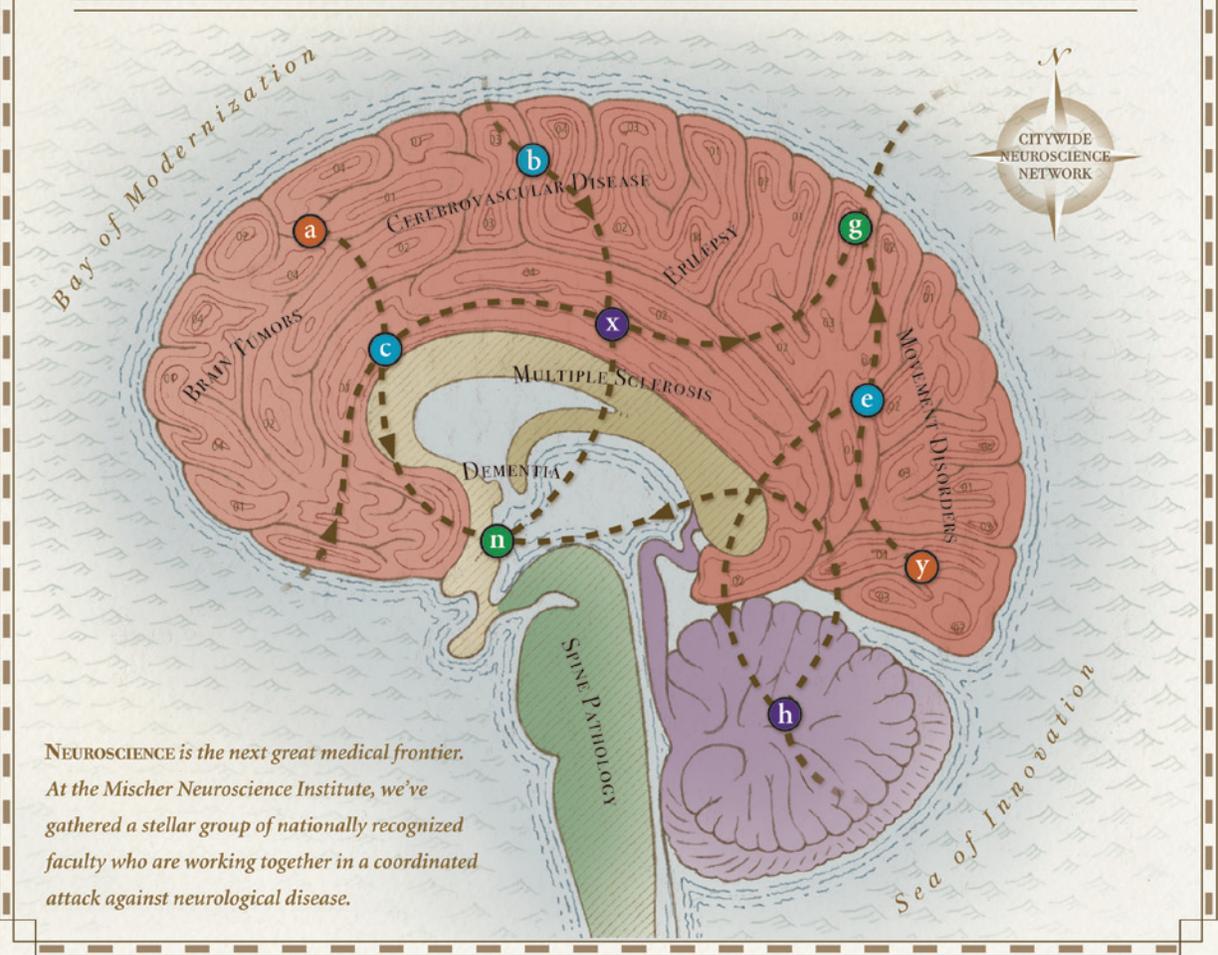


MEMORIAL HERMANN
MISCHER NEUROSCIENCE INSTITUTE
JOURNAL

TEXAS MEDICAL CENTER

NEUROSCIENCE

EXPLORING *the* NEW FRONTIER



NEUROSCIENCE is the next great medical frontier. At the Mischer Neuroscience Institute, we've gathered a stellar group of nationally recognized faculty who are working together in a coordinated attack against neurological disease.

In This Issue

Features

02 Building a Citywide Neuroscience Network

05 Telemedicine Technology Extends Neurology Expertise to the Community

News of Note

07 Jay-Jiguang Zhu, M.D., Ph.D., Joins the Mischer Neuroscience Institute

Anita Madan, M.D., Brings Expertise in Movement Disorders to Outlying Memorial Hermann Facilities

Accolades

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

James C. Grotta, M.D., Honored with Academic Mentorship Award

Research Update

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

10 Safety/Feasibility of Autologous Mononuclear Bone Marrow Cells in Stroke Patients

11 Chronic Cerebrospinal Venous Insufficiency and Its Relationship to Multiple Sclerosis

Detection of Multiple Sclerosis-Related Cognitive Impairment: In Search of MRI Surrogate Markers

12 Behavioral Responses Due to Chronic High-Frequency Stimulation of the Subthalamic Nucleus in the Hemi-Parkinsonian Rat *in vivo* and Electrophysiologic Properties *in vitro*

13 Clinical Outcomes in Acute Stroke: Predictors of the Next Level of Care

14 Insights into Neuroprotection Against Hypoxic/Ischemic Stress

15 The Role of Zinc Transporter ZIP4 in Human Cancer Pathogenesis and Progression

In Print

16 Dissociation Between Diffusion MR Tractography Density and Strength in Epilepsy Patients with Hippocampal Sclerosis

17 Pharmacological Deep Vein Thrombosis Prophylaxis Does Not Lead to Hematoma Expansion in Intracerebral Hemorrhage with Intraventricular Extension

THE NEXT GREAT FRONTIER

For more than 60 years, Houston has led the way in pioneering innovations to conquer heart disease. Now, neuroscience is the next great medical frontier. At the Mischer Neuroscience Institute (MNI), we've gathered a stellar group of nationally recognized faculty who are working together in a coordinated attack against neurological disease, including brain tumors, cerebrovascular disease, epilepsy, multiple sclerosis, neuromuscular disorders, spine pathology, movement disorders and dementia.

We're also building a citywide neuroscience network using the Memorial Hermann Healthcare System's strong acute care presence throughout the Greater Houston metropolitan area, and will soon be adding three new neurosurgeons to our team. Neuroscience centers of excellence at four Memorial Hermann community hospitals bring distinctive subspecialty services to the community, and when combined with the specialized skills of neurosurgeons and neurologists at MNI, they offer suburban patients comprehensive consultation, evaluation and treatment for a range of disorders.

We would like to extend our thanks to Nita Stephens of Silsbee, Texas, for sharing the story of her life-saving encounter with telemedicine. As an emergent patient at Memorial Hermann Baptist Beaumont Hospital, she benefited from MNI's remote presence robotic technology, which is playing a vital role in our strategic plan to extend stroke expertise across the city and ultimately, across the state.

Finally, we would like to recognize the terrific work of our physicians and researchers, whose commitment to research and publication resulted in MNI's high ranking in a study of academic impact that appeared in the September issue of the *Journal of Neurosurgery*. We're proud of the dedication of our team of physicians and staff, and the impact they have on the lives of our patients.

With best wishes,

FOR MORE THAN 60 YEARS, HOUSTON HAS LED THE WAY IN PIONEERING INNOVATIONS TO CONQUER HEART DISEASE. NOW, NEUROSCIENCE IS THE NEXT GREAT MEDICAL FRONTIER.



Dong H. Kim, M.D.

DIRECTOR
MISCHER NEUROSCIENCE INSTITUTE AT MEMORIAL HERMANN

PROFESSOR AND CHAIR
THE VIVIAN L. SMITH DEPARTMENT OF NEUROSURGERY
THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT
HOUSTON (UTHEALTH) MEDICAL SCHOOL



James C. Grotta, M.D.

Co-DIRECTOR
MISCHER NEUROSCIENCE INSTITUTE AT MEMORIAL HERMANN

PROFESSOR AND CHAIR
DEPARTMENT OF NEUROLOGY
THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT
HOUSTON (UTHEALTH) MEDICAL SCHOOL

BUILDING A CITYWIDE NEUROSCIENCE NETWORK

Before the 2008 arrival of neurosurgeon Scott Shepard, M.D., on the Memorial Hermann Southwest Hospital Campus, the facility's Emergency department had to divert patients sporadically to the Mischer Neuroscience Institute (MNI) at Memorial Hermann-Texas Medical Center due to a lack of neuroscience coverage. Today, thanks to Dr. Shepard's full-time practice, occasional backup from other members of the Mischer Neurosurgical Associates (MNA) and the presence of affiliated neurosurgeons in private practice, the hospital provides consistent 24/7 neuroscience coverage to the highly populated Southwest Houston community and outlying suburbs.

“MEMORIAL HERMANN’S ACUTE CARE PRESENCE ACROSS HOUSTON HAS ALLOWED US TO EXTEND OUR NEUROSCIENCE EXPERTISE AND CAPABILITIES OUTSIDE THE TEXAS MEDICAL CENTER THROUGH THE DEVELOPMENT OF NEUROSCIENCE CENTERS OF EXCELLENCE AT FOUR MEMORIAL HERMANN COMMUNITY CAMPUSES.”

