appreciably and if a reduction in intake is not advised then weight increase is likely, for diabetic patients do not appear to compensate by an increase in the thermic response to a meal and noradrenaline stimulation. It is therefore interesting that after a mean of 5.3 months of continuous subcutaneous insulin infusion our subjects gained an average of 3.5 kg.

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Detection of spread of malignant lymphoma to the liver by low field strength magnetic resonance imaging

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Abstract

The accuracy of spin lattice relaxation time (T_1) measurement obtained with a low field strength magnetic resonance imager for the detection of spread of malignant lymphoma to the liver was assessed. The results of histological examination obtained at open liver biopsy were compared with liver T_1 values in 27 patients with lymphoma. The normal range for T_1 was estab-

lished by scanning 61 healthy volunteers. Magnetic resonance imaging was highly sensitive in detecting hepatic lymphoma, all seven patients with liver lymphoma proved by biopsy having considerably higher T_1 values. Specificity was less good. Five out of 20 patients with no histological evidence of hepatic lymphoma had abnormal T_1 values.

This level of sensitivity is considerably better than that reported for other imaging methods and contrasts with the results of one previous study using a different magnetic resonance system. Low field strength magnetic resonance imaging may prove to be a useful screening test in patients with lymphoma. The presence of a normal liver T_1 seems to be a reliable guide to the absence of hepatic disease.

Introduction

Accurate diagnosis of spread of disease to the liver in patients with malignant lymphoma is important for selecting treatment and determining prognosis. Clinical assessment of liver disease is notoriously inaccurate; hepatomegaly is an unreliable guide to the presence of lymphoma,^{1,2} raised serum alkaline phosphatase activities may be found when the results of liver biopsies are normal,^{2,3}

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and, conversely, hepatic lymphoma may occur when the alkaline phosphatase activity is normal.⁴

The sensitivity of imaging methods in the detection of liver lymphoma is poor, mainly because infiltration by lymphoma is usually diffuse rather than focal. Zornosa and Ginaldi obtained a sensitivity of only 57% for the detection of spread to the liver using computed tomography in a study of 65 patients with lymphoma,⁵ and similarly disappointing results have been reported for radio-nuclide scanning.^{5,6} Although no large series on ultrasound have been published, this method is also considered to be a poor detector of diffuse liver lymphoma.^{7,8}

We undertook this study to determine the accuracy of the measurement of spin lattice relaxation time (T_1) with a low field strength magnetic resonance imager in detecting liver lymphoma.

Patients and methods

We studied 27 patients with malignant lymphoma (18 with Hodgkin's disease and nine with non-Hodgkin's lymphoma) aged 18-81 years (median 41) for whom the histological findings of open liver biopsy were available.

FIG 1—Calculated T_1 image of an axial section through the upper abdomen of a volunteer. Cursors are placed peripherally over the liver to avoid major vessels.

Twenty six underwent laparotomy with wedge liver biopsy and in one case tissue was obtained at necropsy. Five patients underwent laparotomy for diagnostic reasons (one with Hodgkin's disease, four with non-Hodgkin's lymphoma), 12 for pretreatment staging (all with Hodgkin's disease), three for post-treatment reassessment (all with Hodgkin's disease), and six for therapeutic reasons (one with Hodgkin's disease, five with non-Hodgkin's lymphoma). Magnetic resonance imaging was performed within two weeks of the histological assessment in all cases, and no treatment was given during this period. Magnetic resonance imaging preceded histological assessment in 20 cases and was performed after laparotomy in seven. Sixty one healthy volunteers (33 men and 28 women), age range 21-60 years, also underwent scanning to establish a normal range of liver T_1 . Liver T_1 values for the 27 patients were compared with the histological findings and with the T_1 values for the volunteers.

Axial sections 16 mm thick were obtained through the liver in all patients using a 0.08 tesla MD 800 resistive magnetic resonance scanner, operating at 3.4 MHz. At least four axial sections were obtained for each normal subject.

