EFFECT OF MULTIPLE SCLEROSIS LESIONS ON THE MTR OF GREY AND WHITE MATTER IN THE CERVICAL SPINAL CORD

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Introduction: The Magnetisation transfer effect is based on the exchange of magnetisation occurring between free protons and those attached to macromolecules, such as in myelin and membranes. This property of exchange between the two proton compartments in tissue can be exploited using selective saturation to indirectly observe the macromolecular protons, which are invisible using conventional MRI techniques. The magnetisation transfer ratio (MTR) is used as a measure of the amount of exchange taking place between the two compartments. MTR is of significance in multiple sclerosis (MS), since high field MRI studies[1, 2] have demonstrated that MTR correlates histologically with demyelination and axonal loss. Pathological studies have shown that demyelination of spinal cord grey matter (GM) occurs[3] and spinal cord GM lesions can be seen on post-mortem MRI studies[5]. A key question is whether MS lesions affecting the GM and white matter (WM) in the spinal cord induce changes in the MTR value of these tissues, which can be measured *in vivo*. This is important, as spinal cord GM MTR in MS has been demonstrated to correlate with physical disability[4].

Aim: To demonstrate the effect of spinal cord MS plaques on MTR values in the spinal cord in GM and WM, and compare these values with those measured in the normal appearing GM (NAGM) and WM (NAWM) in patients with MS and in the GM and WM in healthy subjects.

Methods: We evaluated MRI findings in four female patients (mean age: 44 yrs. range 28-55): three with relapsing remitting MS, one with secondary progressive MS (Expanded disability status score range 0-6) and five healthy controls (mean age: 29 yrs, range 27-31, 4 male, 1 female). Using a 3T Philips Achieva MRI system with RF multi-transmit technology (Philips Healthcare, Best, the Netherlands) and a 16-channel neurovascular coil the following sequences were acquired: 1) 3D fat-suppressed gradient echo (FFE) images (**figure 1**). (TR 23ms; TE 5ms; flip angle 7°; FOV 240x180mm^2; voxel size 0.5x0.5x5mm^3; 10 axial contiguous slices centered at the level of the C2-3 intervertebral disc). 2) MTR data were obtained by acquiring a 3D slab selective spoiled gradient echo sequence with two echoes (TR=36ms, TE1/TE2=3.5/5.9ms, flip angle 9°) with and without Sinc-Gaussian shaped MT saturating pulses of nominal α=360º, offset frequency 1kHz, duration 16ms applied prior to the excitation pulse. 22 5mm slices were acquired in an axial orientation, with FOV=180x240 mm^2 and acquisition matrix 240 x 320 (voxel size 0.75mmx0.75mm, reconstructed to 0.5mmx0.5mm), with SENSE factor 2 in the foot/head direction, with 2 signal averages. The prescribed imaging volume for the MTR sequence was centered at the same level as the FFE sequence. Due to sensitivity to motion artefact a cervical collar was used for immobilisation. Three 5mm slices were selected and regions of interest (ROI) (0.5mm^2) were drawn on each non-MT-weighted (or MT off) image, with reference to the corresponding slices of the FFE images. In the MS cases four ROIs were drawn in the GM and WM affected by lesions and the NAGM and NAWM. In the healthy controls, two identically sized ROIs were positioned in GM and WM. The ROIs were then transferred to the MTR maps to calculate MTR values for each ROI (**figure 2**). A mean MTR value per each ROI and for each case was calculated. An independent samples T test was used to compare mean MTR values between patients and controls.

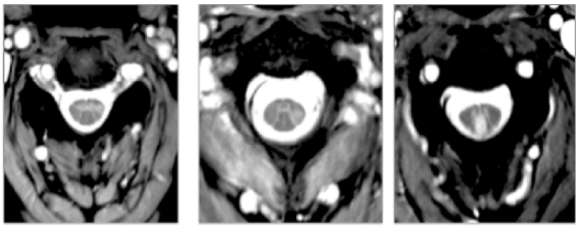

Figure 1. Axial images from three patients with RRMS. FFE sequence NV-coil 0.5x0.5x5mm^3 slices (13min 34sec), showing lesions with different involvement of WM and GM

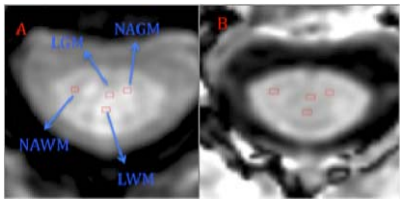

Fig 2A) MT Off with ROIs marked
B) MT MAP with ROIs transferred from MT off

Results: Twelve lesions identified on the FFE images were analysed, all involving WM and nine involving both GM and WM with none involving GM alone. The MTR values in lesional GM (LGM) and WM (LWM) appear to be lower (Mean LGM MTR: 47.4, SD: 0.84; mean LWM: 47.8, SD 2.8) than those in the NAGM and NAWM of patients (mean NAGM MTR: 48.9, SD 1.9: mean NAWM MTR: 49, SD 3.6) and in the GM and WM of healthy controls (GM MTR mean: 51.6, SD 2.5; WM MTR mean 52.3, SD 1.9) (see **Table 1**). A statistically significant difference was found in mean MTR values between LGM (p=0.013) and LWM (p=0.024) and controls.

Table 1. Mean MTR values in the spinal cord of patients and controls

Case No	*MS patient MTR values*		*Healthy control MTR values*	*MS patient MTR values*		*Healthy control MTR values*
	LGM	NAGM	GM	LWM	NAWM	WM
1	47.9	48.7	49.7	47.2	52.4	51.7
2	46.1	47.2	53.5	44.3	45.3	54.8
3	47.6	51.6	49.7	50.4	51.8	51.3
4	47.8	48	54.9	50	46.5	53.8
5			50			50.1

Conclusion:
A method has been demonstrated for imaging GM and WM *in vivo* in the cervical cord of patients with MS. The acquisition of high-resolution FFE images enabled positioning of ROIs in the lesional and NAGM and NAWM of the cervical cord in MS patients. The MTR of both GM and WM affected by lesions was reduced compared controls, although the sample size was small. These findings suggest that spinal cord tissue in MS is affected by demyelination and axonal loss. This confirms brain post-mortem studies, which showed decreased MTR in T2 lesions[6] and NAWM and NAGM[7]. This study represents the first attempt to characterise MTR changes in lesional and NAGM and NAWM in the cervical cord in MS patients. Further investigation with larger patient groups and in different types of MS is warranted.

References: **1** Bot *et al*. Radiology 2004; 233:531-40 **2** Mottershead *et al*. J Neurol 2003; 250:1293-1301 **3** Gimore *et al*. Brain Pathol 2006; 16:202-208 **4** Agosta *et al*. Arch Neurol 2007; 64:1302-1305 **5** Gilmore *et al*. Mult Scler 2009; 15:180-188 **6** van Waesberghe *et al*. Ann Neurol 1999; 46:747-54 **7** Filippi *et al*. Neurology 1999; 52:588-94