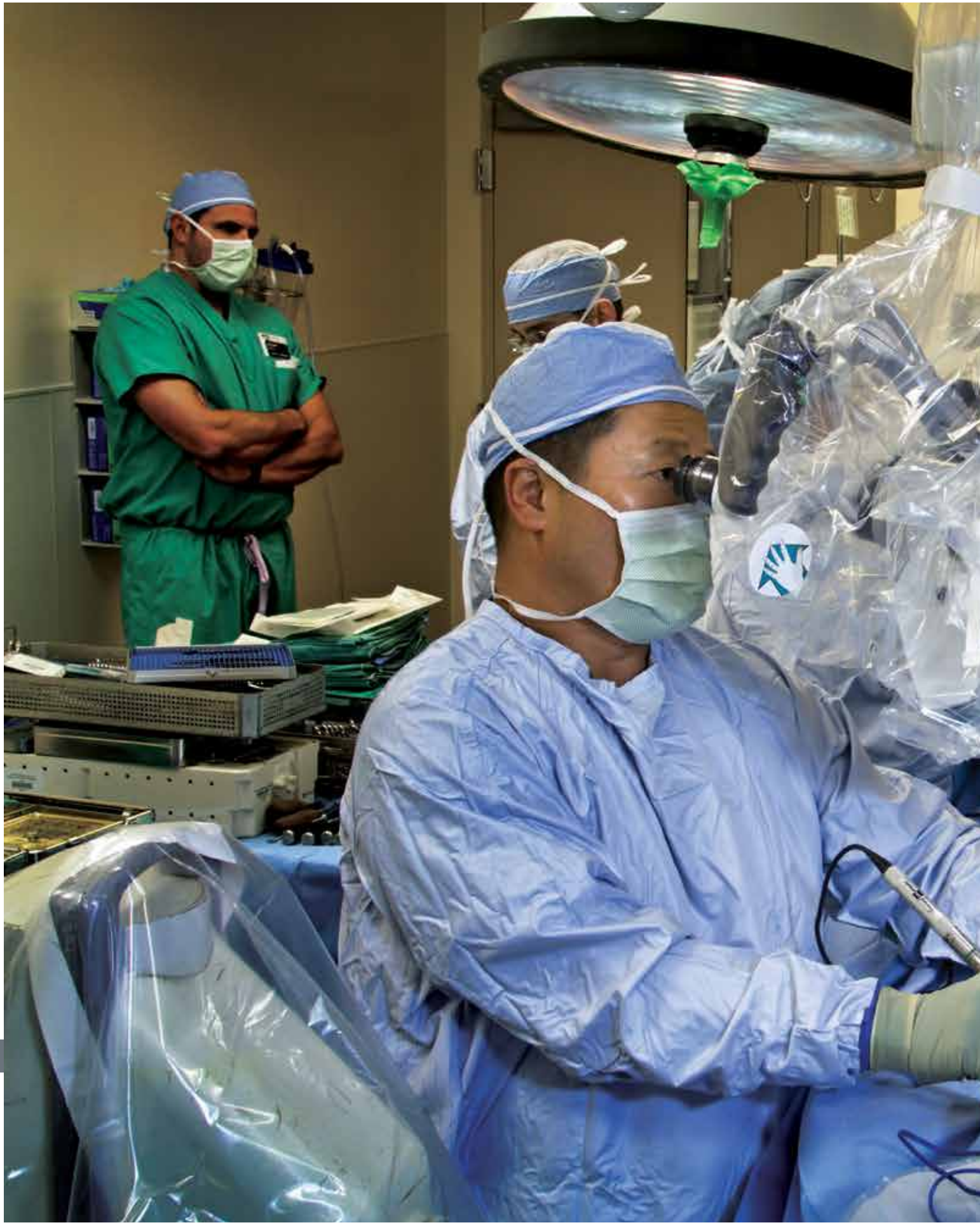
A native of Los Angeles, Dr. Yatsu moved with his family to Cleveland, Ohio, in the mid-1940s. As a Boy Scout in Cleveland, he received a full scholarship to Phillips Academy in Andover, Massachusetts. At Andover, he quickly became popular with his gregarious sense of humor and wit, and was referred to as the "walking dictionary." He went on to receive his baccalaureate from Brown University on a full four-year wrestling scholarship, and completed medical school at Case Western Reserve University. He completed an internal medicine residency at University Hospital in Cleveland and a neurochemistry fellowship at Albert Einstein College of Medicine in New York.

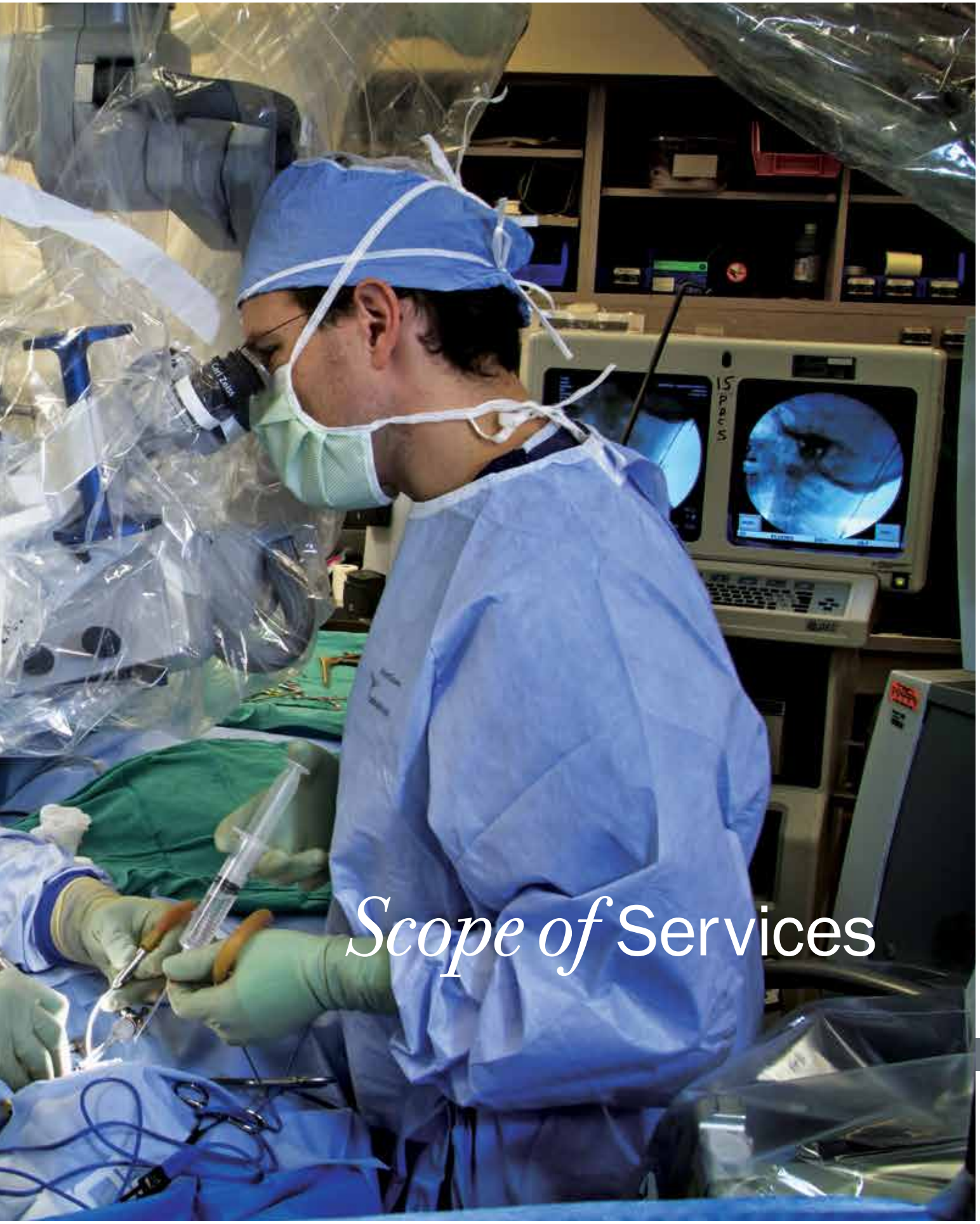
From 1965 to 1967, Dr. Yatsu served as a lieutenant commander at the U. S. Naval Academy in Great Lakes, Illinois, and later went to work for the department of Neurology at the University of California Medical Center, where he became the vice chair of the department and chief of neurology at San Francisco General Hospital. From 1969 to 1974, Dr. Yatsu was appointed a trustee of Brown University, the first Asian-American in the history of the university to receive the honor. He was named chair of neurology at the University of Oregon Health Sciences Center in Portland in 1975, a position he maintained until moving to Houston in 1982.

After stepping down as chair of the department of Neurology in 1995, he continued his clinical and research activities while at the same time turning his attention to global stroke issues. In 2004, he served as the director of the Global Stroke Initiative, a joint enterprise of the World Stroke Organization and the World Health Organization.

Dr. Yatsu is widely recognized as one of the pioneers of the modern era of cerebrovascular disease. He was the principal investigator of one of the first National Institutes of Health-funded Stroke Centers at Oregon Health and Science University. He was one of the few neurologists studying the molecular basis of lipid metabolism underlying cerebrovascular atherosclerosis, research that continues to this day. He was the leading investigator of some of the first clinical trials of acute stroke therapy and was one of the founding editors of the most highly regarded textbook in stroke, *Stroke: Pathophysiology, Diagnosis and Management,* now in its fifth edition. He was widely recognized as an outstanding teacher.

The annual Yatsu Day Symposium, sponsored by the Mischer Neuroscience Institute and the UTHealth Medical School each fall, was established in his honor. The day-long CME conference, which focuses on current issues in stroke management, will be continued in his memory.





Scope of Services

Brain Tumor

The arrival of fellowship-trained neurologist and neuro-oncologist Jay-Jiguang Zhu, M.D., Ph.D., in 2010, added strength to the Mischer Neuroscience Institute's Brain Tumor Center. Dr. Zhu joined MNI from Boston, where he trained at Massachusetts General Hospital and served on the faculty of Tufts University. He focuses his practice on primary brain tumors – gliomas, meningiomas and pituitary adenomas – and primary CNS lymphomas, as well as brain metastases and leptomeningeal spread of systemic malignancies. He is also interested in quality of life, including cognitive function during and after radiotherapy and chemotherapy; neurological complications of systemic chemotherapies; and clinical trials focused on developing new treatment options for primary brain tumors and CNS metastasis. He currently serves as principal investigator in two trials that give eligible study participants access to new and advanced treatments.

The first is a Phase III, multicenter, randomized, controlled trial designed to test the efficacy and safety of a medical device called Novo TFF-100A for newly diagnosed glioblastoma multiforme (GBM) patients in combination with temozolomide, compared to temozolomide alone. The device, which patients wear on the scalp, emits a constant, safe, low-voltage signal 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 of the safety and efficacy of the vaccine ICT-107 for newly diagnosed GBM patients following resection and chemoradiation, which began enrollment in August 2011.

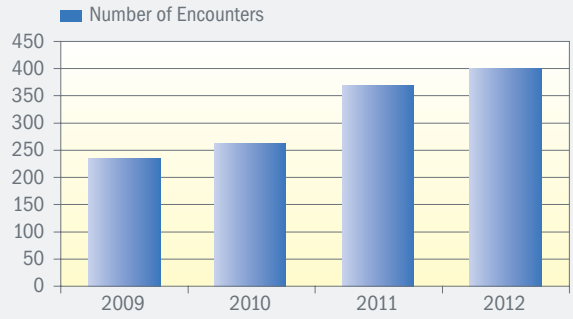
MNI expanded its neuro-oncology team with the addition of Sigmund H. Hsu, M.D., in 2012. Dr. Hsu served as assistant professor in the department of Neuro-oncology, division of Cancer Medicine at The University of Texas MD Anderson Cancer Center, where he completed a fellowship in neuro-oncology. His 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. In his new role, Dr. Hsu

will lead the new Cancer Neurology Clinic, designed to help cancer patients overcome the neurotoxicity associated with chemotherapy. He will also lead the new Brain Metastases Clinic.

In 2011, we opened our Pituitary Tumor and Vision Change Clinic to ensure 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. Led by Arthur L. Day, M.D., vice chair in neurosurgery at MNI, the clinic uses the same integrative approach that has brought national acclaim to MNI. Physicians at the clinic incorporate neurology, endocrinology, neuro-ophthalmology, stereotactic radiosurgery with Gamma Knife® technology, diagnostic radiology, interventional neuroradiology, radiation oncology and neuropathology for a comprehensive diagnosis and treatment plan. They are highly experienced in state-of-the-art microscopic and endoscopic skull-base procedures, including both transsphenoidal – the safest and most effective first-line treatment route for pituitary adenomas – and transcranial approaches.

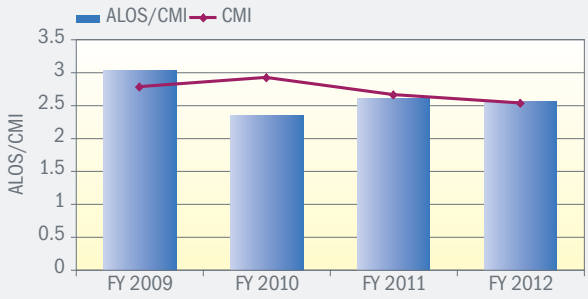
QUALITY & OUTCOMES MEASURES

Brain Tumor Volume



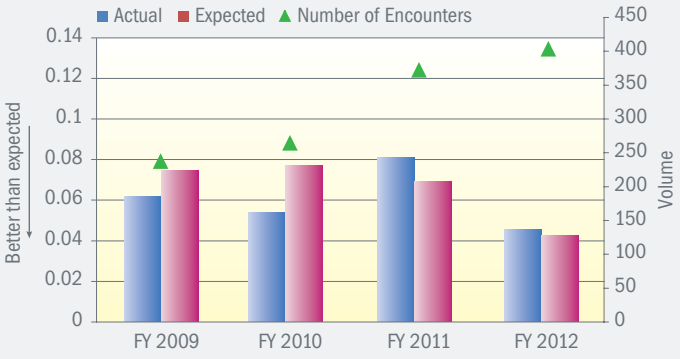
Source: chart data based on ICD-9 coded diagnoses and procedures, per fiscal year

Brain Tumors: Length of Stay



Source: chart data from the University HealthSystem Consortium

Brain Tumors: Inpatient Mortality



Source: chart data from the University HealthSystem Consortium

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

We acquired the region's first Leksell Gamma Knife® in 1993, and are 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.

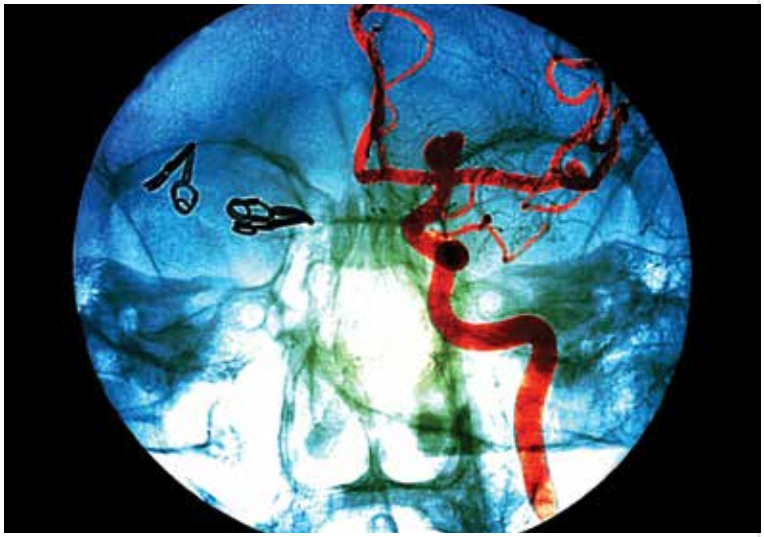
Our clinical team works closely with referring physicians throughout the Gamma Knife treatment process. A neurosurgeon and a radiation oncologist assess each candidate to determine whether radiosurgical treatment is the best option. Our Gamma Knife nurse navigators work directly with patients on scheduling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

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

Cerebrovascular

Opened in 1988 as one of the first dedicated stroke programs in the world, Mischer Neuroscience Institute's Stroke Center is home to the 10-county Greater Houston area's largest onsite stroke team. Neurologists at the Center use leading-edge technology to diagnose and treat more than 1,000 patients annually, ensuring that each patient gets the appropriate treatment as quickly as possible. By working closely with the Houston Fire Department and local EMS services, our stroke team has logged an impressive record of success in the administration of clot-dissolving tPA – more than 10 times the national average of 2 percent. The Center was the first Joint Commission and state of Texas-designated Primary Stroke Center in the region.

Our Telemedicine Program extends our stroke and neurology expertise far beyond our walls, helping emergency physicians in community hospitals throughout Southeast Texas make accurate diagnoses and save lives. Remote presence robotic technology has enhanced MNI's telemedicine program by linking outlying hospitals electronically to the Neurology department, providing real-time visual interaction between neurologists and patients, and allowing MNI neurologists to review CT scans and advise local physicians on treatment outcomes. Through telemedicine, we can now offer patients in outlying 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. Nine hospitals in Southeast Texas went live with the technology in 2012: Huntsville Memorial Hospital, Bellville General Hospital, Matagorda Regional Medical Center, Memorial Livingston Hospital, Citizens Medical Center in Victoria, Cleveland Regional Medical Center, Baptist Orange Hospital, the Medical Center of Southeast Texas in Port Arthur, and St. Joseph Hospital-Downtown in Houston.



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

The Argatroban and Tissue-Type Plasminogen Activator Stroke Study Final Results of a Pilot Safety Study

Barreto AD, Alexandrov AV, Lyden P, Lee J, Martin-Schild S, Shen L, Wu T-C, Sisson A, Pandurengan R, Chen Z, Rahbar MH, Balucani C, Barlinn K, Sugg R, Garami Z, Tsivgoulis G, Gonzales NR, Savitz SI, Mikulik R, Demchuk AM, Grotta JC

ABSTRACT

Background and Purpose: Argatroban is a direct thrombin inhibitor that safely augments recanalization achieved by tissue-type plasminogen activator (tPA) in animal stroke models. The Argatroban tPA Stroke Study was an open-label, pilot safety study of tPA plus Argatroban in patients with ischemic stroke due to proximal intracranial occlusion.

Methods: During standard-dose intravenous tPA, a 100-μg/kg bolus of Argatroban and infusion for 48 hours was adjusted to a target partial thromboplastin time of 1.75× baseline. The primary outcome was incidence of significant intracerebral hemorrhage defined as either symptomatic intracerebral hemorrhage or Parenchymal Hematoma Type 2. Recanalization was measured at 2 and 24 hours by transcranial Doppler or CT angiography.

Results: Sixty-five patients were enrolled (45% men, mean age 63±14 years, median National Institutes of Health Stroke Scale=13). The median (interquartile range) time tPA to Argatroban bolus was 51 (38–60) minutes. Target anticoagulation was reached at a median (interquartile range) of 3 (2–7) hours. Significant intracerebral hemorrhage occurred in 4 patients (6.2%; 95% CI, 1.7–15.0). Of these, 3 were symptomatic (4.6%; 95% CI, 0.9–12.9). Seven patients (10%) died in the first 7 days. Within the 2-hour monitoring period, transcranial Doppler recanalization (n=47) occurred in 29 (61%) patients: complete in 19 (40%) and partial in another 10 (21%).

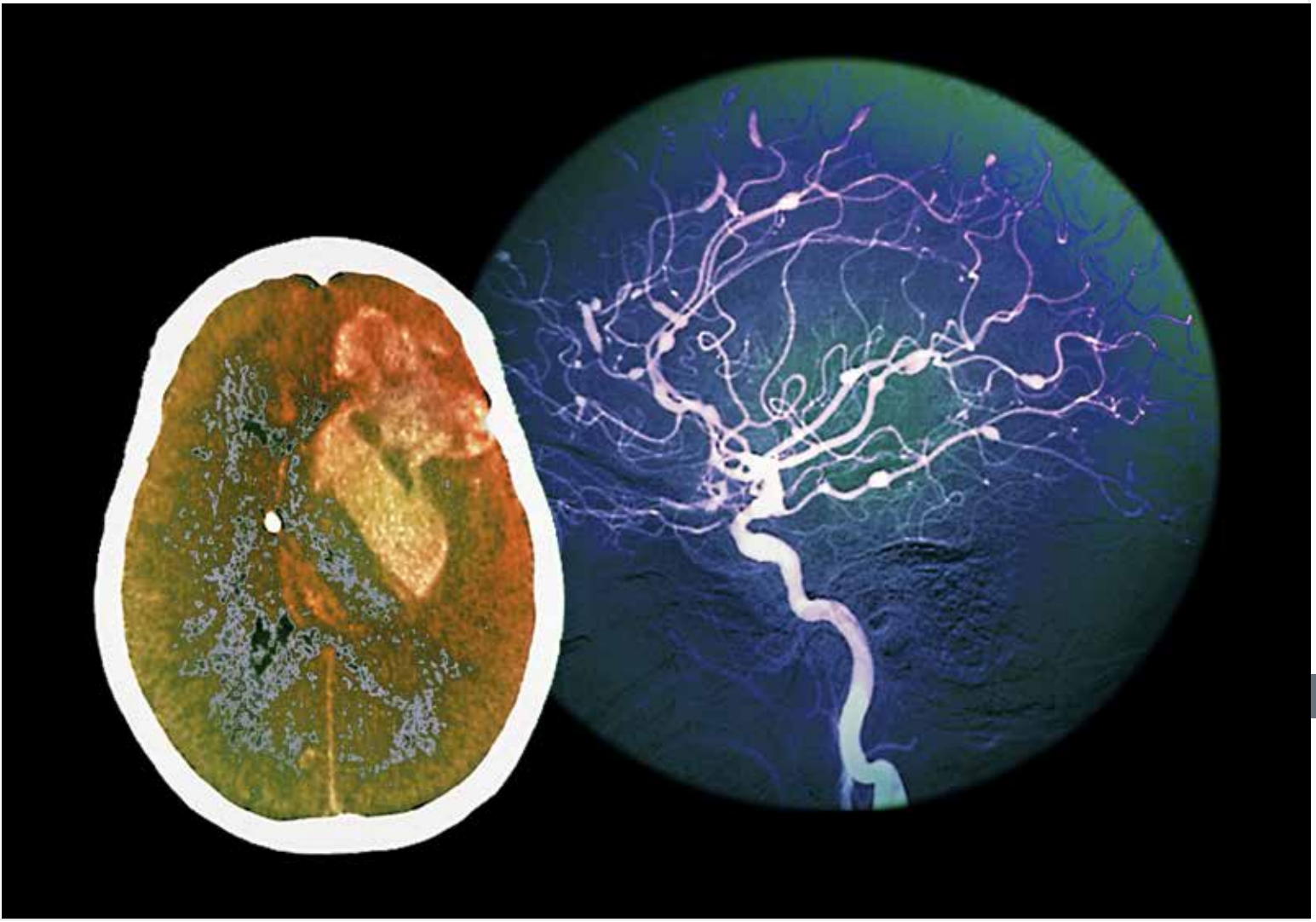
Conclusions: The combination of Argatroban and intravenous tPA is potentially safe in patients with moderate neurological deficits due to proximal intracranial arterial occlusions and may produce more complete recanalization than tPA alone. Continued evaluation of this treatment combination is warranted.

