Upstate Outlook

News on education, biomedical research & health care at SUNY Upstate Medical University
Volume 6, Number 2 Summer 2006

The Brain

At brain-powered SUNY Upstate, teams of neurosurgeons, neurologists, psychologists, scientists, nurses and others decipher, heal and harness our most intriguing organ.

IT TAKES ONE TO KNOW ONE

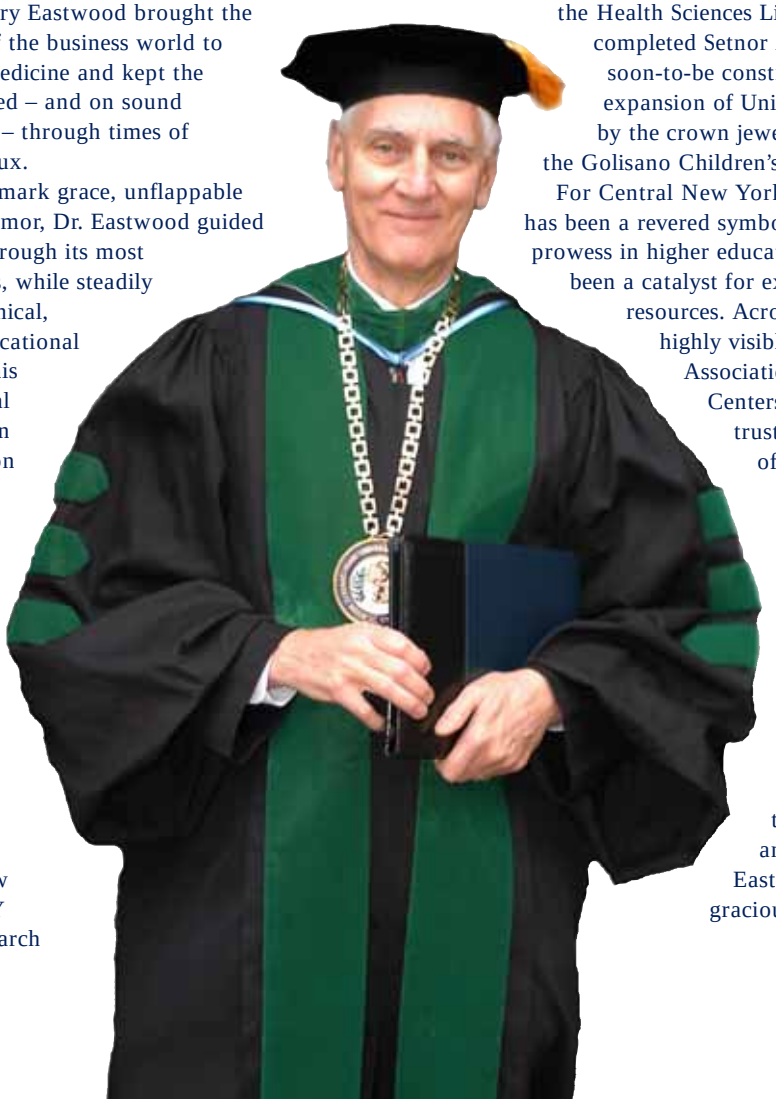
GREGORY L. EASTWOOD, M.D.

On His Watch

He arrived at SUNY Upstate Medical University in 1993, when the disparate cultures of medicine and commerce threatened to collide.

While maintaining Upstate's unflinching focus on superior patient care, President Gregory Eastwood brought the best principles of the business world to the practice of medicine and kept the university centered – and on sound financial footing – through times of unprecedented flux.

With his trademark grace, unflappable calm and wry humor, Dr. Eastwood guided this university through its most challenging years, while steadily expanding its clinical, research and educational enterprises. On his watch, the annual budget has grown from $325 million to more than $700 million. The endowment has increased from $25 to $64 million, and external research funding from $15 million to a projected $40 million in 2007, with Upstate now leading all SUNY campuses in research growth.



Across the campus stand monuments to his leadership: the spectacular Institute for Human Performance, the Health Sciences Library, the soon-to-be completed Setnor Academic Building and soon-to-be constructed East Wing expansion of University Hospital, topped by the crown jewel of his presidency – the Golisano Children's Hospital.

For Central New York at large, Dr. Eastwood has been a revered symbol of our community's prowess in higher education. He has likewise been a catalyst for expansion of our cultural resources. Across the nation, he's been highly visible, as president of the Association of Academic Medical Centers and a measured, trusted voice in the politics of medicine.

But first and foremost, Dr. Eastwood has been a committed physician and scientist, a deeply ethical man, a team player, and an inspiring role model for those who study, train and work at Upstate Medical University.

It has been an honor to serve on his watch, and we wish Dr. Eastwood, and his gracious family, Godspeed.

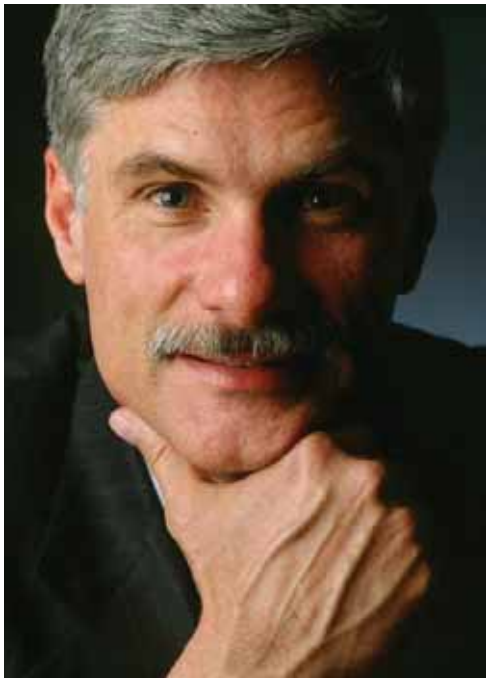
DAVID R. SMITH, M.D.

Taking the Baton

The incoming president of SUNY Upstate Medical University is a pediatrician whose first assignment – at a community clinic on the Texas-Mexico border – taught him "the difference between health and medicine."

Working for the National Health Service Corps in Brownsville, Tex., David R. Smith MD recognized that his patients most challenging problems were more societal than medical, according to a profile in *MedHunters* magazine.

That distinction changed the direction of Smith's career, steering him toward posts that influence public health policy as well as medical care delivery. "I knew that I could do more by changing the way things were done," he explains.



National Prominence

Smith most recently served as chancellor of Texas Tech University, a system with 31,000 students and a budget of almost $1 billion. Under his leadership, the system saw unprecedented growth in enrollment, student quality and fundraising. Innovations included the development of the nation's first four-year medical school on the U.S./Mexico border and a geriatric program with a "teaching nursing home."

En route to his position as chancellor, Smith served as medical director of the Brownsville Community Health Center; a deputy director with the Department of Health and Human Services in Washington DC; and senior vice president and CEO of Parkland Memorial Hospital in Dallas. One of Smith's initiatives there – moving primary care delivery out of the emergency department and into the community – earned a chapter in Bill Moyer's 1993 book, *Healing and the Mind*.

Smith also served as Texas Commissioner of Health, an agency with a $7 billion annual operating budget. In addition to campaigning for childhood vaccinations and folic acid for pregnant women, Smith was the plaintiff in the state's landmark case against the tobacco industry.

Texas won a $17 billion settlement in that case.

He also served for five years as president of the Texas Tech University Health Sciences Center and Dean of the School of Medicine and Graduate School of Biomedical Sciences.

An Ohio native, Smith is said to "carry himself with the air of a Texan. He has a warm handshake and a warmer heart."

Homecoming

Smith and his wife, Donna Bacchi MD, a New York State native, pediatrician – and equally adamant public health advocate – met as undergraduates at Cornell University. "So in a way," Smith said, "coming back to New York is like coming home."

Speaking briefly at Upstate when his appointment was announced, Smith said he prefers to be called Dave, and listening more than speaking. "I believe that's why we have two ears and one mouth," he said.

Smith will assume the Upstate presidency on September 1.

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From the Publisher

Our second issue on the brain features more of the enormous brainpower within the walls of this academic medical center.

