

## MR relaxometry and diffusion tensor imaging of normal appearing white matter in mild traumatic brain injury.

C. J. Cowie<sup>1,2</sup>, B. S. Aribisala<sup>1</sup>, J. He<sup>1</sup>, J. Wood<sup>1</sup>, A. D. Mendelow<sup>2</sup>, P. Mitchell<sup>2</sup>, and A. M. Blamire<sup>1</sup>

<sup>1</sup>Newcastle Magnetic Resonance Centre, Newcastle University, Newcastle upon Tyne, Tyne & Wear, United Kingdom, <sup>2</sup>Department of Neurosurgery, Newcastle General Hospital, Newcastle upon Tyne, Tyne & Wear, United Kingdom

### Introduction

Mild traumatic brain injury (TBI) accounts for approximately 90% of those who present to hospital after head injury [1]. Recovery from mild TBI may be complicated by long term cognitive and affective symptoms. However, conventional MR imaging findings often do not account for these symptoms [2]. Magnetic resonance relaxometry is an established technique which has been little used in the evaluation of mild TBI. We investigated patients with mild TBI using T<sub>1</sub> and T<sub>2</sub> quantitative MR relaxometry as well as with diffusion tensor imaging (DTI), to determine whether we could detect changes in normal appearing white matter (NAWM).

### Methods

**Subject Description:** The study group consisted of twenty four patients with a history of mild TBI (GCS 14-15, mean age 38y, range 18-68y) while the control group consisted of 20 healthy adults (mean age 41y, range 19-67y) with no clinical evidence of neurological disease. Patients were recruited from the accident and emergency and neurosurgery departments, and scanned within 10 days of injury (mean 4.9, range 1-10). Patients with a history of previous head injury, neurological or psychiatric illness and alcohol or drug abuse were excluded from the study. Inclusion was limited to those who could be transferred to a research MRI scanner outside the main clinical area. As part of their clinical evaluation all patients were scanned using computed tomography (CT) prior to recruitment to the study. The study was approved by the local ethical committee and all subjects gave written informed consent.

**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) *T<sub>1</sub> weighted anatomical scan* (TE/TR=4.6/8.3ms, matrix 256x256x180, 1x1x1 mm, SENSE factor 2), (b) *quantitative T<sub>1</sub> measurement* using a custom IR-EPI sequence (TE/TR=24/15000 ms, TI=0.25-2.5s in 12 steps, matrix 128x128x72, 2x2x2 mm, SENSE factor 2), (c) *quantitative T<sub>2</sub> measurement* using a MSE sequence (TE/TR=20ms/4.7s, 8 echoes, echo spacing 20 ms, matrix 128x128x72, 2x2x2 mm), (d) *DTI* (SE EPI sequence, TE/TR=71/2524ms, matrix 128x128x24, 2x2x6 mm, 16 directions, b value 1000 smm<sup>-2</sup>, SENSE factor 2) and (e) *3D dual echo field map* (TE<sub>1</sub>/TE<sub>2</sub>/TR=2.5/5.8/27ms, matrix 128x128x72, 2x2x2 mm, SENSE factor 1.5) which was applied to all EPI data to correct for spatial distortion.

**Image Analysis Algorithm:** The analysis method operates in the subject's space as this approach has reduced partial volume errors compared with analysis in standard space [3]. Regions of interest (ROIs) were manually defined on each subject's high resolution T1 weighted image according to anatomical landmarks, in a non-blinded fashion. Areas of haemorrhage, contusion, oedema or any visible lesions were excluded from the ROIs. The 6 regions of interest used in this study were the brain stem, left and right hemispheres, left and right frontal lobes and the whole brain. All the datasets were brain extracted from the surrounding non-brain tissues using a standard algorithm [4]. Subjects' high-resolution anatomical scans were re-sampled to the native resolution of the image being analysed (e.g. quantitative T1 or T2 maps) and the resultant transformation matrix was applied to the ROI masks to transform them to the native resolution of that same image. Finally, each subject's white matter regions were identified using a standard segmentation algorithm [5] and these were applied on the ROI masks to remove non-white matter tissues from the ROIs. ROI masks were then applied to quantify the dataset to be analysed.

