medicine at MICHIGAN

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Body and Soul

ABOVE THE HURON
News and research from the Medical School

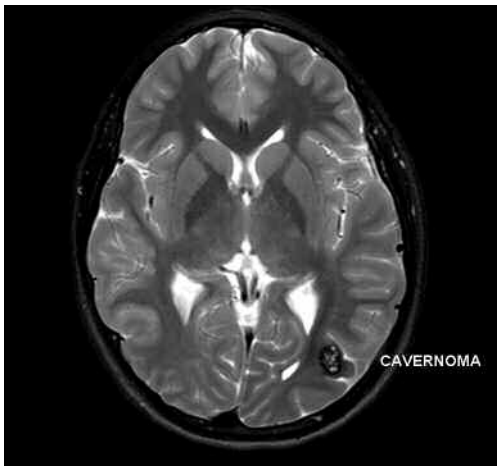
Revealing the Unseen

New imaging helps surgeons navigate complex brain fibers

Left: **A regular brain scan shows a cavernoma, or blood vessel malformation, in the patient's brain.**

Center: **This image, made using tractography techniques, shows white-matter tracts that have never before been visible.**

Far right: **Using a combined image, the neurosurgeon can see important tracts located near the cavernoma that need to be avoided during surgery.**



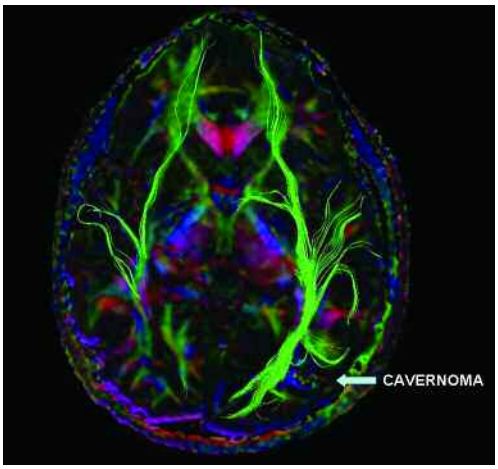


Photo: Scott Galvin

Oren Sagher consults the new MRI imagery in the operating room

From the outside, the brain looks like a gray lump of tissue, covered with ridges and bumps. But inside, a complex network of thread-like white fibers carries signals back and forth between areas of the brain and the spinal cord. Each fiber is crucial to a particular aspect of how the mind communicates with the body.

Until recently, neurosurgeons couldn't see these fibers — called white-matter tracts. Invisible to the naked eye and impossible to see on normal brain scans, they are easily damaged during brain operations to remove tumors or treat severe epilepsy. The result can be permanent damage to the senses, movement or cognitive ability.

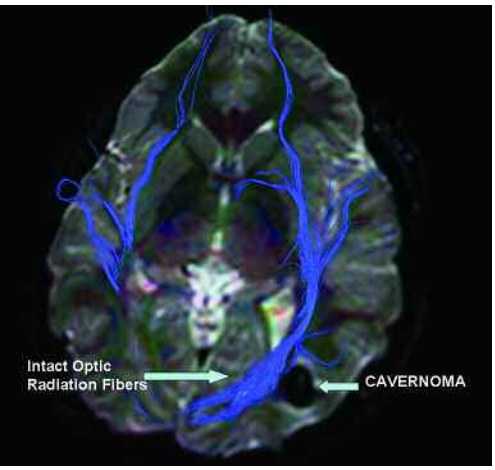
"In the past, we've never been able to see the direct connections from one part of the brain to another, or from one part of the brain to the spinal cord," says Suresh Mukherji, M.D., who directs the Division of Neuroradiology. "Now we can see those connections by looking at the sub-cellular level to see how water molecules move in brain tissue." Mukherji is a professor of radiology, of otorhinolaryngology and of radiation oncology.

The Health System is one of the first medical centers to offer image-guided surgery using a new white-matter imaging technique called tractography. Brain-imaging specialists like Mukherji work closely with U-M neurosurgeons, who perform thousands of brain and spine operations each year, and with neurologists who diagnose and treat brain and nerve disorders.

Oren Sagher, M.D., an associate professor of neurosurgery and of anesthesiology, says this teamwork makes it possible for him to operate with the best possible information about each patient's brain. "Thoroughly imaging the brain is one of the keys to successful brain surgery," Sagher says. "We have to be able to see all the structures we're going after and all the structures in our way that need to be avoided."

