# Localized Constant-Time Correlated Spectroscopy (LCT-COSY) of Human Muscle Using a Clinical 3T MRI Scanner 

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Introduction: Ongoing effort is directed to developing methodology for improving spectral resolution at clinical field strengths. Recently, the constant-time approach has been applied in conjunction with localized MRS techniques towards this goal (1-3). Here, we have implemented and validated a two-dimensional single-voxel constant-time (CT) spectroscopic method based on COSY for resolving the overlapping resonances of IMCL and EMCL within the soleus muscle.
Methods: The localized constant-time COSY experiment (LCT-COSY) was implemented on a 3T MRI/MRS scanner with a transmit / receive extremity coil. The sequence utilizes three slice-selective RF pulses $\left[90^{\circ}-\left(\mathrm{T}_{\text {ct }}\right.\right.$ $\left.+t_{1}\right) / 2-180^{\circ}-\left(T_{\text {ст }}-t_{1}\right) / 2-90^{\circ}-$ acquisition] to achieve volume localization. With $t_{1}$ defined by $t_{1}=k \bullet \Delta t_{1}$, where k indicates the $\mathrm{kth} \mathrm{t}_{1}$ step, the interval between the first $90^{\circ}$ pulse and the following $180^{\circ}$ pulse was incremented by $t_{1} / 2$ and was given by $\left(T_{C T}+k \bullet \Delta t_{1}\right) / 2$, while the interval between the $180^{\circ}$ pulse and the final $90^{\circ}$ pulse was given by $\left(T_{C T}-k \bullet t_{1}\right) / 2$ and was correspondingly decremented by $t_{1} / 2$. The first evolution interval, ( $\left.T_{C T}+t_{1}\right) / 2$, was placed after the first slice selection pulse while the second evolution interval, ( $\left.T_{C T}-t_{1}\right) / 2$, was placed after the crusher gradients surrounding the $180^{\circ}$ pulse. The position of the $180^{\circ}$ refocusing pulse was, in effect, stepped through the fixed delay of $\mathrm{T}_{\text {ст }}$. By design, the sequence exhibits spin-spin decoupling along the F 1 dimension along with improved spectral separation for both diagonal and off-diagonal resonances. The method was validated by simulations as well as phantom experiments, and was further applied to ten healthy subjects using a 27 ml voxel centered in the soleus muscle. The experiments were performed with TR/T Ст of $2 \mathrm{~s} / 56 \mathrm{~ms}, 40 \mathrm{t} 1$ increments, and 16 averages for each experiment, resulting in a total acquisition time of $\sim 21$ minutes.
Results: Figure 1A shows a LCT-COSY spectrum recorded from a soleus muscle of a healthy subject. Various resonances from IMCL and EMCL are assigned in the spectrum. Note the separation of olefinic protons arising from IMCL ( 5.3 ppm ) from those arising from EMCL ( 5.5 ppm ) and also the cross peaks between olefinic protons and allylic, bi-allylic methylene protons from IMCL at (5.3,2.0 ppm), (5.3,2.7 ppm) and (5.5,2.2 ppm), (5.5, 2.9 ppm ) for EMCL, respectively. Figure 1B shows the clear separation of the methyl, n-methylene, and allylic methylene protons from IMCL and EMCL.


Discussion: The spectral separation between the IMCL and EMCL resonances are less than 0.2 ppm in the soleus muscle (4), and therefore remain a challenge to separate at clinical field strengths. The LCT-COSY sequence performs this separation due to its incorporation of constant-time evolution, resulting in spin-spin decoupling along the F1 dimension. In addition the separation of cross peaks between olefinic, allylic and bi-allylic methylene protons within IMCL and EMCL permits an estimate of the degree of lipid unsaturation in these pools.

Fig.1. 2D LCT-COSY spectra recorded in soleus muscle
Conclusion: We have implemented and validated the LCT-COSY technique in soleus muscle of healthy subjects. We believe that this is the first in vivo demonstration of resolving the indicated resonances from IMCL and EMCL at clinical field strengths.

## References

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