# In-Vivo Lactate Detection Using Selective MQ Coherence Spectroscopy: Signal Enhancement Using Spectral-Selective Binomial RF pulses (SS-SelMQC)

**S. B. Thakur[1], J. Yaligar[1], and J. A. Koutcher[1,2]**

[1]Medical Physics, Memorial Sloan Kettering Cancer Center, New York, NY, United States, [2]Medicine, Memorial Sloan Kettering Cancer Center

## INTRODUCTION

Lactate is an important metabolite which reflects elevated tumor glycolysis and poor tissue perfusion, both of which are related to tumor development. The detection of lactate in tissues is difficult due to the presence of high concentrations of co-resonant lipid signals. In our previous work (1) using the SelMQC (2) method, varying lactate signal intensities were observed in rodent prostate R3337 tumors with increasing volumes. Here we report a novel modification of the SelMQC sequence using binomial spectral-selective pulses (SS-SelMQC) (Fig.1). Frequency selective excitation pulses were employed with suitable phase cycling of a binomial sequence $\left[(\pi/4)_{\phi 1} - \Delta - (\pi/4)_{\phi 2}\right]$ to selectively excite either lactate methyl $CH_3$ resonances ($\phi_1$, $\phi_2$=x, -x) or methylene CH resonances ($\phi_1$, $\phi_2$=x, x). Frequency selective inversion was achieved using $\left[(\pi/2)_x - \Delta - (\pi/2)_{-x}\right]$ for the lactate methyl $CH_3$ resonances. Chemical shift selection was achieved by adjusting the interpulse delay equal to the inverse of twice the difference in the center frequencies of maximum and null excitation bands (Fig.2). In a lipid enriched environment, the modified pulse sequence yielded enhanced lactate signal of 200-300% compared to SelMQC. Non-localized proton spectra and 2D CSI-lactate images were obtained from 30mM lactate/lipid phantoms and *in-vivo* R3327 prostate animal tumors.

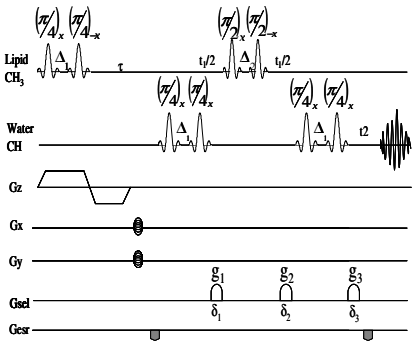


**Fig.1** The SS-SelMQC pulse sequence; The ZQ →DQ coherence transfer path way is selected with the $G_{sel}$ gradients in a ratio of 0:-1:2. τ=72 ms and MQ evolution period $t_1$= 26ms.

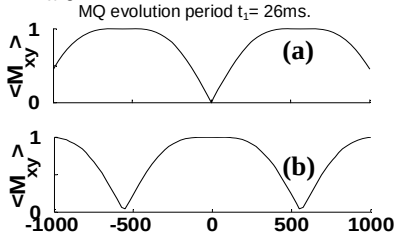


**Fig.2** Theoretical excitation profile as a function of resonance frequency employing $\left[(\pi/4)_{\phi 1} - \Delta - (\pi/4)_{\phi 2}\right]$ with ($\phi_1$, $\phi_2$=x, -x) (a) and ($\phi_1$, $\phi_2$=x, x)(b)

## NUMERICAL SIMULATIONS AND EXPERIMENTAL METHODS

Performance of the selective pulses were evaluated using computer simulations of these pulse blocks using AX spin system representing lactate (A=CH3; X=CH). Numerical simulations were generated using spin density matrix calculations. Selective excitation profile of binomial spectral-selective pulse is shown for CH3 (-560Hz) without disturbing CH (0 Hz) resonance (Fig.2a) and vice versa (Fig. 2b). The numerical simulations were carried out using MATLAB signal processing package.