Mukherji, Sagher and their colleagues predict that tractography will change brain surgery and the way we see the brain's function.

Tractography uses powerful magnetic resonance imaging (MRI) scanners that create images of the patient's brain one thin slice at a time. Then, ultra-fast computers equipped with special software compile all the slices into a three-dimensional image of the brain. Lastly, the neuroimaging team uses special techniques to see how water molecules are oriented and move inside every area of the virtual 3-D brain. The end result is a series of spectacular images that show the entire network of white-matter tracts with their individual nerve fibers.



These images become a roadmap for surgeons like Sagher, especially when they're superimposed on other images that show the specific areas of "gray matter" where epileptic seizures begin or where tumors lurk.

This cross-registration fuses information about two areas of the brain: areas the surgeon needs to remove or destroy to treat the patient's condition and areas the surgeon needs to avoid to preserve a patient's vision, for instance, or her ability to move her right arm.

Mukherji, Sagher and their colleagues predict that tractography will change brain surgery and the way we see the brain's function forever, just like the first CT and MRI scans changed the diagnosis and treatment of many brain disorders. The team is pursuing research to improve the technique and show how it can best be used — and how it helps spare patients from unintended consequences.

"Instead of imaging the brain, we're essentially imaging the mind," says Mukherji. "We're able to image how a person's thoughts and brain impulses travel, and this is just the beginning."

—Kara Gavin

For an expanded version of the story:
www.med.umich.edu/opm/newspage/2007/hmepilepsy.htm

NIH Awards U-M $55 Million for Translational Research Initiative

The University of Michigan has received a $55-million Clinical and Translational Science Award (CTSA) from the National Institutes of Health to support a new University-wide initiative in interdisciplinary research aimed at improving human health.

Photo: Paul Jaronski

Daniel Clauw

Translational research takes promising discoveries from the laboratory and moves them to the clinic where they can be tested for use in patients. It's the often-missing link between traditional biomedical research and medicine.

The five-year grant is the third-largest NIH award in the University's history. Competition for CTSA grants is intense. With this award, the U-M becomes part of the national CTSA consortium made up of 24 leading academic medical centers in the United States. When fully implemented in 2012, the consortium will include about 60 institutions.

The Michigan Institute for Clinical and Health Research — directed by Daniel Clauw (M.D. 1985), professor of internal medicine — is the administrative umbrella for the grant. Many U-M schools, colleges, institutes and divisions are participating in CTSA-driven initiatives through the institute.

"A Clinical and Translational Science Award is the superhighway of the NIH roadmap — it's the ultimate resource an institution needs to deliver cures and treatments to our patients," Clauw says. "The U-M has been building infrastructure for nearly five years. We are ready to use the award to help people do their best research, as well as to attract people who weren't previously thinking about a career in clinical or translational research."

The initiative grew out of an NIH commitment to re-engineer the nation's clinical research enterprise, one of the key objectives of the NIH Roadmap for Medical Research.

—Sally Pobojewski and Mary Beth Reilly

For an expanded version of the story: www.med.umich.edu/opm/newspage/2007/ctsa.htm

Hospitals Make *U.S. News*

In 2007, for the 12th consecutive year, the U-M Hospitals and Health Centers were included in the *U.S. News & World Report* honor roll of "America's Best Hospitals." The U-M was named 14th among the top 18 hospitals in the country, and fourth among hospitals affiliated with public universities.

In addition, C.S. Mott Children's Hospital was named one of the top 30 pediatric hospitals in the nation in *U.S. News & World Report*'s first edition of "America's Best Children's Hospitals." Ranked 22nd, it was the only children's hospital in Michigan to make the list.

Predicting Risk in Aortic Dissection

Each year, 10,000 Americans suffer a sudden and often lethal tear in the lining of the body's largest blood vessel, the aorta, which carries blood from the heart to the lower half of the body.

Patients today are far more likely to survive this medical crisis, called aortic dissection, thanks to improved medical imaging and treatment. But after they leave the hospital, they face a one-in-four chance of dying within the next few years. Doctors don't have a reliable way of predicting which patients have the highest risk of death and who might benefit most from surgery or additional treatment.