Stroke. 2012;43:770-775 published online before print January 5, 2012 doi:10.1161/STROKEAHA.111.625574

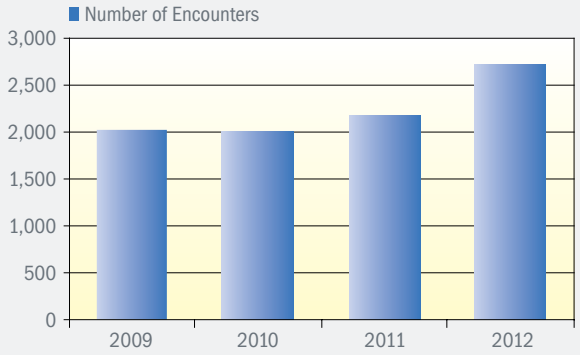
microvascular clipping of aneurysms, endovascular embolization, extracranial-intracranial bypass and carotid endarterectomy.

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

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

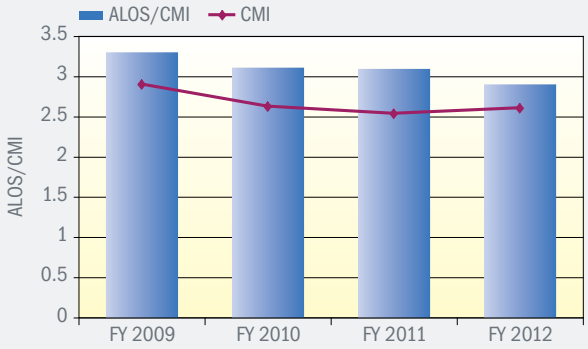


Cerebrovascular Volume



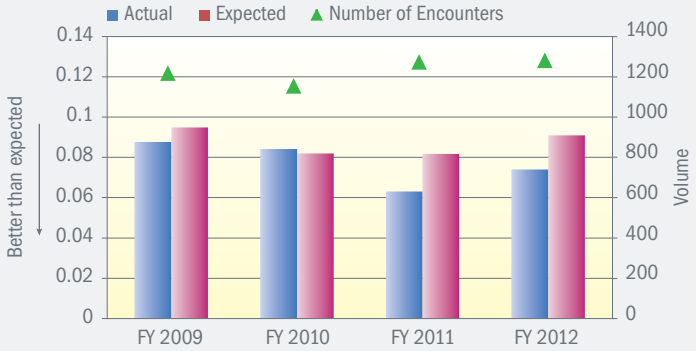
Source: chart data based on ICD-9 coded diagnoses and procedures, per fiscal year

Acute Ischemic Stroke: Length of Stay



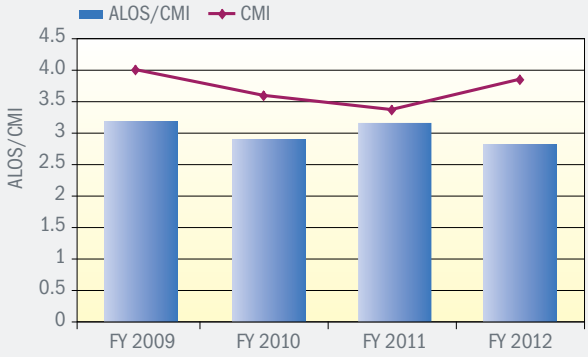
Source: chart data from the University HealthSystem Consortium

Acute Ischemic Stroke: Inpatient Mortality



Source: chart data from the University HealthSystem Consortium

Intracerebral Hemorrhage: Length of Stay



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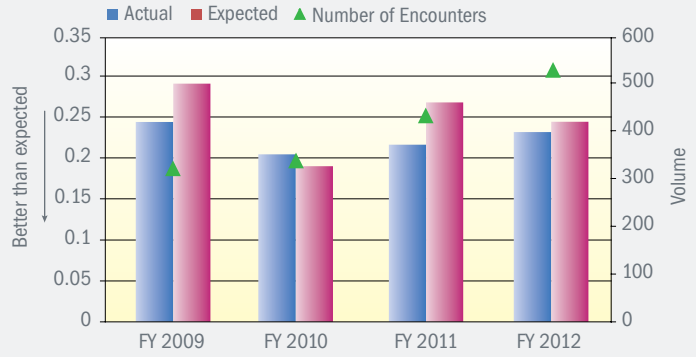
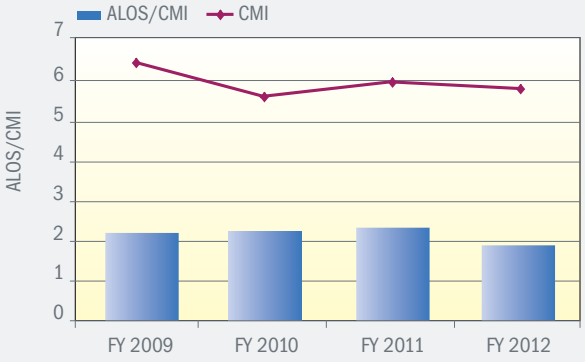
Intracerebral Hemorrhage: Inpatient Mortality



Source: chart data from the University HealthSystem Consortium

Sub-arachnoid Hemorrhage: Length of Stay



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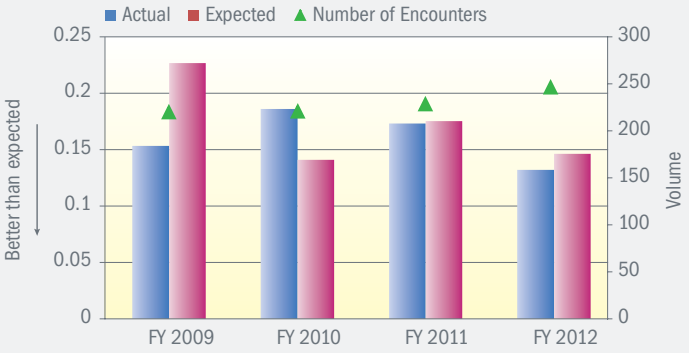
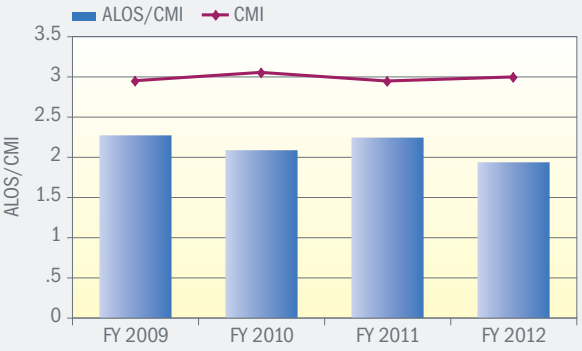
Sub-arachnoid Hemorrhage: Inpatient Mortality



Source: chart data from the University HealthSystem Consortium

Aneurysm Unruptured: Length of Stay



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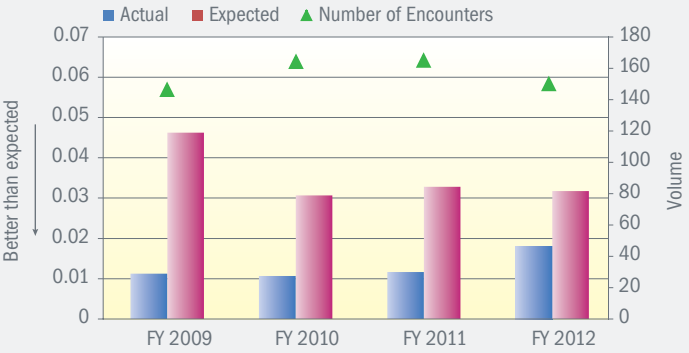
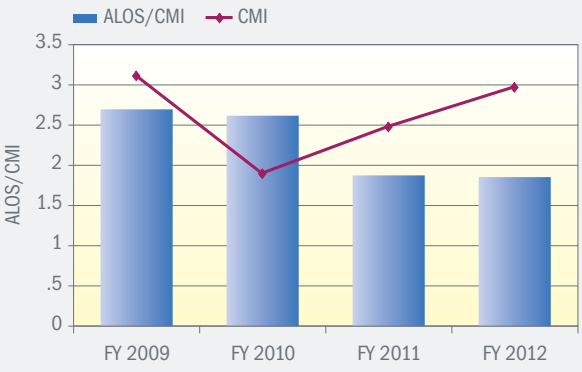
Aneurysm Unruptured: Inpatient Mortality



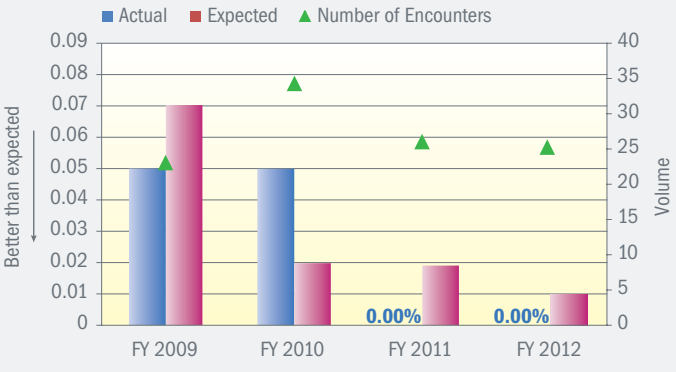
Source: chart data from the University HealthSystem Consortium

Arteriovenous Malformation: Length of Stay



Source: chart data from the University HealthSystem Consortium

Arteriovenous Malformation: Inpatient Mortality



Source: chart data from the University HealthSystem Consortium

Children's Neuroscience

With the arrival of David Sandberg, M.D., F.A.C.S., F.A.A.P., in June 2012, the Mischer Neuroscience Institute added significant strength to its Children's Neuroscience Center. Dr. Sandberg joined the MNI team as director of pediatric neurosurgery from Miami Children's Hospital and the University of Miami Miller School of Medicine, where he was a voluntary associate professor of clinical neurological surgery and pediatrics. His major clinical interests include pediatric brain tumors, minimally invasive endoscopic approaches to brain tumors and hydrocephalus, congenital spinal anomalies, vascular malformations, spasticity and craniofacial disorders in children. Dr. Sandberg is a national leader in developing novel techniques to treat malignant brain tumors in children. Prior to arriving in 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 the initiation of a pilot clinical trial in collaboration with The University of Texas MD Anderson Cancer Center, which Dr. Sandberg is leading as principal investigator.

In addition to introducing novel treatment options for pediatric brain tumors, Dr. Sandberg has published extensively and lectured nationally and internationally on minimally invasive endoscopic techniques to treat both brain tumors and hydrocephalus. To avoid the many complications of ventriculoperitoneal shunting for children with hydrocephalus, our pediatric neurosurgeons frequently perform 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.

Our 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 our center for fetal myelomeningocele repair from throughout Texas and a number of surrounding states.

In collaboration with nationally recognized craniofacial plastic surgeons, pediatric neurosurgeons at Children's Memorial Hermann Hospital perform both conventional and minimally invasive endoscopic surgeries to repair craniosynostosis and other complex craniofacial anomalies. Our 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.

Our 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, we 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 we also use video EEG, PET, SPECT, memory and speech (Wada) testing and neuropsychological testing. We are one of only a few inpatient units 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.

We provide 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. We also offer 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.

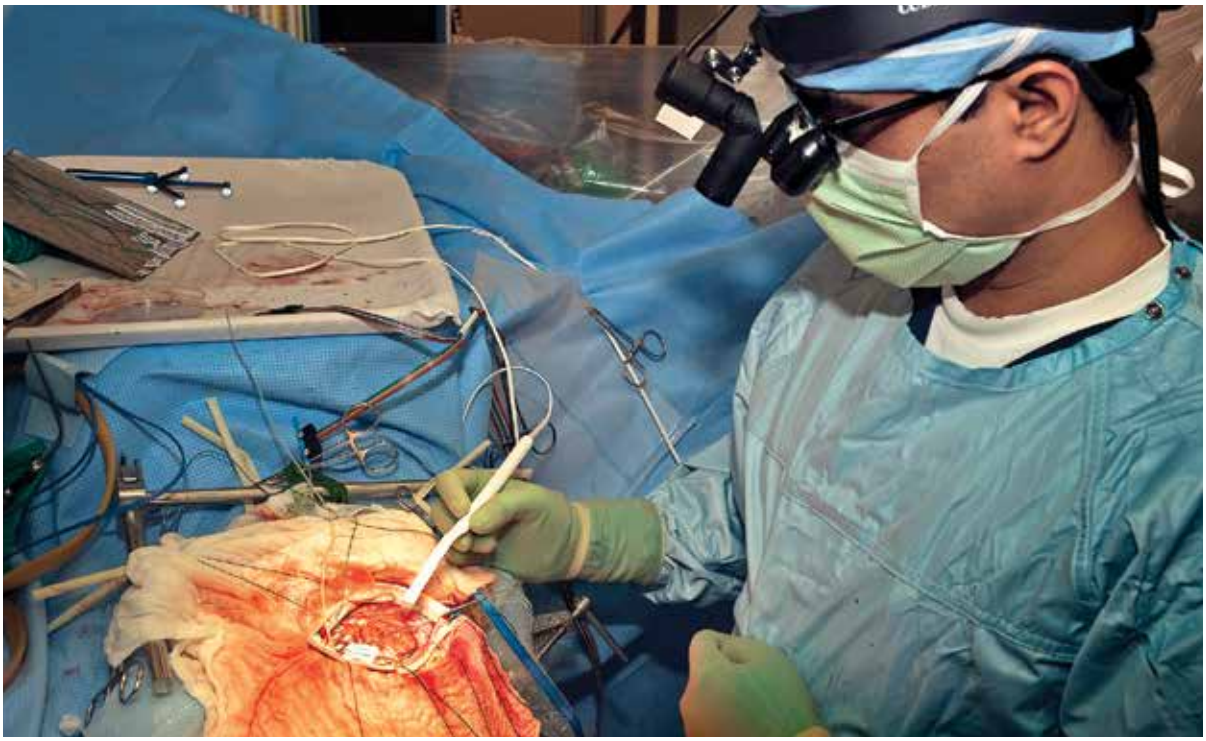
Care at Children's Memorial Hermann Hospital is delivered in a friendly, reassuring environment to promote wellbeing and the best possible outcomes. When surgery is required, we use advanced imaging techniques and minimally invasive procedures that lower patient risk. Onsite sedation is available for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

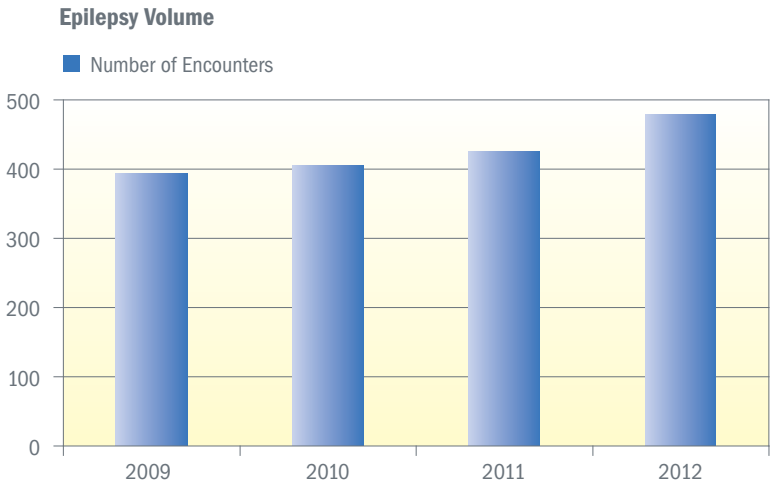
Epilepsy

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

At the heart of our program is a state-of-the-art Epilepsy Monitoring Unit (EMU), the largest and most comprehensive unit of its kind in the region. Patients are referred to the EMU when they have seizures of unknown cause, medically uncontrolled seizures, or are being evaluated for epilepsy surgery. They typically stay in the unit an average of five to seven days. We are one of only a few inpatient units in the country with a comprehensive set of diagnostic technologies that include routine application of a variety of techniques, which, taken together, provide us with datasets that help define and localize the seizure network in the brain.

Our full suite of diagnostic tools includes magneto-encephalography (MEG) to map neurological function, video EEG, 3-Tesla structural MRI, functional MRI





The Texas Comprehensive Epilepsy Program has shown a dramatic increase in volumes in 2012. In the past year, we have treated more than 450 pediatric and adult patients for seizures and epilepsy. Diagnostic tools that localize the origin of seizures and map brain function, and advanced surgical procedures, including laser ablation and stereo EEG, have allowed us to complete even more successful resective surgeries in fiscal year 2012.

and diffusion tensor tractography, positron emission tomography (PET), single photon emission computed tomography (SPECT), memory and intracarotid amytal (Wada) testing and in-depth neuropsychological testing. We are a national leader in combining the use of MEG and functional MRI to map the brain and record brain activity. Each year, we perform more than 150 MEG procedures on pediatric and adult patients. We are also one of only a few inpatient units in the country with the capability to perform electroencephalography and polysomnography simultaneously.

The number of patients we treat annually continues to grow. Today, our board-certified neurologists and neurosurgeons diagnose and treat more than 450 pediatric and adult patients each year for seizures and epilepsy. Genetics, brain trauma, structural abnormalities, stroke and brain tumor rank among the top underlying causes, but because epilepsy and other types of seizures manifest differently among individuals, determination of the origin of seizures is crucial to planning the most effective treatment.

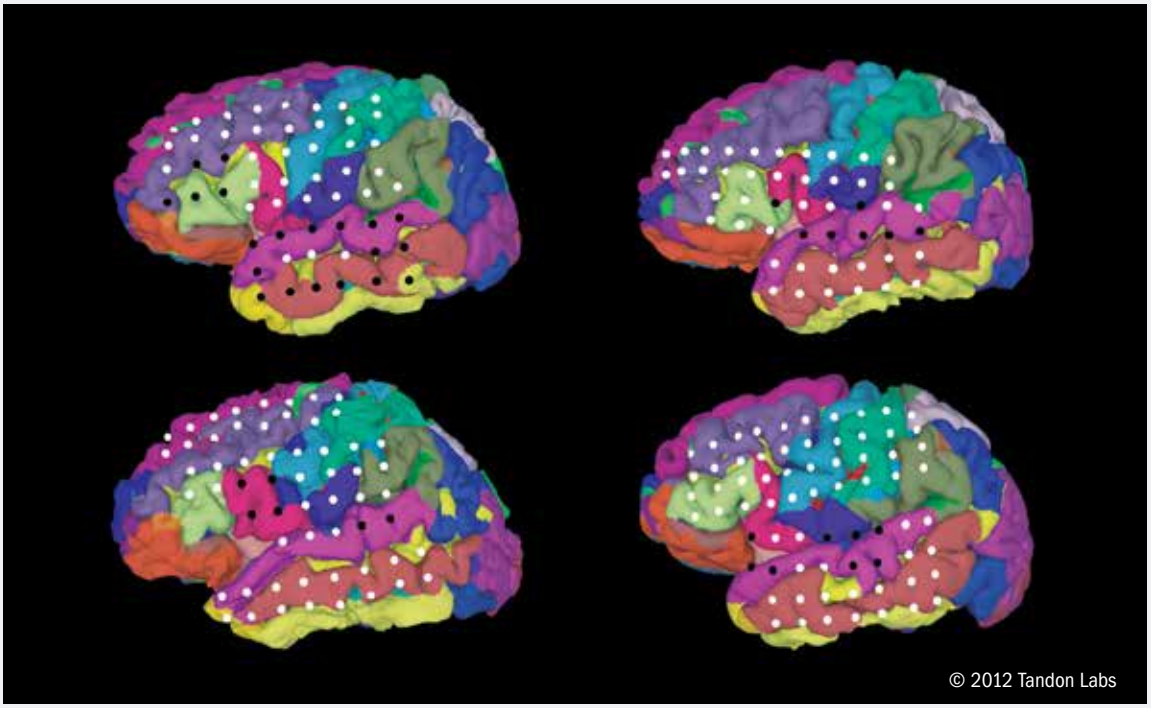
Once a diagnosis is made, we offer the most advanced treatment options available, including drug therapy, the ketogenic diet, vagus nerve stimulation (VNS), focal cortical resection, lobectomy, hemispherectomy and corpus callosotomy. Our surgical complication rates have remained extremely low over the past eight years. At the current time, our epilepsy surgeon has performed

Recursive Grid Partitioning on a Cortical Surface Model: An Optimized Technique for the Localization of Implanted Subdural Electrodes

Pieters TA[1], Conner CR[1], Tandon N[1,2]

[1] The Vivian L. Smith Department of Neurosurgery, The University of Texas Health Science Center at Houston (UTHealth) Medical School

[2] Mischer Neuroscience Institute, Memorial Hermann-Texas Medical Center



ABSTRACT

Objective: Precise localization of subdural electrodes (SDEs) is essential for the interpretation of data from intracranial electro-corticographic (ECoG) recordings. Blood and fluid accumulation underneath the craniotomy flap leads to a nonlinear deformation of the brain surface and of the SDE array on post-operative CT scans, and adversely impacts the accurate localization of electrodes located underneath the craniotomy. Older methods that localize electrodes based on their identification on a post-implantation CT, with co-registration to a pre-implant MRI, can result in significant problems with accuracy of the electrode localization. We report here three novel methods that rely on the creation of a set of 3D mesh models to depict the pial surface and a smoothed pial envelope.

