High Resolution Diffusion Imaging of the Brain Stem for Non-Gaussian Diffusion Analysis at High b-Values

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INTRODUCTION: A high b-value non-Gaussian diffusion model, known as the fractional calculus (FROC) model (1,2), has been proposed and demonstrated on healthy subjects and cancer patients (3–5). The model produces two new parameters β and μ, which are capable of revealing intravoxel tissue heterogeneity and microstructural information (2,3). Like all other diffusion models, the FROC model is susceptible to a number of adverse factors, including (a) partial volume effect arising from insufficient spatial resolution, (b) image distortion caused by magnetic susceptibility and other off-resonance effects, and (c) poor signal-to-noise ratio (SNR) particularly at high b-values and high spatial resolution. In a typical diffusion brain scan utilizing diffusion-weighted single shot EPI (DW-ssEPI), a full FOV is used even when only a small region is of interest (e.g., the brain stem). Additionally, magnitude images are typically averaged to increase the SNR in order to avoid phase inconsistencies between different acquisitions. A large FOV can lead to low spatial resolution and considerable image distortion (on the order of mm). The problems are particularly severe in the brain stem where the magnetic field is highly inhomogeneous and the need for high spatial resolution is pressing. While magnitude averaging can increase the SNR needed for higher spatial resolution, it produces a non-zero background, which biases the signal values and underestimates the diffusion parameters (6,7). To address these issues, we have developed an integrated high-resolution, multi b-value diffusion acquisition approach with reduced FOV and phase-sensitive signal averaging. Our technique relies on a uniquely designed 2D RF pulse to excite a limited spatial region while effectively suppressing lipid signals (8–10), together with a phase-sensitive image reconstruction method to allow complex signal averaging. Using this integrated approach, distortion-free brain stem diffusion images with an in-plane resolution of ~0.6×0.6 mm^2 were obtained and successfully fitted to the FROC model.

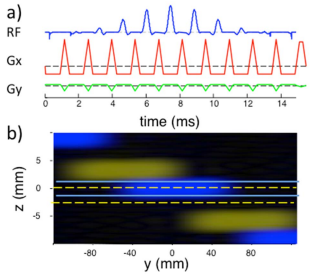

Fig. 1 (a) A 2D RF pulse for reduced FOV and (b) its simulated excitation profile of water (blue) and fat (yellow). The slice profiles for the subsequent refocusing pulse are shown as solid blue lines for water and dash yellow lines for fat.

METHODS: ***2D RF Design:*** The 2D RF excitation pulse (Fig. 1a) for reduced FOV was designed using tilted excitation by rotating the trajectory of excitation k-space. A fly-back echo planar gradient was adopted for robustness (11) with RF sub-pulses playing out only during odd gradient lobes. The duration between two consecutive sub-pulses was set at 1.4 ms so that the fat signal (yellow areas in Fig. 1b) was shifted outside the water profile (blue areas in Fig. 1b) and not refocused by the subsequent 180° pulse in a DW-ssEPI sequence (The blue solid lines and the yellow dash lines in Fig. 1b show the refocusing pulse slice profiles for water and fat, respectively.) In order to achieve a thin slice with a longer sub-pulse, the duration of the fly-back lobes was minimized by utilizing the maximal slew rate allowed by the Reilly's curve (12). Eleven sub-pulses with a time-bandwidth product (TBP) of 3.2 were modulated by an envelope pulse with a TBP of 3.3 and pulse length of 14.7 ms. ***Imaging Protocol:*** The pulse sequence was implemented on a 3T GE MR750 scanner. Two diffusion MR experiments were conducted using a 32-channel head coil (Nova Medical, Inc., Wilmington, MA). First, to demonstrate the high resolution capability, the brain stem of healthy volunteers was scanned with an in-plane resolution of 0.6×0.6 mm^2, FOV = 6×6 cm^2, 20 slices, slice thickness = 3 mm, b = 750 s/mm^2, TR/TE = 3100/87 ms, 3 orthogonal diffusion directions (NEX = 40) in a total scan time of 7 min. Second, a set of diffusion images from the brain stem was acquired using 10 b-values (50 - 4000 s/mm2) to evaluate the FROC model. The image acquisition parameters included: in-plane resolution = 1×1 mm^2 (to maintain an adequate SNR at the highest b-value), FOV = 7.2×7.2cm^2, NEX = 16, and total scan time = 27 min. ***Image Reconstruction:*** Prior to signal averaging, the low frequency phase variation in each acquisition was calculated and subtracted using the triangle window approach (13). The phase corrected complex images were then averaged. ***Model Fitting:*** The FROC model (Eq. 1) was used to fit over 10 b-values using both magnitude- and complex-averaged images for comparison. Parametric maps (D_0, β, and μ) were produced from the trace and 3-directional images separately.

