High Spatial Resolution MRI Unveils the Mystery of Moderate Traumatic Brain Injury

Qiang Shen[1], Lora Talley Watts[1], Shiliang Huang[1], Michael O'Boyle[1], Justin Alexander Long[1], and Timothy Q Duong[1]
[1]*Research Imaging Institute, The University of Texas Health Science Center at San Antonio, San Antonio, TX, United States*

Target audience: Researchers in high resolution imaging, traumatic brain injury and functional MRI.

Purpose: Although traumatic brain injury (TBI) has been investigated using variable imaging techniques, including MRI, the relatively low spatial resolution (>200x200 μm^2) has limited the ability to determine tissue injury type and to predict the tissue fate. Results previously reported are controversial, and are seemingly dependent on the severity of injury, e.g. increased or decreased apparent diffusion coefficient (ADC).[1, 2] Furthermore, prediction of tissue fate in TBI using low resolution data is very difficult. The goal of this study was to employ high spatial resolution (<100x100 μm^2) MRI to investigate moderate TBI longitudinally up to one month post injury. Diffusion, perfusion, T_2, angiography and functional MRI (hypercapnic challenge) were used to determine the anatomical, blood flow, vascular and functional changes after TBI. This study provides a better delineation of tissue injury types and assists in the prediction of tissue fate following TBI.

Methods: An open-skull, controlled cortical impact (CCI) model was used to mimic a moderate TBI in anesthetized rats (N=4).[3] The exposed dura was impacted directly using a pneumatic cortical impactor with an impact velocity of 5.0m/s, a 250**μ**s dwell time, and 1mm depth. Longitudinal high resolution MRI (diffusion tensor image, perfusion using continuous ASL, T_2 mapping, angiography and hypercapnic challenge fMRI) was performed on the day of the TBI (Day-0), and again on days 3, 7, 14 and 28 after TBI onset. A small surface image coil (ID=1.0cm) was used to achieve a small field of view (14.4x14.4 mm^2). The matrix size was 144x144 and the data was reconstructed to 256x256. Three 1 mm thick slices were acquired. Double shorts-EPI was used for DTI and cASL. MRA used 3D FLASH (192x192x192 matrix and 19.2x19.2x19.2 mm^3 FOV). Apparent diffusion coefficient (ADC), fractional anisotropy (FA), CBF, T_2 and hypercapnic challenge percent change maps were generated.[3] Maximum intensity maps were generated for MRA. Behavioral outcomes were assessed using cylinder and foot fault tests. Paired T-test was used for statistical analysis.

Results: **Figure 1** shows representative multi-slice ADC, FA, CBF and T_2 maps on Day-0. End point (Day-28) T_2-weighted image is also shown. Two types of MRI patterns were identified. The type-1 pattern tissue was located at surface of the brain in the impact area and showed reduced ADC, increased FA, reduced CBF and significantly increased T_2 (90±10%). The type-2 pattern tissue was located in deeper cortical regions and showed increased ADC, decreased FA, decreased CBF and slightly increased T_2 (17±3%). Group averaged (n = 4) Day-0 ADC, FA, CBF and T_2 differences from normal values of contralesional hemisphere for type-1 and type-2 patterns are plotted in **Figure 2**. Representative ROIs are shown in the insets. The normal values were $0.75x10^{-3}$ mm^2/s (ADC), 0.23 (FA), 1.1 ml/gram/min (CBF) and 38 ms (T_2). CBF deficits of type-1 and type-2 were not significantly different (p=0.6). T_2 increases of the type-2 tissue were significantly larger than those of the type-1 tissue (P=0.01). The end point T_2-weighted images indicated that the type-1 injury tissue died and the type-2 injury tissue survived.

