^{1}H and ^{31}P Spectroscopy of the Liver in Patients undergoing long-term Total Parenteral Nutrition (TPN)

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Introduction

Patients with intestinal failure require intravenous feeding, or total parenteral nutrition (TPN). The parenteral feed contains lipid emulsions, but unfortunately it is not possible to replicate the complex lipoproteins that are produced *in vivo* by the cells (enterocytes) lining the intestine. Patients undergoing TPN can suffer liver complications, including liver failure, which are thought to be linked to the lipid emulsions used in the parenteral feed. The liver complications comprise steatosis (fat accumulation in the liver) leading to inflammation and fibrosis, and cholestasis due to diminished excretion of bile. Steatosis is also believed to be associated with the absence of choline in the parenteral feed; and a recent pilot study has demonstrated that steatosis can be corrected by choline supplementation [1].

^{1}H MR spectroscopy (MRS) can be used to detect choline-containing compounds (Cho), as well as the CH, CH_2 and CH_3 groups of lipids lipid species in the liver [2]. Levels of the lipid peaks in the normal population vary with body mass index (BMI) and with gender [3]. Additionally, ^{31}P MRS is able to detect phosphomonoesters (PME) and phosphodiesters (PDE), whose relative concentrations can change with liver diseases such as cirrhosis and hepatitis C.

The aims of this pilot study were to demonstrate the feasibility of liver spectroscopy in patients undergoing TPN and to investigate any differences between these patients and control subjects.

Methods

Liver spectra were acquired from 6 female patients receiving long-term TPN (ages 50±13, BMI 20.5±3.1, length of TPN 9±4 years) and from 6 healthy female volunteers (ages 35±13, BMI 23.0±2.9). All 6 patients were receiving <1g/kg lipid per day, with intralipid as the fat source. The scans were acquired after fasting, and were approved by our local research ethics committee. A 1.5 Tesla scanner was used (Signa Excite III, GE Healthcare, Waukesha, WI).

^{1}H spectra were acquired using 8 channels of a torso array coil, using respiratory triggering and with the patient supine. A PRESS sequence (PROBE, GE) contained VSS pulses for out-of-voxel saturation and CHESS water suppression. Scan parameters were TE =35 ms, TR = 1 respiratory cycle (typically 4–5 sec), 2048 data points, dwell time 0.4 ms. The 3×3×3 cm^3 voxel was positioned in the posterior right lobe of the liver. Automatic shimming was performed during an expiratory breathold, corresponding to the diaphragm position for data acquisition. 64 signal averages were acquired, preceded by 16 reference lines without water suppression.

^{31}P spectra were acquired, during free breathing, using a 12cm square-loop transmit/receive coil (R. Hashoian, Clinical MR Solutions) with an additional proton loop pair for acquiring localised images. A right decubitus position was used to minimise respiratory motion. Automatic followed by manual shimming was performed. A slice-selective spin echo sequence was used in sagittal orientation with TE = 2.5 ms, TR = 2 sec, 256 signal averages, slice thickness 40mm, 2048 data points, dwell time 0.4 ms. The slice-select direction was approximately perpendicular to the coil plane. The patient was carefully positioned to ensure that the sensitive region of the coil coincided with the liver; this provided the only in-plane spatial localisation.

For ^{1}H data, initial data processing was performed using SAGE (GE Healthcare). The full dataset was processed using a PROBE SVQ reconstruction, consisting of optimal recombination of the multi-coil data, line-by-line phase correction using the residual water peak, and then water peak subtraction and phase unwarping of the summed data. A separate and additional reconstruction was performed on the reference data (coil combination, line-by-line frequency and phase correction) to allow measurement of the unsuppressed water peak area. Peak areas were estimated with time-domain analysis using the AMARES method [4] in jMRUI [5]. From reference data, the water peak area was determined, then the water peak was removed using an HLSVD filter, and the CH, CH_2 and CH_3 lipid peak areas were determined; these were summed to give the total lipid peak area. From the full dataset, the lipid peak areas were again determined, then lipid and residual water peaks were removed using an HLSVD filter, then the Cho peak area was also determined. The HLSVD filters were necessary to avoid the influence from the tails from water and also the strong lipid peaks found for some subjects. Total lipid / water, choline / lipid and choline / water peak area ratios were estimated.

