Comparison of spin echo and steady-state free precession sequences for diffusion tractography of whole, ex-vivo human brains

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Introduction. Despite the extensive number of published studies using diffusion tractography to trace white matter pathways, there is a paucity of data establishing the link between diffusion imaging and the rich dissection literature. Ex vivo tractography would provide the opportunity to make direct comparisons to post-mortem analyses in the same brain. Our group aims to develop imaging protocols suitable for integration with human brain banks, which might realistically have overnight access to clinical scanners. This kind of study in human brains has been constrained by the unique challenges of diffusion imaging of fixed tissue. We present a comparison of ex vivo data acquired using two different sequences: conventional diffusion-weighted spin echo (DW-SE) and diffusion-weighted steady-state free precession (DW-SSFP) [1]. We previously reported lower uncertainty on fiber direction with DW-SSFP, which effectively indicates higher contrast-to-noise ratio (CNR) in the parameter of interest in tractography [2]. We now demonstrate that a 6-hour scan on a clinical 3T scanner is sufficient to trace major pathways, and show that tract fidelity (anatomical accuracy) is superior with DW-SSFP.

Background. Diffusion imaging of fixed tissue is complicated by profound reductions in the apparent diffusion coefficient (ADC) and T_2. Reduced ADC requires an increased b-value for sufficient diffusion contrast, which lengthens the echo time (T_E) in DW-SE. Combined with reduced T_2, this causes DW-SE to have poor signal-to-noise ratio (SNR). DW-SSFP is more compatible with short T_E because diffusion contrast is accumulated over multiple repetition times (T_R). DW-SE and DW-SSFP protocols were optimized to maximize SNR efficiency at b=4500 s/mm^2 for fixed white matter (T_1/T_2= 340/45 ms, ADC=$5{\cdot}10^{-5}$ mm^2/s). SNR efficiency, which normalizes SNR by the square root of the scan time, allows direct comparison of sequences or protocols independent of scan duration. In DW-SSFP, b-value is not defined, so these protocols are designed to achieve an "effective b-value" with equivalent signal attenuation to DW-SE. DW-SSFP protocol optimization searches all T_R, flip angle, and diffusion gradient duration triplets achieving this effective b-value. For DW-SE, the b-value determines T_E, and we optimize T_R and flip angle. Both methods were optimized at short T_R (DW-SE: 600 ms, DW-SSFP: 34 ms), and are therefore suited to 3D k-space acquisitions. As shown in Table 1, although DW-SSFP has lower absolute signal, it also dedicates a much greater percentage of T_R to acquisition (high readout efficiency). The net effect is ~50% higher SNR efficiency in DW-SSFP over DW-SE.

Methods. Diffusion-weighted images were acquired of a whole, ex-vivo human brain with no known pathology using a clinical 3T system with 40 mT/m and a standard 12-channel human head coil. DW-SE and DW-SSFP acquisitions both used a 3D stack-of-segmented EPI acquisition [1,2] achieving the same resolution (0.94x0.94x0.94 mm^3), effective b-value (4500 s/mm^2) and scan time (6 hours each). A preliminary account of this data was given in [2], where the uncertainty on the fitted principal diffusion direction was found to be lower in DW-SSFP, indicating higher CNR. Here, we extend these results by comparing tractography obtained from these scans. Probabilistic tractography was performed using the FDT package (FSL) [3], including a modified version implementing the DW-SSFP signal model [2]. The analysis was also matched for DW-SE and DW-SSFP, using the same MCMC fit to estimate a single-fiber per voxel, the same seed mask following alignment of each data set to a structural scan, and tractography with 5000 streamlines per seed voxel. To emphasize the differences in the raw data quality, no curvature thresholds or exclusion masks were used to refine the tractography. Two sets of seed masks were generated: (a) masks dividing the corpus calloum (CC) into 5 sub-regions in the mid-sagittal plane [4], and (b) masks for the right and left posterior limb of the internal capsule (corticospinal tract, CST) in an axial plane 5mm superior to the ACPC line.

	Signal (% M_0)	Readout efficiency	SNR efficiency
DW-SE	5.15 %	6.73%	1.33%
DW-SSFP	3.45 %	32.65%	1.97%

Table 1: Signal for optimized DW-SE and DW-SSFP.

