

# Noninvasively Diffusion Basis Spectrum Imaging (DBSI): A Phantom Study

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## Introduction:

Although diffusion tensor imaging (DTI) has been successfully applied to noninvasively evaluate white matter integrity, it is recognized that DTI fails to correctly track crossing fibers, or accurately evaluate axon integrity in the presence of CSF contamination or edema, i.e., isotropic component<sup>1,2</sup>. Various diffusion MRI methods (DSI, Q-ball imaging, etc) were proposed recently to resolve the primary orientation of crossing fibers requiring large number of diffusion weighted images with high b-values limiting their practical applications. Up to date, relatively few have attempted to quantify the diffusion property of the crossing fibers. It is our hypothesis that appropriate model selection would enable multi-tensor model to resolve crossing fibers as DSI and other high angular resolution and high b-value methods while only moderate b-value would be required. In this study, a novel multi-tensor approach, diffusion basis spectrum imaging (DBSI), was developed and applied to resolve crossing fibers in the presence of confounding

## Method:

**Phantom:** Two groups of phantoms were built using the fixed mouse trigeminal nerves. In the first group, 10 trigeminal nerves were organized into five pairs in parallel. Each pair were scanned and then embedded in gel for a repeated scan. In the second group, 14 trigeminal nerves are used. The first 8 nerves were directly scanned without gel embedding to obtain the control axon directional diffusivities. The other 6 nerves were divided into 3 pairs, and each pair of nerves were aligned in 32°, 58°, 91°, then embedded in gel.

**MRI:** Diffusion weighted spectroscopy was performed on the trigeminal nerve phantom on a Varian 4.7T Direct Drive console. 99 distinct diffusion-weighting gradients expanding 3D grids were employed:  $[G_x, G_y, G_z] = [0, 0, 0]$ ,  $[1, 0, 0]$ ,  $[0, 1, 0]$ ,  $[1, 0, 0]$ ,  $[0, 1, 1]$ ,  $[1, 0, 1]$ ,  $[1, 1, 0]$ ,  $[1, 1, 1]$ , ...  $[3, 0, 0]$ . Maximal diffusion weighting factor  $b = 3200$  (s/mm<sup>2</sup>). TR= 2s, TE=48.8ms,  $\Delta = 24$ ms,  $\delta = 8$ ms, NT=5. The total acquisition time was 16 minutes 40 seconds. Using the same TR and TE, a T2 weighted image (64\*64) was acquired.

For crossing fiber phantoms, a DSI scheme with 515 diffusion weighted images on a bigger 3D grids with max diffusion weighting factor  $b = 6000$ (s/mm<sup>2</sup>) was acquired within the same amount of scanning time: 16 minutes 40 seconds.

**DBSI:** DBSI employs multi-tensor model as described by equation [1]. Where,  $b_k$  is  $k^{th}$  diffusion gradient weighting factor;  $S_k$  is the measured diffusion weighted signal at direction  $b_k$ .  $N_{Aniso}$  is the number of anisotropic tensors;  $\theta_i$  is the angle between the diffusion gradient  $b_k$  and the primary direction of  $i^{th}$  anisotropic tensor;  $\lambda_{\parallel i}$  and  $\lambda_{\perp i}$  are the axial and radial diffusivity of  $i^{th}$  anisotropic tensor under the assumption of cylindrical symmetry;  $S_i$  and  $S_j$  are the T1/T2 weighted volume ratio of  $i^{th}$  anisotropic and  $j^{th}$  isotropic tensor respectively.  $N_{Iso}$  is the number of isotropic tensors;  $d_j$  is the diffusivity of  $j^{th}$  isotropic tensor.

For each measured MRI signal,  $N_{Aniso}$  were determined based on the optimized diffusion basis coefficients as described previously<sup>3</sup>. After  $N_{Aniso}$  was computed,  $N_{Iso}$  was determined using nonnegative least-squares (NNLS) analysis<sup>4</sup>. Direct pattern search<sup>5</sup> was employed to conduct the global nonlinear optimization on equation [1].