Here at SUNY Upstate Medical University, we take great pride in the contributions made by our neuroscience teams and by physician/scientists such as Dr. Robert King, professor emeritus; Dr. Charles Hodge, chair of neurosurgery; and Dr. Jeremy Shefner, chair of neurology.

Lay people like myself marvel at these masters of the brain and their knowledge, skill and unyielding pursuit of excellence. When one considers the vital role of the brain, spinal cord and peripheral nerves, we soon realize the critical importance of safeguarding what is collectively called the nervous system.

This *Outlook* continues the journey of exploring and understanding this intriguing puzzle and sharing advancements in the treatments of brain injuries, diseases and disorders. It is no wonder that, when we describe something relatively easy to comprehend, we say 'it's not brain surgery.'

–Ronald R. Young
Publisher and
Vice President
for Public and
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Summer 2006

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ON THE COVER AND ABOVE
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The Brain

What lies within

The more we learn, the more questions we raise.

Q: What do you get when you cross an insomniac, an agnostic and a dyslexic?

A: Someone who's up all night worrying if there's a dog.

This is the riddle used by Louis Pellegrino MD, University Hospital neurodevelopmental pediatrician, to punctuate his presentations on brain plasticity. It breaks the ice beautifully. It also foreshadows the remarkable complexity of the organ under discussion, for the human brain is the seat of medical problems such as insomnia; cognitive disorders such as dyslexia; and higher-level reasoning skills, such as an agnostic's quest to prove there is no god.

The multitasking brain is also the organ often invaded by tumors, debilitated by strokes, rocked by seizures, flooded by hemorrhages and confused by concussion. In other words: profoundly vulnerable to illness and injury.

At University Hospital, it is a daily challenge to address these medical problems without compromising the brain's critical functions.

"Think of the brain as a Monopoly board, with high- and low-priced properties," suggests Associate Professor of Neurosurgery Gregory Canute MD. "The areas that control speech and movement are examples of prime real estate. We constantly weigh the risks of losing these functions against the benefits of treating brain disease."

The Last Frontier

In the 1970s, Nobel Prize laureates predicted that brain research would be the ultimate intellectual challenge in the last quarter of the 20th century.

But when Dr. Eric Kandel won the 2000 Nobel Prize for his work on learning and memory, he said the brain was far from understood. "The danger is that we're at the foot of a mountain range that people think we've already scaled," he said. "It's a huge mountain. It's going to take a century."

"While central questions remain, our understanding of the brain has increased dramatically in the past several decades," notes Charles Hodge MD, professor and chair of neurosurgery at SUNY Upstate. "When I was a resident, neurosurgery was considered a pioneering field. You were lucky to leave the hospital alive after surgery

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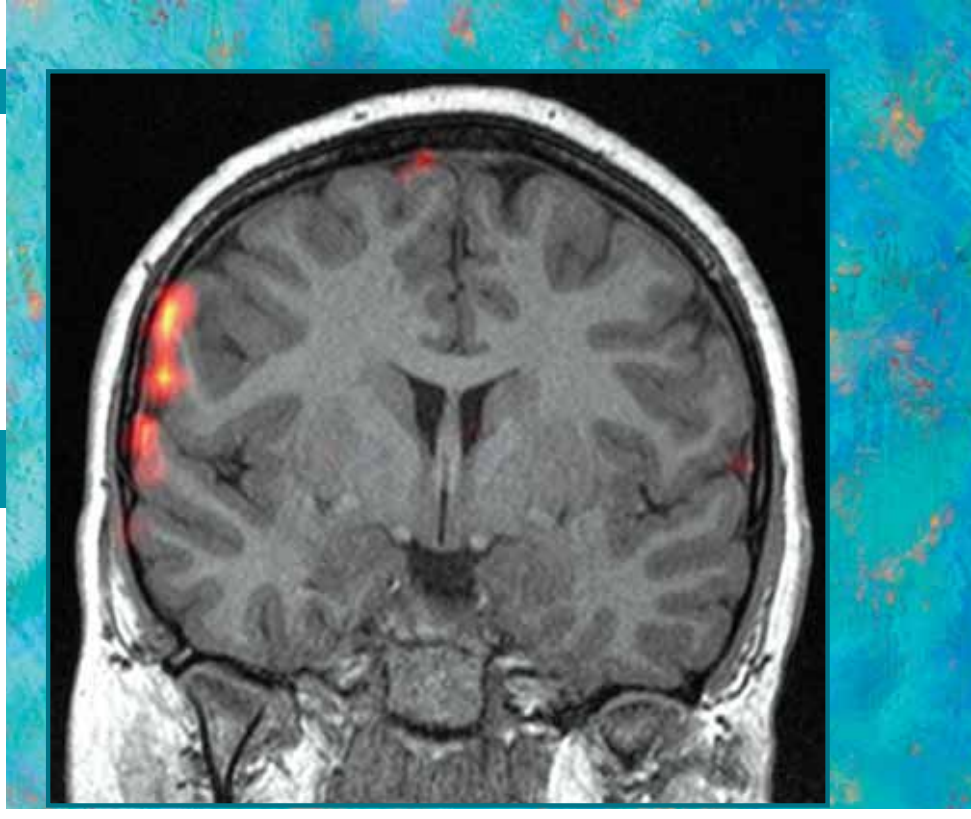

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for a major hemorrhage or brain tumor."

Hodge believes the most profound advance is awareness of the brain's plasticity. "The brain not only controls behavior, behavioral feedback controls some aspects of brain structure," he explains.

"The brain is a machine designed to learn. It's softwired (plastic) rather than hard-wired," according to a recent article in *The New York Times*. "Whenever you learn something new, new neurological connections are believed to form."

Window

Credit for insights into brain plasticity is due largely to advances in brain imaging.

"For most of history, the idea of watching the mind at work was as fantastical as documenting a ghost, *The New York Times* article continues. With X-rays, CT scans and magnetic resonance imaging (MRI), "You could break into the haunted house, but all you could find would be the house itself, the brain's architecture, not its occupant."

But the latest neuroimaging tools such as functional MRI – fMRI – have finally captured this elusive ghost – the brain in action.

Imaging Revolution

Professor Emeritus Robert King MD, Upstate's neurosurgery chair from 1957 through 1996, remembers when there was little technology to light his path.

"As neurosurgeons, we knew much less about the areas we were entering and the changes we were inducing," he explains. "You had to surmise which elements of the brain were not to be invaded. Today, neuronavigational tools help you know when to stop and when to go. These tools keep extending what can be accomplished."

"Neuroimaging is exploding," reports Kent Ogden PhD, a medical physicist in University Hospital's Department of Radiology. "In the past 35 years, the diagnosis – and treatment – of brain disorders has been revolutionized by the development of computed tomography

"Think of the brain as a Monopoly board, with high- and low-priced property. The areas that control speech and movement are prime real estate. We weigh the risks of losing these functions against the benefits of treating the disease."

–Gregory Canute MD
associate professor of neurosurgery

(CT), magnetic resonance imaging (MRI), fMRI, PET, SPECT, angiograms and more."

What Lies Beneath

Armed with these images, neurosurgeons now approach procedures – such as tumor removal and hemorrhage repair – with far greater precision. During the surgery itself, they can move a wand over the patient's head and 'see' on a computer screen what lies beneath the skull. They can also refer to fMRI scans, which identify the function, such as speech or movement, of specific brain tissue.

When these images are combined, the benefits are exponential.

"Today, the biggest trend is multimodal imaging – fusing the data from the various technologies into a single set of images," explains Ogden. Pointing to a vivid image on his computer monitor, he zeroes in on an area that is the likely source of a patient's epilepsy (above left, page 4). "In this image, we've combined the data from an MRI scan, which shows anatomical landmarks, and a series of SPECT scans, which show where the metabolism is higher during seizures," he says. "The increase in activity helps pinpoint the source of the seizures – and guides the neurosurgeon performing resection.

"The benefits to the patient are tremendous," says Ogden.

Access Point

In addition to more accurate diagnoses, the new imaging opens the door to less-invasive treatment options, such as Gamma Knife radiosurgery, or surgery without a scalpel. Since the year 2000, 1,500 University Hospital patients have had computer-guided, ultra-precise Gamma Knife treatment for hard-to-access brain tumors and other neurological conditions.

