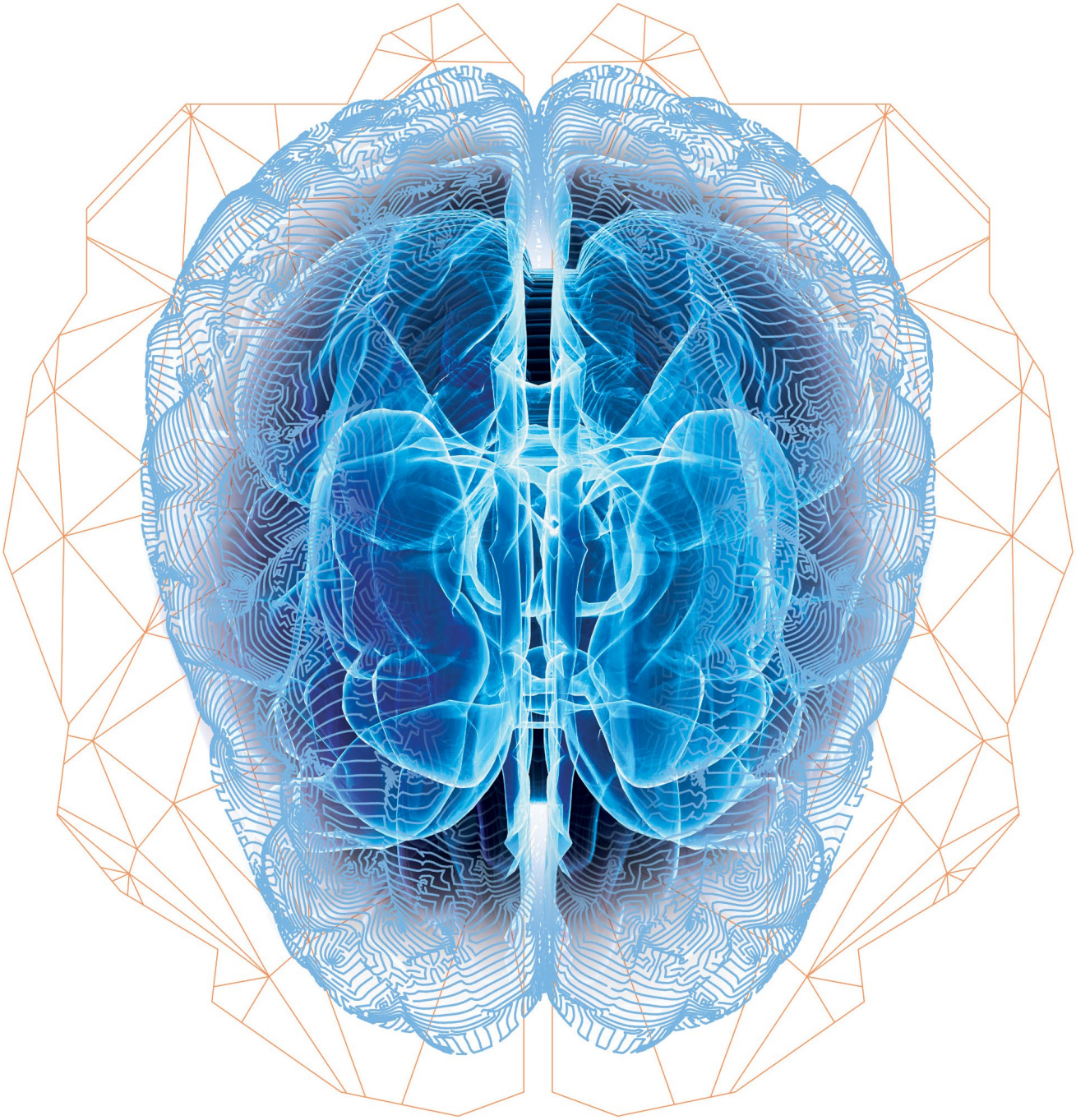
UTHEALTH NEUROSCIENCES

OUTCOMES REPORT 2020



UTHealth®
Neurosciences
The University of Texas Health Science Center at Houston

Outcomes Report 2020

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2020 was an unprecedented year, and the world of health care was no exception. To reduce the risk of COVID-19 infection to patients and clinicians and conserve critical resources, most hospitals in the U.S. enacted periodic temporary bans on elective surgeries resulting in drastic reductions in patient volumes. At the same time, many people postponed non-emergent procedures, such as those for brain tumors, deep brain stimulation, spine surgeries, and pain management procedures. We also saw an increase in patients delaying or avoiding emergent care for conditions like stroke, due to fear of contracting COVID-19. Across the nation, these factors contributed to lower volumes and reduced patient care. You will see this decline reflected in the 2020 data we present for these conditions.

According to the *Harvard Business Review*, deferment of medical care has had a broad impact on the national economy, as "approximately half of the annualized 4.8% decline in the U.S. gross domestic product in the first quarter of 2020 is attributed to health care services, especially delayed elective procedures."

Thankfully, for the people in our community, we have seen a rebound as patients return to us for care.

[1]Jain A, Dai T, Bibee K, Myers CG. Covid-19 Created an Elective Surgery Backlog. How Can Hospitals Get Back on Track? Harvard Business Review. 2020 Aug 10.

Forward Together

Greetings from UTHealth Neurosciences and best wishes for a healthy 2021. In spite of COVID-19, 2020 was a year of growth for us. We brought together two departments at McGovern Medical School at UTHealth, both of which have rich histories of accomplishment in clinical care, teaching, and research: the Department of Neurology and the Vivian L. Smith Department of Neurosurgery. In the process, we streamlined operations and improved efficiency to better serve our patients.

UTHealth Neurosciences now has 141 clinical providers at 15 locations across Greater Houston, 41 research faculty based primarily at the Texas Medical Center, and robust residency and fellowship programs training 113 physicians and physician-scientists. We continue to deliver excellent outcomes for our patients, as evidenced by the mortality and length of stay data you'll see in this report.

In 2019, the Department of Neurosurgery was ranked No. 8 nationally in research funding awarded by the National Institutes of Health to neurosurgery departments, based on data compiled from the NIH Research Portfolio Online Reporting Tools by the Blue Ridge Institute for Medical Research. The Department of Neurology was also ranked No. 22 nationally, and our combined departments have an annual budget of $31 million. Our congratulations to Claudio Soto, PhD, professor and director of the George and Cynthia W. Mitchell Center for Alzheimer's Disease and Other Brain-Related Illnesses, and to Georgene Hergenroeder, PhD, associate professor in the Department of Neurosurgery and director of the Innovation and Quality (IQ) Program at UTHealth Neurosciences, both of whom ranked high in NIH research funding. Soto is No. 6 among principal investigators of NIH-funded clinical science research studies in neurology, and Hergenroeder is ranked No. 7 in NIH funding for all neurosurgery research funding.

This year's outcomes report gives perspective on the strength, depth, and breadth of UTHealth Neurosciences. GQ Zhang, PhD, Samden Lhatoo, MD, and Nitin Tandon, MD, are using big data to expand our patient care footprint, creating a new clinical care and research paradigm for our group. We have redefined fast treatment for acute stroke by creating a citywide network of accessibility for patients. Along with the downside of COVID-19, the pandemic has given us an opportunity to communicate with our patients in new and more convenient ways, thanks to robust technological support from UTHealth.

Our team of clinicians and scientists at UTHealth Neurosciences has taken us well down the road to our destination: to be the premier provider of neurosciences services in the nation. We are grateful to our providers, researchers, staff, and patients for pulling together during the pandemic to make all this possible.

With best wishes,

Louise D. McCullough, MD, PhD

Professor and Chair, Department of Neurology
Roy M. and Phyllis Gough Huffington Distinguished Chair
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Co-Director, UTHealth Neurosciences

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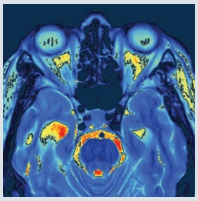
World-Class Neuroscience with Exceptional Patient Experiences



UTHEALTH NEUROSCIENCES has a long-standing reputation for innovation, high-quality outcomes, and the best possible health care experiences, which draws patients from around the world. Our clinicians, researchers, and educators are nationally recognized as leaders in medicine and consistently ranked by quality benchmarking organizations as leaders in clinical quality and patient safety. Their insights, technological innovations, and success at bringing research findings to the bedside quickly are helping to transform neuroscience.

Our clinician team is part of McGovern Medical School at UTHealth. We are Houston's undisputed leader in neuroscience care and the foremost neuroscience provider in the southern half of Texas. We have extended our continuum of care by creating a citywide network of neurologists, neurosurgeons, neurointerventionalists, neuro-oncologists, radiation oncologists, interventional pain management specialists, neurocritical care physicians, neuropsychologists, and advanced practitioners. By building a new structure for the practice of neurology in the community, we have reduced referral wait times. Our clinicians in Houston's suburbs analyze quality data and track outcomes as a group using the same standards employed by their counterparts at UTHealth Neurosciences locations in the Texas Medical Center. We continually modify our clinical practice to ensure exceptional patient experiences.

For 13 years, our physicians have reported mortality rates well below the national expected benchmark, with a 50 percent reduction in length of stay, despite the increased acuity of our patients. Through the Innovation and Quality (IQ) Program, the Texas Institute for Restorative Neurotechnologies, and other initiatives, our leaders are organizing data to improve physician and service performance. We're also measuring quality and tracking long-term outcomes through clinical trials, and using big data – the enormous amount of information available in the medical datasphere – to advance patient care.

At a Glance

PHYSICIAN TEAM

Staff Physicians	**104**
Clinical Residents and Fellows	**113**
Medical Students on Rotation	**315**
Research Fellows	**41**
Advanced Practice Providers	**37**

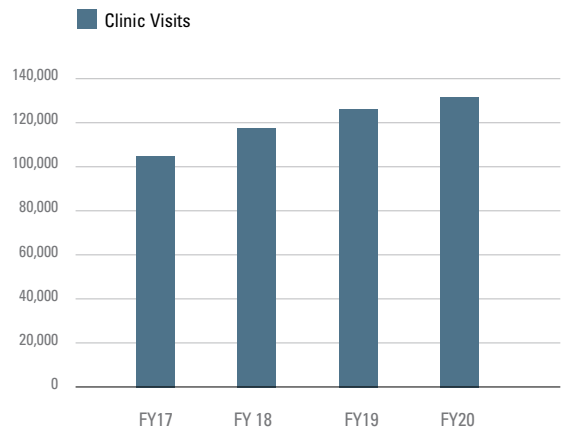
RESEARCH

Research Projects in Progress	**More than 200**
Grants Awarded	**Over $50 million** (Neurology and Neurosurgery)

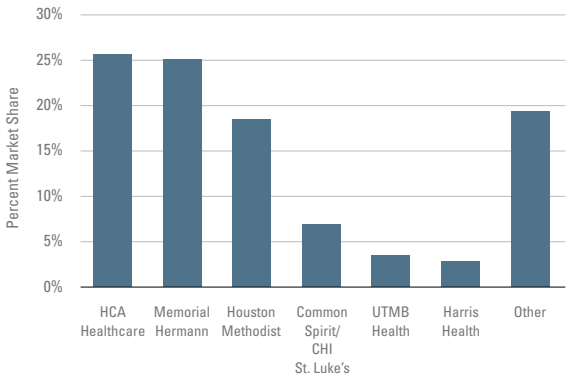
SPECIALTY EQUIPMENT INCLUDES:

- Leksell Gamma Knife® Perfexion™ and Icon™
- Varian Trilogy™ and Edge™ 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
- Nihon Kohden EEG 1200 machine with NeuroWorkbench® data management software
- Viking Nicolet EMG machines (2 freestanding) & Viking NicVue EMG machine (1 portable)
- Phillips CX50 sonography machine (4)
- LivaNova VNS Therapy® devices
- Allergan BOTOX Injection Amplifier®
- Medtronic DBS programmer – Samsung tablet

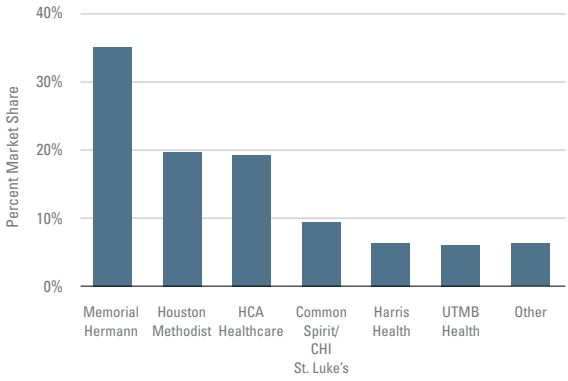
Patient Volumes in Clinic



Neurology Market Share FY20



Neurosurgery Market Share FY20



Source: Texas Hospital Association Patient Data System provided by Truven, formerly Thomson Reuters. Texas Hospital Inpatient Discharge Public Use Data File provided by Texas Department of State Health Services, Center for Health Statistics; 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.

FELLOWSHIPS

McGovern Medical School at UTHealth offers multiple postgraduate fellowships in neurology and neurosurgery.

Department of Neurology

Clinical Neurophysiology Fellowship

Epilepsy Fellowship

Movement Disorders Fellowship

Multiple Sclerosis Clinical/Research Fellowship

Neurocognitive Disorders Fellowship

Neurohospitalist Fellowship

Neuropsychology Postdoctoral Fellowship

Vascular Neurology Fellowship

For more information, please visit
go.uth.edu/neurology-fellowship

Vivian L. Smith Department of Neurosurgery

Cerebrovascular/Skull Base Fellowship

Neurocritical Care Fellowship

Neuroendovascular Surgery Fellowship

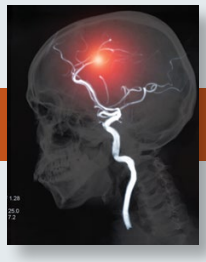
Pediatric Neurosurgery Fellowship

Spinal Neurosurgery and Peripheral Nerve Surgery

For more information, please visit
go.uth.edu/neurosurgery-fellowship

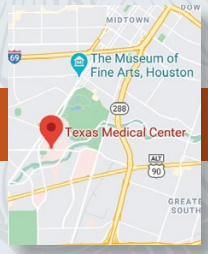
A History of Innovation

Physicians at McGovern Medical School at UTHealth established one of the first dedicated stroke programs in the world in 1988.



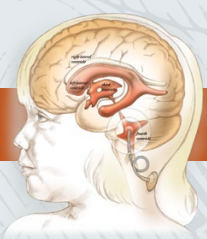
UTHealth was the first in Houston and one of the first in the United States to test the clot-dissolving drug tPA for acute stroke.

The first stroke program in Texas, at Memorial Hermann-Texas Medical Center, the teaching hospital for UTHealth Neurosciences, became the only one in the region to meet The Joint Commission's rigorous standards for the highly coveted Comprehensive Stroke Center certification.



UTHealth Neurosciences developed the first integrated acute stroke transfer network in the region with protocols for evaluating and seamlessly routing patients to one of four Memorial Hermann Comprehensive Stroke Centers, ensuring better outcomes. Complex cases are transferred rapidly to Memorial Hermann-TMC.

Children's Memorial Hermann Hospital is the site of the first single-center clinical trials for recurrent medulloblastoma, ependymoma, and atypical teratoid-rhabdoid tumors using the direct infusion of chemotherapy into the fourth ventricle of the brain.



The UTHealth Institute for Stroke and Cerebrovascular Disease sustains highly successful research in acute stroke treatment and is developing new areas of research in stroke recovery, prevention, population health, and vascular cognitive impairment.

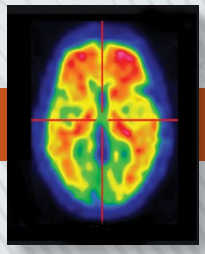
Researchers at McGovern Medical School were the first to discover a genetic mutation linked to intracranial aneurysms.

UTHealth Neurosciences physicians were the first in the region to offer all advanced modalities of treatment for complex lesions: microsurgery, interventional neuroradiology/endovascular surgery, and Leksell Gamma Knife® Icon™.

Neurosurgeons at UTHealth Neurosciences were the first in Texas to use robotic stereoelectro-encephalography (SEEG) for 3D mapping of epileptic seizures.

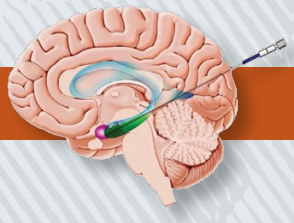
Physicians at UTHealth Neurosciences were the first in the south-central United States and among only a few in the country offering intra-arterial chemotherapy for retinoblastoma, the most modern treatment for the disease.

The Multiple Sclerosis and Neuroimmunology Program is a North American leader in studies of primary progressive multiple sclerosis and the most active center in Texas for organized clinical trials of new therapies for MS.



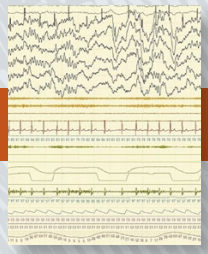
The UTHealth Neurosciences Neurocognitive Disorders Center was the first in Houston to use amyloid-sensitive PET imaging to determine whether patients have Alzheimer's disease.

Physicians at UTHealth Neurosciences were among the first in the nation to offer MR-guided laser interstitial thermal therapy (MRgLITT) using the Visualase® system for the treatment of well-delineated focal epilepsies.



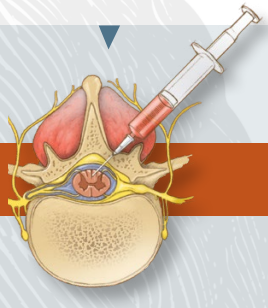
Physicians at UTHealth Neurosciences also were the first in the region to use the NeuroPace® RNS® System, an FDA-approved technique for responsive neurostimulation to treat adult patients with medication-resistant epilepsy.

Memorial Hermann-TMC brought the first clinical magneto-encephalography (MEG) sensor to Houston and has updated the technology to the Elekta Neuromag® TRIUX.



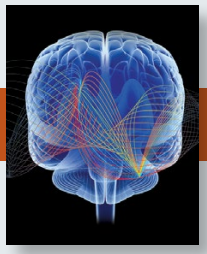
Memorial Hermann-TMC houses one of only a few adult and pediatric inpatient Epilepsy Monitoring Units in the country with the capability of simultaneously performing electro-encephalography and polysomnography.

Physicians at UTHealth Neurosciences are injecting human central nervous system stem cells into the spines of spinal cord injury patients in the hope of restoring a level of function.



The National Center for Testing Treatments for Chronic Spinal Cord and Traumatic Brain Injury (NCTT) is an innovative multicenter research network focused on reducing premature mortality rates and improving the function of people living with spinal cord injury or traumatic brain injury.

Experts at The Will Erwin Headache Research Center at UTHealth, established with a $20 million pledge from The Will Erwin Headache Research Foundation, are dedicated to the study of cluster headaches and other debilitating headaches and facial pain diseases.



Physicians and big-data scientists co-direct the Texas Institute for Restorative Neurotechnologies (TIRN), which integrates efforts across specialties and schools at UTHealth to advance clinical care for epilepsy and other functional neurological disorders.

Expanding the Patient Footprint: Big Data Creates a New Clinical Care and Research Paradigm at UTHealth Neurosciences

EVERY TWO DAYS humans generate as much data as were generated from the dawn of civilization through the year 2003. With hospitals gaining a greater footprint in the collection of biomedical and health data, the repository of clinical information is now growing at a rate of about 50 percent annually. The enormous amount of information available in the medical datasphere has the potential to advance patient care dramatically, if clinicians can access the knowledge it generates. How to organize data and derive value from it is the area of expertise of GQ Zhang, PhD, professor of medicine, biomedical informatics, and public health, and vice president and chief data scientist at The University of Texas Health Science Center at Houston (UTHealth).

"Big data is changing the entire way we practice medicine," says Zhang, who also is co-director of the Texas Institute for Restorative Neurotechnologies (TIRN) at UTHealth Neurosciences, which integrates efforts across specialties and schools at UTHealth to advance clinical research and patient care for epilepsy and other functional neurological disorders. "A couple of decades ago, the digital footprint for patient care was virtually nonexistent, and how a physician treated his or her next patient was based solely on education, training, personal experience, and the medical literature, or on the experience of other physicians via consultation. This type of empirical knowledge cannot be shared quickly and widely. Health information technology, artificial intelligence (AI), and big data have the potential to empower caregivers with very precise knowledge at their fingertips to help them make the right intervention decisions in the right context. And this is just the beginning. The possibilities are limitless."

What Zhang is developing with neurologist Samden Lhatoo, MD, FRCP (Lon), neurosurgeon Nitin Tandon, MD, and others at UTHealth Neurosciences, leverages their prior experience with epilepsy at TIRN and applies it to other areas such as cerebrovascular disease and stroke. "In the current paradigm, physicians see patients in the traditional office setting and enter data into the electronic health record (EHR). We extract it, clean it up, and load it into a registry database to be used in research. This is an expensive, time-consuming process with a long lag time and less value," says Lhatoo, who is professor and John P. and Kathrine G. McGovern Distinguished Chair in the Department of Neurology at McGovern Medical School at UTHealth, director of the Texas Comprehensive Epilepsy Program (TCEP), and co-director of TIRN. "Instead, we're leveraging data and providing innovative interfaces around those data so that they can be captured more efficiently and used to drive clinical care. Our interfaces are developed based on physician input and physician experience, so they save physicians time. With the current EHR system, physicians struggle with all kinds of issues. We're making that process more efficient so that clinicians can spend more time caring for patients and physician scientists have more time for research."

Most of us are familiar with gigabytes, and some may have heard of terabytes, petabytes, and exabytes. In 2015, the scale of the entire datasphere – all the digital information available – was four zettabytes. By 2025, the datasphere is projected to exceed 75 zettabytes, according to Lhatoo.

"That kind of exponential growth in digital information is a huge boon to the way we provide patient care," he says. "For cerebrovascular disease and stroke, there are big questions we'll eventually be able to answer, for instance, how best to respond to stroke with a precise diagnosis that can save people's lives. We're deriving data from the care we provide to help us understand disease outcomes and the efficiency and effectiveness of care delivery systems, from the time a stroke patient arrives at the hospital all the way through rehabilitation."

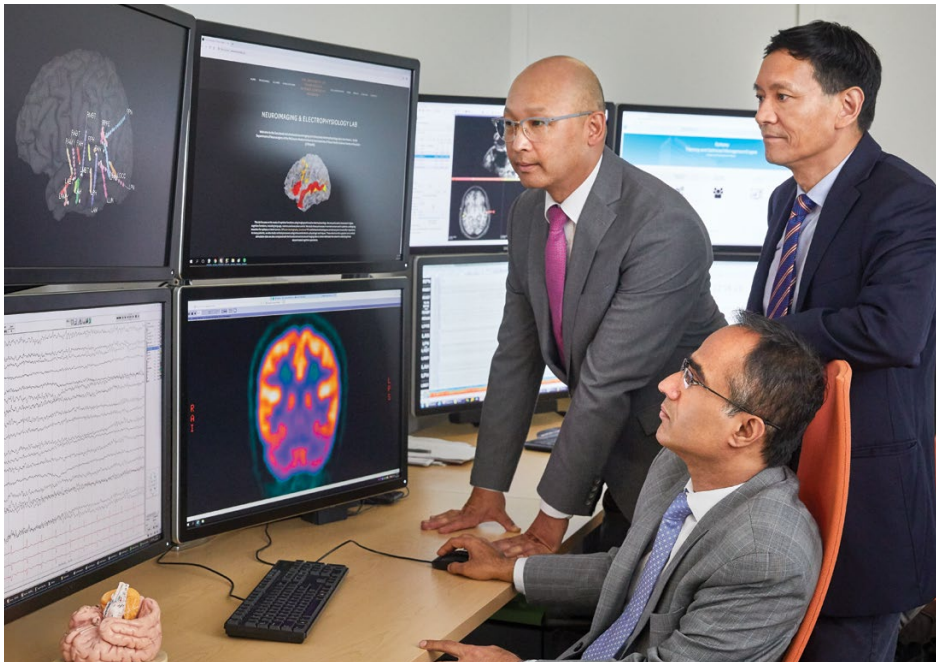
Zhang describes the system they are developing as a

spectrum of specialty-specific vertical systems. "To generate high-quality data in the context of patient care and make that data immediately available to researchers, we use a custom-tailored EHR approach specific to each specialty," he says. "We can quickly customize our general architecture design to disease areas to fill gaps in our database system that prevent us from capturing and integrating valuable real-time information. Our goal is to break down traditional barriers and better leverage information holistically across our entire academic medical system for greater patient benefit. Our system is patient centric and improves the quality, velocity, and experience of the patient journey, taking physician needs into consideration."

Big data is about more than the traditional three Vs: volume, veracity, and velocity. Zhang adds "value" as the fourth V.

"We're talking about a frame of mind," he says. "It's about being open minded, having a bigger vision, thinking globally, and asking a bigger question. This bigger vision will allow us to perceive the health care landscape on a grander information scale and gain more collective value. Data can be replicated an infinite number of times. It can be transported at the speed of light. The value of big data can be much more than the sum of its parts. We're making data findable, accessible, interoperable, reusable, and more importantly interactable. Data is a commodity that should be carefully curated for the common good."

There also is the concept of the Internet of Things – the network of physical objects embedded with sensors, software, and other technologies for the purpose of connecting and exchanging data with other devices and systems through the Internet. "Everything is connected, whether it's your electronic health record, the data from your smart watch, or data in the cloud," Lhatoo says. "These things will eventually all connect with each other. It's a mind-boggling concept to grasp but it isn't inconceivable that one day the computer in your car will be able to monitor some aspect of your physical health, like how long you've had to sit in traffic and how that relates to your stress level. There is every reason to believe that these platforms eventually will interact with the platforms your doctor uses. The concept has been with us for some time. We're now getting the processing power to create what previously has been a science-fiction scenario.



Neurologist Samden Lhatoo, MD, chief data scientist GQ Zhang, PhD, and neurosurgeon Nitin Tandon, MD, (seated), co-directors of the Texas Institute for Restorative Neurotechnologies, are breaking down barriers and leveraging information holistically across UTHealth and Memorial Hermann for greater patient benefit.

"We have a world-class informatics team," Lhatoo adds. "We have world-class researchers who understand how to leverage biomedical informatics expertise for research and health care delivery. What is unique about UTHealth, TIRN, and the School of Biomedical Informatics is that we already are using this expertise in the everyday delivery of patient care. A good understanding of disease processes is what informs preventive health care. In the U.S. today, we are very good at disease care, but we're not necessarily where we need to be with preventive care, which is the real 'health' care. But big data is helping us get much closer."

UTHealth Neurosciences Creates a Citywide Network of Accessibility for Acute Stroke Patients

UTHealth Neurosciences and Memorial Hermann have created a citywide network for stroke care, linking suburban hospitals to Comprehensive Stroke Centers located strategically across Houston.

UTHEALTH NEUROSCIENCES has redefined fast when it comes to timely treatment for people who suffer stroke in the Greater Houston area. Working with Memorial Hermann Health System's four Comprehensive Stroke Centers (CSCs), the cerebrovascular team at UTHealth Neurosciences has developed an integrated transfer network with protocols for evaluating and seamlessly routing acute ischemic stroke patients to one of four CSCs located strategically around the city.

The CSCs provide a network of accessibility staffed by nine academically advanced neurosurgeons, 18 neurologists, and a neuroradiologist, all fulltime academic faculty at McGovern Medical School at UTHealth, who are available 24/7 to provide fast advanced stroke care for better outcomes. Complex cases are transferred rapidly to Memorial Hermann-Texas Medical Center, the quaternary care academic medical center affiliated with UTHealth Neurosciences and the first hospital in the Memorial Hermann system to receive the coveted Comprehensive Stroke Center designation.

"From a clinical care perspective, this network of physicians allows us to extend our neuroscience expertise from the Texas Medical Center to every corner of Houston," says neurosurgeon Arthur Day, MD, co-chair, professor, and program director in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School. "Patients can access equitable acute stroke care close to home provided by the same group of physicians with seamless coordination. We've been working toward this for quite some time, but now the pieces are in place. Patients receive a standardized level of care, either at the facility where they arrive, or through rapid transfer to a Comprehensive Stroke Center."

This translates to substantially advanced stroke care. "No one else in the country has accomplished what we have at UTHealth Neurosciences – providing high-level stroke care at numerous Comprehensive Stroke Centers within a system of 14 community hospitals," says Sean Savitz, MD, director of the UTHealth Institute for Stroke and Cerebrovascular Diseases, professor of neurology at McGovern Medical School, and the Frank M. Yatsu, MD, Chair in Neurology. "Suburban hospitals within the Memorial Hermann system have increased their level of cerebrovascular expertise and can move quickly to identify stroke and other conditions. Our neurologists and neurosurgeons are working together under one system, using best-practices protocols and meeting regularly to review their outcomes. This is a better way to provide stroke care."

UTHealth Neurosciences also is training the next generation of physicians and nurses. "Residents and fellows have exposure to care provided in an academic medical center and also at suburban hospitals," says Meredith Wells, vice president of operations for UTHealth Neurosciences at McGovern Medical School. "This is important experience because not all of our residents and fellows will work in academic medical centers. Our network of accessibility also allows nurses at community hospitals to develop a higher level of expertise in the treatment of stroke. With our commitment to academic research and training, we're continually pushing the envelope to identify and share best practices."

Physicians at UTHealth Neurosciences are leading clinical trials to gain knowledge that will establish new national guidelines for the treatment of cerebrovascular disease. "What we're doing impacts population health," Dr. Day says. "We are now in the planning stages of extending our outreach further across Houston and the periphery of the city. We began with our central core at Memorial Hermann-TMC, but needed to be more accessible because stroke is so time sensitive. We've completed the first level of our stroke care expansion plan, and there's more to come."

STUDY FINDS TRANSPORT BY MOBILE STROKE UNIT GET PATIENTS QUICKER TREATMENT THAN TRADITIONAL AMBULANCE

Researchers at McGovern Medical School at UTHealth published findings in Stroke that show patients transported to the hospital by a mobile stroke unit instead of a standard ambulance received a clot-busting procedure an average of 10 minutes faster.

In 2014, McGovern Medical School was the first in the nation to launch a mobile stroke unit, an ambulance specially equipped for diagnosing and treating stroke rapidly before hospital arrival. "The quicker we restore cerebral blood flow to stroke victims, the more brain tissue we save," says Alexandra Czap, MD, a board-certified neurologist with expertise in vascular neurology and an assistant professor in the Department of Neurology. "This study shows that mobile stroke units like ours can be effective in streamlining time to treatment, potentially saving neurological function and ultimately improving quality of life for stroke patients."

The study looked at data from 161 patients from Houston and two other locations from 2014 to 2018 who underwent intra-arterial thrombectomy after suffering an acute ischemic stroke. The only medical therapy known to treat ischemic stroke, tissue plasminogen activator (tPA), cannot always clear a large clot. To perform endovascular thrombectomy, a vascular neurologist threads a catheter usually through a groin artery up to the blockage, where a small device inserted into the catheter is used to remove the clot.

"This is a hallmark paper because it shows that pre-hospital evaluation and management on a mobile stroke unit can significantly reduce time to endovascular treatment for patients with large artery clots," says Amanda Jagolino-Cole, MD, a teleneurologist and assistant professor in the Department of Neurology at McGovern Medical School.

While on board the unit, an interdisciplinary team begins the process to assess whether the patient needs a thrombectomy, which includes diagnostic imaging, neurological exam, and the administration of tPA. This gives the treatment team a headstart. Upon arrival at the hospital, the patient can be taken quickly to the endovascular suite for the procedure.

"Our mobile stroke unit allows us to bring the hospital to the patient," Czap says. "We can complete diagnostic testing and notify the hospital that we're coming, so that the appropriate teams can be ready. Streamlining this process allowed for one of our recent patients to complete treatment in less than two hours from onset of symptoms. Going forward, identification of possible thrombectomy candidates on the unit can increase the accuracy of triage and increase the number of patients who have the procedure, which we hope will lead to better outcomes."

The research is part of the ongoing "Benefits of Stroke Treatment Delivered Using a Mobile Stroke Unit" (BEST-MSU) study, a prospective comparative effectiveness trial investigating the benefits of stroke treatment delivered using a mobile stroke unit compared to standard management by emergency medical services. The primary outcomes are patients' functional status at 90 days and long-term health care utilization. The estimated primary completion date for the study is July 2021.

Texas Comprehensive Spasticity Center Offers Families a One-Stop Multidisciplinary Experience – Virtually

THE COVID-19 PANDEMIC and resources available at McGovern Medical School at UTHealth have given physicians an opportunity to communicate with their patients in new, more convenient ways. At the Texas Comprehensive Spasticity Center, a multidisciplinary team of physicians sees children with spasticity, movement disorders, or cerebral palsy, whose parents typically take them to multiple providers for different opinions before making a treatment decision. Since its inception, the team has offered parents a new model, gathering specialists together to provide carefully coordinated care in a single location. During the COVID-19 pandemic, they have offered the same multidisciplinary care through InTouch, UTHealth's secure platform for providing virtual care.

