Localization and quantification of injured regions and affected pathways in the 3D head-space of individual TBI subjects using DTI tractography with automatically generated ROIs

M. Singh[1], and J-W. Jeong[1]

[1]Radiology and Biomedical Engineering, University of Southern California, Los Angeles, CA, United States

Introduction

Axonal damage is a common occurrence in Traumatic Brain injury (TBI), likely to change local diffusivity and anisotropy measures such as FA in DTI. A *decrease* in FA and an *increase* in mean diffusivity (MD) have been reported by several authors [e.g., [Arfanakis et al. AJNR 23:794,2002] whereas an *increase* in FA and a *decrease* in MD have also been reported [Bazarian et al. J Neurotrauma 24:1447,2007]. Most previous studies rely on a comparison of FA and other anisotropy metrics in hand-drawn Regions of Interest (ROIs) or conduct a voxel based comparison in a normalized space such as the SPM MNI space. Subjectively drawn ROIs are prone to large errors and relating normalized space ROIs to an individual's anatomy is not straightforward. With the emphasis on not requiring any *a priori* hypotheses or manually drawn ROIs, the objectives of this work were to: a) identify and quantify injured regions in a TBI patient in terms of DTI anisotropy metrics changes, and b) identify and quantify the impact of injury on affected brain pathways (tracts). Also as neurosurgical or other interventions rely on the anatomy of the patient's own brain, one of the key goals was to visualize and quantify tractography changes in the patient's own 3D head space.

Method

Whole-brain single shot EPI DTI data were acquired from 12 TBI subjects (traffic accidents, mean age:28 years, mean interval between injury and DTI:1 month) and 10 age-matched normal control human volunteers on a 1.5 T GE EXCITE scanner at TR=10.3s, field-of-view 26cm, 128x128 matrix, 28 contiguous 4mm thick slices using 25 isotropic gradient directions with b=1000s/mm^2, one b=0 acquisition, and number of excitations (NEX)=2 for a total acquisition time of 7min 50s. A customized FA template in MNI space was created by normalizing FA maps of the 10 NC subjects. The center coordinates of MNI space voxels were inverse mapped to each subject's native space to generate an equal number of seeds located at anatomically equivalent locations in each subject for whole-brain tractography (streamline tractography, 0.2mm step size, FA>0.15, deflection<45°). Based on the Jacobian of the transformation matrices, every tract in each control subject was individually transferred first to MNI space and then to the head space of each individual TBI subject. Thus the number of tracts remains unchanged from each control subject to MNI to an individual TBI subject's head. Also this procedure maintains the continuity of individual tracts, does not introduce any additional smoothing, and the inverse seeding strategy normalizes for different head sizes, shapes and individual white-matter variations. An example of normalization is shown in **Fig. 1** where all tracts from 10 controls were transformed to a TBI subject's head and sorted by a common set of filters to extract fronto-occipital tracts. The superposition is excellent in the body of the tracts with expected inter-subject variations as tracts propagate toward cortical areas. To generate ROIs automatically, the FA map of each TBI subject was compared voxel-by-voxel to the FA maps of the control group in MNI space by computing a modified *t*-score defined as: t_i = [FA$_i$ (control) – FA$_i$ (individual)] /σ_i (control) where FA$_i$ (control), FA$_i$ (individual) and σ_i represent mean FA of the control group, FA of an individual and the standard deviation in the FA values of the control group respectively for the *i*-th voxel. This *t*-score distribution in MNI space was then mapped back to the individual subject's head by using inverse normalization, thresholded ($t \geq 3.0$, cluster size $k \geq 12$) and clustered automatically into ROIs relying on contiguity of voxels. In addition to FA, other diffusion anisotropy metrics, e.g., DA, DR, MD were also computed. These ROIs were also used to sort and quantify tracts from the control group and individual TBI subjects where all control group tracts reside in each TBI subject's head. Tract-counts (which reflect connectivity) of a given ROI in each TBI subject were compared to group mean for the same ROI to quantify impact of injury along affected pathways.

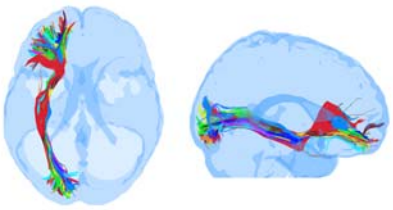


Fig. 1: Normalized fronto-occipital tracts from 10 controls superposed in a TBI subject's head-space.

Results and Discussion

An example of t-score maps corresponding to significant reduction in FA ($t \geq 3.0$, cluster extent $k \geq 12$) between a TBI subject (subject 1) and 10 controls is presented in **Fig. 2**. **Table 1** summarizes the anisotropy metrics and the tract-count reductions in the top 5 ROIs of this subject. Similar results were generated for all TBI subjects and affected pathways were quantified using ROIs as filters. As an example, pathways and corresponding DTI metrics (bar-graph) for the highest *t*-score ROI in TBI subject 1 are shown in **Fig. 3** at FA ≥ 0.15. No regions were found where FA would have increased due to injury in this study.