The Experience Factor

No matter how advanced the technology, experience is the most critical factor when dealing with brain disease and disorders.

At University Hospital, highly experienced health care profession-

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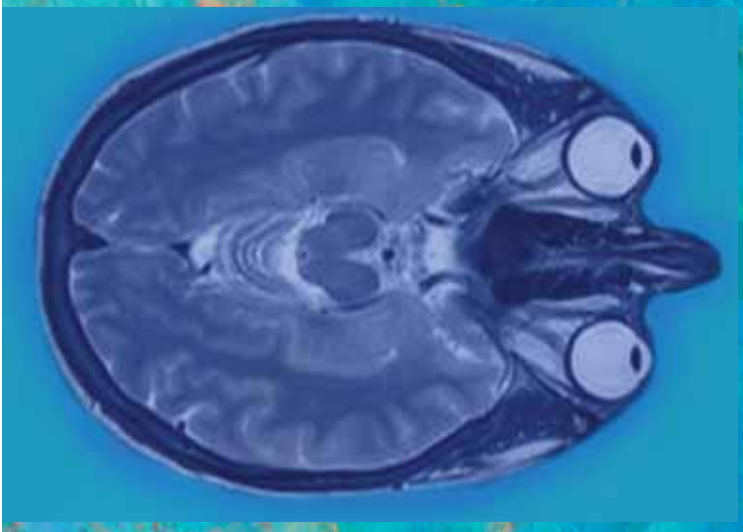

Functional magnetic resonance imaging (fMRI) captures specific brain activity, whereas x-rays and CT scans reveal only brain architecture.

The Brain – *continued from page 7*

als work in interdisciplinary teams to tackle complex conditions, such as brain tumors, Lou Gehrig's Disease (ALS) and even concussion – a "mild brain injury" with potentially severe consequences.

To strike back against stroke – the nation's second leading cause of death – University Hospital has developed a stroke response team that's alerted the minute the patient arrives in or is reported en route to the emergency department. Its seamless delivery of stroke intervention recently earned University Hospital the prestigious designation "Stroke Center" from the New York State Department of Health. In Central New York, only University Hospital holds this designation.

Uncharted Territory

Despite major advances, those who study the brain or treat brain-related disorders agree: the more we learn, the more questions we have.

Thirty years ago, these endless questions prompted King to build two years of bench research into Upstate's five-year neurosurgery residency. Most of the nation's academic medical centers have since followed his lead.

"My own lab experience made such a difference in my understanding of the nervous system," King explains. "The research makes residents much more secure with uncertainty. In a laboratory, it's all about uncertainties. Your research is primarily a vehicle for learning to ask better questions."

The Research Factor

Long beyond their residencies, Upstate's neurosurgeons continue their research, in labs now located in the Institute for Human Performance on Irving Avenue, adjacent to the main SUNY Upstate campus. Hodge and his research team, for example, continue their investigation of cortical plasticity – the brain's remarkable ability to repair itself. Their studies focus on the brain's motor and sensory realms. But Hodge predicts even greater plasticity in the executive and associative areas.

Hodge considers his laboratory research – and the clinical trials it inspires – both a responsibility and a privilege. "As neurosurgeons," he says, "we are the only group that is able to directly handle the human brain, to understand the disastrous consequences of many neurological diseases and to bring modern biological findings to the operating room."

Striking Back at Stroke

Sometimes bad news leads to good news. In response to reports that Onondaga County has the second highest stroke mortality rate in New York State, University Hospital resolved to strike back at stroke with all its resources.

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"We need to treat stroke with the urgency of trauma."

–Tarak Ramachandran MD

Stroke – *continued from page 9*

Now its efforts have earned the prestigious designation "Stroke Center" from the New York State Department of Health. University Hospital, the only Central New York Hospital with this stroke status, has also received the 2006 Specialty Excellence Award for Stroke Care from Health Grades, Inc., a leading healthcare ratings organization. The award ranks University Hospital's stroke care with the top 10 percent of hospitals nationwide.

But University Hospital is far from finished with its assault on stroke – the third leading cause of death and the leading cause of disability in the US. Stroke education and prevention especially require major attention.

Spread the Word

Misinformation is the greatest barrier to timely stroke intervention, according to neurologist Tarak Ramachandran MD, stroke director at University Hospital.

"There seems to be a nihilistic attitude that nothing can be done for stroke," he says. In fact, organized stroke care already results in a 21 percent reduction in early mortality, 18 percent reduction in 12-month mortality and decreased stays in hospitals and rehabilitation centers.

Studies show that nurses are the most proactive about sending family members with stroke symptoms to the hospital. The general public is prone to delay, misunderstanding stroke symptoms or believing that damage to brain tissue is irreversible.

Three-Hour Window

"We need to treat stroke with the urgency of trauma and spread the word that time is of the essence," insists Ramachandran. "Certain interventions must begin within three hours of symptom onset."

Tarak Ramachandran MD, stroke director at University Hospital

Stroke Warning Signs

Act FAST! Call 911 at any sign of stroke:

Face
Does the FACE look uneven? Ask the person to smile.

Arms
Does one ARM drift down? Ask the person to raise both arms.

Speech
Does their SPEECH sound strange? Ask the person to repeat a simple phrase, like "The sky is blue."

Time
If you observe ANY of these signs, it's TIME TO CALL 911!

Credit: MA Dept. of Health.

Often the public does not recognize stroke symptoms, says Ramachandran, citing a recent report that fewer than five percent of patients who could benefit from timely stroke therapy receive that treatment, simply because they arrive at a hospital too late.

Clot Buster

More than 80 percent of strokes are caused by blood clots which disrupt the flow of oxygen to the brain. Many of these ischemic strokes can be treated with tissue plasminogen activator (tPA), an enzyme which dissolves blood clots. But tPA must be administered within three hours of symptom onset.

A second type of stroke – hemorrhagic strokes – cause bleeding in the brain and are not appropriate for tPA. But they may often be treated by a neurosurgeon, with surgical clipping or endovascular coiling.

Ready and Waiting

Diagnosis of ischemic or hemorrhagic stroke requires a hospital with a CT scanner and a coordinated stroke protocol. University Hospital's multidisciplinary stroke team follows a protocol developed by the National Institutes of Health.

Members of the stroke team evaluate patients within 10 minutes of arrival at the hospital and begin a CT scan with 25 minutes, to determine if the stroke is ischemic or hemorrhagic. Within one hour of arrival at the hospital, the appropriate patient is cleared for tPA.

FAST Response

With its clinical response aligned, University Hospital is reaching out to educate the community about stroke symptoms and the need for a FAST response (see page 8).

"We want to inspire the same sense of urgency that people associate with chest pain," explains University Hospital's stroke coordinator Rochele Clark RN.

"Stroke symptoms, like facial droop and slurred speech, tend to be vague," she says. "People often lay down to see if the symptoms go away. The average person waits 22 hours before seeking medical attention for stroke.

"But a stroke is a medical emergency," Clark insists. "You need to call 911 right away."

Ready & Waiting

University Hospital's immediate response stroke team includes an emergency department physician and nurses, neurologist, neurosurgeon (as needed), radiologist, CT scanner technician and administrative supervisor, all prepared to respond within minutes of a patient's arrival at University Hospital.

After patients have been diagnosed and admitted, the stroke team expands to include certified neuroscience nurses (AANN), physical therapists, occupational therapists, speech therapists and others.

Rochele Clark RN, stroke coordinator

Stroke epidemiology*

Stroke is the third leading cause of death and the leading cause of adult disability in the US.

- 50 percent of stroke deaths occur before reaching the hospital.
- Stroke mortality is higher for women (61 percent) and African Americans (87 percent male, 78 percent female).
- Onondaga County has the second highest stroke mortality rate in New York State (55.5 per 100,000 vs. the NYS average of 38.4)

*Epidemiology is the study of disease cause, control and distribution in specific populations.

AFTER STROKE

Once stroke patients receive the necessary medical and surgical care, the focus turns to damage caused by oxygen-deprived brain tissue. The most common deficits include speech, motor and memory problems – addressed at University Hospital through intensive regimens of physical, cognitive, speech and other therapies.

