Stimulated-echo DTI with magnetization transfer contrast for myelin specificity

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Introduction

Diffusion tensor imaging (1,2) provides complementary information to other MR methods by characterizing the local diffusion pattern of water molecules in living tissue. However, because of the complexity of brain microanatomy the tensor characterization is often a composite result of the various participating components and does not directly correlate to changes in individual and specific neuronal microstructure. The combination of DTI with one of the tissue selective techniques, therefore, would provide critical information for earlier diagnosis of a particular white matter pathology (i.e. demyelination). In this work a magnetization transfer (MT) pulse (3,4) was incorporated in a stimulated echo DTI sequence and a theoretical model was developed to analyze the anisotropy of the water molecules involved in exchange of magnetization. Furthermore, an additional multi-TE experiment was sufficient to obtain tensor estimates of the diffusion in the low and high T2 compartments in white matter (5).

Methods

Pulse Sequence: A MT prepared stimulated echo DTI SENSE sequence was developed on a 3T Signa Excite GE scanner to preserve the low T2 spins (e.g. myelin water <50 ms) and image their diffusion properties with sufficient SNR. For a diffusion weighting of 500 s/mm^2, a TE of 24ms was achieved using a center-out partial k-space EPI trajectory to acquire the stimulated echo signal in a single shot. A clinical spatially non-selective MT preparation module (Fermi pulse, 15ms, Δ=3kHz, and θ=1100^o) was used to saturate the longitudinal magnetization in the restricted proton pool in macromolecules (e.g. phospholipids in myelin sheath) prior to slice excitation, allowing magnetization transfer with nearby myelin water protons. Two DTI data sets – S_i without MT; S_i^{MT} with MT on – were acquired with b=500 s/mm^2, TE=24ms, TR =4s, 15 directions, scan-time 1:30 min each, NEX=15. In addition, multi-TE images were acquired (TE/TR=10,15,20,25,30,35,40,45,50, 60,70,80, 90,100,150,200,250/10000 ms) and used to estimate the contributions in the anisotropy measurements for different tissue components (low and high T2).

Theoretical Model: The theoretical framework used to estimate the anisotropy properties of the low T2 pool (myelin water) and residual high T2 pools (parenchyma) is based on the linearity of the quantity ρ*log(S_i/S_0) where ρ is the proton density. Assuming Gaussian diffusion (central limit theorem) in the two proton pools and the independence of T2 decay and diffusion, the anisotropy of the union / difference of the two pools can be characterized by the sum / difference of their ρ*log(S_i/S_0) quantities as shown below. A tensor estimate for the spins that have participated in the transfer of magnetization ($D_{\Delta MT}$) was obtained from the DTI and PD images (TE/TR =10/10000ms) using Equation 1. The multi-TE data was fitted for three compartments (at T2=25/80/2000ms) corresponding to myelin water, parenchyma and CSF peaks. The volume fractions (ρ_{LT2}, ρ_{HT2} for MT off and ρ^{MT}_{LT2}, ρ^{MT}_{HT2} for MT on) were then used to characterize the effect of the MT pulse in white matter and to derive the tensor properties of the low and high T2 water compartments (D_{LT2}, D_{HT2}) based on the previous diffusion measurements in voxels with ρ_{CSF}<5% (Equations 2-3).

$$\rho_{A\cup B}\overline{D}_{A\cup B} = \rho\frac{\left\langle \vec{r}^{\,T}\vec{r}\right\rangle_{A\cup B}}{2\tau} = \frac{N_A+N_B}{V}\frac{\sum_{k=1}^{N_A+N_B}\vec{r}_k^{\,T}\vec{r}_k}{2\tau} = \frac{1}{2V\tau}\sum_{k=1}^{N_A+N_B}\begin{pmatrix} x_k^2 & x_k y_k & x_k z_k \\ y_k x_k & y_k^2 & y_k z_k \\ z_k x_k & z_k y_k & z_k^2 \end{pmatrix} = \frac{1}{2V\tau}\sum_{k=1}^{N_A}\vec{r}_k^{\,T}\vec{r}_k + \frac{1}{2V\tau}\sum_{k=1}^{N_B}\vec{r}_k^{\,T}\vec{r}_k = \rho_A\overline{D}_A + \rho_B\overline{D}_B$$