"We were already at the forefront of virtual care in following patients who have undergone selective dorsal rhizotomy, many of whom come from surrounding states," says Manish N. Shah, MD, FAANS, an associate professor of pediatric neurosurgery who directs the Texas Comprehensive Spasticity Center. Providers at the Center, part of McGovern Medical School, see patients in clinic at UT Physicians Pediatric Surgery. "When UTHealth implemented InTouch to minimize our risk of exposure to the virus, it allowed us to continue our group evaluations with multiple clinicians on a video call, each safely in their own space, with parents at home with their child. Many of our kids are medically fragile. Some use wheelchairs or require transport by ambulance. It's a challenge for parents to get to physician offices under the best of circumstances. Virtual visits are especially valuable now with pandemic measures in place that allow only one parent at an office visit."

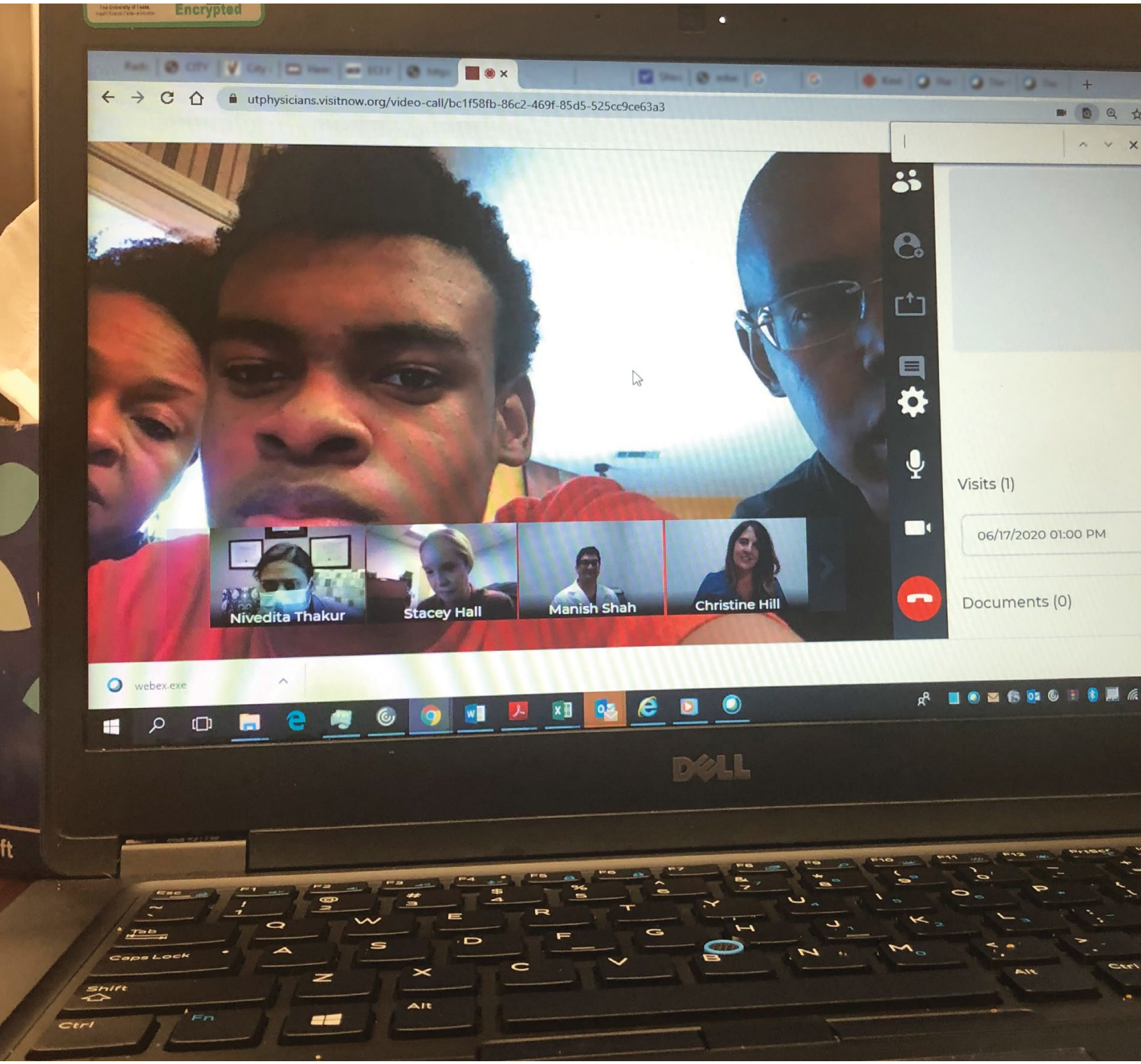
Virtual visits via InTouch also allow home therapists and home nurses to share their input during the video call. "The pandemic has done that one small favor for us – advanced our video capability. We have found it to be very helpful, and families from out of town appreciate not having to drive to Houston and stay in a hotel," Shah says.

Christine Hill, PT, coordinator of the Texas Comprehensive Spasticity Center, points to an additional benefit. "It's difficult for children to move freely in a small exam room," she says. "If we can see them active at home, we can better evaluate their ability to crawl and walk. Parents can take their kids outside, and we can watch them play when they don't know they're being observed. It gives us a broader look at them in motion."

Once Shah and his colleagues determine that a child would benefit from a virtual visit, Hill works with parents to schedule it. "They download the InTouch app from the app store, and our office sends them an invitation with a link for a secure HIPAA-compliant patient visit," she says. "They click the link, and we initiate the visit. We can add other participants, including family members, multiple physicians and the home care team."

Shah commends UTHealth for providing extra support during COVID-19. "I'm very proud to work for an institution that gives us the resources we need to create a good experience for our patients, even during a pandemic," he says.

Virtual visits at the Texas Comprehensive Spasticity Center offer patients convenience while minimizing potential exposure to the SARS-CoV-2 virus.



Research and Innovation at UTHealth Neurosciences

PHYSICIANS AND SCIENTISTS at UTHealth Neurosciences are engaged in a broad and intensive research program focused on the mechanisms, treatment, and cure of neurological disease and injury.

Oncolytic HSV-Infected Glioma Cells Activate NOTCH in Adjacent Tumor Cells

THERAPEUTIC VIRUSES are used increasingly to treat cancer. In the laboratory of Balveen Kaur, PhD, UTHealth Neurosciences researchers have discovered that malignant brain tumor cells treated with an engineered herpes virus can signal adjacent cells, making them responsive to a class of investigational drugs called gamma secretase inhibitors (GSIs). The engineered virus has the potential to increase the effectiveness of GSIs in arresting tumor growth.

The results of the study were published as the cover story in the May 15, 2020 issue of Clinical Cancer Research.[1] "Nearly 24,000 people will be diagnosed with malignant tumors of the brain or spinal cord in 2020, and treatment options are limited. Most people diagnosed with glioblastoma multiforme (GBM) do not survive beyond two years," says Kaur, professor and John P. and Kathrine G. McGovern Distinguished Chair and vice chair for research in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth. "My team researched how viruses change the biology of brain tumors, and how to leverage that knowledge to create strategic therapies that can eradicate cancer."

The NOTCH signaling pathway, a mechanism known to initiate crosstalk between cells, is a core pathway exploited by glioma cells for survival, tumor progression, stem cell maintenance, angiogenesis, and development of resistance to chemotherapy and radiation. Herpes simplex viruses express molecules called micro-RNA that activate the NOTCH signaling pathway. While the oncolytic herpes simplex virus (oHSV) is now a U.S. Food and Drug Administration-approved therapy for metastatic melanoma, its impact on NOTCH signaling has not been investigated.

"We have discovered a novel role for the HSV-1-encoded miR-H16 as an activator of the NOTCH signaling pathway in GBM and shown that this natural HSV-1 mechanism can be exploited to sensitize neighboring uninfected glioma cells to GSI therapy," Kaur says. "This opens the door to a new combination therapy using GSI and oHSV, which has not been investigated and tested previously, and highlights the potential therapeutic efficacy of the two applications on GBM. We're now investigating the immunological aspects of this signaling on brain tumor response to treatment. How it will affect antitumor immune response in the brain is uncharted territory. Continued research in this area is critical to take advantage of the therapeutic benefit of combining these agents for cancer patients."

Kaur's study was supported by a multi-institutional program project grant from the National Cancer Institute and a research scholar grant from the American Cancer Society.

[1]*Otani Y, Yoo JY, Chao S, Liu J, Jaime-Ramirez AC, Lee TJ, Hurwitz B, Yan Y, Dai H, Glorioso JC, Caligiuri MA, Yu J, Kaur B. Oncolytic HSV-Infected Cells Activate NOTCH in Adjacent Tumor Cells Sensitizing Tumors to Gamma Secretase Inhibition. Clinical Cancer Research. 2020 May 15;26(10):2381-2392. Epub 2020 Mar 5.*

Clinical Trial of High-Dose MTX110 Begins After Safe Administration into the Fourth Ventricle in a Non-Human Model

A NOVEL clinical trial of MTX110, a new formulation of soluble panobinostat from Midatech Pharma, is now enrolling patients. According to the American Cancer Society, about 500 children are diagnosed every year with medulloblastoma, the most common malignant brain tumor in children. Current treatments are often associated with considerable toxicity, and when tumors reoccur despite these treatments, survival rates are low.

"The current treatments for children and adults with medulloblastoma are inadequate," says David Sandberg, MD, FAANS, FACP, FAAP, professor of pediatric neurosurgery at McGovern Medical School at UTHealth and director of pediatric neurosurgery at Children's Memorial Hermann Hospital. "Children have low survival rates despite salvage therapy, and novel approaches are needed. This is a new trial of a novel drug, and we are very hopeful that we can help patients overcome this devastating disease."

The clinical trial follows a successful study led by Sandberg in an animal model, which demonstrated that MTX110 can be safely infused in the fourth ventricle and can achieve drug levels dramatically higher than intravenous or oral administration of the same drug. The study team at McGovern Medical School found no neurological deficits after fourth-ventricle infusions.

"Our objective was to test the safety and pharmacokinetics of short-term and long-term infusions of MTX110, a chemotherapeutic agent that inhibits the growth of medulloblastoma, the most common malignant brain tumor in children," Sandberg says. "In the animal study group there were no MRI signal changes in the brainstem, cerebellum, or elsewhere in the brain. In addition, the cytoarchitecture of the brain was preserved in all of the animals, with only mild postsurgical changes."

"We are really excited about the promising data from these experiments," says Sandberg, who is lead author of an article detailing results in the Journal of Neurosurgery: Pediatrics.[1]

The pilot study, which has been approved by the U.S. Food and Drug Administration, will enroll five patients with recurrent medulloblastoma at Children's Memorial Hermann Hospital.

[1]*Sandberg DI, Kharas N, Yu B, Janssen CF, Trimble A, Ballester LY, Patel R, Mohammad AS, Elmquist WF, Sirianni RW. High-dose MTX110 (soluble panobinostat) safely administered into the fourth ventricle in a nonhuman primate model. J Neurosurg Pediatr. 2020 May 1;1-9. Online ahead of print.*

The study is listed at clinicaltrials.gov at https://clinicaltrials.gov/ct2/show/NCT04315064. For more information, please contact Bangning Yu, MD, PhD, at bangning.yu@uth.tmc.edu or 713-500-7363.

Neurologists Test Novel Compound for Lung and Brain Injury in Severe COVID-19

NEUROLOGISTS are researching whether a novel immunomodulatory treatment, OP-101, can lessen lung and brain injury in hospitalized COVID-19 patients through a clinical trial at McGovern Medical School at UTHealth. UTHealth is one of several sites across the country for the Phase II trial, called PRANA, which will enroll 24 patients.

OP-101 is an investigational compound developed by Ashvattha Therapeutics to selectively attack proinflammatory macrophages and microglia – immune cells responsible for hyperinflammation, lung injury, and multi-organ failure caused by infections.

"We see this type of hyperinflammation in a number of neurological disorders, including Parkinson's and Alzheimer's disease," says Aaron Gusdon, MD, an assistant professor in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School and principal investigator at the Houston study site. "Now we're seeing the same activation of the innate immune system in COVID-19 patients that drives production of proinflammatory cytokines, which can contribute to patients becoming rapidly critically ill. OP-101 has been shown to robustly suppress hyperinflammation in a number of different disorders, so we're investigating if this targeted approach can help patients with severe cases of COVID-19 as well."

Unlike single-agent approaches, such as antibodies that address only one pathway, the treatment is intended to seek out and selectively shut down cells that

are proinflammatory and restore the macrophages to a normal state. "The hope is that since OP-101 targets only the activated component of the innate immune system, it will have fewer side effects and less risk of a concurrent infection compared with some steroids and antibodies that broadly suppress the entire immune system," says Gusdon, a neurologist at UTHealth Neurosciences.

"In COVID-19 patients, we know the lungs and sometimes the brain become severely inflamed," says Louise McCullough, MD, PhD, professor and Roy M. and Phyllis Gough Huffington Distinguished Chair in the Department of Neurology at McGovern Medical School and co-investigator at the OP-101 Houston site. "We're seeing that trend play out in the long-hauler patients, as the inflammation can lead to long-term symptoms like confusion, fatigue, and depression. We're interested in seeing if selectively targeting the activated cells in the lungs, blood, and brain can help dampen the cytokine storm and possibly prevent the consequences of lung and brain injury for these patients down the road."

McCullough, who is also co-director of UTHealth Neurosciences and chief of neurology at Memorial Hermann-Texas Medical Center, is treating patients with neurological long-hauler symptoms at the UT Physicians Post-COVID-19 clinic, part of the UTHealth COVID-19 Center of Excellence and the first post-coronavirus clinic in Houston.

The research builds on a strong foundation of COVID-19 neurological research that McCullough and H. Alex Choi, MD, have conducted since the start of the pandemic.

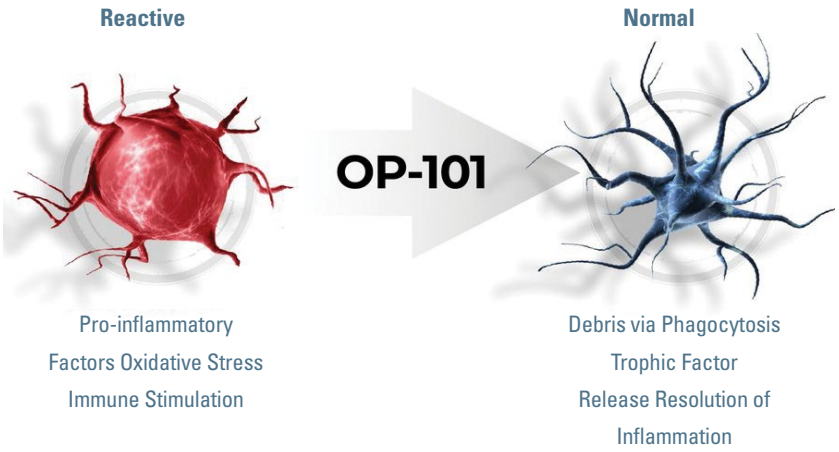
"We're a good fit to be on the frontlines of coronavirus research, because in addition to being neurologists, we're intensivists," says Choi, an associate professor and vice chair for neurocritical care at McGovern Medical School and a neurologist at UTHealth Neurosciences.

"We're interested in how systemic changes like sepsis and respiratory failure impact long-term cognitive functioning. We have established a prospective longitudinal study of COVID-19 patients to understand how severe systemic inflammation can cause brain injury and long-term symptoms. We want to be a part of the solution and understand how coronavirus affects patients long term." Choi is also the director of neurocritical care for the Memorial Hermann Health System and director of the Neuroscience Intensive Care Unit at Memorial Hermann-TMC. Both he and McCullough see patients at the UT Physicians Post-COVID-19 clinic.

Participants at the Houston site were recruited from Memorial Hermann Memorial City Medical Center and Memorial Hermann Southwest Hospital. They were randomized to one infusion of OP-101 or placebo, in addition to standard-of-care therapy. In their review of the data, researchers will evaluate whether the treatment reduced inflammation, improved fever and oxygenation, and reduced the number of days without a ventilator, or time in intensive care.

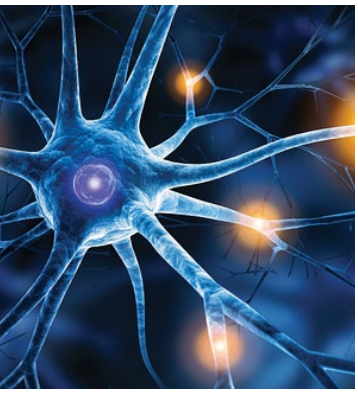
For more information about the PRANA Phase II study, call 713-500-UTHN (8846) or visit clinicaltrials.gov and search NCT04458298.

The investigational compound OP-101 is designed to selectively attack the immune cells responsible for hyperinflammation, lung injury, and multi-organ failure caused by infections.



Discovery of Biomarker Signature Prognostic for Neuropathic Pain After Spinal Cord Injury

CHRONIC NEUROPATHIC PAIN is a debilitating condition that occurs in 10 percent of the general population and 40 to 70 percent of people after a spinal cord injury (SCI). With funding from the National Institute of Neurological Disorders and Stroke, principal investigator Georgene Hergenroeder, PhD, and her research team aim to identify a biomarker signature prognostic for the development of neuropathic pain after spinal cord injury.



Neuropathic pain occurs due to inflammation, irritation, or compression of the neural tissue. Hergenroeder's research aims to discover why some people with spinal cord injury develop neuropathic pain and others do not.

"Our goal is to discover why one person with spinal cord injury will develop neuropathic pain while another with similar injuries will not," Hergenroeder says. "To date, we know of no distinguishing characteristics that identify patients who will develop neuropathic pain. If we can find a biomarker signature that will predict the future development of SCI-induced neuropathic pain, we will be one step closer to identifying new non-opioid treatments with the potential to prevent it."

The researchers are using plasma samples from consenting patients with spinal cord injury, as well as from healthy controls. Their goal is to identify autoantibodies in patients with acute SCI and determine the relationships between autoantibody levels and the development of neuropathic pain. In addition, they will characterize pain phenotypes.

"Using patient samples from early after injury, we will identify the autoantibody combination with the highest prognostic accuracy for the future development of neuropathic pain within six months after a spinal cord injury," says Hergenroeder, an associate professor in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth.

Hergenroeder and her team will use techniques capitalizing on antibody-antigen binding to establish a phenotype-driven panel. This will help them refine the prognostic value of the autoantibodies as biomarkers. "If we can determine, with high reliability, which patients are vulnerable to developing neuropathic pain, it may lead to the future development of non-addictive pain medications," she says.

The project began in September 2019 and is funded through Aug. 31, 2022.

Researcher's Technology Differentiates Between Parkinson's Disease and Multiple System Atrophy

SCIENTISTS believe they have found a way to distinguish between two progressive neurodegenerative diseases, Parkinson's disease (PD) and multiple system atrophy (MSA), using a technology developed at McGovern Medical School at UTHealth. The discovery, which could allow doctors a look into the future to help select the right treatment, was published in February 2020 in Nature.[1]

"It is challenging to distinguish between the two diseases because the early signs are similar – disturbances in movement, tremors, uncontrollable movements during sleep, impaired speech, etc. – but the two diseases progress differently and require distinctive treatment plans," says Claudio Soto, PhD, professor in the Department of Neurology at McGovern Medical School, director of the George and Cynthia W. Mitchell Center for Alzheimer's Disease and Other Brain-Related Illnesses, and senior author of the article in Nature. "Physicians need an objective way to differentiate between PD and MSA to provide patients with the best care. Currently we differentiate them by watching how the disease progresses. By the time people show progressed symptoms of MSA, which advances more rapidly than PD, a substantial amount of brain cells are already damaged or dead, and they can't be brought back. It has been difficult to develop treatment for both diseases because of the high rates of misdiagnosis, so we had to find a way to distinguish between the two at the onset of early symptoms."

Both diseases are characterized by deposits of a protein known as alpha-synuclein (αSyn) in the nervous system. The protein can change shape in a process called misfolding. Misfolded proteins clump together and poison surrounding healthy nerve cells responsible for brain functioning, particularly in motor skills.

"These misfolded clumps can form for many years, even decades, before doing enough damage that a person shows signs of motor impairment," Soto says.

Soto developed Protein Misfolding Cyclic Amplification (PMCA) technology, shown in previous studies to detect misfolded proteins associated with diseases such as Creutzfeldt-Jakob and Alzheimer's disease, after targeting misfolded αSyn aggregates as a way of developing

a sensitive biochemical diagnosis for PD. His latest research in Nature shows that the αSyn-PMCA can successfully discriminate between PD and MSA with an overall sensitivity of 95.4 percent, which gives doctors more information that they need to address. The study also helps shed light on the basis of these diseases at the molecular level.

"Our latest research shows that the αSyn aggregates of PD and MSA have different properties, so by amplifying the abnormal aggregates, we can detect with high efficiency which disease the patient has," Soto says. "This has huge implications for clinical care of the patient, and the development of new specific treatments for both diseases. Since cerebrospinal fluid is collected through spinal taps, the hope is that future research would enable optimization of the PMCA test to detect αSyn in blood or urine.

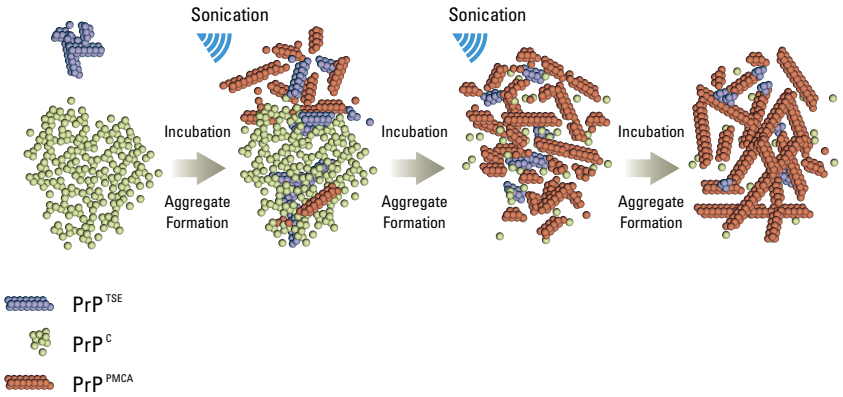
"I envision a world without these diseases, but the only way to achieve that is to couple early diagnosis with good and safe treatment," he adds. "That means we have to detect the abnormal proteins before they produce diseases and use safe preventive treatments. Many diseases like smallpox, diphtheria, and polio have been eliminated by scientific advances. I hope the same will happen with devastating brain diseases, like Alzheimer's and Parkinson's."

The research was funded in part by grants from the Michael J. Fox Foundation for Parkinson's Research and the National Institute on Aging. Soto is an inventor of patented PMCA technology and is the co-founder and chief scientific officer of Amprion, Inc., a biotech company focusing on the commercial utilization of PMCA for early diagnosis of Parkinson's, Alzheimer's, and other neurodegenerative diseases. Soto and Mohammad Shahnawaz, PhD, assistant professor of neurology, are the inventors of patented technology on the use of αSyn-PMCA for PD diagnosis.

The U.S. Food and Drug Administration has granted a Breakthrough Devices designation to Amprion's proprietary technology PMCA for its potential to diagnose Parkinson's disease at a much earlier stage than current diagnostic methods.

[1]*Shahnawaz M, Mukherjee A, Pritzkow S, Mendez N, Rabadia P, Liu X, Hu B, Schmeichel A, Singer W, Wu G, Tsai A-L, Shirani H, Nilsson KPR, Low PA, Soto C. Discriminating α-synuclein strains in Parkinson's disease and multiple system atrophy. Nature. 2020;578:pp. 273-277.*

Protein Misfolding Cyclic Amplification (PMCA)



Claudio Soto, PhD, developed PMCA as a way of distinguishing Parkinson's disease from multiple system atrophy.

UTHealth Neurosciences Clinical and Research Faculty Receive Accolades Across Neuroscience Specialties

Manish N. Shah, MD, FAANS

Dr. Manish N. Shah Receives UTHealth Benjy R. Brooks, MD, Outstanding Clinical Faculty Award

MANISH N. SHAH, MD, FAANS, associate professor of pediatric neurosurgery, is the 2020 recipient of the Benjy F. Brooks, MD, Outstanding Clinical Faculty Award. Shah is director of pediatric spasticity and epilepsy surgery at McGovern Medical School at UTHealth.

"I was surprised and thrilled to receive this award," he says. "Who knew one could get an award for such an intrinsically rewarding and fun activity like teaching?"

Established in 1991 by the Alumni Association of McGovern Medical School, the Benjy Brooks award is presented by McGovern Medical School's Student Surgical Association to recognize individuals "who complement and enhance the education program by serving as role models for students." The award is named in honor of Benjy Brooks, MD, the first board-certified woman pediatric surgeon in the United States, who joined the McGovern Medical School faculty in 1973 and remained active in the life of the medical school until her death in 1998. Medical students may nominate faculty or residents for the award.

Shah molds his teaching philosophy around the words of poet Rabindranath Tagore who wrote, "A teacher can never truly teach unless he is still learning himself. A lamp can never light another lamp unless it continues to burn its own flame." He credits his parents with guiding him down the path he has been on. "My mother, Mayuri, was a retired pediatrician who taught me about service, and my father, Narendra, taught me about lifelong scholarship," he says. Throughout the COVID-19 quarantine, Shah and his father have spent 30 minutes each day learning Sanskrit together.

"I can name all of my teachers from kindergarten onward, and they all had a meaningful impact on my career choice," says Shah, who joined the faculty at McGovern Medical School in 2014. "I learned a great deal from my mentors in medical school, and in residency and fellowship. I also continue to learn from the outstanding students, residents, and faculty here at McGovern Medical School."

Article by Dr. Balveen Kaur and Her Team Selected as Cover Story for Clinical Cancer Research

The results of research conducted in the laboratory of Balveen Kaur, PhD, at McGovern Medical School at UTHealth were published as the cover story of the May 15, 2020 issue of Clinical Cancer Research.[1] Titled "Oncolytic HSV-Infected Glioma Cells Activate NOTCH in Adjacent Tumor Cells," the article describes how researchers have discovered that malignant brain tumor cells treated with an engineered herpes virus can signal adjacent cells, making them responsive to a class of investigational drugs called gamma secretase inhibitors (GSIs). The engineered virus has the potential to increase the effectiveness of GSIs in arresting tumor growth.

The NOTCH signaling pathway, a mechanism known to initiate crosstalk between cells, is a core pathway exploited by glioma cells for survival, tumor progression, stem cell maintenance, angiogenesis, and development of resistance to chemotherapy and radiation. Herpes simplex viruses express molecules called micro-RNA that activate the NOTCH signaling pathway. While the oncolytic herpes simplex (oHSV) virus is now a U.S. Food and Drug Administration-approved therapy for metastatic melanoma, its impact on NOTCH signaling has not been investigated. "My team researched how viruses change the biology of brain tumors, and how to leverage that knowledge to create strategic therapies that may one day eradicate cancer," says Kaur, professor and John P.

and Kathrine G. McGovern Distinguished Chair and vice chair for research in the Vivian L. Smith Department of Neurosurgery at McGovern Medical School. "Our work opens the door to a new combination therapy using GSIs and oHSV, which has not been investigated and tested previously, and highlights the potential therapeutic benefit of combining these agents for patients with glioma."

Kaur says she was excited to see the article on the cover. "It's really thrilling to see the image of brain tumor cells showing NOTCH activation after infection," she says. "What I liked most about the study was watching one cell infected with the virus tell its neighboring cell to watch out. The cover is a great depiction of cell-to-cell communication."

[1]Otani Y, Yoo JY, Chao S, Liu J, Jaime-Ramirez AC, Lee TJ, Hurwitz B, Yan Y, Dai H, Glorioso JC, Caligiuri MA, Yu J, Kaur B. Oncolytic HSV-Infected Cells Activate NOTCH in Adjacent Tumor Cells Sensitizing Tumors to Gamma Secretase Inhibition. Clinical Cancer Research. 2020 May 15;26(10):2381-2392. Epub 2020 Mar 5.

The image depicts glioma cells infected with the oncolytic herpes virus in green. The red stain indicates activation of the NOTCH signaling pathway adjacent to infected cells. The blue-purple stain shows the nuclei of cells. This photo, which appeared on the cover of the May 15, 2020 issue of Clinical Cancer Research, was taken through a high-end fluorescence microscope funded by The University of Texas System Science and Technology Acquisition and Retention (STARs) Program, created to purchase state-of-the-art equipment to help attract and retain highly qualified faculty.

UTHealth Researchers Receive Grant from the Michael J. Fox Foundation to Extend Parkinson's Study to Phase II

THE MICHAEL J. FOX FOUNDATION has awarded Mya C. Schiess, MD, and her team a $2.25 million grant to continue their investigation of the safety of allogeneic adult bone marrow-derived mesenchymal stem cells (MSCs) in patients with idiopathic Parkinson's disease. The current study is titled "Allogeneic Bone Marrow-Derived Mesenchymal Stem Cells as a Disease-Modifying Therapy for Idiopathic Parkinson's Disease: A Phase II Double-Blind, Randomized Controlled Trial."


Mya C. Schiess, MD

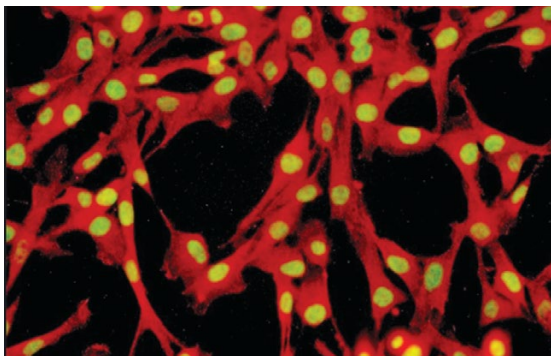
"Chronic brain inflammation plays a critical role in the development and progression of Parkinson's disease, damaging the brain, disrupting the blood-brain barrier and creating a proinflammatory condition," says Schiess, professor of neurology and director of the Movement Disorders and Neurodegenerative Diseases Program at UTHealth Neurosciences, and director of UT*MOVE* at McGovern Medical School at UTHealth. "Mesenchymal stem cells can modulate immune response and are capable of migrating to sites of injury. Once there, they can recognize and react to the environment by secreting several molecules, including anti-inflammatory molecules and growth factors that interact with the surrounding cells, allowing damaged brain cells to regenerate. Our hypothesis is that multiple intravenous infusions of mesenchymal stem cells from the bone marrow of a healthy donor will significantly slow the progression of Parkinson's disease when compared to placebo over the duration of a year."

Schiess presented the results of the Phase I trial, the first in the nation to use donor stem cells in Parkinson's patients, at the International Parkinson and Movement Disorder Society Virtual Congress 2020 held in September.[1] She and her team followed participants after a single infusion for a year and performed a number of safety tests to ensure there was no immune system reaction. They also measured inflammatory markers and quality of life.

"No participant had a serious adverse event, and clinical measures showed significant improvement from baseline to finish during the year we followed the participants," says Schiess, who holds the Adriana Blood

Distinguished Chair in Neurology. "The highest dose had the greatest effect on clinical measures."

The researchers aim to recruit 45 to 50 participants with early-to-moderate Parkinson's disease and assign them to one of three treatment arms. Group 1 will receive three infusions of placebo every 3 months; group 2 will receive two infusions of 10 X 106 MSC/Kg every 3 months and one placebo infusion; and group 3 will receive three infusions of 10 X 106 MSC/Kg every 3 months. All participants will receive three infusions, with three-month intervals between them. They will be monitored for adverse reactions and clinical improvement for a year after the last infusion.



Researchers are investigating if mesenchymal stem cells, shown here labeled with fluorescent molecules, have potential as a disease-modifying therapy for idiopathic Parkinson's disease.

"Cell-based therapy may be a transformative approach in the treatment of Parkinson's disease. By repeating an infusion up to 3 times a year at 3-month intervals, we're hoping to dramatically reduce symptoms of Parkinson's disease when we compare baseline to endpoint," Schiess says. "Because of the high cost of mesenchymal stem cells, we are applying for additional funding beyond the very generous gift of the Michael J. Fox Foundation."

The Phase II study opened in early November 2020. "We hope that people interested in participating will not be intimidated by COVID-19," Schiess says. "We're taking every recommended safety precaution to avoid the spread of the virus."

For more information, please visit https://clinicaltrials.gov/ct2/show/NCT04506073 or contact Vanessa K. Thyne, MS, clinical research coordinator, at 713-500-7127 or vanessa.k.thyne@uth.tmc.edu.

[1]Schiess M, Suescun J, Doursout M, Adams C, Green C, Saltarrelli J, Savitz S, Ellmore T. Allogeneic bone marrow-derived mesenchymal stem cells safety and tolerability in idiopathic Parkinson's disease. Meeting Abstract presented at the MDS Virtual Congress 2020. https://www.mdsabstracts.org/abstract/allogeneic-bone-marrow-derived-mesenchymal-stem-cells-safety-and-tolerability-in-idiopathic-parkinsons-disease.

