Surface Based Analysis of Diffusion Orientation for Identifying Architectonic Domains in the In Vivo Human Cortex

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Introduction. Interrogating microstructure of the *in vivo* human cortex is a long-sought-after goal due to its relevance to brain function, development, aging and disease. The human cortex is characterized not only by distinct laminae of cell bodies but also by the orientation and density of axons extending from these cell bodies. Several groups have recently presented evidence of coherent cortical diffusion anisotropy patterns in the human cortex, mainly radial to the cortical surface[1,2]. A recent study also found patterns of tangential orientations that seem to be associated with primary somatosensory cortex (S1)[2]. The convoluted nature of the cortex makes it difficult to quantify the orientation of detected diffusion directions relative to the local laminar orientation using a standard DTI representation. Hence we developed a surface-based analysis that provides an accurate estimate of the cortical surface normal vector and characterizes the principal diffusion eigenvectors from 1 mm isotropic diffusion measurements relative to this surface normal. We also investigate DTI changes as a function of cortical depth, local surface curvature and partial volume effects. We find that much of the cortical region studied is predominately radial in orientation, but replicate the previous finding that S1 cortex is strongly tangential. Also, cortical regions related to somatosensory cortex, such as S2 and primary auditory cortex share S1's tangential orientation. The ability to obtain high quality 1mm isotropic data and parcellate folded cortex by diffusion metrics provides new possibilities for studying brain organization as it relates to function in the healthy and diseased brain.

Methods. Data were acquired from 5 healthy subjects scanned after Institutional Review and informed consent on a 3T Siemens Tim Trio using a 32ch receive coil. Each acquisition consisted of an 1 mm isotropic MEMPRAGE(TI/TR/TE1/TE2/TE3/TE4/α=1200/2510/1.6/3.5/5.4/7.2ms/13°, 2x GRAPPA, T_{acq} = 6min and 2D single-shot 1mm isotropic resolution DW-SE-EPI (TR/TE= 6360/100ms, matrix size = 218 x 218, iPAT =3, partial Fourier = 6/8, 34 slices, BW = 1146 Hz/px, 2 averages of 256 directions at b=1000 s/mm$_2$, and 50 b=0 images interspersed every 10 volumes. Total diffusion acquisition was 1hr. Slices were prescribed coronally for 3 subjects and axially for 2 subjects. In all subjects the slices covered the primary motor and somatosensory cortices. Surface reconstructions of the inner and outer boundaries of cortical gray matter (GM) were generated by FREESURFER[3] from the MEMPRAGE, and a family of intermediate surfaces evenly spaced throughout the cortical depth were computed. The DTI were co-registered using to correct for motion, and fit to a tensor using FSL[4]. The b=0 diffusion data was aligned to the surfaces with a boundary-based registration method[5]. A radiality index (1=radial, 0=tangential) (Fig.1) was calculated from the dot product of the surface normal vector and the principal eigenvector of the diffusion tensor. Masks of gyri, sulci and banks were created by curvature thresholding. A GM/WM/CSF partial volume map was generated and used to exclude contamination from WM or CSF.

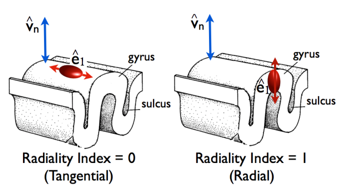

Fig. 1: The radiality index is computed as the magnitude of the dot product of the vector normal to the cortical surface ($\hat{v}_n$) and the principal eigenvector ($\hat{e}_1$) of the measured diffusion tensor.

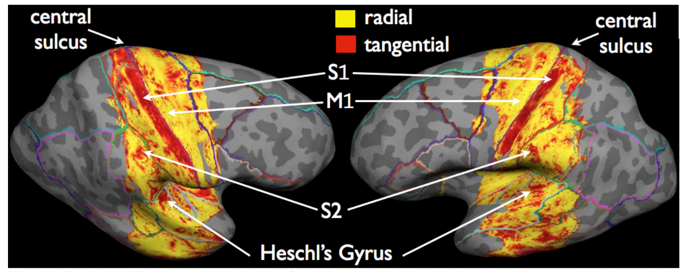

Fig. 2: Cortical diffusion radiality index for left and right hemisphere's of one subject overlaid on an inflated brain surface. Also overlaid is FREESURFER's automatic parcellation. The sharp division between the highly tangential primary somatosensory cortex (S1) and the highly radial primary motor cortex (M1) corresponds with FREESURFER's automatic parcellation's delineation of the central sulcus. The heavily myelinated Heschl's gyrus also appears tangential as does the secondary somatosensory cortex (S2).

