

Left-right bias in triglyceride composition of adipose tissue measured by ¹H MRS

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Target Audience: The abstract is aimed at radiologists and physicists with an interest in adipose tissue characterization.

Purpose. *In vivo* Proton Magnetic Resonance Spectroscopy (¹H MRS) can be combined with an understanding of triglyceride chemical structure to quantitatively examine human adipose tissue triglyceride composition. One assumption of triglyceride characterization is that spectral response across the spectral range of interest is uniform - that is, a unit of signal from the water and fat 'ends' of the spectrum will produce peaks of equal area after allowing for relaxation and j-coupling effects. In this study we examine whether, at clinical field strengths, the location of the MRS voxel within the body has an effect on spectral uniformity and hence the measured composition of triglyceride, and whether using a reduced spectral range removes spatially introduced bias.

Methods. *In vivo* ¹H MR spectra were acquired at 3 Tesla (GE Signa EXCITE HD, GE Healthcare, Waukesha, WI) using an 8-channel torso array coil in 41 subjects (18 adult, 23 pediatric). The Stimulated Echo Acquisition Mode (STEAM) sequence was chosen with minimum TE (10 ms) and mixing time (TM 5 ms) to minimize j-coupling effects. A TR of 3500 ms was chosen to minimize T1 effects. Sixteen signal averages were obtained without water or spatial saturation. After conventional imaging, a spectrum was acquired from the posterior deep right subcutaneous adipose tissue (RSCAT) using a 15 x 15 x 15 mm voxel. The same sequence was repeated with identical parameters in posterior deep left subcutaneous adipose tissue (LSCAT). The LSCAT position was chosen to mirror as closely as possible the RSCAT location. Spectra from the individual channels were combined using a singular value decomposition based approach (1). A single experienced observer analyzed the spectra using the AMARES algorithm (2) included in the MRUI software package (available from www.mrui.uab.es). A detailed description of the technique used to calculate number of double bonds (*ndb*) and number of methylene-separated double bonds (*nmidb*) in adipose tissue has already been published (3). The relative area of each of the peaks was found by adding the number of hydrogen nuclei with its associated type of bond in the triglyceride molecule. Values of *ndb* and *nmidb* were calculated by non-linearly minimizing the difference between the measured areas and that given by the theoretical model (Table 1). The chain length (*CL*) was fixed at 17.5, as allowing *CL* to vary freely can produce *CL* values well outside the narrow range seen *in vivo*. Values of *ndb* and *nmidb* were calculated for two different cases: a 5-peak model which used peaks 1, 3, 4, 5 and 6 to estimate saturation, and a 4-peak model which used only peaks 3, 4, 5 and 6, to investigate whether using reduced spectral range gives different results. Assuming there is no intrinsic left-right bias in deep SCAT, any systematic difference must be related to the acquisition.

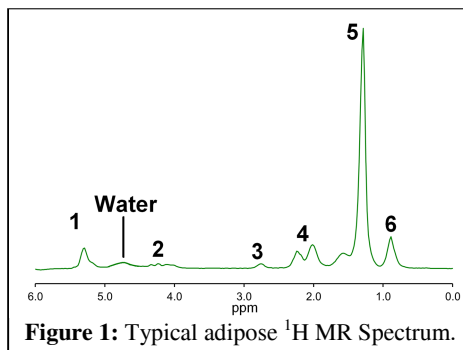


Figure 1: Typical adipose ¹H MR Spectrum.

Table 1: Relative magnitude of triglyceride peaks given by theory. *ndb* – mean number double bonds, *nmidb* – mean number of methylene-interrupted double bonds and *CL* – mean chain length.

Peak	Location	Assignment	Expected Spectral Peak Area
1	5.29 ppm	-CH=CH-	2* <i>ndb</i> + 1
	5.19 ppm	-CH-O-CO-	
2	4.2 ppm	-CH ₂ -O-CO-	4
3	2.75 ppm	-CH=CH-CH ₂ -CH=CH-	2* <i>nmidb</i>
4	2.20 ppm	-CO-CH ₂ -CH ₂ -	6 + (<i>ndb</i> - <i>nmidb</i>)*4
	2.02 ppm	-CH ₂ -CH=CH-CH ₂ -	
5	1.6 ppm	-CO-CH ₂ -CH ₂ -	(CL-3)*6 - <i>ndb</i> *8 + <i>nmidb</i> *2
	1.3 ppm	-(CH ₂) _n -	
6	0.90 ppm	-(CH ₂) _n -CH ₃	9

Results. A comparison of left and right *ndb* and *nmidb* values is shown in Table 2. The (full range) 5-peak model shows significant left-right differences in LSCAT and RSCAT for both *ndb* and *nmidb*. There is no significant difference for the 4-peak model. Figure 2 shows Bland-Altman plots for *nmidb* measured by the 4- and 5-peak models. There is a systematic shift in the 5-peak model which is absent in the 4-peak model, and there is greater scatter in the 5-peak model compared to the 4-peak model.

Table 2: Mean values of *ndb* and *nmidb* in RSCAT and LSCAT as measured using the 4- and 5-peaks models.

	RSCAT	LSCAT	p
5-peak model <i>ndb</i>	2.766	2.931	<0.0001
4-peak model <i>ndb</i>	2.762	2.796	0.1
5-peak model <i>nmidb</i>	0.710	0.859	<0.0001
4-peak model <i>nmidb</i>	0.707	0.719	0.25

Conclusion and Discussion. Non-uniform spectral response due to MRS voxel location introduces left-right bias in triglyceride composition measurements that can be reduced by using the smaller spectral range of a 4-peak model. Positional dependence of measured composition of triglyceride will introduce artificial differences in *ndb* and *nmidb* in different fat depots and possibly introduce a value dependent on patient size. Hence it vital that spatially introduced bias is minimized.

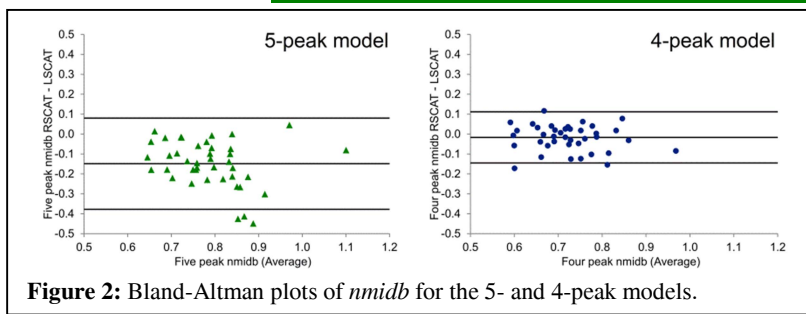


Figure 2: Bland-Altman plots of *nmidb* for the 5- and 4-peak models.

- Refs:**
- 1) Bydder M, Magn Reson Imag 2008; 26: 847.
 - 2) Vanhamme L, J Magn Reson 1997; 129: 35.
 - 3) Hamilton G, JMRI 2011; 34: 468.