Congratulations to Our 2020 Neuroscience Dean's Teaching Excellence Award Winners

EIGHTEEN FACULTY from the Department of Neurology, the Vivian L. Smith Department of Neurosurgery, and the Department of Pediatric Surgery are recipients of 2020 Dean's Teaching Excellence Awards at McGovern Medical School at UTHealth. The awards, given every May during Teaching Excellence Month at the medical school, recognize select faculty who provide exemplary teaching to medical students, residents, and graduate students.

Neurologists recognized include **Hammad Bokhari, DO**, assistant professor; **Kristin Brown, MD**, assistant professor; **Shivika Chandra, MD**, assistant professor and chief of neurology at Harris Health Lyndon B. Johnson Hospital and Outpatient Neurology Clinics at UTHealth; **Amanda Jagolino-Cole, MD**, assistant professor and co-director of the Vascular Neurology Fellowship Program; **Haris Kamal, MD**, assistant professor; **Fudong Liu, MD, MSNS**, associate professor and director of translational stroke research; **Rodrigo Morales, PhD**, associate professor; **Thy Nguyen, MD**, associate professor; **Anjail Sharrief, MD, MPH**, associate professor and director of stroke prevention at the UTHealth Institute of Stroke and Cerebrovascular Disease; **Shaun Smart, MD**, assistant professor and director of the Neurohospitalist Fellowship Program at UTHealth, and chief of the general neurology service at Memorial Hermann-Texas Medical Center; **Erin Furr-Stimming, MD**, associate professor and director of the Huntington's Disease Program; **Melissa Thomas, MD**, assistant professor; **Tzu-Ching "Teddy" Wu, MD**, associate professor and director of the UTHealth Telemedicine Program; and **Alicia Zha, MD**, assistant professor.

Faculty recognized from the Vivian L. Smith Department of Neurosurgery were **H. Alex Choi, MD**, associate professor and director of neurocritical care at McGovern Medical School and Memorial Hermann-TMC; and **Ying Liu, MD, PhD**, assistant professor who runs a laboratory pursing basic and translational research in stem cell biology, regenerative medicine, and pathogenesis of neurodegenerative disease and central nervous system injury.

From the Department of Pediatric Surgery are


Hammad Bokhari, DO


Kristin Brown, MD


Shivika Chandra, MD


Amanda Jagolino-Cole, MD


Haris Kamal, MD


Fudong Liu, MD, MSNS


Rodrigo Morales, PhD

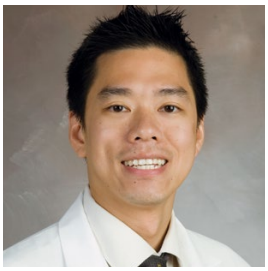

Thy Nguyen, MD

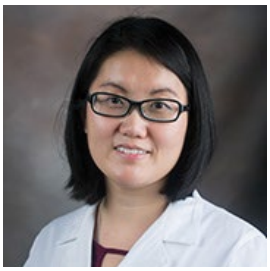

Anjail Sharrief, MD, MPH


Shaun Smart, MD

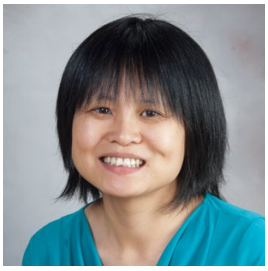

Erin Furr Stimming, MD


Melissa Thomas, MD


Tzu-Ching "Teddy" Wu, MD


Alicia Zha, MD


H. Alex Choi, MD


Ying Liu, MD, PhD


Phuong Nguyen, MD


Manish N. Shah, MD

Phuong Nguyen, MD, chief of pediatric plastic surgery, director of craniofacial surgery and assistant professor in the Division of Plastic Surgery; and **Manish N. Shah, MD**, director of the Texas Comprehensive Spasticity Center at UT Physicians Pediatric Surgery and McGovern Medical School and associate professor in the Division of Pediatric Neurosurgery.

A Guide to Interpreting Incidental Brain and Spine Imaging Findings

BEFORE THE PUBLICATION in June 2020 of Incidental Findings in Neuroimaging and Their Management: A Guide for Radiologists, Neurosurgeons, and Neurologists, there was no definitive guide to help neuroradiologists, neurosurgeons, and neurologists interpret incidental brain and spine imaging findings and make clinically informed, complex treatment decisions. The new 346-page book presents a streamlined, case-based approach to 50 commonly seen incidental findings in neuroimaging, presented in an easily accessible format.

Edited by neuroradiologist Kaye Westmark, MD, neurosurgeon Dong Kim, MD, and neuroradiologist Roy Riascos, MD, the hardbound book provides the knowledge to manage significant unexpected findings, from identification and analysis to effective interventions. The guide includes a broad spectrum of incidental findings, with collaborative contributions from neuroradiologists, neurosurgeons, neurologists, otolaryngologists, body and musculoskeletal imaging experts, endocrinologists, and hematologists/oncologists.

"This is a multidisciplinary effort of faculty members at McGovern Medical School at UTHealth, who worked closely together to create a product that will be helpful for neuroscience professionals," says Riascos, professor of radiology and neurosurgery, and chief of neuroradiology at the medical school. "There is a lot of widely dispersed literature about incidental brain and spine findings, but we were unable to find a centralized source that used a multidisciplinary approach. It was a true effort of leadership beyond the scope of what we typically do in our areas of expertise. Dr. Westmark served as project lead, and Dr. Kim organized the neurosurgery section while I worked on the neuroradiology section. The project took us two years to complete. Huge kudos to Dr. Westmark!"

With the increase in patients undergoing MRIs and concomitant rise in incidental findings, the three

physicians saw a need for an easy-to-use resource. "The majority of incidental findings are benign conditions that won't require intervention," says Westmark, an assistant professor of diagnostic and interventional imaging at McGovern Medical School. "My role as organizer was to act as liaison between radiology and the clinical services to connect imaging results with management of the condition, and to ensure a consistent, readable format throughout the book. We presented the information in bullet points, with pearls and pitfalls that guide physicians to the most likely diagnosis, which was Dr. Riascos' vision. The book required collaboration between departments that wouldn't have happened without Dr. Kim's leadership. He did a fantastic job of organizing the neurosurgery department, and brought together a stunning number of contributing authors."

Amrou Sarraj, MD

The book begins with normal variants important to recognize to avoid unnecessary testing and stress for patients. Later sections focus on abnormalities that require extensive clinical evaluation to determine best-practices management. The final section outlines CT and MR imaging artifacts that mimic more dangerous pathologies, degrade imaging quality, and obscure real findings.

"I usually have an idea of the diagnosis based on what I see on a scan, but not a lot has been published concisely on management guidelines," says Kim, professor and Nancy, Clive, and Pierce Runnells Distinguished Chair of the Vivian L. Smith Department of Neurosurgery at McGovern Medical School, and director and chief of neurosurgery at Mischer Neuroscience Institute at Memorial Hermann-Texas Medical Center. "Early in my training I didn't find books that gave long lists of differential diagnoses to be very helpful, and thought others may have the same problem. We organized the book so that clinicians can scan it and find what they need."

Key findings and differential diagnoses, with imaging "pearls" that help narrow the differential, are listed for each abnormality. Diagnostic and management decision trees present algorithms in an easy-to-understand manner. Clinical question-and-answer sections give extensive background literature, which provided the basis for actual case management decisions.

"Neuroradiologists hold one piece of the puzzle," Westmark says. "Our findings impact patient care, but often we don't know the details of the patient's subsequent workup and management. In compiling this book, we brought together a range of specialists and demonstrated how we work together to determine the management of numerous incidental findings in neuroimaging."

American Stroke Association Honors Dr. Sarraj with Emergency Medicine Award

AMROU SARRAJ, MD, associate professor of neurology at McGovern Medical School at UTHealth, received the prestigious Stroke Care in Emergency Medicine Award from the American Stroke Association in February 2020 for his research, "Optimization Methodologies to Enhance Endovascular Thrombectomy Access in the United States." The award encourages investigators to undertake or continue research in the emergent phase of acute stroke treatment and submit an abstract to the International Stroke Conference.

This is the second major award Sarraj has received from the American Heart Association and American Stroke Association; previously he won the Mordecai Y.T. Globus New Investigator Award in 2012 for his research on predicting poor outcomes in stroke patients undergoing thrombectomy. Sarraj received his most recent award at the American Stroke Association's International Stroke Conference in Los Angeles, the world's premier meeting dedicated to the science of stroke and brain health.

"I am honored to receive this recognition from the American Stroke Association," Sarraj says. "Endovascular thrombectomy is a highly effective treatment for stroke patients, and currently less than a fifth of the U.S. population has timely access to this treatment. We hope that this research is helpful in planning and infrastructure development at the local, state, and national levels to prioritize allocation of resources.

The study, published in *Stroke*,[1] assessed the current state of access to endovascular thrombectomy (EVT) in the United States and, using a simulated model, evaluated two different strategies to optimize access. Model A used an algorithm that captured the largest population with direct access when flipping 10 percent and 20 percent to centers that currently have the capability to perform EVT. Model B used bypassing methodology to directly transport patients to the nearest EVT center if the drive-time difference to the hospital was within 15 minutes to the closest non-EVT center.

"Optimization methodologies that increase EVT centers or bypass non-EVT to the closest EVT center both showed enhanced access," Sarraj says. "Results varied by states, but bypass showed more potential for maximizing direct EVT access. We concluded that national and state efforts should focus on identifying gaps and tailoring solutions to improve EVT access."

Sarraj's work is focused on optimizing stroke outcomes by developing methods to select patients who will benefit maximally from acute stroke therapies. He joined the McGovern Medical School faculty in 2012.

[1]Sarraj A, Savitz S, Pujara D, Kamal H, Carroll K, Shaker F, Reddy S, Parsha K, Fournier LE, Jones EM, Sharrief A, Martin-Schild S, Grotta J. Endovascular Thrombectomy for Acute Ischemic Strokes: Current US Access Paradigms and Optimization Methodology. Stroke. 12 Feb 2020;51:1207-1217.

Dr. Patton Named American Medical Association Alternate Delegate

EDDIE L. PATTON JR., MD, MBA, MS, was selected as an alternate delegate to the American Medical Association (AMA) by the Texas Medical Association House of Delegates at its 2020 virtual session in September.

Patton, a clinical assistant professor of neurology at McGovern Medical School at UTHealth, was nominated as a candidate for alternate delegate by the Harris County Medical Society. In the nomination, the society described Patton as an "established leader with wide-ranging public policy experience and with the youthful exuberance to be a leader in the AMA for years to come."

Delegates and alternate delegates to the American Medical Association offer a direct link between the organization and grassroots physicians by providing information on activities, programs, and policies of the AMA to individual members. Using a two-way relationship between the AMA and its physician members, delegates and alternate delegates also serve as direct contacts for individual members to contribute to AMA policy and communicate situations that may be addressed through policy implementation efforts.

Board certified by the American Board of Psychiatry and Neurology, Patton sees patients at UTHealth Neurosciences. He currently serves on the Harris County Medical Society Board of Medical Legislation and in 2018 was named to the Texas Council on Alzheimer's Disease and Related Disorders by Gov. Greg Abbott. The following year he was elected to serve as vice chair of the council.

Patton chaired the Federal Advocacy Work Group of the American Academy of Neurology (AAN) from 2015 to 2018 and has worked on numerous lobbying campaigns with the AAN's Neurology on the Hill and with the Texas Medical Association's First Tuesdays at the Capitol. "There is no doubt that public policy decisions made in Washington, D.C., exert tremendous influence on our practices and on the lives of patients," Patton wrote in his nomination letter. "Conversely, Texas physicians have a proud history of exerting as much influence as we can on the policy-making process. I believe the AMA would benefit from that spirit of Texas advocacy.


Eddie L. Patton Jr., MD, MBA, MS

"It is time that MDs take a more prominent position in guiding changes in health care. My education and experiences give me a unique view of all aspects of health care policy, including the impact on physicians, patients, and the economy. I want to see the AMA take a more forceful role in health care policy development and implementation in Washington, just like the TMA has done so effectively in Texas, and I want to be a part of the Texas delegation that leads the AMA to the position of influence it should hold."

Patton received his medical degree from Wayne State University in 2005, where he also earned the Distinguished Service Award and the Marjorie Edwards Award for Scholarship and Community Service. During his time at Wayne State, he was co-founder and co-director of the Young Doctors of Detroit High School and Middle School Mentoring Program.

Following neurology residency training at Baylor College of Medicine, Patton completed neuromuscular fellowship training at the same institution. He earned a Master of Business Administration in 2018 at Rice University.

UTHealth Neurosciences Welcomes New Recruits

ELEVEN FACULTY MEMBERS joined UTHealth Neurosciences in the 2020 academic year.

John Caridi, MD, who specializes in complex reconstruction of adult and pediatric cervical, thoracic, and lumbar spinal deformity, joined McGovern Medical School as chief of the neurosurgical spine division and associate professor in the Vivian L. Smith Department of Neurosurgery. After graduating with honors from Indiana University School of Medicine, where he was inducted into Alpha Omega Alpha Honor Medical Society, Caridi completed his internship and neurosurgical residency at the University of Maryland Medical Center and R. Adams Cowley Shock Trauma Center. He completed a one-year orthopedic fellowship in adult and pediatric spinal deformity surgery at the Hospital for Special Surgery in New York City, and trained in advanced minimally invasive spine surgery at the Schoen Klinik in Munich, Germany. Prior to joining McGovern Medical School, he developed and directed the neurosurgical spinal deformity program for the Mount Sinai Health System in New York City. In 2019, he was honored with the prestigious Scoliosis Research Society international traveling fellowship.

Krishanthan Vigneswaran MD, focuses primarily on spine surgery and also sees patients with brain and spinal cord tumors. Vigneswaran received his medical degree at The University of Texas Southwestern School of Medicine in Dallas with distinction in research, and was inducted into Alpha Omega Alpha Honor Medical Society. He completed residency training in neurological surgery at Emory University School of Medicine in Atlanta, and subsequently completed a fellowship in neurosurgical oncology at The University of Texas MD Anderson Cancer Center in Houston. He is a clinical assistant professor in the Department of Neurosurgery.

Kristin A. Brown, MD, an assistant professor of neurology, received her medical degree at SUNY Downstate College of Medicine in 2012 and completed residency training in 2016 at McGovern Medical School. She went on to complete fellowships in stroke prevention, neurophysiology, and neurology at McGovern Medical School. Board certified in neurology, Brown specializes in neurology and clinical neurophysiology. She is a National Institutes of Health StrokeNet Fellow.

Alexandra Czap, MD, is a board-certified neurologist with expertise in vascular neurology and neuro-oncology. She focuses on the neurological and vascular complications of cancer and the treatment of adult brain and spinal cord tumors, in collaboration with neurosurgeons and radiation oncologists. Czap graduated from the University of Connecticut School of Medicine and completed neurology residency training at the University of Pittsburgh Medical Center. She is dual fellowship trained in neuro-oncology at Massachusetts General Hospital/Dana Farber Cancer Institute/Brigham and Women's Hospital and in vascular neurology at McGovern Medical School. Czap is an assistant professor in the Department of Neurology.

Katherine M. J. Harris, MD, received her medical degree at McGovern Medical School in 2014. She completed neurology residency training at the same institution, and completed a Healthcare Management Certificate at the University of Houston-Clear Lake in 2018. An assistant professor in the Department of Neurology, Harris is dual fellowship trained in epilepsy and intracranial EEG at McGovern Medical School.

Indira Kommuru, MD, specializes in pediatric neurology and pediatric epilepsy. She received her medical degree at Rangaraya Medical College in Andhra Pradesh, India, in 2007 and completed residency and fellowship training at SUNY Downstate College of Medicine. An assistant professor in the Department of Pediatrics, Kommuru is certified by the American Board of Psychiatry and Neurology.

Sandipan Pati, MD, joined UTHealth Neurosciences from the University of Alabama at Birmingham, where he was an associate professor of neurology and saw patients in the Epilepsy Neuromodulation Clinic. Pati received his medical degree at the Jawaharlal Institute of Postgraduate Medical Education and Research in Pondicherry, India, and is a member of the Royal College of Physicians (MRCP) in the United Kingdom. He completed residency training in the U.K. in internal medicine at the University of Birmingham NHS Hospitals; in neurology at John Radcliffe Hospital, Oxford University Hospitals NHS in Oxford; and in epilepsy at the National

Epilepsy Center, National Hospital for Neurology and Neurosurgery of University College London Hospitals. After moving to the United States, he completed additional residency training in neurology at Barrow Neurological Institute at St. Joseph's Hospital and Medical Center in Phoenix. He went on to complete fellowship training in epilepsy and clinical neurophysiology at Massachusetts General Hospital/Harvard Medical School in Boston in 2014. Pati is dual board certified in neurology and epileptology. An associate professor of neurology at McGovern Medical School, Pati is a member of the team at the Texas Comprehensive Epilepsy Program and the Texas Institute for Restorative Neurotechnologies at UTHealth Neurosciences. His career goal is to improve the lives of people with epilepsy.

Swati Pradeep, DO, graduated from Philadelphia College of Osteopathic Medicine in 2015. In 2019, she completed her residency training in neurology at the University of Kentucky, where she was chief resident. Pradeep completed fellowship training in movement disorders at McGovern Medical School in 2020 and joined the faculty as an assistant professor. She is board certified in neurology.

Ali Reza Shoraka, MD, received his medical degree at Shahid Beheshti University of Medical Sciences in Tehran, Iran. He completed residency training in neurology at McGovern Medical School, where he received the Senior Resident Teaching Award. He went on to complete a fellowship in clinical neurophysiology at The University of Texas Medical Branch in Galveston. Shoraka is a clinical assistant professor in the Department of Neurology.

Luis F. Torres, MD, received his medical degree magna cum laude at Universidad Iberoamericana in Santo Domingo, Dominican Republic. He completed neurology residency training at the University of Miami Miller School of Medicine and Jackson Memorial Hospital, where he was chief resident. He completed a vascular neurology fellowship at the same institution, followed by a neurocritical care fellowship in the Vivian L. Smith Department of Neurosurgery. Torres is a clinical assistant professor in the Department of Neurology and the Vivian L. Smith Department of Neurosurgery.

Roy X. Zhang, MD, is dual fellowship trained in vascular neurology at Barrow Neurological Institute in Phoenix, Arizona, and in neurocritical care at McGovern Medical School and Memorial Hermann-Texas Medical Center. Zhang is a graduate of Sanford School of Medicine at the University of South Dakota in Vermillion. He completed adult neurology residency training at Barrow Neurological Institute, where he was chief resident. Zhang is a clinical assistant professor in the Vivian L. Smith Department of Neurosurgery.


John Caridi, MD


Krishanthan Vigneswaran, MD


Kristin A. Brown, MD


Alexandra Czap, MD


Katherine M. J. Harris, MD

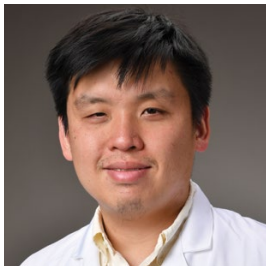

Indira Kommuru, MD


Sandipan Pati, MD


Swati Pradeep, DO


Ali Reza Shoraka, MD


Luis F. Torres, MD


Roy X. Zhang, MD

Scope of Services and Quality Outcomes

Brain Tumor

Cerebrovascular

Children's Neuroscience

Epilepsy

Memory Disorders and Dementia

Movement Disorders and Neurodegenerative Diseases

Multiple Sclerosis and Neuroimmunology

Neuromuscular Disorders

Neurotrauma and Neuroscience Critical Care

Pain Management

Sleep Disorders

Spine Disorders

Brain Tumor

NEURO-ONCOLOGISTS at UTHealth Neurosciences continue to expand the reach of the Brain Tumor Center across Houston. Neuro-oncology services are now available in the Texas Medical Center and at UTHealth Neurosciences clinics in Memorial City, Southwest Houston, and Sugar Land.

Director of neuro-oncology Jay-Jiguang Zhu, MD, PhD, is a fellowship-trained, board-certified neurologist with expertise in neuro-oncology and neurology. He focuses his practice on primary brain tumors, including gliomas, meningiomas, pituitary adenomas, and primary central nervous system lymphomas, as well as brain metastases and leptomeningeal spread of systemic malignancies. In collaboration with other clinicians and research scientists, Zhu and his team are working on the discovery of biomarkers for glioblastoma at recurrence, as well as identifying factors that may improve care and longevity of patients with gliomas using the National Cancer Database.

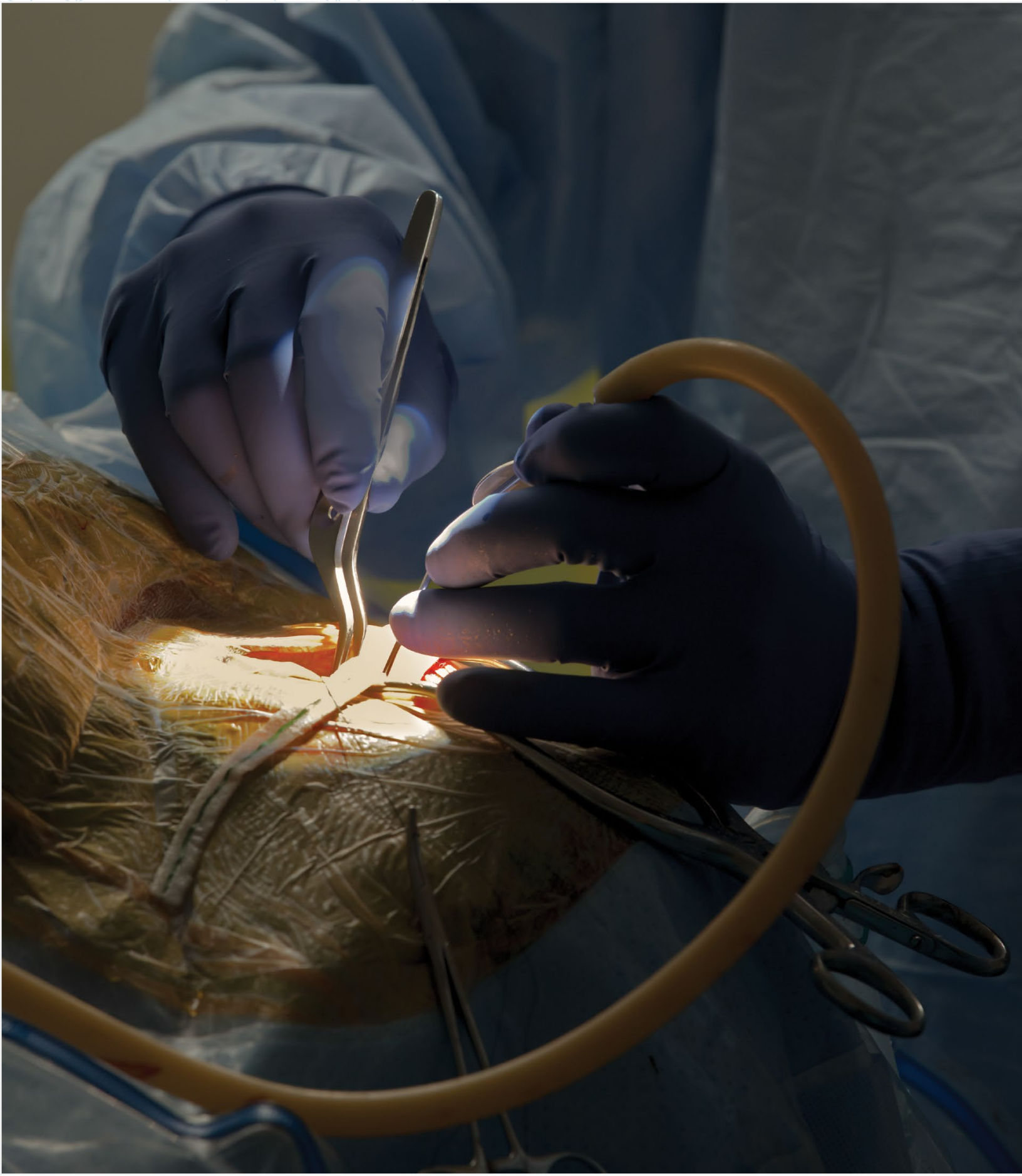
Sigmund Hsu, MD, is fellowship trained and certified by the American Board of Psychiatry and Neurology, with extensive experience in the evaluation and treatment of neurological disorders in cancer patients. He focuses his practice on primary brain tumors, metastatic cancer of the brain and spinal cord, brain cancer neurology, and the treatment of chemotherapy neurotoxicity.

UTHealth Neurosciences has expanded neuro-oncology from the Texas Medical Center to the community with the addition of Alexandra Czap, MD, who is dual fellowship trained in neuro-oncology at Massachusetts General Hospital/Dana Farber Cancer Institute/Brigham and Women's Hospital and in vascular neurology at McGovern Medical School at UTHealth. Czap focuses on the neurological and vascular complications of cancer and the treatment of adults with brain and spinal cord tumors, working closely with neurosurgeons and radiation oncologists. She provides neurological services for benign and malignant brain and spinal cord tumors, brain and leptomeningeal metastases, neurological complications in cancer, and vascular disease of the brain and spine at UTHealth Neurosciences locations in Memorial City, Southwest Houston, and Sugar Land.

Joining Czap in neuro-oncology at UTHealth Neurosciences-Southwest and UTHealth Neurosciences-Sugar Land is Krishanthan Vigneswaran, MD, a fellowship-trained neurosurgeon with expertise in neurosurgical oncology and spine surgery. His practice focuses on the surgical treatment of patients with brain and spinal cord tumors, using the latest neurosurgical tools and working closely with neuro-oncologists and radiation oncologists. While at Emory University as a resident, Vigneswaran worked in the neurosurgical oncology lab on independent research for which he received an NINDS R25 Research Education Grant and a Neurosurgery Research and Education Foundation Research Fellowship to study new drugs to treat glioblastoma and conduct clinical trials. He completed a fellowship in neurosurgical oncology at The University of Texas MD Anderson Cancer Center in Houston.

All UTHealth Neurosciences, neuro-oncologists maintain a strong focus on 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 tumor and central nervous system metastases.

Angel Blanco, MD, director of radiation oncology and stereotactic radiosurgery at UTHealth Neurosciences, performs procedures at Memorial Hermann-Texas Medical Center. During 2020, the academic teaching hospital upgraded its stereotactic radiosurgery equipment to the Leksell Gamma Knife® Icon™. The Icon gives clinicians the option to perform single or fractionated frame-based or frameless treatments,



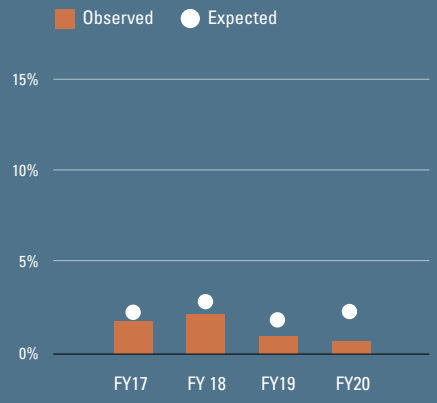
enabling more personalized delivery of cranial radiation with precision and accuracy. Using upgraded sources, it also allows for shorter treatment times. The addition of onboard imaging guidance via conventional CT scan expands clinical usability, and the incorporation of a sophisticated mask system allows some patients to receive frameless image-guided radiosurgery, rather than using a stereotactic frame, depending on the location and size of the tumor and the patient's clinical condition.

At the newly expanded Radiation Oncology Clinic, a team of specialists offers a broad range of treatment modalities for brain and spine tumors, from standard external beam radiation to the Varian Edge® with HyperArc™ capability for intracranial targets. The Edge treatment delivery system is designed to allow for more precise radiation doses to tumors, tracking tumor position in real time. A second LINAC customizes high-energy electrons to conform to a tumor's shape and destroy cancer cells while sparing surrounding normal tissue. For patients who require chemotherapy, UTHealth Neurosciences recently opened an outpatient Infusion Center in the same building. UTHealth Neurosciences radiation oncologist Mark Amsbaugh, MD, treats patients at the Texas Medical Center and at Memorial City. Shariq Khwaja, MD, also expands these services to the community, caring for patients at Memorial Hermann Memorial City Medical Center.

Neurosurgeons Nitin Tandon, MD, and Yoshua Esquenazi Levy, MD, are using 5-ALA (5 aminolevulinic acid) to remove infiltrative gliomas. Patients swallow 5-ALA in a liquid solution that causes malignant glioma cells to fluoresce. Using a modified neurosurgical microscope, they can more easily identify and remove the main tumor mass, in addition to small clusters of tumor cells outside the margins.

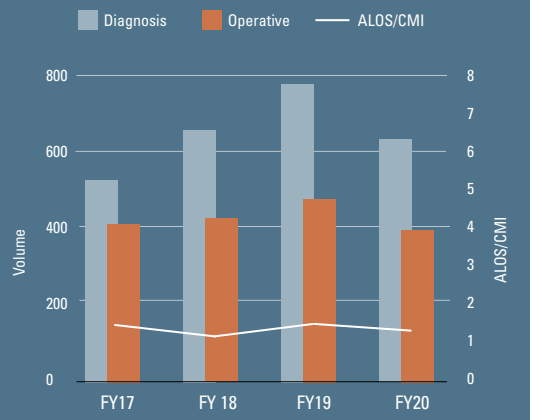
QUALITY & OUTCOMES MEASURES

Brain Tumor: Inpatient Mortality



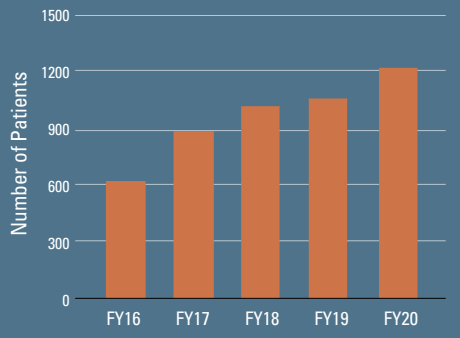
Source: Chart data from Vizient

Brain Tumor Volume & Length of Stay
(CMI Adjusted)



Source: Chart data from Vizient

Radiation Oncology Volume



Source: Chart data from professional billing claims

UTHEALTH NEUROSCIENCES OPENS STATE-OF-THE-ART INFUSION CENTER

Launched in April 2020, the UTHealth Neurosciences Infusion Center is a welcoming space located in the Texas Medical Center. Here, patients receive personalized infusion care, including intravenous fluids and therapies to manage neurological conditions such as neuro-oncological diseases, various headache and pain management therapies, multiple sclerosis, and neuromuscular and other neurological disorders.

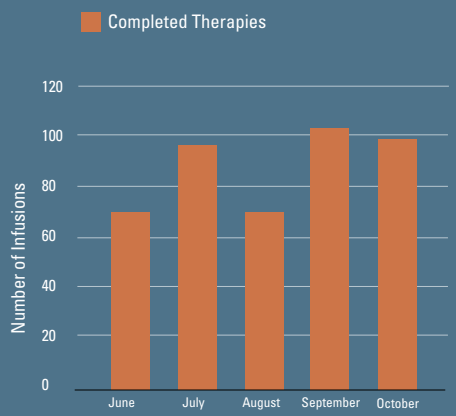
Our team of experienced clinicians offers care and support to promote the best possible health outcomes. Patients receive personalized treatment plans and medical monitoring while undergoing infusion therapy. Infusions are performed in a clean, comfortable setting with reclining chairs, heated linens, complimentary refreshments, television, and Wi-Fi.

At the Infusion Center, a physician oversees each care plan, and the care team remains consistent, allowing for streamlined communication. Medications are provided in a timely manner, their effectiveness is closely monitored, and treatments are adjusted as needed. The Infusion Center provides infusions of prescribed medications, including those for chemotherapy treatment, neurological treatment, and hydration therapies. We also oversee, as needed, maintenance of central-line catheters, outpatient therapy, and many other FDA-approved parenteral medications.

