Anisotropic magnetic susceptibility induced R2* anisotropy of human brain in vivo

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TARGET AUDIENCE: This study is targeted to those researchers who are using gradient echo MRI-derived contrasts, especially T2* or R2*, to characterize brain tissue, and are interested in knowing the dependence of R2* on magnetic field directions due to isotropic and anisotropic magnetic susceptibility distributions.

PURPOSE: It is known that T2* relaxation of brain tissues, especially white matter, depends on brain orientation with respect to the main magnetic field. Recently, Lee et al have suggested that this orientation dependence is determined by both isotropic and anisotropic magnetic susceptibility contributions of the white matter (1). So far, most studies on R2* anisotropy have been conducted on postmortem tissues. In this study, we performed a voxel-wise analysis of the R2* anisotropy of the human brain in vivo. We evaluated the contribution of anisotropic magnetic susceptibility to the R2* anisotropy, and demonstrated the potential use of this susceptibility anisotropy induced R2* variation for the characterization of brain white matter. We also compared the results to parameters determined by diffusion tensor imaging (DTI).

MATERIALS AND METHODS: *Brain Imaging*: One healthy adult was scanned using a GE MR750 3T scanner, using a multi-gradient echo sequence. The parameters were: flip angle = 20º. TE1=4 or 5 ms, echo spacing = 1.8~2.4 ms, TR = 55 ms, 16 echoes and 1.5 mm isotropic resolution. A quadrature head coil or a body coil was employed to allow for a wider range of head orientations. A total of 16 orientations were acquired. In addition, Diffusion tensor images were acquired using an 8-channel head coil and a standard single-shot EPI sequence with a parallel-imaging acceleration factor of 2. The parameters were: TE = 82 ms, TR = 8 s, b-value = 800 s/mm^2, 5 non-diffusion weighted images, 25 diffusion encoding directions and 2 mm isotropic resolution. The DTI images were resampled to 1.5 mm isotropic resolution to align with the reference gradient echo image.

Data Analysis: R2* values were calculated by fitting the logarithm of the image magnitude with a linear model. The gradient echo images from different orientations were nonlinearly registered to the reference gradient echo image using FNIRT tool in FSL (FMRIB). A region of interest (ROI) was selected in corpus callosum to evaluate the relationship between R2* and fiber orientation determined by DTI (Fig. 1). The orientation dependence was fitted using the theory of NMR signal behavior in magnetically inhomogeneous tissues (1, 2), with minor modifications considering the isotropic and anisotropic magnetic susceptibility contributions (2, 3):

$$R2^* = c0 + c1 \cdot \chi \cdot \sin^2\alpha = c0 + c1 \cdot (\chi_0 + \Delta\chi \cdot \sin^2\alpha) \cdot \sin^2\alpha \qquad [1]$$

where c0 and c1 are tissue specific parameters. χ_0 and $\Delta\chi$ are the isotropic and anisotropic susceptibility, respectively. For comparison, the relationship was also fitted to a simplified model with only contributions from isotropic magnetic susceptibility:

$$R2^* = c0 + c1 \cdot \chi_0 \cdot \sin^2\alpha \qquad [2]$$

The multiple orientation R2* dataset were then fitted on a voxel-by-voxel basis to quantify the R2* anisotropy. Due to the limited number of head orientations, a constant ratio of isotropic and anisotropic susceptibility contributions ($\chi_0/\Delta\chi$) was assumed during data fitting to improve the numerical stability. The ratio was determined based on pooled analysis of the corpus callosum. The resulting R2* anisotropy was then median filtered with 6 nearest neighbors.

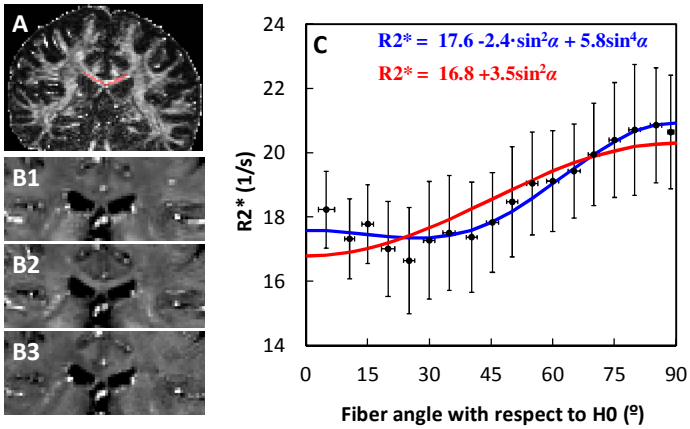

Fig. 1. Dependence of R2* on the fiber angle with respect to the main magnetic field (H0). A: DTI fractional anisotropy (FA) showing the ROI. B1-B3: the R2* map at 3 different head orientations. C: R2*-fiber angle relationship.