“Scott’s arrival on our Campus provided a significant benefit to the population we serve,” says George Gaston, CEO of Memorial Hermann Southwest. “When an academic physician affiliated with a Texas Medical Center institution opens a practice at a community hospital, there’s potential for a contentious relationship with private physicians. I’ve been impressed with how harmonious the neurosurgeons’ working relationships are. Scott’s presence bolsters and supports our private neurosurgeons by allowing them to attend CME conferences or take time off, knowing that they have a fellowship-trained neurosurgeon to provide backup should one of their patients require an urgent admission.”

MNA, a group practice affiliated with

the Mischer Neuroscience Institute, recruited its first two neurosurgeons in 2008 – Dr. Shepard at Memorial Hermann Southwest and Paul Boone, M.D., whose primary practice is located at Memorial Hermann Memorial City Medical Center. MNA is the vision of Dong H. Kim, M.D., who was appointed director of MNI and professor and chair of the Vivian L. Smith department of Neurosurgery at The University of Texas Health Science Center at Houston (UTHealth) Medical School in late 2007. Since his arrival, Dr. Kim has expanded MNI’s infrastructure with financial support from Memorial Hermann and UTHealth, adding new clinical and academic programs and more than 30 nationally recognized faculty.

“That infrastructure expansion and Memorial Hermann’s acute care presence across Houston have allowed us to extend our neuroscience expertise and capabilities outside the Texas Medical Center through the development of neuroscience centers of excellence at four Memorial Hermann community Campuses,” Dr. Kim says. They are Memorial Hermann Memorial City, Memorial Hermann Southwest, Memorial Hermann The Woodlands Hospital and Memorial Hermann Northeast Hospital.

At Memorial Hermann Memorial City, Dr. Boone, an associate clinical professor in the Neurosurgery department at the UTHealth Medical School, reports tremendous growth in his practice over the last three years. “When I first arrived, we were seeing one or two patients in clinic a week,” he says. “Now, we’re seeing 30 or more. I’ve been very pleased with the support we’ve received from local neurologists and neurosurgeons and with the impact we’re making in the community. Our patients can now access tertiary spine and intracranial medicine in the community setting. Having that care available close to home makes it easier

MISCHER NEUROSCIENCE ASSOCIATES: CITYWIDE NEUROSCIENCE NETWORK



Memorial Hermann Katy



Memorial Hermann Memorial City Medical Center



Memorial Hermann Southwest



Memorial Hermann The Woodlands



Memorial Hermann Texas Medical Center



Memorial Hermann Northeast



Dong H. Kim, M.D.
Texas Medical Center
Intracranial aneurysms, arteriovenous malformations, carotid disease, brain tumors, skull base tumors and meningiomas, and trigeminal neuralgia



Paul Boone, M.D.
Katy and Memorial City
Complex spinal surgery, minimally invasive surgery, and general neurosurgery



Anita Madan, M.D.
Memorial City; Northeast, Texas Medical Center and The Woodlands
Deep brain stimulation, Parkinson's disease, essential tremor, spasticity management, and dystonia



Scott Shepard, M.D.
Southwest and Texas Medical Center
Neuro-oncological brain surgery, spine, and general neurosurgery



Jay-Jiguang Zhu, M.D., Ph.D.
Texas Medical Center
Primary brain tumors, brain metastases and leptomeningeal spread of systemic cancers, and neurological complications of systemic chemotherapies



Juan Ortega-Barnett, M.D.
The Woodlands
Neuro-oncological brain surgery, minimally invasive spine surgery, and cranial and peripheral nerve disorders



Albert J. Fenoy, M.D.
Memorial City; Northeast, Texas Medical Center, and The Woodlands
Deep brain stimulation for movement disorders and psychiatric diseases, spinal cord stimulation, and intrathecal therapies

for them to maintain their relationship with their primary care physician during subspecialty treatment.”

Dr. Boone’s practice encompasses all aspects of general neurosurgery with special expertise in spinal procedures, including minimally invasive surgery. After he was recruited to Memorial Hermann Memorial City, the medical center invested in a 5,850-square-foot, state-of-the-art Spine Center. “Dr. Kim has brought tremendous energy and leadership at the System level,” says Keith Alexander, CEO at Memorial Hermann Memorial City. “We put together our neuroscience strategy three years ago. Since then we’ve worked it aggressively

and are seeing tremendous results. We’re in a growth pattern, and every six to nine months we’ve been able to add another feather to our cap. We’re currently recruiting a physical medicine and rehabilitation specialist and expect to bring in other neurological specialties to create a multidisciplinary spine center. This level of service is unheard of outside the Texas Medical Center.”

Dr. Boone also spends a half day each week in a newly built MNA clinic at Memorial Hermann Katy Hospital. MNA is currently recruiting a second neurosurgeon to build the neuroscience market in Memorial City and Katy.

Three fellowship-trained physicians are

now onsite at Memorial City for weekly half-day clinics: neurosurgeon Albert J. Fenoy, M.D., neurologist and neuro-oncologist Jay-Jiguang Zhu, M.D., Ph.D., and neurologist Anita Madan, M.D. They provide the same services at Memorial Hermann Northeast and Memorial Hermann The Woodlands.

Dr. Fenoy, an assistant professor in the Neurosurgery department at the UTHealth Medical School, has expertise in deep brain stimulation for movement disorders, including Parkinson’s disease, dystonia and tremors, and he also specializes in surgery for neck and back pain, including minimally invasive techniques. Dr. Madan, a movement disorders

specialist, complements Dr. Fenoy's expertise with clinical and research interests that include Parkinson's disease, dystonia, Huntington's disease, Wilson's disease, essential tremor, Tourette syndrome, progressive supranuclear palsy, restless leg syndrome, multiple system atrophy, REM behavior sleep disorder, ataxia, deep brain stimulation and spasticity management.

"I came to MNI because I was impressed with the Institute's growth," says Dr. Fenoy, who runs a full-time practice at Memorial Hermann Northeast, in addition to providing specialty neurosurgery in deep brain stimulation at the other hospitals in the neuroscience network. "I was looking for an academic position in functional neurosurgery and wanted the opportunity to do research. My position at MNI gives me the time and stability to accomplish those goals, as well as the resources to start my own lab and develop a deep brain stimulation program, which is an area of growth."

Dr. Zhu, who started at Memorial Hermann-TMC in September 2010, is the sole neuro-oncologist at the UTHealth Medical School. "I joined MNI because of the tremendous potential for growth in neuro-oncology under the visionary leadership of Drs. Kim and Grotta," he says. "I was surprised to learn about the Memorial Hermann System's total bed volumes during my interview. Memorial Hermann's dominance of the Houston healthcare market gives us a high volume of brain tumor patients, and there are strong and growing neurosurgery, neurology and oncology teams here. Because we're still discovering how brain tumors initiate and progress while under radiation and chemotherapies, there's a lot of opportunity for new discovery and excitement in the field of neuro-oncology." Dr. Zhu is an associate professor in the departments of Neurosurgery and Neurology at the medical school. His clinical interests include primary brain tumors; primary central nervous system lymphomas; brain metastases and leptomeningeal spread

of systemic malignancies; quality of life, including cognitive function during and after radiotherapy and chemotherapy; and neurological complications of systemic chemotherapies.

Juan Ortega-Barnett, M.D., was recruited in 2009 to extend neurosurgical expertise to The Woodlands. "Our group of affiliated neurosurgeons dissolved in 2009, leaving us without a neurosurgery program," says Steve Sanders, CEO of Memorial Hermann The Woodlands. "Out of adversity comes opportunity. Through the efforts of Dr. Kim we recruited Dr. Ortega and rebuilt our program from the ground up. Neuroscience is now an important, fast-growing service line for us, and it's been advantageous to have a close working relationship with MNI and the UTHealth Medical School. Ultimately, that collaboration brings us the highest quality of subspecialty services and allows our patients to access top-quality care close to home."

Dr. Ortega, who also practices at Memorial Hermann-TMC and is an assistant professor of Neurosurgery at the UTHealth Medical School, focuses on cervical, thoracic and lumbar spine pathology, which represents 50 to 75 percent of his caseload. "The remainder of my practice is cranial surgery, including tumors, trauma, trigeminal neuralgia, pain syndrome, arteriovenous malformations and aneurysms," he says. "I'm also very interested in neuro-oncology, in which I did my fellowship, and am seeing patients in conjunction with Dr. Zhu."

At Memorial Hermann Northeast, Dr. Fenoy reports that his clinic volume has doubled and surgical volumes have grown dramatically. "We started up in May 2009 with no instruments and zero cases," he says. "We anticipate a 30 percent increase over our 2010 volumes - about 120 cases." Dr. Fenoy treats lower back pain, degenerative disk disease, herniated disks, lumbar and cervical stenosis and performs complex spine surgery.