Methods: The first method involves manually picking the location of each electrode using digital photographs obtained at surgery. This is highly accurate, but requires time-intensive, operator-dependent input. The second uses four electrodes localized manually in conjunction with an automated, recursive partitioning technique to localize the entire electrode array constituting a particular subdural grid. We evaluated the accuracy of previously published

methods by applying them to our data and comparing them against the photograph-based localization. Lastly, we further enhanced the usability of our new methods by using automatic parcellation techniques to assign anatomic labels to individual electrodes as well as by implementing a strategy to generate an inflated cortical surface model while still preserving electrode locations relative to the cortical anatomy.

Results: The recursive grid partitioning had the least error in comparison to older methods (672 electrodes, 6.4 mm maximum single electrode error, 1.97 mm mean error, $p < 10^{-18}$). The maximum errors derived using prior methods of localization ranged from 8.20 mm to 11.73 mm for an individual electrode, with mean errors ranging between 2.9 and 4.1 mm depending on the method used. We also noted a larger error in all methods that used CT scans alone to localize electrodes as compared to those that used both post-op CT and post-op MRI. The large mean errors reported with these methods are liable to affect inter-modal data comparisons (e.g., with functional mapping techniques) and may impact surgical decision-making.

Conclusion: We have presented several aspects of using a new technique to visualize electrodes implanted for localizing epilepsy. The ability to use automated labeling schema to denote which gyrus a particular electrode overlies is potentially of great utility in planning resections, and in corroborating the results of extra-operative stimulation mapping. Dilation of the pial mesh model provides, for a first time, a sense of the cortical surface not sampled by the electrode, and the potential roles this "electrophysiologically hidden" cortex may play in both eloquent functions and seizure onsets.

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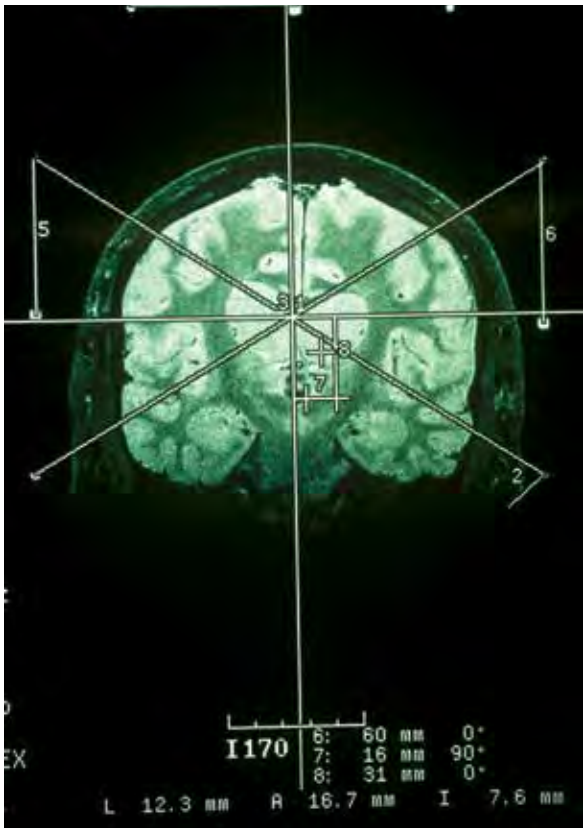
more than 350 craniotomies for the treatment of epilepsy, with a zero percent mortality rate and a very low rate of permanent morbidity from such operations. We also go beyond diagnosis and treatment of epilepsy by counseling patients in ways to cope with their diagnosis. Specialized counselors ensure that recently diagnosed patients have the emotional support they need.

Our team has been involved in research related to most epilepsy treatments approved in the United States in the last 15 years, including a number of drug and intravenous therapies and VNS therapy. Current research includes lacosamide monotherapy and adjunctive therapy for partial-onset seizures; an open-label extension study of rufinamide as an adjunctive therapy in patients with refractory partial-onset seizures; 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. Another new innovation is the application of stereoencephalography for the localization of epilepsy arising in deep foci in the brain. This technique blends the use of frame based stereotaxy with the 3D planning capabilities of modern neuro-navigation software, to help localize epilepsy in a minimally invasive fashion.

MNI is a pioneering site for the application of laser surgery to the treatment of well-delineated focal epilepsies, with carefully selected patients being treated with this highly advanced, minimally invasive approach to the ablation of the seizure focus.

Movement Disorders and Neurodegenerative Diseases

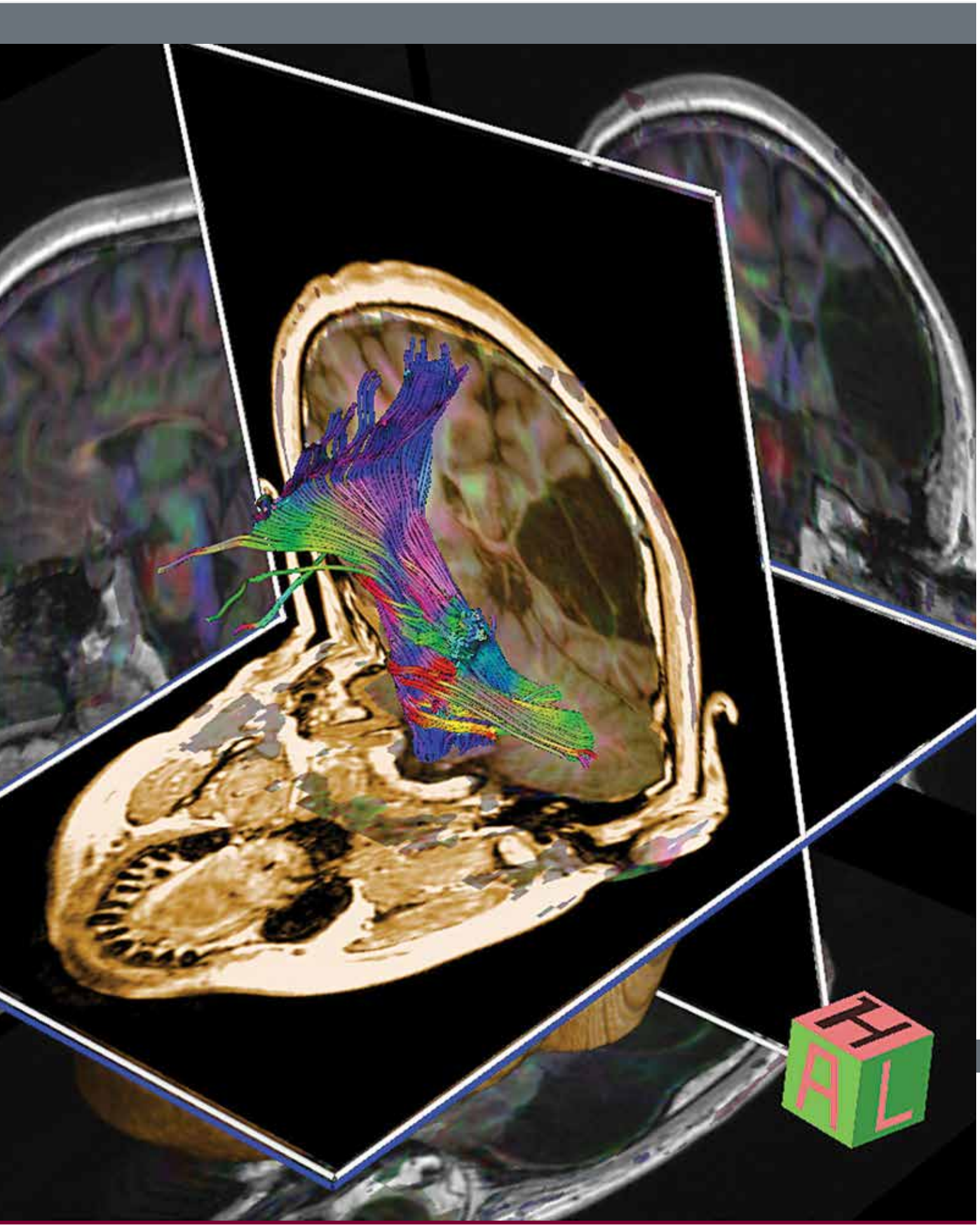
Using pioneering techniques to diagnose, evaluate, manage and treat adult and geriatric patients, the Movement Disorders and Neurodegenerative Diseases Program has established a track record of providing outstanding care with excellent outcomes. In 2012, we nearly doubled our number of patient visits.



Our medical team uses proven and investigational medications and interventional methods to manage Parkinson's disease, Parkinsonian disorders, generalized and focal dystonia, essential tremor, Huntington's chorea, Alzheimer's disease, cortical and subcortical dementias, cerebral palsy, spasticity, ataxias, gait disorders, spinal and brain trauma-related movement abnormalities, multiple sclerosis-related movement abnormalities and other inherited and acquired neurodegenerative diseases.

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

Our deep brain stimulation (DBS) program for Parkinson's tremor, dystonia and essential tremor is known for low complication rates and outstanding outcomes. Based on the skill of our neurological and neurosurgical teams and our expertise in DBS programming, we advocate for early use of deep brain stimulation in appropriate patients.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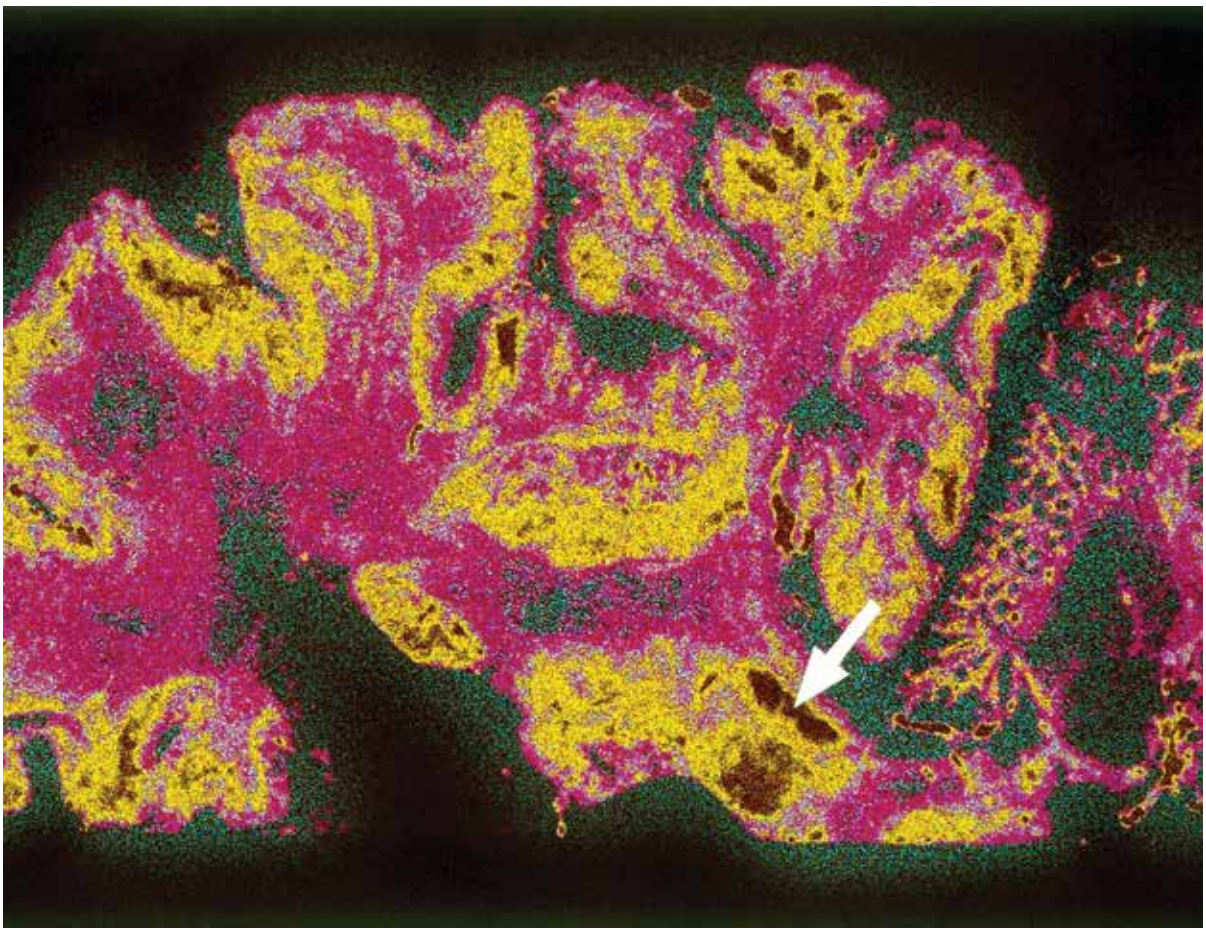
In 2012, we recorded record growth in our DBS program. The Movement Disorders and Neurodegenerative Diseases Program is a collaborative effort of the Mischer Neuroscience Institute and UT MOVE, with specialty clinics that include Spasticity Management, DBS Selection and Programming, Botox® Injection and Intrathecal Baclofen Pump Therapy. Because rehabilitation is integral to our outcomes, we work closely with the physical and occupational therapists and speech-language pathologists in our inpatient and outpatient clinics and at TIRR Memorial Hermann to research new approaches to improving treatment.

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. We regularly take part in clinical trials of devices for deep brain stimulation and are unique in our participation in worldwide registry databases for both DBS stimulation implants and intrathecal baclofen pumps.



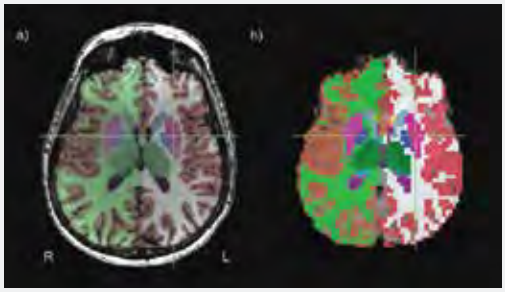
Reduced Resting State Functional Connectivity as an Imaging Pre-symptomatic Biomarker of Parkinson's Disease

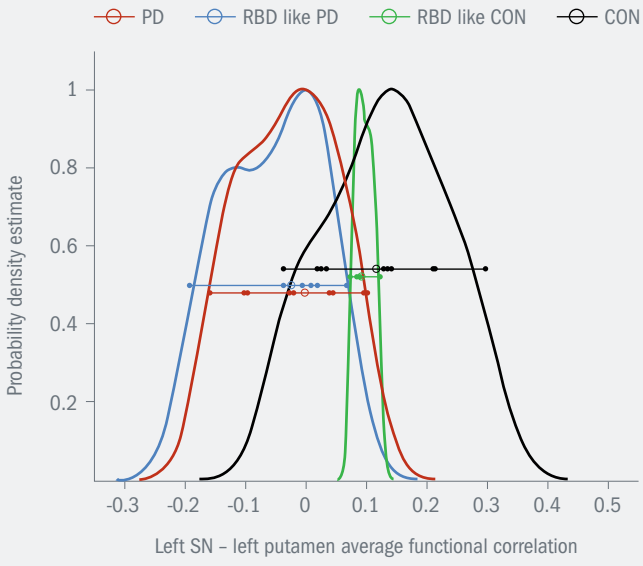
PRINCIPAL INVESTIGATOR: **Mya C. Schiess, M.D.**
Professor and Adriana Blood Chair in Neurology
Department of Neurology
The University of Texas Health Science Center at Houston (UTHealth) Medical School

Rapid eye movement sleep disorder (RBD), a sleep disturbance, is one of the most common non-motor complications of Parkinson's disease (PD). RBD frequently arises as an early manifestation in PD, likely reflecting the anatomical areas affected by the neurodegenerative process. While specific neuropathological aspects shared by RBD and PD have yet to be fully documented, further characterization is critical to discovering reliable biomarkers that predict PD onset.

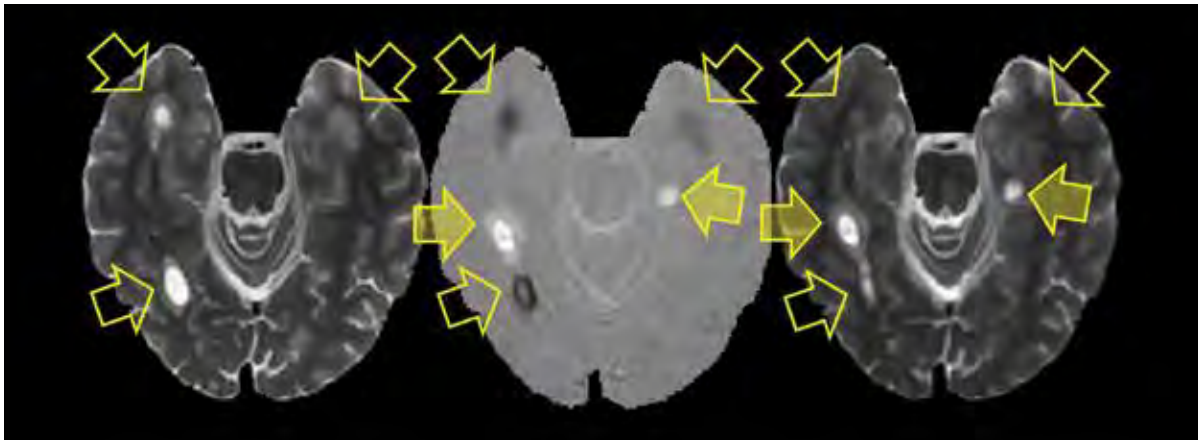
In a recent study, we tested the hypothesis of a diminished functional connection between substantia nigra and striatum in patients diagnosed with RBD. We measured functional correlations of substantia nigra using rest-state blood oxygen level-dependent functional magnetic resonance imaging (BOLD-fMRI) in a group of idiopathic RBD patients at risk for developing PD, a group of diagnosed PD patients and a group of aged controls. Significantly reduced correlations ($p<0.01$, corrected) in RBD and PD patients compared to controls were found between substantia nigra and putamen using voxelwise tests and single-subject region of interest analyses indicating impairment of nigrostriatal functional connectivity.

Individual Subject Left SN – Left Putamen Average Correlation Values and Modeled Distributions





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. Our scope of expertise is broad and includes patients in all stages of MS, as well as those with neuromyelitis optica, transverse myelitis and optic neuritis. We are experienced in the appropriate use of aggressive therapies in severe cases.

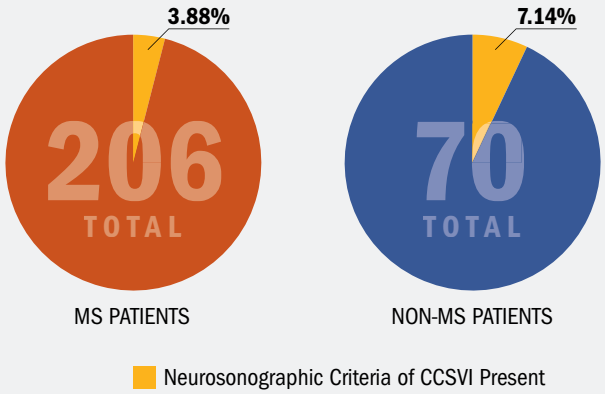
Organized in 1983, the Multiple Sclerosis Research Group (MSRG) has participated in numerous clinical trials of novel disease-modifying therapies, serving as the lead center for numerous international studies, several of which were pivotal in gaining FDA approval of currently available treatments for MS. 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).

We were the first center in the world to conduct preclinical studies on the effects of combined therapy with immunomodulating drugs and to explore the effects of oral cytokines in modulating MS and Type 1 diabetes. We are the first and only center in Houston to direct national and international clinical trials in MS, and we remain the North American leader in studies of primary progressive multiple sclerosis, as well as the most active center in Texas in the conduct of organized clinical trials of new therapies for MS. Our physicians are at the forefront of investigator-initiated research

Prospective Case-Control Study of Chronic Cerebrospinal Venous Insufficiency: Neurosonography Results

PRINCIPAL INVESTIGATOR: **Jerry S. Wolinsky, M.D.**
Professor, Bartels Family Professor and Opal C. Rankin *Professor in Neurology,* Department of Neurology
The University of Texas Health Science Center at Houston (UTHealth) Medical School

Many centers have postulated that there is a significant impairment of cerebral venous drainage in multiple sclerosis (MS), which has led to increased utilization of imaging for chronic cerebrospinal venous insufficiency (CCSVI). Our facility participated in a prospective case-control study to evaluate the association of CCSVI with MS. The study evaluated imaging of extracranial and intracranial venous drainage among 276 patients: 206 had MS and 70 did not. Overall, 82 subjects (29.7 percent) fulfilled one of five criteria for CCSVI; 13 (4.7 percent) fulfilled two criteria and none fulfilled greater than two criteria. The distribution of subjects with zero, one or two criteria did not differ significantly across all diagnostic groups, between patients with or without multiple sclerosis. No significant differences emerged between MS and non-MS subjects for extracranial or intracranial venous flow rates. Our findings described as CCSVI are much less prevalent than previously reported and do not distinguish MS subjects from other subjects. The findings do not support the postulate that CCSVI is causally associated with MS.



On May 10, 2012, the U.S. Food & Drug Administration released a safety communication alerting people with MS to the risk of serious injury and death associated with procedures to treat CCSVI. According to the FDA, "The benefits of these experimental procedures have not been proven, and their promotion as a treatment for MS may lead people with the disease to make treatment decisions without being aware of the serious risks involved."

in immune regulation in MS, infection as a cause of MS, MS-related cognitive impairment and MS-related MRI findings.

In our state-of-the-art Magnetic Resonance Imaging Analysis Center, we use spectroscopic and diffusion tensor imaging with tractotomy, as well as other advanced diagnostic tools. Following diagnosis, patients benefit from breakthrough treatment options that include injectable immunomodulators, immunosuppressives and other agents designed to treat the debilitating symptoms of MS. Investigators also use the MRI Analysis Center to monitor the effects of promising oral drugs in pivotal efficacy trials.

