Voxel selective Lactate editing at high magnetic field strengths using Sel-MQC

Gerd Melkus[1], Myriam M Chaumeil[1], Sharmila Majumdar[1], and Sabrina M Ronen[1]
[1]*Radiology and Biomedical Imaging, University of California, San Francisco, San Francisco, CA, United States*

Introduction: Lactate (Lac) is commonly used as an important metabolic marker of tumor status in the clinic. The evaluation of Lac level may help assess the effects of chemo- and radiotherapy [1,2]. However, the unequivocal detection of Lac in tissues is often difficult as the Lac CH_3 resonance can be overlapped by co-resonant signals from lipids. To address this problem, several localized spectral editing methods were developed. One of theses methods is the Selective Multiple Quantum Coherence (Sel-MQC) filter proposed by He et al. [3], which enables a robust and single scan editing of Lac. Sel-MQC filtering of Lac was used in different studies, where the filter is combined with spectroscopic imaging acquisition schemes to image Lac levels [4-6]. When single-voxel localization is necessary, the selective pulses in the Sel-MQC sequence could be replaced by spatial-spectral pulses to achieve localization and frequency selection [7,8]. However, especially at high magnetic field strength, spatial-spectral pulses impose high demands on the gradient switching rate and additional artefacts from eddy currents can occur. It has been shown that chemical shift selective imaging in spin echo sequences could be performed when a spatial mismatch between resonances is applied [9]. Based on these concepts, this study aimed to develop and optimize a single-voxel localization technique for the Sel-MQC sequence, less hardware demanding, that would provide an improved localized detection of Lac.

Material and Methods: Fig. 1 shows the proposed method for single voxel localization using the Sel-MQC filter. The Sel-MQC sequence is based on four frequency selective pulses, alternating applied on the CH_3 and CH Lac groups. Pulsed field gradients (G1, G2) select the MQC-path; spoiler gradients (Sp) dephase the magnetization resulting from the imperfections of the 180˚ refocusing pulse [3]. Voxel localization is achieved by slice selective gradients applied during the first three frequency selective pulses. To achieve the necessary condition of chemical shift selectivity of the pulses while a localisation gradient is on, the pulse bandwidths ($\Delta\omega_{HF}$) must be smaller than the chemical shift difference between the Lac CH and the CH_3 group ($\Delta\omega_{CS}$): $\Delta\omega_{HF} < \Delta\omega_{CS}$ (Fig. 2). Only then the spins in the selected voxel pass through the complete Sel-MQC filter whereas magnetization outside the voxel is not refocused or is spoiled.
The sequence was tested on a 14.1T vertical and a 7T horizontal magnet (Agilent Technologies, Palo Alto, CA) equipped with the VnmrJ 3.1 imaging software. Experiments at 7T were performed using a 20 mm diameter linear birdcage resonator. Lac spectra from a phantom containing 100 mM Lac in water were acquired in a 2 x 2 x 2 mm^3 voxel. The Lac signal from the Sel-MQC localization was compared to the Lac signals measured using PRESS- (using sinc- or mao-refocusing pulses, duration (d) = 1 ms, $bandwidth_{SINC}$ (BW_{SINC}) = BW_{MAO} = 4.7 kHz) and LASER-localization (adiabatic hyperbolic secant pulses: d = 1 ms, BW_{LASER} = 25 kHz) (all sequences: TR = 10 s, TE = 136 ms, averages = 4). For the Sel-MQC sequence, sinc pulses where applied: d = 12 ms, BW = 495 Hz (at 7T), d = 8 ms, BW = 740 Hz (at 14.1T). As *in vivo* proof of principle of the sequence, a localized Sel-MQC Lac spectrum was acquired at 14.1T from an orthotopic glioblastoma (GBM) tumor in mice using a 40 mm diameter volume coil (TR = 4 s, TE = 136 ms, NA = 640, voxel = 3 x 3 x 3 mm^3).

