

# Longitudinal changes in apparent diffusion coefficient value predicts prognosis for mTBI patients

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## Introduction:

Early return to activity from traumatic brain injury (TBI) and a secondary injury days or weeks after the primary injury may result in prolonged disability or even mortality for patients. Almost 40% of patients with secondary injury have poorer prognosis [1]. Accurate prognosis prediction for TBI patients would improve outcome, quality of life and reduce associated medical cost of a secondary injury. ADC maps have been used as a predictor of outcomes in TBI [3, 6, 7, 8, 9]. Higher ADC values have been associated with vasogenic edema, and lower ADC values with a predominantly cellular form of edema [3]. None of these studies however have used ADC maps as a prognostic biomarker for mild TBI (mTBI) patients. In this work, longitudinal changes in the ADC map from automatically parcellated white matter regions of the brain are used to predict prognosis for mTBI patients.

## Methods:

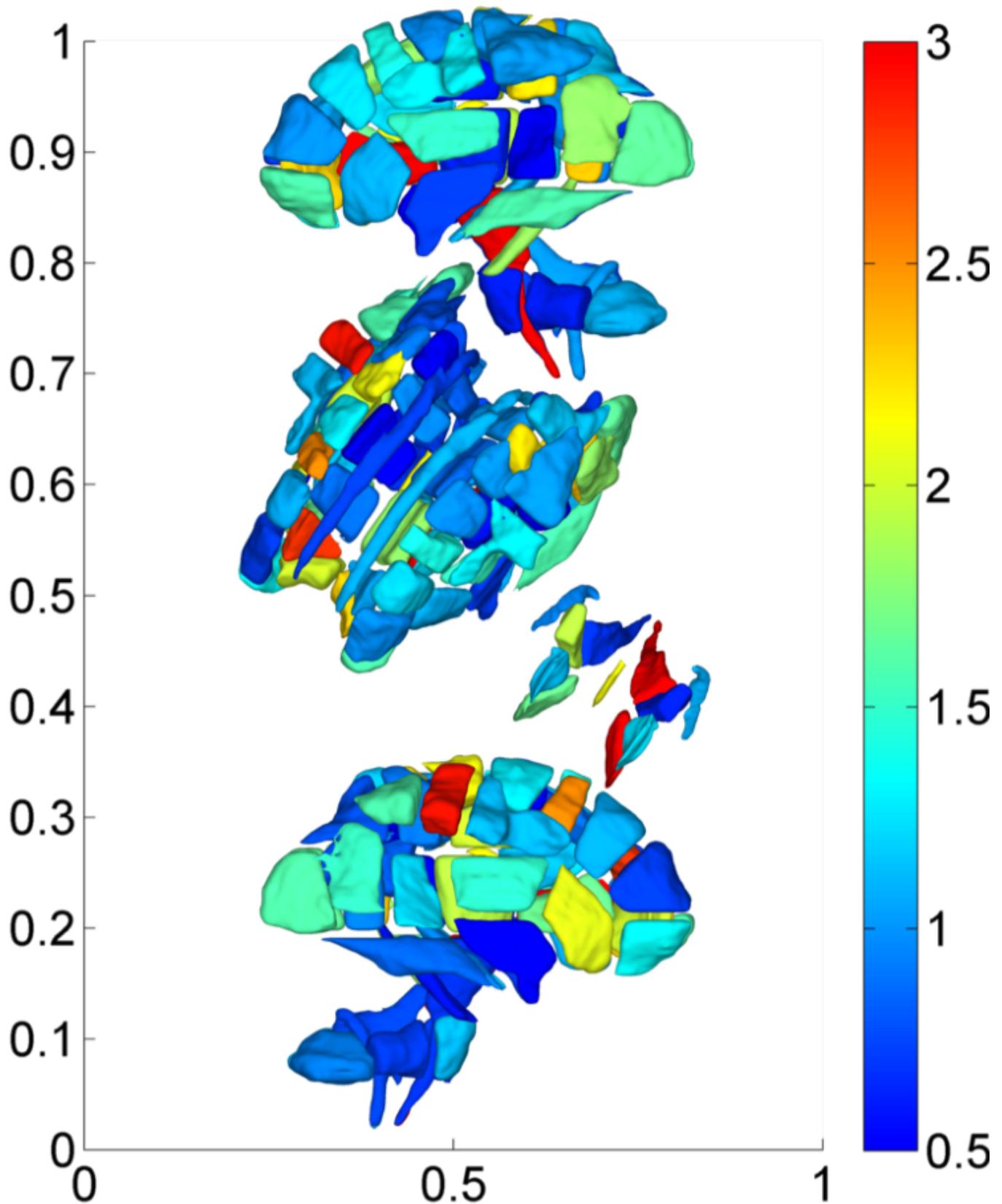
Longitudinal diffusion MRI data were acquired for n=267 mTBI subjects with no structural MRI abnormalities at 3, 7, 21, and 90 days post-injury over three clinical sites using 3T GE MR750 scanners (GE Healthcare, Milwaukee, WI).