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

Neurocognitive Disorders

Physicians in the Neurocognitive Disorders Center at the Mischer Neuroscience Institute are dedicated to evaluating and treating people with an array of diseases that produce cognitive, behavioral, mood and interpersonal symptoms, and to performing leading-edge research into the diseases that produce these disorders. In 2012, we were the first program in Houston to offer a new tool that enables physicians to diagnose Alzheimer's disease (AD), and to give researchers insights into how they might one day prevent the disorder. The tool is a PET scan that uses florbetapir, which attaches to amyloid deposited in the brains of patients with Alzheimer's disease. A positive or negative scan is very helpful to physicians considering a diagnosis of AD. The technique was approved in April of 2012 by the Food and Drug Administration.

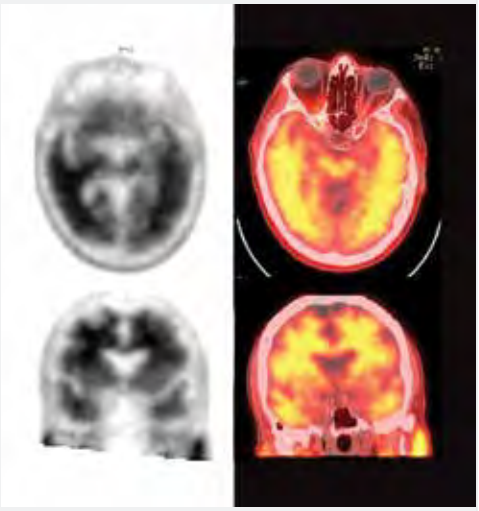
Our Center expanded this year with the addition of two new neuropsychologists who are experts at assessing cognitive function – Jacqueline Phillips-Sabol, Ph.D., and Bethany Williams, Ph.D., and we are moving to a new building to accommodate the expansion of our faculty and support staff.

We have several foci of evaluation, treatment, and investigation.

Greater Prevalence and Incidence of Dementia in Older Veterans with Post-Traumatic Stress Disorder

Qureshi SU, Kimbrell T, Pyne JM, Magruder KM, Hudson TJ, Petersen NJ, Yu H-J, Schulz PE, Kunik ME

A recent article demonstrated that the odds of being diagnosed with dementia are 2.3 times as high in veterans with post-traumatic stress disorder (PTSD). That was true even when comparing veterans with PTSD, a psychologic trauma, to veterans with combat-related injuries, which produce both physical and psychologic stress. Other factors related to dementia risk were gender, race and medical illnesses, including diabetes mellitus, elevated cholesterol, high blood pressure, coronary artery disease, stroke, traumatic brain injury, smoking, alcohol abuse and dependency, and drug abuse and dependency. This study, then, suggests that severe psychologic stress can cause long-lasting changes in the brain that put people at very increased risks for developing dementia. This finding is also important to civilians, who develop PTSD at comparable rates to service men and women after stressful events, such as serious car accidents.



Importantly, it was also found that one risk factor can increase the chances of having another risk factor for dementia. For example, mild TBI at the time of a stressful event increases the odds of developing PTSD from 23 to 60 percent. In the other direction, we have demonstrated that controlling risk factors for dementia, like hypertension, reduces the risk of developing the disorder.[1]

Current approaches to treating dementia are to implement treatment after a patient has been diagnosed with dementia. At the Neurocognitive Disorders Center, we are investigating screening tools that may predict dementia prior to its onset. In 2012, we were the first program in Houston to offer a new tool approved by the FDA that enables physicians to diagnose Alzheimer's disease (AD). A florbetapir PET scan demonstrates amyloid plaques in the brains of patients with AD, thereby allowing a diagnosis of AD in a living patient, which formerly was possible only at autopsy. This powerful tool may allow us to diagnose amyloid deposition before the symptoms of dementia start. Additional research is being conducted to identify how to prevent or delay dementia in patients in whom amyloid is visualized, and replacing lost neurons with stem cells.

[1] Johnson ML, Parik N, Kunik ME, Schulz PE, Patel JG, Chen H, Aparasu RR, Morgan RO. Antihypertensive Drug Use and the Risk of Dementia in Patients with Diabetes Mellitus. Alzheimer's and Dementia, 2012, 1-8.

Journal of the American Geriatrics Society, 2010, 58:1627-1633

Our Memory Disorders and Dementia Clinic is dedicated to assessing and treating all the known causes of dementia, including infections, trauma, medications, vitamin or hormone deficiencies, vascular disease and strokes, and neurodegenerative disorders, such as AD, frontotemporal dementia (FTD) and Parkinson's disease. Research efforts in the MNI Memory Disorders and Dementia Clinic are directed at developing ways to provide early diagnosis and treatment for these devastating illnesses. This includes determining which individuals will develop dementia, finding accurate tools to diagnose dementia and determine the type from which a person suffers, and finding ways to stop the progression of dementing illnesses.

A second focus is in neuropsychiatry, in which we determine whether patients with psychiatric symptoms have an underlying neurologic cause, or whether patients with neurologic symptoms may have an underlying psychiatric disorder. The major foci of our research in this area are traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD), both of which cause neurologic and psychiatric symptoms. Together with the Center for Translational Injury Research, we are investigating treatments for TBI and the causes, treatments and prevention of PTSD.

A third area of focus is our Stroke and Dementia Prevention Program, which is dedicated to reducing the risk of developing dementia and to developing new diagnostic and treatment tools. Our team has identified multiple risk factors for dementia, including family history, head trauma, high blood pressure, high cholesterol or triglycerides, diabetes, obesity, smoking, post-traumatic stress disorder and many others. In this clinic, physicians evaluate individuals at risk for dementia who are asymptomatic, and treat their risk factors. Risk factor reduction is associated with a significant decrease in a person's risk for developing dementia. Research efforts in this clinic are focused on investigating new treatments to delay or ameliorate the development of dementia. We believe that treatment interventions will be much more effective if introduced early in the molecular cascade of events that lead to these diseases – before dementia symptoms develop.

A fourth area of focus is frontotemporal dementia. FTD typically onsets in the 50s and causes devastating behavioral changes in people at the prime of their lives. Our clinic is dedicated to evaluating and treating patients with FTD, and investigating the environmental and genetic causes of FTD. We are also investigating its relationship to amyotrophic lateral sclerosis, a devastating disorder that produces progressive weakness.

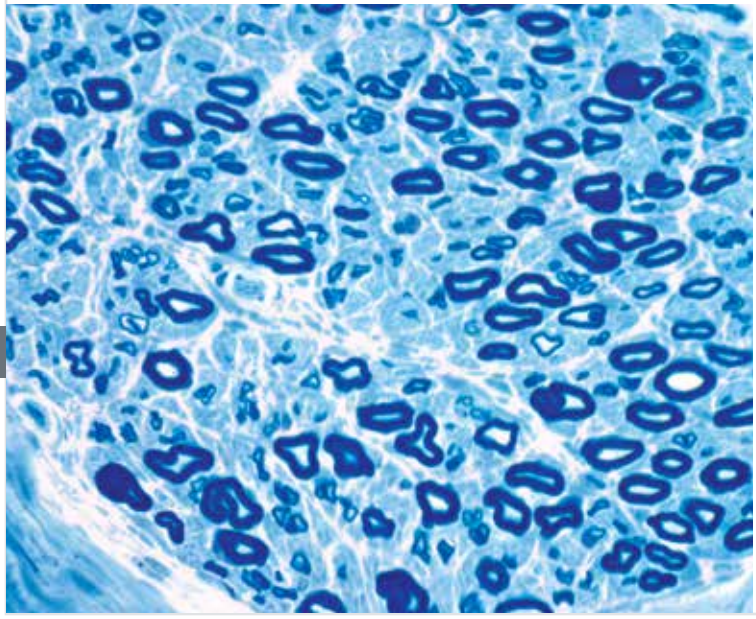
Our laboratory partner is the George P. and Cynthia W. Mitchell Center for Research in Alzheimer's disease and Related Brain Disorders under the direction of Claudio Soto, Ph.D. Findings are taken from the clinic to the laboratory and from the laboratory to the clinic to develop new diagnostic methods and treatments for dementia. For example, together we are identifying biomarker changes in animals that can be studied as diagnostic tools in humans, and we are testing medications to treat these diseases.

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

Neuromuscular Disorders

The GBS/CIDP Foundation International has designated the Mischer Neuroscience Institute's Neuromuscular Disorders Program a center of excellence for the diagnosis and treatment of Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP) and other inflammatory peripheral neuropathies. The designation was awarded in recognition of the high standards maintained and quality of patient care provided through the program, which is one of only 10 such centers of excellence in the United States and abroad.

Physicians affiliated with the Neuromuscular Disorders Program are subspecialized in complex neuromuscular disorders that are difficult to diagnose and treat, including neurodegenerative disorders, inflammatory nerve and muscle disorders, autoimmune neuromuscular junction disorders, traumatic nerve injuries and toxic metabolic disorders of the peripheral nerves and muscles. The program records more than 2,000 patient visits annually, primarily adults age 18 and older. About two-thirds of our patients are over the age of 50.



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

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

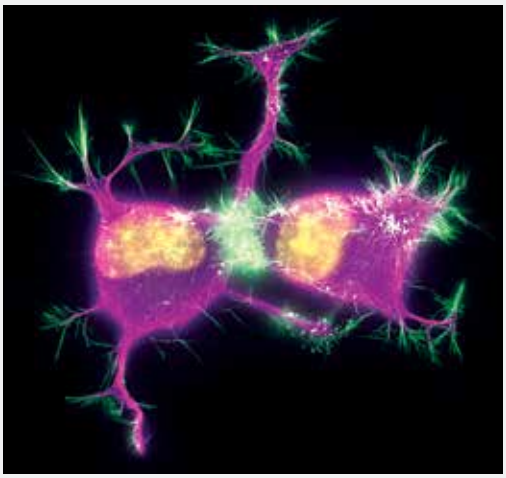
Erythropoietin Enhances Nerve Repair in Anti-Ganglioside Antibody-Mediated Models of Immune Neuropathy

Zhang G[1], Lehmann HC[2], Bogdanova N[1], Gao T[1], Zhang J[3], Sheikh KA[1]

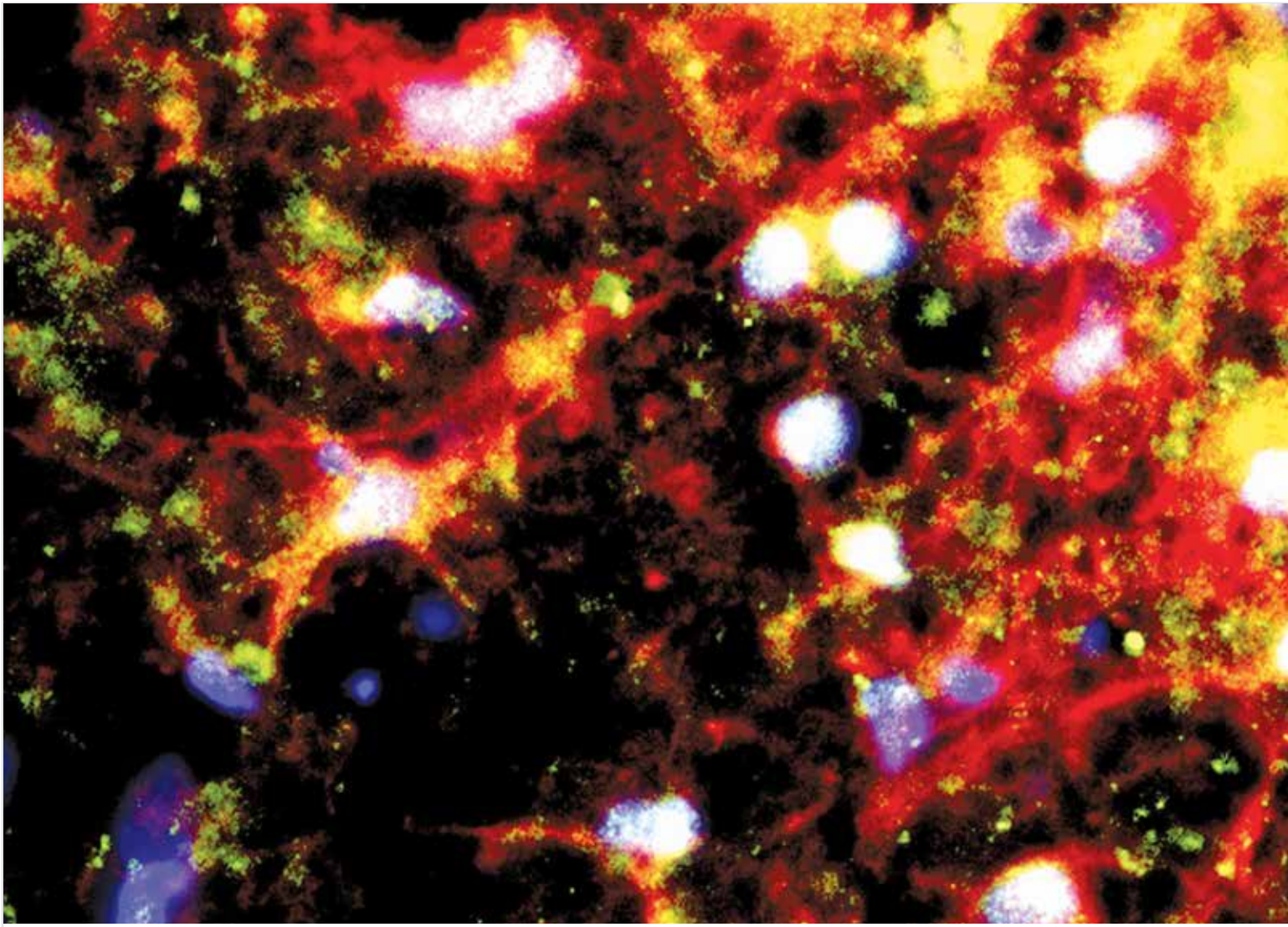
[1]Department of Neurology, The University of Texas Health Science Center at Houston (UTHealth) Medical School, United States of America; [2]Department of Neurology, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany; [3]Department of Radiology, Johns Hopkins University, Baltimore, Maryland, United States of America

ABSTRACT

Guillain-Barré syndrome (GBS) is a monophasic immune neuropathic disorder in which a significant proportion of patients have incomplete recovery. The patients with incomplete recovery almost always have some degree of failure of axon regeneration and target reinnervation. Anti-ganglioside antibodies (Abs) are the most commonly recognized autoimmune markers in all forms of GBS and specific Abs are associated with the slow/poor recovery. We recently demonstrated that specific anti-ganglioside Abs inhibit axonal regeneration and nerve repair in preclinical models by activation of small GTPase RhoA and its downstream effectors. The objective of this study was to determine whether erythropoietin (EPO), a pleiotropic cytokine with neuroprotective and neurotrophic properties, enhances nerve regeneration in preclinical cell culture and animal models of autoimmune neuropathy/nerve repair generated with monoclonal and patient derived Abs. Primary neuronal cultures and a standardized sciatic crush nerve model were used to assess the efficacy of EPO in reversing inhibitory effects of anti-ganglioside Abs on nerve repair. We found that EPO completely reversed the inhibitory effects of anti-ganglioside Abs on axon regeneration in cell culture models and significantly improved nerve regeneration/repair in an animal model. Moreover, EPO-induced proregenerative effects in nerve cells are through EPO receptors and Janus kinase 2/Signal transducer and activator of transcription 5 pathway and not via early direct modulation of small GTPase RhoA. These preclinical studies indicate that EPO is a viable candidate drug to develop further for neuroprotection and enhancing nerve repair in patients with GBS.



PLoS ONE 6(10): e27067. doi:10.1371/journal.pone.0027067



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.

Our Muscle and Nerve Laboratory helps improve diagnosis in cases with limited neuromuscular findings by locating abnormalities at a pathologic/microscopic level. Affiliated subspecialists perform muscle, nerve and skin biopsies, which are further processed by highly experienced staff. Our preferred technique is open biopsy under local anesthesia, which reduces the likelihood of missing abnormalities in cases of patchy involvement, such as in inflammatory myopathies. In 2012, we added skin biopsies for the diagnosis of small-fiber neuropathy to our comprehensive list of diagnostic tests. The Neuromuscular Disorders Program 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, our investigators are studying the pathogenesis of autoimmune neuropathies, immune effectors and nerve repair, novel strategies to enhance axon regeneration and nerve repair, and the development of MRI technology to assess neuromuscular disorders in preclinical and clinical studies.

Neurorehabilitation

Patients recovering from neurological illness or injury benefit from innovative neurorehabilitative technology and integrated care at the Mischer Neuroscience Institute (MNI) and TIRR Memorial Hermann. Subspecialists affiliated with both facilities are expert in the treatment of 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 our Neurorehabilitation Program. Upon admission, they discuss their goals with our interdisciplinary team and together, we develop a treatment plan designed to help them reach their highest level of function. Mischer Neurorehabilitation provides innovative and evidence-driven rehabilitation by blending manual and technologic therapies, including Korebalance™, Bioness® and IREX® Virtual Reality.

Our affiliated physicians conduct groundbreaking research on the underlying conditions that impact rehabilitation progress, applying knowledge gained directly to the care of each patient they serve. 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 research innovation and clinical excellence makes Mischer Neurorehabilitation a leader in the post-acute treatment of neurologic conditions.

Brain-Machine Interface Control of a Therapeutic Exoskeleton

PRINCIPAL INVESTIGATOR AT UTHEALTH:
Gerard E. Francisco, M.D.
Professor and Chair, Department of Physical Medicine and Rehabilitation
The University of Texas Health Science Center at Houston (UTHealth) Medical School
Chief Medical Officer, TIRR Memorial Hermann
Director, UTHealth Physical Medicine and Rehabilitation Motor Recovery Lab

PRINCIPAL INVESTIGATOR AT RICE UNIVERSITY:
Marcia O'Malley, Ph.D.
Associate Professor of Mechanical Engineering and Materials Science
Director, Mechatronics and Haptic Interfaces (MAHI) Lab
Rice University
Director of Rehabilitation Engineering,
TIRR Memorial Hermann

PRINCIPAL INVESTIGATOR AT THE UNIVERSITY OF HOUSTON: **José Contreras-Vidal, Ph.D.**
Professor of Electrical and Computer Engineering
Director of the UH Laboratory for Noninvasive Brain Machine Interface Systems
The University of Houston

$1.17 million collaborative grant from the National Institutes of Health (NIH) and the President's National Robotics Initiative (NRI) will enable four Houston institutions to create and validate a human-robot interface with a noninvasive brain-machine to help stroke patients recover use of their upper limbs to the fullest extent possible. Awarded to Rice University, the University of Houston (UH) and The University of Texas Health Science Center at Houston (UTHealth) Medical School, the grant will fund the development of neurotechnology that will interpret the brainwaves of stroke patients, allowing them to use their thoughts to operate an exoskeleton that wraps around the arm from the fingertips to the elbow. The device will be validated by UTHealth physicians and scientists at TIRR Memorial Hermann in up to 40 volunteer patients during the final two years of the four-year R01 award.

When set into motion, the intelligent exoskeleton will use thoughts to trigger repetitive motions and retrain the brain's motor networks. Marcia O'Malley,

TIRR MEMORIAL HERMANN

A national leader in medical rehabilitation and research, TIRR Memorial Hermann is a model for interdisciplinary rehabilitation services, patient care, education and research. The hospital has more than 50 years of experience in rehabilitation and research and is one of only six in the nation designated as a model system by the National Institute on Disability and Rehabilitation Research (NIDRR) for its traumatic brain injury program. For 23 consecutive years, *U.S.News & World Report* has named the hospital to its list of "America's Best Hospitals." In 2012, TIRR Memorial Hermann rose from fourth in the nation to third.

Research done at the hospital is conducted by physicians and scientists, and also by our therapists, nurses, chaplain and the residents who rely on us to advance their knowledge in specialized areas of rehabilitation medicine. Our Brain Injury Research Center (BIRC) brings together world-renowned researchers to study the many complicated facets

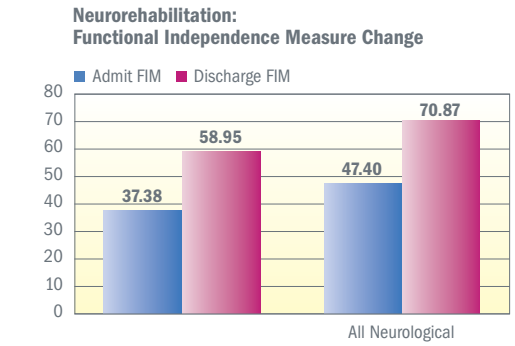
Ph.D., and her Rice University team are developing the exoskeleton in the Mechatronics and Haptic Interfaces (MAHI) Lab. At the University of Houston, a team led by principal investigator José Contreras-Vidal, Ph.D., is developing the electroencephalograph-based neural interface. Dr. Contreras-Vidal's team was the first to successfully reconstruct 3-D hand and walking movements from brain signals recorded noninvasively using an EEG brain cap. The technology allows users to control robotic legs with their thoughts and also permits below-elbow amputees to control neuroprosthetic limbs. The new project will be one of the first to design a brain-machine interface (BMI) system for stroke survivors.

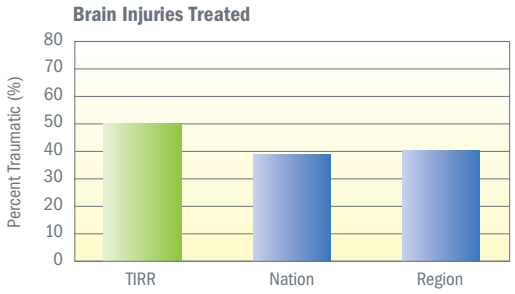
Rice University's robotic devices and UH's neural interfaces will make it possible for principal investigator Gerard Francisco, M.D., and his team to facilitate translational research that will fast track engineering findings into clinical practice.