**Scan Analysis:** Quantitative T<sub>1</sub> and T<sub>2</sub> times and mean diffusivity (MD) values were calculated on a pixel by pixel basis and analysed to determine the mean values for each of the ROIs. Group comparisons were made by t-test (SPSS 17). The first statistical analysis compared the entire patient group with the control population. Further statistical analysis comprised of comparison of the control population with patients grouped according to visible lesion location (either on CT, anatomical MRI or both) in either right or left hemisphere to determine whether the quantitative mapping revealed hemispheric diffuse damage extending beyond any discrete lesion. T<sub>1</sub> and T<sub>2</sub> values are presented in milliseconds, and MD values in  $\times 10^{-6} \text{mm}^2 \text{s}^{-1}$ .

ROI	Control Group n=20			Patient Group n=24			Patients with left sided lesion n=7			Patients with right sided lesion n=13		
	T <sub>1</sub> WM	T <sub>2</sub> WM	MDWM	T <sub>1</sub> WM	T <sub>2</sub> WM	MDWM	T <sub>1</sub> WM	T <sub>2</sub> WM	MDWM	T <sub>1</sub> WM	T <sub>2</sub> WM	MDWM
brainstem	952±26	94±4	1043±105	957±49	92±4	1056±147	964±28	92±3	991±174	964±58	92±4	1072±134
left frontal	843±30	81±3	739±24	854±40	81±3	745±54	<b>881±37</b>	83±4	<b>765±21</b>	851±33	81±2	732±72
right frontal	839±30	82±3	729±21	849±41	82±2	744±15	878±39	83±3	<b>747±10</b>	845±38	81±2	<b>744±15</b>
left hemisphere	893±31	82±2	779±23	900±42	82±2	787±29	929±41	84±3	797±36	893±36	81±2	779±29
right hemisphere	891±33	82±2	766±22	899±46	82±2	777±18	927±42	83±3	782±26	894±44	81±2	775±12
whole brain	892±32	82±2	772±22	900±44	82±2	782±22	928±41	83±3	789±31	893±40	81±2	777±19

### Results

No significant differences were found between the controls and the patient group as a whole. Statistical analysis performed on patients grouped according to visible lesion location revealed a significant increase ( $p \leq 0.05$ ) in the mean diffusivity of NAWM in the frontal lobe on the side containing the lesion, when compared to controls. There was a significant increase in the T<sub>1</sub> value in the frontal lobes of those with a left sided lesion, but not in those with a right sided lesion. There was no significant difference in T<sub>2</sub> values between either group and the controls.

### Discussion

In mild TBI patients with a visible lesion, DTI has revealed changes in frontal lobe NAWM on the ipsilateral side. These changes were not detected using T<sub>1</sub> and T<sub>2</sub> quantitative MR relaxometry, and were not visible on CT or anatomical MRI scans. The increase in MD observed is consistent with the findings of other investigators and may represent damage to neuronal tissue [6]. Frontal lobes play a major role in executive function, and this damage may account for the symptoms commonly seen in these patients such as memory loss, inability to concentrate, irritability and depression.

**References:** [1] NICE Clinical Guideline 56. Head Injury: Full Guideline. 2007, NIH & CE. [2] Lee, H., et al., Journal of Neurotrauma, 2008. **25**(9): p. 1049. [3] Aribisala et. al., ISMRM 2009,4771. [4] Jenkinson et. al., Eleventh Annual Meeting of the Organization for Human Brain Mapping, 2005. [5] Zhang et. al.; *IEEE Trans. on Medical Imaging*, 20(1):45-57, 2001. [6] Lipton et al., Journal of Neurotrauma, 2008. **25**(11): p. 1335-1342.

**Acknowledgments** Sir Jules Thorn Charitable Trust for funding, Carol Smith, Louise Morris and Tim Hodgson for assistance with scanning.