An Optimization Protocol for Generalized Diffusion Tensor Imaging with Higher Order Tensors

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INTRODUCTION: Resolving multiple fiber orientations within one imaging voxel is critical for accurate quantification of tissue microstructure and faithful reconstruction of the complex neural fiber pathways. It is recognized that the diffusion process in brain tissues is generally non-Gaussian. Recently there have been multiple methods developed specifically to account for this non-Gaussian property (1, 2, 3). However, many of these efforts have been largely focused on improving fiber tracking algorithms rather than providing a quantitative assessment of the deviation from Gaussian diffusion. Consequently, fast and quantitative assessment of this non-Gaussian property is critically needed. Developing quantitative measurement of non-Gaussian diffusion processes may provide powerful tools to assess changes in white matter that are due to axonal damage or degeneration. Generalized DTI (GDTI) with the use of higher order tensors (HOT) (4) provides one such method to identify, characterize and visualize underlying fiber structures. An optimal scan protocol required to estimate the forth order diffusion tensors is needed in order to maximize the efficiency and speed of the data acquisition. This was investigated for a phantom that models crossing white matter fibers and compared to *in vivo* scans. We identified the minimum number of b-values and gradient directions sufficient to estimate fourth order diffusion tensors.

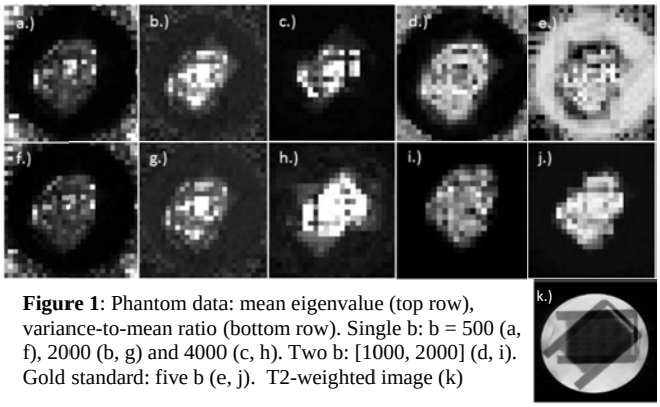

Figure 1: Phantom data: mean eigenvalue (top row), variance-to-mean ratio (bottom row). Single b: b = 500 (a, f), 2000 (b, g) and 4000 (c, h). Two b: [1000, 2000] (d, i). Gold standard: five b (e, j). T2-weighted image (k)

METHODS: The phantom consisted of sheets of parallel plastic capillaries with an inner diameter of 50μm and an outer diameter of 350μm (PTFE ultramicrobore tubing P-06417-70, Cole-Parmer Instrument, Vernon Hills, IL). Two sets of capillaries were overlapped at a 45° angle. Imaging was performed on a 3T MRI system with scan parameters; FOV = 25×25, TR = 1900ms, TE = 13.8ms, single slice, NEX = 4 (non-averaged), and matrix size = 32×32. Diffusion-weighted images were acquired with a stimulated echo for 160 diffusion encoding directions and for b-values of 500, 1000, 2000, 4000, and 8000s/mm^2. A healthy adult was also scanned on a 3T MRI system using an FOV = 256×256, TR = 10200 ms, and TE = 98.5ms for 73 slices. The diffusion-weighted images were acquired with a dual echo sequence for 30 diffusion encoding directions and b-values of 1000 and 2500s/mm^2.

The fourth order generalized diffusion tensors were calculated using a variety of set-up parameters for both the subject and phantom data. Tensors were calculated for single b-value, two b-value and five b-value set-ups. The large difference in the number of diffusion encoding directions between the phantom and subject data provided another basis for comparison. In each case, the calculated tensors were converted to a 9×9 matrix upon which eigenvalue decomposition could be applied. The fourth order tensor was then estimated by calculating the mean eigenvalue of the three largest eigenvalues produced by the decomposition. The variance-to-mean ratio was also calculated giving a second method for comparison.

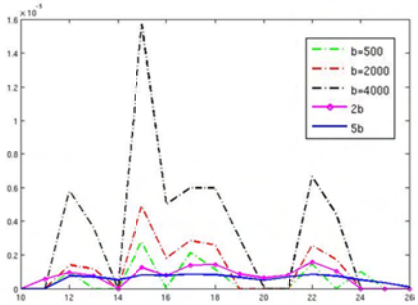

Figure 2: Line profile through row 16 of the phantom data in figure 1

RESULTS & DISCUSSION: The last column in Fig.1(e,j) provided a gold standard for comparison as the phantom data was acquired with five b-values and 160 diffusion direction and is not realistic for a *in vivo* scan. The single b-value phantom acquisitions (Fig. 1a, b, c, f, g, h) had widely fluctuating values as seen in the central line profile shown in Fig. 2 and had poor agreement. The two b-value calculation compared well with the gold standard, with a percent difference of 0.72% along that line.

We also found that a single b-value was not sufficient to generate a quality image *in vivo*. This was consistent with the results from the phantom data. The two b-value patient data shown in Fig. 3 (c,f) generated an excellent image with 30 diffusion directions compared to the 160 used for the phantom.

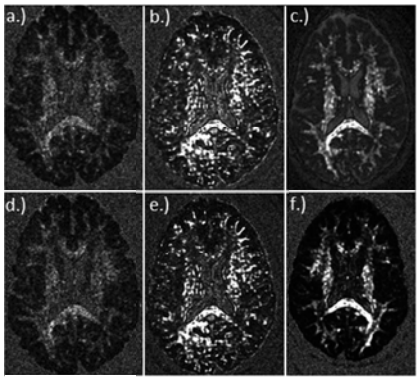

Figure 3: Patient data: mean eigenvalue (top row), variance-to-mean ratio (bottom row). Single b: b = 1000 (a,d), 2500 (b,e) Two b: [1000, 2500] (d,f).

CONCLUSION: A single b-value is not sufficient for the calculation of higher order diffusion tensors. Two b-values, however, give a significantly better image that, in the case of the phantom, had high agreement with the gold standard. We also found that two b-values with only 30 diffusion encoding directions will generate a quality fourth order diffusion tensor image *in vivo*.

ACKNOWLEDGMENTS: NIH R00EB007182.

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