Proton Spectral Editing for Separation between Lactate and Threonine in Human Brain In Vivo

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INTRODUCTION

Prior measurements of lactate (Lac) in human brain *in vivo* by either conventional spectroscopy or spectral editing have commonly focused on the resonance at 1.31 ppm. However, Lac overlaps with threonine (Thr) at this resonance. While Lac has resonances at 1.31 (C3) and 4.10 (C2) ppm (J = 6.93 Hz), Thr has five water non-exchangeable protons resonating at 1.31 (C4), 4.25 (C3), and 3.56 (C2) ppm [1]. The coupling strength between C2 and C3 protons is 4.92 Hz, and that between the C3 proton and the C4 methyl protons is 6.35 Hz. Thus, a simple detection of the resonance at 1.31 ppm will always record an overlap of Lac and Thr, as shown in Fig. 1. Here, we report proton MRS discrimination between Lac and Thr in human brain *in vivo*. A preliminary result from the human occipital cortex is presented.

METHODS

The resonances of the Lac C2 and Thr C3 protons, to which their 1.31 ppm resonances are coupled, differ by 0.15 ppm, which is ~19 Hz at 3.0 T. This difference affords an opportunity to separate the Lac and Thr signals at 1.31 ppm by means of spectral editing. Three separate scans have been employed to extract the Lac and Thr signals through J-difference editing. Three spectrally-selective 180° RF pulses were designed, see Fig. 2, and implemented within a single-voxel adiabatic-refocusing sequence; *i.e.*, 90 – HS180 – HS180 – editing 180 – HS180 – HS180. First, a double-band 180° pulse (D180) gave selective refocusing at 1.31 and 3.02 ppm for generating positive doublets of both Lac and Thr and for acquiring the Cr singlet simultaneously for use as a reference in phase correction. Second, a triple-band 180° pulse (T180-Lac) was designed for refocusing at 1.31 and 3.02 ppm, longitudinal inversion at 4.10 ppm, and no effect on 4.25 ppm, in order to induce a negative Lac doublet and a positive Thr doublet. The Cr singlet was refocused 180° out of phase. Third, another triple-band 180° pulse (T180-Thr) was designed for excitation at 1.31 and 3.02 ppm, longitudinal inversion at 4.25 ppm, and no effect on 4.10 ppm, in order to induce a negative Thr doublet and a positive Lac doublet. The refocusing of the Cr resonance was in the opposite direction. It follows that, at TE = 1/J, subtraction between the first (D180) and the second (T180-Lac) spectra will reveal the Lac signal, canceling the Thr signal, while the difference between the D180 and T180-Thr spectra will provide a Thr peak, canceling the Lac portion, Fig. 3. The Cr 3.02 ppm singlet is entirely recovered in both difference spectra. The echo time was optimized at 160 ms for all three types of scans.

In vivo tests of the filtering sequence were conducted on four healthy subjects. A 25×30×30 mm^3 voxel was positioned in the parieto-occipital cortex. Experiments were carried out at 3.0 T in an 80-cm bore magnet, interfaced to a SMIS console. A 28-cm diameter quadrature birdcage coil was used for RF transmission and reception. The density-matrix simulation was programmed with Matlab.

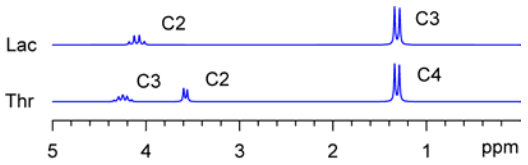

FIG 1. Calculated proton spectra of Lac and Thr, following a 90°-acquire sequence, for an identical concentration. Spectra are broadened to 2 Hz.

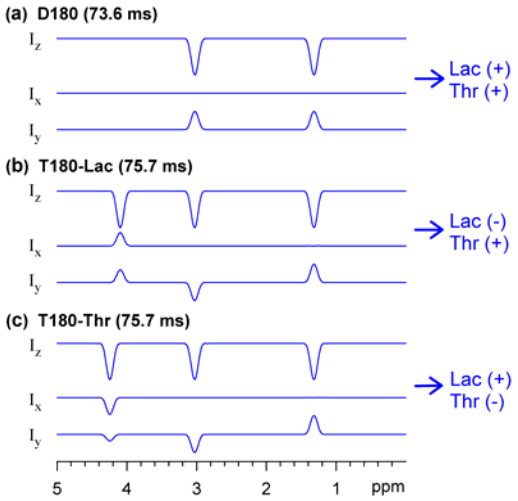

FIG 2. Inversion (I_z) and refocusing (I_x, I_y) profiles of 180° editing pulses used for selective detection of Lac and Thr are shown, together with the predicted sign of the doublet of Lac and Thr at TE ≅ 1/J.

