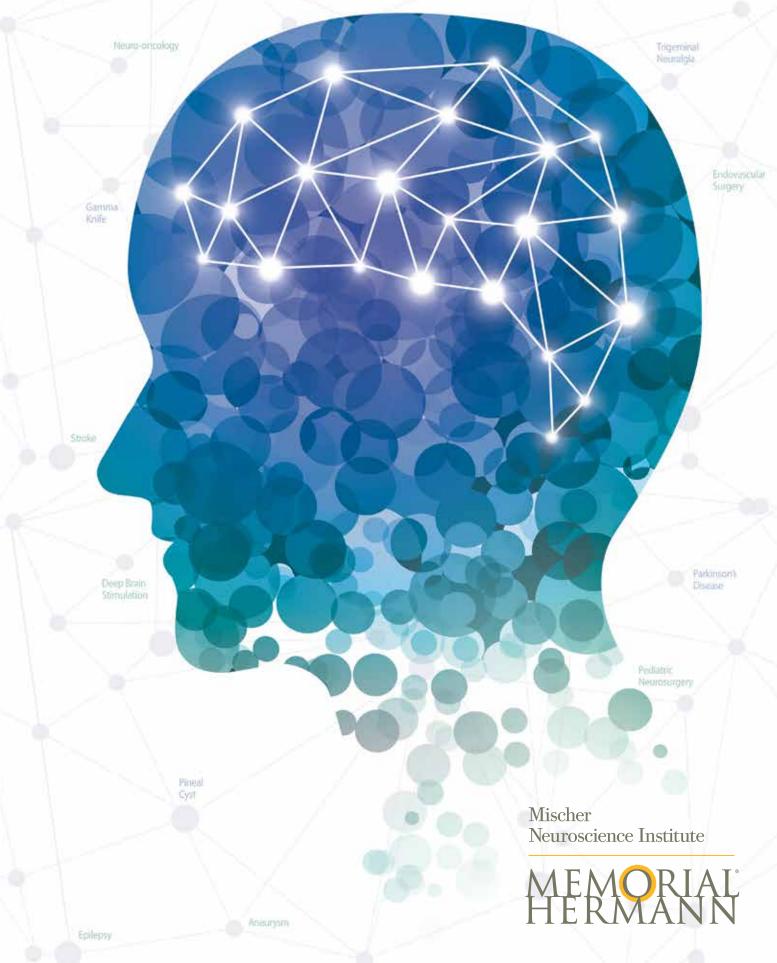
MISCHER NEUROSCIENCE INSTITUTE REPORT 2017



The Mischer Neuroscience Institute is a collaboration between Memorial Hermann-Texas Medical Center – part of the Memorial Hermann Health System – and McGovern Medical School at UTHealth. The Institute draws patients from around the world.

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Dear Esteemed Colleagues,

As we approach a decade of growth at the Memorial Hermann Mischer Neuroscience Institute, Mischer Neuroscience Associates, and UTHealth, we are looking to the future. We are planning the continued expansion of comprehensive clinical care across the Greater Houston area, training the next generation of physicians and enhancing our research infrastructure to support even more studies that we can quickly translate to clinical practice.

We opened our first MNA practice at the Texas Medical Center in 2007. Since then, we have established 24 locations that include 87 physicians: 22 neurosurgeons, four interventional pain management specialists, two neuro-oncologists, two radiation oncologists, nine neurocritical care specialists and 23 neurologists, and 25 residents and fellows. In addition, MNA employs 36 advanced practice providers and 174 other staff.

During the past year, we welcomed another 15 recruits. They include interventional pain management specialist Joseph Amos, M.D.; vascular neurologist Ritvij Bowry, M.D.; neurologist Guy Burrows, M.D.; neurosurgeon Joseph Cochran, M.D.; neurologist Michael Chachere II, M.D.; interventional pain management specialist Divya Chirumamilla, M.D.; neurologist Mimi Dang, M.D.; neurologist Megan Davis, M.D.; neurologist Edward Escobar, D.O.; neurosurgeon Yoshua Esquenazi, who completed his fellowship training in epilepsy surgery with us; radiation oncologist Shariq Khwaja, M.D.; spine surgeon Joseph Martinez, M.D.; neurologist Justin Morgan, M.D.; vascular neurologist Sunil Sheth, M.D.; and neurointerventional surgeon Gary Spiegel, M.D., who is director of endovascular and interventional neurology at UTHealth.

In the realm of education, residents and fellows come to the Institute and UTHealth to work with outstanding teachers and mentors, to access cutting-edge research and to treat the broad range of patients who seek care at the nation's largest medical center. Highlights of our training programs include a world-renowned stroke and cerebrovascular service, a 38-bed Neurotrauma ICU – the largest in the area and second busiest in the nation – nine dedicated ORs, one of the country's largest and most comprehensive epilepsy programs, and a large and innovative brain tumor program.

We are pleased to share with you the Mischer Neuroscience Institute Clinical Achievements Report for fiscal year 2016, which highlights our ongoing efforts in quality, safety, clinical care and research from July 2015 through June 2016. As always, our report includes a section recognizing the accomplishments of our terrific nurses.

We are especially grateful to the donors who have provided \$18.6 million in philanthropic research support, which allows us to continue to make a difference in the lives of our patients. They include the Vivian L. Smith Foundation, the Staman Ogilvie Fund, Mission Connect, The William Stamps Farish Fund, Randa Duncan and Charles Williams, The Moody Foundation and The Will Erwin Headache Research Foundation.

We're proud of our team of neuroscience providers, who are doing their very best, and consistently asking questions about how to make things better.

Please feel free to contact me directly if you would like more information about our services, research and programs.

With best wishes,



Dong H. Kim, M.D.

DIRECTOR MEMORIAL HERMANN MISCHER NEUROSCIENCE INSTITUTE AT THE TEXAS MEDICAL CENTER

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About the Institute

The Memorial Hermann Mischer Neuroscience Institute's reputation for innovation, high-quality outcomes and the best possible healthcare experiences draws patients from around the world. The Institute's team of clinicians, researchers and educators is nationally recognized and consistently ranked by quality benchmarking organizations as a leader in clinical quality and patient safety. Their insights, technological innovations and success at applying research findings at the bedside are transforming the field of neuroscience.

A collaborative effort between Memorial Hermann-Texas Medical Center and McGovern Medical School at UTHealth, the Mischer Neuroscience Institute is Houston's

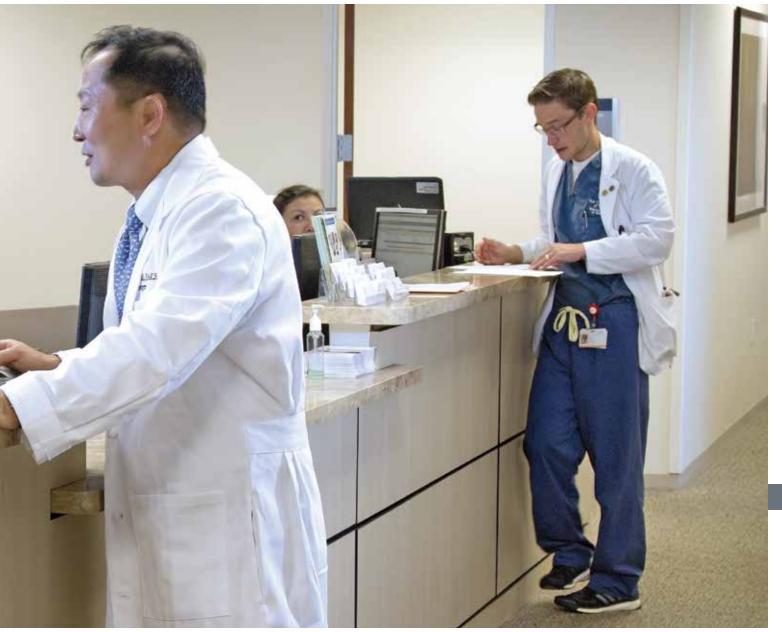


undisputed leader in neuroscience care and the foremost neuroscience provider in the southern half of Texas. As the first stroke program in Texas and the only one in the region to meet The Joint Commission's rigorous standards for Comprehensive Stroke Center certification, and one of the few hospitals in the country recognized with the American Heart Association's Get With The Guidelines[®]-Stroke Gold Plus Achievement Award, the Institute stands among an elite group of providers focused on complex stroke care.

This same comprehensive, integrated approach led to the creation of the Southwest's leading epilepsy program, a highly ranked neurotrauma program, a cerebrovascular center where affiliated physicians treat more aneurysms

and arteriovenous malformations than any other center in the region, an established pediatric neuroscience program in collaboration with Children's Memorial Hermann Hospital, an unmatched spinal neurosurgery and reconstructive peripheral nerve surgery program and a Brain Tumor Center where physicians diagnose and treat hundreds of new tumor patients each year. Affiliated physicians are also innovators in the treatment of multiple sclerosis, movement disorders, neurocognitive disorders, memory disorders and dementia, neuromuscular diseases, chronic pain and traumatic brain injury.

The Institute has extended these comprehensive services across the city through the strategic expansion of



ABOUT THE INSTITUTE

Mischer Neuroscience Associates, a citywide network of neurologists, neurosurgeons, neurointerventionalists, neuro-oncologists, interventional pain management specialists and advanced practitioners – and reduced referral wait times by building a new structure for the practice of neurology in the community. These providers analyze quality data and track outcomes as a group, using the same standards employed at the Texas Medical Center to modify clinical practice and ensure exceptional patient experiences.

Through its telemedicine program, the Institute offers patients in outlying communities access to stroke and neurology expertise and opportunities to participate in clinical trials. Nineteen community hospitals in Southeast Texas are now linked to the Institute through remote presence robotic technology. In addition, affiliated physicians are reaching larger numbers of people and engaging them in a powerful way through patient access portals on the group's website, neuro.memorialhermann.org.

Through the Innovation and Quality (IQ) Program, the Institute's leaders are organizing data to improve physician and service performance, fostering innovative ways to measure quality and track long-term outcomes, and increasing infrastructure support to enable faculty at McGovern Medical School to conduct more clinical trials and patient-centered research. The results of these novel treatments are quickly transitioned to clinical practice.

These efforts have led to a strong nine-year growth trend in consumer preference for neuroscience care at Memorial Hermann. During that time, affiliated physicians have reported mortality rates well below the national expected benchmark and have seen a greater than 50 percent reduction in length of stay, despite the increased acuity of the patients they treat.





At a Glance

Physician Team

Staff Physicians	101
Clinical Residents and Fellows	63
Medical Students on Rotation	310
Research Fellows	20
Advanced Practice Providers	20

Inpatient Facilities

Total Neuro Beds	172
Neuro ICU Beds	38
Neuro IMU Beds	12
Neuro Acute Care Beds	74
Stroke Unit Beds	12
Neurorehabilitation Beds	23
Dedicated Operating Rooms	9
EMU Beds – Pediatric & Adult	13

Research

Research Projects in	Progress More than 200
Grants Awarded	Over \$20 million
(Neurology and Neurosurgery)	

Specialty Equipment includes:

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

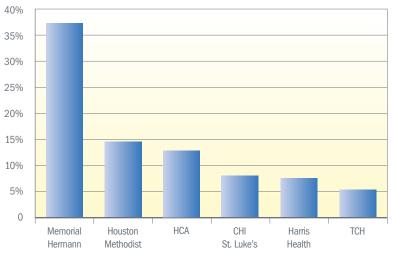
30% 25% 20% 15% 10% 5% 0 HCA Memorial Houston CHI Harris Tenet Methodist St. Luke's Health Hermann

Neurology Market Share FY16

Percent Market Share

Percent Market Share





Source: Texas Hospital Association Patient Data System (FY2014 Q1 – FY2016) provided by Truven, formerly Thomson Reuters. Texas Hospital Inpatient Discharge Public Use Data File (FY2015 Q2 – FY2016 Q1) provided by Texas Department of State Health Services, Center for Health Statistics; FY2016 Q2 – FY2016 Q4 discharges estimated by using historical data by hospital. Excludes Normal Newborns and SNF and any hospital not reporting to THA or Truven. 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

As institutions across the country struggle to improve outcomes and satisfaction while reducing costs, the Mischer Neuroscience Institute is achieving both goals. The close cooperation of affiliated physicians and an innovative administrative structure allows nurses to spend more time coordinating patient care, which has led to an upward trend in patient satisfaction over the last nine years. Data gathered by the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey shows consistent improvement in domains considered critical to ensuring a high level of patient satisfaction.



Source: Press Ganey, national hospital survey vendor, for all surveys received from patients discharged from (7 Jones, EMU, 5 Jones, NIMU, Stroke, Spine added as of FY14, NVICU added as of FY16). HCAHPS scores have not been adjusted to account for a survey mode administration change.

A History of Firsts

- The first center to discover a genetic mutation linked to intracranial aneurysms.
- The first stroke program in Texas and the only one in the region to meet The Joint Commission's rigorous standards for the highly coveted Comprehensive Stroke Center certification.
- Site of the first single-center clinical trial for recurrent medulloblastoma, ependymoma and atypical teratoid-rhabdoid tumors using the direct infusion of chemotherapy into the fourth ventricle; the first trial of infusion of 5-AZA into the fourth ventricle or resection cavity in children with recurrent posterior fossa ependymoma; and the first trial of combination intraventricular chemotherapy (methotrexate and etoposide) infusions into the fourth ventricle or resection cavity in children with recurrent posterior fossa brain tumors.
- The first neurosurgery center to offer all advanced modalities of treatment for complex lesions: expert microsurgery, interventional neuroradiology/ endovascular surgery and Gamma Knife[®] radiosurgery.
- The first hospital in the south-central United States and one of only a few in the country offering intraarterial chemotherapy for retinoblastoma, the most modern treatment for the disease.
- The first in Texas to use robotic stereoencephalography (SEEG) for 3-D mapping of epileptic seizures.
- The first in Houston to offer amyloid imaging, a new diagnostic tool that enables physicians to diagnose Alzheimer's disease and will give researchers insights into how they might one day prevent the disorder.
- The first center to conduct a national, multicenter trial for hypothermia in head injury.

- The 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 stroke center in Houston and one of the first dedicated stroke programs in the world.
- One of the first centers in the nation to offer MRguided laser interstitial thermal therapy (MRgLITT) using the Visualase[™] system for the treatment of well-delineated focal epilepsies.
- The first center in the region to use the NeuroPace[®] RNS[®] System, a new FDA-approved technique for responsive neurostimulation to treat adults with medication-resistant epilepsy.
- The Mischer Neuroscience Institute brought the first clinical magnetoencephalography (MEG) sensor to Houston and has updated the technology to the Elekta Neuromag[®] TRIUX[™].
- The Institute houses one of only a few adult and pediatric inpatient Epilepsy Monitoring Units in the country with the unique capability of simultaneously performing electroencephalography and polysomnography.
- The first in the region to inject human central nervous system stem cells into the spines of spinal cord injury patients.
- 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.





An Eye to the Future at Mischer Neuroscience Institute

A model for best practices in clinical care, the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center actively supports the next generation of physicians through teaching and learning. Through a robust research program, physician investigators at the Institute discover new treatments and move advances in neuroscience quickly to the bedside.

"Our goal at Mischer Neuroscience Institute is to instill a culture of accountability and adaptability in a

time of unprecedented change in health care," says Dong Kim, M.D., director of the Institute and professor and chair of the Vivian L. Smith Department of Neurosurgery at UTHealth. "Performance improvement tools and strategies keep progressing, which allows us to sharpen our focus on collaboration and results."

Strategies used at the Texas Medical Center are also in place at all Mischer Neuroscience Associates (MNA) practices located across the Greater Houston area. "As healthcare reform moves the focus of medicine toward keeping patients healthy, MNA's quality and accountability effort has expanded," says Rahil Tai, manager of clinical quality review for the Memorial Hermann Health System. "By proactively looking at our own data and continuously improving our practice, we remain among the topperforming hospitals."

"We are fortunate to have outstanding teachers and mentors, cutting-edge research and a large, diverse patient population in Houston, which gives our residents and fellows exposure to an exceptionally broad range of cases." - Arthur L. Day, M.D. MNA practices now hold regular Morbidity and Mortality (M&M) Conferences in which all neurosurgery operative cases with complications, excessive length of stay or unexpected outcomes are reviewed – just one example of how the Institute has moved quality initiatives used in academic medical centers to the community. "M&M Conferences allow physicians to sit down as partners and have cases presented to them," Tai says. "If an outcome was unexpected, they look at it analytically and discuss what could have been

done differently, which allows us to identify small problems before they become larger, and implement practices to prevent future occurrences."

The result has been positive. "We're doing great," Tai says. "Every year we have fewer complications. If there's a variance in practice or a complication we can identify it. It's a collegial peer-review process. The objective is not punitive but educational, so that physicians in MNA practices can learn from these cases."

Mischer Neuroscience Institute's relentless focus on quality is transferred to the next generation through education. Through its affiliation with the Vivian L. Smith Department of Neurosurgery and the department of Neurology at UTHealth, the Institute offers both neurosurgery and neurology residencies and fellowships.



"We are fortunate to have outstanding teachers and mentors, cutting-edge research and a large, diverse patient population in Houston, which gives our residents and fellows exposure to an exceptionally broad range of cases," says Arthur L. Day, M.D., director of clinical education in neurosurgery at the Institute and professor and vice chair of neurosurgery at UTHealth. "Multiple neuroscience subspecialties are well represented in our educational programs and supported by the latest technology."

Fellowships offered include cerebrovascular/skull base, neurocritical care, neuroendovascular surgery, stroke and stroke interventional track, multiple sclerosis, movement disorders, neuro-oncology, neuromuscular diseases and epilepsy. The Institute is currently training 16 neurosurgery residents and one fellow through a program started in 2008; in the department of Neurology there are 28 neurology residents and 13 fellows. "We've developed a system to help residents clearly understand the responsibilities they'll have after they complete their programs," Dr. Day says. "They include the basics of quality patient care from the physician standpoint – promptness, doing dictations on time and including the correct information, checking up on patients within a few hours after surgery, and strategies to keep infection rates low."

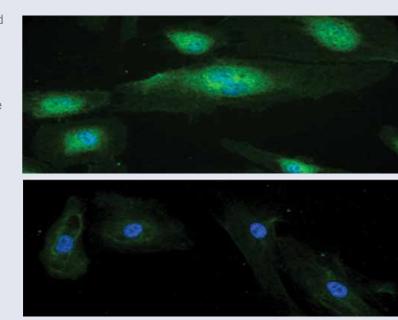
Senior residents present quality projects at the end of their seventh year of training. "They spend their last year polishing up the areas they need to refine and some may even start a fellowship while still in residency," he says. "They develop projects in areas where they see opportunities for improvement, implement them and present their results and conclusions." With high quality scores, the citywide infrastructure of MNA, and residencies and fellowships in place, Dr. Dong Kim has turned more of his focus to the discovery of new knowledge that will change the face of patient care. Clinical research is critical to optimizing care and providing patients with state-of-the-art options. Under Dr. Kim's leadership, physicians affiliated with the Mischer Neuroscience Institute are bridging research and clinical practice. Patients are evaluated and those who meet qualifying criteria are invited to participate in innovative research studies.

Among those under way are the HOPES trial (Hypothermia for Patients Requiring Evacuation of Subdural Hematoma), a randomized, prospective trial studying the effect of very early cooling in patients undergoing evacuation of acute subdural hematomas, and the National Center for Testing Treatments in Chronic Spinal Cord Injury and Traumatic

On the Cutting Edge

A research team led by Dr. Dong Kim has discovered a genetic mutation linked to intracranial aneurysms (IA). After studying more than 500 people, including a large family with multiple incidents of IA, the team identified a specific protein coding gene, THSD1, whose mutation is suspected to lead to the formation of weak or thin spots in cerebral arteries. The defect can cause the artery to rupture, leading to bleeding in the subarachnoid space, which can result in disability or death. After pinpointing the mutation, the researchers investigated the consequences of a loss of function of THSD1, using genetically modified mice and zebrafish. They discovered cerebral hemorrhage and increased mortality in both animal models when the gene's function was switched off. In mice, the bleeding was located in the subarachnoid space, providing new insight and understanding into the function of a gene that has not been widely studied. The study results were published in the Nov. 17, 2016, issue of Stroke.

For the first time in humans, principal investigator David I. Sandberg, M.D., FACS, FAAP, and his team demonstrated in a previous pilot clinical trial that chemotherapy can be delivered directly into the



fourth ventricle of the brain in children with recurrent, malignant brain tumors. Promising results from a pilot trial with low-dose methotrexate infusions has led to an ongoing Phase I dose-escalation trial. To date, seven patients with medulloblastoma have received methotrexate infusions. All patients had progressive disease prior to enrollment in the trial despite surgery, chemotherapy and radiation therapy. Three of the seven patients had a partial response (at least 50 percent Brain Injury (NCTT), which is unique in its focus on research to improve the lives of people who have passed the acute phase of spinal cord injury and are living with the injury as a lifelong condition.

Through the NCTT and The Will Erwin Headache Research Center, leadership at the Mischer Neuroscience Institute has committed to investment in discovery in two areas that affect Americans profoundly. Recruiting physicians who will spend 75 percent of their time focused on research is a new direction for the Institute.

"Our culture encourages asking questions," Dr. Dong Kim says. "In our search for answers we create new research infrastructures that provide substantial data on long-term outcomes. We tie that data to the decisions we make about future research. In this way we continue down the path to revolutionize neuroscience."

reduction in disease burden), two patients had stable disease, and two had disease progression. There were no serious adverse events or new neurological deficits caused by the methotrexate infusions. Dr. Sandberg's research has led to a new trial, recently approved by the FDA and about to open. In the new trial, two agents – methotrexate and etoposide – will be infused into the fourth ventricle simultaneously in patients with recurrent malignant brain tumors. The researchers hope for continued demonstration of safety and even more robust clinical responses. Dr. Sandberg is professor and director of pediatric neurosurgery and holds the Dr. Marnie Rose Professorship in Pediatric Neurosurgery in the departments of Pediatric Surgery and Neurosurgery at UTHealth.

A research team led by neuro-oncologist Jay-Jiguang Zhu, M.D., Ph.D., associate professor of neurosurgery, continues its study of the effectiveness of the NovoTTF-100A device in treating glioblastoma multiforme (GBM), the most aggressive and common glial tumor. Historical data shows that median overall survival is 14.6 months with maximum safe resection followed by radiation and chemotherapies. A recent trial of triple chemotherapies plus TTFields demonstrated superior overall survival benefit compared to historical data: For patients who received a combination of thiotepa, busulfan and cyclophosphamide (TBC) plus TTFields at tumor recurrence, the median overall survival is 32.8 months. For patients who received TTFields with standard of care or alternative therapy, the medial overall survival is 17.9 months.

Daniel H. Kim, M.D., FACS, FAANS, and his fellow investigators are developing a steerable telerobotic microcatheter with life-changing potential for stroke patients worldwide. "Stroke is a time-sensitive emergency, and for those living in remote locations, access to fast care may not be possible," Dr. Kim says. "With telerobotics, an emergency physician in a rural community can access the femoral artery, and a skilled endovascular neurosurgeon working in a telerobotic hub can manipulate the microcatheter via computer to retrieve the clot." The first-of-its-kind endovascular telerobotic microcatheter-based robotic system is ready for testing in an animal model to prove safety before the researchers initiate a clinical trial.



FEATURE

Using an Innovative Delivery Model, Mischer Neuroscience Associates Extends High-Level Care Across the Region

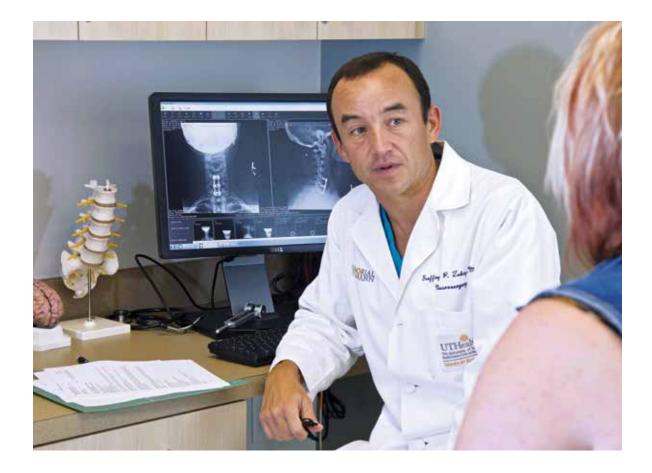
Mischer Neuroscience Associates (MNA) has enjoyed a highly successful year of recruitment, which brings the organization's total count of physicians practicing in MNA clinics in the Greater Houston area to 61. That number includes 21 neurosurgeons, four pain management specialists, two neuro-oncologists, two radiation oncologists, nine critical care intensivists and 23 neurologists. These specialists work together in an innovative model that ensures high-quality, cost-effective care with a strong focus on the patient experience. In addition, 36 advanced practice providers, 16 residents and eight fellows at McGovern Medical School at UTHealth are now providing care at the 24 MNA practices located across the city.

"The reputation of Mischer Neuroscience Institute and UTHealth has helped us recruit high-quality, high-service physicians who deliver outstanding care at Memorial Hermann's network of hospitals," says Amanda Spielman, President of Mischer Neuroscience Associates and Vice President of Neurosciences at Memorial Hermann Health System. "Building on a core group of expert academic physicians at Memorial Hermann-Texas Medical Center and UTHealth, we've created multidisciplinary teams that work across our 24 MNA locations to serve our patients, hospitals and the medical staff. They collaborate closely to develop consistent care protocols, regardless of the site of service, and look for ways to improve on the quality of care they deliver." To arrive at this point, Spielman and Mischer Neuroscience Institute director Dong Kim, M.D., took a close look at the complement of physicians within the Institute, and asked the question, "How do we develop a comprehensive network of neuroscience providers, both specialists and generalists, with a connection to the Texas Medical Center and access to its tertiary-care resources?"

The solution was a citywide group practice, grounded in best practices and protocols, that allows patients to access neurological care, including complex spine and intracranial medicine, often closer to home. "The large recruitment of providers that followed allowed us to think strategically about the specific needs of each hospital and the community it serves," Spielman says.

Among them is a multicenter, coordinated neuroendovascular program focused on getting the right patients to the right hospital, depending on their needs. "Without the expansion of MNA and the ability to leverage our existing team of providers for full coverage, we would have had to hire two neurointerventionalists to serve each area of the city," Spielman says. "Instead, with a large group of physicians and other providers who work closely together and rotate at MNA clinics and hospitals, we've created coverage that extends our team's expertise across the Greater Houston area."

FEATURE



The innovative practice model also made possible the extension of neurocritical care to Memorial Hermann Southwest Hospital. As a Primary Stroke Center certified by The Joint Commission, the hospital was already equipped for rapid diagnosis and treatment of stroke. Thanks to MNA, its new state-of-the-art Neuroscience ICU is staffed 24/7 by physicians affiliated with the Mischer Neuroscience Institute and UTHealth, all of whom are fellowship trained in neurocritical care. These neurointensivists work hand in hand with neurosurgeons and neurologists to provide superior care. Also through its affiliation with Mischer Neuroscience Associates. the hospital now has full emergency department call coverage for all neurosurgery specialties. Critical care fellows started rotating at Memorial Hermann Southwest last July; by next summer, the hospital will be on the rotation list for critical care residents.

The hospital is also adding a state-of-the-art hybrid operating room where neurosurgeons can perform emergent or elective endovascular and skull base procedures. Diagnostic angiography is available onsite, and patients of referring physicians have access to a spectrum of neuroendovascular services through the hospital's affiliation with the Mischer Neuroscience Institute. The expanded neuroscience program supports Memorial Hermann Southwest Hospital's application for certification as a Level II trauma center – the facility serves a large population in an area with a shortage of higher-level trauma care.

MNA is also building out complete neuroscience programs at Memorial Hermann Memorial City Medical Center and Memorial Hermann The Woodlands Hospital. "Each program is slightly different based on the needs of the local community," Spielman says. "Memorial City has added neurocritical care and diagnostic angiography to complement its existing neurosurgery and inpatient and outpatient neurology programs, which have been in place for many years. High-level services are also available through the MNA practice in The Woodlands, which means that residents of North Houston and The Woodlands no longer have to make the long drive to Houston for certain procedures."

At Memorial Hermann Memorial City, "we're growing up and evolving," says Meredith Wells, RN, NEA-BC, associate vice president for neurosciences. "We already have 19 beds dedicated to neuroscience – a mix of ICU and acute care beds – which gives us a competitive advantage because it allows patients to stay on the same floor as they get closer to discharge with consistent expert nursing care. We also now have in-house nighttime

"Having a coordinated team of physicians and advanced practice providers is really good overall for a hospital campus and its medical staff, but most important, we bring the services to our patients in a coordinated manner." - Amanda Spielman

neuroscience coverage, which gives us 24/7 availability of neuroscience provider expertise. When you put that together with our MNA neurosurgeons and neurologists, two neurointensivists and six advanced practice providers supporting critical care, you have a dedicated neuroscience unit that is uniquely capable of taking care of higher-acuity patients in a community hospital setting."

Memorial Hermann The Woodlands Hospital is now served by 12 MNA providers, including a newly recruited pain management specialist who joined the team in summer 2016. The multidisciplinary team includes neurosurgery, inpatient and outpatient neurology, neuroendovascular services, pain management and neuro-oncology. In-house nighttime neuroscience coverage and Neuro 1, a one-stop number that allows referring physicians to access the appropriate on-call neuroscience provider quickly, have been added. The hospital is gearing up for certification as a Level II trauma center.

