Proton T_2 measurement of Lactate in Brain Tumors at 3T

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TARGET AUDIENCE: MR spectroscopists and Neuro-oncologists/radiologists.

PURPOSE: Lactate (Lac) is elevated in tumors and has been extensively studied because of its potential use in clinical diagnosis. Lac has a prominent resonance at 1.31 ppm which appears as a doublet at short echo times. This signal is overlapped with lipid signals which are also elevated in many tumors, thus Lac is often measured using long echo times, at which the Lac signal at 1.31 ppm becomes an inverted doublet while the lipid signal remains positive and is markedly attenuated due to the effects of short lipid T_2[1]. We aim to accomplish precise measurement of Lac T_2 and absolute quantification of its concentration with corrections for the T_2 relaxation effects.

METHODS: *In vivo* T_2 of Lac was measured in 18 glioma patients, the set of gliomas comprised 10 low grade (4 grade II oligodendrogliomas, 4 grade II astrocytomas and 2 grade II oligoastrocytomas) and 8 high grade gliomas (5 grade III anaplastic oligodendrogliomas, 2 grade III anaplastic oligoastrocytomas and 1 grade III anaplastic astrocytoma). Written informed consent was obtained prior to *in vivo* scans. All experiments were carried out on a 3T scanner (Philips Medical Systems Inc) using a body coil for RF transmission and an 8-channel phased-array coil for reception. Water-suppressed metabolite data and unsuppressed water data were acquired using single voxel PRESS sequence from a T_2w FLAIR hyperintensity region at 8 echo times (TE = 58, 88, 118, 148, 178, 208, 238, 268 ms). The voxel size was 20x20x20 mm^3 and TR = 2 s. The number of sampling points were 2048 with a spectral width of 2500 Hz. For each TE, 16 signal averages were recorded. Water signal was suppressed using a four-pulse scheme. The total scan time for T_2 measurement was 5 minutes. Residual water signal was removed using the HL-SVD filter of JMRUI[2]. Data was apodized with a 2-Hz exponential filter. Eddy current compensation and frequency drift corrections were performed using in-house Matlab programs. Spectral fitting was performed using the LCModel software[3]. The basis function for fitting included numerically calculated model spectra of 22 brain metabolites calculated using published chemical shift and J coupling constants[4] with volume localization RF and gradient pulses. The metabolite signal estimates from LCModel were fitted to a monoexponential curve as a function of TE's to obtain the T_2 value. A two tailed unpaired t-test was performed to determine whether the estimated T_2 values differed between the tumor grades and subtypes.

RESULTS AND DISCUSSION: Figure 1 (**a**) and (**b**) shows the phantom and *in vivo* spectra respectively along with LCModel fits and residuals. The *in vivo* data was obtained from a FLAIR enhancing region (tumor mass) in a subject with grade III anaplastic oligoastrocytoma. The signal strength of the singlets (NAA, Cr, Cho) reduced with increasing TE due to T_2 relaxation whereas for Lac the signal strength as well as the spectral pattern varied with TE due to T_2 signal decay and the J coupling effects. The calculated Lac signals at 1.31 ppm shown in Figure 1 (**c**) are nearly identical with the spectral pattern in the phantom and *in vivo* data. The experimental spectra were well reproduced by LCModel fit at all TE's with very small residuals. Figure 2 (**a**) and (**b**) shows the monoexponential fittings for the singlets and the Lac multiplet for the data in Figure 1.Signal decay vs. TE was well represented by monoexponential fits, giving coefficients of determination (R^2) close to unity. The T_2 of Lac in phantom was 621ms. The T_2's of Lac, tCr and tCho in the tumor were estimated to be 252 ms, 153 ms and 291 ms, respectively. Figure 3 (**a**) and (**b**) shows the estimated Lac T_2 in each of the 18 subjects and the mean Lac T_2 in low grade and high grade gliomas respectively. The estimated T_2 value for Lac was 246 ± 18 ms (mean ± SD) in low grade and 245 ± 22 ms in high grade gliomas. The Lac T_2 values did not show statistically significant difference between tumor grades or tumor subtypes. Previous studies reported the T_2 of Lac in conditions like chronic infarction[5], stroke[6] and developing brain[7] but in tumors there has been no report yet to our best knowledge. In the previous studies data were acquired only at 2 TE's and was either reported from a small patient population (< 5) or with large variations in T_2 estimate (i.e., 186 - 2110 ms). In the present study, 8 echo times were used for T_2 elevation which could improve the precision in Lac T_2 estimation.

CONCLUSION: The Lac T_2 was similar between tumor grades and subtypes. The T_2 of Lac was estimated to be 246 ± 20 ms, which can be used to correct for the T_2 relaxation effects and quantify Lac in all tumors.

