Evaluation of 2D L-COSY to study lipid composition in mouse fatty liver at 7T

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Target audience: This paper could be of interest to the researchers doing either applications or development in magnetic resonance spectroscopy (MRS) or to physicians working on fatty liver disease

Purpose: Recent studies [1,2,3] have demonstrated the ability of 1D MRS to assess in vivo hepatic fatty composition. However depending on the chosen volume of interest, the shim system and technique performance, B0 field inhomogeneity can lead to large spectral line-width which hampers strongly peak assignment and quantification and thus derivation of lipid composition indexes. In this study, we evaluate the use of the 2D Localized Correlation Spectroscopy (LCOSY)[4] to analyze lipid composition and compare it to 1D MRS in fatty liver of mice, at 7T, in condition where the resulting shim were not always optimal.

Methods: Animal experiments were performed using five weeks old male C57BL/6J-ob/ob mice (n=3) weighting 31 to 37g and presenting severe hepatic steatosis. The experiments were conducted according to the procedures approved by the Institutional Animal Care and Ethical Committee of our University. Liver MRS was performed with a respiratory trigger method [5] using a 7T Bruker Biospec sytem at two time points (S1 = week 5 and S2 = week 7). 1D PRESS and 2D LCOSY were used with the following parameters: TR= 3s, for 1D: TE = 16 ms, 4096 data points (BW=4000Hz) were acquired with NA=64 for an acquisition time of ~5 min. For LCOSY, the 2D raw matrix consisted of 4096 data points along the direct dimension and 256 t1 increments (BW=4000Hz in both dimensions), NA=1, acquisition time was ~20 min. The voxel used for MRS was 3x3x3 mm and placed in the right lobe of the liver. Figure 1 shows typical spectra acquired with the two techniques in the liver. Peak assignment is described in Table 1. Quantification was performed for 1D spectrum using a voigt model employing 14 lines [6]. 2D spectra were post-processed using a sinebell filter in both dimension and zero-filling to 1024x1024 points and the volume of diagonal peaks and cross peaks were integrated using TopSpin 2.1. No correction for T2 was used. From the quantification results , indexes on the lipid composition were calculated.

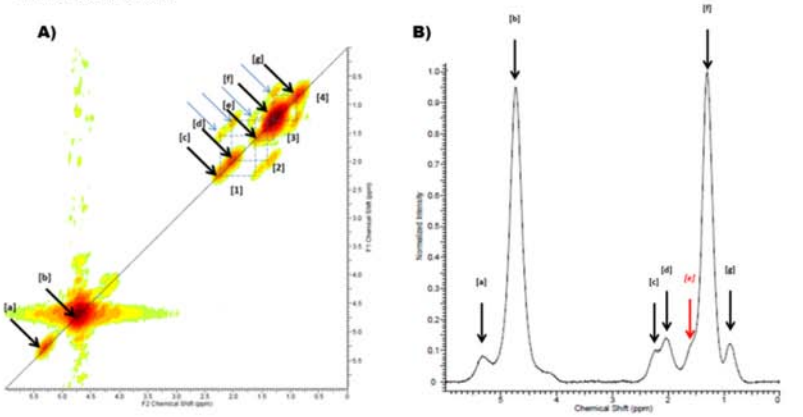

Figure 1: A) Typical 2D LCOSY spectrum of ob/ob mouse liver. A better dispersion is obtained compared to 1D and allow to visibly distinguish fatty resonances. Coupled fatty show characteristic cross-peak linked to resonance on the diagonal. Assignement is made in table 1. B) Typical PRESS spectrum obtain in ob/ob mouse liver . Line-width of water peak is 70 Hz. Compared to 2D spectrum the 1.6 ppm resonance is overlapped. Report to table 1 for assignement.

	Location (ppm)	Assignement	Cross-correlation	
[a]	5.3	-CH=CH-	[1]	2.25x1.6
[b]	4.7	H20	[2]	2.0x1.3
[c]	2.25	-CO-CH2-CH2-	[3]	1.6x1.3
[d]	2.0	-CH2-CH=CH-CH2-	[4]	1.3x0.9
[e]	1.6	-CO-CH2-CH2-		
[f]	1.3	-(CH2)n-		
[g]	0.9	-(CH2)n-CH3		

Table 1: Resonance Assignment of 1D & 2D spectrum

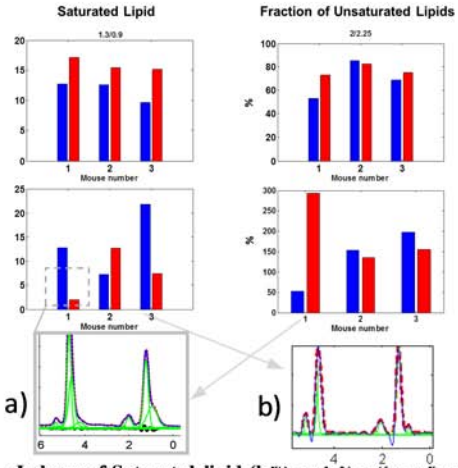

Figure 2 : Indexes of Saturated lipid (left) and Fraction of unsatured lipids (right) derived from quantification for 2D and 1D MRS at S1 (blue) and S2 (red) for the n=3 mice. Results found show good concordance with the literature for 2D MRS [3]. In these cases, 1D MRS suffers either from a) overlapping with poor shimming and b) dephasing due to motion to correctly discriminate and quantify resonances as highlighted in the displayed fitted spectra (a) mouse n°1 S2 b) mouse n°3 S1)

Result: Figure 2 shows the results obtained for two indexes (fraction of unsaturated lipid-fUL= 0.5*2ppm/2.25ppm- and saturated lipid component-SL=3/2*1.3ppm/0.9ppm- as defined in [3]) that are difficult to derive in 1D spectrum at 7T due to insufficient spectral dispersion compared to achievable line width (here between 65Hz and 90 Hz measured on the water peak). Also (results no shown) cross-peak analysis showed to have quantitative interest: cross-peak volumes [2] and [4] of table 1 are significantly proportional to the methylene resonance (1.3 ppm) and cross peaks [1] are proportional to the methyl resonance (0.9 ppm).

Discussion/ Conclusion: Our results show that the L-COSY can be used for the study of fatty liver to derive quantitative indexes. In this study, despite the use of a respiratory trigger technique, 1D MRS averaging could be sensitive, in some cases, to motion artifact, whereas even for a longer acquisition time 2D MRS quantitative results were more robust and consitent with expected range of values (0<SL<16 and 50%<fUL<100%).

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References: [1]: Hamilton,G *et al*. (2009), J Magn Reson Imaging 30(1): 145-52. [2] Lundbom, J. *et al* (2009), J Magn Reson 201(1): 39-47. [3] Ye, Q *et al*(2012), Magn Reson Mater Phy 25(5):381-9. [4] Thomas MA, et al. Magn Reson Med 2001;46:58-67 [5] Garbow, J. R et al. (2004), Concepts Magn. Reson., 21B: 40–48 [6] Ratiney, H, et al, *Proceedings of IEEE ISBI*. 2008; 1529-1532.