Improved data analysis for two-dimensional J-resolved 1H-MRS: Application in brain tumors

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INTRODUCTION: Two-dimensional (2D) J-resolved spectroscopy may provide improved resolution for J-coupled resonances. Since data are acquired following a series of echo times, the method can be easily incorporated into an existing sequence, such as point-resolved spectroscopy (PRESS). When theoretical model spectra are available, phase-sensitive data analysis of *in vivo* data is feasible, giving detailed metabolic information, as demonstrated in recent studies in which spectral fitting was performed in brain 2D data using basis sets created from an idealized RF pulse sequence (1,2). Here, we present 2D J-resolved data analysis, on the data from tumor patients, which incorporated basis sets that were generated incorporating the 3D volume localization.

METHODS: 2D J-resolved spectroscopy was investigated for measurement of metabolites in 3 patients with glioblastoma multiforme (GBM). Experiments were carried out on a whole-body 3T scanner (Philips Medical Systems). Written informed consent was obtained prior to *in vivo* scans. A body coil was used for RF transmission and an 8-channel phased-array coil for reception. Volume localization was obtained with a 9.8-ms 90° RF pulse (BW = 4.2 kHz) and a 13.2-ms 180° RF pulse (BW = 1.3 kHz). Following survey image scans, T_2w FLAIR images (axial and sagittal) were acquired for identifying tumor masses. A 2×2×2 cm^3 voxel was positioned within the tumor region. Water-suppressed single-voxel localized PRESS data were acquired at 32 echo times (TE_1 = 32 ms; TE_2 = 26 - 491 ms, with increments (Δt_1) of 15 ms), using TR = 2 s, sw = 2500 Hz, number of sampling points = 2048, number of averages = 4 for each TE. Data were apodized with a 1-Hz exponential function along the FID time axis (t_2) and zero filling along the t_1 direction. The resulting 2048×64 matrix was Fourier transformed along the t_1 dimension, leading to a data matrix $D(t_2, \nu_1)$. These 64 FIDs were analyzed with LCModel software, using 64 basis sets constructed as follows: FIDs of 25 metabolites were calculated numerically for the 32 TEs, incorporating the PRESS slice-selective RF and gradient pulses and assuming T_2 of 200 ms for all metabolites. For each metabolite, a frequency-domain 4096×64 data matrix $D(\nu_2, \nu_1)$ was created with zero filling and 2D Fourier transformation. The phase undulation of the spectra across ν_1 was removed with zero-order phasing in the ν_2 domain. The resulting matrices of 25 metabolites were individually inverse Fourier transformed along the ν_2 dimension to obtain 64 LCModel basis sets in t_2 and ν_1 domains. Following LCModel analyses of *in vivo* 2D data, metabolite concentrations were estimated using the brain water signal as a normalization reference and assuming a normal-brain tCr concentration at 8 mM. Relaxation effects were assumed to be identical between metabolites and between normal brain and tumors.

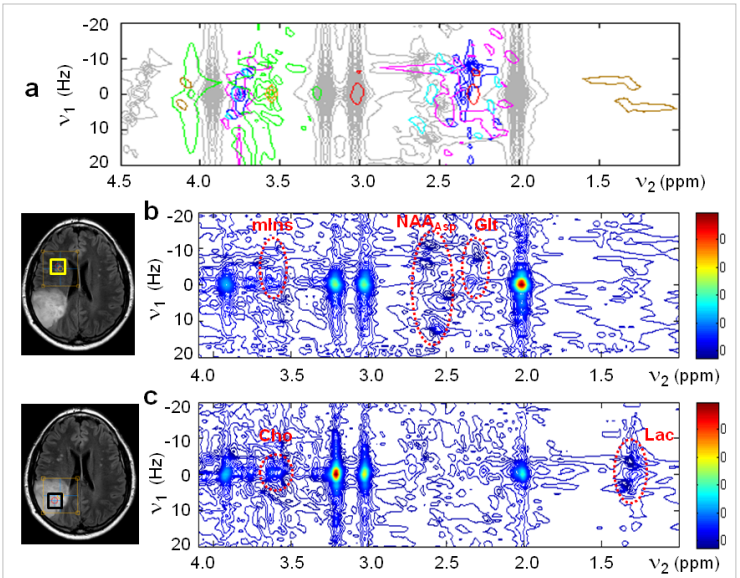

FIG. 1. (a) A contour plot of numerically-calculated 2D J-resolved spectra of Cr+NAA+Cho (gray), Glt (blue), Gln (magenta), GSH (cyan), GABA (red), mIns (green), Gly (orange), and Lac (brown) for physiological concentrations of the normal brain. Line broadening to singlet FWHM at 5 Hz was applied along the ν_2 direction. (b,c) Contour plots of *in vivo* brain 2D J-resolved data from (b) normal-appearing brain and (c) a tumor mass of a GBM patient.