## Results and Discussion:

In the trigeminal nerve + gel, mimicking vasogenic edema, DBSI accurately identified single nerve population and recovered axial ( $\lambda_{\parallel}$ ) and radial ( $\lambda_{\perp}$ ) diffusivities reporting comparable values as nerve alone (Fig.1A). But DTI failed to recover fiber's directional diffusivity due to the partial volume effect from gel (Fig.1A). In addition, DBSI derived Gel% agreed with the Gel% by weight (Fig.1B) suggesting the potential of DBSI to quantify the extent of edema. For the crossing fiber phantoms, DBSI accurately identified two crossing nerve populations and detected the crossing fiber angle as 28° (bias 4°, 13% relative error), 55° (bias 3°, 5% relative error), 92° (bias 1°, 1% relative error) respectively (Fig.2). DBSI quantified mean fiber  $\lambda_{\parallel} = 1.14 \pm 0.06 \mu m^2/ms$ ,  $\lambda_{\perp} = 0.12 \pm 0.02 \mu m^2/ms$  in the crossing fiber with gel agreed with the single fiber  $\lambda_{\parallel} = 1.07 \pm 0.05 \mu m^2/ms$ ,  $\lambda_{\perp} = 0.14 \pm 0.02 \mu m^2/ms$ , without gel. The DBSI derived crossing fiber volume ratios were 0.94, 1.18, and 1.0 for 32°, 58°, and 91° phantoms respectively agreeing with T2 weighted MRI determined fiber ratios of 0.88, 1.04, and 1.02. The DSI studio<sup>6</sup> was used to analyze the DSI data acquired from the three crossing fibers applying DSI and general q-sampling imaging (GQI)<sup>7</sup> method (Fig.2). Both DSI and GQI derived orientation density function (ODF) correctly estimated two fibers crossing at 90°. For 58° phantom, both DSI and GQI derived ODF estimated the two fibers crossing at 13°. For the 32° fibers, DSI estimated the two fibers crossing at 13° while GQI did not resolve the crossing fibers. The preliminary findings of this study suggest that using low b-value DBSI has the potential to correctly determine the angle of crossing fibers as well as the diffusion properties of individual crossing fiber with gel, mimicking the presence of edema.

**References:**  
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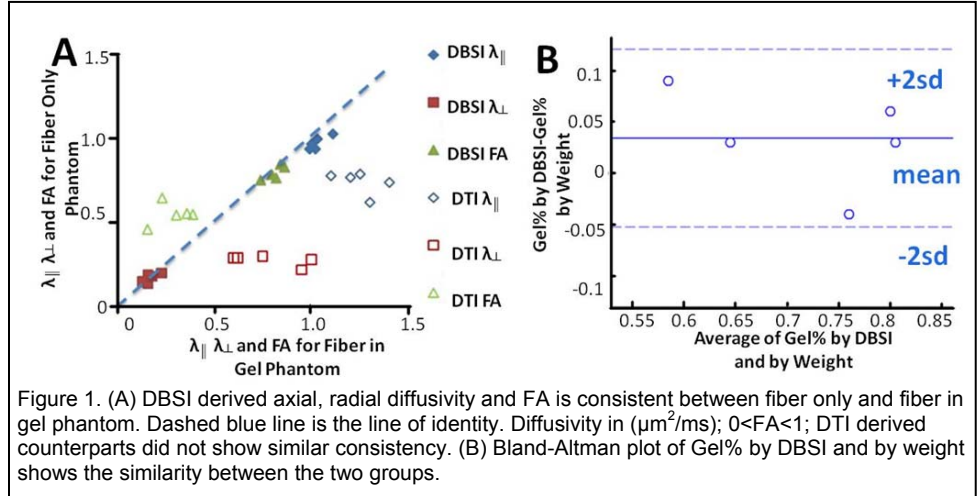


Figure 1. (A) DBSI derived axial, radial diffusivity and FA is consistent between fiber only and fiber in gel phantom. Dashed blue line is the line of identity. Diffusivity in ( $\mu m^2/ms$ );  $0 < FA < 1$ ; DTI derived counterparts did not show similar consistency. (B) Bland-Altman plot of Gel% by DBSI and by weight shows the similarity between the two groups.

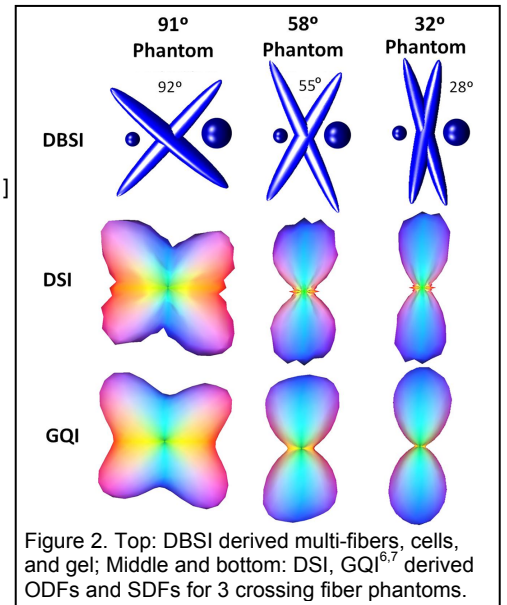


Figure 2. Top: DBSI derived multi-fibers, cells, and gel; Middle and bottom: DSI, GQI<sup>6,7</sup> derived ODFs and SDFs for 3 crossing fiber phantoms.