Title: Insights of Contemporary Diffusion MRI Modeling Techniques in Mild Traumatic Brain Injury: A TRACK-TBI Study

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Introduction

The majority of traumatic brain injuries are categorized as mild (mTBI), and in up to 82% of cases, neuroimaging is ordered, with only ~9% of studies revealing intracranial pathology. Novel advanced neuroimaging techniques such as diffusion-weighted magnetic resonance imaging (DWI) are sensitive to subtle white matter changes following injury, but the natural history of these changes in recovery have yet to be fully defined. Inconsistencies in observed patterns of change with the common modeling technique diffusion tensor imaging (DTI) may be due to limitations of the model, and in this study, we explore novel modeling techniques that take advantage of high angular resolution multishell data collected during the TRACK-TBI study at UCSF.

Methods

DWI data at b-values of 1300 mm/s^2 and 3000 mm/s^2 from two-weeks and six-months post-injury were analyzed with MRtrix3's constrained spherical deconvolution and fixel-based analysis. Post-Hoc comparisons were conducted on white matter tracts constructed with TractSeg a deep learning algorithm trained on human connectome project data. Tract average metrics computed with DTI, diffusion kurtosis imaging (DKI), and neurite orientation dispersion and density imaging (NODDI) for projection fibers, long association fibers and commissural fibers were compared with fixel-based analysis metrics. The analysis scheme is summarized in Figure 1.

Results

Significant differences in all fixed-based metrics observed at the two-week timepoint remained at the six-month timepoint Figure 2. Differences between mTBI and control means decreased between timepoints, but a greater number of significant fixels were present for fiber density (FD), fiber cross-section (FC), and fiber density cross-section (FDC) at the six-month timepoint. There were no significant differences in any change images. Initially, a decrease in FD drove differences, whereas, at later time points, there was a greater contribution of decreased FC as well.

Conclusion

Fixel-based analysis revealed damage to white matter that was observed at two-weeks post mTBI remained at six-months post injury. This would suggest there is a difference in the time course of biological recovery and resolution of symptoms that should be the target of future study and interventions. Fixel-based analysis and NODDI metrics demonstrated similarities in sensitivity to white matter change, and there were no differences observed for the DTI metric FA. This adds further evidence it should not be used as the sole modeling technique when studying mTBI.

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Figure 1. Graphical Representation of Fixel-Based Analysis Pipeline

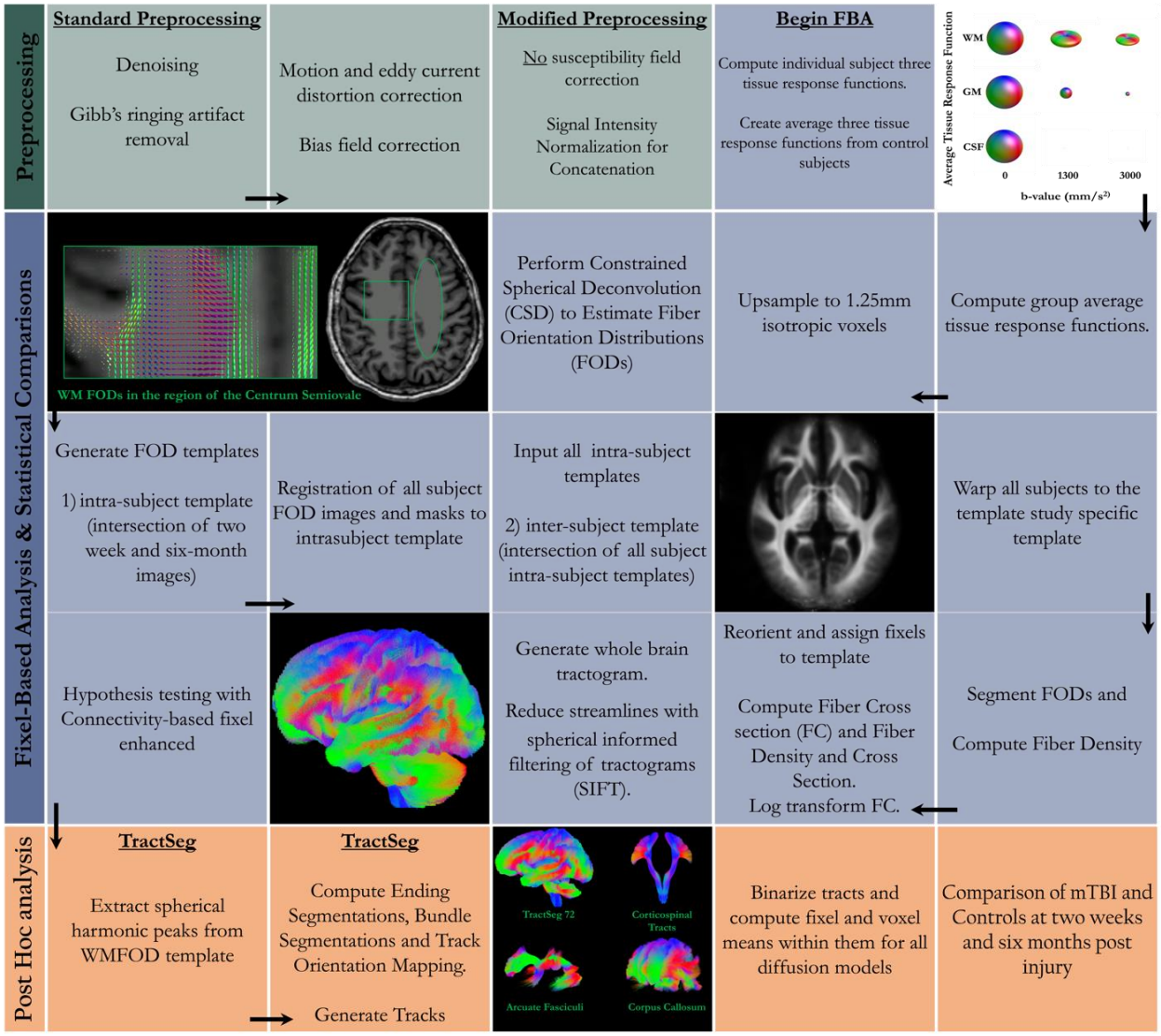

Figure 2. Fixel-Based Analysis Results for Fiber Density Cross-Section