RESULTS: Consistent with previous postmortem studies by Lee et al (2), *in vivo* R2* shows obvious orientation dependence (Fig. 1 B1-B3). For the selected segments of corpus callosum, an apparent derivation from sine-squared relationship (Eq. 2) was observed (red line). In contrast, the relationship is much better fitted using Eq. 1, which considers the contribution of both isotropic and anisotropic susceptibility (Fig. 1C, blue line). Since the amount of data is not sufficient to fit three model parameters, a constant ratio ($\chi_0/\Delta\chi \equiv -0.4$ determined based on Fig. 1C) were assumed for subsequent voxelwise R2* anisotropy quantification**.**

Fig. 2 shows the R2* anisotropy caused by the anisotropic susceptibility, which exhibits clear contrast between gray and white matter, with higher R2* anisotropy in white matter. R2* anisotropy shows similar contrast to DTI FA map in many ways. The plot of R2* anisotropy against DTI FA shows an excellent correlation (Fig. 3). Interestingly, R2* anisotropy increases monotonically with DTI FA, indicating the similar white matter origins of these two distinct type of anisotropies.

DISCUSSION: Our *in vivo* data showed that R2* have a profound dependence on the fiber orientation with respect to the main magnetic field. These results agrees with Lee et al's finding that the R2* is influenced by both isotropic (χ_0) and anisotropic ($\Delta\chi$) magnetic susceptibility. From our results, the R2* variation resulting from the anisotropic magnetic susceptibility is on the order of 2~6 s^{-1}, which is approximately 10~30% of the R2* value of the white matter tissue. Further, the anisotropic susceptibility induced R2* variation is predominantly observed in the brain white matter, and is highly correlated with DTI FA values. With the advent of high and ultra-high magnetic field MRI systems, R2* maps can be obtained with much higher spatial resolution and signal-to-noise ratio, which may allow it to become a promising tool for the study of brain myelination and white matter microstructure.

REFERENCES: (1) Yablonskiy and Haacke, MRM, 1994.32,749. (2) Lee et al, NeuroImage, 2011, 57: 225. (3) Li et al, NeuroImage, 2012, 59: 2088

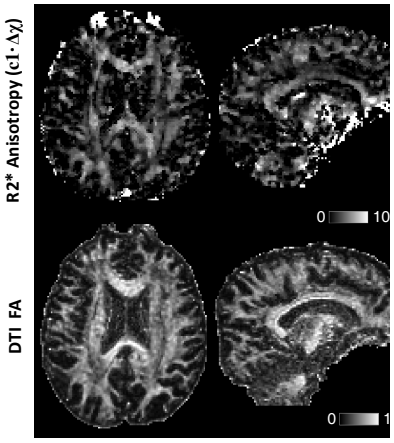

Fig. 2. R2* anisotropy v.s. DTI FA. R2* is calculated assuming $\chi_0/\Delta\chi \equiv 0.4$.

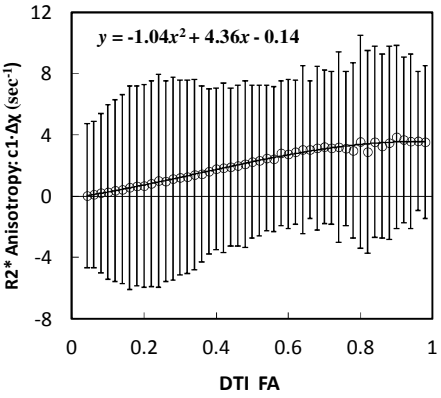

Fig. 3. Relationship between R2* anisotropy and DTI FA.