In a *New England Journal of Medicine* study directed by physicians in the Cardiovascular Center, researchers propose a new way to predict post-hospital death risk for aortic dissection survivors, and present a new model for the mechanism behind that risk.

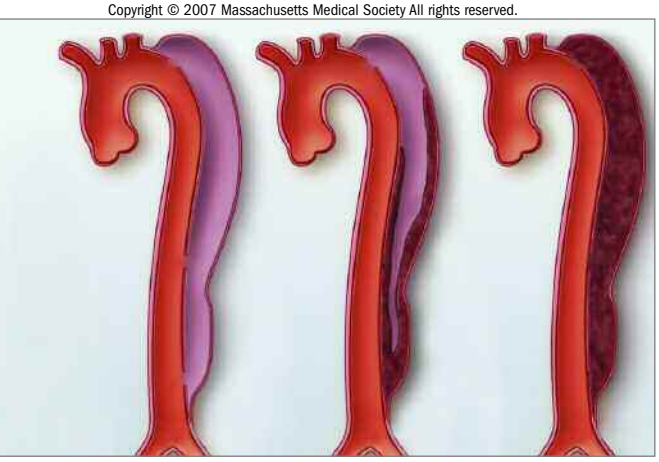
The model focuses on the presence of blood clots in a channel created when the layers of the aorta separate like two layers of an onion. This channel, called the "false lumen," runs alongside the "true" lumen – the hollow middle of the aorta, which is the pipeline for blood flowing out of the heart and down through the abdomen.

As blood enters the false lumen from the top of the torn aorta, it gets trapped inside the new channel where blood clots can form. The study showed that the risk of post-hospital death was more than two-and-a-half times greater for patients with partial clotting of the false lumen, than for those whose false lumen contained no clots. If the false lumen was completely filled with clotted blood – something that happens infrequently – the patient had an intermediate risk of death.

"This could be a predictor of patients most at risk – knowledge that might help guide decisions about when it's wise to proceed with more aggressive treatment and when we can hold off," says lead author Thomas Tsai (M.D. 1998), a fellow in cardiovascular medicine.

The study involved data from 201 patients with dissections in their descending aortas, who were followed for up to three years or until death, as part of IRAD – the International Registry of Acute Aortic Dissection. IRAD is headquartered at the Cardiovascular Center and includes data from 22 large medical centers in 11 countries. Kim Eagle, M.D., a director of the Cardiovascular Center, also helps direct IRAD.

–Kara Gavin



These three cross-sectional illustrations of the aorta illustrate the different states of blockage that might occur within the "false lumen" or secondary channel created by an aortic dissection. In each case, the false lumen is in purple, and the "true" aorta is red. At left, the channel is clear (also called patent), a state that was associated with lower risks of post-hospital death in the new study. In the middle, the false lumen is partially blocked by clots, a state that was associated with a much higher risk of death. At right, the false lumen is entirely thrombosed, or filled with clots. This state was associated with an intermediate risk of death.

Photo: Martin Vloet

Thomas Tsai

For an expanded version of the story:
www.med.umich.edu/opm/newspage/2007.aorta.htm

For patient information on aortic dissection:
www.med.umich.edu/1libr/aha/aha_aortdiss_car.htm

Music for Deaf Ears

Scientists at the Kresge Hearing Research Institute have shown in animals that a tiny, ultra-thin electrode array implanted directly in the auditory nerve can transmit a wide range of sounds to the brain. U-M scientists believe the new hearing-assist technology could one day be a superior alternative to current cochlear implants.

Electrode array implants could improve the ability of profoundly and severely deaf people to hear low-pitched sounds common in speech, hear conversation in a noisy room, identify high and low voices, and appreciate music — areas where current cochlear implants have significant limitations, says John C. Middlebrooks, Ph.D., a professor of otolaryngology and of biomedical engineering.