Stroke rehabilitation accounts for about 20 percent of patients treated in University Hospital's Acute Brain Injury Rehabilitation Program on 2 North.

Rehabilitation is very function-oriented, according to Cenk Pekis MD, assistant professor of medicine and rehabilitation. "Our goal is to find functional solutions for patients who are impaired or disabled – and to get patients back home or back to work." For example, a patient with weakness on one side of the body may learn to stand with special devices and walk with assistance.

Pekis says the role of the rehabilitation physician is to "orchestrate a large circle of professionals – physical, speech, cognitive and recreational therapists; counselors; educators; nurses; and even therapy dogs – whatever helps and motivates patients to adapt to their limitations and disabilities.

"Physical rehabilitation is a team sport – it's very democratic, interdisciplinary, labor-intensive – and costly," Pekis adds. "We bring in whatever medical professionals can help patients adapt to their limitations and disabilities.

"It used to be considered dogma, that brain tissue could not be repaired or replaced," he says. "But this is no longer valid. Cortical function is very complex. Recovery is not black and white, it's measured by degrees. But intensive therapy can lead to functional improvement."

A BETTER WAY?

Eagerly anticipated at University Hospital is a clinical trial that may help stroke patients recover more motor function after stroke damage.

The EVEREST multicenter stroke treatment trial tests the use of implanted electrical brain stimulation with rehabilitation therapy, to see if patients develop better control of stroke-damaged upper extremities.

The trial, led at Upstate by Neurosurgery Chair Charles Hodge MD, involves implantation of an electrical pulse generator in the cerebral cortex. According to Hodge, "This is an important site for neuroplasticity – a process of reorganization in which new areas of the brain take over the function of brain-damaged areas."

Previous studies have established that cortical stimulation therapy is safe and more effective in increasing motor function than rehabilitation alone.

Patients who receive the implant will also undergo six weeks of physical therapy. Control group patients will receive therapy only.

The Upstate trial exemplifies the interdisciplinary nature of stroke care at University Hospital, with a research team that includes Charles Bradshaw PhD, neuropsychologist; Margaret Turk MD of Physical Medicine and Rehabilitation; Michael Vertino MD, neurologist; and Lorraine Padden CNRN, ANP, study coordinator.

EVEREST

"We need to approach this problem not as competitors, but as one giant hospital meeting this community's serious need for stroke care."

Striking Back As a Community

Satish Krishnamurthy MD, Associate Professor of Neurosurgery

Only a small fraction of strokes require intervention by a neurosurgeon, but that hasn't stopped University Hospital neurosurgeon Satish Krishnamurthy MD from rallying the community to strike back at stroke.

In 2003, Krishnamurthy agreed to chair the CNY Regional Stroke Task Force, assembled by the American Heart Association.

His motivation? "Better stroke care for our community. At that point, Onondaga County had the second highest stroke mortality rate in New York State and no standardized stroke care."

At 7 a.m. monthly meetings, the task force first identified deficits in local stroke awareness and care. The group gathered strength as Krishnamurthy recruited his peers at other hospitals and stroke-related organizations.

"Our first question," he reports, "was why are so many people dying from stroke?

"It turned out that close to 50 percent of mortality was related to not getting to the hospital in time," he says. "People do not recognize the severity of stroke symptoms or the importance of prompt intervention."

But local hospitals also needed to fine-tune their stroke response. University Hospital, the region's Level 1 trauma center, was first to mobilize its stroke response team and earn certification by the New York State Department of Health.

Now it's helping other local hospitals develop their stroke protocols.

"We need to approach this problem not as competitors, but as one giant hospital meeting this community's serious need for stroke care," Krishnamurthy says.

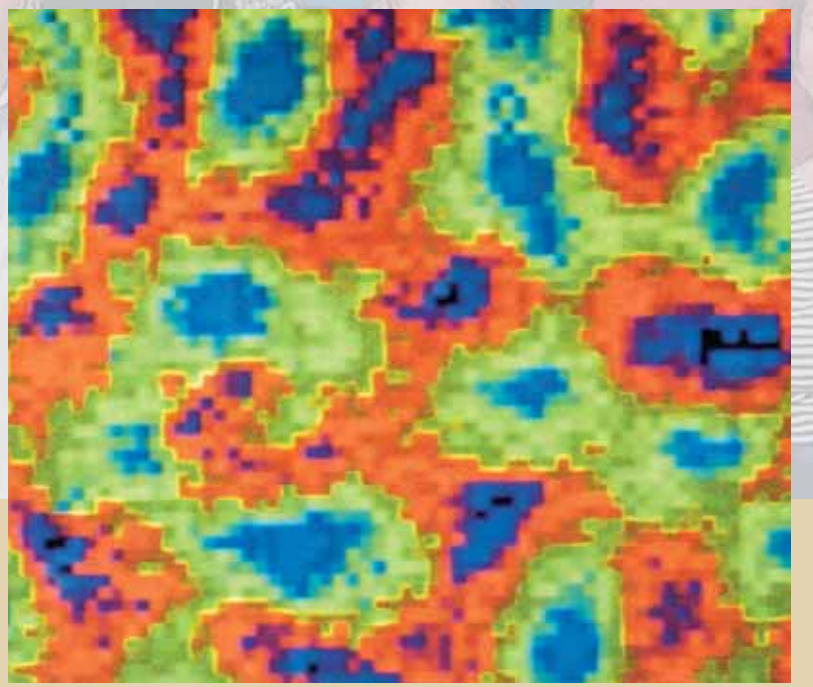
"Stroke is a problem that requires lots of resources, lots of attention," he adds. "But there's so much synergy and enthusiasm in this group. It's the most exciting thing I've done in this community."

Krishnamurthy believes that education is key to effective stroke management – and that physicians must be the most adamant educators. "We have to warn our patients who are at risk of stroke from obesity, diabetes, smoking, hypertension – and age. Age-related stroke is an epidemic just waiting to happen."

Krishnamurthy is encouraged by the medical community's evolution from reactive to proactive stroke response. "This generation is moving from treating stroke after it's happened to addressing the problem before it happens, which is how it should be."

Brain Trust

SUNY Upstate research teams take on the elusive organ



It takes one to know one. Never was this more true than in the realm of brain research, where it takes decades of investigation – and an almost unfathomable understanding of medical science – to decipher the workings of this intricate organ. That's why SUNY Upstate assembles entire teams – of neurosurgeons, research scientists, residents, doctoral and postdoctoral students, lab technicians and lab assistants – to tackle the questions posed in its brain research laboratories.

BOOSTING BRAIN REPAIR

In the Cortical Plasticity Lab, the questions concern the brain's remarkable ability to repair itself.

For almost four decades, Professor and Chair of Neurosurgery Charles Hodge MD has led studies identifying the intricacies of this self-repair, known as plasticity.

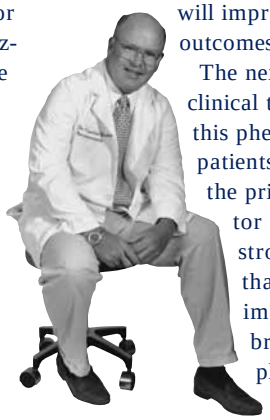
"It is abundantly clear that the brain and nervous system are not static," Hodge explains. "The fact that we can adapt to new environments and recover function after brain injury are indicators of that plasticity.

"As neurosurgeons, we have the opportunity to personally witness how the brain responds to disease or injury," he says.

When stroke kills brain cells, for example, the brain often reorganizes, with healthy cells assuming the dead cells' functions.

In recent laboratory studies – funded by the National Institutes of Health – Hodge and his team have demonstrated that certain stimulants alter the brain's self-repair mechanisms.

"In the lab," Hodge explains, "we have pretty good evidence that these drugs improve recovery. They ramp up the brain and stimulate more neurons to fire. Our hypothesis is that such stimulation, plus physical therapy, will improve long-term outcomes."



The next step is a clinical trial to explore this phenomenon in patients. Hodge is also the principal investigator on a multisite stroke recovery trial that employs an implanted electrical brain stimulator plus physical therapy.

