Researchers look into mechanisms of multiple sclerosis using 7T MRI

OSU is using Achieva 7.0T hoping ultrahigh field imaging may help understand progression of MS
Physicist Petra Schmalbrock, PhD, is Associate Professor of Radiology at the Ohio State University Department of Radiology, Wright Center of Biomedical Imaging. She explains how MR is being studied for its usefulness in diagnosing and assessing MS. “Sequences that are typically used are FLAIR, pre- and post-contrast T1W, and T2W. On FLAIR, MS lesions are well visible as bright spots. In the T1-weighted images, MS lesions appear dark, and there aren’t as many as on FLAIR. Eventually, the T1 images show a persistent black lesion, and the assumption is that the tissue has been destroyed. The inflammatory process is considered to be most active when lesions are seen bright (enhanced) on post-contrast images. This is thought to occur because the disease begins around small vessels, and gadolinium will leak out of these small vessels into the active lesion. However, the enhancing lesions come and go rather quickly, usually within a few weeks, yet the inflammatory process continues probably much longer.”

Dr. Schmalbrock is collaborating with neurologist/pathologist David Pitt, MD, Assistant Professor of Neurology at the Ohio State University and using Achieva 7.0T to gain understanding of the mechanisms of MS progression. The ultimate goal is to help better develop treatment plans.

**White matter lesions with different iron content**

“In order to study MS, we characterize white matter lesions. The most widely accepted mechanism is that small vessels break open, and inflammatory cells (macrophages and T cells) can enter the brain tissue and cause an inflammatory response,” says Dr. Schmalbrock. “We study MS brain specimens to characterize these cells. The macrophages can either be pro-inflammatory or anti-inflammatory and contain different amounts of iron depending on their polarization state. The anti-inflammatory cells have less iron than the pro-inflammatory macrophages. That’s where the ultrahigh field MR imaging comes in: it’s more sensitive than low field to the effects of iron, and it provides higher resolution to see more of the structural detail in these MS lesions.”

There are several aspects to the white matter lesions study. Active, demyelinating inflammation occurs during the early, so-called relapsing remitting phase of the disease while
We found significantly more iron lesions in the relapsing remitting patients than in the secondary progressive patients. It is absent in the later phase, called secondary progression. “We’re studying the two stages of the disease,” says Dr. Schmalbrock, “And we’ve found significantly more iron lesions in the relapsing remitting patients than in the secondary progressive patients. This supports our hypothesis that iron lesions tell us something about the inflammation mechanism.”

The other aspect is comparing the gadolinium-enhancing lesions with the iron-containing lesions. “Interestingly, these might reflect different aspects of inflammation. The gadolinium enhancement reflects active demyelination and the iron longstanding, chronic inflammation process which leads ultimately to tissue degeneration and cannot be seen with gadolinium enhancement.”

**Basal ganglia are also affected**
It has been shown that iron also accumulates in the basal ganglia of MS patients. Dr. Schmalbrock is now studying whether iron in basal ganglia can be an indicator for disease advancement and perhaps can serve as a predictor. The mechanism of this iron accumulation is not fully understood. “We are just beginning some follow-up studies.”

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White matter lesion characterization
Example images of a 31-year-old female RRMS patient. The high-pass filtered phase image is reconstructed from the third echo of the 3D-FFE sequence. The Gd-enhancing lesion (red arrow) is also seen on FLAIR, but not or only partially on the phase image reflecting iron content, unlike the two clearly depicted dark “iron” lesions on the phase image (blue arrows). The green arrows depict a lesion seen on FLAIR, but not on the T1 image. Phase images were computed off-line from the scanner generating real and imaginary images, by homodyne reconstruction of the complex data using a Gaussian filter with a pixel width of 4% of the xy-matrix size. All images were spatially registered using FSL.
“We have developed a 7.0T white matter attenuated sequence, which may increase sensitivity and allow us to count the cortical MS lesions.”

**Cortical lesion**

Achieva 7.0T images of a 30-year-old male. A cortical lesion is marked. Other potential lesions that were only visible by the readers on the color-indexed image are marked by the arrows. The color magnitude phase images were computed off-line from the scanner reconstructed real and imaginary components by the bright-to-dark setting from the magnitude and the color by assigning each color of a color wheel to the different phase angles.

**Acquisition parameters:**

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Coil</th>
<th>TR [ms], flip, TE [ms]</th>
<th>TS / TI [ms]</th>
<th>Acq voxel [mm³]</th>
<th>Scan time [min.]</th>
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<tr>
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<tr>
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</table>

WHAT = white matter attenuated, TS = shot interval, TI is inversion time.

*7T-WHAT, 7T GM attenuated, and 7T-T1-TFE use an adiabatic inversion pulse with a pulse setting of 2000 selected under control parameters.
We enrolled patients before they started their treatment and they will regularly come back over the next year, to see how they’ve changed.”

**Multiple sclerosis also affects the cortex**

The third study involves cortical lesion imaging. Initially, MS was thought to be only a white matter disease, but more recent pathology studies have also found disease activity in the cortex. Cortical lesions are thought to develop at later stages in the disease. “How that happens is not understood, but it may relate to the progression of cognitive function problems and permanent damage. Cortical lesions are almost impossible to visualize with conventional MRI because the spatial resolution is insufficient and contrast is weak between lesions and normal gray matter.”

“We have developed a 7.0T sequence that we call White Matter Attenuated sequence, which may increase sensitivity and allow us to count the cortical lesions. We are comparing this method with high-resolution susceptibility weighted imaging that was shown to be successful for cortical lesion imaging by researchers from the Massachusetts General Hospital. We are currently developing a model that estimates how well a given MRI technique may visualize cortical lesions.”

“Ultrahigh field MRI has some practical limitations, such as lack of homogeneity because the RF waves do not evenly propagate through the brain, and adjacent air and brain tissue, which can lead to artifacts. But the advantage is that ultrahigh field MRI can help detect more subtle changes that couldn’t be visualized in conventional MRI,” says Dr. Schmalbrock. “I would say MS is really the most promising application for ultrahigh field MRI right now.”

“7.0T MRI is more sensitive than low field to the effects of iron, and provides higher resolution to see more structural detail in MS lesions.”

**Reference**