Fiber-Orientation Dependent White Matter Contrast in Gradient Echo MRI.

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Introduction: Gradient-echo (GE) MRI is widely used for producing diagnostic images of the human brain, since both the phase and magnitude of the complex NMR signal measured using GE sequences can be used to create high-resolution images that show strong contrast between different types of brain tissue. Recent studies at high magnetic field strengths (3T and above) have shown that there is a direct link between the orientation of white matter (WM) fibers to the B_0-field and the contrast observed in magnitude and phase images [1-4]. Although the origin of this link is currently not understood, fibre-orientation-dependent contrast in GE images is of great interest, since it could offer researchers easy access to a new diagnostic tool for investigating tissue microstructure using MRI. Here, we show that fibre-orientation-dependent contrast in magnitude and phase images can be fully explained by modelling nerve fibers as long, hollow cylinders of myelin, within which: (i) myelin-water [5] generates a rapidly-decaying signal and (ii) the magnetic susceptibility is anisotropic. Based on the orientation and shape of the lipid chains in the myelin sheath [6], the model assumes that the susceptibility tensor is cylindrically symmetric and that the principal component of the tensor is always radially oriented.

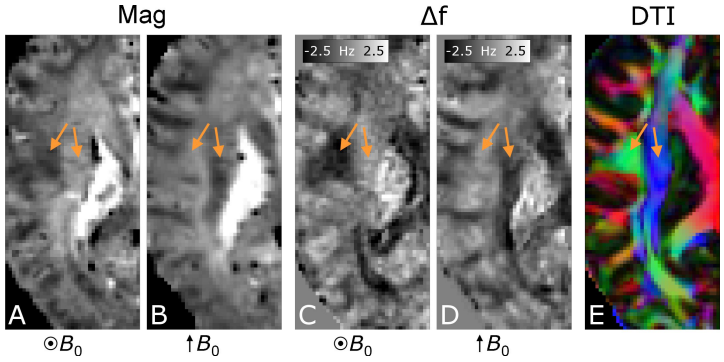

***Fig.1** Magnitude and FDM data (TE= 60.5 ms) from supine (A&C) and sphinx (B&D) positions. DTI colour-coded fiber orientation map (E).*

Methods: Three healthy subjects were imaged on a Philips whole-body 3T scanner using a spoiled, multi-echo GE sequence (TR = 70 ms, 1.4 mm isotropic resolution, FOV = 200×200×50 mm^3) yielding 13 TE-values, spread evenly between 4.7ms and 60.5ms. Each subject was imaged twice, once in a standard supine position, and once in the sphinx position, so as to produce a data-set in which the major fiber tracts were oriented at a range of angles to B_0. Flexible receiver coils positioned on either side of the head were used to allow imaging in the two positions. DTI data were also acquired for each subject with 2 mm isotropic resolution and 32 diffusion-gradient directions. These data were used to calculate the angle, β, between fiber axis and B_0 in WM voxels. For the detailed analysis, voxels with a fractional anisotropy > 0.25 were divided into six β-value ranges equally spread between 0 and 90°. Frequency maps were produced by scaling the phase data by TE. Frequency difference (Δf) maps (FDMs) [7] were used in further analysis so as to eliminate the effect of non-local fields (e.g. due to macroscopic susceptibility variation and incorrect shimming). FDMs were created by subtracting the frequency map measured at TE=4.7ms from data acquired with longer TE-values, followed by weak high-pass filtering.

