Too Many Peanuts Makes You Fat: Sensitivity of Diffusion Weighted Steady State Free Precession to Anisotropic Diffusion in *Ex Vivo* Brain Tissue

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Introduction Diffusion-weighted steady-state free precession (DW-SSFP) has been shown to have a strong sensitivity to the self-diffusion of water within tissues. Since DW-SSFP acquires signal from multiple echoes simultaneously it requires only modest gradients and short imaging times, making it a promising option for high spatial and angular resolution diffusion imaging. In DW-SSFP, however, signal attenuation due to diffusion weighting is dependent not only on the diffusion-encoding gradient but also on flip angle (α), TR, T_1 and T_2. Using DW-SSFP, a quantitative measurement of the diffusion coefficient (D) is possible for free diffusion in phantoms[1,2] and a non-quantitative fractional anisotropy map has been produced in the *in vivo* human brain[3], but a b-matrix is ill-defined for this pulse sequence making it unclear whether it can be used to measure anisotropic diffusion. Simulations presented previously[4], indicate that DW-SSFP should be sensitive to anisotropic diffusion, but that its signal profile for a single fiber population is fundamentally different than that produced by diffusion-weighted spin echo (DW-SE) pulse sequences. This study aims to validate the signal model for DW-SSFP in a single fiber population through measurements in an *ex vivo* macaque brain. As a secondary goal, the potential benefits of using DW-SSFP for *ex vivo* imaging experiments will be assessed.

Methods DW-SSFP, DW-SE, T_1 and T_2 data were acquired in an axial slice at the level of the corpus callosum (CC) of an *ex-vivo* perfuse-fixed macaque brain using a 4-channel array of surface coils for signal reception in a 3T clinical MR scanner. Diffusion measurements included 29 isotropically sampled directions ($\Delta\theta$ = 6°) in the 2D plane of the slices, using optimised 3D segmented DW-SE-EPI (TE/TR=111/590 ms, BW= 801Hz/px, 21 lines per segment, matrix size = 120x94x52) and 3D segmented DW-SSFP-EPI (TE/TR=12/40 ms, α = 37°, BW = 942 Hz/pixel, 25 lines per segment, matrix size = 120x166x52). DW-SE and DW-SSFP protocols had 720 µm x 720 µm in-plane resolution and 52 matched 1.4 mm slices. Diffusion weighting was always applied with the maximum available gradient strength = 40 mT/m. T_1 and T_2 were measured in the centre two slices of the 3D diffusion acquisitions using 2D SE single-shot EPI (720 µm x 720 µm in-plane resolution, matrix = 120x104, BW = 772 Hz/pixel, 2.8 mm slice) with 8 different TEs (43-200 ms) and a slice-selective inversion pulse applied for T_1 measurement using 8 TIs =50-3000 ms. To compare the sensitivity of each pulse sequence to anisotropic diffusion, the variance of the mean profile for ROI 2 ($\sigma_p^2=p^Tp$) was divided by the variance of the noise (σ_n^2) in each voxel in the ROI to obtain an estimation efficiency[5] ($\sigma_p/(\sigma_n)$ which should be a predictor of contrast–to-noise ratio (CNR).

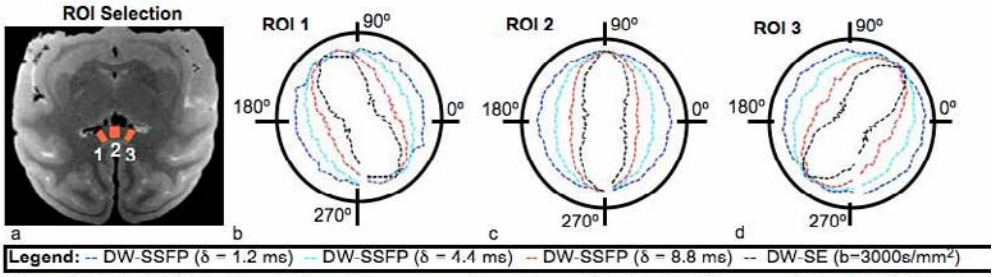

Figure 1: a)The 3 ROIs in the splenium of the corpus callosum from which signal profiles were obtained. b-d) Signal profiles for DW-SSFP at 3 different diffusion weightings and DW-SE (b=3000s/mm^2) for ROIs 1-3 respectively.