(See page 12)

CURBING A LETHAL FOE

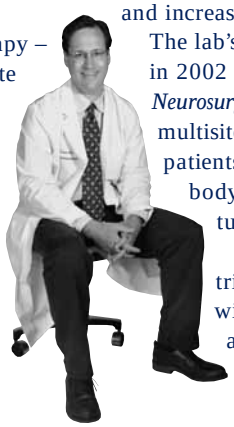
In Upstate's Brain Tumor Laboratory, there is a sense of quiet urgency, inspired by the glioblastoma multiforme brain tumor (GBM).

"It's the most lethal tumor known to man," according to the lab director and Associate Professor of Neurosurgery Gregory Canute MD. Every year he surgically removes 50 to 60 GBM tumors, but the standard treatments – surgery plus radiation and chemotherapy – "don't work very well," Canute reports. "Almost all patients die within a year of diagnosis."

In the U.S., about 9,000 patients a year are diagnosed with GBM. In patients age 15 to 34, GBM is the third leading cause of cancer death.

Since 1993, Canute and his research team have been studying the molecular characteristics of GBM tumors and experimenting with agents that might thwart their growth. Several of their studies have led to clinical trials.

Recently the lab has been focused on the monoclonal antibody cetuximab, which has been approved for use against colon cancer. It has also shown promise, in the Upstate lab's studies, in curbing GBM cell growth and increasing cell death.



The lab's findings – published in 2002 and 2005 in the journal *Neurosurgery* – have inspired a multisite Phase I clinical trial of patients infused with the antibody prior to surgery for tumor recurrence.

Patients enrolled in the trial have GBM tumors with a genetic mutation – amplified epidermal growth factor receptor (EGPR) – which seems to make the tumor cells more vulnerable to cetuximab. About 40 percent of GBM patients – especially older patients, with poorer prognoses – have this amplified EGPR.

One of the questions the trial will answer is "Can the antibody penetrate the tumor?"

"It has big, heavy molecules and is hard to spread outside vessels and past the blood tumor barrier," Canute explains. "But we've shown it can be done in the laboratory."

If the drug can reach the tumor, be tolerated by patients and eventually be added to the current GBM regimen, "This could represent a huge jump forward," says Canute. "Our standard chemotherapy – BCNU – is theoretically not even close to as effective as this antibody."

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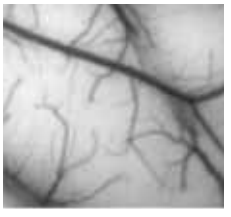
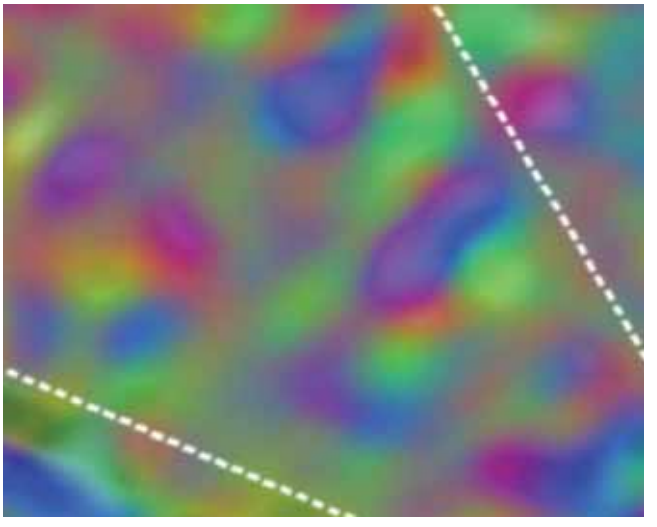
Research – *continued from page 15*





Optical imaging analysis of a section of the brain's visual cortex. Above left: the same section, without optical imaging analysis.

READING THE SIGNALS

With another NIH research grant, Upstate's vision research team is tracing the brain's ability to process visual input. It is painstaking work – as demonstrated by Neurosurgery Research Director Daniel Tso PhD, who has been on this research trail for more than 25 years. His current studies build on the work of his Harvard University mentors: Nobel Prize winners David Hubel and Torsten Wiesel. "They made major inroads into the working of the brain and the visual cortex," Tso explains. "As researchers, we all stand on the shoulders of such giants.

Daniel Tso PhD

"Visual information entering the brain from the retina undergoes a series of remarkable transformations," Tso continues, "including separation into channels that process color, form, depth and motion. Our research concerns the organization and processing of this information."

Tso and his research team use optical imaging to identify how and where this processing occurs. "When a part of the brain is active, it blushes," Tso explains. "Optical imaging captures that blushing by measuring changes in blood oxygenation."

Tso's discoveries about the visual cortex have broad implications. "When you look at the neocortex, it all looks rather similar," he says. "What largely defines the visual, auditory or sensory cortex is the input it gets from the eyes, ears and skin. Our research should lead to a better understanding of overall brain function and architecture," he says. "Our insights into disorders of the visual cortex apply to other diseases involving neuronal connectivity, such as Alzheimer's and epilepsy."

Gaining Ground on Concussion

For psychologist Brian Rieger PhD, concussion has become a crusade, fueled by a huge gap in community awareness and concussion care.

Rieger was enlisted by University Hospital to work with brain injury patients almost 10 years ago, and has seen – over and over – how a so-called 'mild traumatic brain injury,' also known as concussion, can have serious consequences.

"Many people have no idea of the symptoms or how disruptive they can be," explains Rieger. "The symptoms wax and wane. The cultural message is 'You will be fine.' On the other hand, people who have suffered concussion often say, 'I feel like garbage. I'm really tired. I feel foggy all the time. Nobody understands.'"

High Alert

Fortunately, Rieger understands, and he's alerting physicians, coaches, trainers, teachers and others to the realities and dangers of concussion – especially the fact that concussion can sometimes cause lingering, and even disabling, symptoms.

Several years ago, Rieger established the Concussion Management Program and CNY Sports Concussion Center at University Hospital. A team of physicians, psychologists, nurses and physical and occupational therapists provides coordinated concussion care.

The programs, which diagnose and treat concussion patients, have doubled in size in the past year, and remain unique in the region and the state for focusing specifically on mild traumatic brain injury. The services continue to expand, and the team now includes Neuropsychologist Dominic Carone PhD, who specializes in the effects of brain injury and illness.

Psychology Realm

"When I'm out 'preaching' about concussion," notes Rieger, "audiences will ask, 'What do psychologists have to do with concussion?'

"Concussion causes a chemical crisis in the brain and alters its ability to function," he explains. "Long-term symptoms are often cognitive and emotional – things like anxiety and difficulty concentrating. These are areas in which psychologists specialize.

Brain Rieger PhD

"Patients are referred with labels like 'lazy' and 'irritable.' Sometimes they think they're crazy, because concussion is such an invisible injury," says Rieger. "They need a lot of reassurance and education."

Front Lines

Yet physicians play a key role in diagnosing concussion, notes Rieger, who often collaborates with James Callahan MD of University Hospital's dedicated Pediatric Emergency Department.

"Concussion can be elusive to diagnose," admits Callahan, another impassioned concussion crusader. "There is no objective test. A CT scan looks normal," he says. "Concussion is a clinical diagnosis, based on symptoms. Sometimes those symptoms don't appear until 24-48 hours post-injury. So when we discharge patients from the emergency department, we often refer them for follow up by the Concussion Program."

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Gathering Evidence

Because pediatric concussion is under-researched, Callahan and Rieger are collaborating on a clinical research study tracking young patients' symptoms for a year after concussion. "We know that the majority of adults will recover completely from concussion within two weeks, but up to 20 percent may still have symptoms a year after injury," says Callahan. "We don't yet have statistics on children."

Rieger is also collaborating with Lawrence Lewandowski PhD from Syracuse University on a study examining the academic effects of concussion in high school students. Students who still have symptoms of a concussion are asked to keep track of symptoms with a personal digital assistant (PDA).

At What Cost?

"When some students return to school, they have trouble with memory and attention," explains Rieger. "They get headaches and can get very tired from mental exertion. The PDA helps us to track their symptoms over the course of a school day.

"We can't just look at what these students force themselves to do," he says. "We have to consider the price they pay to do it."

Inside Look

Rieger is also working with Upstate research psychologist Wendy Kates PhD and neuropsychologist Carone to image concussion patients' brains.The proposed study will utilize functional magnetic resonance imaging technology in the Institute for Human Performance and will be "a huge step forward in our research," according to Rieger.