$$-\rho\log\frac{S_i}{S_0} + \rho^{MT}\log\frac{S_i^{MT}}{S_0^{MT}} = \vec{g}^{\,T}\left(\rho\overline{D} - \rho_{MT}\overline{D}_{MT}\right)\vec{g} = \vec{g}^{\,T}\rho_{\Delta MT}\overline{D}_{\Delta MT}\vec{g} \quad (1)$$

$$\begin{cases} -\rho\log\dfrac{S_i}{S_0} = \vec{g}^{\,T}\rho_{LT2}\overline{D}_{LT2}\vec{g} + \vec{g}^{\,T}\rho_{LT2}\overline{D}_{LT2}\vec{g} & (2) \\ -\rho^{MT}\log\dfrac{S_i^{MT}}{S_0^{MT}} = \vec{g}^{\,T}\rho^{MT}_{LT2}\overline{D}_{LT2}\vec{g} + \vec{g}^{\,T}\rho^{MT}_{LT2}\overline{D}_{LT2}\vec{g} & (3) \end{cases}$$

Results and Discussion

The multi-TE experiments confirmed that the MT pulse acts mainly on the low T2 water compartment. Moreover, the tensor characteristics of the macromolecular water pool appear to be similar to those of the low T2 water compartment validating that anisotropy in white matter is due mainly to the motion of hydrogen spins in the proximity of macromolecular structures such as myelin sheaths, cellular membranes, etc, where water is assumed to be more structured. In the Corpus Callosum the average volume fractions were 24% low T2, 74% high T2 and <2% CSF while the mean MT effect was 6% (14% in low T2 and 4% in high T2). The SNR of the calculated tensors is reduced because of the difference operation and lower signal in specific compartments relative to the regular DT image where all spins contribute. The multiplication with the proton density maps only slightly reduces the SNR of the data (5%) and preserves the anisotropy information at the cost of adding uncertainty with respect to diffusivity values. In practice the SNR is greatly improved in multi-slice acquisitions in which the MT pulses are repeated (6), making this pulse sequence highly feasible for whole brain applications.

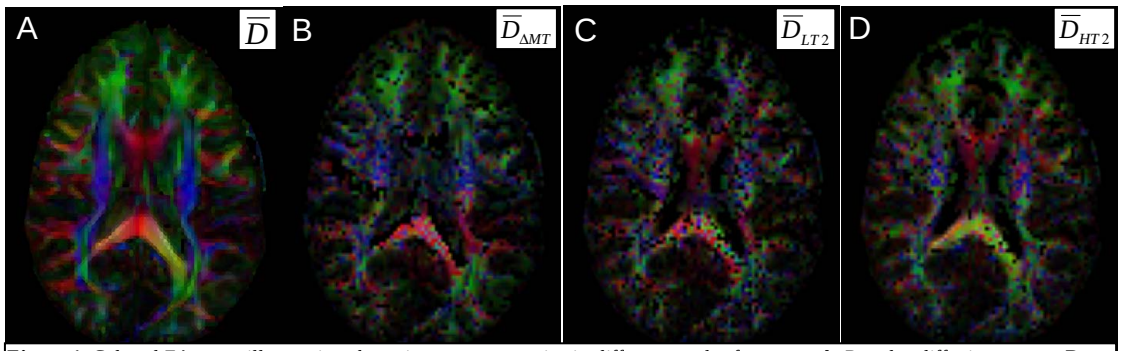

Figure1: Colored FA maps illustrating the anisotropy properties in different pools of protons. **A**. Regular diffusion tensor, **B**. Tensor of exchanged magnetization (Equation 1), **C**. Low T2 (myelin) water tensor derived from A, **D**. High T2 (e.g. axonal) water tensor derived from A. Equations 2-3 were solved for C and D.

Conclusion

We present a new method for estimating the anisotropy of myelin water proton pools using their magnetization exchange with macromolecular proton pool during off-resonance irradiation. Our theoretical model can further separate the low T2 and residual high T2 water compartments that are associated, respectively, with myelin water and intra/extracellular water in white matter. We anticipate that these measurements may be used as clinical markers for detecting pathological changes associated with specific white matter structures such as myelin.

References:
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