Comparison of *In Vivo* Human, *In Vivo* Macaque and *Ex Vivo* Human Measurements of Diffusion Orientation in the Cerebral Cortex

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INTRODUCTION. Recently, we characterized *in vivo* human cerebral cortical diffusion anisotropy in the cortical reference frame using a surface-based, laminar analysis[1]. Cortical diffusion anisotropy was detected reliably *in vivo* with both radial and tangential orientation nrelative to the cortical surface. Much of the cortex appeared radial in orientation, but S1, S2 and A1 were tangential. Unfortunately, the sensory cortices are thinner (e.g.~2mm in S1 compared to ~5mm in M1) and are therefore more prone to partial volumes of the underlying white matter (WM). In an attempt to limit partial volume contamination we analyze 1mm isotropic human data and higher spatial resolution diffusion data in *in vivo* macaque (0.7 mm iso) and in an *ex vivo* human tissue specimen (0.5 mm iso).

METHODS. ***In vivo* human data** consisted of 6 healthy adults scanned on a 3T Siemens Tim Trio using a 32ch receive coil. Each acquisition consisted of a 1 mm iso 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 iso DW-SE-EPI (TR/TE=6360/100ms, matrix = 218 x 218, R=3, partial Fourier = 6/8, 34 coronal slices, BW = 1146 Hz/px, 2 avgs. of 256 directions at b=1000 s/mm^2, and 50 b=0 images, T_{acq}=1hr. Surface reconstructions of the inner and outer boundaries of cortical gray matter (GM) were generated by FreeSurfer[2,3] using the MEMPRAGE. A family of intermediate surfaces evenly spaced throughout the cortical depth were computed. The DTI were co-registered 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 was calculated from the dot product of the surface normal vector and the principal eigenvector of the diffusion tensor.

***In vivo* macaque data** were acquired on 1 male, 4 year old, anesthetized Macaca mulatta on a 3T Siemens Tim Trio using an insert head gradient (AC88, 80mT/m, slew rate = 400T/m/s) and a custom-built, surgically implanted 8-channel head receive coil[6]. The acquisition was 0.6 mm iso MPRAGE (TI/TR/TE= 900/2100/36.5 ms, α=9°, Tacq = 9min.) and 2D single-shot 0.7mm iso DW-SE-EPI (TR/TE= 6960/77ms, matrix size = 148 ×148, R=3, partial Fourier = 6/8, 61 axial slices, BW = 1408 Hz/px, 5 avgs. of 256 directions at b=1000 s/mm^2, and 50 b=0 images, Tacq=3 hrs.) Macaque cortical surface reconstructions required a higher number of iterations and a careful selection of the stopping threshold for the bias correction, manual definition of the brain center and radius for skull stripping and manual definition of the pons, corpus callosum as well as many control points throughout the WM for tissue segmentation.

***Ex vivo* human data** were acquired on a left hemisphere of a 79 yr old male with no history of disease. For surface reconstruction, FLASH (TR=20ms, TE=1.8ms-15.92ms, flip angle = 5:5:30°, 1mm iso)[7] data were acquired on the whole hemisphere using a 1.5T Siemens. Prior to FreeSurfer analysis, the embedding fluid was masked using methods described in Fischl 2004[7]. The hemisphere was then sectioned and 0.5 iso diffusion data were acquired on a sample containing M1 and S1 with a 4.7T Bruker Biospec Avance system equipped with 400 mT/m gradients using 3D DW-SE (TR/TE =350/25 ms , matrix size = 128 x 112 x 88, 20 directions at b = 4500 s/mm^2, 2 b=0, Tacq.= 20 hrs.

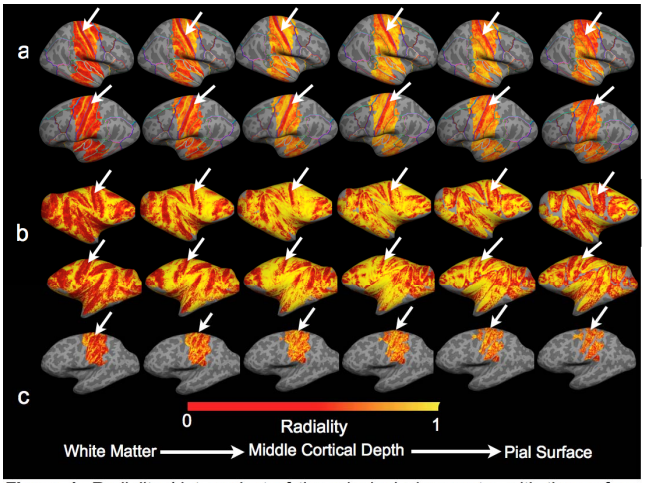

Figure 1: Radiality (dot product of the principal eigenvector with the surface normal) overlaid on inflated surfaces for a) *in vivo* human data (N=6), b) *in vivo* macaque (N=1) and c) *ex vivo* human tissue (N=1). Left to right increases in cortical depth from the WM to the pial surface. White arrows point to S1.