Heath Rushing, service line administrator for neuroscience at Memorial

Hermann Northeast, says the hospital has expanded the service line in several ways. "Neuroscience is important in our market," Rushing says. "Before the arrival of Dr. Fenoy, we were underserved in subspecialty and surgical care in our primary service area. We were the first in our market to offer neurosurgery, and being first to market sets the stage well for continued growth. Physicians in the community wanted local options for their patients. Our neuroscience program fulfills their needs as well as provides exceptional care and convenience for their patients." Memorial Hermann Northeast has invested more than \$500,000 in neurosurgical instruments and equipment, including specialty equipment for minimally invasive surgery. Like the other hospitals in the neuroscience network, the facility has plans to expand its program to include other subspecialties of neurosurgery and neurology.

"Growth is occurring at an unprecedented rate," notes Dr. Ortega. "What Dr. Kim is doing to build a citywide neuroscience network is extraordinary. I get a lot of feedback from physicians who are amazed at how the program has taken off."

TELEMEDICINE TECHNOLOGY EXTENDS NEUROLOGY EXPERTISE TO THE COMMUNITY

Nita Stephens had occasional insomnia and was up late playing a computer game when she suddenly felt very hot. “I went to the bathroom and washed my face, then headed to the bedroom,” the 59-year-old Silsbee, Texas, resident remembers. “I reached up to adjust the air conditioning to a lower temperature and found that I couldn’t turn the knob. Then I fell to the floor.”

Stephens recalls being conscious but unable to move. When her fiancé Thomas Jones saw the characteristic

Neurologist William J. Hicks II, M.D., who is completing his first year of a two-year fellowship in stroke at MNI, was on-call for telemedicine the night Stephens presented at the Emergency department in Beaumont. “They paged me at my home in Houston around 3:20 a.m.,” Dr. Hicks recalls. “The ER physician gave me a rundown of her symptoms – left-sided weakness and facial droop that began around 2 a.m. Her CT scan did not show bleeding.”

From his laptop control station at home, Dr. Hicks logged on to Memorial Hermann-TMC’s RP-7™ Remote Presence Robotic System, a teleconferencing technology that links the MNI Stroke Center to three outlying Memorial Hermann facilities: Memorial Hermann Southwest Hospital, Memorial Hermann Sugar Land Hospital and Memorial Hermann Baptist Beaumont Hospital. Pioneered by InTouch Health, the RP-7 system is a robot that can be remotely maneuvered by the stroke team member on call. Equipped with two-way video capability, it allows physicians to consult with specialists, see patients and view monitors and other clinical data sources firsthand from remote locations.

When Dr. Hicks activated his computer at home, the emergency center staff in Beaumont directed the remote presence robot toward Stephens, allowing physician and patient to view each other on the screen and talk. “Her speech was slurred, and she had a hard time communicating,” he says. “I could see the facial droop on the computer screen, and she demonstrated left arm and left leg weakness. Based on her CT results, the physical exam conducted by the emergency physician and my observations via computer, we thought she would be a good candidate for tPA.”

“TELEMEDICINE HAS TAUGHT US THAT YOU DON’T NEED A MAJOR MEDICAL CENTER TO PROVIDE GOOD STROKE CARE. WHAT YOU DO NEED IS AN EXPERT PHYSICIAN AND A STRONG TELEMEDICINE PROGRAM.”

droop on the left side of her face, he recognized the symptoms of a stroke and called 911. The EMS team arrived quickly and transported her to the nearest acute care medical facility, Memorial Hermann Baptist Beaumont Hospital, located about 25 miles away in Beaumont, Texas.

The emergency physician in charge of her case ran through the standard medical protocols for stroke – and followed a relatively new one. He paged the physician on call for telemedicine at the Mischer Neuroscience Institute (MNI) Stroke Center. Founded at Memorial Hermann-Texas Medical Center in 1988 by neurologist James C. Grotta, M.D., the MNI Stroke Center operates the 10-county Greater Houston metropolitan area’s largest and busiest dedicated 24/7, onsite stroke team and is the United States leader in number of acute stroke patients treated with tPA.

Stephens consented to treatment, and the thrombolytic agent was administered onsite.

Dr. Hicks also assisted in arrangements for Stephens' transfer to MNI's dedicated Stroke Unit by Memorial Hermann Life Flight®. She arrived at 6:15 on the morning of October 25, 2010. Following a two-day hospitalization, she was released to inpatient rehabilitation at HealthSouth Rehabilitation Hospital of Beaumont for a three-week inpatient stay.

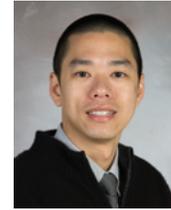
"This is a clear-cut example of the value of telemedicine," says Dr. Grotta, who is chief of neurology at Memorial Hermann-TMC, professor and chair of the Neurology department at The University of Texas Health Science Center at Houston (UTHealth) Medical School and co-director of MNI. "Without telemedicine capabilities at Memorial Hermann Baptist Beaumont Hospital, Ms. Stephens might have expected a dramatically different outcome. She suffered a major stroke, was aphasic and hemiplegic when she presented at the hospital, but thanks to Dr. Hicks' accurate assessment and the fast action of our team, she made a good recovery."

"What's most amazing to me is that we can provide protocol-based care quickly and efficiently - even from home," Dr. Hicks says. "Most emergency physicians want access to neurology expertise and another set of eyes to examine the patient. Telemedicine technology is invaluable in this regard. It's been shown in the literature to be a safe practice, and to diminish morbidity and mortality in stroke patients in the community setting. It's also been a major asset in my training as a fellow."

"Much can be done for stroke patients in community hospitals, especially if the emergency center is set up for telemedicine," Dr. Grotta says. "Our remote presence robotic technology is playing a vital role in Memorial Hermann's system-wide neuroscience strategic plan, which is extending our expertise to the suburbs through neuroscience centers of excellence at Memorial Hermann Memorial City, Memorial Hermann Northeast, Memorial Hermann Southwest and Memorial Hermann The Woodlands hospitals."

The RP-7 system is enhancing MNI's existing telemedicine program, which

has been used to help some of Memorial Hermann's community hospitals achieve stroke center designation, and extends emergency expertise on all neurological conditions to community hospitals throughout the state of Texas. The hospitals are linked electronically to the Neurology department, providing real-time visual interaction between neurologists and patients, and allowing neurologists to review CT scans and advise local physicians on treatment outcomes.



"Our goal is to expand telemedicine coverage and MNI's reach deeper into outlying communities," says Tzu-Ching (Teddy) Wu, M.D., who

will assume the role of telemedicine director for MNI on July 1, following completion of his two-year stroke fellowship. "Telemedicine has taught us that you don't need a major medical center to provide good stroke care. What you do need is an expert physician and a strong telemedicine program. We can now offer patients in outlying communities an opportunity to participate in clinical trials that would otherwise be unavailable to them, which helps the entire medical community by expanding knowledge. In the future we hope to move beyond stroke to offer multiple services from the same telemedicine center. The possibilities are limitless."

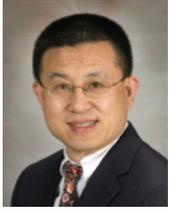
For more information about the telemedicine program, call Wrenne West, program coordinator, at 713.704.4802. For emergencies, call 713.704.4000 and ask for the stroke physician on call.

Nita Stephens wishes to thank the physicians who provided care for her in Houston and Beaumont, and her daughter Lisa Ard, who took leave from her job in Dallas to stay by her side during two hospitalizations and later provided care for her in her home.



NEWS OF NOTE

Jay-Jiguang Zhu, M.D., Ph.D., Joins the Mischer Neuroscience Institute



Fellowship-trained neurologist and neuro-oncologist Jay-Jiguang Zhu, M.D., Ph.D., has joined the medical staff of the Mischer Neuroscience Institute at Memorial Hermann-Texas Medical Center from Boston's Tufts Medical Center and Tufts University School of Medicine, where he served as an assistant professor and attending physician in neurology, hematology and oncology. In his new position, he also serves as an associate professor in the Vivian L. Smith department of Neurosurgery and in the department of Neurology at The University of Texas Health Science Center at Houston (UTHealth) Medical School.

Dr. Zhu earned his medical degree at McGill University in Montreal, Quebec, Canada. He completed his residency training in neurology at Tufts University School of Medicine and subsequently completed his fellowship in neuro-oncology at Massachusetts General Hospital and Harvard Medical School in Boston. Prior to entering medical school, Dr. Zhu received his doctorate in molecular biology at the State University of New York in Buffalo, and completed his postdoctoral training in central nervous system (CNS) tumorigenesis research at Children's Hospital, Brigham and Women's Hospital and Harvard Medical School.

Dr. Zhu's clinical interests include primary brain tumors - gliomas, meningiomas and pituitary adenomas - and primary CNS lymphomas; brain metastases and leptomeningeal spread of systemic malignancies; quality of life, including cognitive function during and after radiotherapy and chemotherapy; clinical trials focused on developing

new treatment options for primary brain tumors and CNS metastasis; and neurological complications of systemic chemotherapies.

