Concentrations of Glycogen and Choline Compounds in Human Liver Measured with 1H-MRS at 3T

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Introduction

^{1}H-MRS of the liver is widely used to study lipid content of the liver. To better understand changes in lipid and glucose metabolism due to metabolic disorders such as altered insulin sensitivity we want to observe other metabolites such as choline and glycogen. Both choline and glycogen are present in the normal liver in very high concentrations. The total concentration of choline containing compounds (CCC) in animal livers is about 30 mmol/kg_ww (1,2) and glycogen glycosyl unit concentration is somewhere between 100 and 300 mmol/kgww (3). Moreover, the choline TMA group resonating at 3.24 ppm has nine equivalent protons. In spite of that, choline and glycogen are rarely identified in human liver ^{1}H-MR spectra. High lipid content and large line widths as a result of poor B0 field homogeneity and breathing motion reduce the choline peak to a broad signal and water suppression (WS) often obliterates all glycogen signals. In this paper we show feasibility of measuring choline and glycogen in the human liver with navigator gated single volume PRESS ^{1}H-MR spectroscopy (4).

Materials and Methods

Experiments were performed on a Siemens Verio 3T MRI scanner using TIM phased-array coils. B_0 shim parameters were optimized with an expiration breath hold B_0 mapping method (5). Navigator gated T_2 weighted (T2w) and expiration breath-hold T_1 weighted (T1w) images in coronal and axial orientations were used to prescribe a 20x20x20 mm^3 spectroscopy volume in an area with high signal to noise ratio, free of fatty structures or blood vessels. Coronal T1w and T2w images were used to verify that the expiration breath hold B_0 field map was valid for navigator-gated acquisitions. After additional manual shimming, and optimization of transmit power and WS RF level 32 signals were averaged with a minimum repetition time (TR) of 3s with WET WS followed by 4 signals averaged with WS RF power set to zero (non-WS). The WET pulse bandwidth was set to 35 Hz to avoid saturation of glycogen. For metabolite quantification the water T_2 was measured in six subjects with five expiration breath hold non-WS spectra averaging two signals each at TR 3s and TE 24, 36, 48, 96 and 144 ms. The apparent T_2's of summed lipid CH_2 and CH_3 resonances, CCC and of summed glycogen H5, H3, and H2,4' resonances were determined with navigator gated spectra in six subjects at TE 35, 45, 60, 90 and 120 ms each with 32 signal averages. Spectra were corrected for eddy current distortions (6) and residual water signals between 4.5 and 4.9 ppm were filtered with HSVD (7) in jMRUI. Time domain signals were fitted with AMARES (7) to Gaussian line shapes, 0.2 to 0.5 ppm soft constraints regions around the initial estimates on chemical shift and phases of all signals constrained to the fitted zero order phase. Glycogen concentration was calculated from the summed area of three fitted resonances in the area labeled glyc in fig. 2.

Results and discussion

Spectra with quantifiable signals from glycogen and choline can be routinely obtained with expiration breath hold B_0 field mapping followed by manual shimming. Sample spectra are shown in figs. 1 and 2. Sample linear regression results on T_2 measurements are shown in figure 3. The T_2 of water protons was 33.8±3.5 ms (N=6), the T_2 of lipid 54±11 ms (N=13, WS + nonWS), the T_2 of CCC was 93±29 ms (N=6: range 76-130) and glycogen 34.8±8.5 ms (N=4: range 23-45). The CCC concentration was 16.9±4.5 mmol/kg ww (72% water). Assuming human liver contains 30 mmol/kg_ww total CCC as found in other mammals (2,3) this suggest that almost half the CCC may be MRS invisible (membrane lipids). The glycogen concentration of 78±36 mmol/kg ww we found is lower than expected (4). The cause of this discrepancy is unknown but direct or indirect saturation as a result of WS is unlikely. The glycogen concentration from a non-WS spectrum (4 signal averages) was 52 versus 53.5 mmol/kg ww in the WS spectrum of the same subject. Further validation is required, but we have shown that T_2 corrected quantification of glycogen and choline in the human liver is feasible with ^{1}H-MRS at 3T. This is likely to provide much more information on the mechanisms of metabolic disorders than liver lipid content alone.

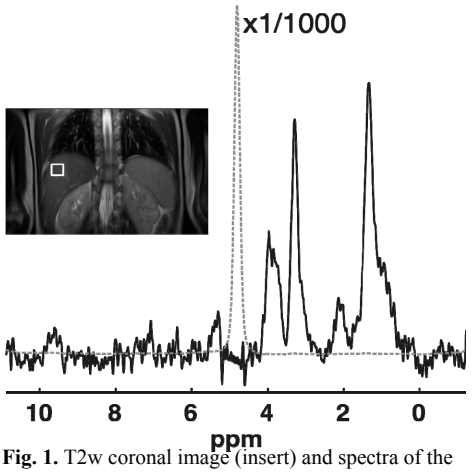

Fig. 1. T2w coronal image (insert) and spectra of the liver of a healthy 22 y.o. woman. The non-water suppressed spectrum is displayed as dashed gray line with the water suppressed spectrum superimposed, magnified 1000 fold in black solid line.

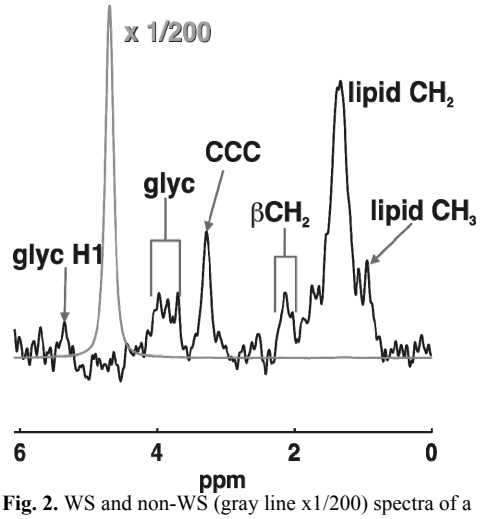

Fig. 2. WS and non-WS (gray line x1/200) spectra of a 23 y.o. healthy female subject. Peak assigments glyc H1: glycogen H1 (plus lipid) glyc: H2,4' H3 and H5 of glycogen, CCC: choline ompounds, βCH_2: lipid and amino acid beta-CH_2, lipid CH_2, CH_3 lipid methylene and methyl.

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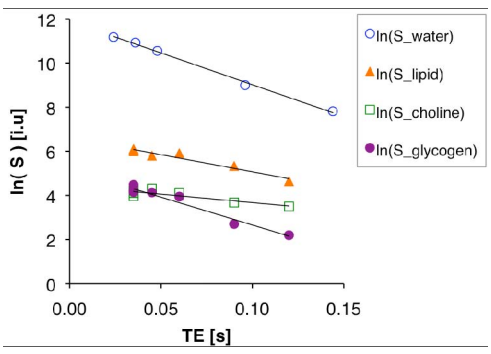

Fig. 3. Log of the time domain signal amplitudes (S) as a function of echo time for one subject (23 y.o. female). Linear regression lines are shown for water T_2=34.7ms (r^2 = .997), lipid T_2=64ms (r^2 = .95), choline T_2=130ms (r^2 = .77), glycogen H5+H3+H2,4' T_2=40ms (r^2 = .96).

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