## 2D Correlated MRS as a quantitative method to asses liver fatty acid composition of ob/ob mouse

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Target Audience: This paper could be of interest to the researchers doing methodological development in magnetic resonance spectroscopy (MRS) acquisition and quantitative analysis.

Introduction: Magnetic Resonance Spectroscopy (MRS) is a well suited method for in vivo characterization of lipid content [1,2]. However, due to short T2 relaxation time and B0 field inhomogeneity, classical methods such as STEAM/PRESS MRS, with clinical or medium preclinical B0 field (B0<9.4T), can be limited by their spectral resolution, leading to quantification ambiguity and thus lipid composition assessment error. The aim of this work is to demonstrate the use of a 2D MRS method called L-COSY [3] and its quantification by a proper dedicated time domain quantification procedure using prior knowledge on triglyceride chemical groups and their connectivity.

Material and Methods: Acquisitions were performed on the liver of three male C57BL/6J-ob/ob mice on a 7T Bruker System at two different weeks (W1 & W2, respectively five and seven weeks after birth). Experiments were conducted according to the procedures approved by the Institutional Animal Care and Ethical Committee of our University. Mice averaged mass were for W1, m = 33.5±1.7 g and W2, m = 37.2±1.5 g. LCOSY acquisitions were performed in N-type mode leading to phase dispersive 2D spectra with TEmin = 16 ms, n2/n1 = 2048x256 Pts, Fe = 4000x4000 Hz. Acquisition time was about ~20min. The acquisitions were respiratory triggered as described in [4]. The quantification procedure consists in adjusting a model function describing the acquired signal with  $\widehat{S_{2D}}(t_1, t_2) = \sum_m a_m \widehat{x}_{Tri\,m} (t_1, t_2) R_m (t_1, t_2, T_{2inh}, T_{2m}) f_m (t_1, t_2, \Delta \omega_m, \phi_0)$  and which gives triglyceride coupled spin system ( $\widehat{x}_{Tri}$ ) contribution in term of amplitude ( $a_m$ ), relaxation ( $R_m$ ) and frequence & phase ( $f_m$ ) modulation. Relaxation time was estimated as two main contributions: T2 and T2inh due to B0 inhomogeneities which are assumed to impact in the same way the different chemical groups and leading to a mean linewidth of 69.4±9.7 Hz (W1) and 71.9±4.5 Hz (W2) on the water peak. A metabolite simulation basis set was use as prior knowledge using SPINACH simulation package [5]. Basis simulation was designed to describe (sub) spin system of triglyceride group using coupling values found in [6] and is represented in figure 1.

**Results**: A typical COSY spectrum acquired on liver is shown on Fig 2 with the corresponding fit. The spin group annotated as G was not integrated in our procedure since it was not detected in the acquired spectra.

Discussion/ Conclusion: Results show that respiratory triggered LCOSY can be used to acquire spectrum with sufficient resolution regarding the quantification, despite: important inhomogeneities, i.e poor shim conditions and a moving organ. 2D COSY Spectrum can be quantified via a dedicated time domain fitting procedure using prior knowledge. This quantification approach has the advantage of handling the phase twisted lineshape of LCOSY spectrum with dispersive tails. Results obtained by this method allow assessing fatty liver composition indexes equivalently to 1D MRS [7]. These later are in agreement with mice model evolution used (increased steatosis leading to increase of total lipid and saturated component indexes [8]). The quantification method allows to access T2 relaxation of each sub-spin systems in disadvantageous experimental condition. More acquisition are planned to corroborate these preliminary results.

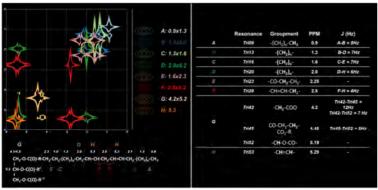
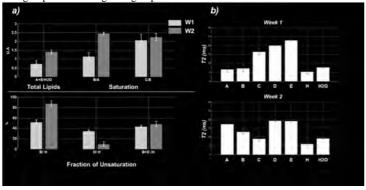


Figure 1: Parameters used in the simulation and basis set simulation corresponding to sub spin system of triglyceride group annotated with the molecule (TriXX refers to 1D MRS assessment). Liver fatty acid is composed of a triglyceride chain beginning with group *A* and ending with group *E*.



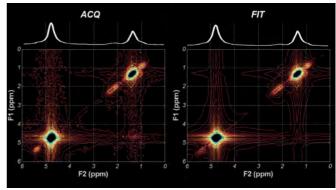


Figure 2: Acquired LCOSY spectrum (ACQ) and its quantification (FIT)

Figure 3: Results of Quantification between the two weeks. a) Evolution of calculated index: Total lipid was defined as the ratio of mean number of liver triglyceride chain and water (A+E / H2O). Saturated component as the ratio B/A and E/C. Fraction of Unsatured Lipids (fUL). fUL is relevant to B and D groups. Index B/H is relative to number of unsaturation at beginning of the chain and D/H the number at the end, their combination gives the proportion of fatty unsaturated chain.

b) T2 estimation of each compound

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