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> *****Magnetic resonance spectroscopy scans body metabolism.

DALLLAS -- Researchers at The University of Texas Health Science Center at Dallas are among a handful of scientists in the world who are using powerful magnets to monitor certain aspects of human body metabolism. This ability to monitor how well living cells are meeting their energy needs without surgery or withdrawing fluids was thought impossible in the past. Now it is possible, and possible without exposure to any ionizing radiation.

The non-invasive technology, called magnetic resonance spectroscopy, allows doctors to examine biochemical signals produced by the brain tissue of stroke victims, tumor tissue of cancer patients and heart tissue of those who have suffered a heart attack. The resulting information points toward new clinical arenas for MR, which has already revolutionized medicine's ability to see inside the human body through MR imaging. MR spectroscopy gives scientists a tool for determining whether a disorder is permanent or temporary and whether or not it warrants aggressive therapeutic intervention.

Among the health science center projects under investigation:

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**Pediatric researchers are monitoring babies who have suffered an interval of oxygen deficiency (asphyxia) at birth. Also, they are helping to explain childhood metabolic disorders, such as rickets, which interfere with muscle strength and growth.

**Stroke researchers are analyzing patients who have suffered a single stroke and have lost their ability to speak.

**Cancer researchers are detecting better tumor response to radiation therapy when the treatments are combined with injections of fluosol, a blood substitute and oxygenator.

**Heart researchers are performing intricate base-line studies on the beating hearts of normal individuals. Soon they will begin comparing these values with those of patients with heart disease.

"We have a window on the biochemistry of the body that we never had before because the technology hadn't existed before," says Dr. Ray Nunnally, director of the Biomedical Magnetic Resonance Center at UTHSCD.

During an MR spectroscopic exam, persons are positioned within the core of a magnet, just as they are for MR imaging. But the MR imaging technology, used to create CAT scan-like pictures of human anatomy, is altered with spectroscopy to produce a "spectrum" of chemical amounts in the form of a graph. This graph is a measure of various biological chemicals present in the tissue or organ under examination. The MR machine's radio pulse is changed to a different frequency in order to detect specific chemical elements, which appear as spikes or peaks in a graph according to their quantities in a particular tissue area. The graphs can be displayed on a television screen or printed out on paper.

After determining normal amounts of various body chemicals, UTHSCD scientists are able to tell how efficiently cells are metabolizing and producing energy. Abnormalities are often revealed by a reduction in chemicals, with a subsequent shortening of peaks on the graph. One stroke patient, for example, had a 50 percent reduction in all chemicals on one side of the brain but not on the other. This indicated a loss of tissue viability in the area affected by stroke, Nunnally said. Completely dead tissue produces a totally flat line graph.

From information provided by the spectra, researchers can assess how drugs influence the performance of unhealthy tissue and whether drug treatment should be altered. In some cases it is even possible to detect the drug itself and follow its fate in the body.

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"We know with certainty what most of the peaks represent," says Nunnally. "We can measure compounds used to make cell membranes and compounds that represent the primary fuel of cells. We can monitor changes in the overall pattern that drug therapy produces, and can see the spectrum go from one that indicates disease to one that looks normal."

MR spectroscopy is offering UTHSCD pediatric researchers a way to assess the damage to a newborn's brain cells when its oxygen supply is decreased in the uterus during the birth process or after birth. Says neonatologist Dr. Abbot Laptook, "Because of a lack of information about the effects of asphyxia, we have been confined in therapy to supportive care and controlling seizures. Now we have the means to address new questions.

"If we can study enough sick babies who have suffered some interval of asphyxia, we may be able to understand why some babies tolerate a lack of oxygen better than others. We may also be able to determine when therapy, such as the use of certain drugs, may be helpful -- for example, in controlling brain swelling," Laptook says.

Pediatric nutritionists Dr. Charles Mize and Dr. Ricardo Uauy have been monitoring the progress of "Baby Raul," who at ten months of age was unable to raise his head or roll over. He was diagnosed as having rickets. In the past, pediatricians have been unable to identify the cause of muscle problems in the disease that affects mainly the bones. However, using spectroscopy the doctors were able to assess that Baby Raul's muscle weakness problem was one of muscle cell phosphorus, and they watched him recover as a result of phosphorus repletion in his muscle after vitamin D treatment.

Stroke researchers are studying the brain tissue of a group of patients who are recovering from a single stroke but who still have speech difficulties. The researchers, including Drs. Frederick Bonte, Michael Devous and Delaina Batson, have found a decrease in chemical levels within tissue on the stroke side of the brain, as one would expect with the presence of scar tissue. In addition, they have found lower than normal levels on the opposite side of the brain as well.

"This means that the energy needs of cells throughout the brain are not being met," said Bonte. "Probably this generalized pattern indicates the presence of an underlying blood vessel disease, similar to that in persons with atherosclerosis leading to a heart attack."

Cancer experts are using a blood substitute, fluosol, as an agent to enhance a patient's response to radiation therapy, according to physicist Dr. Peter Antich. He and radiation oncologist Dr. Phuc Nguyen are performing clinical trials using fluosol as an oxygen transport agent. They have found that the agent accumulates in blood vessels surrounding tumors and that it helps to delineate tumor from normal tissue. Using MR spectroscopy, they hope to find how best to use the agent therapeutically to penetrate tumor tissue and increase a tumor's vulnerability to therapy.

Heart researcher Dr. Craig Malloy will soon begin using spectroscopy to analyze treatment in patients with cardiac myopathy, which is heart failure for unexplained reasons, and in patients with ischemic heart disease who have suffered a heart attack. His studies now concentrate on normal individuals, establishing base-line values. Also, with the arrival of new equipment later this year, Malloy and others will begin integrating MR imaging information with that of MR spectroscopy from the same heart region to pursue a combined approach.

The MR center is supported in part by a \$2.7 million research grant from the National Institutes of Health's Division of Research Resources. The grant, under Nunnally's direction, has enabled the center to purchase its second spectroscopy unit -- a state-of-the-art MR unit that, when functioning sometime this year, will operate at a magnetic field more than double that of other MR machines. This stronger magnet is the second such unit in the country to be installed. The NIH support makes the health science center facility a regional biotechnology resource to which investigators from Texas and surrounding states have access. It is one of only nine such federally funded facilities for MR research in the United States.

Nunnally who is a biochemist, directed a team of engineers and physicists at the health science center in building the clinical MR spectroscopy system. After completing the project, they have been working on a number of developing areas within

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the field of MR technology. One of these areas includes a specialized MR device called a surface coil. The round coil is placed on the surface of the patient's body and helps to amplify and focus the radio pulse within a given location, thereby producing a stronger signal. The health science center research team developed the first surface coil in the United States to be approved by the U.S. Food and Drug Administration.

"The most important application for MR spectroscopy is to see early on if therapy is having an affect. This would especially hold true for cancer, liver disease, metabolic diseases, heart disease and episodes of stroke," Nunnally said.

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NOTE: The University of Texas Health Science Center at Dallas comprises Southwestern Medical School, Southwestern Graduate School of Biomedical Sciences and the School of Allied Health Sciences.