Echo planar spectroscopic imaging based temperature calibration at 7T and 3T for whole brain temperature measurement in rodents and humans

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

PURPOSE: Whole brain temperature mapping is of great interest for investigating traumatic brain injuries. Elevated body and brain temperature are linked to poor prognosis in patients with brain injury. The noninvasive measurements of brain temperature with magnetic resonance spectroscopy (MRS) have been developed [1, 2] and is considered as one of the most accurate method of measuring region specific temperature distribution in the brain. Earlier studies investigated brain temperature using either single voxel or CSI approaches to map the temperature. Experimental studies in phantoms [1] and experimental models [2] have shown close correlation between temperatures measured by MRS and temperatures measured using implanted probes. The chemical shift between the water and NAA has been used for calculating the temperature. Single-voxel-spectroscopy (SVS) and CSI approaches provides limited spatial coverage in the brain, whereas 3D Echo-planar spectroscopic imaging (EPSI), covers the entire brain for investigating the metabolite concentrations and temperature. Our study aims at implementation of EPSI, calibration and validation of the temperature measurement in brain phantoms using EPSI and SVS at pre-clinical and clinical scanners.

METHODS: ***Brain Phantom:*** Two-compartment glass phantoms (Fig. 1) were designed and fabricated to conduct the temperature calibration [3]. A phosphate buffer solution containing 61.25 mM NAA, 39.25 mM Creatine & 8.5 mM Choline, adjusted to physiological pH of 7.2 was filled in the inner chamber of the pre-clinical phantom. The inner chamber of the clinical phantom had metabolite concentration of 12.25 mM NAA, 7.85 mM Creatine & 1.7 mM Choline that was also adjusted to physiological pH of 7.2. ***Scanners:*** The pre-clinical and clinical scanners used for the study were 7T Bruker Clinscan using Siemens IDEA VB15, with 1H system frequency of 300.4 MHz, gradient engine BGA – 12 SA having maximum gradient amplitude 80 mT/m, and 3T Siemens MAGNETOM Tim Trio running Siemens IDEA VB17, with 1H system frequency of 123.2 MHz, with gradient system TQ-engine (45 mT/m @ 200 T/m/s) respectively. ***Temperature calibration setup:*** A 4-channel phased array coil (Rapid Biomedical, Germany) was used for the study at 7T, whereas a Tx/Rx CP Extremity coil was used for the study at 3T Clinical scanner to achieve a higher form fill factor. The phantoms were placed inside the coil and the temperature-controlled water was circulated in the outer compartment to calibrate the chemical shift differences of NAA and water at different temperatures using a high precision water circulation pump at a constant rate. An optical temperature probe (Neoptix®), 400 microns in diameter with outer protective jacket of pure virgin PTFE Teflon™ having a diameter of 1.15 millimeters, response time of less than 500 milliseconds; operating temperature range from -270 ^{O}C to 250 ^{O}C and a resolution of 0.1^{O}C was placed at the center of the inner chamber to measure the temperature of the phantom. 3D EPSI and single voxel PRESS was performed on the phantom using the pre-clinical 7T and 3T clinical scanners at different temperatures (30 ^{O}C – 40 ^{O}C at ~1^{O}C step). ***EPSI:*** - A 3D spin echo based EPSI sequence [4] was implemented on both 3T Siemens Clinical scanner and 7T Bruker Clinscan pre-clinical scanner using Siemens IDEA VB15 and spectroscopic data, with interleaved water reference acquisition. ***For 7T*** preclinical scanner EPSI sequence was modified to acquire signal with a voxel resolution of 2 x 2 x 2 mm, FOV- R >>L -100mm, A >> P - 40mm and F >> H - 10mm respectively, and TR1 / TR2 / TE of 3000/ 1200 / 70 ms, with 84º flip angle followed by 180º for re-focusing, and water excitation pulse of 20º flip angle. ***For 3T clinical scanner*** in plane resolution of 5.6 x 5.6 mm and 7.5 mm slice thickness; TR1 / TR2 / TE of 2000/ 700 / 70 ms; 2 averages, FOV- R >>L - 280mm, A >> P - 180mm and F >> H - 60mm respectively and Flip angle of 73^{O}. ***EPSI processing*** - 3D T1 weighted MPRAGE or T2 weighted turbo spin echo data was acquired to register the spectroscopic data for spatial reference. EPSI sequence was tested and validated on a brain phantom; K-space raw data was collected during the acquisition and post processed with MIDAS software [4]. Post processing included re-gridding of the K-space data from non-Cartesian to Cartesian co-ordinates, followed by a 4D Fourier transformation, for quantitation of metabolites and creation of NAA, Cr, and Cho metabolite maps [4]. Metabolite and water spectral signals were acquired in a single TR in an interleaved fashion. Phase correction and eddy current compensation was performed using the unsuppressed water data during pre-processing stage in MIDAS [4]. In addition to EPSI, we also performed SVS with TR/TE – 4000/13 ms; 7 x 7 x 7 mm voxel placed at the centre of the inner compartment; water-suppressed (with 16 averages) and water-unsuppressed (with 2 averages) were acquired. The SVS acquisition in 3T was performed with TR/TE – 2000/30 ms; 15 x 15 x 15 mm voxel, water-suppressed (24 averages) and water-unsuppressed (2 averages) acquisition. The relation between NAA – Water chemical shift difference in ppm and temperature in ^{O}C of the brain metabolites was derived (Fig.2) using the experimental values (eq. 1) for both EPSI and SVS based spectra.

