White matter fiber orientation mapping based on T2* anisotropy

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Introduction

Recent studies have shown that T2* relaxation may be anisotropic [1-4]. This anisotropy has been attributed to the microscopic (sub-voxel level) anisotropic distribution of susceptibility perturbers. In white matter fiber bundles, these anisotropic perturbations could originate from compounds such as lipid and ferritin that may align with axons, and could generate magnetic field variations whose magnitude depends on axonal orientation (θ) relative to B0 [5]. In the current study, we used post-mortem brain tissue to examine the dependence of T2* on θ and explored the possibility if this dependence could be exploited to map the orientation of white matter fibers analogous to DTI. For these purposes, models were fitted to T2* measurements at a range of θ values and the fiber orientation map was compared to that derived from DTI.

Background and Method

In gradient echo MRI of brain tissue, transverse relaxation is accelerated by an amount of R2 (R2* = R2 + Rχ) due to local field inhomogeneity caused by microscopic field perturbers. In white matter fiber bundles, the distribution of perturbers may be approached by parallel cylinders causing an angular dependent change of R2* = cAχ sin2θ or cAχ sin2θ [4-5]. An additional angular dependence may arise from the recently observed “magnetic susceptibility anisotropy” in white matter [7-8]; when susceptibility anisotropy is included, Δχ can be written as ηχ + χsin2θ (planar approximation). Hence, R2* becomes (ηχ + χsin2θ sin2θ) and R2* will show both sin2θ and sin4θ angular dependence.

Two coronal slabs of a fixed human brain were cut into circular shapes and put in a container. Then cylindrical axis of the container was placed perpendicular to B0. A 7 T human scanner (GE) with a 3-inch coil was used. The tissues were scanned at 18 different orientations in 10° steps of rotation in the x-z plane. The rotation was performed only in 2D. The sequence was a 3D multi-echo GRE and the scan parameters were TR = 700 ms, TE1 = 4.6 ms, echo spacing = 2.7 ms (Tissue 1) or 3.0 ms (Tissue 2), # of echoes = 12, FA = 60°, FOV = 8 x 8 x 1.2 cm², res. = 0.625 x 0.625 x 0.75 mm³. Each orientation took 23.9 min. For analysis, R2* values were calculated from multi-echo data and all orientations were realigned to the first image volume using linear and nonlinear registration. Two ROIs were drawn in the corpus callosum area (Fig. 1a) and the average R2* value was calculated in each ROI in each orientation. The mean R2* values were fitted with two sinusoidal models: A “sin2θ model” with a constant, sin2θ and cos2θ components and a “sin4θ model” with a constant, sin2θ, cos2θ, sin4θ, and cos4θ components. Least-square fit results were obtained in each model.

To generate a T2* fiber orientation map, the model fitted T2* curve (normalized) was cross correlated on a voxel-by-voxel basis with a 4D T2* data set (3D space + 18 orientations). The angle of the peak correlation coefficient in each voxel was saved for an angular map. A ΔT2* map was also generated. Finally, a T2* orientation map, which color coded the angular map the same as a DTI map and multiplied it by the ΔT2* map, was generated. For comparison, DTI was acquired at a 7 T animal system with the same resolution and FOV was used and TR = 1000 ms, TE = 57.43 ms, FA = 70°, diffusion gradient direction = 20, b-value of 3,000 s/mm². The total scan time was 13.1 hours. The reconstructed DTI results were projected to 2D space to generate a pseudo-2D DTI (a 2D V1 map multiplied by a 2D FA map) and compared to the T2* orientation map.

Results

The orientation dependent R2* variation is shown in Fig. 1. The R2* curves clearly demonstrate orientation dependency yielding maximum R2* value when the fibers are oriented perpendicular to B0. Fitted curves for a sin2θ model (red lines) deviate from the measurement (adjusted R2* = 0.80 ± 0.03) whereas a sin4θ model (blue lines) tightly matches to the measurement (adjusted R2* = 0.95 ± 0.01). The positive peak of sin2θ coincides with the positive peak of sin4θ (Fig. 2) indicating phase coherence between the two. The ΔT2* values were fitted with two sinusoidal models: A “sin4θ model” with constant, sin4θ and cos4θ components and a “sin4θ model” with constant, sin4θ, cos4θ, sin4θ, and cos4θ components. Least-square fit results were obtained in each model.

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Conclusion and Discussion

In this study, we demonstrated orientation dependent T2* in ex-vivo white matter and generated a T2* fiber orientation map. The R2* curves revealed a sin4θ component as well as a sin2θ component with phase coherence between the two. A model based on magnetic susceptibility anisotropy yielded a good fit for the measurement. Extension for 3D is straightforward and can be done by rotating tissue in two directions.

Although the sin4θ term suggest that susceptibility anisotropy is a significant contributor to R2*, there may be alternative or additional explanations. One possibility is the contribution of “magic angle” effects. When R2* is modeled by the susceptibility and magic angle effect, the resulting adjusted R2 was 0.89 ± 0.03. This is lower than that of the anisotropism yielding maximum R2* value when the fibers are oriented perpendicular to B0. Fitted curves for a sin2θ model (red lines) deviate from the measurement (adjusted R2* = 0.95 ± 0.01). The positive peak of sin2θ coincides with the positive peak of sin4θ (Fig. 2) indicating phase coherence between the two. The ΔT2* values were fitted with two sinusoidal models: A “sin4θ model” with constant, sin4θ and cos4θ components and a “sin4θ model” with constant, sin4θ, cos4θ, sin4θ, and cos4θ components. A great similarity between T2* orientation results and DTI can also be observed at the bottom rows of Fig. 3 where DTI like color coded T2* orientation map (Fig. 3c) and pseudo-2D DTI results (Fig. 3f) are shown.

References

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