In conjunction with UTHealth, telemedicine services are now available at nine Memorial Hermann hospitals, connecting them with stroke experts at the Mischer

> Neuroscience Institute. At Memorial Hermann Katy Hospital, this has resulted in a wait time of less than 10 minutes for a patient to come face to face with a stroke expert on a remote monitor. Before the implementation of telemedicine, Memorial Hermann Katy Hospital logged 0 to 1 cases of acute ischemic stroke treated with tPA each month. Post-implementation, the hospital has had as many as nine. Collaboration with emergency care team providers, standardizing access and escalation protocols and providing a common language to request a consult through

Neuro 1 has also improved the quality of care.

The expansion of MNA has also led to the opening of new practices in Sugar Land and Cypress. Pain management specialists have been added at MNA-Katy, MNA-Memorial City and MNA-The Woodlands.

"Having pain management specialists in our spine clinics improves service for patients and offers them comprehensive care." Spielman says. "Having a coordinated team of physicians and advanced practice providers is really good overall for a hospital campus and its medical staff, but most important, we bring the services to our patients in a coordinated manner."

Capabilities Across the City

MEMORIAL HERMANN SOUTHWEST HOSPITAL

- Neurosurgery, neurology, neuroendovascular, pain management and rehabilitation
- A new Neuroscience ICU staffed 24/7 by fellowship-trained physicians affiliated with the Mischer Neuroscience Institute and UTHealth
- Recognized by The Joint Commission as a Primary Stroke Center
- Full emergency department call coverage for all neurosurgery specialties
- Continuous EEG available for inpatients
- A state-of-the-art hybrid operating suite for emergent endovascular and general neurosurgical procedures
- Support from rotating critical care fellows
- Neuro 1, a one-stop number to access the appropriate neuroscience physicians for inpatient consultations
- Telemedicine with face-to-face access to stroke experts at the Texas Medical Center
- Hospital is pursuing Level II trauma center status
- Seizure Clinic
- Memory Loss and Alzheimer's Disease Clinic

MEMORIAL HERMANN GREATER HEIGHTS HOSPITAL

- Neurology
- Recognized by The Joint Commission as a Primary Stroke Center
- Seizure Clinic
- Telemedicine with face-to-face access to stroke experts at the Texas Medical Center

MEMORIAL HERMANN KATY HOSPITAL

- Neurosurgery, neurology and pain management
- Recognized by The Joint Commission as a Primary Stroke Center
- Neuro 1, a one-stop number to access the appropriate neuroscience physicians for inpatient consultations
- Telemedicine with face-to-face access to stroke experts at the Texas Medical Center

MEMORIAL HERMANN MEMORIAL CITY MEDICAL CENTER

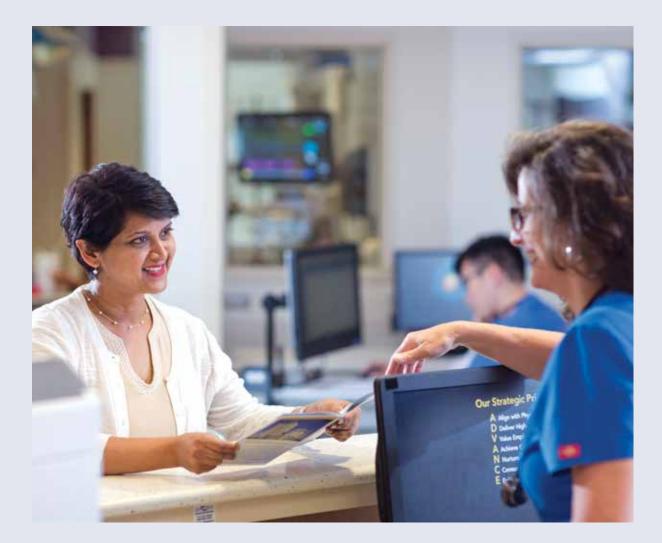
- Neurosurgery, neurology, neuroendovascular, neuro-oncology, pain management, radiation oncology and rehabilitation
- 19-bed dedicated neurocritical care unit combining intensive and acute care, with the ability to expand in the future to 23 additional beds for a total of 40 dedicated neuroscience beds
- Recognized by The Joint Commission as a Primary Stroke Center
- Neuroscience ICU staffed 24/7 by fellowship-trained physicians affiliated with Mischer Neuroscience Associates and UTHealth
- Full emergency department call coverage for all neurosurgery specialties
- · Continuous EEG available for inpatients
- A state-of-the-art Neuroendovascular IR suite for emergent and diagnostic endovascular procedures
- Neuro 1, a one-stop number to access the appropriate neuroscience physicians for inpatient consultations
- Telemedicine with face-to-face access to stroke experts at the Texas Medical Center
- Hospital is pursuing Level IV trauma center status
- In-house nighttime neuroscience advanced practice provider coverage

MEMORIAL HERMANN PEARLAND HOSPITAL

- Neurology
- Telemedicine with face-to-face access to stroke experts at the Texas Medical Center

MEMORIAL HERMANN SOUTHEAST HOSPITAL

- Neurosurgery and neurology
- Recognized by The Joint Commission as a Primary Stroke Center
- Telemedicine with face-to-face access to stroke experts at the Texas Medical Center



MEMORIAL HERMANN SUGAR LAND HOSPITAL

- Neurosurgery with a focus on elective spine surgery
- Telemedicine with face-to-face access to stroke experts at the Texas Medical Center
- Neuro 1, a one-stop number to access the appropriate neuroscience physicians for inpatient consultations

MEMORIAL HERMANN THE WOODLANDS HOSPITAL

- Neurosurgery, neurology, neuroendovascular, pain management and neuropsychology
- Recognized by The Joint Commission as a Primary Stroke Center

- Neuro 1, a one-stop number to access the appropriate neuroscience physicians for inpatient consultations
- Telemedicine with face-to-face access to stroke experts at the Texas Medical Center
- Hospital is pursuing Level II trauma center status

NEW MISCHER NEUROSCIENCE ASSOCIATES CLINICS

- MNA-Sugar Land Neurosurgery Clinic
- MNA-Cypress Neurosurgery and Neurology Clinic
- MNA-Pearland Neurosurgery Clinic



ACCOLADES

Dr. Arthur Day Awarded the Highly Coveted Harvey Cushing Medal, Receives UTHealth Dean's Teaching Excellence Award



Arthur L. Day, M.D., vice chair, program director and director of clinical education in neurosurgery at the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center and professor of neurosurgery at

McGovern Medical School at UTHealth, has received the prestigious Harvey Cushing Medal, the highest honor awarded by the American Association of Neurological Surgeons. Dr. Day was selected as recipient of the honor for his many years of outstanding leadership, dedication and contributions to the field of neurosurgery.

"I am incredibly honored to be recognized with the Harvey Cushing Medal," Dr. Day says. "Many world-renowned, well-respected physicians have received this award in the past, and it is deeply humbling to be added to a group with such great medical legacies."

A fellowship-trained and board-certified neurosurgeon with specific expertise in cerebrovascular and skull base neurosurgery, Dr. Day also specializes in microsurgical treatments of brain tumors and minimally invasive spinal surgery.

Dr. Day received his medical degree at Louisiana State University in New Orleans. He completed his neurological surgery and fellowship in brain tumor immunology at the University of Florida College of Medicine in Gainesville.

Before joining the Mischer Neuroscience Institute and UTHealth, Dr. Day practiced at the University of Florida for 25 years, ultimately rising to the positions of professor, co-chair and program director of the department of Neurosurgery. In 2002, he moved to Boston to assume a position as a professor of surgery at Harvard Medical School with a clinical practice at Brigham and Women's Hospital.

While there, he served as the associate chair and residency program director of the department of Neurological Surgery at Brigham and Women's and Children's Hospital Boston. Later, he was the chairman of the department, and was also the director of the cerebrovascular center and the neurologic sports injury center at Brigham and Women's Hospital.

Dr. Day has held leadership positions in many medical professional societies, and received numerous awards and honors, including the Medal of Honor from the Neurosurgical Society of America (NSA) and the Founders' Laurel Award from the Congress of Neurological Surgeons for his "exceptional service, lifelong dedication and meritorious accomplishments in the field of medical education."

In 2011, he was appointed as president of the Society of Neurological Surgeons. He has also been named multiple times to Best Doctors in America. Dr. Day has published nearly 180 journal articles and book chapters, and co-edited two books about neurological sports injuries.

This year he was also recognized with McGovern Medical School's Dean's Teaching Excellence Award. The award is an annual recognition presented to faculty and volunteers for outstanding teaching performance. Those chosen to receive the award have exhibited outstanding teaching; incited intellectual curiosity in their medical students, residents and graduate students; engaged them in the learning process; and helped them develop lifelong skills.

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Dr. Bob Fayle Named Physician of the Year by the Texas Neurological Society



Neurologist Robert W. Fayle, M.D., has been honored as Physician of the Year by the Texas Neurological Society. The society promotes the interest of patients with neurologic disease by supporting the development

and delivery of quality medical care to these patients.

Board certified in adult neurology and sleep medicine, Dr. Fayle is a past-president of the Texas Neurological Society and currently serves as chair of the organization's Education Committee. He has held multiple leadership positions with Memorial Medical Center in Livingston, Memorial Clinics, the Harris County Medical Society, the Texas Medical Association, the American Academy of Sleep Medicine, the Diagnostic Center Hospital Board of Trustees, the Diagnostic Clinic of Houston Executive Committee and the Park Plaza Hospital Medical Executive Committee.

Dr. Fayle received his medical degree at the McGovern Medical School at UTHealth and completed his residency in neurology at UTHealth-affiliated hospitals in Houston. His research in the field of sleep and stroke, including CPAP compliance and adherence, treatment of insomnia and the role of sleep apnea in diabetic patients, has been published widely.

Dr. Fayle, who is on the medical staff at Memorial Hermann Southeast Hospital, provides neurological consultations and follow-up at the Houston Neurological Institute's Pasadena and Pearland locations.

Harris County Medical Society Installs Dr. Kimberly Monday as President



The Harris County Medical Society (HCMS), the professional society for physicians in Harris County and the largest county medical society in the nation, installed into office boardcertified neurologist Kimberly

E. Monday, M.D., as the 115th President on Jan. 22, 2016, in Houston. Dr. Monday is in private practice at the Houston Neurologic Institute (HNI), which she co-founded in 1997. HNI is affiliated with Memorial Hermann Mischer Neuroscience Associates.

Dr. Monday completed her medical training, neurology residency and chief residency at Baylor College of Medicine in Houston, followed by fellowship training in clinical neurophysiology at Emory University in Atlanta where she specialized in intra-operative monitoring, diagnostic sleep medicine, EMG and EEG. Board certified by the American Academy of Psychiatry and Neurology in adult neurology, clinical neurophysiology and sleep medicine, she provides state-of-the-art electrophysiological therapy for movement disorders, including deep brain stimulation programming, baclofen pump programming and vagal nerve stimulation for epilepsy treatment. She provides neurological consultation for patients with epilepsy, movement disorders and sleep disorders, and directs both the EEG and sleep laboratories at the Houston Neurological Institute.

Dr. Monday has been named a Super Doctor by *Texas Monthly* magazine and Top Doctor by both *H Magazine* and *The Consumer's Guide to Top Doctors*. She serves on the Board of the Texas Neurological Society, is a delegate to the Texas Medical Association and chairs the Clinical Ethics Care Committee for MHMD, the Memorial Herman Physician Network. In addition, she serves on the Medical Advisory Board for the Houston Area Parkinson's Society. She also is a clinical assistant professor in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth. She was recently appointed to serve on the Harris Health System Board of Managers and is chair of compliance. In 2015, she was appointed to The University of Texas College of Liberal Arts Advisory Council.

During her medical career, Dr. Monday has held many hospital and leadership positions, including chair of the Bioethics Committee at Bayshore Medical Center (1999-2002) and chair of the Bioethics Committee at Memorial Hermann Southeast Hospital (2003-2010).

She has hospital affiliations with Memorial Hermann Southeast Hospital, Memorial Herman-Texas Medical Center, Memorial Hermann Southwest Hospital, Memorial Hermann Memorial City Medical Center, Memorial Hermann Greater Heights Hospital, St. Luke's Patient Medical Center, Bayshore Medical Center and Clear Lake Regional Medical Center.

HCMS, established in 1903, is the professional society for physicians in Harris County. It is the largest county medical society in the nation, with a membership of more than 11,000 physicians and medical students. Its mission is to be the leading advocate for its member physicians, their patients and the community, in promoting the highest standards of ethical medical practice, access to quality medical care, medical education, research and community health.

McGovern Medical School Designated Huntington's Disease Center of Excellence by National Organization



The comprehensive Huntington's Disease Program at McGovern Medical School at UTHealth has been named a Huntington's Disease Society of America (HDSA) Center of Excellence for 2016.

The new HDSA Center of Excellence is part of the Movement Disorders and Neurodegenerative Diseases Program, called UT MOVE, at UTHealth and the Mischer Neuroscience Institute. Led by Erin Furr-Stimming, M.D., associate professor in the department of Neurology at McGovern Medical School, the Huntington's Disease Program is one of 39 centers of excellence across the country and the only one in Texas to receive the prestigious designation.

"HDSA Centers of Excellence represent an elite team approach to providing comprehensive and expert Huntington's disease care to families, while simultaneously committing to the clinical science that will bring treatments for HD forward," says Louise Vetter, president and CEO of the Huntington's Disease Society of America. "We are proud to recognize the excellence in Huntington's disease care made possible by Dr. Erin Furr-Stimming and the team at UTHealth."

Huntington's disease (HD) is a fatal inherited disorder that causes degeneration of brain cells. Symptoms of the disease, which progressively worsen, include uncontrolled movements, abnormal body postures and changes in behavior, emotion, judgment and cognition. The disease typically begins in the prime of life, between the ages of 30 and 50. Eventually HD affects the ability to reason, walk and speak.

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More than 30,000 Americans have HD. Every child of a parent with HD has a 50/50 chance of carrying the altered gene, placing 200,000 Americans at risk. Although there is no cure or FDA-approved neuromodulatory therapy, novel basic science and translational research is under way at the Mischer Neuroscience Institute and other centers around the world.

Dr. Nneka Ifejika Spotlighted in National Physical Medicine and Rehabilitation Publication



The Physiatrist, the official membership publication of the American Academy of Physical Medicine and Rehabilitation (AAPM&R), featured Nneka Ifejika, M.D., M.P.H., in its inaugural June 2015 member spotlight.

Dr. Ifejika is director of neurorehabilitation at McGovern Medical School at UTHealth, where she holds joint appointments as an associate professor in the department of Neurology and the department of Physical Medicine and Rehabilitation.

A former AAPM&R Leadership Program Fellow (2013-2015), Dr. Ifejika completed a dual M.D./M.P.H. program at the University of North Carolina at Chapel Hill with a focus in health policy and administration. She is currently pursuing a Master of Science degree in clinical research at McGovern Medical School, where her research program focuses on stroke outcomes and health disparities with a goal of closing the disability gap between minorities and non-minorities in patients with cerebrovascular disease. Dr. Ifejika is principal investigator of a National Institutes of Health-funded clinical trial called Swipe Out Stroke, which uses a mobile application to monitor diet and physical activity in high-risk stroke patients and their family members.

"Minority compliance with obesity management has been a longstanding concern in the stroke community," Dr. Ifejika says. "Unfortunately, structured weight loss programs are expensive, and compliance significantly decreases after completion of the program. At the same time, minorities spend more than \$4.5 billion annually on consumer electronics, making studies that use media ideal for health outreach and health promotion efforts in minority communities. We believe that many patients will benefit from a low-cost smartphone-based application that facilitates personal contact, provides positive reinforcement and gives support."

Dr. Ifejika, who is an active member of the AAPM&R, recently began a three-year term on the Health Policy and Legislation Committee. She volunteers on the Medical Education Committee as a question writer and reviewer for the AAPM&R Certification Exam Prep Question Bank. She recently completed a webinar presentation on evidence-based medicine (EBM) for the EBM Committee and serves as a manuscript reviewer for *PM&R*, the official scientific journal of the AAPM&R.

Thirty Neuroscience Specialists Named to Top Doctors Lists for 2015

A total of 30 neurologists, neurosurgeons and pediatric neurosurgeons affiliated with the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center and McGovern Medical School at UTHealth were named to top doctors lists for 2015.

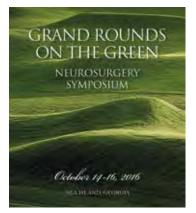
Twenty-five physicians were named to Houstonia magazine's 2015 listing of Top Doctors in Houston. Their selection was based on nominations solicited from nearly 16,000 medical professionals practicing in eight counties in the Greater Houston area. Neurosurgeons included on the Houstonia magazine list are Peng Roc Chen, M.D., Arthur L. Day, M.D., Daniel H. Kim, M.D., Dong Kim, M.D., and Nitin Tandon, M.D. Pediatric neurosurgeons among the Top Doctors are David I. Sandberg, M.D., and Manish Shah, M.D. Neurologists on Houstonia magazine's list are Andrew Barreto, M.D., Suur Biliciler, M.D., José M. Diaz, M.D., William G. Irr, M.D., Giridhar P. Kalamangalam, M.D., John A. Lincoln, M.D., Raymond A. Martin, M.D., Ankit Patel, M.D., Sean I. Savitz, M.D., Mya C. Schiess, M.D., Jeremy D. Slater, M.D., Sudha S. Tallavajhula, M.D., and Mary Ellen Vanderlick, M.D. Pediatric neurologists listed are Ian J. Butler, M.D., Mary Kay Koenig, M.D., Jeremy Lankford, M.D., Pedro Mancias, M.D., and Gretchen Von Allmen, M.D.

Nine physicians affiliated with the Mischer Neuroscience Institute were selected by their peers as Texas Super Doctors. Following an extensive nomination and research process conducted by Key Professional Media Inc., the results were published in the June 2015 issue of *Texas Monthly* magazine. They include Dr. Dong Kim, Dr. Ian Butler, Dr. Mya Schiess, Dr. John Lincoln, and Dr. Raymond Martin, who were also named to *Houstonia*'s Top Doctors list., and neurologists James Ferrendelli, M.D., Nicole Gonzales, M.D., Omotola Hope, M.D., and Jerry Wolinsky, M.D. Recognized as a Texas Super Doctors Rising Star was neurologist Melissa Thomas, M.D.

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NEWS OF NOTE

Grand Rounds on the Green Recap



Seventy-two invited guests attended the Grand Rounds on the Green neurosurgery symposium, held Oct. 14-16, 2016, in Sea Island, Georgia. Hosted by the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center and McGovern Medical School at UTHealth, Emory University School of Medicine and Washington University School of Medicine, the intimate gathering was held at The Cloister at Sea Island and its sister hotel The Lodge.

The weekend of continuing neurosurgery education drew top speakers from the three sponsoring medical schools, who presented on topics including cerebrovascular procedures, neuro-oncology, spine surgery, neurotrauma, functional techniques and peripheral nerve treatments, including case study discussions.

The audience participated in lively discussions on current hot topics in neurosurgery, forged new connections with peers and enhanced their knowledge in an intimate, scholarly environment. Attendees also participated in a golf tournament on the Seaside Course, Sea Island's top course, ranked routinely among the top 100 courses in the United States.

Watch for news of the next Grand Rounds on the Green in future Mischer Neuroscience Institute publications.

Mischer Neuroscience Institute Hosts Fourth Annual Neuro ICU Symposium

More than 360 physicians, nurses, fellows, residents and medical professionals working in neurology, neurosurgery, critical care, trauma, emergency medicine and anesthesiology attended the Memorial Hermann Mischer Neuroscience Institute's Fourth Annual Neuro ICU Symposium, held at the JW Marriott in Houston in March 2016. Participants from 13 states and Canada attended the two-and-a-half-day meeting, which had the highest attendance of any Neuro ICU Symposium to date.

This year's event, "Cutting-edge Management of Neurological and Neurosurgical Emergencies and Critical Care," placed a strong emphasis on prehospital care as well as ultra-early brain resuscitation beginning in the field and continuing in the emergency room. Highlights included "Bringing the Stroke Unit to the Field: Cutting Down Symptom-Onset-to-Needle Time" and "Neuro ICU in the Emergency Room." "Time is brain and the brain does not wait for a Neuro ICU bed to open up," says course director and committee chairman Kiwon Lee, M.D., FACP, FAHA, FCCM, vice chairman of neurosurgery for critical care, director of neurocritical care at Memorial Hermann-Texas Medical Center, director of the Neuroscience, Neurotrauma and Neurovascular Intensive Care Unit at the Mischer Neuroscience Institute and an associate professor in the department of Neurology and the Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth. "The injury is ongoing, and it must be stopped right from the

onset. Neurointensivists have been thinking about bringing cuttingedge neurocritical care right down to the emergency room for years now. At the 2016 symposium we discussed specifically how to do that and achieve ultra-early brain resuscitation."

Invited faculty speakers included Claudia Robertson, M.D., professor of neurosurgery at Baylor College of Medicine. Speakers from McGovern Medical School and Memorial Hermann-Texas Medical Center included Wamda Ahmed, M.D., assistant professor of neurosurgery; Tiffany Chang, M.D., assistant professor of neurosurgery and neurology and director of the Neurocritical Care Fellowship Program; P. Roc Chen, associate professor of neurosurgery; Charles S. Cox Jr., M.D., the George and Cynthia Mitchell Distinguished Chair in Neurosciences, director of the Children's Regenerative Medicine Program at Children's Memorial Hermann Hospital and professor of pediatric surgery; Arthur Day, M.D., professor of neurosurgery and director of the Neurosurgery Residency Training Program: Pratik B. Doshi, M.D., assistant professor of emergency medicine and internal



medicine at the medical school and director of emergency critical care and medical director of the Transplant Intensive Care Unit at Memorial Hermann-TMC; Nicole Gonzales, M.D., associate professor of neurology; Naveet Grewal, M.D., assistant professor of anesthesiology; James C. Grotta, M.D., director of the Mobile Stroke Unit Consortium. director of Stroke Research at the Clinical Innovation and Research Institute and vascular neurologist at Memorial Hermann-TMC; Caroline Ha, M.D., assistant professor of internal medicine, division of Geriatric and Palliative Medicine; Nicole Harrison, B.S.N., M.B.A., RN, administrative director of the Mischer Neuroscience Institute and Central Monitoring at Memorial Hermann-TMC; Ryan Kitagawa, M.D., assistant professor of neurosurgery; Sara K. Miller, M.D.,

assistant professor of emergency medicine and chief of the division of Ultrasound and director of the Ultrasound Fellowship Program; Samuel J. Prater, M.D., assistant professor of emergency medicine at the medical school and medical director of the Emergency Department at Memorial Hermann-TMC; Jeremy Ragland, M.D., assistant professor of neurosurgery; Kunal Sharma, M.D., assistant professor of emergency medicine; Scott R. Shepard, M.D., assistant professor of neurosurgery; Gary Spiegel, M.D., professor of neurosurgery and neurology; Robert Wegner, M.D., assistant professor of anesthesiology; and George Williams, M.D., assistant professor of anesthesiology and assistant program director of the Residency and Critical Care Fellowship Programs in anesthesiology.

The Practice of Nursing





Life in the Fast Lane: Great Teamwork, High Morale and High Patient Satisfaction on the Neuroscience Intermediate Care Unit

It's not uncommon for patients on the Neuroscience Intermediate Care Unit (NIMU) to tell their nurses they don't want to leave when they're discharged to another inpatient area.

"That says a lot about our NIMU nurses. Even though we're a very busy unit and hardly ever have an open bed, we work hard to provide our patients with a good experience," says Shannon Bednarczyk, B.S.N., RN, a charge nurse in the NIMU. "Patients with a variety of neurological conditions at various stages of recovery come to us from the ICU, emergency department, post-anesthesia care, the stroke unit and medicine, which means we work with multidisciplinary affiliated physician teams. We don't see the intensivists as often as nurses in the ICU do, so we have a lot of responsibility to keep close watch over patients and communicate our observations to the physicians. We really strive for excellence, and the main reason we succeed is that we work so well together as a team."

The NIMU's success is evident in the unit's 2016 scores in the "patient experience of care" domain on the HCAHPS patient satisfaction survey, which is required by the Centers for Medicare and Medicaid for adult in patients. Ranked in the 77th percentile, the unit easily surpassed the Memorial Hermann Health System's target – the 67th percentile. The NIMU also logged the sixth highest score across all services lines at Memorial Hermann-Texas Medical Center for 2016, and scores high every year on the hospital's employee engagement survey, placing in Tier 1, the highest ranking.



"It's actually hard for the NIMU to get high scores in the patient experience domain because we're the middle unit between the ICU and the Neuroscience Acute Care Unit, where patients are discharged home," says Gesno Ulysse, M.S.N., RN, NIMU clinical nurse manager. "HCAHPS surveys are tied to the floor of discharge, so we had to think outside the box and use creative ways to improve the experience for patients and raise our scores."

Ulysse started by asking a unit secretary to serve as a patient liaison and guide other unit secretaries in the new role. "The secretaries round on all patients and families, and introduce themselves as the person who will be calling them to follow up after their discharge," he says. "Our managers also round, and we have customer service champions who make sure patients and families have everything they need. We also do environmental rounds to ensure that the rooms are clean and comfortable. When a patient is discharged from our unit, we send personal notes thanking them for letting us provide care during their stay. And every patient gets a follow-up call after discharge."

The NIMU is one of two units at Mischer Neuroscience Institute where nurses have increased their skills to provide care for high-acuity patients, including stable ventilator patients, stable external ventricular drain patients, and those who are on intravenous drips that don't require frequent titration.

"Increasing the capability, knowledge and critical thinking skills of our NIMU staff has allowed us to decompress the ICU, which always has a high census, and move patients who come in through the emergency department into the ICU faster," Ulysse says. "It also gives our nurses options to use their higher-level skills to advance their careers. As a unit we're very versatile. If the ICU needs additional help, it's my nurses who fill in." In 2016, the NIMU team implemented a triage process to further improve patient flow through the 12-bed unit. Patients are triaged every four hours; if they no longer need to be on a monitored unit, they're transferred to the acute care unit.

The Neuroscience Intermediate Care Unit will be expanded to 15 beds by the end of 2016. "The NIMU nurses do a great job of organizing care for patients in a situation where they don't have physicians living on the unit like they do in the ICU," says Nicole Harrison, M.B.A., B.S.N., RN, administrative director of the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center. "There's rarely a day when their foot is not on the gas pedal. They get patients from neurology and neurosurgery so they need expertise in all types of disease processes. Their occupancy is in the 90th percentile, and many of their patients would be in the ICU at a lower-acuity facility. Despite the fact that they have patients with significant medical and surgical needs, they provide high-quality care that produces great outcomes. There's high morale on the unit and their outstanding teamwork has been instrumental in ensuring that patients have a great environment in which to heal."

Even with the fast pace, Ulysse encourages his nurses to develop themselves professionally. "Our nurses are big on career growth," he says. "They go to critical care classes and come up with initiatives and projects that keep them growing professionally. Many come in and sharpen their skills and move on to the ICU."

But some choose to stay in the NIMU. Bednarczyk, who has worked on the unit for two and a half years, is among them. "Many of our nurses set their sights on the Neuroscience ICU, and working here does provide a good path for them. I'm still here because I feel very valued, and also because working as part of a good strong team makes nursing so much easier."

Nurse-led Initiatives Improve Patient Safety on the Neuroscience Acute Care Unit

Identifying potential problems quickly, before they become emergent situations, has improved safety on Mischer Neuroscience Institute's Neuroscience Acute Care Unit. On the 51-bed unit, process improvement initiatives have led to a dramatic reduction in preventable serious safety events – from three in fiscal year 2015 to one in 2016. The nursing team's goal for 2017 is zero.

"We're doing a better job of identifying patients who need a higher level of care and transferring them to monitored units before their condition escalates into a rapid response situation." – Janelle Headley, B.S.N., RN Among those spearheading the safety improvement effort is intensivist H. Alex Choi, M.D., medical director of the Neuroscience Acute Care Unit and an assistant professor in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth. "A strong partnership between nurses, physicians and other caregivers is essential in ensuring patient safety," says Dr. Choi, who views his role as a facilitator, bringing staff members

"We're doing a better job of

identifying patients who need a higher level of care and transferring them to monitored units before their condition escalates into a rapid response situation," says Janelle Headley, B.S.N., RN, clinical nurse manager of the Neuroscience Acute Care Unit. "Many of our new initiatives came out of the Rapid Response and Higher Level of Care Transfer Committee, a large group that includes medical directors, neuroscience service line managers, stroke coordinators, educators and other staff members who review our data on a daily and weekly basis. If we discover a problem, we resolve it quickly to make things safer for our patients. Nurses complete a debriefing post-rapid response worksheet that identifies opportunities for improvement, and the information is shared during our regular shift huddles." together to enhance collaboration. "Out of the Rapid Response Committee came several initiatives that led to new processes. None of them would have been possible without the collaborative work of Gabby Edquilang, our quality improvement coordinator, and Stephanie Cooper, our stroke coordinator; Kim Vu, our complex care specialist; Janelle Headley, the unit manager; and Dr. Andrea Xavier, our hospitalist."

Working together, the Neuroscience Acute Care Unit team implemented a post-procedure algorithm specific to the unmonitored med/surg unit. "By examining our data, we noticed that some patients were leaving the unit for procedures and returning with hemodynamic instability," says Gabby Edquilang, B.S.N., RN, SCRN.