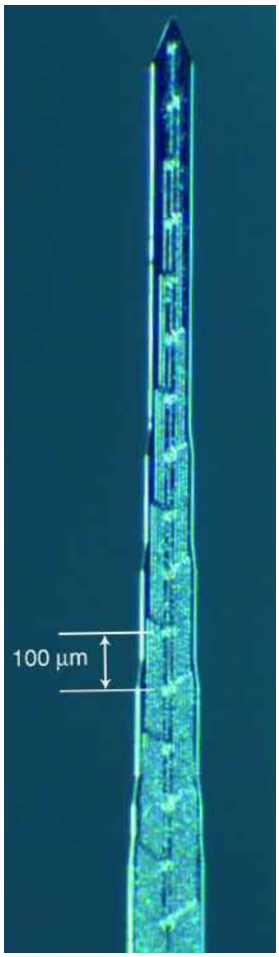
Middlebrooks explains that cochlear implants are designed to stimulate the auditory nerve and other cells to produce a sensation of hearing. But their location, separated from auditory nerve fibers by fluid and a bony wall, is a limitation.

"Access to specific nerve fibers is blunted," Middlebrooks says. "The effect is rather like talking to someone through a closed door. Because the electrode array is in intimate contact with nerve fibers, it achieves more precise activation."

The next step will be testing the device over time to see if it is safely tolerated by the auditory nerve, according to Middlebrooks. If the initial success in animals is borne out in further tests, he says that a human auditory nerve implant is probably five to 10 years away.

—Anne Rueter

For an expanded version of the story:
www.med.umich.edu/opm/newspage/2007/hd.htm



A magnified image of the U-M electrode array that transmitted sounds to the brain when it was implanted in the auditory nerves of research animals. Initial results suggest the device could have advantages over cochlear implants, the technology currently used to restore partial hearing in people with profound to severe hearing loss. The array has 16 stimulating sites spaced 100 micrometers apart — about the width of a human hair.

Fish Oil Beats Vegetable When It Comes to Inflammation

Consuming more fish oil and less vegetable oil could help reduce inflammation by decreasing the body's production of chemicals called prostanoids, according to William L. Smith (Ph.D. 1971), professor and chair of biological chemistry.

In recent research, Smith found that prostanoids made from vegetable oil caused more pain, swelling and redness in body tissues, while prostanoids made from fish oil led to fewer inflammatory symptoms.

Both fish oils and vegetable oils are converted into prostanoids through chemical reactions involving enzymes called COX-1 and COX-2. Increased understanding of how these enzymes regulate prostanoid production could lead to more effective anti-inflammatory drugs with fewer side effects.

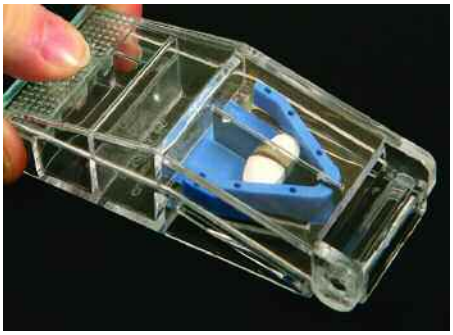
For an expanded version of the story:
www.newswise.com/p/articles/view/531827

Photo: ©iStockphoto.com/Murat Koc

Splitting the Difference

Cutting cholesterol-lowering pills in half could slice a hefty amount off of America's prescription drug costs without interfering with cholesterol control, according to a study led by U-M pharmacist Hae Mi Choe.

Photo: Martin Vloet



Many medicines are manufactured in tablet formulations that contain different doses of the active ingredient, but the wholesale cost of half of a high-dose pill usually is much lower than the cost of a whole low-dose pill. While only some types of pills can be split effectively, the practice could be used by millions of Americans — including many who take popular cholesterol-lowering drugs called statins.

The findings have already had an impact on the prescription drug plan for U-M employees and retirees. In just the first year, a new pill-splitting program saved the University $195,000, and saved individuals more than $25,000 in co-pays.

—Kara Gavin

For an expanded version of the story:
www.med.umich.edu/opm/newspage/2007/split.htm

Strain of "Pale Tremor" Mice Leads to Gene Discovery

Thanks to the chance appearance of a strain of mutant mice in their research laboratory, U-M scientists have identified the gene responsible for one type of Charcot-Marie-Tooth disorder, common among inherited neurological diseases.

The discovery means a genetic test will be possible for people with a less common subtype of the disorder — one that until now was unidentified and had an unknown genetic basis, says Miriam Meisler, Ph.D., a professor of human genetics in the Medical School.

