用質子(1H) 磁性共振分光鏡作體內肝脂定量所帶來的問題

Problems associated with using in vivo proton (^{1}H) magnetic resonance spectroscopy to quantify liver fat

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In-vivo ^{1}H magnetic resonance (MR) spectra of the liver were obtained in 8 patients admitted for liver biopsy. These patients had abnormal liver function and the presumptive diagnosis of fatty liver prior to biopsy. Two patients with NIDDM were also studied but liver biopsies were not performed as liver function was normal. The MR spectra, obtained on a 60 cm clear-bore 1.9 tesla superconducting magnet showed two ^{1}H resonances, one from water and the other from repeating methylene protons – (CH_2)n – in triglyceride. The lipid: water signal ratio was used to characterize tissues as subcutaneous fat (high lipid:water ratio), normal liver (low lipid: water ratio) and fatty liver (intermediate lipid: water ratio). The spectra obtained at the greatest depth from the probe surface ~4.5 cm) was used as it was most likely to represent liver tissue.

Although all 8 patients were expected to have fatty liver only 2 had evidence of significant fatty changes on microscopy. This was assessed by counting the vacuoles of fat over the area of the biopsy specimen and quantitated as 'fat vacuoles per high power field' (f/hpf).

In the 2 patients with NIDDM, unusual stack plots suggested technical difficulties with ^{1}H MR spectroscopy for in-vivo assessment of fatty liver. The first patient, PT had a significant increase in lipid:water ratio on the spectra thought to represent liver (lipid:water ~ 65% cf levels <3% in norma liver and 12.6% + 26.5% in those patients subsequently found to have fat on biopsy). This was later found on MR imaging to represent omental fat lying between the liver and muscle layer. The second patient, OM had a large amount of subcutaneous fat overlying the area assessed. As seen on the stack plot, the probe depty was not great enough to pass through the subcutaneous fat and muscle layer to penetrate liver tissue.

There was a significant correlation between the lipid:water signal ratio and visible fat on biopsy in those patients who underwent liver biopsy. Difficulties experienced with probe depth suggests imaging would be necessary prior to spectroscopy to ensure liver tissue is actually assessed.

Introduction

Fatty infiltration of the liver is seen in many clinical situations such as obesity and non-insulin-dependent diabetes as well as in ethanol excess[1]. Diagnosis from liver function tests is difficult although the degree of fatty liver can be correlated with the degree of abnormality of enzyme testing[2]. In some patients, such as those with non-insulin-dependent diabetes, liver function may be normal and thus fatty liver may go undetected. Ultrasound is not specific for fatty infiltration although it is sensitive in detecting localized areas of fat[3]. Computed tomography (CT) can identify moderate and severe fatty infiltration, however, other factors such as oedema or drug therapy can alter hepatic density making CT scanning neither sensitive nor specific. As fatty liver may obscure or mimic another disease process on imaging techniques available routinely[4,5] often liver biopsy is required.

Conventional MR images using spin-echo techniques are also relatively insensitive for identifying fatty liver. Newer phase-contrast methods produce separate water and fat images with good spatial resolution and provide a sensitive method to detect fatty infiltration of the liver quantitatively[6]. This method, known as the Dixon method, requires a pulse sequence which, unfortunately, is not readily available as commercial MRI software.

^{1}H-Magnetic resonance spectroscopy (MRS) has recently been used to analyse human fat in vivo as it can easily detect water and lipid protons[7]. The phase-modulated rotating frame imaging technique[8] has been used in the human liver for quantifying phosphorus-containing metabolites[9] and for investigating iron overload by ^{1}H MR spectroscopy[10]. We have applied this technique to obtain one-dimensional chemical shift images of the liver, in order to detect and quantify hepatic fatty infiltration in eight patients. Two patients with non-insulin-dependent diabetes were also studies although technical difficulties prevented adequate penetration to liver tissue.

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Methods

Subjects

^{1}H MR spectra of the liver were obtained in eight patients with abnormal liver function tests admitted for liver biopsy (6 m/2 f). The age range was 41–78 years (mean 62) and only five of the patients admitted to consuming alcohol (between 1–18 standard drinks/day). Three patients smoked. Body mass index (BMI) ranged from 20.5–32.5 kg/m^2 (mean 24.5 kg/m^2) although there was evidence of abdominal obesity in the men with a mean waist to hip ratio (WHR) of 0.99. Percent body fatness as estimated by four skinfold thicknesses was 22.8 ± 4.

