ANALYSIS OF HIGH *B*-VALUE DIFFUSION IMAGES USING A FRACTIONAL ORDER DIFFUSION MODEL WITH DENOISING IMAGE RECONSTRUCTION

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Introduction In biological tissues, diffusion-induced MR signal attenuation does not follow the classical mono-exponential decay at high *b*-values. To characterize this anomalous diffusion behavior, several models have been proposed, such as the bi-exponential model [1], the distributed diffusion model [2], the stretched exponential model [3], the fractal model [4], and a recently proposed model based on fractional order (FO) calculus [5,6]. A challenge common to all these models is that images acquired at high *b*-values (e.g., > 2,000 s/mm^2) are typically of very low signal-to-noise ratio (SNR; e.g., ~5). This adversely affects quantitative estimation of diffusion parameters and makes it difficult to evaluate these models. Conventionally, two approaches have been used to address the issue with low SNR. One is to increase the number of signal averages (NSA or NEX), which results in longer scan times; the other is to increase the voxel size, which reduces the spatial resolution and accentuates partial volume effects. Recently, Haldar *et al.* proposed a statistical model for joint reconstruction and denoising of images acquired with different diffusion-weightings [7]. This algorithm provides an effective way to remove noise without the need for signal averaging, while recognizing and preserving image features with a negligible compromise of spatial resolution. In this study, we have applied the denoising technique to high *b*-value (up to 3,300 s/mm^2) diffusion-weighted (DW) images of the human brain and demonstrate the substantial improvement in diffusion parameter quantification using an FO diffusion model [5, 6].

Methods Diffusion-weighted images were acquired from the human brain using a customized single-shot echo planar imaging (EPI) sequence on a 3T GE Signa HDx scanner with a quadrature coil. Fifteen *b*-values were used, ranging from 0-3,300 s/mm^2, with the diffusion gradient applied successively along the three orthogonal axes to minimize the effect of diffusion anisotropy. The other acquisition parameters were: TR/TE = 4,000/102.2 ms, FOV = 22 cm, image matrix = 128 × 128, and slice thickness = 4 mm.

Statistical joint image reconstruction of the whole image sequence was performed on *k*-space data by utilizing a quasi-Bayesian prior model to preserve correlated edge features while reducing noise [7]. Phase correction process was built into the statistical reconstruction model. For comparison, images were also reconstructed using a homodyne technique without denoising.

Images reconstructed with and without denoising were analyzed using an FO model by fitting the data to the following equation: $S/S_0 = \exp\{-D\mu^{2(\beta-1)}(\gamma G_d\delta)^{2\beta}[\Delta-(2\beta-1)\delta/(2\beta+1)]\}$ [5, 6], where G_d, δ, and Δ are the gradient amplitude, pulse width, and pulse separation of a Stejskal-Tanner gradient pair, β is the fractional order ($0<\beta<1$) with respect to space, and μ is a spatial parameter in units of μm. A non-linear least-squares algorithm was used, yielding spatially resolved maps of D, β, and μ. In the fitting, the initial D values were obtained from the data acquired at b values < 1,000 s/mm^2 using the classical mono-exponential model.

Results Figure 1 displays a set of representative diffusion images with b = 3,300 s/mm^2 and gradient direction along the superior/inferior (S/I) direction. The SNR [8] calculated from a region of interest (ROI) in the genu was 6.3 without denoising (Fig. 1a) and 11.9 with denoising (Fig. 1b). This SNR improvement was equivalent to that obtained with 4 averages (SNR=12.0; Fig. 1c). Figure 2 shows the diffusion-induced signal attenuation together with the fitting curves using the FO diffusion model from three ROIs selected in white matter (WM), gray matter (GM) and cerebrospinal fluid (CSF) without (Fig. 2a) and with (Fig. 2b) denoising. The variable b^* in the figure was defined as $b^* = (\gamma G_d\delta)^2[\Delta-(2\beta-1)\delta/(2\beta+1)]$. The goodness-of-fit was evaluated by χ^2, which improved from 0.163 (WM), 0.061 (GM), and 0.063 (CSF) to 0.021 (WM), 0.006 (GM), and 0.019 (CSF) after denoising. With noise reduction, the anomalous diffusion behaviors of the brain parenchyma were well described by the FO diffusion model (Fig. 2b). Figure 3 compares the maps of D, β and μ produced by the FO diffusion model before (first row of images) and after (second row of images) denoising, where the improvements afforded by noise reduction were visually evident. The improvements were also quantified in Table 1, where the standard deviations (STD) of D, β, and μ in three representative ROIs were substantially reduced after denoising. In addition, the mean values of all three parameters were consistent with the results in [5] where much longer scan time was used for signal averaging.

