A Comparison of *In Vivo* and *Ex Vivo* Diffusion Tensor Imaging in the Same Patient

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Introduction There exist few methods by which one can study the structure of human brain white matter. Most histological tract tracing depends on active-transport mechanisms that are unsuitable for human studies and laborious classical dissections are subjective and often limited to a single tract per specimen. *In vivo* DTI is an exciting non-invasive alternative but *ex vivo* DTI is also increasingly gaining recognition. The long scan times permitted and the absence of motion allows visualisation of more intricate fibre structures. Unfortunately, *ex vivo* tissue suffers decreased diffusion rates, mandating higher b-values and decreased T_2 and proton density, which reduces SNR. These properties have restricted DTI of fixed tissues to research scanners with high main field strengths and powerful gradients. In this study, we present a method for high-resolution 3D DTI in whole, human, fixed brain on a clinical scanner. Whereas previous post-mortem studies have focused on animal brains or small sections of human tissue, we present the highest resolution, whole human brain DTI yet reported. Using a rare case study that includes *in vivo* and *ex vivo* DTI in the same patient, we directly compare *in vivo* and *ex vivo* anisotropy patterns, illustrating the visualisation of additional structure in the high resolution post-mortem images.

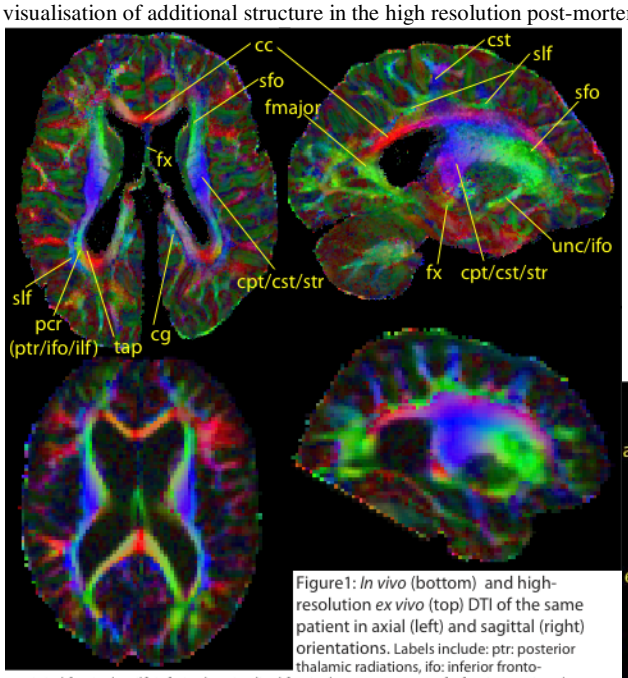

Figure1: *In vivo* (bottom) and high-resolution *ex vivo* (top) DTI of the same patient in axial (left) and sagittal (right) orientations. Labels include: ptr: posterior thalamic radiations, ifo: inferior fronto-occipital fasciculus, ilf: inferior longitudinal fasciculus, tap: tapetum, fx: fornix, cg: cingulum, cpt: coritcopintine tract, cst: corticospinal tract, str: superior thalamic radiation, sfo: superior fronto-occipital fasciculus, cc: corpus callosum, fmajor: forceps major, slf: superior longitudinal fasciculus, unc: uncinate fasciculus, pcr: posterior corona radiata.

Methods *In vivo* imaging of a 62 year old man was performed using 2D single-shot DW-SE-EPI on a Siemens 1.5T scanner with 3×60 directions at b = 1000 s/mm^2 and 9 $\times$ b = 0, TE/TR = 89/141 ms, BW = 1860 Hz/pixel, matrix = $128 \times 104 \times 64$, partial Fourier = 6/8, voxel size = 8 mm^3. The patient died of natural causes 2 years after the *in vivo* acquisitions. The brain was extracted from the cranium 24 hours post-mortem and soaked in a 10% neutral buffered formalin for 6 weeks then immersed in a proton-free fluid called Fomblin LC/8 (Solvay Solexis Inc.) for imaging. Post-mortem imaging was performed on a Siemens 3T using 3D segmented DW-SE-EPI, 5×64 directions at b = 3000 s/mm^2 and $27 \times$ b = 0, TE/TR = 114/670 ms, BW = 820 Hz/pixel, 32 lines per EPI segment, matrix = $254 \times 254 \times 192$, partial Fourier = 5/8, voxel size = 0.73 mm $\times$ 0.73 mm $\times$ 0.73 mm = 0.39 mm^3 for a total acquisition time of 99 hours 11 minutes. Averages were co-registered using FLIRT[8] to correct for B_0 drift and eddy-current distortions before combining the data and fitting to a tensor.

