A novel approach to generate a B0 orientation dependent R2* (= 1/T2*) map: a potential biomarker for myelin

Se-Hong Oh[1,2], Sung-Yeon Park[2], John A. Detre[1], Young-Bo Kim[2], Zang-Hee Cho[2], and Jongho Lee[1]

[1]*Department of Radiology, University of Pennsylvania, Philadelphia, Pennsylvania, United States,* [2]*Neuroscience Research Institute, Gachon University of Medicine and Science, Incheon, Korea, Republic of*

Introduction

The ability to assess the integrity of myelin in brain white matter (WM) is important for the diagnosis of brain disorders and injury (e.g. multiple sclerosis). Until now, several MRI methods such as DTI, Magnetization Transfer (MT), and Myelin Water Fraction (MWF), have been proposed as a potential biomarker for myelin (1-3). However, DTI and MT have shown to be less specific to myelin (4, 5) whereas MWF suffers from a low SNR and a long scan time. Recently, studies at high fields have demonstrated that T_2^* values in major WM fibers are B_0 orientation dependent (6-8). The amount of a voxel-wise T_2^* change ($\Delta T_2^* = T_2^*$@fibers parallel to B_0 - T_2^*@fibers perpendicular to B_0)) is quite substantial at 7 T (e.g. 23.5 ms when perpendicular to B_0 vs. 38 ms parallel to B_0) (9, 10). The origin of this T_2^* change has been attributed to myelin and a recent study has revealed a good match between a myelin-based susceptibility model and the measured B_0 orientation dependent T_2* contrast (8). Additionally, a ΔT_2^* image has shown similarity to a FA map in DTI (8). Since the orientation dependent T_2^* is primarily from myelin, this ΔT_2^* map (or a ΔR_2^* map) may provide more specific information of myelin content compared to a FA map of DTI, which is shown to be more specific to axonal membrane (4). Despite this advantage, the application of a ΔT_2^* map or (ΔR_2^* map) for in-vivo studies is significantly limited by the need to rotate a head multiple times in MRI which is time consuming and is not practical. In this study, we developed a new approach to generate a $\Delta_{0°\text{-}90°}R_2^*$ map (= R_2^*@parallel to B_0 - R_2^*@perpendicular to B_0 in each voxel) from one rotation (i.e. two GRE scans) and one DTI scans. This new approach may enable us to generate a new myelin specific map from *in vivo* in a reasonable scan time.

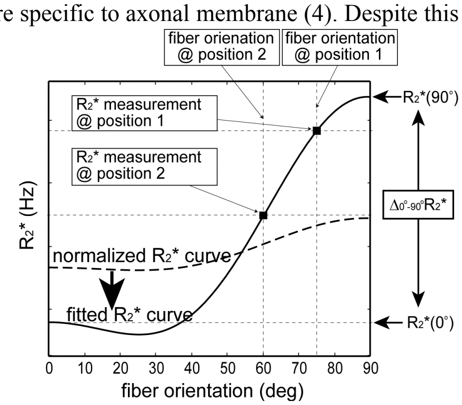

Figure 1: Normalized B_0 orientation dependent R_2^* curve and fitted (or calculated) curve

Materials and Methods

Procedure for a new $\Delta_{0°\text{-}90°}R_2^*$ mapping method: A minimum two GRE data for T_2^* and one DTI is necessary to generate a $\Delta_{0°\text{-}90°}R_2^*$ map using this method. Multi-echo GRE and DTI data are acquired in a normal supine position (position 1) and then the head of a subject is rotated in x-axis and y-axis (logical coordinate) by certain degrees (e.g. 15° to 30°) for the second multi-echo GRE data (position 2). The resolutions are matched between GRE and DTI. After data acquisition, GRE data from position 2 are aligned to position 1 and R_2^* values are calculated in each data. From DTI, the primary fiber orientation of each voxel is calculated for position 1. For position 2, the primary fiber orientation is estimated by DTI data and the registration information of the two GRE data. Only the relative angle to B_0 field (not x-y-z angles) is necessary. At this point, each voxel has four values: R_2^* value and voxel fiber orientation relative to B_0 in position 1, and R_2^* and voxel fiber orientation relatively to B_0 in position 2. Using these four values, a B_0 orientation dependent R_2^* curve ($= c_0 + c_1*(-3.05\cdot\sin(2\theta + \pi/2)+ 1.21\cdot\sin(4\theta))$; ref. 8) is calculated (for more than two orientations, the curve can be fitted to the data.). After that, R_2^* values at 0° and 90° are calculated from the resulting curved and the final $\Delta_{0°\text{-}90°}R_2^*$ value is obtained by $|R_2^*(0°) - R_2^*(90°)|$.

