Assessment of Whole Brain Temperature in Brain Injuries by 3D Echo-Planar Spectroscopic Imaging

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Target Audience: For researchers in the area of Imaging and Spectroscopic Biomarkers for Traumatic Brain Injury

Purpose: Traumatic brain injuries (TBI) result from a blow or jolt to the head. Mild traumatic brain injury may cause temporary dysfunction of brain cells. TBI can also result in bruising, torn tissues, bleeding and other physical damage to the brain that results in long-term complications or death. TBI increases brain temperature due to the incidence of neurogenic fever and raised brain temperature is linked to poor outcome. Large deviations between the brain and body temperature is observed after TBI [1]. Diffuse axonal injury and frontal lobe injury of any type increases the risk of neurogenic fever development following severe TBI [2]. A body temperature of 35 to 35.5 ^{O}C will reduce intracranial hypertension, maintains sufficient cerebral perfusion pressure without cardiac dysfunction or oxygen debt suggesting that this temperature range seems to be the optimal temperature to treat patients with mild and severe traumatic brain injury [3]. For many clinical applications single or multislice acquisition based proton MR spectroscopic imaging of the brain is limited in information for diagnostic assessment due to insufficient spatial coverage. A 3D MRSI approach with larger spatial coverage is highly desirable for assessing changes in cerebral metabolism and temperature; however, conventional 3D MRSI techniques require long acquisition times, resulting in limited clinical translation. 3D Echo-planar spectroscopic imaging (EPSI) permits rapid acquisition of MRS data from the entire brain [4]. Using the chemical shift separation between the water and NAA at each voxel of the brain, we can derive the whole brain temperature. In this study, we have implemented EPSI on a pre-clinical scanner to evaluate the brain temperature changes in rodents with mild TBI.

Materials and Methods: Adult male Sprague Dawley rats (280 – 300g) were subjected to focal brain injury using the lateral fluid percussion device. Animals were subjected to either 1) Sham (4mm-diameter hole, in the skull), 2) Mild (22.75 ± 0.75 psi) or 3) Severe (64.04 ± 1.49 psi) injury at 2mm lateral and 3.8mm posterior to bregma. The study set had three shams, 6 mild and 6 severe rats. MR imaging was performed on baseline (BL), hour -3, day-1, 3, 7, 14 and 28 to study the effect of TBI on brain temperature. ***In-vivo data collection: EPSI -*** A 3D EPSI sequence was implemented on 7T Bruker Clinscan pre-clinical scanner using Siemens IDEA VB15 and 3D spectroscopic data (Fig-1) was collected using spin echo (SE) based EPSI sequence, with interleaved water reference acquisition. A 4-channel phased array head coil (Rapid Biomedical, Germany) was used for the study. EPSI sequence was modified to acquire signal with a voxel resolution of 2 x 2 x 2 mm^3, FOV- R >>L - 100mm, A >> P - 40mm and F >> H - 10mm respectively, and TR1 / TR2 / TE of 3000/ 1200 / 70 ms, with 80º flip angle followed by 180º for re-focusing of metabolites. Metabolite and water spectral signals were acquired in a single TR in an interleaved fashion. The trapezoidal readout gradient lobes consisted of up and down ramp sampling (duration 20µs respectively) and plateau duration of 100 µs . Additional single voxel based MRS acquisition was performed with PRESS sequence at all time time points for validation. The MRS data was collected using a short TE/TR/TA=13 ms/4 s/~8 mins, voxel size of 3.5 × 2.0 × 3.5 mm^3, with (128 averages) and without (8 averages) water suppression. Eddy current compensation and scaling were performed using the water-unsuppressed spectrum for the calculation of spectral shift between the NAA and water peaks at every time point. The hippocampus temperature was computed using calibrated chemical shifts between water and NAA. We performed temperature calibration using brain phantom, EPSI sequence and derived the relation between temperature and chemical shift of NAA and water before in-vivo measurements. ***Imaging and Data processing*** **-** A 3D T1 weighted MPRAGE or T2 weighted turbo spin echo data was acquired to register the spectroscopic data for spatial reference of anatomical regions. K-space raw data was collected during the acquisition and post processed with MIDAS software [3]. Post processing included re-gridding of the K-space data from non-Cartesian to Cartesian co-ordinates, followed by a 4D Fourier transformation, quantitation of metabolites and creation of NAA, Cr, and Cho metabolite maps [3]. Phase correction and eddy current compensation was performed using the unsuppressed water data during pre-processing stage in MIDAS.

