Multi-echo time approach for study of metabolic profiles in brain tumors at 3T

C. Choi[1], I. Dimitrov[1,2], D. Douglas[1], A. Patel[1], H. Huang[1], R. Deberardinis[3], J. Pascual[4], R. Bachoo[5], C. Malloy[1], and E. Maher[6]

[1]Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, Texas, United States, [2]Philips Medical Systems, Cleveland, Ohio, United States, [3]Pediatrics, University of Texas Southwestern Medical Center, Dallas, Texas, United States, [4]Neurology, Physiology and Pediatrics, University of Texas Southwestern Medical Center, Dallas, Texas, United States, [5]Neurology, University of Texas Southwestern Medical Center, Dallas, Texas, United States, [6]Internal Medicine and Neurology, University of Texas Southwestern Medical Center, Dallas, Texas, United States

INTRODUCTION

Proton MRS has been widely used for detecting abnormalities in metabolic profiles in brain tumors [1]. Spectra from healthy brains are characterized by prominent singlets from N-acetylaspartate (NAA), creatine (Cr), and choline (Cho). However, precise measurement of other metabolites is often elusive due to their relatively low signal strengths and spectral overlap between neighboring resonances. These complexities in ^{1}H-MRS can be alleviated with long TE approaches, with an advantage that TE optimization can improve the specificity of metabolite signals and suppresses the underlying macromolecule signals. Here, we present preliminary *in vivo* results of short- and long-TE approaches from different grades of malignant gliomas. Differentiation between glutamate (Glu), glutamine (Gln), glycine (Gly), myo-inositol (mIns), lactate (Lac) and lipids is discussed.

METHODS

The TE dependence of coupled-spin metabolites following point-resolved spectroscopy (PRESS) at 3T has been investigated with computer simulations that included the effects of slice-selective RF and gradient pulses. Single-voxel localization was obtained with a 9.8-ms 90° RF pulse (BW = 4.2 kHz) and a 13.2-ms 180° RF pulses (BW = 1.3 kHz), at an RF field intensity of 13.5 μT. Three pairs of PRESS subecho times, (TE_1, TE_2) = (32, 22), (32, 80), and (32, 214) ms, were selected for optimum selectivity of Glu and Gln, and used for *in vivo* measurements of metabolites in brain tumors. Experiments were carried out on a whole-body 3T scanner (Philips Medical Systems, Cleveland, Ohio, USA). A body coil was used for RF transmission and an 8-channel phased-array head coil for signal reception. For metabolite measurements, a single voxel was placed within tumor mass and normal tissues, based on MP-RAGE and T2-FLAIR images. The number of averages was 32, 64, and 128 for the three TEs, respectively. Acquisition parameters included sweep width = 2.5 kHz and number of sampling points = 2048. LCModel software [2] was employed to analyze the *in vivo* spectra. Published chemical shift and coupling constants were used in the simulation [3].

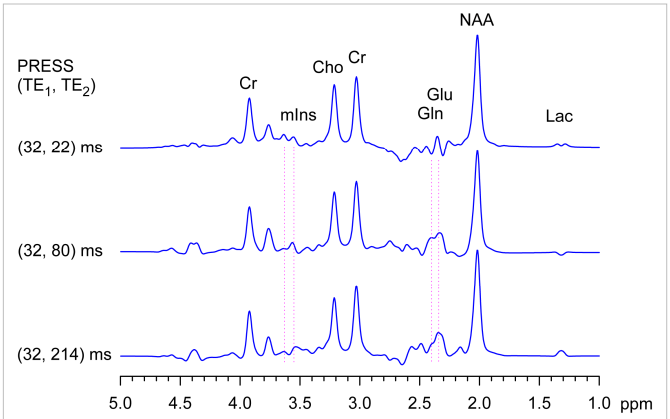

FIG. 1. Computer simulated ^{1}H-MRS spectra of brain metabolites at physiological concentrations for three PRESS subecho time pairs. Spectra are broadened to singlet linewidth of 6 Hz, relevant to *in vivo*.

RESULTS AND DISCUSSION

Figure 1 presents simulated spectra of brain metabolites at a physiological concentration ratio [3] for the three pairs of PRESS subecho times. For [Gln]:[Glu] of 3:10, Glu and Gln are not well resolved in the spectrum at (TE_1, TE_2) = (32, 22) ms, which was the shortest possible for the given RF and gradient pulses. However, at (TE_1, TE_2) = (32, 80) ms, the C4-proton spins of Glu and Gln give peaks at 2.35 and 2.4 ppm, respectively, leading to a composite multiplet pattern as shown in the figure. The lactate (Lac) signal at 1.3 ppm appears as a negative peak at (TE_1, TE_2) = (32, 80) ms and a positive peak at (TE_1, TE_2) = (32, 214) ms. For 3.5 – 3.7 ppm, the multiplet of mIns dominates the spectral pattern over the Gly singlet for [mIns]/[Gly] = 6.