Liver histology

Liver biopsies were obtained from the initial eight patients by the standard Menghini technique within two days of the ^{1}H MRS study. The specimens were sectioned and stained with haematoxylin and eosin and were graded by an independent histopathologist. Vacuoles (left by lipid droplets) were counted and documented as fat vacuoles per high power field (f/hpf).

^{1}H MR spectroscopy

Magnetic resonance spectra were obtained on a 1.9 T 60 cm bore magnet (Oxford Research Systems, Oxford, UK) interfaced to a Biospec 1 spectrometer (Bruker, Karlsruhe, Germany) operating at 80 MHz for protons. The patient lay on his or her right side with the liver positioned over a double surface coil tuned to ^{1}H. The diameter of the receiver coil was 7 cm and this dimension defined the lateral extent of the volume from which signals were collected. One dimensional chemical shift images of the protons in the liver and overlying intercostal muscle were obtained by the phase-modulated rotating frame imaging technique[11]. The image involved 32 phase-encoding steps of eight scans (and two dummy scans) each, with an interpulse delay of 2.28 s. Each image took 13 minutes to acquire. The images were processed by two-dimensional Fourier transformation. A Lorentzian windowing function was applied in the frequency dimension, and a Gaussian function in the depth dimension.

Analysis

The MR spectra showed two H resonances, one from water and the other from repeating methylene protons — $(CH_2)n$ — in triglyceride. The lipid:water ratio was manually determined by counting the 'area under the curves' and the ratio used to characterize tissue as subcutaneous fat (high lipid:water ratio), muscle (low lipid:water ratio), normal liver or fatty liver (intermediate lipid:water ratio). The spectrum obtained at the greatest depth from the probe surface (~4.5 cm) was considered to be most likely to represent liver tissue although no imaging was performed.

Statistical methods

A Spearman Rank correlation was performed using the number of fat vacuoles per high power field as an index of liver fat severity and the lipid:water ratio calculated from the spectrum obtained at the greatest depth from the probe surface. This gave a correlation co-efficient of r = 0.88, P <0.001.

Discussion

In this small study there was a strong correlation between fat seen on liver biopsy and an increased lipid:water ratio on ^{1}H MRS (r=0.88). Patients with fatty liver on biopsy had a second fat peak which persisted through to the maximum depth (Fig. 1). Those with no evidence of fatty liver had a low lipid:water ratio at the maximum depth and had only one peak of fat (Fig. 2). This correlation is similar to that seen by Longo et al.[12] who presented the results of 26 patients using ^{1}H MR imaging spectroscopy to quantify hepatic fat.

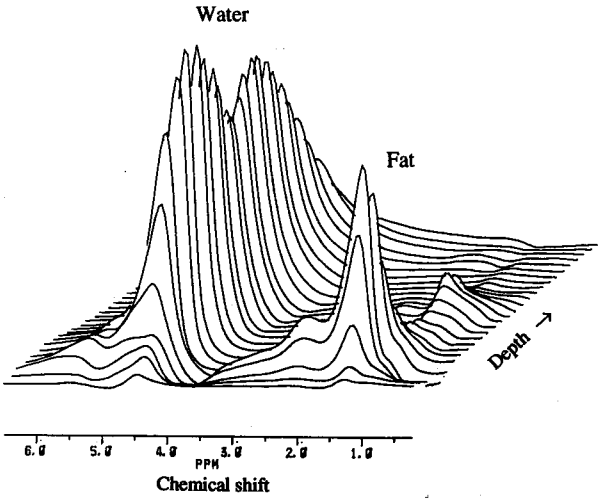

Figure 1. Stack plot from a patient with fatty liver showing persistence of a second fat peak through to the maximum depth.

