

# Diffusional Kurtosis Imaging and Perfusion of the Thalamus and White Matter during the First Month of Mild Traumatic Brain Injury

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**Introduction:** Mild traumatic brain injury (MTBI) is major public health problem for which conventional imaging does not detect damage sufficient to account for long-term or permanently disabling cognitive impairment (1). In a previous cross-sectional study we reported that diffusion tensor imaging (DTI) and diffusional kurtosis imaging (DKI) (2) can supply complimentary information that may serve as a sensitive marker for possible early detection of injury in the thalamus and white matter regions of MTBI patients (3). The purpose of this study is to examine baseline structural and physiological differences in the thalamus and white matter regions of MTBI patients from controls within the first month of injury in a currently ongoing longitudinal investigation that is employing DTI, DKI, and arterial spin labeling (ASL) to better understand the pathophysiology of MTBI. These studies are the first to examine MTBI using DKI which, unlike DTI, measures non-Gaussian water movement and therefore provides unique information unattainable with DTI about tissue microstructural organization (2). Furthermore, we have employed a newly developed ASL sequence to measure perfusion in deep gray matter at high spatial resolution (4). The thalamus has also only been infrequently studied in MTBI despite its influence over many neural pathways that, if impaired, could produce much of the clinical non-focalized sequelae associated with this condition.

**Methods:** Fourteen adult patients with MTBI (11 male, 3 female; mean age 35.7 yrs  $\pm$  10.4) were recruited within an average of 24.9 days  $\pm$  17.3 since injury in accordance with diagnostic criteria of the American Congress of Rehabilitative Medicine (5) along with six gender and age matched controls (5 male, 1 female; mean age 35.5 yrs  $\pm$  13.2). The study was IRB approved and all participants provided informed written consent. Experiments were conducted on a Siemens 3T whole-body MR scanner (Magnetom Trio, A Tim System). DKI was applied to 28 axial slices with thickness = 2.7 mm, TR = 3700 ms, TE = 96 ms, FOV = 222 x 222 mm<sup>2</sup>, and voxel size = 2.7 x 2.7 x 2.7 mm<sup>3</sup>. Image acquisition was performed by means of a twice-refocused spin echo diffusion sequence (6) using six b-values (0, 500, 1000, 1500, 2000, and 2500 s/mm<sup>2</sup>) and 30 different diffusion encoding directions for each nonzero b-value. Segmented True-FISP ASL was applied to one axial slice positioned at the level of the basal ganglia with thickness = 8 mm and included a FAIR preparation with TI = 1200 ms and a steady-state precession readout with FA = 50°, TR = 4.2 ms, TE = 2.1 ms, FOV = 256 x 256 mm<sup>2</sup>, and voxel size = 1 x 1 x 8 mm<sup>3</sup>. A FOCI pulse was applied every 3 s to allow for recovery of longitudinal magnetization and a pair of images were also obtained at TI<sub>0</sub> = 100 ms to correct for off-resonance effects. Data analysis was conducted by a single reader blinded to subject group.

Three-dimensional motion correction and spatial smoothing was applied to DKI data using a Gaussian filter (FWHM = 3.875 mm) and mean kurtosis (MK), fractional anisotropy (FA), and mean diffusivity (MD) maps

Brain region	Measure	Controls	MTBI	Controls vs MTBI
		Mean $\pm$ SE	Mean $\pm$ SE	P-values
Thalamus	MK	0.89 $\pm$ 0.03	0.73 $\pm$ 0.02	< 0.01
	FA	0.30 $\pm$ 0.01	0.25 $\pm$ 0.01	< 0.01
	MD	0.90 $\pm$ 0.05	0.99 $\pm$ 0.03	< 0.01
Internal capsule	MK	1.11 $\pm$ 0.06	0.95 $\pm$ 0.03	< 0.01
	FA	0.55 $\pm$ 0.05	0.46 $\pm$ 0.02	< 0.01
	MD	0.85 $\pm$ 0.02	0.87 $\pm$ 0.02	< 0.01
Splenium of corpus callosum	MK	1.21 $\pm$ 0.04	1.09 $\pm$ 0.03	< 0.01
	FA	0.73 $\pm$ 0.03	0.70 $\pm$ 0.03	0.10
	MD	1.01 $\pm$ 0.04	1.09 $\pm$ 0.05	0.06

