Quantification of myelin in the cervical spinal cord using inhomogeneous magnetization transfer imaging

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Purpose Magnetization transfer (MT) imaging has been explored as a potentially sensitive marker to myelin in neurological disorders[1]. However, MT is not a specific marker of axonal damage concurrent with demyelination. Recently a technique was proposed to extract the 'inhomogeneous' component of MT[2] (ihMT), which was shown to be specific to myelin in brain[3,4]. The ihMT component is thought to come from more mobile macromolecular pools that cause asymmetrical line broadening about the center frequency, and can be extracted by applying MT saturation pulses with alternating (positive/negative) off-resonance frequencies. The goal of this study was to summarize myelin content along the length of the cervical spinal cord by using the ihMT imaging technique to acquire a myelin-specific image of the SC in the sagittal plane. A myelin-specific MT imaging technique may accurately and specifically reflect axonal damage in the event of spinal cord injury.

Methods Images were acquired on a 3.0 T scanner (GE Healthcare, Waukesha, WI) using the upper half of a twelve-channel spine receive coil. Inhomogeneous MT images were acquired by applying a pulsed saturation scheme for 500 ms, consisting of 35 mG (rms), 500 μs Hanning-shaped pulses applied every 1.5 ms with a +/- 7.0 kHz frequency offset to acquire four images in each set, as follows: positive frequency offset (A), alternating dual frequency offset (B), negative frequency offset (C), alternating dual frequency offset (D). Following the saturation, a single slice was acquired using single-shot spin-echo echo planar imaging (EPI) in the sagittal plane comprising the brainstem and cervical spinal cord, with the following imaging parameters: TR/TE = 2500/23 ms, FOV = 18 cm, phase FOV = 0.5, acquisition matrix 96 × 48 (reconstructed to 128 × 64), slice thickness = 10 mm, with 54 averages of each set and an additional eight averages of the unsaturated EPI image, for a total scan duration of ~ 9 minutes.

The images were combined to yield the ihMT component image, given by: ihMT = (A + C) – (B + D). Inhomogeneous MT ratios (ihMTR) were calculated by normalizing the ihMT images by the unsaturated EPI images. For comparison, the MT ratio (MTR) was also calculated using image 'A' as the saturated image. A mask was applied to select only the brainstem and spinal cord, and was used to calculate ihMTR as a function of position along these regions.

Results Figure 1 demonstrates the result of this experiment on a representative volunteer. The unsaturated EPI image is shown in Fig. 1a, Fig. 1b shows the MT ratio, and the ihMT ratio is shown in Fig. 1c, clearly illustrating the specificity of this measure to myelin. The ihMTR ranges from ~5% in the brainstem up to ~6.5% around C3, and decreases to ~4% at the C7/T1 level (Fig. 1d), although some of this signal decrease may also be due to RF field inhomogeneity. Corresponding conventional MTR values range from ~32% in the brainstem to ~27% in the cervical spinal cord, and arise not only from the saturation of other macromolecules along with myelin in the cord but also from direct saturation effects. Similar results were seen on a second volunteer.

Discussion and Conclusions Inhomogeneous MT imaging is clearly sensitive to regions within the cerebellum, brainstem, and cervical spinal cord. Its specificity to myelin in white matter is evidenced by the absence of signal in cerebellar gray matter, vertebrae, intervertebral disks, subcutaneous fat, and cerebrospinal fluid. Signal differences in ihMT between the spinal cord and the brainstem (particularly the medulla oblongata) are expected due to fractional differences in white matter between these regions. Although several averages were acquired to improve the signal to noise ratio (SNR), the ihMT quantification remained the same even with 1/4th the number of averages (data not shown). This, along with the consistency of the values across volunteers, indicates the robustness of the measure.

A disadvantage of the current acquisition is large distortion due to EPI, which limited the imaging FOV to 18 cm in the sagittal plane. A move to the rapid acquisition with relaxation enhancement (RARE) sequence is expected to improve signal, reduce spatial distortions, and allow better visualization of the entire spinal cord. The technique is expected to be applied to patients with spinal cord injury and may aid in the evaluation of axonal damage in the neighborhood of the injury.

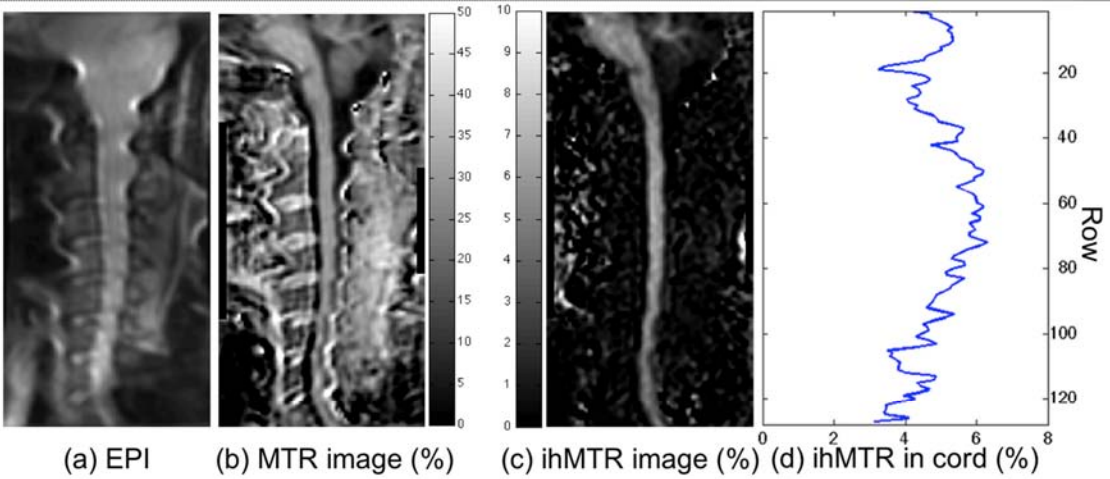

FIGURE 1 shows (a) unsaturated EPI, (b) MTR, and (c) the inhomogeneous MTR. Note the specificity of the ihMTR image to white matter in the cerebellum (the arbor vitae can be seen), brainstem, and cervical spinal cord. The ihMTR is shown as a function of its location along the brainstem and cord (not including the cerebellar white matter) in (d).

References (1) Filippi *et al*., *J Neuroimg*, 14:p303, 2004 (2) Alsop *et al.*, *ISMRM* 2004, p2324 (3) Alsop *et al.*, *ISMRM* 2005, p2224 (4) Alsop *et al.*, *ISMRM* 2007, p2188