Dr. Zhu is a member of the Massachusetts Medical Society, the American Academy of Neurology, the Society of Neuro-Oncology, the American Society of Clinical Oncology and the European Association of Neuro-Oncology. He is an ad hoc reviewer for the *Journal of Neuro-Oncology*, the *Chinese Medical Journal* and *Neurosurgical Focus*. His research has been published in *Molecular and Cellular Biology*; *Chromosoma*; *Journal of Clinical Endocrinology and Metabolism*; *Neurosurgery*; *Cancer Research*; *Oncogene*; *Genes, Chromosomes and Cancer*; *American Journal of Pathology*; *Neuro-Oncology*; and the *Journal of Neuro-Oncology*, among others.

Anita Madan, M.D., Brings Expertise in Movement Disorders to Outlying Memorial Hermann Facilities



Anita Madan, M.D., has joined the medical staff of the Mischer Neuroscience Institute (MNI), concomitant with her appointment as assistant professor in the Neurology department at The University of Texas Health Science Center at Houston (UTHealth) Medical School. In her new role she will be involved in the extension of MNI's neurology expertise to three Memorial Hermann community hospitals: Memorial Hermann Memorial City Medical Center, Memorial Hermann Northeast Hospital and Memorial Hermann The Woodlands Hospital.

Dr. Madan received her medical degree from Saba University School of Medicine in Saba, Netherlands Antilles, in 2004. She completed her internship in internal medicine at the University of Missouri-Kansas City and her residency at the UTHealth Medical School, where

she served as chief resident during the 2007-2008 academic year. She completed a fellowship in movement disorders in 2010 at the same institution.

As part of her extensive training in movement disorders, Dr. Madan has clinical expertise in intraoperative recording for deep brain stimulation electrode placement and deep brain stimulation programming. She also specializes in spasticity management, including botulinum toxin injection and patient selection and programming of intrathecal baclofen pumps.

She has served as co-investigator on several studies with principal investigator Mya Schiess, M.D., professor and vice chair of the Neurology department. Dr. Schiess holds the Adriana Blood Endowed Chair at the UTHealth Medical School and is director of UT MOVE, a program focused on clinical care, education and basic science research on the neurological conditions of motor systems disruption.

Dr. Madan's clinical and research interests include Parkinson's disease, dystonia, Huntington's disease, Wilson's disease, essential tremor, Tourette syndrome, progressive supranuclear palsy, restless leg syndrome, multiple system atrophy, REM behavior sleep disorder, ataxia, deep brain stimulation and spasticity management. She is board certified, fluent in French and a member of the Texas Neurological Society and the Movement Disorders Society.

ACCOLADES

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

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

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

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

the department was ninth nationally. These rankings are the highest of any neurosurgery program in Texas.

"We're proud of the work of our physicians and researchers," says Dong H. Kim, M.D., director of the Mischer Neuroscience Institute and professor and chair of the Neurosurgery department at the UTHealth Medical School. "These are terrific rankings - the result of our shared commitment to advancing medical knowledge by reporting the results of our basic science studies and participation in clinical trials."

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

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

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

James C. Grotta, M.D., Honored with Academic Mentorship Award



The American Heart Association presented one of its highest honors, the Eugene Braunwald Academic Mentorship Award, to

James C. Grotta, M.D., co-director of the Mischer Neuroscience Institute (MNI) at Memorial Hermann-Texas Medical Center and professor and chair of the Neurology department at The University of Texas Health Science Center at Houston (UTHealth) Medical School. He was recognized for exceptional achievement in guiding and inspiring young trainees throughout his career in research and administration.

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

Dr. Grotta, who holds the Roy M. and Phyllis Gough Huffington Distinguished Chair, has played a leadership role in many clinical research studies of both thrombolytic drugs and cytoprotective agents following stroke, and has been funded by the National Institutes of Health (NIH) for laboratory studies on the biology of brain injury and recovery in animal stroke models. He is currently funded by the NIH for a project to carry out a series of novel pilot studies aimed at amplifying the existing benefits of intravenous tPA and achieving clinically



meaningful neuroprotection using hypothermia.

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

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

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

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

RESEARCH UPDATE

Noninvasive Imaging to Quantify Peripheral Nerve Injury and Repair in Clinic

Researchers at the Mischer Neuroscience Institute (MNI) and The University of Texas Health Science Center at Houston (UTHealth) Medical School are investigating the use of noninvasive imaging techniques in the early assessment of regeneration following traumatic nerve injury. Currently, such techniques are unavailable in clinical practice.

“Civilian and combat trauma to limbs often results in serious injury to the peripheral nerves, leading to significant morbidity,” says Kazim Sheikh, M.D., professor of neurology at the UTHealth Medical School, director of the Neuromuscular Program at MNI and principal investigator of the single-center study. “While advances in trauma management have reduced overall mortality, many patients are left with disability as a result of peripheral nerve injury. Our aim is to develop and validate noninvasive magnetic resonance-based diffusion tensor imaging (DTI) technology capable of monitoring the degenerative and regenerative response in nerves after traumatic injury. We hope that early assessment of regeneration will ultimately lead to timely decisions,

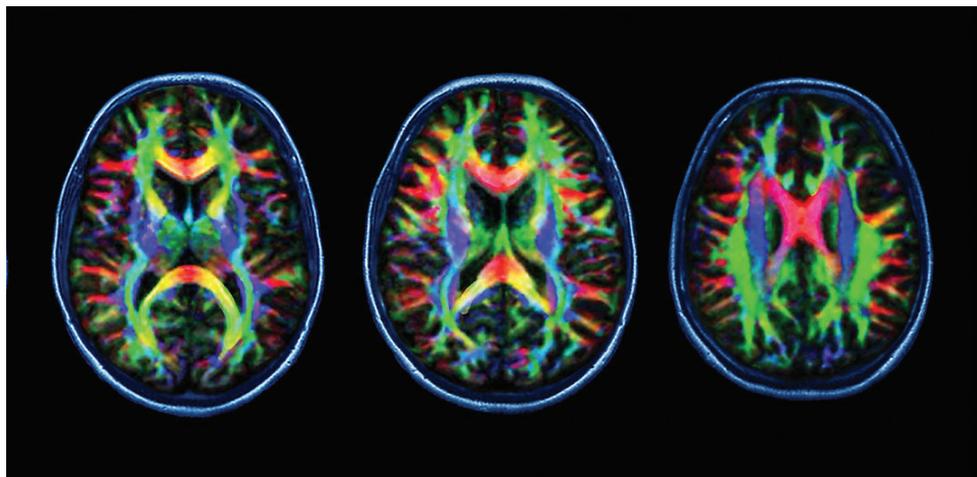


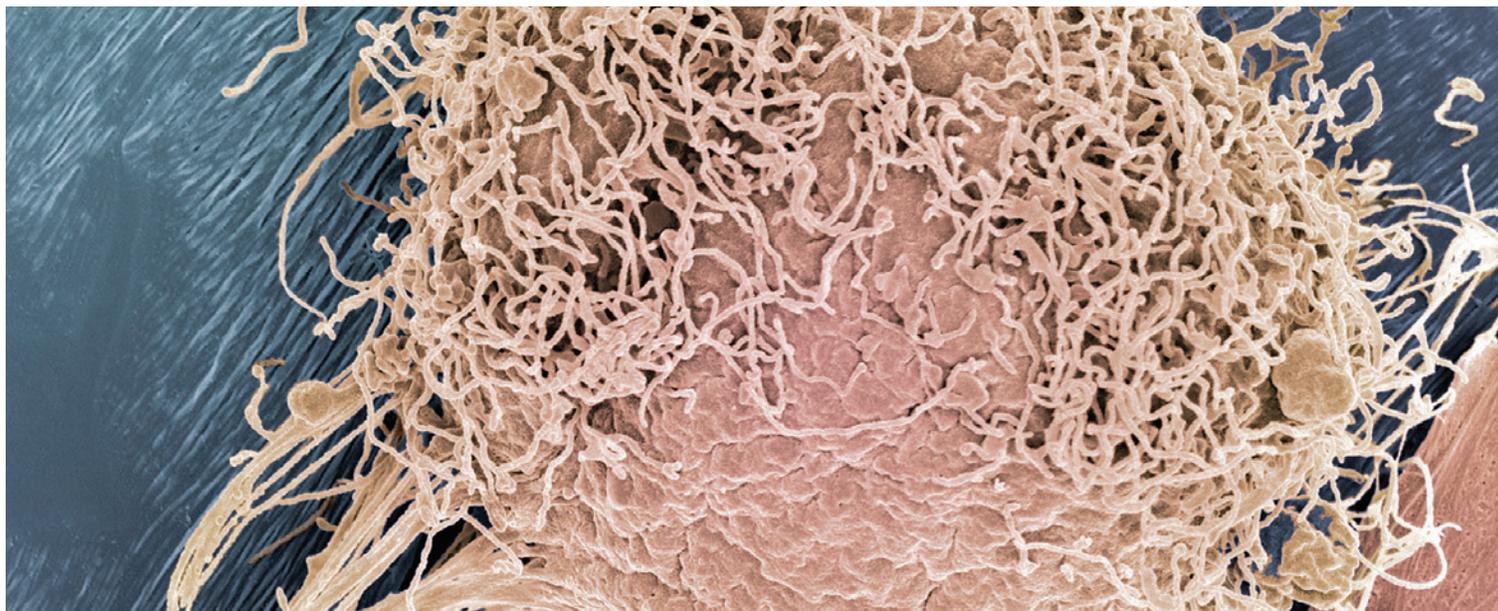
improved management and improved rehabilitation outcomes.”

