Analysis of Inhomogeneous Magnetization Transfer Applied In Patients with Multiple Sclerosis

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Target audience: Basic and clinical researchers interested in the application of new techniques for characterizing multiple sclerosis and myelin.

Purpose: Inhomogenous Magnetization Transfer (IHMT) is a refinement of MT that that appears more specific to myelin[1]. Although the nature of this contrast remains under study, it is believed to originate from inhomogeneous broadening of rotationally restricted protons within myelin's ample phospholipid bilayers[2]. The apparent specificity to myelin demonstrated in IHMT images of the brain and spine, in mice and humans[3, 4], lends itself to studies involved with degradation of myelin. Prior studies relating to MT such as MS have shown mixed results in application to studies of demyelination and the associated normal appearing white matter (NAWM)[5]. As a technique based on MT, it is hoped that IHMT might provide additional insight into the nature and/or progression of such diseases. Indeed earlier study of IHMT applied to a small subset of MS patients showed a correlation between IHMT and the expanded disability status scale[6].

Methods: As with MT, the IHMT technique is applied using a series of RF applied off-resonance in a series of four experiments, with RF pulses applied: at a positive offset frequency of 7kHz (POS); at the negative offset (NEG); and with successive RF pulses alternating between the positive and negative offset frequency (DUAL). These preparatory schemes were applied before a 2D spin-echo EPI sequence at 3T with parameters: FOV=25x25cm^2; matrix=128x128; NEX=32; slice thickness=6mm; TE/TR=18/2000. Data acquired with the RF pulse amplitude set to zero were used as a measure of M_0 to provide the IHMT ratio: IHMTR = ([POS+NEG]-2*DUAL)/M_0. In acquiring IHMT images, maps of the MT ratio were also produced from the same data: MTR = 1-([POS+NEG]/[2*M_0]). The imaging slice was placed axially at the mid-ventricular level, with the slice repositioned in MS patients (where possible) to include any lesion(s). IHMT data acquired from 30 MS patients and 8 healthy volunteers were analyzed based on NAWM ROIs placed in the: frontal white matter (FWM); posterior internal capsule (PIC); and parietal-occipital white matter (POWM).

Results: Figure 1 provides a comparison of the IHMT and MT values from analysis of the same ROIs within the subjects. The IHMTR values from volunteers appear inter-mixed with those from patients in FWM and PIC ROIs. However the IHMTR from within the POWM ROI appears greater in volunteers than in the patient population. The IHMTR in POWM ROI also shows a statistically significant difference, following a 2-tail heteroscedastic t-test, between the volunteer and patient values (Fig. 2). The p-value is much better than that obtained from MTR data alone (p~0.037). A similar trend is found in statistical analysis with respect to type of MS (see Table).

Discussion and Conclusion: IHMTR from POWM ROIs shows a more significant difference between the volunteer and patient populations than traditional MTR. Although MTR changes would also be expected based on previous literature[5], the results suggest IHMT might serve as an improvement over MT in such studies. Limitations of this study include the use of a single slice with slightly variable position. However the enhanced sensitivity of IHMTR over MTR merits a more comprehensive study of IHMTR in MS over the whole brain using newer 3D techniques[7].

References: [1] Proc. ISMRM (2004) 2324; [2] JACS 95(1973) 7541-53; [3] Proc. ISMRM (2013) 2535; [4] Proc. ISMRM (2013) 350; [5] JMRI 33(2011) 713-8; [6] Proc. ISMRM (2007) 2188; [7] Proc. ISMRM (2013) 4224
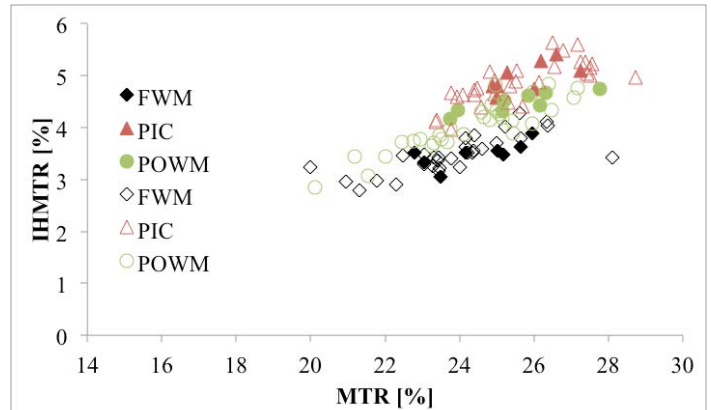
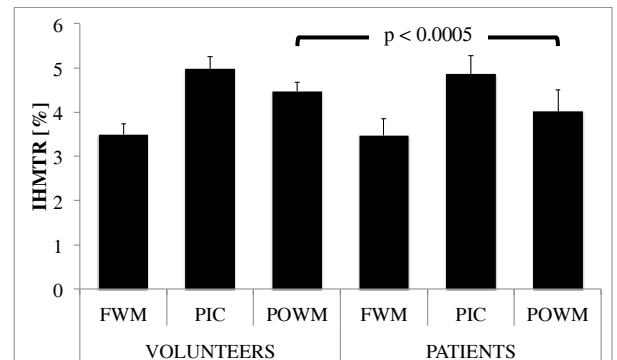**Figure 1** Plot of MTR versus IHMTR values from ROIs in MS patients (hollow) and healthy volunteers (solid).

Figure 2 Chart of average IHMTR values from ROIs.

Groups compared in 2-tail heteroscedastic t-test	p-value from POWM	
	IHMTR	MTR
Primary/secondary-progressive (n=6) and volunteers	0.0823	0.1887
Relapsing-remitting (n=24) and volunteers	0.0093	0.0568
Primary/secondary-progressive and relapsing-remitting	0.4065	0.5468
MS and volunteers	0.0004	0.0374