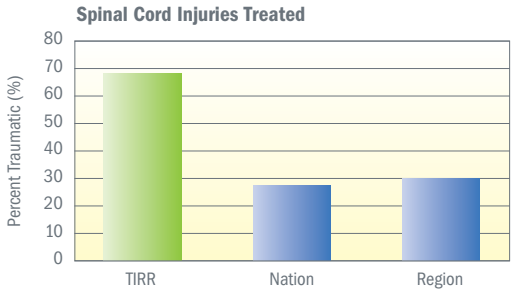
The project, funded through the National Institute of Neurological Disorders and Stroke (NINDS), is one of only a few projects selected by the NRI, a collaborative partnership of the NIH, National Science Foundation, NASA and the Department of Agriculture to encourage the development of the next generation of robots that will work closely with humans.

of recovery from brain injury, leveraging resources from NIDRR to conduct research identifying effective treatments. In 2012, our Spinal Cord Injury Research Center (SCIRC) broadened our team with the addition of experts in cognitive and psychosocial research. These new faculty allow us to 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. Ongoing research at the UTHealth Motor Recovery Lab at TIRR Memorial Hermann revolves around spasticity management, robotic therapy, neural interface and noninvasive brain stimulation.

TIRR Memorial Hermann has added 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 to its growing list of innovative rehabilitation technologies. A new inpatient sleep lab provides diagnosis of sleep-disruptive disorders in patients recovering from stroke or traumatic brain injury.







Source: chart data based on calendar year 2011

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

Steady growth in the pediatric program at TIRR Memorial Hermann Adult and Pediatric Outpatient Rehabilitation led to an expansion of services in a newly constructed space adjacent to the facility. The expansion adds 2,900 square feet designed solely for the use of pediatric patients.

Adult and Pediatric Outpatient Rehabilitation logged more than 60,000 outpatient therapy visits during the fiscal year. Innovative technology in use at the center includes Bioness equipment and the Lokomat®, the world's first driven-gait orthosis. We are one of only two facilities in Texas with pediatric legs for the Lokomat. The outpatient center provides comprehensive physical, occupational and speech therapy as well as support groups, counseling and individualized training to prepare families and caregivers for taking on the additional responsibilities of caring for patients after inpatient discharge.

Considered one of the nation's premier brain injury rehabilitation programs, the Challenge Program at TIRR Memorial Hermann Adult and Pediatric Outpatient Rehabilitation 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.

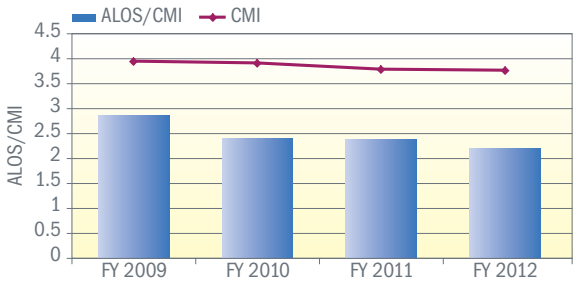
Although our patients are much higher acuity than most rehabilitation facilities nationwide, TIRR Memorial Hermann consistently has significant, positive functional independence measure (FIM) change scores.


TIRR MEMORIAL HERMANN
TIRR MEMORIAL HERMANN

Neurotrauma/Critical Care

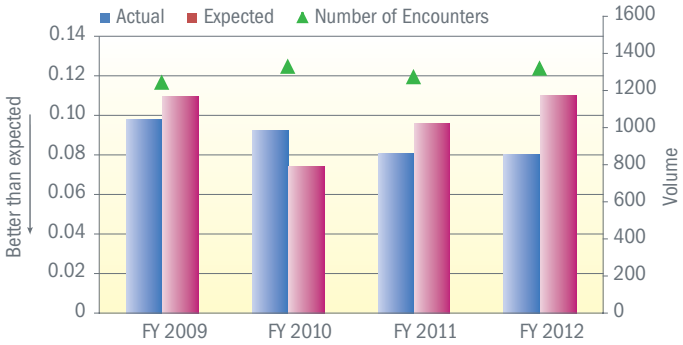
The Mischer Neuroscience Institute's Neurotrauma/Critical Care Program is internationally recognized for the treatment of high-acuity brain and spinal cord injuries. We manage more neurotrauma cases than any other center in the southwestern United States, with neurointensivists and experienced mid-level practitioners staffing our dedicated Neuro ICU around the clock to provide ongoing intensive care to critically ill patients. Our faculty and program continue to grow, with more than 1,300 traumatic brain injury patients alone diagnosed in fiscal year 2012.

Traumatic Brain Injury: Length of Stay



Source: chart data from University HealthSystem Consortium

Traumatic Brain Injury: Inpatient Mortality

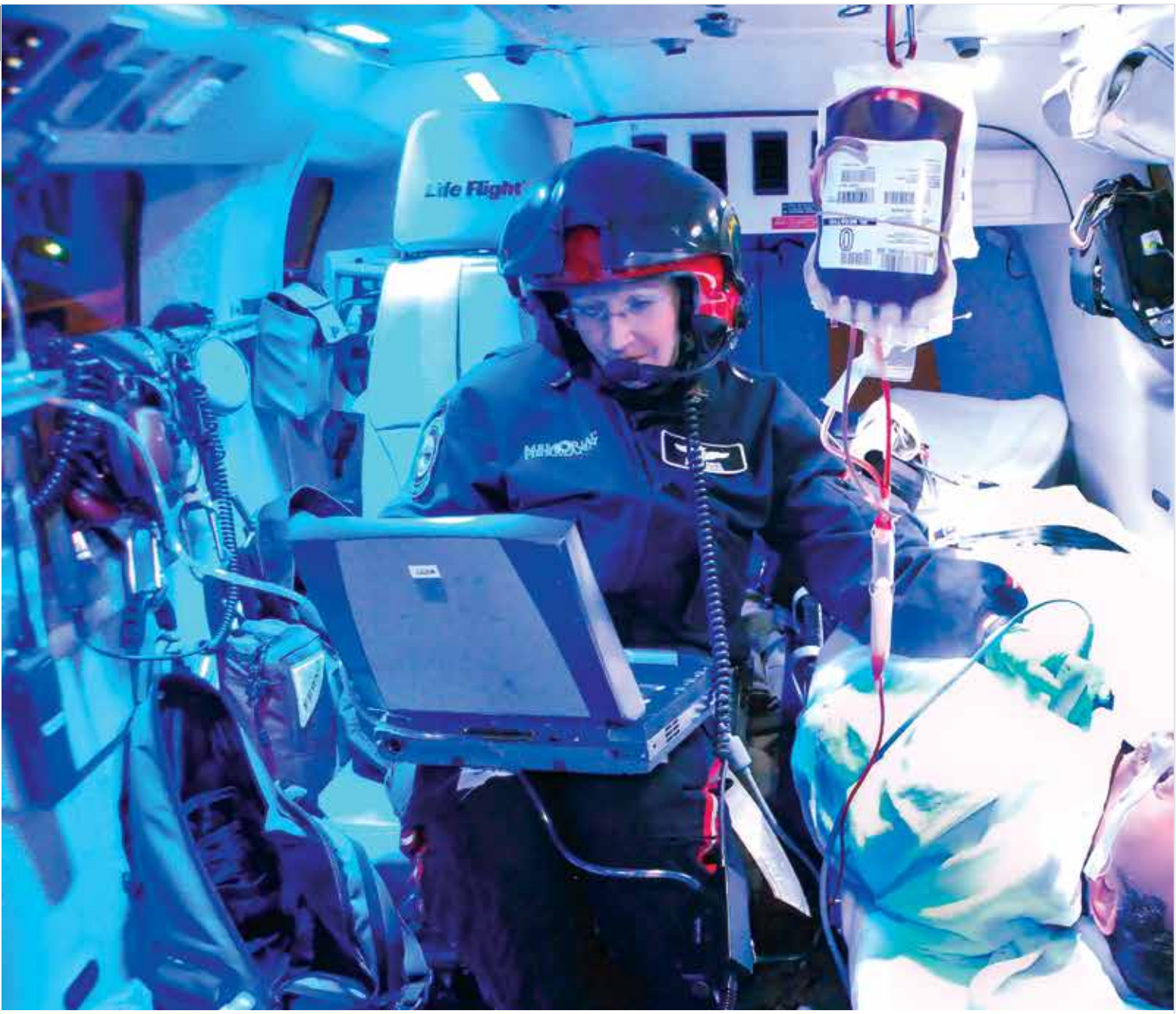


Source: chart data from the University HealthSystem Consortium

MNI's Neurotrauma/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.

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

Memorial Hermann Life Flight provides high-quality care and safe air transport for critically ill and injured patients via helicopter and fixed-wing aircraft. Our helicopter service responds within a 150-mile radius of Memorial Hermann-TMC. Fixed-wing service is available beyond 150 miles with world operating authority. Memorial Hermann Life Flight, the only hospital-based air ambulance service in Houston, operates 24 hours a day, 365 days a year, weather permitting. Since its inaugural flight, the medical transport service has flown more than 130,000 missions.



In 2012, Memorial Hermann-Texas Medical Center established the 200-bed Texas Trauma Institute, built on the hospital's long-term affiliation with The University of Texas Health Science Center at Houston (UTHealth) Medical School. The Institute provides high-quality care to both adult and pediatric trauma patients and offers a full spectrum of service including access to Memorial Hermann Life Flight and Houston's only verified burn center. Physicians at the Institute drive innovations in trauma care by moving research quickly from the laboratory to the bedside.

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

Spine

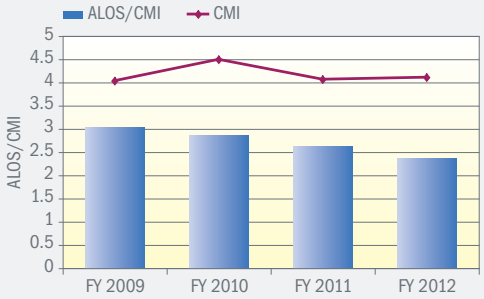
The highly skilled spine surgeons at the Mischer Neuroscience Institute performed more than 1,400 surgeries in 2012 in new, state-of-the-art facilities equipped with advanced instruments and dynamic imaging systems. These physicians are known for their expertise in minimally invasive spine procedures and innovative treatment options for patients with back pain resulting from trauma, degenerative disc disease, osteoporosis and related stress fractures, and deformity, including kyphosis and scoliosis.

Our clinicians provide exceptional care for patients with traumatic spine injury, including the 10 to 20 percent of admissions through our Level I Trauma Center that involve neurological damage. Based on benchmark University HealthSystem Consortium data, the Spine Center's inpatient mortality for spine trauma, degenerative spine disease and elective spine surgery has been consistently lower than expected for the past five years.

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

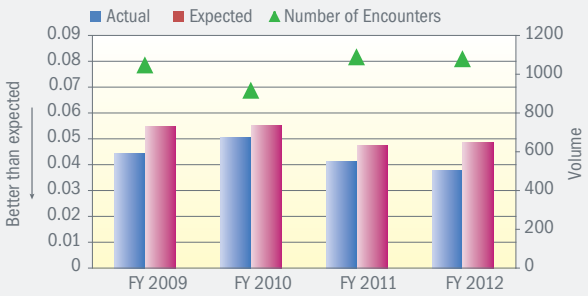
Research under way at the MNI Spine Center is focused on bringing promising therapies for spinal cord injury (SCI) patients from the laboratory to clinical trials in a manner that will provide evidence of effectiveness, with maximum safety, to patients undergoing treatment. Investigators are currently engaged in a Phase 2 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 Trauma: Length of Stay



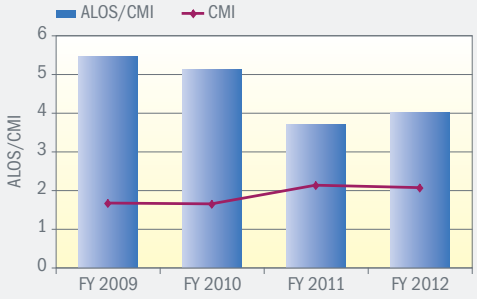
Source: chart data from the University HealthSystem Consortium

Spine Trauma: Inpatient Mortality



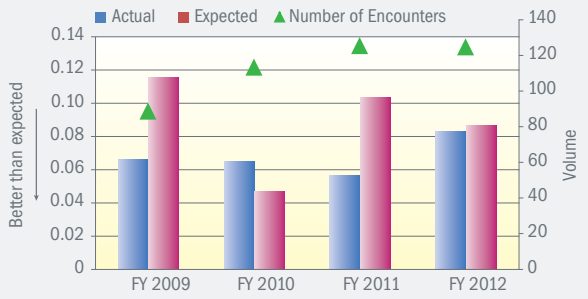
Source: chart data from the University HealthSystem Consortium

Spine Tumors: Length of Stay



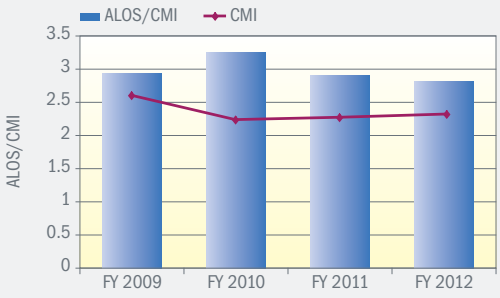
Source: chart data from the University HealthSystem Consortium

Spine Tumors: Inpatient Mortality



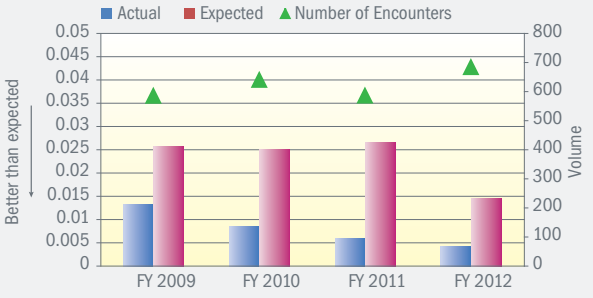
Source: chart data from the University HealthSystem Consortium

Spine Degenerative/Elective: Length of Stay



Source: chart data from the University HealthSystem Consortium

Spine Degenerative/Elective: Inpatient Mortality



Source: chart data from the University HealthSystem Consortium

Research and Innovation


HyClone

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

Our projects are supported by the National Institutes of Health, the Vivian L. Smith Foundation for Neurologic Disease, the American Stroke Association and other granting agencies. They cover major areas of neurological disease, including stroke, aneurysm, spinal cord injury, brain tumor, stem cell therapies, neuroprotection, hypoxic encephalopathy, epilepsy, traumatic brain injury and Parkinson's disease. During the 2012 calendar year, researchers at the Institute and the UTHealth Medical School received more than $10.5 million in 200 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.

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

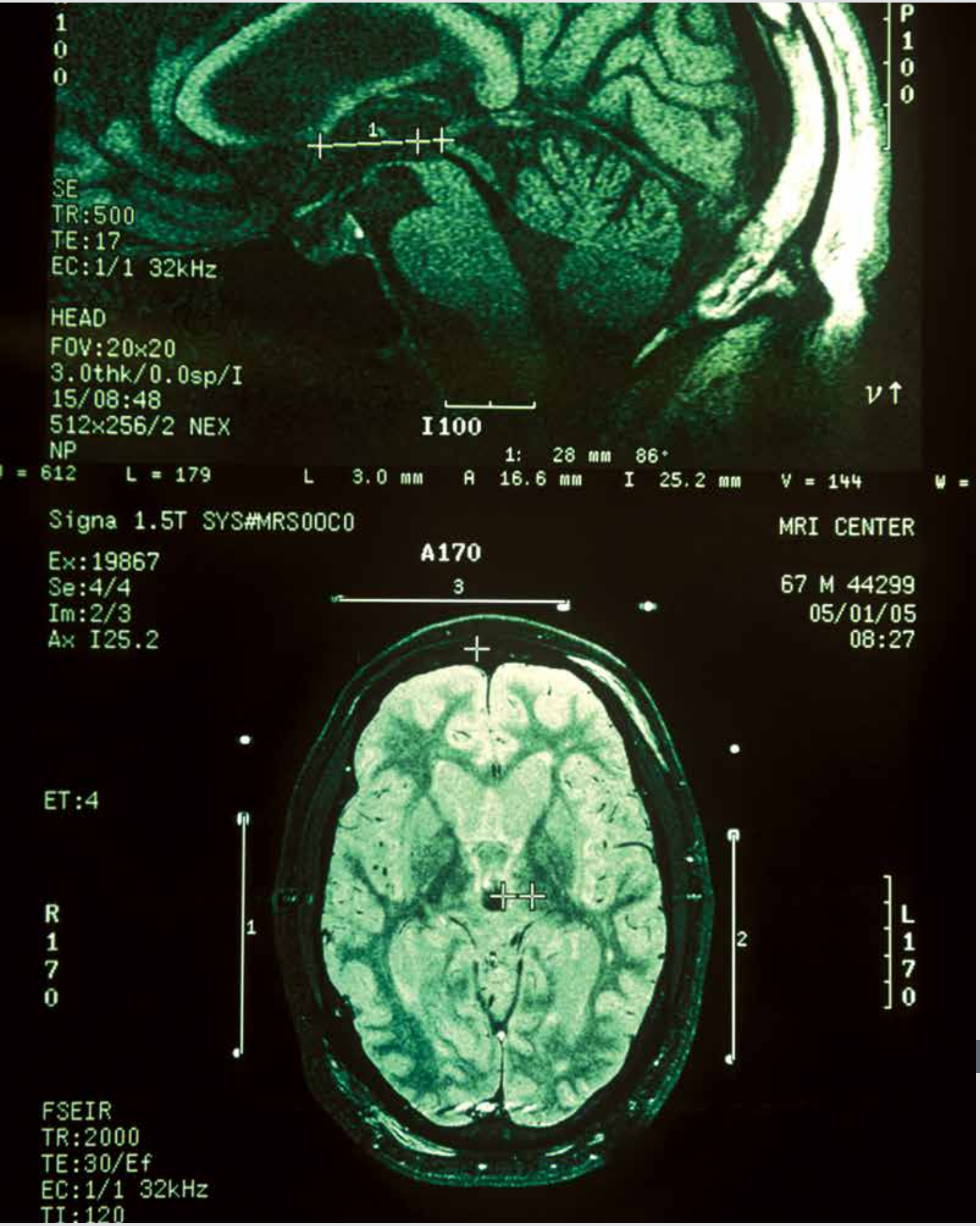
PRINCIPAL INVESTIGATOR**: P. Roc Chen, M.D.**

ARUBA is an FDA- and institutional IRB-approved randomized multicenter international clinical trial designed to determine whether medical management improves long-term outcomes of patients with unruptured brain AVMs, compared to interventional therapy (with endovascular procedures, neurosurgery or radiotherapy, alone or in combination). This trial tests whether medical management or interventional therapy will reduce the risk of death or stroke due to hemorrhage or infarction by at least 46 percent (an absolute magnitude of about 9.5 percent over five years). A total of 400 patients will be enrolled in order to detect the hypothesized 46 percent reduction in event rate, analyzed using the intention-to-treat principle. This sample size supports a test of non-inferiority if medical management is not superior to interventional therapy. Patients are followed for a minimum of five years and a maximum of 10 years from randomization.

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.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MRI CENTER
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Se:4/4
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ET:4
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FSEIR
TR:2000
TE:30/Ef
EC:1/1 32kHz
TI:120

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 relative effectiveness of both treatments in preventing stroke, myocardial infarction and death in the 30-day period immediately following the procedure.

Combination Treatment of rtPA and Apyrase for Stroke

PRINCIPAL INVESTIGATOR: **Jaroslaw 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: **Jaroslaw 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

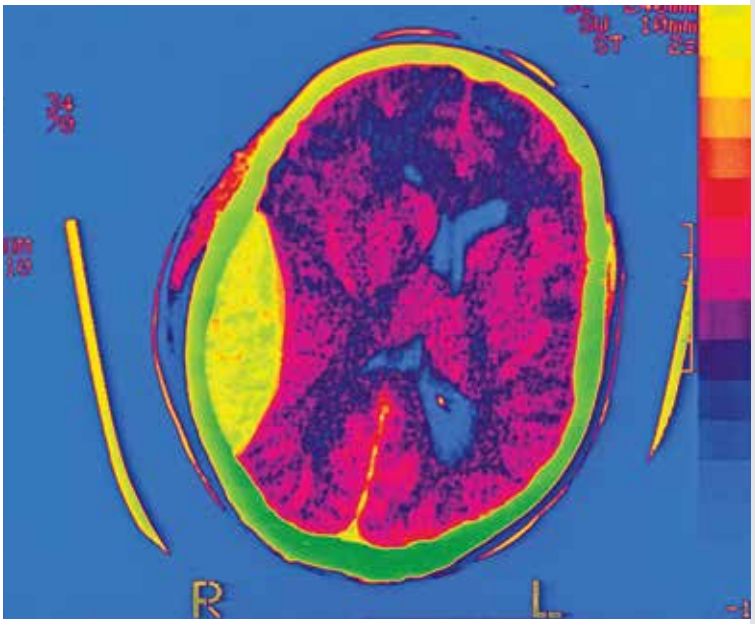
PRINCIPAL INVESTIGATOR: **P. Roc Chen, M.D.**

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.



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).

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

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

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

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.

Neurofluctuations in Patients with Subcortical Ischemic Stroke (NISS)

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

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

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.

**Amrou Sarraj, M.D., won the Mordecai Y.T. Globus New Investigator Award at the 2012 International Stroke Conference for his work on this project.*

Pleiotropic Transcription Factors as a Target for Intracerebral Hemorrhage Treatment

PRINCIPAL INVESTIGATOR: **Jaroslaw 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

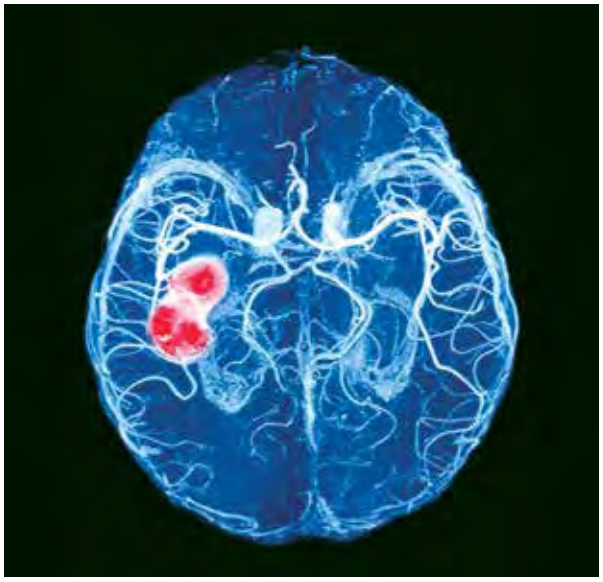
PRINCIPAL INVESTIGATOR: **Amrou Sarraj, M.D.**

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

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

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



Safety of Intravenous Thrombolysis for Wake-up Stroke

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

This is a safety study of acute treatment with IV tPA in ischemic stroke patients who wake up with their stroke symptoms. The administration of tPA must occur within three hours of awakening from sleep. The primary aim of this study is to demonstrate the safety of IV tPA in ischemic stroke patients who present to the Emergency department after awakening.