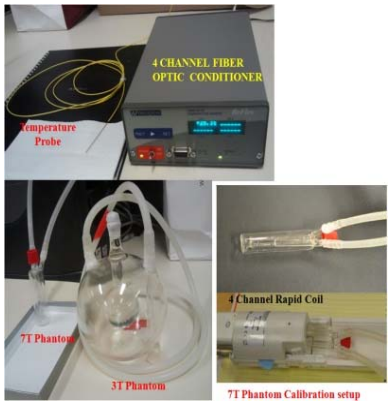

Fig. 1 Brain phantoms for 3T and 7T, Temperature probe and Signal conditioner

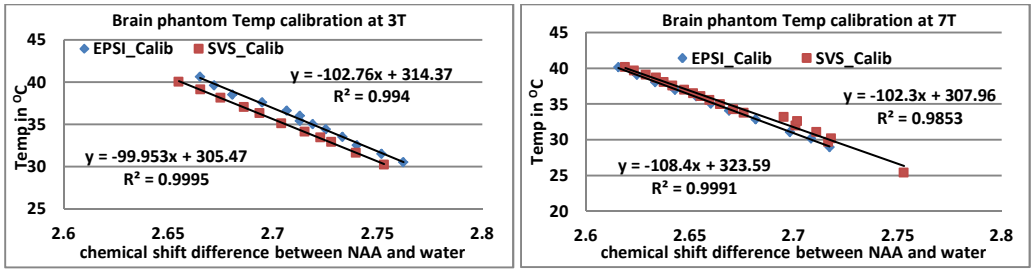

Fig. 2 Temperature calibration plots for 3T and 7T using EPSI and SVS based analysis

EPSI_3T : $\boldsymbol{Temp} = -102.76 * \delta_{(Water-NAA)} + 314.37$	SVS_3T : $\boldsymbol{Temp} = -99.53 * \delta_{(Water-NAA)} + 305.47$
EPSI_7T : $\boldsymbol{Temp} = -108.4 * \delta_{(Water-NAA)} + 323.59$	SVS_7T : $\boldsymbol{Temp} = -102.3 * \delta_{(Water-NAA)} + 307.96$

Table 1. Equations derived from the analysis of brain temperature calibration by EPSI and SVS on 3T and 7T

RESULTS: The chemical shift difference between water and NAA peaks were calculated from the spectra of EPSI and SVS for each temperature point for both EPSI and SVS as measured at 3T and in 7T. A least square error based linear relation between chemical shift differences of NAA and water and temperature was derived from the experimental results and is tabulated in Table – 1. The correlation coefficients between the actual and calculated temperature (using the equations) by spectroscopy were 0.9926 and 0.9995 for SVS and EPSI respectively at 7T, 0.9998 for SVS and 0.9970 for EPSI on 3T. We observed a shift of -0.0096 ppm/^{O}C between water and NAA in both EPSI and SVS at 3T and in 7T. Our results are in agreement with earlier work published by Zhu et al [5].

CONCLUSIONS: We have modified and implemented the 3D EPSI on pre-clinical scanner and calibrated the brain phantom for temperature measurement on both 3T (Clinical) and 7T (Pre-clinical) MRI/MRS scanners. The water – NAA chemical shift showed a linear dependence with respect to temperature as shown in the graphs. These calibration equations are used in our study to analyze the change in body and brain temperature due to brain injury in rodents and humans [6]. The EPSI additionally allows acquiring whole brain metabolite maps, which can be used for the study of changes in brain metabolism due to brain injury.

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