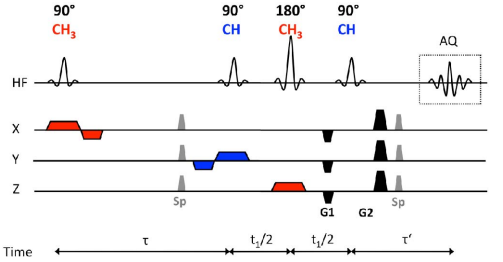

Fig. 1: Pulse sequence for Sel-MQC voxel localization

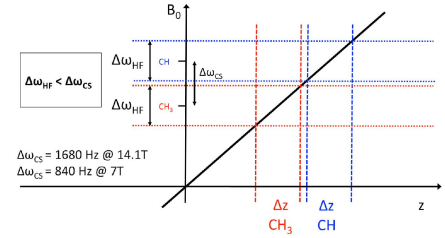

Fig. 2: Pulse bandwidth conditions to achieve chemical selectivity

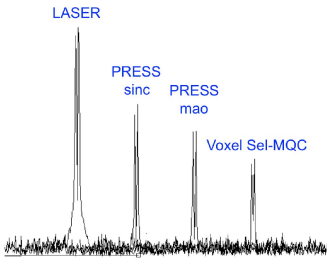

Fig. 3: Lac signal comparison between different localization schemes (phantom)

Results and Discussion: The comparison of localized Lac signal between Sel-MQC method, PRESS and LASER is shown in Fig. 3. The LASER localization results in the highest signal for Lac, the signal being lower using PRESS localization (with either sinc- or mao-refocusing pulses). The signal intensity of the Lac detected using the Sel-MQC acquisition scheme is about 50% of the signal obtained by LASER localization. This result is in line with the theory, because only one of the two coherence pathways is refocused by the MQC-gradient (G1, G2) combination [3]. The signal difference between LASER and PRESS results from the improved localization performance of LASER, where - because of the broadband (BW = 25 kHz) adiabatic pulses - the chemical shift error between the CH and CH_3 group is smaller than using sinc or mao pulses. Due to the reduced chemical shift artefact, the effects of the J-modulation between the CH and the CH_3 at TE = 136 ms are significantly reduced in LASER versus PRESS. Using the Sel-MQC voxel localization, the effects of the chemical shift related signal drop is also minimized. Fig. 4 shows a Sel-MQC localized ^{1}H spectra obtained *in vivo* in an orthotopic GBM tumor in a mouse. As expected, the Lac CH_3 peak is detectable at 1.3 ppm, while other resonances are suppressed by the editing scheme.

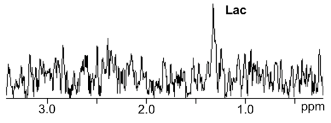

Fig. 4: *In vivo* tumor Lac editing from 3x3x3 mm^3 voxel using Sel-MQC

Conclusion: The voxel localization combined with Sel-MQC editing scheme has low demands on the gradient system performance, because low amplitude gradients are used in combination with long selective pulses. This sequence does not suffer from chemical shift based localization artefacts for J-coupled spin-systems (like Lac) and is therefore also usable with low-power HF-amplifiers, where high broadband pulses are not reachable due power limitations. Several studies are underway to further evaluate this sequence *in vivo*. We believe that this sequence should prove useful for the unequivocal detection of lactate, especially in glioblastoma tumors.

Acknowledgement: This work was supported by a Seed Grant from the Department of Radiology and Biomedical Imaging at the University of California, San Francisco.

References: [1] Rofstad EK. Int J Radiat Biol. 2000; 76:589-605 [2] Quennet V. Radiother Oncol. 2006; 81:130-5. [3] He Q et al. J Magn Reson B. 1995; 106: 203-11 [4] Thakur et al. Magn Reson Med. 2009; 62:591-98 [5] Stephen P et al. Magn Reson Med. 2008; 60:299-305 [6] Melkus et al., NMR Biomed. 2008; 21:1076-86. [7] Thakur et al. ISMRM 2003, p.1141 [8] He et al. ISMRM 2005, p. 728 [9] Park HW et al. Magn Reson Med. 1987; 4:526-36.