Validation of Diffusion Tensor MRI in the Central Nervous System using Light Microscopy

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Introduction Diffusion tensor imaging is routinely used to characterize tissue microstructure noninvasively [1]. In an effort to validate the structural information from DTI on a microscopic level, we used multi-step registration scheme to correlate fiber geometry information from DTI with high magnification light microscopy in non-human primates.

Methods A fixed owl monkey brain was scanned on a Varian 9.4 Tesla, 21 cm bore magnet using a multi-slice, pulse gradient spin echo sequence (22 weighting directions, b = 0 and 1309 s/mm^2 , TE = 31.15 ms, TR = 17.1 s, 128 x 128 x 132 image volume matrix, .3 x .3 x .3 mm^3 voxels resolution). It was then frozen and sectioned on a microtome at 50 micron thickness in the coronal plane. The frozen tissue block was digitally photographed prior to cutting every third slice. Tissue sections were processed for myelin (Gallyas, 1979) and mounted for light microscopy analysis. A digital camera mounted on a microscope was used to take images of the stained sections at 0.5x, 1x, 2x, 4x, 10x, and 20x magnifications. One iteration of an anisotropic smoothing algorithm [3] was performed to improve SNR. Both the blockface and microscopy images were rescaled to match the in-plane DTI resolution. Registration was performed using rigid [4] and nonrigid registration with the Adaptive Bases Algorithm (ABA) [5] . First DTI images were transformed to the tissue block image space, and then the blockface images were transformed to the microscopy image space. Finally a set of in-plane registrations were performed in order to find the coordinates of the high-resolution micrographs (1x, 2x, 4x, 10x, 20x) within the low-magnification micrograph (0.5x) of the same section. The preservation of principal direction (PPD) reorientation strategy proposed by Alexander *et al* [6] was utilized to transfer the diffusion tensors into the high resolution microscopy image space in a way such that the principal direction of the tensors was preserved, and the tensors were overlaid on top of the high resolution micrographs. The registered tensors were diagonalized in-plane and the new eigenvectors were calculated in order to measure the in-plane tensor orientation. The spread of myelin stained fibers as well as their directionalities were measured using Fourier domain filtering [7] of the micrographs. Rose plots were used to visualize fiber orientation histograms which reveal the dominant orientation and coherence of stained fibers.

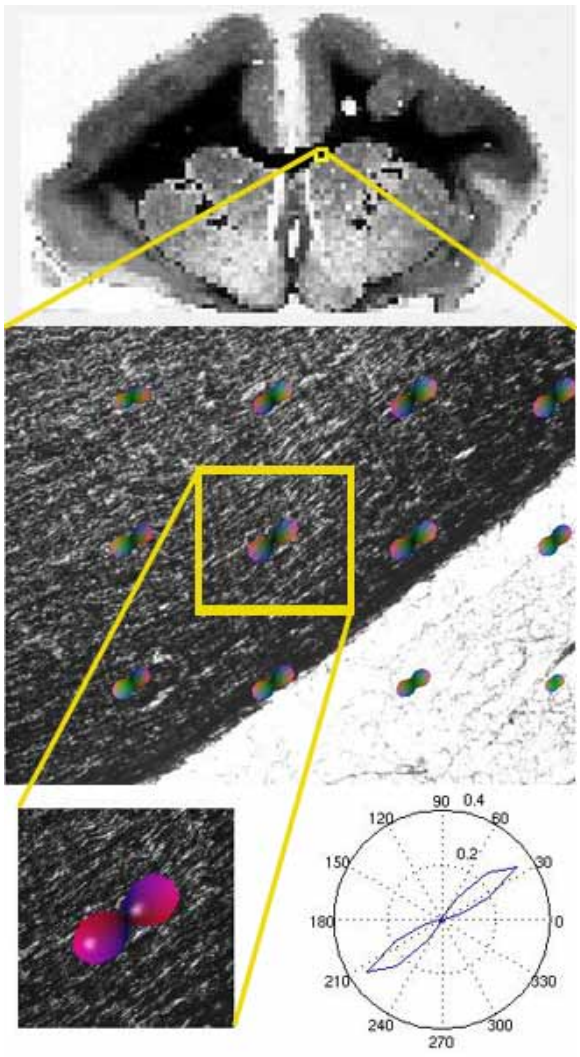

Figure 1. Fiber orientation comparison between DTI (lower left) and the orientations of myelinated fibers revealed in a high resolution micrograph (lower left & right).

Results The registration process correctly reoriented, translated, scaled, and corrected for global shearing. It also corrected for nonlinear shrinkage arising from the staining and mounting process. Overall alignment of the tensors with the myelin stained fibers was very good. A diffusion surface ("peanut") overlaid on a high resolution micrograph and the rose plot of the myelin stained fiber orientation distribution are shown in Figure 1. The principal eigenvector of the tensor is at 35.8 degrees to the horizontal axis, and the dominant fiber orientation in the micrograph is 36.3 degrees.

Conclusion In this study, fiber orientation information from DTI was validated on a microscopic level by direct comparison with light microscopy data. To the best of our knowledge, this is the first such study in the central nervous system. The overall agreement of the principal direction of tensors and that of myelin stained fibers was very good. The degree of anisotropy characterized by tensors also showed high correlation with the width of the Rose plot.

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References

[1] Basser, P.J. Biophys J, 1994. 66(1):p. 259-67.
[2] Sun, S.W. Magn Reson Med, 2005. 53(6): p. 1447-51.
[3] Ding, Z. Magn Reson Med, 2005. 53(2): p. 485-90.
[4] Maes, F. IEEE Trans Med Imaging, 1997. 16(2): p. 187-98.
[5] Rohde, G.K. IEEE Trans Med Imaging, 2003. 22(11): p. 1470-9.
[6] Alexander, D.C. IEEE Trans Med Imaging, 2001. 20(11): p. 1131-9.
[7] Rangayyan, R.M. 2004, CRC Press.