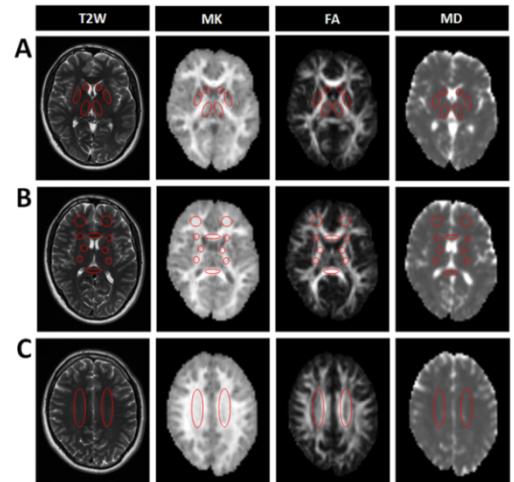
**Table 1.** DTI and DKI measurements in regions where MTBI patients showed significant differences from controls.

**Results:** Examples of MK, FA, MD, and qualitative perfusion maps obtained from MTBI patients are shown in Figs. 1 and 2. DTI and DKI measurements in regions where MTBI patients displayed significant differences from controls are reported in Table 1; these included the thalamus, the internal capsule, and the splenium of the corpus callosum. Deep gray matter regions where MTBI patients displayed significant differences in perfusion from controls are reported in Fig. 3; this included only the thalamus. Regression analyses showed that in MTBI patients thalamic perfusion was significantly correlated with MK in frontal white matter ( $r = 0.77$ ,  $P < 0.01$ ) and the centrum semiovale ( $r = 0.75$ ,  $P < 0.01$ ).

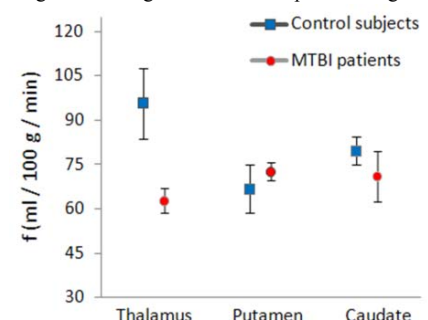
**Conclusions:** We have shown the feasibility of using DKI and ASL to investigate changes in MTBI patients within one month of injury. DKI appears to provide additional and complementary information to DTI about the degree of diffusional heterogeneity in tissue. Our results suggest that alterations of perfusion in the thalamus are associated with structural changes in frontal white matter and the centrum semiovale and may be of primary and/or secondary origin related to direct vascular damage, injury to axons that innervate blood vessels, and modifications in neuronal microcirculation requirements. Certain regions, such as the thalamus, the internal capsule, and the splenium of the corpus callosum may be important to identifying individuals at high risk of developing a complex persistent long-term condition. We plan to further evaluate these preliminary results as part of an ongoing longitudinal study with respect to diagnostic measures for post-concussion syndrome and neurocognitive performance.

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**References:** 1. Report to Congress on mild traumatic brain injury in the United States, Atlanta, GA: CDC; 2003; 2. Jensen JH, et al, NMR Biomed 2010;23:698-710; 3. Grossman EJ, et al, Proc ISMRM 2010;18:4484; 4. Grossman EJ, et al, JMIR 2009;29:1425-1431; 5. Esselman PC, et al, Brain Injury 1995;9:417-424; 6. Reese TG, et al, MRM 2003;49:177-182; 7. Buxton RB, et al, MRM 1998;40(3):383-96.



**Fig 1.** Representative T2W images and corresponding MK, FA, and MD maps (A, B, C) from one 36 year old male MTBI patient. Locations of ROIs are indicated in red.



**Fig 3.** Means and standard errors for perfusion measured in deep gray matter ROIs. The only region where MTBI patients significantly differed from controls was in the thalamus, where  $P < 0.01$ .