Lactate Edited 3D MR Spectroscopic Imaging of Gliomas at 3T Using Ellipsoidal SENSE with BASING Pulses

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Introduction: Lactate is a metabolite with the methine resonance detected as a quartet at 4.1 ppm and three magnetically equivalent methyl protons detected as a doublet at 1.3 ppm using MR spectroscopic imaging. Lactate is formed in ischemia as a result of the pyruvate turnover, and it has been detected in high-grade brain tumors and stroke cases. Lactate detection requires a special editing scheme like the J-difference technique using dual BASING pulses [1], which requires two cycles of spectral data acquisition. In the first acquisition, BASING 180 bands are placed to include the methine quartet resulting in an inverted lactate methyl doublet at 144ms. In the second acquisition, the methine quartet is excluded from the inversion band resulting in an upright lactate methyl doublet. The sum of these two cycles results in spectra including the Cho, Cr, NAA and lipid signals, and their difference results in edited lactate spectra. The main limitation of this method is the 2-fold increase in scan time for a given phase-encode matrix. Previous studies reported the application of flyback EPSI for fast lactate editing [2]. In this study, we have applied fast data acquisition using the ellipsoidal SENSE technique [3] with BASING pulses to acquire 3D lactate edited MRSI of brain tumor patients with the clinically feasible scan time of 9 min at 3T.

Methods: An MRS phantom containing brain metabolites (Cho, Cr, NAA and lactate) and six glioma patients were scanned on a 3T MR scanner (GE Healthcare, Waukesha, WI) equipped with an eight channel RF coil (MRI Devices Inc, Gainesville, FL). The imaging protocol included the acquisition of axial T2 weighted FLAIR and proton-density weighted coil sensitivity images. FLAIR abnormality regions excluding surgical cavity areas (FL) were segmented using an in-house region growing algorithm. Ellipsoidal SENSE spectral data acquisition was implemented in a custom PRESS MRSI sequence with BASING pulses. Two cycles of 16x16x8 ellipsoidal SENSE (R_x=2, R_y=2, total scan time =9 min) data were acquired (TR/TE = 1100/144 ms). VSS outer volume suppression pulses were employed to minimize the lipid contamination in the spectra. Data reconstruction for ellipsoidal SENSE spectra was implemented using Matlab 7.0 (The Mathworks Inc., Natick, MA). Two sets of the ellipsoidal SENSE spectra were first placed on a respective rectangular grid, and pre-processed [4] to generate aliased spectra. These spectra were unaliased 2 fold in both x and y directions. Tikhonov's simple regularization was utilized to condition the inversion problem (λ=1). The spectra from the first and second cycles were added to generate Cho, Cr, NAA and lipid spectra, and they were subtracted from each other to generate the lactate spectra. The sum and difference spectra were quantified using a frequency domain analysis [4]. The signal to noise ratio (SNR) of Cho, Cr, NAA, lipid and lactate were estimated by normalizing their heights with the standard deviation of the spectral noise calculated from the left end of the spectrum. Geometry factor (g) maps were computed to estimate the noise amplification. A Mann-Whitney rank sum test was utilized to assess if the FL regions had significantly different Cho/NAA ratios than normal appearing white matter (NAWM) regions for the patients.

Results: Figure 1 shows spectra from a high grade glioma patient where clear lactate peaks were observed. The spectra of the first and second cycle from the red grid are shown at the top, and the sum and the difference spectra are shown at the bottom. The FLAIR abnormality region had high Cho, low NAA and small lipid in the sum spectra, and definite lactate peaks were observable in the difference spectra. The median g-factor (Table 1) ranged from 1.24 to 1.6 with a minimum of 1.05 in patient 5 and a maximum of 2.52 in patient 3. The median SNR for the phantom data was 56.5 for Cho, 107.25 for Cr, 176.41 for NAA, 2.95 for lipid, and 33.86 for lactate. The presence of a small lipid measurement in the phantom data indicated a small phase difference between the two cycles of spectra, since the phantom did not contain any lipids. Table 2 shows the median SNR values for all the metabolites in the FL and NAWM regions of the patients. The Cho/NAA ratio was significantly (p=0.02) higher in FL than NAWM for this patient population.

Discussion and Conclusion: The main limitation found for the ellipsoidal SENSE spectra was the residual lipid peaks due to insufficient unaliasing. However, these residual lipid peaks did not interfere with an accurate lactate estimate, because taking the difference of the spectra from the two cycles canceled out the lipid peaks given that they had the same phase. This meant that it was important to ensure that the spectra from the two cycles had the same phase. Although subtraction based spectral editing schemes are also susceptible to motion artifacts, there were minimized by acquiring the two cycles as the inner data acquisition loop, as well as by the fast data acquisition. Incorporating the ellipsoidal SENSE technique into the PRESS MRSI sequence with BASING pulses provided spectra with good data quality and high SNR, allowing lactate editing within only 9 minutes of scan time.

Figure 1. A glioma patient's FLAIR image and spectra from the two cycles, their sum and difference.

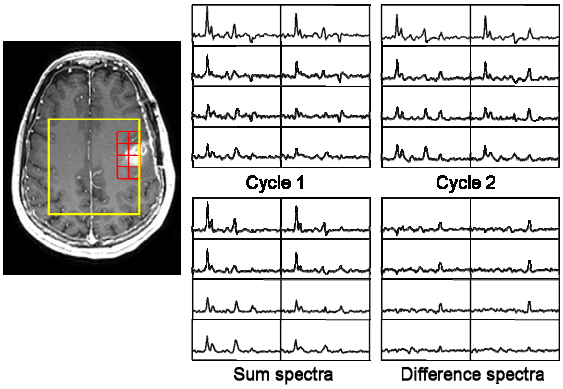

Table 1. The median, minimum and maximum of the g factor for all the subjects.

G-factor	median	min	max
Phantom	1.48	1.13	2.14
Patient1	1.38	1.06	2.27
Patient2	1.24	1.08	2.31
Patient3	1.6	1.16	2.52
Patient4	1.25	1.09	1.81
Patient5	1.29	1.05	1.97
Patient6	1.45	1.13	2.21

Table 2. The SNR of the metabolites in NAWM and FL regions for the 6 patients studied.

SNR	NAWM					FL				
	Cho	Cr	NAA	Lip	Lac	Cho	Cr	NAA	Lip	Lac
Patient1	21.83	17.64	24.23	3.03	1.76	22.44	17.5	24.42	2.52	1.43
Patient2	23.66	24.05	48.3	2.9	1.8	-	-	-	-	-
Patient3	11.54	11.77	20.25	3	1.58	5.72	4.74	6.68	2.12	1.41
Patient4	27.83	24.38	43.07	1.21	1.72	23.69	19.3	28.03	1.28	3.3
Patient5	18.51	14.77	25.78	1.56	1.45	38.14	20.83	27.25	2.14	3.52
Patient6	14.22	12.68	22.41	1.13	1.21	9.01	8.94	9.88	0.96	1.46

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