High Resolution Probablistic Tractography in Whole, Fixed, Human Brain Using Diffusion-Weighted Steady-State Free Precession

J. A. McNab[1], S. Jbabdi[1], S. C. Deoni[1,2], G. Douaud[1], T. E. Behrens[1], and K. L. Miller[1]

[1]Oxford Centre for FMRI of the Brain, University of Oxford, Oxford, United Kingdom, [2]Centre for Neuroimaging Sciences, Institute of Psychiatry, King's College, University of London, London, United Kingdom

Introduction Diffusion-weighted steady-state free precession (DW-SSFP)[1-4] is a unique alternative to standard diffusion-weighted spin-echo (DW-SE) imaging. Since DW-SSFP acquires signal from multiple echoes simultaneously it requires only modest gradient areas and short repetition times, making it a promising option for reducing distortions and achieving high spatial and angular resolution diffusion images. One difficulty in using DW-SSFP *in vivo* is the strong sensitivity to motion, which has previously been addressed using navigation[5]. A second obstacle for DTI and tractography is the complicated dependencies of its diffusion sensitivity on T_1, T_2, TR and flip angle, which invalidates the mathematical relations used in conventional DTI analysis. In this study we present a robust method for estimating the principal diffusion direction from multi-angle DW-SSFP data and demonstrate probabilistic tractography at sub-millimeter resolution in a whole, fixed human brain (where the *in vivo* confound of motion has been removed).

Methods

DW-SSFP, T_1 and T_2 data were acquired in a fixed, whole, human brain of a 65 year old man in accordance with the ethics approval at our institution. Data were acquired on a Siemens 3T using a 12-channel head coil for signal reception. 3D DW-SSFP-EPI data were acquired with TE/TR = 28/42 ms, $\alpha = 37°$, BW = 924 Hz/pixel, 17 lines per EPI segment, matrix size = 246×246×176, partial Fourier factor = 5/8, voxel size = 0.8 mm isotropic and acquisition time TA = 113 s per volume. 17 averages of 63 isotropically distributed diffusion directions were acquired with diffusion gradient duration and magnitude (δ/G) = 16.7 ms / 40 mT/m. 107 averages with low diffusion weighting along a single direction (δ/G = 1.2 ms / 40 mT/m) were also acquired. Quantitative whole brain T_1, T_2 and B_1 maps were acquired alongside the DW-SSFP data using the DESPOT methods[6-8]. The DESPOT and DW-SSFP acquisitions were interleaved for a total imaging time of 50 hours, 49 minutes. Individual acquisitions of the DW-SSFP data were co-registered using FLIRT[9] to correct for B_0 drift and eddy-current distortions before averaging the data. The analytical expression for the DW-SSFP signal[10] (which describes only isotropic diffusion along a single direction) was modified to account for conditions of diffusion anisotropy using a partial volume model[11]. The anisotropic DW-SSFP signal model was then integrated into a probabilistic tractography framework[11]. Markov Chain Monte Carlo (MCMC) sampling was used to estimate the posterior probability density functions (*pdfs*) for each of the unknown parameters in the model, which include: the orientation of the principal diffusion axis in polar coordinates (θ, ϕ), the equilibrium magnetization (M_0), the anisotropic fraction (f), the diffusion coefficient along the principal diffusion axis (D), the variance of the noise (σ^2), and the longitudinal and transverse relaxation times (T_1 and T_2). Uninformative priors were used with the exception of T_1 and T_2, which were given a tight Gaussian prior distribution centered at their measured value. MCMC sampling applied a "burn-in" period of 200 steps prior to sampling 50 of a total of 2000 steps. Each step consisted of independent changes of each parameter. The estimated *pdfs* for the principal diffusion orientation at each voxel were then used to perform tractography using Probtrack[11] with a single seed mask, loop-check to terminate pathways that loop back on themselves, a step-length equal to 0.2 mm, 5000 steps per sample, 1000 samples and no curvature threshold.

