Cross contamination of IMCL signals through loss of Bulk Magnetic Susceptibility Shift (BMS) differences in Human Muscle detected using ^{1}H-MRSI at 4T

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Introduction

Intramyocellular lipid (IMCL) and extramyocellular lipid (EMCL) signals are separated by 0.2 ppm[1]. This difference in bulk magnetic susceptibility has been determined to be due to the compartmentation of lipid stores within muscle – bulk EMCL lipids arise from adipocytes and are linearly arrayed alongside muscle fibers, while IMCL droplets are spherical and thus anisotropic. Experimental and theoretical analysis has determined that maximization of spectral resolution requires preservation of the BMS shift within the voxel of interest [2-4]. This in turn is dependent upon correct orientation of bulk muscle fibers along B_0, and avoidance of large EMCL deposits that might overlap with the IMCL signal. Almost all studies to date have been performed either at routine clinical field strengths (1.5T) and/or have used large voxel sizes of 1-8 mls where both problems are predicted to degrade spectral resolution. The goal of this study therefore, was to determine whether the measurement error of IMCL measurement could be reduced under optimal conditions by controlling the voxel size from 1.0 to 0.063 ml size using a multivoxel (spectroscopic imaging) approach.

Methods

Subjects: 8 sedentary lean (BMI 25.6 ± 3.5, mean ± SD), and 12 obese non-diabetic subjects (BMI 32.1± 1.8) were studied. *[1]HMRS:* A 4T Varian Inova whole body MR system with a TEM ^{1}H resonator was used in all studies. After scout images, SI localization was performed by slice selective excitation (10 mm). In-plane phase encoding (16x16, 32x32 and 64x64) over 16.0^2 cm^2 resulted in nominal voxel resolutions of 1.0, 0.25, and 0.063 ml. Water suppression was achieved using a semi-selective refocusing pulse. The acquisition time of ^{1}H SI (TR/TE=1000/24 ms for 16x16 and 32x32 PE, and 600/24 ms for 64x64 PE) was 5 min, 17 min or 43 min. For internal reference purposes, water SI (TR/TE=5000/24 ms) on the same slice was also acquired with 16x16 phase encoding (acquisition time= 21 min). For each muscle group (soleus S; tibialis anterior TA; tibialis posterior TP), all 32x32 MRSI spectra were inspected and the best resolved 3-4 voxels per muscle were selected and processed. Smaller size of voxels, e.g., 0.25 ml, or 0.063 ml, were chosen from within bigger sized voxels, e.g., 1.0 ml or 0.25 ml. Spectral Processing: Spectra were processed using a 10 Hz Lorentzian-Gaussian transformation and 250 Hz convolution difference. The IMCL resonance at 1.3 ppm was curve-fit using a Gaussian model and the linewidth of t-Cr as reported previously [5].

Results and Discussion

Table 1. IMCL (mmol/kg wet wt) (Mean±SD) obtained from 1.00 ml voxels and 0.25 ml voxels *via* 16x16 and 32x32 phase encoding

	S		TA		TP	
	1.00 ml	0.25 ml	1.00 ml	0.25 ml	1.00 ml	0.25 ml
Normal (n=6)	6.23±2.74	5.27±2.67$^{\phi}$	2.09±1.00	1.96±0.73	3.45±0.98	3.54±1.10
Obese (n=5)	11.0±5.30	8.57±3.51*	2.09±0.54	2.04±0.49	5.65±1.92	5.62±1.41

Normal (2F,4M): BMI=26.3±1.6, Obese (4F,1M): BMI=32.0±0.6. $^{\phi}$, p=0.11; *, p<0.05; 1.0 ml vs 0.25 ml.

Table 2. IMCL (mmol/kg wet wt) (Mean±SD) obtained from 0.25 ml voxels and 0.063 ml voxels *via* 32x32 and 64x64 phase encoding

	S		TA		TP	
	0.25 ml	0.063 ml	0.25 ml	0.063 ml	0.25 ml	0.063 ml
Normal (n=5)	7.12±1.72	7.09±1.39	1.88±0.74	1.88±0.72	3.26±2.12	3.44±2.21
Obese (n=9)	5.52±3.75	5.65±3.75	2.84±1.65	2.47±0.87	4.95±2.82	4.41±2.73

Normal (5M): BMI=26.0±1.5, Obese (7F,2M): BMI=31.4±0.90.

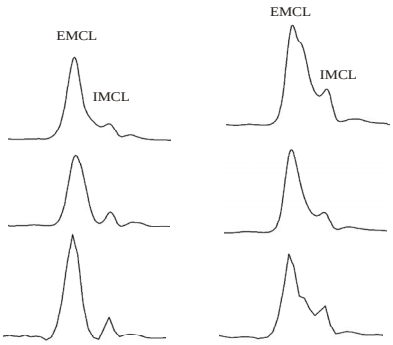

Figure 1. Proton NMR spectra in soleus obtained from sedentary lean (left column) and obese (right column) volunteers with different nominal voxel sizes: 1.00 ml, 0.25 ml, and 0.063 ml from top to bottom

The IMCL peak resolution from 0.25 ml vs. 0.063 ml voxels show no differences in soleus, TA or TP, but is better compared to 1.00 ml in soleus (Fig. 1). The IMCL (mmol/kg wet weight) obtained from 0.25-ml MRSI strongly correlates with that from 0.063-ml MRSI for both sedentary lean subjects (r =0.944, p<0.001) and obese subjects (r = 0.951, p<0.001) (Table 2). The acquisition time to obtain MRSI with voxel sizes of 0.063 ml is 43 min. This is barely practical due to the necessity for keeping the limb immobile during the entire acquisition. MRSI acquisition using a 0.25 ml voxel size is a practical alternative as this provides reasonable IMCL resolution for those subjects with non-ideal oriented muscle fibers and can be obtained in 17 min. When the voxel size is increased to 1.00 ml from 0.25 ml, IMCL content in TA and TP regions are not different for both sedentary and obese subjects. This may be due to our acquisition approach, as only the best resolved spectra, and thus voxels containing the best oriented muscle fibers, are analyzed. In addition, it is well known that fibers in TA are naturally oriented parallel to each other and thus easily align along B_o for optimum IMCL resolution. This same phenomenon may also be occurring in TP. The less uniformly oriented muscle fibers in the soleus region result in worse IMCL resolution as voxel size is increased. In Table 1, when the voxel size is increased from 0.25 to 1.00 ml, IMCL increases by nearly 20% in sedentary lean subjects (p=0.11), and is 30% higher for obese subjects (p<0.05). Multiple component and/or broad EMCL peaks were detected confirming EMCL myofibril heterogeneity likely arising from disparate fiber orientation along B_0.

We conclude that optimum IMCL resolution can be obtained from soleus muscle from voxels of 0.25 ml or smaller using a MRSI approach at 4T. Larger volumes up to 1.0 ml may be appropriate in TA or TP muscles, provided care is taken to analyze only well resolved voxels.

References

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