We used the standard pulse sequence for this scanner.⁹ This consists of alternating saturation recovery and inversion recovery sequences with a repetition time of 1000 ms and an inversion time of 200 ms. A calculated T_1 image is generated from a computed algorithm. T_1 is measured by placing a cursor over a 4 cm² region of interest (fig 1). A minimum of 12 readings (three from each of four slices) were taken for each study and the mean T_1 calculated. Care was taken to avoid measuring areas containing hepatic or

portal veins. Reproducibility of T_1 measurement was assessed by scanning a standard phantom over three months, which is reported elsewhere.¹⁰ In the relevant range for the liver the standard deviation of measurements was less than 2% of the mean.

Results

Figure 2 shows the liver relaxation times for patients and volunteers. Mean relaxation times for the 61 healthy volunteers ranged from 166 to 222 ms (mean (SD) 191 (13) ms).

FIG 2—Mean liver T_1 values for patients with lymphoma and volunteers.

Seven patients (five with non-Hodgkin's lymphoma, two with Hodgkin's disease) showed histological evidence of spread of the lymphoma to the liver. All of these had noticeably longer mean relaxation times (>3 SD above the normal mean), range 238-278 ms. All seven showed increased T_1 throughout the liver, but with additional focal lesions with even higher T_1 values in one case.

Nineteen patients yielded normal results on liver biopsy. Fifteen of these had liver T_1 values within the normal range established by this study. Two of the other four patients showed a slightly higher T_1 (223 and 226 ms) and two had noticeably longer times (241 and 243 ms). Biopsy specimens from the liver of the remaining patient showed chronic active hepatitis but no evidence of hepatic lymphoma. The patient's serum was positive for hepatitis B surface antigen. His liver T_1 was slightly increased (228 ms).

Twelve patients therefore had liver relaxation times outside the normal range for the healthy volunteers. Seven of these had hepatic lymphoma confirmed by biopsy, one had chronic active hepatitis, and four yielded normal biopsy specimens. T_1 was considerably longer in most patients with hepatic lymphoma than in those who yielded negative results on liver biopsy (fig 2). Two patients in whom histological examination of the liver yielded normal results, however, had T_1 values within the range for patients with hepatic lymphoma.

The patients with normal results of histological examination had liver T_1 values around 15 ms longer than the volunteers (fig 2). This difference was highly significant (Student's t test = 4.12, $p < 0.0001$) and remained significant when the two patients in this group with considerably higher liver T_1 values were excluded from the analysis ($p < 0.001$).

Discussion

These findings indicate that measurement of T_1 by this low field strength magnetic resonance imager is a very sensitive detector of

liver lymphoma. Magnetic resonance imaging missed none of the seven patients with hepatic lymphoma confirmed by biopsy despite the fact that six patients had only diffuse disease. Furthermore, the relaxation times of the patients with proved hepatic lymphoma were more than three standard deviations above the normal mean.

The high level of sensitivity found in this study contrasts with the results from the only other study of magnetic resonance imaging in the detection of hepatic lymphoma, which was performed by Weinreb *et al* using a 0.35 tesla magnetic resonance imager.¹⁰ Twelve of their 13 patients with histologically proved lymphoma had mean liver T_1 values within one standard deviation of the normal mean established in the study. As T_1 varies with magnetic field strength absolute times reported from centres using different imagers may be expected to differ. The range of liver relaxation times for the 20 normal subjects in the study by Weinreb *et al* (195–1112 ms) was relatively much wider than that found in this study. This discrepancy has not been explained but may reflect the differences in the pulse sequence and in the method of calculating T_1 . The technique of adiabatic fast passage in the inversion recovery sequence used in our type of scanner is said to give very accurate measurements,¹¹ and we have verified their reproducibility.¹² Weinreb *et al* used spin echo sequences with long and short repetition rates to calculate T_1 . The lower magnetic field strength used in our study may also be important; differences between the T_1 values of normal and malignant tissues may be greatest at lower magnetic field strengths.^{13,14} It is unlikely that differences between the populations of patients or volunteers in the two studies could have accounted for the pronounced difference in the results.

