Multivoxel Lactate Editing in Glioma Patients at 3.0T

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Introduction: Neuro-radiologists and oncologists are constantly looking for improved means to characterise brain tumours and assess response to treatment. The concentration of lactate in gliomas could potentially act as a prognostic biomarker for patients. The level of lactate in tumours is a marker of anaerobic glycolysis which in turn could be an indication that the tumour is becoming stressed by its environment, and is likely to initiate a proliferative response[1]. Lipid and lactate are known to commonly coexist in gliomas, yet both resonate at around 1.3ppm. Unfortunately the large amounts of lipid often found in high grade gliomas obscure the smaller lactate signal causing cancellation effects in the lipid peak and total loss of quantification for lactate. However, at 144ms echo times, lactate presents as an inverted doublet due to J-coupling while lipid can be seen as an upright singlet, providing a mechanism to separate them using a simple editing scheme. Here we demonstrate the feasibility of lactate edited multivoxel spectroscopy in clinically acceptable times with quantification of lactate.

Methods: Sixteen patients with diagnosed gliomas (7 high grade (pathological), 9 low grade (radiological)) were scanned using a multivoxel PRESS editing sequence with interleaved BASING pulses[2] on a GE 3.0T MR750 system using a dedicated eight channel phased array head coil. The 2D-MRSI was planned from axial T_2 FLAIR imaging and acquired before contrast. The volume of interest was positioned to cover as much of the lesion in a single slice while avoiding contamination from skull based lipid and susceptibility effects along with a half voxel buffer zone to improve slice profile. Two additional SAT bands were used to help supress susceptibility and spurious signal. Spectroscopic scan parameters included 16x16cm field of view with 16x16x1 phase encodings, 0.8NEX and 10mm slice thickness for a nominal voxel size of 1ml, with TE/TR=144/1000ms. The frequency of the BASING pulses was alternated between 0Hz (on) and -198Hz (off) from water to minimise movement effects. Broadband pulses[3] replaced the 137° refocusing pulse used in the standard 3.0T PRESS sequence reducing the effects of chemical shift displacement and ensuring full excitation of both lactate regions given their differing spectral separation from the centre frequency. Total scan for the 2D-MRSI was 7 minutes and higher order shimming was run twice before acquiring the data. Spectra were processed offline using Spectral Analysis by GE (SAGE). Data were automatically split into BASING on and off data. The BASING off data was coil combined using a sum of the squares signal weighting method and phased using the residual water signal. Coil weightings and phasing were duplicated for the BASING on data where the residual water is completely supressed. Summing the BASING off and on produces a singlet spectrum while subtracting them produces an edited spectrum with an antiphase lactate signal. Spectra were quantified in LCModel[4] using a 'tumor' control file for the singlet data to quantify choline, creatine, NAA and lipid. A 'csf' control file was used to quantify the lactate only spectra due to the absence of NAA, creatine and choline normally used for spectral referencing (figure 1). Cramer Rao lower bound filtering was applied to all data with a threshold of 20% applied. Lactate concentrations were mapped back onto T_2 FLAIR images (figure 2) using software developed in MATLAB. A mirrored T_1 post contrast image has been added to show areas of necrosis.

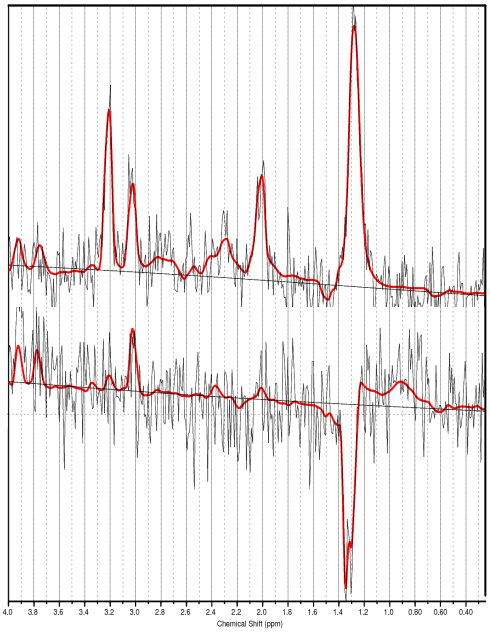

Figure 1: Top spectrum shows the LCModel fitting and quantification of choline and the 1.3ppm lipid peak. Bottom shows lactate edited spectrum from the same voxel fitted with LCModel using the 'csf' control file scaled separately. Cramer Rao lower bounds were 8% for lipid13b, 7% for choline, 13% for creatine, 14% for NAA and 9% for lactate.

Results: Lactate was successfully quantified in the presence of lipid using a multivoxel PRESS editing sequence where both metabolites were present in the same voxel of interest (Figure 1). A large resonance was present at 1.3ppm in 5 of the 7 high grade lesions and none of the low grade lesions. In the 5 high grade tumours a significant component of the 1.3ppm pseudo-concentration was lactate (33-60%). LCModel lactate pseudo-concentrations ranged from 1.69-5.99mM. The within patient lactate/lipid pseudo-concentration ratio varied between 2 and 24 percentage points. For individual patients, lipid was observed in 40-75% of the voxels that contained lactate.

Discussion: This study demonstrates that lactate quantification can be achieved using a PRESS editing sequence that uses interleaving BASING pulses to modulate the lactate doublet between the inphase and antiphase positions. An important aspect of the scheme used here is that in the BASING off condition, the residual water remains unaffected and can be used to determine the coil weightings and phase for both parts of the data. The advantages of broadband pulses include better excitation of the whole volume while removing the risk of unintentionally exciting skull based lipid. Consequently there is no requirement for voxel oversizing techniques such as OVERPRESS as used in some other spectral editing sequences.

Conclusions: Quantifiable lactate edited multivoxel spectroscopy were acquired in clinically acceptable times. The implementation of this simple editing scheme combined with the automated processing will allow the systematic investigations of lactate concentration heterogeneity in glioma patients that may indicate signs of transformation and response to therapy.

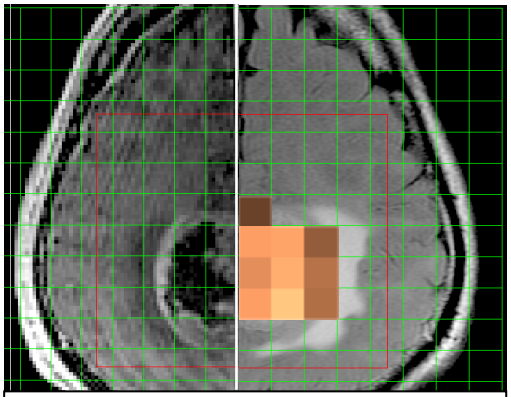

Figure 2: Lactate map of a glioblastoma using LCModel for concentration quantification superimposed on T_2 FLAIR imaging. Processing shows quantifiable levels of lactate with Cramer Rao lower bounds less than 20% throughout the tumour. (Yellow = Highest Concentration). Post contrast T_1 imaging is mirrored on the left to show the solid tumour.

References: *1.* Kaur *et al.* Neuro Oncol. 2005; 7(2):134-53. *2.* Star-Lack *et al*. Magnetic Resonance in Medicine 1997; 38:311–321. *3.* Janich *et al.* Journal of Magnetic Resonance. 2011; 213(1):126–135 *4.* Provencher.Magnetic Resonance in Medicine 1993; 30:672-679.