For ^{31}P spectra, AMARES was used to fit the PME and PDE peaks (each as two separate peaks); also Pi and the NTP multiplets.

For all spectra, fixed sets of prior knowledge and soft constraints were used to minimise operator dependence. Each resonance was modelled as an exponentially decaying sinusoid. Results were inspected visually to ensure acceptable fits and small residuals.

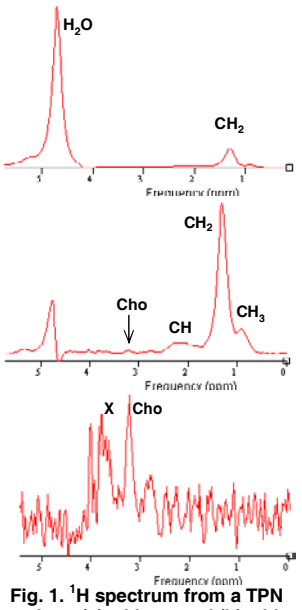

Fig. 1. ^{1}H spectrum from a TPN patient: (a) without and (b) with water suppression; (c) after filtering out water and lipid peaks. Amplitude scale varies between graphs.

Results

Example spectra are shown in Figures 1 and 2. Table 1 shows results from the analysis of both ^{1}H and ^{31}P spectra. Lipid/water and Cho/lipid ratios showed significant differences between the groups (Mann-Whitney U test).

Three of the patients had significantly higher (≥3 s.d.) levels of lipid than the control subjects (lipid/water = 0.113, 0.154 and 0.478); two of these patients had confirmed fatty infiltration on ultrasound. Choline peaks were visible in spectra from all control subjects and four of the patients, but no choline peak was visible in the remaining two.

No significant differences were seen between the ^{31}P spectra from controls and patients as a group. However, the two patients for whom PME/PDE falls outside the control group mean by ≥3 s.d., were the two in whom liver fibrosis had been identified at biopsy.

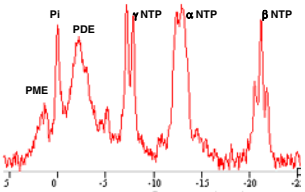

Fig. 2. ^{31}P spectrum from the same patient.

Discussion and Conclusions

MR liver spectroscopy data was obtained from patients receiving parenteral nutrition, demonstrating the feasibility of the technique in these patients. Despite their low BMIs, three patients had substantially higher lipid levels than the controls (or than normal data in ref. 3); this method could be used for quantitative assessments of steatosis and allow monitoring of lipid changes during therapeutic interventions such as choline supplementation (in a similar fashion to imaging based methods of fat assessment).

Levels of choline itself (relative to water) could be reliably assessed in controls, who all had relatively low lipid levels. However, the very large neighbouring lipid peaks in some patients make it difficult to be confident that the relatively small Cho peaks are genuine in all cases. Our results for Cho/water in patients should therefore be treated with caution; future studies may be able to avoid this problem by using increased echo times and/or lipid suppression methods, which reduce spectral contributions from lipids.

With the current sample size and the heterogeneous nature of this patient group, there were no significant differences between the phosphorus spectra for the two groups as a whole; however as expected the two patients with known liver fibrosis showed an elevated PME / PDE ratio. Future investigations will investigate this link further in these patients. Such studies could achieve improved spectral quality using higher field strengths, and the ISIS sequence could be used to give improved localisation.

	Controls	Patients
lipid / water	0.020 ± 0.019	0.143 ± 0.173 *
Cho / lipid	0.14 ± 0.13	0.02 ± 0.02 *
10^3 × Cho / water	1.58 ± 0.56	0.88 ± 0.71
PME / PDE	0.205 ± 0.042	0.262 ± 0.076
PME / NTP	0.130 ± 0.017	0.132 ± 0.035
PDE / NTP	0.647 ± 0.082	0.525 ± 0.127
Pi / NTP	0.181 ± 0.020	0.161 ± 0.024

Table 1: results from ^{1}H and ^{31}P spectra (mean ± standard deviation). * denotes $p<0.05$

Acknowledgements

We would like to thank Timo Schirmer for practical advice on liver spectroscopy, and the FFA for funding.

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