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

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

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

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

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

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

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.

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

A 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.

A 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.

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.

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.

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.

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.

MULTIPLE SCLEROSIS

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

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

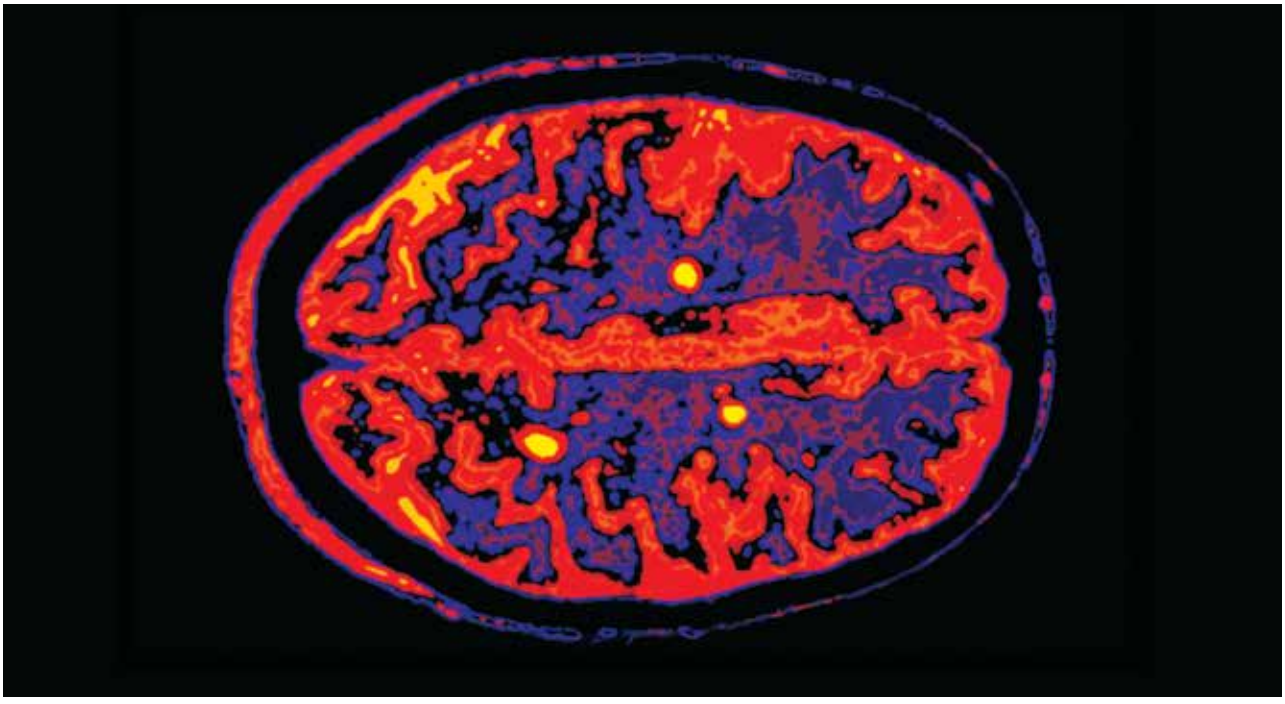
This study aims to develop and apply a multimodal MRI approach to the evaluation of cognitive impairment in patients with multiple sclerosis.

Phase III 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

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.

MRI Analysis Center for Protocol LTS 6050 – A Long-term Extension of the Multinational, Double-blind, Placebo-controlled Study EFC6049 (HMR1726DI3001) to Document the Safety of Two Doses of Teriflunomide (7 and 14 mg) in Patients with Multiple Sclerosis with Relapses

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

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

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.**

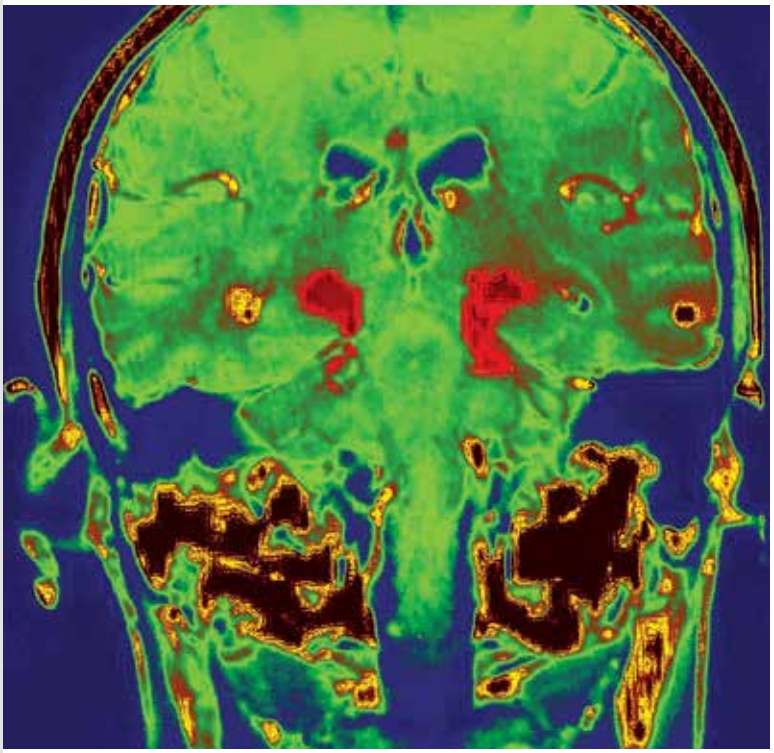
Researchers are using serial magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) to gather data to better understand disease processes in patients with multiple sclerosis.

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.**

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.

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.

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.

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 in September to the U.S.-China Program for Biomedical Collaborative Research in cooperation with the National Institutes of Health.

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 over time.

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), and the outcome of patients with GBS, and will 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

Novo TTF-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 4-7 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. 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/dendric 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.

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.

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.

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

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

PRINCIPAL INVESTIGATOR: **Nneka Ifejika-Jones, 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, R.N.**

Investigators in this clinical trial believe that spinal cord injury (SCI) patients who develop chronic pain have biomarkers in their blood that can predict their condition. 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

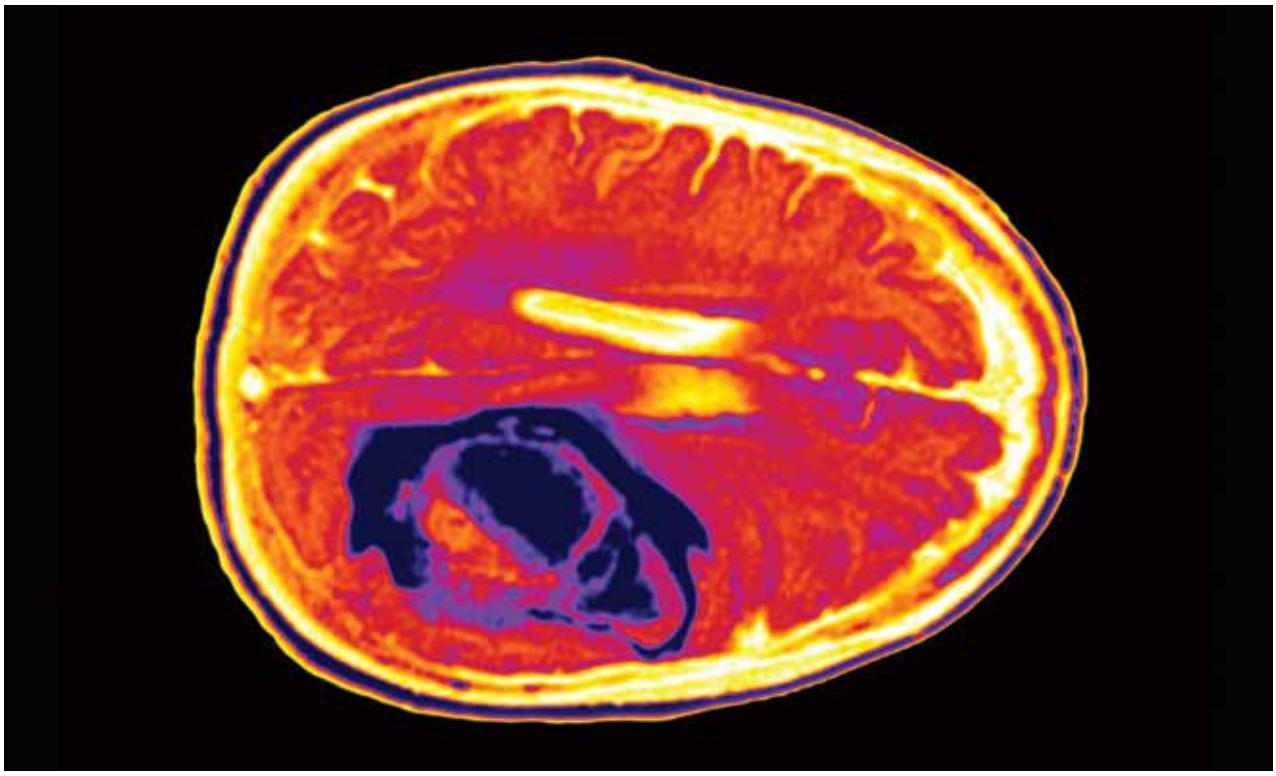
PRINCIPAL INVESTIGATOR: **Kiwon Lee, M.D.**

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.

Effects of Erythropoietin on Anemia and Need for Transfusion (a Component of the Program Project "Vascular Mechanisms of Secondary Injury after Traumatic Brain Injury")

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

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



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 and Hispanic patients, 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 studies of the regulatory networks of hematopoietic precursor cell self-renewal and differentiation using the multipotent EML (erythroid, myeloid and lymphocytic) cell 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.

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 subrachnoid hemorrhage.

Intrathecal Nicardipine Injection via External Ventricular Drain in Aneurysmal Subarchnoid 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

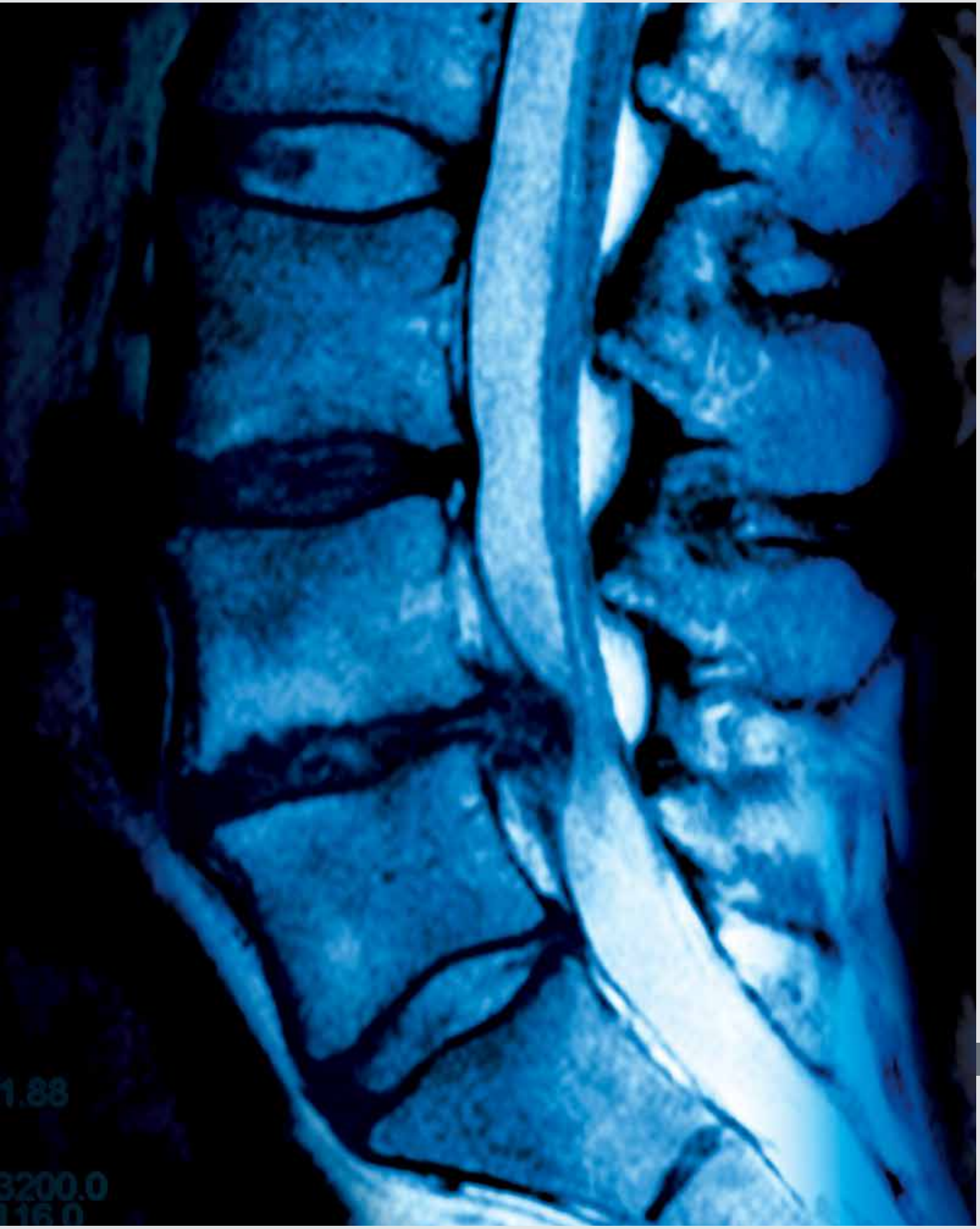
PRINCIPAL INVESTIGATOR: **Nitin Tandon, M.D.**

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, R.N.**

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



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

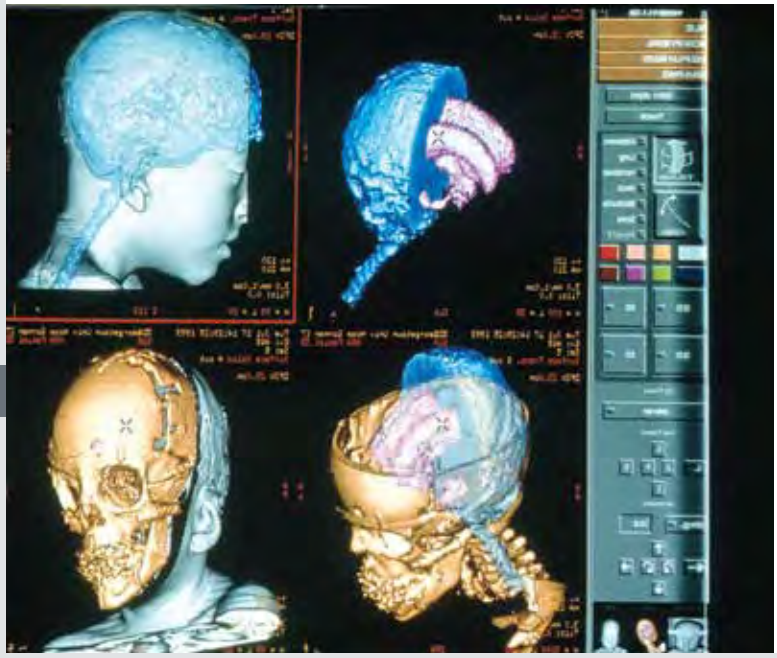
PRINCIPAL INVESTIGATOR: **Nitin Tandon, M.D.**

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

Fronto-Basal-Ganglia Circuits for Selective Stopping and Braking

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

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



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 electro-corticography 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

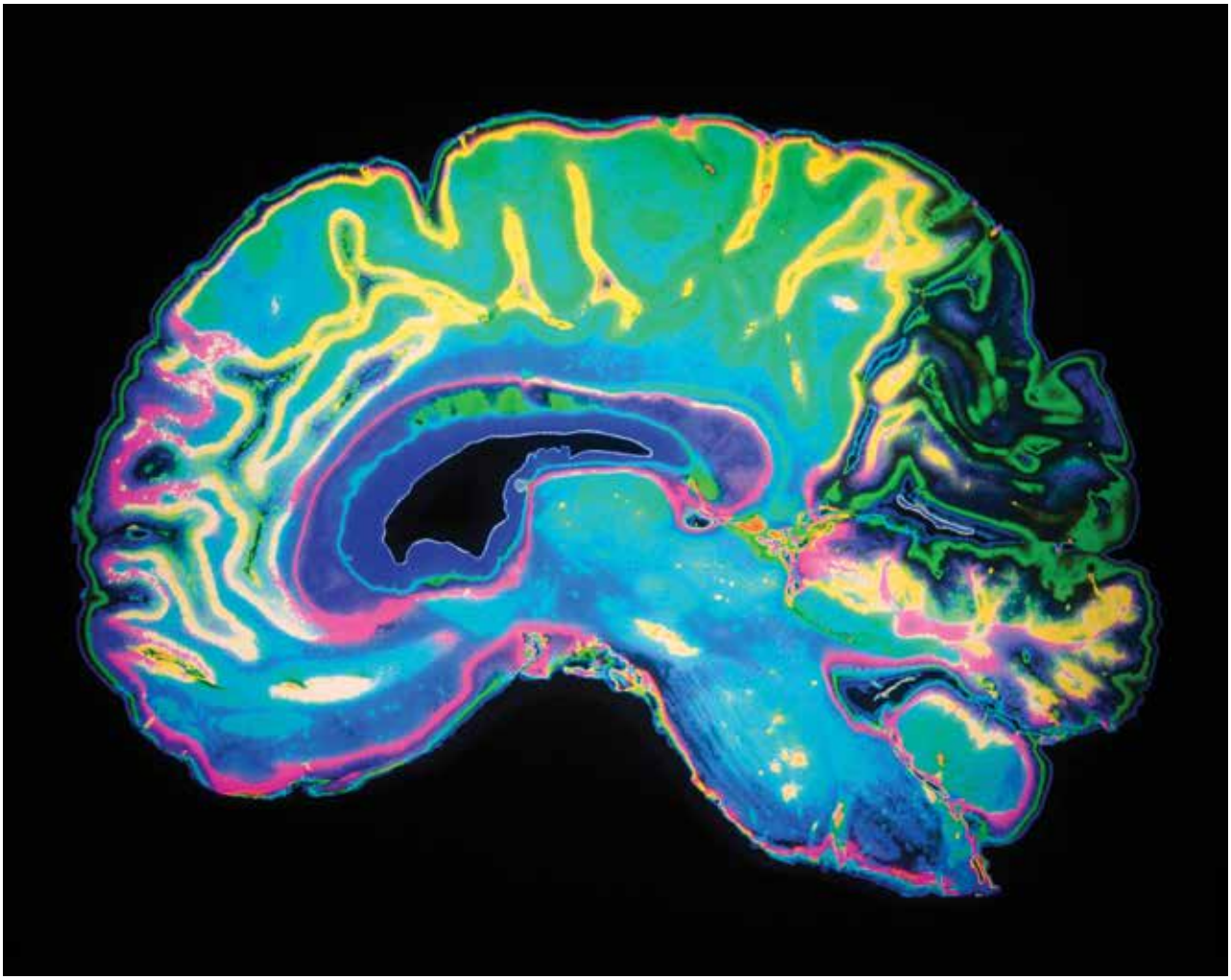
PRINCIPAL INVESTIGATOR: **Qi Lin Cao, Ph.D.**

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).