Computer simulation: A computer simulation was performed to test the new method. A DTI data acquired from an *in-vivo* experiment was used. A $\Delta_{0°\text{-}90°}R_2^*$ value of each voxel was set to the FA value. Each voxel R_2^* value for position 1 was calculated from the B_0 orientation dependent curve and DTI fiber orientation (Fig. 2A). For position 2, a rotation of 30° in x-axis and 30° in y-axis was assumed and each voxel R_2^* value was calculated by a new fiber orientation and the B_0 orientation dependent curve (Fig. 2B). Then the $\Delta_{0°\text{-}90°}R_2^*$ is calculated as described above. For an infinite SNR, this will result in the FA map since the $\Delta_{0°\text{-}90°}R_2^*$ was assumed to be the same as the FA values. In our processing, we assumed a threshold of 6% of the maximum range of the orientation dependent R_2^* curve and voxels below the threshold were masked out to simulate an SNR effect. This covered 84% of all the white matter voxels.

Experimental data: To test the feasibility of this new method, a subject was scanned at 7 T using a single channel Tx/Rx coil. A multi-echo 3D GRE sequence was used to measure R_2^*. The scan parameters were TR = 100 ms, TE = 4:6:40 ms, resolution = 2 x 2 x 2 mm^3, matrix size = 128 x 128 x 48, and scan time = 7m 42s. For DTI, a single echo diffusion-weighted sequence was used. The scan parameters were TR/TE = 6900/64 ms, resolution = 2 x 2 x 2 mm^3, b-value = 900 s/mm^2, 30 diffusion directions and the total scan time was 7m 44s. The same procedure described above was used to calculate a $\Delta_{0°\text{-}90°}R_2^*$ map.

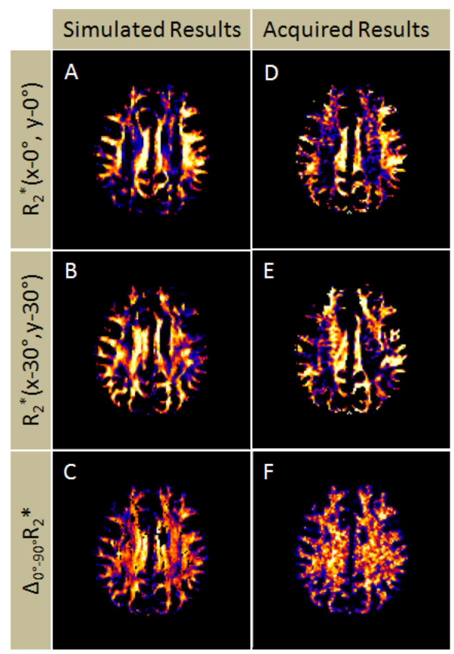

Figure 2. (A-C) Simulated results from DTI and (D-F) *in-vivo* results

Results

Figure 2 shows the results of computer simulation (Fig. 2A-C) and experiment (Fig. 2D-F). The R_2^* images of positions 1 and 2 show a good similarity between the two. The final results, $\Delta_{0°\text{-}90°}R_2^*$ maps (Fig. 2C *vs.* 2F), also reveal a certain level of similarity despite speckle-type noise observed in *in-vivo* data. This artifact may arise from SNR deficiency and/or fiber estimation errors.

Discussion and Conclusion

Our computer simulation and preliminary results suggest that a $\Delta_{0°\text{-}90°}R_2^*$ map can be obtained from this new method that only requires two orientation GRE data and one DTI. The similarity in the R_2^* maps between the simulation and the acquired data confirms that B_0 orientation dependence of R_2^* is significant in white matter. The quality of a $\Delta_{0°\text{-}90°}R_2^*$ map can be improved by correcting large scale field inhomogeneity artifacts (11) and using a multi-channel coil. The coverage of white matter with the two orientations was 84% based on our simulation assuming a 6% threshold mentioned above. Additional measurement or higher SNR will increase this coverage.

References: [1] Mackay,MRM,1994,31:673 [2] Klingberg,Neuroreport,1999,10:2817 [3] Cercignani,2001,AJNR,22:952 [4] Beaulieu,NMR Bio,2002,15:435 [5] Vavasour,JMRI,2011 [6] Wiggins,ISMRM2008;p237. [7] Schäfer, ISMRM,2009;p955. [8] Lee,NeuroImage2011,57;225 [9] Wiggins,ISMRM,2011;19:13 [10] Sati,NeuroImage,2011 [11] Ferna´ndez-Seara,MRM,2000,44,358 **Acknowledgements:** This work was supported by an NCRR-funded Research Resource RR002305.