

Simultaneous MSC-SelMQC Mapping of Polyunsaturated Fatty Acids (PUFA), Lactate and Choline in Tissues Containing High Concentration of Mobile Lipid

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INTRODUCTION. The MRS detection of choline has improved the diagnostic specificity of human breast cancer.² However, choline level may also increase in lactating breast. Therefore, multiple metabolite markers may enhance the accuracy of breast cancer diagnosis. We have developed the Sel-MQC sequence for lactate detection in breast cancer and other tissues containing high concentration of mobile lipid with complete suppression of lipid and water signals in a single scan.³⁻⁶ Using the Sel-MQC technique, polyunsaturated fatty acids (PUFA) were found to have different distribution patterns in individual human breast tissues and breast malignancy.¹ The Sel-MQC method has been used to detect antineoplastic agent Iproplatin and adapted for simultaneous measurement of lactate and Iproplatin.⁵ The T₁- and T₂-Sel-MQC sequences have been developed to determine the relaxation times of the edited lactate signals for tissue metabolite quantification.⁷ The volume selective Sel-MQC techniques using 1331 composite pulses,⁸ a multi-slice Sel-MQC method for 3D mapping of metabolites using the Hadamard matrix approach,⁹ and a 3D volume SelMQC spectroscopic imaging technique using spatial-spectral (SPSP) selective RF pulses were also developed.¹⁵ Recently, we have demonstrated the modified Sel-MQC sequences for simultaneous detection of PUFA and lactate in different multiple quantum coherence transfer pathways, as well as the DSE-SelMQC for simultaneous detection of choline and lactate or choline and PUFA.¹⁰ In this report, we will present a novel pulse sequence Molecular Specific Coherence (MSC)-SelMQC that permits simultaneous detection of PUFA, lactate and choline in tissues containing high concentration of mobile lipid, with complete suppression of water and unwanted lipid resonances in a single scan. The method will be applied to detect malignant changes in human breast tissues or other organs containing high concentration of fat.

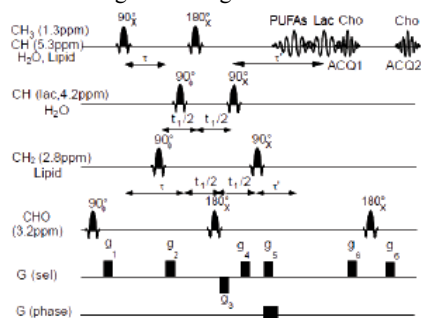


Fig. 1 MSC-SelMQC pulse sequence for PUFA, lactate and choline detection in a single scan for lipid and water suppression by coherence transfer gradient combination $g_1: g_2: g_3: g_4: g_5: g_6 = -5.25: -3: 5.25: -7.5: -6: -8$.

to generate PUFA MQC. The PUFA MQC echo is refocused ($g_2: g_5 = 1:2$) via the ZQ→DQ coherence transfer pathway, where $g_3+g_4=2.28$ serves as a t₁-crusher. The cosine modulated sinc 180° of 10ms duration is applied at the lactate CH₃ 1.3 ppm and PUFA at 5.3 ppm to inter-converts the DQ and ZQ coherence transfer pathways for both lactate and PUFA. Both are converted into single-quantum (SQ) states respectively by the last lactate CH 90° sinc pulse at 4.2ppm and the last PUFA CH₂ 90° pulse at 2.8ppm for detection in the first acquisition window (ACQ1). Choline signal were refocused twice for 1st and 2nd echo acquisition in window ACQ1 and ACQ2, respectively. To obtain images shown in Fig. 2, a 1-lobe sinc pulse (10 ms) was employed as the frequency-selective 90° and 180° pulses for lactate CH, PUFA and Cho excitation (~100 Hz bandwidth). A 12 mm two-compartment phantom containing a mixture solution of 50 mM choline and 100 mM lactate in saline in the outer tube and pure vegetable oil in the inner 5mm NMR tube was used. A home-built RF coil was constructed to fit the phantom. All experiments were carried out on a Bruker 7T horizontal bore MRI spectrometer (Paravision 4.0).