"Our unit standard is to round hourly and check vitals every four hours. We aimed to increase the monitoring of vital signs once patients returned to the unit after a procedure."

The patient's primary nurse now alerts the physician when the patient returns. Nurses check vitals every 15 minutes for the first hour and every 30 minutes for the second hour. After the two-hour post-procedure window, they return to their normal schedule. Since the team implemented the algorithm, care of all unstable patients has been escalated quickly to attending physicians.

To prevent aspiration pneumonia, the Acute Care team also introduced an oral care protocol that was trialed in the Neuroscience Intermediate Care Unit and rolled out to the Neuroscience ICU and Stroke Unit in fall 2016. "The number one line of defense against aspiration pneumonia is obvious: to prevent aspiration of food or liquid into the lungs," Edquilang says. "Whether they're independent or dependent, patients now have oral care completed every six hours."

Multiple physician teams guide patient care on Mischer Neuroscience Institute's largest unit, making it challenging for nursing staff to get in touch with the appropriate physician. To solve the problem, all team members now enter their pager numbers in one centralized location – the patient record. To improve nurse-physician communication, they also instituted two new protocols: Code 1, for emergent situations, and Code 2, for non-emergent situations. Code 1 is nurse driven and ensures that attending physicians, as well as residents, are notified of changes in a patient's neurological, respiratory or hemodynamic status. Code 2 is bedside-nurse driven; if a non-emergent change in status renders the plan of care inappropriate, the nurse communicates with the attending physician.

"It's a great process," says Headley, whose unit has a strong culture of teamwork. "It helps ensure that the attending physician is always in the loop and that we're all on the same page for better management of the patient."

Frances Jaime, RN-BC, is the Neuroscience Acute Care Unit's patient experience ambassador, a position created in 2014. "I'm an extension of all the nurses on the unit, letting patients know we're here to meet their needs," she says. "I visit everyone on the unit, and if a patient or family member needs help, I make it happen. My long-term goal is to make every nurse on the unit a patient ambassador."

As medical director, Dr. Choi acknowledges the importance of this kind of teamwork. "Nurses know our patients best because they're at the bedside," he says. "They're also very good at determining where and how processes can be improved. We've found that empowering nurses at the bedside to implement quality initiatives has led to dramatic improvement in our quality metrics. The next step for our team is to share what we've learned with the rest of the medical community to influence care on an international stage. Many of our initiatives have been submitted for abstracts at national conferences with nurses as the primary presenters."



PRECOG 1: A Nurse-Physician Study Examines Provider Differences in Prognostication for Patients with Subarachnoid Hemorrhage

Neurocritical care nurses Christina Luther, B.S.N., RN, and Jenna Snow, B.S.N., RN, presented the results of an observational study conducted at Mischer Neuroscience Institute at the 13th Annual Meeting of the Neurocritical Care Society held in Scottsdale, Arizona, in October 2015. The study compared the accuracy of nurse and physician outcome prognostication in patients with subarachnoid hemorrhage (SAH).

"Prognostication after acute brain injury is an important aspect of decision-making in neurological care," says Luther, orientation coordinator in the Neuroscience Intensive Care Unit at the Institute. "Medical and surgical decisions depend on the ability of providers to make an accurate prognosis for thoughtful discussions with patients and their families about medical choices and future care decisions. Many studies have looked at predictors of poor outcomes in neurologically injured patients, but few have examined the accuracy of physician prognostication, and even fewer have investigated the accuracy of nursing prognostication."

To evaluate the differences between physician and nurse prognostication, the researchers asked neurocritical care nurses, attending physicians and fellows who were directly involved in patients' care for their best-guess outcome prognosis using the Modified Rankin Scale, which measures the degree of disability and dependence after a stroke. Because significant



neurological changes are common during the first two weeks after admission, the providers were asked to predict outcomes at three different time intervals during the patients' hospitalizations: days 1-3, days 5-9 and days 10-14. Between November 2014 and May 2015, 900 prognosis values were collected on 48 patients during their hospital stays and through follow-up telephone calls at three, six and 12 months post-discharge.

The study grew out of the Neuroscience ICU's Research and Evidence-based Practice Committee. "We were looking for research ideas to fuel quality and process improvement projects that would benefit our unit," Luther says. "On reviewing our data, we found that we had some really sick patients for whom we didn't expect a good clinical outcome. But at three and six months after discharge, it turned out that they were doing well. We'd like to be able to take this information back to the unit and remind our patients and families not to lose hope. Even though things may look grim during the hospitalization, we know that some patients in the same condition have done well over time. We don't want to give false hope, but we believe the prospect of a good outcome helps patients, families and nurses stay positive, which benefits the healing process."

Snow says the study helped increase providers' understanding of the accuracy of their ability to prognosticate outcomes after acute brain injury. "It's a common question from patients and families: 'Will they be able to walk or talk again?' Our population has varied outcomes, but we hoped the study would enable us to tell them what may happen with some accuracy," she says. "Because nurses spend a significantly longer period of time with families than physicians do, we thought the impact of nurses' communication with families might be equal to or more important than physician communications with the family."

Both Luther and Snow credit neurointensivist H. Alex Choi, M.D., an assistant professor with dual appointments in the departments of Neurology and Neurosurgery at McGovern Medical School at UTHealth, with providing support and direction for the research study. "Perhaps the most important interactions patients and families have during their hospital stay are with the bedside nurse," Dr. Choi says. "This makes it so vitally important to include bedside nurses in quality improvement and research endeavors." Snow says the researchers found that the prognoses of neurocritical care physicians, nurses and fellows were highly correlated in the short term, with no statistically significant difference between types of healthcare providers for patients with SAH.

The research team will continue the study to determine the accuracy of long-term prognostication out to one year; they plan on presenting their findings at an upcoming national conference. The results of PRECOG have led to a follow-up study led by Wamda Ahmed, M.D., a neurointensivist and assistant professor of neurology and neurosurgery, which extends tracking to neurocritically ill patients who have had a palliative care consult in the last two years. The goal of the study is to understand the palliative care experience from the family members' points of view to improve end-of-life care.

"In the interim, the information we've gathered has helped guide our discussions with families and helped with the decision-making progress for patients," Snow says. "In the long run, it may change nursing interactions with family members and patients."

Both nurses welcomed the opportunity to participate in process improvement research. "Traditionally research is the purview of nurse practitioners, but our neurocritical care physicians are very inclusive," Snow says.

"There's a special relationship between the doctors and nurses on our unit," Luther adds. "I could talk about how wonderful our hospital and service line are all day long. The fact that prognoses from physicians and nurses are highly correlated supports the fact our communication about patients is really good."



Neuroscience Nursing Academy Gives New Nurses a Boost in Knowledge and Skills

Nurses are expanding their knowledge of their specialty at the new Neuroscience Nursing Academy at Mischer Neuroscience Institute. The program was launched in January 2016 for new nurses and those with less than a year of experience in the discipline.

"As nurses become more involved in the direction of patient care, proficiency in neuroscience is even more important," says Heather Webster, B.S.N., RN, CCRN, CNRN, SCRN, neuroscience clinical education specialist, who "As nurses become more involved in the direction of patient care, proficiency in neuroscience is even more important, in nursing school, students have minimal exposure to neuroscience. Our goal is to give novice nurses a solid foundation so they can grow their practice and excel in their specialty.." - Heather Webster, B.S.N., RN, CCRN, CNRN, SCRN was instrumental in designing the Neuroscience Nursing Academy curriculum. "In nursing school, students have minimal exposure to neuroscience. Our goal is to give novice nurses a solid foundation so they can grow their practice and excel in their specialty."

Through the Academy, a multidisciplinary team of nurses, affiliated attending physicians, residents, neurorehabilitation specialists and pharmacists provides instruction in four-hour sessions held once a week for eight weeks. Each year, four



groups of 50 nurses go through the program, which is mandatory for nurses with less than a year of experience in neuroscience.

"The response to the program has been excellent," Webster says. Our annual employee survey scores are already high in the areas of engagement and staff development at Memorial Hermann-Texas Medical Center. What we've seen in the last year is more participation of our nurses in hospital committees, unit practice councils and education committees. In the long run, we believe the Academy will lead to improved outcomes, greater staff retention and higher all-around satisfaction."



Susan Nevada, M.S.N., RN, CNRN, SCRN, neuroscience clinical education specialist for the Stroke Unit, Neuroscience ICU and Neuroscience Acute Care Unit, notes a high number of positive reviews on postacademy evaluations. "I also believe that physicians enjoy working with new graduates now that they have added knowledge," she says. "It helps build relationships and trust between physicians and nurses. What nurses have learned at the Academy clarifies issues at the bedside, giving them a clear idea of what to communicate to physicians and appropriate questions to ask. We've also found that the supportive relationships they develop with other nurses make them more inclined to pursue certifications in their particular specialties." Over the past half-decade, Mischer Neuroscience Institute has expanded its reach across the city of Houston. With this broad geographical presence, the Neuroscience Nursing Academy is now open to nurses from other campuses around the Memorial Hermann Health System.

"Many of our physicians at the Texas Medical Center also hold clinics at outlying practices, so we're all working with the same doctors," Webster says. "By bringing neuroscience nurses to the TMC campus, they have an opportunity to interact with each other and learn how we've honed our processes here. Eventually the protocols we use in the medical center will be the norm at all hospitals within the Memorial Hermann system. What we're doing is encouraging nurses to engage in their specialty more deeply."

Innovation in the Neuroscience OR: Epilepsy Monitoring and Deep Brain Stimulation

Neurosurgeons at Mischer Neuroscience Institute are innovators in high-tech surgical approaches to the treatment of epilepsy, and in the use of deep brain stimulation (DBS) therapy for the FDA-approved indications of Parkinson's disease, tremor and dystonia. The nurses and surgical techs who work with them in dedicated neuroscience operating rooms are crucial to the success of the surgeries and play an important role in ensuring high-quality patient outcomes.

Abigail Paz, RN, and Kasandra Hernandez, CST, work with neurosurgeon Nitin Tandon, M.D., professor of neurosurgery at McGovern Medical School at UTHealth, who uses the ROSA™ robot to perform precision epilepsy surgery. An advanced robotized surgical assistant, ROSA allows Dr. Tandon to create 3-D maps of the patient's brain and plan the best approach to those areas to implant depth electrodes, place probes for laser ablation or perform brain biopsies.

"Surgery with the robot is minimally invasive," says Paz, who has worked with Dr. Tandon for more than two years. "Dr. Tandon uses needle-thin instruments to place micro-recording depth electrodes into the brain through a tiny hole. After the electrodes are placed, patients are transferred to the Epilepsy Monitoring Unit where the team records electrical activity from the cerebral cortex. Patients in the EMU are taken off their anticonvulsants to induce



seizures in hopes of localizing the focus. If they succeed, some patients are eligible for resective surgery."

Kasandra Hernandez has worked with Dr. Tandon long enough to observe his transition from subdural electrode implantation via craniotomy – the placement of electrodes directly on the exposed surface of the brain – to the use of minimally invasive depth electrodes. "We're always adding more advanced technology, and Dr. Tandon does whatever he can to innovate and improve processes and outcomes. It's exciting to work in an environment that's constantly changing. We have the opportunity to observe patients full circle, in clinic with the surgeons and rounding on them after surgery. We also get to interact with the epileptologists in the OR and the EMU. The willingness of all these doctors to take the time and effort to teach us is very rewarding."

Nasha Parker, RN, and Jamie Bielat, CST, work with neurosurgeon Albert Fenoy, M.D., an assistant professor of neurosurgery, and movement disorders specialist Mya Schiess, M.D., professor of neurology and director of the Movement Disorders and Neurodegenerative Diseases Program at Mischer Neuroscience Institute. The two physicians use proven and investigational methods to manage Parkinson's disease, Parkinsonian disorders, generalized and focal dystonia, essential tremor and other tremor states. Based on their excellent outcomes over time, both Dr. Schiess and Dr. Fenoy support early deep brain stimulation (DBS) surgery in appropriate patients based on their status and the results of their presurgical workup.

"We see patients before surgery as well as during surgery," says Parker, a circulating nurse with the DBS team. "From a nursing standpoint it's important to be compassionate with our patients, who are awake during the placement of the DBS leads. They're scared, and it's important that

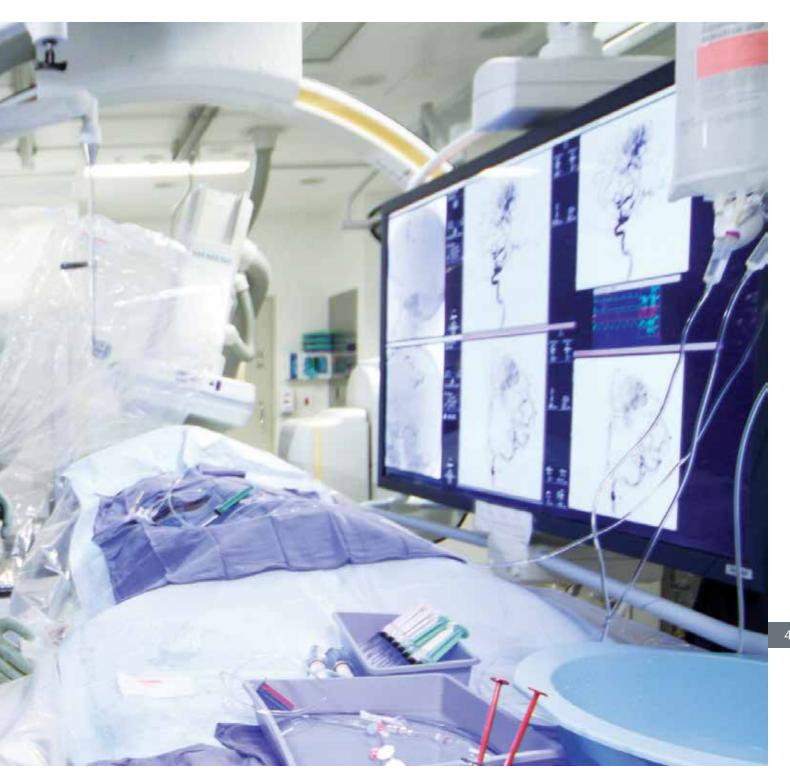


they participate in the process to ensure the ideal results. It's a pleasure to work with Dr. Fenoy and Dr. Schiess because we collaborate very well as a team. I've seen patients with movement disorders regain the ability to write their names or drink a cup of coffee – abilities they'd lost, and important things that we take for granted."

Bielat considers the neuroscience OR an exciting environment. "We think on our feet constantly," she says. "We're always busy, and the new equipment and innovation fascinates me. What we can do as healthcare professionals to help patients keeps getting better. The OR is a supportive environment. We help everybody, including new nurses who join the team. We want them to learn. The biggest thing I would say to nurses with an interest in working in the OR is, 'Be ready to learn.' The work we do for patients is important, and from the nursing perspective it's stimulating and fun."

Scope of Services and Quality Outcomes







BrainTumor

Neuro-oncologists Jay-Jiguang Zhu, M.D., Ph.D., and Sigmund H. Hsu, M.D., continue to expand the capabilities of the Brain Tumor Center at the Memorial Hermann Mischer Neuroscience Institute and in Mischer Neuroscience Associates practices across the city. Dr. Zhu, fellowship trained at Massachusetts General Hospital, focuses his practice on primary brain tumors - gliomas, meningiomas and pituitary adenomas - and primary CNS lymphomas, as well as brain metastases and leptomeningeal spread of systemic malignancies. He is also interested in quality of life, including cognitive function during and after radiotherapy and chemotherapy; neurological complications of systemic chemotherapies; and clinical trials focused on developing new treatment options for primary brain tumors and CNS metastases. Dr. Hsu, fellowship trained at The University of Texas MD Anderson Cancer Center, has clinical and research interests in the discovery of new and more effective therapies for patients with primary brain tumors, treatment of metastatic cancer to the brain and spinal cord, and the evaluation and treatment of neurological problems in cancer patients.

Dr. Zhu is the site principal investigator in several trials that give eligible study participants access to new and advanced treatments. With funding from the National Cancer Institute, he is leading a Phase II/III clinical trial studying the efficacy of veliparib with temozolomide compared to temolozomide alone in treating patients with glioblastoma multiforme (GBM) or gliosarcoma. The trial, which will run through June 2022, is currently enrolling patients at Mischer Neuroscience Institute; more than 400 patients will be enrolled in the eight-year study at sites located around the country.

Dr. Zhu was principal investigator in a randomized, double-blind, controlled Phase IIB clinical trial testing the safety and efficacy of the vaccine ICT-107 for newly diagnosed GBM patients following resection and chemoradiation. The trial, which began enrollment in August 2011 and was completed in December 2015, showed improved, progressive-free survival of patients who are human leukocyte antigen (HLA) A2 positive. HLA genes are key to the activity of the immune system in identifying the body's own proteins versus proteins of foreign origin. A Phase III trial for HLA A2-positive GBM patients has just opened at Memorial Hermann-Texas Medical Center, and patients are now being enrolled.

Mischer Neuroscience Institute is the only Houston site for a study of 4-Demethyl-4-cholesteryloxycarbonylpenclomedine (DM-CHOC-PEN) in patients with brain tumors, led by Dr. Zhu. DM-CHOC-PEN is a polychlorinated pyridine cholesteryl carbonate, which exerts antineoplastic activity through cross-linking DNA strands in patients with brain tumors. The trial is open to patients with advanced lung, breast and melanoma cancers that have spread to the central nervous system as well as those with primary CNS malignancies. The trial is on hold pending FDA approval of adding nivolumab, a checkpoint inhibitor (immune modulator) to the DM-CHOC-PEN for the same groups of patients.

RESEARCH HIGHLIGHT

Survival Benefit with Triple Chemotherapy and TTFields for Glioblastoma

INVESTIGATORS: Guangrong Lu, MBBS; Mayank Rao, MBBS; Lauren C. Delumpa, FNP-C; Zheyu Liu, MS; Sigmund H. Hsu, M.D.; Jay-Jiguang Zhu, M.D., Ph.D.; McGovern Medical School at UTHealth

Background: Glioblastoma multiforme (GBM) is the most aggressive and common glial tumor. Historical data shows that median overall survival (OS) is 14.6 months with maximum safe resection followed by radiation and chemotherapies. We have been treating recurrent GBM patients with triple chemotherapies [temozolomide (TMZ), bevacizumab (BV) and Irinotecan (CPT-11)] since 2010. We also offer patients tumor treating fields (TTFs) for recurrent GBM following FDA approval and participated in the EF-14 clinical trial for newly diagnosed GBM from 2011. Here we report OS data of our institute's patients on TTFs treatment, with or without the triple chemotherapy, from February 2011 to June 2016.

Methods: Data review was approved by the Committee for the Protection of Human Subjects at The University of Texas Health Science Center (UTHealth) at Houston. Kaplan-Meier survival curve and log rank test were used for statistical analysis. Primary objectives were OS and adverse events.

Results: Fifty-two GBM patients (21-76 years old, average $age=54\pm11.6$) received TTF treatment, 32 of which expired, 17 patients are alive, and the survival status of 3 patients remains unknown. For patients who received triple chemotherapies plus TTFs (average TMZ cycles=17.9±11.2; BV infusion times=23.5±10.8; CPT-11 infusion times=13.7±6.8), median OS is 34.5 months (n=29, 95% CI: 27.8-49.7). Median OS is 14.0 months (n=23, 95% CI: 11.5-17.90) for patients receiving BV/CPT-11 (average TMZ cycles=4.9±7.2; BV infusion times=6.6±6.2) plus TTFs (Log rank test, p<0.05). For patients who started TTFs within 125 days from their initial diagnosis, OS is 39.4 months (n=15, 95% CI: 11.8-53.1). Major adverse events are chemotherapy-related thrombocytopenia (grade III in 2 cases), neutropenia, anemia and TTFs-related scalp lesions. Molecular profile will be provided at the time of presentation.

Conclusion: Treating recurrent GBM with triple chemotherapies (BV, TMZ, and CPT-11) is reasonably well tolerated with manageable side effects. Triple chemotherapies plus TTFields demonstrates superior OS benefit compared to historical data.

First presented at the Society of NeuroOncology annual meeting, Scottsdale, Arizona, in November 2016.

BRAIN TUMOR • SCOPE OF SERVICES

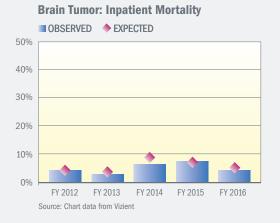


Two other trials led by Dr. Zhu are ongoing but not currently enrolling participants. A Phase III multicenter, randomized, controlled trial is testing the efficacy and safety of a medical device called Novo TTF-100A for newly diagnosed GBM patients in combination with temozolomide, compared to temozolomide alone. The device, which patients wear on their scalp, provides a constant, safe, low-voltage electric field that has been shown to reduce tumor cell survival and division capacity. The device was approved by the FDA for progressive GBM in April 2011. Interim analysis of the trial data showed significant improvement of progression survival time and overall survival duration in participants randomized to the treatment arm of the study. Based on this trial result, the FDA approved the device for newly diagnosed GBM in October 2015.

The study was completed in July 2016. The results from 83 participating institutions showed significant improvement of progression survival time and overall survival duration in patients randomized to the treatment arm versus the control arm with temozolomide alone. The results were first presented at the annual meeting of the Society of NeuroOncology in November 2016.

Dr. Zhu is also leading an open-label Phase I/II (safety lead-in) study of trans sodium crocetinate (TSC) with concomitant treatment of fractionated radiation therapy and temozolomide in newly diagnosed GBM patients. The trial examines the safety and efficacy of TSC as a radiation sensitizer for the treatment of malignant tumors. The study is closed, and the results demonstrated the benefit to patients in the trial. A Phase III randomized trial is pending FDA approval.

QUALITY & OUTCOMES MEASURES



Brain Tumor:



Dr. Sigmund Hsu is principal investigator in several studies, including the trial of a novel taxol chemotherapy compound, TPI 287, which crosses the blood-brain barrier and is administered in combination with bevacizumab versus bevacizumab alone in adults with recurrent glioblastoma. In addition, he is leading a Phase II dose-escalation study of TPI 287 in combination with bevacizumab in adults with recurrent or progressive glioblastoma following a bevacizumab-containing regimen.

Dr. Hsu is also the lead physician in the FoundationOne[™] Registry study, a prospective observational study to examine practice patterns and the impact on clinical decision-making associated with the FoundationOne next-generation sequencing test. The study allows physicians affiliated with Mischer Neuroscience Institute to recommend optimal advanced technologies, including motor and language mapping, functional neuroimaging, frameless stereotactic navigation in surgery and awake craniotomies performed under local anesthesia, as well as minimally invasive procedures, including neuroendoscopy and stereotactic radiosurgery.

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

Mischer Neuroscience Institute added a new radiation oncologist, Shariq Khwaja, M.D., to its neuro-oncology team in 2016. Together with Angel Blanco, M.D., director of Radiation Oncology and Stereotactic Radiosurgery and associate professor in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth, they provide radiation oncology services at the Brain Tumor Center. The Institute acquired the region's first Leksell Gamma Knife[®] in 1993, and is now using the more advanced Leksell Gamma Knife® Perfexion[™]. Patients who benefit from the Perfexion's sophisticated software with dose-to-target conformation include those with meningiomas and vestibular schwannomas, arteriovenous malformations, medically refractory trigeminal neuralgia, and metastases. Multiple intracranial metastases can usually be treated in a single outpatient procedure. Neurosurgeons affiliated with the Institute have performed more than 4,100 Gamma Knife procedures.

The Varian Trilogy linear accelerator is the first in a powerful new generation of cancer-fighting technologies, offering the highest dose rates for shorter sessions. The system delivers 3-D conformal radiotherapy, IMRT, extracranial and intracranial stereotactic radiosurgery, fractionated stereotactic radiation therapy, stereotactic body radiosurgery (SBRT), and intensity-modulated radiosurgery for cancer and neurosurgical treatment. The Brain Tumor Center is led by Dong Kim, M.D., director of Mischer Neuroscience Institute and professor and chair of the Vivian L. Smith Department of Neurosurgery. The team works closely with referring physicians throughout the radiosurgical treatment process. A neurosurgeon and a radiation oncologist assess each candidate to determine whether radiosurgical treatment is the best option. Nurse navigators work directly with patients on scheduling and pretreatment education, and provide support and care on the day of treatment. The Center also sponsors a well-attended brain tumor support group that meets the second Wednesday of every month.

Breakthrough approaches to treatment provided by specialists affiliated with Mischer Neuroscience Institute have led to an increase in the number of patients treated for brain tumors. Since 2009, volumes have increased by nearly 50 percent.

Cerebrovascular

The Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center is home to the first stroke center in Texas to receive the highly coveted Comprehensive Stroke Center (CSC) certification from The Joint Commission (TJC) and the American Heart Association/American Stroke Association. Under the leadership of Sean Savitz, M.D., the Memorial Hermann Comprehensive Stroke Center remains the only facility in the Greater Houston area with TJC-accredited CSC certification, solidifying its position among an elite group of providers in the country focused on complex stroke care. Within a year, the AHA had also recognized Memorial Hermann-Texas Medical Center with the Get With The Guidelines®-Stroke Gold Plus Achievement Award. TJC and the AHA recertified the hospital in 2015.

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

The Comprehensive Stroke Center's cerebrovascular services span the continuum of care, from prehospital ambulance care to the emergency center setting, and extends through a 12-bed dedicated inpatient stroke unit, to neurorehabilitation provided in a 23-bed inpatient unit at Memorial Hermann-Texas Medical Center and its sister hospital TIRR Memorial Hermann, an international leader in rehabilitation and research. Patients benefit from comprehensive inpatient and outpatient services. state-of-the-art technology, and innovative therapies and techniques. They also have access to comprehensive outpatient stroke management through clinics, including the Stroke Transitions Education and Prevention (STEP) Clinic directed by Anjail Sharrief, M.D. In the STEP Clinic, practitioners aim to reduce risk of stroke while improving the quality of life of stroke survivors through risk-factor control and post-stroke complication management. They are also developing novel interventions to improve stroke care and outcomes.

The Memorial Hermann Comprehensive Stroke Center consistently achieves excellent metrics for quality of care and outperforms national and peer-based benchmarks. Under the direction of Farhaan Vahidy, M.D., Ph.D., a robust data core is provided to physicians by a team of programmers, data scientists and medical abstractors, enabling CSC leadership to monitor quality data in real time and use it to plan and implement evidence-based quality improvement measures.

The CSC also has the largest stroke fellowship program in the country, led by Amrou Sarraj, M.D. The program has a rich history of preparing leaders in the field of stroke care by providing comprehensive clinical and academic training that covers all aspects of cerebrovascular disease.



In addition to breakthrough treatment for stroke, the cerebrovascular team provides coordinated care for patients with aneurysms, carotid occlusive disease and intracranial vascular malformations, including open surgical and endovascular treatments such as angioplasty, stenting and embolization. Also available is the Pipeline[™] endovascular flow-diverting stent, a device that reconstructs the parent vessel lumen of difficultto-reach aneurysms as an alternative to clipping or endovascular coiling. Affiliated neurosurgeons are skilled at microvascular clipping of aneurysms using the best skull base approaches to minimize brain manipulation, extracranial-intracranial bypass procedures, carotid endarterectomy and hemicraniectomy for severe strokes. State-of-the-art radiosurgery using the Leksell Gamma Knife[®] Perfexion[™] is used regularly for vascular malformations that are best treated non-surgically.

A research team led by Dong Kim, M.D., director of Mischer Neuroscience Institute and professor and chair of the Vivian L. Smith Department of Neurosurgery at UTHealth, has conducted a 15-year study on a large family with numerous reported aneurysms. The team found that a genetic mutation of THSD1 is linked to intracranial aneurysms. This finding provides new insight into what causes aneurysms and provides new understanding of THSD1 function.

The Comprehensive Stroke Center is staffed by four full-time academic neurosurgeons dedicated to cerebrovascular practice: Arthur L. Day, M.D., P. Roc Chen, M.D., Spiros Blackburn, M.D., and Mark Dannenbaum, M.D. Drs. Chen, Blackburn and Dannenbaum are dually trained in both open and endovascular neurosurgery and have extensive experience in skull base surgery. With the addition of a fourth experienced endovascular neuroradiologist, neurosurgeon Gary Spiegel, M.D., Mischer Neuroscience Associates has extended its cerebrovascular program to Memorial Hermann Memorial City Medical Center and Memorial Hermann The Woodlands Hospital.

RESEARCH HIGHLIGHT

THSD1 Mutation in the Pathogenesis of Intracranial Aneurysm and Subarachnoid Hemorrhage

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

Director, Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center *Professor and Chair,* Vivian L. Smith Department of Neurosurgery, McGovern Medical School at UTHealth

Background and Purpose: A ruptured intracranial aneurysm (IA) is the leading cause of a subarachnoid hemorrhage (SAH). This study seeks to define a specific gene whose mutation leads to disease.

Methods: More than 500 IA probands and 100 affected families were enrolled and clinically characterized. Whole exome sequencing was performed on a large family, revealing a segregating THSD1 mutation. THSD1 was sequenced in other probands and controls. THSD1 loss-of-function studies in zebrafish and mice were used for in vivo analyses, and functional studies performed using an in vitro endothelial cell model.