TACKLING SPORTS CONCUSSION

Sports cause only a fraction of concussions, yet sports concussion gets plenty of attention, in the media and at University Hospital.

One driving force is second impact syndrome, which places younger athletes at greater risk, should they suffer a second concussion.

At all ages, repeat concussions may take longer to heal and can increase the chances of lifelong symptoms.

In recognition of this risk, the National Federation of State High School Associations passed a new mandate: players with suspected concussion must now have physician clearance for return to play.

"It's not law, but it makes school districts liable," says Brian Rieger PhD, who has also addressed the NYS Athletic Trainers Association about the perils of concussion.

"The mandate underscores two key messages: that it takes medical experience to diagnose concussion and that young athletes are more susceptible – and take longer to heal – than professional athletes. We suspect it's because their brains are still developing."

"In rare cases, the consequences are fatal," James Callahan MD warns. "There is massive brain swelling and nothing we can do to stop it."

Rieger and Callahan recently addressed local Section III athletic directors about second impact syndrome and other potential consequences of concussion.

"Coaches, athletic trainers and student athletes were also invited, to learn about recent findings in head injuries," reports Karissa Graham (at right), assistant director of athletics with the Marcellus Central Schools. "Dr. Rieger and Dr. Callahan left a strong impression on this group. We're still receiving compliments about their program.

"As an athletic trainer, I have also referred a patient to Dr. Rieger," she continues. "The entire family – after months of trying to deal with a concussion on their own – found the program to be tremendously helpful."

Bench to Bedside

ACUTE NEED FOR ALS CARE STEERS NEUROLOGY CHAIR FROM LAB TO CLINIC

Propelled by a fascination with the physiology of the brain, Jeremy Shefner completed a PhD, medical degree and two post-doctoral fellowships to prepare for a research career. But when he was finally ready to settle into his own lab, he discovered a flaw in his plan. "I missed the patient contact and the opportunity to be immediately useful," explains Shefner.

Jeremy Shefner MD/PhD, chair, Department of Neurology

"(Someday) ALS will be...a chronic disease that can be managed through drug therapy."

–Jeremy Shefner MD/PhD

Joining the faculty at Harvard Medical School, the young neurologist tried to tackle both patient care and research, but he encountered another obstacle: Shefner was increasingly drawn to patients with Amyotrophic Lateral Sclerosis (ALS) – a challenging and time-consuming disease to treat.

ALS, also known as Lou Gehrig's disease, attacks motor neurons, causing degeneration throughout the brain and spinal cord – and leading to paralysis and death.

Diverse Demands

"A lot of these patients' demands are emotional and social. But I discovered I like giving that support," says Shefner. "I get along well with these patients. I find it rewarding to make them more comfortable and functional, minimize their suffering, look for ways to extend their lives."

After establishing an ALS clinical and research program at Harvard, Shefner was recruited to SUNY Upstate in 1996.

"I came here to develop ALS resources for Central New York," he says. "There were five major ALS centers in Boston. Creating an ALS program here was a real service. Otherwise patients had to go to Vermont, Boston or NYC."

Before leaving Boston, Shefner – a researcher at heart – established the Northeast ALS (NEALS) Trials consortium, to rapidly identify and clinically test promising treatments for ALS. He currently cochairs NEALS.

Hope Ahead

"Patients with ALS are always clamoring for new drugs and clinical trials. With clinical trials, there is hope ahead," Shefner explains.

"There is no real disease modifying treatment for ALS," he continues. "Only one drug – Riluzole – is FDA approved. It's not dramatic. It extends life 10 to 20 percent."

The NEALS consortium now includes 60 U.S. academic health centers and has conducted four large multicenter clinical trials. For three of those trials, Shefner was principal investigator or co-investigator.

Shefner is currently involved in five ALS trials that have brought more than a million dollars in research funding to Upstate. These studies are testing the safety and efficacy of drug compounds that may slow the progression of ALS, as well as respiratory and nutritional treatments.

Genetic Connection

Recent discoveries on the ALS front include identification of a mutation of the SOD1 gene, believed to make a defective protein that is toxic to motor nerve cells, as well as genes that appear to serve as ALS markers.

These findings have inspired in increase in funded studies.

"Given the knowledge we currently have, I believe ALS will someday be considered a chronic disease that can be managed through drug therapy," Shefner says.

On the other hand, he notes that ALS is not a lucrative focus for drug development, since it affects about 5 out of every 100,000 people "More often, ALS appeals to smaller companies or companies looking to expand use of existing drugs."

Change in Approach

The most positive change in ALS treatment is a change in attitude. "Physicians take a more active role in management of the disease. The patient's emotional needs are a big part of the practice," Shefner says.

Under Shefner's leadership, SUNY Upstate offers one of 33 ALS Research and Treatment Centers designated by the Muscular Dystrophy Association.

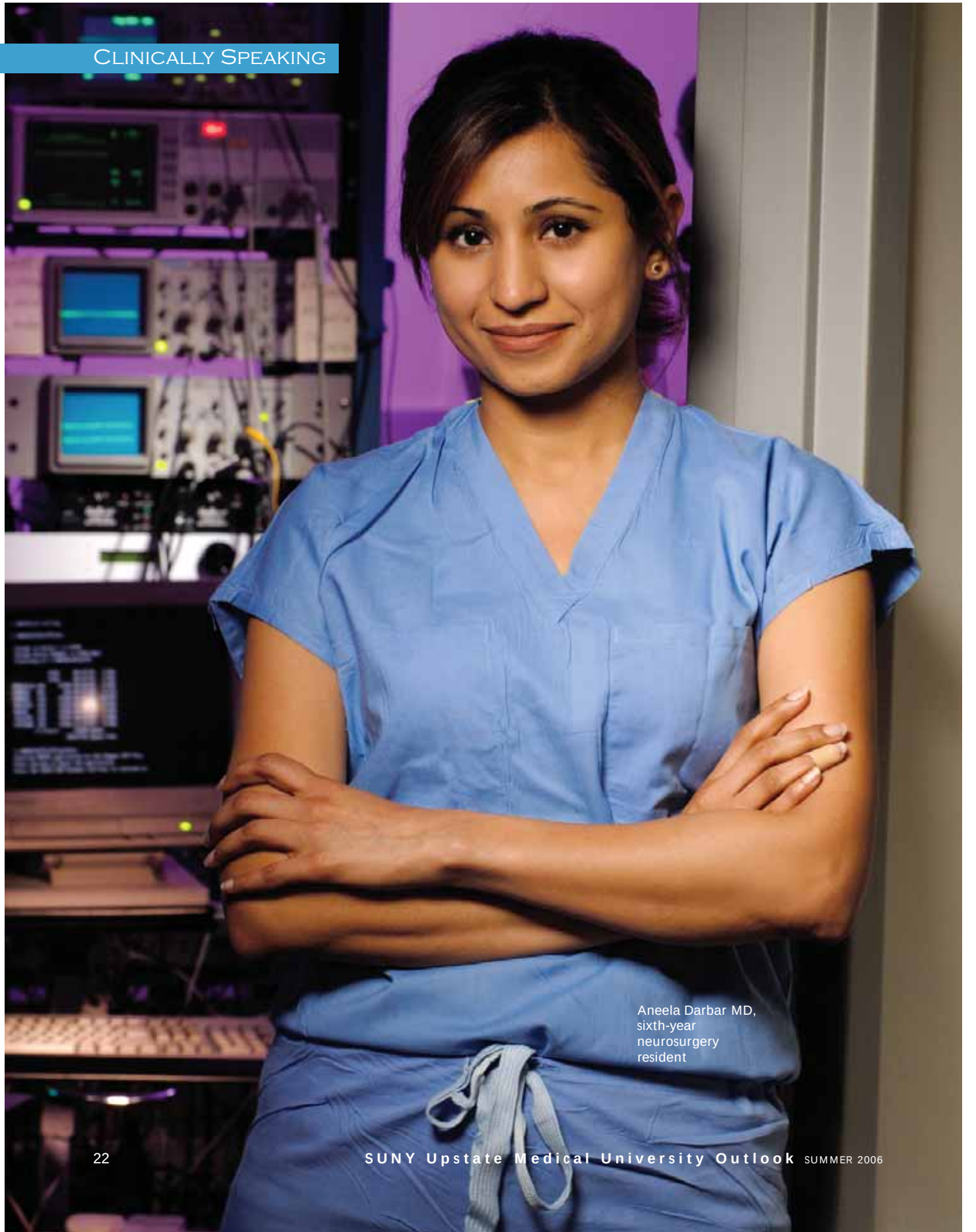
About 120 CNY patients receive their care at the SUNY Upstate center, receiving integrated treatment from a respiratory therapist, occupational therapist, social worker, pulmonologist, neurologist, nutritionist, speech and language specialist and physician's assistant.

