Magnetization Transfer DTI in Multiple Sclerosis

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Introduction

Diffusion tensor imaging (DTI) provides unique information about the tissue and cellular microstructure in the human brain. However, because all protons in a voxel contribute to the diffusion signal, DTI has little tissue specificity. Magnetization transfer (MT) preparation applies off-resonance irradiation to preferentially saturate water in the vicinity of structures with high macromolecular content such as myelin. In this work we present a MT based technique for increasing the myelin specificity of DTI and illustrate its prospective clinical applicability in a patient diagnosed with relapsing remitting multiple sclerosis (MS). Two stimulated-echo based DTI acquisitions are used to derive the diffusion anisotropy of myelin water. When compared to a clinical dual-spin echo DTI, the FA values of the derived tensor varied more significantly across lesions with different degrees of demyelination, thus providing a more accurate differentiation of myelin abnormalities in early disease progression. Our preliminary results corroborate the potential of myelin water anisotropy to become a biomarker for early detection of demyelination.

Methods & Results

Pulse sequence

Magnetization transfer preparation was implemented in a single-shot stimulated echo based DTI EPI sequence. With this sequence adequate diffusion weighting can be achieved even with short TE (~30ms), thus preserving most of the myelin water low T2 signal. Sensitization to myelin water is then achieved by the MT preparation. The diffusion signal of the myelin water spins saturated by the MT preparation can be retrieved from two stimulated echo DTI acquisitions (one with MT on and one with MT off) and a regular magnetization transfer ratio (MTR) map. Because the amount of incoherent dephasing due to the diffusion of the saturated spins can be calculated for each direction independently, no prior assumptions of Gaussianity are needed until the last step.

$$\begin{cases} \rho_\Delta e^{-b*D_\Delta} = \rho\frac{S_i}{S_0} - \rho_{MT}\frac{S_i^{MT}}{S_0^{MT}} \\ MTR = \frac{\rho - \rho_{MT}}{\rho} = \frac{\rho_\Delta}{\rho} \end{cases} \rightarrow D_\Delta = -\frac{ln\left(\frac{1}{MTR}\frac{S_i}{S_0} - \frac{MTR-1}{MTR}\frac{S_i^{MT}}{S_0^{MT}}\right)}{b_i};$$

Comparison in MS patient

A patient diagnosed with relapsing-remitting multiple sclerosis was scanned with the DTI sequence both with and without the MT preparation while all other scan parameters were kept constant: TE/TR=38/4500ms, 15 slices with 2x2x5 mm^3 resolution, b=500 s/mm^2, 15 directions, 8 averages. The parameters of the off-resonance Fermi shaped MT pulse were: offset=2.5kHz, flip=1080 degrees. Spin echo based proton density images with the same MT preparation on and off were used to compute the MTR map (TE/TR=20/10000ms). The MTR map along with the DTI data sets was then used to retrieve the diffusion tensor of the myelin water spins that have exchanged magnetization during the off-resonance MT irradiation. In addition, diffusion tensors were fitted separately to the two stimulated echo DTI acquisitions (with and without MT). The SNR of the calculated myelin water tensor was MTR dependent and ranged between 40% and 60% of the SNR of a single stimulated echo DTI acquisition. Finally, for comparison, a standard clinical dual spin echo (DSE) single-shot EPI DTI measurement was performed with similar parameters as the stimulated echo sequences: TE/TR=70/4500ms, resolution 2x2x5mm^3, b=500s/mm^2, 15 directions, NEX=1.

Region of Interest Analysis

Four regions of interest (ROI) were drawn on the T2 weighted images: three in white matter lesions with different degrees of demyelination and one in normal appearing white matter (Figure 2A). was performed on several regions of white matter with different stages of demyelination. The mean FA values were computed in those regions for each of the four calculated tensors (clinical DSE diffusion tensor, stimulated echo DTI without MT, stimulated echo DTI with MT and myelin water diffusion tensor). As expected, in all four ROIs average FA values in the stimulated echo DTI acquisition were larger than those in the clinical DSE DTI measurement, suggesting that indeed a shorter TE provides increased contribution from myelin water. Furthermore, when the MT was turned on thus cancelling the contribution of most myelin water to the diffusion tensor, a decrease in the average FA was observed. Most importantly, the FA values in the estimated diffusion tensor due to the myelin water spins vary more significantly across lesions with different degrees of myelination (MTRs). Because the calculated myelin water anisotropy is more specific to the changes in myelin microstructure it could provide a more accurate differentiation of white matter lesions in early stages.

ROI	*Volume (uL)*	*MTR(%)*	*FA*			
			DSE	stDTI	MTstDTI	MWDTI
NAWM	12.79	30.64	0.47	0.51	0.49	0.56
LA	2.06	26.08	0.28	0.26	0.25	0.40
RP	10.1	23.91	0.22	0.25	0.24	0.29
LP	9.49	23.4	0.22	0.25	0.23	0.32

Table 1: ROI comparison of mean FA values of calculated tensors: stimulated echo DTI (**stDTI**), MT prepared stimulated echo DTI (**MTstDTI**), myelin water tensor (**MWDTI**) and clinical DTI (**DSE**)

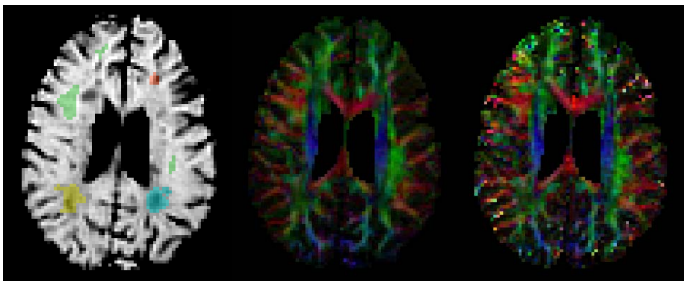

Figure 1: A. MTR with ROIs: NAWM (green), LA (red), RP (yellow), LP (blue) **B.** Colored FA of clinical DSE DTI **C.** Colored FA of myelin water diffusion tensor

Conclusion

Our preliminary results, based on a new DTI pulse sequence with greatly shortened echo times, demonstrate that it is possible to preserve sufficient myelin signal. Moreover, the myelin water anisotropy shows a clear reduction in FA in the lesions as compared to the healthy white matter. There is also a better differentiation in FA values within the three lesions that can potentially be correlated to the disease progression. In comparison, the FA values in conventional DTI did not indicate any significant differentiation, most likely due to the lack of myelin signal.

References

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