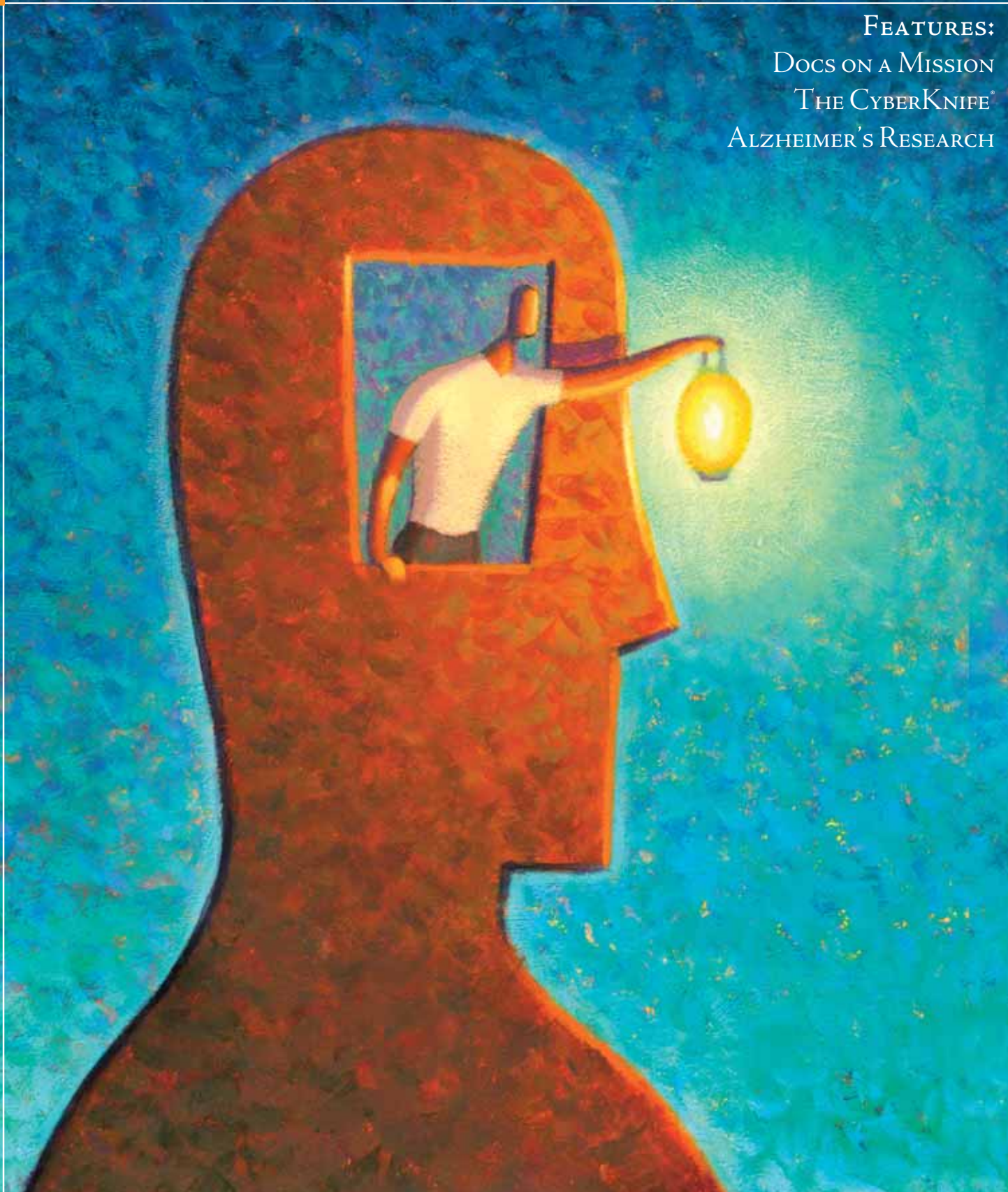


FRONTIERS

FEATURES:
DOCS ON A MISSION
THE CYBERKNIFE®
ALZHEIMER'S RESEARCH



The University of Tennessee Medical Center and the University of Tennessee Graduate School of Medicine Frontiers

3rd Quarter 2005

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Frontiers is a quarterly magazine produced by The University of Tennessee Medical Center and The University of Tennessee Graduate School of Medicine. This publication was designed to showcase the unique benefits of having an academic medical center in East Tennessee.

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THE UNIVERSITY of TENNESSEE | **UT**
Graduate School of Medicine

UT THE UNIVERSITY OF TENNESSEE
MEDICAL CENTER

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SETTING OURSELVES APART...

Compassionate Care • Academic Excellence • Comprehensive Research



 **THE UNIVERSITY OF TENNESSEE
MEDICAL CENTER**

EXPANDING THE FRONTIERS OF MEDICINE.®



August 2005

On behalf of the members of our Board, our medical staff, our nurses and other health professionals and our other employees, I am pleased to welcome you to the first edition of *Frontiers*.

The University of Tennessee Medical Center is one of only 161 academic medical centers in the United States and we are extremely proud of our almost 50 year history of providing exceptional patient care, respected medical education, and innovative research for the citizens and medical community of East Tennessee. We take our responsibilities seriously and look forward to continuing this role in the years ahead.

Our objective in publishing *Frontiers* is to share with you the many facets of an academic medical center. Our patient care, teaching and research programs compliment and support each other and, as a result, the University of Tennessee Medical Center is recognized as the region's Level I Trauma Center, home to the region's kidney and pancreatic transplant programs, the Tom and Katherine Black Neonatal Intensive Care Unit, the Heart Lung Vascular Institute, the Brain and Spine Institute and the Cancer Institute. Each of these initiatives contributes to our strength and the services we provide.

Frontiers will provide you with a unique look at the people and programs of the University of Tennessee Medical Center. This first edition focuses on issues related to the brain and spine. Welcome and thank you for your continuing support.

Sincerely,

Joseph R. Landsman, Jr.
President & CEO



August 2005

Dear Friends:

The University of Tennessee Graduate School of Medicine is pleased to be a part of the University of Tennessee Medical Center and we want to welcome you to the first edition of *Frontiers*. The strength of the University of Tennessee Medical Center is in the unique combination of outstanding patient care, advanced medical education and complimentary world-class research. The University of Tennessee Medical Center physicians have a strong base because they teach and care for patients. Our research is recognized for its practical and clinical applications and the result is the highest level of care for those patients and families we serve.

Frontiers provides us an opportunity to share with our many communities and constituencies the advances in patient care, the breakthroughs in research and the people and programs that make this a truly outstanding academic medical center.

We hope you enjoy learning more about the University of Tennessee Medical Center and the University of Tennessee Graduate School of Medicine through this and future issues of *Frontiers*.

Sincerely,

Michael R. Caudle, MD
Dean
UT Graduate School of Medicine

From left, Dr. John Parham, Dr. Greg Blake, and Dr. David Stockton



Docs on a Mission

Across Town...and Across the Globe

Sickness, pain, and suffering know no geographic boundaries.

Fortunately, neither do many concerned doctors and nurses at

The University of Tennessee Graduate School of Medicine.

These dedicated medical professionals know that medicine, and those who practice it, are needed not only here at home but also around the world, and they stand ready to respond.

For many people, the idea of providing medical care to foreign areas conjures up vivid images of a rain forest or the sweltering heat of the tropics. Surprisingly, these images sometimes are quite accurate. Answering the call to help the sick, injured and hopeless can take these professionals anywhere—including just around the corner.

Associate professors of family medicine in the UT Graduate School of Medicine are among those that answer the call right here at home. Larry Davis, MD, MPH, shares his knowledge to help the working uninsured at downtown Knoxville's InterFaith Clinic.

For others, like Ken Bielak, MD, MPH, the need at Child and Family Tennessee is greatest. Steve Roscos, MD, MPH, helps refugees receive medical care and establish themselves in East Tennessee through a local Bridge Program. These doctors and other UT personnel regularly stand stalwart in the “trenches” of their own city’s needs.

Other countries’ trenches, however, are more muddy, and answering the call means much more primitive conditions.

Imagine working in a 10-bed makeshift hospital in an abandoned schoolhouse.

Imagine trying to meet the needs of thousands in a canvas clinic on a tsunami-ravaged coast.

Imagine confronting patients with malaria, undiagnosed cancers, limbs deformed from broken bones that were not properly treated, and babies that have never received immunizations or vitamins—problems that rarely occur in the United States.

These images are just a few of many challenges that assault medical professionals who travel to remote areas around the world. They bring humanitarian aid, develop healthcare programs, teach local residents and perhaps even offer spiritual hope to despairing people. In return, they come back as better doctors.

