In vivo investigation of choline compounds with 1H and 31P MRS in the patients with liver disorders.

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Purpose

Measurements of hepatocellular lipid content (HCL) with ^{1}H MR spectroscopy are useful in understanding a number of liver disorders (e.g. obesity, steatosis, cirrhosis) whereas the measurements of choline containing compounds (CCC) lack the clean conclusion [1,2]. Phosphorus ^{31}P MR spectroscopy enables the observation of energy metabolism and intracellular compartmentation through the signals of phosphomonoesters (PME), phosphodiesters (PDE), inorganic phosphate (Pi) and nucleotide triphosphates (ATP) *in vivo* [3]. The metabolites that contribute to the CCC ^{1}H MR spectroscopic peak (choline, phosphocholine (PC), and glycerophosphorylcholine (GPC)) and can partly be resolved by ^{31}P MRS [4] are either cell membrane precursors (choline and PC) or cell membrane degradation products (GPC). Thus the concentration of these substances in tissues is expected to change with changing cell turnover [2]. In this study the link between ^{1}H & ^{31}P MRS regarding to CCC and HCL in patients with non-alcoholic fatty liver disorders - fatty liver (NAFLD) and steatohepatitis (NASH) was examined.

Methods

Eleven patients with suspicion for NAFLD or NASH (6 males, 5 females, median age 51, average BMI 29.7±5.2 kg.m^{-2}) were included in the study. Measurements were performed on 3T MR scanner (TimTrio, Siemens Healthcare, Germany) using spine and body array ^{1}H coil (Siemens) and 7T MR scanner (Magnetom, Siemens) using 9 cm circular double-resonant ^{1}H/^{31}P surface coil (Rapid Biomedical GmbH, Germany). HCL and CCC were measured by PRESS sequence (TE=30ms, TR=2s, no water suppression, 30x30x30mm, NS= 6) in 3T scanner. HCL was calculated with correction on relaxation times [5]. HCL and CCC signals were fitted by AMARES in jMRUI package and calculated as ratio to water signal [6]. Phosphorus metabolites were assessed by 2D CSI sequence (12x12, TE*=1ms, TR=1.8s, 200x200x30mm) in 7T scanner. 4x4 voxels from ^{31}P CSI with sufficient SNR were selected and phosphorus metabolites (PC, PE, Pi, GPC, GPE, γATP & α ATP) were fitted by AMARES and calculated as ratio to sum of all signals. After the MRS, liver biopsy from all patients was obtained. According to histology four patients were diagnosed with steatosis (NAFLD) and seven with steatohepatitis (NASH). Fibrosis staging score was calculated according to Kleiner et al [7]. Data were analysed for group differences between NASH and NAFLD and linear correlation between respective variables. Differences and correlations were considered significant with Pearson coefficient (r) at p<0.05.

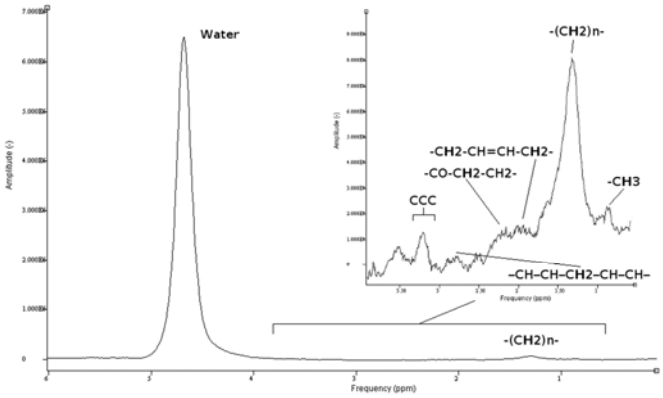

Fig. 1 Example of the liver ^{1}H MRS at 3T with choline region in more detail (water removed from detailed spectra, NAFLD patient).

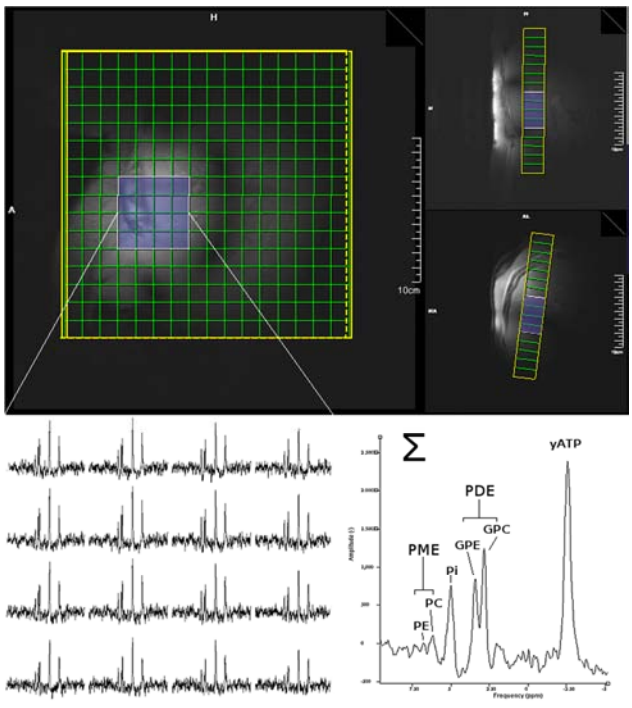

Fig. 2 Example of 2D CSI data from ^{31}P MRS at 7T and processed spectra from liver parenchyma (NAFLD patient).

Results/Discussion

In the ^{31}P MRS data there was minimal phosphocreatine contamination in the liver tissue Strong correlation between the CCC and HCL in all patients (r=0.89, p<0.001) has been found. HCL correlated also with steatosis grading of biopsy (r=0.82, p<0.001). The patients with NAFLD didn't have significantly different CCC signals than the patients with NASH. No significant difference was found in case of GPC and PC between these two groups. PE correlated with CCC (r=0.72, p<0.012) and PME correlated with histological steatosis (r=0.61, p<0.047) in all patients as well. Also PME/gamaATP [8] ratio correlated with Kleiner score (r=0.69, p<0.019) in all patients.

Conclusion

The measurements at 7T magnetic field strength allowed to resolve the resonances of choline containing metabolites in ^{31}P MRS. Even-though we could find certain links between ^{1}H- and ^{31}P- MRS derived measures of hepatic metabolism status, further investigation of differences between NAFLD and NASH on larger patient groups is needed.

References

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