All experiments were performed on a 4.7 Tesla Bruker Biospin spectrometer (40 cm horizontal bore). Animal studies were conducted in compliance with protocols approved by the animal care protocols in Memorial Sloan-Kettering Cancer Center. The rat was anesthetized using a mixture of isoflurane and air (20% $O_2$) and placed in the animal holder. The tumor was placed inside a 2 turn home built coil (25mm diameter) tuned and matched at 200MHz and MR experiments were initiated. The tumor volume was 857mm3 (using vernier calipers). The modified pulse sequence was tested using phantoms (cylinder 30mM lactate doped with 25uM Gd-DPTA/Crisco Fat), and demonstrated in vivo using a R3327-AT prostate tumor subcutaneously implanted on the thigh of a Copenhagen rat. MR spectroscopy acquisition parameters for SelMQC were taken from ref (1). In SS-SelMQC , we used high power three-lobe sinc shaped RF pulses for both 45° (200 us duration) and 90° (400us duration) flip angles, a pulse repetition of 2 s and spectral width of 12.5 ppm; $\Delta_1$=693us; $\Delta_2$=493us; Although we can use hard RF pulses, we used shaped pulses for low RF power dissipation and slice selection. Due to finite pulse widths, the interpulse delay was calculated by taking them into consideration. Transmitter was set at the CH frequency. Non-localized spectra were obtained with 16 transients. The 2D $^1$H CSI was performed with a voxel size of 2.5×2.5x5 $mm^3$ (FOV=4.0cm). Total time for 2D CSI experiment was ~1 hr 15 minutes (ns=8). The $^1$H-MRS images were reconstructed using 3DiCSI processing software. The intensity of each CSI voxel is proportional to the corresponding lactate spectral intensity. The anatomical T2 -$^1$H reference images were acquired using the same setup with a multiple spin-echo sequence.

## RESULTS AND DISCUSSION

Fig 3 shows the non-localized spectra obtained from the phantom (MR image shown in (Fig.3a)) using SS-SelMQC showing lactate signal with complete suppression of lipid and water (Fig. 3b). Integrated lactate signal area is 3 times stronger than the signal obtained using SelMQC with same amount of water suppression level (Fig.3c). The same effect was demonstrated using R3337 tumor (Fig. 4). From this summed spectrum, the lactate signal to noise with SS-SelMQC is more than 200% that obtained with the SelMQC. Experimental 16 x 16 2D-CSI lactate maps (Fig.5) were obtained from a 5 mm sagittal slice in the tumor region which was coregistered with a T2-weighted image. Varying amounts of lactate signal were present at different positions within the tumor In *in-vivo* situations with shorter T2 relaxation times, enhancement of signal to noise would be critical for accurate measurements and for absolute quantification of tissue lactate concentrations. This effect will be dominant in studies with small tumor volumes, where lactate concentrations may be low (1).

## CONCLUSION

Lactate signals detected by SS-SelMQC have a 2-3 times higher signal to noise compared to conventional SelMQC. The sequence is currently being implemented for lactate detection from volume of interest, which will be used to image the internal organs of transgenic animal tumor models.

**REFERENCES:** 1) Yaligar J, et al, PISMRM 5138 (2007). 2) He Q, et al, J Magn Reson B **106,** 203 (1995).

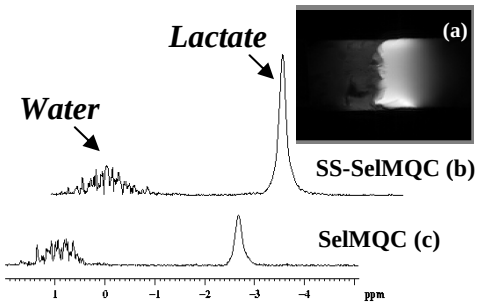


**Fig.3** Experimental non-localized $^1$H spectra obtained from lactate/lipid phantom (MR image shown in (a)), using SS-SelMQC (b) and SelMQC (c). Note excellent lipid and water suppression

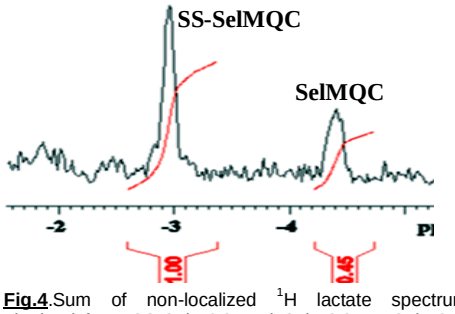


**Fig.4**.Sum of non-localized $^1$H lactate spectrum obtained from SS-SelMQC and SelMQC. In SelMQC, lactate frequency is shifted to -4.4ppm before adding to SS-SelMQC signal. Integrated areas are labeled in red

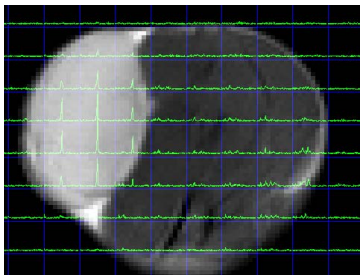

**Fig.5** Localized 2D CSI $^1$H spectra of lactate using SS-SelMQC