Detection of Tissue Changes in Traumatic Brain Injury Patients Using Automatic Regional Analysis of Quantitative MR Scans

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Introduction
Traumatic brain injury (TBI) is a major cause of death and disability with more than 112,000 people per year in the UK admitted with a primary diagnosis of head injury. Around 90% of these admissions are classed as mild (Glasgow Coma Scale 14–15) [1], but a significant proportion of these patients have ongoing symptoms which do not correlate with conventional MRI or CT findings. Here we investigated a cohort of patients with mild TBI using multi-parametric, quantitative MRI to assess whether it is a more sensitive technique for detecting parenchymal damage.

Methods
Patients: Twenty subjects with history of mild TBI (GCS, 14–15, mean age 38±15 yrs) were scanned within 10 days of injury (mean 4.9, range 1–10 days) and compared against 20 healthy adults (41±16 yrs) with no clinical evidence of neurological diseases.

MR Protocol: Subjects were imaged using a 3.0T whole body system (Philips Achieva) equipped with an 8-channel head coil. Scan data included (a) T1 weighted anatomical scan (SENSE factor 2, TE/TR=4/6.8 ms, matrix 256x256x180, 1x1x1 mm3), (b) quantitative T1 measurement using a custom IR-EPI sequence (SENSE factor 2, TE/TR=24/15000 ms, TI=0.25-2.5 s in 12 steps, matrix 128x128x72, 2x2x2 mm3), (c) quantitative T2 measurement using a MSEQ sequence (TE/TR=20ms/4.7s, 8 echoes, echo spacing 20 ms, matrix 128x128x72, 2x2x2 mm3), (d) DTI (SE EPI sequence, SENSE factor 2, TE/RE/Volume=71/252/528ms, Matrix 128x128x24, 2x2x2 mm3, 16 directions, b value 1000 mm²/s) and (e) 3D dual echo field map (SENSE factor 1.5, TE2/TE1/TR=2.5/5.8/27 ms, Matrix 128x128x72, 2x2x2 mm3) which was applied to all EPI data to correct for spatial distortion.

Image Analysis Algorithm: We applied our previously proposed method whereby the whole brain is automatically divided into 16 regions of interest (ROI) for each tissue type [2]. This analysis method operates in patient space and was demonstrated to significantly reduce partial volume errors compared to the same analysis performed in standard space [3]. In brief, the method uses a standard space brain ROI template which is transformed into patient space based on a multi-step registration using the patient’s high resolution T1-weighted anatomical scan. Next, the same anatomical scan is segmented into white matter, grey matter and CSF masks [4] and combined with the brain region template to generate tissue specific anatomical ROIs which are applied to the quantitative images under analysis. Multi-spectral analysis is applied to the quantitative data to improve classification [5].

Scan Analysis: Quantitative T1 and T2 times and mean diffusivity (MD) values were calculated on a pixel by pixel basis and subsequently analysed to determine the grey and white matter T1, T2 and MD histograms for each of the ROIs. Patients whose lesions were still visible after brain extraction and segmentation were excluded from the analysis. Group comparisons were made by t-test although heterogeneity of patient injury is expected to influence the power of such group statistics. We therefore determined the Z-score for each individual ROI in each patient against the mean and the standard deviation of the control group. In each patient the number of ROI with Z > 1.65 (p<0.05) were counted and the patient was considered abnormal if at least 3 out of 7 regions had significant Z scores (p<0.05 correct for multiple comparisons).

Results and discussions
Significant group differences (p<0.05) were found in White matter T2 (left parietal), White matter MD (left frontal superior, left temporal parietal and right frontal superior), Grey matter T1 (right temporal, right occipital and left temporal parietal) and Grey matter T2 (right temporal and right occipital). Values for T1WM, T1GM, T2GM and MDWM were elevated in controls (table). Z-score analysis of individual ROI data showed areas of significant difference in most patients. However, 12 patients had significant Z-scores for at least 3 regions in T1GM with 4 patients having significant Z-scores in 6 of 7 regions.

Conclusions
We have shown that a fully automatic real space method of analysing quantitative MR parameters can be used to detect changes in normal appearing tissues in patients suffering mild TBI. These changes may represent damage to neuronal tissue and further work is needed to determine whether this is responsible for the cognitive and affective symptoms commonly seen following mild head injury, which include memory loss, inability to concentrate, irritability and depression (data collected but not presented).


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Fig. : (a) Anatomical T1W image, (b) MD, (c) and (d) quantitative T1 and T2 images.