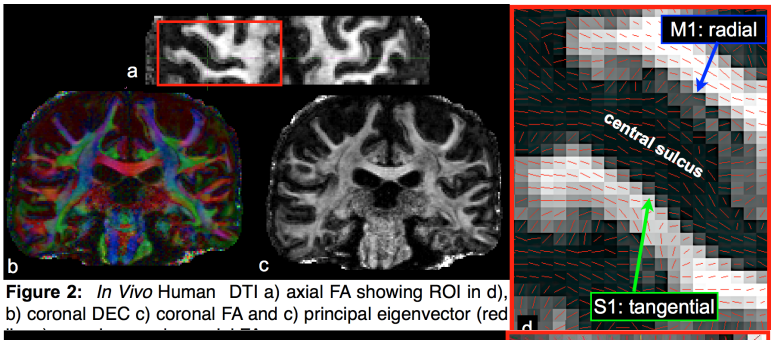

Figure 2: *In Vivo* Human DTI a) axial FA showing ROI in d), b) coronal DEC c) coronal FA and c) principal eigenvector (red

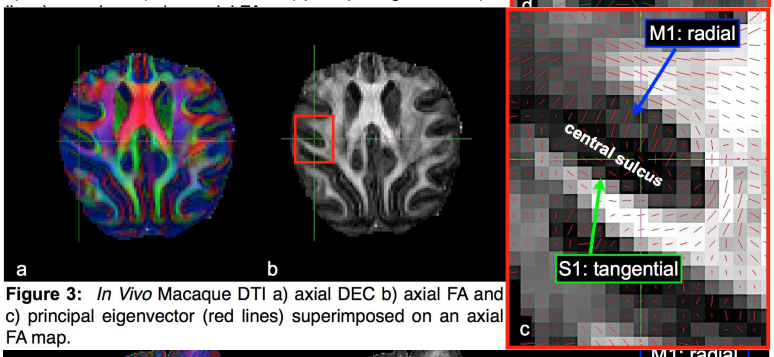

Figure 3: *In Vivo* Macaque DTI a) axial DEC b) axial FA and c) principal eigenvector (red lines) superimposed on an axial FA map.

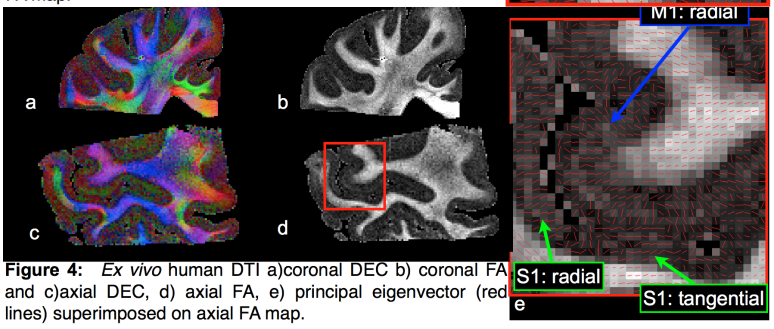

Figure 4: *Ex vivo* human DTI a)coronal DEC b) coronal FA and c)axial DEC, d) axial FA, e) principal eigenvector (red lines) superimposed on axial FA map.

RESULTS AND DISCUSSION. The cortical diffusion observed in the *in vivo* monkey corresponds closely with the *in vivo* human observations at 1mm isotropic (i.e. radial M1/tangential S1). Interestingly, *ex vivo* human data exhibits some regions of S1 with tangential diffusion and some regions of S1 with radial diffusion. While the source of the observed cortical diffusion remains unclear, the close agreement between data acquired in different species, *in vivo* and *ex vivo* and using different acquisition protocols demonstrates that the radial and tangential diffusion patterns are highly robust. **References:** [1] McNab JA. et. al. ISMRM 2011 [2] Dale, A.M. et. al. NI 9:179-194 (1999). [3] Fischl et. al. NI 9:195-207 (1999). [4] FMRIB Software Library, www.fmrib.ox.ac.uk/fsl [5] Greve & Fischl *NI* 48:63-72 (2009). [6]Janssens T. et. al. ISMRM 2012. [7] Fischl B. et. al. 2004. **Acknowledgements** Funding provided by the Canadian Institute of Health Research, NIH Blueprint for Neuroscience Research Grant: U01MH093765, NIH NCRR P41RR14075 and NIBIB R01EB006847.