Results: A nonsense mutation in THSD1 (thrombospondin type-1 domain-containing protein 1) was identified that segregated the 9 affected (3 suffered SAH; 6 had unruptured IA) and 13 unaffected family members (LOD score 4.69). Targeted THSD1 sequencing identified mutations in 8 of 507 unrelated IA probands, including 3 who had suffered SAH (1.6% [95% CI, 0.8%-3.1%]). These THSD1 mutations/rare variants were highly enriched in our IA patient cohort relative to 89,040 chromosomes in ExAC database (p<0.0001). In zebrafish and mice, THSD1 loss-of-function caused cerebral bleeding (which localized to the subarachnoid space in mice) and increased mortality. Mechanistically, THSD1 loss impaired endothelial cell focal adhesion to the basement membrane. These adhesion defects could be rescued by expression of wild-type THSD1 but not THSD1 mutants identified in IA patients.

Conclusions: This report identifies THSD1 mutations in familial and sporadic IA patients, and shows that THSD1 loss results in cerebral bleeding in two animal models. This finding provides new insight into IA and SAH pathogenesis and provides new understanding of THSD1 function, which includes endothelial cell to extracellular matrix adhesion.

CEREBROVASCULAR • SCOPE OF SERVICES



The UTHealth Telemedicine Program, directed by Teddy Wu, M.D., extends stroke and neurology expertise far beyond the Institute's walls, helping emergency physicians in suburban and community hospitals throughout Southeast Texas make accurate diagnoses and save lives. Remote presence robotic technology has enhanced the telemedicine program by linking outlying hospitals electronically to the Neurology department at McGovern Medical School, providing real-time visual interaction between neurologists and patients, and allowing affiliated neurologists to review CT scans and advise local physicians on treatment protocols. Through telemedicine, physicians can now offer patients in outlying communities an opportunity to participate in clinical trials that otherwise would be unavailable to them, which expands medical knowledge as it saves lives. Baptist Beaumont Hospital and Memorial Hermann Southwest Hospital were early

adopters of telemedicine. Since then, 15 more sites in southeast Texas have gone live with the technology: Memorial Hermann Memorial City Medical Center, Memorial Hermann Greater Heights Hospital, Memorial Hermann The Woodlands Hospital, Memorial Hermann Katy Hospital, Memorial Hermann Pearland Hospital, Huntsville Memorial Hospital in Huntsville, Matagorda Regional Medical Center in Bay City, Baptist Orange Hospital in Orange, the Medical Center of Southeast Texas in Port Arthur, Citizens Medical Center in Victoria, St. Joseph Hospital-Downtown in Houston, DeTar Healthcare System in Victoria, Tomball Regional Medical Center in Tomball, UTHealth Northeast in Tyler and Brazosport Regional Health System in Lake Jackson. The Telemedicine Program is a flagship training program for residents and fellows in the stroke academic community, led by Amanda Jagolino, M.D.

RESEARCH HIGHLIGHT

Efficient Resource Utilization for Patients with Intracerebral Hemorrhage (EnRICH)

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

Assistant Professor, Department of Neurology, McGovern Medical School at UTHealth

Enhancing quality of care has been one of the focus areas for stroke care delivery over the past decade. This involves evaluating strategies for effective implementation and dissemination of proven therapies, as well as optimizing the availability of these therapies and resources to all stroke patients. This has led to regionalization of stroke care, in which a large number of stroke patients are transferred to designated comprehensive stroke care centers (CSC) from smaller community hospitals. The elements of effective care at a CSC are relatively well established for ischemic stroke patients. However, there is a dearth of evidence for patients with a brain hemorrhage. Intracerebral hemorrhage (ICH), or brain hemorrhage, is a devastating disease that unfortunately does not have any proven treatment modalities. As the search for new therapies continues, evaluation of the effectiveness of current care metrics remains critically important.

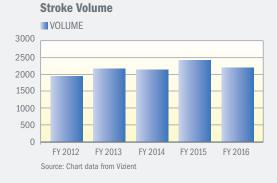
The investigators of EnRICH aim to study the potential benefits for care provision at a CSC for ICH patients. The study will further help identify brain hemorrhage patients who may benefit from transfer to a CSC. The results of this study can provide evidence necessary for decision-making during the triage and transfer process for brain hemorrhage patients across healthcare systems. As a secondary aim, the study will compare resource utilization for ICH patients at various levels of care. The Memorial Hermann Health System, which includes an academic teaching hospital and a network of hospitals across Greater Houston, provides the infrastructure necessary to implement EnRICH. The study has been funded by the Lone Star Stroke Consortium of Texas and will also be conducted simultaneously at medical centers in San Antonio, Austin and Dallas.

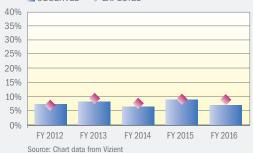
Physicians at Mischer Neuroscience Institute and UTHealth conduct more research than any other stroke program in the south or southwestern United States, participating in multicenter and single-center clinical trials testing new treatments for patients who cannot be treated elsewhere. The medical school, in partnership with the Memorial Hermann Comprehensive Stroke Center, was chosen as the only regional coordinating center in Texas and the Southwest United States to serve in StrokeNet, a national network funded by the National Institute of Neurological Disorders and Stroke to conduct clinical stroke trials across the country. The Stroke Center serves as the flagship to coordinate clinical stroke trials throughout the region. Pioneering stroke research at UTHealth and Mischer Neuroscience Institute has included thrombolytic treatment for wake-up stroke, the safety of pioglitazone for hematoma resolution in intracerebral hemorrhage, multi-agent vasodilator infusion therapy versus current typical single-agent therapy for cerebral vasospasm, and stem cell-based therapies for acute ischemic stroke. Dr. Savitz is leading pioneering studies in stroke recovery with the use of stem cells with promising



QUALITY & OUTCOMES MEASURES



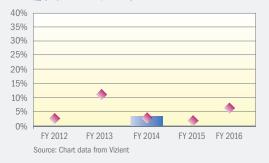




Acute Ischemic Stroke: Volume & Length of Stay (CMI Adjusted)







Arteriovenous Malformation: Volume & Length of Stay (CMI Adjusted)

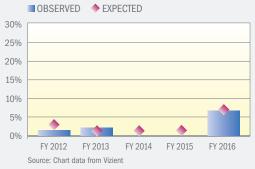




Subarachnoid Hemorrhage: Inpatient Mortality

Intracerebral Hemorrhage: Inpatient Mortality





Unruptured Aneurysm: Inpatient Mortality

Subarachnoid Hemorrhage: Volume & Length of Stay (CMI Adjusted)



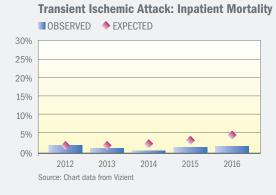
Intracerebral Hemorrhage: Volume & Length of Stay (CMI Adjusted)

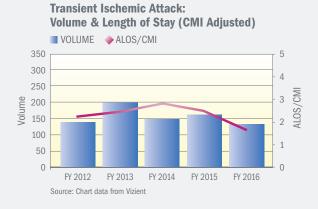


Unruptured Aneurysm: Volume & Length of Stay (CMI Adjusted)



QUALITY & OUTCOMES MEASURES





Stroke Core Measures

GWTG Measure	MHH Measure Goal	2011	2012	2013	2014	2015	2016
STK-1 - VTE Prophylaxis	85%	97.90%	99.7%	99.1%	99.9%	100%	100%
STK-2 - Discharged on Antithrombotic Therapy	85%	100%	100%	98.8%	99.5%	100%	99.7%
STK-3 - Anticoagulation Therapy for Atrial Fib.	85%	100%	100%	97.9%	98%	97.2%	98.3%
STK-4 - Thrombolytic Therapy	85%	95.2%	100%	97%	94.6%	100%	100%
STK-5 - Antithrombotic Therapy by End of Hospital Day 2	85%	98.1%	99%	92.8%	97.8%	99.2%	98.7%
STK-6 - Discharged on Statin Medication	85%	94.2%	98.3%	98.2%	99.2%	100%	99.4%
STK-8 - Stroke Education	85%	92.9%	94.9%	96.1%	97.3%	98.4%	99.5%
STK-10 - Assessed for Rehabilitation	85%	98.7%	99.4%	99.2%	99.8%	99.7%	99.9%

Source: Chart data based on fiscal year

results. Investigations led by Andrew Barreto, M.D., seek to increase the effect of standard-of-care treatment by combining tPA and other blood thinners to enhance recanalization of large artery clots in acute stroke.

Optimizing stroke patients' outcomes is one of the most important areas in acute stroke care. The Memorial Hermann Comprehensive Stroke Center is conducting the largest multicenter study on refining selection methods to determine how best to triage acute ischemic stroke patients prior to endovascular therapy (SELECT), led by Amrou Sarraj, M.D.

By supporting collaborative research from neuroscience, clinical neurology, vascular biology, immunology, cerebrovascular diseases and aging, the Cerebrovascular Research Group is developing effective strategies for the diagnosis and treatment of stroke and brain injury - and moving new discoveries quickly from the bench to the bedside. Led by Louise D. McCullough, M.D., Ph.D., the Group, which consists of four other independent investigators - Jun Li, Ph.D., Fudong Liu, M.D., Venu Venna, Ph.D., and Akihiko Urayama, M.D. is funded by the National Institutes of Health and the American Heart Association to study aspects of stroke and vascular disease, with programs ranging from neonatal stroke to post-stroke dementia. Active research programs are investigating sex differences in stroke, how social factors such as depression and social isolation affect stroke outcomes, the mechanisms underlying pregnancy-associated stroke risk, the impact of aging of the immune system on stroke-related cognitive decline, chromosomal and hormonal contributions to sex differences in ischemic stroke, the hypothesis that microchimeric cells home to the site of injury as part of the immune response to stroke, the role of calcium signaling in stroke, the effects of X chromosome-linked

proteins on sexual dimorphism in ischemic stroke, and how manipulation of the brain's resident immune cells may help limit ischemic injury and promote tissue repair after stroke. Dr. Liu examines how sex differences in inflammation alter outcomes after neonatal stroke, and Dr. Venna is working on understanding the role of an emerging cytokine, macrophage migration inhibitory factor, in post-stroke depression, cognitive impairment and post-stroke recovery. New work by Dr. Urayama in collaboration with Claudio Soto, Ph.D., a worldrenowned expert in neurodegenerative diseases, has shown that transfer of blood from young animals to older ones can reduce age-related inflammation. The group also is invested in training, and has numerous postdoctoral fellows and M.D./Ph.D. students actively engaged in research.

Led by Jaroslaw Aronowski, M.D., Ph.D., and funded by multiple grants from the National Institutes of Health, studies in intracerebral hemorrhage - the stroke subtype with the highest mortality - are focused on the development of new treatments. Dr. Aronowski's group is examining various anti-oxidative and anti-inflammatory therapeutic strategies with a particular focus on how to reprogram immune cells to reduce inflammation, improve clearance of debris and ultimately improve brain repair after intracerebral hemorrhage (ICH) in experimental models. Discoveries from this research led to a clinical trial directed by Nicole Gonzales, M.D., investigating factors linked to hematoma clearance as a new therapeutic approach in patients with ICH. Lastly, Farhaan Vahidy, M.B.B.S., Ph.D., is leading studies comparing functional and quality-of-life outcomes in patients with intracerebral hemorrhage transferred to the Memorial Hermann-TMC campus with those patients who remain at outside hospitals to determine which patients can benefit most from transfer.

Children's Neuroscience

Pediatric neurosurgeons David Sandberg, M.D., FAANS, FACS, FAAP, Stephen Fletcher, D.O., and Manish Shah, M.D., bring a broad range of clinical and research expertise to the Children's Neuroscience Center at Children's Memorial Hermann Hospital.

Translational studies conducted by Dr. Sandberg have demonstrated the safety of infusing chemotherapeutic agents directly into the fourth ventricle to treat children with recurrent malignant tumors in this location in the brain. The results of these studies led to a methotrexate dose-escalation study available only at Children's Memorial Hermann Hospital, in collaboration with Mischer Neuroscience Institute and McGovern Medical School. Dr. Sandberg is also conducting two new single-center trials: "A Combination Intraventricular Chemotherapy Pilot Study," investigating methotrexate and etoposide infusions into the fourth ventricle in children with recurrent posterior fossa brain tumors, and "Infusion of 5-Azacytidine (5-AZA) into the Fourth Ventricle or Resection Cavity in Children with Recurrent Posterior Fossa Ependymoma."

Dr. Fletcher leads fetal pediatric neurosurgery efforts at The Fetal Center at Children's Memorial Hermann Hospital, a national leader in providing diagnosis, treatment and complete care for mothers with high-risk pregnancies and infants with congenital anomalies or genetic conditions. The multidisciplinary team performed the first fetal spina bifida repair in the region, and patients are now being referred to the Center for fetal myelomeningocele repair from throughout Texas and a number of surrounding states. The fetal surgery team continues to refine efforts at improving neurological outcomes in children with spina bifida with a robust research effort to determine the best method of repairing the abnormality; they also aim to reduce the risk to the mother by performing the procedure endoscopically. The combined efforts of basic scientists, general and fetal surgeons, neurosurgeons, pathologists and radiologists has led to a novel method to close the spinal defect, which remains under study. Their goal is to enroll more patients in ongoing studies to improve outcomes for children with spina bifida.

Dr. Shah, who has special expertise in the surgical management of spasticity and dystonia in children, directs the Texas Comprehensive Spasticity Center at McGovern Medical School at UTHealth, Children's Memorial Hermann Hospital and Mischer Neuroscience Institute. Dr. Shah performs selective dorsal rhizotomies, baclofen pump placement and advanced deep brain stimulation. He is also an expert in pediatric epilepsy, craniofacial surgery and craniocervical spine surgery. His research focuses on advanced imaging-based classifications of cerebral palsy and epilepsy patients.

To avoid the many complications of ventriculoperitoneal shunting for children with hydrocephalus, pediatric neurosurgeons affiliated with the Institute routinely perform minimally invasive endoscopic techniques such as third ventriculostomy, septostomy, choroid plexus coagulation and fenestration of arachnoid cysts. Selected brain tumors can be biopsied or removed completely via endoscopic techniques. All of these procedures are





performed through very small incisions with minimal hair shaving. In collaboration with otolaryngologists affiliated with Memorial Hermann-Texas Medical Center, neurosurgeons also remove some tumors via endoscopic transnasal approaches without an external incision. Together with nationally recognized craniofacial plastic surgeons, pediatric neurosurgeons affiliated with Children's Memorial Hermann Hospital perform both conventional and minimally invasive endoscopic surgeries to repair craniosynostosis and other complex craniofacial anomalies. The multidisciplinary Texas Cleft-Craniofacial Team was established in 1952 and has been a regional leader for pediatric craniofacial surgery for decades.

Children's Memorial Hermann Hospital is also a center of excellence for pediatric epilepsy surgery and comprehensive specialized care for children with refractory epilepsy. The pediatric Epilepsy Monitoring Unit is the largest and most comprehensive of its kind in the southwestern United States. In addition to MRI and CT with low radiation dose protocols for pediatric patients, affiliated physicians use the Elekta Neuromag® for noninvasive functional mapping of brain activity with magnetoencephalography (MEG) to locate the source of epileptic seizures and minimize risk for children undergoing resective surgery for refractory epilepsy. For the most accurate diagnosis they also use stereo EEG, video EEG, PET, SPECT, memory and speech (Wada) testing, and neuropsychological testing. Interventions include medical management and the ketogenic diet as well as surgery, including vagus nerve stimulation and laser ablation procedures. Manish N. Shah, M.D., directs the pediatric epilepsy surgery program. Gretchen Von Allmen, M.D., is chief of pediatric epilepsy for the Texas Comprehensive Epilepsy Program and medical

RESEARCH HIGHLIGHT

Infusion of Chemotherapy into the Fourth Ventricle to Treat Recurrent Malignant Brain Tumors in Children: A Summary of Clinical Trials

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

Director, Pediatric Neurosurgery, Mischer Neuroscience Institute *Professor,* Vivian L. Smith Department of Neurosurgery and Department of Pediatric Surgery; *Dr. Marnie Rose Professorship in Pediatric Neurosurgery,* McGovern Medical School at UTHealth

For the first time in humans, our center demonstrated in a previous pilot clinical trial that chemotherapy can be delivered directly into the fourth ventricle of the brain in children with recurrent, malignant brain tumors. Promising results from a pilot trial with low-dose (2 milligram) methotrexate infusions has led to an ongoing Phase I dose-escalation trial. In enrolled patients, a catheter was surgically placed into the fourth ventricle and attached to a ventricular access device. Cerebrospinal fluid (CSF) flow was confirmed by CINE MRI postoperatively. Patients were then given sequential infusions of methotrexate. Disease response was monitored with serial MRI scans and CSF cytologic analysis.

To date, seven patients with medulloblastoma have received methotrexate infusions. All patients had progressive disease prior to enrollment in the trial despite surgery, chemotherapy and radiation therapy. Three of the seven patients had a partial response (at least 50% reduction in disease burden), two patients had stable disease, and two had disease progression. There were no serious adverse events or new neurological deficits caused by methotrexate infusions.

In conclusion, methotrexate can be infused into the fourth ventricle without causing neurological toxicity, and some patients with recurrent medulloblastoma experience a beneficial anti-tumor effect from these infusions.

These trials have led to two new single-center trials: "A Combination Intraventricular Chemotherapy Pilot Study," investigating methotrexate and etoposide infusions into the fourth ventricle in children with recurrent posterior fossa brain tumors, and "Infusion of 5-Azacytidine (5-AZA) into the Fourth Ventricle or Resection Cavity in Children with Recurrent Posterior Fossa Ependymoma." Both trials are open to qualifying patients age 1 to 21. The researchers hope for continued demonstration of safety and even more robust clinical responses.

RESEARCH HIGHLIGHT

Resting State Signal Latency Predicts Laterality in Pediatric Medically Refractory Temporal Lobe Epilepsy

PRINCIPAL INVESTIGATOR: Manish Shah, M.D.

Assistant Professor, Departments of Pediatric Surgery and Neurosurgery, Director, Pediatric Spasticity and Epilepsy Surgery McGovern Medical School at UTHealth

Temporal lobe epilepsy (TLE) affects resting state brain networks in adults. In a similar fashion, the researchers correlated resting state functional MRI (rsMRI) signal latency in pediatric TLE patients with their laterality.

From 2006 to 2016, 26 surgical TLE patients (12 left, 14 right) with a mean age of 10.7 years (range 0.9-18) were prospectively studied. Preoperative rsMRI was obtained in patients with concordant lateralizing structural MRI, EEG and PET studies. After standard preprocessing techniques, the latency in rsMRI signal between each 6-millimeter voxel sampled was examined, compared to the global mean signal, and projected onto standard atlas space for individuals and the cohort.

All but one of the 26 patients showed improved seizure frequency postoperatively with a mean follow-up of 2.9 years (range 0-7.7), with 21 patients remaining seizure free. When grouped for epileptogenic laterality, the latency map qualitatively demonstrated that the right TLE patients had a relatively early signal pattern (blue-green) compared to the global mean signal in the right temporal lobe, whereas the left TLE patients had a relatively late signal pattern (red-orange) in the right temporal lobe. The majority of the individual left (7/12) and right (9/14) TLE patients followed this qualitative pattern.

There are functional MR signal latency changes in medically refractory pediatric TLE patients. Specifically, signal latency in the right temporal lobe precedes the mean signal in right TLE patients and is delayed in left TLE patients. Preoperative rsMRI signal latency analysis could offer an inexpensive, noninvasive adjunct modality to lateralize pediatric TLE.



director of the Children's Memorial Hermann Hospital Pediatric Epilepsy Monitoring Unit. Along with pediatric epileptologists Jeremy Lankford, M.D., and Michael Watkins, M.D., they work together with other adult and pediatric epilepsy specialists to manage patients over their entire lifespan for a seamless transition of care.

Three other centers of excellence focus on West syndrome, dysautonomia, and neurometabolic and mitochondrial disorders. The West Syndrome Center of Excellence opened in 2014, with a generous philanthropic gift from the West Syndrome Foundation, and now attracts patients from around the world for treatment of West syndrome. Co-directors Ian J. Butler, M.D., and Gretchen Von Allmen, M.D., lead research on the causes of the syndrome and related pediatric epilepsy disorders and work to increase awareness of the disease. Dr. Butler and pediatric cardiologist Mohammed Numan, M.D., are co-directors of the Dysautonomia Center of Excellence. The two physicians work together to create individualized treatment plans for each patient based on the most advanced modalities. Mary Kay Koenig, M.D., directs the Mitochondrial Center of Excellence, where affiliated physicians provide comprehensive services to aid in the diagnosis and management of neurometabolic and mitochondrial disorders. Hope Northrup, M.D., is director of the UTHealth Tuberous Sclerosis Center of Excellence, which has been designated by the national Tuberous Sclerosis Alliance and brings together all the subspecialists required to treat the manifestations of tuberous sclerosis complex.

RESEARCH HIGHLIGHT

Cryopreserved Human Umbilical Cord for Repair of Fetal Spina Bifida Defects

PRINCIPAL INVESTIGATOR: **Ramesha Papanna, M.D.** Assistant Professor of Fetal Surgery, Department of Obstetrics, Gynecology and Reproductive Sciences, McGovern Medical School at UTHealth

CO-INVESTIGATOR: Stephen Fletcher, D.O.

Associate Professor, Division of Pediatric Neurosurgery, McGovern Medical School at UTHealth

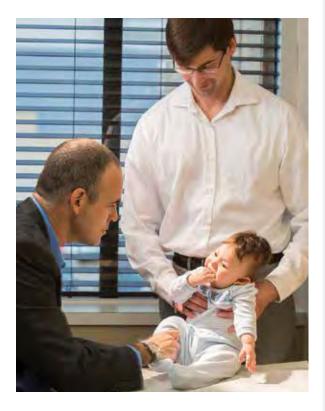
In utero repair has been shown to improve neurological outcomes in children with open neural tube defects. In Dr. Papanna's lab, researchers are investigating the various tissues used to repair these defects in the spines of infants.

Preliminary data in various animal models suggest that the use of human umbilical cord for repair offers many advantages over commercially available products. Two patients were enrolled in an FDAapproved clinical trial and are being followed one year after surgery. Outcomes appear promising, and the fetal team at Children's Memorial Hermann Hospital is seeking approval for a study using this material in future fetal surgeries.

The research has been expanded to include an even more detailed analysis of the molecular and biochemical changes that occur with human umbilical cord, and the researchers are studying all options, from open fetal repair to endoscopic fetal repair for selected patients with open neural tube defects. Children's Memorial Hermann Hospital is a leading center for the treatment of retinoblastoma, a rare pediatric eye malignancy that affects only 250 to 350 new patients each year. It is one of a handful of hospitals in the United States at which physicians routinely administer intra-arterial chemotherapy, the most modern treatment for the disease, which enables children to have chemotherapy injected into the artery that feeds the eye, eliminating the side effects of systemic chemotherapy and maximizing the dose to the eye. Intra-arterial chemotherapy is a complex treatment that involves close collaboration among a 50-person retinoblastoma team at Children's Memorial Hermann Hospital. In addition to ocular oncologist Amy Schefler, M.D., and neurointerventionalist Mark Dannenbaum, M.D., the team includes pediatric oncologist Deborah Brown, M.D., pediatric anesthesiologist Michael Lin, M.D., neuroradiologists and other physicians. Specialty trained nurses in the oncology pharmacy, pediatric operating room, pediatric recovery area and angiography suite all play a role in caring for these special patients, as well as social workers, genetic counselors and Child Life specialists. Physicians affiliated with Mischer Neuroscience Institute and Children's Memorial Hermann Hospital are also engaged in research investigating new ways to save eyes that have failed conventional therapies.

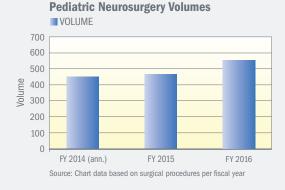
The Children's Neuroscience Center provides a broad range of diagnostic and treatment services for children with complex neurological problems including autism, brachial plexus disorders, brain tumors and malformations, cerebral palsy, congenital hydrocephalus, craniofacial disorders, developmental disorders, epilepsy, chronic headache and migraine, head trauma, learning disabilities, movement disorders, myopathy, neurofibromatosis, neurometabolic disorders,

QUALITY & OUTCOMES MEASURES



neuromuscular disorders, pediatric stroke, peripheral nerve disorders, sleep disorders, spina bifida, Tourette syndrome and tuberous sclerosis complex. Physicians affiliated with the Center have specialized pediatric neurosurgical expertise in congenital malformations, including Chiari malformation; endoscopic neurosurgery; and treatment for pediatric stroke, spinal deformities and traumatic brain and spine injury.

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



Pediatric Surgical Site Infection Rate (Per 100 Procedures)



Source: Chart data is based on surgical procedures per fiscal year

Epilepsy

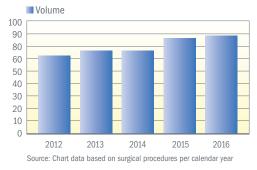
Over the past four years, the Texas Comprehensive Epilepsy Program (TCEP), a Level 4 National Association of Epilepsy Centers-certified center, has seen accelerated growth in volumes of medically and surgically treated patients and in numbers of faculty physicians. Affiliated providers now include six full-time adult and three full-time pediatric epileptologists and an adult and pediatric epilepsy surgeon. A collaborative effort between Memorial Hermann-Texas Medical Center, Children's Memorial Hermann Hospital and McGovern Medical School at UTHealth, the program is the premier destination for the diagnosis and treatment of epilepsy in patients of all ages in the southwestern United States. A host of etiologies, including genetic anomalies, brain trauma, structural abnormalities, stroke and brain tumors, can cause epilepsy, and a specific determination of the cause of seizures by experts in the field is crucial to planning the most effective treatment plan for individual patients.



At the heart of the program is a state-of-the-art sevenbed adult Epilepsy Monitoring Unit (EMU) and a six-bed pediatric EMU, together making up the largest and most comprehensive monitoring unit of its kind in the region. Board-certified physicians employ a complete set of advanced diagnostic technologies that provide comprehensive datasets to help define and localize brain seizure networks. Diagnostic tools include high-definition MRI employing specialized sequences to probe grey and white matter and eloquent function, including double-inversion recovery, diffusion tensor imaging and functional MRI; magnetoencephalography (MEG) coupled to high-density electroencephalography (EEG) for spike localization and cognitive function mapping; state-of-the-art video-EEG for epilepsy electro-clinical classification; positron emission tomography (PET) and single photon emission computed tomography (SPECT) for probing cerebral metabolism; intracarotid amytal (Wada) testing for language and memory lateralization; and epilepsy-specific neuropsychological testing. The Institute's video-EEG monitoring unit is one of a few inpatient units in the country with simultaneous electroencephalography/ polysomnography capability.

Once a diagnosis is made, TCEP physicians offer the most advanced medical treatment options available, including combination drug therapy, the ketogenic and modified Atkins diet, and specialized measures for special populations (for example, hormonal manipulation for catamenial epilepsies). Under the leadership of Nitin Tandon, M.D., the program is a world

Epilepsy Surgery Volumes



leader in epilepsy surgery. Dr. Tandon has performed more than 700 cranial procedures for the localization and treatment of epilepsy, with a zero percent mortality rate and a very low rate of permanent morbidity. In addition to the conventional procedures of focal cortical resection, lobectomy, hemispherectomy and corpus callosotomy, physicians affiliated with the program have adopted several innovative surgical procedures for epilepsy. Prominent among these are robotic stereo-electro-encephalography (SEEG) for 3-dimensional investigation of epileptic foci in the brain with a stereotactic placement of intracerebral electrodes, MR-guided laser interstitial thermal therapy (Visualase[®]) and Responsive Neural Stimulation (RNS - NeuroPace[®]). The program was the second in the country to adopt robotic SEEG, and Dr. Tandon recently performed his 100th robotic SEEG implantation with zero percent morbidity from the placement of nearly 1,500 electrodes.

The Institute is a pioneering site for Visualase, the application of laser surgery for well-delineated focal epilepsies, which is used to ablate seizure foci in a minimally invasive fashion. In addition to the conventional use of Visualase for the treatment of temporal lobe epilepsy associated with hippocampal sclerosis, affiliated physicians use it in novel ways, including the treatment of deep-seated periventricular nodular heterotopia and hypothalamic hamartoma. More than 50 Visualase procedures have been completed at the Institute, with zero complications. The program also offers responsive neurostimulation therapy (RNS - NeuroPace®) to selected patients whose refractory disease is not amenable to conventional or laser surgery. Finally, the Institute's program goes beyond the medical and surgical treatment of epilepsy to offer general supportive measures via a network of community counselors who help patients cope with the psychosocial and emotional aspects of their condition. An active patient support group, overseen by physicians, a specialist nurse and coordinating administrative staff, meets every month at Memorial Hermann-Texas Medical Center.

The TCEP has been involved in drug-trial research related to most of the new epilepsy treatments approved in the United States in the last 15 years, including lacosamide monotherapy and adjunctive therapy for partial-onset seizures, and an open-label extension study of rufinamide as an adjunctive therapy in patients with refractory partial-onset seizures. Current drug trials include vigabatrin therapy with magneticresonance spectroscopy (MRS) for refractory partial epilepsy. Physicians have also contributed patient data to nationwide trials in epilepsy genetics (the Epilepsy Phenome-Genome Project) and epidemiology (Human Epilepsy Project). The program is a member of the National Critical Care EEG Monitoring Research Consortium. TCEP faculty, all of whom hold academic appointments at McGovern Medical School, pursue several other lines of investigator-initiated clinical and scientific research. Research funding comes from a variety of sources, including major National Institutes of Health and National Science Foundation grants. In addition, they pursue collaborative interdisciplinary research with numerous local, national and international institutions. Prominent research interests are in the area of the neuroimaging and electrophysiology of epilepsy and human cognitive function, such as the neurophysiology of human language and memory processing and the sleep-wake cycle; advanced MRI techniques to localize epilepsy when conventional methods fail; and signal processing of EEG to understand brain networks and the more fundamental aspects of how seizures arise and propagate using existing cognitive networks.

