Glutamate and Glutamine spectroscopic imaging in brain tumors at 3.0 T

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INTRODUCTION

Glutamate (Glu) and glutamine (Gln) metabolism (glutaminolysis) is important in glioma growth [1, 2]. Alterations in Glu and Gln concentrations in brain tumors were reported using single-voxel spectroscopy with optimized echo-time (TE) recently [3], but such techniques do not provide regional distribution information over the tumor mass, which is critical for understanding the proliferation of tumors. Here we report PRESS-based chemical shift imaging (CSI) of Glu and Gln with optimized-TE and present preliminary in-vivo brain data from a healthy volunteer and tumor patients.

METHODS

PRESS CSI with TE = 112 ms (TE1 = 32 ms and TE2 = 80 ms) was used for optimum differentiation of Glu and Gln. Experiments were carried out on a 3.0 T whole-body scanner (Philips Medical Systems) equipped with a body transmit coil for excitation and an 8-channel phased array head coil for signal reception. The method was tested in a spherical phantom with N-acetyl-aspartate (NAA) (20mM), creatine (Cr) (16 mM), Glu (20mM), Gln (6mM), myo-Inositol (mI) (8mM) and glycine (Gly) (2mM). The method was validated in a healthy volunteer. Clinical application included brain tumor patients. Written informed consent was obtained prior to scans. Following survey scans, T2w FLAIR images (axial and sagittal) were acquired to identify tumor regions. Acquisition parameters of CSI were: spatial resolution of 1 cm x 1 cm; data matrix of 20x16; slice thickness of 15mm; TR=1.2 s; 1024 complex sampling points; spectral width of 2000 Hz; number of averages=2. Water suppression was achieved using a four-pulse variable flip angle scheme. Signals from subcutaneous regions were suppressed using slice-selective signal suppression schemes. For scans in tumor patients, PRESS volume localization was adjusted to include most of the enhanced-FLAIR region and normal tissues. During the post-processing, residual water signals were removed using the HL-SVD tool of JMRUI [4] software. Frequency-drift corrections were carried out using in-house Matlab programs. LCModel software [5] was employed to analyze the spectra and estimate the metabolite concentrations. Basis sets for LCModel analysis were created using density matrix simulations [3] employing published chemical shift and coupling constants [6]. The metabolite levels in tumors were obtained with reference to NAA at 10 mM.

RESULTS AND DISCUSSION

Figure 1 displays CSI spectra obtained from the phantom. The spectral pattern from this phantom with metabolites at approximately physiological concentration ratios agrees with that of the single-voxel MRS data from normal brain [3]. The concentration maps, shown in Figs. 1c and 1d, gave uniform metabolite distribution within the phantom. Figure 2 presents in vivo CSI data from healthy brain. The spectral pattern in Fig. 2b agrees well with that in Fig. 1b. LCModel fits reproduced the in vivo data well, giving relatively low fit errors (CRLB). The CRLBs of Glu and Gln were in most spectra less than 10% and 20%, respectively. The concentration maps of NAA and Glu are shown in Figs. 2c and 2d, respectively. The NAA map indicated a uniform distribution of the metabolite throughout the brain, in consistent with a prior study [7]. The Glu map showed clearly a regional difference between gray and white matter. The concentration of Glu was estimated to be ~10 mM and ~5 mM in GM and WM, respectively, in good agreement with prior studies [7]. Figure 3 presents CSI data from a patient with malignant glioma (GBM). The spectra in Fig. 3b showed an abnormal pattern of Cho, Cr and NAA, which is commonly observed in brain tumors. In addition, the Glu-Gln composite signal exhibited an abnormal spectral pattern, most likely due to decreased Glu and increased Gln. For the center of the enhanced-FLAIR region, where the Cho (GPCPC) level was 3.7 mM (~ 6-fold higher than normal), the Glu and Gln concentrations were estimated to be 7.2 and 6.5 mM, with CRLB 4% and 5%, respectively. In conclusion, the optimized-TE PRESS CSI method can be used for imaging of Glu and Gln in the human brain.

