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 laborsome 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 T₂ and proton density, which reduces SNR. These properties have restricted DTI of fixed tissues to research scanners with high magnetic 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.

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/mm² and 9 × b = 0, TE/TR = 89/141 ms, BW = 1860 Hz/pixel, matrix = 128 × 104 × 64, partial Fourier = 6/8, voxel size = 8 mm³. 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/mm² and 27 × b = 0, TE/TR = 114/670 ms, BW = 820 Hz/pixel, 32 lines per EPI segment, matrix = 254 × 254 × 192, partial Fourier = 5/8, voxel size = 0.73 mm × 0.73 mm × 0.73 mm = 0.39 mm³ for a total acquisition time of 99 hours 11 minutes. Averages were co-registered using FLIRT to correct for B₀ drift and eddy-current distortions before combining the data and fitting to a tensor.

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 ×10⁻³ mm²/s vs. 1.6 × 10⁻⁵ mm²/s), in agreement with previously reported values. 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 mm³ 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).

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 achievable 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).