Comparative 3D Anatomy of the Prosimian Brain: DTI and Histological Studies

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INTRODUCTION - We have used computational models of white matter trajectories based on 3D DTI data to examine intact fixed brains of two rare primate species, the mouse lemur and the aye-aye (*Microcebus murinus* and *Daubentonia madagascariensis*). The 3D DTI data were acquired at approximately 70 µm isotropic resolution using an 11.7 T microimaging system. The 3D fiber tract trajectories were examined using streamtubes and streamsurfaces, a visual representation of linear and planar anisotropy [1]. After acquisition of the DTI, histology sections were prepared in the same brains and stained for white matter fibers. The histology was used to provide feedback about the fidelity of DTI-based models of fiber tracts.

METHODS AND RESULTS - A mouse lemur from a colony at Caltech was perfused and fixed using 4% paraformaldehyde. The aye-aye died of natural causes at the Duke University Primate Center and was immediately frozen at -80 ºC. Later it was thawed and the brain removed and fixed in 4% paraformaldehyde. Before imaging, brains were rinsed in PBS, immersed in Fluorinert (Sigma Inc.), and positioned in a 30 mm ID birdcage coil. Images were acquired using an 11.7 T, 89 mm vertical-bore, Bruker microimaging system. The 3D DTI data were built from three overlapping packets of 32 contiguous slices acquired using a PGSE protocol. Each slice packet was translated along the slice direction by one third of the slice thickness. Post-processing interleaved the slices for a final isotropic voxel size of approximately 70 µm. A total of 29 volumetric images were used in fitting the diffusion tensors. The diffusion gradients were applied along 7 different directions, and four values of b-matrix were used along each direction (maximum b≈2000 mm^2/s). Images were acquired with TR/TE=2000/19 ms and 512×256×96 image points. The tensors were fit using a laboratory-written non-linear fitting algorithm [2]. Streamtube representations were generated by creating integral curves in the vector field defined by the direction of fastest diffusion and choosing a representative subset within regions of significant linear diffusion. Points on each tube are colored according to linear anisotropy; redder regions have higher anisotropy. Similarly, points on each green surface have a color saturation that scales with planar anisotropy [1]. After imaging, histology was performed on the same brains by embedding in celloidin, serially sectioning at 40 µm using a sliding microtome, and staining with the Gallyas technique; digital micrographs of the sections were recorded. Exemplary DTI and visualization results are shown in Figures 1-2. Figure 1 shows three representative orthogonal slices taken from a 3D DTI dataset in the mouse lemur brain. The data were rendered in such a way that the diagonal elements of the effective diffusion tensor are displayed as a single composite image, where each color channel (red, green, blue) is assigned to a diagonal tensor element. Regions showing predominantly a single color represent fiber tracts with a high degree of coherence. Gray matter regions appear gray due to the diffusion isotropy in this material. Figure 2 shows a 3D model using a streamtubes and streamsurfaces of the major fiber tracts using the same DTI data shown in Figure 1.

DISCUSSION - The mouse lemur is one of the world's smallest primates (<90 grams total body weight). The total brain size is only slightly bigger (~25 %) than a mouse brain. From a DTI technology development perspective, these animal subjects are ideal. These brains easily fit into the bore of the microimaging system and have a substantially larger volume fraction of white matter compared to the rodent brain. The methods used to acquire the 3D DTI data using overlapping slices, followed by interpolation to give isotropic voxels, is a reasonably time efficient approach and yields artifact-free data. Data in these rare primates are important because they closely resemble the primitive primates living millions of years ago. Thus, they can provide unique insights into primate brain evolution, including the evolution of the human brain.

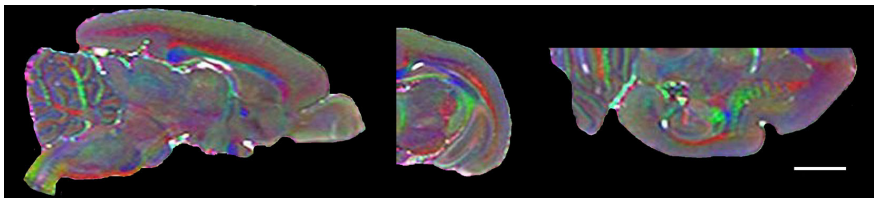

Figure 1. Sections of 3D DTI in the intact brain of the mouse lemur. Shown are hemi-segments of para-sagittal, coronal, and horizontal slices taken from the 3D volume. A composite RGB image was formed from the diagonal tensor elements, where red=rostral-caudal, green=dorsal-ventral, and blue=lateral. A dominant color in a region indicates the directionality of a track. Scale= 5 mm.

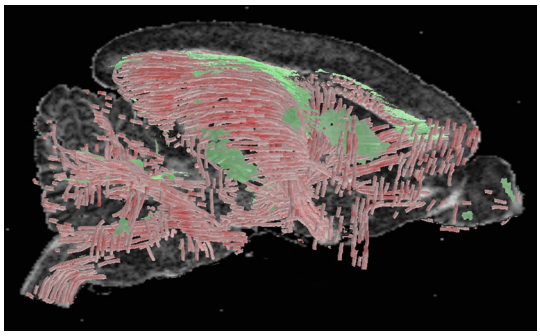

Figure 2. 3D model of major fiber tracts in the mouse lemur brain (para-sagittal view). Shown is one hemisegment from the same data as Fig. 1. Streamtubes, derived from the diffusion tensor, represent a sampling of pathways of linear anisotropic diffusion. The trajectories sweep along the principle eigenvector field and begin from seed points. The amount of diffusion anisotropy is rendered in red (i.e. red=strong anisotropy). Streamsurfaces (green) represent planar anisotropy. Several hundred representative streamtubes were chosen for display from ~10^5 that were calculated. For anatomical context, a single T_2-weighted grayscale slice from the 3D volume is shown.

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