“We shipped tens of thousands of medicines to El Salvador to treat acute illnesses, parasites, wounds and other conditions. We go and we care.”

David Stockton, MD, MPH, and UT Graduate School of Medicine associate professor of family medicine, recently trekked to Indonesia to bring medical aid to Banda Aceh, a small town in Sumatra nearest the epicenter of the tsunami that struck countries bordering the Indian Ocean on December 26, 2004. This tsunami is now recognized as the third largest natural disaster in world history, killing more than 310,000 people.

“It was relief Olympics,” Stockton recalls. “There were 3,000 relief workers in Banda Aceh, alone.”

Stockton went with a group associated with International Medical Corps. They were equipped with an emergency health kit packed with enough medications and supplies to help 10,000 people for three months.

“I found the organization on the Internet, and I volunteered to go,” Stockton explains.

Most of these physicians use personal leave during their medical mission trips. But, when teaching opportunities arise, doctors and other professionals find that their classrooms or labs have shifted to another time zone—and a different reality.

On a recent trip to China, Stockton and Dr. Moses Benevidas, a third-year medical resident, formed a professional exchange program with Qingdao Municipal Hospital. This affiliation allows UT residents to train in the Chinese hospital, while medical professionals from the Chinese hospital can visit UT Medical Center to observe and learn. Both sides benefit from experiencing other cultures and sharing their knowledge.



Resident Dr. Andrew Deroo brings a moment of delight to a child seeking medical treatment in El Salvador.



Dr. Fletcher Goode (left) explains eye exam procedures to residents Dr. Andrew Deroo (back) and Dr. Darby Miller during their medical mission trip to El Salvador.



Dr. Ann Lankford holds a young Salvadoran girl after treating her leg for burns.

Sharing a spiritual message also is important to some, including Jon Parham, DO, MPH, associate professor, and Gregory Blake, MD, MPH, professor and chairman of UT Graduate School of Medicine's Department of Family Medicine. Parham has embarked with medical mission groups to places as diverse as Albania, St. Kitts, Nevis, Montserrat, and Guyana. Most recently, he joined more than 40 healthcare professionals to travel to El Salvador with the volunteer agency, Christian Medical and Dental Association.

"In four and a half days, we saw 2,550 patients," Parham says. "We shipped tens of thousands of medicines to El Salvador to treat acute illnesses, parasites, wounds, and other conditions. We go and we care."

Parham, like other medical volunteers, tries to educate patients about their own health. "If you show people you care, maybe they will take their own healthcare more seriously. Maybe patient education will last longer than medicines," he reflects.

"Sometimes medicine is not as important as the touch we give to people," said Blake, who shares Parham's interest in spiritually based medical support. "Many patients don't need medical treatment at all. They are thirsty for spiritual or emotional help, so we show them that someone cares."

Simple compassion can be taken for granted in the modern hospitals in the United States, where having a chaplain available to patients is commonplace. Not true in other parts

of the world. Blake once led a team of professionals and residents to Chile, where in addition to teaching Advanced Cardiac Life Support (ACLS) to medical personnel there, the team educated religious leaders about starting a clinical pastoral care program in the local hospital.

"Many patients in the Chilean hospital have traveled for hundreds of miles and are alone," Blake says. "They have no one to provide support, so a pastoral care program will help doctors care for the patient physically and spiritually."

Residents and those holding fellowships often accompany UT physicians on medical mission trips. They provide medical assistance, but they also gain knowledge and experience to be better prepared for the time when they will practice medicine independently. In El Salvador, residents got first-hand experience working with patients in difficult circumstances.

"They will carry these experiences with them, which will make them better doctors," Parham says. "Many will continue to provide humanitarian aid both locally and in foreign areas."

On a mission to Thailand, Tamara Davis, MD, Geriatric Fellow, UT Graduate School of Medicine, worked with Blake to treat patients of all ages. Davis observed diseases in advanced stages and learned to rely on clinical skills rather than technology to diagnose and treat patients—an important

lesson for an American physician.

"Sometimes medicine is not as important as the touch we give to people."

The eyes of young survivors of the Indonesian tsunami often told the tale of the terrible destruction.



Medical professionals worked to ensure young and old were immunized to avoid infections long after the physical evidence of the Indonesian tsunami had vanished.



Dr. Greg Blake (far left) listens as his translator (back to camera) conveys health information from an elderly patient (in hat) during a medical mission trip to Sumatra.

Doctors and nurses pay for their own trips, and if the medicines they need are not donated, they purchase those as well. On one particular venture to Brazil, the doctors arrived but the medicines did not, so Blake and others had to purchase a massive amount of medicine from pharmacies in the area. Although these professionals may come home with empty pockets, they do not seem to feel a sense of loss from the experience. As Parham says, "I leave a much richer person than when I arrived."

"I leave a much richer person than when I arrived."

"The need for basic healthcare in these destinations is so much greater than here in the States," Stockton says. "I leave realizing that I shouldn't take for granted the technology and knowledge we have. At the same time, though, I gain from watching doctors practice the art of medicine without technology. Real medicine is more than technology."

"When you see the joy in an elderly man's face whom you've helped to walk without a crutch, that's joy," Parham points out.

"When you leave knowing you immunized thousands of children, you know you've made a difference," Stockton adds.

The effect humanitarian trips can have on physicians is felt in their hometown. "When we are in the field, we remember why we went into medicine," Blake says. "Back home, in an environment of intense focus on medical costs and insurance constraints, seeing and filling dire human need softens our response to people."

So whether they are providing for needs around the block or around the world, one simple truth is clear: they emerge as better doctors.

-LL

Gregory H. Blake, MD, MPH

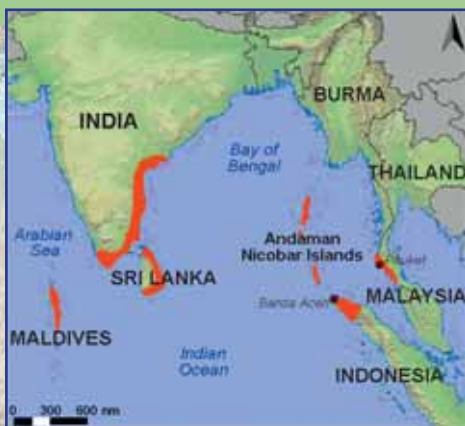
UT Graduate School of Medicine physician Greg Blake received his Bachelor of Arts from Texas Tech University, his MD from the University of Texas Health Science Center, Southwestern Medical School, and a master's degree in public health from the University of Oklahoma Health Sciences Center's College of Health. A professor and chairman for the UT Graduate School of Medicine, Department of Family Medicine, Blake lives in Knoxville with his wife, Mary Helen, and has three children: Bryan, 31; Denise, 27; and Karen, 25.

Jon S. Parham, DO, MPH

UT Graduate School of Medicine physician Jon Parham earned a Bachelor of Arts degree in general science from Harding University in Arkansas, a Master of Public Health from Boston University's School of Public Health, and his DO from the University of Health Sciences of Osteopathic Medicine in Missouri. Currently, he serves as associate professor in the UT Graduate School of Medicine, Department of Family Medicine. Parham, his wife, Dianna, and their children, Alex, 8 and Cameron, 6, live in Knoxville.



In the aftermath of the tsunami that struck Indonesia and other areas in December 2004, parents and children sought treatment from medical missionaries.