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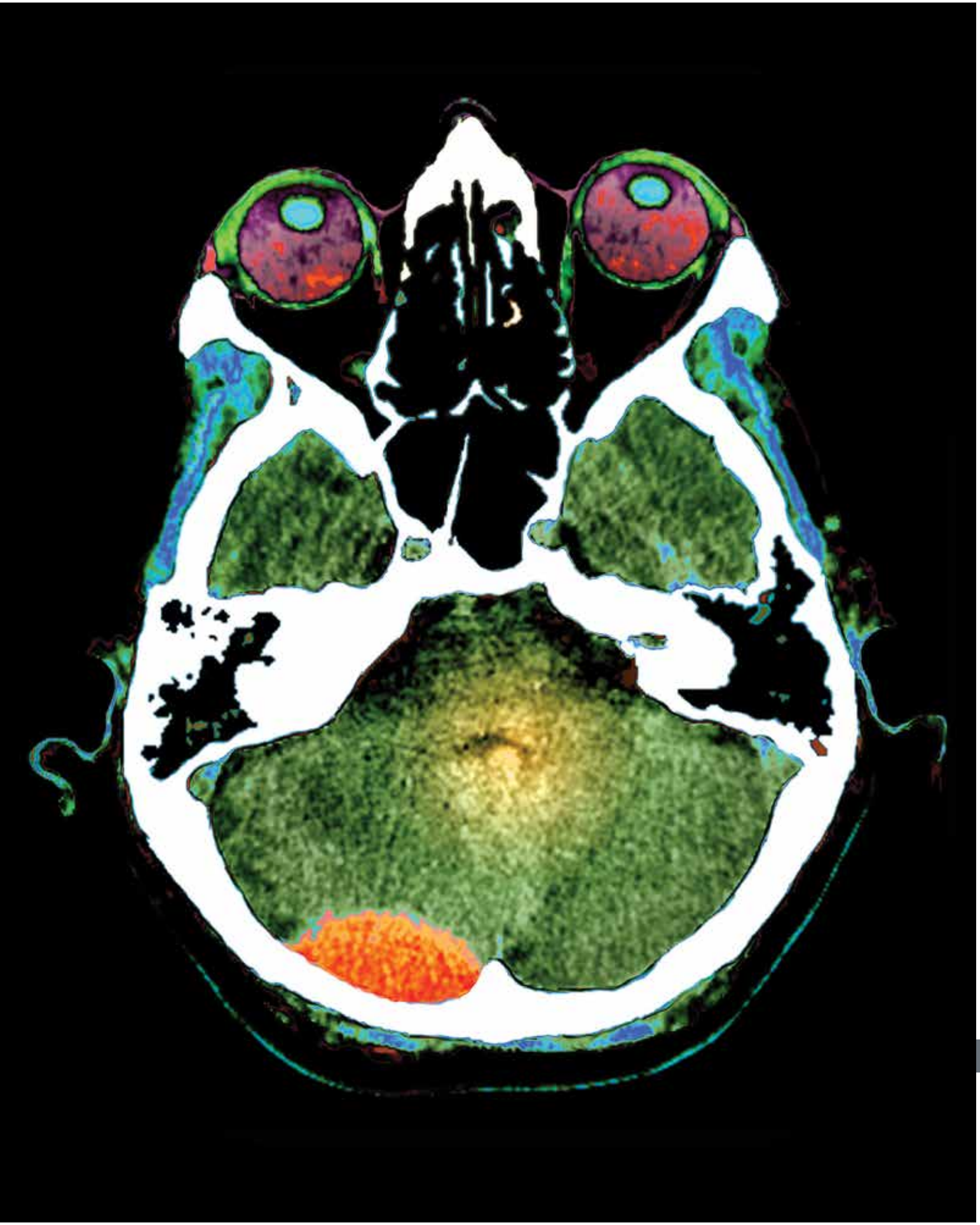

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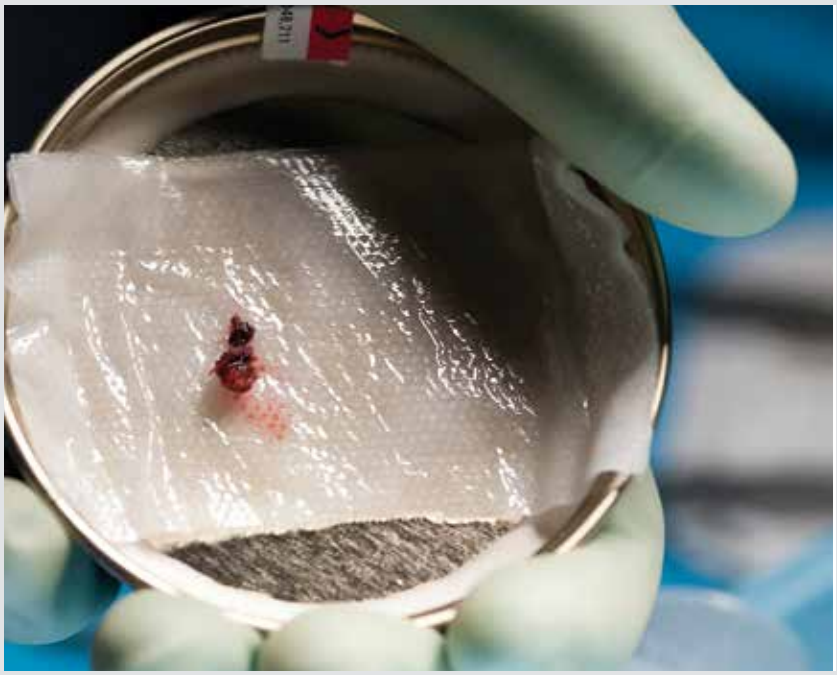

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EXIT
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CRITICAL CARE
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Patient Stories

Lenord Lewis:
Beating the Glioblastoma Multiforme Odds

Van Buren, Arkansas, resident Lenord Lewis was working in Houston when his recurrent headaches became so bad that a co-worker drove him to Bayshore Medical Center in Pasadena, Texas. After reviewing the results of an MRI and CT scan, the emergency physician called an ambulance to transport the 55-year-old to the Mischer Neuroscience Institute (MNI) at Memorial Hermann-Texas Medical Center.

"When I got there, they told me they were operating on Monday," says Lewis, who repairs electrical generators for General Electric's hydro and nuclear power operations. On April 12, 2010, Dong Kim, M.D., director of MNI and professor and chair of the Vivian L. Smith Department of Neurosurgery at The University of Texas Health Science Center at Houston (UTHealth) Medical School, performed a craniotomy and resected a golf ball-sized brain tumor. The pathology report confirmed glioblastoma multiforme (GBM).

Of the estimated 19,000 primary brain tumors diagnosed in the United States each year, approximately 60 percent are gliomas, a heterogeneous group of neoplasms that differ in location within the central nervous system, growth potential, invasiveness and response to treatment. With the exception of brainstem gliomas, GBM has the worst statistical prognosis of any central nervous system malignancy – a median survival of 14.6 months. Only 3 to 5 percent of patients survive for more than three years, and they are classed as long-term survivors.

Following the surgery, Lewis was seen by Jay-Jiguang, Zhu, M.D., Ph.D., a fellowship-trained neuro-oncologist at MNI and an associate professor in the department of Neurosurgery at the UTHealth Medical School. Dr. Zhu had recently joined the MNI team from Boston, where he trained at Massachusetts General Hospital and served on the faculty of Tufts University. He worked with Lewis to develop a plan of care.

Lewis received standard-of-care treatment – temozolomide chemotherapy for 42 days with concurrent radiation. But the tumor recurred. An MRI scan in August 2010 showed a change at the surgical cavity in his left temporal lobe. This small area of progression was treated with Gamma Knife® radiosurgery by Dr. Kim, then Lewis resumed chemotherapy with temozolomide until February 2011. At that time, Dr. Zhu offered him the opportunity to try a new technology that generates an electric field to the brain through electrodes applied to the scalp. Made by NovoCure, the NovoTTF-100A has been approved by the FDA for treatment of recurrent GBM and is being tested for safety and efficacy as an adjuvant treatment in newly diagnosed GBM patients.

A locally or regionally delivered treatment, tumor treating fields (TTF) therapy uses electric fields within the human body to disrupt the rapid division and spread of cancer cells. Developed to provide physicians and patients with a fourth treatment option for cancer in addition to surgery, radiation therapy and chemotherapy, TTF therapy is designed for continuous use during the day and night, with portable battery packs that allow

patients to maintain their normal daily routine while undergoing treatment.

"Studies have shown that low-intensity, intermediate frequency electric fields stunt the growth of tumor cells," Dr. Zhu says. "The device is designed to administer alternating electric fields to the region of the malignant tumor by means of insulated surface electrode arrays."

Lewis will wear the NovoTTF-100A for two years while continuing the standard chemotherapy regimen of temozolomide five days out of every 28, following an initial four cycles of Avastin® once every two weeks. Four pads, each of which contains nine electrodes, cover his head. He wears the pads for three days, then removes them, washes and shaves his head, and applies a clean set of electrodes.

"With a median survival of 14.6 months, the odds of making it three years after a diagnosis of GBM are low," Dr. Zhu says. "Lenord is able to maintain normal activities of daily living, and he's very upbeat. That's the key to success in addition to therapies. His wife and family provide excellent care and support for him, which has allowed him to keep up the long-distance medical care. We feel that our care is top quality, and he and his wife feel that it's worth the travel time and expense to be treated at MNI."

Lewis and his wife, Celeste, participated in the 5K Run for the Rose in Houston in March 2012, an event that funds brain cancer research. "There are so many cancer patients," he says. "I hurt for the others. If I can show how good life is and how other people can enjoy it despite cancer, that's what I want to do. We don't view Dr. Zhu and Dr. Kim as just doctors. We feel like they're family helping us. If I can pull a couple more years with the device and then a couple more years after that – and a couple more years after that – that's what I'm going for. You've just got to bite the bullet and keep going."

Kellee Hearne:
Relief from 14 Years of Headaches

Twenty-four-year-old Kellee Hearne had suffered severe headaches from the age of 10. Over the course of those 14 years, several physicians diagnosed her with migraines, but none of the medications they prescribed eliminated the pain.

It was her Ob/Gyn who first suggested that the location of the headaches indicated they might be something other than migraines and referred her to a neurologist, who ordered an MRI. Based on the results, he diagnosed her with Chiari I malformation, a neurological disorder in which the cerebellum – the part of the brain that controls balance – descends out of the skull and into the spinal area.

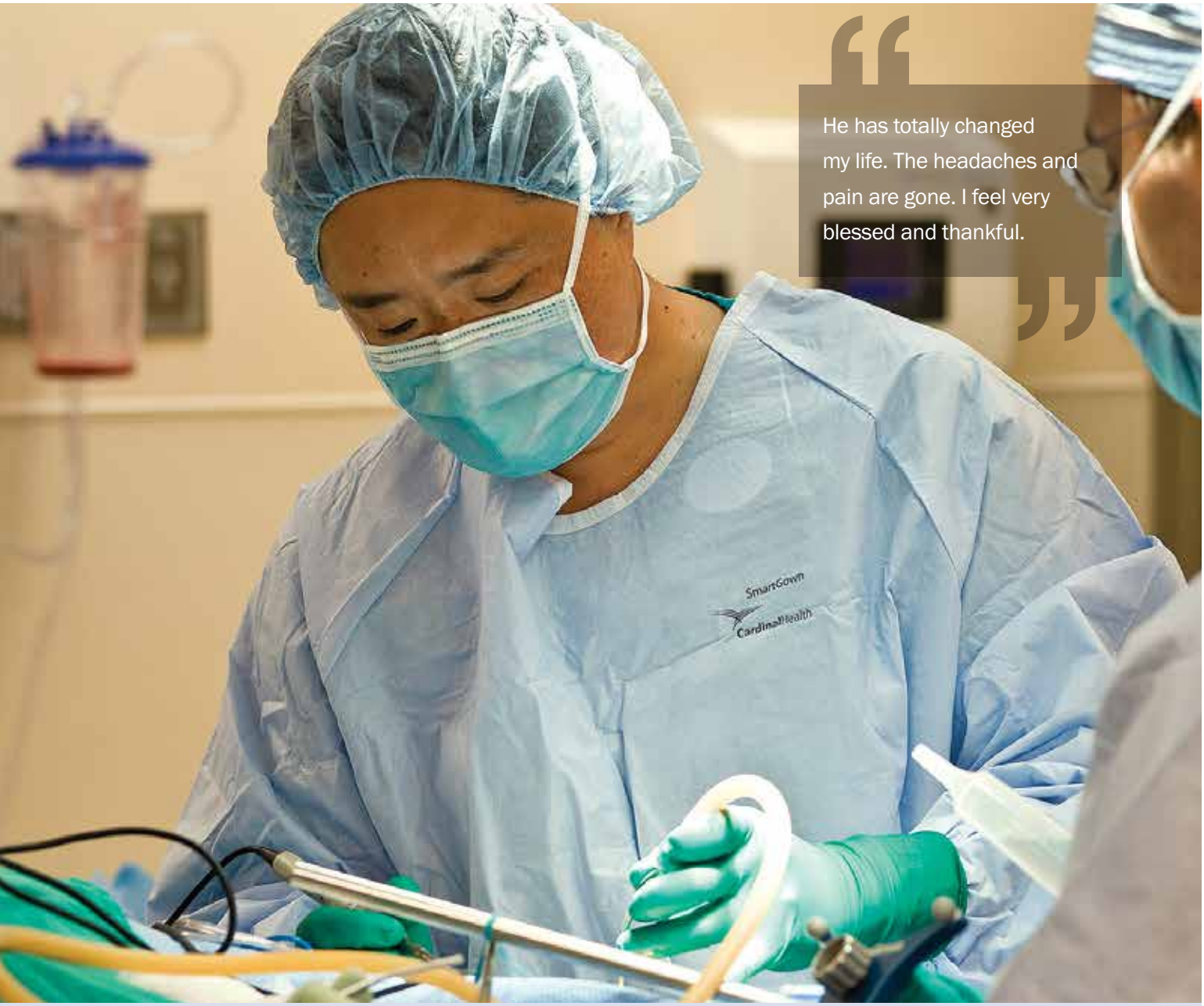
Normally, the cerebellum and parts of the brain stem sit in an indented space at the lower rear of the skull above the foramen magnum, a funnel-like opening to the spinal canal. Chiari malformation is diagnosed when part of the cerebellum is located below the foramen magnum. The most common Chiari malformation is Type I, which involves the extension of the lower part of the cerebellum into the foramen magnum, without involving the brain stem. Chiari I can affect adolescents and adults, and often causes severe symptoms.

Hearne's mother learned about the Mischer Neuroscience Institute's Face Pain, Trigeminal Neuralgia and Chiari Clinic during an Internet search. The clinic was started by Dong Kim, M.D., director of MNI and professor and chair of the Vivian L. Smith Department of Neurosurgery, with neurologist Anita Madan, M.D., an assistant professor of neurology, both at The University of Texas Health Science Center at Houston (UTHealth) Medical School. "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. Madan 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 neck pain, muscle weakness, numbness, balance problems, vision problems or difficulty swallowing, in addition to headaches.

When Hearne and her mother saw Dr. Madan and Dr. Kim at the clinic, they discussed surgical options and what to expect during recovery. "They left the decision up to me, but I'd already decided on surgery because I wanted to be here for my 2-year-old son," Hearne says.

When working with patients, Dr. Kim listens carefully to their 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. Eventually, as the symptoms worsen, medications begin to fail."

Hearne's surgery took place on June 20, 2012. "It's a straightforward procedure," Dr. Kim says. "The goal of



> He has totally changed my life. The headaches and pain are gone. I feel very blessed and thankful.

surgery is to provide more space in the foramen magnum without affecting the brain. We open the skull and cut a window in the dura, the outermost of the three layers of meninges surrounding the brain and spinal cord. To prevent a postoperative cerebrospinal fluid leak, we're now using a synthetic membrane that we carefully sew in under a microscope to ensure a watertight seal."

Like most patients who undergo the surgery, Hearne was hospitalized for three days and returned to work four weeks later. "Everyone made me feel at ease, from the doctors to the nurses to the nursing assistants," says Hearne. "Dr. Kim is amazing. He has totally changed my life. The headaches and pain are gone. I feel very blessed and thankful."

"The most important thing is to seek early treatment," says Dr. Kim, who does approximately 25 Chiari I malformation repairs every year. "The longer patients endure their symptoms, the most likely they are to have at least some residual symptoms after the surgery."

Tom Tinn:
From Stroke to a New Life Abroad

Tom Tinn's stroke led him to rearrange his life in some very interesting ways. The journey began on September 14, 2011. The 55-year-old had just finished breakfast when his wife looked at him and noticed the telltale droop of stroke on the left side of his face. "Why don't you go lie down and I'll call 911," he remembers her saying. When he tried to stand up, he fell to the floor.

About two weeks earlier, he'd returned home following surgery for prostate cancer at Memorial Hermann Memorial City Medical Center. After the procedure, he went back to the hospital twice to be treated for allergic reactions to the antibiotics he was prescribed."When I had the stroke, the EMS team told me, 'We're taking you to the best place to treat it.'"

The "best place" is Mischer Neuroscience Institute (MNI) at Memorial Hermann, whose Stroke Center opened in 1988 as one of the first dedicated stroke programs in the world. Today, the Center is home to the 10-county Greater Houston area's largest onsite stroke team. Neurologists at the Center use leading-edge technology to diagnose and treat more than 1,000 patients annually, ensuring that each patient gets the appropriate treatment as quickly as possible. By working closely with the Houston Fire Department and local EMS services, the stroke team has logged an impressive record of success in the administration of clot-dissolving tPA – more than 10 times the national average of 2 percent.

On arrival at Memorial Hermann-Texas Medical Center's Emergency Center, Tinn was seen by Osman Mir, M.D., a member of the MNI stroke team. He was completely paralyzed on the left side and his score on the National Institutes of Health Stroke Scale (NIHSS) was 11, indicating a moderate-sized stroke. The NIHSS is a neurologic assessment used to evaluate the severity of stroke on a scale from 0, indicating no deficits, to 39.

Tinn was treated with tPA, the standard of care for acute ischemic stroke, but he didn't respond to the therapy. "In fact, he got worse," says George A. Lopez, M.D., Ph.D., a neurologist affiliated with MNI and an associate professor in the department of Neurology at The University of Texas Health Science Center at Houston (UTHealth) Medical School, who saw Tinn the next morning and directed his care during his hospitalization. "When his stroke scale score went from 11 to 13, we asked if he would be interested in participating in an ongoing stroke clinical trial called MR RESCUE."

Begun in May 2004, the study, "Mechanical Retrieval and Recanalization of Stroke Clots Using Embolectomy," nicknamed MR RESCUE, compares the effectiveness of treating acute ischemic stroke with mechanical embolectomy using a clot retriever within eight hours of symptom onset to standard medical treatment. The researchers also aim to identify people who might benefit from mechanical embolectomy by the appearance of the stroke on CT or MRI.

Tinn consented to participate in the study and was assigned to the interventional arm. He was taken to MNI's angiography suite by neurointerventionalist

> "I can walk and talk and I'm back at work. I thank God and the people at Memorial Hermann. They really saved me."

Roc Chen, M.D., an assistant professor in the Vivian L. Smith Department of Neurosurgery at UTHealth Medical School, who performed a cerebral arteriogram showing a blockage of the right middle cerebral artery. Dr. Chen guided a small catheter into the artery and used a retrieval device to extract the clot.

Immediately following the procedure, Tinn's stroke scale score dropped to 7. He was seen daily by a physical therapist while in the hospital and discharged seven days later on September 21. On November 1, after six weeks of outpatient rehabilitation, he returned to his job as a business development director for a global service provider in the oil industry.

"I still have some issues that Dr. Lopez is aware of but I consider myself 100 percent recuperated," he says. "It does take time to come back after a stroke. But I can walk and talk and I'm back at work. I thank God and the people at Memorial Hermann. They really saved me."

Tinn and his wife relocated to Milan, Italy, at the end of July 2012. "My wife is Italian, and our family is there," he says. "The events of the past year had an enormous psychological effect on me. I've always put my work before my family, but I feel I need to put them first now."

Dr. Lopez considers Tinn's recovery remarkable. "He went back to work in a high-functioning environment a little more than a month after the stroke," he says. "We don't typically see recoveries like that. Usually, patients have many more deficits to overcome."

In an email Tinn sent to Dr. Lopez in June 2012, he wrote, "Both my wife and I would like to offer our deepest and sincere thanks to you and all the members of the stroke team. Your kindness and professionalism is something I'll always treasure and remember in my life. I'm here today because of them and God."

Lauren Lackey: **A Life-Saving Endovascular Procedure for Complex Brain Arteriovenous Fistulae**

Nine-year-old Lauren Lackey began displaying odd behavior just before Thanksgiving in 2010. A straight-A student, she was now struggling with routine assignments and tests. She danced competitively – tap and jazz – but was having difficulty concentrating and following simple instructions.

"At first we thought she just needed some extra help from her teachers," says Lauren's mother, Sandy Lackey, who is a fifth-grade teacher. But shortly after the New Year, Lackey was helping her daughter with her homework when Lauren started writing random, nonsensical letters and broke down crying. "As an educator and a parent, I knew that all these things didn't add up, but never would we have expected what was to come."

A few days later, on January 26, 2011, Lauren complained to her teacher of a headache and stomachache. The school nurse examined Lauren and called her father, Mark Lackey, to pick her up at her elementary school in Cypress, Texas. But before they could leave the school parking lot, Lauren's condition deteriorated to the point that she couldn't walk or talk.

By the time she arrived at Children's Memorial Hermann Hospital, Lauren was in status epilepticus, had lapsed

She couldn’t move, and she couldn’t speak. Dr. Chen told us that her vessels were like a 10-lane highway with eight or nine lanes closed. We were praying for a miracle.

into a coma and had to be intubated. Her MRI and CT scans were reviewed by Ian Butler, M.D., a pediatric neurologist affiliated with the hospital and professor and Adriana Blood Chair in Neurology at The University of Texas Health Science Center at Houston (UTHealth) Medical School. When he saw an alarming blood vessel abnormality, he called P. Roc Chen, M.D., to consult on the case. A cerebrovascular neurosurgeon affiliated with the Mischer Neuroscience Institute (MNI), Dr. Chen specializes in adult and pediatric patients with congenital vascular anomalies of the brain and spine, and endovascular surgery for aneurysms.

"Dr. Butler and I were concerned about two things that weren't clear from the initial scans," says Dr. Chen, who is an assistant professor in the Vivian L. Smith Department of Neurosurgery at the UTHealth Medical School. "We had to determine if we were dealing with an intracranial venous occlusion or a diffused neuro arteriovenous fistula." He accompanied Lauren to the neurointerventional suite for a diagnostic angiogram, where testing revealed that she had both conditions.

"She had lost her blood outflow channels almost completely and was left with only one complete outflow through her face. In addition, there were diffused dural arteriovenous fistulae (AVF), which significantly increased venous pressure to prevent blood flow out of her brain," he says. "Her brain was engorged with blood, which caused the seizure, her cognitive dysfunction and coma. The disease was so widespread that every artery was shortcutting shunting to the venous sinus [outflow channel]. Her condition was extremely dire."

The neurosurgeon injected 10 cubic centimeters of Onyx® glue into the abnormal vessels to repair the dural arteriovenous fistulae. He stopped after 70 minutes when his team had reached the single-day radiation and contrast safety limit, and brought her back the following day to finish the procedure.

"When I first got to the hospital, Lauren was not in good shape," her mother says. "She couldn't move, and she couldn't speak. Dr. Chen told us that her vessels were like a 10-lane highway with eight or nine lanes closed. We were praying for a miracle."

Less than two weeks after she was admitted, Lauren was discharged – walking and talking. She completed a short course of outpatient rehabilitation at TIRR Memorial Hermann Adult and Pediatric Outpatient Rehabilitation. Her long-term prognosis is positive, and her life has returned to normal.

"She lives with a single venous flow channel, but she has done remarkably well," says Dr. Chen, who credits Lauren's outcome to the experience and professionalism of the multidisciplinary team that provided her care. "Our expertise at MNI gives us the ability and confidence to aggressively and swiftly treat some of the most serious cerebral vascular conditions, which, if not treated immediately, would result in a devastating prognosis or death."

