T1rho MR is sensitive to changes in normal appearing white matter and gray matter in multiple sclerosis

Jay Gonyea1, Christopher G. Filippi2, Angela Applebee2, Trevor Andrews3,4, Lindsay Kan4, Scott Hipko4, and Richard Watts4

1Department of Radiology, University of Vermont College of Medicine, Burlington, VT, United States, 2Department of Radiology, University of Vermont College of Medicine, Burlington, VT, United States, 3Department of Radiology, Columbia University Medical Center, New York, NY, United States, 4Philips Healthcare, Cleveland, OH, United States, 5University of Vermont College of Medicine, Burlington, VT, United States

Purpose
To determine if quantitative T1ρ MRI is sensitive to the demyelinating process, or protein leakage found in the brains of Multiple Sclerosis (MS) patients31, and to compare to normative values of T1ρ in white matter (WM) and cortical gray matter (GM).

Methods
This IRB-approved cross-sectional study compared 13 MS patients to 17 age-matched controls (demographics in Table 1). Data was acquired using a Philips 3T Achieva TX scanner and an 8-channel head coil. Whole-brain T1ρ-weighted images were acquired using a fluid attenuated variable flip angle 3D turbo spin echo technique (spatial resolution 1.8x1.8x1.8mm³). Images were acquired with a spin lock frequency of 500Hz and spin lock durations of 0, 20, 40, 60, 80 and 100ms. Each T1ρ map was calculated based on a single exponential fit to the coregistered T1ρ-weighted images. The T1ρ map was then itself coregistered to a T1-weighted 3D TFE anatomical scan. Using unified segmentation12 (SPM8) of the T1-weighted image, the T1ρ maps were segmented into WM and GM, and spatially normalized to MNI space. Major WM tracts were defined using the JHU atlas13, while cortical GM and juxtacortical WM were defined by an intersection of the Harvard-Oxford cortical atlas (dilated by 5mm) with the subject-specific GM and WM masks respectively. In addition, 3D FLAIR (spatial resolution 1.2x1.2x1.2mm³) and 3D DIR (spatial resolution 1.2x1.2x1.3mm³) images were obtained for lesion identification.

Results
The new T1ρ technique produced high SNR whole-brain T1ρ maps. Table 1 shows the measured T1ρ values, with significant differences in T1ρ values for cortical GM (p=0.007), WM (p=0.003) and juxtacortical WM regions (p=0.002).

Figure 1 shows an example of the defined regions-of-interest using the WM/GM segmentation of the T1-weighted image and predefined MNI templates. The T2-FLAIR shows periventricular lesions that are clearly delineated on the T1ρ map. These lesions demonstrate substantially increased T1ρ values (typically 100ms or greater) compared to the surrounding tissue (75-80ms).

Discussion and Conclusions
T1ρ MRI has been previously shown to reflect the macromolecular content of tissue, due to chemical exchange. Limited brain studies have shown T1ρ to be sensitive to the changes associated with Alzheimer’s and Parkinson’s disease44, but it has not been investigated in relation to MS. MS is known to cause disruption of the blood-brain barrier, which in turn leads to increased levels of blood serum proteins in the brain31; this increase in protein content can increase chemical exchange locally. Abnormal epithelial tight junction (TJ) proteins found in MS may participate in this exchange to a different degree, than do normal TJ proteins.

Our results demonstrate that both normal-appearing WM and GM have different T1ρ values in MS compared to age-matched controls. Lesions have low signal intensity on the T1-weighted images, leading to their exclusion from the WM/GM masks generated by the segmentation. Thus our results are not biased by lesion load, which would otherwise increase the T1ρ values within the defined regions. Including lesions in the analysis would likely increase differentiation between the MS and control groups due to their higher T1ρ values. In addition, although this study found significant differences between non-focal regions of interest, it is possible that specific brain regions show greater changes which would increase the diagnostic utility of this approach.

MS is known to result in early stage cortical lesions, although these lesions are often not visible on standard imaging56. T1ρ may provide a quantitative measure of cortical GM changes that are not seen with other methods. While the difference in T1ρ values is relatively small (~1-2ms), our technique has sufficient sensitivity to detect this subtle change.

References

Table 1. Subject demographics and T1rho estimates. (Mean±SD)

<table>
<thead>
<tr>
<th>Sex</th>
<th>Sex</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>MS Patients</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>44.5±10.3</td>
<td>44.6±1.2</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>78.0±1.1 ms</td>
<td>79.1±1.0 ms</td>
</tr>
<tr>
<td>GM</td>
<td>76.2±1.4 ms</td>
<td>78.2±1.8 ms</td>
</tr>
<tr>
<td>WM Tracts</td>
<td>75.0±1.0 ms</td>
<td>76.7±1.5 ms</td>
</tr>
</tbody>
</table>

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