Mapping of glucose concentration in mild traumatic brain injury via glucoCEST

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Introduction

Tramatic brain injury (TBI) results in an instant increase in cerebral metabolic rates to fulfill the cellular energy requirements to maintain transmembrane potential. Glucose is the main energy souce of brain but after traumatic insult levels decrease dramatically. The energy substrate supply and consumption is crucial for the survival of traumatized brain tissue after TBI. In this study, we conducted the asymmetry analysis of non-chemical exchange saturation transfer (CEST) MRI experiments on 9.4T scaner to study the glucose distribution after mild TBI. Our results indicate that the CEST asymmetry analysis could be a sensitive marker to measure glucose distribution non-invasively after brain trauma.

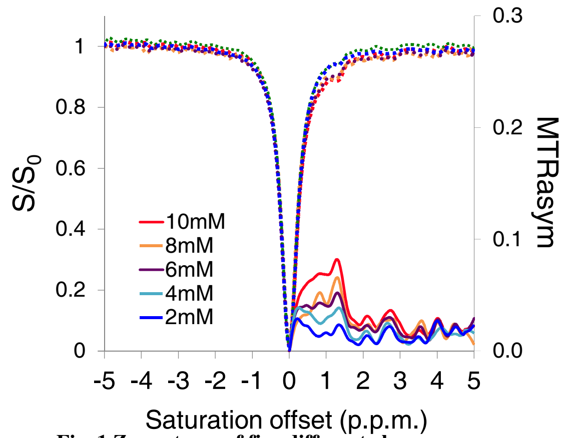

Fig. 1 Z-spectrum of five different glucose concentrations. The asymmetry curves separate the difference of glucose concentration from 2mM to 10mM.

Materials and Methods

To explore the feasibility and sensitivity of the glucoCEST on 9.4T scanner, we first conducted a phantom experiment including five tubes of different glucose concentrations (2mM~10mM). MR imaging was done using a volume coil as transmiter and a 8-channel surface coil as receiver in a Bruker 9.4T spectrometer. CEST data were acquired by 2D fast spin echo with (M_T) and without (M_0) MT preparation pulses: TR 2.5s, TE 10.39ms; resolution 200µm, slice thickness 0.8mm; MT preparation pulse: amplitude 1.5µT, duration 2ms. The MT offset frequences ($\Delta\omega$) were set from −1.6kHz to +1.6kHz with 100Hz stepping to detect the proton metabolites glucose (1.0~3.0 ppm)[1]. CEST magnetization transfer ratio (MTR) were derived by $1 - M_T/M_0$ and the MT asymmetry analysis is calculated by subtracting right ($-\Delta\omega$) and left ($\Delta\omega$) MT signal intensity around the water resonance frequency (0Hz) in unit of percentage. Procedure similar to the WASSR method[2] was applied to the CEST data processing to correct the B0 and B1 field inhomogenety[3]. After phantom experiment, the glucoCEST technique was conduct on a rodent TBI model to examine the glucose distribution before and after TBI. Three female 10-week-old Sprague Dawley rats were undergone TBI via a 2m height/450g diffuse injury weight drop model without focal injury. All imaging data were processed by in house Matlab scripts and ImageJ.

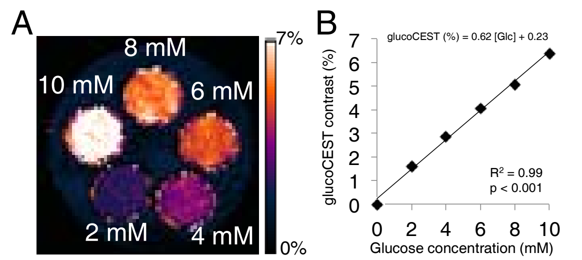

Fig. 2. The glucoCEST generates a linear relation to the glucose concentration. A strong correlation is seen between the glucoCEST contrast and the glucose concentration.

Results

The Z-spectrum of the five gluco tube is showing in figure 1, demonstration the feasibility of measuring glucose concentration via asymmetry analysis of the glucoCEST data. The asymmetry analysis of the glucoCEST sucessully differentiated five different glucose concentraion. The contrast measured from the glucoCEST is linear to the glucose concentration (Fig.2). For the in vivo study, the anatomical T2W images clearly show the consequence of mild TBI. The injured brain show the significant increase of ventricle size at 1 day post injury (Fig. 3A). The glucoCEST map clearly show the decrease of glucose concentration in the cerebral cortex of the brain post injury. glucoCEST asymmetry curves derived from z-spectrum of CEST MRI are capable of reflecting the changes of glucose following TBI (Fig. 3B).

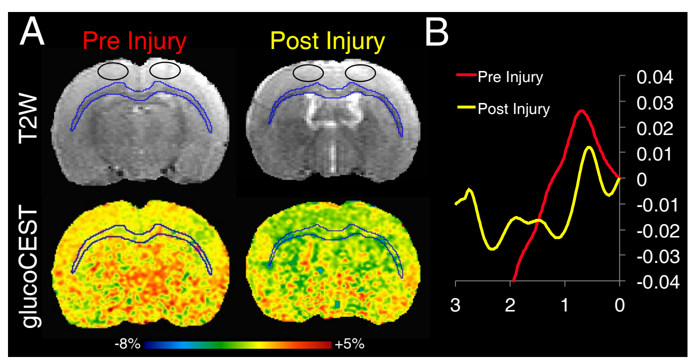

Fig. 3. glucoCEST detects the glucose distribution in a TBI rat brain. Glucose contrast is significantly lost in the cerebral cortex of the injured brain, indicating the decrease of glucose concentration after TBI. Acquiring from the circular ROIs in A, the glucoCEST asymmetry analysis differentiates the glucose concentration before and after TBI. Blue lines outline the area of white matter.

Discussion

The current study shows that the assymetry analysis of CEST effects is sensitive in the detection of glucose distribution after mild TBI. The immediate decrease of MT effects on all metabolites post injury also indicates that the water content significantly increased from edema immediately after injury. The results of MT assymetry analysis are comparable to previous reports that glucose largely decreases after traumatic insult. Further histological and molecular analysis are underway to confirm the findings.

Reference 1. Walker-Samuel et al., Nature Medicine, 2013, 18:1067-74. 2. Kim et al. MRM, 2009 61:1441-1450. 3. Stancanello et. Al, NMR Biomed, 2008, 3 136-49