Detection of TBI-Related Anomalies in Single-Subject DTI Scalar Images

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Introduction. Group studies of DTI scalar images in traumatic brain injury (TBI) patients demonstrate group differences at the regional level but with insufficient sensitivity to detect lesions in single subjects. These regional results could be driven by relatively small lesions that could be detectable in single subjects. This would assist in the diagnosis of mild TBI in individual subjects. We extend the work of Kim et al [1] by detecting such anomalous white matter regions using scalar DTI images (FA, AD, RD, MD) and either t-statistics or Hotelling T^2 statistics.

Methods. Diffusion tensor data were acquired from 20 male and 13 female controls (32.5 +/- 8.5 yrs) with (TR=10s, TE=85ms, FA=90, 2x2x2mm voxels, b=1000, 48 gradient directions, 70 128x128 slices). Reproducibility study: data were acquired in repeated sessions at 6 month intervals from 47 TBI subjects (43 male, 4 female, age=30.1+/-9.1 years, 36 mild TBI, 8 moderate TBI, 3 severe TBI. subjects had two scanning sessions, 6 had 3 sessions and 1 had four sessions. Median time since injury was 141 days. A second data set consisting of 34 mild, 27 moderate and 7 severe TBI patients (65 male, 5 female, 30.2 +/- 8.1yrs) was imaged. Diagnoses were assigned at intake to our facility. A tensor-based custom template was constructed from the 33 control subjects using DTI-TK. Data were preprocessed with DTIPrep, tensors were reconstructed using the Camino implementation of the RESTORE algorithm, and the tensor was transformed to standard space using DTI-TK. Control data were processed for each subject by first reconstructing the tensor using only those gradient directions that survived preprocessing for that subject, applying a Box-Cox normality transformation, and computing means, standard deviations, and covariance matrices. Test statistics include a t-test using FA and Hotelling T^2 tests using vectors formed from axial and radial diffusivities (ADRD) and mean-diffusivity and FA (MDFA). Regions were defined by thresholding the F- and t- statistics maps with height and extent thresholds determined with AFNI's alphasim program for p<.05. Regions are designated as replicated if, after dilation by one voxel, the union of their voxels is nonempty.

The probability of replication (PR) was approximated by the probability of an anomalous region detected in the second scanning session also being detected in the first. It was calculated as the number of replicated regions summed across subjects over the total number of detected regions. We refer to these regions as anomalies rather than lesions because we have not clearly shown them to be a result of injury. If it is assumed that replicated anomalies are true anomalies, the specificity can be approximated by the square root of PR. Detection probability can be approximated by the ratio of the number of detected anomalies (NA) to the total number of actual anomalies. The denominator is unknown but fixed, so we use the number of detected anomalies as a proxy for the detection probability. Hence a plot of the probability of replication vs. the number of anomalies can be used to select optimum parameters much as an ROC curve – the optimum parameter detects the greatest number of anomalies with the highest probability of replication.

Results. An image acquired from a subject with mild TBI is shown in Figure 1. With the exception of the region in the corpus callosum, all anomalies overlaid T1 hypointensities and were detected with the ADRD statistic but not FA. This suggests that these anomalies are due to injury. The proxy ROC curve in Figure 2 suggests 1) That the optimum threshold is 2.5 (with it's corresponding extent threshold); 2) That t-statistics formed from FA are most sensitive; and 3) The Hotelling T^2 statistics are less sensitive but roughly as replicable as FA. Interestingly, the anomalies detected with FA do not always overlap with those detected with the ADRD, suggesting that a combination of both statistics might be optimum. This is also true for MDFA but to a lesser extent. Figure 3 shows the mean value and spread of each statistics as a function of diagnosis. Volumes for mild and moderate TBI patients were well separated from those of severe TBI patients, suggesting that the detected anomalies largely correspond to lesions. The results do not clearly distinguish between patients with mild and moderate TBI. This might result more from the difficulty of clinical diagnosis and the vagaries of self-report data than a failure of the method.

Conclusions. These results suggest that scalar DTI data can be used to detect anomalous lesions in individual subjects. Although the method cannot determine whether these anomalous regions result from injury or are due to processing artifacts or normal variations in anatomy it might serve as a useful adjunct in the diagnosis of traumatic brain injury.

References: 1. Kim N, Branch CA, Kim M, and Lipton ML, PLoS ONE 8(3) 2013 e59382.

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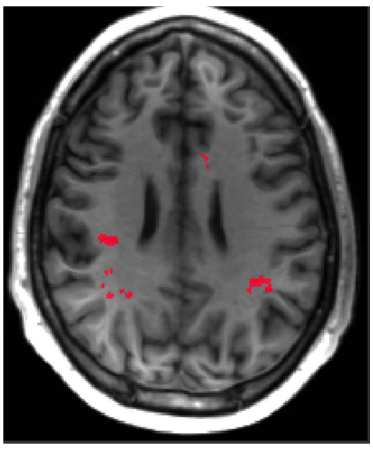

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Anomalous regions overlaid on a T1 weighted image. All regions except that in the corpus callosum corresponded to hypointensities in the T1 image.

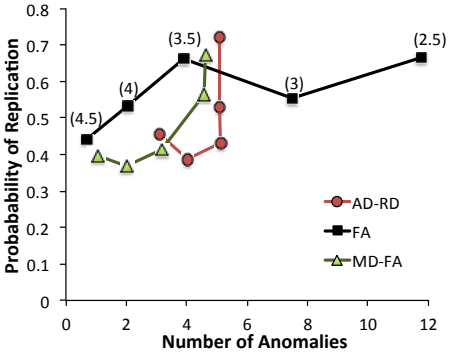

Figure 2. Proxy for an ROC curve. Numbers in parentheses are thresholds as z statistics. Thresholds are in the same order for the AD-RD and MD-FA Hotelling statistics.

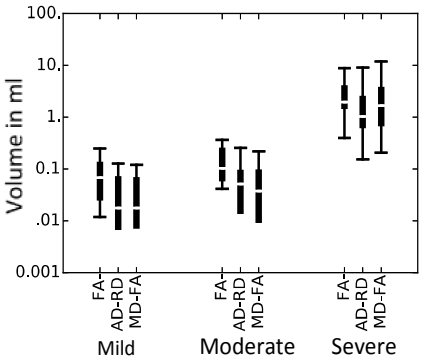

Figure 3. Whisker barrel plots for the total volume of anomalies per subject. Note the logarithmic scale.