MEDICATIONS ADMINISTERED INCLUDE:

Acthar® Gel Injection
Avastin®
Cyclophosphamide
Depakote®
Dexamethasone
Dihydroergotamine (DHE)
Irinotecan
IV Immunoglobulin (IVIG)
Lemtrada®
Nivolumab (Opdivo®)
Ocrevus®
Reglan®
Remicade®
Rituxan® (rituximab)
Soliris®
Toradol®
Tysabri®
Zofran®

Infusion Center Volume

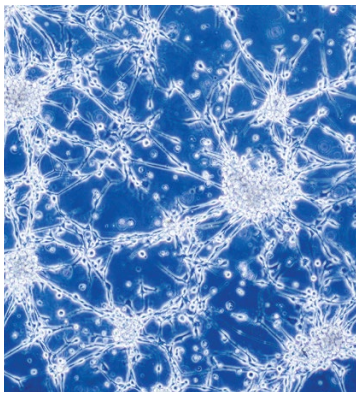


Source: Chart data from professional billing claims

RESEARCH HIGHLIGHT

DEVELOPMENT OF ARTIFICIAL INTELLIGENCE FRAMEWORK FOR ASSESSMENT OF RESPONSES TO TREATMENT AND AUTOMATED TUMOR VOLUME MEASUREMENT IN GLIOBLASTOMA

PRINCIPAL INVESTIGATOR: Jay-Jiguang Zhu, MD, PhD
Professor, Vivian L. Smith Department of Neurosurgery
McGovern Medical School at UTHealth
Director, Neuro-oncology, Memorial Hermann-Texas Medical Center



Abstract:

Poor prognosis with a short median overall survival of 11 months in glioblastoma patients (GBM WHO grade IV) has been a significant problem in the brain cancer field. A major challenge is the lack of accurate tools for identification of GBM status post-chemo-radiation (SOC), which is often ambiguous. The limited reliability of MRI scans in determining GBM progression has been a significant issue for physicians in deciding when to alter treatment. Although advanced brain tumor imaging MRI technologies (ABTI MRI) help, their cost and availability render them inaccessible to most patients, especially in non-academic centers.

There also are data, such as electronic health records and molecular biomarkers, which are not jointly utilized in the determination of GBM patient care. Recognizing the challenge and the technological gap, Zhu and his team are devising artificial intelligence (AI) technologies to connect the dots by fusing complementary information to build a stronger and better model for GBM responses to SOC. Focusing on co-teaching algorithms to learn from ABTI MRI and multi-modality learning algorithms to identify hybrid biomarkers, as well as obtaining tumor volume with no or minimal human supervision, they are piloting novel solutions to push the frontiers of GBM research and improve patient care. As a group of highly dedicated and experienced physicians and informaticians, they plan to develop integrated AI solutions with humans in the loop.

Built on the clinical knowledge and biological findings, their novel machine-learning algorithm goes beyond off-the-shelf tools, offering inherent connections between health care data and designed to learn from fragmented information. If successful, the project will profoundly improve GBM patient care, biomarker research, and clinical trials. It also will open the door to applying AI in other brain tumor research. The research grant was awarded in August 2020 by the Cancer Prevention and Research Institute of Texas.

Cerebrovascular

THE UTHEALTH NEUROSCIENCES Stroke Center, led by the Department of Neurology and the Vivian L. Smith Department of Neurosurgery at McGovern Medical School at UTHealth, has long been a leader in the treatment of stroke and other cerebrovascular diseases. Physicians at UTHealth helped Memorial Hermann-Texas Medical Center become the first facility in Texas to earn The Joint Commission's Comprehensive Stroke Center (CSC) certification in 2013, the highest quality standard for stroke care in the United States at the time.

In addition to breakthrough treatment for stroke, the cerebrovascular team has developed an integrated transfer network with protocols for evaluating and seamlessly routing acute stroke patients to one of four Memorial Hermann Comprehensive Stroke Centers. This network of accessibility is staffed by 6 neurosurgeons, 21 neurologists, 2 interventional neurologists, and a neuroradiologist. All are faculty at McGovern Medical School, and are available 24/7 to provide a high level of stroke care across Greater Houston, ensuring better outcomes. Complex cases are transferred rapidly to Memorial Hermann-TMC.

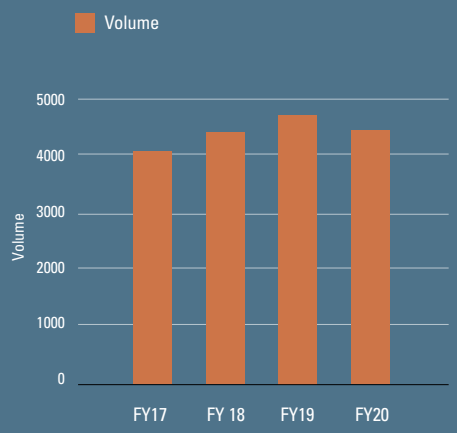
UTHealth neurosurgeons also provide coordinated care for patients with aneurysms, carotid occlusive disease, and intracranial vascular malformations, including open surgical and endovascular treatments such as angioplasty, stenting, and embolization. They are skilled at microvascular clipping of aneurysms using the most advanced 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® Icon™ is used regularly for vascular malformations best treated nonsurgically. Also available is the Pipeline™ endovascular flow-diverting stent, a device that reconstructs the parent vessel lumen of difficult-to-reach aneurysms as an alternative to clipping or endovascular coiling.

The UTHealth Neurosciences Cerebrovascular Surgery Program is staffed by nine specialists: Arthur L. Day, MD; P. Roc Chen, MD; Spiros Blackburn, MD; Mark Dannenbaum, MD; Gary Spiegel, MD; Joseph Cochran, MD; Wes Jones, MD; Yazan Alderazi, MD; and Sunil A. Sheth, MD. Day, Chen, Blackburn, and Cochran have extensive experience in skull base surgery; Chen, Blackburn, Dannenbaum, and Cochran are trained in both open and endovascular neurosurgery. Spiegel is an experienced neuroradiologist and neuroendovascular surgeon, and Sheth is trained as both a vascular neurologist and neuroendovascular surgeon. Alderazi is trained as a critical care and vascular neurologist, as well as a neuroendovascular surgeon. This multidisciplinary group has extended the UTHealth cerebrovascular program to locations across the city. Patients at UTHealth Neurosciences and benefit from a comprehensive array of procedures ranging from diagnostic angiograms to thrombectomies and endovascular coiling.

Our physicians stand among an elite group of providers in the country focused on complex stroke care. Opened in 1988 as one of the first dedicated stroke programs in the world, the Memorial Hermann-TMC Comprehensive Stroke Center is home to the 10-county Greater Houston area's largest onsite stroke team. UTHealth neurologists and neurosurgeons use leading-edge technology to diagnose and treat more than 2,000 stroke and aneurysm patients annually, ensuring that each patient receives the appropriate treatment quickly. By working closely with the Houston Fire Department and local EMS services, the stroke team has logged an impressive track record of success in the administration of tPA – more than five times the national average of 5 percent.

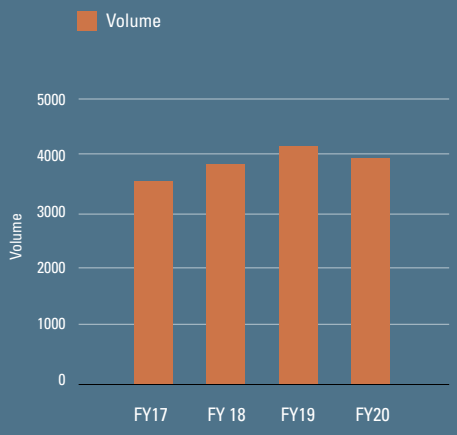

UTHealth
McGovern
Medical School

Cerebrovascular Volume



Source: Chart data from Vizient for Memorial Hermann-Texas Medical Center, Memorial Hermann Memorial City, Memorial Hermann Southwest, and Memorial Hermann The Woodlands

Stroke Volume



Source: Chart data from Vizient for Memorial Hermann-Texas Medical Center, Memorial Hermann Memorial City, Memorial Hermann Southwest, and Memorial Hermann The Woodlands

Sean Savitz, MD, is director of stroke program development for the Memorial Hermann Health System and also heads two parallel efforts that extend stroke research and clinical expertise beyond the Texas Medical Center to Memorial Hermann hospitals across Houston: the UTHealth Institute for Stroke and Cerebrovascular Disease and Memorial Hermann's Stroke Systems of Care. With funding from UTHealth, the Institute serves as a multidisciplinary hub for research and best practices in acute stroke treatment, stroke prevention, stroke recovery, population health, and health services. As the research infrastructure at the Texas Medical Center expands, the network for stroke research will be extended to Memorial Hermann's 14 acute care hospitals.

UTHealth Neurosciences' cerebrovascular continuum of care spans the gamut from pre-hospital ambulance care to the emergency center setting, and extends through a dedicated inpatient stroke unit, to neurorehabilitation at Memorial Hermann-TMC and at its sister hospital TIRR Memorial Hermann, an international leader in rehabilitation and research. Patients benefit from comprehensive outpatient stroke management through clinics, including the Stroke Transitions Education and Prevention (STEP) Clinic directed by Anjail Sharrief, MD. In the STEP Clinic at UTHealth Neurosciences, practitioners aim to reduce the 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-TMC Comprehensive Stroke Center consistently achieves excellent-to-perfect metrics for quality of care and outperforms national and peer-based benchmarks. A robust data core is provided to physicians by a team of programmers, data scientists, and medical abstractors, enabling leadership to monitor quality data in real time and use it to plan and implement evidence-based quality improvement measures.

The Department of Neurology at McGovern Medical School also has the largest stroke fellowship program in the country, led by Amanda Jagolino-Cole, MD. 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. Cochran, who specializes in endovascular and cerebrovascular surgery, leads a neurosurgery residency rotation at Memorial Hermann Southwest Hospital that has promoted further growth in treatment of arteriovenous malformations, intracerebral hemorrhage, and aneurysms at that site.

The UTHealth Neurosciences Telemedicine Program, directed by Teddy Wu, MD, extends stroke and neurology expertise far beyond the hospital'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 Department of Neurology at McGovern Medical School, providing real-time visual interactions between neurologists and patients, and allowing UTHealth 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. The Telemedicine Program is a flagship training program for residents and fellows in the stroke academic community, led by Jagolino-Cole; Alicia Zha, MD; and Tiffany Cossey, MD.

Physicians at UTHealth conduct more research than any other stroke program in the southwestern United States, participating in multicenter and

STROKE CORE MEASURES

GWTG Measure	MEASURE GOAL	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
VTE Prophylaxis	85%	97.9%	99.7%	99.1%	99.9%	100%	100%	99.9%	99.9%	99.8%	99.8%
Discharged on Antithrombotic Therapy	85%	100%	100%	98.8%	99.5%	100%	99.5%	99.5%	99.9%	99.8%	99.7%
Anticoagulation Therapy for Atrial Fib.	85%	100%	100%	97.9%	98%	97.2%	98.3%	99.2%	97.8%	93.4%	93.7%
Thrombolytic Therapy	85%	95.2%	100%	97%	94.6%	100%	100%	99.2%	99.2%	98.4%	95.6%
Antithrombotic Therapy by End of Hospital Day 2	85%	98.1%	99%	92.8%	97.8%	99.2%	98.8%	98.9%	98.2%	98.6%	98.6%
Discharged on Statin Medication	85%	94.2%	98.3%	98.2%	99.2%	100%	99.4%	99.7%	99.5%	99.7%	99.3%
Stroke Education	85%	92.9%	94.9%	96.1%	97.3%	98.4%	99.5%	99.4%	99.5%	98.1%	97.7%
Assessed for Rehabilitation	85%	98.7%	99.4%	99.2%	99.8%	99.7%	99.9%	99.7%	99.4%	99.6%	99.5%

Source: Chart data based on fiscal year

single-center clinical trials testing new treatments for patients who cannot be treated elsewhere. McGovern Medical School, in partnership with the Memorial Hermann-TMC Comprehensive Stroke Center, was chosen as the only regional coordinating center in Texas and the southwestern 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. UTHealth serves as the flagship coordinating clinical stroke trials throughout the region.

Pioneering stroke research at McGovern Medical School includes 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. Savitz is leading pioneering studies in stroke recovery using stem cells, with promising results. Investigations led by Andrew Barreto, MD, 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. McGovern Medical School 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 2), led by Amrou Sarraj, MD.

Cerebral aneurysms are a significant cause of morbidity and mortality, and at McGovern Medical School, physicians collaborate on research to improve outcomes after brain bleeding. Blackburn has done National Institutes of Health-funded work investigating the role of hyperactive platelets causing strokes after brain bleeding. In addition, though his efforts, the medical school is the leading national enroller for a sponsored clinical trial investigating the use of spinal fluid filtration to remove the toxic breakdown products of red blood cells before they cause strokes after aneurysm bleeding. To address the delayed strokes that occur following aneurysm bleeding, Chen is leading a multicenter clinical trial investigating the use of vasodilators to open brain arteries and improve brain blood flow.

By supporting interdisciplinary collaborative research from neuroscience, clinical neurology, vascular biology, immunology, cerebrovascular diseases, and aging, the UTHealth BRAINS Research Laboratory 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, MD, PhD, the lab consists of 11 other independent investigators. Funded by the National Institutes of Health and the American Heart Association to study aspects of stroke and vascular disease, the lab has programs ranging from neonatal stroke to post-stroke dementia. Fudong Liu, MD, examines how sex differences in inflammation alter outcomes after neonatal stroke, and Venu Venna, PhD, is working on understanding the role of an emerging cytokine, macrophase migration inhibitory factor, in post-stroke depression, cognitive impairment, and post-stroke recovery. New work by Akihiko Urayama, PhD, in collaboration with Claudio Soto, PhD, a world-renowned expert in neurodegenerative diseases, has shown that transfer of blood from young animals can reduce age-related inflammation. The group also is invested in training, and has numerous postdoctoral fellows and MD/PhD students actively engaged in research.

Led by Jaroslaw Aronowski, MD, PhD, and funded by multiple grants from the National Institutes of Health, studies in intracerebral hemorrhage (ICH) – the stroke subtype with the highest mortality – are focused on the development of new treatments. 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 in experimental models. Discoveries from this research led to a clinical trial investigating factors linked to hematoma clearance as a new therapeutic approach in patients with ICH.

RESEARCH PROGRAMS AT THE BRAINS RESEARCH LABORATORY 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
- How manipulations of the microbiome can improve stroke recovery and disease progression in animal models of dementia
- The role of calcium signaling in stroke
- How manipulation of the brain's resident immune cells may help limit ischemic injury and promote tissue repair after stroke
- G-quadruplex DNA in senescence
- Effect of genetic sex and aging on atrial fibrillation and cardioembolic strokes
- Aging-associated changes in the neurovascular unit involved in brain health and disease

UTHEALTH BRAINS RESEARCH LABORATORY INVESTIGATORS

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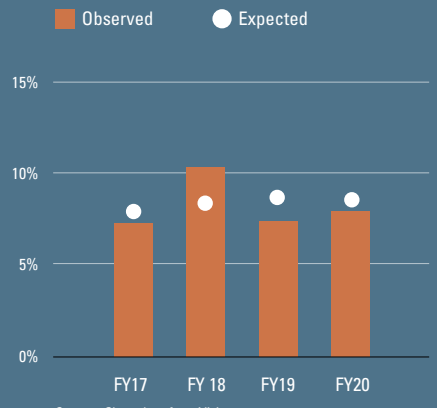
Gab Seok Kim, PhD
Jun Li, PhD
Fudong Liu, MD
Bharti Manwani, MD, PhD
Sean Marrelli, PhD
Jose Felix Moruno-Manchon, PhD
Andrey Tsvetkov, PhD
Akihiko Urayama, PhD
Venu Venna, PhD

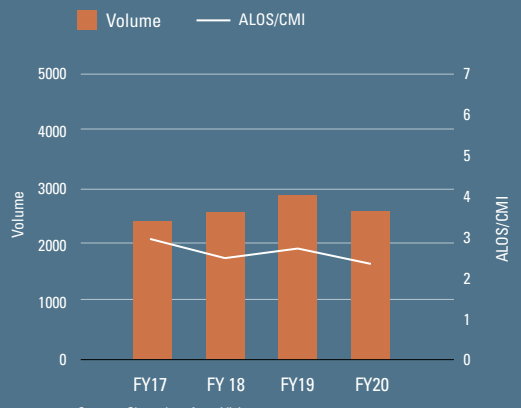
QUALITY & OUTCOMES MEASURES

Acute Ischemic Stroke: Inpatient Mortality



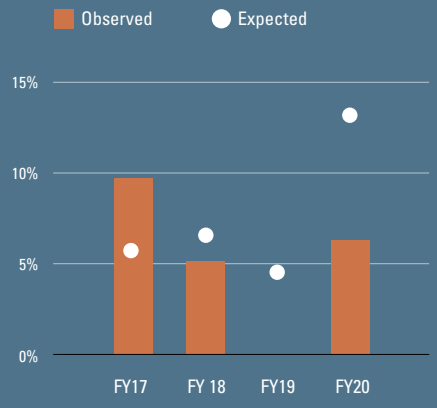
Source: Chart data from Vizient

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



Source: Chart data from Vizient

Arteriovenous Malformation: Inpatient Mortality



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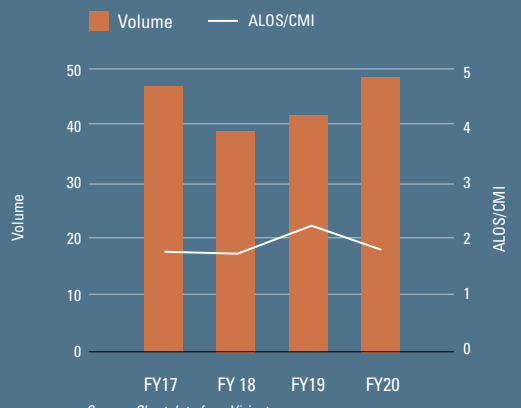
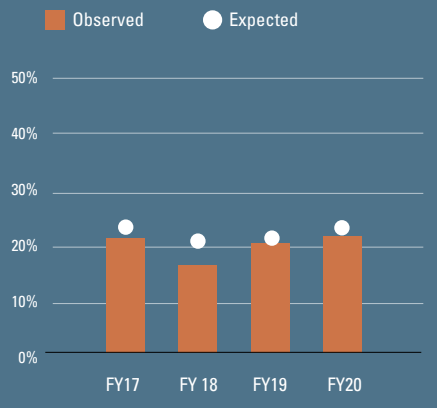
Arteriovenous Malformation: Volume & Length of Stay (CMI Adjusted)



Source: Chart data from Vizient

Subarachnoid Hemorrhage: Inpatient Mortality



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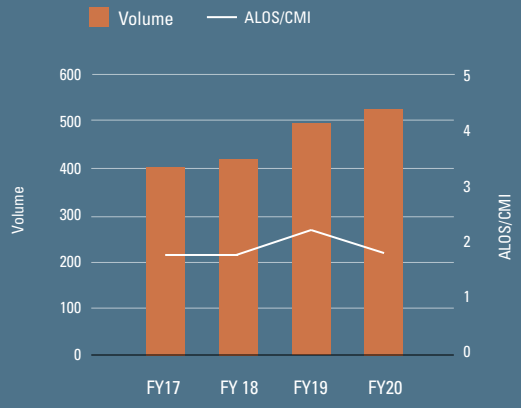
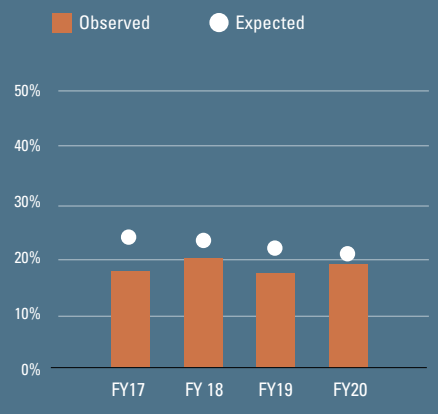
Subarachnoid Hemorrhage: Volume & Length of Stay (CMI Adjusted)



Source: Chart data from Vizient

Intracerebral Hemorrhage: Inpatient Mortality



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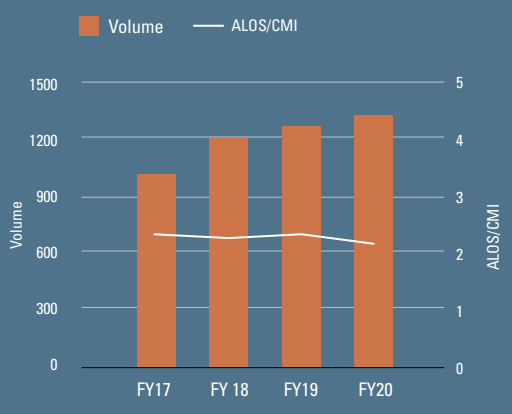
Intracerebral Hemorrhage: Volume & Length of Stay (CMI Adjusted)



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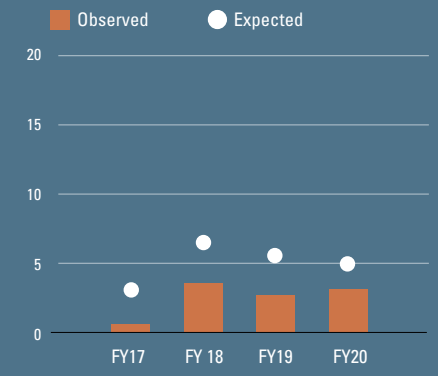
Unruptured Aneurysm: Inpatient Mortality



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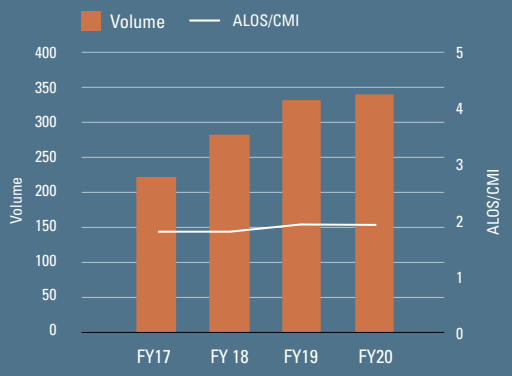
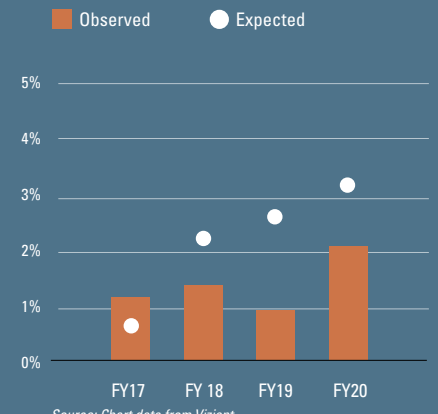
Unruptured Aneurysm: Volume & Length of Stay (CMI Adjusted)



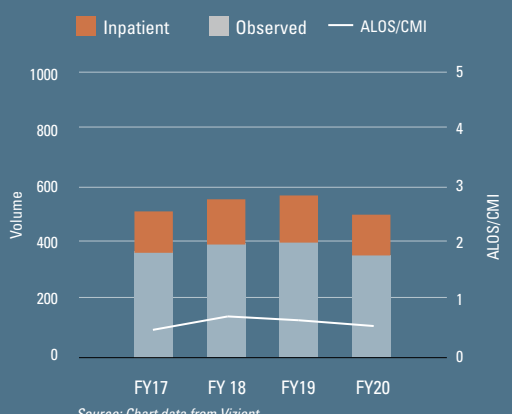
Source: Chart data from Vizient

Transient Ischemic Attack: Inpatient Mortality



Source: Chart data from Vizient

Transient Ischemic Attack: Volume & Length of Stay (CMI Adjusted)



Source: Chart data from Vizient

RESEARCH HIGHLIGHT

OPTIMIZED LACTOFERRIN AS PROMISING TREATMENT FOR INTRACEREBRAL HEMORRHAGE

PRINCIPAL INVESTIGATOR: Jaroslaw Aronowski, MD, PhD
Professor and Vice Chair for Research
Roy M. and Phyllis Gough Huffington Chair in Neurology
Department of Neurology
McGovern Medical School at UTHealth

Intracerebral hemorrhage (ICH) is the deadliest form of stroke, with the highest mortality among all stroke subtypes. Rapid accumulation of immune cells results in oxidative stress, inflammation and the accumulation of toxic products of hemolysis (e.g., heme, hemoglobin, and iron) at the site of the ICH, leading to a massive injury to the brain tissue and deadly perihematomal edema. There are no effective treatments currently available for ICH and brain edema.

Overview of Therapeutic Technology: Lactoferrin is an endogenous glycoprotein with anti-microbial and immunoregulatory functions, with the potential to curtail the inflammatory response and promote repair. It is also a potent iron toxicity neutralizing protein. However, endogenous lactoferrin has limited therapeutic potential due to its short half-life in the blood and its limited capacity for blood-brain barrier penetration. Researchers at UTHealth Neurosciences have optimized lactoferrin by creating a novel fusion protein (PRC14) that has been demonstrated to combat multiple aspects of ICH pathogenesis.

Stage of Development: Studies of PRC14 in rodents, including hypertensive rats and aged mice, have shown reduction in neurological deficit, reduction in edema, and faster hematoma clearance with a uniquely long 24-hour window of treatment opportunity. Promising results have also been demonstrated in a pig model of ICH. This technology is well positioned to advance into clinical studies. Stroke care is a primary area of expertise at UTHealth Neurosciences and its affiliated quaternary hospital Memorial Hermann-Texas Medical Center, where there is a large cohort of ICH patients as well as significant expertise available for future clinical studies in this area.

For more information:

Zhao X, Kruzel M, Ting S-M, Sun G, Savitz SI, Aronowski J. Optimized lactoferrin as a highly promising treatment for intracerebral hemorrhage: Pre-clinical experience. Journal of Cerebral Blood Flow & Metabolism. 2020 May 21;271678X20925667. doi: 10.1177/0271678X20925667. Online ahead of print.

RESEARCH HIGHLIGHT

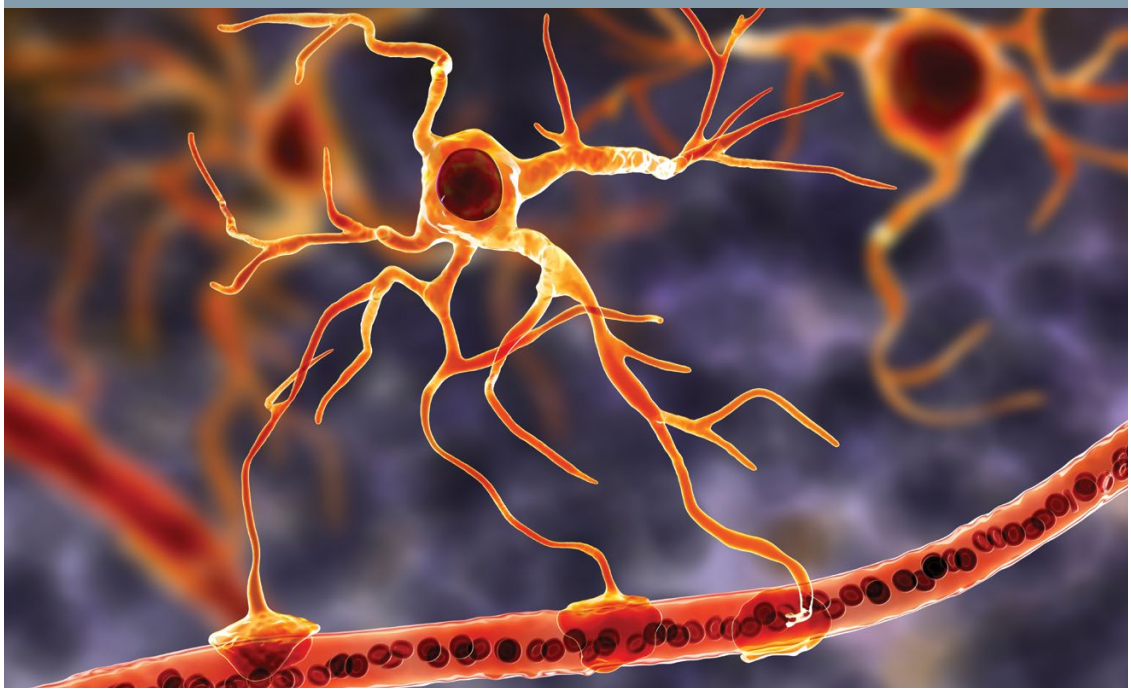
UNDERSTANDING AND TARGETING EPIGENETIC REGULATION OF BLOOD-BRAIN BARRIER FORMATION

PRINCIPAL INVESTIGATOR: Peeyush K. Thankamani Pandit, PhD
Assistant Professor, Vivian L. Smith Department of Neurosurgery
McGovern Medical School at UTHealth

The blood-brain barrier (BBB) acts as a strict barrier to separate ions, molecules, and cells in the blood from neuronal cells. The integrity of this barrier is compromised in several pathological conditions, including stroke, edema, brain trauma, and multiple sclerosis. Despite the importance off the BBB in maintaining brain homeostasis, the fundamental genetic mechanism that regulates the formation and maintenance of this specialized structure remains elusive.

Endothelial cells that line the blood vessels are a major contributor to BBB properties. Epigenetic mechanisms are central to their development and differentiation via control of gene expression. With the support of a career development grant from the American Heart Association, the researchers are using a combination of cellular, molecular, and genetic approaches to understand the epigenetic mechanisms in endothelial cells that support the formation and maintenance of the blood-brain barrier. They also are targeting the epigenetic mechanisms in endothelial cells to repair post-stroke leaks in the BBB.

The long-term goal of their research is to clarify these epigenetic mechanisms of the BBB during health and disease in order to develop epigenetic drugs to reestablish the barrier and treat neurological diseases.



Astrocytes connect neuronal cells to blood vessels to create the blood-brain barrier.

RESEARCH HIGHLIGHT

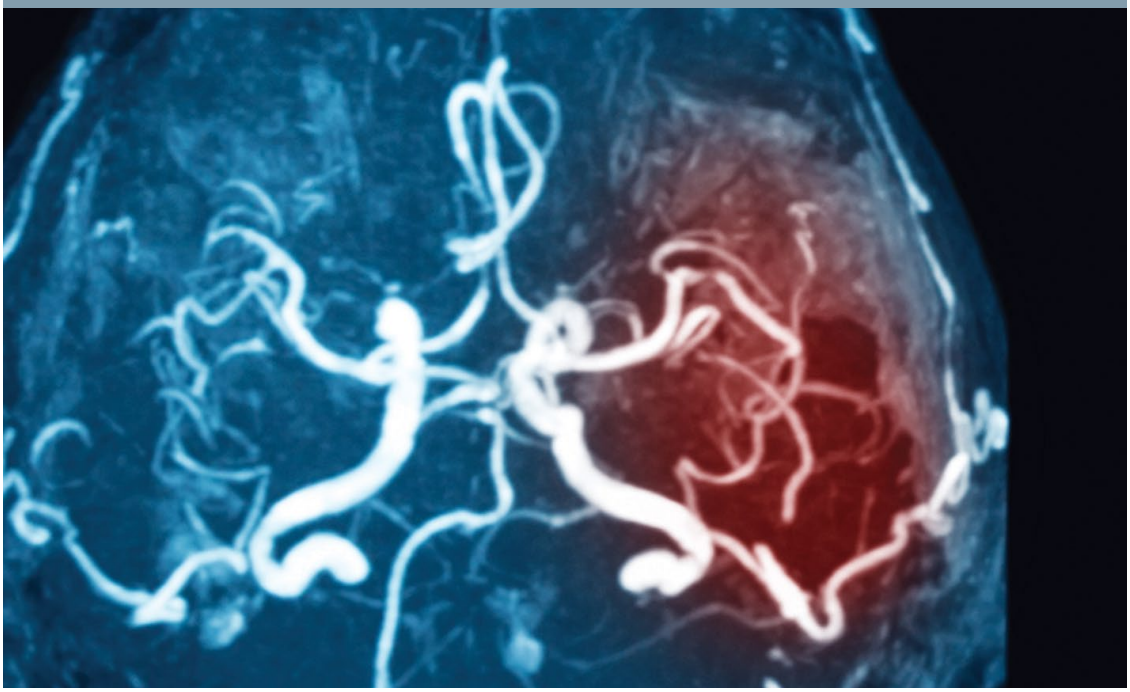
ROLE OF AUTOPHAGY IN THSD1-MEDIATED INTRACRANIAL ANEURYSM

PRINCIPAL INVESTIGATOR: Yanning Rui, PhD
Assistant Professor, Vivian L. Smith Department of Neurosurgery
McGovern Medical School at UTHealth

An intracranial aneurysm (IA) is a focal dilatation of an arterial blood vessel in the brain. The rupture of IA causes subarachnoid hemorrhage, a major cause of death and disability in patients. Unfortunately, no drugs are available to treat IA. Lack of knowledge about the underlying pathogenic mechanisms further impedes attempts to find new therapeutic targets.

Recently, our research team found that autophagy, a self-eating system in the cells, is involved in IA disease. Importantly, genetic inactivation of the autophagy pathway rescues defects in cerebrovascular integrity in animal models and focal adhesion assembly in endothelial cells. It is well established that in the vascular system, focal adhesion can mediate interactions between endothelial cells and the extracellular matrix that are critical for cerebrovascular integrity, which is compromised during IA pathogenesis. Our work supports that autophagy negatively regulates endothelial focal adhesion by degrading its essential components, and thus plays a pathogenic role in IA development. As numerous compounds targeting autophagy have been developed, including several FDA-approved drugs (e.g., verteporfin, clomipramine, and chloroquine), our research may establish anti-autophagy as a novel therapy for IA disease.

The study was funded by a National Institutes of Health R21 grant.



An MRI scan of the brain reveals intracerebral hemorrhages.