RESULTS AND DISCUSSION

With a large bandwidth (5 kHz) of the adiabatic 180° pulses, signal loss and experimental errors due to voxel shift effects are negligible. Coherence evolution during the long editing RF pulse results in signal loss. The reduction of the signal is significant when a (negative) doublet is induced following the refocusing of two coupled resonances. Moreover, the positive doublets to be eliminated through subtraction are not identical, leading to incomplete cancellation and consequently partial contribution to the difference spectra. The signal retention ratios of Lac and Thr, numerically evaluated with a density-matrix simulation, are shown in Fig. 3. *In vivo* edited spectra are presented in Fig. 4. The 1.31 ppm signals of the *in vivo* difference spectra, labeled (A-B)/2 and (A-C)/2, were measured as 4.5±0.6% and 5.3±0.4% (mean±SD, n = 4) relative to Cr, respectively. With the contribution ratios in Fig. 3, assuming identical T_1 and T_2 between Lac, Thr and Cr, the concentrations of Lac and Thr were estimated to be 0.50±0.06 and 0.59±0.04 (mean±SD) µmol/g, with reference to Cr at 8 µmol/g.

REFERENCE

1. V. Govindaraju *et. al.*, NMR Biomed **13**, 129 (2000).

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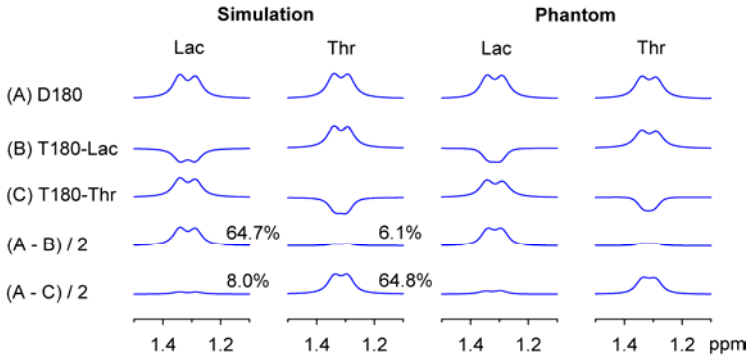

FIG 3. Calculated and phantom edited spectra of Lac and Thr for an identical concentration. Spectra are broadened to 6.7 Hz, identical to that of *in vivo* spectra in Fig. 4. The percentages in the difference spectra represent the peak area ratio with respect to the Cr 3.02 ppm singlet.

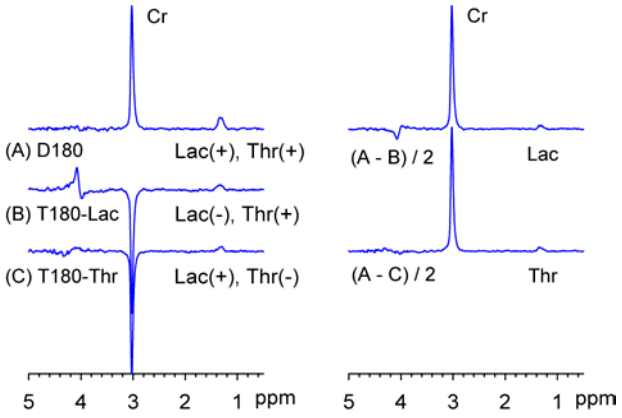

FIG 4. *In vivo* spectra from the human occipital cortex; subspectra on the left and difference spectra on the right. TR = 2.4 s. NT = 256 for subspectra. Difference spectra were obtained from subtraction between the FIDs of the subscans. The FIDs were filtered with a 1-Hz exponential and 2-Hz Gaussian function before Fourier transformation.