T_1 Measurement of the Myelin Water Fraction

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Purpose of study: To investigate the T_1-relaxation of the myelin water fraction.
Myelin water imaging is important for its potential in studying demyelinating diseases and may help understanding MR signal contrast in the brain in the complex structure of myelinated nerve fibers. Analysis of T_2 and T_2^* [1-3] relaxation characteristics with multi-echo MRI has shown promise in separating the signal contribution of myelin water from that of other tissue compartments. In addition, attempts have been made to distinguish myelin water based on T_1 relaxation [4-9]. However, T_1 based approaches may have reduced specificity, possibly because of substantial exchange between the water compartments on the T_1 time scale. Here, we further investigate T_1 relaxation by combining an inversion recovery (IR) preparation with a multi-gradient-echo (MGRE) readout. Importantly, the effect of the short T_2 of myelin water spins on inversion efficiency was considered.

Theory

The signal (S) in an ordinary MGRE (in white matter) can be described as the sum of three complex exponential decays [3]:

$$S = A_1 e^{-R_{2,1}^* t + i\omega_1 t} + A_2 e^{-R_{2,2}^* t + i\omega_2 t} + A_3 e^{-R_{2,3}^* t + i\omega_3 t} \quad [1]$$

corresponding to water between the myelin layers, interstitial water and axonal water, each with its own amplitude, R_2^* decay rate ($=1/T_2^*$) and frequency (ω). When the IR preparation is added, the amplitude of each of the components becomes a function of the inversion delay time (TI):

$$A_i(TI) = A_{i,0}\frac{1 + (e^{-R_{1,i}TI} - e^{-R_{1,i}TR})\cos\beta - e^{-R_{1,i}TI}}{1 - \cos\alpha\cos\beta e^{-R_{1,i}TR}}\sin\alpha \quad [2]$$

which describes the steady state of the magnetization in an IR experiment with total repetition time TR, excitation flip angle α, inversion flip angle β and relaxation rate $R_{1,i}$ ($=1/T_{1,i}$); $A_{i,0}$ is the signal amplitude of component i without inversion. Assuming the T_1 relaxation is slow compared to the T_2^* decay ($T_1 >> T_2^*$), the two equations can be considered independently. This model of T_1 relaxation ignores any exchange between compartments.

Methods

Experiments were performed on healthy subjects (n=11, age 22-49), under IRB approval. Five slices encompassing the splenium of the corpus callosum (SCC) were acquired sequentially; their order was varied on successive repetitions to cycle through the various TI's [10]. Relevant imaging parameters were: resolution 90x60, 2.7mm isotropic voxels, 80 echoes, TE 2.16-45.3ms, TR 3s, nominal excitation flip angle 70°, 10ms adiabatic inversion (hyperbolic secant, FWHM about 3.5ms, total flip angle =1210°), TI 9, 199, 448, 812, 1500ms. An acquisition without inversion (called reference) was also performed. Only the 41 odd-numbered echoes were used to avoid possible odd-even gradient artifacts. The phase of the images was high pass filtered to remove effects of macroscopic field inhomogeneity. A region of interest was drawn on each reference set to select the SCC and signals in this region were averaged. The reference data were fitted with Eq 1. Keeping the relaxation and frequency parameters from this fit constant (per subject), the amplitudes were then fitted to the IR data. The data with TI 812ms were discarded, as the phase filtering of this data close to the zero crossing introduced artifacts in the decay curves. The resulting amplitudes, including those obtained from the reference, were fitted with Eq 2., with α fixed to 70°, the nominal experimental flip angle.

Results

Fitting results (see Table and Fig. 2) indicated an excellent model fit to the data. The average of the ratio of the variance after and before fitting ($=1-R^2$) of the reference data for the T_2^* decay was $5\bullet10^{-5}$, for the fitting of the T_1 of the components was (7, 4 and 1)$\bullet10^{-3}$. T_2^* values and frequency shifts of the 3 water components are consistent with previous work [3] confirming the ability to distinguish between the various water signals. A substantial difference in inversion flip angle between the components was found with the myelin water angle being 32% below the target value. Apparent T_1 values were similar for all components.

Table 1. Mean (n=11) and standard error (SE) of relaxation characteristics of the three water components; amplitudes were normalized to 1.

Type	A	R_2^* [Hz]	Freq. [Hz]	R_1 [Hz]	Inv. angle
Myelin	0.0833	142.5	35.7	0.975	121.5
(SE)	(0.0066)	(5.1)	(1.1)	(0.058)	(2.5)
Interstitial	0.5323	42.55	1.29	0.971	147.2
(SE)	(0.0059)	(0.58)	(0.11)	(0.032)	(0.9)
Axonal	0.3844	28.60	-5.16	0.808	154.7
(SE)	(0.0077)	(0.62)	(0.16)	(0.023)	(2.3)

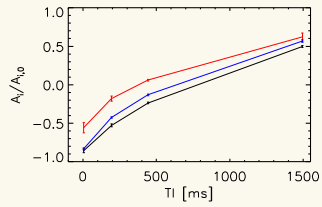

Figure 1. Normalized mean signal as function of inversion delay time, with standard errors. Although myelin water (red) has an incomplete inversion, it shows similar T_1 relaxation as interstitial (blue) and axonal (black) water.

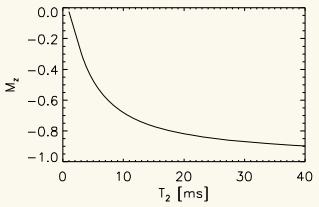

Figure 2. Simulation of M_z after a 10ms adiabatic inversion pulse for a range of T_2 values. Short T_2 components are less effectively inverted.

Discussion

The apparent T_1 in distinct white matter water compartments was determined based on each compartment's characteristic T_2^* signal decay in a major white matter fiber bundle. The results were highly reproducible over subjects, and indicated apparent T_1 values that were similar between myelin water and water in the other compartments. A plausible explanation for this is a rapid (relative to T_1) inter-compartmental water exchange. In fact, this would be consistent with reported exchange times in the order of a few 100ms [3,5,6,9,11] (but see [10], reporting exchange times of 1-4s). The results further suggest that it may be difficult to perform myelin water imaging based on T_1 relaxation characteristics alone, and that effects of imperfect inversion may confound interpretation of IR-based T_1 measurement of myelin water. Simulation of the inversion pulses used here confirmed a reduced efficiency at T_2's typical of myelin water (Fig. 2).

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