Children's Neuroscience

PEDIATRIC NEUROSURGEONS David Sandberg, MD, FAANS, FACS, FAAP; Stephen Fletcher, DO; and Manish N. Shah, MD, FAANS, bring a broad range of clinical and research expertise to the Children's Neuroscience Center at UTHealth Neurosciences.

Translational studies conducted by Sandberg have demonstrated the safety of infusing chemotherapeutic agents directly into the fourth ventricle of the brain to treat children with recurrent malignant brain tumors. Three studies are currently enrolling at Children's Memorial Hermann Hospital: Clinical Trial of High-Dose MTX110 (Soluble Panobinostat), A Combination Intraventricular Chemotherapy Pilot Study, and Infusion of 5-Azacytidine.

Fletcher participates in fetal neurosurgery efforts at The Fetal Center at Children's Memorial Hermann Hospital, affiliated with McGovern Medical School at UTHealth and UT Physicians. The Fetal Center is a national leader in 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 in-utero spina bifida repair in the region, and patients are now being referred to the Center for fetal myelomeningocele repair from throughout Texas and across the United 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 mothers by performing the procedure endoscopically. The combined efforts of basic scientists, general and fetal surgeons, neurosurgeons, pathologists, and radiologists have led to a novel method to close the spinal defect using cryopreserved human umbilical cord. A recent Food and Drug Administration clinical trial was approved to perform the procedure using endoscopic repair.

Shah, who has special expertise in the surgical management of spasticity and dystonia in children, directs the Texas Comprehensive Spasticity Center. Providers at the center, part of McGovern Medical School, see patients in clinic at UT Physicians Pediatric Surgery. Dr. Shah performs selective dorsal rhizotomies, baclofen pump placement, and deep brain stimulation. He also has expertise in pediatric epilepsy, craniofacial surgery and craniocervical spine surgery. His National Institutes of Health-funded laboratory focuses on advanced imaging-based enhancement of patient selection and surgical outcomes in cerebral palsy, epilepsy, and hydrocephalus.

Shah recently worked with a team of scientists to develop cap-based transcranial optical tomography (CTOT), the first wearable, high-resolution, whole-brain functional imaging device that does not require anesthesia in infants. Using night-vision goggle technology, near-infrared light and high-resolution detectors, CTOT helps physicians accurately diagnose the severity of an infant's brain injury and diagnose treatment that will optimize quality of life throughout childhood.

To avoid the many complications of ventriculoperitoneal shunting for children with hydrocephalus, UTHealth pediatric neurosurgeons routinely perform minimally invasive techniques such as endoscopic 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 UTHealth 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 UTHealth craniofacial plastic surgeons, pediatric neurosurgeons perform both conventional and minimally invasive endoscopic surgeries to repair craniosynostosis and other complex craniofacial anomalies. The multidisciplinary Texas

Cleft-Craniofacial Team, established in 1952, has been a regional leader in pediatric craniofacial surgery for decades.

Children's Memorial Hermann Hospital is also a renowned center for pediatric epilepsy surgery and comprehensive specialized care for children with refractory epilepsy. The pediatric Epilepsy Monitoring Unit is one of 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, UTHealth physicians use the Elekta Neuromag® for noninvasive functional mapping of brain activity with magnetoencephalography (MEG) to help locate the source of epileptic seizures and minimize risk for children undergoing resective surgery for refractory epilepsy. For the most accurate diagnosis, they may 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. Shah directs the Pediatric Epilepsy Surgery Program at Children's Memorial Hermann Hospital. Gretchen Von Allmen, MD, is chief of pediatric epilepsy for the Texas Comprehensive Epilepsy Program and medical director of the Children's Memorial Hermann Hospital Pediatric Epilepsy Monitoring Unit. Along with pediatric epileptologists Jeremy Lankford, MD, and Michael Watkins, MD, they work with other adult and pediatric epilepsy specialists to manage patients over their entire lifespan for a seamless transition of care.

UTHealth physicians provide treatment for retinoblastoma, a rare pediatric eye malignancy that affects only 250 to 350 new patients each year. They were the first in Texas and one of only a handful of physicians in the United States to administer intra-arterial chemotherapy, the most modern treatment for the disease, by which chemotherapy is injected

THE CHILDREN'S NEUROSCIENCE CENTER AT UTHEALTH PROVIDES A BROAD RANGE OF DIAGNOSTIC AND TREATMENT SERVICES FOR CHILDREN WITH COMPLEX NEUROLOGICAL PROBLEMS INCLUDING:

- Autism
- Brain tumors and malformations
- Cerebral palsy
- Chiari malformation
- Congenital hydrocephalus
- Craniofacial disorders
- Developmental disorders
- Endoscopic neurosurgery
- Epilepsy
- Chronic headache and migraine
- Learning disabilities
- Movement disorders
- Myopathy
- Neurofibromatosis
- Neurometabolic disorders
- Neuromuscular disorders
- Pediatric stroke
- Peripheral nerve disorders
- Sleep disorders
- Spasticity
- Spina bifida
- Spinal deformities
- Tourette syndrome
- Traumatic brain and spine injury
- Tuberous sclerosis complex

RESEARCH HIGHLIGHT

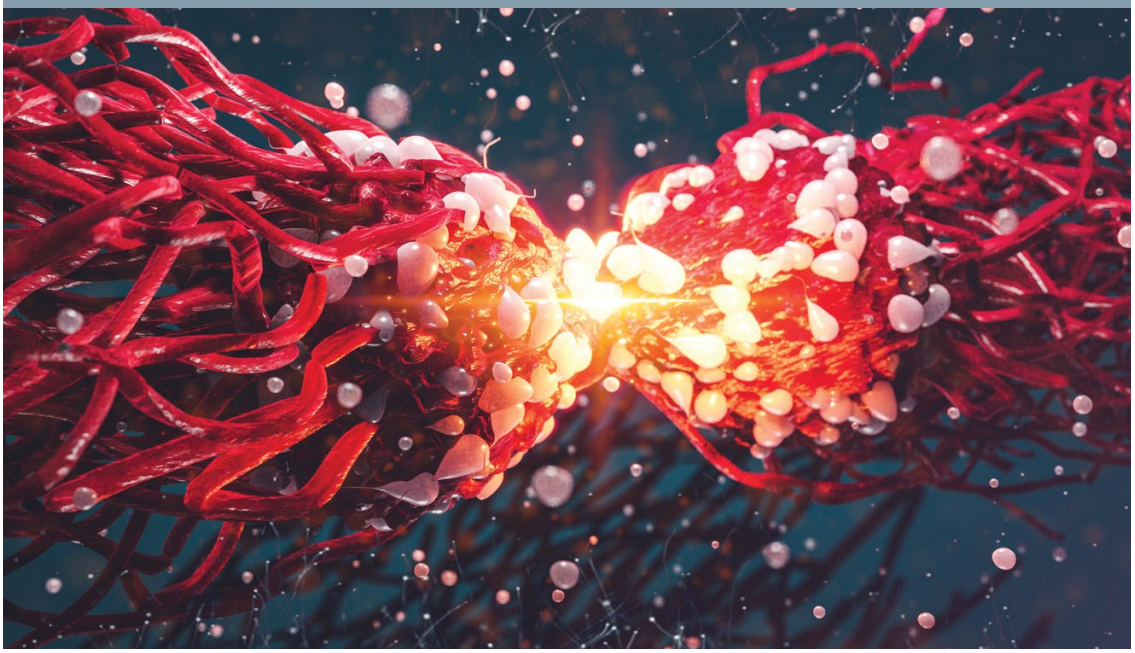
CLINICAL TRIAL OF HIGH-DOSE MTX110 (SOLUBLE PANOBINOSTAT) FOR THE TREATMENT OF MEDULLOBLASTOMA

PRINCIPAL INVESTIGATOR: David I. Sandberg, MD
Professor, Vivian L. Smith Department of Neurosurgery and Department of Pediatric Surgery
Dr. Marnie Rose Professor in Pediatric Neurosurgery
McGovern Medical School at UTHealth
Director, Pediatric Neurosurgery, Children's Memorial Hermann Hospital

A novel clinical trial of MTX110, a new formulation of soluble panobinostat from Midatech Pharma, is now enrolling patients. Current treatments for children and adults are often associated with considerable toxicity, and when tumors recur after treatment, survival rates are low, despite salvage therapy. In this new trial of a novel drug, the researchers hope to help patients overcome this devastating disease.

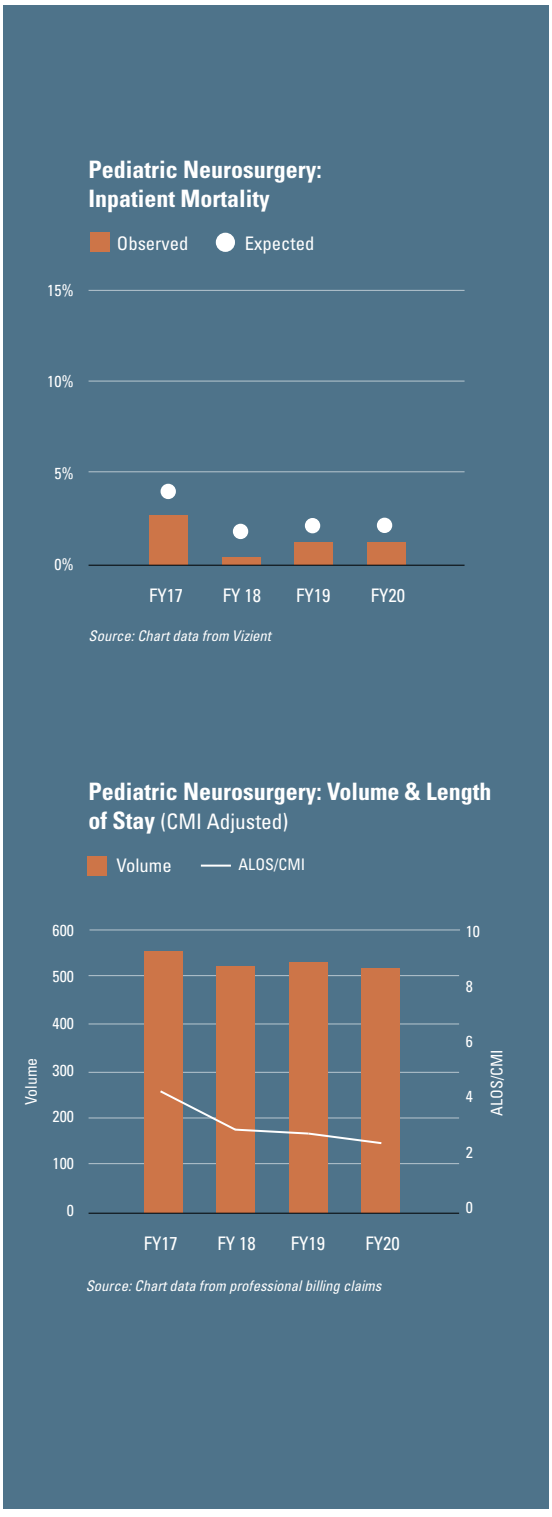
The trial follows a successful study led by David Sandberg, MD, in an animal model, which demonstrated that MTX110 can be safely infused in the fourth ventricle and can achieve drug levels dramatically higher than intravenous or oral administration of the same drug. The study team found no MRI signal changes in the brainstem, cerebellum, or elsewhere in the brain after fourth-ventricle infusions in the animal study group. In addition, the cytoarchitecture of the brain was preserved in all of the animals, with only mild postsurgical changes.

The pilot study, which has been approved by the U.S. Food and Drug Administration, will enroll five patients with recurrent medulloblastoma at Children's Memorial Hermann Hospital.



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 UTHealth ocular oncologist Amy Schefler, MD, and UTHealth neurointerventionalist Mark Dannenbaum, MD, the team includes pediatric oncologist Deborah Brown, MD, 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 are also engaged in research investigating new ways to save eyes that have failed conventional therapies.

UTHealth physicians 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. When surgery is required, physicians use advanced imaging techniques and minimally invasive procedures that lower patient risk.




DAVID I. SANDBERG M.D.
PEDIATRIC NEUROSURGERY

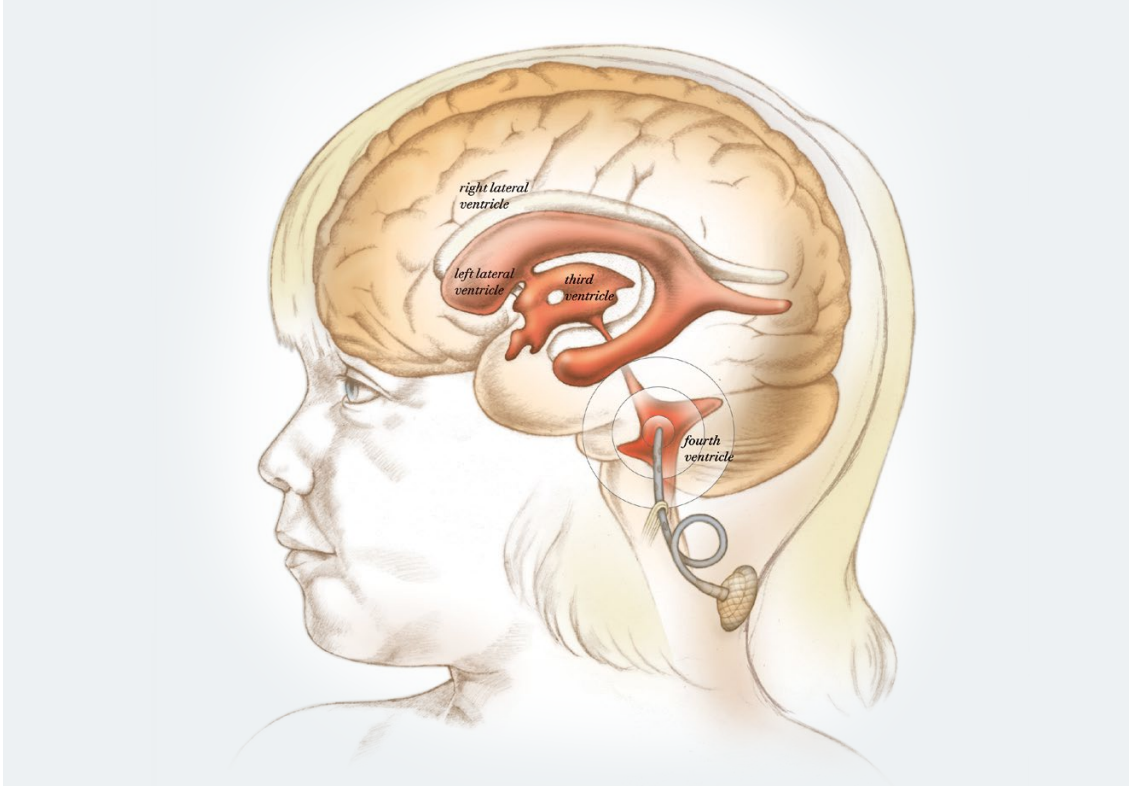
RESEARCH HIGHLIGHTS

INFUSION OF 5-AZA INTO THE FOURTH VENTRICLE OR RESECTION CAVITY IN CHILDREN WITH RECURRENT POSTERIOR FOSSA EPENDYMOMA

PRINCIPAL INVESTIGATOR: David I. Sandberg, MD
Professor, Vivian L. Smith Department of Neurosurgery and Department of Pediatric Surgery
Dr. Marnie Rose Professor in Pediatric Neurosurgery
McGovern Medical School at UTHealth
Director, Pediatric Neurosurgery, Children's Memorial Hermann Hospital

This clinical trial at Children's Memorial Hermann Hospital involves infusion of 5-Azacytidine (5-AZA) into the fourth ventricle or resection cavity in children with recurrent posterior fossa ependymoma. The study is open to participants age 1 to 21 years old.

5-AZA is a DNA methylation inhibitor that has been infused in an animal model with no neurological toxicity, while achieving substantial and sustained cerebrospinal fluid levels. Recent studies demonstrated that 5-AZA kills ependymoma cells. The researchers hope to establish the safety of direct administration of 5-AZA into the fourth ventricle, and also demonstrate the clinical efficacy of the infusions. Because low-dose infusions in their pilot trial showed shrinkage of some tumors in the brain, they hope that higher and more frequent doses will lead to even more robust responses.



COMBINATION INTRAVENTRICULAR CHEMOTHERAPY PILOT STUDY: METHOTREXATE AND ETOPOSIDE INFUSIONS INTO THE FOURTH VENTRICLE OR RESECTION CAVITY IN CHILDREN WITH RECURRENT POSTERIOR FOSSA BRAIN TUMORS

PRINCIPAL INVESTIGATOR:
David I. Sandberg, MD
Professor, Vivian L. Smith Department of Neurosurgery and Department of Pediatric Surgery
Dr. Marnie Rose Professor in Pediatric Neurosurgery
McGovern Medical School at UTHealth
Director, Pediatric Neurosurgery, Children's Memorial Hermann Hospital

David Sandberg, MD, and his research team are investigating combined methotrexate and etoposide infusions into the fourth ventricle in children and adults with recurrent posterior fossa brain tumors. The trial is open to patients age 1 to 80 years with recurrent medulloblastoma, recurrent ependymoma, or recurrent atypical teratoid/ rhabdoid tumors of the brain and/or spine. The study builds on translational models of direct infusion chemotherapy into the fourth ventricle of the brain in animal models, developed by Sandberg.

The researchers' primary objective is to determine if combination intraventricular infusions of these two agents are safe. They are also assessing the antitumor activity of the infusions in the hope that they will yield even more robust treatment responses than those observed in previous single-agent trials. They hope for continued demonsration of safety and even more robust clinical responses than in previous trials, which produced promising results.

DYNAMIC NEAR-INFRARED FLUORESCENCE IMAGING OF CSF OUTFLOW: A TOOL TO MANAGE PEDIATRIC HYDROCEPHALUS

CO-PRINCIPAL INVESTIGATOR:
Manish N. Shah, MD
Associate Professor, Division of Pediatric Neurosurgery, Department of Pediatric Surgery and Vivian L. Smith Department of Neurosurgery
William J. Devane Distinguished Professor
McGovern Medical School at UTHealth
Director, Texas Comprehensive Spasticity Center

CO-PRINCIPAL INVESTIGATOR:
Eva Sevick-Muraca, PhD
Professor and Director, Center for Molecular Imaging
Nancy and Rich Kinder Distinguished Chair in Cardiovascular Disease Research
McGovern Medical School at UTHealth

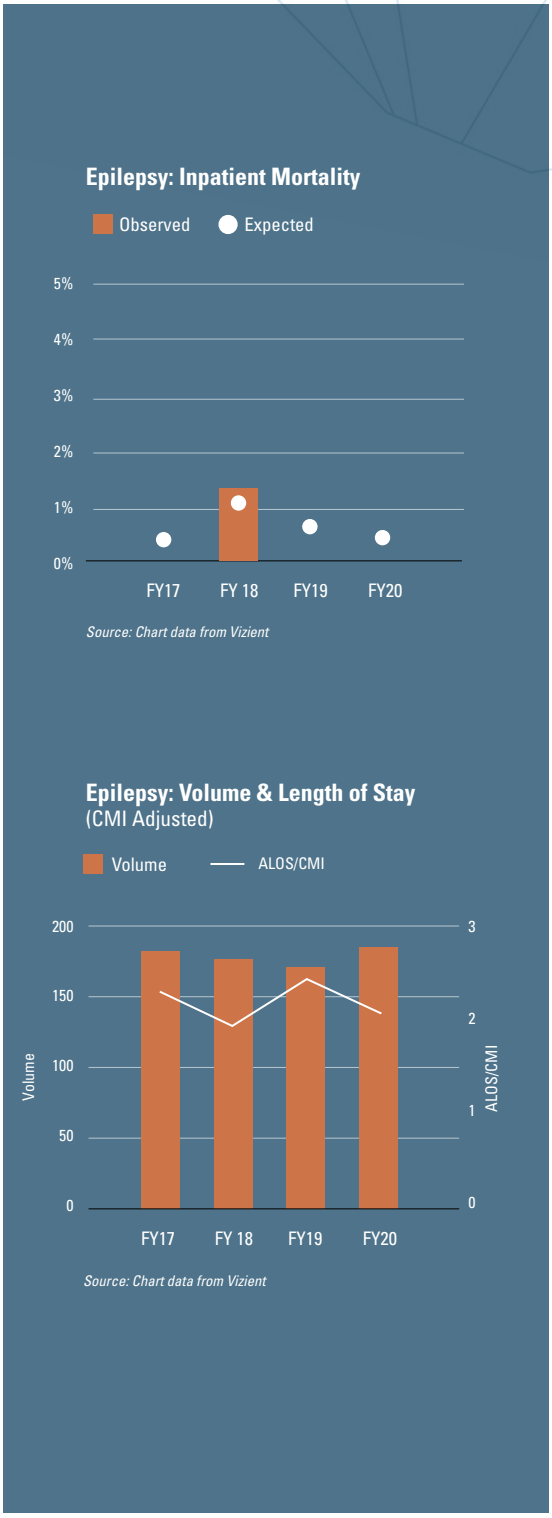
Funded by an R21 grant from the National Institute of Neurological Disorders and Stroke, the co-principal investigators, along with collaborator Banghe Zhu, PhD, will assess fluorescence-based cerebrospinal fluid flow in an animal model using their whole-brain optical imaging technology: cap-based transcranial optical tomography (CTOT). CTOT is the first wearable, high-resolution, whole-brain functional imaging device that does not require infants to be put under anesthesia. Using night-vision goggle technology, near-infrared light and high-resolution detectors, CTOT helps physicians accurately diagnose the severity of an infant's brain injury and prescribe treatment that will optimize quality of life throughout childhood.

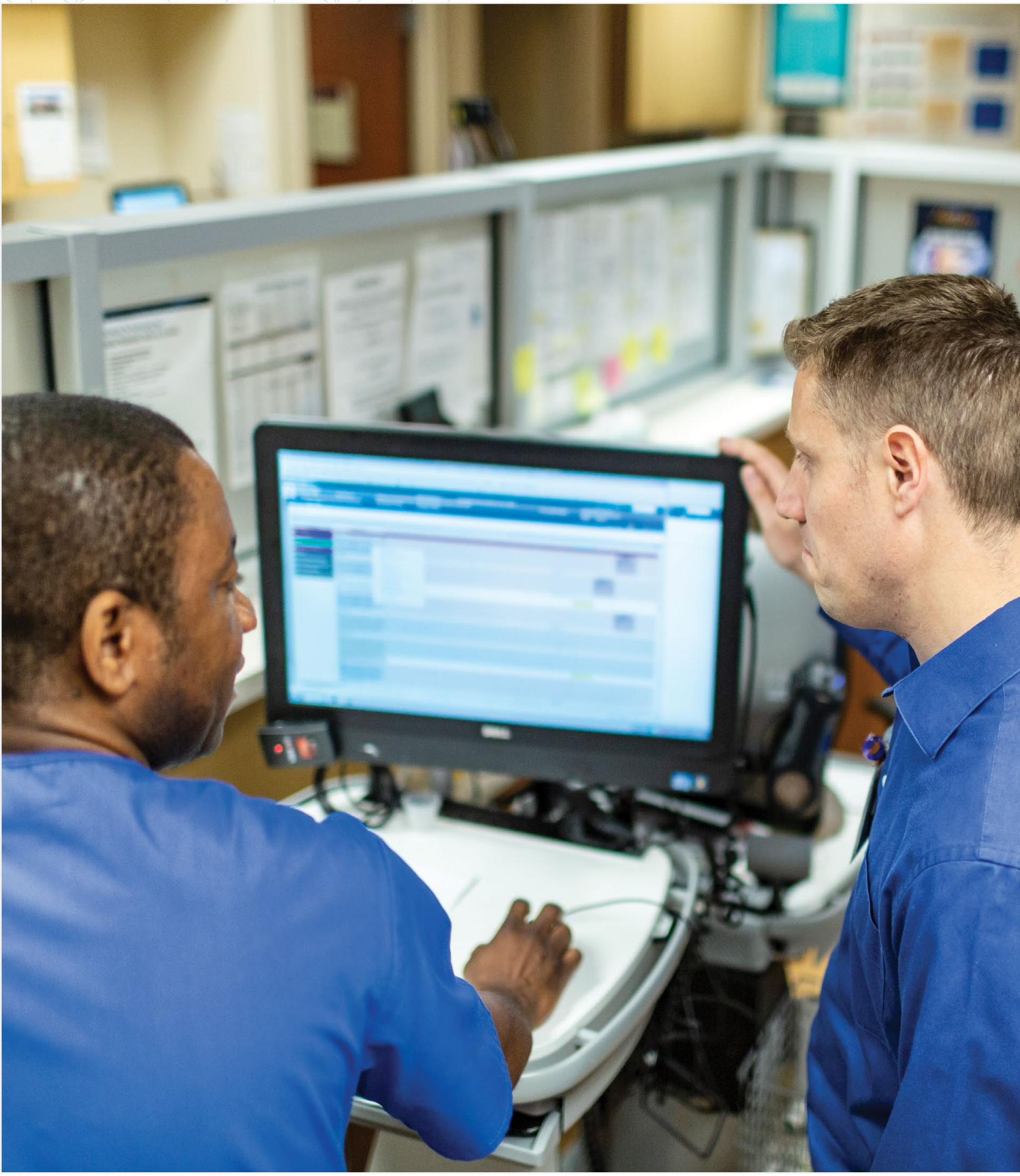
Epilepsy

A COLLABORATIVE effort between UTHealth Neurosciences at McGovern Medical School at UTHealth and Memorial Hermann-Texas Medical Center, the Texas Comprehensive Epilepsy Program (TCEP) is a Level 4 National Association of Epilepsy Centers-certified center. TCEP now includes 10 adult and three pediatric epileptologists and an adult and pediatric epilepsy surgeon, making the program 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 for each patient.

TCEP is led by Samden Lhatoo, MD, executive vice chair of the Department of Neurology at McGovern Medical School. At the heart of the program is a state-of-the-art seven-bed adult Epilepsy Monitoring Unit (EMU) and a six-bed pediatric EMU, together comprising the largest and most comprehensive monitoring unit of its kind in the region. The 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 neurosurgeon Nitin Tandon, MD, the program is a world leader in epilepsy surgery. Tandon has performed more than 900 cranial procedures for the localization and treatment of epilepsy with a zero 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, UTHealth Neurosciences physicians have developed several innovative surgical procedures for epilepsy. Prominent among these are robotic stereoelectroencephalography (SEEG) for 3D investigation of epileptic foci in the brain with 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 Tandon recently performed his 200th robotic SEEG implantation with less than 1 percent morbidity from the placement of nearly 3,000 electrodes.

UTHealth Neurosciences physicians are pioneering the use of 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, UTHealth physicians use it in novel ways, including the treatment of deep-seated periventricular nodular heterotopia and hypothalamic hamartoma. More than 125 Visualase procedures have been completed 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. The 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.

The TCEP has been involved in clinical trials related to most of the new epilepsy treatments approved in the United States in the last two decades. UTHealth Neurosciences physicians have also contributed patient data to nationwide trials in epilepsy genetics and epidemiology. The program is a member of the National Critical Care EEG Monitoring Research Consortium.

Tandon and Lhatoo, together with big data scientist GQ Zhang, PhD, direct the Texas Institute for Restorative Neurotechnologies (TIRN), which integrates efforts across specialties and schools at UTHealth to advance clinical care for epilepsy and other functional neurological disorders. TIRN brings together the imagination and energy of these three leaders in the fields of neurology, neurosurgery, neuromodulation, and neurodata, who aim to leverage systems neuroscience, neurotechnology, and neuroinformatics to develop transformative treatments for functional disorders of the brain.

ADVANCED DIAGNOSTIC TECHNOLOGIES

- Board-certified physicians employing advanced diagnostic technologies that provide comprehensive datasets to help define and localize brain seizure networks.
- High-definition MRI employing specialized sequences to probe gray and white matter and eloquent function, including double-inversion recovery, diffusion tensor imaging, and functional MRI
- Magnetoencephalography (MEG) coupled with high-density electroencephalography (EEG) for spike localization and cognitive function mapping
- State-of-the-art video-EEG for epilepsy electroclinical classification
- Positron emission tomography (PET) and single-photon emission computed tomography (SPECT) for probing cerebral metabolism
- Intra-carotid amytal (Wada) testing for language and memory lateralization
- Epilepsy-specific neuropsychological testing

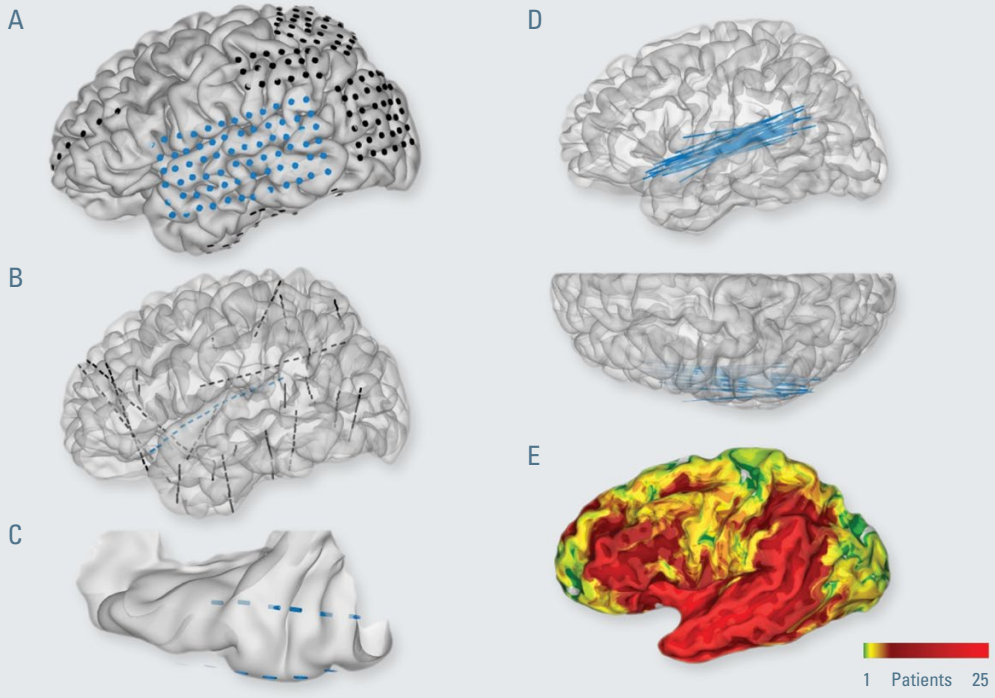
RESEARCH HIGHLIGHT

LANGUAGE PREDICTION MECHANISMS IN HUMAN AUDITORY CORTEX

Forseth KJ, Hickok G, Rollo PS, Tandon N. Nature Communications. 2020 Oct 16;11(1):5240. doi: 10.1038/s41467-020-19010-6.

Abstract:

Spoken language, both perception and production, is thought to be facilitated by an ensemble of predictive mechanisms. We obtained intracranial recordings in 37 patients using depth probes implanted along the anteroposterior extent of the supratemporal plane during rhythm listening, speech perception, and speech production. These reveal two predictive mechanisms in early auditory cortex with distinct anatomical and functional characteristics. The first, localized to bilateral Heschl's gyri and indexed by low-frequency phase, predicts the timing of acoustic events. The second, localized to planum temporale only in language-dominant cortex and indexed by high-gamma power, shows a transient response to acoustic stimuli that is uniquely suppressed during speech production. Chronometric stimulation of Heschl's gyrus selectively disrupts speech perception, while stimulation of planum temporale selectively disrupts speech production. This work illuminates the fundamental acoustic infrastructure – both architecture and function – for spoken language, grounding cognitive models of speech perception and production in human neurobiology.



A. Grid electrodes localized relative to patient-specific cortical model, including a lateral temporal grid.
B. The same patient with a second implant using stereotactic depth electrodes, including an anteroposterior supratemporal trajectory.
C. Dorsal view of the supratemporal plane in the same patient with depth electrodes in Heschl's gyrus and planum temporal, as well as the closest grid electrodes over lateral superior temporal gyrus.
D. All anteroposterior supratemporal trajectories superimposed in Talairach space relative to the MN127 atlas.
E. Recording zone density from all electrodes on an inflated MN127 atlas.

Memory Disorders and Dementia

PHYSICIANS at the UTHealth Neurosciences Neurocognitive Disorders Center evaluate and treat patients with cognitive issues, such as challenges with memory, language, finding one's way around, and judgment. Symptoms are often associated with mood and behavior concerns, and have a range of potential causes, including normal aging, early dementia, mini-strokes, infections, vitamin deficiencies, and sleep disorders, among others. As a result, patients seen at the Center are evaluated fully to ensure that their treatment is the best possible for their symptoms. Important advances are allowing physicians at the UTHealth Neurosciences Neurocognitive Disorders Center to determine a specific diagnosis in most patients, leading to more personalized treatments.

