Whole Brain FA Histogram analysis for improved detection of DAI

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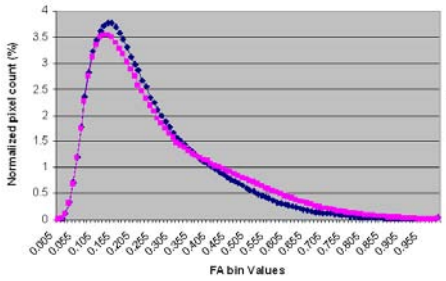
Introduction: Each year in the U.S. 1.5 million people sustain traumatic brain injuries (TBI). Closed head injury, caused by acceleration and deceleration of the head and brain, is associated with a core clinical syndrome which varies in severity. The underlying pathology is the shearing of white matter fibers, i.e., diffuse axonal injury (DAI). Conventional MRI is typically negative in mild TBI and may appear near normal in moderate injury. Thus, there is a need for new methods of grading severity and predicting neurological outcome from TBI. DWI and DTI have demonstrated potential utility in TBI using ROI analysis. The aim of the current study was to evaluate the ability of whole-brain fractional anisotropy (FA) to distinguish between controls and TBI patients ranging in severity and time to imaging. The underlying hypothesis is that FA is decreased (decreased anisotropy) in affected areas due to decreases in long-axis (i.e., parallel to fiber orientation) diffusion and possibly increases in short axis diffusion.

Materials and Methods: 12 recent and remotely injured patients with mild to severe closed head injury (mean age of 37+/-15 years) were scanned 3 days to 15 years after closed head injury, along with 13 healthy volunteers (mean age = 27+/-3). DTI was performed on a Siemens Sonata 1.5 T scanner. Single shot spin-echo planar DTI was acquired in 6 directions with the following parameters: FOV=256x256, resolution=2x2x4, 35 contiguous slices, TR/TE = 5800/97, b=0 and 1000 sec/mm^2, NEX = 10. Other images included: high-resolution 3D FLASH T1, T2, fluid-attenuated inversion recovery (FLAIR), arterial spin-labeled (ASL) perfusion, diffusion-weighted (DWI) and susceptibility-weighted (SWI). Corresponding FA and eigenvalue maps were generated using DTI studio software (http://cmrm.med.jhmi.edu) with noise suppression threshold of 50. Custom Matlab scripts were invoked through SPM2 (http://www.fil.ion.ucl.ac.uk) to create group-averaged whole-brain FA histograms for the controls and patients. An FA 'sum' was generated by computing the area under the tail of the histogram above a threshold value. The whole-brain FA sum computed for each subject was normalized to the intracranial volume to correct for brain size differences. The group-averaged histograms were then compared using absolute and percentage difference plots. Based on these results, three different FA thresholds (0.4, 0.55, 0.7) were compared statistically for maximum group separation of the individual FA sums. The optimal threshold was then used to threshold the group-averaged spatially normalized FA maps to locate the white matter areas which were most affected by DAI. These areas were then interrogated for FA component eigenvalues, trace and ADC between the groups.

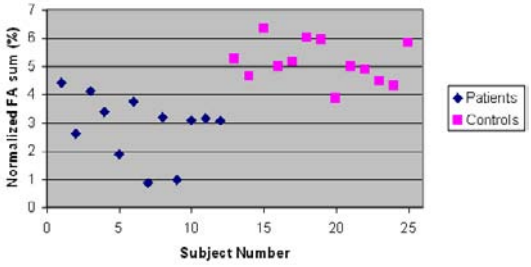
Results:



Histogram of FA for Patients and Controls
Fig. 1

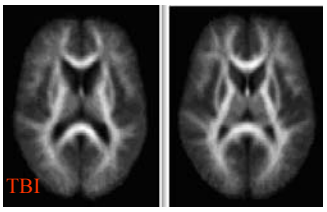
	FA threshold 0.4	FA threshold 0.55	FA threshold 0.7
T value	4.59	5.71	5.30
P value	0.0001	<0.0001	<.0001

Statistical comparison of FA index between the three thresholds
Table 1

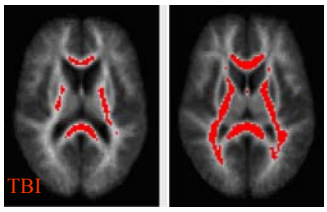


FA index scatter plot of the two groups using a threshold of 0.55
Fig. 2

Figure 1 plots the averaged whole-brain FA histograms for the groups. As can be seen, there is a cross-over point at about 0.4 representing the FA value above which the patients have fewer voxels than normals, i.e, there is a leftward shift. Table 1 gives the statistical results for the three different FA thresholds used to generate the FA sums. A FA of 0.55 gave the greatest separation between FA sums of the two groups (defined as the FA index). Figure 2 plots the FA index for all subjects at a threshold of 0.55. Note the near complete separation of the groups. Preliminary results suggest association of cognitive outcome with FA index (in progress). Figure 3 gives the group-averaged unthresholded FA map for a single slice. Note the similar appearance of the two images. Figure 4 displays all voxels with FA $\geq$0.55 as red. Note the reduced number suprathreshold voxels for the TBI averaged image. Note also that the location of these higher FA values are in large periventricular white matter fascicles which is concordant with reported postmortem literature of commonly affected sites of shear injury. The histogram and FA image differences are also apparent for single subjects (not shown) Table 2 compares diffusion in long axis (λ_1) and short axis (λ_2, λ_3) for the groups. Note the decrease in long axis and increase in short axis diffusion for the TBI group compared with controls consistent with a priori hypothesis. Overall diffusivity did not differ significantly between the groups but trended higher in the TBI group. A single subject was scanned three times (3 months, 6 months, 1 year) post severe injury with little change in FA index or eigenvalues.



Mean FA map unthresholded
Fig. 3



Mean FA map thresholded at 0.55
Fig. 4

		Control	Patient	P value	T value
ROI (0.55 threshold mask)	FA	0.55/0.04	0.48/0.08	0.0128	2.71
	λ1	1.45/0.16*	1.29/0.17*	0.0236	2.42
	λ2	0.57/0.07	0.68/0.10	0.0015	3.12
	λ3	0.34/0.06	0.49/0.10	0.0002	4.45
	Trace	2.36/0.17*	2.46/0.21*	0.1	1.32
	ADC	0.79	0.82		

Reduction in FA and significant change in the diffusion pattern in the patient group
Table 2

* Data are the mean/SD. The eigenvalues λ1, λ2, λ3 and trace are in 10^{-3} mm^2/s

Conclusions:

Using a whole brain rather than an ROI approach we were able to differentiate normals and temporally heterogeneous TBI cases using thresholded histograms of FA. TBI cases had a leftward shift of highest FA values owing to an overall loss of anisotropy of damaged and/or absent axons. Location of significantly differing FA between groups was in corpus callosum, internal capsule, centrum semiovale, i.e., major white matter tracts. Distribution of pathology was sufficiently distributed that a whole brain index differentiated the groups. Further, the loss of anisotropy for the patients is apparently due to long axis decreased diffusion and short axis increased diffusion, presumably due to impairment in axonal transport and breakdown of myelin or axon loss. We are currently investigating the relationship of these DTI indices with injury outcome and temporal variables along with multimodality MR data (e.g., SWI, MRS, fMRI) acquired in the same subjects. Thus MR, and in particular DTI, will likely provide improved methods by which brain injury can be evaluated and neurological outcome can be predicted.