**31P-MRS reveals biliary phosphatidylcholine in the liver**

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**Target audience:** General audience and researchers dealing with metabolism and MR spectroscopy.

**Purpose:** In previous in-vivo 31P MRS studies of the human liver the resonance at 2.06 ppm was hardly resolved due to the overlap with phosphomonoesters (PME). Due to optimized sequences and the higher field strength of recent studies, this peak at 2.06 ppm can now be detected at 7T and in decoupled and NOE enhanced spectra at 3T (1). Most references assign the 31P resonance at 2.06 ppm to be phosphoenolpyruvate (PEP), an important intermediate in glycolysis and gluconeogenesis (2,3). Recent publications link this resonance also to phosphatidylcholine (PtdCh), which is the main compound of bile and thus present in the gall bladder and bile ducts (4). The aim of this study is to determine the contribution of PtdCh to the metabolite resonance at 2.06 ppm in the phosphorus spectrum of the human liver.

**Methods:** To investigate the impact of gall bladder contamination on liver spectra, 25 healthy volunteers [mean age: 51.3 years; mean body mass index (BMI): 25.8 kg/m²] were divided in 3 subgroups, i) infiltration of the gall bladder in the VOI (N = 4), ii) small distance (≤ 2 cm) (N = 11) and iii) large distance (> 2 cm) between gall bladder and VOI (N = 7). The liver spectra of 5 subjects lacking gall bladder (cholecystectomy) was also measured (BMI: 26.0 kg/m², age: 60.4 years). An additional 4 young healthy subjects were used to study intra- and interday reproducibility (age: 25.2 years, BMI: 21.2 kg/m²). Finally, 39 subjects were included to study the correlations between liver spectra and metabolic parameters (age: 25.6 years, BMI: 24.5 kg/m²). All MRS measurements were performed on a 3T scanner (Philips Achieva, Best, The Netherlands). 31P spectra were acquired using a 14 cm circular 31P surface coil and the 1H body coil for 1H-decoupling and NOE enhancement. A 6×6×6 cm³ voxel of interest (VOI) was placed within the liver avoiding muscle. Localized liver spectra [TR = 4 s, number of signal averages = 192] were used to study intra- and interday reproducibility (age: 56.8 years, BMI: 24.5 kg/m²). All MRS measurements were performed on a 3T scanner (Philips Achieva, Best, The Netherlands). 31P spectra were acquired using a 14 cm circular 31P surface coil (Philips Healthcare, Best, The Netherlands) and the 1H body coil for 1H-decoupling and NOE enhancement. A 6×6×6 cm³ voxel of interest (VOI) was placed within the liver avoiding muscle. Localized liver spectra [TR = 4 s, number of signal averages = 192] were used to study intra- and interday reproducibility (age: 56.8 years, BMI: 24.5 kg/m²).

**Results:** In phantom measurements the broad PtdCh peak resonated at 2.8 ppm, while PEP resonated at -0.6 ppm, indicating PtdCh as the better candidate for the in vivo metabolite detected at 2.06 ppm. The in vivo peak at 2.06 ppm (PtdCh) was reproducible with a coefficient of variation of 4.8% (intraday) and 7.2% (interday). The PtdCh concentration in liver spectra lacking gall bladder infiltration (c = 0.78 ± 0.11 mmol/l) differed from the two other groups (c_infiltration = 1.32 ± 0.27 mmol/l, c_small dis. =1.19 ± 0.11 mmol/l) (p < 0.0001, p = 0.001). Additionally the exact distances between the VOI and the gall bladder of the subjects without gall bladder infiltration (N = 18) correlated with the concentration of PtdCh (r² = 0.68, p < 0.001). There was a difference in PtdCh concentration (p < 0.05) between persons with a history of cholecystectomy (c = 1.03 ± 0.23 mmol/l) and subjects with no gall bladder infiltration (c = 0.78 ± 0.11 mmol/l) (Fig. 1). There was also a correlation between bile duct diameter and PtdCh concentration (N = 10, p = 0.026, r = 0.69) and between PtdCh and cholesterol (N = 39, p = 0.01, r = -0.4) (Fig. 2)

**Discussion:** The correlation between the distance to the gall bladder and PtdCh concentration suggests that the resonance at 2.06 ppm arises from breathing motion shifting the VOI into the gall bladder. Contrary to this finding is the high concentration of PtdCh in the liver of cholecystectomy subjects and the low inter- and intraday variability. This leads to the assumption that bile in intrahepatic bile ducts in addition to bile in the gall bladder is contributing to the signal at 2.06 ppm. The 24% higher PtdCh concentration in cholecystectomy subjects compared with subjects without gall bladder infiltration could be explained by the widening of the bile ducts.

**Conclusion:** We suggest that the peak at 2.06 ppm originates from Phosphatidylcholine from bile in the liver as well as in the gall bladder. The association between liver PtdCh and serum cholesterol levels warrants further study.