RESEARCH HIGHLIGHT

A Unified Cognitive Network Model of Language

LEAD PHYSICIAN: Nitin Tandon, M.D.

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

Researchers at McGovern Medical School aim to remedy current limitations of research into cognitive processes by using icEEG to study the processes involved in reading from an integrative and unified perspective. The study is funded by a \$3 million grant from the National Institutes of Health BRAIN Initiative, awarded to Dr Tandon. His collaborators include Nathan Crone, M.D., Johns Hopkins School of Medicine; Greg Hickok, Ph.D., University of California, Irvine; Stanislas Dehaene, Ph.D., Collège de France; and Xaq Pitkow, Ph.D., Baylor College of Medicine and Rice University.

Most current research into the neural basis of the human language function and other cognitive processes is done using fMRI or MEG/EEG. These imaging modalities possess limited spatial and temporal resolution that do not allow researchers to capture relevant dynamics, which occur on the millisecond time scale. Another limitation of most approaches is the generally fragmented approach to the study of cognitive processes. Language, a seamless and fluent process, is typically studied as a conglomeration of separate subsystems: perception, pattern recognition, categorization, response selection, cross-modal integration, motor control and sensorimotor integration.

The researchers selected reading because it is a complex task that involves visual pattern recognition; visual-auditory and visuo-motor integration; semantic, syntactic and phonological access; and in reading aloud, response selection and motor sequencing. They propose that understanding is achieved not by information passing through a sequence of discrete processing stages in individual modules but through a distributed network.

Dr. Tandon and his colleagues will recruit 80 patients in whom they will quantify local and inter-regional cortical dynamics during word reading – from early primary visual perception, through selection, to word output. With their combined expertise in language, reading, icEEG signal analysis, population level network modeling from intracranial recordings and neural networks, the team members believe the results of the study will dramatically improve scientific understanding of reading and language systems, as well as developing and testing a new way to model neural computation.

Memory Disorders and Dementia

Physicians affiliated with the Neurocognitive Disorders Center evaluate and treat patients with concerns about memory, language, judgment, mood, behavior and related issues. Because symptoms may have a range of causes – normal aging, early dementia, mini-strokes, infections, vitamin deficiencies, depression, hormonal deficiencies and sleep disorders, among others – they evaluate symptoms fully to ensure correct treatment. Several important advances are allowing them to determine a specific diagnosis in most patients, leading to better treatments. Research at the Center focuses on three key areas for dementia: improving diagnosis, determining its causes, and improving treatment, either by preventing dementia or treating it in the early symptomatic stage.

Under the direction of neurologist Paul Schulz, M.D., Mischer Neuroscience Institute was the first in Houston to diagnose Alzheimer's disease (AD) using amyloid-sensitive PET imaging, which is helpful in determining whether patients do or do not have AD. Now physicians are working with laboratory scientists to develop new spinal fluid and blood tests for AD and Parkinson's disease (PD), and new imaging agents that will help diagnose other forms of dementia and provide insights into their underlying processes. They are also using blood and spinal fluid to investigate the role of genetic mutations and chemical modifications of genes in dementia. Neurodegenerative diseases affect millions of Americans, and their causes remain uncertain. While there is a known hereditary component to AD, PD, amyotrophic lateral sclerosis (ALS) and frontotemporal disease (FTD), most patients with these disorders do not have a family history. Based on this knowledge, physicians suspect that environmental risk factors may increase vulnerability to the disorders. Investigators at the Neurocognitive Disorders Center are examining how certain risk factors may lower the threshold for dementia, including traumatic brain injury, posttraumatic stress disorder (PTSD) and transmissible components. They are also investigating whether chemical modifications of genes, caused by these risk factors, may lead to dementia.

Several pioneering studies are under way at the Center, including multicenter clinical trials of two promising medications added to the treatment regimen of patients currently taking donepezil; both medications have unique mechanisms of action previously unstudied. Other trials are investigating the efficacy of deep brain stimulation in patients with major depressive disorder who have not responded to other treatments; developing stem cells for use in patients with neurodegenerative disorders; and determining whether removing amyloid, a protein deposited abnormally in the brains of people with AD, from the blood of patients with early AD will reduce the overall amount of amyloid in the brain.



Movement Disorders and Neurodegenerative Diseases

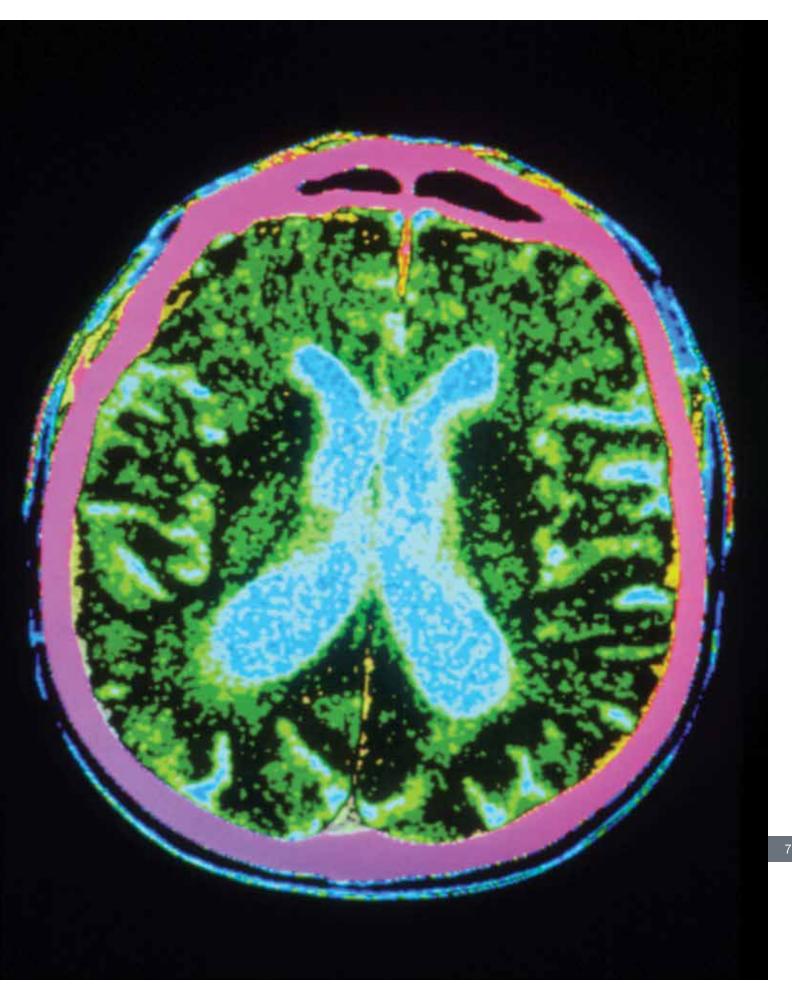
Using pioneering techniques and clinical expertise to diagnose, evaluate, manage and treat adult and geriatric patients, the Movement Disorders and Neurodegenerative Diseases Program, called UT MOVE, has established a track record of providing outstanding care for patients. A collaboration of the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center and McGovern Medical School at UTHealth, UT MOVE provides patients with specialty clinics and faculty expertise in spasticity management, deep brain stimulation, neurotoxin injection therapy, Huntington's disease, Parkinsonian disorders, and disorders of tremor, ataxia, and those caused by traumatic brain or spine injury.

The Spasticity Management Clinic offers pharmacological and surgical therapies, including the use of intrathecal baclofen pump therapy. Through the Deep Brain Stimulation (DBS) Clinic, candidates are selected for DBS therapy for the FDA-approved indications of Parkinson's disease, tremor and dystonia, which includes team management and programming of DBS therapy. At the Neurotoxin Injection Therapy Clinic, physicians use Botox[®], Xeomin[®], Myobloc[®] or Dysport[®] as indicated for abnormal states of dystonia, spasticity, chronic migraine and limb spasticity.

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

Neuroscience Institute at the Texas Medical Center and through Mischer Neuroscience Associates in the community, is known for low complication rates and outstanding outcomes. Based on the skill of neurological and neurosurgical teams and their expertise in DBS programming, Mya Schiess, M.D., director of the Movement Disorders and Neurodegenerative Diseases Program, and her team advocate for early use of deep brain stimulation in appropriate patients.

In 2015, the DBS program recorded record growth, and Dr. Schiess was the only representative from the United States participating in the international Consensus Panel to Formulate Criteria for the Selection of Parkinson's Disease Patients for DBS Therapy. Based on the panel's now published work, she is helping to develop and launch a version of the EARLY STIMULUS assessment tool for use in the United States. In addition, she is the U.S. spokesperson for an expanded FDA indication for the Activa® neurostimulator for DBS therapy in Parkinson's disease, a groundbreaking approval that will allow some patients to be eligible for DBS therapy earlier – at four years from disease onset with a minimum of four months of motor complications. DBS therapy continues to be appropriate for longerduration motor complications in advanced disease, but there is no longer an upper-age restriction.



RESEARCH HIGHLIGHT

Pilot Phase 1 Study of Allogeneic Bone Marrow-derived Mesenchymal Stem Cell Therapy for Idiopathic Parkinson's Disease

PRINCIPAL INVESTIGATOR: **Mya C. Schiess, M.D.** *Professor and Adriana Blood Chair*, Department of Neurology, McGovern Medical School at UTHealth

This study is the first step in investigating the safety of using escalating doses of allogeneic adult bone marrow-derived mesenchymal stem cells (MSCs) delivered intravenously to patients with idiopathic Parkinson's disease (PD). The target population includes men and women of any ethnic, racial or socioeconomic background with sporadic late-onset clinically diagnosed Parkinson's disease with onset of motor symptoms > 4 years and \leq 7 years between the ages of 45–70 years old at the start of the trial. Twenty-four men who meet the UK Brain Bank criteria for idiopathic PD and who have a Hoehn and Yahr of < 3 in the OFF medicine state will be recruited to participate. Each cohort of 5 study subjects will receive one of four doses of MSC; 1 X 106 MCS/kg of body weight, 3 X 106 MCS/kg, 6 X 106 MCS/kg, or 10 X 106 MCS/kg.

The researchers' primary outcomes will be safety, defined as the absence of an immediate transfusion reaction, adverse events or organ damage. Secondary outcomes will measure therapy impact on PD progression as defined by changes on UPDRS, MDS-UPDRS, TUG, PDQ-39, H&Y, C-SSRS and immunologic profile. A greater goal envisions additional studies using repeated MSC dosing to address progression in typical and atypical Parkinson's neurodegeneration.

Impact on Health Care: MSC therapy has the potential to slow the rate of PD progression and restore homeostasis to the neuronal-glial populations damaged by the degenerative process. Currently our PD therapies focus on symptom relief. If intravenous adult-derived mesenchymal stem cell therapy proves to be neuroprotective or neurorestorative, it would truly advance our care, which is the mission of UTHealth and Mischer Neuroscience Institute.

UT MOVE faculty member Raja Mehanna, M.D., has added depth and understanding to the program's legacy in DBS with numerous publications of reviews, articles and a book on DBS therapy and outcomes. In addition, UT MOVE's referral program is thriving. Today, 25 percent of Stage 1 electrode-placement surgeries performed on patients referred to UT MOVE and Mischer Neuroscience Institute's DBS team are referred by community physicians.

UT MOVE's comprehensive Huntington's Disease Program was named a Huntington's Disease Society of America

(HDSA) Center of Excellence for 2016. Led by Erin Furr-Stimming, M.D., the program is one of 39 centers of excellence across the country and the only one in Texas to receive the prestigious designation. Affiliated physicians operate the only specialty clinic for the diagnosis, management and support of patients and their families with Huntington's disease in the Houston area.

In addition, expertise in the management of traumatic brain injury is available in collaboration with the Halle Center for Traumatic Brain Injury and the joint appointment of Allison Boyle, M.D., to the UT MOVE team of physicians. The bimonthly, full-day UT MOVE clinic established at Memorial Hermann The Woodlands Hospital in 2015 has expanded to three clinic days a week with the addition of movement and sleep disorders specialist Sarah Hoque, M.D. The Woodlands clinic provides the same expert care available in the Texas Medical Center to this fast-growing community.

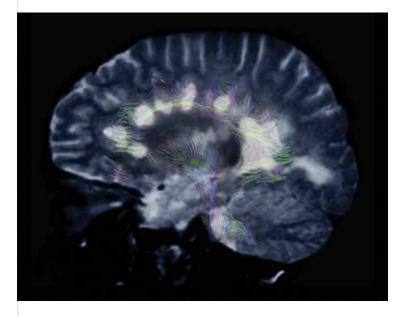
The movement disorders medical team uses proven and investigational medications and interventional methods to manage Parkinson's disease, Parkinsonian disorders, generalized and focal dystonia, essential tremor and other tremor states, Huntington's chorea, restless leg syndrome and other sleep disorders like REM sleep behavior disorder, cortical and subcortical dementias, cerebral palsy, spasticity, ataxias, gait disorders, spinal and brain trauma-related movement abnormalities, multiple sclerosis-related movement abnormalities, and other inherited and acquired neurodegenerative diseases. The team's treatment philosophy is grounded in the early identification of disease and early use of neuromodulating or neuroprotective approaches. Physicians maintain patients at the highest level of function possible, based on symptom-driven therapeutic goals set by the physician and patient. In developing and adjusting treatment plans, they consider the whole person, as well as the patient's environment and support groups. They also emphasize education, and encourage patients to stay mentally and physically active, to work at having fun and to create a positive environment with friends and family.

UT MOVE supports and partners with the Houston Area Parkinson's Society (HAPS), which has been crucial in providing educational, exercise and social programs as well as support groups to Parkinsonian patients. The program partners with TIRR Memorial Hermann in a comprehensive UT MOVE/Neurorehabilitation Program that incorporates neurological-driven rehabilitation as part of the treatment approach.

Research within the division of Movement Disorders and Neurodegenerative Diseases at UTHealth is substantial, with partnerships and collaborations among clinical and basic science studies and multiple disciplines, and funding from federal, pharmaceutical and philanthropic sources. Faculty in the program are members of the Movement Disorders Society, the Parkinson's Study Group, Huntington's Study Group, Tremor Research Group, Dystonia Coalition and Restless Legs Syndrome Study Group. Ongoing established research includes a longitudinal prospective study on biomarkers and presymptomatic biomarkers for Parkinsonian syndromes, which led in 2013 to the discovery of immune-mediated markers of disease activity and proposed cell therapy intervention for Parkinsonism.

Dr. Schiess is the primary architect and principal investigator for an FDA-approved Phase IA/B pilot safety study of the use of adult bone marrow-derived mesenchymal stem cells in Parkinson's disease. The trial, which began in January 2016, will evaluate the safety and tolerability of neuroimmune modulation with allogeneic stem cells in patients with Parkinson's disease. The UT MOVE program continues as a participating site for the multicenter National Institute of Neurological Disorders and Stroke/Parkinson Study Group (NINDS/PSG) trial of isradipine as a neuroprotective drug in Parkinson's disease. In addition, the UT MOVE program is recruiting for the Sure PD-3 clinical trial sponsored by NINDS/PSG to explore the manipulation of uric acid as a neuroprotective molecule in Parkinson's-mediated neurodegeneration.

Multiple Sclerosis



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

Organized in 1983, the Multiple Sclerosis Research Group (MSRG) has participated in numerous clinical trials of novel disease-modifying therapies, serving as the lead center for international studies, several of which were pivotal in gaining FDA approval of currently available treatments for MS. Recently completed clinical research includes two international randomized, controlled studies in primary progressive MS: INFORMS, which investigated the potential benefits of fingolimod, a drug that did not limit progression, and ORATORIO, which examined the effects of anti-CD20 (B-cell) therapy with the monoclonal antibody ocrelizumab and is the first study to show a positive outcome with this form of MS. Paired studies of the same drug in relapsing MS were favorable in a controlled, blinded study that used interferon beta-1a as the active comparator. The MSRG participated at multiple levels in both clinical trials.

Léorah Freeman, M.D., Ph.D., joined the MSRG in 2016. An experienced neurologist, multiple sclerosis expert and imaging experimentalist from Paris, France, Dr. Freeman is completing a transitional fellowship supported in part by the National Multiple Sclerosis Society.

Led by Jerry S. Wolinsky, M.D., the Multiple Sclerosis Program was the first in the world to conduct preclinical studies on the effects of combined therapy with immunomodulating drugs. It is the first and only center in Houston to direct national and international clinical trials in MS, and remains the North American leader in studies of primary progressive multiple sclerosis, as well as the most active center in Texas in the conduct of organized clinical trials of new therapies for MS. Affiliated physicians are at the forefront of investigator-initiated research in immune regulation in MS, infection as a cause of MS, MS-related cognitive impairment and MS-related MRI findings. In the department of Neurology's state-of-the-art Magnetic Resonance Imaging Analysis Center, physicians use spectroscopic and diffusion tensor imaging with tractotomy, as well as other advanced diagnostic tools. Following diagnosis, patients benefit from breakthrough treatment options that include injectable immunomodulators, immunosuppressives, monoclonal antibodies and all of the newer oral 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 efficacy trials. The Center was pivotal in providing quantitative imaging data that supported the regulatory approval of the oral agent teriflunomide for use in relapsing forms of MS in the United States, Europe and a growing number of countries worldwide, determining the optimal drug dose and extending the results of its benefits when used in first symptom-onset disease.

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

RESEARCH HIGHLIGHT

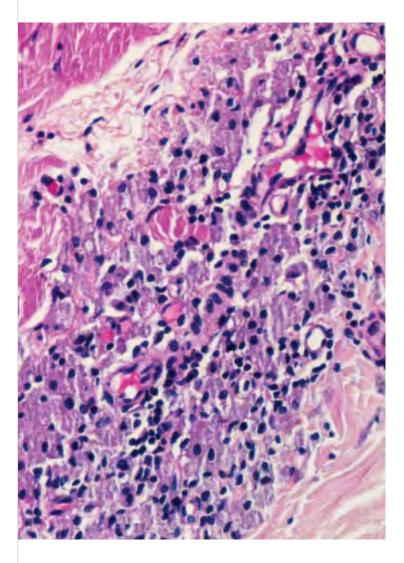
The Impact of Enhanced Cerebral Perfusion on the Evolution of Multiple Sclerosis Lesions

LEAD PHYSICIAN: John A. Lincoln, M.D., Ph.D. Assistant Professor, Department of Neurology, McGovern Medical School at UTHealth

Global and regional changes in blood flow to the brain (cerebral perfusion) have been seen early in multiple sclerosis (MS) patients with both relapsing and progressive forms. Previous research in our laboratory has shown that reduced small-vessel perfusion is associated with the formation of gliotic lesions (lesions with permanent damage). Studies have suggested that virtual hypoxia resultant from the combination of diminished cerebral perfusion and increased energy demand contributes to permanent tissue damage that strongly correlates with clinical disability in persons with MS.

There are currently several potent anti-inflammatory medications available to treat patients with MS, though none are known to enhance cerebral perfusion. Acetazolamide (ACZ) is a generic medication with a well-established safety and tolerability profile that is known to enhance cerebral perfusion in healthy subjects. Improving cerebral perfusion might improve energy supplies as well as reduce buildup and improve clearance of toxic metabolites, thereby decreasing permanent tissue injury. The goal of this project is to determine if daily therapy with ACZ improves cerebral perfusion in MS patients and if improved perfusion enhances repair of previously formed and newly formed MS lesions, reducing irreversible neurological damage and disability.

Neuromuscular Disorders



Physicians affiliated with the Neuromuscular Disorders Program at UTHealth 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. Led by Kazim A. Sheikh, M.D., the program is a designated center of excellence for Guillain-Barré syndrome (GBS) and chronic inflammatory demyelinating polyneuropathy (CIDP) and records more than 4,000 patient visits annually, primarily adults age 18 and older. About two-thirds of patients seen by affiliated physicians are over the age of 50.

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

Because electrodiagnostic evaluation is an extension of clinical findings, affiliated 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

RESEARCH HIGHLIGHT

Fluorescently-tagged Anti-ganglioside Antibody Selectively Identifies Peripheral Nerve in Living Animals

PRINCIPAL INVESTIGATOR: Kazim Sheikh, M.D.

Professor, Department of Neurology, McGovern Medical School

Selective in vivo delivery of cargo to the peripheral nervous system (PNS) has broad clinical and preclinical applications. An important applicability of this approach is systemic delivery of fluorescently conjugated ligands that selectively label PNS, which could allow visualization of peripheral nerves during any surgery. We examined the use of an anti-ganglioside monoclonal antibody (mAb) as a selective neuronal delivery vector for surgical imaging of peripheral nerves.

Systemic delivery of an anti-ganglioside mAb was used for selective intraneuronal/axonal delivery of fluorescent agents to visualize nerves by surgical imaging in living mice. In this study, we demonstrated that intact motor, sensory and autonomic nerve fibers/paths are distinctly labeled following a single nanomolar systemic injection of fluorescently labeled anti-ganglioside mAb. Tissue biodistribution studies with radiolabeled mAb were used to validate neuronal uptake of fluorescently labeled mAb.

Implications of this proof of concept study are that fluorescent conjugates of anti-ganglioside mAbs are valuable delivery vectors to visualize nerves during surgery to avoid nerve injury and monitor nerve degeneration and regeneration after injury. These findings support that antibodies, and their derivatives/ fragments, can be used as selective neuronal delivery vector for transport of various cargos to PNS in preclinical and clinical settings.

Cynthia A. Massaad, Gang Zhang, Laila Pillai, Ali Azhdarinia, Weiqiang Liu, Kazim Sheikh. Fluorescentlytagged anti-ganglioside antibody selectively identifies peripheral nerve in living animals. Scientific Reports. 2015 Oct 30;5:15766. neuropathies; and traumatic nerve injury, including evaluation of the brachial plexus and facial neuropathy. The Neuromuscular Disorders Program is the only program in Houston that provides single-fiber EMG.

Studies conducted in the Muscle and Nerve Laboratory help improve diagnosis in cases with limited neuromuscular findings by locating abnormalities at a pathologic/microscopic level. Affiliated subspecialists perform muscle, nerve and skin biopsies, which are further processed by highly experienced staff. Their preferred technique is open biopsy under local anesthesia, which reduces the likelihood of missing abnormalities in cases of patchy involvement, such as in inflammatory myopathies. They also perform skin biopsies for the diagnosis of small-fiber neuropathy, and the lab is the only center in Houston that processes skin biopsy specimens for the diagnosis of small-fiber neuropathies. Current research is focused on developing new strategies to treat neuropathic disorders and enhance nerve repair. With funding from the National Institutes of Health and the GBS/CIDP Foundation International, affiliated investigators are evaluating the role and pathogenic mechanisms of anti-ganglioside antibodies in autoimmune neuropathy; using diffusion tensor imaging to assess and quantify nerve degeneration and regeneration in patients with traumatic nerve injuries; investigating modulation of FcRn as a strategy to prevent autoantibody-mediated nerve injury; examining the pathobiologic effects of anti-ganglioside antibodies on nerve regeneration; and using monoclonal antibodies for delivery of cargo to nerve cells for peripheral nerve imaging and modulation of function. The group is also involved in clinical studies examining the predictors of short- and long-term outcomes in Guillain-Barré syndrome and comparing the efficacy of current treatments in the management of neuropathic pain.

Neurorehabilitation

Patients recovering from neurological illness or injury benefit from innovative neurorehabilitative technology and integrated care at the Memorial Hermann Mischer Neuroscience Institute and TIRR Memorial Hermann. Subspecialists affiliated with both facilities are experts 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

Nneka Ifejika, M.D., an award-winning author, mentor and reviewer in the fields of neurology and physiatry, leads the only neurorehabilitation team in the United States that is part of a Comprehensive Stroke Center certified by The Joint Commission. Under her direction, Memorial Hermann-Texas Medical Center's 10-bed inpatient neurorehabilitation unit provides comprehensive rehabilitation care, including an intensive program of physical therapy, occupational therapy and speechlanguage pathology. The program is distinguished from others by its focus on incorporating clinical research in stroke prevention and health disparities in the rehabilitation setting.

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

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

Research led by Dr. Ifejika includes Swipe Out Stroke, a regional study focused on decreasing the disability gap present in minority populations through culturally competent interventions using mobile health technologies, and Rehab MATRIX, a multicenter pilot study under way across the Memorial Hermann Rehabilitation Network, which uses a novel patient assignment tool to decrease patient falls and improve patient safety and healthcare quality.



TIRR MEMORIAL HERMANN

An international leader in rehabilitation and research, TIRR Memorial Hermann traces its roots back to the early 1950s when polio was at the height of its epidemic in the United States. Over the past 50 years, TIRR Memorial Hermann has moved far beyond only treating patients with polio to providing leading comprehensive rehabilitation services.

TIRR Memorial Hermann is the best rehabilitation hospital in Texas and the second best in the United States, according to *U.S. News & World Report's* Best Hospital rankings for 2016-2017. This marks the 27th consecutive year TIRR Memorial Hermann has been included in the rankings. Using a team approach, the hospital's affiliated physicians, therapists, nurses, neuropsychologists and allied health professionals serve patients with a variety of diagnoses and conditions. TIRR Memorial Hermann has been named among the National Institute on Disability and Rehabilitation Research Traumatic Brain Injury Model Systems since 1987. Recently the hospital was designated as a Spinal Cord Injury Model System as well.

Many of the world's leading physicians in rehabilitation medicine provide care at TIRR Memorial Hermann, a sister hospital to Memorial Hermann-Texas Medical Center. The patient care environment, which blends passionate staff, exemplary care and a commitment to overall quality of life, distinguishes TIRR Memorial Hermann. Rehabilitation teams at the facility transform lives and inspire hope in people whose lives have been significantly altered by an illness or injury. Because the hospital is part of the Memorial Hermann Health System, patients also have access to Texas Medical Center specialists.

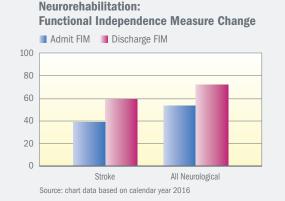
QUALITY & OUTCOMES MEASURES

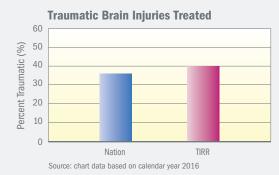
Inpatient Rehabilitation

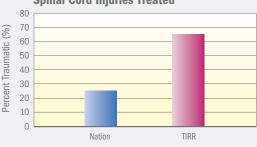
Patients can benefit from this interdisciplinary approach at the inpatient level. Upon admission, patients discuss goals with an interdisciplinary team and, together, develop a treatment plan. Support groups, counseling and individualized training prepare families and caregivers for caring for the patient after discharge. Inpatient rehabilitation programs and services include treatment of stroke, brain injury, spinal cord injury, neurological disorders, Guillain-Barré syndrome, limb loss, trauma, neurodegenerative diseases and debilitation. Patients can continue regaining skills through TIRR Memorial Hermann outpatient rehabilitation.

Outpatient Rehabilitation

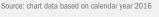
TIRR Memorial Hermann has extended its top-notch rehabilitation to many outpatient locations throughout Greater Houston. These outpatient programs are changing patients' lives by helping them regain the skills and confidence they need to reintegrate into the community. The Outpatient Medical Clinic at TIRR Memorial Hermann is a physician-based clinic designed to meet the needs of individuals who require initial or continuing rehabilitation care with a physician The Challenge Program is a comprehensive community re-integration program for brain injury survivors, 14 years of age or older. The program assists individuals in returning to community activities such as work, school or volunteering, or to a higher level of independence. Once rehabilitation is complete, exercise plans tailored to the individual are available through TIRR Memorial Hermann's Strength Unlimited, a community-based wellness and recovery program for lifelong health and wellbeing.













Programs and services include:

- Physical, occupational and speech therapies
- Balance/vestibular rehabilitation
- Cancer rehabilitation
- Challenge program, community re-entry
- Cognitive rehabilitation
- Decondition
- Neuropsychology
- Swallowing and voice therapy
- Vision rehabilitation

Pediatric Rehabilitation

TIRR Memorial Hermann offers specialized pediatric therapy programs at our inpatient and outpatient locations; outpatient programs serve newborns through adolescence and inpatient programs serve children age ten and up. For children and adolescents newly released from intensive care and those whose recovery from neurological illness or injury is already underway, affiliated physicians and therapists have one goal: getting young people back to school and play surrounded by family and friends.

TIRR Memorial Hermann has a dedicated international team that works with patients of diverse backgrounds and nationalities. The team accommodates a variety of dietary, language and religious needs. Staff members work closely with embassies, consulates and other governmental entities to assist in the admission process.

TIRR Memorial Hermann's recognition as a national leader in rehabilitation is based on a solid history of



accomplishment in clinical care, backed by a 56-year legacy of innovation through research. Research has always been an integral part of TIRR Memorial Hermann's name. Founded in 1959 as the Texas Institute for Rehabilitation and Research, the hospital evolved from providing treatment to people who survived the polio epidemic in the 1950s to providing rehabilitation for people with spinal cord and brain injuries. Today, with over 46 researchers receiving \$21.5 million in total research funding, we are breaking the boundaries of rehabilitation one study at a time.