140 diffusion weighted volumes (25-40-75 gradient directions with  $b = 700, 1000, 2800 \text{ mm}^2/\text{s}$ , respectively) and eight  $b=0$  images were acquired with 2.5mm isotropic resolution. Presence of diffusion imaging and at least two scans and corresponding RPQ scores were used as inclusion criteria. Final number of patients after imposing the inclusion criteria was 177.

White matter was automatically parcellated into 76 anatomical ROIs by registering to the MNI atlas [6]. Statistics (mean, median, standard deviations, skewness and kurtosis) within each of these 76 parcellated ROIs were computed. Temporal changes in the ADC map of these 76 ROIs were quantified by calculating the gradient of the statistics. For computing the gradient, statistical values of each ROIs for an encounter were subtracted from the consecutive encounter and divided by the number of days between the encounters. Last three encounters were taken to compute second order derivative and quantify the rate of changes in gradient. In absence of an encounter, values from the previous encounter was imputed. Ground-truth for patient outcome was created from Rivermead post-concussion symptom questionnaire (RPQ13) scores. Gradient of the RPQ13 score computed from the first and the last encounter was used to automatically cluster the patients into 4 classes (fast recovery, slow recovery, mildly symptomatic and not-recovered) in a k-means clustering framework [7]. An 8-fold-cross-validation was performed to predict patient outcome by predicting each class for the patient from the diffusion imaging features. Random forest classifier [8] was used inside cross-validation to automatically select the important features to reduce feature dimension and reduce overfitting. The reduced number of features were used in a support vector machine [9] classifier to predict each of the four classes inside the cross-validation step.

