Microstructure of the Marmoset Cerebral Cortex Observed using High Resolution Diffusion Weighted Imaging

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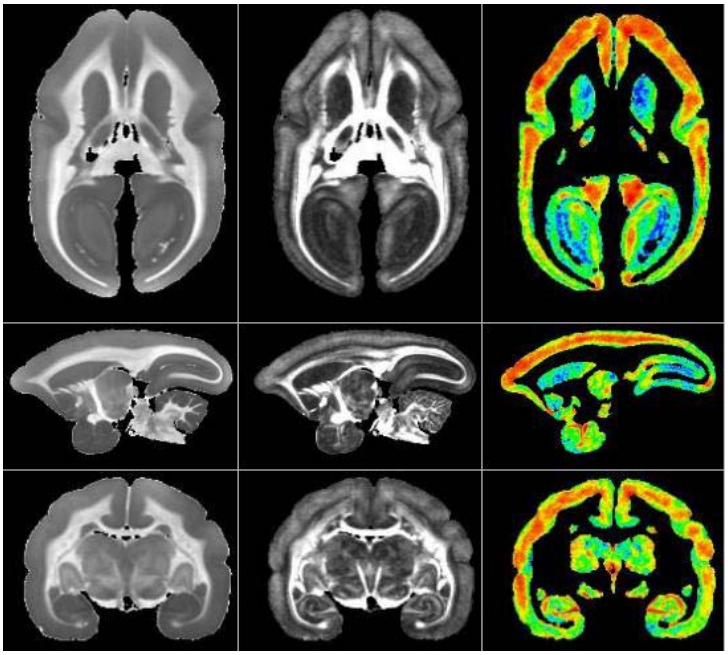
Introduction Diffusion-weighted MRI allows for the characterization of white matter microstructure based on the anisotropic diffusion profile in each voxel. Anisotropy is often taken as the basis for large-scale white matter connectivity in the form of tractography. By contrast, diffusion anisotropy in the cerebral cortex is small in magnitude and its basis is poorly understood. Several factors may contribute to the difficulties in evaluating cortical anisotropy. First, gray matter contains more cell bodies and fewer thick fiber bundles than the white matter, thus the diffusion is less restricted. Second, the diffusion profile in gray matter might be too complex for the popular tensor model to handle. Third, the density and orientation of fibers can differ among cortical layers, leading to partial volume effects in low resolution imaging. Fourth, measuring the low diffusion anisotropy requires particularly high SNR, which is incompatible with the small voxels needed to overcome the partial volume effects. The study described here attempts to overcome these difficulties by using ultra-high resolution diffusion-weighted imaging in the ex-vivo marmoset brain. The marmoset (Callithrix jacchus), like the human, is a primate. However, its much smaller brain size allows for the usage of a smaller RF coil for high SNR as well as a smaller FOV to achieve high spatial resolution. In the present study, these advantages were pushed to the extreme by using an ex-vivo fixed brain sample scanned at the high field strength of 7T. Q-ball diffusion imaging [1] and spherical harmonic decomposition of the diffusion orientation distribution function (dODF) is chosen over the simple tensor model to better model the diffusion profile. A ghosting-free, segmented, spin-echo EPI sequence running in 3D acquisition mode was used to deliver high SNR and high quality diffusion-weighted images.

Methods A formalin fixed brain of a healthy marmoset was placed in a plastic tube filled with Fomblin. It was scanned in a 40 mm diameter birdcage transmit-receive RF coil on a 7T Bruker Biospec scanner. A spin-echo, diffusion weighted, multi-segmented EPI sequence was used, in a phase-encoded 3D acquisition mode: TR=700 ms, TE=40 ms, 16 segments, matrix size 256 x 192 x 180, 150 μm isotropic voxel size. Even echoes were phase encoded the same as the odd ones and they are combined together in reconstruction to avoid EPI ghosting artifacts. Large b-value (4800 s/mm^2, δ/Δ = 6.4/16ms) images were collected for 126 directions on a single shell in the q-space. Six b=0 image were acquired which also served as T2-weighted images. The total scan time was about 75 hours.

The raw DWI volumes were preprocessed using TORTOISE (Pediatric Neuroimaging Diffusion Tensor MRI Center, NIH) to remove eddy-current-induced image misalignment. Using Camino Diffusion Toolkit [2], spherical harmonic decomposition was first carried out to reconstruct the dODF. Then peaks on dODF were searched and ranked according to their dODF magnitude in each voxel. We normalized the peak magnitude using the mean dODF magnitude in the same voxel. A gray matter mask was created based on the T2-weighted image and the FA map.



Results The three-dimensional orientation distribution function (i.e. the dODF) was obtained over the marmoset brain at 150 μm isotropic spatial resolution. Focusing on the cerebral cortex, we found that the summary statistics of the dODF, obtained using spherical harmonics, resulted in high quality parameter maps. For example, characterizing the magnitude of the largest peak revealed significant areal specificity, as shown in the accompanying figure. The peak magnitude was highest in the prefrontal cortex and lowest in the ventral temporal cortex. The left column in the figure shows the inverted T2-weighted images in axial, sagittal, and coronal sections. The middle and right columns show the dODF magnitude at the dominating peak, normalized by the voxel mean. In this peak search analysis, about 46% gray matter voxels were characterized by a single diffusion peak, 41% voxels by double peaks, and 12% voxels by triple peaks. Additional parameter maps, or "stains", were obtained using other methods to characterize the dODF distribution.

Discussion The long-term goal of this research is to develop methods to parcellate the gray matter based upon the diffusion properties of different cerebral cortical areas. The cortex contains both radial and tangential fibers, which are apparent in the raw 3D orientation distribution functions. The cortex is also a laminated structure, with different layers containing a different combination of radial and tangential components. Our results highlight the fact that combining high spatial and angular resolution in diffusion imaging can reveal marked patterning in the cerebral cortex. Lower resolution images would be hampered by partial volume effects, whereas simple tensor models are unable to capture multiple diffusion peaks, as are observed due to combined radial and tangential diffusion. It is important to point out that while the multi-dimensional dODF is inherently rich in information, it is a challenge to fully utilize all the information in a concise and easy-to-understand format. Present research in the laboratory is investigating other means by which to summarize the dODF into different parameter maps, or "stains".

Reference: [1] Tuch DS, MRM 52:1358-1372, 2004. [2] Cook PA, et. al., ISMRM Proceedings, p.2759, 2006.