Looking at Magnetization Exchange in Human White Matter Structures In Vivo

S. Kalantari[1], C. Laule[2], T. Bjarnason[3], and A. MacKay[1,2]

[1]Department of Physics and Astronomy, University of British Columbia Hospital, Vancouver, BC, Canada, [2]Department of Radiology, University of British Columbia Hospital, Vancouver, BC, Canada, [3]Department of Electrical and Computer Engineering, University of Calgary

Introduction

It has previously been shown that T_2 relaxation measurements can distinguish two water components in healthy white matter: myelin water and intra/extra cellular (I/E) water based on their T_2 values[1]. Myelin water signal from human brain has previously been measured in vivo[2,3] and the quantitative correlation of myelin water fraction (MWF, the proportion of water trapped in the myelin bilayers) with histological staining for myelin in central nervous system tissue[4] validates MW as a reliable marker for myelin. Current *in vivo* measurement of MWF relies upon the assumption that there is negligible exchange of magnetization between the myelin water and the I/E water pools. If exchange occurs during the time scale of the measurement, then the measured MWF could be inaccurate. Using a four pool (myelin, myelin water, I/E water, non- myelin) model[5-7] to fit T_2 decay curves acquired after a magnetization transfer (MT) pulse, we measured exchange (or cross relaxation) times between myelin water and I/E water (T_{cr}^D) in five white matter structures from healthy human brain *in vivo*.

Subjects and Methods

Fifty seven normal volunteers were scanned at 1.5T with a combined MT – T_2 relaxation sequence. The MT portion of the sequence consisted of a 19 ms sinc MT pulse (2000Hz off-resonance) followed by delay times of 0, 33, 66, 100, 200, 300, 450, 600, 750 ms prior to the T_2 relaxation sequence. The T_2 relaxation sequence consisted of a 90° slice selective pulse followed by 48 rectangular composite 180° pulses. Sequence parameters were TR=3800 ms, TE=10 ms, FOV=22cm, matrix size = 64x64, slice thickness = 5mm, 2 averages. ROIs were drawn for the genu (GU) and splenium (SP) of the corpus callosum, posterior internal capsules (IC), minor forceps (MN), and major forceps (MJ). The T_2 decay curve for each white matter structure were fit using a non-negative least squares (NNLS)[8] algorithm. The Bloch equations that govern the dynamics of water signal in each of these 4 pools were solved analytically and signals from the aforementioned five white matter structures were fitted to these solutions in order to extract cross relaxation times (T_{cr}^D). Due to uncertainties[9-11] regarding the assignment of T_1 to the considered pools, we examined three different T_1 scenarios (T_1^m, T_1^{mw}, T_1^{iew}, T_1^{nm} denote the spin-lattice relaxation times of myelin, myelin water, I/E water, and non- myelin proton pools): **Scenario I**[9] the same T_1 for all pools (T_1^m=T_1^{mw}=T_1^{iew}=T_1^{nm}=670 ms), **Scenario II**[10] (T_1^m= T_1^{nm} = 150 ms, T_1^{mw}= T_1^{iew} =1250 ms), **Scenario III**[11] (T_1^m= T_1^{mw} = 250 ms, T_1^{nm} = T_1^{iew} = 1250 ms).

Results

The cross relaxation times between aqueous pools (myelin water and intra-extra cellular water) for each of the five white matter structures using three T_1 scenarios are shown in Table 1. Myelin water fractions corrected for cross relaxation from each scenario are reported in Table 2.

Table 1. Cross relaxation times between aqueous signal pools for each of the five examined white matter structures corresponding to scenario I (T_1^m=T_1^{mw}=T_1^{iew}=T_1^{nm}=670 ms), scenario II (T_1^m= T_1^{nm} = 150 ms, T_1^{mw}= T_1^{iew} =1250 ms) and scenario III (T_1^m= T_1^{mw} = 250 ms, T_1^{nm} = T_1^{iew} = 1250 ms). Error estimates are indicated by a +/- symbol.

	GU	IC	MN	MJ	SP
T_{cr}^D (ms)- Scenario I	1303^{+312}_{-302}	1246^{+313}_{-317}	1402^{+282}_{-271}	1375^{+325}_{-302}	1321^{+381}_{-391}
T_{cr}^D (ms)- Scenario II	2692^{+953}_{-768}	2785^{+936}_{-752}	2802^{+916}_{-811}	3584^{+915}_{-829}	3257^{+921}_{-955}
T_{cr}^D (ms)- Scenario III	4652^{+711}_{-724}	4564^{+731}_{-767}	4239^{+747}_{-754}	3988^{+792}_{-747}	4329^{+742}_{-765}

Table 2. Measured and cross relaxation corrected Myelin Water Fractions (%) for 5 white matter structures corresponding to the three considered T_1 scenarios. Standard deviations are shown in brackets.

	GU	IC	MN	MJ	SP
Measured	**9.86 (0.96)**	**15.00 (0.95)**	**8.40 (0.89)**	**10.11 (0.51)**	**13.05 (0.96)**
Corrected-Scenario I	**11.24 (1.28)**	**17.25 (1.31)**	**9.40 (1.11)**	**11.52 (0.92)**	**14.74 (1.21)**
Corrected-Scenario II	**10.65 (1.23)**	**16.05 (1.25)**	**9.07 (1.19)**	**10.76 (0.96)**	**13.89 (1.19)**
Corrected-Scenario III	**10.15 (1.25)**	**15.45 (1.12)**	**8.69 (1.24)**	**10.51 (0.94)**	**13.51 (1.10)**

Discussion/Conclusion

Our findings define the role of exchange and measure its impact on the magnetizations of all four proton pools in white matter. The spin-lattice relaxation time had a strong affect on all T_{cr}^D values. The T_{cr}^D's measured in all five structures were long (> 1200 ms) compared to spin-spin relaxation times of the proton pools. The cross relaxation times for the five white matter structures were not significantly different for a given scenario. Corrections to the MWF values (due to magnetization exchange) were 12-15% for scenario I, 6-8% for scenario II and 3-4% for scenario III. This study was unable to determine which of the considered T_1 scenarios was the most realistic one as all considered scenarios fit the data equally well. Further investigation is required to look into the T_1 ambiguity.

References

1. Whittall, K.P. et al.. *Magn Reson Med* **37**, 34-43(1997).
2. Mackay, A. et al. *Magnetic Resonance in Medicine* **31**, 673-677(1994).
3. MacKay, A. et al. *Magn Reson Imaging* **24**, 515-525(2006).
4. Laule, C. et al. *Mult. Scler* **12**, 747-753(2006).
5. Stanisz, G.J. et al.. *Magn Reson Med* **42**, 1128-1136(1999).
6. Bjarnason, T.A. et al. *Magn Reson Med* **54**, 1072-1081(2005).
7. Levesque, I.R. & Pike, G.B. *Magn Reson Med* (2009).doi:10.1002/mrm.22131
8. Whittall, K.P. et al.. *Magnetic Resonance in Medicine* **37**, 34-43(1997).
9. Vavasour, I.M. et al. *Neuroimage* **32**, 637-642(2006).
10. Kamman, R.L. et al. *Magn Reson Med* **6**, 265-274(1988).
11. Labadie, C. *et al. Proc. Intl. Soc. Mag. Reson. Med. 17 (2008)*