In Vivo Measurement of Blood Flow After Traumatic Brain Injury in Rats Using Susceptibility Weighted Imaging

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Introduction: Magnetic resonance imaging offers a non-invasive means to study brain trauma. In this paper, we evaluate the use of susceptibility weighted imaging (SWI) to study changes in the vasculature of the rat brain after mild traumatic brain injury. Previous methods of evaluating brain trauma have included MR spectroscopy, diffusion weighted imaging (DWI), MR angiography and perfusion weighted imaging (PWI). Each method offers its own advantages. MR spectroscopy successfully predicts the state of the tissue in terms of neuronal function, DWI shows areas of cellular disruption, MR angiography offers information about the presence of intact arterial vessels, and PWI can potentially show regions of reduced perfusion. On the other hand, SWI offers information about the intact structure of the venous system and about the oxygen saturation as well. These two added pieces of information can be used to improve the diagnosis of the state of the brain tissue.

Materials and Methods: Prior to TBI male Sprague-Dawley rats (350-400g) were anesthetized. The skull was exposed and a steel helmet was placed at bregma using dental cement. To induce brain injury, a 450 g weight was dropped from 2 m onto the helmet (1). A total of 6 rats were imaged in groups of two. The MRI scans were repeated over 4 days at 4 time points: Baseline scans, 4h, 24h, and 48h post TBI. One of the 6 rats died. All of the MRI measurements were performed on a 4.7-T Bruker AVANCE scanner. Four sequences were run: T_2 and T_1 weighted imaging, arterial spin labeling as a means to measure flow (2), and susceptibility weighted imaging. For all sequences, FOV= 40x40x24 mm^3. The SWI parameters were as follows: TR = 36 ms, TE = 15 ms, FA = 20°, with a matrix size 512 x 512 x 24, Nacq = 2. SWI is based on a fully flow compensated, high resolution, 3D gradient echo method (3,4). The flow compensation ensures that there is no flow induced phase in the SWI filtered phase images. The relative changes in flow are associated with the relative changes in oxygen saturation in veins (measured from the susceptibility changes). Therefore, blood flow can be measured indirectly using the SWI phase filtered images (5). We define the relative changes in phase between the background and vessel ($\Delta\varphi$) pre and post trauma as: $R_{pc} = -(\Delta\varphi_1 - \Delta\varphi_0) / \Delta\varphi_0$, then the relative change in flow $f = R_{pc} / (1 - R_{pc})$. This fractional change in flow is independent of blood vessel orientation. The change in phase can be measured from a profile along a straight line across blood vessel in the phase images (Fig. 1).

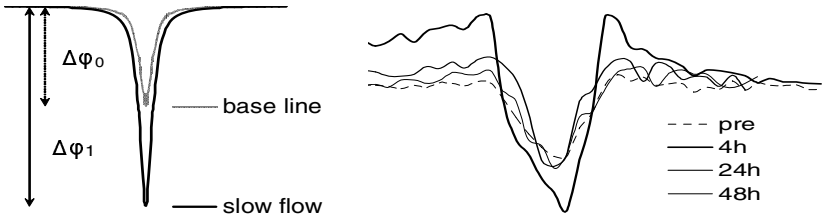

Figure 1: (A) Model profiles of phase across a vessel prior to trauma and post trauma (dark shaded line) on the left. (B) The experimental profiles across all four studies (right). The smallest phase jump is shown in the pre-trauma case, the largest 4 hours post-trauma, while the other two time points show a return to normal phase values.

Results: An example analysis of two vessels pre and post trauma for TBI showed in Figure 1 and 2. We chose 5 large blood vessels for analyses in each rat brain. The relative changes in flow at 4 h, 24 h, and 48 h post trauma are -0.26±0.10, -0.23±0.15, and -0.22±0.17, respectively. The blood flow decreased 20 to 30% in the 5 rats after TBI. The ASL results show that the means of the cbf values of medial dorsal cortex tended to recover but those of the hippocampus got worse.

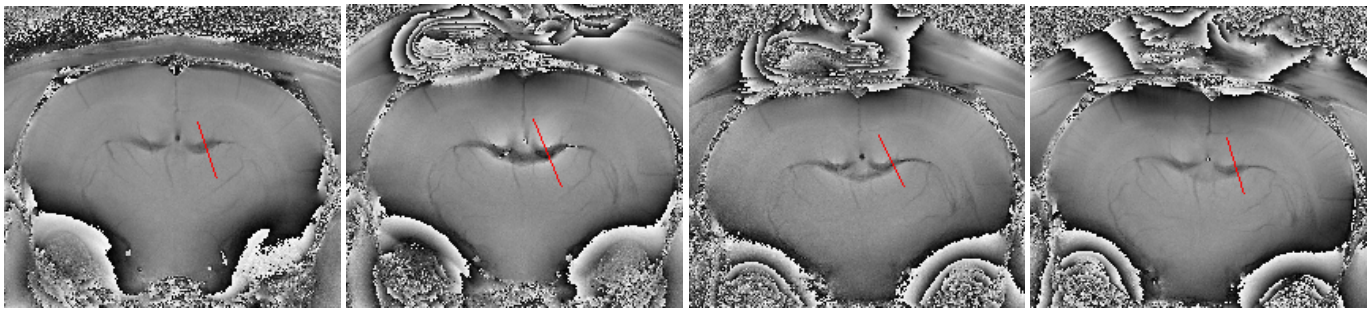

Figure 2: Four time points in a single rat showing the change in phase from pre-trauma to 4 h, 24 h and 48 h post trauma (left to right). It can be seen visually that the phase in the large and small vessels decreases after trauma and have returned to normal at 48h.

Discussion and conclusion: Traumatic brain injury is difficult to follow with most imaging methodologies. We have shown here that it is possible to visualize changes in oxygen saturation in the veins of a rat post-trauma. By assuming a deoupling of the CMRO2 from flow, the changes in phase pre and post trauma have been shown to correlate with expected reductions in flow from the literature and from the ASL changes. SWI should prove to be an important means by which to monitor changes in the rat brain both in terms of vascular damage to the venous system and oxygen saturation changes.

References: 1. Petrov TH, Steiner J, Braun B, Rafols JA., Neuroscience 2002;115(1):275-283; 2. Detre JA, Leigh JS, Williams DS, Koretsky AP., Magn Reson Med 1992;23:37-45; 3. Haacke EM, Lai S, Reichenbach JR, Kuppusamy K, Hoogenraad FGC, Takeichi H, Lin W., Human brain mapping 1997;5:341-346; 4. Reichenbach JR, Barth M, Haacke EM., J Comput Assist Tomogr. 2000;24:949-957; 5. Haacke EM, Brown RW, Thompson MR, Venkatesan R., Magnetic resonance imaging: physical principals and sequence design. New York: A. John Wiley & Sons; 1999. p 741 - 779.