Preliminary studies conducted by Dr. Sheikh's research team in an animal model support the hypothesis that DTI can measure Wallerian-like degeneration and regeneration in injured nerves. “We also know that normal human nerves can be imaged with this technology, which supports the feasibility of the study,” he says.

Funded by a \$1.6 million, three-year grant from the National Institutes of Health (NIH), the study is the first NIH-sponsored study to examine nerve injuries with MRI/DTI technology. Ponnada Narayana, M.D., department of Diagnostic and Interventional Imaging, and Milan Sen, M.D., department of Orthopedic Surgery, are critical collaborators involved in this research study.

The study aims to fill gaps that include a lack of knowledge of normative DTI parameters for various peripheral nerves and a lack of studies demonstrating the utility of DTI technology in detecting peripheral nerve degeneration and regeneration in humans. The researchers will collect normative data in control groups and apply it to patients with complete nerve injuries (Sunderland grade V) undergoing nerve repairs. They believe that validation of DTI technology in patients with complete nerve injuries





will allow broader in-clinic application of the modality in patients with other types of traumatic nerve injuries and neuropathies.

“There is an acute need for reliable measures to monitor nerve injury and repair, allowing physicians to make informed management decisions in clinic,” Dr. Sheikh says. “We expect this technology to facilitate medical management decisions in these patients.”

Dr. Sheikh is renowned for his work in the area of autoimmune and inflammatory neuropathies. He has served as principal or co-principal investigator in studies funded by the NIH, the GBS Foundation, Muscular Dystrophy Association, the National Institute of Environmental Health Sciences, Johns Hopkins University and the National Multiple Sclerosis Society. He expects to begin enrolling patients in April 2011. For more information about inclusion criteria, or to refer a patient, call 713.704.6784.

Safety/Feasibility of Autologous Mononuclear Bone Marrow Cells in Stroke Patients

Can bone marrow containing stem cells be safely removed, purified and then given back intravenously to adults who have suffered an acute ischemic stroke? This hypothesis is under investigation

in a single-center safety and feasibility study underway at Mischer Neuroscience Institute (MNI) and The University of Texas Health Science Center at Houston (UTHealth) Medical School. The study, which will enroll 30 patients over the course of three years, is the nation’s first investigational trial giving stroke patients their own cells.

“Our goal is to determine whether it’s safe and feasible to harvest bone marrow from a patient who has just had a stroke, purify out from the patient’s bone marrow a subpopulation of cells enriched with stem cells and reinfuse them into the patient intravenously,” says principal investigator Sean I. Savitz, M.D., a neurologist affiliated with MNI and an associate professor of neurology at the UTHealth Medical School. Dr. Savitz was recruited to MNI in 2007 based on his clinical interest in stem cell therapies for stroke and his experience using animal models to test potential stroke treatments. As an assistant professor at Harvard Medical School, he was involved in one of the nation’s first studies of fetal progenitor cells in stroke patients.

In the current study, bone marrow aspiration and infusion of stem cells must take place within 24 to 72 hours

following acute ischemic stroke in patients who have passed the window of opportunity for administration of tPA. Dr. Savitz and his team harvest cells from bone marrow in the leg, extract the stem cells and inject them into the patient’s arm.

“The study will progress very slowly,” Dr. Savitz says. “We’re watching each participant very closely during the first 30 days to assess for safety, and we will continue to monitor them over time to see if their deficits change. Extensive animal studies have shown that stem cells improve recovery following stroke by releasing factors that reduce inflammation and ongoing injury, and promote repair of the brain after stroke. We’re hoping the same process will take place in humans.”

The interventional study began in January 2009 with funding from the National Institutes of Health. “We’re a long way from knowing the best method for the use of stem cells to potentially treat stroke patients,” Dr. Savitz says. “We expect this trial to lead to future research in the development of new therapies for stroke.”

For more information about study inclusion criteria, contact Susan Alderman, R.N., at susan.alderman@uth.tmc.edu. To refer a patient, call the stem cell hotline at 713.500.5030.



Chronic Cerebrospinal Venous Insufficiency and Its Relationship to Multiple Sclerosis

The idea that chronic cerebrospinal venous insufficiency (CCSVI) may have a unique role in multiple sclerosis (MS) sparked a firestorm of interest and the embrace of venoplasty as a potential therapy. But until recently, no Level I randomized, controlled clinical trials had been conducted to confirm the phenomenon originally described by Italian vascular surgeon Paolo Zamboni, M.D., and resolve the questions he and others raised about whether CCSVI exists as a cause of MS or is related to MS in another manner.

Last summer, The University of Texas Health Science Center at Houston (UTHealth) Medical School was among three institutions in the United States to receive an initial grant to study CCSVI in MS. The award, which was part of a more than \$2.3-million joint commitment from the National MS Society and the MS Society of Canada, will allow researchers to resolve conflicting data from previous research, such as how frequently CCSVI occurs in MS and how often it occurs in a control group of people who do not have MS. If CCSVI is found in study subjects, the National MS Society wrote in a news release, the findings will speed the way to determining whether therapeutic trials to correct blockages will be helpful in improving or altering the MS disease process.

Dr. Zamboni and his colleagues based their conclusions on a retrospective analysis of 109 MS subjects, 65 of whom underwent selective venography and venoplasty. His team presented evidence based on transcranial color-coded Doppler and high-resolution echocolor Doppler sonography that suggested an unexpected high incidence of abnormalities in the venous outflow of the central nervous system among patients with all major clinical phenotypes of MS

that was not seen among normal controls or among individuals with a variety of other brain diseases.

“As part of our study we’ll attempt to reproduce the ultrasound approach used by Dr. Zamboni and test whether other imaging methods, such as MRI, can confirm the ultrasound findings,” says Jerry Wolinsky, M.D., who is the Bartels Family



and Opal C. Rankin Professor of Neurology at the UTHealth Medical School, director of the Multiple Sclerosis Research Group and principal investigator of the study at the Houston site. “Obtaining validation of a reliable diagnostic approach for CCSVI and demonstrating an MS-specific association of the condition is the first logical step toward determining whether we should proceed with a definitive, blinded and randomized therapeutic trial of venoplasty as an approach to the treatment of MS,” said Dr. Wolinsky. “If evolving data suggests the need, a trial-planning grant proposal will be submitted to the National Institutes of Health during the course of the study.”

Dr. Wolinsky serves or has served on review and advisory committees of the

National Institutes of Health, the National Multiple Sclerosis Society, the Multiple Sclerosis International Federation, the Food and Drug Administration and numerous pharmaceutical houses.

The two other American institutions receiving two-year grants that began July 1, 2010, are the Cleveland Clinic and the University of Wisconsin-Madison. Four institutions in Canada have also been awarded research grants.

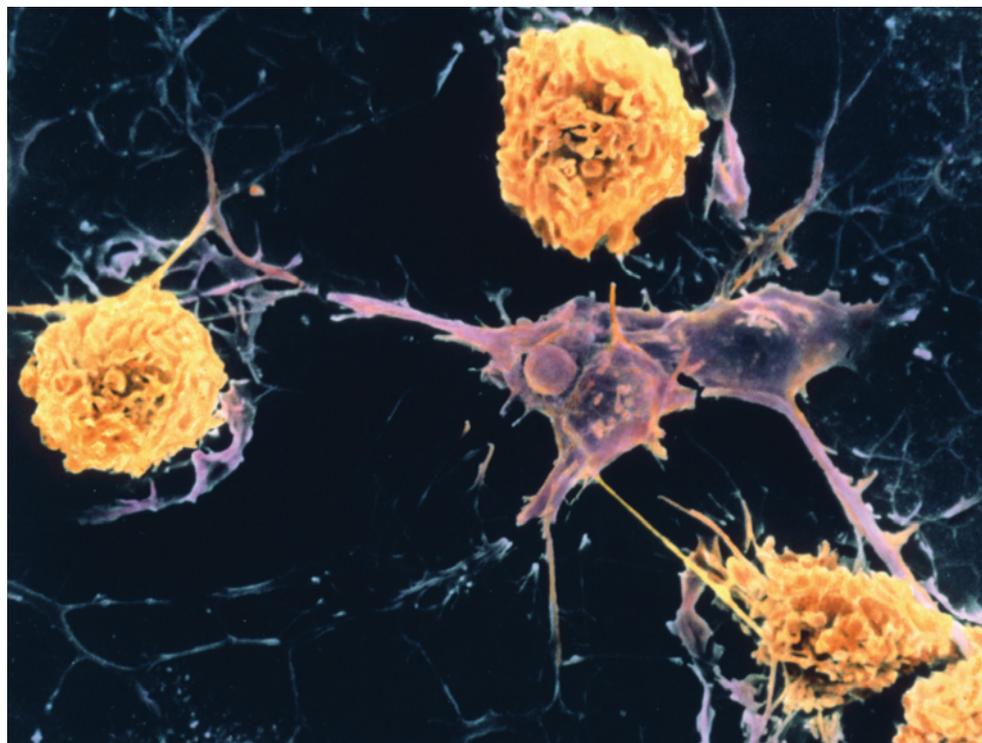
To learn more about the CCSVI study, contact james.r.jemelka@uth.tmc.edu.