Results: The 3D EPSI was implemented on the 7T pre-clinical scanner. The temperatures of the brain at different locations were calculated using the chemical shift between NAA and water. The temperature distribution obtained form 12 different locations on a slice (Fig-2a) and the mean temperature from different locations of the brain at different time points (BL, Hour-3, and Day-3) for mild and severe TBI rats for one animal in each group are shown in Fig-2b. Paired samples T- test and independent samples Mann-Whitney test were conducted to check the correlation of temperature distribution on different days with respect to baseline and all the results are significant with $p < 0.05$. The brain temperature decreased with respect to baseline until day-3 in mild injury whereas the temperature increased at hour -3 and decreased to the baseline after day-14 in the case of severe injuries. Fig.3a shows mean temperature as observed at different time points and Fig.3b shows the variation in temperature across the hippocampal area in mild and severely injured rats. The results of EPSI were cross-validated using the SVS measurements.

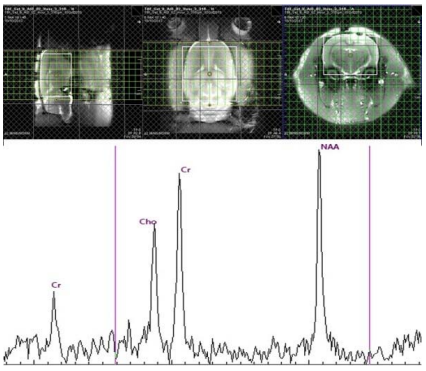
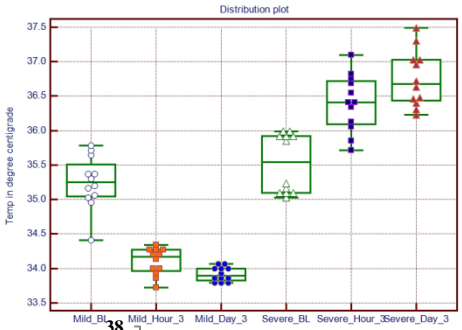


Fig. 1 EPSI data acquisition and the spectrum



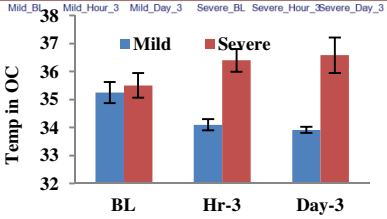
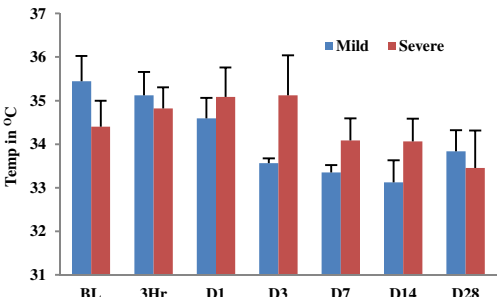


Fig. 2 Distribution plot of 12 different locations in the brain and the mean temperature in mild & severe TBI rats.



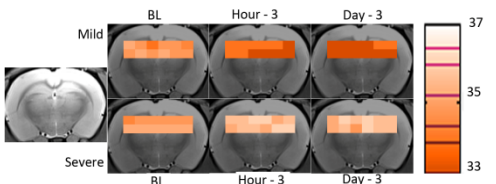


Fig. 3. Plot of mean temperature at time points and temperature maps for mild and severe at BL, hr-3 & day-3

Conclusions: We have implemented and validated a 3D EPSI sequence on a 7T Bruker Clinscan MRI/MRS scanner for mapping the brain temperature in mild and severe injuries. The spectra and the metabolite maps were computed using MIDAS Software. The feasibility of mapping whole brain temperature is demonstrated on the rat brain. The 3D EPSI sequence significantly reduces the acquisition time and permits investigation of brain temperature using smaller voxels. Reduction in acquisition time along with high spatial resolution allows translation of this technology within a clinical setting for investigating brain injuries. This technology can be used for whole brain metabolic imaging in animal models and in human for investigation of brain temperature due to stroke, traumatic brain injury, cancer, epilepsy.

References: [1] Childs C et al. Neurocrit Care. 2006; 5(1):10-4. [2] H J Thompson et al. J Neurol Neurosurg Psychiatry 2003; 74: 614–619. [3] Tokutomi T et al. Neurosurgery 2003 Jan; 52(1):102-11. [4] Andrew A. Maudsley et al. Magnetic Resonance in Medicine. 2001; 46(6):1072–78.