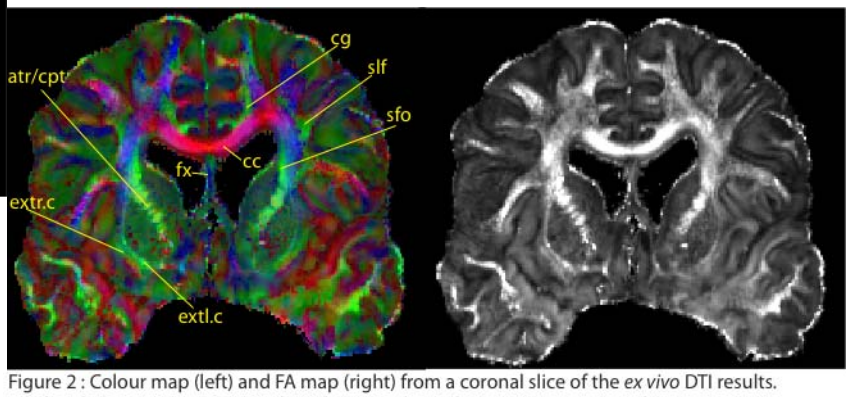

Figure 2 : Colour map (left) and FA map (right) from a coronal slice of the *ex vivo* DTI results. Labels include: extr.c: extreme capsule, extl.c: external capsule, atr: anterior corona radiata, cpt: corticopontine tract, fx: fornix, cc: corpus callosum, cg: cingulum, slf: superior longitudinal fasciculus, sfo: superior fronto-occipital fasciculus.

Results At the genu of the corpus callosum the principal eigenvalue was an order of magnitude less *ex vivo* compared to *in vivo* (1.7×10^{-4} mm^2/s vs. 1.6×10^{-3} mm^2/s), in agreement with previously reported values[1]. *Ex vivo* fractional anisotropy (FA) was also slightly lower, (0.5 vs. 0.7) but this could be indicative of the reduced rates of diffusion rather than alterations in tissue structure. Figure 1 shows matched axial and sagittal slices of *in vivo* and *ex vivo* DTI. Similar anisotropy patterns are observed in both, but the 0.39 mm^3 resolution of the *ex vivo* data provides a visibly sharper delineation of major white matter tracts, particularly at the posterior horn of the lateral ventricles where the superior longitudinal fasciculus, posterior corona radiata and tapetum are more easily distinguished. Even the external and extreme capsules can be resolved *ex vivo*, as can the striatal cell bridges connecting the caudate and putamen (Fig. 2). Whereas gray matter (GM) anisotropy is seldom observed in *in vivo* acquisitions, the principal eigenvector of the post-mortem data displays a strong coherence in cortical GM, oriented perpendicular to the adjacent white matter and following the sulcal folds (Fig. 3). This may indicate that it is the radial cortical fibres which dominate the measured anisotropy at this resolution. The *ex vivo* FA maps (Fig. 2 and 3) also show a band of very low anisotropy at the white-gray matter interface which has been observed previously[1] but is not well understood.

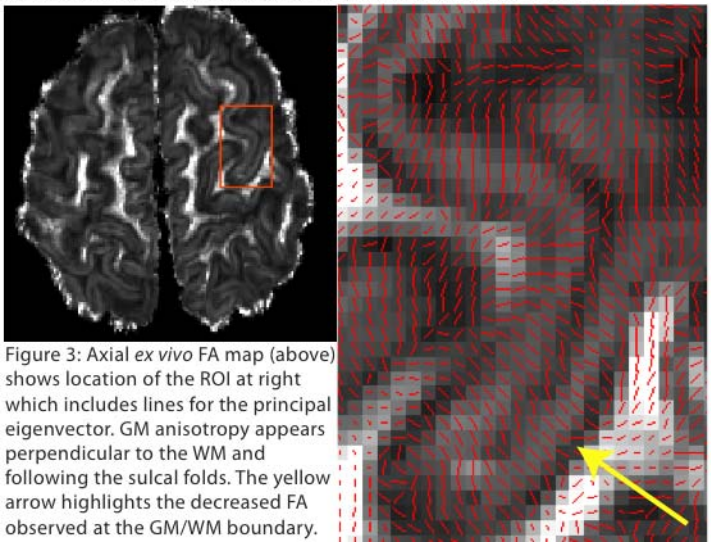

Figure 3: Axial *ex vivo* FA map (above) shows location of the ROI at right which includes lines for the principal eigenvector. GM anisotropy appears perpendicular to the WM and following the sulcal folds. The yellow arrow highlights the decreased FA observed at the GM/WM boundary.

Discussion Since the results of animal studies are not directly transferable to human anatomy, it is important to extend the benefits of post-mortem DTI to human brain samples. We have shown that high-resolution, whole, fixed human brain DTI is achieveable on a clinical scanner. Further, the enhanced detail which can be gleaned from the high resolution DTI strongly supports efforts to improve *in vivo* diffusion scanning through both hardware and ingenious pulse sequence development.

Acknowledgments and References Funding provided by the Charles Wolfson Charitable Trust. The authors would like to thank Dr. Steven Chance for his assistance preparing the specimen for imaging. (1) D'Arceuil HE .et. al. NeuroImage 36:64-68 (2007). (2) Guilfoyle DN et. al. NMR in Biomed. 16:77-81 (2003) (3) Sun SW et. al. MRM 53:1447-1451 (2005).