Correlation of Fractional Anisotropy with Histology for Diffuse Axonal Injury in a Rat Model

Z. Kou[1,2], Y. Shen[1], N. ZAKARIA[3], S. Kallak[3], J. Cavanaugh[3], Y. Yu[1], J. Hu[1], and E. M. Haacke[1,2]

[1]Radiology, MR Research Facility, Wayne State University, Detroit, MI, United States, [2]MRI Institute for Biomedical Research, Detroit, MI, United States, [3]Biomedical Engineering, Wayne State University, Detroit, MI, United States

Introduction: Traumatic brain injury (TBI) is a leading cause of death and disability that affect young people in the prime of their lives. Diffuse axonal injury (DAI) is a significant pathology of TBI and is very difficult to identify using conventional neuroimaging techniques. DAI is characterized by initial swollen axons that eventually disconnect and form axonal retraction balls (RB) in white matter tracts. Diffusion Tensor Imaging (DTI), specifically fractional anisotropy (FA), has been reported as being a sensitive means to detect axonal injuries in human TBI subjects [1-3]. However, a number of pathologies may account for a decrease in FA as well, thus making FA a non-specific marker for specific DAI pathology. To date, few results have been presented correlating DTI with histological validations. The objective of this study was to investigate axonal injury pathology by using DTI in MR with histological validation in an experimental TBI rat model.

Materials and Methods: DAI was induced in six male Sprague Dawley rats utilizing the Marmarou impact acceleration model [4,5]. DTI images were acquired *ex vivo* 6-7h post injury using a Bruker 4.7Tesla scanner. At this time, perfusion fixed brain tissue was harvested. A body coil was used as the radio frequency signal transmitter and a surface coil as the receiver. The diffusion tensor images were acquired with a 3D spin echo DTI sequence with TR= 850ms, TE=24ms, b=0 and 1200 mm/s^2, direction number=6, FOV=26x26x20mm^3, acquisition matrix=128x80x32, NA=1, and a total imaging time of 4h 14m. After imaging, the brain specimens were processed with silver staining and beta-amyloid antibody precursor protein (beta-APP) immunostain was used to validate the pathology. The numbers of retraction balls on the histology images were quantified via IMAGEJ software (http://rsb.info.nih.gov/ij). The retraction ball quantification was then compared to the DTI measurements in order to determine if any correlation existed between DAI and DTI index changes.

Results: Prominent βAPP stained RB were observed in the corpus callosum (cc), cingulum (cg), optic chiasm (OX), and other brainstem regions as well. In all animals, the optic chiasm consistently has RBs. No significant cytotoxic or vasogenic edema was found. A region of interest analysis in the OX demonstrated a negative linear correlation between the number of RBs and FA decrease (R^2=0.9816) as well as axial diffusivity (λ_0) (R^2=0.5526) (Figure 1). No change of radial diffusivities or mean apparent diffusion coefficient (ADC) was found. Figure 2 presents the RBs in red dots in the OX, and Figure 3 shows its corresponding anatomical location on a DTI FA map with OX shown by the red boundary.

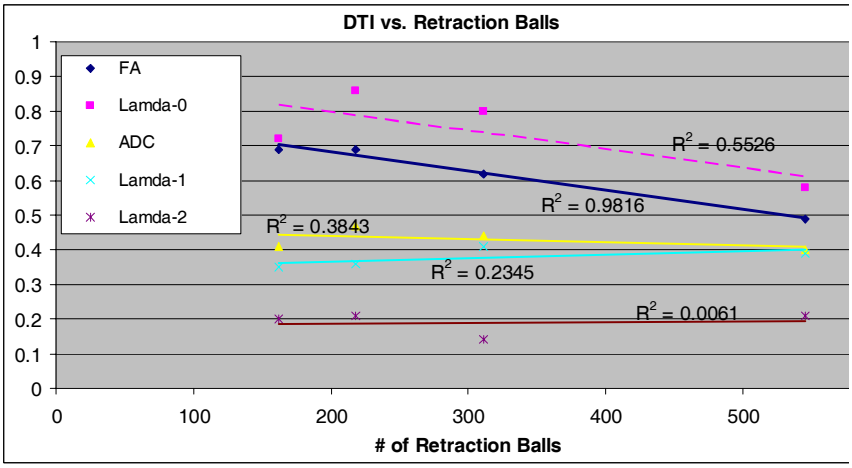

Figure 1. Correlation between the number of axonal retraction balls and DTI Measurements.

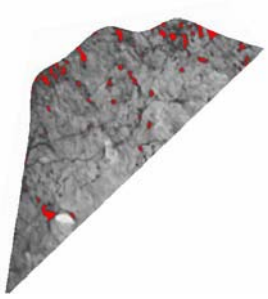

Figure 2. Histology confirmation of axonal retraction balls (red).

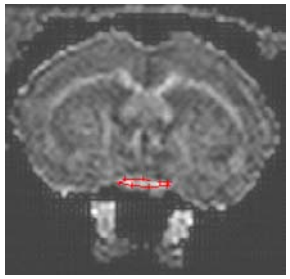

Figure 3. DTI FA map (OX is in red).

Discussion: Our work represents the first reported data regarding the direct correlation between DTI and histologic findings in traumatic brain injury in an animal model. Many injury pathologies could induce the decrease of FA, including, but not limited to, the disruption of axons, the impaired axonal plasmatic transport, the increase of axonal membrane permeability, and the enlargement of extracellular space caused by a change in the blood brain barrier, etc. In our data, the linear correlation between FA and the number of RBs as well as the decease of main directional diffusivity suggest that axonal disruption, and possibly the impaired cytoplasmatic transport, are the major reasons of FA decrease. Furthermore, the fact that no change of mean ADC or radial diffusivity occurs suggests that neither the increased permeability of the axonal membrane nor the enlargement of the extracellular space in vasogenic edema causes the FA change. This has been confirmed by histology on the rats in the same study with very limited extent of edema.

Conclusions: DTI may effectively characterize the pathology of diffuse axonal injury. Axonal disruption appears to be the major pathology of the optical chiasm 6-7h post injury in a weight-impact rat model. A larger sample size and the study of more brain regions are warranted in future investigations.

References:

1. M. Inglese et al., Journal of Neurosurgery 103:298-303. 2005.
2. K. Arfanakis et al., American Journal of Neuroradiology, vol. 23, pp. 794-802, 2002.
3. R. Benson et al., Journal of Neurotrauma, 2006, to appear.
4. A. Marmarou et. al, Journal of Neurosurgy 80: 291-300, 1994.
5. F. Abd-Elfattah et. al, Journal of Neurosurgery 80:301-313, 1994.