CBF data (**Figure 3**) showed marked CBF reduction (-85±4%) on Day-0 and significant hyperperfusion (+161±31%) on Day-3 in the impacted area, which was associated with significant T_2 increases. By contrast, hypoperfusion (-56±9%) was widespread in areas surrounding and beyond the impacted region after Day-3, which could still be observed on Day-28. MRA data (**Figure 4**) further confirmed the observations of hyper-perfusion (green arrow) and hypo-perfusion (red and blue arrows).

While no significant anatomical (ADC, FA and T_2) changes were observed in the hypo-perfused regions on Day-28, hypercapnic challenge (5% CO_2) results showed significant cerebrovascular reactivity disruption (7% *vs* 62% CBF increases of normal tissue). Behavioral tests also showed significant motor functional deficits of the right forepaw (impact was over the left hemisphere) on Day-28.

Discussion & Conclusion: High spatial resolution MRI enabled clear identification of different types of tissue injuries in TBI and tissue fate predictions possible. Type-1 tissues are most likely found within the directly impacted tissue and cannot be rescued. In contrast, type-2 tissues are most likely the indirectly impacted tissue and may survive if the CBF is restored. Wide spreading hypoperfusion and vascular reactivity deficits were observed within the chronic phase and did not recover until one month post impact. Though hypoperfusion may not cause anatomical changes, it could cause functional and behavioral deficits. Histological studies need to be included to further confirm tissue fate. More sensitive behavior tests are needed to assess cognitive changes. In conclusion, longitudinal high resolution MRI provides the possibility of identifying types of tissue injury and to predict tissue fate following TBI.

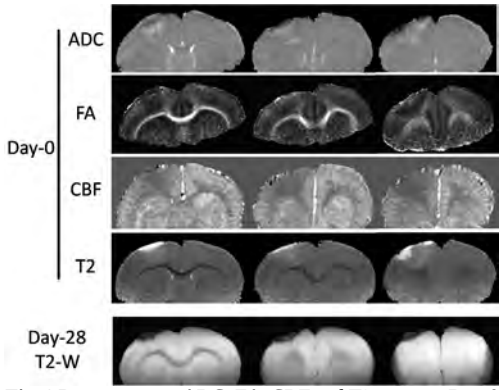

Fig. 1 Representative ADC, FA, CBF and T2 maps on Day-0 and end point (Day-28) T2-weighted image.

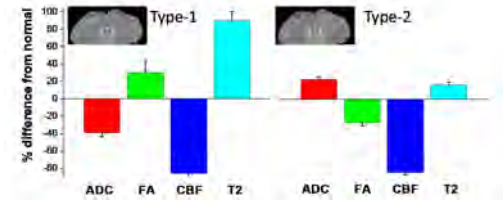

Fig.2 Group averaged Day-0 ADC, FA, CBF and T_2 differences from normal values of contralateral hemisphere for type-1 and type-2 patterns.

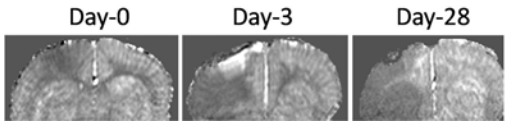

Fig.3 CBF maps of Day-0, Day-3 and Day-28 of a representative rat.

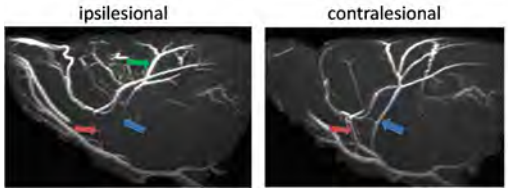

Fig.4 MRA of Day-3 showed hyper-perfusion (green arrow) and hypo-perfusion (red and blue arrows) in ipsilesional hemisphere.

References: 1. Barzo P, et al., J Neurosurgery 1997; 87: 900. 2. Xu S, et al., J Neurotrauma 2011; 28: 2091. 3. Watts LT, et al., J Neurotrauma 2014; 31: 1063. 4. Shen Q, et al., JCBFM, 2011; 31: 2076.