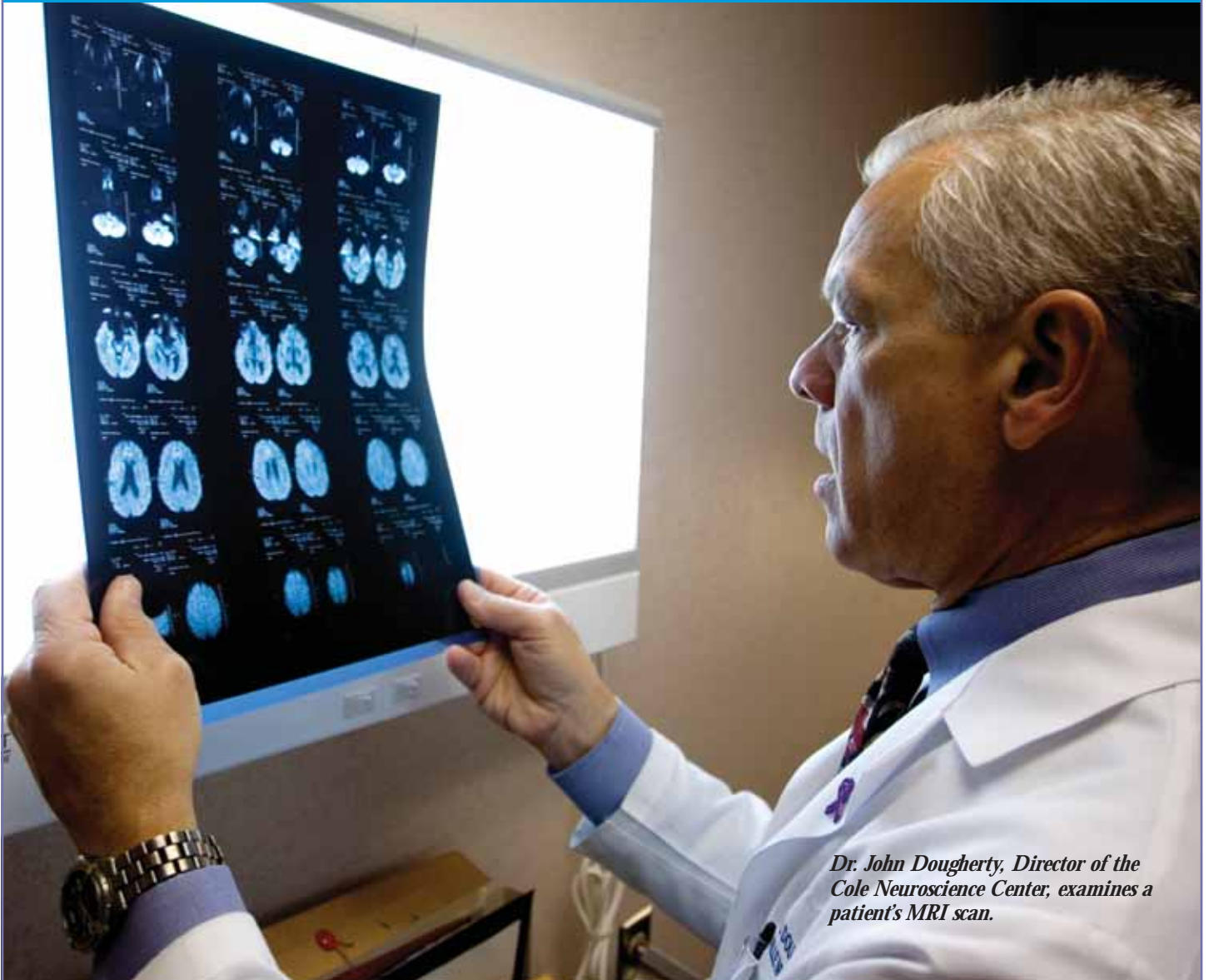
The areas in orange were most affected by the tsunami.

M. David Stockton, MD, MPH

Physician David Stockton serves the UT Graduate School of Medicine as associate professor of Family Medicine and director of the Division of Preventive Medicine. He received Bachelor of Arts and Master of Public Health degrees from the University of Tennessee in Knoxville and his MD from the University of Tennessee in Memphis. Residing in West Knoxville, Stockton and his wife, Lisa, have three children: Ben, 23; Betsy, 20; and Jess, 17.

A Cure May be Just a Tremor Away

*Cole Neuroscience Center Discovers Breakthrough Research
that Leads to Management of Parkinson's Disease*



*Dr. John Dougherty, Director of the
Cole Neuroscience Center, examines a
patient's MRI scan.*

Robert Cole's Dream

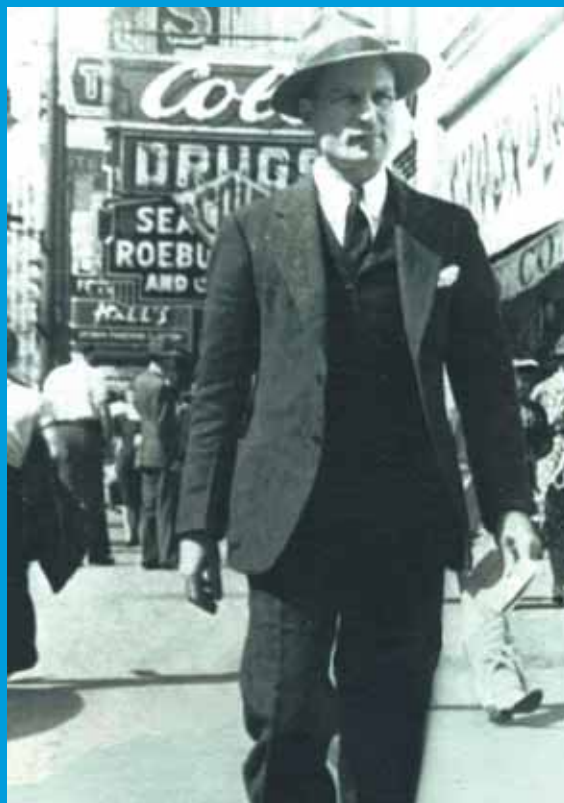
He was the first to admit it. He had lived the American dream. After business school, a cash-poor Robert Cole moved to Knoxville and opened a drug store. Four decades of relentless work and sacrifice followed, resulting in owning 35 stores and socializing with the region's rich and powerful. He didn't think much about the little hand tremor when he first noticed it, but over the next few months, it appeared more frequently. He tried laughing it off, thinking it was stress or too much coffee during his hectic days. After six months of the constant tremor, it spread to his other arm, and the jokes stopped.

Cole went to his internist, who thought it probably was a mild aging tremor. He then consulted a neurologist, who listed several diagnostic possibilities, some worrisome. Increasingly uneasy about his future, Cole talked to another neurologist for a second opinion. This time he received an answer. He had Parkinson's disease, an enigmatic, progressive, neurodegenerative, and fatal disease. There was no treatment and no cure in sight. Cole's American dream was about to become a nightmare.

Parkinson's disease principally is caused by the degeneration of a key neuronal circuit originating in the brain stem, which projects to many parts of the brain and influences posture, movement, mood and autonomic function. These neurons communicate with other neurons in the circuit by releasing a neurotransmitter called dopamine. As the neurons die and brain levels of dopamine decline, the critical input of the neurons wanes and the circuit malfunctions, resulting in the characteristic symptoms of the disease.

As with Cole and, more recently, Pope John Paul II, Parkinson's disease usually presents as a rhythmic resting tremor in an arm or leg. With time, muscle rigidity (known as the cogwheel phenomenon), slowness of movement, stooped posture, and loss of facial expression develop. Approximately 25 percent of patients also develop dementia.

Some would say Cole was well prepared for his struggle against the disease. Opening a drugstore in the middle of the Depression had been a battle. He had won that one, creating an empire of 35 stores serving three Southern states. But this fight would be different. As a businessman, he wrestled with budgets and suppliers—things he understood and could see. Now he was fighting an unseen foe that had defied the efforts



Robert Cole walks down Gay Street in downtown Knoxville. The Cole drugstore sign is behind him.

Image courtesy of the Cole family.

of physicians for centuries. He brought the skills he had learned in business to his new struggle. After reading and consulting all he could, he finally recruited others to join him in his battle. Initial recruits included the late neurosurgeon Frank Turney, M.D., and neurologists John Dougherty, M.D., and Michael Eisenstadt, M.D. With their help, he became one of the first in the region to try the revolutionary new treatment, L-dopa and carbidopa (Sinemet). This treatment gave him some good years and more time to plan.

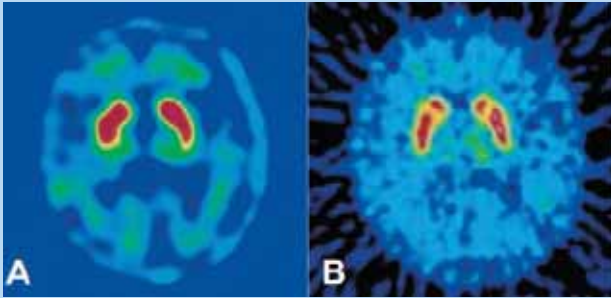
In 1970, Cole and his wife, Monica, funded the creation of the Cole Neuroscience Center that bears his name. The center's mandate is to promote: 1) patient care regardless of ability to pay, 2) physician education, and 3) research in Parkinson's disease.

The prevalence of Parkinson's disease in the U.S. is 150-200 per 100,000 or 0.3 percent of the population. This increases exponentially after age 65, jumping to 3 percent of those at or over retirement age. Although Parkinson's exists worldwide, it is more common in whites than in blacks or Asians.



