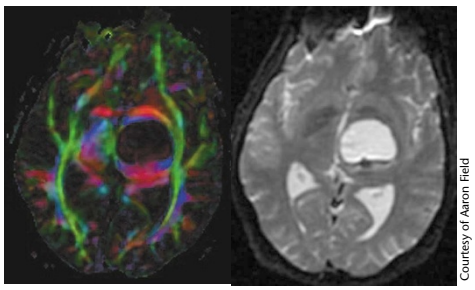
NIH commercializes new imaging technique

Last month saw additional evidence that the National Institutes of Health (NIH) is increasing its activities in the area of biomedical engineering and bioimaging. The National Institute of Child Health and Human Development (NICHD) has signed a major deal with GE Medical Systems, licensing them to produce and market a new imaging technology it has developed. The new method gives high-quality views of nerve-fiber pathways, blood vessels, skeletal muscle, heart and other soft tissues, allowing the construction of detailed three-dimensional tissue maps.



Courtesy of Aaron Field

Conventional MRI (right) and DR-MRI (left) in a patient with a ganglioglioma displacing white matter fiber tracts. Only the DT map localizes individual fiber tracts, allowing their preservation during tumor resection

Called diffusion tensor magnetic resonance imaging (DT-MRI), the system produces images noninvasively and painlessly. For certain scans, conventional MRI uses exogenous contrast agents, such as an intravenously administered gadoliniun-based compound. In contrast, DT-MRI exploits the effects of tissue microstructure on the diffusion of water to generate endogenous tissue contrast scans.

The motion of water molecules in tissues varies between tissues and according to their disease state. For example, in brain gray matter, water diffuses in an approximately spherical pattern, whereas in tissues with a large number of parallel fibers, such as brain white matter, skeletal and cardiac muscle, water diffuses fastest along the direction of the fibers, and slowest at right angles to them. Based on these differences, DT-MRI produces intricate 3-D images of the tissue's architectural organization and local structure. Changes in tissue water diffusion can be correlated with processes that occur in development, degeneration, disease and aging.

According to DT-MRI's principal inventor, Peter Basser, "The most important clinical application of DT-MRI to date has been the ability to follow the progression of cerebral ischemia during acute stroke, and to follow the subsequent neural degeneration in chronic stroke." Basser, NICHD's Chief of the Section on Tissue Biophysics & Biomimetics, says "the first applications are likely to be in surgical planning, since DT-MRI can provide the neurosurgeon with additional information about brain anatomy and architecture that conventional MRI methods do not."

Indeed, DT-MRI's use in imaging fiber tracts may cause a modest revolution in neurosurgery. Aaron Field, assistant professor of Radiology at the University of Wisconsin Medical School, is exploiting this property of DT-MRI to study cerebral tumor infiltration. His group has found that DT-MRI patterns indicate whether a tumor is displacing, invading or destroying white matter tracts. "Diffusion tensor properties differ between tumor types and even between different regions of the same tumor. We've used DT-MRI to map the displacement of functionally critical white-matter tracts, such as the corticospinal tract, by an enlarging tumor, enabling the surgeon to preserve the tract during resection."

Massimo Filippi, director of the Neuroimaging Research Unit at the Scientific Institute and University in Italy, is using DT-MRI to study the brains of patients with multiple sclerosis (MS) and Alzheimer disease (AD). In AD patients, for example, Filippi's group found cortical gray matter abnormalities that correlate with the patients' clinical symptoms: "Diffusion changes in white matter (corpus callosum, white matter of the frontal, temporal and parietal lobes) are present in AD patients and are strongly correlated with mental state examination score."

The only drawback to the technique appears to be artifact production. "DT-MRI data suffers from artifacts as do other imaging modalities," says Basser. "The primary sources of these are background noise, image distortion due to eddy-currents, and rigid and non-rigid patient motion." But Basser insists that DT-MRI is still an improvement over conventional MRI in this regard.

The NIH's interest in biomedical imaging and engineering has grown visibly since 2000 when Congress pronounced this an area in which the Institutes' efforts have been "inadequate" (*Nature Med.* **6**, 7; 2000). Congress called for the creation of an Office of bioimaging/bioengineering that has now become the newest, full-blown Institute, called the National Institute for Biomedical Imaging and Bioengineering (NIBIB). This month, Roderick Petigrew takes over as NIBIB's first permanent director. In addition, Congress chose to elect Elias Zerhouni, an expert in MRI, as the new NIH Director.

Caitlin Smith, Oregon

Trial tests chelation's effect on heart disease

Last month, the National Center for Complementary and Alternative Medicine (NCCAM) and the National Heart, Lung and Blood Institute (NHLBI) launched a $30 million clinical trial to investigate the efficacy of chelation therapy in heart disease—a treatment for which many experts say there is no experimental evidence that it works.

Chelation therapy consists of a series of intravenous infusions of the synthetic amino acid EDTA (ethylene diaminetetraacetic acid). A clinical trial published this January concluded that it has no benefit for patients with heart disease (*JAMA* **287**, 481; 2002). But that study has been criticized by proponents of the therapy for being too small and inconclusive. The NCCAM/NHLBI study is over 20 times larger than any previous trial of chelation therapy, and is sufficiently large to detect even mild or moderate effects or risks.

The American Heart Association's official position on chelation therapy for heart disease is that there is "no scientific evidence to demonstrate any benefit," a sentiment echoed by many in the scientific community. Even Gervasio Lamas of the Mount Sinai Medical Center and Miami Heart Institute, who will lead the new five-year trial admits, "the state of the evidence is somewhat flimsy." Most studies that report any benefit for chelation therapy are case reports and a few small trials.

"The reason for doing the clinical study," says Lamas, "is the positive reports and the massive public usage [of chelation therapy]." Indeed, the American College