High-End Technologies for High-Powered Research

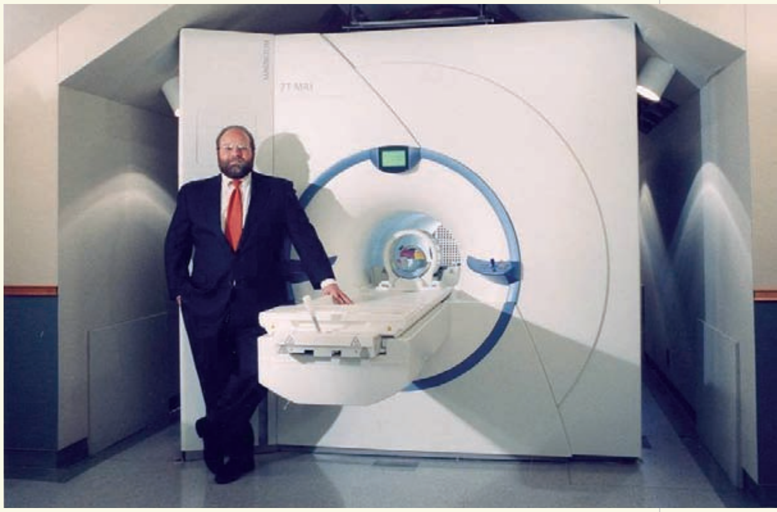
Grants for high-end instruments give a boost to imaging studies, and more.

Imagine having to deliver a 33-ton package in the middle of Manhattan, containing a magnet so powerful that it could draw every metal object in a three-mile radius. It happened two years ago, when New York University (NYU) School of Medicine became home to one of the world's most powerful magnetic resonance imaging (MRI) machines. Around the same time, another large device, one that churns out radioactive elements, was delivered to the opposite coast, at the University of Washington in Seattle.

Both machines came with hefty price tags, paid in part by a new class of NCRR grants for High-End Instrumentation (HEI). NCRR has long been supporting the purchase of instruments costing up to $500,000 through its Shared Instrumentation Grant (SIG) Program (see *NCRR Reporter*, Fall 2004, pages 8-9). But many devices used in biomedical research are much more expensive. "We were getting applications for the maximum amount of the SIG award, but the total cost of the instrument was well over $1 million," says Marjorie Tingle, who oversees the HEI and SIG Programs for NCRR's Division of Biomedical Technology. "We realized there was a need for high-end instrumentation that was not being met." And this realization proved to be correct. In 2002, the first year the HEI grants were made available for instruments costing more than $750,000, NCRR received close to 100 applications.

Joseph Helpern was among the successful applicants. As director of NYU's Center for Biomedical Imaging, Helpern received a $2 million HEI grant to purchase a new MRI machine. MRI allows researchers to visualize almost every tissue in the body. When undergoing an MRI scan, the patient lies inside a large, cylinder-shaped magnet as waves—thousands of times stronger than the Earth's magnetic field—are sent through the body, forcing the nuclei of atoms to wobble. A scanner records the nuclei's movement, and a computer then turns this information into a three-dimensional picture.

A unique aspect of the NYU machine is the strength of its magnet, which measures at 7 tesla, nearly 5 times as powerful as the 1.5-tesla MRI systems used routinely at most medical centers. "It is equivalent to having built a new telescope to look into space. You can see things that you never saw before," Helpern says.



Joseph Helpern used HEI funding to purchase a robust MRI system, nearly 5 times more powerful than most clinical MRI machines. This high-end instrument will aid studies of Alzheimer's disease, breast cancer, and other conditions.

Although other 7-tesla MRI systems are used for clinical research, these scanners are limited, for technical reasons, to imaging the head. But Helpern worked closely with Siemens Medical Solutions in Erlangen, Germany, to create an instrument that could image the entire human body. Initially, the idea was met with some skepticism. "It took a lot of conference calls and discussions with engineers, but we did it," says Helpern. "This is an example of a unique cooperation between a private institute, a vendor, and the National Institutes of Health."