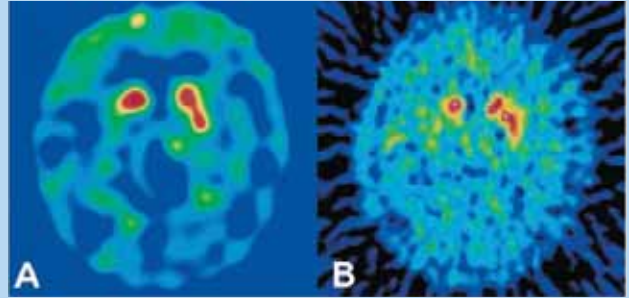
A patient prepares for a PET scan.

Single Photon Emission Computerized Technology (SPECT) and Positron Emission Technology (PET) identify changes in metabolic activity in the brain.



Healthy Patient

Normal brain activity is seen on (a) representative transverse SPECT image (b) PET image



Patient with Parkinson's Disease

Decreased brain activity is seen on (a) representative transverse SPECT image (b) decreased brain activity in area controlling movement is seen in a PET image

Images courtesy Dr. Yongxia Xongxia

Cole Neuroscience Center

Each year the Cole Neuroscience Center serves more than 1,000 patients with Parkinson's disease, 1,500 with Alzheimer's disease, and numerous others with neurodegenerative diseases, including epilepsy, movement or sleep problems, and various types of brain attack commonly referred to as "stroke."

The Cole Center has expanded to a staff of seven, including a social worker and consulting dietician. Providing early diagnosis, state-of-the-art care, and individualized treatment plans are key goals of the center. The results have been well worth the effort.

"With efficacious drugs, we have been able to prolong life and reduce the comparative death rate (of Parkinson's patients) to that of the normal population," Dr. Dougherty notes.

The armory used in the diagnosis and treatment of Parkinson's includes drug therapies and state-of-the-art brain-imaging techniques. The use of positron emission tomography (PET) is central to the center's mission. In 1982, PET was so new that its use with Parkinson's disease made headlines of the *New York Times*.

Monica Cole became aware of its potential and asked if PET could be brought to the Cole Neuroscience Center.

"Monica's determination was the driving force to get PET here," Dr. Dougherty recalls.

Led by George Kabalka, Ph.D., and collaborator Hildegard Schuller, D.V.M., Ph.D., the Cole Center is developing a series of single photon (SPECT) and positron emission tomography (PET) imaging agents that can be used for the diagnosis and study of Parkinson's and Alzheimer's disease.

This is being done in conjunction with new radio-labeling facilities established at UT Medical Center adjacent to the PET facilities. An early success was the radio-labeling of L-dopa for the detection of early Parkinson's disease.

Currently under development are radio-labeled cyclooxygenase-2 inhibitors, which stick to COX-2 in the brain. These will take advantage of the recent finding that COX-2 is elevated in Alzheimer's disease. Thus, radio-labeled COX-2 inhibitors, infused into the blood, should help identify early changes in Alzheimer's disease and facilitate diagnosis and research on its pathogenesis. The recent addition of Dr. Yongxia Zhou, an expert on multimodality imaging, expands the center's diagnostic and research capabilities to include integrated PET and magnetic-resonance imaging analysis.



George Kabalka, Ph.D.

With an expanding staff and new therapies and imaging techniques, the Coles' dream of conquering Parkinson's disease continues as ongoing research yields progress toward earlier diagnosis and better treatment. Like its founder, the Cole Center hopes to see its own American dream—a cure for Parkinson's disease—someday become a reality. -MJ

Cole Center Services

Senior Assessment Clinic

Provides diagnosis and treatment options for seniors with behavioral or cognitive impairment, including Alzheimer's disease and other types of dementia.

Treatment/medical management:

- Clinical trials with new medications
- Diagnostic imaging

Movement Disorders Clinic

Provides diagnosis, treatment and management of disorders such as Parkinson's disease, chorea, Huntington's disease, tremors and other movement disorders, and dystonias (Torticollis).

Treatment/medical management:

- Treatment planning to optimize patient functioning and quality of life
- New surgical therapies for Parkinson's disease
- Botulinum injections
- Clinical trials with new medications
- Neuro-imaging with the latest technology, including positron emission tomography (PET) scanning to image the brain

Comprehensive Epilepsy Clinic

Encompasses diagnosis, medical and neurosurgical treatment, and management of adults and children with epilepsy.

Treatment/medical management:

- Complete evaluation
- Medical management
- Surgical intervention
- Long-term seizure monitoring unit
- Complete range of diagnostic techniques, including PET and functional magnetic resonance imaging (MRI)

The Sleep Center

Provides comprehensive treatment and evaluation of unexplained problems with sleep that last over a significant time period. Disorders include sleep apnea, narcolepsy, restless legs syndrome, sleepwalking, nightmares, night terrors, and insomnia.

Treatment/medical management:

- Complete medical evaluation of diagnostic testing, including sleep studies, multiple sleep latency tests, and management of wake/sleep problems
- Conservative management of mild sleep-disordered breathing
- CPAP for sleep apnea
- Surgical treatment for upper airway problems
- Treatment of restless legs syndrome
- Treatment of narcolepsy
- Help with sleep hygiene



Mrs. Monica M. Cole with a portrait of her husband, Robert H. Cole

Cole Neuroscience Center Gift Funds

Cole Neuroscience Gift Fund

Established by the Robert H. and Monica M. Cole Foundation to provide resources to ensure continued excellence in research and education related to neurological diseases.

Thompson Alzheimer's Research

Supports Alzheimer's disease care, research and education.

William Edward Booker, Jr.

Neuroscience Endowment

Provides support for a lectureship in neuroscience.

Robert H. Cole Endowed Chair

in Neuroscience

Supports programs and research of the chair focused on neuroscience.

Cole Neuroscience Clinic Gift Fund

Supports training, educational materials, research grants and staff of the Cole Neuroscience Center.

Monica M. Cole Neuroscience Endowment

Supports neuroscience teaching, research and public service initiatives.



Healthcare Coordinator Erin Dean

1-877-UT-CARES

Healthcare Coordinators

Not many things in life are free *and* easy...

The University of Tennessee Medical Center is unique in its own way for more than one reason. We know life is hectic and when it comes to scheduling doctor appointments it can become overwhelming. We are here to change that.

In May 2004, the Healthcare Coordination program began with the goal of simplifying access to healthcare. The University of Tennessee Medical Center provides healthcare coordinators, similar to personal assistants, to make the process of arranging appointments as easy as one phone call.

For example, suppose it's time for your annual mammogram but you also need to find a dermatologist to take a look at a new spot on your face. How are you going to find time to do both? Our healthcare coordinators will try to arrange both of your appointments on the same day, so you can make just one trip.

When you call one of the qualified coordinators, they will collect all your information and take care of the rest. Whether it's requesting to have your old records sent to a new provider, or letting you know which specialists require a referral, the healthcare coordinators help set the University of Tennessee Medical Center apart.

"Although our service is for anyone, those who are new to the area probably benefit the most," says healthcare coordinator Jeremy Welch. "It always takes time to become familiar with a new community, so just think of how daunting it might be to

find a pediatrician, a primary care physician, or specialists like an OB/GYN or a cardiologist in a brand new place. One of the ways we can make things easier is by sending maps of the hospital and giving detailed directions. Hospitals can sometimes be confusing places to get around so, if needed, we'll even meet you at the front door of the Medical Center to lead you to the right place."

Modeled around the concept of a concierge service, this program seeks to provide top-notch customer service in a personal way.

"One of the things our patients appreciate is having one person to talk to. We often hear how much easier it makes the experience when they could turn to one person to coordinate needs with several providers. We are here for our patients and they know we want to help with simple requests or complex needs," adds healthcare coordinator Erin Dean. "It's a big time saver and people love it. We also mail patients the paperwork that they are usually asked to complete in the office. That way, they can fill it out in advance and bring it with them at their first appointment."

"We are here for our patients and they know we want to help with simple requests or complex needs."


While UT Medical Center is the only hospital in the area with this type of service, there are other programs like this across the country. Medical centers such as the Cleveland Clinic, Johns Hopkins, and Cedars-Sinai have similar services. In each setting, as is the case at UT Medical Center, coordinators are very knowledgeable about what makes their hospital unique and can tell you more about the specialty services available.

Call toll-free to 1-877-UT-CARES. After talking to one of the healthcare coordinators, you'll see why they were given this memorable telephone number—because they really do care.

-PI

The Revolutionary Technology of
CyberKnife®
Radiosurgery





While most patients don't understand the meaning of stereotactic, fiducials or linear accelerators, they can relate to the idea of a fast, painless, and non-invasive medical procedure. A revolutionary radiation procedure called CyberKnife now provides an alternative to surgery or conventional radiation for treatment of chronic pain and tumors.

