Refocused Double Quantum editing for lactate detection in the human calf muscle at 7T

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Introduction:
Lactate is an important marker for anaerobic glucose metabolism, and of particular interest in cerebral ischemia, skeletal muscle disorders and monitoring of cancer treatment. However, the in vivo detection of lactate with MR spectroscopy is complicated by the overlap of the low intensity lactate methyl resonance with strong lipid signals at 1.3 ppm. Double quantum filters have been employed to dephase the overlapping lipid signal, since they allow for a very high lipid suppression efficiency. But for reliable lactate detection in a lipid rich environment, very long and strong crushing gradients have to be employed to dephase the lipid signal below the noise level. Unfortunately, double quantum filters are generally associated with signal loss. Half of the lactate signal is lost by selecting either the double or zero quantum coherences. On top of that, due to incomplete refocusing, traditional double quantum filters with very large crusher gradients show additional loss of the already low lactate signal [1]. Especially at ultra-high field, with increased susceptibility artifacts, very long crushing gradients are required, leading to severe signal loss. In this work we have added additional 180 degree pulses in the double quantum filter, which refocus the additional source of signal loss, making it possible to detect lactate at lower concentrations in lipid rich environments. Lactate measurements are shown in human calf muscle at 7T.

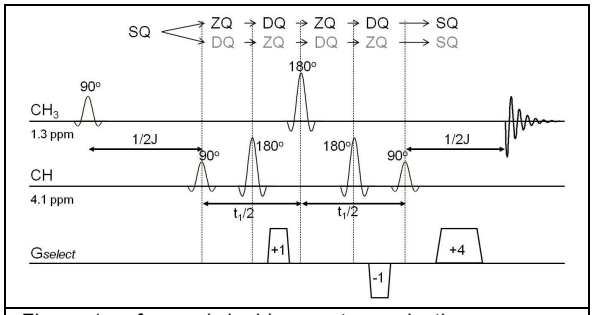

Figure 1; refocused double quantum selection sequence. The lactate signal is converted to a double quantum state where it is twice as sensitive to dephasing gradients. The overlapping (single quantum) lipid signal experiences asymmetric gradients and shows a reduced signal intensity, dependent on the effective spoiling area. The first excitation pulse was made slice selective to generate signal from a single slice.

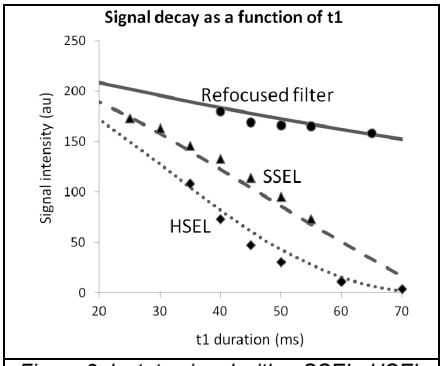

Figure 2; lactate signal with a SSEL, HSEL or refocused double quantum filter. The refocused filter shows no additional signal loss (apart from T2 decay)

Methods:
Experiments were performed on a whole body 7T MRI system (Philips, Cleveland, OH, USA). A volume birdcage coil was used (Nova Medical, Inc, Burlington, MA, USA). Experiments were performed on both phantoms and in calf muscle of a healthy volunteer.
Traditional multiple quantum filters use asymmetric gradients, where the double quantum period is used to double the effective dephasing of the spins of interest. In SSEL or HSEL multiple quantum filters, a single hard or selective refocusing pulse is added to the double quantum evolution period (t1) to refocus chemical shift of the resonance of interest. An extension of this principle was used, where additional refocusing pulses are added to a SSEL-MQC selection filter [1] to refocus both the chemical shift and J-coupling evolution in the multiple quantum t1 time (figure 1). This cancels the additional $\cos(\pi*J*t1)$ or $\cos^2(\pi*J*t1)$ term of signal loss originating from the incomplete refocusing (figure 2).
The required dephasing gradient strength was determined by measuring a spectrum (single transverse slice through the calf muscle) with the double-quantum read pulse turned. In this case, no lactate signal was detected. With increasing crusher strength, the residual lipid signal was decreased to below the noise level. With this dephasing strength the double-quantum read pulse was turned back on to facilitate conversion of the lactate signal to an observable state.

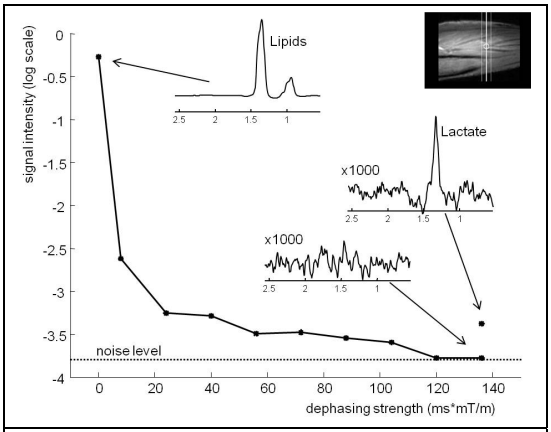

Figure 3; measurements were performed with the double-quantum read pulse turned off, and with increasing dephasing strength. After the lipid residual signal was reduced to below the noise level, the double-quantum read pulse was turned back on, and a clear lactate signal was detected.

Results:
High dephasing areas (>120 ms*mT/m) were required to reduce the lipid signal from the human calf muscle to below the noise level (figure 3). After enabling the double quantum read pulse, the lactate signal was clearly visible above the noise. Alterations in lactate signal in the calf muscle were observed during exercise (700N applied to the toes, figure 4).

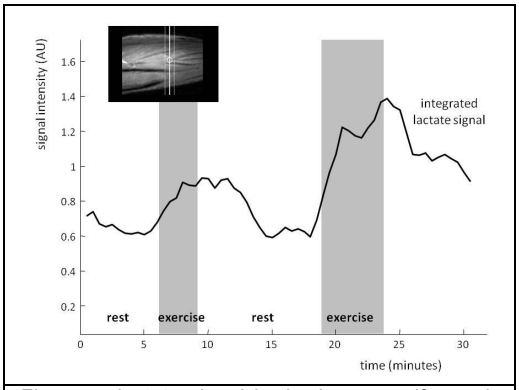

Figure 4: lactate signal in the human calf muscle before, during and after exercise.

Conclusion:
The refocused double quantum allows for double quantum filtering of coupled spin systems with long t1 times, as is required for the complete dephasing of overlapping resonances at the expense of additional T2 loss during this t1 time. The low lactate signal at rest and exercise was detected in the human calf muscle at 7T, even without optimizing the sequence to possible varying J-coupling values dependent on fiber orientation [2], nor with inclusion of more selective spatial localization.

References: [1] He J Magn Reson B 1995;106:203 [2] J Magn Reson 1999;139:213