Detection of Multiple Sclerosis-Related Cognitive Impairment: In Search of MRI Surrogate Markers



Neurologist Flavia Nelson, M.D., is the recipient of a funded National Institutes of Health (NIH) Career Development Award for the study of dementia in multiple sclerosis (MS) patients. Her study is the first to use functional MRI (fMRI) to evaluate the effect of cortical lesions on cognitive function.

“Cognitive impairment is an important cause of disability in multiple sclerosis patients,” says Dr. Nelson,



who is an assistant professor of neurology at The University of Texas Health Science Center at Houston (UTHealth) Medical School and associate director of the medical school's MRI Analysis Center. "Diagnosis of impairment is usually made by neuropsychological testing, which is limited in availability, expensive and often not covered by insurance, preventing many patients from being diagnosed and treated," says Dr. Nelson. "The Multiple Sclerosis Research Group at Mischer Neuroscience Institute and UTHealth Medical School has developed imaging techniques that can detect cortical lesions. Using these techniques we hope to better understand the relationship between lesions and cognitive impairment. By identifying better diagnostic tools for cognitive impairment, we hope to improve the prognosis for MS patients."

The single-center study, which began in February, will enroll 50 patients during

its first two years. The remaining two years of the four-year grant will be focused on analysis of data. "We're using multiple technologies to explore the relationship between cortical lesions and cognitive impairment, including fMRI, MRI diffusion tensor imaging (DTI) and advanced techniques - double-inversion recovery and phase-sensitive inversion recovery - for detection of cortical lesions, which will give us a large body of data to analyze before we can begin to draw conclusions."

To evaluate the efficacy of fMRI in patients with cognitive abnormalities, the researchers will compare imaging studies with the results of standard neuropsychological testing. They will also compare results gathered from traditional MRI with those from fMRI and DTI.

The new study is a continuation of work Dr. Nelson has done previously on cortical lesions. Also NIH funded, her first study investigated which type of cortical lesion was the greatest contributing factor in

MS-related cognition issues. "Lesions present in the brain cortex extending into the sub-cortical white matter were found to have a strong correlation with measures of decreased cognition, but other MRI metrics of tissue damage also contribute, which is why we will use a multimodal approach to evaluating cortical function in the new study," she says.

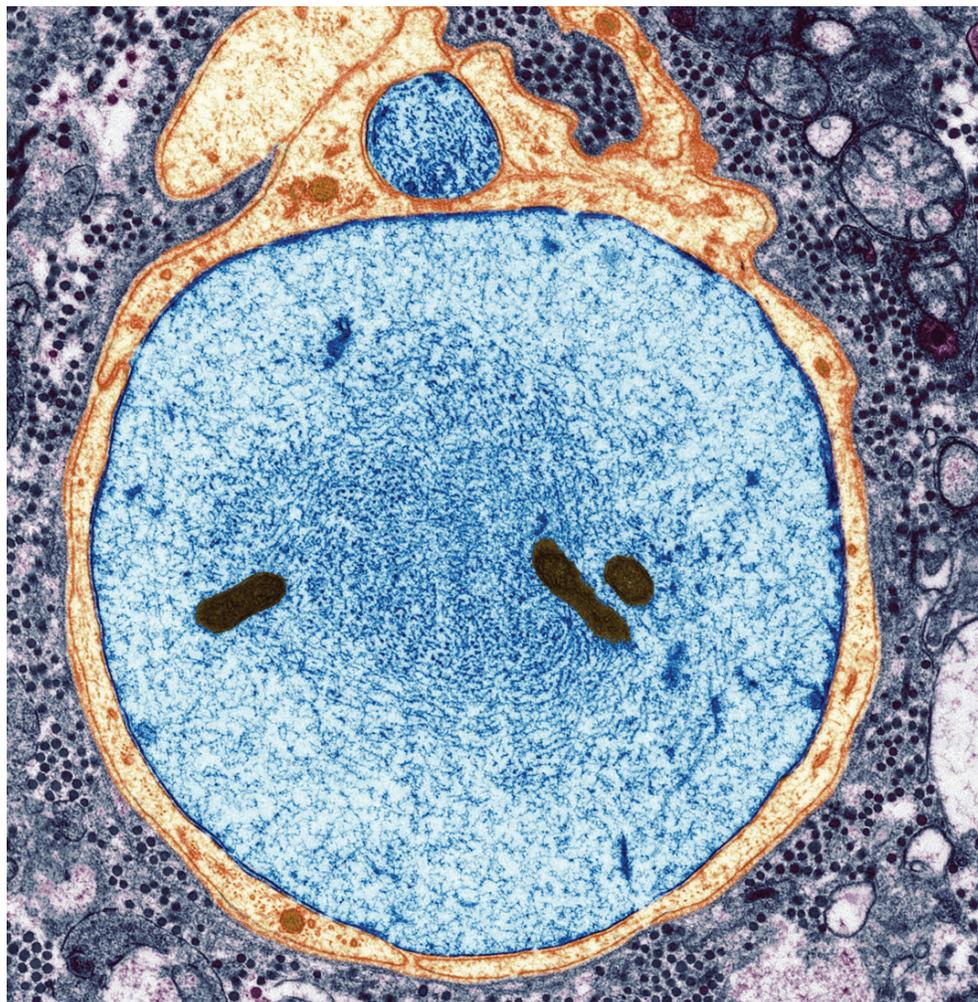
"As the first study of its kind, detection of MS-related cognitive impairment is exciting research," she adds. "Cognitive impairment can cause major disability and greatly diminish the quality of life of MS patients. We hope to gather more information about the neural structures damaged by MS and find effective diagnostic tools that are accurate and eventually more cost effective than neuropsychological testing."

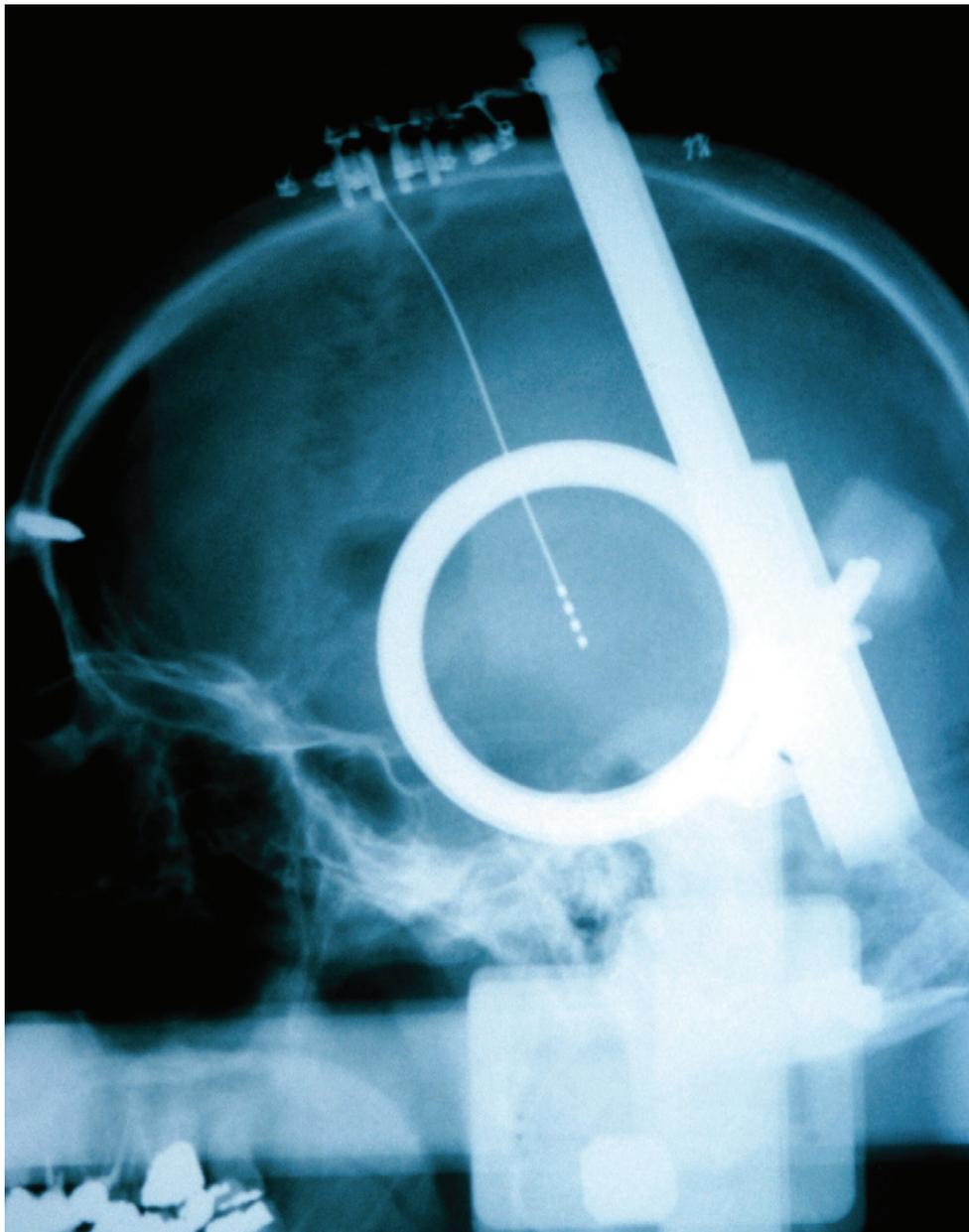
Behavioral Responses Due to Chronic High-Frequency Stimulation of the Subthalamic Nucleus in the Hemi-Parkinsonian Rat *in vivo* and Electrophysiologic Properties *in vitro*

A variety of therapeutic treatments for Parkinson's disease (PD) have been developed, but the most common is administration of the drug levodopa, which improves motor symptoms but produces severe side effects, such as dyskinesias, in long-term treatment. The Food and Drug Administration approved deep brain stimulation (DBS) as a treatment for essential tremor in 1997, for Parkinson's disease in 2002 and for dystonia in 2003. Despite its successful 14-year history, how DBS works to control the motor symptoms associated with these three disorders remains a mystery to physicians and researchers.