The CyberKnife system consists of three components—a linear accelerator, a robotic arm and an X-ray guidance system. The linear accelerator produces the beams of radiation used to treat diseased areas, while the robotic arm precisely aims the radiation beam directly at the tumor or other problem area. Three-dimensional X-ray cameras compile frequent images of the patient during treatment to guide the radiation beam and adjust for patient movement. University of Tennessee Medical Center Neurosurgeon Dr. William Snyder, Jr. notes that “because of its pinpoint accuracy, the CyberKnife system offers hope to patients who cannot receive further conventional radiation therapy. Patients who are poor surgical candidates or who have inoperable tumors may also be treated with CyberKnife. It also can treat tumors of the spine with the same level of accuracy as in the brain.”

Although other systems such as Gamma Knife can deliver stereotactic radiosurgery, they are generally limited to treatments for the head only and require attaching a metal frame to the skull. In contrast, CyberKnife requires no frame and can deliver treatment in other areas of the body.

The CyberKnife procedure consists of three steps that can be completed in one day or spread across five days—all on an outpatient basis. Step one is the set-up. For head treatments, a soft mesh facial mask is custom made, which effectively holds the head steady during the treatment. For spine or body treatments, fiducials (metal markers) are placed near the tumor to guide the beam of radiation. Next, a computed tomography (CT) scan provides detailed information regarding the exact size, shape and location of the area to be treated. From this image, the CyberKnife team—consisting of a neurosurgeon, radiation oncologist and medical physicist—develops a customized radiation delivery plan.

The treatment plan tells the CyberKnife robotic arm the number, direction, and intensity of beams to deliver to the affected area. Dr. Robert Bertoli, a UT Medical Center radiation oncologist, explains, “The physicians outline the tumor or lesion to be irradiated, and mark the surrounding area where radiation should be minimized or avoided. The high-speed CyberKnife computer then performs millions of calculations to generate the optimal radiation delivery plan. Never in my career did I dream I'd be able to use this type of technology.”

Physicians and nurses alike praise the CyberKnife technology because it dramatically affects the quality of life for their patients.

Stereotactic Timeline

- 1951 — In Stockholm, Lars Leksell describes radiosurgery



- 1958 — In Uppsala, Sweden, B. Larsson applies a proton beam to neurosurgery

- 1965 — In Moscow, proton irradiation is used by V. Koroshkov

- 1967 — In Stockholm, Lars Leksell develops the first gamma knife procedures

- 1970 — In Stockholm, gamma knife is used for brain arteriovenous (AVM) malformation

- 1982 — Linear accelerator applied to radiosurgery

- 1992 — First commercial radiosurgery linear accelerator installed

- 1994 — Stanford, CA
First CyberKnife treatment of a brain lesion



- 1997 — Stanford, CA
CyberKnife used for arteriovenous malformation of the brain

- 2000 — CyberKnife used for lung diseases

Step three is treatment. The patient lies on a table while the robotic arm moves the linear accelerator around him, stopping at preset positions to fire a small beam of radiation at the offending area or tumor. The room is surprisingly quiet, with only the hum of the equipment and the buzzing noise of the invisible radiation beam. The patient feels nothing.

The radiation beams are delivered from different angles, but all intersect on the targeted area which receives a very high total radiation dose. The surrounding healthy tissue receives a very low, non-toxic dose. A typical treatment can be composed of 100 to more than 150 beams.

“The Cyberknife system offers hope to patients who cannot receive further conventional radiation therapy.”

**Dr. William Snyder, Jr.
Neurosurgeon**

Because the treatment is non-invasive, the patient can return home and resume a normal routine, generally with no pain or lengthy recovery process. There is no risk of hemorrhage or infection and there are rarely any side effects.

Physicians and nurses alike praise the CyberKnife technology because it dramatically affects the quality of life for their patients. As Dr. Daniel Green, medical director of Radiation Oncology says, “It is very gratifying to see such immediate pain relief for a patient who had such debilitating pain for 20 years.”

With the CyberKnife system in place, the University of Tennessee Medical Center now offers the latest advances in stereotactic radiosurgery. Physicians with the CyberKnife Center at the Brain and Spine Institute include a group of five board-certified neurosurgeons and two board-certified radiation oncologists who are familiar with the newest techniques in stereotactic radiosurgery. In addition, they collaborate with board-certified neurologists, neuropathologists and neuroradiologists, creating a multidisciplinary team that offers the best treatment options for patients throughout the East Tennessee region.

-BT

Dr. Robert Bertoli and members of the CyberKnife team discuss treatment with a patient.



Understanding Tumor Treatments

Stereotactic Techniques:

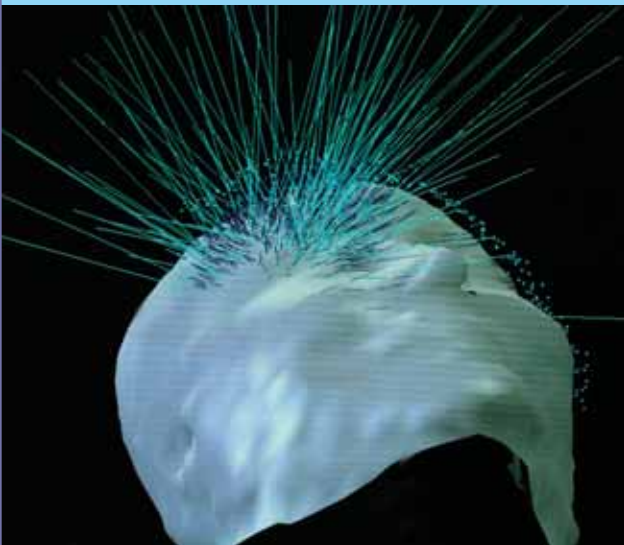
Computers are used to produce a three-dimensional image of the tumor. This 3-D view offers the physician a precise and accurate view of a tumor as well as its relationship to other vital parts. The 3-D image is obtained with the aid of pins, a compass (or Sextant) system, or C-arm equipment.

Radiosurgery:

Radiosurgery is not really surgery because no incision is required. Focused radiation is used to destroy a tumor. Because the radiation is more tightly focused on the tumor, a smaller dose can be used with far less damage to surrounding tissue.

Minimally Invasive Surgery:

While performed by surgeons, there is no incision, but only a series of small punctures, less than a quarter inch in size. Small cameras, tubes and equipment work through the incisions to reach the tumor. X-ray machines provide the surgeon with a three-dimensional enlarged view of the tumor and surrounding area. Once the appropriate treatment is performed, the incisions are sealed with an adhesive, called Permabond. No stitches needed.



*Illustration of radiation beams
Image courtesy of Accuray*



"It's a miracle in my life. God has blessed me," she smiles.

Wanda Thrasher sips iced tea with friends after enjoying a full day shopping, walking, and talking. It may seem like an unremarkable scene, but for Thrasher, it's like a dream come true. After living for almost two decades with excruciatingly severe pain in her face, Thrasher has been rescued by the CyberKnife team at UT Medical Center.

In 1986, Thrasher suffered severe injuries throughout her body when she was involved in an automobile accident. The head trauma caused a condition known as trigeminal neuralgia or tic douloureux, a disorder characterized by repeated episodes of severe facial pain. The intense pain she experienced could be triggered by any touch to her face: chewing or swallowing food or drink or even a gentle breeze of cool air could cause the trigeminal nerve in her face to erupt with the speed and severity of lightning.

"I was on several medications and still was in tremendous pain," Thrasher recalls. When the pain hit, she could not eat, drink or talk. Doctors had suggested brain surgery, but that frightened her even more than the pain and medications. Eventually, she found the CyberKnife treatment through her son.


Thrasher's procedure took approximately one hour and 30 minutes, although she says it didn't seem that long. "I felt relief right on the table," she remembers. The first question the team asked her was, "Do you have any pain or numbness?" Astonished, she replied, "I have none." The pain of almost twenty years was gone.

Thrasher's treatment was a success, and she actually could start thinking about a life with no more pain. "Without incisions or blood, I was able to get up and go home," Thrasher states, still amazed. "It's a miracle in my life. God has blessed me."

-WB

Minimally Invasive Surgery

and the Alleviation of Back Pain



In 2004, the office of the U.S. Surgeon General issued its first-ever report on the nation's bone health. It warned that by 2020, one in two Americans over the age of 60 would be at risk for fractures—primarily in the wrist, hip and spine—from osteoporosis or low bone mass.

