Multi-echo Susceptibility Weighted Imaging of Blast Induced Traumatic Brain Injury in Rodent Model

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Introduction: Traumatic brain injury (TBI) due to blasts by improvised explosive devices (IEDs), is increasingly seen in several countries. It causes various neuropsychological dysfunctions such as attention deficit, working function, motor skills etc in both animals and humans. Susceptibility weighted imaging (SWI) $^{[1, 2]}$ allows improved detection of paramagnetic hemorrhagic blood components based on their magnetic susceptibility effects. SWI is sensitive to venous blood and can be used to visualise the micro vessels, which is useful in the analysis of TBI. SWI with multiple echoes yields good signal to noise ratio (SNR) as well as contrast-to-noise ratio (CNR)^[3]. In the present study, we explore the blast induced TBI using multi- echo SWI on rodent model.

<u>Methods:</u> <u>Blast Test Set-up</u> 5 kg of 2,4,6-trinitrotoluene (TNT) with a penta-erythritol tetra-nitrate (PETN) booster was detonated at 1 m height in each blast. Blast sensors were used to monitor the intensity and duration of blast over pressure (BOP) exposure. Metal cages along with the pressure transducer were set up at 2 m and 3 m alternately from the blast source. All the animals were randomly grouped into 1) Sham: where the subjects were not exposed to blast but anaesthetized; 2) High Blast (HB): where subjects were exposed to a single blast at ~480 kPa BOP at 2 m from blast source; 3) Low Blast (LB): where subjects were exposed to a single blast at ~180 kPa at 3 m from the blast source ^[4].

<u>MRI Data Acquisition</u> SWI and high resolution MPRAGE images were acquired on 7T ClinScan (Bruker BioSpin, Germany) equipped with 4 channel RAPID phased array coil before blast (Baseline, BL), on day 1, 3, 5, 14 and 28 after blast (# HB Rat = 6, #LB Rat = 6). Multi echo SWI was performed using TR/flip angle/slice thickness/#slice/FOV/matrix size/# average = 45 ms /20°/0.8 mm/64/36 mm × 27 mm/512×384/2. A total of 5 echoes with a central-echo time of 14.95 ms and an echo-spacing of 4.008 ms (the 5 acquired echo times used were: 6.79, 10.87, 14.95, 19.03, 23.11 ms) were acquired. MPRAGE images were acquired with TR/TE/flip angle/slice thickness/#slice/FOV/matrix size/# average = 2000 ms/1.6 ms/20°/0.5 mm/52/35 mm × 28.44 mm/256×208 (zero filled to 512 × 512)/2.Western blot for Hypoxia-inducible factor (HIF)-1a was also performed to see the changes in deoxygenation at cortex. A Java based ImageJ (National Institute of Health, USA) plugin was developed to quantify the R2* maps of the entire brain. The 5 echo data were fit to mono-exponential to obtain the R₂* maps ^[5].

<u>Results</u>: Minimum intensity projection (mIP) over 7 slices of 1st and 2nd echo at different time points are shown in Fig. 1 (top and middle rows respectively). The filtered phase images of 2nd echo at different time points are shown in the Fig. 1 (bottom). Calculated R_2^* map at day 3 is shown in the Fig. 1 (last image of bottom row). The phase profiles of vessels along the red line on phase images in Fig. 1 are shown in the Fig. 2. The largest jump is shown at day 1 and day 3 and the smallest is in BL. The decrease in signal in veins after blast is indicated by arrows (red and purple) in Fig 1. The arrows show the injury and dilation of vessels during the acute phase and recovery in the later phase. The smaller venous structures are better visualized in the 2nd echo (Fig.1 middle row). Western blot graph of HIF-1a for blast cortex is shown in Fig 3 which shows the significant change in de-oxygenation after blast.

Conclusions and Discussions: MPRAGE images at different time points showed no visible trauma where as the SWI show the change in veins in Fig. 1^[6]. Multi-echo SWI provides phase and R_2^* with better SNR and CNR, making it a sensitive technique to image blast induced TBI^[3, 7]. SWI at longer TE has stronger susceptibility effect yielding greater venous contrast, whereas SWI at shorter TE provides higher SNR and less off-resonance artefact^[7]. Larger veins are clearly shown at shorter TE, and smaller venous structures are better visualized at longer TE as in shown in Fig. 1^[7]. Multi-echo SWI may help to detect and classify the types and patters of blast induced TBI. The decrease in the signal in the veins after blast is due to the increase in deoxyhomoglobin^[7]. The HIF-1a result shows the same fact. From the phase profiles in Fig. 2, we can conclude that relative change in cerebral blood flow (CBF) in the post blast trauma is higher than compared to sham^[6,8]. R_2^* maps calculated from multi-echo SWI data may be used to measure of iron deposition in the brain. Also the calcification and haemorrhage can be easily differentiated with the help of filtered phase images. Overall, the multi-echo SWI is sensitive and very useful technique for TBI imaging and analysis^[6,7,8].



Fig. 1. mIP of 1^{st} (top) and 2^{nd} (middle) echo over 7 slices at different time points for LB. The darkening in the veins post blast is indicted by the arrows. The filter phase images (bottom) at different time points. R_2^* map (last image at bottom) at day 3.

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