"Deep brain stimulation provides high-frequency stimulation to normalize brain circuitry functioning, which has been shown to be a powerful treatment for Parkinsonian motor syndrome," says Mischer Neuroscience





Institute neurosurgeon Albert Fenoy, M.D., who is principal investigator of a laboratory study investigating behavioral responses to high-frequency stimulation (HFS) of the subthalamic nucleus (STN) in rats. “As a result of this study, we hope to better understand exactly how the mechanism of high-frequency stimulation of the subthalamic nucleus exerts its beneficial effects, and why there is often a potentiation of effects even after the stimulator is turned off.”

More than four million people have been diagnosed with PD worldwide; this number is expected to more than double in less than 20 years due to increased life expectancy. Neurologists have long

viewed DBS as a last-resort treatment for patients who have failed medication. As a result, many have not had access to the intervention until they are older and have more advanced disease.

“Prior studies in animal models have shown that subthalamic nucleus DBS leads to an increase rather than a decrease in glutamate output, and a regulation in basal ganglia firing pattern,” Dr. Fenoy says. “It remains to be seen how this causes such local as well as widespread brain effects.”

In this study, Dr. Fenoy and his team will study the effects of STN-HFS on motor behavior in freely moving rats and in a rat model of Parkinson’s disease

over a chronic progressive application period. They will also investigate the effects of local injections of specific drugs on behavior during STN-HFS in the same awake PD model rats to determine whether certain neurotransmitters mediate the effects of STN-HFS. Finally, postmortem tests will be conducted to determine the physiologic effects of the stimulation alone and stimulation after applying agents that can impact cellular functioning.

Funding for the study is provided by the Vivian L. Smith Center for Neurologic Research/Neurosurgery department at the UTHHealth Medical School. For more information, contact Dr. Fenoy at albert.j.fenoy@uth.tmc.edu.

Clinical Outcomes in Acute Stroke: Predictors of the Next Level of Care



“It’s well documented that patients who receive intravenous tPA after ischemic stroke have better outcomes at six months,” says neurorehabilitation specialist Nneka Ifejika-Jones, M.D., who is principal investigator of a two-year study of clinical outcomes of acute stroke funded by the National Institute of Neurological Disorders and Stroke (NINDS). “We would also like to know if we can predict stroke outcomes earlier than six months in the same subpopulation of patients. To that end we’re examining the discharge level of care after acute stroke, which is directly related to clinical outcomes, including functional status, activity tolerance and medical acuity.”

Dr. Ifejika-Jones, who is medical director of neurorehabilitation at Memorial Hermann-Texas Medical Center and assistant professor and director of neurorehabilitation at The University of Texas Health Science Center at Houston (UTHealth) Medical School, gathered preliminary data in a retrospective study of 2,225 patients who were treated at the



Mischer Neuroscience Institute (MNI) between 2004 and 2009 and discharged to levels of care that included home, inpatient rehabilitation, skilled nursing facilities and sub-acute care facilities.

In her current study, she is investigating two hypotheses: that patients who receive intravenous tPA within the three-hour window of opportunity following ischemic stroke are more likely to have improved outcomes, evidenced by discharge disposition to home or inpatient rehabilitation, and that patients with post-stroke complications are more likely to have worse outcomes, evidenced by discharge disposition to skilled nursing or sub-acute care facilities.

“Cerebrovascular disease is the leading cause of long-term disability, increasing the costs of post-acute care and caregiver burden,” Dr. Ifejika-Jones says. “Sixty percent of stroke survivors have moderate or severe disability, rendering

them dependent for even basic activities of daily living. A significant number of high-risk stroke survivors are members of minority groups, a population with a higher tendency to be uninsured and lacking in access to primary stroke preventive care. Outcomes research is critically important in this population, particularly related to post-stroke discharge disposition.

“It’s also very important to view acute stroke treatment and post-stroke treatment as separate entities,” she says. “Patients may have presented at the hospital early enough to receive the appropriate IV therapy but to get a true picture of outcomes, we’ll have to monitor patients for months or years because stroke predisposes patients to other forms of cardiovascular disease.”

For more information on the study, e-mail Dr. Ifejika-Jones at nneka.l.ifejika@uth.tmc.edu.

Insights into Neuroprotection Against Hypoxic/Ischemic Stress



Ying Xia, M.D., Ph.D., and his team joined the Vivian L. Smith Center for Neurologic Research/Neurosurgery department in May 2009

from Yale University School of Medicine, where he was known for his work on hypoxic/ischemic injury and other neurological damage and disorders. A professor and vice chair for research in the Vivian L. Smith department of Neurosurgery at The University of Texas Health Science Center at Houston (UTHealth) Medical School, Dr. Xia is investigating brain protection from ischemia, hypoxic dysfunction of neurons and inhibition of epileptic hyperexcitability with two R01 grants from the National Institutes of Health. He and his team hope to provide new clues for better solutions for stroke, hypoxia encephalopathy and specific neurodegenerative disorders.

“Prolonged oxygen deprivation and/or insufficient blood supply are not uncommon in the clinical setting,” Dr. Xia says. “In-utero hypoxia, intraventricular hemorrhage in premature infants, respiratory distress syndrome in neonates, heart attack and stroke in adults and other conditions that limit oxygen and blood supply to the central nervous system for a prolonged period can be devastating, and may lead to a variety of neurological disorders. Although the relationship between hypoxic/ischemic stress and various disorders has been explored in the literature, the cellular and molecular mechanisms that underlay the neuronal pathophysiology are largely unclear.”

To close the knowledge gap, Dr. Xia is investigating the functional integrity of the neuronal membrane related to physiological condition and its regulation - via membrane protein interaction and intracellular pathways - in hypoxic and/or ischemic circumstances. Toward

this goal, he and his team report several interesting findings.

“For example, although we do not intend to simply link particular neurological diseases to a single factor, our data suggest that cortical dysfunction due to hypoxic/ischemic disruption of ionic homeostasis resulting from ionic channel dysregulation may play a contributing role in some neurological disorders, while activation of a specific membrane receptor-intracellular signal pathway attenuates such pathological change,” he says. “Our goal is to transform the new scientific knowledge we’re gaining into tangible benefits for patients by shedding light on a novel strategy against hypoxic dysfunction in the brain.”

The Role of Zinc Transporter ZIP4 in Human Cancer Pathogenesis and Progression

Although zinc is an important trace element for healthy growth and development, researchers have also linked it to pancreatic cancer and glioblastoma multiforme (GBM), the most common and aggressive type of glioma in humans. Too much ZIP4, a molecule that enables



the transport of zinc into cells, promotes the growth and spread of pancreatic and brain tumor cells, says Min Li, Ph.D., a researcher at the Mischer Neuroscience Institute and director of the Cancer Research Program at the Vivian L. Smith Center for Neurological Research at The University of Texas Health Science Center at Houston (UTHealth) Medical School.