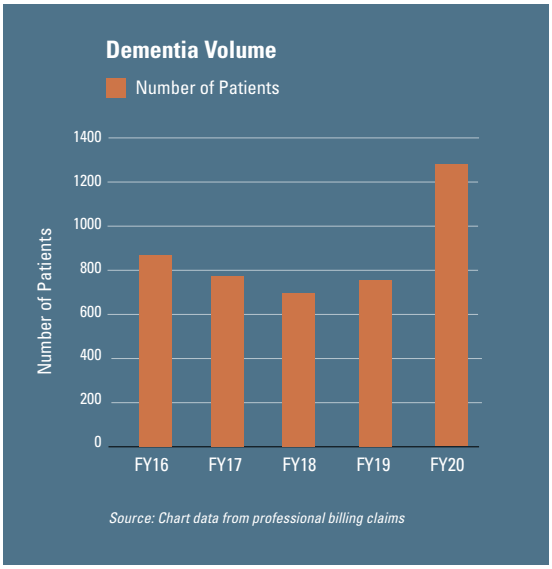
Research at the Neurocognitive Disorders Center focuses on three key areas:

- Improving dementia diagnosis
- Determining causes and risk factors for dementia
- Developing new, highly innovative treatments for dementia

UTHealth Neurosciences physicians were the first in Houston to diagnose Alzheimer's disease (AD) using amyloid-sensitive PET imaging. They are now working with laboratory scientists to develop blood and spinal fluid tests to diagnose AD and other neurodegenerative disorders (NDD) more easily and noninvasively. Other NDDs include frontotemporal dementia (FTD), Parkinson's disease, Lewy body disease, and Huntington's disease. The physicians are also working with imaging specialists to develop better PET and magnetic resonance imaging tools to diagnose NDDs. Finally, physicians at the center are investigating the role of genetic mutations and chemical modifications of genes in the development of dementia.

Paul Schulz, MD, and David Hunter, MD, are currently enrolling patients with mild cognitive impairment in anti-amyloid and anti-tau antibody trials. They are also doing very early phase investigations into progressive supranuclear palsy and FTD due to progranulin mutations using genetic approaches. Current treatments for the NDDs are based on symptoms, but our new generation of medications shows promise at modifying the underlying disease processes. In other trials at the center, physicians are investigating the efficacy of deep brain stimulation in patients with major depressive disorder who have not responded to other treatments, are developing stem cells for use in patients with AD, and are using genetic approaches to Huntington's disease.

Schulz and Hunter consider it an exciting time to be investigating neurodegenerative disorders because decades of work appear to be producing positive signals in treatment trials, which suggest that disease-modifying therapies may be within sight. UTHealth Neurosciences welcomes the partnership of other physicians in this critical journey.



Movement Disorders and Neurodegenerative Disease

USING PIONEERING TECHNIQUES and clinical expertise to diagnose, evaluate, manage, and treat adult and geriatric patients, UT*MOVE*, a division of UTHealth Neurosciences, has established a track record of outstanding care for patients. Part of UTHealth Neurosciences, UT*MOVE* provides patients with specialty clinics and faculty expertise. Conditions seen and treatments available include 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.

UT*MOVE* offers pharmacological and surgical therapies, including intrathecal baclofen pump therapy. Through the Deep Brain Stimulation (DBS) Program, 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.

Deep brain stimulation for Parkinson's tremor, dystonia, and essential tremor is known for low complication rates and outstanding outcomes. Based on the skill of the neurological and neurosurgical team and their expertise in DBS programming, Mya Schiess, MD, director of UT*MOVE*, and her team advocate for early use of deep brain stimulation in appropriate patients. Surgeries are performed by Albert Fenoy, MD, who leads the Deep Brain Stimulation Surgery Program at McGovern Medical School. Raja Mehanna, MD, adds depth to the program's legacy in DBS through publications of reviews, articles, and a book on DBS therapy and outcomes.

Led by Erin Furr-Stimming, MD, UT*MOVE*'s comprehensive Huntington's Disease Program is one of 50 Huntington's Disease Society of America centers of excellence in the United States and the only one in Texas to receive the prestigious designation. UTHealth Neurosciences faculty operate the only specialty clinic in the Houston area for the diagnosis, management, and support of patients and their families with Huntington's disease.

Shivika Chandra, MD, who completed residency training at McGovern Medical School and is UT*MOVE* certified, provides expertise in movement disorders for the Harris Health community at the system's Lyndon B. Johnson Hospital and Smith Clinic. As chief of neurology at Harris Health LBJ and Harris Health Clinics, Chandra has established an infrastructure of accessible, comprehensive, quality care.

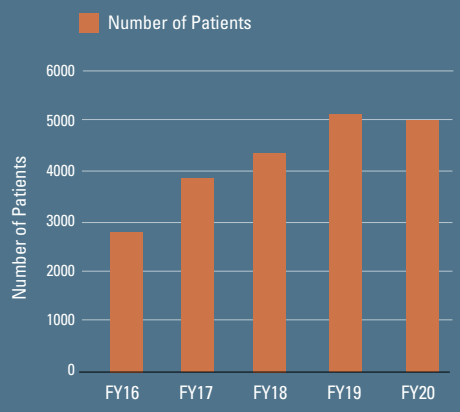
UT*MOVE*'s large patient population benefits from the addition of Swati Pradeep, DO, who joined the team in July 2020 and is board certified and fellowship trained in movement disorders.

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 plans, they consider the whole patient, as well as the patient's environment and support groups. They also emphasize education and encourage patients to stay mentally and physically active, and to have fun and create a positive environment with family and friends.

UT*MOVE* supports and partners with the Houston Area Parkinson's Society (HAPS), which provides educational, exercise, and social programs, and 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 in movement disorders and neurodegenerative diseases at UT*MOVE* is substantial, with collaborations among multiple disciplines and institutions, and funding from federal, pharmaceutical, and philanthropic sources.

Movement Disorders Volume



Source: Chart data from professional billing claims

Diagnoses Contributing to DBS Procedures

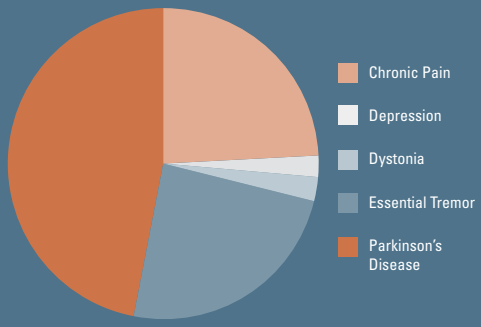
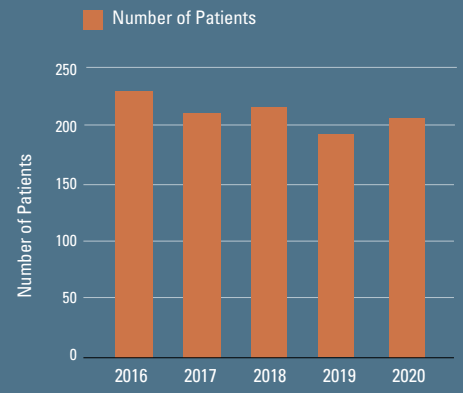


Chart data from ICD10 diagnosis code description

DBS Procedure Volume



Source: Chart data from professional billing claims

RESEARCH HIGHLIGHTS

EFFICACY, SAFETY, AND TOLERABILITY OF VALBENAZINE FOR THE TREATMENT OF CHOREA ASSOCIATED WITH HUNTINGTON'S DISEASE (KINECT-HD)

PRINCIPAL INVESTIGATOR:
Erin Furr-Stimming, MD
Associate Professor, Department of Neurology
McGovern Medical School at UTHealth

In this Phase III randomized, double-blind, placebo-controlled study, investigators at multiple centers are evaluating the efficacy, safety, and tolerability of valbenazine to treat chorea in subjects with Huntington's disease. Patients ages 18 to 75 years with a clinical diagnosis of Huntington's disease with chorea are eligible to enroll. They must be able to walk, with or without the assistance of a person or device. The study will enroll 120 participants at sites in the United States and Canada.

ALLOGENEIC BONE MARROW-DERIVED MESENCHYMAL STEM CELLS AS A DISEASE-MODIFYING THERAPY FOR IDIOPATHIC PARKINSON'S DISEASE

PRINCIPAL INVESTIGATOR:
Mya C. Schiess, MD
Professor, Department of Neurology
Adriana Blood Distinguished Chair in Neurology
McGovern Medical School at UTHealth

Mesenchymal stem cell therapy has the potential to slow the rate of Parkinson's disease progression and restore homeostasis to the neuronal-glial populations damaged by the degenerative process. By ending the destructive inflammatory process, mesenchymal stem cells may re-establish an equilibrium that promotes cell regeneration. This could slow or stop the disease process and restore health to the brain.

This Phase IIa double-blind, randomized, controlled trial will recruit 45 patients with early to moderate Parkinson's disease and assign them to one of three treatment arms. Group 1 will receive three infusions of placebo every 3 months; group 2 will receive two infusions of 10 X 106 MSC/Kg every 3 months and 1 placebo infusion; and group 3 will receive three infusions of 10 X 106 MSC/Kg every 3 months. All subjects will receive three infusions, with 3-month intervals in between. They will be monitored for adverse reactions and clinical improvement for a year after the last infusion.

ELUCIDATING THE TEMPORALITY OF STRUCTURAL AND FUNCTIONAL CONNECTIVITY CHANGES IN ESSENTIAL TREMOR AFTER SUCCESSFUL DEEP BRAIN STIMULATION TO THE DENTATO-RUBRO-THALAMIC TRACT

PRINCIPAL INVESTIGATOR:
Albert Fenoy, MD
Associate Professor, Vivian L. Smith
Department of Neurosurgery
McGovern Medical School at UTHealth

CO-PRINCIPAL INVESTIGATOR:
Mya C. Schiess, MD
Professor, Department of Neurology
Adriana Blood Distinguished Chair in Neurology
McGovern Medical School at UTHealth

Essential tremor, the cause of which is unknown, is the most common movement disorder in adults. When medications are no longer effective, deep brain stimulation (DBS) can be an option for patients. Although DBS is a very effective treatment strategy to control tremor, efficacy can wane over time and side effects can develop. In this study, researchers aim to verify what is occurring during stimulation through tractography, which uses diffusion magnetic resonance imaging to illuminate the dentato-rubro-thalamic tract to understand how brain connectivity patterns change in patients with essential tremor after deep brain stimulation. The study, funded with a $2.1 million R01 grant from the National Institutes of Health, will recruit 72 patients who are planning to undergo DBS for essential tremor and follow them for two years after the surgery.

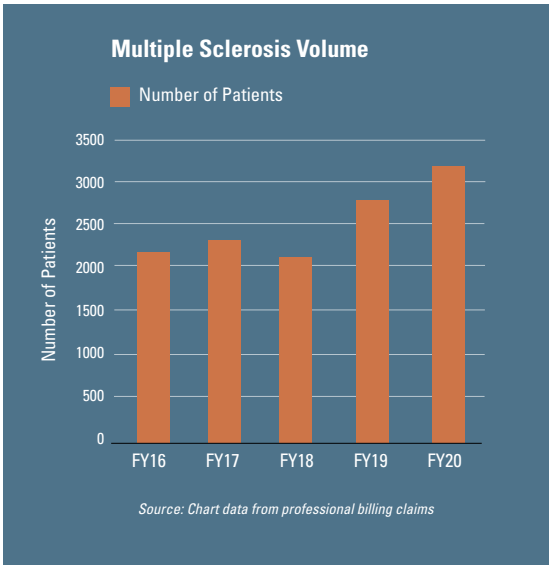
Multiple Sclerosis and Neuroimmunology

THE MULTIPLE SCLEROSIS and Neuroimmunology Program at UTHealth Neurosciences has established a track record of leading-edge care using groundbreaking techniques to diagnose, evaluate, manage, and treat adult patients with multiple sclerosis (MS) and other demyelinating disorders. The scope of expertise of UTHealth physicians is broad and includes patients in all stages of MS, as well as those with neuromyelitis optica, transverse myelitis, and optic neuritis. Led by neurologist J. William Lindsey, MD, director of the Division of Multiple Sclerosis and Neuroimmunology, they are experienced in the appropriate use of aggressive therapies in severe cases.

Organized in 1983 as the Multiple Sclerosis Research Group, the program's subspecialists have 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. In addition to Lindsey, faculty members include John Lincoln, MD, PhD; Rohini Samudralwar, MD; and Rajesh Gupta, MD. They practice at UTHealth Neurosciences clinics for patients with MS and related disorders, participate in multiple clinical trials of new medications for MS, and engage in research on imaging of MS and in basic science research aimed at defining the cause of MS.

In the Department of Neurology's state-of-the-art Magnetic Resonance Imaging Analysis Center, physicians use spectroscopic and diffusion tensor imaging with tractography, as well as other advanced diagnostic tools. Following diagnosis, patients benefit from breakthrough treatment options, including injectable immunomodulators, immunosuppressives, monoclonal antibodies, and 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 and Neuroimmunology Program's goal is to maintain patients at the highest level of function possible, with early use of immunoactive agents to prevent disease progression. Because rehabilitation is integral to each patient's treatment plan, physicians work closely with the physiatrists and therapists at TIRR Memorial Hermann, a national leader in medical rehabilitation and research.



RESEARCH HIGHLIGHTS

PIVOTAL PHASE III TRIAL FOR INVESTIGATIONAL EVOBRUTINIB IN RELAPSING MULTIPLE SCLEROSIS

LEAD PHYSICIAN: J. William Lindsey, MD
Professor, Department of Neurology
Opal C. Rankin Professor in Neurology
McGovern Medical School at UTHealth

Bruton's tyrosine kinase (BTK) is an enzyme important for the activation and regulation of two kinds of white blood cells that cause tissue damage in patients with multiple sclerosis. Evobrutinib is the first oral highly selective BTK inhibitor to show clinical proof of concept in adult patients with relapsing multiple sclerosis (RMS). Researchers at McGovern Medical School at UTHealth are enrolling participants with RMS in a Phase III trial following the results of the Phase II clinical trial, which met its primary endpoint over 24 weeks of treatment, where the total cumulative number of T1 gadolinium-enhancing (Gd+) lesions was reduced with evobrutinib compared with placebo. Further data show that the effect on relapse reduction observed at week 24 was maintained through 48 weeks.

PHASE III CLINICAL TRIAL OF FENEBRUTINIB IN PROGRESSIVE MULTIPLE SCLEROSIS

LEAD PHYSICIAN: J. William Lindsey, MD
Professor, Department of Neurology
Opal C. Rankin Professor in Neurology
McGovern Medical School at UTHealth

Researchers at McGovern Medical School at UTHealth are investigating fenebrutinib, with the ultimate goal of halting progression of multiple sclerosis (MS). Fenebrutinib is an investigational oral Bruton's tyrosine kinase (BTK) inhibitor in relapsing MS and primary progressive MS (PPMS). BTK is an enzyme important for the activation and regulation of two kinds of white blood cells that cause tissue damage in patients with multiple sclerosis. Fenebrutinib is a dual inhibitor of both B-cell and myeloid lineage-cell activation, which may offer a novel approach to suppress disease activity and slow disease progression by targeting both acute and chronic inflammatory aspects of MS. Preclinical data have shown that fenebrutinib is highly selective and acts as a non-covalent agent with a slow release rate from its target.

Neuromuscular Disorders

PHYSICIANS with the UTHealth Neurosciences Neuromuscular Program subspecialize in complex neuromuscular disorders that are difficult to diagnose and treat, including neurodegenerative diseases, 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, MD, 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 the patients seen by physicians are over the age of 50.

Neurodiagnostic facilities at UTHealth Neurosciences include a state-of-the-art Electromyography (EMG) Laboratory and a Muscle and Nerve Laboratory. The EMG Lab, directed by UTHealth neurologist Thy Nguyen, MD, provides comprehensive nerve conduction studies and EMG evaluations performed by experienced staff.

Because electrodiagnostic evaluation is an extension of clinical findings, medical specialists perform a focused neuromuscular exam, 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. The UTHealth Neurosciences Neuromuscular Program is the only program in Houston that provides single-fiber EMG.

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

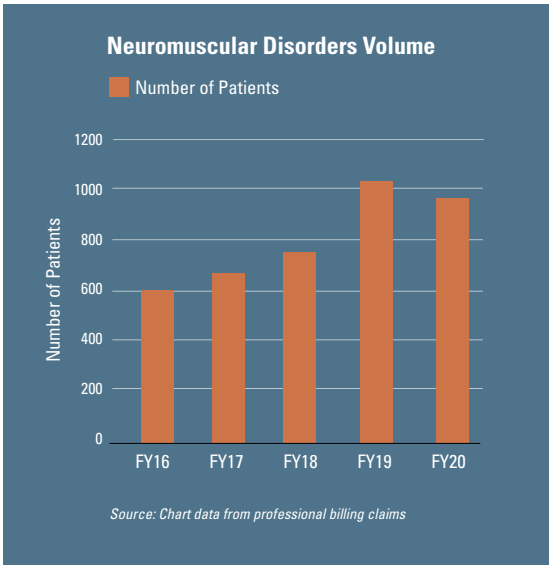
AN INVALUABLE DIAGNOSTIC TEST, EMG PROVIDES EVIDENCE IN SUPPORT OF DIAGNOSES OF:

- Peripheral neuropathies
- Motor neuron diseases such as amyotrophic lateral sclerosis and spinal muscular atrophy
- Muscle disorders such as myopathy and muscular dystrophy
- Neuromuscular junction disorders such as myasthenia gravis
- Entrapment neuropathies such as carpal tunnel syndrome, ulnar, and peroneal neuropathies
- Traumatic nerve injury, including evaluation of brachial plexus and facial neuropathy

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. The laboratory provides technical services to regional neuromuscular experts as well. The Muscle and Nerve Lab is co-directed by Sheikh and Suur Biliciler, MD.

New to the program this year is Kristin Brown, MD, who specializes in neurology, EMG, and clinical neurophysiology. Brown sees patients at UTHealth Neurosciences Neurology in the Texas Medical Center and at Sienna Village in Missouri City, Texas.

At the Neuromuscular Disorders Clinic at UTHealth Neurosciences Memorial City, neurologist Eddie Patton, MD, provides patients with a personalized medical experience tailored to their health issues and lifestyle goals. In addition to offering tertiary care in Memorial City, his mission is to provide quality, compassionate care to his patients, based on trust and good communication.



Source: Chart data from professional billing claims

RESEARCH HIGHLIGHT

GUILLAIN-BARRÉ SYNDROME

Continuum. 2020 Oct;26(5):1184-1204.

PRINCIPAL INVESTIGATOR: Kazim A. Sheikh, MD
Director, Neuromuscular Program
Professor, Department of Neurology
McGovern Medical School at UTHealth

Abstract:

Purpose of review: This article reviews the clinical features, diagnosis and differential diagnosis, prognosis, pathogenesis, and current and upcoming treatments of Guillain-Barré syndrome (GBS).

Recent findings: GBS is an acute inflammatory neuropathic illness with striking clinical manifestations and significant morbidity. A substantial proportion of patients with GBS do not respond to current immunomodulatory therapies (e.g., plasma exchange and IV immunoglobulin [IVIg]), highlighting the need for new therapies. Prognostic models that can accurately predict functional recovery and the need for artificial ventilation have emerged. These models are practical, and online calculators are available for clinical use, facilitating early recognition of patients with poor outcome and the opportunity to personalize management decisions. Clinical and experimental studies have identified innate immune effectors (complement, macrophage lineage cells, and activating Fcγ receptors) as important mediators of inflammatory nerve injury. Two complement inhibitors are undergoing clinical testing for efficacy in GBS.

Summary: GBS is the most common cause of acute flaccid paralysis in the United States and worldwide. New treatments for GBS have not emerged since the 1990s. Our understanding of the pathogenesis of this disorder has progressed, particularly over the past decade; as a result, new therapeutic agents targeting different components of the complement cascade are at advanced stages of clinical development.

Neurotrauma and Neuroscience Critical Care

THE NEUROTRAUMA and Neuroscience Critical Care Program is internationally recognized for the treatment of high-acuity brain and spinal cord injuries. UTHealth Neurosciences physicians manage severe neurotrauma cases, with neurointensivists and experienced mid-level practitioners staffing the 32-bed Neuroscience ICU (NSICU) at Memorial Hermann-Texas Medical Center around the clock to provide ongoing intensive care to critically ill patients. The program now operates a total of 74 NSICU beds in three hospitals: Memorial Hermann-TMC, Memorial Hermann Southwest Hospital, and Memorial Hermann Memorial City Medical Center, making it one of the largest programs in the country.

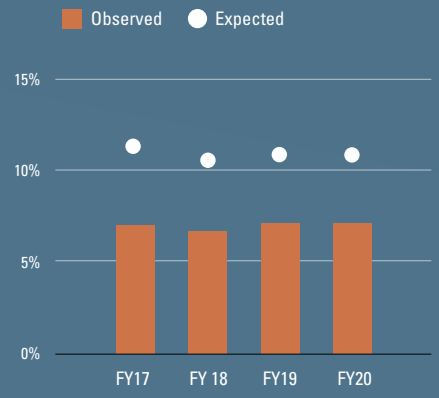
UTHealth Neurosciences is an international leader in research on innovative treatments following neurotrauma and participates in multicenter trials. Led by H. Alex Choi, MD, director of neurocritical care and an associate professor in the Vivian L. Smith Department of Neurosurgery, the program utilizes the most advanced medical technologies and devices. The NSICU is equipped with multimodal monitoring capability including ICP, CPP, continuous video EEG monitoring, continuous cardiac output, noninvasive cerebral blood flow monitoring, and brain oximetry.

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 ambulance service established in Texas and the second in the nation. Built on the hospital's long-standing affiliation with McGovern Medical School, the 200-bed institute provides high-quality care to adult and pediatric patients and offers a full spectrum of service.

At Memorial Hermann Southwest Hospital, the state-of-the-art Neuroscience ICU is staffed 24/7 by UTHealth faculty members, all of whom are fellowship trained in neurocritical care. Memorial Hermann Memorial City Medical Center operates a 19-bed dedicated neurocritical care unit combining intensive and acute care. Memorial City's NSICU is also staffed 24/7 by fellowship-trained UTHealth Neurosciences physicians. The unit sees a large volume of neurotrauma and stroke patients and is equipped with continuous EEG capabilities. Both centers have 24/7 neuroendovascular surgical care available for immediate stroke care and the treatment of complex cerebral vascular diseases. Both are equipped with tele-robot capabilities allowing experts to be at the virtual bedside in minutes.

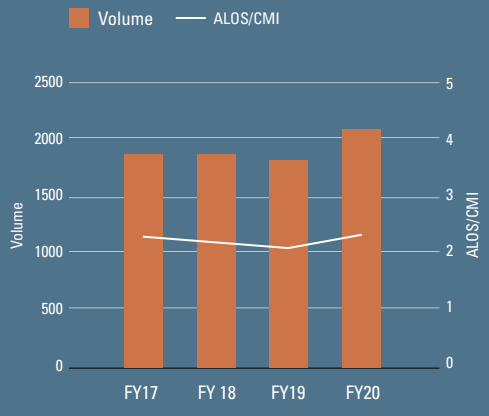
McGovern Medical School offers a two-year neurocritical care fellowship to physicians who are board certified or eligible in neurology, emergency medicine, anesthesia, or internal medicine. A one-year fellowship track is open to eligible candidates who have completed postgraduate training in neurosurgery, medical critical care, anesthesia critical care, or surgical critical care.

Traumatic Brain Injury: Inpatient Mortality



Source: Chart data from Vizient

Traumatic Brain Injury: Volume & Length of Stay (CMI Adjusted)



Source: Chart data from Vizient

Pain Management

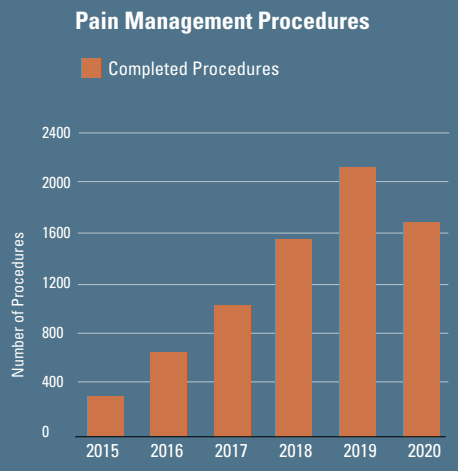
PAIN MANAGEMENT is an integral part of the overall patient care program at UTHealth Neurosciences. Specialists in interventional pain management and physical medicine and rehabilitation treat patients with acute and chronic pain arising from trauma, nerve damage, degenerative conditions, cancer, and systemic metabolic disorders such as diabetes. The multidisciplinary team works in close collaboration to provide a variety of interventions and strategies for pain self-management to help people return to their daily activities. As clinicians, researchers, and educators, they work to transform and advance the specialty of pain management.

UTHealth faculty members Nadya Dhanani, MD; Mark Burish, MD, PhD; Joseph Amos, MD; Ashley Amsbaugh, MD; and Hiral Patel, MD, are key members of the UTHealth Neurosciences Pain Management Program. Dhanani, who heads the program, is well versed in all aspects of pain medicine and focuses her practice on treating spine and cancer-related pain. She sees patients at the Texas Medical Center and Greater Heights locations.

Burish directs The Will Erwin Headache Research Center at UTHealth Neurosciences. Established with a $20-million pledge from The Will Erwin Headache Research Foundation, the Center includes experts dedicated to the study of cluster headaches and other debilitating headaches and facial pain diseases. Physicians and researchers who work with The Will Erwin Headache Research Center include neurosurgeon Dong Kim, MD, professor and chair of the Vivian L. Smith Department of Neurosurgery at McGovern Medical School; researcher Georgene Hergenroeder, PhD, associate professor in the department; and researcher Pramod Dash, PhD, professor and chair of the Department of Neurobiology and Anatomy at McGovern Medical School. Because cluster headache and other debilitating types of headaches affect relatively small numbers of people, the group works with centers across the country to identify patients with the goal of better understanding and treating the disorders.

PAIN DISORDERS TREATED

- Carpel tunnel syndrome
- Cervical and lumbar radiculopathy
- Facet arthropathy
- Degenerative disc disease
- Joint disorders
- Headache, migraine disorders, and occipital neuralgia
- Myofascial disease
- Neuropathic pain conditions
- Sacroiliac dysfunction
- Spinal stenosis
- Vertebral compression fractures



Source: Chart data from professional billing claims

Amos practices at the group's Memorial City and Katy locations and serves as an expert panelist in pain management for the Texas Medical Board. Amsbaugh practices at the Texas Medical Center and Northeast Houston locations, and Patel has expanded Texas Medical Center expertise to UTHealth Neurosciences clinics in Southeast Houston, Pearland, and Sugar Land.

RESEARCH HIGHLIGHT

HIGH-DOSE VITAMIN D PLUS MULTIVITAMIN IN THE PREVENTION OF CLUSTER HEADACHE

PRINCIPAL INVESTIGATOR:
Mark Burish, MD, PhD
Assistant Professor, Vivian L. Smith
Department of Neurosurgery
McGovern Medical School at UTHealth

This study is investigating the use of high-dose vitamin D3 plus a multivitamin in the prevention of cluster headache attacks. Participants may be enrolled at any location in the United States that has access to a participating lab for blood work.

The study will include screening – interview, examination, survey response, and blood work. The first week will be a baseline period, with no added medications. Weeks 2 through 4 are a double-blinded experimental period during which participants receive either high-dose vitamin D3 plus a multivitamin, or placebo plus a multivitamin. During this time they will fill out a survey and have blood testing. Weeks 5 through 7 are an open-label period during which all participants will receive high-dose vitamin D3 and a multivitamin. The primary outcome is the change from baseline to experimental weeks 1 through 3 in the frequency of cluster headache attacks between placebo and high-dose D3.

To be eligible, participants must be age 18 to 70 years and have a diagnosis of either episodic or chronic cluster headache according to the International Classification of Headache Disorders (3rd edition), as well as cluster periods that are predictable and have a duration of 6 weeks or longer, with a minimum of one attack daily. For more information, visit rebrand.ly/headache-trial

Sleep Disorders

THE UTHEALTH NEUROSCIENCES Sleep Medicine Program offers state-of-the-art care and support to patients struggling with sleep disorders. The multidisciplinary team of physicians diagnoses sleep disorders and develops personalized treatment plans to help patients get a better night's sleep. In addition to somnology, the treatment team includes otorhinolaryngology, psychiatry and behavioral psychology, cardiology, and oral and maxillofacial surgery/dentistry. They offer new patient and follow-up patient consultations, both virtually and in person.

Sleep Medicine Program specialists Sudha Tallavajhula, MD, and Aparajitha Verma, MD, MBA, employ a variety of tools to identify and distinguish between sleep disorders. Using polysomnograms, they measure brainwave activity, breathing effort, airflow and heart rate, eye movements, limb movements, and blood oxygen levels. These traditional sleep studies, which are done on an outpatient basis at a sleep disorders center, evaluate other behaviors, such as sleep-walking, acting out dreams, or sleep talking.

In addition to traditional sleep studies, UTHealth Neurosciences offers the Multiple Sleep Latency Test (MSLT) and Maintenance of Wakefulness Test (MWT). The MSLT is the standard tool to diagnose narcolepsy and idiopathic hypersomnia. The MWT measures alertness during the day, an indicator of how well a person is able to function and remain alert during quiet times of inactivity.

Physicians at UTHealth Neurosciences formulate a report that provides a diagnosis and recommendations for treatment. The sleep medicine physician also will address any coexisting sleep disorders, and when appropriate, prescribe CPAP or BiPAP for patients with obstructive sleep apnea (OSA). UTHealth Neurosciences also provides management of advanced machines, including average volume-assured pressure support (AVAPS), a relatively new mode of noninvasive positive-pressure ventilation for management of hypoventilation in various neuromuscular disorders, including amyotrophic lateral sclerosis (ALS), myasthenia gravis, and muscular dystrophies. Adaptive servo-ventilation (ASV), a noninvasive ventilatory treatment option created for adults with OSA and/or central sleep apnea (CSA), is also available.

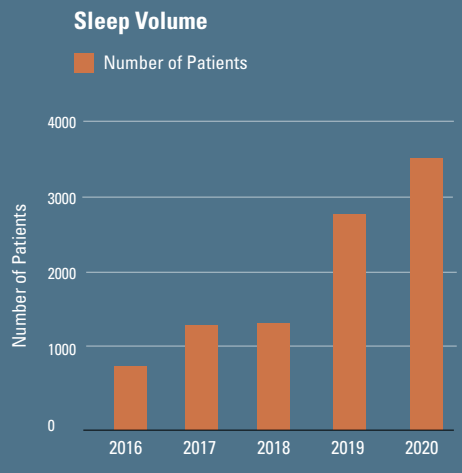
UTHealth Neurosciences offers ambulatory home sleep testing (HST), allowing eligible patients to use the home sleep testing kit for one to three nights and return the device to the clinic. Physicians download the information, formulate a report, and discuss findings with patients. Those who qualify may benefit from WatchPAT®, a revolutionary Food and Drug Administration-cleared portable home sleep apnea test and diagnostic device that uses innovative technology to rule out sleep apnea.

About 50 percent of people diagnosed with OSA by a sleep study are unable to tolerate CPAP or BiPAP. These patients, who are at increased risk of heart attack, stroke, and high blood pressure, may be eligible for Inspire® Upper Airway Stimulation, an implantable nerve stimulator used to treat moderate to severe OSA. An otolaryngologist implants the device, which is designed to detect the patient's breathing pattern and maintain an open airway through mild hypoglossal nerve stimulation. The sleep medicine specialist can configure the stimulation settings using an external programmer. Patients use a remote to start the therapy before they go to sleep and stop it when they awaken.

The UTHealth Neurosciences Sleep Medicine Program also offers the Remedē® system for moderate to severe central sleep apnea in adults. A cardiologist implants a battery pack under the skin in the upper chest area and inserts small, thin wires into the blood vessels in the chest near the phrenic nerve. The device is designed to monitor respiratory signals during sleep and send signals to the diaphragm to stimulate breathing when needed. After the system is implanted, the sleep medicine specialist works with the patient to adjust the settings to ensure that normal breathing is restored.

SLEEP MEDICINE SPECIALISTS TREAT:

- Obstructive sleep apnea (OSA)
- Central sleep apnea (CSA)
- Insomnia
- Narcolepsy
- Restless leg syndrome
- Periodic leg movement
- Hypoventilation related to neuromuscular and skeletal disorders
- Hypoventilation caused by restrictive lung disease
- Hypoxic conditions during sleep
- Parasomnias that include abnormal movements, behaviors, emotions, perceptions, and dreams that occur while falling asleep, sleeping, between sleep stages, or during arousal from sleep



Source: Chart data from professional billing claims

Spine Disorders

THE NEUROSURGEONS at the UTHealth Neurosciences Spine Center provide exceptional patient care and the most advanced nonsurgical and surgical treatments available. They perform more than 2,600 procedures annually, making the spine program the largest in the region. The center is among a handful of select practices in Walmart's elite Centers of Excellence Program for spine surgery.