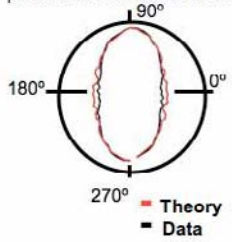

Figure 2: Measured T_1, T_2 and ADC values from ROI2 substituted into theoretical model for DW-SSFP signal profile (red). Empirical DW-SSFP signal profile from ROI 2 (black).

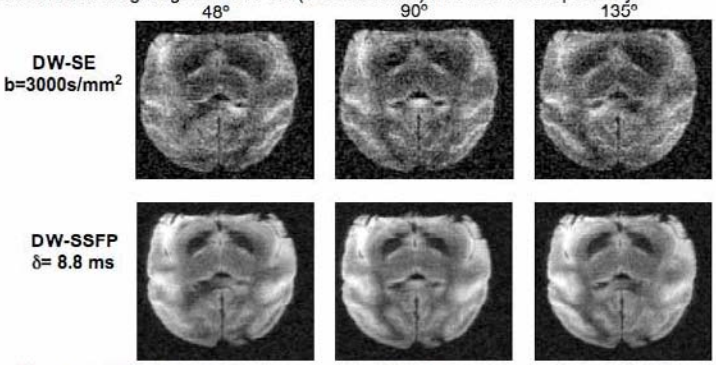

Figure 3: Diffusion-weighted images with diffusion-encoding applied at 48, 90° and 135° in-plane using DW-SE (b=3000s/mm^2) (top) and DW-SSFP (δ=8.8 ms) (bottom).

Table1

	Acquisition Time	SNR	Profile Variance	Noise Variance	Estimation Efficiency
DW-SE (b = 3000 s/mm^2)	6 min.	5	0.243	0.134	1.81
DW-SSFP (δ = 8.8 ms)	3 min.	16	0.189	0.098	1.92

Results and Discussion As expected, DW-SSFP signal profiles display increased sensitivity to anisotropic diffusion with increasing duration of the diffusion gradient (Fig.1b-d). Theoretical values for the DW-SSFP signal profile (Fig. 2) were calculated by subsituting measured T_1/T_2=833/65 ms and ADC values (ranging from 0.00009 to 0.0006 mm^2/s based on SE measurements) into the DW-SSFP model[6,7]. The excellent correspondence between theory and empirical data (Fig. 2) validates that the DW-SSFP profile has a "fatter waist" than its DW-SE counterpart. This is due to the weighted summation of many "peanut-shaped" signal profiles each of which has a different sensitivity to anisotropic diffusion. Since shorter echo pathways with less sensitivity to diffusion are weighted more heavily in the measured DW-SSFP signal than longer echo pathways with stronger diffusion-weighting, the "waistline" (i.e. direction parallel to the length of the fiber) of the resultant profile is larger than that of the DW-SE profile. However, the high SNR and diffusion-weighting efficiency of DW-SSFP more than compensates for the lack of definition in its profile. Each DW-SSFP image in Figure 3 took half as long to acquire as its DW-SE counterpart (3 min. vs. 6 min.) and yet the DW-SSFP images have more than 3x greater signal-to–noise ratios (SNR = 16 vs. SNR = 5) and similar estimation efficiency (Table 1). It is clear from the DW-SSFP signal profiles (Fig. 2b-c) and the raw DW-SSFP images (Fig. 3) that information about anisotropic diffusion is present. Due to the high SNR efficiency of DW-SSFP and the relatively small diffusion gradients required to sensitize the signal to diffusion, DW-SSFP is an optimal choice for diffusion imaging in *ex vivo* brain tissue which has characteristically short T_2 values and low diffusion coefficients. An appropriate method for analyzing DW-SSFP signal profiles such that quantitative measures of anisotropic diffusion may be determined is still required and comprehensive motion correction methods will be mandatory to implement this pulse sequence *in vivo*, however, the potential benefits of such a rapid and efficient diffusion imaging pulse sequence is clearly evident.

Acknowledgments and References Funding provided by the Charles Wolfson Charitable Trust. (1) Buxton RB. MRM. 29:235-243 (1993). (2) Deoni SC. et. al. MRM 51:428-433 (2004). (3) Miller KL, Pauly JM. MRM 50:675-683 (2003). (4) McNab J.A. Miller KL. Proc. ISMRM #1630 (2006). (5) Dale, A.M. HBM 8:109-114 (1999). (6) Kaiser R. et. al. J. Chem. Phys. 60:2966-2980 (1974). (7) Wu EX., Buxton RB. JMR. 90:243-253 (1990).