Results and Discussion. Results are shown in Figs. 1 and 2. For all seed regions, tractography of DW-SSFP data dispersed less along the tracts and tracked further into the cortex (yellow boxes). This is consistent with the greater uncertainty (lower CNR) on principal diffusion direction in DW-SE reported previously [2]. This effect is particularly notable for the CST, where the DW-SE tracts die out in the region where the CST crosses the superior longitudinal fasciculus (SLF) and CC [5]. At reduced display threshold, the tracts can be seen to pick up the SLF and CC with both DW-SE and DW-SSFP. We therefore expect multiple fiber estimation to improve both the DW-SE and DW-SSFP tractography. This functionality exists for DW-SE [3] and will be implemented for DW-SSFP in future work. The improved tracking fidelity with DW-SSFP is directly related to lower uncertainty on the principal diffusion direction, ultimately driven by higher SNR efficiency.

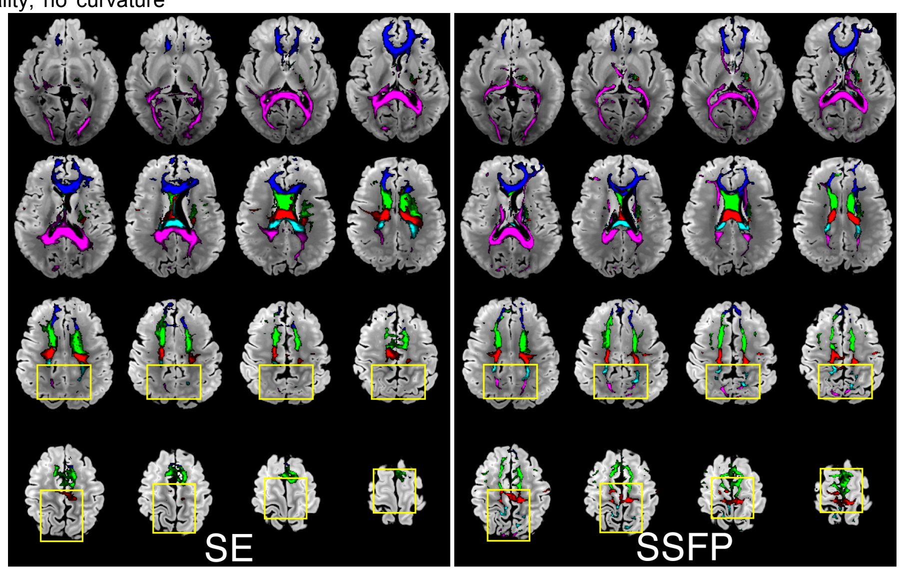

Figure 1: Tractography seeded from 5 sub-regions of the corpus callosum (CC) for SE and SSFP with identical thresholding (2000 fibers). Tracts reach the cortex more reliably in SSFP.

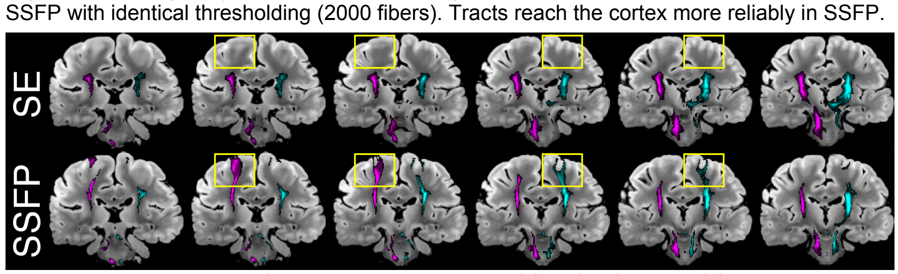

Figure 2: Tractography of the corticospinal tract (CST) for SE and SSFP with identical thresholding (1000 fibers). Tracts reach the cortex more reliably in SSFP, whereas the SE tracts end where the CST crosses the superior longitudinal facsciculus (SLF) and CC.

Conclusions. In this work, we demonstrate diffusion tractography in whole, ex-vivo human brains from data acquired in a 6-hour scan. Our data indicate that DW-SSFP may be a better option than DW-SE due to its high SNR efficiency. Ultimately, this kind of imaging could be performed overnight on a clinical scanner, offering a powerful tool for routine use in brain banks.

[1] McNab and Miller, MRM 2008.
[2] McNab et al, NeuroImage 2009.
[3] www.fmrib.ox.ac.uk/fsl/fdt/
[4] Hofer and Frahm, NeuroImage 2006.
[5] Wedeen et al, NeuroImage 2008.