While statistics about the future are alarming, even today back pain is second only to colds and upper respiratory infections as the main reason people visit a physician. And as the country's population ages, conventional surgical techniques for the treatment of chronic back pain are receiving scrutiny. Advanced technologies are facilitating new surgical methods, and more patients are now able to find relief from what had been thought to be untreatable medical problems.

Our doctors are embracing these emerging technologies and utilizing them in new and dramatic ways. When neurosurgeons and nurses speak passionately of new high-tech procedures and the stunning results they see in their patients, their enthusiasm warrants a closer look.

Here are two examples of how neurosurgeons are revolutionizing spinal surgery with minimally invasive techniques.

Balloon Kyphoplasty

Often, what people think of as everyday back pain and stooped posture that is said to be “just a normal part of aging,” could actually be a compression fracture in a vertebra. This pain is now only a memory for patients who have experienced balloon kyphoplasty.

Osteoporosis, a condition in which bones become weak or brittle, and certain types of cancer can cause vertebrae to fracture and collapse. Traditional treatments for fractured vertebrae include bed rest, pain medication and back braces. While these treatments temporarily relieve some of the pain, they do not address the underlying cause of the discomfort and frequently reduce a person’s ability to participate in daily activities.

Balloon kyphoplasty, in contrast, is a minimally invasive treatment that requires only two needle size incisions. The procedure usually takes less than an hour for each fractured vertebra, and most of that time is devoted to the precise positioning of equipment. Neurosurgeon James A. Killeffer, M.D., demonstrated how two X-ray cameras—a very specialized “C-Arm”—are positioned around the patient to generate 3-dimensional images on a computer to help guide precise placement of tools during the procedure.

These small incisions are made on the patient’s back and needles are inserted into the site of the fracture. An orthopedic balloon is then inserted through a needle and guided into the fractured or collapsed vertebra. “When the balloon is inflated,” Killeffer says, “it gently pushes the collapsed vertebra to the correct position. As the balloon is deflated and removed, the cavity in the vertebra is filled with surgical bone cement helping prevent further collapse.”

According to Killeffer, most patients experience a significant reduction in back pain immediately. Because they are able to return to their normal activities, their quality of life can improve dramatically. Former back pain sufferers now can enjoy walking, shopping, working and simply enjoying life without pain thanks to balloon kyphoplasty and surgeons like Killeffer.



*Dr. James Killeffer,
Neurosurgeon*

Balloon Kyphoplasty



*Fractured Vertebra
Spinal fracture, also known as vertebral
compression fracture (VCF)*



*IBT Insert
Through 2 small incisions, the doctor
creates narrow pathways into the fractured
bone and inserts 2 KyphX® balloons*



*IBT Inflated
The balloons are inflated to raise the
collapsed vertebra, then deflated and
removed, leaving a cavity in the bone*



*Filling the Cavity
The cavity is filled with a bone cement to
support the surrounding bone and prevent
further collapse*



*Internal Cast
The cement forms an internal cast that
holds the vertebra in place*

Spinal Fusion

Back and leg pain can be linked to many different causes, including herniated discs, spinal stenosis and spondylolisthesis (instability or abnormal motion between two or more adjacent vertebrae). Spinal fusion surgery can stabilize such conditions and eliminate the patient's pain.

Traditional "open" spinal surgery for spinal fusion requires the surgeon to make a 4- to 6-inch incision over the area of instability, directly exposing the spinal vertebrae by stripping the overlying muscles away from the spine. The fusion is performed by removing bone grafts from the patient's hip (through a separate incision) and layering the graft over the unstable vertebrae. Screws are placed in the affected vertebrae and connected with rods to provide immediate stabilization of the unstable vertebrae. The bone grafts eventually fuse the two vertebrae together to provide permanent stabilization. Although this surgery proves successful in achieving stability, there can be significant blood loss and pain.

Dr. William S. Reid, Jr., Neurosurgeon



Due to recent technical advancements, UT Medical Center neurosurgeons, such as Dr. William S. Reid, Jr., are able to perform a spinal fusion through small, 1/2- to 1-inch incisions, greatly reducing surgical trauma to the back muscles and reducing blood loss. Dramatic progress in this technique has resulted in improved fusion rates, shorter hospital stays, and a more active and rapid recovery as compared to the "traditional way."

One of the most significant technical advances in this arena is frameless stereotactic imaging. Also known as surgical navigation, this technique combines the use of 3-D X-ray images and a computerized guidance system. The 3-D images are created with a specialized fluoroscope that performs a CT scan in the operating room. This fluoroscope is especially unique and is only available in Knoxville at UT Medical Center. Using the 3-D images and the image guidance system, the surgeon can precisely place bone screws through very small incisions.

"The high-resolution video monitor vividly displays the surgical site as we manipulate the precision instruments through an incision that is less than an inch long," Dr. Reid says. "During the procedure, images from repeated X-rays and CT scans help to continuously monitor the surgical site."

Another technical advance used with the image guidance system is the Sextant System, which places stabilizing rods through the tops of the bone screws to lock the screws together. This can also be performed through a 1/2-inch incision, minimizing surgical trauma.

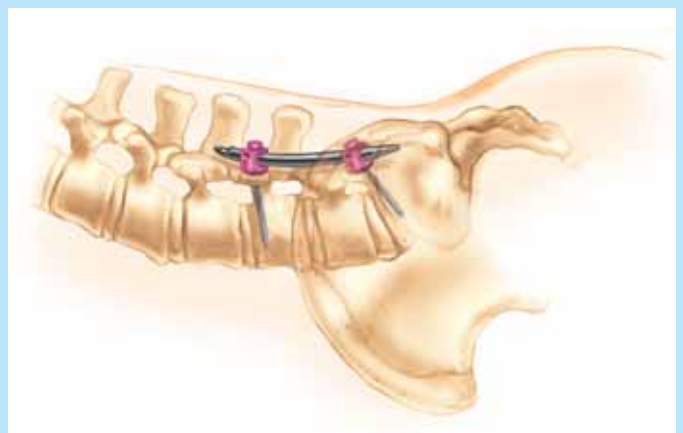
Technical and scientific advances in radiology, computerized surgical navigation and surgical instrumentation are now making it possible for patients to undergo complex spinal surgery with less pain and a shorter recovery—great news for those hoping to find relief from pain.

-BT

Minimally Invasive Spinal Fusion



Percutaneous placement of pedicle screws and connecting rod



Final placement of screws and rod using minimally invasive technique

Images courtesy of Medtronic, Inc.



Stalking a Cure

The artwork on Dr. Wetzel's wall dominates his office.

It tempts visitors to read a great deal of symbolism into the Guy Coheleach painting that depicts a pool of sharks gracefully circling in placid blue water. Ronald Wetzel, Ph.D., laughs about his painting of predators. "It's on loan to me. I chose it because I like it," he explained.

And it is clear that there is no symbolism, only science, in Wetzel's research. He is devoted to the scientific understanding of the underlying causes of neurodegenerative disease.

Wetzel is a world-renowned expert in protein folding, and is regularly featured in medical and scientific journals for his research. He is sought as a lecturer on the topic at universities, research facilities, and conferences around the world. In addition, he is a professor at The University of Tennessee Graduate School of Medicine and an associate professor for the UT Departments of Biochemistry and Chemistry.

For more than twenty-five years, Wetzel has studied protein folding. During that time, he and his network of assistants and colleagues have linked misfolded proteins to Alzheimer's Disease, Huntington's Disease and several other neurodegenerative diseases.

Proteins are biological workhorses that fold into precise, complex shapes required for activities such as supporting the skeleton, controlling senses, moving muscles, digesting food, building new cells and defending against infections. There are tens of thousands of proteins in the human body and each of the different types of proteins fold into the specific shape required for its job. Although this folding process is very complicated and occurs within a split second, it almost always leads to successful formation of the correct shape required for its biological function. That "almost always" is the problem. Wetzel and colleagues have discovered that occasionally a protein will misfold, and now their challenge is to discover how and why misfolding occurs.

"Misfolded proteins are present in several diseases," he said. "They build up in cells and create problems associated with diseases such as Alzheimer's, Huntington's, Parkinson's, Lou Gehrig's, and Creutzfeld-Jacob, which is a disorder related to mad-cow disease."

But understanding proteins and how they fold—or misfold—is only part of the equation. Wetzel is also concerned with how aggregates (groupings of misfolded proteins) kill cells or alter their function. One area of interest is a series of housekeeping molecules, appropriately called chaperones, which are responsible for overseeing the folding of proteins.