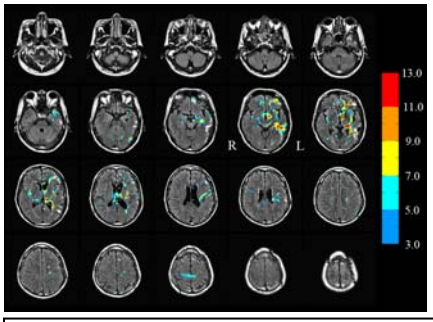
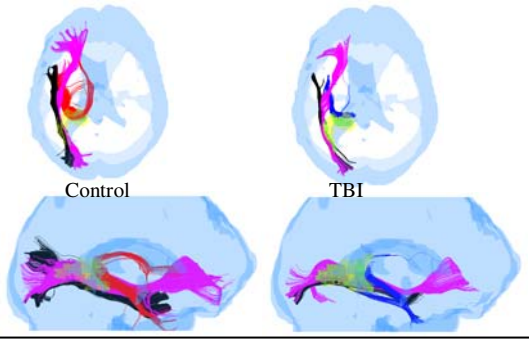


Fig. 2: FA change (t-score in color bar) between TBI subject and 10 controls super-posed on TBI subject's FLAIR images.



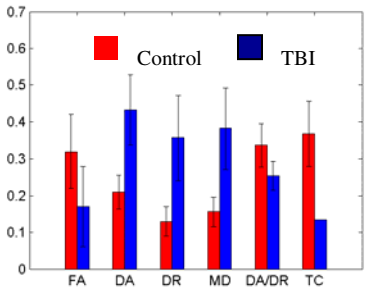


Fig. 3: Three pathways, hippocampal/fornix (HC/FX: red), inferior fronto-occipital (IFO:magenta) and inferior longitudinal fasciculus (ILF: black) in a control and a TBI subject identified by the highest t-score ROI in the TBI subject. DTI metrics incorporating mean and st. dev. of all controls are shown in the graph.

Table1: Summary of DTI and Tract-count (TC) metrics for the top 5 (out of 13) ROIs localized in TBI subject 1 by FA change. t-score is average over ROI.

t-score	Pathway	FA		DA		DR		MD		TC	
		Control	TBI	Control	TBI	Control	TBI	Control	TBI	Control	TBI
	HC/FX-l	0.32(0.10)	0.17(0.11)	1.05(0.23)	2.16(0.48)	0.65(0.20)	1.78(0.58)	0.78(0.20)	1.91(0.55)	367.80(88.58)	135
5.35	IFO-l-1	0.47(0.08)	0.21(0.12)	1.28(0.20)	2.14(0.49)	0.61(0.21)	1.67(0.64)	0.83(0.20)	1.83(0.59)	421.50(114.29)	119
	ILF-l-1	0.49(0.08)	0.24(0.09)	1.18(0.14)	1.84(0.39)	0.53(0.11)	1.35(0.47)	0.74(0.11)	1.51(0.44)	404.30(180.02)	121
5.29	IFO-l-2	0.28(0.06)	0.11(0.04)	0.94(0.07)	1.34(0.18)	0.61(0.07)	1.15(0.18)	0.72(0.06)	1.21(0.18)	409.60(150.97)	62
5.00	CC-g	0.47(0.03)	0.33(0.01)	1.17(0.04)	1.13(0.01)	0.52(0.03)	0.66(0.01)	0.74(0.03)	0.81(0.01)	238.00(55.04)	171
	UF-r	0.42(0.04)	0.31(0.02)	1.12(0.06)	1.10(0.02)	0.56(0.04)	0.67(0.02)	0.75(0.03)	0.81(0.01)	113.80(41.11)	55
4.84	CC-s-2	0.45(0.05)	0.28(0.07)	0.97(0.07)	0.92(0.04)	0.47(0.03)	0.62(0.05)	0.64(0.03)	0.72(0.03)	375.80(116.83)	169
	FX-l	0.29(0.10)	0.16(0.09)	1.24(0.24)	1.85(0.50)	0.83(0.24)	1.54(0.52)	0.97(0.24)	1.64(0.51)	253.50(110.68)	91
4.80	IFO-l-3	0.47(0.07)	0.28(0.07)	1.17(0.11)	1.41(0.23)	0.55(0.07)	0.96(0.26)	0.76(0.07)	1.11(0.24)	347.80(108.94)	74
	ILF-l-2	0.48(0.06)	0.29(0.07)	1.15(0.11)	1.31(0.22)	0.52(0.07)	0.87(0.22)	0.73(0.07)	1.02(0.21)	410.10(181.88)	115