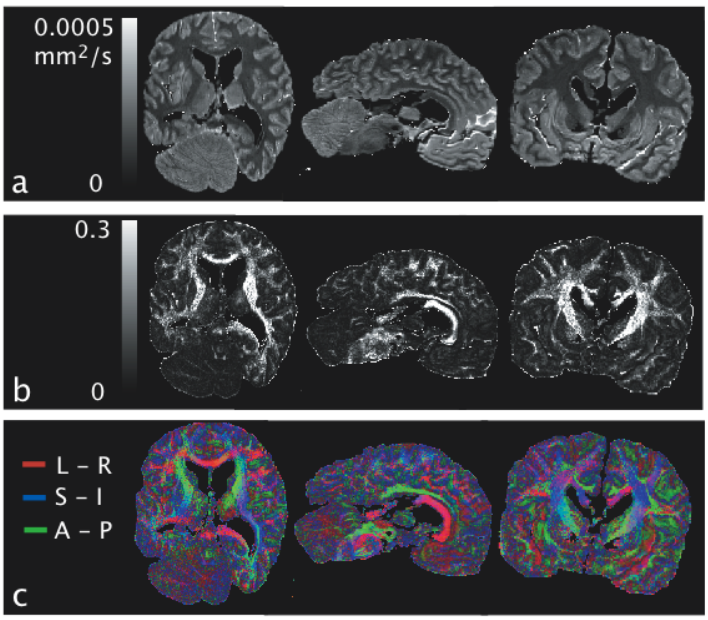

Figure 1: Results from the voxel-wise estimation of diffusion parameters. The mean of the posterior distribution for a) the apparent diffusion coefficient (ADC), b) the anisotropic fraction and c) the principal diffusion direction at each voxel. Left to right are axial, sagittal and coronal views. The mean of the principal diffusion direction is displayed using directionally-encoded colour with red, blue and green indicating left-right, superior-inferior and anterior-posterior respectively.

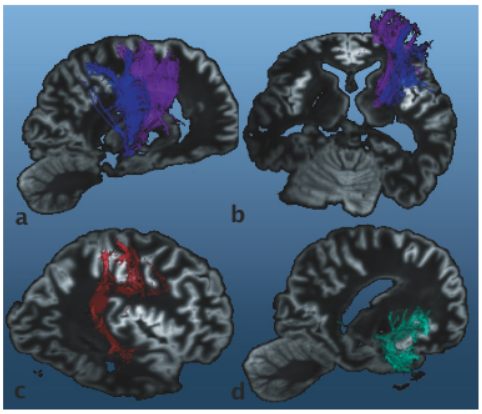

Figure 2: Volume rendered DW-SSFP tractography results superimposed on structural images. The corticospinal tract (blue) and the anterior-superior thalamic radiations (purple) are shown relative to a) a sagittal and b) axial orientations. The arcuate fasciculus (red) and the uncinate fasciculus (turquoise) are displayed in c) and d) respectively in relation to sagittal slices.

Results and Discussion The average values for diffusion in white matter (along the principal diffusion axis) (Fig. 1a) ranged from 7×10^{-5} to 3×10^{-4} mm^2/s which is in good agreement with ADC values determined previously in fixed human brain[12]. As anticipated, the map of mean anisotropic fraction (Fig. 1b) clearly demarcates the white matter in the brain and the directionally-encoded colour map (Fig. 1c) displays an accurate representation of known white matter tracts such as the corpus callosum, internal capsule, cingulum and superior longitudinal fasciculus. The methods used here also allowed for the faithful reconstruction of the corticospinal tract, anterior-superior thalamic radiations and the arcuate and uncinate fasciculi (Fig. 2) without the use of any exclusion or through-point masks. Motion-corrected DW-SSFP pulse sequences have already been demonstrated *in vivo*[11] and thus the results presented here should be applicable to *in vivo* studies. The very long acquisition times in the current study are primarily a consequence of the decreased T_2 relaxation times, diffusion coefficient and proton density levels that are characteristic of fixed tissues. Post-mortem diffusion imaging is also a useful technique in its own right since it permits the comparison of diffusion tractography results with histological measures. DW-SSFP offers significant advantages for the purposes of *ex vivo* imaging due to its high SNR and CNR efficiency. The diffusion images presented here with 0.8 mm isotropic voxels, high-angular resolution diffusion sampling (63 directions) and whole brain coverage represent a significant advancement from previous post-mortem human brain studies which have either used only small samples of tissue[7] or achieved only low spatial and angular resolutions.

Acknowledgments and References Funding provided by the Charles Wolfson Charitable Trust. (1) Kaiser R. et. al. J Chem Phys 60:2966-2979 (1974). (2) LeBihan D. MRM 7:346-351 (1988). (3) Merboldt KD. et .al. MRM 9:423-429 (1989). (4) Wu E. et. al. JMR 90:243-253 (1990). (5) Miller KL, et. al. MRM 50:675-683 (2003). (6) Deoni SC. et. Al. MRM 53:237-241 (2005). (7) Deoni S. ISMRM #42 (2007). (8) Deoni S. ISMRM #1783 (2007). (9) Jenkinson M. Medical Image Analysis 5:143-156 (2001). (10) Buxton RB. MRM. 29:235-243 (1993). (11) Behrens TEJ et. al. MRM 50:1077-1088 (2003). (12) D'Arceuil H. et. al. ISMRM Workshop on Methods for Quantitative Diffusion MRI of Human Brain 1 (2005).