"One possible explanation for the toxicity of protein aggregates might be their ability to overwhelm the molecular chaperones. In addition, decreases in the efficiency of molecular chaperones, due to aging or the result of disease, might help explain why large amounts of misfolded proteins accumulate in some disease states in the first place," Wetzel explained.

Glossary of Terms

Aggregation – the formation of deposits; a concentration of unfolded or partially folded proteins

Assays – to analyze in search of one or more valuable compounds

Amyloid – clumps of abnormal proteins

Amyloid Fibrils – twisted strands of proteins in nerve cells

Chaperones – specialized molecules that accompany proteins and oversee their folding

In Vitro – experiments in the laboratory

In Vivo – experiments in the living cell

In Silico – experiments using computer models

Plaques – clumps of dead nerve cells containing abnormal protein called amyloid

Prions – normal human protein particles when folded properly; when folded abnormally leads to disease

Therapeutics – a branch of medical science dealing with the application of remedies for diseases

Ongoing research support comes from:

- The National Institute of Aging of the National Institutes of Health
- The American Health Assistance Foundation
- The Alzheimer's Association
- The Heredity Disease Foundation

Dr. Wetzel's Amyloid and Neurodegeneration Research Labs were initiated in 1997 by a gift from Mr. Lindsay Young of Knoxville in support of the Center for Research and Treatment of Alzheimer's Disease and Amyloid-Related Disorders.

Alzheimer's Disease Research Gift Fund has been established to provide "seed" money for promising research ideas. Donations to this fund help pay for equipment, supplies and graduate level and post-doctoral students to assist in Alzheimer's research initiatives. For more information, contact the UT Medical Center Development Office at 865-544-6611.



The advanced technology in his laboratory helps speed the research. The nuclear magnetic resonance spectroscopy (NMR) and mass spectrometry (MS), conducted in collaboration with other scientists at UT, help Wetzel and his team analyze the structures of misfolded proteins. Various kinds of microscopy make it possible to observe aggregates in cells and tissue.

The pressure is on Wetzel as he and his colleagues probe into the fundamental beginnings of neurodegenerative diseases. The goal of this research is to eradicate or at least slow the progress of these debilitating neurological diseases. More than ten percent of people over the age of 65, and perhaps half of those over 85, are affected by Alzheimer's Disease—a disease that kills 100,000 Americans yearly and costs society over \$82 billion annually to care for its victims.

Wetzel understands the urgency of his research. He is dedicated to the quest for answers that will offer prevention and treatment of these diseases. His challenge is to keep searching—one molecule at a time.



UT Graduate School of Medicine researcher Dr. Ronald Wetzel received his Bachelor of Science degree in chemistry from Drexel University and his Ph.D. in organic chemistry from the University of California, Berkeley. He completed postdoctoral work at Max Planck Institute, Goettingen, Germany, and at Yale University. He joined The University of Tennessee Graduate School of Medicine in 1997.



Diagram A
Credit: Ronald Wetzel, UT Graduate School of Medicine



Diagram B
Credit: Ronald Wetzel, UT Graduate School of Medicine, and Ying Xu and Jun-tao Guo, University of Georgia

Like a string of beads that is dropped, healthy proteins fold into a complex pattern (see **Diagram A**) to accomplish their biological functions. Each of the different types of proteins in the body has to fold into a specific shape to do its job. Unhealthy proteins take on a much simpler, repeating pattern of folding (see **Diagram B**).



Diagram C
Credit: Angela Williams & John Duncan, UT Graduate School of Medicine

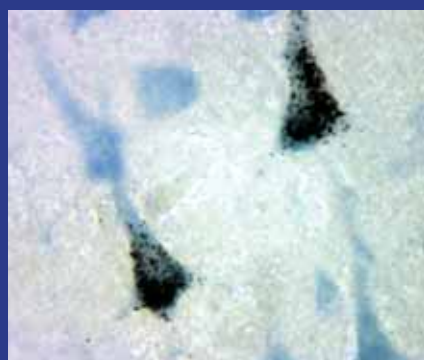


Diagram D
Credit: Alex Osmand & Stuart Wilson, UT Graduate School of Medicine

Several misfolded proteins together resemble twisted threads (as seen in **Diagram C**). Collections of misfolded proteins are called aggregates, which can kill cells or alter their function. **Diagram D** shows a microscopic view of aggregates (the black dots) in brain cells of a person who had Huntington's disease.

Is Your Doctor Still Learning?

According to research published recently in the highly-regarded *Annals of Internal Medicine*, people generally assume that knowledge and skills accumulated by physicians during years of practice lead to superior clinical abilities. However, since medical advances occur frequently, physicians' knowledge and skills may become out of date unless they continue to seek new information through journals, research, and quality continuing medical education (CME).

CME is Important to Us

The University of Tennessee recognizes the importance of providing physicians with ready access to the latest research findings, national experts, and medical developments. That's why UT Graduate School of Medicine's Office of Continuing Medical Education provides UT Medical Center and regional healthcare professionals with continuing medical education activities.

A staff of professionals organizes and presents continuing medical education that meets rigid national standards for physician continuing education. And that's important to all citizens in our region.

Why is CME important to you?

In a nutshell, CME allows physicians to maintain their level of competence in an evolving body of knowledge that deals with improving the quality of medical care for patients and their

communities. By continuing to learn, physicians are able to provide higher quality healthcare to you and your family.

"People who choose to graduate from medical school and practice medicine make a commitment to be lifelong learners of medicine," explains Dr. Michael R. Caudle, Dean of the UT Graduate School of Medicine. "Physicians and other healthcare professionals as well, have long recognized the need to continually upgrade their skills, expand their knowledge base, and generally search for the best treatment options for their patients. It's a lifetime commitment to education."

"People who choose to graduate from medical school and practice medicine make a commitment to be lifelong learners of medicine."

Dr. Michael R. Caudle, Dean
UT Graduate School of Medicine

UT provides scores of comprehensive, state-of-the-art educational courses that allow physicians to learn new strategies for disease prevention and detection, discuss issues that are important to health maintenance, and observe

techniques to enhance medical skills throughout the year. Last year alone, UT's statewide CME programs educated more than 100,000 healthcare professionals enrolled in 574 courses totaling more than 6,200 hours of certified medical education instruction.

From weekly educational meetings to annual national conferences, there's a whole lot of learning going on here. The next time you visit your physician, why not ask him or her about what they are learning in "school." You hope they will have lots to share.

-LL



Soul Speak: Physician-Patient Communication

UT Launches Unique Health Literacy Conference

One of the most important issues in the world of healthcare today is health literacy. The manner in which patients and physicians communicate with one another and the clear, correct understanding of that communication is key to quality physical and mental healthcare for patients, physician decisions about treatment protocol, and the public's education about disease prevention.

Physician-patient communication will be the focus of the University of Tennessee's new continuing medical education series, the Annual Health Literacy Conference. The UT Graduate School of Medicine and the UT Health Science Center College of Medicine present the inaugural conference, "Soul Speak: Plain Talk about Health Literacy in the Physician-Patient Partnership," February 8-11, 2006, at the Snake River Lodge & Spa in Jackson Hole, Wyoming. Physicians, researchers, clinicians, administrators, health literacy professionals and authors will explore the prevalence of limited health literacy and its impact on healthcare.

U.S. Sen. Bill Frist, M.D. has been invited to open the conference with UT Health Science Center Chancellor Dr. Bill Owen. UT researchers and faculty who are experts in health literacy will join visiting faculty and nationally-known authors for conference discussions about the importance of our nation's health literacy. Participants will also participate in American Medical Association Train-the-Trainer Workshops in which sound principles for improved health communication techniques in verbal and written communications are demonstrated.

Featured speakers for the conference include:

Dr. Barry Weiss, author of the American Medical Association's handbook on health literacy, *Manual for Physicians*

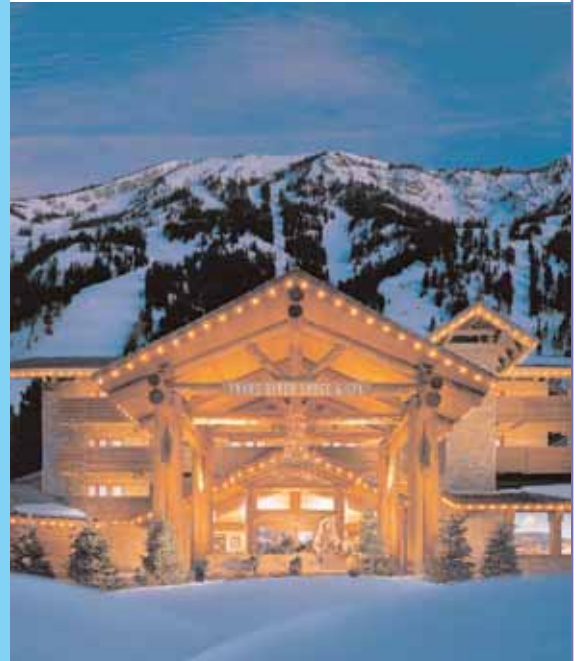
Dr. Thomas Moore, theologian, philosopher, former monk, and internationally known best-selling author of *Care of the Soul*

Dr. Mahlon Johnson, UT Medical Center neuropathologist, who has been featured on "60 Minutes," "The Today Show," and in *USA Weekend*, *Paris Match*, and *Newsweek* for his book, *Working on a Miracle*

The February 2006 conference is the first in a series of the five upcoming events. UT Graduate School of Medicine faculty and staff plan to present the conference annually for many years and have discussed the possibilities of establishing an institute dedicated solely to health literacy research and education for healthcare professionals.