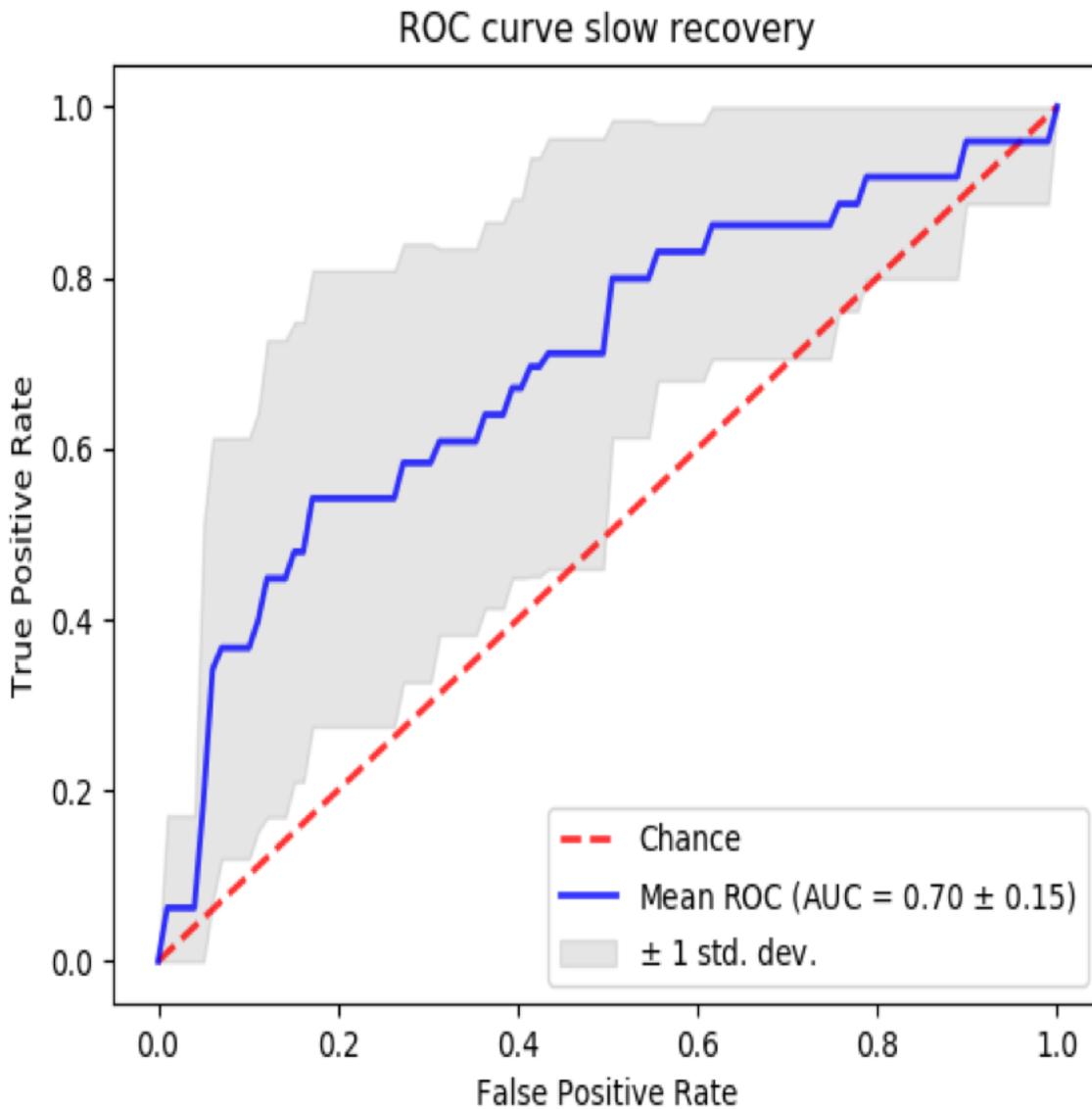
## Results:

Gradient of median and standard deviation of the ADC maps of the brain regions in body of corpus callosum, corona radiata, middle cerebellar peduncle, sagittal stratum, hippocampus, external capsule were consistently ranked as top features in predicting the outcome (Fig 1). The prognosis prediction accuracy for slow recovery patient was (AUC=0.70) (Fig. 2) for fast recovery (AUC=0.59), mildly-symptomatic (AUC=0.67) and not-recovered (AUC=0.38). We suspect that lack of samples for not recovered class ( $n=14$ ) resulted in a poor prediction score.



**Figure 1 Brain regions important for mTBI prognosis prediction from ADC maps.**

·Brain regions important for mTBI prognosis prediction from ADC maps.



**Figure 2 ROC curve for slow recovery patients.**

·ROC curve for slow recovery patients.

#### Conclusions:

ADC values were found to be different between mTBI patients and controls in literature. In this work we have used longitudinal changes in the ADC map to predict prognosis (slow, fast, symptomatic etc.) for mTBI patients. This preliminary analysis may facilitate building a prediction model of prognosis for mTBI patients from diffusion images and aid in patient management and rehabilitation.

#### Disorders of the Nervous System:

Traumatic Brain Injury <sup>1</sup>

#### Imaging Methods:

Diffusion MRI

### Modeling and Analysis Methods:

Classification and Predictive Modeling <sup>2</sup>

### Keywords:

Machine Learning

MRI

Trauma

WHITE MATTER IMAGING - DTI, HARDI, DSI, ETC

<sup>1|2</sup>Indicates the priority used for review

### My abstract is being submitted as a Software Demonstration.

No

### Please indicate below if your study was a "resting state" or "task-activation" study.

Other

### Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

Patients

### Are you Internal Review Board (IRB) certified? Please note: Failure to have IRB, if applicable will lead to automatic rejection of abstract.

Yes

### Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.

Yes

### Was any animal research approved by the relevant IACUC or other animal research panel? NOTE: Any animal studies without IACUC approval will be automatically rejected.

Not applicable

### Please indicate which methods were used in your research:

Structural MRI

Diffusion MRI

### For human MRI, what field strength scanner do you use?

3.0T

## Which processing packages did you use for your study?

Other, Please list - SimpleITK, Scikit

## Provide references using author date format

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