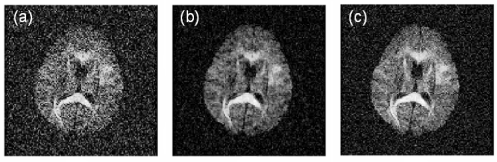

Fig. 1 Normalized DW images in the S/I direction at b = 3300s/mm^2. (a) NEX = 1 without denoising; (b) NEX = 1 with denoising; (c) NEX = 4 without denoising.

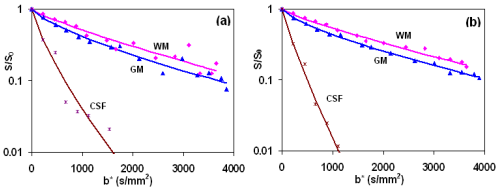

Fig. 2 Experimental diffusion signals and fitting curves vs. b^* in ROIs of three different tissues without (a) and with (b) denoising.

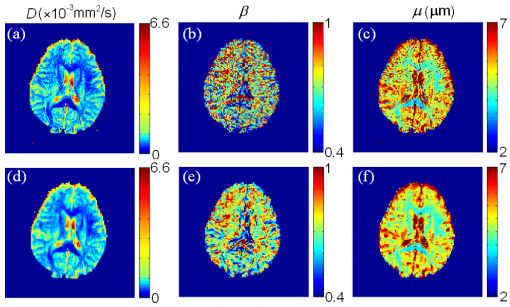

Fig. 3 Maps of D (×10^{-3}mm^2/s), β and μ (μm) obtained without (a, b, c) and with (d, e, f) denoising.

Table 1 Mean and STD of Diffusion Parameters in Three ROIs

Tissues	without denoising			with denoising		
	D (×10^{-3}mm^2/s)	β	μ (μm)	D (×10^{-3}mm^2/s)	β	μ (μm)
WM	0.39±0.09	0.70±0.08	4.11±0.20	0.44±0.03	0.61±0.03	4.18±0.07
GM	0.62±0.20	0.80±0.16	5.10±0.14	0.71±0.03	0.74±0.04	5.09±0.08
CSF	3.05±0.96	0.85±0.14	6.15±0.41	3.09±0.36	0.92±0.08	6.28±0.09

Discussion and Conclusions We have shown that noise is a major source of error in quantitative diffusion analyses with high *b*-values. The adverse effect of noise can be substantially reduced using a statistical image reconstruction technique where denoising can be accomplished with negligible loss of spatial resolution. With denoising, the accuracy of the diffusion parameters of an FO diffusion model has been considerably improved. The substantial increase in SNR without signal averaging opens the possibility of using the FO diffusion model with high *b*-values for patient studies.

References [1] Mulkern RV, et al., MNR Biomed 1999; 12:51-62. [2] Yabloskiy DA, et al., MRM 2003; 4:664-669. [3] Bennett KM, et al., MRM 2003; 50:727-734. [4] Ozarslan E, et al., JMR 2006; 183:315-323. [5] Magin RL, et al., JMR 2008; 190:255-270. [6] Zhou XJ, et al., ISMRM abstracts, p.38, 2008. [7] Haldar JP, et al., IEEE ISBI 2008; 752-755. [8] Gudbjartsson H, et al., MRM 2005; 34:910-914.