Cortical profile of mean kurtosis and fractional anisotropy with high resolution DKI and DTI of macaque brains

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Target Audience: MR physicists and radiologists

Purpose:

The primate cerebral cortex is characterized with complicated cytoarchitecture including neurons, glial cells, dendrites and small axons. It is difficult to delineate these complicated cellular components with only diffusion tensor imaging (DTI). Diffusion kurtosis imaging (DKI) [1], measuring non-Gaussian diffusion, has the potential to delineate the cortical microstructural complexity and provide complementary microstructural information to DTI since there are a significant amount of diffusion barriers in the cerebral cortex [1-3]. Integrating cortical MK and FA map from high resolution DKI and DTI could offer a refreshing insight into the cellular microstructure noninvasively across the cerebral cortex. In this study, we aimed to reveal the MK and FA profile across different cortical areas and explore the relationship of cortical MK and cortical FA with high resolution DKI and DTI of macaque brains.

Methods:

<u>High resolution DTI and DKI acquisition</u>: 3 normal rhesus macaque brains were fixed with perfusion fixation. During DKI, they were put into a custom-made plastic tube containing Fomblin. Diffusion MRI (dMRI) was acquired with a 3T Philips Achieva MR system using an 8 channel knee coil. Diffusion imaging parameters were: FOV=130x130x74mm, in-plane imaging matrix/resolution=148x150 / 0.76x0.75mm, slice thickness=2mm, single-shot EPI with SENSE parallel imaging scheme (R=2), TR/TE=2100/84ms, two b-values=1500, 4500 s/mm^2, 30 diffusion-encoded orientations [4], NSA=32. Total acquisition time was 18 hours. *<u>Diffusion tensor and kurtosis fitting</u>*: Tensor fitting was conducted with dMRI of b 1500s/mm^2 by using DTIstudio. With dMRI of two b values (b=1500, 4500 s/mm^2), kurtosis was fitted with in-house Matlab code using constrained linear least square fitting. *<u>Cortical mapping of MK and FA values:</u>* A median-sized macaque brain was used as a template. Cortical MK and FA of all macaque brains were obtained after segmentation with dual-channel FAST in FSL (fsl.fmrib.ox.ac.uk) using contrasts of both FA and averaged diffusion weighted image (aDWI). Cortical FA and MK maps of all macaque brains were transferred to the template with affine and large deformation diffeomorphic metric mapping (LDDMM) [5] transformations and then averaged in the template space. All transformations were conducted with Diffeomap (mristudio.org). The cortical surface of the template brain was rendered with Amira software (FEI). At a given cortical vertex, the mapped averaged cortical MK and FA values were the ones closest to this cortical vertex. *<u>Relationship of cortical MK and cortical FA:</u>* These 3 macaque brains were part of the 10 brains used for establishing comprehensive macaque brain atlas. This digital macaque brain atlas in coronal slices is shown in Fig. 1, including the comprehensive labeling of all major cortical gyri. In the template space, the cortical labeling of atlas was applied to obtain the lobe-level cortical MK and FA of each macaque brain. A linear regression model was applied to test if there is a significant interaction effect of lobe-level cortical FA on lobe-level cortical MK.

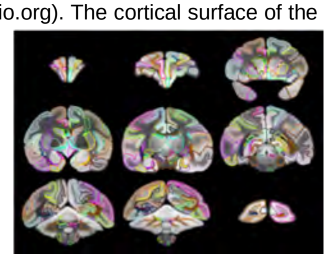
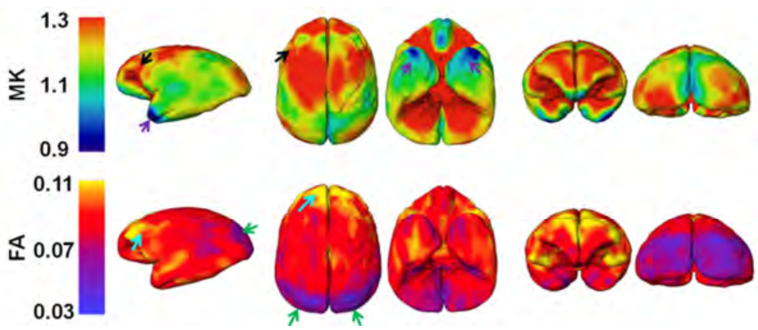


Figure 1: Macaque brain atlas labeling overlaid on the template aDWI. Top left to bottom right is from anterior to posterior.

Results

Fig. 2 shows the heterogeneous averaged MK and FA maps on the cortical surface of the template brain. Lower MK can be clearly observed in the temporal cortex (pointed by purple arrows) with high MK observed in the frontal cortex (pointed by black arrows). MK is also higher in occipital cortex. For cortical FA map, lower cortical FA at occipital areas (pointed by green arrows) and higher cortical FA at prefrontal areas (pointed by cyan arrows) are prominent. Fig. 3 shows the relationship of cortical MK and cortical FA at the lobe level. It can be observed that in many cortical regions, high FA values correspond to high MK values with $p<0.05$ from linear regression test; however, the distribution of the measurement points is quite spread and not clustered around a major linear line.



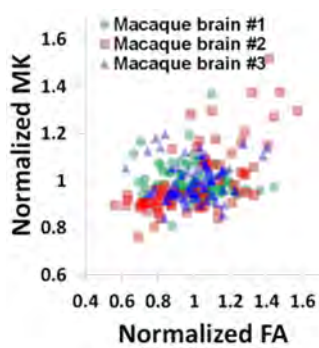


Figure 2 (left): Averaged cortical MK and FA values mapped onto the template macaque brain cortical surface from lateral, superior, inferior, anterior and posterior view from left to right. Color bars encode varying MK and FA values.

Figure 3 (right): Relationship of normalized cortical MK and normalized cortical FA at lobe level. Each point represents normalized MK and FA of a lobe from a specific macaque brain.

Discussion and conclusion:

To our knowledge, we have delineated, for the first time, cortical MK and FA profile of macaque brains using the high resolution DKI and DTI. With the small cortical thickness of macaque brains, sub-millimeter high resolution (0.76x0.75mm^2) DKI data was required to reveal the cortical microstructures. Heterogeneous cortical MK distribution indicates heterogeneous cortical microstructures, including various neuronal density, glial cell density, dendritic density and extracellular matrices across the cortical surface. We also revealed relationship of cortical MK and cortical FA, suggesting that complementary microstructural information not detected with FA may be provided by cortical MK. For example, the prefrontal cortical MK and the occipital cortical MK are both high, implying similar level of diffusion barriers in both cortical areas; however, the prefrontal cortical FA values are higher than occipital cortical FA values, implying more organized microstructure in the prefrontal cortex compared to the occipital cortex. It is noteworthy that the cortical FA or MK variability across different macaque brains is small. Despite that, more samples will be added in this study to increase the statistical power. Further investigations on underlying neuroanatomy of the cortical MK and FA based on histology and contributions of cortical MK and FA to estimating neuroanatomical parameters such as dendritic density are underway.

References: [1]. Jensen JH, et al. (2005) Magn Reson Med 53:1432-1440. [2]. Jensen JH and Helpern JA (2010) NMR Biomed 23:698-710. [3]. Wu EX and Cheung MM (2010) NMR Biomed 23:836-848. [4]. Jones DK, et al. (1999) Magn Reson Med 42:515-525. [5] Miller MI, et al. (2002) Annu Rev Biomed Eng 4: 375. **Acknowledgement:** This study is sponsored by NIH MH092535 and NIH EB009545.