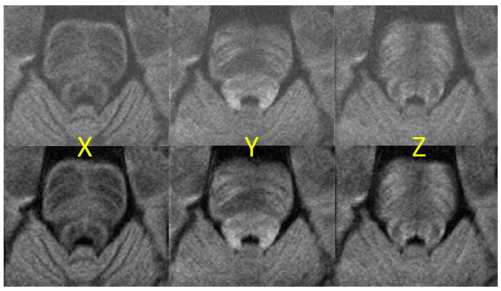

Fig. 2 A set of representative diffusion images from the brain stem (b = 750 s/mm^2, voxel size = 0.6×0.6×3.0 mm^3). The haze background in magnitude-averaged images (top) was eliminated in complex-averaged images (bottom).

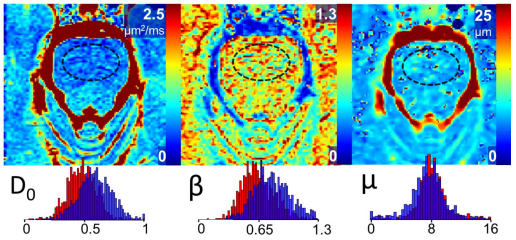

Fig. 3 D_0, β, and μ maps computed from complex-averaged trace images. Histograms were calculated over ROIs (black circles) from complex- (blue) and magnitude- (red) averaged images.

RESULTS: Fig. 2 shows a set of representative diffusion images of the brain stem with diffusion gradient along the three orthogonal directions. The increased spatial resolution and reduced image distortion allowed clear visualization of the structures in the pons. The haze background in magnitude-averaged images (top row) was eliminated in the complex-averaged images (bottom row). Fig. 3 displays D_0, β, and μ maps computed form complex-averaged trace images, together with the histograms (bottom of Fig. 3) over an ROI (black circle). The means of the histograms on complex (C) and magnitude (M) averaged images were: D_0 = 0.59±0.15 um^2/ms (C) and 0.48±0.13 um^2/ms (M); β = 0.80±0.23 (C) and 0.65±0.21 (M); μ = 7.7±1.2 um (C) and 8.2±0.8 um (M). D0, β, and μ were underestimated by 18.6%, 18.8%, and -6.5% respectively in the magnitude averaged images.

CONCLUSION: By combining a 2D RF excitation pulse with phase-corrected complex averaging, high-resolution, distortion free diffusion images from the brain stem have been achieved at b-values up to 4000 s/mm^2. This ability allowed us to successfully extend the FROC diffusion model to the brain stem, a challenging anatomic area which was not able to be reliably analyzed using high b-value non-Gaussian diffusion models. This study also demonstrates the potential for extending the applications of high b-value non-Gaussian diffusion models to other fine brain structures.

$$S = S_0 exp\left\{-D_0\mu^{2(\beta-1)}(\gamma G_d\delta)^{2\beta}\left[\Delta-(2\beta-1)\delta/(2\beta+1)\right]\right\}$$

Eq.1 D_0: diffusion coefficient, β: degree of tissue heterogeneity, and μ (in um): mean free length. G_d, δ, and Δ are diffusion gradient amplitude, duration and separation, respectively.

REFERECES: **1.** Magin et al., JMR, 2008. **2.** Zhou et al., MRM, 2010. **3.** Sui et al., ISMRM, 2012. **4.** Sui et al., ISMRM; 2012. **5.** Liu et al., ISMRM, 2013. **6.** Newbould et al., ISMRM, 2008. **7.** Dietrich et al., MRM, 2001. **8.** Finsterbusch, ISMRM, 2011. **9.** Banerjee et al., ISMRM; 2013. **10.** Saritas et al., MRM, 2008. **11.** Finsterbusch, JMRI, 2012. **12.** Reilly, MBEC, 1989. **13.** Pipe et al., MRM, 2002.