# Inhomogeneous Magnetization Transfer Imaging of Myelin Concentration in Multiple Sclerosis

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**Introduction**: Myelination and dysmyelination play a crucial role in brain development, decreased function with aging, and especially pathologies of the white matter, including trauma and multiple sclerosis (MS). Quantification of myelin concentration could serve a valuable role in the study of these diseases and the management of patients. While MR measures such as T1, magnetization transfer (MT) ratio, and diffusion are affected by myelin concentration, they are also affected by numerous other factors that limit their specificity to myelin. We have previously reported a new MT subtraction experiment that appears selectively sensitive to tissues with myelin[1]. Here we describe initial experience with this technique in patients with MS.

**Methods**:

MT subtraction experiment: Our MT method compares three images acquired with different off-resonance irradiation. One image is acquired with off-resonance at a positive frequency offset, f, one is acquired with the negative of this frequency offset, -f, and one is acquired with equal total power but divided between positive and negative offset. The dual frequency image is subtracted from the average of the two individual frequency images to produce an MT subtraction image. This subtraction image should be zero for homogeneously broadened lines but will be nonzero if the line is inhomogeneously broadened. We refer to this difference image as an Inhomogeneous MT (IMT) image, figure 1.

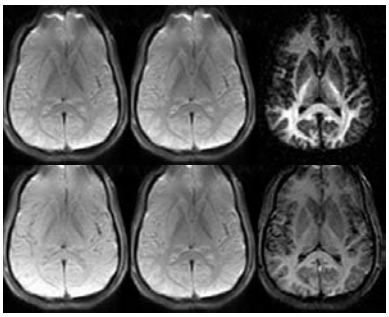

Figure 1: IMT image, top right, is the difference between single frequency, top left, and dual frequency, top middle, MT prepared images. Conventional MT images, bottom right, are the difference between zero power, bottom left, and nonzero power single frequency irradiation, bottom middle. Note the higher contrast between gray and white matter, the absence of difference signal within the scalp, and the higher intensity in heavily myelinated regions, such as the internal capsule, on the IMT images.

In this study, off-resonance irradation was performed with 500μs Hanning shaped pulses applied every 1.5 ms at either positive or negative 7kHz offset. The amplitude of the pulses was adjusted such that the average power was equivalent to a constant 35 mG irradiation. For the dual frequency MT image, pulses were alternated between positive and negative frequency. MT pulses were applied for 500ms prior to image acquisition. Imaging was performed with a single slice, spin echo echoplanar sequence in the axial plane. A TR of 2 s, a FOV of 24 cm, a matrix of 128x128 and a slice thickness of 6 mm were employed. All imaging was performed on a 3T GE Twinspeed system using the 8 channel head array coil. 32 averages of each single frequency image and 64 averages of the dual frequency image were acquired for a total scan time of 4min 16 s.

Subjects: 6 patients diagnosed with MS and 5 normal controls were imaged after giving written consent following an institutionally approved protocol. The MS patients were 2M/4F, mean age 39.7 years, mean Expanded Disability Status Scale (EDSS) score 3.1, mean duration of disease 8.0 years, 4 relapsing/remitting, 1 primary progressive, 1 secondary progressive. The controls were 3M/2F, mean age 39.9 years.

Analysis: Regions of Interest (ROI) were manually drawn in the internal capsule bilaterally, the occipital parietal white matter, excluding lesions, and the frontal white matter. Average values within the IMTR images were calculated for each region in each subject.

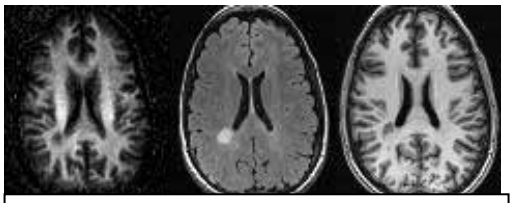

Figure 2: IMTR image, left, in a patient with a long T2 and T1 lesion. Reduced IMTR in the lesion is clearly apparent.

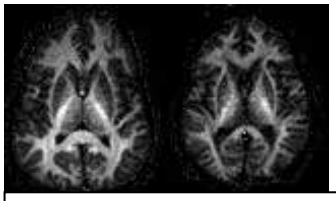

Figure 3: Comparison of IMTR images in a normal control, left, and a patient with EDSS of 6.5. IMTR is diffusely lower in the patient.

**Results:** Good image quality was obtained in all subjects. In patients with T1 hypointense lesions within the slice, the lesion showed marked decrease in the IMTR images, figure 2. IMTR was significantly reduced in the parietal-occipital white matter, $p<0.02$, of the patients ($2.37\pm0.14\%$) relative to the controls($2.74\pm0.20\%$) but not the internal capsule or frontal white matter. EDSS score was significantly inversely correlated (Spearman's rank correlation) with IMTR in the internal capsule, $\rho= -0.90$, $p<0.015$, and the parietal-occipital white matter, $\rho= -0.93$, $p<0.008$, but not the frontal white matter.

**Discussion:**These results provide further support for a strong relationship between IMTR and myelin concentration. The significant difference in IMTR between groups and the correlation between EDSS and IMTR are both impressive, though a larger study will be required to compare to other MR correlates of EDSS[2]. The posterior cerebral white matter seems especially vulnerable to clinically relevant myelin loss. While the IMTR effect is smaller than the overall MT effect, improved specificity may make it desirable for quantitative studies of myelination.

References:[1] Proc ISMRM 2005 p. 2224 [2] Acta Neurol Scand. 2001 104:24-30