Results. Figure 2 provides compelling evidence of spatial homogeneity of cortical radiality across the cortical surface. Regions exhibiting coherently low radiality (i.e. tangential organization) appear in several clusters including S1, S2 and Heschl's gyrus. The agreement between the tangentially organized regions and the freesurfer parcellation suggests a close relationship between the local cortical fibre orientation and large-scale anatomical features such as the folding pattern. Figure 3 shows the 3 subjects with coronal slices. The spatial pattern of the radiality index is apparent in all subjects but more pronounced in subjects 2 and 3 than in subject 1. To investigate the pattern of radiality across multiple cortical depths we performed a laminar analysis of radiality relative to curvature (Fig. 4). Even though only voxels containing 100% GM were included in this analysis we still see a strong effect of cortical depth on the incidence of tangentially dominated voxels. The histograms in Fig.4b demonstrate a difference of the proportion of radially and tangentially dominated voxels between the sulci, gyri and banks of the cortical folding pattern, particularly near the WM surface---despite that this analysis excluded voxels that were identified to contain non-GM compartments.

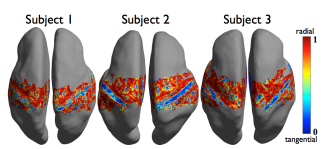

Fig. 3: **a)**: Cortical diffusion radiality indices for the middle cortical depth plotted on inflated brain surfaces for 3 subjects show that the strongly tangential S1 region is consistently identified.

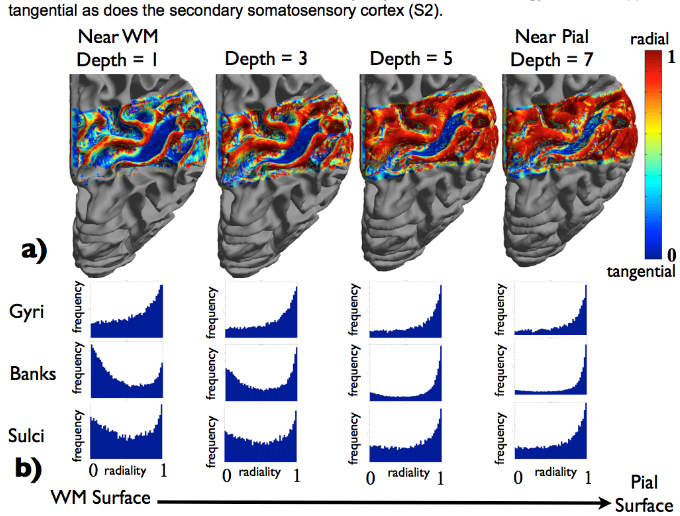

Fig. 4: **a)**: Cortical diffusion radiality indices at four different cortical depths, incrementing left-to-right from just above the WM surface towards the pial surface. **b)** Laminar and curvature analysis indicate that a significant proportion of the fibres at the GM/WM boundary of the banks and sulci tend to be orientated tangentially (i.e. parallel to the cortical surface) whereas the gyri appear predominantly radial throughout the different depths. Histograms represent all cortical regions encompassed by our data.

Discussion Surface-based analysis is well-suited to analyzing cortical diffusion data because it provides a frame of reference to the intrinsic laminar framework of the cortex as well as cortical thickness and partial volume estimates which could be potential confounds if unaccounted for in the interpretation of such data. Radiality maps depend on both accurate diffusion estimates and surface rendering. Small isotropic voxels and low distortion are essential characteristics of the diffusion acquisition and excellent GM/WM contrast in the MEMPRAGE is critical to obtaining accurate surfaces. By limiting the brain coverage of our diffusion acquisition we were able to significantly reduce our TR and therefore acquire sufficient averages to support the low SNR associated with the 1 mm isotropic voxels. GRAPPA 3x was also critical to mitigating distortions. Our results confirm earlier findings of tangential orientation in S1. We also find additional cortical areas (S2 and A1) that appear to be dominated by tangentially oriented fibres.

References: [1] McNab JA. et. al. NI 46:775-785 (2009). [2]Heidemann RM. et. al. *MRM* 64:9-14 (2010). [2] Anwander A. et. al. ISMRM 2010. [3]. Dale, A.M. et. al. NI 9:179-194 (1999). [4] FMRIB Software Library, www.fmrib.ox.ac.uk/fsl. [5] Greve & Fischl *NI* 48:63-72 (2009). **Acknowledgements** Funding from Canadian Institute of Health Research, NIH NCRR P41 RR14075 and NIBIB R01EB006847. Many thanks for assistance and helpful discussions with Dr. Christina Triantyfllou and Thomas Witzel.