Centers of Research include:

- Brain Injury Research Center
- Spinal Cord Injury and Disability Research Center
- · Center for Research on Women with Disabilities

- NeuroRecovery Research Center
- Independent Living Resource Utilization

TIRR Memorial Hermann has expanded access to rehabilitation programs through the Memorial Hermann Rehabilitation Network. Team members within this network are among the best trained and most experienced rehabilitation professionals. With a total of 258 inpatient beds and locations across the area, TIRR Memorial Hermann and the Memorial Hermann Rehabilitation Network help both adults and children with a variety of diagnoses/treatments, restoring independence and helping patients reintegrate into the community.

TIRR is a registered trademark of TIRR Foundation.

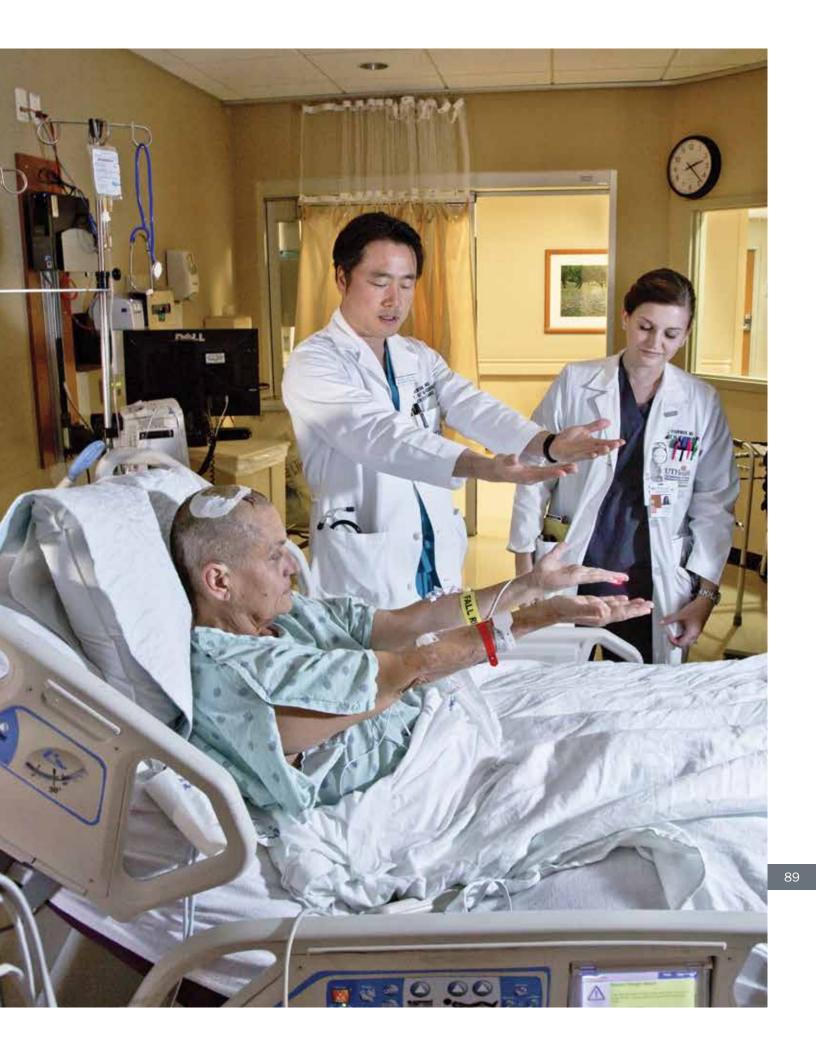
Neurotrauma and Neuroscience Critical Care



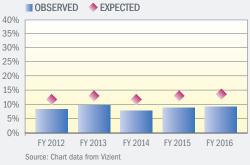
The Neurotrauma and Neuroscience Critical Care Program at the Memorial Hermann Mischer Neuroscience Institute is internationally recognized for the treatment of highacuity brain and spinal cord injuries. Affiliated physicians manage more neurotrauma cases than any other center in the United States, with neurointensivists and experienced mid-level practitioners staffing the 32-bed Neuroscience and Neurotrauma ICU (NSICU) around the clock to provide ongoing intensive care to critically ill patients. The program continues to grow and now operates the largest and busiest Neuro ICU in the region and the second largest in the nation.

The Neurotrauma and Neuroscience Care Program is an international leader in research conducted on innovative treatments following neurotrauma, including participation in several multicenter trials. Investigators at Mischer Neuroscience Institute, McGovern Medical School at UTHealth 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; the safety and pharmacokinetics of riluzole in patients with traumatic acute spinal cord injury; coagulation and outcome from acute neurologic injury using thrombelastography; perihematomal response to tissue injury and outcomes from intracerebral hemorrhage (ICH); inflammation and global cerebral edema after subarachnoid hemorrhage (SAH); and other basic science research and clinical trials. The Neuroscience and Neurotrauma Critical Care Program, led by Kiwon Lee, M.D., FACP, FAHA, FCCM, associate professor and vice chair of neurosurgery and neurology for critical care, utilizes the most advanced medical technologies and devices, including a multimodal monitoring system.

Mischer Neuroscience Institute and McGovern Medical School offer a two-year neurocritical care fellowship for applicants who are board certified or eligible in neurology, emergency medicine, anesthesia or internal medicine. A one-year fellowship track is open to eligible candidates who have completed postgraduate training in neurosurgery, medical critical care, anesthesia critical care or surgical critical care. The educational curriculum is specifically designed to train physicians with a strong base in general critical care, with an emphasis



QUALITY & OUTCOMES MEASURES



Traumatic Brain Injury: Inpatient Mortality



Traumatic Brain Injury:

on neurological and neurosurgical emergencies. The Neuroscience ICU (NSICU) is equipped with multimodality monitoring capability including ICP, CPP, continuous video EEG monitoring, continuous cardiac output, SjvO2 monitoring and the country's first use of the latest model of digitalized brain oxymetry (PbtO2) with monitors connected to patient bedside monitoring. The NSICU is a truly academic training environment where fellows work with neurosurgery, neurology, anesthesia and emergency medicine residents, as well as rotating fellows from other critical care programs. Fellows may rotate through the medical, surgical/ trauma and cardiovascular ICUs and are offered a number of electives including anesthesiology, stroke, EEG, TCD, neuroradiology and burns. They also have the opportunity to work on the nation's first Mobile Stroke Unit.

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

In March 2016, Mischer Neuroscience Institute sponsored the fourth annual Neuro ICU Symposium, a three-day course designed to educate physicians and other healthcare professionals on optimal management of patients using a team approach. The symposium emphasizes early treatment of neurotrauma patients, starting in the emergency room.

Patients with acute neurological injuries benefit from the Memorial Hermann Red Duke Trauma Institute – one of only two Level 1 trauma centers in the area and one of the busiest in the nation – and from Memorial Hermann Life Flight[®], the first air medical transport service established in Texas and the second in the nation. A long-term collaboration with McGovern Medical School, the 200-bed Red Duke Trauma Institute provides high-quality care to both adult and pediatric trauma patients and offers a full spectrum of service, including access to Houston's only verified burn center. Physicians affiliated with the Institute drive

RESEARCH HIGHLIGHT

innovations in trauma care by moving research quickly from the laboratory to the bedside.

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

Mischer Neuroscience Institute has expanded the division's active role in saving the lives of critically ill patients through a new neurotrauma and neuroscience critical care service at Memorial Hermann Southwest Hospital. The hospital's new state-of-the-art Neuroscience ICU is staffed 24/7 by physicians affiliated with Mischer Neuroscience Institute and the medical school, all of whom are fellowship trained in neurocritical care. These neurointensivists work hand in hand with neurosurgeons to provide superior care after neurological surgery.

Diagnostic angiography is available onsite, and patients of referring physicians have access to the full spectrum of neuroendovascular services, including endovascular surgery for aneurysms, arteriovenous malformation, skull base tumors and stroke, through the hospital's affiliation with Mischer Neuroscience Institute. Comprehensive neuroendovascular services will be available at Memorial Hermann Southwest Hospital by the summer of 2017 as the hospital moves toward certification by the American College of Surgeons as a Level II trauma center.

Acute Effects of Intraventricular Nicardipine on Cerebral Hemodynamics: A Preliminary Finding

In an article published in *Clinical Neurology and Neurosurgery*,¹ researchers reported on a study investigating the acute effects of intraventricular nicardipine (IVTN) on cerebral hemodynamics when used as a treatment option for severe vasospasm in patients with subarachnoid hemorrhage (SAH).¹ Over a two-and-a-half-year period, IVTN was administered to 11 patients with SAH with multimodality monitoring for refractory vasospasm. The study team analyzed physiological parameters retrospectively from baseline up to six hours after the IVTN injection.

Statistical analysis revealed that mean intracranial pressure increased slightly for 20 minutes following the injection and decreased gradually during the next hour, and that mean cerebral perfusion pressure decreased transiently 20 to 30 minutes after injection. Other signs, including mean arterial pressure, partial pressure of brain oxygen tension, cerebral blood flow and autoregulation indices showed no significant change. The investigators concluded that the vasodilatory effect of IVTN increased intracranial pressure transiently but did not significantly affect the other parameters or oxidative glucose metabolism immediately after injection.

¹ Ko SB, Choi HA, Helbok R, Kurtz P, Schmidt JM, Badjatia N, Claassen J, Connolly ES, Mayer SA, Lee K. Acute effects of intraventricular nicardipine on cerebral hemodynamics: A preliminary finding. Clin Neurol Neurosurg. 2016 May; 144:48-52.

Pain Management

Pain management is a critical part of the Institute's overall program. Specialists in interventional pain management and physical medicine and rehabilitation treat acute and chronic pain arising from trauma, nerve damage, degenerative conditions, cancer, and systemic metabolic disorders such as diabetes. The multidisciplinary team works in close collaboration to provide a variety of interventions and strategies to help people regain control of their lives.

The recruitment of Joseph Amos, M.D., in 2016 added strength to the Pain Management Program at the Memorial Hermann Mischer Neuroscience Institute at



the Texas Medical Center. Dr. Amos is a fellowshiptrained interventional pain management specialist who was in private practice in Houston prior to joining the Institute. He serves as an expert panelist in pain management for the Texas Medical Board.

The Pain Management Program also includes Nadya Dhanani, M.D., and Mark Burish, M.D., Ph.D. A boardcertified anesthesiologist and interventional pain management specialist, Dr. Dhanani joined the team in 2014 after completing her residency training in anesthesiology at Massachusetts General Hospital and a fellowship in pain medicine at The University of Texas MD Anderson Cancer Center. Dr. Burish was recruited in 2015 after completing his neurology residency and pain management fellowship at the University of California at San Francisco.

In addition to treating patients with spine and neuropathic pain, Dr. Burish directs The Will Erwin Headache Research Center at Memorial Hermann and McGovern Medical School at UTHealth. Established with a \$20 million pledge from The Will Erwin Headache Research Foundation, the Center includes a group of experts dedicated to the study of cluster headaches and other debilitating headaches and facial pain diseases.

Physicians and researchers working with The Will Erwin Headache Research Center include neurosurgeon Dong Kim, M.D.; researcher Georgene Hergenroeder, B.S.N., M.H.A., RN, CCRC; researcher Pramod Dash, Ph.D.; and genetic counselor Krista Qualmann, M.S. The group will work with other institutions across the country to

RESEARCH HIGHLIGHT

The Will Erwin Headache Research Center Study of Cluster Headache: Building a Registry of Cluster Headache Patients

PRINCIPAL INVESTIGATOR: **Mark Burish, M.D., Ph.D.** Assistant Professor, Vivian L. Smith Department of Neurosurgery, McGovern Medical School at UTHealth

The Will Erwin Headache Research Center Study of Cluster Headache is a large observational repository of information related to cluster headache. The researchers' goal is to collect clinical data from consenting patients through online questionnaires and biological samples such as blood and saliva, which will be studied in the lab and shared with other researchers interested in greater access to cluster headache samples. Currently in its first year, the study will continue for 10 years with pledged funding from the Will Erwin Headache Research Foundation.

Previous research into cluster headache has been limited by access to large samples of patients: cluster headache affects only 1 in 1,000 people. The registry at Mischer Neuroscience Institute is the first of its kind in the United States devoted to cluster headache, and can be used to study genetics, biomarkers and pain signaling. The researchers hope to gain insights that will be used to develop new treatments for the disorder.

develop a consortium of centers to identify patients with cluster headache and other debilitating types of headaches, with the goal of better understanding and treating the disorders. Projects under way at the Center include clinical research into cluster headache features and treatments, as well as an investigation of genetics, epigenetics and metabolomics of cluster headaches through collaborations with basic science researchers.

Disorders treated by the Institute's pain management specialists include cervical and lumbar radiculopathy and facet arthropathy; sacroiliac dysfunction; spinal stenosis; carpal tunnel syndrome; vertebral compression fractures; and neuropathic pain conditions, including peripheral neuropathy, diabetic neuropathy, post-herpetic neuralgia and central post-stroke pain. Treatment is highly individualized and may consist of kyphoplasty and vertebroplasty for vertebral compression fractures; stellate, celiac plexus, lumbar sympathetic, superior hypogastric, and ganglion impar blocks and neurolysis; facet injections, medial branch nerve blocks and radiofrequency ablation; sacroiliac joint blocks and strip lesioning using radiofrequency ablation; transforaminal, interlaminar and caudal epidural steroid injections; greater and lesser occipital, supraorbital and suprascapular nerve blocks; joint and muscle injections; and spinal cord stimulation.

Spine Disorders

The renowned spine surgeons affiliated with the Spine Center at Mischer Neuroscience Institute offer the most advanced treatments available today, both surgical and nonsurgical. They perform more than 2,600 procedures annually, making the spine program the largest in the region.

Nationally and internationally renowned neurosurgeon Daniel H. Kim, M.D., FACS, FAANS, has expanded the spinal neurosurgery program and added expertise in reconstructive peripheral nerve surgery, complex spinal reconstruction and minimally invasive spinal surgery, both endoscopic and robotic. A clinical and educational leader in his field, he has authored hundreds of papers and published 20 surgical textbooks, many of which are used at leading medical schools to teach standardof-care techniques for neurosurgery. Dr. Kim is a pre-eminent researcher in peripheral nerve repair through nerve transfer and nerve graft, and is also recognized for his work in neurorehabilitation through robotics and cortical stimulation, spinal biomechanics and innovative neuromodulation treatments for chronic pain. With the addition in 2016 of fellowship-trained neurosurgeon Joseph Martinez, M.D., the program has expanded further. Dr. Martinez has expertise in complex minimally invasive spine surgery.

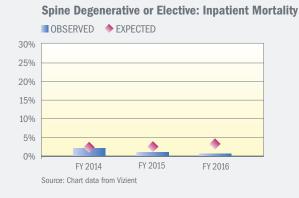
At the Spine Center a multidisciplinary team works in new state-of-the-art facilities equipped with advanced instrumentation and dynamic imaging systems. They are skilled in minimally invasive spine procedures and innovative treatment options for patients with back pain resulting from trauma, degenerative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

In 2015, Mischer Neuroscience Institute opened a stateof-the-art 16-bed Neuroscience Elective Unit with 10 beds dedicated to patients who choose to have spine surgery. Six beds are ICU level, reserved for patients admitted for brain surgery – for conditions such as trigeminal neuralgia, Chiari malformation, pineal cysts and brain tumors.

Pain management is a critical part of the Institute's spine program, and neurosurgeons work closely with specialists in physical medicine and rehabilitation and interventional pain management to help patients manage chronic back and neck pain. The multidisciplinary team works together to provide a variety of interventions and strategies for self-management to help people regain control of their lives. Anesthesiologist and interventional pain management specialist Nadya M. Dhanani, M.D., joined the Spine Center team in 2014 after completing her fellowship in pain medicine at The University of Texas M. D. Anderson Cancer Center. Pain management specialist Mark Burish, M.D., Ph.D., joined the team in 2015 after completing his neurology residency and pain medicine fellowship at the University of California at San Francisco. Interventional pain management specialist Joseph Amos, M.D., was recruited in 2016. He completed his fellowship in pain medicine at the University of Washington in Seattle and was in private practice in Houston prior to joining Mischer Neuroscience Institute.



QUALITY & OUTCOMES MEASURES



Spine Degenerative or Elective: Volume & Length of Stay (CMI Adjusted) VOLUME ALOS/CMI 1000 5 800 4 ALOS/CMI 600 Aolume 400 3 2 200 0 0 FY 2014 FY 2015 FY 2016 Source: Chart data from Vizient

Spine Trauma: Inpatient Mortality

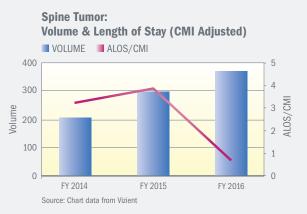


Spine Tumor: Inpatient Mortality



Spine Trauma: Volume & Length of Stay (CMI Adjusted)





SPINE DISORDERS • SCOPE OF SERVICES



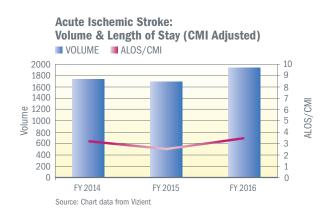
The Center's clinicians provide exceptional care for patients with traumatic spine injury, including the 10 percent to 20 percent of admissions through the Level I Red Duke Trauma Institute that involve neurological damage. Based on benchmark University HealthSystem Consortium data, the Spine Center's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

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

As faculty at UTHealth, neurosurgeons at the Center educate the next generation of spine experts and shape the future of medicine through basic science research, clinical discovery and the development of new, breakthrough treatments. Research under way at the Spine Center is focused on bringing promising therapies for spinal cord injury (SCI) patients from the laboratory to clinical trials in a manner that will provide evidence of effectiveness, with maximum safety, to patients undergoing treatment. Investigation is currently focused on tissue engineering matrices and axon regeneration, gene transmission and regulation of stem cell differentiation, the safety of the anticonvulsant drug riluzole in patients with SCI, and novel neuroprotection therapeutic approaches to SCI, among other projects.

SYSTEM CLINICAL OUTCOMES

Mischer Neuroscience Institute's infrastructure includes more than 100 nationally recognized faculty members. This allows the Institute to extend its neuroscience expertise and capabilities outside the Texas Medical Center through its network of Mischer Neuroscience Associates clinics. Physicians in these clinics are focused on providing superior care and exceptional service to their patients. As is done at Memorial Hermann-Texas Medical Center, quality is tracked closely at all system campuses in order to provide the best possible patient outcomes.



Transient Ischemic Attack: Volume & Length of Stay (CMI Adjusted) VOLUME \Rightarrow ALOS/CMI



Volume & Length of Stay (CMI Adjusted)

5

4

3

2

1

0

FY 2016

ALOS/CMI

Spine Neurosurgery:

VOLUME ALOS/CMI

Hemorrhagic Stroke: Volume & Length of Stay (CMI Adjusted) VOLUME ALOS/CMI





FY 2015

0 FY 2014 Source: Chart data from Vizient

1000

800

600



FY 2015



Volume 400 200

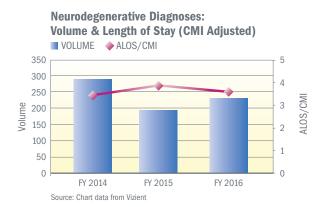
1

0

FY 2016

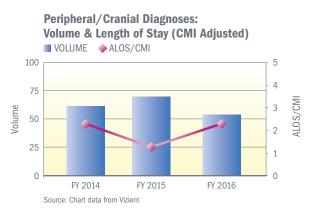
FY 2014

Source: Chart data from Vizient

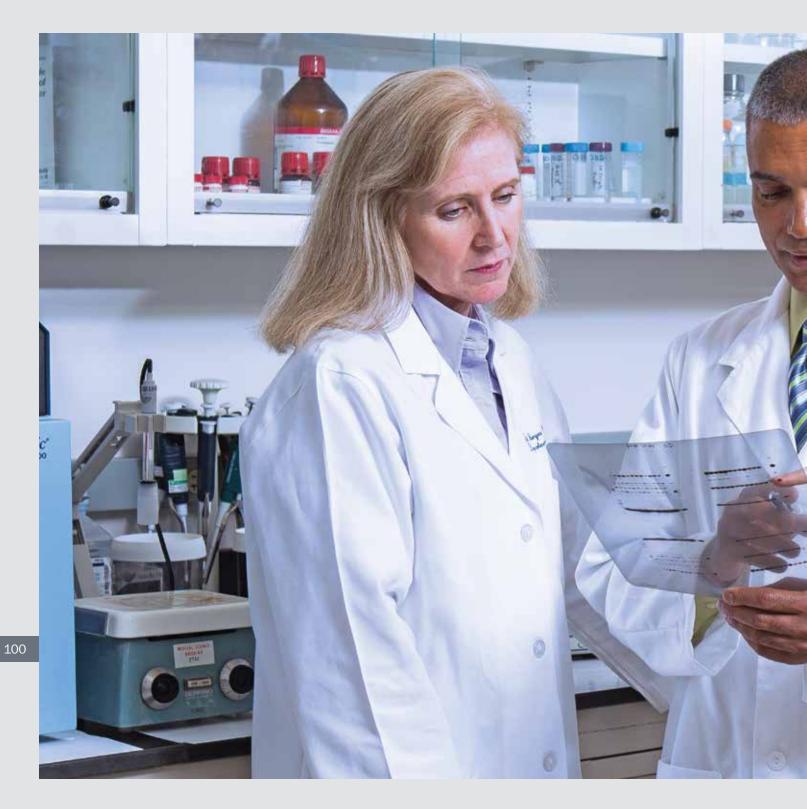


Multiple Sclerosis: Volume & Length of Stay (CMI Adjusted)





Research and Innovation





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

Research is supported by the National Institutes of Health, the Vivian L. Smith Foundation for Neurologic Disease, the American Stroke Association and other granting agencies. Investigations 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 2015-2016 fiscal year, researchers at the Institute and McGovern Medical School received more than \$10 million in 70 grants and contracts. The following listing is a sample of ongoing or recently completed research projects.

CEREBROVASCULAR

A Double-Blind, Multicenter Study to Evaluate the Efficacy and Safety of Alteplase in Patients with Mild Stroke: Rapidly Improving Symptoms and Minor Neurologic Deficits (PRISMS)

LEAD PHYSICIAN: Nicole R. Gonzales, M.D.

The primary objective of this study is to determine the efficacy of intravenous (IV) alteplase for treatment of acute ischemic stroke (AIS) in patients with mild stroke (also known as "minor neurologic deficit" and "rapidly improving stroke symptoms"), defined as a National Institutes of Health Stroke Scale (NIHSS) score \leq 5 and not clearly disabling, within 3 hours of last known well time.

Advanced Artificial Extracellular Matrix for Treatment of Chronic Stroke

PRINCIPAL INVESTIGATOR: Louise D. McCullough, M.D., Ph.D.

There is considerable evidence from both clinical and experimental studies that outcomes after stroke differ in males and females. New experimental data has shown that brain cells die differently in the male versus the female brain, and each sex responds differently to neuroprotective strategies. New sex-based treatments are being explored.

Clinical Trial Evaluating Carotid Revascularization (CAS or CEA) Plus Best Medical Management vs. Best Medical Management Only for Patients with Asymptomatic Internal Carotid Artery Stenosis (CREST-2)

LEAD PHYSICIAN: Nicole R. Gonzales, M.D.

CREST-2 is multicenter randomized, clinical trial designed to assess treatment differences between intensive medical management alone compared to revascularization (carotid endarterectomy or carotid artery stent) plus intensive medical management. Intensive medical management will involve control of blood pressure, LDL cholesterol, cigarette smoking and other vascular risk factors.



Cognitive Impairment in Mild Stroke

CO-INVESTIGATORS: Susan Alderman, Ph.D., RN, and Sean Savitz, M.D.

In this prospective study, researchers are identifying severity and predictors of impairment in patients with mild stroke.

Efficient Resource Utilization for Patients with Intracerebral Hemorrhage (EnRICH)

CO-INVESTIGATORS: Farhaan Vahidy, M.D., Ph.D., and Sean Savitz, M.D.

The goal of this study is to establish a prospective cohort of intracerebral hemorrhage patients and compare outcomes between patients managed at various levels of stroke care hospitals.

Endovascular Therapy for Acute Ischemic Stroke With Occlusion of the Middle Cerebral Artery M2 Segment

LEAD PHYSICIAN: Louise D. McCullough, M.D., Ph.D.

A pooled retrospective cohort of 500 patients enrolled at 10 centers was analyzed to evaluate EVT safety and effectiveness in M2 occlusions in a cohort of patients with acute ischemic stroke. The results of this study indicate patients treated with



EVT have 3 times the odds of a good outcome as those who received medical management (odds ratio [OR], 3.1; 95% Cl, 2.1-4.4; P<.001). Although a randomized clinical trial is needed to confirm these findings, available data suggest that EVT is reasonable, safe and effective for LVO of the M2 segment relative to best medical management.

Extracorporeal Filtration of Subarachnoid Hemorrhage via Spinal Catheter

LEAD PHYSICIAN: Spiros Blackburn, M.D.

In this pilot study, researchers are assessing the safety of rapid spinal fluid filtration using a lumbar drain catheter, which may lead to improved outcomes for patients with ruptured cerebral aneurysms.

Fetal Microchimeric Responses to Ischemic Stroke

PRINCIPAL INVESTIGATOR: Louise D. McCullough, M.D., Ph.D.

Events that occur during pregnancy can have lasting implications on both the mother and fetus for decades after parturition. In particular, fetal microchimerism, the bidirectional exchange and persistence of cells between a pregnant female and her fetus has been shown to play a role in various disease pathologies but has not been well studied in the brain. This study hypothesizes that microchimeric cells (MCs) home to sites of injury as part of the immune response to stroke and display a stem cell phenotype with potential to aid in repair.

Imaging Analysis Center of Stroke Patients in a Stem Cell Trial

CO-INVESTIGATORS: Sean Savitz, M.D., and Pan Narayana, Ph.D.

Through prospective analyses of imaging endpoints in a randomized, sham-controlled trial, researchers are testing the safety and efficacy of stem cells in stroke patients with chronic disability.

Immunomodulatory Effects of Inter-alpha Inhibitors in Attenuating Ischemic Stroke

PRINCIPAL INVESTIGATOR: David Sandberg, M.D.

Researchers in this prospective multicenter cohort trial are evaluating outcomes in children with probable isolated calvarial Langerhans cell histiocytosis.

Immunomodulatory Effects of Inter-alpha Inhibitors in Attenuating Ischemic Stroke

PRINCIPAL INVESTIGATOR: Louise D. McCullough, M.D., Ph.D.

Unfortunately, current stroke therapies approved for human use are very limited. Preliminary work performed in collaboration with Dr. Yow-Pin Lim using exogenously administered blood-derived human IAIP, has found that this agent is strikingly neuroprotective after experimental stroke, even when given six hours after ischemic onset to aged mice. This research project proposes to further explore the potential neuroprotective efficacy of IAIP to determine if this is a viable therapeutic target to develop as a treatment for ischemic stroke.

Improving Rapid Diagnosis of Posterior Circulation Stroke

CO-INVESTIGATORS: Jazba Soomro, M.D., and Amrou Sarraj, M.D.

This prospective study is designed to develop predictive models of posterior circulation stroke.

Intracerebral Hemorrhage Deferoxamine Trial (iDEF Trial)

LEAD PHYSICIAN: Tzu Ching Wu, M.D.

Investigators are collecting data on all telemedicinetreated stroke patients through the Lone Star Stroke Consortium Telestroke Network to understand how stroke care is delivered and how outcomes are achieved.



Longitudinal Imaging Assessments to Identify Markers of Stroke Recovery

CO-INVESTIGATORS: Sean Savitz, M.D., and Muhammad Haque, Ph.D.

This observational study is characterizing the natural history of recovery after stroke and identifying imaging markers and predictors of outcome.

Microbiota Manipulation to Enhance Stroke Recovery

INVESTIGATOR: Venugopal Reddy Venna, Ph.D. MENTOR: Louise D. McCullough, M.D., Ph.D.

This study investigates the role of age-associated changes in the microbiome in age-related diseases such as stroke. Preliminary findings suggest stroke ages gut microbiome and these changes influence stroke outcomes. In this project we are studying how manipulation of the gut biome can promote recovery after stroke and reduce the mortality.



Optimizing Patient Selection for Endovascular Treatment in Acute Ischemic Stroke (SELECT)

LEAD PHYSICIAN: Amrou Sarraj, M.D.

This prospective study is designed to develop predictive models of stroke patients' clinical and radiographic outcomes in acute ischemic strokes treated with endovascular therapy.

Psychosocial Stress and the Response to Stroke PRINCIPAL INVESTIGATOR: Louise D. McCullough, M.D., Ph.D.

Social isolation (SI) is associated with increased mortality and morbidity in patients with established vascular disease, including stroke. Emerging evidence from experimental and clinical studies show that isolation is not only a risk factor for stroke, but also contributes to increased stroke severity and delayed functional recovery. This research project investigates miRNAs that are differentially expressed after post-stroke isolation in aged males and females, and is attempting to determine common gene targets and attempt to block or mimic their effects.

R21: Regulation and Implication of Hemoglobin Clearance in Subarachnoid Hemorrhage

LEAD PHYSICIAN: Spiros Blackburn, M.D.

With funding from the National Institutes of Health, researchers are evaluating biomarkers related to hemoglobin breakdown in the CSF, and correlating these findings with cerebral vasospasm and clinical outcomes after aneurysmal subarachnoid hemorrhage.

