Measurement of Brain Metabolites using a Lactate Enhanced Detection Chemical Shift Imaging (LED-CSI) Pulse Sequence

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INTRODUCTION: Numerous reports indicate that the elevated brain lactate levels are present in patients with psychiatric disorders such as bipolar disorder, schizophrenia, and depression. The pathophysiologic mechanism that underlies this metabolic change is uncertain. One hypothesis is that oxidative metabolism using glucose is dysfunctional. Therefore, glycolytic conversion of pyruvate to lactate acid is activated to compensate for an insufficient energy supply in order to maintain normal brain activity. Currently 3T magnetic resonance scanners are widely available and considered to be the clinical high-field standard. Since the lactate resonance appears in a region which often contains overlapping signals from lipid and macromolecules, short echo time acquisitions are not a good choice to detect lactate. The intermediate (TE=135 ms) and long echo times (TE=288 ms) are preferred. However, long echo time acquisition will reduce spectral signal to noise ratio due to T_2 decay. To get reasonable spectral signal to noise ratios and avoid lactate resonance overlap with macromolecules, intermediate echo time (TE=135 ms) acquisition would be advantageous. Moreover at TE=135 ms, the lactate doublet resonance is negative in phase which is easy to recognize and fit. However, the challenge associated with lactate detection at TE=135 ms is signal nulling due to the four compartment artifact [1]. This makes the lactate concentration evaluation difficult. Single voxel spectroscopy (SVS) with lactate detection improvement has been investigated by others [2, 3] and the BASING technique [4] has been implemented in chemical shift imaging to improve the lactate signal but, in this instance, signal detection is limited by the selective BASING pulse bandwidth. A lactate enhanced detection chemical shift imaging pulse sequence (LED-CSI) is developed by applying a nonselective RF pulse to minimize the four compartment artifact and enhance lactate and glutamate/glutamine signal detection without the disadvantage of BASING.

METHOD: Fig. 1a illustrates LED-CSI sequence diagram. A non-selective adiabatic B_1 independent rotation-4 (BIR4) pulse is added to a conventional CSI pulse sequence. The BIR4 is placed in the middle of time interval between the first and the second selective 180^0 RF pulses. This BIR4 re-phases the phase dispersion resulting from J-coupling between the lactate methyl group protons and the methine group proton. Fig. 1b demonstrates the molecular structure of the lactate. The red circle includes methyl group protons while the green cycle contains the methine group proton. Methyl group protons give rise to a doublet resonance at 1.31 ppm while the methine group proton resonates at 4.1 ppm. In conventional CSI, the sinc-shaped selective 180^0 RF pulse (duration of 7.4 ms) has a bandwidth of 811 Hz. The chemical shift displacement between the methyl group protons (red matrix) and the methine group proton (green matrix) at 3T is about 342 Hz, which is 84 mm with respect to the 200 mm field of view shown in Fig. 1c. Assuming perfect excitation of the 90^0 RF pulse along the slice selection direction is achieved, illustrated by blue pane (A zone), both methyl group protons (CH_3) and the methine group proton (CH) are simultaneously excited by two selective 180^0 RF pulses. However, in the purple pane (B zone), CH is solely observed by the 2^{nd} selective 180^0 RF pulse while in the brown pane (D zone) CH is only observed by the 1^{st} selective 180^0 RF pulse. In the black pane (C zone), neither of two selective 180^0 RF pulses sees the methine proton. Therefore, the phase evolution from J-coupling between CH_3 and CH in the four zones (A, B, C and D zones) are different and summation of signals with various phases minimizes the lactate signal. The BIR4 pulse plays an important role in refocusing phase dispersion resulting from J-coupling during the phase evolution between two selective 180^0 RF pulses. Phase dispersion evolves between the 90^0 RF pulse and the 1^{st} selective 180^0 RF pulse and from the 2^{nd} selective 180 to echo time still exists. All studies were performed on a 3 T clinical MRI system (Verio-Tim, Siemens Medical Solutions, Erlangen, Germany) with gradients (43 mT/m strength and 180 T/m/s slew rate) using a Siemens 12-channel volume head coil. ^{1}H spectra were acquired from a Braino phantom (containing 5 mM lactate acid) using the LED-CSI pulse sequence. Acquisition parameters were FOV 20x20x2 cm^3, receiver bandwidth 2 kHz, TR/TE 2000/135 ms, single average, vector size 1024, matrix size 16x16, and BIR4 pulse duration/bandwidth 5.12 ms/13.96 kHz, 75% Hamming filter was applied on LED-CSI matrix to suppress signal leaking from neighbor voxels.

