

Peri-lesional White Matter Changes in Clinically Isolated Syndrome Suggestive of Demyelination on MTR and MPRAGE at 7T

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Introduction Many MR studies have reported changes in the normal appearing white matter (NAWM) in multiple sclerosis. However histological and MR evidence suggests that these changes are not uniform, but rather are localized close to gross lesions [2]. Better identification of diffuse areas of damage in WM may be important in studying the progression of MS and possible responses to therapy. MTR is a marker of the density of macromolecules including myelin, but the MT sequence can also be sensitized to the chemical exchange saturation transfer (CEST) in amides. This may have particular sensitivity to myelin and can be detected with good sensitivity at 7T. Here, we have acquired T1w, MTR and MT sensitive to CEST (MTR_c) images acquired at high spatial resolution at 7T and have developed software to characterise peri-lesional changes in NAWM in patients with clinically isolated syndrome (CIS) suggestive of MS. **Aim:** to characterise peri-lesional changes and compare MT and T1 changes in a series of lesions from CIS patients.

Methods Images were acquired from 10 patients with CIS (age=36.7±10.8, EDSS mean=2.3±0.8) on a 7T Philips Achieva scanner using an MPRAGE sequence for T1w images (0.6x0.6x0.6mm³, FOV=192x163x156mm³, TR/TE=15/5.9ms, 12:05min) and an MT-TFE sequence for MTR and MTR_c (0.86x0.86x1.5mm³, TR/TE=9.8/5.7ms, FOV=220x220x30mm³, 8:22min). For MT-TFE, Magnetization Transfer preparation was applied before each TFE readout, with either 20 off-res pulses applied at +1100Hz for CEST sensitivity (MT₁), -1100Hz (MT₂), or no saturation (MT₀). MT₁ and MT₂ scans were registered to MT₀ scans and processed to obtain MTR_c=(MT₀-MT₁)/MT₀ and MTR=(MT₀-MT₂)/MT₀ maps. B1 correction was performed to reduce contrast inhomogeneity [1]. Both data-sets were linearly registered with 6 degrees of freedom (DOF) to the MPRAGE images using FLIRT (FSL). Lesions were segmented manually by an experienced radiologist on the MPRAGE images using NeuRoi. The MPRAGE images were normalised and masks of the NAWM were obtained by thresholding the WM probability maps in SPM5. As lesions were often classified by SPM5 as in GM, dilated lesion masks were added to the NAWM masks. These masks were then eroded to ensure all GM was removed. For each subject a map of distance from the voxel to the closest lesion was calculated using the ImageJ cortical thickness plugin. For a preliminary test of the software, ten lesions lying at least 2cm from any other lesion and not touching the ventricles were chosen. Values of MTR_c, MTR and T1w signal were plotted against the distance from the lesion boundary for each lesion to give a peri-lesional profile, binned at 1mm spatial resolution. The function

(x represents distance), was fitted to the peri-lesional profile to parameterize the width of the rim proximal to the lesion (*W*) and any slope changes distal to the lesion (*S*).

Results Figure 1 shows an example of a lesion where the MTR/MTR_c signals increase slowly in the lesion rim (*W*=0.6/0.8mm), whereas the T1w signal changes only within ≤1mm of the lesion (*W*= 0.3mm). Figure 2 shows that *W* for MTR and MTR_c correlated well with *W* for T1w (and values also correlated with each other, *r*² = 0.66) although *W* was significantly higher for MTR and MTR_c than T1w (*p*<0.01 in both cases). For the lesion shown in Fig. 1, the T1w signal was flat distal to the lesion (*S*= 0.001 mm⁻¹) whereas the MT signal decreased (*S*=+0.003/0.011mm⁻¹). Such a decrease in MT distal to the lesion (positive *S*) was observed in about a third of the lesions (Fig. 3). Figure 3 shows that in general if *S* was positive for one parameter (e.g. MT) then it was generally also positive for the other parameters and that the absolute value of *S* was generally larger for MTR and MTR_c than for the T1w signal (*p*<0.05).

Discussion This new method of characterizing peri-lesional changes shows that all lesions display a proximal rim which is wider on MTR and MTR_c than on T1w scans. More distally, most lesions show increases in MTR or T1w signal (negative *S*), but a significant fraction show a decrease (positive *S*) which indicates the presence of a ring around the lesion. The values of *S* suggest that MTR and MTR_c maps were more sensitive to distal peri-lesional changes than T1w scans. A previous study that characterised peri-lesional changes in a similar way [2] found MT to be less sensitive than T1w, but this difference may be due to the increased sensitivity of MT, or the better spatial resolution available at 7T. Future work will include analysis of lesions from different types of MS patients, using T1 maps instead of T1w images, and determination of a method for dealing with neighbouring lesions. The peri-lesional changes will also be related to other features of the lesion, in particular the relationship between the ring apparent on some lesions here and the ring observed on some MS lesions in phase maps will be investigated [3].

References [1] Ropele et al., MRM, 2005, 53:134-14; [2] Vrenken et al., AJNR Am J Neuroradiol, 2006, 27:2005-11; [3] Hammond et al, Annals of Neurology, 64, 6, 2008. *Funded by the MRC.*

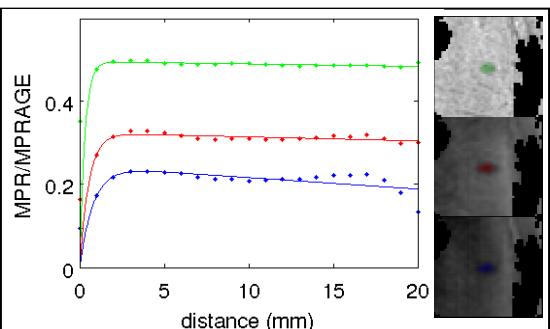


Fig. 1: Example peri-lesional profiles for MTR_c (red), MTR (blue) and MPRAGE (green) with overlaid fits described in the text.

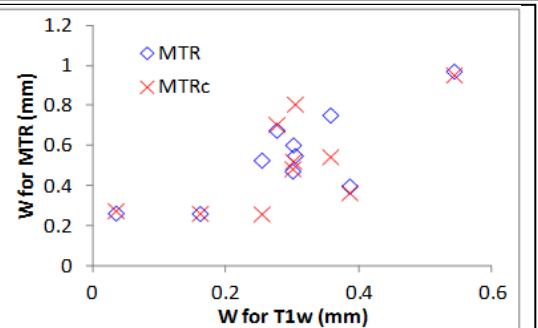


Fig. 2: Coefficient *W* for MTR_c and MTR plotted against *W* for T1w (mm) showing linear correlation (MTR *r*² = 0.66 and MTR_c *r*²=0.48).

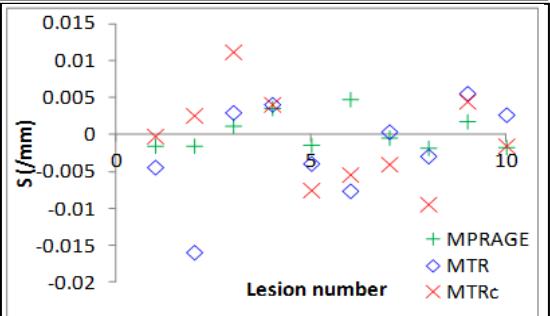


Fig. 3: *S* plotted for each image contrast, for each lesion.