Rejuvenating the Aging CNS: Reversing Age-Related Changes in Microglia Phenotype and Function

LEAD PHYSICIAN AND MENTOR: Louise D. McCullough, M.D., Ph.D. M.D./PH.D. TRAINEE: Edward (Ted) Koellhoffer

This research focuses on how microglia, the innate immune cells residing in our brains, transition from being a protective cell into a damaging pro-inflammatory cell with age. With funding from a NRSA fellowship awarded by the NIH, it has been identified that the aging brain has changes in the structure of some of its genes and that these changes determine how proteins are expressed (called epigenetic modifications). However, using unique animal models we have shown that these changes are actually reversible. We can "rejuvenate" older microglia to look and act like those of a younger individual. This project is now working to identify the factors in the blood responsible for these changes with age so that therapeutic intervention can be developed and improved outcomes in patients suffering from age-related diseases like Alzheimer's disease and stroke.

Restore: Droxidopa in Neurogenic Orthostatic Hypotension

LEAD PHYSICIAN: Raja Mehanna, M.D.

In this placebo-controlled trial, researchers are assessing the impact of droxidopa in neurogenic orthostatic hypotension.

Reversing Age Related Inflammation

PRINCIPAL INVESTIGATOR: Louise D. McCullough, M.D., Ph.D.

This study investigates and manipulates the mechanisms by which chronic inflammation impacts the response to ischemic stroke, the leading cause of long-term disability in the elderly. Experimental, clinical and epidemiological studies demonstrate that peripheral immune challenges lead to detrimental effects in the CNS such as sickness behavior and delirium. New treatments targeting ageassociated inflammation in ischemic injury are being explored in the laboratory. Findings from this preclinical work will be used to guide future investigations and target validation in stroke patients.

Role of MIF in Depression and Post-stroke Recovery

PRINCIPAL INVESTIGATOR: Venugopal Reddy Venna, Ph.D.

Clinical data suggests that older age and depression are risk factors for poor outcome in stroke patients, and the incidence of both stroke and depression increase with age. Aging is also associated with poor recovery and high mortality after stroke. We have found that macrophage migration inhibitory factor (MIF) levels decline with age, and mice with genetic deletion of MIF have a depressive phenotype at baseline, and have significantly impaired functional recovery after stroke compared to wild-type mice. This work will determine the role of MIF in post-stroke recovery and the mechanism by which aging and depression interact to contribute to impaired stroke recovery in animals, and in clinical samples from stroke patients.

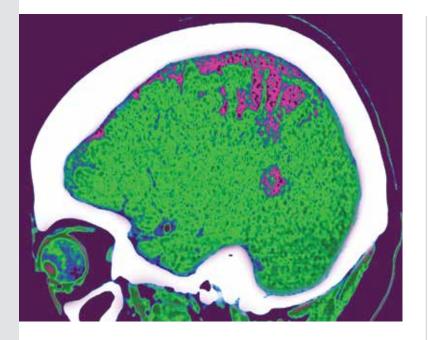
Role of P450 Aromatase After an Acute Ischemic Stroke

INVESTIGATORS: Louise D. McCullough, M.D., Ph.D., and Bharti Manwani, M.D., Ph.D.

This study investigates the contributions of sex steroids to the etiology of sex differences in stroke. We have measured sex steroid levels after ischemic stroke and found increased aromatase levels in post-menopausal women. Ongoing work is assessing correlation of functional outcomes after stroke with hormone (estrogen, testosterone and aromatase) levels in women and men with stroke.



RESEARCH



Sex Differences in Fat Inflammation, Diet-Induced Obesity and Stroke

LEAD PHYSICIAN AND MENTOR: Louise D. McCullough, M.D., Ph.D. POSTDOCTORAL TRAINEE: Hilda Ahnstedt

Stroke incidence is rising disproportionally in middleaged women, with rates increasing dramatically following menopause. Abdominal obesity is an important risk factor for stroke and is up to 10 times more common in women. This project studies sex differences in fat tissue and systemic inflammation with aging and how this affects outcome after stroke.

Sex Differences in Immune Responses to Hypoxic Ischemic Encephalopathy

PRINCIPAL INVESTIGATOR: Fudong Liu, M.D.

The innate immune response has a fundamental role in the pathophysiology of HIE. Microglial activation is regulated by the endogenous inhibitory signals, primarily CX3CL1/CX3CR1 signaling pathway. Recent studies have found that sexual dimorphism exists in microglia number, activation and expressed membrane receptors in the neonatal brain under normal conditions. It is hypothesized that microglia are differentially activated after HIE in male and female neonates, leading to differential immune responses and ischemic outcomes. These exploratory studies will lead to better understanding of sex-specific mechanisms underlying HIE and will help identify and optimize biological targets for therapeutic intervention in children.

Stroke-induced Respiratory Dysfunction: Effects of Age and Sex

LEAD PHYSICIAN AND MENTOR: Louise D. McCullough, M.D., Ph.D. PREDOCTORAL TRAINEE: Anthony Patrizz

This research project focuses on the effects of strokeinduced respiratory dysfunction on cognitive decline. In addition to determining the efficacy of pharmacologically targeting a specific brainstem respiratory control site to stabilize instability and ultimately improving post stroke cognitive outcomes.

Soluble CD163 as a Prognostic Marker for Perihematomal Edema Formation and Functional Outcomes in Intracerebral Hemorrhage

LEAD PHYSICIAN AND MENTOR: Louise D. McCullough, M.D., Ph.D. M.D./PH.D. TRAINEE: Meaghan Roy-O'Reilly

Intracerebral hemorrhage (ICH) injures the brain in two phases, initially via mass effect and secondarily via toxic blood products and subacute inflammation and edema formation. Macrophages are the predominant cell capable of removing toxic hemoglobin, and CD163 has been recognized as the hemoglobin scavenger receptor present on the macrophage cell surface. In this study, we explored the levels of soluble CD163 (sCD163) in the serum and cerebrospinal fluid (CSF) of ICH patients to ascertain whether sCD163 was associated with clinic-radiologic features and long-term functional outcomes.

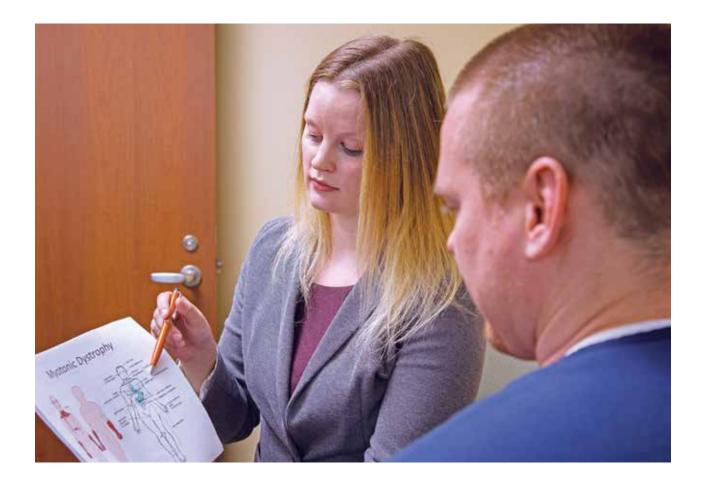
Targeting Perivascular Fibrosis to Prevent Cognitive Decline in Stroke Survivors

LEAD PHYSICIAN AND MENTOR: Louise D. McCullough, M.D., Ph.D. M.D./PH.D. TRAINEE: Matthew Howe

This study looks at how stroke induces progressive cognitive decline in older patients. This research shows that stroke induces widespread scarring and damage to the outer surface of cerebral small vessels, impairing their ability to circulate cerebrospinal fluid and remove toxic waste products from the brain. This could lead to neurodegenerative disease and cognitive impairment in stroke survivors. The ultimate goal of this research is to target the molecular and cellular mechanisms underlying this impairment, allowing for the development of new therapies to improve waste clearance, stabilize cognitive function and improve quality of life in stroke survivors.

The IRF5-IRF4 Regulatory Axis: A New Target for Stroke PRINCIPAL INVESTIGATOR: Fudong Liu, M.D.

Microglial activation is a key element in initiating and perpetuating innate immune responses to cerebral ischemia. Microglial responses are characterized as either M1, classical activation (pro-inflammatory), or M2, alternative activation (anti-inflammatory). This study hypothesizes that the IRF5-IRF4 regulatory axis balances the TLR4-MyD88-IRF5 and IL4R-Jmjd3-IRF4 pathways to direct microglial M1/M2 polarization after stroke, and that manipulation of the IRF5-IRF4 regulatory axis confers neuroprotection by suppressing/promoting pro-/ anti-inflammatory responses respectively. Manipulation of the IRF5-IRF4 regulatory axis in microglia/infiltrating leukocytes may help limit ischemic injury and promote tissue repair after stroke.



The Intra-arterial Vasospasm Trial

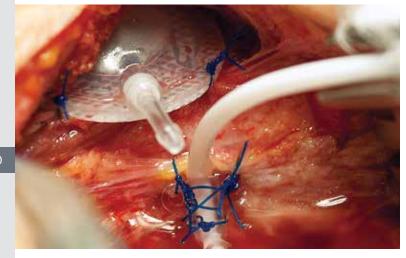
LEAD PHYSICIAN: Peng R. Chen, M.D.

The primary objective of the study is to determine the optimal intra-arterial (IA) drug treatment regimen for arterial lumen restoration post cerebral vasospasm following aneurysmal subarachnoid hemorrhage. The secondary objective is to evaluate clinical outcome at 90 days post discharge following optimal IA drug treatment for cerebral vasospasm. The researchers hypothesize that IA infusion of a combination of multiple vasodilators is more efficacious than single-agent treatment cerebral vasospasm therapy.

The Neuroprotective Potential of TGF-beta Activated Kinase Inhibition in Acute Stroke

PRINCIPAL INVESTIGATOR: Louise D. McCullough, M.D., Ph.D.

Outcomes after stroke differ in the elderly. Experimental studies are needed to test promising therapies in a variety of animal models before attempting to move them into clinical trials. New data from the bench has identified a novel signaling pathway involved in the response to stroke (TAK-1). This will be tested to see if inhibition of this pathway is protective in aging and will explore potential mechanisms for its protective actions using cell specific knockout models.



The Role of CaMK Cascade in Stroke

PRINCIPAL INVESTIGATOR: Jun Li, Ph.D.

It has been recently discovered that CaMKK signaling is an important contributor to the protection induced by the brain during injury. In this study, a focused investigation on the functional role of the CaMKK signaling pathway in stroke will be performed in an attempt to develop novel treatments for stroke.

The Role of GDF in Stroke Recovery

LEAD PHYSICIAN AND MENTOR: Louise D. McCullough, M.D., Ph.D. POSTDOCTORAL TRAINEE: Anjali Chauhan, Ph.D.

This project examines GDF, a rejuvenating factor, on stroke recovery in young and aged mice. Increasing GDF by the use of a monoclonal antibody enhances new neuron growth and survival after stroke.

The Stroke Transitions, Education, and Prevention (STEP) Clinic for Blood Pressure Reduction

LEAD PHYSICIAN: Anjail Sharrief, M.D.

In this randomized clinical trial, the primary objective is to evaluate the effectiveness of a multidisciplinary stroke clinic at improving blood pressure control after stroke.

The Treatment of Ischemic Stroke in Aged Populations: Sex-specific Targeting of the Neutrophil Response

LEAD PHYSICIAN AND MENTOR: Louise D. McCullough, M.D., Ph.D. M.D./PH.D. TRAINEE: Meaghan Roy-O'Reilly

This study will try to determine the influence of age and sex on the detrimental effects of infiltrating neutrophils following ischemic stroke. In addition, this study will determine the efficacy of specific anti-neutrophil monoclonal immunotherapy for the treatment of ischemic stroke.

CHILDREN'S NEUROSCIENCE

A High-resolution Near-infrared Pediatric Functional Brain Imaging System

LEAD PHYSICIAN: Manish Shah, M.D.

The major aim of this study is to develop a near-infrared imaging system to assess functional brain networks in children.

Combination Intraventricular Chemotherapy Pilot Study: Methotrexate and Etoposide Infusions into the Fourth Ventricle or Resection Cavity in Children with Recurrent Posterior Fossa Brain Tumors

LEAD PHYSICIAN: David I. Sandberg, M.D.

This study was recently approved by the IRB and an IND was granted from the FDA. Following up on the promising results from prior trials with single-agent infusions into the fourth ventricle, children (age 1 to 21 years) with recurrent malignant brain tumors that originated in the posterior fossa of the brain (including medulloblastoma, ependymoma and atypical teratoid/rhabdoid tumor) are eligible. Patients will receive simultaneous infusion of two chemotherapy agents, methotrexate and etoposide, into the fourth ventricle. Safety as well as disease responses will be assessed.

Infusion of 5-Azacytidine (5-AZA) into the Fourth Ventricle or Resection Cavity in Children with Recurrent Posterior Fossa Ependymoma: A Pilot Study

LEAD PHYSICIAN: David I. Sandberg, M.D.

Children with recurrent posterior fossa ependymoma are eligible for this study of 5-Azacytidine (5-AZA), which has been approved as an Investigational New Drug by the FDA . Participants will receive infusions of 5-AZA, a chemotherapy agent that targets DNA methylation, into the fourth ventricle or tumor resection cavity. Safety as well as disease responses will be assessed.



Phase I Study of Methotrexate Infusion into the Fourth Ventricle in Children with Recurrent Malignant Fourth Ventricular Brain Tumors

LEAD PHYSICIAN: David I. Sandberg, M.D.

Under an IRB-approved protocol, for the first time in humans, methotrexate is being infused into the fourth ventricle in patients with recurrent malignant fourth ventricular tumors (including medulloblastoma, ependymoma and atypical teratoid/rhabdoid tumor). Preliminary results of this study are extremely promising, as no patients have suffered any new neurological problems and some patients have had decreased tumor burden or stable disease after infusions.

The Use of Cryopreserved Human Umbilical Cord as a Skin and Dural Patch for In-utero Surgery in Children with Open Neural Tube Defects

INVESTIGATORS: Ramesha Papanna, M.D., Saul Snowise, M.D., Lovepreet Mann, Ph.D., Stephen A. Fletcher, D.O., and Kenneth Moise, M.D.

This study provides further analysis of the researchers' use of human umbilical cord for fetal surgery in patients who have cutaneous defects on the back too large to close by conventional means. An ovine and rodent model have enabled extensive experience with this technique; further refinements of technique and investigation into the understanding of the inflammatory mechanism are under way in the laboratory.

EPILEPSY

A Study of the Structure and Function of the Retina in Adult Patients with Refractory Complex Partial Seizures Treated with Vigabatrin (Sabril[®])

LEAD PHYSICIAN: Jeremy Slater, M.D.

The purpose of the study is to evaluate the change in visual fields by means of automated static perimetry and to evaluate the change in retinal structure by means of spectral domain optical coherence tomography (SD-OCT) in adult patients with refractory complex partial seizures (CPS) being treated with vigabatrin.



Diffusion Tensor and Functional Connectivity Imaging in Pediatric Epilepsy: Imaging/Histology Correlation

LEAD PHYSICIAN: Manish Shah, M.D.

This study is determining if diffusion tensor and functional connectivity magnetic resonance imaging are helpful in better understanding and diagnosing intractable epilepsy in children.

Exploring Sparsity and Spectral-temporal Decomposition in Real-time Network Modulation for Intractable Epilepsy

LEAD PHYSICIAN: Nitin Tandon, M.D.

The researchers are developing algorithms to capture the dynamic, frequency-dependent connectivity of the brain from real-time monitoring of the brain using electrocorticography, identifying the optimal parameters for the low-frequency electrical stimulation to modulate the connectivity of the epilepsy network with temporal and spatial precision.

Noninvasive Measurement of Vigabatrin-induced Changes in Brain GABA Levels Utilizing Magnetic Resonance Spectroscopy (MRS)

LEAD PHYSICIAN: Jeremy Slater, M.D.

The GABA-MRS trial is an attempt to use magnetic resonance spectroscopy to measure levels of different neurotransmitters in the brain before and after starting an anti-epileptic drug. The drug under study is vigabatrin (Sabril[®]), chosen because it blocks the breakdown of gamma-Aminobutyric acid (GABA) in the brain and, as a result, should trigger extremely high levels. Researchers know that too much excitation or too little inhibition can contribute to seizures in the brains of patients suffering from epilepsy. This study looks at levels of the inhibitory neurotransmitter GABA, the excitatory neurotransmitter glutamate and several others. Patients will have a baseline study; the study is repeated 6 hours after their first dose of the new drug, and then again after they have been taking the medication for 6 weeks.

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

LEAD PHYSICIAN: Jeremy Slater, M.D.

Researchers in this multicenter trial are obtaining baseline clinical outcome data (stage 1) upon which to base a subsequent study (stage 2) of the Model 106 VNS implantable pulse generator.

MEMORY DISORDERS AND DEMENTIA

Effect of Youthful Systemic Milieu on Alzheimer's Disease Pathology

PRINCIPAL INVESTIGATOR: Akihiko Urayama, Ph.D.

In this pilot study, researchers are investigating the effect of youthful systemic milieu on brain tau pathology. Prior studies found that young plasma is capable of rejuvenating the brain and other peripheral organs, including the liver, heart, and muscle. This study explores the potential mechanisms of young blood to ameliorate tauopathy. Ongoing studies include the assessments of the brain tau pathology, cytokine profiles in the plasma and cerebrospinal fluid from P301S mice receiving young blood. This study also looks at relating findings in the Tau model mice and clinical human samples, thereby developing a clinical research database and sample collection to move the field forward.

MOVEMENT DISORDERS AND NEURODEGENERATIVE DISEASES

ADAMAS PD302

LEAD PHYSICIAN: Erin Furr-Stimming, M.D.

The primary objective of this study is to evaluate the safety and tolerability of ADS-5102, an extended-release formulation of amantadine, administered at a dose of 340 milligrams once nightly at bedtime for the treatment of levodopa-induced dyskinesia (LID) in subjects with Parkinson's disease (PD). The secondary objective of this study is to evaluate duration of ADS-5102 effect on dyskinesia as assessed by the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part IV, and to evaluate the progression of Parkinson's disease as assessed by MDS-UPDRS Combined Score Parts I, II and III. Enrollment is closed.

An Open-Label, Long-term Safety Study of SD-809 ER in Subjects with Chorea Associated with Huntington Disease (ARC-HD)

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

In this study, researchers are evaluating the long-term safety and tolerability of SD-809 ER (deuterated analog of tetrabenazine). Investigators will look at what the body does to the study drug and whether the study drug lessens chorea in Huntington's disease. The study will also look at the general safety and tolerability of adjusting and maintaining the dose of SD-809 ER, as well as switching some people from tetrabenazine to SD-809 ER. Enrollment is closed.

Deep Brain Stimulation for Parkinson's Disease

LEAD PHYSICIAN: Albert Fenoy, M.D.

Investigators are studying the non-motor effects of deep brain stimulation to the subthalamic nucleus in Transgenic Hemizygous Parkin-Q311x9A mice to further characterize such behavioral changes before evident motor changes.

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

LEAD PHYSICIAN: Erin Furr-Stimming, M.D.

The primary objective of this worldwide observational, prospective, multicenter study is to improve our understanding of Huntington's disease (HD). Researchers are collecting information about cognition, behavior and motor function to estimate how HD progresses in patients; collecting blood samples and data to identify genetic and environmental factors that affect HD phenotype and disease progression; and promoting interrogatory studies that may provide clues to the pathogenesis of HD. Enrollment is open.

LEGATO-HD

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

In the LEGATO-HD trial, researchers are determining the effect of different doses of an investigational drug called laquinimod on people with Huntington's disease. In addition, information will be collected about the safety and possible side effects of laquinimod in people with HD.

National Device Product Surveillance Registry for DBS, ITB and Neural Stimulators

LEAD PHYSICIAN: Mya Schiess, M.D.

This worldwide registry creates a database for products, performance and outcome measures.

Pilot Phase I Study of Allogeneic Bone Marrow-derived Mesenchymal Stem Cell Therapy for Idiopathic Parkinson's Disease

LEAD PHYSICIAN: Mya Schiess, M.D.

In this FDA/IND-approved study, researchers aim to prove the safety of escalating doses of intravenously administered mesenchymal stem cells.

STEADY-PD III: Multicenter Study on the Effectiveness of Isradipine on Early Parkinson's Disease

LEAD PHYSICIAN: Mya Schiess, M.D.

In this randomized, placebo-controlled clinical trial, investigators are evaluating Isradipine in slowing the progression of Parkinson's disease.

SURE-PD: A Phase 3 Study of Urate Elevation in Parkinson's Disease

LEAD PHYSICIAN: Mya Schiess, M.D.

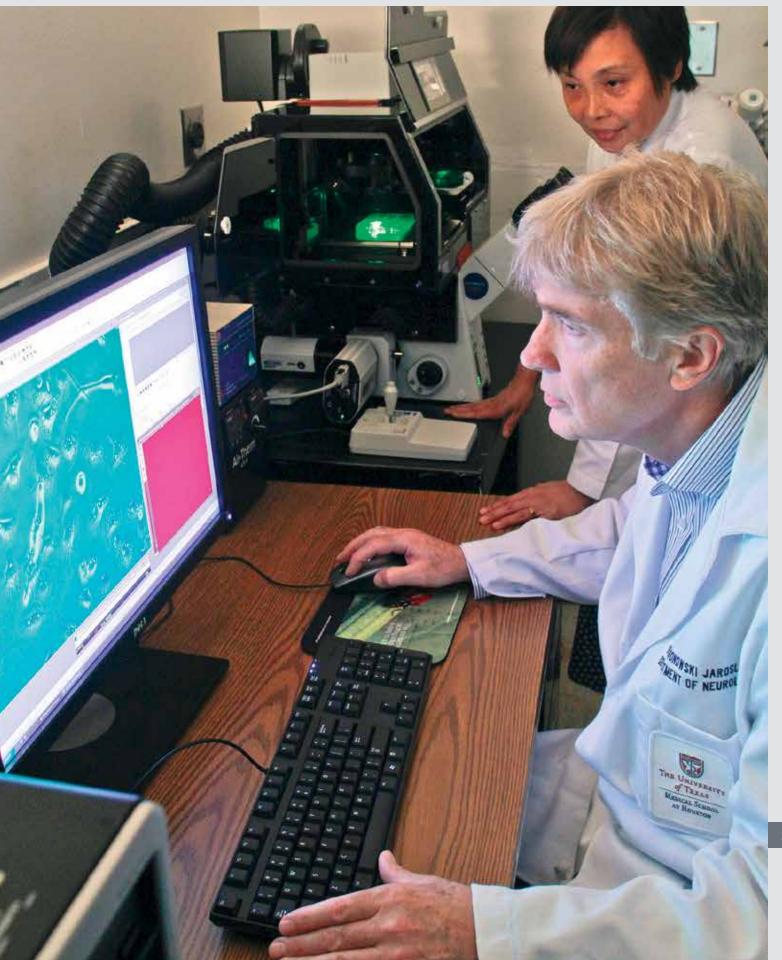
The major goal of this study is to show the effectiveness of uric acid in reducing the symptoms of Parkinson's disease, compared to placebo.

MULTIPLE SCLEROSIS

DTI-based Whole Brain Sulcal CSF is Associated with Cognitive Impairment in Multiple Sclerosis

LEAD PHYSICIAN: Flavia Nelson, M.D.

MS patients develop brain atrophy at a faster rate than healthy controls, and brain and cortical atrophy have been associated with cognitive impairment. In this cross-sectional NIH/NINDS- funded study a new diffusion tensor imaging (DTI) based approach, developed by Khader Hasan, Ph.D., in the department of Interventional and Diagnostic Radiology, to calculate brain and cortical atrophy, was found to correlate with measures of cognitive impairment in a study of 46 patients with MS. The study was presented at the American Neurological Association Meeting in Baltimore MD and will be highlighted by Medscape Neurology online. Keser et al., J Neuroimaging 2016;00:1-6. DOI: 10.1111/jon.12406.



Multiple Sclerosis-related Cognitive Impairment and Correlations with BOLD Activation by fMRI LEAD PHYSICIAN: Flavia Nelson, M.D.

Task-related fMRI studies of cognitive function in MS show more widespread patterns of blood oxygenation level-dependent (BOLD) activation in some cognitively non-impaired MS patients vs. HC, suggesting that functional reorganization may be an early adaptive mechanism to limit early cognitive impairment. In this study of 50 MS patients, a novel fMRI working memory paradigm was found to detect cognitive impairment based on magnitude of BOLD signal. These findings were validated by a Standard Neuropsychological Battery. Nelson et al. DOI: 10.1177/1352458516666186.

The Impact of Enhanced Cerebral Perfusion on the Evolution of Multiple Sclerosis Lesions

LEAD PHYSICIAN: John A. Lincoln, M.D., Ph.D.

Previous research by the investigators, led by Flavia Nelson, M.D., has shown that reduced small-vessel perfusion is



associated with gliotic lesions. The goal of the project, which is currently enrolling, is to determine if daily therapy with a generally well-tolerated oral medication that improves cerebral perfusion can repair previously formed and newly formed MS lesions, reducing irreversible neurological damage and disability.

NEUROMUSCULAR DISEASES

Fluorescently-tagged Anti-ganglioside Antibody Selectively Identifies Peripheral Nerve in Living Animals LEAD PHYSICIAN: Kazim Sheikh, M.D.

In this proof of concept study, researchers found implications that fluorescent conjugates of antiganglioside monoclonal antibodies (mAbs) are valuable delivery vectors to visualize nerves during surgery to avoid nerve injury and monitor nerve degeneration and regeneration after injury. These findings support that antibodies, and their derivatives/fragments, can be used as selective neuronal delivery vector for transport of various cargos to PNS in preclinical and clinical settings.

International GBS Outcome Study (IGOS): A Prospective INC Study on Clinical and Biological Predictors of Disease Course and Outcome in Guillain-Barré (GBS)

LEAD PHYSICIAN: Kazim Sheikh, M.D.

This study aims to identify clinical and biological determinants and predictors of disease course and outcome in individual patients with Guillain-Barré syndrome, as early as possible after the onset of disease. This information will be used to understand the diversity in clinical presentation and response to treatment of GBS. It will also be used to develop new prognostic models to predict the clinical course and outcome accurately in individual patients with GBS.

NEURO-ONCOLOGY

A Phase 2 Trial of SMO/AKT/NF2 Inhibitors in Progressive Meningiomas with SMO/AKT/NF2 Mutations

LEAD PHYSICIAN: Jay-Jiguang Zhu, M.D., Ph.D.

This study tests how well vismodegib, an SMO inhibitor, and the focal adhesion kinase (FAK) inhibitor GSK2256098 work in treating patients with meningiomas. FAK activity is related to NF2 gene mutation, which occurs in about 50 percent of patients; while SMO gene mutation is much rarer.

A Phase II/III Randomized Trial of Veliparib or Placebo in Combination With Adjuvant Temozolomide in Newly Diagnosed Glioblastoma With MGMT Promoter Hypermethylation

LEAD PHYSICIAN: Jay-Jiguang Zhu, M.D., Ph.D.

This randomized Phase II/III trial studies how well temozolomide and PARP inhibitor (veliparib) function compared to temozolomide alone in treating patients with newly diagnosed glioblastoma multiforme.

A Phase 2/3 Randomized, Open-Label Study of Toca 511, a Retroviral Replicating Vector, Combined With Toca FC versus Standard of Care in Subjects Undergoing Planned Resection for Recurrent Glioblastoma or Anaplastic Astrocytoma

LEAD PHYSICIAN: Jay-Jiguang Zhu, M.D., Ph.D.

This is a multicenter, randomized, open-label Phase 2/3 study of Toca 511 virus and Toca FC versus standard of care that comprises Investigator's choice of single-agent chemotherapy (lomustine or temozolomide) or bevacizumab administered to subjects undergoing resection for first or second recurrence (including this recurrence) of GBM or AA.

A Phase 1A/1B Study of FPA008 in Combination with Nivolumab in Patients with Selected Advanced Cancers LEAD PHYSICIAN: Jay-Jiguang Zhu, M.D., Ph.D.

This study plans to evaluate safety, tolerability, PK and clinical benefit of FPA008 in combination with nivolumab, both of which are monoclonal antibodies, in patients with six types of advanced cancers including glioblastoma multiforme.

A Phase III Randomized, Double-blind, Controlled Study of ICT-107 With Maintenance Temozolomide (TMZ) in Newly Diagnosed Glioblastoma Following Resection and Concomitant TMZ Chemoradiotherapy

LEAD PHYSICIAN: Jay-Jiguang Zhu, M.D., Ph.D.

Researchers are testing the efficacy of the ICT-107 vaccine in treating GBM. The vaccine is made from dendritic cells, prepared from autologous mononuclear cells that are pulsed with six synthetic peptides derived from tumor-associated antigens (TAA) present on glioblastoma tumor cells.

A Phase 3, Randomized, Controlled, Double-arm, Open-label, Multicenter Study of VB-111 Combined with Bevacizumab versus Bevacizumab Monotherapy in Patients with Recurrent Glioblastoma

LEAD PHYSICIAN: Sigmund Hsu, M.D.

The researchers are testing VB-111, a non-replicating adenoviral vaccine vector with anti-angiogenic properties.

A Phase 2 Dose-escalation Study of TPI 287 in Combination with Bevacizumab in Adults with Recurrent Glioblastoma

LEAD PHYSICIAN: Sigmund Hsu, M.D.

