Cortical Depth Dependence of the Diffusion Anisotropy in the Human Cortical Gray Matter in vivo

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Introduction: While diffusion tensor imaging (DTI) has primarily been used to assess white matter (WM) microstructure, its application for the investigation of diffusion anisotropy in cortical gray matter (GM) may provide valuable biomarkers for the diagnosis of various neurological disorders. To date, however, such studies have mostly been performed in fixed tissue, in animals, or at ultra-high field strength (7T), because the current DTI methodology based on single-shot echo-planar imaging (EPI) is inherently limited by a low spatial resolution, low signal-to-noise ratio (SNR), and high vulnerability to geometric distortions.

The goal of the present study is to investigate the cortical depth dependence of diffusion anisotropy in cortical GM in the human brain in vivo on a clinical (3T) scanner. To this end, we use a novel multi-shot constant-density spiral DTI technique with inherent correction of motion-induced phase errors to achieve a high resolution, SNR, and spatial fidelity, without requiring a variable-density spiral trajectory or a navigator echo, and hence an excessively long scan time.

Methods: Healthy volunteers were studied on a 3T MR750 GE scanner with a 32-channel head coil. T_1-weighted anatomical images were acquired with a 3D inversion-prepared spoiled gradient-echo sequence and a 1 mm isotropic voxel size. Multi-shot spiral DTI data were acquired with a single spin-echo, 6-shot, constant-density spiral sequence and TR = 2 s, TE = 51 ms, FOV = 16 cm, matrix = 256×256, in-plane resolution = 0.625×0.625 mm, slice thickness = 5 mm, 6 axial slices, *b*-factor = 800 s/mm^2, 7 *b*=0 images + 60 diffusion directions, and NEX = 1.

In multi-shot DTI, subject motion causes phase errors among different shots, leading to signal loss and aliasing artifacts. Such phase errors were inherently estimated from the central k-space data of each shot by using a sensitivity encoding (SENSE) reconstruction algorithm[1] and subsequently corrected by using an iterative conjugate gradient algorithm[2]. Blurring artifacts due to susceptibility effects and eddy currents were also corrected with a dynamic off-resonance correction method[3]. The DTI images were then registered to the anatomical images with FLIRT[4] before derivation of the diffusion tensor.

A cortical GM mask was segmented from the anatomical images with FreeSurfer[5] and divided into 11 surfaces evenly spaced along the cortical depth from the pial surface to the GM/WM interface. Three additional surfaces extending into cerebrospinal fluid or WM were generated beyond each of these two interfaces. Cortical profiles of the fractional anisotropy (FA) were computed by averaging the FA within each surface. To account for regional heterogeneity across the brain, separate profiles were computed in different cortical regions. Furthermore, to minimize partial volume effects along the slice direction, the analysis was restricted to voxels for which the normal vector to the GM/WM interface (also generated from the anatomical images with FreeSurfer) remained within ±20° of the axial plane.

Results and Discussion: The DTI data obtained with the proposed multi-shot spiral DTI technique benefit from a high resolution, SNR, and spatial fidelity (**Fig. 1**), revealing a high level of anatomical detail typically not seen in low-resolution DTI data acquired in vivo at 3T with single-shot EPI.

In particular, the FA map shows a clear diffusion anisotropy in cortical GM (**Fig. 2**), with a band of low FA in the deep cortical layers adjacent to the GM/WM interface, most prominently along the sulci (arrows) but not the gyri (stars). Such a low-FA band has also been observed in the human brain ex vivo[6] and the cat brain in vivo[7], and is thought to reflect a lower microstructural coherence in layer VI, which, unlike other cortical layers, contains pyramidal cells oriented both parallel and perpendicular to the cortical surface[6].

Furthermore, the color-coded principal eigenvector map clearly shows that the diffusion anisotropy in cortical GM has a different orientation than that of adjacent WM (**Fig. 3**), primarily along the sulci (arrows) but not the gyri where the WM tracts continue straight into GM (stars), which has also been observed in the human brain ex vivo at 3T[6] and in vivo at 7T[8].

Finally, cortical profiles of the FA in three representative regions (#1–3 in Fig. 2) clearly show that the FA is consistently higher in the middle cortical layers and lower in the superficial and deep cortical layers (**Fig. 4**). More systematic studies performed with a higher resolution and SNR are currently underway to further investigate the observed variability across different cortical regions.

Conclusion: The proposed multi-shot constant-density spiral DTI technique with inherent correction of motion-induced phase errors can achieve a high resolution, SNR, and spatial fidelity, thereby revealing a clear cortical depth dependence of diffusion anisotropy in cortical GM in the human brain in vivo at 3T, which may find broad applications in basic and clinical neurosciences.

References: 1. Pruessmann KP et al. MRM 2001;46:638–51. 2. Liu C et al. MRM 2005;54:1412–22. 3. Truong TK et al. NeuroImage 2011;57:1343–47. 4. www.fmrib.ox.ac.uk/fsl 5. surfer.nmr.mgh.harvard.edu 6. Miller KL et al. NeuroImage 2011;57:167–81. 7. Ronen I et al. MRM 2005;54:317–23. 8. Heidemann RM et al. MRM 2010;64:9–14.

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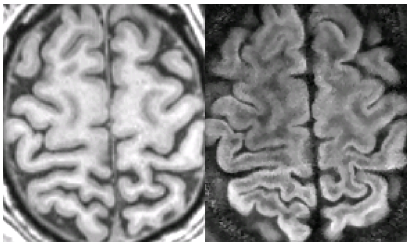

Fig. 1: Anatomical and DTI images.

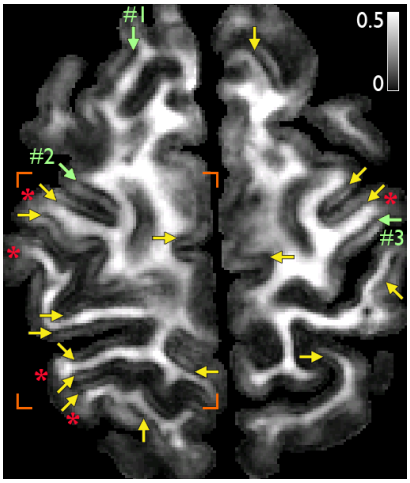

Fig. 2: FA map.

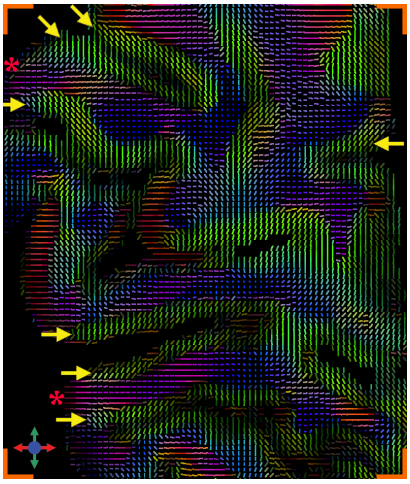

Fig. 3: Principal eigenvector map.

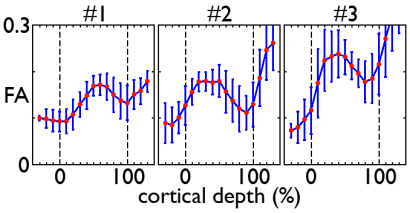

Fig. 4: FA (mean ± SD) vs. cortical depth.