Lactate Detection for Gliomas Patients Using Lactate-Edited 3D 1H MR Spectroscopic Imaging with Flyback Echo-Planar Readout Gradient at 3T

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Introduction: Lactate is a product of anaerobic glycolysis and an indicator of reduced cellular oxygenation. It is therefore expected to be an important metabolic marker in many brain pathologies. In brain tumor patients the detection of lactate is of interest for both evaluating prognosis and response to therapy. The lactate molecule has two weakly coupled resonances in ^{1}H MRSI: a doublet at 1.3 ppm from the methyl protons and a quartet at 4.11 ppm from the methane protons. The doublet at 1.3 ppm may be difficult to quantify because of overlapping lipid peaks in the range of 0.9 to 1.3 ppm. Spectral editing techniques based on J-difference modulation with BASING (band selective inversion with gradient dephasing) pulses [1] allows for detection of the lactate peak at 1.3 ppm as well as choline (Cho), creatine (Cr), NAA and lipids. In this case the lactate at 1.3 ppm is upright at the 1st cycle, and inverted at the 2nd cycle so that summing the datasets gives Cho, Cr, NAA and lipids, while subtracting them gives lactate [1]. The use of a flyback echo-planar readout gradient provides the possibility for acquiring MRSI data with high spatial resolution and large coverage in a short scan time at 3T [2]. The purpose of this study is to develop and implement lactate-edited 3D ^{1}H MRSI for 3T and using flyback echo-planar readout gradient to allow a scan time appropriate for use in a clinical setting.

Materials and Methods: A new 3D PRESS-MRSI sequence was developed incorporating shortened, higher-bandwidth 180^o pulses, new 3T dual BASING lactate-editing pulses specially designed for this study, new high bandwidth Very Selective Suppression (VSS) pulses [3] and a flyback echo-planar readout [2]. The 8.8 KHz, 2ms VSS pulses, optimized for 3T, were applied on all sides to define the edges of the selected volume with an over-PRESS factor of 1.7 in order to minimize the effects of chemical shift mis-registration. Lactate edited MRSI data were obtained from phantoms, five volunteers, and fourteen patients with glioblastoma multiforme (GBM) using a 3T MR scanner (GE Healthcare, Milwaukee, WI) with an 8-channel phased array head coil. The spectral quantification was performed as published previously [4]. In order to estimate the feasibility of implementing flyback echo-planar gradient into a lactate editing sequence and compare the signal-to-noise ratios (SNR) with the conventional phase encoding chemical shift imaging (CSI), two phantoms and two volunteers were scanned using both the conventional CSI with lactate editing (TR/TE=1104/144 ms, 1 cm^3 resolution, 12x12x8 phase encoding matrix, TA=18:59, elliptical k-space sampling) and the flyback echo-planar method with lactate editing (TR/TE=1104/144 ms, 1 cm^3 resolution, 16x16x16 for readout coverage, TA=9:34). All the other exams were scanned using the flyback method. Since the two methods have different acquisition times, normalized SNR was calculated in order to compensate for the signal drop in the shorter acquisition. SNR for the CSI method was normalized and compared to SNR of the flyback method based on the following formula:

$$nSNR_{CSI} = SNR_{CSI} \cdot \frac{\Delta V_{flyback}\sqrt{TA_{flyback}}}{\Delta V_{CSI}\sqrt{TA_{CSI}}}$$

where ΔV is the voxel resolution, and TA is the total acquisition time for each method. An additional factor of 2.2 was used to correct for effective spatial resolution of the elliptical k-space sampling as described in a previous study [5].

Results: The lactate-edited MRSI spectra from phantom and volunteer data demonstrated excellent detection of the uncoupled spin in the summed spectra and lactate in the subtracted spectra throughout the selected region with minimal chemical shift mis-registration effects due to the high bandwidth VSS pulses. Figure 1 shows an example of a spectroscopic voxel in a phantom and a volunteer. In the subtracted spectra (a2, b2), the lactate doublet at 1.3 ppm was observed in the phantom data (a2). Cho, Cr, and NAA were removed (a2, b2) or summed (a1, b1) for both phantom and volunteer. Median normalized SNR values of brain metabolites between the traditional CSI and flyback-gradient lactate editing imaging for phantoms and volunteers are given in table 1, and an example of spectra from a volunteer comparing two methods is shown in figure 2. The lactate doublet was quantified separately (Lac1 and Lac2) for the phantom data. Four patients showed lactate in their lesions, and an example is shown in figure 3. The red, blue and green voxels corresponds to voxels (a), (b), and (c) respectively. The first two (a, b) were taken from the contrast enhancing lesions in the T1-weighted post contrast image, and voxel (c) was taken from the normal tissue from contralateral hemisphere. The voxels in the first row shows the summed spectra. High Cho levels are observed in voxels (a1) and (b1) as expected for the tumor characteristics, and high lipid level in voxel (b1) may indicate a necrotic region. The voxels in the second row show the subtracted spectra and lactate doublets are visible in the lesions.

