

# Whole-brain oxygen extraction fraction is decreased in pediatric traumatic brain injury patients

D. K. Ragan<sup>1</sup>, and J. A. Pineda<sup>1</sup>

<sup>1</sup>Department of Pediatrics, Washington University School of Medicine, St. Louis, MO, United States

## Introduction

Traumatic brain injury (TBI) affects approximately half a million children each year and may result in death or significant long-term disability [1]. Impairments in brain oxygen metabolism have deleterious consequences on outcome. When studying such abnormalities, oxygen extraction fraction (OEF) measurements allow investigators to distinguish between perfusion deficits (high OEF) and abnormal oxygen utilization (low OEF) [2]. This distinction is fundamental when selecting and testing therapies aimed at improving oxygen metabolism after TBI. OEF is classically measured with using invasive techniques such as jugular bulb blood sampling or imaging techniques that involve radiation exposure (PET). Both approaches involve significant risks to children and make MR-based measurements preferable. We report our initial results using susceptibility weighted imaging to calculate OEF using measurements of brain deoxygenated blood, in both the macro[3]- or micro[4]-vasculature. We investigated the feasibility of using this method to test the hypothesis that children with TBI have abnormal brain oxygen utilization as reflected by low global OEF.

## Methods

All procedures were approved by our local institutional review board. Informed consent was obtained from the parent or legal guardian of study participants. Children who had suffered TBI were imaged within two weeks of injury. Studies were performed on Siemens 3.0T whole-body clinical MR scanners. Magnetic field maps were acquired with a three-dimensional dual-echo gradient-echo sequence with acquisition parameters: TE = 5.5 ms and 12.3 ms, TR = 25 ms, flip angle = 25°, FOV = 256 x 192 x 90 mm, matrix size = 128 x 96 x 60. A low-resolution image was constructed by filtering the longer-TE image. This was used to remove the background phase contribution, leaving only the smaller-scale vascular contribution. Rectangular regions of interest were drawn on sagittal images in the processed phase map. The regions were placed in the straight section of the sagittal sinus venosus at the inferior portion of the brain (Fig. 1). The phase change was converted to magnetic susceptibility according to [3]. Vessel orientation was only measured if it was greater than 15° from the magnetic field; otherwise the angle was assumed to be 0°. This would only produce a maximum error of 5% and the uncertainties in the measured angle would introduce more error than was avoided. An arterial blood saturation of 100% and hematocrit of 0.42 were assumed.

Injury severity classification was performed according to the Glasgow Coma Scale (GCS) at admission. A total of eight children with severe TBI (GCS 8 or less; ages 3 months to 17 years) and five children with mild-moderate TBI (GCS 9 or higher; ages 1 month to 17 years) were included in the study. Three healthy children (9 weeks, 11 years, and 17 years) with no history of head injury were scanned as controls. Statistical analysis was performed using ANOVA and Student's t-test.

## Results

Whole-brain OEF measurements were obtained for all patients. Mean  $\pm$  SD OEF in patients with severe TBI was 20.5  $\pm$  4.7%, while the mild-moderate TBI patients had an OEF of 31.4  $\pm$  7.9%. Control subjects had a mean OEF of 45.7  $\pm$  3.2% (Fig. 2). ANOVA revealed a statistically significant difference between the groups ( $p < 0.01$ ). Mild-moderate TBI subjects displayed a tendency towards lower OEF ( $p < 0.10$ ), and severe TBI patients had significantly lower OEF when compared to both mild-moderate TBI and control patients ( $p < 0.005$ ).

## Discussion

We found that OEF decreases during the subacute phase of recovery after TBI in pediatric patients, with a significant decrease in severe TBI patients. These results suggest ongoing metabolic dysfunction after TBI and are consistent with mitochondrial abnormalities and the resulting low oxygen utilization previously described in pre-clinical and adult human TBI studies [5]. Ongoing longitudinal studies including MRI measurements of cerebral blood flow will further test our hypothesis and will also explore the implications of our pathological findings on clinical outcome. Better understanding of the underlying metabolic abnormalities in children with TBI may facilitate future therapy development.

## References

- [1] Faul, et al., Centers for Disease Control and Prevention, National Center for Injury Prevention and Control, 2010.
- [2] Vespa, PM. *Curr Opin Crit Care*, 2006, 12(2):119-123.
- [3] Jain, et al., *J Cerebr Blood F Met*, 2010, 30(9):1598-1607.
- [4] He and Yablonskiy, *Magn Reson Med*, 2007, 57(1):115-126
- [5] Kawai, et al., *Acta Neur S*, 2009, 102:241-245.

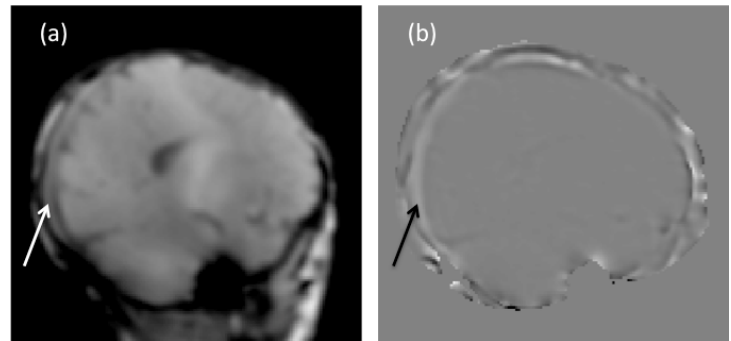


Figure 1: Anatomical image (a) and the corresponding field map (b) for one subject. An oblique sagittal slice is acquired to maximize visibility of the vessel. The superior sagittal sinus is highlighted in each image by the arrow. The field map in the brain is homogenous, except for the larger venous structures and the skull.

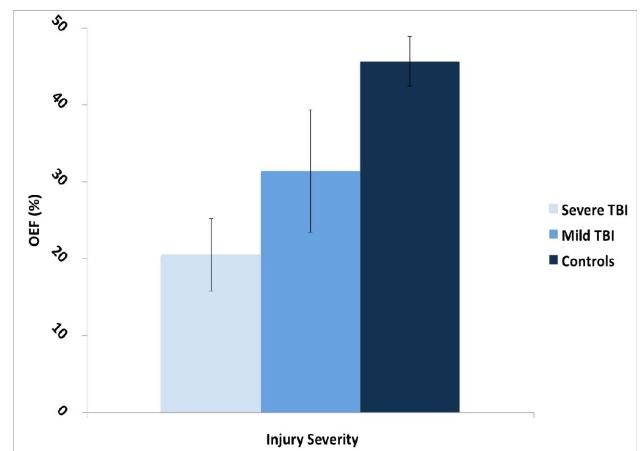


Figure 2: OEF values for TBI and control patients. We found that even mild-moderate TBI was associated with a decrease in OEF, which was statistically significant in children with severe TBI.