Prognosis

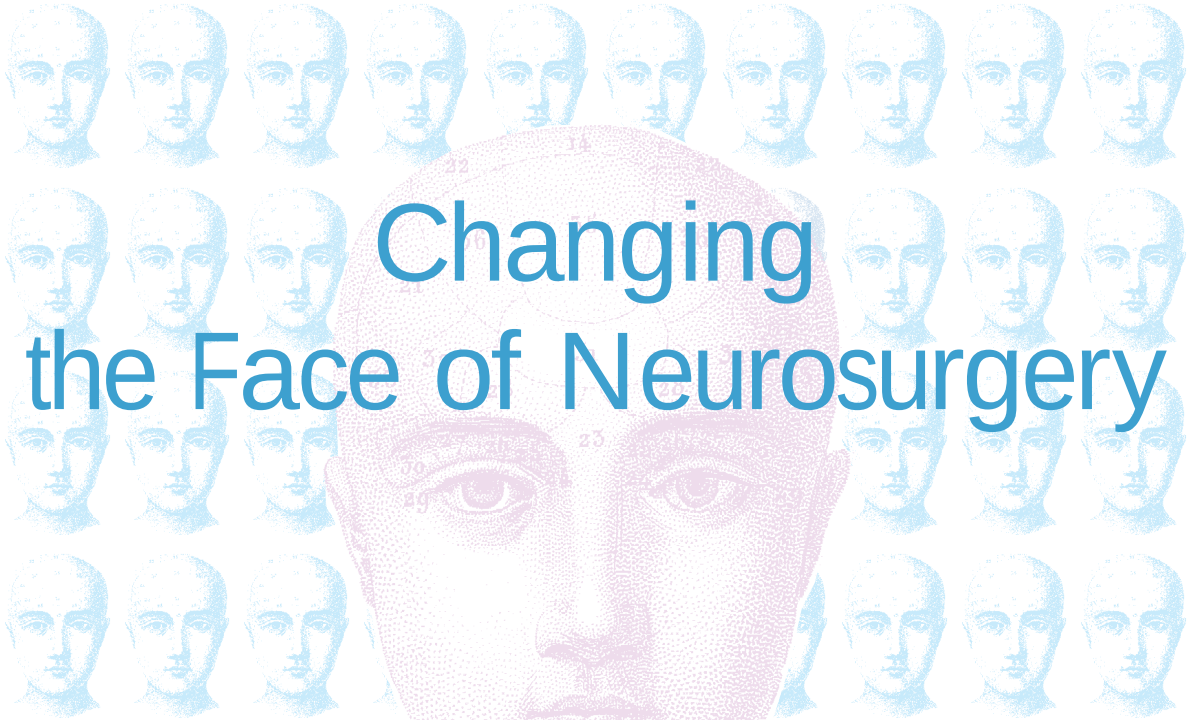
Shefner concedes that it requires great patience and persistence to take on ALS. "We have to accept that progress toward new treatment will be slow and incremental. It's frustrating for patients and for me."

As chair of the Department of Neurology, Shefner continues his campaign to expand research. That's a real challenge in a community where demand for clinical neurologists is high. "For now, our clinical focus is on the complicated diseases: epilepsy, active muscular dystrophy, muscular sclerosis. We also treat stroke, the most common neurological disease.

"We have 12 full-time neurologists and four PhDs, as well as 15 residents and three neurophysiology fellows," Shefner reports. "We need to double our faculty in a market where the supply of academic neurologists is very limited. So we're competing with major markets. But we offer neurologists the opportunity I had: the freedom to build their own programs."



Aneela Darbar MD, sixth-year neurosurgery resident



Changing the Face of Neurosurgery

One of SUNY Upstate's female neurosurgery residents has been enthralled by the brain since she was a small girl. The other fell under its spell unexpectedly, enroute to a career in primary care. Both prove that "When women are in neurosurgery, neurosurgery wins."*

While women now fill more than half of American medical schools, women in neurosurgery remain a rarity. Of the nation's 4,000 neurosurgeons, fewer than 5 percent are female. It's a rigorous specialty, with a seven-year residency, grueling hours, daunting diseases and relentless stress. An added deterrent, especially for women, is neurosurgery's reputation as not family friendly.

SUNY Upstate's neurosurgery residency program, however, has a reputation as being women-friendly. Thirty years ago, it was the training ground for one of the first women to enter the specialty: Elisabeth Post MD, now practicing in New Jersey. (SUNY Upstate also traces its roots to Geneva Medical College, which graduated the first American female physician, Elizabeth Blackwell MD, in 1849.)

Absence of Bias

When Upstate's Jennifer Jennings MD, now a fourth-year resident, looked at Upstate's neurosurgery program in 2003, she found a "refreshing" absence of bias against women. "I had the sense in my interview that I would not be treated any differently," says Jennings.

**motto of the national organization, Women in Neurosurgery (WINS)*

continued on page 24

Residents – *continued from page 23*

"...if I can do something for 36 hours straight and still love it – I know I'm in the right place."

–Jennifer Jennings MD, fourth-year neurosurgery resident

"That was not necessarily the case in other interviews."

"Being a woman is not an issue in this program," adds Aneela Darbar MD, a sixth-year resident. "The only issue is 'Are you competent enough to become a neurosurgeon?'"

Detour

Stanford University graduate Jennifer Jennings decided on a career in medicine while working as an Americorps volunteer – in a South Dakota clinic providing free prenatal care to homeless women.

"I assumed it would be primary care," says Jennings, "until my neurosurgery rotation in my third year.

"I loved the intricacy of the surgery and found the nervous system fascinating," she explains. "I knew it wouldn't be an easy specialty. Out of 200 students in my medical school, at the University of Texas at San Antonio, I was the only person to choose neurosurgery. My parents – my father is a computer programmer and my mother, a preschool teacher – are still trying to make sense of my decision. "

Jennings describes her interviews for a neurosurgery residency as "daunting" – until she visited Upstate and found its program both welcoming and highly ranked, with "a strong chair, a wide variety of cases, the latest minimally invasive technology and a neuro-intensive care unit."

For Darbar, the path to neurosurgery had other major obstacles. She is a graduate of a foreign medical school – Dow Medical College in Karachi, Pakistan – and from a culture that is more restrictive for women.

"Everyone at home challenged my dream of becoming a neurosurgeon," says Darbar, who, as a young girl, amused herself by sculpting PlayDough® models of the brain.

Gray Area

"I have always been fascinated by the novelty and mystery of the brain and its diseases," says Darbar. "There is so much gray area – so many things we have yet to figure out."

As a medical student, Darbar completed a visiting clerkship at SUNY Upstate. Once she earned her medical degree, she returned to Upstate to fortify her credentials for a neurosurgery residency.

"Neurosurgery is the most competitive area of medicine," she explains. "If you're a graduate of a foreign medical school, you need a CV that's better than the competition."

As a postdoctoral research fellow at Upstate, Darbar worked with pain pioneer Vania Apkarian PhD, using fMRI to document how the brain processes pain. With her research published in the *Journal of Neurophysiology*, she then completed an internship in surgery and pre-residency fellowship in neurosurgery at University Hospital. In 2001, after six additional months of study in Oxford, England, she secured a residency in Upstate's Department of Neurosurgery.

Now heading into the home stretch of her training, Darbar assumes she will go onto a fellowship in minimally invasive neurosurgery. Her fascination with the brain continues to grow.

She recently completed two more years of bench research – a departmental mandate – in the NIH-funded laboratory of Neurosurgery Chair Charles Hodge MD. The focus here is on the brain's plasticity – its remarkable ability to compensate for damaged cells.