Open to bevacizumab-naïve patients with recurrent glioblastoma, this study is examining TPI 287, a taxane derivative with alkylating properties that work against tumor cells. A Phase III Clinical Trial Evaluating DCVax[®]-L Autologous Dendritic Cells Pulsed With Tumor Lysate Antigen for the Treatment of Glioblastoma Multiforme

LEAD PHYSICIAN: Jay-Jiguang Zhu, M.D., Ph.D.

The primary purpose of the study is to determine the efficacy of an investigational dendritic cell-generated vaccine called DCVax(R)-L in patients with newly diagnosed GBM for whom surgery is indicated.

A Randomized, Placebo-controlled Phase 2B/3 Study of ABT-414 with Concurrent Chemoradiation and Adjuvant Temozolomide in Subjects with Newly Diagnosed Glioblastoma (GBM) with Epidermal Growth Factor Receptor (EGFR) Amplification

LEAD PHYSICIAN: Sigmund Hsu, M.D.

This Phase 3 study is recruiting newly diagnosed GBM patients with tumor tissue that has EGFR mutation. The researchers are investigating the drug ABT-414, an EGFR antibody conjugated to anti-mitotic cytotoxin monomethyl auristatin F (MMAF).

Detection of Structural and Cognitive Changes in Patients with Gliomas Undergoing Chemoradiation

LEAD PHYSICIAN: Yoshua Esquenazi, M.D.

Researchers are using structural brain imaging to identify patients who are more susceptible to brain injury from chemoradiation.

Effect of NovoTTF-100A Together With Temozolomide in Newly Diagnosed Glioblastoma Multiforme (GBM)

LEAD PHYSICIAN: Jay-Jiguang Zhu, M.D., Ph.D.

This clinical trial, which has led to FDA approval of NovoTTF Optune device, is still active but not enrolling. Indium analysis results were published in the *Journal of the American Medical Association*.

Gamma Knife Stereotactic Radiosurgery for Focally Recurrent Glioblastoma

LEAD PHYSICIAN: Yoshua Esquenazi, M.D.

The goal of this study is to evaluate the efficacy, indications and outcomes of patients undergoing stereotactic radiosurgery for focally recurrent glioblastoma.

NEUROREHABILITATION

Comparison of Inpatient Neurorehabilitation at a Comprehensive Stroke Center with Community-based Facilities

LEAD PHYSICIAN: Nneka Ifejika, M.D.

A retrospective study of FIM efficiency in an integrated stroke model of care at a comprehensive stroke center versus community-based inpatient rehabilitation facilities.

Rehab MATRIX

LEAD PHYSICIAN: Nneka Ifejika, M.D.

This prospective quality project is designed to improve patient safety and healthcare quality through nurseidentified acuity variables on inpatient neurorehabilitation services.

NEUROTRAUMA/CRITICAL CARE

Application of Machine-learning Techniques to Improve Outcomes after Aneurysmal Subarachnoid Hemorrhage

LEAD PHYSICIAN: H Alex Choi, M.D.

Delayed cerebral ischemia is an important contributor to poor outcome after subarachnoid hemorrhage. Using machine-learning techniques with panels of inflammatory biomarkers, the researchers are developing methods to predict neurologic deterioration before it occurs.

Coagulation and Outcome from Acute Neurologic Injury Using Thrombelastography

PRINCIPAL INVESTIGATOR: Tiffany Chang, M.D.

This prospective, observational study will evaluate coagulation disturbances in the setting of intracerebral hemorrhage, subarachnoid hemorrhage and traumatic brain injury using thrombelastography.

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

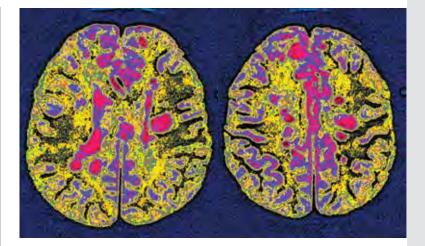
LEAD PHYSICIAN: Dong Kim, M.D.

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

Hypothermia for Patients Requiring Evacuation of Subdural Hematoma: Effect on Spreading Depolarizations

CO-INVESTIGATOR: Ryan Kitagawa, M.D.

This randomized, controlled trial for hypothermia for surgically evacuated subdural hematomas is currently under way. This support is for a supplemental study to determine the role of cortical spreading depolarizations in this patient population and the effects of hypothermia.



MISTIE III: Minimally Invasive Surgery Plus rt-PA for Intracerebral Hemorrhage Evacuation

LEAD PHYSICIAN: Tiffany Chang, M.D.

MISTIE III is Phase 3, randomized, multicenter clinical trial to evaluate the recovery of participants with intracerebral hemorrhage who receive minimally invasive surgery with r-tPA, compared to participants who receive standard medical care. This study is supported by the National Institute of Neurological Disorders and Stroke (NINDS).

Subarachnoid Hemorrhage Recovery and Galantamine (SAHRANG): A Randomized Clinical Trial of Galantamine for SAH

LEAD PHYSICIAN: H Alex Choi, M.D.

In this placebo-controlled randomized clinical trial, researchers are studying the safety of galantamine for the treatment of brain injury after subarachnoid hemorrhage. Preclinical studies have shown that galantamine is neuroprotective after acute brain injury. This study is the first to translate these promising results into human clinical trials. Treatment of Adult Severe Traumatic Brain Injury Using Autologous Bone Marrow Mononuclear Cells

LEAD PHYSICIANS: Charles Cox, M.D., and Ryan Kitagawa, M.D.

This study will assess the safety and functional outcomes following treatment of severe TBI in adults using autologous bone marrow mononuclear cells.

SPINE

Evaluation of Elective Spine Outcomes with a Clinical Registry

LEAD PHYSICIAN: Joseph C. Hsieh, M.D.

This project studies clinical outcomes for the most common cervical and lumbar elective spine procedures through use of a comprehensive spine registry with a focus on pain, patient satisfaction, quality of life, disability and functional status.

STEM CELL

Long Non-coding RNAs: Novel Regulators in Stem Cell Neural Differentiation and Candidates for RNA-based Therapy

PRINCIPAL INVESTIGATOR: Jiaqian Wu, Ph.D.

The major goal of this study is to investigate the functions and mechanisms of long non-coding RNAs (IncRNAs) in neural stem cell differentiation and neural cell fate determination.

Optimization of Tissue Engineering Matrices for SCI Treatment

PRINCIPAL INVESTIGATOR: Laura Smith Callahan, Ph.D.

The main objective of this study is to identify the optimal stiffness and bioactive signaling for n-cadherin and laminin to support human induced stem cell therapy treatments for spinal cord injury.

Patient-specific iPSC Neural Derivatives in Treating Spinal Cord Injury

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

The major goal of this study is to develop a combinatorial stem cell biology and genetic engineering strategy for potential treatment for acute and chronic spinal cord injury.

To Optimize the Scaffold for OPC Transplantation After Spinal Cord Injury

PRINCIPAL INVESTIGATOR: Laura Smith Callahan, Ph.D.

The main objective of this study is to identify the optimal bioactive signaling to support the transplant of oligodendrocyte progenitor cells for stem cell therapy treatments in the central nervous system.

OTHER

Deep Brain Stimulation for Treatment-resistant Depression

LEAD PHYSICIAN: Jair Soares, M.D.

Researchers are studying the effects of deep brain stimulation to the medial forebrain bundle in treatmentresistant depression patients in this clinical trial.

Deep Brain Stimulation for Treatment-resistant Depression in an Animal Model

LEAD PHYSICIAN: Joao Quevedo, M.D.

This study examines the effects of deep brain stimulation to the medial forebrain bundle in an animal model of depression, to elucidate involvement or modulation of the dopamine-reward pathway.

Development of Steerable Robotic Microcatheter Systems

LEAD PHYSICIAN: Daniel H. Kim, M.D.

The aim of this research is to develop state-of-art steerable robotic microcatheters for treating lifethreatening conditions such as cerebral stroke. Through tele-robotic capabilities, our patients can be treated remotely when living in areas of the world where special surgical procedures are not otherwise readily accessible.

Development of Surgical Robots for Microsurgery

LEAD PHYSICIAN: Daniel H. Kim, M.D.

The aim of this research is to develop minimally invasive microsurgical robots to perform surgical procedures in delicate regions of the body that cannot be accessed by current technology, such as the brain, or in pediatric populations as well as fetal procedures.

Reward Expectation in the Subthalamic Nucleus

LEAD PHYSICIAN: Albert Fenoy, M.D.

Investigators are recording local field potentials during intra-operative microelectrode recording in the subthalamic nucleus during a reward application paradigm, and analyzing of differences between anticipation, rewarded and unrewarded cued responses.

The American Registry for Migraine Research

LEAD PHYSICIAN: Mark Burish, M.D., Ph.D.

In collaboration with the Mayo Clinic and the American Migraine Foundation, researchers in this nationwide study are recording headache characteristics and collecting blood samples from patients with migraine and other headache disorders. UTHealth is the second site to be activated.



Treating Neuropathic Pain by In Vivo Reprogramming of Astrocytes After SCI

PRINCIPAL INVESTIGATOR: Qilin Cao, M.D.

Researchers are testing whether reprogramming pronociceptive reactive astrocytes into antinociceptive GABAergic interneurons will attenuate SCI-neuropathic pain.

Will Erwin Headache Research Center Study of Cluster Headache

LEAD PHYSICIAN: Mark Burish, M.D., Ph.D.

In collaboration with several scientists across the city of Houston, this study investigates headache mechanisms to find new targets for the treatment of cluster headache.

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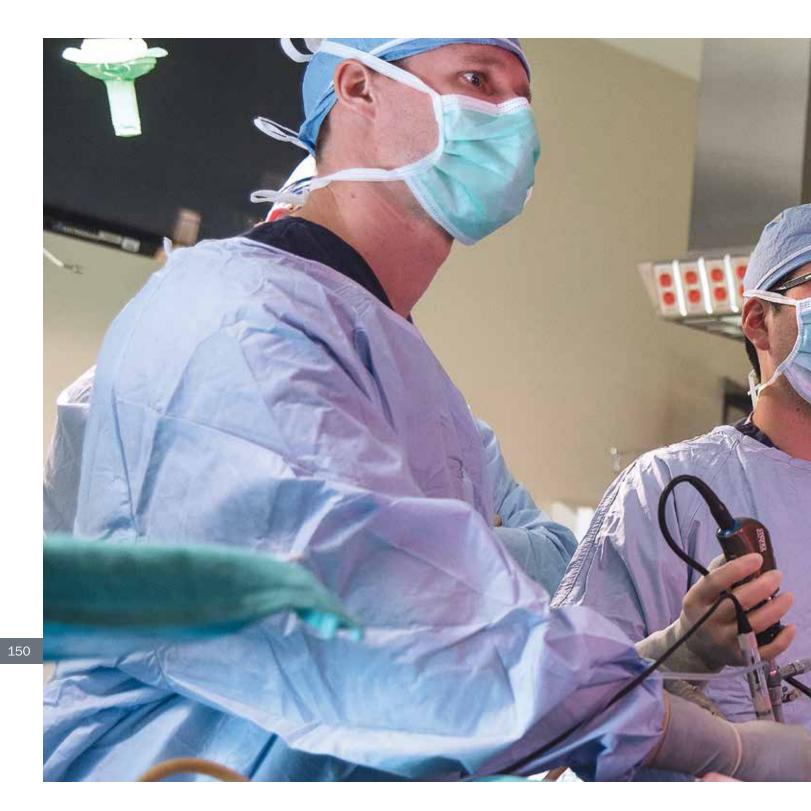
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Patient Stories





Maria Flores: Defying the Odds

For those diagnosed with glioblastoma multiforme (GBM), one of the most common and deadly types of malignant brain tumors, the outlook for long-term survival can be devastatingly grim. The average life expectancy after diagnosis hovers near 15 months, and the five-year survival rate is less than 4 percent. But for 57-year-old Maria Flores, succumbing to the disease without a fight was not an option. Her loved ones say that through her strong faith, positive outlook and the exceptional care she has received at the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center, she is still here today – an astounding seven years after her original diagnosis.

In December 2009, the sudden onset of a crushing headache brought Flores to the emergency center at Memorial Hermann-Texas Medical Center, where an MRI revealed a mass that was consistent with GBM. The next day, Dong Kim, M.D., director of Mischer Neuroscience Institute and chair of the Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth, performed surgery to remove the tumor.

"These tumors are extremely infiltrative and aggressive. The more tumor we can remove surgically, the better the prognosis," says Jay-Jiguang Zhu, M.D., Ph.D., a neurooncologist at Mischer Neuroscience Institute who has overseen Flores' care since her diagnosis. "All visible areas of the tumor, including the core, were removed during surgery. However, with GBM, there are surrounding cells that remain beyond detection." Chemotherapy and radiation are the standard treatments for most patients following surgery to shrink the tumor and prevent further tumor progression. After a successful surgery, chemotherapy and radiation, Flores remained stable without evidence of GBM until January of 2013 when an MRI showed tumor activity once again. This time, she underwent Gamma Knife stereotactic radiosurgery, performed by Angel I. Blanco, M.D., director of radiation oncology and stereotactic radiosurgery at Mischer Neuroscience Institute. Mischer Neuroscience Institute has successfully treated more than 3,400 patients since acquiring the region's first Gamma Knife in 1993.

"After the Gamma Knife, we used a combination of three different chemotherapy drugs, which included bevacizumab, irinotecan and temozolomide, versus the standard one-drug treatment, with the total treatment cycle taking a little over a year," Dr. Zhu says. "Mrs. Flores tolerated the treatment very well. She's a strong, determined and positive woman, and wanted to treat her GBM as aggressively as possible."

In February 2016, Flores successfully underwent a second surgery by Dr. Kim after an MRI revealed tumor progression yet again. "This is the pattern of this disease, and why GBM patients must be closely monitored," Dr. Zhu says. "We conduct an MRI every two months, and I review the results very carefully with the multidisciplinary team on our tumor board, and then again with Mrs. Flores during every visit." Surprisingly, pathology reports after her surgery showed no active GBM tumor cells in the tissue removed, according to Dr. Zhu, and the reason why remains a mystery – although a welcome one.

"Mrs. Flores tolerated the treatment very well. She's a strong, determined and positive woman, and wanted to treat her GBM as aggressively as possible."

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"Mrs. Flores' case is very unique in that she has tolerated treatment so well," he adds. "Perhaps her genes give her a better prognostic disposition, but in any case, she is unflappable and unwavering in her positive attitude, and she has refused to be intimidated by this diagnosis." Flores' daughter-in-law and husband, both of whom accompany her to every appointment, agree wholeheartedly. "She's very smart, very brave and is definitely a survivor," says her daughter-in-law Paulina. "Throughout all of this, she has carried on with her life, continuing to cook and do all the things she loves." As for Flores, her explanation of defying the odds are decidedly more humble. "How lucky am I to have found Dr. Kim, Dr. Blanco and Dr. Zhu," she says. "I am truly blessed."

Riley Lentz: No Stone Unturned

Fifteen-year-old Riley Lentz is no stranger to hospitals. Diagnosed with malignant medulloblastoma in 2008, she underwent two open brain surgeries to remove the tumor and later, two non-invasive radiosurgical CyberKnife[®] procedures. When the tumor recurred in 2013, she was given high-dose chemotherapy and received a stem cell transplant to help her body bounce back after the infusions.

"After the chemo, we went until April or May of 2015 before they found another small spot and opted to try the CyberKnife for the second time," says Riley's mother, Melissa Saban. "At her three-month follow-up MRI, we learned that the procedure didn't help."

Somewhere along the way, Saban joined a Facebook group called Parents of Kids with Medulloblastoma, a forum for parents who want to share their knowledge and experience. "I had heard about a clinical trial of direct infusion of chemotherapy into the fourth ventricle around the time Riley had the stem cell transplant in 2013," she says. "After her oncologist told us her body wouldn't tolerate any more systemic chemo, I started looking for other options. I was fortunate to find another parent on the Facebook page whose child had just finished the clinical trial in Houston."

Through Parents of Kids with Medulloblastoma, Saban connected with Marcia Kerr, RN, CCRC, research coordinator for pediatric neuroscience at McGovern Medical School at UTHealth. Among the trials Kerr coordinates is one led by David I. Sandberg, M.D., FAANS, FACS, FAAP, director of pediatric neurosurgery at Children's Memorial Hermann Hospital, the Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center, and the McGovern Medical School.

Before his arrival in Houston in 2012, Dr. Sandberg conducted translational studies that demonstrated the safety of infusing chemotherapeutic agents directly into the fourth ventricle to treat children with recurrent malignant brain tumors in this location. The promising results of those studies led to a pilot clinical trial completed in August 2015 and a new methotrexate dose-escalation study available only at Children's Memorial Hermann Hospital in collaboration with the Mischer Neuroscience Institute.

"Delivering chemotherapeutic agents directly to the site of disease minimizes the side effects for children like Riley by decreasing systemic drug exposure," says Dr. Sandberg, an associate professor with dual appointments in the Vivian L. Smith Department of Neurosurgery and the Department of Pediatric Surgery at McGovern Medical School. "After we determined that methotrexate can be infused into the fourth ventricle without causing neurological toxicity, and that some patients with recurrent medulloblastoma experience a beneficial anti-tumor effect both within the fourth ventricle and at distant sites, our next step was a dose-escalation study to determine the optimum dose of the agent."

Riley was among the first participants enrolled in the clinical trial at Children's Memorial Hermann Hospital, the only such study under way in the world. In a surgery that

"Riley came to us from Arkansas and had a dramatic response. Her parents are unbelievably dedicated, leaving no stone unturned to help their daughter."

PATIENT STORIES

took place on Nov. 3, 2015, Dr. Sandberg removed as much of the tumor as possible and placed a reservoir for the direct delivery of chemotherapy – a catheter and plastic disk covered by a rubber balloon underneath the skin at the back of Riley's neck.

Riley and other children who participate in the trial undergo three cycles of chemotherapy and an MRI before and after treatment. Each cycle includes an infusion on Monday and Thursday for three weeks, followed by a rest week.

Over the next three months, Saban and her former husband, Jeff Lentz, made the 16-hour round trip twice a week from their home in Greenbriar, Arkansas, to Houston. "Riley's dad didn't want me to make the trip alone," she says. "Both of us have remarried and have other kids, which made it difficult to find childcare that would allow us to stay in Houston during Riley's treatment. So we chose to drive down and back the same day."

On January 29, 2016, just before Riley completed the clinical trial, Saban posted an update on her Facebook page. "The treatment is working – THE TUMOR IS ALMOST COMPLETELY GONE!!!!! The plan is to continue the same treatment and then start another round at Arkansas Children's Hospital. We are beyond excited!!!!"

"Once we've shown that the treatment is safe and the child is responding to it, we're happy if we can find a pediatric oncologist to continue it," Dr. Sandberg says. "Riley came to us from Arkansas and had a dramatic response. Her parents are unbelievably dedicated, leaving no stone unturned to help their daughter, including making the 16-hour round-trip drive to Houston twice a week. They're good people, and Riley is the sweetest kid. We're thrilled to get this kind of positive response to the treatment without the toxicity of systemic chemotherapy, and we're grateful to Riley's oncologist for continuing the treatment in Little Rock."

Saban describes the family's experience in Houston as very positive. "I loved Dr. Sandberg," she says. "He's personable and caring and extremely passionate about what he's doing to help kids. And he was great with Riley."

As for Riley, she takes it all in her stride. "We've been fighting cancer for so long that it's become a part of her daily life," Saban says. "We've always been honest with her, and we always listen to what she tells us. She's never said, 'Okay, I'm done with this.' She takes it with a grain of salt and is doing amazingly well considering how much she's been through and how different her life is from the lives of other kids. And the tumor is almost gone! What Dr. Sandberg is doing is working."

For more information about the clinical trial, visit neuro. memorialhermann.org/research/brain-tumor/phase-istudy-of-methotrexate-infusion-into-the-fourth-ventriclein-children-with-recurrent-malignant-fourth-ventricularbrain-tumors, or contact Marcia Kerr at 713.500.7363 or via email at marcia.l.kerr@uth.tmc.edu.

Robin Schroeder: Woman on Fire

Opportunity often arrives disguised as misfortune. After Robin Schroeder was diagnosed with multiple sclerosis, she set out to ride the MS 150, a two-day cycling event organized by the National MS Society to raise funds for research. Her success led to an even greater accomplishment.

"I'd never done anything that athletic before," says the 38-year-old, who started training in 2013 for the 2014 Houston-to-Austin ride. "But when April rolled around, I wasn't where I needed to be in terms of endurance and was having a lot of trouble building muscle."

Schroeder continued to train with an eye on the 2015 ride, without making any real progress toward her physical goals. When her neurologist stopped seeing patients in 2014, she found her way to the office of Philip Blum, M.D., a general neurologist with Patient Centered Neurology at Mischer Neuroscience Associates. Dr. Blum has specialty interests in electromyography, nerve conduction studies and neuroimmunology, as well as diseases of the peripheral nervous system like chronic inflammatory demyelinating polyneuropathy (CIDP) and central nervous system diseases like MS.

"Robin is an outgoing and energetic person, and when she came to us, she was losing the ability to realize her dreams," Dr. Blum says. "We listened to her goals, reviewed her medical records, did a thorough physical exam and discovered that the symptoms preventing her from meeting her goals were related not to MS but to her medication." Schroeder was taking teriflunomide, a once-daily tablet prescribed to treat relapsing-remitting MS. "Dr. Blum and I were willing to try going without medication for a few months because I hadn't had an MS attack in a while," she says. "He prescribed a medication to flush the teriflunomide out of my body, but after a month without medication my body was not reacting well. So we switched to monthly intravenous steroids to keep my white cell count under control so I could continue to train and build muscle."

Schroeder signed up for the Houston MS 150 in April 2015. When day one of the bike ride was canceled due to weather conditions, she registered for the Amarillo MS 150, scheduled for July.

"It was an amazing experience," she recalls. "I did the whole ride and it went great – and it's really hot in Amarillo in July. To be able to get to the point where I could do it was a very emotional and rewarding experience."

After Amarillo, Schroeder returned to her normal workout routine and set her sights on competing in an Ironman 70.3 in the fall of 2016 – a 1.2-mile open water swim, 56-mile bike ride and a 13.1-mile run. Around the same time, Dr. Blum switched her medication to daily injections of glatiramer acetate, hopeful that it wouldn't interfere with her ability to build muscle. She started training in January 2016, allowing herself nine months.

PATIENT STORIES

"I couldn't swim, so I had to take swimming lessons. I'd never run more than a 5K so I had a lot of building up to do. I set my mind to it, and nothing was going to stop me," she says.

In June, during a sprint triathlon – a quarter of the Ironman 70.3 – she had a panic attack in open water and failed to finish. In July, she competed in an Olympic triathlon – 50 percent of the Ironman 70.3.

"I finished it – the first triathlon I'd ever finished," she says. "The open water swim was in a river. I was nervous but I did it, and that motivated me to keep progressing with my training."

By August of 2016, she was working out 30 hours a week. On glatiramer acetate, she was able to build even more muscle than she'd built while training for the MS 150.

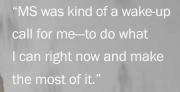
The Ironman 70.3 was held in September in Augusta, Georgia. She describes it as "a really hard day but not because of MS." She lost a contact during the open water swim, was bitten by fire ants, and hit a bump on her bicycle and lost all of her race nutrition. "But I finished every inch of it, and that's what I set out to do," she says. "There's no way I could have done that before I met Dr. Blum."

Late last fall, Schroeder wore her Ironman medal to a routine physician office visit. "I got some looks in the waiting room, but I was so excited that I wanted to show Dr. Blum. I'd been working for so long to achieve the goals I set for myself. I pushed myself to do things I'd never done before. MS was kind of a wake-up call for me – to do what I can right now and make the most of it."



For his part, Dr. Blum believes that success in treating MS lies in never presuming that symptoms can't be controlled without a thorough investigation of the case.

"Robin deserves most of the credit because she was very clear about her goals," he says. "We pride ourselves on helping patients achieve the goals they've set for themselves. As soon as we know their priorities, we start to work on improving their quality



of life. When I saw her again after she completed the Ironman competition, she was very fit and all smiles. She had really blossomed." Schroeder's husband, Craig, completed the Houston MS 150 in 2016, the year after her successful Amarillo ride. In 2017, their daughter Avianna will be 12, the minimum sign-up age for the MS 150, and the family will ride together for the first time.

EST.1978

"I don't know what the future holds for me medically, but my life has changed for the better since I learned I have MS," she says. "I can't say enough about Dr. Blum. From my first visit with him it was all about what I could do, not what I couldn't do. The focus was on how to make it happen. I consider myself very lucky to have found a great MS doctor."

Photographed by Katherine DeVillier

Alan Benson: A Successful Nonsurgical Fix for Back Pain

Alan Benson had suffered from very painful sciatica for six long weeks by the time he arrived in the office of interventional pain management specialist Divya Chirumamilla, M.D. He came by way of Geoffrey Zubay, M.D., FACS, a board-certified neurosurgeon with fellowship training in complex spinal reconstructive surgery. The two physicians work together at Mischer Neuroscience Associates-The Woodlands to ensure their patients access to fast, comprehensive spine care with effective pain management.

In Benson's case, "fast" is the first operative word. Last fall, he saw Dr. Zubay on Oct. 4 and was evaluated by Dr. Chirumamilla the following day. One day later, on Oct. 6, she performed a fluoroscopically guided transforaminal epidural injection of a long-acting steroid between his third and fourth lumbar vertebrae, the location of a herniated disk. The procedure was done at Memorial Hermann Surgery Center-The Woodlands.

"I've worked in public service for 37 years and recognize compassion when I see it," says Benson, who is 60. "Dr. Zubay believed I was a candidate for the most conservative treatment possible, and Dr. Chirumamilla concurred. She explained exactly what she would be doing during the office visit, and then dropped in and visited with me again before the procedure while a nurse was taking my vital signs. The procedure went like clockwork, and she saw me again when they took me to recovery to check my blood pressure. Considering her background and high level of training, I didn't expect that kind of exemplary doctor-patient interaction." Fellowship trained in pain medicine, Dr. Chirumamilla is a Diplomate of the American Board of Anesthesiology, with primary certification in anesthesiology and subspecialty certification in pain medicine. She joined Mischer Neuroscience Associates from Harvard Medical School, where she served as clinical faculty in the department of Anesthesia, Critical Care and Pain Medicine.

To her, compassion is second nature. "I talk to all of my patients about the risks of procedures and ask them if they have any questions beforehand. Not all of it sinks in so I also spend time with them the day of surgery to make sure they have a good understanding of the procedure," she says. "I use a lot of numbing medication to avoid anesthesia and its associated risks, so I like to see them after the procedure in recovery to make sure they're doing okay before they head out."

Benson's pain was relieved after the first injection, but when he returned for a follow-up visit in November, he had some lingering discomfort. A second injection resolved it; going forward, Dr. Chirumamilla will see him on an as-needed basis.

"For Alan things worked out really well," she says. "As a multidisciplinary spine care group, we try to make it as easy as possible for our patients. Alan's case was particularly fast. For other patients we work to get treatments scheduled as quickly as possible within the limitations of insurance authorizations.

"I've worked in public service for 37 years and recognize compassion when I see it. Dr. Zubay believed I was a candidate for the most conservative treatment possible, and Dr. Chirumamilla concurred."

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PATIENT STORIES

"Dr. Zubay does the initial evaluation. If he feels they will respond to conservative management, he refers them to me," she adds. "I do an evaluation from the pain management perspective and develop an appropriate treatment plan. We work closely together, and our teams communicate well."

Benson, an avid golfer, has returned to his active lifestyle. "The whole experience was so positive for me that I wrote Dr. Chirumamilla a personal note to thank her and her staff," he says. "I was in so much pain that I was actually excited to have the opportunity to have a needle stuck into my spine. It's not something I'd wish on anyone, but if you do have back pain, you can expect a good experience with her."

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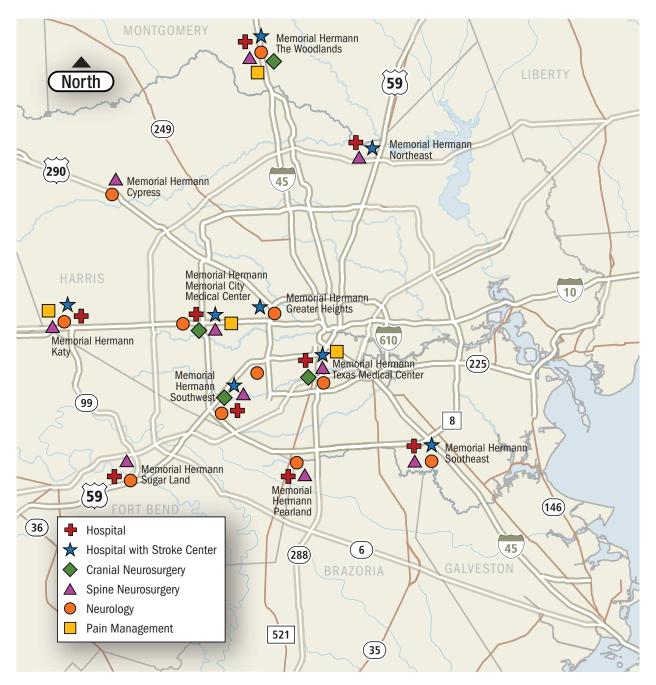
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The physicians and researchers at the Mischer Neuroscience Institute stand at the threshold of breakthrough discoveries that will transform how to treat and cure neurological diseases and disorders. In partnership with the philanthropic community,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

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

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



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