

Specific Inhomogeneous MT Contrast in White Matter. Application to Spinal Cord Imaging.

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Target audience: MR physicists and physicians interested in novel endogenous contrast mechanisms and specific white matter imaging.

PURPOSE: Myelin specific imaging has become an growing research area because of the high clinical relevance of myelin-associated diseases such as multiple sclerosis. Advanced MR techniques such as Myelin Water Fraction (MWF), Magnetization Transfer (MT) and Diffusion Tensor imaging (DTI), as well as more recent applications using quantitative susceptibility mapping or ultrashort TE imaging, have enabled the assessment of myelin content and white matter (WM) fiber integrity directly *in vivo*. Although these techniques all rely on some specific features of the myelin MR signal, related to water compartmentalization between the myelin sheaths, susceptibility, ultrashort T2 signature, or bound/semi-solid proton pool, they are also affected by multiple other factors which limit their specificity. Recently a novel MT contrast, known as inhomogeneous MT - ihMT, has demonstrated very high specificity toward WM tissue, likely due to the lipid layered structure specific to myelin [1-3]. Inhomogeneous broadening of a resonance line may occur in semi-solids whose proton magnetization do not exchange rapidly throughout the molecule. In such circumstances the saturation induced by an off-resonance RF irradiation pulse and subsequent transfer effect to the mobile water pool, strongly depend on the way the RF energy is deposited over the spectrum, and this can be exploited to generate specific inhomogeneous MT contrast. Previous studies have been performed at 3T on human brain. In this work an ihMT sequence was developed on a 1.5T clinical scanner, and its specificity to WM was demonstrated on the human cervical spinal cord (SC).

METHODS: All experiments were performed on a 1.5T MRI scanner (Siemens, Erlangen, Germany) on healthy volunteers. **ihMT sequence design:** A 500ms pulsed MT preparation module (333 Hann shaped saturation pulses, 500 μ s duration each, repeated every 1.5ms), was implemented in combination with a product HASTE readout module for imaging. The ihMT contrast was generated from 4 sets of images acquired with varying offset-frequency scheme for the 333 saturation pulses: 1/ MT^{+f}: all pulses applied at the same positive offset frequency +f. 2/ MT^{+f,-f}: pulses applied at alternated offset frequencies +f, -f, +f etc... 3/ MT^{-f}: all pulses applied at negative offset frequency -f, and 4/ MT^{-f,+f}: pulses applied at alternating offset frequencies -f, +f, -f etc... The specific ihMT contrast obtained by linear combination of the generated images, $ihMT = MT^{+f} + MT^{-f} - MT^{+f,-f} - MT^{-f,+f}$, suppresses the homogeneous MT signal and reveals the inhomogeneous component only [1,2]. The sequence also provided measurement of the M₀ signal (i.e. with RF saturation power set to zero) in order to enable calculation of MT ratios: $MTR = 1 - MT/M_0$ and $ihMTR = ihMT/M_0$. In all the following a ± 7 kHz offset saturation and an average B1 of 3.5 μ T over the whole 500ms saturation duration (equivalent to 7.4 μ T RMS) were used. Finally data were averaged over 132 NEX (4x M0, and 32x for each of the four frequency conditions). **Brain MR experiment:** In order to compare with previously reported ihMT results, our sequence was initially tested on the brain with the following imaging parameters: TR/TE = 2.5s/14 ms, BW_{/pixel} = 797 Hz, 20 cm FOV for a 128x128 Mx, 5mm slice thickness, 150 $^\circ$ refocusing angle for a total scan time of 5min 30s. For comparison, DTI was assessed on the same slice and at the same in-plane resolution using a DTI-EPI sequence (TR/TE = 4s/89ms, 20 diffusion directions and b-values of 0 and 1000 s.mm⁻² for a total scan time of ~3min).

