Measurement of Deep Gray Matter Perfusion in Acute Mild Traumatic Brain Injury Using Segmented True-FISP ASL

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Introduction: Mild traumatic brain injury (MTBI) is a significant public health problem with potentially serious long-term or permanently disabling impairments **(1).** Biomarkers are missing for MTBI since conventional imaging approaches usually fail to reveal evidence of damage and the few lesions sometimes detected are localized to brain regions that cannot account for the origin of clinical non-focalized sequelae experienced by patients **(2).** The purpose of the current study is to examine if the thalamus and other functionally related deep gray matter structures play a potential role in the pathological development of acute MTBI and can provide a prognostic measure of subsequent brain damage by identifying physiological changes in blood flow that may occur even when lesions are absent from standard imaging techniques **(3)**. The thalamus, which has been sparsely investigated, influences many diverse neural pathways and, if impaired, could produce much of the morbidity associated with MTBI **(4)**. To conduct our assessment we have employed segmented True-FISP ASL, a technique we recently developed to measure perfusion in deep gray matter at high spatial resolution **(5, 6)**. In the following we present some preliminary results of our investigation.

Methods: Seven adult patients with acute MTBI (6 male, 1 female; mean age 38.9 yrs ± 10.4; range 25-56 yrs) were recruited in accordance with diagnostic criteria of the American Congress of Rehabilitation Medicine **(7)** and underwent MR imaging within a mean interval of 23days (range 3-56 days) after their traumatic incident. The same scanning protocol was administered to six age and gender matched healthy controls (5 male, 1 female; mean age 38.7 yrs ± 14.2; range 25-57 yrs). The study was IRB approved and all participants provided proper informed written consent. Experiments were conducted on a Siemens 3T whole-body MR scanner (Magnetom Trio, A Tim System). A segmented True-FISP ASL sequence was performed in which acquisition was from an 8 mm thick oblique axial slice positioned parallel to the AC-PC line at the level of the basal ganglia. The pulse sequence included a FAIR **(8, 9)** preparation in which TI = 1200 ms. A FOCI pulse was applied every 3 s to allow for recovery of longitudinal magnetization and had a slice thickness 2.5 times that of the imaging slice to compensate for imperfect slice profile. Other sequence parameters for the segmented True-FISP steady-state precession readout included: FA = 50°, TR = 4.2 ms, TE = 2.1 ms, image matrix size = 256 x 256, FOV = 256 mm, and a spatial resolution of 1 mm x 1mm x 8 mm. One label and one control image were acquired with eight averages. A pair of images were also obtained at TI_0 = 100 ms to correct for off-resonance effects using an approach described by Figueiredo et al. **(10)**. A separate scan was performed in the absence of IR pulses to obtain an M_0 estimate. During postprocessing analysis ROIs of uniform size were placed bilaterally in the thalamus, putamen, and caudate by a single reader blinded to subject group. Absolute perfusion in each localized region was quantified using a general kinetic model described by Buxton et al. **(11)** and T_1 values obtained from published works **(12)**.

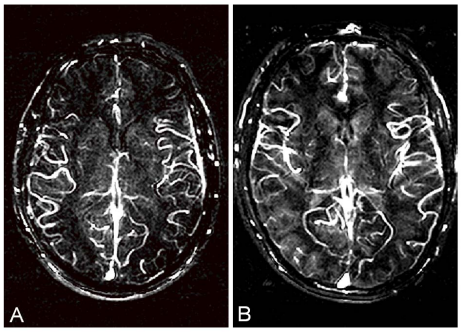

Figure 1. Qualitative perfusion maps acquired from (A) acute MTBI and (B) control subjects using segmented True-FISP ASL.

Results: Examples of qualitative perfusion maps obtained using the current technique are shown for acute MTBI and control subjects in Fig. 1A and B. Regions with a brighter signal denote greater local perfusion. Table 1 shows the mean and standard deviations for perfusion in each ROI. A student t-test for nonpaired data was used to compare acute MTBI and control subject groups for each ROI. Acute MTBI patients demonstrated significantly lower perfusion than controls in right ($p < 0.03$), left ($p < 0.01$), and both sides (bilateral mean) ($p = 0.01$) of thalamus and in left ($p < 0.01$) and both sides ($p < 0.01$) of caudate.

Regions		f (ml/100g/min)		p-values
		Acute MTBI	Controls	
Thalamus:	Right	60.6 ± 10.6	87.2 ± 25.7	**< 0.03**
	Left	56.7 ± 14.2	95.2 ± 28.9	**< 0.01**
	Both	58.6 ± 11.12	91.2 ± 26.0	**0.01**
Putamen:	Right	71.2 ± 17.0	72.8 ± 18.8	0.88
	Left	74.8 ± 18.1	63.7 ± 23.1	0.35
	Both	73.0 ± 14.3	68.2 ± 20.6	0.63
Caudate:	Right	61.6 ± 13.1	79.1 ± 17.7	0.07
	Left	64.6 ± 9.9	98.9 ± 15.7	**< 0.01**
	Both	63.1 ± 9.0	89.0 ± 16.2	**< 0.01**

Table 1. Mean and standard deviations for perfusion measured in deep gray matter ROIs.

Conclusions: We have shown the feasibility of using a segmented True-Fisp ASL sequence to detect differences in deep gray matter perfusion between symptomatic acute MTBI patients and healthy control subjects. Results indicate that a state of hypoperfusion may exist in the thalamus and caudate of such patients. These regions may be important to understanding the pathology of syndromatic MTBI and the identification of biomarkers. A larger sample size is required before drawing further conclusions. This research is part of an ongoing longitudinal study in which we intend evaluate changes in blood flow with respect to sensitive non-conventional MR measures of structural damage as well as diagnostic indicators of post-concussion syndrome and neurocognitive performance.

References: **(1)** Report to Congress on mild traumatic brain injury in the United States, Atlanta, GA: CDC; 2003; **(2)** Hammoud DA, et al, Neuroimaging Clin N Am 2002;12:205-216; **(3)** Ichimi K, et al, Neurol Res 1999;21:579-584; **(4)** Sherman SM, et al, J Neurophysiol 1996;76:1367-1395; **(5)** Grossman EJ, et al, Proc ISMRM 15, 2007:1417; **(6)** Grossman EJ, et al, JMRI 2009;29:1425-1431; **(7)** Esselman PC, et al, Brain Injury 1995;9:417-424; **(8)** Kim SG, MRM 1995;34(3):293-301; **(9)** Kwong KK, et al, MRM 1995;34(6):878-87; **(10)** Figueiredo PM, et al, JMRI 2005;21(6):676-82; **(11)** Buxton RB, et al, MRM 1998;40(3):383-96; **(12)** Lu H, et al, JMRI 2005;22(1):13-22.