Although we found liver T_1 to be highly sensitive to spread of lymphoma, the specificity of this measurement was less good. Five of the patients who had higher T_1 values did not have hepatic lymphoma. One of these patients had chronic active hepatitis, which is known to produce higher T_1 values.¹⁵ The explanation for the remaining four patients (two with slightly higher T_1 values and two with considerably higher values) is unknown. It seems unlikely, though possible, that these represent false negative results of liver biopsies. Although it is recognised that lymphoma may frequently be missed by percutaneous liver biopsy, the incidence of positive results of biopsies is higher at peritoneoscopy and further increased by open wedge biopsy.¹⁶ Open liver biopsy is thus the best available method for detecting hepatic lymphoma (albeit the most invasive) and was therefore used as the yardstick in this study.

The difference between the results for healthy volunteers and for the group of patients with normal results of histological examination was unexpected. Although most of the patients (15 of 19) with normal liver biopsy specimens had liver T_1 values within the normal range, the patients as a group had significantly longer times than the volunteers. This may be because of a non-specific hepatic response to the presence of lymphoma elsewhere, as has been suggested by Bagley *et al* as the cause of false positive alkaline phosphatase measurements.³ The four patients with liver T_1 values outside the normal range but with normal results on histological examination may be the most pronounced examples of this phenomenon. In this

study the increase in liver T_1 was generally less among those with negative results on biopsy than among those with positive results. Further evaluation is needed to establish whether there is a level of liver T_1 above which histological evidence of lymphoma is found in all cases.

These results, showing a higher level of sensitivity than has been observed with any other imaging method, suggest that measurement of liver T_1 by low field strength magnetic resonance imaging may be a useful non-invasive screening test in patients with lymphoma. As Castellino pointed out, in patients with a disease where the overall incidence of hepatic disease is low the sensitivity is the most important index by which to judge a technique.¹⁷ If the results obtained in this study are confirmed low field strength magnetic resonance imaging may prove to be a reliable method for excluding hepatic lymphoma. Invasive biopsy procedures might then be reserved for those patients with higher T_1 values, for whom a definite diagnosis of liver disease is clinically important.

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100 YEARS AGO

There can certainly be no doubt that the state of the labour-market and the weather has brought many more people face to face with starvation this winter, than for many years past. But still it may be doubted whether they have mastered the use of all weapons of defence against that deadly foe. A valiant vegetarian correspondent, who has never for eight years betrayed his dietary in prosperity or in adversity, writes to us to point out that in vegetarianism lies an escape from some of the pressure of poverty, inasmuch as the healthy vegetarian, in full exercise of his powers, can support himself on 5d. a day, which may suffice for three meals, such as shall thoroughly fit him for the duties of life. During an eight years' experience of a life of hard work, involving nine or ten, or even twelve hours' work a day, this slender tax has proved sufficient for nutrition. Some details of the mode of its application to the poorest classes are required; and it must not be forgotten

that one of the main difficulties which has to be met is the clumsiness in cooking, and almost total absence of kitchen utensils, which obtains among the poor. If they have a frying-pan as well as a kettle, that is all that can be expected; and that increases their tendency to struggle after animal food, expensive though it may be, and, if they cannot get it, to fall back on dry bread with perhaps a dash of treacle, instead of the cheaper and more appetising preparations that can be made from greens, potatoes, lentils, oatmeal, arrowroot, rice, sago, and the like, which need a saucepan, or better still, a stock-pot. Important as it is that they should realise the worth of vegetables, it is almost more important that they should appreciate in the French fashion the value of a *pot au feu*, and not rank it contemptuously as "slops." There is a great field for instruction in this matter by penny dinners and public kitchens. (*British Medical Journal* 1886;i:512.)