chemical shift imaging of glycogen storage disease patients showing increased liver fat contents at young age only

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Purpose Phosphylase-b deficient patients suffer from glycogen storage disease (GSD IXa) leading to liver enlargement which usually resolves during puberty and adolescence. Presented is the first characterization of this pathology by ^{1}H MR spectroscopy (MRS) investigation.

Introduction MRS of 8 GSD IXa patients was performed in this study to assess whether or not liver fat content is elevated in GSD IXa and decreases with aging. An improvement in our MRS method compared with previous liver fat MRS studies is that we measured a plane of liver voxels at once rather then a single MRS voxel, yielding a reliable determination of liver fat content.

Methods We used hydrogen (^{1}H) MRS to determine the lipid concentration in the livers of 8 lean GSD IXa patients and 2 healthy control subjects (body mass index 18.9-23.7). MRI and MRS were performed using a 1.5 T Siemens Sonata system . A flexible liver coil placed over the liver region in the right side of the subject in the supine position was used for receiving the MRS signals. Movement of the liver with breathing was not suppressed as in the past it was shown that the quality of liver MR spectra is not affected by this (3). Hybrid 2D-chemical shift imaging (CSI), using PRESS with a TR of 5000 ms and a TE of 30 ms, was performed using a field of view of 16x16 cm^2 and a volume of interest of 5x8x4 cm^3 positioned inside the liver (Fig.1). The CSI measurement lasted 16x16x5s = 1280 sec or approximately 21 min. Water suppression was not applied in order to be able to calculate the fat-water ratio distributions in liver directly. The water-fat analysis was restricted to those (anterior) 4x6=24 voxels which were closest to the coil used for MRS. Fat to water ratios, defined as usual by the ratio of the curve fitted -CH_2- lipid signal (1.3 ppm) divided by the sum of the same lipid signal and that of H_2O (4.7 ppm), are equal to the weight fat/(fat+water) ratio because the relative hydrogen contents of water and fat are identical (approximately 11%). Determination of the fat contents for each of the above mentioned 24 MRS voxels thus led to estimates of the mean value and heterogeneity (standard deviation) in the liver fat content of patient and volunteers. At the used TR of 5 sec T1 saturation of the water and fat signals is negligible and at TE = 30 ms the correction required to compensate for the fact that the fat signal has a longer T2 than that of water should be in the order of 10% [1,2]. Our data have not been corrected for this. In one control and in one patient the CSI measurement was repeated with the use of a different receiver coil (a phased-array spine coil) and all other MRS parameters kept the same. The obtained liver fat contents were 0.57 ± 0.18 % in the control (0.92 ± 0.33 % with the flexible liver coil) and 4.90 ± 1.91 % in the patient (4.81 ± 1.80 %), indicating a good reproducibility of liver fat contents obtained by our method.

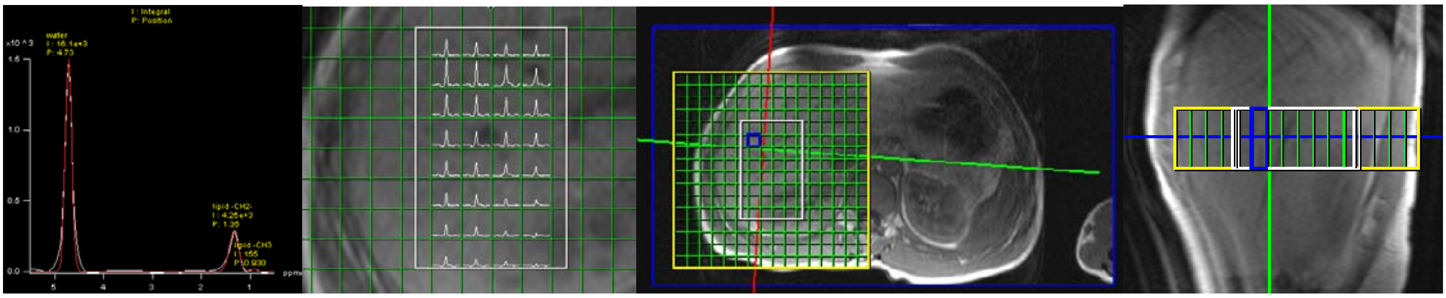

Fig.1. Liver MR spectrum of GSD IXa patient showing water, (–CH_2-)n and -CH_3 lipid signals resonating at 4.7, 1.3 and 0.9 ppm, respectively , and spectral map showing the distribution of the lipid signals within the 5x8x4 cm3 volume of interest.

Results The two control subjects had liver fat contents of less than 1%. The eight GSD IXa patients had liver fat contents varying between 0.39 and 9.99%. The spectrum of the liver voxel with the highest fat content, fat/(fat+water) = 4250/(4250+16100) = 21%, was chosen for illustrating the signals of water and fat in one plot (Fig.1). In the 8 GSD IXa patients the heterogeneity (standard deviations) in the fat contents in the transverse plane of 20 quantified liver voxels varied between 0.17 and 3.22%. No correlation with body mass index (BMI) was found. Four patients had an increased liver fat content compared to controls and three of them a palpable liver. In one patient, whose liver did not show an increased fat content, the liver was also palpable and in the other low-fat liver GSD IXa patients the liver was not palpable. Consistent observations paralleling the changes in liver fat content in GSD IXa were increases of the levels of triglycerides and of low-density-lipoprotein-cholesterol in blood.

Discussion Observed in young GSD IXa patients were fat contents of 3.4 to 10%, as compared with 0.5-0.9% in controls, that dropped to control level in patients past age 40 ($r = -0.82$; $P < 0.01$). We conclude that liver fat content is increased in glycogen storage disease (GSD IXa) and normalizes with aging. Assessing liver fat levels in this population is novel and is interesting not only for assessment of this population, but for an increased understanding of liver function which may be applicable to the approximate 20% of the population who have increased liver fat.

References 1. Longo R, Ricci C, Masutti F, Vidimari R, Crocé LS, Bercich L, Tiribelli C, Dalla Palma L. Fatty infiltration of the liver. Quantification by ^{1}H localized magnetic resonance spectroscopy and comparison with computed tomography. Invest Radiol 1993: 4: 297-302. 2. Thomsen C, Becker U, Winkler K, Christoffersen P, Jensen M, Henriksen O. Quantification of liver fat using magnetic resonance spectroscopy. Magn Reson Imaging 1994;12: 1994;12:487-495. 3. Sijens PE, van Dijk P, Dagnelie PC, Oudkerk M. Non-T_1 weighted ^{31}P MR chemical shift imaging of the human liver. Magn Reson Imaging 1995;13:621-628.

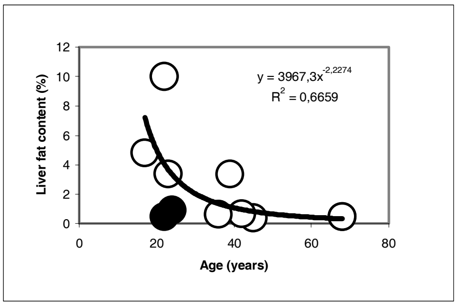

Fig.2. MR spectroscopy determined liver fat content in GSD XIa patients (open circles) and controls (closed circles) as a function of age. The equation represents the result of power fitting of the patient data ($P < 0.01$).