Internationally known neurosurgeon John Caridi, MD, was recruited in fall 2020 as chief of the Neurosurgical Spine Division, with the goal of expanding the Spine Center and building its reputation. Caridi's area of expertise is complex reconstruction of adult and pediatric cervical, thoracic, and lumbar spinal deformity. He joins John Quinn, MD, who has expertise in complex reconstructive surgery in children and adults; Karl Schmitt, MD, who has expertise in traumatic spinal injury; and Jessica Stark, MD, who specializes in minimally invasive spine surgery and spinal trauma. They provide care in a state-of-the-art 16-bed Neuroscience Elective Unit at Memorial Hermann-Texas Medical Center, which has 10 beds dedicated to patients who undergo spine surgery.

Krishanthan Vigneswaran, MD, joined the spine program in August 2020 and practices at UTHealth Neurosciences locations in Memorial City, Southwest Houston, and Sugar Land. Vigneswaran focuses on the surgical treatment of patients with brain and spinal cord tumors, using the latest neurosurgical tools and working closely with neuro-oncologists and radiation oncologists. Cyrus King, MD, who was recruited to UTHealth Neurosciences in 2018 and practices at the group's Memorial City and Katy locations, has expertise in complex spine and deformity surgery. King extends Texas Medical Center expertise to the Katy area. Wesley Jones, MD, who joined UTHealth Neurosciences in 2019, specializes in endovascular neurosurgery and complex spine surgery in Memorial City.

New operating rooms at the Spine Center are equipped

SPINE DISORDERS TREATED

- Adolescent idiopathic scoliosis
- Cervical and thoracolumbar deformity
- Congenital spine disorders
- Degenerative disc disease
- Flatback syndrome
- Herniated disc
- Kyphosis
- Nerve sheath tumors
- Peripheral nerve injuries
- Piriformis syndrome
- Scheuermann's kyphosis
- Scoliosis
- Spinal arteriovenous malformations
- Spinal stenosis
- Spine and spinal cord tumors
- Spine deformity
- Spine fractures
- Spine infection
- Spondylolisthesis
- Spondylosis
- Tethered spinal cord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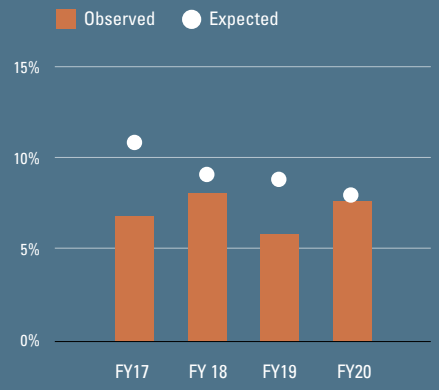
with advanced instrumentation and dynamic imaging systems, allowing neurosurgeons to perform minimally invasive spine procedures and innovative treatments for patients with pain resulting from degenerative disease, trauma, and spinal deformity.

Pain management is a critical part of the spine program. Neurosurgeons collaborate closely with interventional pain management specialists Ashley Amsbaugh, MD, and Nadya Dhanani, MD, seeing patients side by side in the Spine Center. The team works with patients and families to devise personalized pain management plans to help people return to their daily lives.

The center's neurosurgeons provide exceptional care for patients with traumatic spine injury, including the 10 to 20 percent of admissions through the Level 1 Memorial Hermann Red Duke Trauma Institute. Based on benchmark Vizient data, spine surgeons at UTHealth Neurosciences have consistently lowered inpatient mortality outcomes for spine trauma, degenerative spine disease, and elective spine surgery for the past decade.

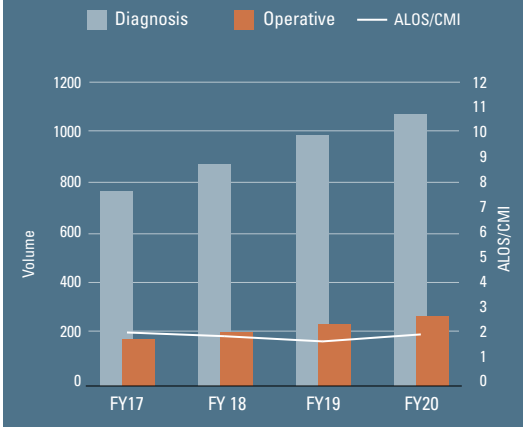
As faculty at McGovern Medical School at UTHealth, neurosurgeons at the Spine Center educate the next generation of spine experts and shape the future of medicine through basic science research, clinical discovery, and the development of breakthrough treatments.

Spine Trauma: Inpatient Mortality



Source: Chart data from Vizient

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



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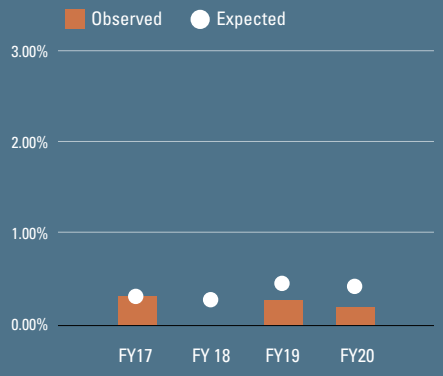
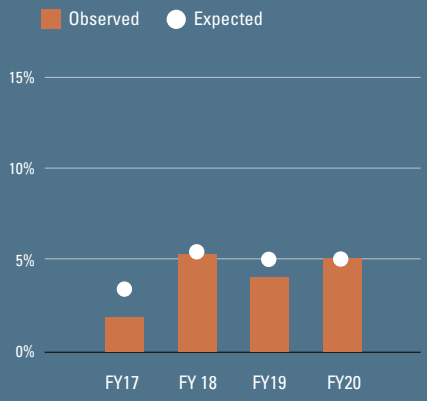
Spine Degenerative or Elective: Inpatient Mortality



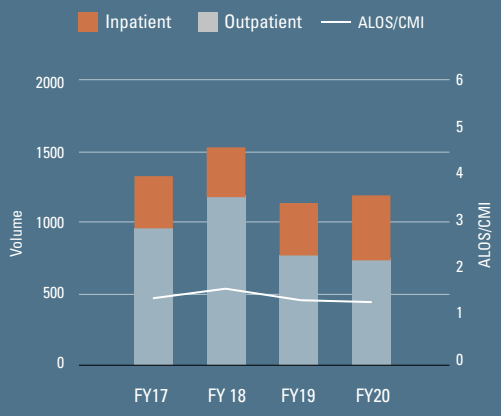
Source: Chart data from Vizient

Spine Tumor: Inpatient Mortality



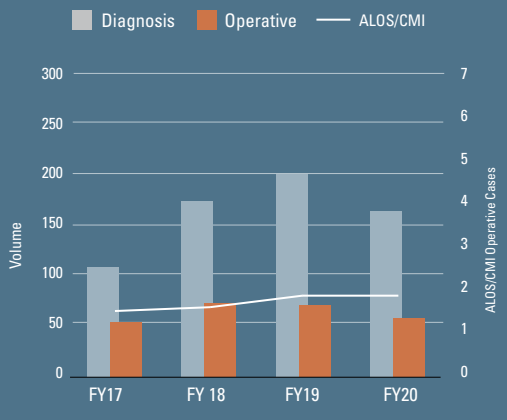
Source: Chart data from Vizient

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



Source: Chart data from Vizient

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



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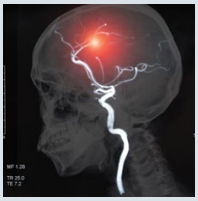
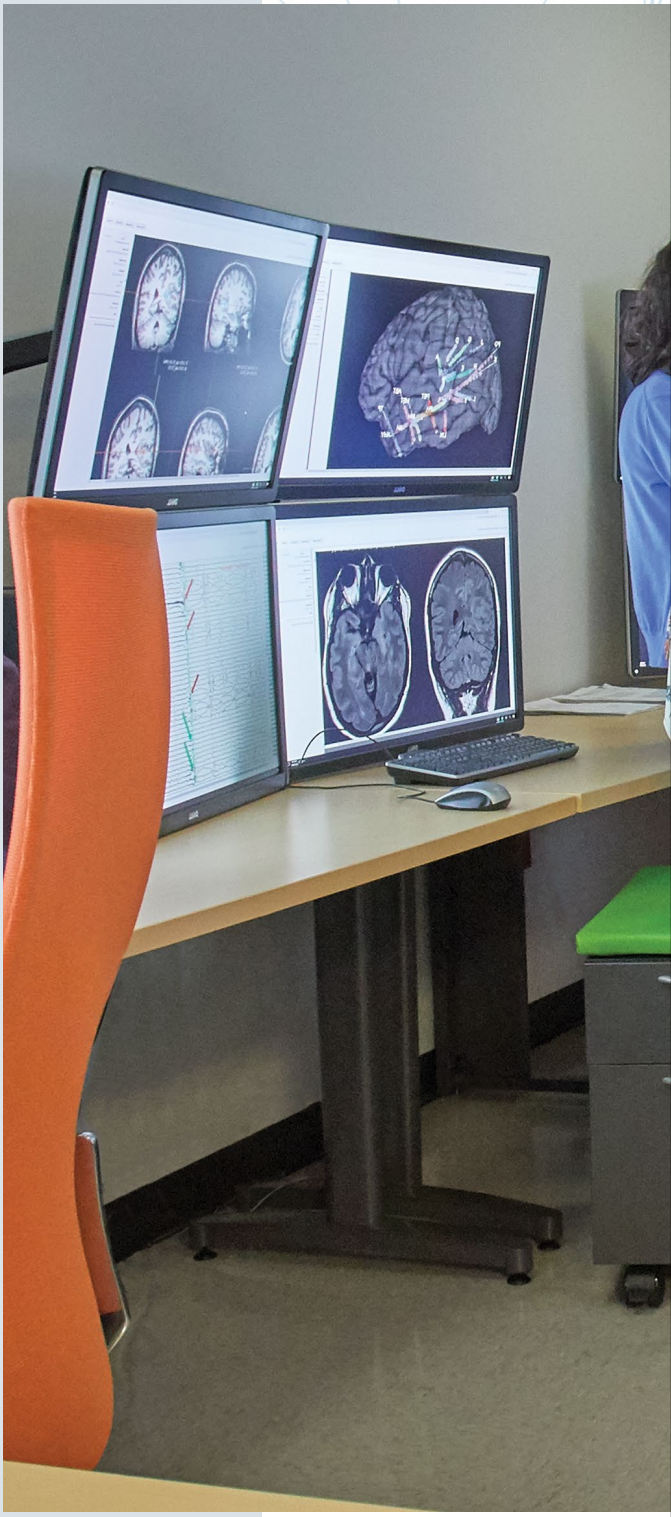
Research and Innovation



PHYSICIANS AND SCIENTISTS at UTHealth Neurosciences are engaged in a broad and intensive research program focused on the mechanisms, treatment, and cure of neurological disease and injury. They use molecular, transgenic, and electrophysical approaches in biomedical studies, translational research, clinical trials, and technology development and assessment.

During the 2018-2019 fiscal year, UTHealth researchers in the Department of Neurology and the Vivian L. Smith Department of Neurosurgery received more than $27.4 million in 158 grants and contracts. The following listing is a sample of ongoing or recently completed research.



Brain Tumor and Neuro-Oncology Research

A Randomized Phase II/III Open-Label Study of Ipilimumab and Nivolumab versus Temozolomide in Patients with Newly Diagnosed MGMT (Tumor O-6-Methylguanine DNA Methyltransferase) Unmethylated Glioblastoma (NRG-BN-007)

Investigator: Jay-Jiguang Zhu, MD, PhD

The researchers are determining if combining ipilimumab and nivolumab with fractionated radiation therapy significantly prolongs overall survival versus standard of care of temozolomide with fractionated radiation therapy in patients with new diagnosed GBM without MGMT promoter methylation.

Genomically Guided Treatment Trial in Recurrent Brain Metastases

Investigator: Ankush Bhatia, MD

This study is designed to determine if patients with brain metastases harboring CDK, P13K, or NTRK/ROS1 inhibitors will predict sensitivity to these inhibitors, with targeted therapies. Participants must have histologically confirmed metastatic disease to the brain from any solid tumor and no known leptomeningeal involvement. Patients who have concurrent administration of anticancer therapies and chemotherapy within 14 days before entering the study are excluded.

NeMeRe Neoplastic Meningitis Registry

Investigator: Jay-Jiguang Zhu, MD, PhD

Researchers are collecting information about adults with neoplastic meningitis to better understand the condition. Participants in this collaborative study with Pennsylvania State University must be 18 years or older with a diagnosis of neoplastic meningitis.

TRIDENT/EF-32 for Newly Diagnosed Glioblastoma Multiforme

Principal Investigator: Jay-Jiguang Zhu, MD, PhD

This study is testing the efficacy and safety of tumor treating fields (TTFields) with radiation therapy and temozolomide compared to radiation therapy and temozolomide followed by TTFields and temozolomide in newly diagnosed GBM patients.

Cerebrovascular

A Multicenter, Double-Blind, Multi-Dose, Placebo-Controlled, Randomized, Parallel-Group, Phase II Study to Evaluate the Efficacy and Safety of Intravenous BIIB093 for Patients with Brain Contusion

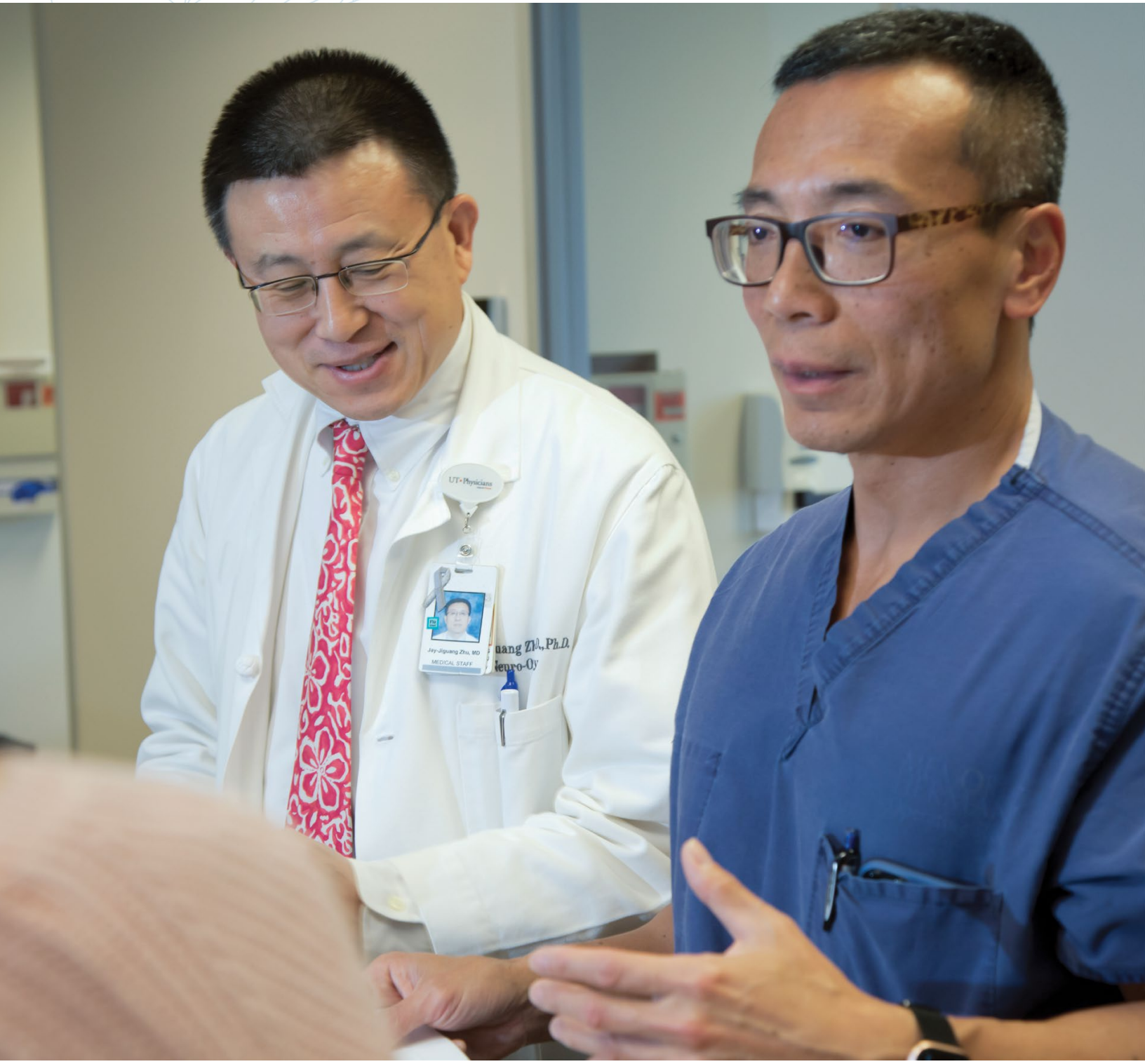
Investigators: Ryan Kitagawa, MD, and Swathi Kondapalli, MD

The primary objective of the study is to determine if BIIB093 reduces brain contusion expansion by Hour 96 when compared to placebo.

A Randomized, Controlled Trial to Optimize Patient Selection for Endovascular Treatment in Acute Ischemic Stroke (SELECT-2)

Investigator: Amrou Sarraj, MD

Researchers are evaluating the efficacy and safety of endovascular thrombectomy compared to medical management alone in acute ischemic stroke patients with a large vessel occlusion in the distal ICA and MCA M1, who have large core on either CT or advanced perfusion imaging, or both, and are treated within 24 hours from the last known well.


UT Physicians
Jay-Jiguang Zhu, MD
MEDICAL STAFF

A Study of NCS-01 in Patients With Acute Ischemic Stroke

Investigator: Anjail Sharrief, MD

This Phase I/II dose-finding, double-blind, placebo-controlled, multicenter study of 116 patients is evaluating the safety and tolerability of intracarotid artery administration of human bone marrow-derived mesenchymal stem cells (NCS-01) in patients with acute ischemic stroke. The primary objective is to assess the safety and tolerability of intracarotid artery administration of rising doses of NCS-01 with or without preceding thrombolysis/thrombectomy in patients with acute ischemic stroke.

A Study on BMS-986177 for the Prevention of a Stroke in Patients Receiving Aspirin and Clopidogrel

Investigator: Anjail Sharrief, MD

This study is a global Phase II, randomized, double-blind, placebo-controlled, dose-ranging study of BMS-986177, an oral factor XIa inhibitor for the prevention of new ischemic stroke or new covert brain infarction in patients receiving aspirin and clopidogrel following acute ischemic stroke or transient ischemic attack. Up to 2,350 participants will be enrolled at 30 sites around the world. Participants must be 40 years of age or older and identified by MRI within 48 hours of onset of signs and/or symptoms of stroke or TIA.

aBnormal motION capture In aCute Stroke (BIONICS)

Investigator: Sean Savitz, MD

In this pilot study, investigators are using machine learning to observe and identify abnormal or compensatory movements in subjects after stroke during hospitalization. Two hundred subjects will be enrolled over 6 months. Participation includes video recording of daily standard of care rehabilitation sessions during acute stroke hospitalization. Participation ends at hospital discharge.

Atrial Cardiopathy and Antithrombotic Drugs in Prevention After Cryptogenic Stroke

Investigator: Anjail Sharrief, MD

ARCADIA is a multicenter, biomarker-driven, randomized, double-blind, active-control, Phase III clinical trial of the medication apixaban (Eliquis®) versus aspirin in patients who have evidence of atrial cardiopathy and a recent stroke of unknown cause. Eleven hundred subjects will be recruited over 2.5 years at 120 sites in the National Institutes of Health StrokeNet consortium. Participants will be evaluated by the primary investigator for 1.5 to 4 years.

CBAF 312X

Investigator: Alex Choi, MD, MS

In this Phase II, patient- and investigator-blinded, randomized, placebo-controlled study, investigators are evaluating the efficacy, safety, and tolerability of BAF312 (siponimod) in patients with stroke due to intracerebral hemorrhage (ICH).

Cerebral Edema

Investigator: Alex Choi, MD, MS

Cerebral edema (CE) after subarachnoid hemorrhage is associated with poor outcomes. The pathomechanism of global cerebral edema (GCE) is unclear. GCE may represent in a range from vulnerable tissue status to microcirculatory ischemia. Patients with CE are at risk of developing delayed cerebral ischemia (DCI) and vasospasms. The investigators will develop a novel cerebral edema scoring system based on admission status to build a predictive system for DCI and vasospasm.

Clinical Outcomes and Patient Factors in Patients Admitted to an Inpatient Rehabilitation Facility

Investigator: Sean Savitz, MD

In this retrospective study, researchers are evaluating the multifactorial impact of stroke characteristics and treatment paradigms on clinical outcomes in patients undergoing inpatient rehabilitation. The data collected will be used to predict rehabilitation potential and factors that affect it in 1,000 acute stroke patients treated at a Memorial Hermann acute care hospital and inpatient rehabilitation facility.

Efficient Resource Utilization for Patients with Intracerebral Hemorrhage (EnRICH)

Investigator: Sean Savitz, MD

This prospective, observational study is open to adult patients with primary intracerebral hemorrhage who present and are managed at various hospitals across Greater Houston and other participating institutions across the country. The researchers are assessing regional patterns of care for adult patients with primary intracerebral hemorrhage (ICH). Approximately 1,000 participants will be enrolled over five years.

Extracorporeal Filtration of Subarachnoid Hemorrhage via Spinal Catheter Extension (PILLAR-XT)

Investigator: Spiros Blackburn, MD

Patients with subarachnoid hemorrhage (SAH) have delayed cerebral ischemia (DCI) secondary to the toxic effects of hemolysis in the cerebrospinal fluid (CSF). Clearance of red blood cells (RBCs) from the CSF can prevent delayed cerebral ischemia. The researchers are investigating the safety of a novel filtration device to remove RBCs and lysed blood by-products from hemorrhagic CSF in patients following aneurysmal SAH.

Hemostasis and Intracranial Hemorrhage

Principal Investigator: Tiffany Chang, MD

This prospective, observational study looks at measures of hemostasis, hematoma expansion, and outcomes in patients with bleeding in the skull.

Impact of Fever Prevention in Brain-Injured Patients (INTREPID)

Investigator: Alex Choi, MD, MS

The objective of this study is to assess fever burden and the impact on outcomes of fever prevention using the Arctic Sun 5000 Temperature Management System as compared to standard fever care in brain-injured patients.

Inflammatory Cytokine Pathways After SAH

Investigator: Alex Choi, MD, MS

Uncontrolled neuroinflammation after acute brain injury is a significant contributor to secondary brain injury and poor outcomes. The researchers plan to experimentally determine inflammatory cytokine levels in serum and cerebral spinal fluid collected from subarachnoid hemorrhage patients in the NICU. Using novel bioinformatics clustering and network analysis tools, they hope to discover pathways within the inflammatory profile that favor poor patient outcomes versus good outcomes.

Lesion Size and Brain Atrophy Changes in Patients with Hemorrhagic and Ischemic Stroke (LAPHI)

Investigator: Muhammad Haque, MD

In this prospective pilot study, researchers are evaluating changes in stroke lesion volume, loss of brain tissue (atrophy), white matter track integrity, and metabolic status of the brain over two years in a stroke population. The researchers will obtain four follow-up MRIs, in addition to the standard-of-care MRI done at the time of admission, to evaluate the changes. The study will lead to understanding of the microstructural changes and the lesion resolution in the brain over the period of about one year post-stroke.

Machine-Learning Techniques for Prediction of Secondary Complications After SAH

Investigator: Alex Choi, MD, MS

Some subarachnoid hemorrhage patients in the ICU are at increased risk of developing dangerous secondary complications such as delayed cerebral ischemia (DCI). In patients with DCI, a sudden loss of blood flow to vital brain regions can result in severe morbidity or mortality. If these at-risk patients are identified early, a physician can treat them prophylactically and monitor them diligently to mitigate symptoms. Currently, there are no effective methods to assess a patient's risk of developing DCI. The researchers plan to develop novel machine-learning algorithms that can predict whether or not a patient will develop DCI using easily available data such as lab reports, vital signs, and admission status.

Multi-Arm Optimization of Stroke Thrombolysis (MOST)

Investigator: Andrew Barreto, MD

This study is a blinded, randomized, controlled, adaptive, multi-arm, adjunctive-thrombolysis efficacy trial in ischemic stroke. A maximum of 1,200 patients will be enrolled at approximately 110 sites in the United States. The primary goal of the study is to determine the efficacy of two medications used in combination with standard of care for ischemic stroke. The researchers will determine if either medication, argatroban or eptifibatide intravenous infusions, results in improvement in acute ischemic stroke patients.

OP-101

Investigator: Aaron Gusdon, MD

This double-blind, placebo controlled Phase II study will evaluate the safety, tolerability, pharmacokinetics, and efficacy of OP-101 (dendrimer n-acetyl-cysteine) in patients with severe COVID-19.

Perinatal Arterial Stroke: A Multi-Site Randomized, Controlled Trial of Intensive Infant Rehabilitation (iACQUIRE)

Investigator: Nivedita Thakur, MD

In this Phase III clinical trial, researchers are comparing the efficacy of two dosages of a new infant rehabilitation protocol – I-ACQUIRE – to usual and customary forms of rehabilitation in infants who experienced perinatal arterial stroke (PAS).

Predicting Upper-Extremity Motor Recovery in Subcortical Hemorrhagic Stroke Using DTI and TMS (PREDICT ICH)

Investigator: Sean Savitz, MD

This study is designed to determine the predictive value of transcranial magnetic stimulation (TMS), diffusion tensor imaging (DTI), or a combination of the two modalities in upper-extremity motor recovery and rehabilitation after first time-ever spontaneous subcortical intracranial hemorrhage (ICH). Thirty patients will participate in the trial for up to 6 months with diagnostic TMS, MRI, and assessments performed at Day 90 and Day 180.

Quantification of Vasospasm

Investigator: Alex Choi, MD, MS

Cerebral vasospasm is a well-known sequela of aneurysmal subarachnoid hemorrhage (SAH). Investigators are developing novel imaging biomarkers for quantification of early vasospasm and testing its capability to predict delayed cerebral ischemia after SAH.

Recombinant Factor VIIa (RFVIIa) for Acute Hemorrhagic Stroke Administered at Earliest Time Trial (FASTEST)

Investigator: James Grotta, MD

This two-arm, randomized, double-blinded clinical trial will enroll 860 patients at approximately 115 hospital sites and 15 mobile stroke units in the NINDS-funded StrokeNet in the U.S. and key global institutions. The researchers' primary objective is to test the hypothesis that treatment with rFVIIa within two hours of onset in appropriately selected patients with spontaneous intracranial hemorrhage improves outcome as measured by the ordinal distribution of the modified Rankin Scale at 180 days, as compared to placebo.

SEdation versus General Anesthesia for Endovascular Therapy in Acute Ischemic Stroke (SEGA)

Investigator: Peng R. Chen, MD

This study aims to estimate overall treatment benefit (improvement in disability) among acute ischemic stroke patients randomized to general anesthesia compared with sedation during endovascular therapy. Researchers will assess safety as measured by incidence of symptomatic intracranial hemorrhage, rates of endovascular therapy, procedural complications, reperfusion, and quality of life.

Sleep for Stroke Management and Recovery Trial (SleepSmart)

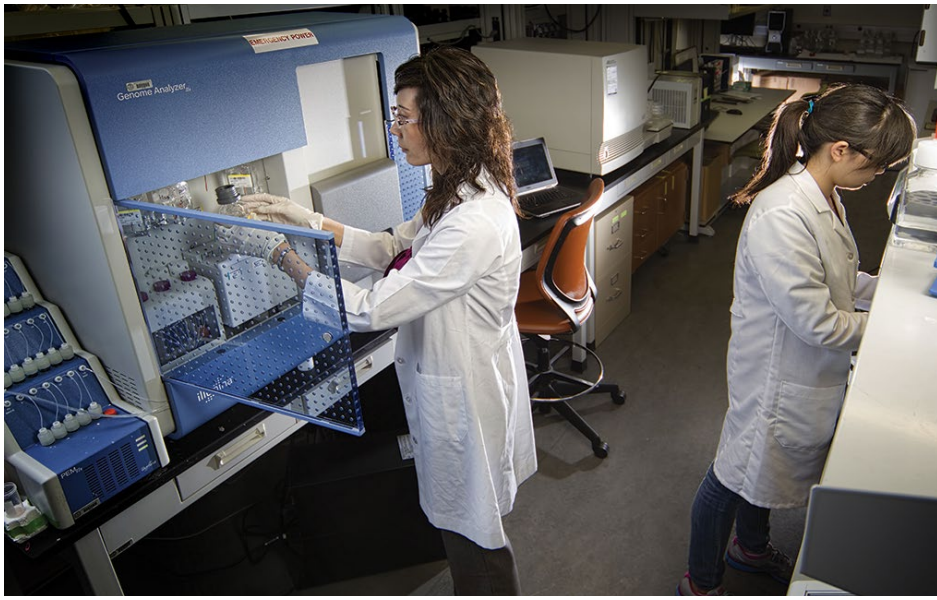
Co-Investigators: Sudha Tallavajhula, MD, and Anjail Sharrief, MD

This investigator-initiated Phase III multicenter, prospective, randomized, controlled trial is testing whether treatment of obstructive sleep apnea (OSA) with continuous positive airway pressure is effective for secondary prevention and recovery after stroke. The primary goals of this study are to determine whether treatment of OSA with positive airway pressure starting shortly after acute ischemic stroke or high-risk TIA (1) reduces recurrent stroke, acute coronary syndrome, and all-cause mortality 6 months after the event; and (2) improves stroke outcomes at 3 months in patients who experienced an ischemic stroke.

Stroke (AIS) Bio-Repository

Investigator: Jaroslaw Aronowski, MD, PhD

This biorepository obtains tissue samples and associated data from patients with acute cerebrovascular diseases, allowing researchers to determine biomarkers and genomic profiles to identify new diagnostics, treatment targets, and predictors of disease. Researchers hope to use the data to identify health trends and stroke recovery, and to improve care.



Stroke Telemedicine Outpatient Prevention Program for Blood Pressure Reduction (STOP STROKE)

Investigator: Anjail Sharrief, MD

Researchers will evaluate the effectiveness of the Stroke Telemedicine Outpatient Program (STOP) in 100 patients over a six-month period, with the goal of identifying any reduction in blood pressure after stroke in patients at risk for high blood pressure.

Tenecteplase in Stroke Patients Between 4.5 and 24 Hours (TIMELESS)

Investigator: Andrew Barreto, MD

In this Phase III blinded, randomized trial of thrombolysis in imaging-eligible, late-window patients, researchers are assessing the efficacy and safety of a clot-dissolving medication, tenecteplase, in patients with acute ischemic stroke (AIS) who arrive in the emergency department in the 4.5- to 24-hour time window. They hope to extend the treatment window from the current 4.5 hours restrictions to up to 24 hours after AIS.

The Intra-Arterial Vasospasm Trial (iVAST)

Investigator: Peng R. Chen, MD

This study is designed to compare outcomes between intra-arterial infusion of a combination of multiple vasodilators and a single agent in treatment of cerebral vasospasm.

Thrombectomy for Emergent Salvage of Large Anterior Circulation Ischemic Stroke (TESLA)

Investigator: Sunil Sheth, MD

This prospective, randomized, open-label, blinded endpoint study will enroll up to 500 participants. Patients who present with symptoms of acute ischemic stroke and have evidence of a moderate-to-large infarct volume (NCCT ASPECTS 2-5) in the anterior circulation will be assigned to either best medical management alone (including intravenous recombinant tissue-type plasminogen activator [IV rtPA]) or intra-arterial treatment (IAT) with mechanical thrombectomy added to best medical management.

Thromboelastographic Correlation with Neurological Complications and Outcome in Subarachnoid Hemorrhage Patients

Investigator: Alex Choi, MD, MS

Thromboelastography (TEG) is the broadly applied method for detecting coagulation, platelet function, and fibrinolysis abnormality of various clinical situations. In several studies on intracranial hemorrhage, ischemic stroke, and traumatic brain injury, TEG correlates with disease severity and complications. In subarachnoid hemorrhage (SAH) patients, long-term outcome and mortality have been determined by complications such as re-bleeding and delayed cerebral ischemia. The researchers are investigating TEG as a tool in SAH patients to determine its association with complications and outcome.

Thromboelastography (TEG) Database

Investigator: Tiffany Chang, MD

This observational study is evaluating coagulation disturbances in the setting of intracerebral hemorrhage (ICH), subarachnoid hemorrhage (SAH), and traumatic brain injury (TBI).

