

## DTI Parameters Predict Outcome in Severe Traumatic Brain Injury Patients

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### Introduction

Diffuse axonal injury (DAI) represents the most common primary intra-axial form of traumatic brain injury (TBI), comprising approximately half of all such injuries<sup>1,2</sup>. Patients presenting with DAI follow a highly variable clinical course, with initial status frequently discrepant from long-term neurological outcome<sup>3</sup>. In this study, we retrospectively compare the average and standard deviations (SD) of DTI parameters ( $\lambda_1$ ,  $\lambda_{\text{PERP}}$ , ADC, and FA) from the whole brain white matter (WM), and at selected regions throughout the brain among severe TBI patients with varying outcome following the Glasgow Coma Scale (GCS) at the time of discharge.

### Materials and Methods

The study was approved by the University of Maryland School of Medicine Institutional Review Board. 74 patients were selected from a list of patients referred for MRI evaluation of the brain as part of routine trauma evaluation. Patients were selected for this study if they had a GCS of 8 or less at the time of MRI, which comprised a severe TBI group, or had a GCS of 15 and their MRI was judged to be negative by a board-certified trauma radiologist, forming the mild TBI reference group. 38 patients were eligible for subsequent analysis (29 male, age=30.5±17, scanned 3.3±4.6 days post admission), of which 8 patients were judged to have mild TBI and with negative MRI, and 30 patients were judged to have severe TBI.

Patient outcomes were classified as death, severe GCS at discharge (poor outcome), mild/moderate GCS at discharge (good outcome), or mild TBI (the reference group). Among the severe TBI group, there were 9 deaths, 10 severe outcomes, 11 mild or moderate outcomes.

### Imaging

All patients were imaged with conventional MRI and DTI. Diffusion tensor images were obtained in 12 directions at an effective b-value of 1000 s/mm<sup>2</sup>. All imaging was performed on a 1.5T Siemens Avanto scanner using a 12 channel head-neck coil. Other imaging parameters were: FOV 23cm<sup>2</sup>; matrix 128x128; slice thickness 2mm with no gap; 3 averages; and a TE/TR of 95/11200ms, parallel imaging (GRAPPA) with a reduction factor of 2 was used. A total of 68 axial images were acquired to cover from top of the brain to the skull base.

### Image Processing and Analysis

DTI images were exported offline and processed using FDT (FMRIB Diffusion Toolbox, Analysis Group, FMRIB, Oxford, UK). For whole brain analysis, the FA maps of all patients and controls were segmented into gray matter, white matter, and CSF categories using SPM5 (Wellcome Department of Imaging Sciences; University College London, UK). The segmented white matter masks were then used to generate whole brain white matter ADC, FA and eigenvalue images. Eigenvalue images were used to calculate parallel diffusivity ( $\lambda_1$ ) and radial diffusivity ( $\lambda_{\text{PERP}}$ ) images. For ROI-level analysis, ROIs were drawn on the genu and splenium of the corpus callosum, and the brain stem using FSL (Analysis Group, FMRIB, Oxford, UK) to obtain the average FA, ADC,  $\lambda_1$ , and  $\lambda_{\text{PERP}}$  in the ROIs.

### Statistical Analysis

Multiple regression was used to examine the relationship of DTI parameters to scan GCS. Non-parametric one-way ANOVAs were used to compare the DTI parameters across groups, due to departures from normality and heterogeneous variance. Logistic regression models were used to determine if DTI parameters add to GCS in their ability to predict patient survival. Furthermore, ordinal logistic regression was used to predict outcome class (death, poor outcome, good outcome, or reference group) given the DTI parameters. Statistical analysis was conducted in SAS 9.2 (SAS Institute, Cary, NC) and R (R Foundation for Statistical Computing, Vienna, Austria).

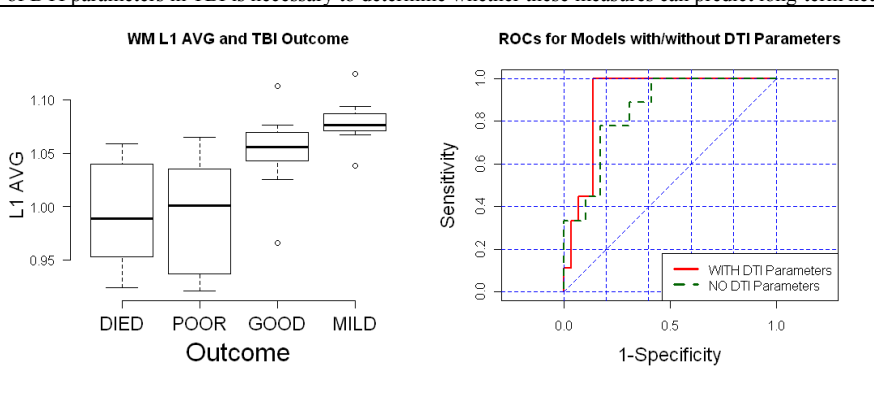
### Results

In multiple regression models whole brain average  $\lambda_1$  was significantly related to scan GCS even after adjusting for age, gender, and scan delay ( $p=0.116$ ). At the whole-brain level, both the averages and variances of ADC and  $\lambda_1$  significantly differed between the four outcome groups ( $p<0.05$  in all comparisons). Radial diffusivity ( $\lambda_{\text{PERP}}$ ) and FA did not significantly differ between groups. At the ROI level, significant group differences were found in average  $\lambda_1$  in the brainstem, genu, and splenium. Differences in FA in the brainstem ROIs were also significant. No significant differences in ADC or  $\lambda_{\text{PERP}}$  were noted at the ROI level.

Parameters that differed significantly between groups were used to predict survival and outcome class membership. In a model including age, gender, and scan GCS, addition of average  $\lambda_1$  and ADC SD resulted in a significantly better model fit when predicting survival ( $\Delta D=6.385$ , 2 DF,  $p=0.041$ ). In addition to predicting survival, average  $\lambda_1$  and ADC SD significantly predicted outcome class membership ( $p<0.0004$  and  $p<0.0236$  respectively) across all classes (death, poor outcome, good outcome, and mild TBI).

### Conclusions

The GCS is a coarse measure of neurological function, with many known limitations<sup>3,4</sup>. Whole Brain and ROI-specific DTI parameters such as average  $\lambda_1$  may be useful in assessing the clinical outcomes of TBI patients. These parameters are significantly related to traditional neurological measures, such as the GCS, but may better predict important clinical outcomes. Such models may be important in clinical decision-making and conveying realistic expectations to the families of traumatic brain injury patients, as well as in the evaluation of patients whose neurological status does not appear to reflect conventional radiological findings. A prospective study of DTI parameters in TBI is necessary to determine whether these measures can predict long-term neurological and cognitive recovery after discharge.



**Figure 1.** Side-by-side box plots showing the differences in median and variance of Average  $\lambda_1$  between the severe TBI outcomes (death, severe discharge GCS, mild/moderate GCS) and the mild TBI reference group.

**Figure 2.** ROC plots demonstrate the improvement in classifying survival in TBI patients when adding Average  $\lambda_1$  and ADC SD to age, gender and scan GCS.

### References:

- [1] Gentry, LR et al. *Am J Roentgenol* 1988 150: 663-612
- [2] Kampfl, A. *J Neurosurg* 1998; 88:809-816
- [3] Cordobes, F. *Acta Neurochirurgia* 1986; 81:27-35
- [4] Gill, M. R. et al. *Ann Emerg Med* 2004 43(2):215-223