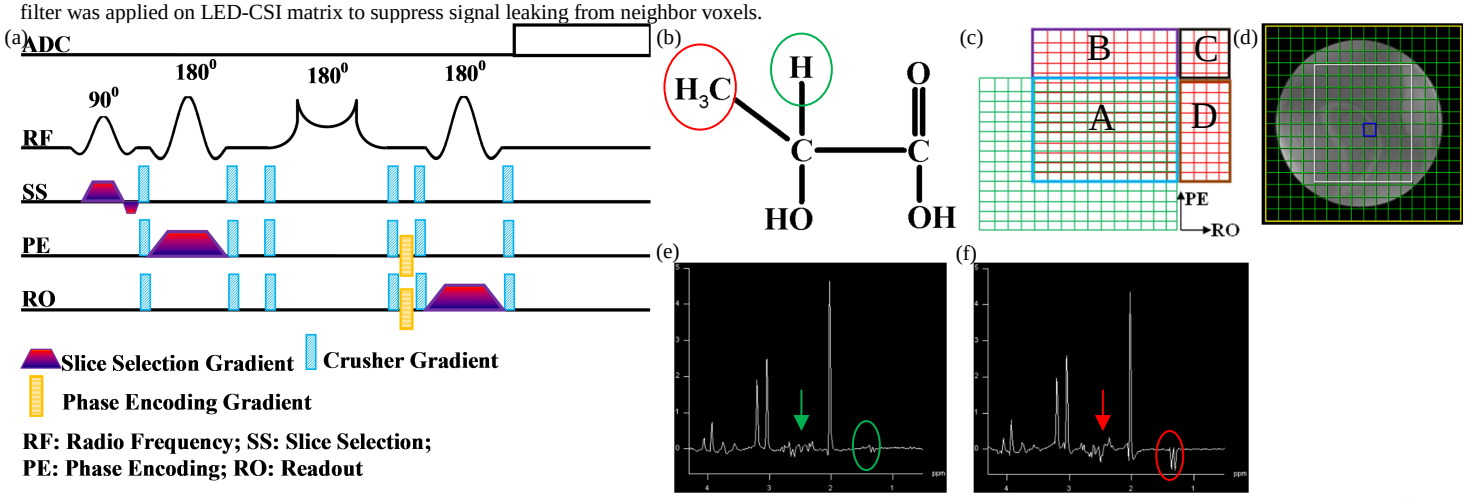

Figure 1: (a) LED-CSI Sequence diagram, (b) Lactate molecule: methyl group is circled in red and the methine group proton is shown in green. (c) Chemical shift displacement of methyl group protons (red) and methine group proton (green). PE: phase encoding; RO: readout direction. (d) Region of Interest. Blue box represents the typical chemical shift imaging voxel. (e) and (f) are spectra acquired using conventional CSI and LEDCSI, respectively.

RESULT & DISCUSSION: Fig. 1e would show almost no lactate signal (green) if the conventional CSI sequence is used at TE=135 ms. With LED-CSI, the lactate signal (red) is greatly recovered as shown in Fig. 1f. In addition, glutamate resonance in LED-CSI is also increased in magnitude compared to Fig. 1e (red and green arrow). Benefits of choosing TE 135 ms include reduced macromolecule and lipid signals. Even with any residual macromolecule/lipid signal, the negative lactate doublet is also easy to be identified and distinguished from macromolecule signals, which are positively phased. In human subjects, field homogeneity will be more variable across the larger field of view. Introduction of the adiabatic BIR4 RF pulse minimizes the signal loss due to the imperfect 180^0 RF pulse. Compared to the conventional LASER pulse sequence, LED-CSI results in less specific absorption rate (SAR) problems and is relatively easy to implement. With respect to the SVS method, LED-CSI shows much stronger Lactate/Glutamate/Glutamine SNR enhancement and has the potential to play a critical role in monitoring lactate and glutamate/glutamine variation.

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