METHODS. The MSC-SelMQC sequence (Fig. 1) is modified from the Sel-MQC CSI pulse sequence for simultaneous mapping of PUFA, lactate and choline.³ The method excites lactate and PUFA into different multiple-quantum (MQ)-states via two different MQ coherence transfer pathways, whereas choline into the spin echo pathway for simultaneous detection in the first acquisition period (ACQ1), leaving unwanted lipid signals and water in the SQ modes to be completely suppressed by the MQC-selection gradient pulses ($g_1: g_2: g_3: g_4: g_5 = -5.25: -3: 5.25: -7.5: -6$). A second choline echo can be obtained using a selective 180° pulse at 3.2ppm and a pair of crusher gradients with amplitude $g_6 = -8$. Experimentally, the choline magnetization was excited by the first 90° choline selective pulse and labeled by gradient g_1 . A cosine modulated 1-lobe 90° sinc pulse in 10ms duration was applied to excite the olefinic methylene protons of PUFA at 5.3ppm and the lactate methyl CH₃ protons at 1.3ppm. The excited lactate and PUFA protons evolved into anti-phase magnetization via J-coupling in the preparation period of $\tau = 1/2J$, where J is the scaling coupling constant of lactate or PUFA coupled spins. The third 90° pulse applied at the lactate CH resonant frequency (4.2 ppm) generated lactate MQ coherence, which was refocused by the coherence labeling gradient g_3 : ($g_4+g_5-g_2 = 1: -2$ in the DQ→ZQ coherence transfer pathway, whereas g_2 serves as a t₁-crusher. The 4th 90° selective pulse excites the allylic methylene protons of PUFA at 2.8 ppm

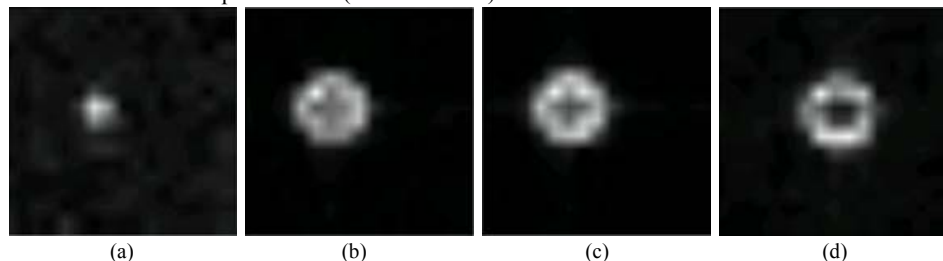


Fig. 2 Two-dimensional 16x16 CSI images of (a) PUFA, (b) lactate, and (c) choline were acquired in the 1st echo in ACQ1 and (d) choline from 2nd echo acquired in ACQ2 using the MSC-SelMQC method on a Bruker Avance 7T MRI spectrometer with a home-made gap-resonator RF coil. FOV = 3 cm. The two-compartment phantom contains a saline mixture of 50mM choline and 100 mM lactate in the outer tube and pure vegetable oil in the inner tube. Unwanted lipid signals and water were suppressed.

RESULTS. Simultaneous detection of PUFA, lactate, and choline spatial distributions with MSC-SelMQC was demonstrated in phantom (Fig. 2). As expected, the PUFA signal at 5.3ppm were detected only from the inner chamber (Fig. 2a), and the lactate and choline signals only from the outer chamber with excellent suppression of unwanted lipid signals and water (Fig. 2b,c) in the acquisition window ACQ1. The choline map was also obtained in the 2nd acquisition window ACQ2 (Fig. 2d). **CONCLUSION.** We have demonstrated the feasibility of simultaneous detection of PUFA, lactate and choline using MSC-SelMQC method with complete suppression of unwanted lipid and water signals. The sequence will be optimized and applied to study animal tumor models and human breast cancer or other extracranial cancers in tissues containing high concentration of fat. **ACKNOWLEDGMENTS.** The work was supported from NIH (grant 1R01 CA109471-01 A1). **REFERENCES:** ¹MRM 58, 1079 (2007). ²Radiology 209, 269 (1998). ³JMR B 106, 203 (1995). ⁴JMR B 112, 18-25 (1996). ⁵MRM 33, 414 (1994). ⁶NMR in Physiology and Biomedicine, ed. R. J. Gillies (Academic Press, San Diego, 1994), pp. 311. ⁷MRM 52, 902 (2004). ⁸Proc. ISMRM, 1141 (2003). ⁹Proc. ISMRM 3, 1447 (1997). Proc. ENC, 2009.