To register or for more information, visit our website at www.tennessee.edu/cme or call 865.544.9190

*Snake River Lodge and Spa,
Jackson Hole, Wyoming*



The UT Graduate School of Medicine's Office of Continuing Medical Education plans ongoing educational activities for physicians and allied healthcare professionals throughout the year.

CME Course Calendar

Fall/Winter 2005-2006

Health Literacy: The Hidden Risk Factor	October 25, 2005 Wood Auditorium Knoxville, TN	<i>Nationally known health literacy advocate, Dr. Barry Weiss of the University of Arizona, will speak at the mini-conference on Health Literacy. A prelude to the inaugural Health Literacy Conference in February 2006, this mini-conference will expose area physicians to the prevalence of limited health literacy in the U.S.</i>
Vital Signs: Advances in Heart Lung Vascular 10th Annual (formerly Cardiology) Update	November 11-12, 2005 UT Conference Center Knoxville, TN	<i>Calling upon the combined faculty of the departments of Cardiology, Medicine and Surgery, this year's 10th annual conference promises to be information rich. In addition, the guest speaker, Javed Butler, M.D. of Vanderbilt University, will discuss the current status and treatments for congestive heart failure with practical tips on using beta-blockers. The conference includes three sets of breakout sessions that will enable participants more focused time with the faculty. Networking opportunities during this UT football homecoming weekend include a talk by UT head football coach Phillip Fulmer, riverboat cruise on the Tennessee River, and the Memphis/UT game.</i>
2nd Annual Hematology Review	January 21, 2006 UT Conference Center Knoxville, TN	<i>This annual review serves as a follow-up and briefing to the American Society of Hematology (ASH) international conference held each year in December. Prominent physicians from across the country will discuss new findings and updates to information presented at the ASH meeting.</i>
Health Literacy Conference: Soul Speak: Plain Talk about Health Literacy in the Physician-Patient Partnership	February 8-11, 2006 Jackson Hole, WY	<i>This conference will allow physicians to learn how to better assess language needs, conduct motivational interviews with patients, break communication and motivation barriers, and maintain the focus of a medical provider. Attendees will participate in plenary sessions, discussions, and the AMA's Train-the-Trainer workshops on health literacy.</i>

Spring/Summer 2006

2nd Annual Diabetes Update	March 2006 Knoxville, TN	<i>This conference is focused on the latest techniques and medicines in the treatment of diabetes. It is a conference designed for the whole office as a team approach for battling this disease. From the front desk staff to the physician, everyone is included in this learning experience.</i>
29th Annual Family Medicine Update	April 27-29, 2006 Park Vista Resort, Gatlinburg, TN	<i>The format of this year's update will follow the human life cycle. The conference will cover the time periods of childhood, adolescence, adult, and senior adult. Each time period will feature experts in the appropriate specialties. The final day talks will be on the inevitability of death and taxes featuring a tax attorney and the nationally known forensic anthropologist Dr. Bill Bass.</i>
Perinatal Update 2006	Early Summer 2006 Asheville, NC	<i>This perinatal conference will focus on the specialties of obstetrics, neonatology and pediatrics. Invited participants will include physicians, physician assistants and nurse practitioners. The faculty will be composed of the top specialists in the region.</i>

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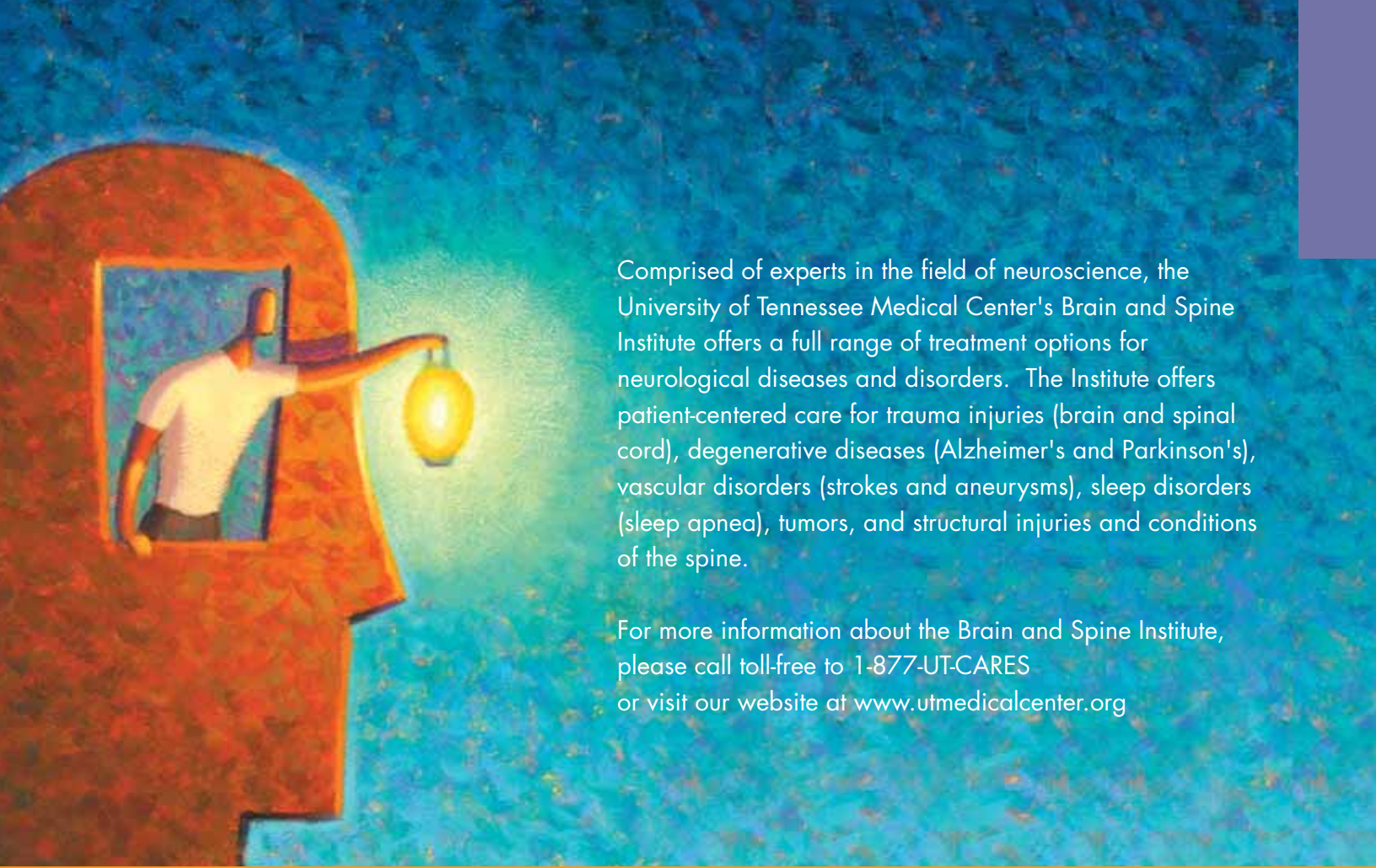


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Image courtesy of Accuray



Comprised of experts in the field of neuroscience, the University of Tennessee Medical Center's Brain and Spine Institute offers a full range of treatment options for neurological diseases and disorders. The Institute offers patient-centered care for trauma injuries (brain and spinal cord), degenerative diseases (Alzheimer's and Parkinson's), vascular disorders (strokes and aneurysms), sleep disorders (sleep apnea), tumors, and structural injuries and conditions of the spine.

For more information about the Brain and Spine Institute, please call toll-free to 1-877-UT-CARES or visit our website at www.utmedicalcenter.org



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