Temporal behavior of diffusion tensor properties in ex vivo human brain hemispheres

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Introduction: Histopathologic verification of in vivo diffusion tensor imaging (DTI) findings can potentially be accomplished by comparing the results of postmortem DTI with histologic data from human brain specimens. This approach minimizes neuronal changes between the time of the MRI scan and the time of histology in a cost efficient manner (as opposed to longitudinal antemortem MRI). However, data acquired with postmortem DTI may be contaminated by postmortem changes in the tissue's MR properties. In this work, human brain hemispheres immersed in formaldehyde were imaged with DTI over time, in order to investigate changes in diffusion tensor properties through time postmortem. Based on previous studies involving mouse brains [1], we anticipated an immediate decrease in diffusivity after death. Based on the same previous report, we expected fractional anisotropy (FA) to remain approximately unchanged immediately after death. However, given the large size of human brain hemispheres and the relatively long time it takes for deep portions of the tissue to become completely fixed [2], we also anticipated partial decomposition of unfixed regions in the days and weeks following death, resulting in reduction of FA.

Methods: Four hemispheres were placed in formaldehyde solution and were imaged with DTI, twice within 48 hours postmortem and approximately once per week thereafter, until one month postmortem. One brain donor had also undergone MRI one year prior to death, so antemortem DTI data were available for this subject. All postmortem imaging was conducted at room temperature using the same clinical 3T Philips Achieva MRI scanner (Best, Netherlands) using the following scan parameters: resolution = 1.8 × 1.8 × 2.0 mm^3, TE = 53 ms, TR = 35.5 s, b = 0, 1000, 2000, 3000, 4000, 5000, 6000 s/mm^2, 15 diffusion directions, scan time = 55 min. All diffusion-weighted volumes from a given hemisphere were registered to the same T_2-weighted volume. Mean diffusivity (MD) and fractional anisotropy (FA) were calculated for each imaging session and the changes in these quantities over time were observed.

Results: For the hemisphere that had been imaged both antemortem and postmortem, voxelwise comparison showed 92% reduction in white matter MD and 78% reduction in gray matter MD just 22 hours after death (the time of the first postmortem scan) compared to 1 year antemortem (Fig. 1, top left). There was little correlation between antemortem and postmortem MD values. Conversely, FA values were not substantially altered in the first 22 hours after death (Fig. 1, right). Antemortem and postmortem FA values gathered from all brain voxels were highly correlated ($r = 0.78$, $p = 10^{-12}$, Fig. 1, bottom left). Following the first postmortem scan of each hemisphere, FA in the major white matter tracts decreased by approximately 30% over a timespan of 1 week (Fig. 2). Over the next 3 to 4 weeks, FA measurements stabilized somewhat and remained lower than the initial postmortem FA (Fig. 2). The noise of the FA measurements increased in the later scan sessions (noise measurements not shown). Results were similar for all four hemispheres.

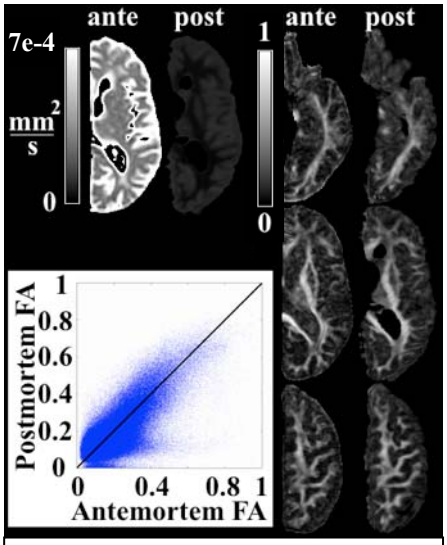

Figure 1. Comparison of ante-mortem and postmortem (22 hours after death) MD and FA values from a single subject.

Discussion: As expected, MD values were reduced by more than 78% in both white and gray matter in the first postmortem DTI session (22 hours postmortem) compared to the antemortem values (1 year antemortem). This is almost double the MD decrease than can be explained by the temperature difference between these two scan sessions alone (37˚ C in vivo versus 21˚ C ex vivo only accounts for 43% reduction in MD). FA values, however, did not undergo large changes in the first 22 hours after death, though there was subsequent reduction of FA in the white matter tracts in the first week postmortem, likely due to partial tissue decomposition. In addition to this FA reduction, T_2 values are also known to decrease by 50% or more within the first two to four weeks postmortem [2], and with this decrease in T_2 comes a reduction in the available SNR for the DTI sequence. Based on these considerations, we conclude that postmortem DTI should be conducted as soon as possible after death, preferably within 24 hours, in order to obtain FA values that are most similar to those that would have been measured in vivo just before death and are most likely to be related to histological data. In future work, we will use the diffusion data gleaned from this study to more accurately model the fixation process in whole human brain hemispheres.

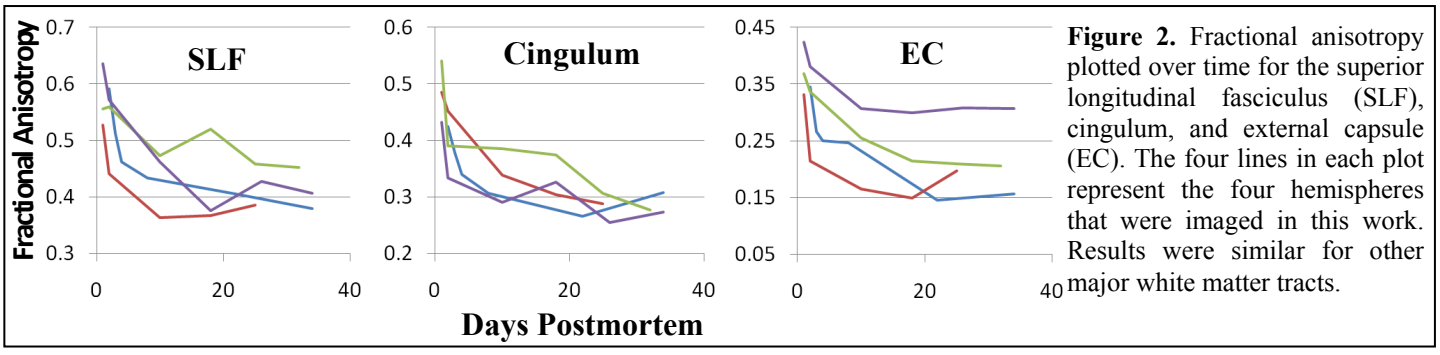

Figure 2. Fractional anisotropy plotted over time for the superior longitudinal fasciculus (SLF), cingulum, and external capsule (EC). The four lines in each plot represent the four hemispheres that were imaged in this work. Results were similar for other major white matter tracts.

References: [1] D'Arceuil H, de Crespigny A. NeuroImage 2007;36:64-68. [2] Dawe RJ, et al. Magn Reson Med 2009;61:810-818.