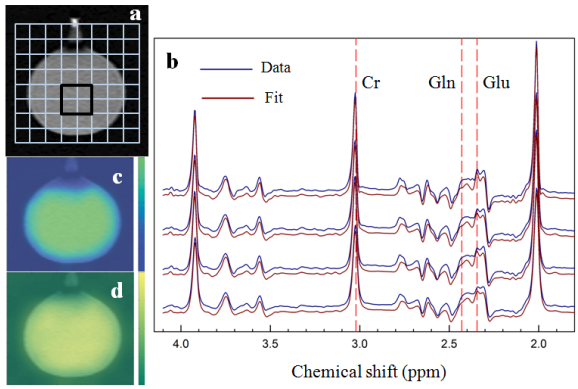

Fig **1**: (**a**) CSI FOV/VOI position in phantom. (**b**) Spectra from the four selected voxels (shown in Fig 1a as a black box) along with LCModel fits shown in brown (vertical lines indicate Glu, Gln, and Cr peak locations). (**c**) and (**d**) are Glu and Cr concentration maps respectively. Concentration maps are from 0-16 mM and 0-20 mM, for Cr and Glu respectively.

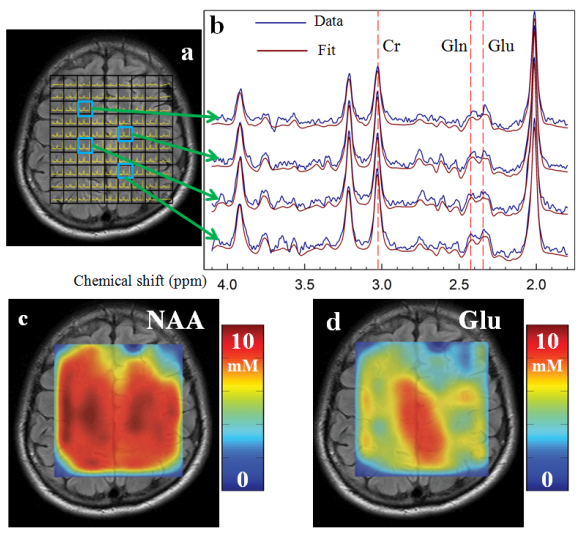

Fig 2: (**a**). Voxel selection in healthy volunteer with spectra. (**b**) shows representative spectra from the four selected voxels (vertical lines indicate Glu, Gln, and Cr peak locations). (**c**), (**d**) and (**e**) are Cr, Glu and NAA concentration maps respectively created from LCModel metabolite estimates.

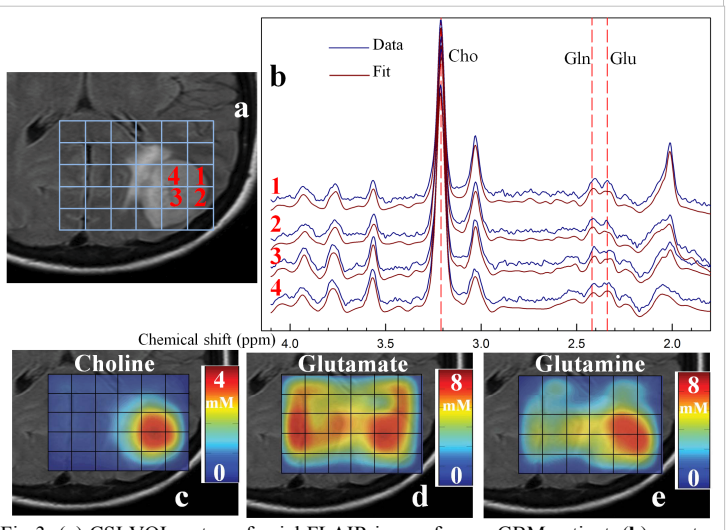

Fig 3: (**a**) CSI VOI on top of axial FLAIR image from a GBM patient. (**b**) spectra from the voxels labeled in (a). Concentration maps of Cho, Glu and Gln are shown in (**c**), (**d**) and (**e**), respectively. Gln is elevated in the tumor region.

REFERENCES

1. Sontheimer H. J Neurochem 2008;105:287-295. **2.** Hoew FA *et al*. NMR Biomed. 2003;16:123–131. **3**. Choi C *et al*. ISMRM 2010. Stockholm. p. 2180. **4**. Naressi A *et al*. MAGMA. 2001;12:141–152. **5**. Provencher SW. Magn Reson Med 1993;30:672-679. **6**. Govindaraju V *et al*. NMR Biomed 2000;13:129-153. **7**. Pan JW *et al*. Magn Reson Med 2010;64:1237–1246.