Another challenge for Helpern was to figure out how to house the massive instrument at NYU. For starters, he designed a 420-ton, octagon-shaped steel shield for it. In addition, the university built a 14-foot-high concrete bed to support the instrument and to protect it from vibrations. Once the MRI was put in place and thoroughly tested, Helpern's team and several collaborators began gathering breathtaking images of different parts of the human body. In one project, Helpern is trying to develop methods to detect the telltale signs of Alzheimer's disease and other disorders that affect the brain.

PHOTO BY RENÉ PEREZ, NEW YORK UNIVERSITY SCHOOL OF MEDICINE

"Other NYU researchers have embarked on a series of breast-imaging studies, with spectacular results," says Helpern. "The possible applications of this machine are endless."

Another type of imaging, positron emission tomography (PET), relies on the detection of positrons, tiny particles emitted from radioactive substances. An instrument called a cyclotron makes short-lived isotopes—such as carbon-11, with a half-life of 20 minutes, or fluorine-18, with a half-life of 110 minutes—which are then used to synthesize different compounds. Once administered to a patient, these radioactive compounds, or tracers, yield chemical information about various tissues. Because the isotopes are short-lived, they need to be manufactured onsite.

The University of Washington has had a thriving PET imaging program for 19 years. But to obtain radioisotopes for PET research, imaging groups originally had to purchase time on a cyclotron belonging to a different university department. In 2002, however, "life got much better," says Kenneth A. Krohn, who heads the university's Cancer Imaging program project. Krohn received a $2 million HEI grant to purchase a cyclotron dedicated to imaging research. "We can now make more radioactive compounds for more studies, with more collaborators, and we can use more complicated protocols," he says. "Since installing the new machine, the center's productivity and the number of investigators using our tracers has increased by about fourfold."

■ *Kenneth Krohn prepares to create radioactive tracers in a state-of-the-art cyclotron acquired through an HEI grant. The tracers are used primarily for cancer imaging in patients.*

PHOTO COURTESY OF UNIVERSITY OF WASHINGTON

PET imaging is primarily used to study cancer. With short-lived isotopes, a researcher can use different tracers in a single imaging session to measure multiple tumor properties at once. "Tomorrow we are going to study a woman with a sarcoma in her shoulder, and we will obtain images using three different tracers," says Krohn. "Carbon-11-labeled thymidine will measure the rate of DNA synthesis in the tumor; fluorine-18-labeled fluoromisonidazole will measure the degree of hypoxia, or lack of oxygen, in the tumor, since tumors that are hypoxic respond poorly to radiation therapy; and carbon-11-labeled verapamil will measure multidrug resistance, another indicator of the response to therapy." A study like this, typical of several done each day at the center, can be completed in about two-and-a-half hours. This technology is critically important for selecting the right treatment for each patient.

Although the cyclotron is primarily used for cancer research, the instrument also is used for other purposes. For example, the NCRR-funded Washington National Primate Research Center makes use of the short-lived tracers for studies on primate models of disease. A major focus of Krohn's research is the development of new tracers. He recently synthesized fluorine-18-labeled annexin V to detect cells undergoing programmed cell death in a rat model of cancer. With further evaluation, the tracer might become a useful tool for detecting a patient's clinical response to cancer therapy.

The researchers acknowledge the importance of the HEI program for their work. "The cyclotron would have been too expensive for us to buy," says Krohn. "It cost $1.7 million, plus $1 million to prepare the site for installation." Helpern concurs. "The HEI is a very significant program," he says, speaking from experience. Sixteen years ago, Helpern's group received a $400,000 SIG from NCRR to build the world's first 3-tesla MRI system specifically for human brain research. "Now the 3-tesla system is exploding in popularity," he says.

—LAURA BONETTA

APPLY FOR FUNDING: Applicants for High-End Instrumentation (HEI) grants may request up to $2 million to cover the purchase of a major piece of equipment, including mass spectrometers, electron microscopes, supercomputers, and more. Institutions are expected to provide support for the associated infrastructure. Grants are available to domestic public and nonprofit health professional schools, other academic institutions, hospitals, health departments, and research organizations. To be eligible, the application must identify three or more NIH-funded investigators who will use the instrument. Applicants are encouraged to contact NCRR program staff at HEI@mail.nih.gov before applying for a grant. Additional information about HEI grants is available at http://www.ncrr.nih.gov/biotech/btheinstr.asp.