Multimodal High Resolution Magnetization Transfer and T1mapping in NAWM of patients with Clinically Isolated Syndrome

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Introduction: Multiple Sclerosis (MS) is known to reduce magnetization transfer ratio (MTR) [1,2] and increase the longitudinal relaxation time (T1) in the white matter (WM) [3,4]. However MS involves multifocal inflammation, demyelination, Oligodendrocytes loss, axonal loss, gliosis and remyelination, and MT and T1 will be differently affected by these processes. We hypothesize that multimodal imaging of MT and T1 will provide increased sensitivity and specificity for characterizing disease progression. Ideally such multimodal comparisons should be spatially specific to allow the effects on normal appearing white matter and perilesional effects to be separated. High spatial resolution maps of T1 and MTR can be formed at 7T due to increased signal to noise ratio; limitations in MTR imaging at 7T due to high Specific Absorption Rate (SAR) can be resolved using an MT prepared turbo field echo sequence (MT-TFE) with pulsed saturation. Here, we measure the distribution of MTR and T1 values in normal appearing white matter (NAWM) at 7T and high spatial resolution, comparing CIS patients with healthy controls.

Methods: Ten patients with Clinically Isolated Syndrome (a condition that is likely to lead to MS) were recruited from Nottingham University Hospital. Six age-sex matched healthy volunteers were also recruited, and both groups were consented according to local ethics approval. Scanning was performed on a 7T Philips Achieva system, equipped with whole body gradients and 16-channel receive coil and head only volume transmit coil. MT images were acquired using a 3D MT-TFE sequence (1x1x1.5mm resolution; TE=5.7 ms; TR=9.8 ms; 20 slices; total scan time =8:22min) [5] for no saturation pulse (S_0) and for pulsed saturation (S_{MT}). The pulsed saturation applied a train of 20 off-resonance pulses (13.5 µT Gaussian-windowed, sinc pulses with a bandwidth of 200 Hz and off-resonance by ±1.05 kHz (3.5ppm), with 50 ms between each pulse). Images were co-registered and MTR maps were calculated on voxel by voxel basis according to $MTR=(S_{MT0}-S_{MT})/S_{MT0}$. The scanning protocol included field map and a B1 map to correct the MT images for the effect B1 inhomogeneity [6,7]. T1 maps were derived from MPRAGE images (1.25 mm isotropic voxels, TE=3.2 ms; TR=6.9 ms; 58 slices; scan time per TI =2 min) acquired at 7 different inversion times (150, 300, 500, 800, 1200, 1800, 2500 ms). T1 maps were then produced using a method described previously [8]. The MPRAGE image with a TI near the null point was used in SPM5 to segment and create a mask of the NAWM [9]. MTR images were then registered to the MPRAGE image, so that the NAWM of the MTR and T1 maps could be segmented with the same mask. The histograms of MTR and T1 of the NAWM were normalised to the number of pixels in the mask and plotted. The mode (peak position), Full Width at Half Maximum (FWHM) and area under the curve of left and right tails of histograms (tails delineated from point where histogram reached half maximum). Voxel values of MTR and T1 within the NAWM were plotted against each other for each subject. The resulting scatter plots from all healthy subjects were then overlaid on the scatter plot for each CIS patient.

Results: Fig 1 shows the average distributions of (A) MTR and (B) T1 values in NAWM of both CIS and healthy subjects. Table 1 summarises the parameters describing the histograms averaged over all subjects. MTR values are reduced for CIS patients compared to controls with the histogram being skewed to lower MTR values (see areas under tails). T1 is similarly increased in patients compared to controls but the effect is less pronounced. Fig 1C shows a scatter plots of MTR+ versus T1 of all controls (black) overlaid on a similar scatter plot for one CIS subject (green). This suggests different populations of abnormal pixels in CIS patients in the MTR/T1 space, but when these voxels are mapped back to the brain they showed no particular clustering. These plots were very variable between our CIS patients but all CIS patients showed larger scatters than controls.

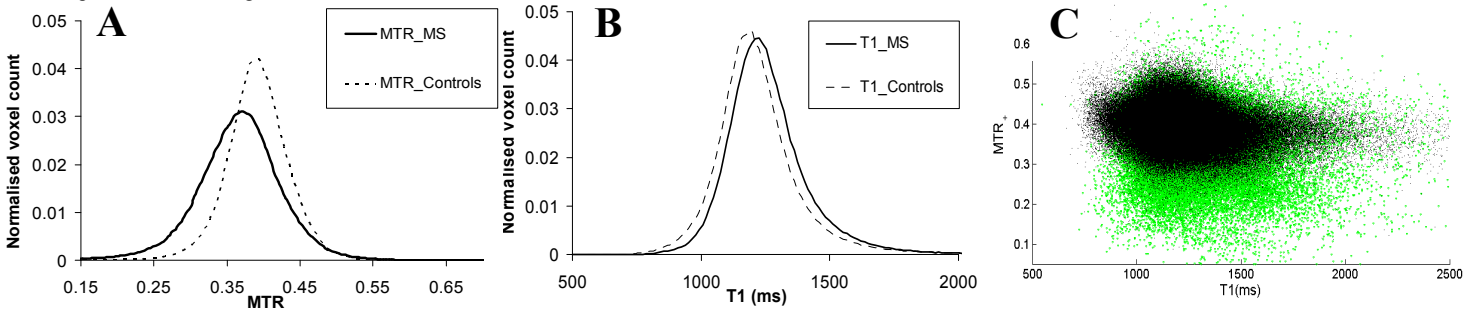

Fig.1(A) Average histograms of MTR in MS and controls (B) Histograms of T1 in MS and controls(C) Scatter plot of MTR-T1 of all controls overlapping MTR-T1 scatter plot of one MS subject

Discussion: MTR and T1 histograms in NAWM show significant differences between CIS patients and controls and the data indicates that MTR parameter can be more sensitive to changes in NAWM than T1. However the scatter plot indicates different populations of abnormal voxels in the MTR/T1 space, and these populations voxels will now be characterized particularly in patients with more advanced MS.

	MTR			T1 (ms)		
	CIS	Controls		CIS	Controls	
	Average±sd	Average±sd	p-value	Average±sd	Average±sd	p-value
Mode (peak position)	0.369±0.026	0.389±0.010	0.032	1218±32	1188±28	0.0425
FWHM	0.103±0.014	0.084±0.014	0.009	257±41	256±51	
Area of low tail	0.159±0.040	0.137±0.013		0.112±0.022	0.119±0.014	0.013
Area of high tail	0.133±0.0131	0.147±0.015	0.032	0.212±0.015	0.199±0.013	

Table 1: Statistical analysis of MTR and T1histograms averaged over MS and controls subject**.**

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