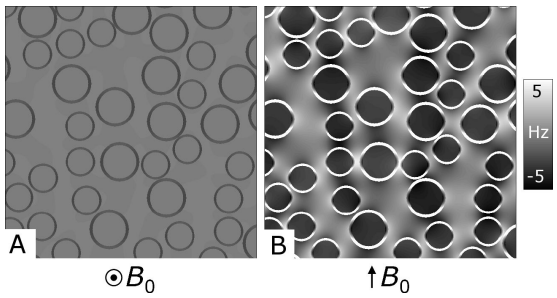

***Fig. 2** Simulated frequency maps for fibers oriented parallel (A) and perpendicular (B) to B_0.*

Model: Analytic expressions describing the field perturbation produced by an anisotropic, hollow cylinder as a function of β, and the isotropic and anisotropic susceptibility coefficients, (χ_I and χ_A), were derived from the magnetic scalar potential, using an appropriate sphere of Lorentz correction. Using these expressions, the frequency offsets generated by arrays of randomly-positioned, non-overlapping, parallel, hollow myelin cylinders could be evaluated for different values of fiber volume fraction (FVF) and g-ratio. Figure 2 shows frequency offset maps produced with fibers parallel (Fig. 2A) and perpendicular to the field (Fig. 2B). The phase and magnitude of the NMR signal from WM was simulated by summing the complex signal contributions from all compartments. Different T_2^* and spin density values were assigned to the myelin compartment, compared to those used for the intra- and extra-axonal compartments.

Results and Discussion: Co-registered magnitude images, along with the corresponding FDMs, are shown in Fig.1, for the two head orientations and TE=60.5ms. Significant intensity variations that are correlated with fiber-orientation are evident in WM in the magnitude images (Fig. 1A&B) and FDM data (Fig. 1C&D); in both cases, fibers perpendicular to B_0 produce a lower intensity than fibers which are parallel to B_0. Figure 2 shows the evolution of the magnitude signal (Fig. 2A) and frequency difference (Fig. 2B) with TE for three different ranges of β (0 -15°, 45-60° & 75-90°). There is a significant variation of Δf (and a lesser variation of signal magnitude) with orientation at long TE. The phase and magnitude of the signal from the hollow cylinder model was fitted to the experimental data over the full range of β-values, producing the dashed lines shown in Fig. 3, which are in very good correspondence with the experimental measurements. In contrast, it was not possible to produce realistic fits to the experimental data by assuming myelin has purely isotropic susceptibility or anisotropic susceptibility with the principal component aligned with the fiber. The combination of parameters that produced the best fit was: T_2*(myelin) = 14ms, T_2*(intra-/extra-axonal)= 60ms, spin density (myelin) = 0.55, g-ratio = 0.85, FVF = 0.5, χ_I (relative to surrounding region) = -0.14ppm and χ_A = -0.18ppm. These biophysically plausible values were also used to produce the simulated frequency maps shown in Fig. 2. It is clear from Fig. 2B that the rapid decay and significant positive frequency offset of the myelin water signal combine to produce the negative Δf-values at long TE for fibers that are perpendicular to B_0, while the negative intra-axonal frequency offset contributes to the elevated rate of signal decay and strong phase effects that are seen in WM tracts with fibers oriented perpendicular to B_0.

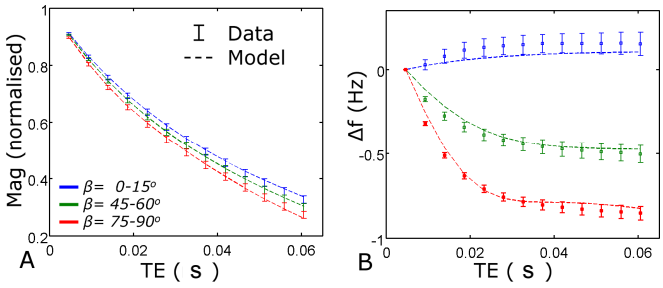

***Fig. 3** Measured variation of signal magnitude (A) and Δf (B) with TE for three different ranges of fiber orientation. Dashed lines = model fits.*

Conclusions The agreement of the predictions of the hollow cylinder model with the experimental data suggests that the anisotropic susceptibility of the myelin sheath is the dominant source of fiber orientation related contrast in WM. The resulting orientation-dependent change of frequency with TE provides a valuable new MRI contrast that carries information about tissue microstructure.

References: [1] Lee et al. 2010. PNAS. (107) 5130-5135. [2] Denk et al. 2010. NMR Biomed. DOI:10.1002/nbm.1581 [3] Lee et al. 2011. Neuroimage. (57) 225-234. [4] Sati et al. 2011. Neuroimage. DOI:10.1016/j.neuroimage.2011.08.064 [5] Mackay et al. 1994. MRM. 673-677 (31) [6] Shäfer et al. 2011. Proc ISMRM. 4238. [7] Schweser et al. 2011. Proc ISMRM. 1428.