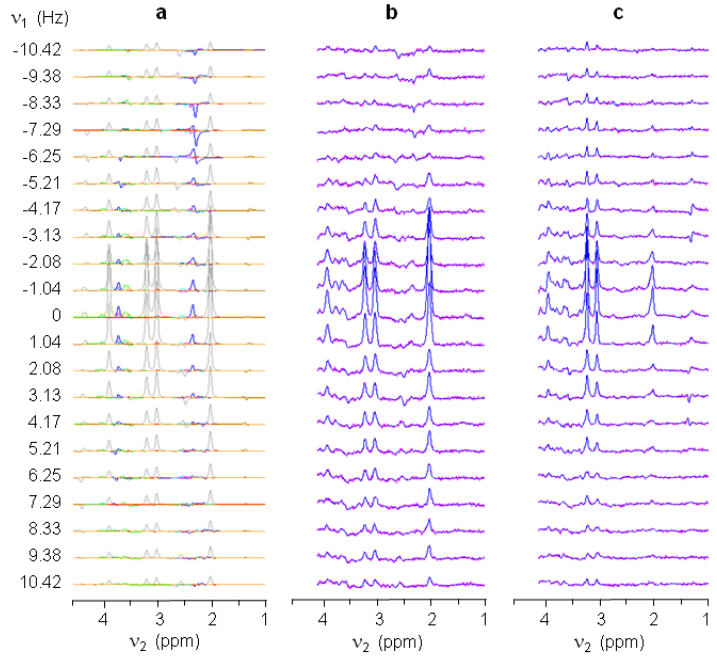

FIG. 2. (a) A stack of spectra (from Fig. 1a) are displayed for ν_1 from -10.42 to 10.42 Hz. Similarly, spectra from Figs. 1b and 1c are displayed in (b) and (c). In (b) and (c), spectra and LCModel fits are shown on top of each other (magenta and blue, respectively). In (a), metabolite signals are colored identically to Fig. 1a.

RESULTS and DISCUSSION: Figure 1 presents contour plots of PRESS 2D J-resolved spectroscopy data obtained from a GBM patient, together with theoretical data calculated for physiological concentrations of the normal brain and the same experimental parameters. While the singlet resonances of Cr, NAA and Cho (3.21, 3.02 and 2.01 ppm, respectively) exhibited high intensity at ν_1 = 0 Hz, J-coupled resonances were pronounced at non-zero ν_1 frequencies. The C4-proton resonances of glutamate (Glt) showed high intensity at (ν_2, ν_1) = (2.3 ppm, -7.5 Hz) compared to an in-phase signal at (2.35 ppm, 0 Hz) in both simulated and *in vivo* data. The NAA aspartate CH_2 resonances exhibited four temporal high-intensity spots between ν_2 = 2.5 - 2.7 ppm in Figs. 1a and 1b. Figure 1c, which was obtained from a tumor mass, showed a pronounced Cho singlet and smaller singlet signals of Cr and NAA. The Glt C4 proton and NAA coupled resonances were reduced due to decreased Glt and NAA levels in GBM. Lac showed clearly two high-intensity spots at $\nu_2 \approx 1.3$ ppm in Fig. 1c, which was not detectable in the normal brain region (Fig. 1b). The high intensity at 3.6 ppm in Fig. 1c is largely attributed to the Cho coupled resonances. Figure 2 displays individual spectra between $\nu_1 \approx \pm 11$ Hz, with increments of 1.04 Hz ($\approx (1/\Delta t_1)/64$)). The spectra in Fig. 2a were phase corrected, thus do not contain phase undulation which arises from Fourier transformation. These spectra represent LCModel basis sets that were used for analyzing *in vivo* spectra in Figs. 2b and 2c. In Fig. 2a, the Glt C4-proton resonance (blue) exhibited positive multiplets at $\nu_1 \approx 0$ Hz but large out-of-phase signals at $\nu_1 \approx$ -7.5 Hz, which correspond to the two temporal high-intensity spots in Fig. 1b. These spectral patterns of Glt were well reproduced in Fig. 2b. The percentage fit errors (CRLB) of Glt in spectra at ν_1 = 0 and -7.29 Hz were 4% and 7%, respectively. In Fig. 2c, Lac showed large signals at $\nu_1 \approx \pm 3.5$ Hz, corresponding to the two temporal spots in Fig. 1c. The concentrations of Glt, Gln and GABA were estimated to be 9.4±1.2, 3.6±1.1, and 1.1±0.8 mM (mean±SD, n = 3) in normal-brain regions. For tumors, Glt was decreased and Gln was increased. The metabolite estimates showed large SD, most likely due to the various tumor subtypes.

REFERENCES: **1.** Schulte RF and Boesiger P. NMR Biomed 2006;19:255-263. **2.** Jensen *et al*. NMR Biomed 2009;22:762-769.