# T1RHO MR IS SENSITIVE TO CHANGES IN NORMAL APPEARING WHITE MATTER AND GRAY MATTER IN MULTIPLE SCLEROSIS

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## Purpose

To determine if quantitative $T_{1\rho}$ MRI is sensitive to the demyelinating process, or protein leakage found in the brains of Multiple Sclerosis (MS) patients[1], and to compare to normative values of $T_{1\rho}$ 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 $T_{1\rho}$-weighted images were acquired using a fluid attenuated variable flip angle 3D turbo spin echo technique (spatial resolution $1.8\times1.8\times1.8mm^3$). Images were acquired with a spin lock frequency of 500Hz and spin lock durations of 0, 20, 40, 60, 80 and 100ms. Each $T_{1\rho}$ map was calculated based on a single exponential fit to the coregistered $T_{1\rho}$-weighted images. The $T_{1\rho}$ map was then itself coregistered to a $T_1$-weighted 3D TFE anatomical scan. Using unified segmentation[2] (SPM8) of the $T_1$-weighted image, the $T_{1\rho}$ maps were segmented into WM and GM, and spatially normalized to MNI space. Major WM tracts were defined using the JHU atlas[3], 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 $1.2x1.2x1.2mm^3$) and 3D DIR (spatial resolution $1.2x1.2x1.3mm^3$) images were obtained for lesion identification.

## Results

The new $T_{1\rho}$ technique produced high SNR whole-brain $T_{1\rho}$ maps. Table 1 shows the measured $T_{1\rho}$ values, with significant differences in $T_{1\rho}$ 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 $T_{1\rho}$ map. These lesions demonstrate substantially increased $T_{1\rho}$ values (typically 100ms or greater) compared to the surrounding tissue (75-80ms).

| | Controls | MS Patients | p-value |
|---|---|---|---|
| Sex | 11M, 6F | 4M, 9F | - |
| Age | 44.5±10.3 | 44.6±11.2 | - |
| Diagnosis | - | 9RR, 3CIS, 1PP | - |
| Cortical GM | 78.0±1.1 ms | 79.1±1.0 ms | 0.007 |
| WM Tracts (JHU) | 76.2±1.4 ms | 78.2±1.8 ms | 0.003 |
| Juxtacortical WM | 75.0±1.0 ms | 76.7±1.5 ms | 0.002 |

**Table 1.** Subject demographics and T1rho estimates. (Mean±SD) RR=Relapsing remitting, CIS=Clinically isolated syndrome, PP=Primary progressive.

## Discussion and Conclusions

$T_{1\rho}$ MRI has been previously shown to reflect the macromolecular content of tissue, due to chemical exchange. Limited brain studies have shown $T_{1\rho}$ to be sensitive to the changes associated with Alzheimer's and Parkinson's disease[4], 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 brain[1]; this increase in protein content can increase chemical exchange locally. Abnormal epithelial tight junction (TJ) proteins found in MS may participate in chemical exchange to a different degree, than do normal TJ proteins.

Our results demonstrate that both normal-appearing WM and GM have different $T_{1\rho}$ 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 $T_{1\rho}$ values within the defined regions. Including lesions in the analysis would likely increase differentiation between the MS and control groups due to their higher $T_{1\rho}$ 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 imaging[5, 6]. $T_{1\rho}$ may provide a quantitative measure of cortical GM changes that are not seen with other methods. While the difference in $T_{1\rho}$ values is relatively small (~1-2ms), our technique has sufficient sensitivity to detect this subtle change.

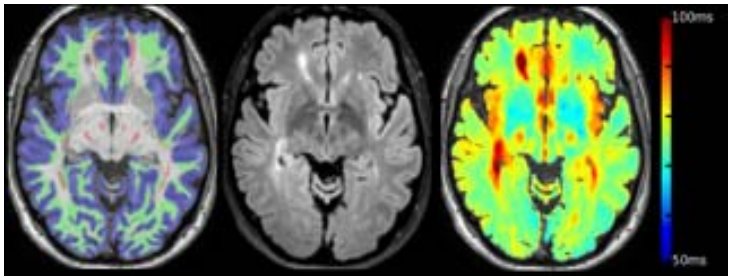


Figure 1. T1-weighted image showing segmentation of cortical gray matter (blue), juxtacortical white matter (green) and major white matter tracts (forceps minor, corticospinal tract, anterior thalamic radiation, inferior longitudinal fasciculus, red); T2-FLAIR showing white matter lesions; T1rho map.

## References

1. Plumb, J., et al., *Abnormal endothelial tight junctions in active lesions and normal-appearing white matter in multiple sclerosis.* Brain pathology, 2002. **12**(2): p. 154-169. 2. Ashburner, J. and K.J. Friston, *Unified segmentation.* Neuroimage, 2005. **26**(3): p. 839-51. 3. Wakana, S., et al., *Reproducibility of quantitative tractography methods applied to cerebral white matter.* Neuroimage, 2007. **36**(3): p. 630-44. 4. Haris, M., et al., *T1ρ MRI in Alzheimer's Disease: Detection of Pathological Changes in Medial Temporal Lobe.* Journal of Neuroimaging, 2011. **21**(2): p. e86-e90. 5. Filippi, M., et al., *Intracortical lesions.* Neurology, 2010. **75**(22): p. 1988-1994. 6. Lucchinetti, C.F., et al., *Inflammatory cortical demyelination in early multiple sclerosis.* New England Journal of Medicine, 2011. **365**(23): p. 2188-2197.