Figure 2 presents ^{1}H spectra at the three PRESS TEs, from normal tissues (2a) and tumor masses (2b – 2d). In Fig. 2a, the spectral pattern is overall in agreement with the simulated spectra in Fig. 1. The composite multiplets of Glu and Gln at 2.2 – 2.5 ppm and the spectral pattern of mIns and Gly at 3.5 – 3.7 ppm are in consistent with those in Fig. 1. The signals at ~1.3 ppm in the short-TE spectrum are largely attributed to lipids. The lipids signals are reduced substantially in the long-TE spectrum due to their relatively short T_2, allowing to detect a small Lac signal. Fig. 2b shows spectra from a glioblastoma multiforme (GBM); NAA and Cr levels are substantially low. Spectra in Fig. 2c, also from a GBM, exhibit several spectral signatures different than normal. First, a large signal at 3.55 ppm is due to elevated Gly [4]. [Gly]/[Cr] was estimated, by LCModel, as ~1.7, with CRLB of 2% from the (32, 80) ms spectrum. Second, a signal at 1.3 ppm is most likely attributable to lipids, not Lac, because the signal is not inverted in the (32, 80) ms spectrum. Third, the Glu-Gln multiplet at ~2.4 ppm is different than normal, indicating an elevated Gln level. LCModel fitting gave [Gln]/[Glu] ≅ 1. Fig. 2d shows spectra from an untreated low-grade glioma. Elevated Lac level is clearly indicated from a negative 1.3-ppm signal in the (32, 80) ms spectrum. Gln is also elevated. From LCModel fitting of this spectrum, [Gln]/[Glu] and [Lac]/[Cr] were estimated as 1.4 and 0.5, respectively, with CRLBs of 6 – 9%. Further patient studies are currently underway.

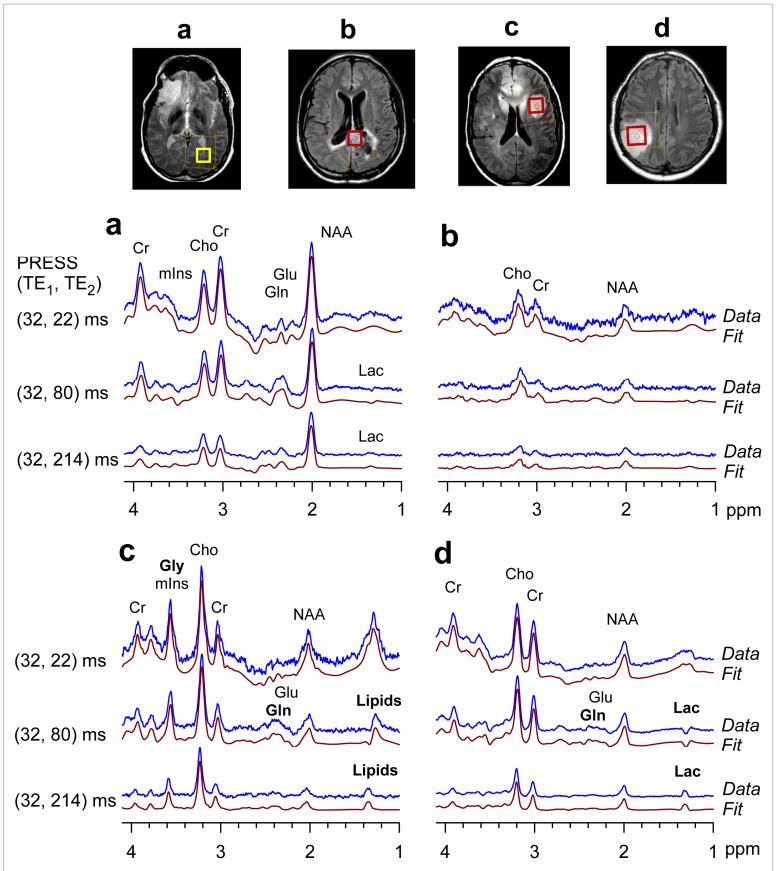

FIG. 2. ^{1}H-MRS spectra from normal (a) and three types of tumor tissues (b, c, d) are shown together with LCModel fits. Voxel size was 20x20x20 mm^3 in a, b, and c, and 25×25×25 mm^3 in d. Repetition time (TR) was 2 s. Spectra are normalized with respect to brain water signals at TE = 14 ms.

REFERENCES

1. Gillies RJ *et al*. Annu Rev Biomed Eng 2005;7:287-326.
2. Provencher SW. Magn Reson Med 1993;30:672-679.
3. Govindaraju V *et al*., NMR Biomed 2000;13:129-153.
4. Lehnhardt FG *et al*. NMR Biomed 2005;18:371-382.