Transcranial Direct Current Stimulation for Post-Stroke Motor Recovery: A Phase II Study (TRANSPORT 2)

Principal Investigator: Gerard Francisco, MD

Co-Investigator: Sean Savitz, MD

TRANSPORT 2 is a Phase II multicenter randomized transcranial direct current stimulation (tDCS) study to determine the efficacy, safety, tolerability, and feasibility of use of tDCS. Participants must be ages 18 to 80 years, with a first-ever unihemispheric ischemic stroke in the past 30 to 180 days resulting in unilateral limb weakness. Intervention sessions last 30-60 minutes per session, and 10 intervention sessions are required over a 14-day period.

Venous Thromboembolism and Complications in Hospitalized Patients

Investigator: Alex Choi, MD, MS

This study is focused on comprehensive analysis of the epidemiologic features, including incidence, complications associated with prophylaxis or management, and outcome in hospitalized patients with venous thromboembolism (VTE). VTE is induced by stasis of venous blood particularly in hypercoagulative condition, such as old age, active cancer, and neurological disease with limb paresis, major surgery, and trauma. VTE is common in hospitalized patients and associated with reduced survival and increased morbidity. An understanding of VTE in hospitalized patients might help prevent it and improve overall outcomes. In this study, researchers are analyzing the data of hospitalized patients retrospectively to find clinical implications of VTE incidence, complications, and outcome for adequate prevention and management.

Virtually Assisted Home Rehabilitation After Acute Stroke (VAST-Rehab)

Investigator: Sean Savitz, MD

This pilot study will assess the feasibility, safety, and efficacy of adding virtual patient learning and video-conference visits with licensed rehabilitation therapists to standard-of-care home therapy. Subjects complete virtual visits with a physiatrist and rehabilitation therapists as well as documentation of daily rehabilitation activity over a period of 12 weeks. Outcome assessments are performed at baseline and end-of-therapy visits.

Epilepsy

Analysis of Multimodal Sensor Data and Algorithms with a Wearable Device in Patients Undergoing Epilepsy Treatment

Investigator: Samden Lhatoo, MD

Patients ages 18 to 80 years undergoing epilepsy treatment, who are willing to wear the device, may enroll in this study.

Autonomic and Imaging Biomarkers of Sudden Unexpected Death in Epilepsy (SUDEP)

Investigator: Samden Lhatoo, MD

Participants in this study to track biomarkers of sudden unexpected death in epilepsy must have a diagnosis of epilepsy and be at least 1 year old.

Comparative Study of Postictal Generalized Electroencephalographic (EEG) Suppression in Surface EEG and Intracranial EEG

Investigator: Samden Lhatoo, MD

Patients ages 18 and older with medically refractory epilepsy who undergo intracranial monitoring in the adult Epilepsy Monitoring Unit at Memorial Hermann-Texas Medical Center and have at least one generalized tonic-clonic seizure during monitoring are eligible for this study.

Genetics in Epilepsy

Investigator: Samden Lhatoo, MD

Researchers are actively enrolling patients who have an established diagnosis of epilepsy and are seen at UTHealth Neurosciences epilepsy and epilepsy surgery clinics, or admitted to the Epilepsy Monitoring Unit at Memorial Hermann-Texas Medical Center.

Human Autonomic and Respiratory Responses to Direct Cortical Stimulation

Investigator: Samden Lhatoo, MD

This study examines human autonomic and respiratory responses to direct cortical stimulation in patients 18 years and older with a diagnosis of epilepsy, who are admitted to the Epilepsy Monitoring Unit for intracranial video EEG evaluation.

Occult Epileptic Seizures and Epileptiform Activity in Patients with Alzheimer's Disease: A Prospective Study Using a Computer-Based Detector, High-Density Electroencephalography, and Magnetoencephalography

Investigator: Samden Lhatoo, MD

This study is actively enrolling patients with Alzheimer's disease, dementia, or presymptomatic AD.

RNS® System Post-Approval Study in Epilepsy

Investigator: Nitin Tandon, MD

This observational study is designed to assess the long-term safety and effectiveness of the RNS System as an adjunctive therapy in reducing the frequency of seizures. Eligible individuals are 18 years of age or older, with partial onset seizures, who have undergone diagnostic testing that localized no more than two epileptogenic foci, are refractory to two or more antiepileptic medications, and have frequent and disabling seizures.

Stereotactic Laser Ablation for Temporal Lobe Epilepsy (SLATE)

Investigator: Nitin Tandon, MD

This study is designed to evaluate the safety and efficacy of the Visualase® MRI-guided laser ablation system for necrotization or coagulation of epileptogenic foci in patients with intractable mesial temporal lobe epilepsy. The study will include approximately 150 adult patients with drug-resistant MTLE treated at select epilepsy centers in the U.S.

Study of Cerebrovascular Reactivity (CVR) to Hypercapnia Using Blood Oxygenation Level-Dependent (BOLD) Magnetic Resonance Imaging

Investigator: Samden Lhatoo, MD

The researchers are studying the relationship between hypercapnic ventilatory response (HCVR), respiratory depression, and sudden unexpected death in epilepsy (SUDEP).

Headache and Pain Management

American Registry for Migraine Research

Investigator: Mark Burish, MD

In this observational study, researchers are collecting biospecimens and longitudinal clinical data from research subjects with primary and secondary headache disorders.

Discovery of Biomarker Signatures Prognostic for Neuropathic Pain After Acute Spinal Cord Injury

Investigator: Georgene Hergenroeder, PhD

The researchers' ultimate goal is to identify a biomarker signature prognostic of spinal cord injury-induced neuropathic pain to develop new non-addictive treatments for the prevention of pain after acute SCI.

Investigation of Clinical Questionnaires in Cluster Headache

Investigator: Mark Burish, MD, PhD

Using existing data from patient charts, the investigators are determining which questionnaires are most useful in the diagnosis of cluster headache.

The Pain Biomarker Study

Investigator: Mark Burish, MD, PhD

This study investigates changes in circulating pain-signaling molecules when pain is provoked, to better understand the molecular and physical biomarkers of headache. A better understanding the mechanism of headache will lead to more effective treatment.

Memory Disorders and Dementia

A Study of Donanemab in Participants with Early Alzheimer's Disease (TRAILBLAZER-ALZ2)

Investigator: Paul Schulz, MD

This interventional clinical trial is assessing the safety, tolerability, and efficacy of donanemab (LY3002813) in early symptomatic Alzheimer's disease. The study is open to participants ages 60 to 85 years with mild symptoms of AD, as well as the ability to undergo PET scans.

Plasma Exchange for the Treatment of Early Alzheimer's Disease

Investigator: Paul Schulz, MD

The researchers' goal is to test the hypothesis that plasma exchange will lower blood Aß, tau, and inflammatory molecules, and that this will improve clinical outcomes in Alzheimer's disease, most likely through reduction of brain levels of these three classes of molecules. This is a single-site, investigator-initiated translational trial from mice to humans.

Stem Cell Therapy for Early Alzheimer's Disease

Investigator: Paul Schulz, MD

Stem cell therapy for Alzheimer's disease involves the systemic introduction of mesenchymal stem cells into the body intravenously to find inflammation and repair it. The study is open to patients ages 50 to 90 years with mild cognitive impairment or early symptoms of AD.

The Oral Microbiome in Patients with Dementia

Co-Investigators: Paul Schulz, MD, and Cameron Jeter, MD

Alzheimer's disease has been linked to the oral microbiome, the composition of which is influenced by diet. This study is enrolling patients aged 50 to 90 years with mild cognitive impairment or early symptoms of AD.

Movement Disorders and Neurodegenerative Diseases

A Randomized, Double-Blind, Placebo-Controlled Trial of Allogeneic Bone Marrow-Derived Mesenchymal Stem Cells as a Disease-Modifying Therapy for Idiopathic Parkinson's Disease (MSCII Study)

Investigator: Mya Schiess, MD

Researchers aim to select the safest and most effective number of repeat doses of mesenchymal stem cells to slow the progression of Parkinson's disease.

Child to Adult Neurodevelopment in Gene Expanded Huntington's Disease (ChANGE-HD)

Investigator: Erin Furr-Stimming, MD

This study evaluates brain structure and function in children, adolescents, and young adults (ages 6 to 30) who are at risk for developing Huntington's disease, i.e., those who have a parent or grandparent with HD.

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

Co-Investigators: Mohammad Shahnawaz, PhD, and Mya Schiess, MD

The investigators are assessing the use of peripheral alpha-synuclein oligomers as a possible biomarker for diagnosis of and progression in Parkinson's disease.

DM/Q for Irritability in Huntington's Disease

Investigator: Erin Furr-Stimming, MD

Researchers are evaluating the efficacy of dextromethorphan/quinidine in treating irritability in Huntington's disease. The study is open to adults ages 18 through 75 who are gene positive for HD with irritability symptoms.

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

Investigator: Erin Furr-Stimming, MD

This study is developing a comprehensive repository of prospective and systematically collected clinical research data and biological specimens from individuals with manifest HD, unaffected individuals known to carry the HD mutation or at risk of carrying the HD mutation, and control research participants (e.g., spouses, siblings, and offspring of HD mutation carriers known not to carry the HD mutation).

HDClarity: A Multi-Site Cerebrospinal Fluid Collection Initiative to Facilitate Therapeutic Development for Huntington's Disease

Investigator: Erin Furr-Stimming, MD

HDClarity will seek at least 1,200 research participants at different stages of Huntington's disease. The primary objective of this study is to collect a high-quality CSF sample for evaluation of biomarkers and pathways that will enable the development of novel treatments for HD. The secondary objective is to generate a high-quality plasma sample collection matching the CSF collections, which will also be used to evaluate biomarkers and pathways of relevance to HD research and development.

KINECT-HD: Efficacy, Safety, and Tolerability of Valbenazine for the Treatment of Chorea Associated with Huntington's Disease

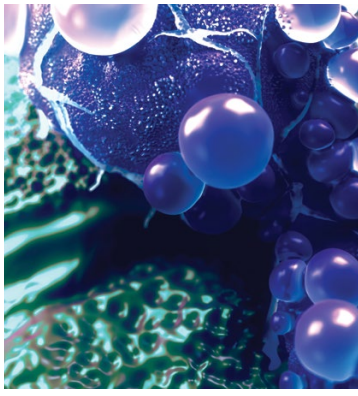
Investigator: Paul Schulz, MD

This is a Phase III, randomized, double-blind, placebo-controlled study to evaluate the efficacy, safety, and tolerability of valbenazine to treat chorea in participants with Huntington's disease. Participants must have a diagnosis of motor-manifest HD at or before screening and be naïve to VMAT 2 inhibitors.

Medtronic Product Surveillance Study for Deep Brain Stimulation

Investigator: Mya Schiess, MD

The Medtronic Product Registry provides continuing evaluation and periodic reporting of safety and effectiveness of Medtronic market-released products to support the interests of patients, hospitals, clinicians, regulatory bodies, payers, and the industry. This world registry of implanted neuromodulation devices includes patients who have received or intend to receive deep brain stimulation or an intrathecal baclofen pump with either a new or replacement neurostimulator or pump.



REM Sleep Behavior Disorder Study

Investigator: Mya Schiess, MD

The researchers' goal is to identify biomarkers of clinical progression and conversion to alpha-synucleinopathies in the population with REM sleep behavior disorder. Participants must be 40 to 80 years of age with a diagnosis of idiopathic RBD by polysomnography, healthy controls, atypical Parkinsonism or Parkinson's disease.

Safety and Proof-of-Concept Study with AMT-130 in Adults with Early Manifest Huntington's Disease

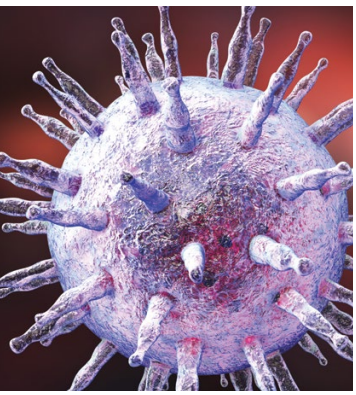
Investigator: Erin Furr-Stimming, MD

This is the first study of AMT-130 in patients with early manifest Huntington's disease and is designed to establish safety and proof of concept. CT-AMT-130-01 is a Phase I/II, randomized, multicenter, dose-escalation, double-blind, imitation surgery, first-in-human study.

Study of the Fecal Microbiome in Patients with Parkinson's Disease

Investigator: Mya Schiess, MD

Researchers are characterizing the intestinal microbiome in subjects with Parkinson's disease and determining the safety and trends in improvements in diversity of colonic microbiome following administration of lyophilized PRIM-DJ2727 or placebo given orally for 12 weeks in subjects with Parkinson's disease.



Study to Assess the Safety and Effectiveness of Pridopidine Compared to Placebo in the Treatment of Levodopa-Induced Dyskinesia in Patients with Parkinson's Disease

Investigator: Raja Mehanna, MD

This is a multicenter, randomized, three-arm, parallel-group, double-blind, placebo-controlled, study to evaluate the efficacy, safety and pharmacokinetics of pridopidine vs. placebo for the treatment of levodopa-induced dyskinesia (LID) in patients with Parkinson's disease.

The INSYTE (Management of Parkinson's Disease Psychosis in Actual Practice) Study

Investigator: Paul Schulz, MD

The researchers are examining the disease progression of Parkinson's disease psychosis; the clinical, economic, and humanistic impact of antipsychotic therapy in the management of the condition in real-world settings; and the burden of the condition on patients and their caregivers.

VY-AADC02 for Parkinson's Disease with Motor Fluctuations (RESTORE-1)

Co-Investigators: Paul Schulz, MD, and David Hunter, MD

This randomized, sham surgery-controlled, double-blind, multicenter study is assessing the efficacy, safety, and tolerability of VY-AADC02 in patients with Parkinson's disease with motor fluctuations.

UTHealth Neurocognitive Disorders Biobank

Investigator: Paul Schulz, MD

The UTHealth Neurocognitive Disorders Biobank is a resource for researchers engaged in studies of neurocognitive and other neurological disorders. Researchers at the NCD Biobank are collecting and archiving whole blood for RNA and DNA extraction, plasma, serum, urine, cerebrospinal fluid, and oral fluids from healthy volunteers and from adult patients who visit the Neurocognitive Disorders Center and the Department of Neurology at McGovern Medical School.

Multiple Sclerosis

A Study to Investigate the Pharmacokinetics, Safety, and Tolerability of Subcutaneous Ocrelizumab Administration in Participants with Multiple Sclerosis

Investigator: J. William Lindsey, MD

This study will test whether Ocrevus® can be given by injection under the skin rather than by intravenous infusion, and determine the most effective dose.

Determining the Effectiveness of Early Intensive versus Escalation Approaches for Relapsing-Remitting Multiple Sclerosis (DELIVER-MS)

Investigator: Rohini Samudralwar, MD

Researchers are enrolling newly diagnosed patients and comparing outcomes in a group started on safer but less effective treatments to the group started on more effective treatments with more potential side effects.

Elezanumab for Neural Regeneration

Investigator: J. William Lindsey, MD

This study will investigate whether elezanumab will promote regeneration and repair of damaged brain tissue when given by monthly intravenous infusion to three treatment groups – placebo, low dose, and high dose. Enrollment and treatment are completed, and results will be available in early 2021.

Enhanced Cerebral Perfusion with Oral Acetazolamide

Investigator: John Lincoln, MD, PhD

This study is determining whether acetazolamide increases brain perfusion. Patients with MS will be treated with oral acetazolamide at different doses, and the effect on brain blood flow will be measured with MRI.

Epstein-Barr Virus and Multiple Sclerosis

Investigator: J. William Lindsey, MD

Researchers are investigating the connection between Epstein-Barr virus and multiple sclerosis and testing whether antibodies to EBV cause damage to brain cells. Current findings indicate that immune cells specific for EBV also recognize brain antigens.

Features and Outcomes of Viral Infections in Sarcoidosis and Other ILDs: A Prospective Study During a Pandemic (INSILD)

Co-Investigators: Rohini Samudralwar, MD, and Pascal Kingah, MD

The investigators are retroactively tracking infectious events that subjects with all forms of sarcoidosis report during prospective follow-up visits. Adult patients with a diagnosis of sarcoidosis or another ILD who are receiving clinical care may enroll.

Hormones and Inflammatory Markers in Relapsing-Remitting Multiple Sclerosis

Investigator: Rohini Samudralwar, MD

In this study, researchers are examining the different stages of life and gender and their influence on hormone changes, and correlating this with levels of inflammatory markers in the blood that may be associated with RRMS. Researchers will also look at functional status in newly diagnosed patients and those who have relapses to see if key hormones have an influence on overall wellbeing.

North American Registry for Care and Research in Multiple Sclerosis (NARCRMS)

Investigator: Rohini Samudralwar, MD

Researchers are creating a national registry and longitudinal database by collecting clinical and patient-based information related to multiple sclerosis.

Phase I Study to Evaluate the Safety and Efficacy of ATA188 in Subjects with Progressive Multiple Sclerosis

Investigator: J. William Lindsey, MD

The purpose of this study is to evaluate the safety and tolerability of ATA188 as a monotherapy, with the long-term goal of using white blood cells specific for EBV as a treatment for MS. This is a Phase I study in progressive multiple sclerosis, with the objective of assessing safety and tolerability of the treatment.

Phase III Study of Fenebrutinib

Investigator: J. William Lindsey, MD

Researchers are comparing the effect of fenebrutinib, a new oral agent, to Ocrevus®, an approved medication for primary progressive multiple sclerosis.

Ravalizumab in Neuromyelitis Optica

Investigator: John Lincoln, MD, PhD

This trial is determining if ravalizumab is effective in treating neuromyelitis optica. Ravalizumab is very similar to eculizamab, which is approved for treatment of NMO, but requires less frequent dosing. Enrollment is complete, treatment is ongoing, and results are expected in 2022.

Study of Evobrutinib in Participants with Relapsing Multiple Sclerosis

Investigator: J. William Lindsey, MD

Researchers are evaluating the efficacy and safety of evobrutinib administered orally twice daily versus Aubagio orally once a day in participants with relapsing multiple sclerosis. Enrollment is ongoing.

Tremor in Multiple Sclerosis

Investigator: John Lincoln, MD, PhD

The goal of this study is to determine which areas and networks in the brain cause tremors in patients with multiple sclerosis.

Nerve Disorders

Restoring Hand Function Utilizing Nerve Transfers in Persons with Cervical Spinal Cord Injuries

Investigator: Wesley Jones, MD

This non-randomized prospective study assesses outcomes after upper-extremity nerve transfer in patients with post-acute cervical spinal cord injury.

Nerve Transfers to Improve Upper-Extremity Function and Quality of Life in Tetraplegic Patients

Investigator: Wesley Jones, MD

The researchers are studying the utility of peripheral nerve transfer surgery to regain hand function in patients with complete spinal cord injury.

Neuromuscular Disorders

A Phase Ib Study to Evaluate the Safety, Tolerability, and Drug-Drug Interactions of ANX005 in Combination with Intravenous Immunoglobulin in Subjects with Guillain-Barré Syndrome

Investigator: Kazim Sheikh, MD

This study is evaluating safety, tolerability, and drug-drug interactions of ANX005, a monoclonal antibody that inhibits complement component C1q and prevents complement-mediated tissue injury. The trial design includes administration of this experimental medication along with standard treatment of Guillain-Barré syndrome with intravenous immunoglobulins (IVIG) during the acute stage of the disease.

A Phase II Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability, and Efficacy of Zilucoplan in Subjects with Immune-Mediated Necrotizing Myopathy

Investigator: Suur Biliciler, MD

This study is evaluating the safety, tolerability, and efficacy of zilucoplan in subjects with immune-mediated necrotizing myopathy. Participants must be 18 to 75 years old with a diagnosis of IMNM, positive for anti-HMGCR or anti-SRP auto-antibodies, and vaccinated against meningococcal infections within three years or prior to the initiation of the study drug.

A Phase III Randomized, Double-Blind, Placebo-Controlled Multicenter Study to Evaluate the Safety and Efficacy of Ravulizamab in Complement-Inhibitor-Naïve Adult Patients with Generalized Myasthenia Gravis

Investigator: Thy Nguyen, MD

This study is evaluating the safety and efficacy of ravulizumab, a long-acting monoclonal antibody that inhibits complement component C5 for approximately 8 weeks. This trial is recruiting adult patients with generalized myasthenia gravis who have not received complement inhibition treatments previously.

A Phase III Study to Evaluate the Efficacy, Safety, and Tolerability of Immune Globulin Infusion with Recombinant Human Hyaluronidase for the Treatment of Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP)

Investigator: Kazim Sheikh, MD

Patients 18 years of age and older with a diagnosis of definite or probable CIDP may be eligible to participate in this study of 10 percent human immune globulin infusion with recombinant human hyaluronidase (HYQVIA/HyQvia) and human immune globulin infusion 10 percent GAMMAGARD LIQUID/KIOVIG for the treatment of CIDP.

Spinal Cord Injury

Nerve Transfers to Improve Upper-Extremity Function and Quality of Life in Tetraplegic Patients

Investigator: Wesley Jones, MD

In this prospective, multi-institutional, non-randomized, single-arm trial, researchers will measure the efficacy of nerve transfer surgery in the treatment of patients with complete spinal cord injuries and no hand function. Their goal is to optimize the efficiency of nerve transfer surgery by evaluating patient outcomes, quality of life, and functional independence. Seventy participants with cervical ASIA A-B and hand function impairment will be enrolled.

Pediatric Neuroscience

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

Investigator: David Sandberg, MD

This trial employs a novel means of treating malignant tumors that originate from the fourth ventricle: infusion of two chemotherapy agents directly into the fourth ventricle rather than systemic intravenous delivery. There will be no simultaneous systemic chemotherapy. Participants must be ages 1 to 21 with recurrent medulloblastoma (PNET), recurrent ependymoma, or recurrent atypical teratoid/rhabdoid tumors involving the brain and/or spine.

Dynamic Near-Infrared Fluorescence Imaging of CSF Outflow: A Tool to Manage Pediatric Hydrocephalus

Co-Investigators: Manish N. Shah, MD, and Eva Sevick-Muraca, PhD

The researchers are assessing fluorescence-based cerebrospinal fluid flow in an animal model using their whole-brain optical imaging technology: cap-based transcranial optical tomography. CTOT is the first wearable, high-resolution, whole-brain functional imaging device that does not require infants to be put under anesthesia. Using night-vision goggle technology, near-infrared light, and high-resolution detectors, CTOT helps physicians accurately diagnose the severity of an infant's brain injury and prescribe treatment that will optimize quality of life throughout childhood.

Infusion of MTX110 into the Fourth Ventricle in Patients with Recurrent Medulloblastoma

Investigator: David Sandberg, MD

This novel trial places MTX110, a new formulation of panobinostat, directly into the fourth ventricle of the brain while avoiding the surrounding healthy tissue. MTX110 is a chemotherapy drug that has shown promise in laboratory models of medulloblastoma, the most common malignant brain tumor in children. The pilot study, approved by the U.S. Food and Drug Administration, will enroll five patients with recurrent medulloblastoma at Children's Memorial Hermann Hospital.

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

Investigator: David Sandberg, MD

This study employs a novel means of treating ependymoma brain tumors that originate from the fourth ventricle: infusion of a chemotherapy agent directly into the fourth ventricle, rather than systemic intravenous delivery. The agent being infused, 5-AZA, has been shown to effectively kill ependymoma cells in the laboratory. The trial is open to patients ages 1 to 21 years old with recurrent ependymoma that originated in the posterior fossa of the brain.

Phase 1 Dose-Escalation Trial

Investigator: David Sandberg, MD

This trial is the only study in the world investigating the direct administration of methotrexate into the fourth ventricle of the brain for the treatment of children with recurrent malignant fourth ventricular brain tumors. A pilot clinical trial completed in August 2015 demonstrated that some patients with recurrent medulloblastoma experience a beneficial anti-tumor effect both within the fourth ventricle and at distant sites. Delivering chemotherapeutic agents directly to the site of disease is particularly advantageous for children because it enables high drug concentrations at the site of disease origin, while minimizing the side effects of chemotherapy by decreasing systemic drug exposure.

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Aronowski, Jaroslaw

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Angel Ignacio Blanco, M.D.
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With Timely Treatment and Determination, Patricia Miata Recovers from Stroke

PATRICIA MIATA couldn't walk or speak after she suffered a left middle cerebral artery (MCA) ischemic stroke in February 2018 at the age of 57. The only thing she could say was her dog Diesel's name. Eight months later she was back at work and her exercise routine, thanks to timely treatment from neurologists at UTHealth Neurosciences.

Miata was home with Diesel when she felt like something was not quite right. "I sat down, and then just fell out of the chair onto the floor," she recalls. "I army-crawled out my front door, across the concrete, yelling for help. A neighbor called 911."

She was taken to Memorial Hermann Memorial City Medical Center, home to one of Memorial Hermann's four Comprehensive Stroke Centers. "We work with EMS crews to recognize the signs of large stroke, so they know to skip small hospitals and go straight to a stroke center where patients have fast access to tPA and endovascular thrombectomy," says Sunil Sheth, MD, a neurologist with UTHealth Neurosciences and an assistant professor at McGovern Medical School at UTHealth. "Every minute counts."

Miata had vision loss, significant weakness in her right arm and leg, and difficulty speaking and understanding. "I was stunned at how quickly Trish was taken care of," says her husband John Miata. "She got the tPA within 16 minutes of her arrival at the hospital – and an immediate thrombectomy. She started physical, occupational, and speech therapy while she was still in the intensive care unit, which made a big difference in her recovery."

Within a few days, Miata had regained some strength and most of her sight. Because she had aphasia and loss of sensation and weakness on her right side, she was referred to Reza Sadeghi, MD, a neurologist and clinical neurophysiologist with UTHealth Neurosciences.

"Dr. Sadeghi helped us work through the stages of Trish's recovery," John Miata says. "His encouragement and awe of Trish encouraged us to keep pushing through. He was easy to talk to and told it like it was."

Eight months after her stroke, thanks to two local inpatient rehabilitation programs and outpatient therapy at TIRR Memorial Hermann, Miata was able to return to her position as registrar at a local high school.

"Trish blew them away at both rehab programs," John Miata says. "She's been active her whole life and was determined to get back to that, so she always asked her therapists for more. She couldn't walk after the stroke, and a little over a year later, we went hiking in Colorado, and there she was, walking the trails."

Miata's stroke was cryptogenic – not clearly attributable to a cardioembolism, atherosclerosis, or small artery disease. "I still have issues comprehending complex directions, and I struggle with spelling, but Dr. Sadeghi recommended software that helps with texting and writing," she says. "I've found ways to work around my limitations and do my job. I never feel like I'm behind. If I can't figure out how to solve a problem, I research it.

"John is very supportive, and Diesel was a lifesaver for me because I walk or run with him to get my two miles in every day," she adds. "I like to keep moving."

"She got the tPA within 16 minutes of her arrival at the hospital – and an immediate thrombectomy. She started physical, occupational, and speech therapy while she was still in the intensive care unit, which made a big difference in her recovery." — John Miata

Isla Ritchie Finds Freedom from Epilepsy

IN MAY 2021, 17-year-old Isla Ritchie will be seizure free for two years, after implantation of a vagus nerve stimulator (VNS). She's an outlier on the bell curve of patients with epilepsy who respond to stimulation of the vagus nerve. Most who decide to move forward with VNS have seizures reduced by half – shorter seizures that are less frequent and more easily managed.

"Every once in a while we have a patient who becomes seizure free after VNS implantation, and Isla is in that group," says Gretchen Von Allmen, MD, chief of pediatric epilepsy for the Texas Comprehensive Epilepsy Program and medical director of the Children's Memorial Hermann Hospital Pediatric Epilepsy Monitoring Unit. "There are people on both sides of the bell curve, but the average response is a 50 percent reduction in seizures, and there are some who have no change at all in seizure frequency. Almost everyone with intractable epilepsy agrees that even a 50 percent reduction makes a significant difference in quality of life."

Isla at 11 and 12

Isla remembers the day she knew something was wrong. "I was 11. I woke up and my arms were shaking. I freaked out and ran to my parents' room and told them I didn't know what was happening," she says.

When she was 12, she had four generalized convulsive seizures in a single night. "We made it to the hospital in time for the fourth seizure," says her mother, Lisa Ritchie. "After that, she had seizures almost weekly for as long as five minutes. She lost her memory, and there were a variety of memories she never recovered, including some of our family trips, which were the most poignant and noticeable to her. It was a rough rollercoaster ride for all of us, especially for Isla."

By the time she saw Von Allmen in 2015, Isla had trialed several anti-convulsive medications. The family came to the epileptologist for a second opinion when medication failed to stop the seizures. She ordered genetic testing, which was positive for mitochondrial disease, and referred her to neurologist Mary Kay Koenig, MD, a mitochondrial specialist with UTHealth Neurosciences. Isla was also diagnosed with dysautonomia, a group of medical conditions caused by dysfunction of the autonomic nervous system, which controls the breathing, the heartbeat, and digestion.

"I had a lot on my plate at the age of 12," Isla says. "I was diagnosed with all these things at the same time and before that, I was very athletic. I swam and did triathlons. Suddenly I was a wreck. I didn't know anyone who had even one of my problems. The big generalized seizures were terrible, and my mitochondria were not producing enough energy for my body. I felt so bad from all the medications that I couldn't get out of bed. I gained 60 pounds and struggled to get through the day. I felt alone and depressed."

From Medication to the Next Level

Isla was having focal seizures with impaired awareness that present as staring episodes, in addition to generalized convulsive seizures. "When people with epilepsy fail two or more medications, there is only a 1 to 2 percent chance that they will have a significant response to additional medications. So we move on to the next level of therapies – epilepsy surgery, the ketogenic diet, or vagus nerve stimulation," Von Allmen says. "First we wanted to see if she was a candidate for focal surgical resection, which offers a more than 70 percent chance of being seizure free."

Isla was admitted to the Epilepsy Monitoring Unit at Children's Memorial Hermann Hospital and evaluated for intractable epilepsy. Testing showed she was not eligible for focal brain surgery because the seizures were originating from both sides of the brain. She tried the ketogenic diet, but it didn't agree with her. Von Allmen recommended vagus nerve stimulation.

Manish N. Shah, MD, director of pediatric spasticity and epilepsy surgery at McGovern Medical School at UTHealth, implanted Isla's VNS in October 2016. "It

"It took Isla about six months to adjust to the VNS. She had at least one seizure every time Dr. Von Allmen turned it up. After a few months, we could see that the seizures were spreading out a bit and then spreading out more and more."— Lisa Ritchie

took her about six months to adjust to the VNS," Lisa Ritchie says. "She had at least one seizure every time Dr. Von Allmen turned it up. After a few months, we could see that the seizures were spreading out a bit and then spreading out more and more. There was an adjustment period, but now we're looking back on it."

Isla at 17

Isla says she's been through a lot, with a lot of tears shed. "I want to deal with my reality and move forward. I exercise more and dance a lot. I've developed an interest in science and health, and know I want to work in the medical field. They've taught me what these disorders are and led me to think in different ways about my future," she says. "I'm still thinking it through, but I know that medicine will keep advancing and I want to be a part of that."

"Since the VNS kicked in, Isla has totally transformed herself," says her father, Norman Ritchie. "I'm amazed at what she has overcome. When I think of myself at her age, I had nothing to deal with compared to what she is dealing with. She's a very determined young lady. There's no 'Woe is me.' It's always 'This is what happened, and this is how I handled it.' She decides what she wants to do, and she does it."

Her mother says Isla can think more clearly and now has a good balance of academics, sports, and social life. "As a parent of a child with epilepsy, I found it helpful to connect with groups," Lisa Ritchie says. "There are plenty on Facebook. Other families are struggling through the same thing. Your friends want to help and mean well, but they don't really know what you're going through."

Isla now sees Von Allmen once a year for a checkup or as needed. "Never would I have imagined that I would do track and field," she says. "I do discus, shot put, dancing, swimming, and bicycling. That physical outlet is important to me, and I didn't have it for many years. It gives me self-confidence."

One in 25 people will develop epilepsy in their lifetime, but stigma still surrounds the disorder. "Because it's so

unpredictable, it has a major effect on quality of life," Von Allmen says. "Two-thirds of people with epilepsy do respond to medication, but then often have to deal with the medication side effects. The other third might be candidates for other therapies if they are properly evaluated, but often they're not."

"Way back in the beginning, it was heartbreaking," Norman Ritchie says. "You try this and try that. As a parent you feel helpless. I remember one teacher talking about her daydreaming when she was younger. She might have been having seizures that we were unaware of. If we'd had better education and awareness, perhaps we would have recognized it. Maybe we had an opportunity to help her earlier that we were unaware of."

Isla has shared her story with friends and peers at school and has advice for kids with epilepsy. "It may feel like you're alone, but you're not. I've overcome many obstacles that I didn't expect to have. I want to tell people what epilepsy is and show it to the world so if you have it, you won't feel alone. It was tough and took a lot out of me. You might struggle, but if you believe in yourself, you can push through any obstacle that comes your way.

"Epilepsy is more common than people realize," she says. "You might pass someone on the street who has it and not know. Have confidence, believe in yourself, and tell the people around you that you have epilepsy. When the people I'm with know about it, I feel safe because I know I'll be taken care of."

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