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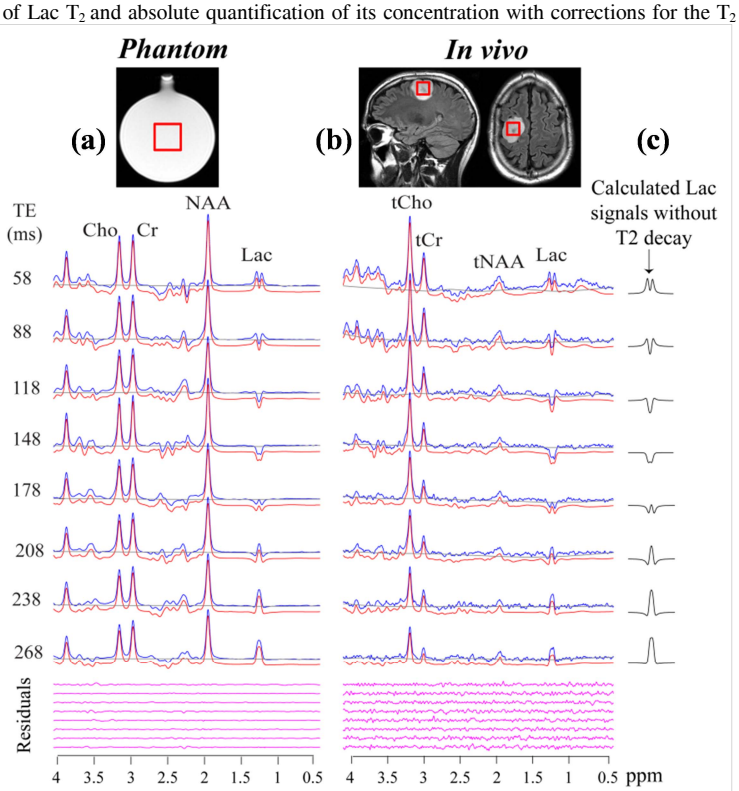

Fig. **1**: Experimental spectra (blue), LCModel fits (red) and residuals (magenta) at TE = 58, 88, 118, 148, 178, 208, 238, 268 ms from (**a**) a phantom containing Lac (6mM), NAA (12.5mM), Cr (10mM), Cho (3mM), Glu (12.5mM) and mIns (7.5mM) (b) from a FLAIR enhancing region (tumor mass) in a subject with anaplastic oligoastrocytoma. (c) Calculated Lac signals at 1.31 ppm without T_2 decay for comparison with phantom and *in vivo*.

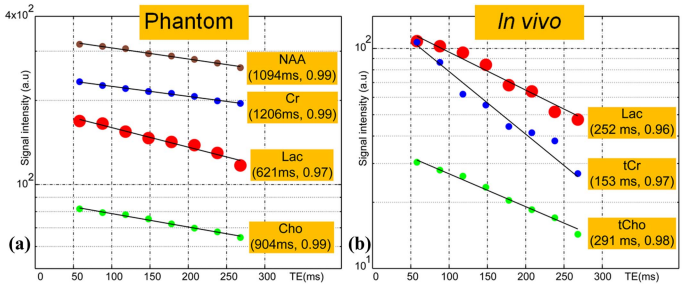

Fig. **2**: Monoexponential fitting of LCModel signal estimates vs TE (**a**) for Lac, NAA, Cr and Cho in phantom and (**b**) for Lac, tCr and tCho in the tumor spectra from figure 1. The T_2 values and the coefficient of determination (R^2) are also shown.

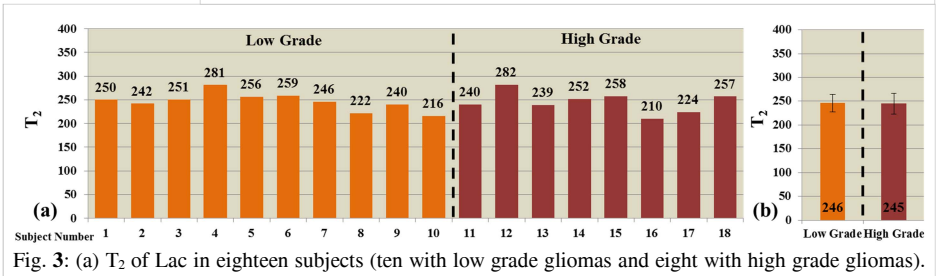

Fig. **3**: (a) T_2 of Lac in eighteen subjects (ten with low grade gliomas and eight with high grade gliomas). (b) Mean T_2 of Lac in low grade and high grade gliomas. Error bars are the standard deviation.