1D and 2D Correlation Spectroscopy of Muscle at 7T

S. Ramadan[1], E. M. Ratai[2], L. L. Wald[2], G. C. Wiggins[2], and C. E. Mountford[3]

[1]Department of Radiology, Brigham and Women's Hospital, Boston, MA, United States, [2]Department of Radiology, Massachusetts General Hospital, Boston, MA, United States, [3]Radiology, Brigham and Womens Hospital, Boston, MA, United States

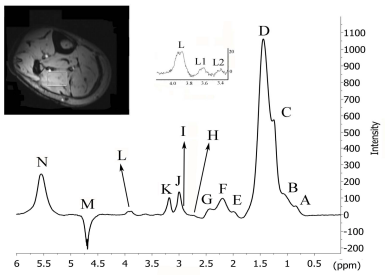

Figure 1. Axial image (voxel positioning). 7 T MR ^{1}H 1D spectrum of soleus muscle (38 yo volunteer). 3.3-4.3 ppm spectral region expanded to show detail. Peak assignment is:

Label/ppm	Assignment
A/0.84	C**H3** (IMCL)
B/1.05	C**H3**(EMCL)
C/1.25	(C**H2**)n (IMCL)
D/1.44	(C**H2**)n (EMCL)
E/2.00	–C**H2**–CH=CH– (IMCL)
F/2.20	–C**H2**–CH=CH– (EMCL)
G/2.43	–C**H2**–(C=O)–OR
H/2.76	–CH=CH–C**H2**–CH=CH– (IMCL)
I/2.93	–CH=CH–C**H2**–CH=CH– (EMCL)
J/3.00	C**H3** (Total Creatine, tCr)
K/3.18	TMA (N(C**H3**)3, e.g.Carnitine and
L2/3.41	C**H3** (Total Creatine, tCr) dipolar
L1/3.63	C**H2** (Total Creatine) dipolar coupling
L/3.92	C**H2** (Total Creatine)
M/4.70	Residual water
N/5.55	–**H**C=C**H**–,–(C=O)–O–C**H**R–

INTRODUCTION

A means of providing a detailed analysis of the chemicals involved in muscle metabolism and subsequent alterations with disease or drugs would be an important advance. Two examples of this include the effect of the cholesterol-lowering drugs, known as statins, that commonly cause muscle pain or weakness and can progress to rhabdomyolysis and mortality[1]. The second is the relationship between skeletal muscle triglycerides and insulin resistance, obesity and exercise[2]. Magnetic resonance spectroscopy (MRS) can provide such information by reporting on the intramyocellular lipids (IMCL) and extramyocellular lipids (EMCL) in muscle. These two types of lipids reside in different compartments in muscle tissue and thus their protons are shielded differently. Non-invasive quantification of IMCL and EMCL by 1D and 2D ^{1}H MRS has been reported at 3T[3]. However at 3T there is significant overlap or the resonances in the 1D and crosspeaks in the 2D MR spectra making assignment and definitive correlations with disease difficult. The goal here is to develop 1D and 2D MRS methods at the higher field strength of 7T in order to provide more detailed chemical information than is available at 3T.

MATERIALS AND METHODS

The technique was developed on apparently healthy volunteers, on no medication, with institutional review board approval. MR data was obtained using a 7T MR scanner (Siemens Medical Solutions, Erlangen, Germany) and a 28 cm diameter de-tunable birdcage coil for excitation and a 8.5 cm diameter surface coil for signal reception. Localizer images were obtained using a gradient-echo imaging sequence. The voxel was placed in the soleus muscle. For the 1D spectrum the spectral width was 4000 Hz, vector size 2048 points, voxel size of 15x19x30 mm^3, averages: 8, repetition time 2000 ms. The "WET" water suppression method[4] was applied before the acquisition sequence. The 1D spectra were processed using the MestReNova program[5]. The L-COSY sequence[6] was applied with a TE (initial)=30ms, TR=2000ms, averages = 8, voxel size: 15x19x30 mm^3, t1 increment size: 0.4 ms, indirect spectral width: 2500 Hz, number of increments:64. The total time for acquisition was 17 min. The processing parameters used were: F2 domain (skewed sine-squared window, 2048 points, magnitude), F1 domain (sine-squared window, linear prediction to 128 points, magnitude)[7]. The tCr(C**H**3) resonance at 3.00 ppm was used as a chemical shift reference.

