ImagE of the month

Magnetization transfer imaging (MTI) assays macromolecular protons through their intimate connection and interaction with surrounding tissue water. "Anywhere it's applied, MTI is very sensitive to macromolecular makeup of the tissue," said Seth Smith, Ph.D., a post-doctoral fellow at the F.M. Kirby Imaging Center at Johns Hopkins University in Baltimore. "It's useful in cases of problems with multiple sclerosis (MS), this means myelin.

"MTI is a much more sensitive myelin marker than any other conventional imaging technique," he said.

Conventional MRI targets only water, making it hard to assess the macromolecular subunits of CNS tissue, like myelin. With MTI, an initial off-resonance radiofrequency pulse is applied to the spin-lattice column. This pulse selectively saturates the magnetization of protons attached to such macromolecules as myelin. Some of this magnetization is transferred to free protons in tissue, which reduces the intensity of the observed water signal. Since MTI's effect depends on the density of macromolecules in the tissue, it's a back-door method for getting at the macromolecular structure," said Dr. Smith.

The researchers then calculate a slightly modified magnetization transfer ratio, based on the difference in the signal intensities with and without an MTI prepulse, to quantify differences between patients with and without disease.

In the past, it was difficult to ascertain whether or not spinal cord lesions were a significant factor in MS. Conventional MR imaging did not reveal the amount of tissue damage that was actually present in the spinal cord, though in MS brain lesions MTI reveals much more MS pathology. It is now hypothesized that a lot of the clinical deficit in MS arises from spinal cord damage. "When we use MT imaging, what we find is that every cord (from patients with MS) is damaged in some way," said Dr. Smith.

The presence of MS spinal lesions on MTI correlates better with the patient's symptoms at presentation than does the presence of brain lesions detected by conventional MRI. A patient with spinal lesions may be walking at presentation. However, "If I look at the spinal cord and see a bunch of lesions, I can guarantee that the patient is not walking well," said Dr. Smith.

The researchers have imaged patients varying ages and at a spectrum of stages in MS: relapsing-remitting, secondary progressive, etc. Since it is difficult to get a patient before he or she has had an attack, information from such studies about the early stages of the disease may prove useful, said Dr. Smith. The researchers also are imaging MS patients periodically (3, 6, 12, and 24 months) to see if they can detect changes in the disease over time.

The researchers are seeking links between MS-induced changes in spinal MTI and brain MTI and the neurologic presentation of patients with MS. The correlation between spinal MTI and the neurologic presentation has been striking.

"We and others find in the brain there is little correlation with clinical presentation. However, the second we look at the spine, everything starts to correlate," said Dr. Smith. The spine is the main pathway for nerves in the body and gets a small lesion in something the size of a quarter, the effects could be massive.

MRI is used to confirm the clinical findings in patients suspected of MS. "We're hoping to make MTI more of a diagnostic tool," Dr. Smith said. A strong enough correlation between MTI spinal imaging findings and clinical presentation could lead to the primary use of MRI to diagnose MS and predict outcome.

MTI also has implications for therapy. Right now, patients with MS often are treated with axonal protection agents, but the effects may take a long time to be seen. "What we hope to see is, can we within a shorter amount of time see that there is any sort of change in the tissue due to therapeutic intervention," said Dr. Smith.

MTI scans can be done with most higher field MRI scanners using a surface (spine) coil that can take only 7 minutes using a 3T magnet. This implies that the technique could easily be integrated into an imaging center or hospital setting.

Dr. Smith's collaborators include Dr. Peter Calabresi; Peter van Zijl, Ph.D.; Craig Jones, Ph.D.; Eliza Gordon-Lipkin; and Kathleen Zackowski, Ph.D.

-Kerry Wachter

Study: Natalizumab Use Poses Limited Risk of PML

Los Angeles — There is limited risk of developing progressive multifocal leukoencephalopathy with the use of natalizumab, according to the results of a safety evaluation presented at the annual Digestive Disease Week.

Researchers from the Mayo Clinic in Rochester, Minn., and Cedars-Sinai Medical Center in Los Angeles evaluated patients who had taken the drug while participating in clinical trials of its use in treating Crohn's disease, multiple sclerosis, and rheumatoid arthritis.

Trials involving natalizumab (marketed as Tysabri) were halted in 2005 after there were two reports of patients who developed progressive multifocal leukoencephalopathy (PML) while taking combination therapy with natalizumab and interferon-beta. A third report described a patient who was taking natalizumab alone and had previously taken the drug in combination with azathioprine. Additionally, this patient had previously been treated with rituximab. The companies funded the safety evaluation.

However, Dr. Sandborn noted that the patients who developed PML had taken natalizumab in combination with either interferon-beta or azathioprine, and physicians were likely to use the drug more aggres- sively until the risk factors were better understood.

It is unclear whether a shortened washout would be effective for PML, according to the researchers.

-May Ellen Schneider

Healthy spine by T2 and T1 3T MRI and MTCSI (top); White T2 and T1 MRI show slight cord atrophy in MS patient; MTCSI shows hyperintensities in the lateral (green arrow) and dorsal (yellow arrow) column (bottom).