Now 11, Lauren is doing "beyond great," in the words of her mother. "She just started the sixth grade. After all she'd been through, it was difficult to think of her going from elementary school to junior high with 1,200 kids and eight different teachers, but she has adjusted well socially and academically, and is taking all above-level classes." Lauren has resumed ballet and tap dancing and this fall joined a community league softball team.

"As a parent you hope you never have to experience anything like this," Mrs. Lackey adds. "But from the initial emergency room visit to her discharge, our experience was absolutely great."

Megan Collins: **Deep Brain Stimulation Changes a Life**

Five years ago Megan Collins' life was marked by pain, social embarrassment and uncertainty about her medical future. Today, the 35-year-old considers herself lucky.

Collins began having balance and coordination problems in 2007 at the age of 30, and they worsened progressively. An employee of the Children's Neurology Clinic in Fort Worth, Texas, she was referred to Mya Schiess, M.D., by two pediatric neurologists who had completed fellowships with the movement disorders specialist at The University of Texas Health Science Center at Houston (UTHealth) Medical School. Dr. Schiess is professor and vice chair of the department of Neurology and holds the Adriana Blood Endowed Chair at UTHealth Medical School. She is affiliated with the Mischer Neuroscience Institute and is also the director of UT MOVE, a program focused on clinical care, education and basic science research on the neurological conditions of motor systems disruption, including movement disorders, cerebral palsy, spasticity, neurodegenerative diseases and dementias.

"We worked with Megan for about a year and responded to the disorder before we knew exactly what we were dealing with," Dr. Schiess says. "It took us some time to reach a conclusive diagnosis. Her father had similar symptoms, so we suspected a genetic disorder. But testing for a full panel of inherited ataxia disorders is expensive, and Megan is a single working mom."

Collins' father eventually underwent testing paid for by the Veterans Administration and was diagnosed with spinocerebellar ataxia type 1 (SCA1). "When a family member tests positive for a disorder and another family member has the same symptomatology, we can narrow down the testing to one relatively inexpensive test," Dr. Schiess says. "Megan also tested positive for the disorder."

Spinocerebellar ataxia type 1 is characterized by progressive problems with movement. Patients with the disorder initially experience problems with balance – ataxia – and coordination. Other signs and symptoms of the disorder may include speech and swallowing difficulties, spasticity, and weakness in the muscles that control involuntary eye movements. Individuals with SCA1 may have cognitive impairment marked by difficulty processing, learning and remembering information. Over time, they may develop numbness, tingling or pain in the arms and legs, muscle wasting, twitches and uncontrolled muscle tensing, known as dystonia.

Over the course of the next year, Collins developed the classic symptoms of craniocervical dystonia, a movement disorder characterized by intermittent spasms of the neck and shoulder muscles that cause abnormal head movements. "Botulinum toxin injections provided relief from the spasms," Dr. Schiess says. "After a lumbar puncture revealed neurotransmitter deficits, we prescribed levodopa and sertraline to target the deficiencies. The medications helped alleviate symptoms, and subsequent analysis of the cerebrospinal fluid showed a normalization of her levels.

We also started her on baclofen for spasticity and clonazepam for her dystonia."

Collins responded favorably to the treatment regimen for almost 18 months. Then her dystonia began to worsen and evolved aggressively for almost a year, despite increased dosage and distribution of botulinum toxin injections. Eventually, her upper limbs and trunk became involved, and her severe dystonic crises became unresponsive to medication changes. She required several emergency department visits and hospitalizations.

"Megan reached the point that she was no longer able to work," Dr. Schiess says. "We kept her out of the hospital as long as possible. She was on very high doses of medication, and we realized that her disorder was not coming under control despite our best efforts."

Collins had read about deep brain stimulation (DBS), which was approved by the FDA in 2003 for the treatment of dystonia. "Dr. Schiess agreed that I could see Dr. Fenoy for a consult," she says. "When I scheduled the appointment with him, I was in the middle of a dystonic storm, never knowing when I was going to have an episode. I ended up having one in his office. It was very scary and crazy but I feel lucky that he could see what was happening to me."

Albert Fenoy, M.D., is a neurosurgeon and deep brain stimulation specialist affiliated with the Mischer Neuroscience Institute and an assistant professor in the Vivian L. Smith Department of Neurosurgery at the UTHealth Medical School. On May 22, 2012, with Dr. Schiess attending in the OR, he placed a DBS electrode into Collins' globus pallidus internus.

"We placed a stereotactic frame on Megan's head and using MRI visualization, we made two burr holes in the skull while she was awake, and descended microelectrodes into the brain to verify neuronal activity and confirm that we'd reached the target area," Dr. Fenoy says. "Then we placed the actual DBS leads and test stimulated to see what kind of response she had and whether there were any side effects." Two weeks later, on June 6, with Collins under general anesthesia, they placed extensions from the electrodes to a pulse generator and implanted the generator in her chest under the clavicle.

On June 7, Dr. Schiess programmed the stimulator for the first time. "It's been a miracle," Collins says. It's amazing what I can do now that I couldn't do before. I can now stand up with my feet together and move better than I've been able to move in years. I would recommend Dr. Schiess and Dr. Fenoy to anyone in the world. They've changed my life."

"When you understand a therapy and are involved in the selection of many candidates over time and have the opportunity to observe the results, you develop a good sense of what it can and can't do. We're very good DBS programmers here," Dr. Schiess says. "We believe that if DBS can help a patient improve in even a single area, it should be applied. When indicated, it can greatly improve a patient's life. Four months out from her surgery, Megan is holding her own, and her dystonia is better controlled. As time goes on, through research, we'll find different targets in the brain and develop more exquisite control. Science is an evolutionary process. We keep driving forward."


It’s been a miracle. It’s amazing what I can do now that I couldn’t do before. I would recommend Dr. Schiess and Dr. Fenoy to anyone in the world. They’ve changed my life.

Staff Listing

NEUROSURGERY

Dong Kim, M.D.
Director
Mischer Neuroscience Institute

Chief of Neurosurgery
Memorial Hermann-Texas Medical Center

Professor and Chair
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

P. Roc Chen, M.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

Mark J. Dannenbaum, M.D.
Associate Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

Arthur L. Day, M.D.
Director of Clinical Education
Mischer Neuroscience Institute

Professor and Vice Chair
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

Albert Fenoy, M.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

Michele M. Johnson, M.D.
Director
Spine Program
Mischer Neuroscience Institute

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

Daniel H. Kim, M.D., F.A.C.S.
Director
Reconstructive Spinal and Peripheral
Nerve Surgery
Mischer Neuroscience Institute

Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

Karl Schmitt, M.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

Scott Shepard, M.D.
Director
Gamma Knife Radiosurgery Program
Mischer Neuroscience Institute

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

Nitin Tandon, M.D.
Associate Professor
Vivian L. Smith Department of Neurosurgery

Associate Professor
Department of Pediatric Surgery
UTHealth Medical School

NEUROLOGY

James C. Grotta, M.D.
Co-Director
Mischer Neuroscience Institute

Chief of Neurology and Director
Stroke Center
Memorial Hermann-Texas Medical Center

Professor and Chair
Department of Neurology
Roy M. and Phyllis Gough Huffington
Distinguished Chair in Neurology
UTHealth Medical School

Parveen Athar, M.D.
Assistant Professor
Department of Neurology
UTHealth Medical School

Andrew Barreto, M.D.
Assistant Professor
Department of Neurology
UTHealth Medical School

Suur Biliciler, M.D.
Assistant Professor
Department of Neurology
UTHealth Medical School

Staley Brod, M.D.
Professor
Department of Neurology
UTHealth Medical School

Randall C. Edgell, M.D.
Associate Professor
Vivian L. Smith Department of Neurosurgery
and Department of Neurology
UTHealth Medical School

James Ferrendelli, M.D.
Professor
Department of Neurology
UTHealth Medical School

Erin Furr-Stimming, M.D.
Assistant Professor
Department of Neurology

Movement Disorders Specialist
UT MOVE Clinic

Director
Neurology Clerkship Program
UTHealth Medical School

Nicole R. Gonzales, M.D.
Assistant Professor
Department of Neurology
UTHealth Medical School

Omotola Hope, M.D.
Assistant Professor
Department of Neurology

Director
Neurology Residency Training Program
UTHealth Medical School

Sigmund H. Hsu, M.D.
Neuro-Oncologist
Assistant Professor
Vivian L. Smith Department of Neurosurgery
Department of Neurology
UTHealth Medical School

Nneka Ifejika, M.D.
Assistant Professor
Department of Neurology

Director of Neurorehabilitation
UTHealth Medical School

Ernesto Infante, M.D.
Assistant Professor
Department of Neurology
UTHealth Medical School

Giridhar Kalamangalam, M.D., D.Phil.
Assistant Professor
Department of Neurology
UTHealth Medical School

Robert Knowlton, M.D.
Associate Professor
Department of Neurology
UTHealth Medical School

John A. Lincoln, M.D.
Assistant Professor
Department of Neurology
UTHealth Medical School

John William Lindsey, M.D.
Professor
Department of Neurology
UTHealth Medical School

George Lopez, M.D.
Associate Professor
Department of Neurology
UTHealth Medical School

Anita Madan, M.D.
Assistant Professor
Department of Neurology
UTHealth Medical School

Raymond A. Martin, M.D., F.A.A.N.
Professor
Department of Neurology

Medical Director
Outpatient Neurology Clinic
UTHealth Medical School

Vivek Misra, M.D.
Clinical Instructor
Department of Neurology
UTHealth Medical School

Flavia Nelson, M.D.
Assistant Professor
Department of Neurology

Associate Director
Magnetic Resonance Imaging Analysis Center
UTHealth Medical School

Elizabeth Noser, M.D.
Medical Director
Neurorehabilitation
Memorial Hermann-Texas Medical Center

Clinical Assistant Professor
Department of Neurology
UTHealth Medical School

Thy Nguyen, M.D.
Assistant Professor
Department of Neurology

Co-Director
Electromyography Laboratory
UTHealth Medical School

William Ondo, M.D.
Professor
Department of Neurology
UTHealth Medical School

Jacqueline Phillips-Sabol, M.D.
Director
Neuropsychology Program
Memorial Hermann-Texas Medical Center

Assistant Professor
Department of Neurology
UTHealth Medical School

Sean Savitz, M.D.
Professor
Department of Neurology

Director
Stroke Program

Director
Vascular Neurology Fellowship
UTHealth Medical School

Mya Schiess, M.D.
Professor and Vice Chair
Department of Neurology
Adriana Blood Endowed Chair
in Neurology

Director
Movement Disorders and
Neurodegenerative Disease

Director
UT MOVE Clinic
UTHealth Medical School

Paul E. Schulz, M.D.
Associate Professor and Vice Chair
Department of Neurology

Director
Dementia Program
UTHealth Medical School

Kazim Sheikh, M.D.
Professor
Department of Neurology

Director
Neuromuscular Program
UTHealth Medical School

Jeremy Slater, M.D.
Medical Director
Epilepsy Monitoring Unit and Neurophysiology
Memorial Hermann-Texas Medical Center

Associate Professor
Department of Neurology
UTHealth Medical School

Sudha Tallavajhula, M.D.
Associate Professor
Department of Neurology
UTHealth Medical School

Melissa Thomas, M.D.
Assistant Professor
Department of Neurology
UTHealth Medical School

Gage Van Horn, M.D.
Professor
Department of Neurology
UTHealth Medical School

Holly Knudsen Varner, M.D.
Assistant Professor
Department of Neurology
UTHealth Medical School

Bethany Williams, M.D.
Assistant Professor
Department of Neuropsychology
UTHealth Medical School

Jerry S. Wolinsky, M.D.
Bartels Family and Opal C. Rankin
Professor
Department of Neurology

Director
Multiple Sclerosis Research Group (MSRG)

Director
Magnetic Resonance Imaging Analysis Center
UTHealth Medical School

Tzu-Ching (Teddy) Wu, M.D.
Telemedicine Director
Mischer Neuroscience Institute

Assistant Professor
Department of Neurology
UTHealth Medical School

Jay-Jiguang Zhu, M.D., Ph.D.
Neuro-Oncologist
Associate Professor
Vivian L. Smith Department of Neurosurgery
Department of Neurology
UTHealth Medical School

CRITICAL CARE

Imo Aisiku, M.D.
Director
Neurocritical Care
Mischer Neuroscience Institute

Associate Professor
Vivian L. Smith Department of Neurosurgery

Vice Chair
Division of Critical Care
UTHealth Medical School

H. Alex Choi, M.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
and Department of Neurology
UTHealth Medical School

Kiwon Lee, M.D.
Co-Director
Neurocritical Care
Mischer Neuroscience Institute

Associate Professor
Department of Neurology and
Vivian L. Smith Department of Neurosurgery

Vice Chair of Clinical Affairs
Department of Neurology
UTHealth Medical School

Bilal Rana, D.O.
Assistant Professor
Vivan L. Smith Department of Neurosurgery
UTHealth Medical School

Hanh Truong, M.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

George W. Williams, II, M.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

Asma Zakaria, M.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
Department of Neurology
UTHealth Medical School

CHILDREN'S NEUROSCIENCE CENTER

Ian Butler, M.D.
Director
Division of Child & Adolescent Neurology
Department of Pediatric Surgery

Professor
Division of Child & Adolescent Neurology
Department of Pediatric Surgery
UTHealth Medical School

Stephen Fletcher, D.O.
Associate Professor
Division of Child & Adolescent Neurology,
Department of Pediatric Surgery
UTHealth Medical School

Michael Gambello, M.D., Ph.D.
Professor
Division of Medical Genetics,
Department of Pediatrics
UTHealth Medical School

Mary Kay Koenig, M.D.
Director
Neurometabolic & Mitochondrial Clinic

Assistant Professor
Division of Child & Adolescent Neurology
Department of Pediatrics
UTHealth Medical School

Pedro Mancias, M.D.
Associate Professor
Division of Child & Adolescent Neurology
Department of Pediatrics
UTHealth Medical School

Hope Northrup, M.D.
Director
Division of Medical Genetics
Department of Pediatrics

Director
Tuberous Sclerosis Complex Clinic

Professor
Division of Medical Genetics
Department of Pediatrics
UTHealth Medical School

David Sandberg, M.D., F.A.A.N.S., F.A.C.S., F.A.A.P.
Director
Pediatric Neurosurgery
Mischer Neuroscience Institute

Associate Professor
Vivian L. Smith Department of Neurosurgery

Associate Professor
Department of Pediatric Surgery
UTHealth Medical School

Nitin Tandon, M.D.
Associate Professor
Department of Pediatric Surgery

Associate Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

Gretchen Von Allmen, M.D.
Director
Pediatric Epilepsy Program

Co-Director
Epilepsy Monitoring Unit
Memorial Hermann-Texas Medical Center

Assistant Professor
Division of Child & Adolescent Neurology
Department of Pediatrics
UTHealth Medical School

RESEARCH FACULTY

Jaroslaw (Jarek) Aronowski, Ph.D.
Professor
Department of Neurology
UTHealth Medical School
Ischemic Stroke and Brain Hemorrhage

Qilin Cao, M.D.
Associate Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School
Stem Cell Therapy

Guy Clifton, M.D.
Director
Vivian L. Smith Center for
Neurologic Research

Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School
Brain Injury

Pramod Dash, M.D.
Professor
Vivian L. Smith Department of Neurosurgery
and Department of Neurobiology and Anatomy
UTHealth Medical School
Brain Injury

Timothy Ellmore, Ph.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School
Neural Substrates of Language and Memory

Georgene Hergenroeder, R.N.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School
Bioinformatics and Translational Research

Nobuhide Kobori, M.D., Ph.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School
Brain Injury and Memory

Min Li, Ph.D.
Associate Professor
Vivian L. Smith Department of Neurosurgery

Director
Cancer Research Program
UTHealth Medical School
Neuro-Oncology

Ying Liu, M.D., Ph.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School
Stem Cell Research

Hariyadarshi Pannu, Ph.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School
Vascular Disease and Genetics

Teresa Santiago-Sim, Ph.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School
Vascular Disease and Genetics

Claudio Soto, Ph.D.
Director
Center for Neurodegenerative Diseases

Professor of Neurology
UTHealth Medical School
Neurodegenerative Disease

Jia Qian Wu, Ph.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School
Stem Cell Research

Ying Xia, M.D., Ph.D.
Professor and Vice Chair
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School
Cellular and Molecular Neuroscience

Rong Yu, Ph.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School
Oxidative Stress and Brain Injury

Gang Zhang, M.D.
Assistant Professor
Department of Neurology
UTHealth Medical School
Peripheral Nervous System

Xiurong Zhao, M.D.
Associate Professor
Department of Neurology
UTHealth Medical School
Ischemic Stroke and Brain Hemorrhage

ACROSS THE SYSTEM

MEMORIAL HERMANN KATY HOSPITAL

Quoc Anh Thai, M.D.
Clinical Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

MEMORIAL HERMANN MEMORIAL CITY MEDICAL CENTER

Paul Boone, M.D.
Clinical Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

Anita Madan, M.D.
Assistant Professor
Department of Neurology
UTHealth Medical School

G. Silky Patel, M.D.
Clinical Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

Scott Shepard, M.D.
Director
Gamma Knife Radiosurgery Program
Mischer Neuroscience Institute

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

MEMORIAL HERMANN NORTHEAST HOSPITAL

Albert Fenoy, M.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

MEMORIAL HERMANN SOUTHEAST HOSPITAL

Kathleen Eberle, M.D.
Neurologist
Houston Neurological Institute

Joseph C. Hsieh, M.D.
Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

Kimberly Monday, M.D.
Neurologist
Houston Neurological Institute

Jack Ownby, M.D.
Neurologist
Houston Neurological Institute

MEMORIAL HERMANN THE WOODLANDS HOSPITAL

Raul J. Cardenas, M.D.
Clinical Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School

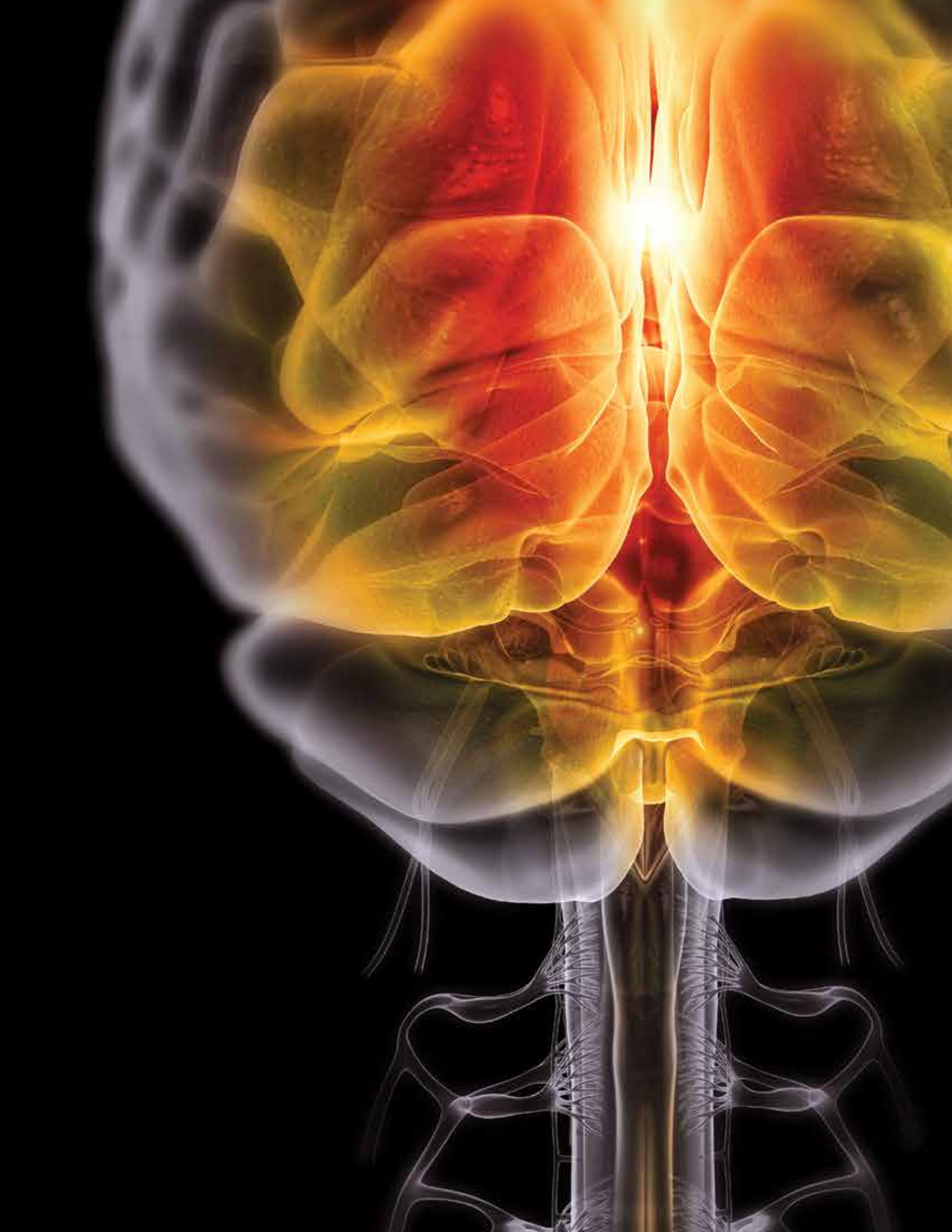
Kevin C. Gaffney, M.D.
Neurologist
Mischer Neuroscience Associates
The Woodlands

Anita Madan, M.D.
Assistant Professor
Department of Neurology
UTHealth Medical School

Ryan McDonald, M.D.
Neurologist
Mischer Neuroscience Associates
The Woodlands

Randall Wright, M.D.
Neurologist
Mischer Neuroscience Associates
The Woodlands

Geoffrey P. Zubay, M.D., F.A.C.S.
Clinical Assistant Professor
Vivian L. Smith Department of Neurosurgery
UTHealth Medical School



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Memorial Hermann-Texas Medical Center
6411 Fannin
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