RESULTS AND DISCUSSION

Typical 7T localized 1D MR spectrum of the soleus muscle, from a healthy volunteer, is shown in Figure 1. The resonances are assigned and listed in the legend. The resonances are similar to those assigned in Velan et al [3] but the spectral dispersion shown at 7T has not been recorded previously in vivo. For example resonances denoted E, F and G in Figure 1 show the splitting of allylic IMCL and EMCL resonances. Resonances A,B,C and D resolved more clearly than reported at 3T[3]. It has been reported that TMA/tCr ratio at 1.5T can vary from one muscle to another in the same person and between healthy and diseased muscles [8]. TMA/tCr ratio at 1.5T was found to be 0.6 when recorded with a TE of 30 ms. In this study, at 7T, and using the same TE value the TMA/tCr ratio is 0.9. This difference in T1 and T2 values of TMA and tCr at 1.5T and 7T is the expected rational for this difference. The L-COSY recorded from the same volunteer is shown in Figure 2. The chemical shifts and assignments of the crosspeaks are listed in the legend.The diagonal peaks at 3.41,3.41 and 3.63,3.63 appear to originate from partially oriented[9] tCr within the muscle tissue [9]. The ratio of resonances at 3.63 and 3.92 ppm n the diagonal in L-COSY spectrum is 22%, an indication of the partially oriented versus free tCr at 7T. Two diagonal peaks for carnosine are seen at F2=F1=6.9 ppm and 7.9 ppm. No residual dipolar coupling was observed, possibly due suboptimal muscle orientation. With optimal spectral dispersion, cross peaks P, Q, R and S can be used to determine the unsaturation level by inspecting ratios P/R (EMCL, 1.2) and Q/S (IMCL, 0.8), which correlate with existing values in literature.

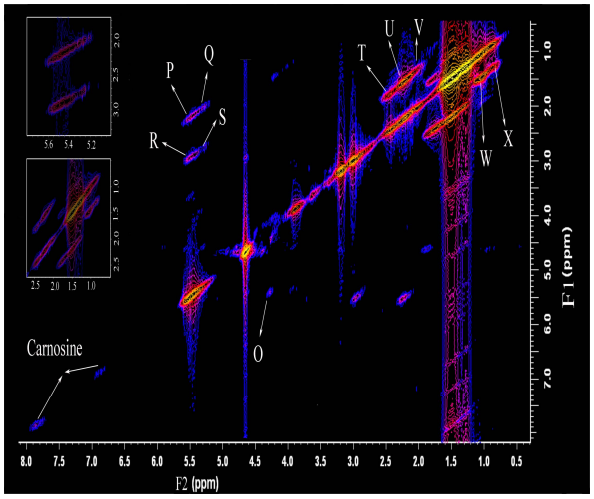

Figure 2. 7T 2D localized ^{1}H L-COSY from tibial bone marrow (same voxel as Figure 1). Following were assigned:

Cross peaks	Assignment
O (4.28,5.42)	Glycerol backbone
P (5.48,2.19)	EMCL Allylic and Olefinic
Q (5.31,2.02)	IMCL Allylic and Olefinic
R (5.50,2.93)	EMCL diallylic and Olefinic
S (5.30,2.76)	IMCL diallylic and Olefinic
T (2.44,1.78)	α-carbonyl and (CH2)n
U (2.23,1.56)	allylic (EMCL) and (CH2)n
V (2.03,1.32)	allylic (IMCL) and (CH2)n
W (1.04,1.47)	CH3 and (CH2)n (EMCL)
X (0.86,1.28)	CH3 and (CH2)n (IMCL)

CONCLUSION

The 1D and 2D L-COSY spectra obtained at 7T from the soleus muscle provide new information on TMA, creatine and lipid chemistry and structure. This method, as developed at 7T, offers an improvement in resolution and sensitivity over 3T and the opportunity to study in detail the effect of disease and drugs on muscle metabolism and chemistry.

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