In neurosurgery – where much remains to be deciphered – research is especially imperative, stresses Darbar, who presents research at national and international neurosurgery meetings. She earned first place for a poster presentation at the 2006 American Association of Neurosurgeons meeting in San Francisco. The abstract – on the efficacy of Gamma Knife radiosurgery for trigeminal neuralgia patients with multiple sclerosis – will be published in the *Journal of Neurosurgery*.

Research represents hope, in a field that can be very challenging for both patient and practitioner. "Many of the diseases we treat are not curable," says Darbar. "Neurosurgery is very difficult, emotionally. In some ways, you learn to detach. But sometimes, no matter how hard you try, you are deeply affected. You are human."

Neurosurgery is also very physically demanding, according to Darbar. "Sometimes you get so tired – but that's residency, not just neurosurgery. And the more you do, the more conditioned you become."

Darbar uses exercise as an antidote for the legendary stress of

neurosurgery. “A lot of my colleagues train for marathons and Iron Man competitions,” she says.

Early in her residency, Darbar worked 120 hours a week. In 2004, the resident’s work week was cut to 88 hours. “With the new limits, life is a little more sane. You can carve out time for a long run.”

Interlude

Now in her fourth year of residency, Jennings is in research mode, investigating neuron signaling in the laboratory of Mary Lou Vallano. Their findings may provide important insights into neurodegenerative disorders.

The orderly rhythm of research offers a welcome interlude before her two final clinical years. Jennings suspects she will subspecialize in pediatric neurosurgery, and her eyes widen with excitement when she describes the ever-expanding array of interventions, from Gamma Knife to deep brain stimulation.

“Sometimes it seems surreal, the things I’m seeing and learning,” says Jennings. “The hours are long, and it’s emotionally demanding. But if I can do something for 36 hours straight and still love it – I know I’m in the right place.”

By Heart

Both Jennings and Darbar take pride in the fact that two 2006 graduates of Upstate’s College of Medicine are studying neurosurgery – at Duke and Mount Sinai – after rotating through their program. “I’m sure we’ll all stay in touch,” says Darbar. “The women in this field know each other by heart.”

Jennifer Jennings MD, fourth-year neurosurgery resident

Trisha Torrey, right, host of HealthLink on Air, interviews University Hospital internist Lisa Kaufmann MD, clinical professor of medicine, about her work with stress reduction and "mindful eating."

UNIVERSITY HOSPITAL LAUNCHES

HealthLink on Air

9 A.M. SUNDAY MORNINGS ON WSYR/570 AM

Since it's impossible to convey the complexity of academic medicine on a billboard – or in a sound bite – University Hospital has launched a one-hour weekly radio program that shares the expertise of its own and other health care professionals.

HealthLink on Air airs 9 to 10 a.m. Sundays on WSYR, 570 AM. Because guests work on the unpredictable front lines of medical care, the program is taped, not live. But listeners are encouraged to leave feedback, topic suggestions and questions at www.healthlinkonair.org or by calling 877-464-4545.

Defining the Academic Difference

"For years, we've been using the phrase 'the academic difference' to distinguish University Hospital from its hospital colleagues," says Patricia Numann MD, medical director of HealthLink on Air. "Now we have an hour every week to talk with the remarkable people – doctors, nurses, scientists, therapists, patients, community activists and more – who help us deliver that academic difference."

SUNY Upstate's educational mission inspired the creation of HealthLink on Air. "We wanted to make the community our classroom, because informed patients are healthier patients," explains Numann. "They are alert to symptoms. They understand the power of prevention. They share responsibility for their own health."

The new radio program also evolved from the popular Health Link seminars at University Hospital's learning center (and also home to the OASIS senior program) in ShoppingTown Mall. Both venues recruit the hospital's medical experts to help the public navigate an increasingly complex health care arena.

Easy to Swallow

While HealthLink on Air addresses serious medical issues, its tone is far from somber. "It's very upbeat, conversational and engaging," reports Trisha Torrey, host of the new program. "Medical news doesn't have to be a bitter pill to swallow – it's fascinating to explore the different perspectives and layers of expertise available at University Hospital."

Torrey, a longtime Syracuse resident, is an authority on medical consumerism and patient advocacy – and author of the biweekly *Post Standard* column, Every Patient's Advocate.

"Our guests are medical experts, but we talk about health and medicine in plain English," says Torrey. "I'm not a medical professional or an insider. I'm 'Every Patient's Advocate,' with lots of questions. My goal is to help listeners become more informed, more discerning and more responsible for their health and health care."

Each episode of HealthLink on Air features an in-depth interview with a University Hospital expert, on topics such as stroke, trauma, depression, aging, concussion or the Golisano Children's Hospital at University Hospital, which is approaching its first phase of construction.

"Our guests bring a wealth of inside information to the radio show," says Melanie Rich, University Hospital's director of Marketing and University Communications and producer of HealthLink On Air. "They are also very engaging. If you practice in an academic medical center, you are very comfortable teaching – medical students, nursing students, residents and patients."

Empowerment

"For most HealthLink on Air guests, teaching is a critical part of their jobs," says Rich. "This program turns Central New York into a huge classroom. Our listeners become students – and empowered patients."

HealthLink on Air shows also include segments covering headlines, health tips, recipes, medical trivia, community conversations and a calendar of health-related events.

Torrey also offers a weekly segment on Patient Tools – strategies for becoming better health care consumers.

Beyond the Headlines

The Health Headlines segment is designed to both update and stimulate listeners. "We are not just parroting what we've all read about health this week," says Torrey. "We're training our listeners to be more discerning about the daily flood of health news. Headlines often oversimplify medical studies, which can be very detailed and applicable to select patients only.

"Breaking news on hormone replacement therapy (HRT) is a good example of the need to dig deeper and ask a lot of questions," Torrey continues. "Several recent HRT studies seem to reach contradictory conclusions. In fact, the studies apply to very specific groups of patients – for instance, women who have been on HRT for 20 years or more. The findings are not universally applicable. That's why we need to read beyond the headlines."

Ultimately, says Torrey, patients are advised to use health news as a springboard for discussions with their own doctors. "We've all heard about women who stopped HRT after reading alarming headlines," she says. "We checked with Dr. Numann, the HealthLink medical director, who said it can be dangerous to discontinue a drug without a discussion with your doctor."

"If there's one overriding takeaway message from this program," Numann stresses, "it's that every significant medical decision merits a discussion with your doctor."

Guests of Honor

Another HealthLink on Air segment features community conversations with Central New Yorkers such as Chris Arnold, whose daughter, Paige Arnold, was a patient at University Hospital's Center for Children's Cancer and Blood Disorders.

Paige died in 1994, from complications of a bone marrow transplant. But her brave spirit inspired Baldwinsville's annual Paige's Butterfly Run.

In the past 10 years, this popular event has raised close to $450,000 for pediatric cancer research and family support services at University Hospital as well as for scholarships in Baldwinsville.

"There are many inspiring stories about University Hospital patients and families," notes Rich. "This weekly radio hour gives us an opportunity to talk personally with families like the Arnolds, who have rallied the community and turned a personal tragedy into positive energy."

Encourage Interaction

Audience interaction is an important goal of HealthLink on Air, so there's a dedicated phone line, where listeners can chime in on the weekly topics, make suggestions, or seek immediate advice from University Hospital's Health Connections service, which is staffed 24 hours a day by registered nurses.

This portrait of Robert B. King MD by C. Schmidt hangs in University Hospital's lobby.

DEDICATED TO ROBERT B. KING, M.D.

As a pioneering neurosurgeon and chair of the Department of Neurosurgery (1957 – 1996), Robert B. King MD has long been a catalyst for brain inquiry at SUNY Upstate Medical University. He established the region's first Neuroscience Intensive Care Unit (NICU) and the nation's first neurosurgery residency program to require two years of laboratory research. He also established the Research Foundation of the American Association of Neurological Surgeons. Dr. King set the bar very high for the practice of neurosurgery, for the relentless pursuit of research and for the education of neurosurgeons nationwide. He continues to enlighten our campus with his compassion for patients and deep understanding of the human brain.

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