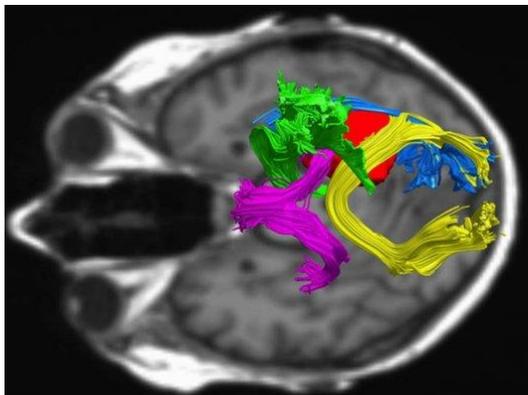


A better road map for neurosurgeons



An example of diffusion tensor imaging shows a tumor in red surrounded by a bundle of critical brain circuitry. (Photo by Arlan Mintz, Capital Health / enhanced at University of Pittsburgh Medical Center)

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While preparing to remove a malignant tumor from the Rev. Michael Prewitt's brain, neurosurgeon Steven Brem of the University of Pennsylvania worried that the surgery could affect his patient's ability to speak or move.

As surgeons have for decades, he studied an MRI that showed the tumor in Prewitt's left parietal lobe. But he also examined a type of scan you've probably never heard of: diffusion tensor imaging. It shows bundles of the fibers that transmit messages from parts of the brain to one another and the brain stem.

Leaving the most important fibers unscathed reduces disability, but surgeons can't see them while they're operating. A DTI helps them better plan a safe way to reach and remove the tumor.

This kind of brain picture, made by mathematically manipulating information captured by a magnetic resonance imaging machine, is colorful and sometimes lushly beautiful. If X-rays, MRIs, and CT scans are sparrows, DTIs are peacocks. Some brain researchers have been using them for years, but they have only recently begun making the leap into clinical practice, where patients might encounter them.

For surgeons like Brem, the new technology is like going from knowing only where a city's major buildings and parking lots are to seeing the network of roads that connect them. If you must destroy something to save City Hall, stay away from I-95 and the Schuylkill Expressway. "That's huge," Brem said. "That is a groundbreaking paradigm shift."

Prewitt's DTI told Brem he could be aggressive in removing the tumor on one of its sides but that he would have to be much more conservative on the other side, where a key bundle of fibers abutted the cancer cells.

"I'll say that worked," Prewitt said good-naturedly during his recovery.

The 68-year-old West Philadelphia man owned a marketing and public relations company before being ordained a Presbyterian minister in 2004. He had his second surgery for glioblastoma, an incurable, invasive form of brain cancer, on April 8. He ate lunch and dinner that day and was up walking the next. He is still getting physical therapy for his balance, but he spoke clearly and passionately last month about his life and pastoral work. "I'd go back and do this surgery again in a minute."

Neurosurgeons at Temple University Hospital, Capital Health, and Abington Memorial Hospital are among those using the scans regularly. Thomas Jefferson University Hospital is using them in research to differentiate tumor types and measure the effectiveness of treatment, but neurosurgeon David Andrews said he didn't think it added that much to surgical planning. Colleagues are using it to evaluate epilepsy patients.

Joshua Levine, codirector of the neurological intensive care unit at the Hospital of the University of Pennsylvania, said his traumatic brain injury patients are getting DTIs as part of a study. The hope is the scans will eventually help doctors predict who has the best chances of recovery.

"I think we're all excited about the potential of this," Levine said. "How to use it and how useful it is has not been established definitively."

Figuring out how the parts of the brain work together - what's being called the "human connectome" - is a hot topic. Psychologists and physicians who have focused for years on the individual parts say untangling this complicated system will help them understand everything from schizophrenia and autism to Alzheimer's and traumatic brain injury. Brem hopes it will also help explain how the brain heals.

President Obama has asked Congress to spend \$100 million next year to map the brain. Advanced forms of diffusion imaging will play a key role.

Diffusion imaging is a way of peering into the white matter of the brain where axons, the threadlike appendages you see in pictures of brain cells, form their communication network. It looks like tapioca pudding to the naked eye.

The scans, also called tractography, are not pictures of the axon fibers themselves but representations of water molecules that move parallel to bundles of fibers.

The technology is still evolving, and many researchers are trying to improve the accuracy of pictures, especially when it comes to following the twists and turns of axons from start to finish. A team at the University of Pittsburgh Medical Center has developed an enhanced form called high-definition fiber tracking that it says does a better job of tracing specific groups of axons. Others also are tweaking the technology.

Van J. Wedeen, an imaging scientist at Massachusetts General Hospital and one of the principle investigators of the Human Connectome Project, is now testing the Siemens Connectom, a powerful MRI scanner he helped develop. To his surprise, the fibers in its pictures are arranged in a three-dimensional grid that "looks like wires on a circuit board."

The imaging techniques have much promise, but the results are not yet definitive. "We literally have no idea how the human brain is wired," Wedeen said, "in fact, how any brain is wired."

Regarding the value of diffusion imaging in clinical practice, Wedeen said, "It's a mistake to say it's ready for prime time."

That said, he added that surgeons may not need as much detail about the fiber tracts as neuroscientists. "In the hands of knowledgeable surgeons," he said, "it would appear that it's useful information even in its current form."

Surgeons say there are some issues. The brain shifts once the skull is opened, so there are problems with precision even when the images are combined with navigation systems in the operating room. Still, the fiber-tract modeling can help surgeons better assess where the connections that control movement, speech, and vision are.

"It's helping to do surgery with more confidence," said Juan Fernandez-Miranda, a UPMC neurosurgeon who uses high-definition fiber tracking.

Surgeons differed over whether DTI allows them to operate on patients who would not have qualified for surgery in the past. Arlan Mintz, a Capital Health neurosurgeon, thinks it does. He also said he had sometimes "changed the entire operation" after seeing a scan during the planning phase.

DTI is not covered by health insurance.

Though Fernandez-Miranda said there was no proof the scans improved surgical outcomes, Brem found some evidence it does when he helped write a review of the science for the journal *Neurosurgical Focus* last month. A 2007 study from Shanghai found the median survival for patients with gliomas, a category of brain tumors that includes the type Prewitt has, was 21 months for patients whose surgeons had seen DTIs before the operation compared to 14 months for other patients.

Surgeons can never remove all the glioblastoma cells. The more they take, the longer patients live, as long as there's no disability, Brem said. Inactivity, he said, may make patients more prone to blood clots and pneumonia.

Prewitt, who had to quit his job in Rhode Island when he was diagnosed last year, said he felt reenergized after the surgery and ready to start helping others again. "I love being a pastor," he said. "It's a great job. I will go back to some kind of pastoral work as soon as I can."