Intracellular sodium imaging in the brain via short-T2 component in bound sodium

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INTRODUCTION

Intracellular sodium concentration (ISC) is a potential endogenous imaging biomarker for noninvasive detection of pathological changes of cells in a wide range of conditions and diseases, from cancers to neurological disorders such as bipolar, epilepsy, and concussion (or mTBI). Change of ISC is typically detected using triple-quantum filtering (TQF) by taking advantage of the bi-exponential decay of T_2 relaxation in sodium binding to macromolecules which are in slow motion and mainly locate in intracellular space in the brain[1]. The TQF sodium imaging, when performed at high fields such as 3T or 7T, produces high specific absorption rate (SAR) and requires long scan times (~40 min) to meet the SAR constraints on humans, which are difficult to tolerate by patients. There is a critical need to develop alternative approaches for imaging the ISC that are adequate for clinical use and produce low SAR. Here we present a new method to meet this need. Our method directly measures the intensity of short component in the bi-exponential T_2 relaxation in bound sodium by subtracting between two single-quantum (SQ) sodium images acquired at ultrashort and long echo times respectively. As a single RF pulse is used in the SQ approach, the SAR limitation is mitigated. In addition, signal intensity from the short-T_2 component is comparable to that in the SQ image and thus has the potential to increase SNR by 10 times over TQF imaging. The subtraction methodology was first proposed by Hilal et al[2,3], but it is different from our method in implementation.

METHODS AND EXPERIMENTS

Methods A single-quantum sodium image at TE1 (e.g., 0.44ms) is used to quantify total (or tissue) sodium concentration (TSC). A second SQ image at TE2 (e.g., 5ms) is subtracted in magnitude from the first SQ image to produce a sodium image related to the short component of bi-exponential T_2 relaxation. The short-T_2 sodium image is used to quantify intracellular sodium concentration (ISC) (more precisely, it is a volume-fraction-weighted ISC or vISC). ***Experiments*** The proposed method was tested on phantoms and brain tumor patients on a 3T MRI scanner (Magnetom Trio Tim, Siemens Medical Solutions, Erlangen, Germany) with a dual-tuned (^{1}H-^{23}Na) volume head coil (Advanced Imaging Research, Cleveland, OH, USA), under an approved IRB protocol. A cylindrical phantom was filled with mixed agarose gel (46.4mM NaCl) and saline water (20.2mM NaCl). Four patients with high grade glioma (age 42-68 years) were scanned at three time points (pre-treatment, 1- and 2-month follow-ups). The TPI sequence[4] was used for the patient and phantom studies: FOV=220mm, matrix size=64, isotropic voxel size=3.44mm, hard RF pulse=0.8ms, flip angle=81° at SAR= 100% and TR=100ms, TE1/TE2=0.44/5ms, p=0.4, TPI projections=1596, averages=4, and TA=10.9min for each TE. For comparison, a lower-resolution TPI trajectory was used on the phantom for both short-T_2 imaging and regular three-90°-pulse TQF imaging: p=0.2, TPI projections=204, averages=4, and TA=3.27min for the short-T_2 imaging and 37.5min for the TQF imaging with 6-step phase cycling. ***Quantification*** An integrated two-point linear calibration (CSF TSC=145mM and the noise-only region TSC or vISC =0mM) was used for the quantifications of both TSC and vISC.

RESULTS AND DISCUSSION

Figure 1 demonstrates a better performance of the short-T_2 (ST2) imaging over the TQF imaging at the same spatial resolution, with 6.6-fold higher SNR (39.7 vs. 6.0) and 11-fold shorter acquisition time (3.27 vs. 37.5 min). The intensity on the short-T_2 image at the higher-resolution TPI acquisition is 41.1% of the SQ-image intensity at TE1 (or 68.5% after the correction for the component intensity fraction of 0.6). This intensity ratio is in good agreement with the concentration ratio of bound to total sodium (46.6 vs. 66.6 mM, or 70.0%). Figure 2 shows the TSC and vISC from a brain tumor patient studied. The vISC has an average value of 43.9 mM in the tumor tissue before treatment, a 2.93-fold increase from normal ISC (15 mM) in the neuron which is comparable to 3.27 folds in the literature[5]. The vISC showed a smaller region of the tumor but larger change in value between the three time points (43.9 -> 47.4 ->30.1 mM) than the TSC, suggesting vISC more specific to tumor tissue and, also, more sensitive to tumor response to treatment. However, the proposed method still needs optimization for clinical use as the subtraction may have distortions from the motion of the head/brain between the two TE acquisitions. The subtraction may also bring in a substantial intensity floor to the short-T_2 image when long component of T_2 relaxation is not long enough (e.g., <30ms). Our next step will be to further improve the technique by minimizing these distortions.

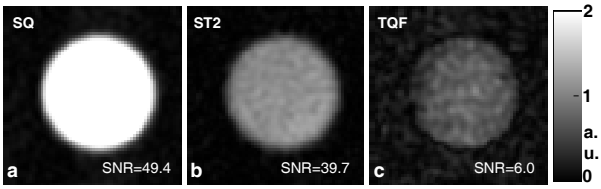

Fig. 1. Sodium images of the phantom: (a) SQ image at TE1 (0.44ms), (b) short-T2 image, and (c) TQF image. The images are displayed at the same window/level.

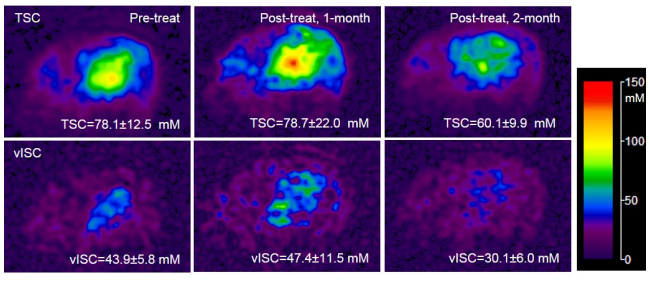

Fig. 2. Total (tissue) sodium concentration (TSC) and volume-fraction-weighted intracellular sodium concentration (vISC) maps (sagittal) of a brain tumor patient at three time points.

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