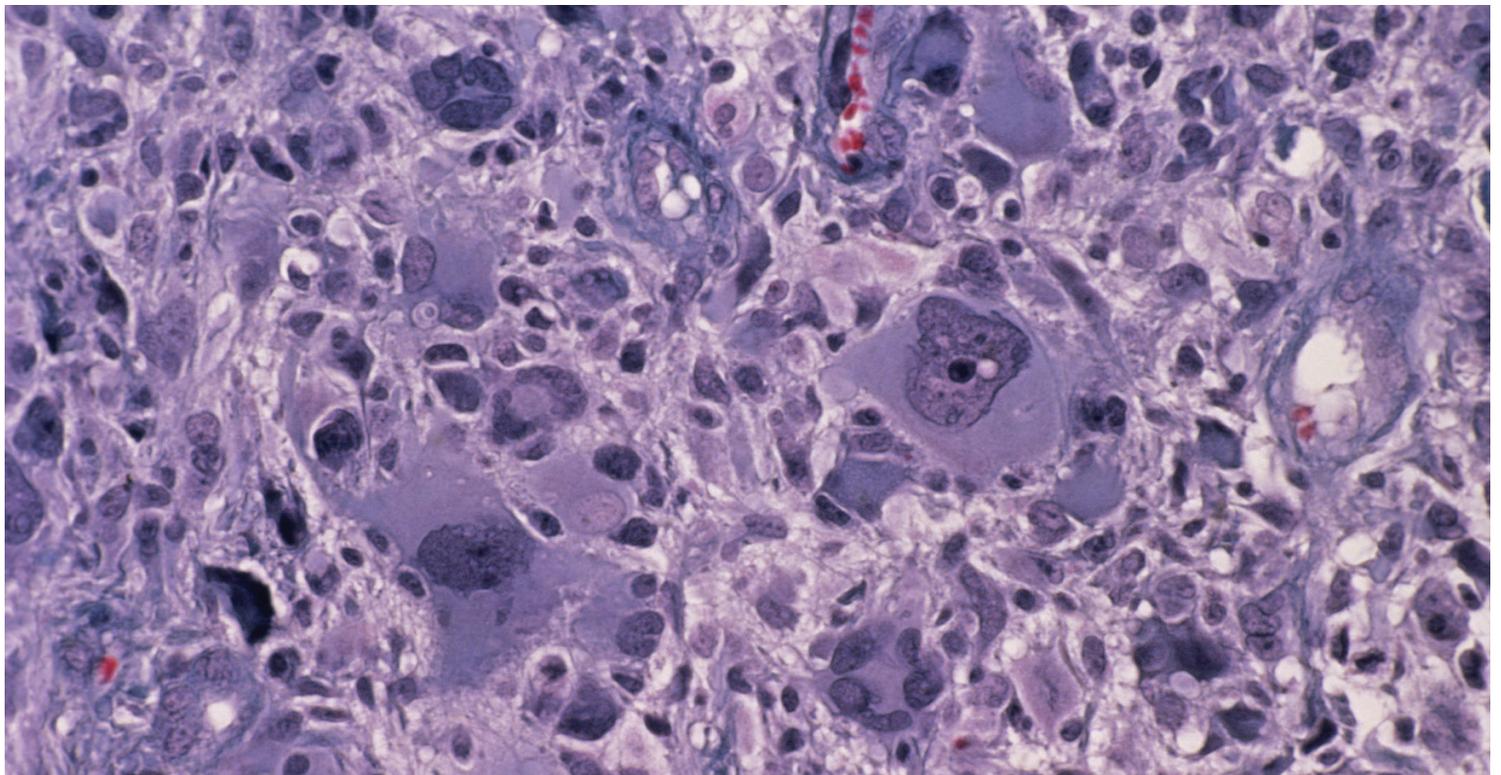
“We’ve found that ZIP4 is substantially overexpressed in clinical pancreatic adenocarcinoma and in glioblastoma multiforme,” says Dr. Li, who is an associate professor of neurosurgery at the UTHealth Medical School. “Based on our published results and the preliminary results of our current research, we are developing a better understanding of the mechanistic role of ZIP4 in the development of human cancers.”

A previous study by one of Dr. Li’s collaborators, Craig Logsdon, Ph.D., professor and Lockton Distinguished Professor for Pancreatic Cancer Research at The University of Texas M. D. Anderson Cancer Center, indicated high levels of zinc transporters in pancreatic cancer

tissues by microarray analysis. Research by Dr. Li confirmed those findings and also showed that overexpressed ZIP4 increases zinc uptake by the cell, resulting in significantly increased tumor growth.

Dr. Li’s team is also investigating the therapeutic potential of ZIP4 short hairpin RNA (shRNA), a sequence of RNA that can be used to silence gene expression. “In pancreatic cancer, we’ve found that silencing of ZIP4 was associated with decreased cell proliferation, migration and invasion. Our preliminary studies also indicate that ZIP4 shRNA can sensitize pancreatic cancer cells to chemotherapy drug treatment. We think a combination therapy using ZIP4 shRNA and chemotherapy may further increase the efficacy of treatment for pancreatic cancer. We hope to kill two birds with one stone by targeting ZIP4 with shRNA therapy in both pancreatic cancer and brain tumor.”

Dr. Li’s laboratory is funded by the National Institutes of Health, the National Cancer Institute and private foundations.



DISSOCIATION BETWEEN DIFFUSION MR TRACTOGRAPHY DENSITY AND STRENGTH IN EPILEPSY PATIENTS WITH HIPPOCAMPAL SCLEROSIS

Ellmore T, Pieters TA, Tandon N

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

ABSTRACT

Mesial temporal lobe epilepsy (MTLE) is hypothesized to involve derangement of long-range limbic connectivity, but *in vivo* evidence is lacking. We used diffusion tractography to investigate the relationship between hippocampal atrophy and connectivity in MTLE patients with hippocampal sclerosis (HS). Atrophy was correlated with relatively decreased connectivity density but increased connectivity strength, suggesting that HS is accompanied by relatively sparse but strong connections as measured by white matter diffusion anisotropy.

BACKGROUND AND PURPOSE. Epilepsy patients with HS show reductions of volume in the hippocampus on one side of the brain. Atrophy has been linked to pyramidal cell loss, granule cell dispersion and axonal sprouting confirmed within the hippocampus during postmortem pathological studies. Less is understood about the connectivity differences of the white matter fiber systems that bring information into and out of the sclerotic hippocampus in the living human brain.

METHODS. White matter hippocampal connectivity was examined in 10 epilepsy patients with HS and 10 age-matched controls using 3-Tesla diffusion-weighted magnetic resonance imaging tractography. This technique allows for reconstruction of coherently organized and myelinated white matter axonal fiber tracts. In each hemisphere, 1) hippocampal volume, 2) the number of hippocampal fiber tracts (connectivity density) and 3) the average diffusion anisotropy (connectivity strength) of each hippocampus' set of tracts were computed.

RESULTS. Patients showed a positive relationship between hippocampal volume and connectivity density asymmetry, with the magnitude of volume loss in the sclerotic hippocampus correlating with significantly fewer pathways. A significant negative relationship was found between hippocampal volume and connectivity strength asymmetry, with volume loss in the sclerotic hemisphere correlating with relatively higher connectivity strength. Matched controls showed no significant relationships between hippocampal volume asymmetry and connectivity density or strength.

CONCLUSIONS. We conclude that hippocampal sclerosis, a pathological finding in many cases of pharmaco-resistant epilepsy, is marked by different structural connectivity between the hippocampus and other regions of the brain. Reduced connectivity density but relatively increased connectivity strength together may be facilitative of seizure spread. These findings provide new insights into the structural brain differences accompanying epilepsy, and supplement existing noninvasive diagnostic techniques for planning the surgical treatment of this disease.

PHARMACOLOGICAL DEEP VEIN THROMBOSIS PROPHYLAXIS DOES NOT LEAD TO HEMATOMA EXPANSION IN INTRACEREBRAL HEMORRHAGE WITH INTRAVENTRICULAR EXTENSION

Wu TC, Kasam M, Harun N, Hallevi H, Bektas H, Acosta I, Misra V, Barreto AD, Gonzales NR, Lopez GA, Grotta JC, Savitz SI

Department of Neurology, The University of Texas Health Science Center at Houston (UTHealth) Medical School

ABSTRACT

BACKGROUND AND PURPOSE. Patients with intracerebral hemorrhage (ICH) are at high risk for development of deep venous thrombosis. Current guidelines state that low-dose subcutaneous low-molecular-weight heparin or unfractionated heparin may be considered at three to four days from onset. However, insufficient data exist on hematoma volume in patients with ICH before and after pharmacological deep venous thrombosis prophylaxis, leaving physicians with uncertainty regarding the safety of this practice.

METHODS. We identified patients from our stroke registry (June 2003 to December 2007) who presented with ICH only or ICH+intraventricular hemorrhage and received either low-molecular-weight heparin subcutaneously or unfractionated heparin within seven days of admission and had a repeat CT scan performed within four days of starting deep venous thrombosis prophylaxis. We calculated the change in hematoma volume from the admission and post-treatment CTs. Hematoma volume was calculated using the ABC/2 method and intraventricular hemorrhage volumes were calculated using a published method of hand-drawn regions of interest.

RESULTS. We identified 73 patients with a mean age of 63 years and median National Institutes of Health Stroke Scale score 11.5. The mean baseline total hematoma volume was $25.8 \text{ mL} \pm 23.2 \text{ mL}$. There was an absolute change in hematoma volume from pre- and post-treatment CT of $-4.3 \text{ mL} \pm 11.0 \text{ mL}$. Two patients developed hematoma growth. Repeat analysis of patients given pharmacological deep venous thrombosis prophylaxis within two or four days after ICH found no increase in hematoma size.

CONCLUSIONS. Pharmacological deep venous thrombosis prophylaxis given subcutaneously in patients with ICH and/or intraventricular hemorrhage in the subacute period is generally not associated with hematoma growth.

Memorial Hermann Healthcare System
7737 Southwest Freeway
Houston, TX 77074

mhmni.com
713.222.CARE

Nonprofit Org.
U.S. POSTAGE
PAID
Permit No. 3156
Houston, TX

4403834