		Cho	Cr	NAA	Lac1	Lac2
phantom	csi	56.8	72.6	96.6	18.1	17.3
	flyback	52.6	64.0	88.9	17.4	15.1
volunteer	csi	11.8	10.7	20.5		
	flyback	8.9	7.6	16.0		

Table 1. Comparison between normalized SNR of CSI lactate editing and SNR of flyback-gradient lactate editing for phantoms and volunteers

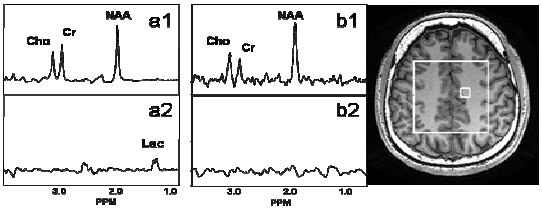

Figure 1. Flyback lactate edited spectra in phantom with lactate (a) and volunteer (b). T1 weighted image shows PRESS and a voxel for spectra (b). (a1) and (b1) show summed spectra (cycle1+cycle2) and (a2) and (b2) show subtracted spectra (cycle1 – cycle2).

Discussion: This study demonstrated the feasibility of detecting lactate at 1.3 ppm as well as Cho, Cr, and NAA using the new 3T lactate edited sequence with a flyback echoplanar readout in 9.5 minutes. The total acquisition was reduced by a factor of two compared to the conventional elliptical phase-encoding CSI (19 min). The median signal reductions in using the flyback rather than conventional phase encoding as measured from the normalized SNR of NAA were 8 % for phantoms and 22 % for volunteers (table 1). These values are similar to previous findings [2] and are due to both the interruption in sampling caused by the rewind gradients in the flyback gradient design and imperfections in the gradient trajectory. The benefit of reduction in acquisition time is expected to make this technique more applicable in clinical settings.

Conclusion: The 3T flyback lactate edited sequence was able to detect lactate in brain tumor patients in a clinically acceptable acquisition time. While further studies are required, the robust lactate detection using this method is expected to play an important role in evaluating these and other brain pathologies.

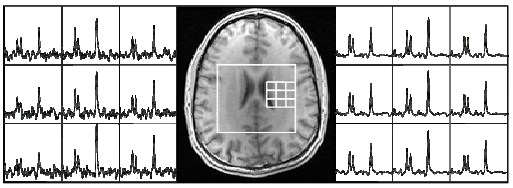

Figure 2. Comparison of lactate edited 3D MRSI between flyback echo-planar (left) and conventional elliptical CSI (right).

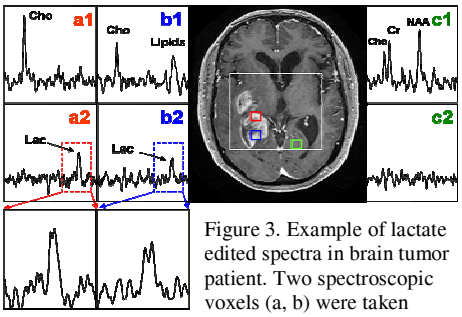

Figure 3. Example of lactate edited spectra in brain tumor patient. Two spectroscopic voxels (a, b) were taken from the contrast enhancing lesions in T1 post contrast image, and a voxel (c) was taken from the normal tissue form the contralateral hemisphere.

References:

[1] Star-Lack J, et al., *J Magn Reson.* 1998;133:243-254. [2] Cunningham CH, et al,. *Magn Reson Med.* 2005 Nov;54(5);1286-9. [3] Tran TKC, et al,. *Magn Reson Med.* 2000;43(1):23-33. [4] Nelson SJ, et al., *Magn Reson Med.2001*;46: 228-239. [5] Ozturk-Isik E, et al., *Proc. ISMRM, 13th Annual Meeting, Seattle*, 2006. p.1779.

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