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

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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 CH₃ lect the MQC-path; spoiler gradients (Sp) dephase the J-coupled spin-systems (like Lac) due to the long T₂ relaxation time of the CH₃ group. Selective pulses, alternating applied on the CH₃ and CH resonances 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 useful with low-power HF-amplifiers, where high bandwidth 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.

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 CH3 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 (ΔωCS) must be smaller than the chemical shift difference between the CH and the CH3 group (ΔωCS: ΔωCS < ΔωCH3 (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 1.4T 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 mm³ 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, bandwidthsinc (BWsinc) = BWMAO = 4.7 kHz) and LASER-localization (adiabatic hyperbolic secant pulses: d = 1 ms, BWLASER = 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 mm³).

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 rephased 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 CH3 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 CH3 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 1H spectra obtained in vivo in an orthotopic GBM tumor in a mouse. As expected, the Lac CH peak is detectable at 1.3 ppm, while other resonances are suppressed by the editing scheme.

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 useful with low-power HF-amplifiers, where high bandwidth 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.

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