SC MR experiment: High resolution imaging was used in order to discriminate SC structures (TR/TE = 4.5s/26ms; BW_{/pixel} = 592 Hz, 12.8 cm FOV for a 192x192 Mx, 10 mm slice thickness, 120 $^\circ$ refocusing angle and a total scan time of ~10min). Moreover, since pulsatile motion of the cerebro-spinal fluid induces motion artifacts around the SC, ECG triggered acquisitions were required to obtain reproducible SC images across the repetitions. In addition, data were registered using the FSL FLIRT algorithm [4] to reduce the impact of patient motion. As for the brain, DTI was assessed on the same slice for comparison (DTI-EPI, TR/TE = 1.7s/73ms, 0.9mm in-plane resolution, 30 diffusion directions, b-values of 0 and 600 s.mm⁻², for a total scan time of 5min 20s).

RESULTS AND DISCUSSION: Fig. 1 and 2 show various axial images of the brain and the cervical SC. Brain ihMT images are similar to those obtained previously at 3T [1-3], with close ratio values (ihMTR around 9% in WM in our experimental conditions). Conventional MTR images show poor and non-specific contrast: a uniform signal was thus obtained in the SC gray and white matter (Fig2. MTR). Moreover, high signal can be seen in muscle tissue surrounding the SC on such MTR image. In contrast, ihMTR images exhibit high specificity toward WM (Fig2). Remarkably, the sensitivity of ihMT and the spatial resolution were sufficient to delineate the gray and white matter SC structures (Fig 2. bottom row, see T2*-w MEDIC for comparison) with contrast comparable to the FA map derived from DTI. As for the brain the ihMT ratio was around 9% in the SC WM. Note that the subtle contrast differences observed between FA and ihMT images underline that both effects arise from different contrast mechanisms, although both are related to WM microstructure.

CONCLUSION: This study was intended as a demonstration of the ihMT contrast in the human SC at 1.5T. This new endogenous contrast demonstrated tremendous specificity towards SC WM. Combining ihMT with other WM specific contrast such as DTI would certainly be of great benefit to assess various aspect of the WM fiber integrity in future studies. This holds great promise for future clinical applications on SC pathologies such as trauma or MS.

REFERENCES: [1]. Alsop et al., Proc. ISMRM 2004; p2324 [2]. Alsop et al., Proc. ISMRM 2005; p2224 [3]. Alsop et al., Proc. ISMRM 2007; p2188 [4]. Jenkinson et al., NeuroImage 2002;17(2):825-841

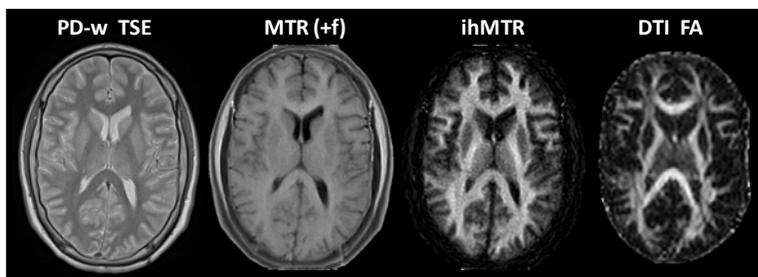


Fig. 1: Illustration of ihMT imaging of the brain. The ihMT contrast exhibits high specificity toward white matter, comparable with more conventional fractional anisotropy maps derived from DTI data.

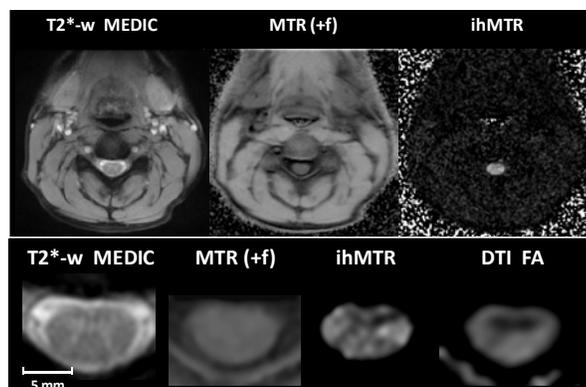


Fig. 2 : Demonstration of the ihMT contrast in the cervical spinal cord. Top row: full size images. Bottom row: corresponding zoom in the SC. Tremendous specificity towards CNS tissues is obtained with the ihMT sequence.