Photo: Clement Chow

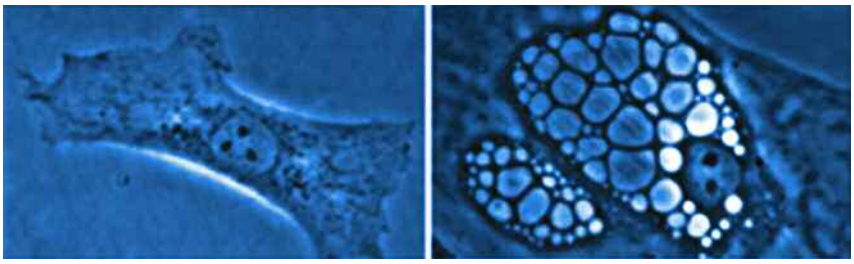
A pale tremor mouse (right) with a normal mouse in Meisler's lab.

It all started when scientists in Meisler's lab noticed that some mice had offspring with a strange, wobbly gait and light coat color. The team named them "pale tremor" mice. Clement Chow, a Ph.D. student in human genetics, identified a gene mutation called FIG4 that was responsible for the animals' symptoms.

Researchers then tested 95 patients with Charcot-Marie-Tooth disorder of unknown cause. In four patients, they found mutations in FIG4, the same gene implicated in the diseased mice. The finding has resulted in a newly identified form of the disease called CMT4J.

Charcot-Marie-Tooth disorder affects one in 2,500 people in the United States. The disease damages peripheral nerves in the feet and legs, causing pain and muscle weakness, foot deformities, and difficulty walking.

—Anne Rueter



Large fluid-filled vacuoles pack cells of mice with the FIG4 gene mutation, shown at right, and interfere with cell function. A normal cell is shown at left.

For an expanded version of the story:
www.med.umich.edu/opm/newspage/2007/charcot.htm

For patient information on Charcot-Marie-Tooth:
www.ninds.nih.gov/disorders/charcot_marie_tooth

Doctor's Orders

Nurses in the Health System's Neonatal Intensive Care Unit (NICU) used to spend a lot of time "hunting and gathering," says Kathrynn Schmidt, who used to work as a clinical nurse in the unit. Tracking down patient charts and processing hand-written, and sometimes illegible, physician orders was a regular part of a nurse's day. But that was before UM-CareLink.

UM-CareLink is a new computerized provider order entry system designed to improve the quality and safety of inpatient care in the Health System. Implementation of the new system began in 2006, and it is now up and running in ob/gyn, Women's Hospital and Mott Children's Hospital.

The system allows physicians to order tests, procedures and medications online from any computer, eliminating the need for paper forms. Nurses can access test results and enter information on a laptop computer next to each patient's bedside.

Photo: Scott Galvin

Kathrynn Schmidt discusses the U-M CareLink system with Pam Manee, a nurse in the Neonatal Intensive Care Unit

"Everybody has access to the same information at the same time from anywhere," Schmidt says. "There's no more searching for charts and no more tracking down physicians to double-check their handwriting. Electronic orders go directly to the pharmacy or the lab, so the turnaround time is much quicker."

One year before the transition to UM-CareLink, Schmidt was asked to serve as the liaison between the NICU nursing staff and the Orders Management Project design team. "It was a big change," Schmidt says. "Some of our nurses had used the old paper system for 30 years. Just getting comfortable with the computer was a big learning curve. But in the end, our nursing staff agreed they would never go back to paper."

UM-CareLink is scheduled to "go live" in University Hospital and the Cardiovascular Center in April 2008.

—Sally Pobojewski

Independence Threatened by Missed Conditions

About half of adults age 65 and older have health conditions that affect their ability to participate independently in daily living activities, such as bathing or dressing, according to a recent U-M study. These conditions are often overlooked by physicians.

Researchers found that 50 percent of the 11,000 older adults studied had a moderate to severe form of at least one of the following conditions: cognitive impairment, falls, incontinence, low body mass index, dizziness, vision impairment or hearing impairment.

The study was the first to investigate the total impact of geriatric conditions on health and disability in the older adult population, notes Christine Cigolle, M.D., a lecturer in family medicine and a physician in the V.A. Ann Arbor Healthcare System.

"Because the focus in medicine has been on diagnosing and treating diseases, these geriatric conditions can be missed by physicians," says Cigolle. "Clinicians need to ask older patients about these issues. In many situations, they may be able to help manage the condition before it leads to disability."

—Katie Vloet

For an expanded version of the story:
www.med.umich.edu/opm/newspage/2007/geriatric.htm