A Longitudinal Study of Magnetization Transfer in Multiple Sclerosis

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Introduction
Magnetization transfer (MT) imaging has been shown to improve the detectability of contrast enhancing multiple sclerosis (MS) lesions [1,2] and pathological specificity [3-6]. Given the variability in appearance of MS lesions on conventional MRI scans, the evolution of MT measures that may more closely reflect lesion demyelination is of considerable interest. We present here a longitudinal study of a group of MS patients and describe the temporal evolution of MT properties in lesions and normal appearing brain.

Methods
We have collected conventional MRI (T1W, T2W, PDW) and MT data in 12 normal volunteers and 30 MS patients (11 relapsing/remitting, 5 primary progressive and 14 secondary progressive). For the MS patients, MRI data were acquired at six time points over a ~5 year period (5 exams at 6-8 month intervals and 1 followup exam ~1.5 years later) while MT data were acquired only during the last 3 time points. MT contrast (MTC) images were calculated as a percent difference \(100 \times \frac{[M_{\text{nosat}}-M_{\text{sat}}]}{M_{\text{nosat}}} \) between SE (TR/TE=940/20 ms) images collected without and with an on-resonance binomial saturation pulse (1 ms, 121, \(|B_1| = 20\mu T \)) [7].

A semi-automated tissue segmentation and analysis package was used to classify all MS lesions seen on T2W and PDW images. All data were spatially registered, using automated software[8], to a single time point to allow temporal tracking of all voxels. ROI's were also manually defined in four white matter (WM) and four grey matter (GM) areas of normal subjects and in normal appearing tissue of the MS patients.

Results
From the ROI analysis, we measured an MTC value of 41.3±1.4% (mean ± standard deviation) for WM in normal subjects. In the MS patients, the mean MTC in both normal appearing WM (NAWM, 38.1±2.3%) and lesions (26.9±2.6%) were significantly \(p < 0.0001 \) decreased. MTC values for GM were unchanged (28.5±1.72% for normal subject and 28.0±2.6% for MS patients).

(0-5 years). The average lesion MTC for each age range per patient is plotted in Figure 1 and reveals a negative correlation between MTC and lesion age \((R=0.47, p < 0.0001)\). The pre-lesion history of voxels identified as new lesions on a single time point can also be extracted from this data. Figure 2 shows a plot of the average MTC versus time over a range of ~1.5 years prior to MRI detection to ~1 year post detection. Again a negative correlation was observed \((R=0.42, p < 0.0001)\). At ~1-1.5 prior to being identified as lesion, WM MTC values (32.9±2.7%) were significantly \(p < 0.0001 \) lower than NAWM in the same patients.

Discussion
The negative correlation between lesion age and MTC reflects the progression of demyelination in MS and provides useful data for the interpretation of the pathological state and evolution of lesions. The decreased MTC in the NAWM of MS patients, previously reported by ourselves and other[6], is likely due to microscopic lesions not directly visualized on conventional MRI. The negative correlation between MTC and time prior to MRI detection as lesion indicates that significant demyelination may be occurring in NAWM without being detected on conventional MRI. The observation of decreased MTC in WM later classified as lesion compared to WM that remained normal on subsequent MRI scans, suggest that MT might provide a predictive index of disease progression in MS.

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References

Fig. 1. Mean MTC versus lesion age in 30 MS patients (o) and the linear regression line.

Fig. 2. Mean MTC versus time since MRI detection of MS lesion (o) and linear regression line.