Evaluation of whole brain and regional DTI parameters on diffuse axonal injury patients in the sub-acute stage

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INTRODUCTION: Traumatic brain injury (TBI) is the primary cause of death and disability in young population under 45 years of age, among which approximately one half suffer diffuse axonal injury (DAI). Patients presenting with DAI follow a highly variable clinical course, with the patient's initial status frequently discrepant from their long-term neurological outcome[1]. Both CT and conventional MRI have been found to have limited sensitivity in the acute to sub-acute trauma setting. Recent studies have attempted to use diffusion tensor imaging (DTI) to evaluate DAI[2,3,4]. However, initial studies have obtained varying, if not conflicting, results regarding the correlation between DTI parameters and clinical measures. In this study, we compare whole brain, whole brain white matter, and regional DTI parameters among a large group of TBI patients and compare them to normal subjects.

METHODS: Imaging: Seventy three TBI patient (Glasgow Coma Scale (GCS): 9.2 ±4.8, age: 40.3±18.3, mean time to imaging following injury: 6 ± 11 days) and 12 healthy adult volunteers (ages 34.4 ± 10.1) were imaged with conventional MRI and DTI. Diffusion tensor images were obtained in 6 non-colinear directions at an effective b-value of 1000 s/mm^2. All imaging was performed on a 1.5T Siemens Avanto scanner. Other imaging parameters were: FOV 23cm^2; matrix 128x128; slice thickness 2mm with no gap; 5 averages; and a TE/TR of 73/7000ms. A total of 72 axial images were acquired to cover from top of the brain to the skull base. 3D T1-weighted high resolution volumetric images that match the DTI slice positioning were also acquired for anatomical reference (TR/TE/flip 21ms/4.6ms/30º).

Data Analysis: FA and ADC maps were generated using DTI task card (courtesy Dr. Benner, MGH). To obtain the whole brain ADC and FA values, the ADC and FA maps were exported to an offline workstation (SGI O200, Sunnyvale, CA) where the skull and the durra were stripped using the brain extraction routine (BET) available in FSL (FRB's Software Library, http://www.fmrib.ox.ac.uk/fsl). The FA maps of all patients and controls were then segmented into gray and white matter, and CSF categories using SPM5 (http://www.fil.ion.ucl.ac.uk/spm). The segmented white matter masks were then used to generate whole brain white matter ADC and FA histograms. All regional measures were carried out by a radiologist by placing a circular ROI of a constant size of 12 pixels centrally within the following regions: bilateral frontal lobe (FL), bilateral temporal lobe (TL), bilateral posterior limb internal capsule (PIC), bilateral basal ganglia (BG), bilateral thalamus, bilateral cerebral peduncle (CP), bilateral midbrain, as well as the genu (CC-G) and splenium (CC-S) of the corpus callosum.

RESULTS: Figure 1 shows the mean and peak ADC/FA values of the TBI patients compare to normal controls for both whole brain and whole brain white matter measures. A significant increase ($p<0.05$) in both FA and ADC values were observed for both measures. Figure 2 shows the relationship between peak ADC and GCS for all patients grouped according to their GCS ($r^2=0.22$, $p=0.13$). Notice the correlation significantly went up ($r^2=0.72$, $p<0.001$) when we removed all mild cases (1 case of GCS 14 and 26 cases of GCS 15) and replaced with normal controls with an assigned GCS of 16. Although there was an increase in the mean and peak FA for the TBI patients, we did not find a strong relationship between these parameters and GCS at the whole brain level. Whole brain white matter measure displayed a same trend as the whole brain measures. Figure 3 shows the regional FA/ADC values for the patients and normal controls. Bilateral regional measures were averaged because we didn't see a significant difference in left compared to right in any of the regions. Significant increases in mean ADC were found in all regions ($p<0.05$) except temporal lobe ($p = 0.52$). A significant decrease in FA was observed in the corpus callosum regions ($p < 0.05$) and a significant increase in FA was observed in basal ganglia ($p = 0.028$).

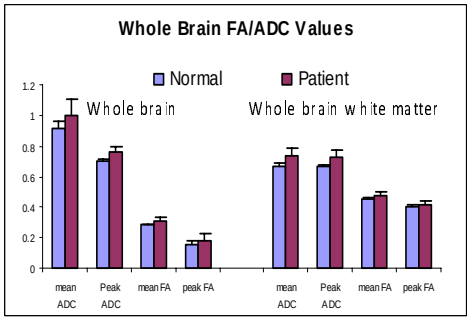


Figure 1. Whole brain and whole brain white matter mean/peak FA and ADC values for TBI patients and normal controls. ADC values are of unit 10^{-3}mm^2/s.

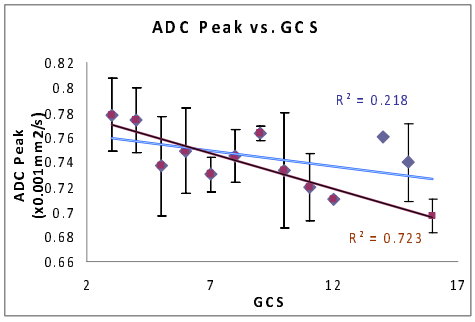
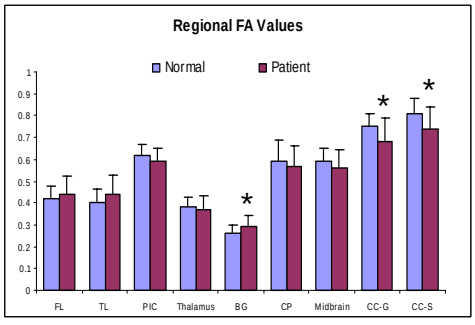


Figure 2. Whole brain peak ADC vs. patient GCS with patient values grouped for each GCS score.



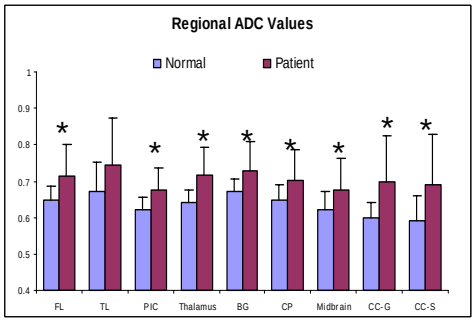


Figure 3 Regional FA and ADC values for TBI patients compare to normal controls. ADC values are of unit 10^{-3}mm^2/s. * shows regions with significant difference ($p<0.05$) between patient and normal control group.

CONCLUSION: In TBI patients, a widespread significant increase in ADC at sites throughout the brain and brainstem was observed that was best appreciated by global markers of ADC from the whole brain DTI data. In contrast to the results of previous studies[4], there was a significant increase in whole brain FA values that we hypothesize reflects an early preservation of axonal integrity in the sub-acute phase following trauma, even in light of the changes in ADC. Whole brain white matter analysis provided essentially similar results as the whole brain analysis suggesting that the extra processing to isolate white matter may not be necessary in a clinical environment. Whole brain analyses demonstrated a strong correlation with GCS for ADC and such correlation is strengthened when removing mild case, which may be an indication that ADC is a better marker describing pathophysiologic changes in mild TBI patients that is not accurately captured by GCS. Regional analysis revealed a significant decrease in FA within the corpus callosum that was not found in other sites in the brain and brainstem, suggesting a possible unique role in the corpus callosum in the detection and assessment of TBI patients.

Reference:

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