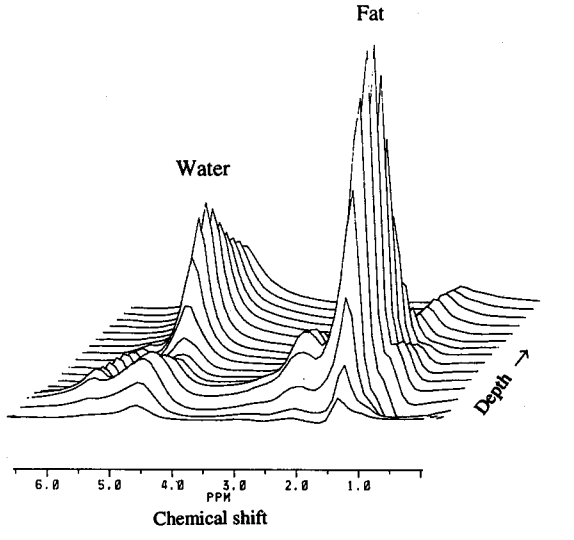

Figure 2. Stack plot from a patient with no fat on liver biopsy. There is an early fat peak (high lipid:water ratio), close to the probe surface resulting form subcutaneous fat. At the maximum depth, there is no fat peak and the low lipid:water ratio is thought to represent normal liver tissue.

In the two subjects who did not have liver biopsy (9 + 10) the lipid:water ratio remained high in the spectrum obtained at the greatest depth from the probe surface. Both subjects had non-insulin-dependent diabetes with normal liver function tests and so liver biopsy was not clinically indicated in these patients. Inspection of the spectra obtained demonstrated some of the difficulties associated with MRS in these patients.

In patient number 9 (see Fig. 3), subcutaneous tissue extended in from the probe surface to approximately 3.5 cm. Intercostal muscle tissue was detected but penetration was not sufficient to allow liver tissue to be demonstrated. This

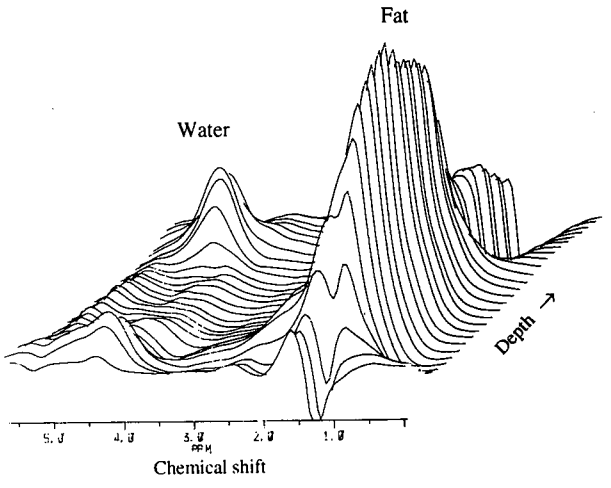

Figure 3. In patient with a large amount of subcutaneous tissue, depth penetration is not sufficient to accurately assess liver tissue.

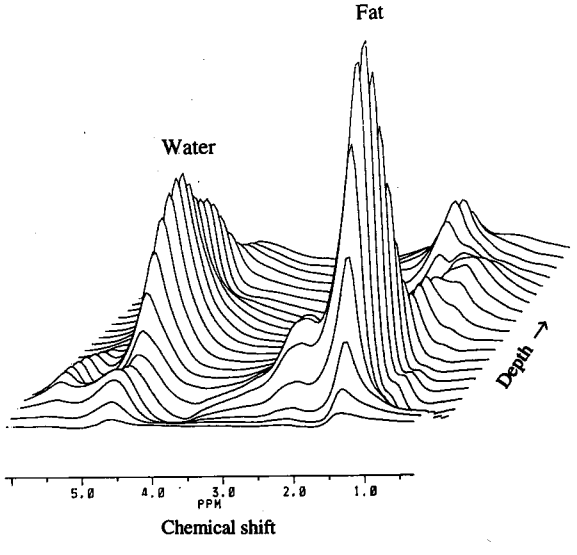

Figure 4. In a patient with significant abdominal obesity, the second fat peak (high lipid:water ratio) was shown to represent omental fat on MR imaging.

finding was subsequently confirmed by use of MR imaging and emphasizes the need for imaging to be performed concurrent with MRS.

In patient number 10 (see Fig. 4) a second peak with a high lipid:water ratio occurred at a depth though to represent liver tissue. At MR imaging this was seen to represent omental fat interfaced between intercostal muscle tissue and liver. This patient had an abdominal distribution of body fatness with a waist:hip ratio of 0.95 and MR imaging showed large amounts of visceral fat.

Thus, ^{1}H spectroscopy is a useful tool to quantitate hepatic fat and as such can be used where liver biopsy is contraindicated. There are, however, situations where increased body fatness either subcutaneous or omental may make interpretation difficult and necessitate imaging using either ultrasound, CT or MR.

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