In-vivo Determination of the Full ^{1}H MR Spectrum of Liver Fat

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Introduction: Determination of the complete liver fat proton (^{1}H) MR spectrum is important for both accurate spectroscopic quantification and for MR imaging-based measurement techniques that incorporate the multi-peak spectral structure of hepatic triglycerides. In-vivo spectroscopy at in-vivo field strengths can not directly measure the full spectrum as there are two fat peaks that overlap the water peak (**Figure 1**). However, it possible to derive the full spectrum from the fat peaks visible in the range 0.5-3 ppm using a triglyceride chemical structure approach (**Table 1**) previously used to find type of fat present in adipose tissue at high field (**1**) and to confirm food oil purity (**2**).

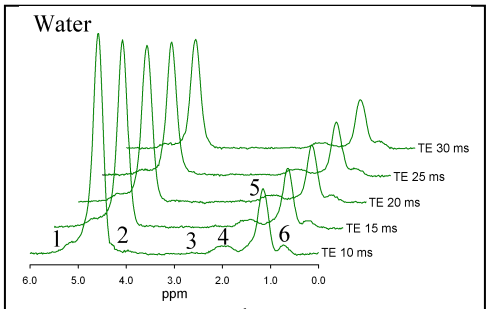

Figure 1: Typical liver ^{1}H MRS acquisition.

Methods: The study was IRB and HIPAA complaint, with subjects giving written informed consent. STEAM spectra were acquired on 121 human subjects with known or suspected NAFLD, at 3 Tesla (GE Signa EXCITE HD, GE Healthcare, Waukesha, WI) using an 8-channel torso array coil. After conventional imaging, a 20x20x20 mm voxel was selected within the liver that avoided liver edges as well as large biliary or vascular structures. Following a single pre-acquisition excitation, five spectra (TR 3500 ms, TM 5 ms) were acquired with a single average at progressively longer TEs of 10, 15, 20, 25 and 30 ms in a single 21 sec breath-hold. STEAM, the short TE range, and minimum TM were all chosen to minimize j-coupling effects. Signals from different array elements were combined using an SVD technique (**3**). A single experienced observer analyzed the spectra using the AMARES algorithm (**4**) included in the MRUI software package (**5**). The T2-values and the T2-corrected peak areas were calculated by non-linear least-square fitting. Peak 3 was only detectable in subjects with the highest levels of fat in the liver, and hence area of this peak in the high fat subjects was used to describe this peaks area relative to the other fat peaks. The relative areas of measureable fat peaks (peaks 3-6) were used in the theoretical model (**Table 1**) to generate mean ndb, nmidb, and CL values for a "mean" liver triglyceride molecule, allowing the areas of peaks 1 and 2 to be extrapolated.

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 Magnitude
1	5.29 ppm 5.19 ppm	-C**H**=C**H**- -C**H**-O-CO-	2***ndb** +1
2	4.2 ppm	-C$\mathbf{H}_2$-O-CO-	4
3	2.75 ppm	-CH=CH-C$\mathbf{H}_2$-CH=CH-	2***nmidb**
4	2.20 ppm 2.02 ppm	-CO-C$\mathbf{H}_2$-CH_2- -C$\mathbf{H}_2$-CH=CH-C$\mathbf{H}_2$-	6 + (**ndb-nmidb**)*4
5	1.6 ppm 1.3 ppm	-CO-CH_2-C$\mathbf{H}_2$- -(C$\mathbf{H}_2$)$_n$-	(**CL**-3)*6 - **ndb***8 + **nmidb***2
6	0.90 ppm	-$(CH_2)_n$-C$\mathbf{H}_3$	9

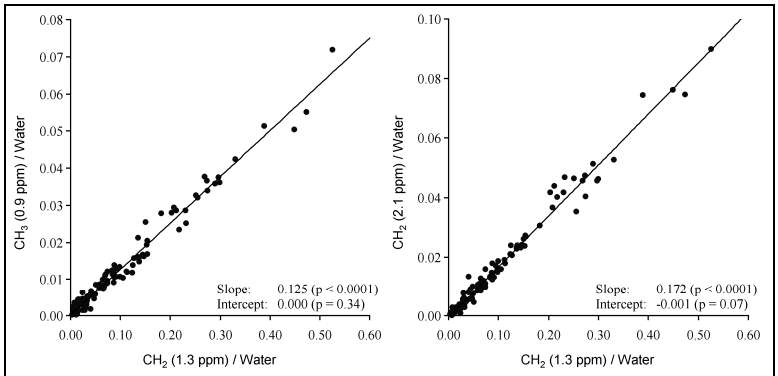

Figure 2: Comparison of areas of peak 6 and peak 5, and the areas of peak 4 and peak 5 in human subjects. A strong linear correlation is evident.

Results: Figure 2 compares T2-corrected peak area of peaks 5 and 6, and the T2-corrected peak area of peaks 4 and 5. There is strong linear correlation evident in both graphs. The ratio of peak areas of 5 to 6 is 0.125, while the ratio of the area of peak 4 to peak 5 is 0.172. For the four subjects with T2-corrected peak 4 area fat ratios ≥ 35%, the mean T2-corrected area of peak 3 (2.75 ppm) peak is determined to be 0.9% (range 0.7 – 1.1%) that of the T2-corrected area of peak 5. This gives CL = 17.45, ndb = 1.92 and nmidb = 0.32 for human liver fat. The area of the full fat spectrum is given in **Table 2.**

Table 2: The liver fat spectrum, using the areas of peaks 3, 4, 5 and 6 to extrapolate the areas of peaks 1 and 2.

Peak	T2 (ms)	% Total Fat
1	**-**	**4.7%**
Water	**23**	**-**
2	**-**	**3.9%**
3	**51**	**0.6%**
4	**52**	**12.0%**
5	**62**	**70.0%**
6	**83**	**8.8%**

Conclusions: The liver fat profile appears uniform regardless of the level of liver fat deposition. The model gives that 8.6% of the total liver fat underlies the water peak.

Refs: 1. Ren J, Dimitrov I, Sherry AD, Malloy CR. J Lipid Res 2008; 49: 2055-2062. **2.** Sacchi R, Addeo F, Paolillo L. Mag Res Chem 1997; 35: S133-S145. 3. Bydder M, Hamilton G, Yokoo T, Sirlin CB. Magn Reson Imaging. 2008; 26: 847-850. **4.** Vanhamme L, van den Boogaart A, Van Huffel S. *J Magn Res* **129**:35-43, 1997. **5.** .Naressi A, Couturier C, Devos JM, Janssen M, Mangeat C, de Beer R, Graveron-Demilly D. *MAGMA* **12**: 168-176, 2001.