Low field strength magnetic resonance imaging of the spleen: results from volunteers and patients with lymphoma

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Summary Low field strength (0.08 Tesla) magnetic resonance imaging (MRI) of the spleen with spin lattice relaxation time (T_1) measurement was performed on a total of 79 healthy volunteers and 62 patients with lymphoma. Inhomogeneity was observed on the T_1 images of the spleen from 25 volunteers. This was therefore considered a normal variant. The normal range of spleen T_1 at 0.08 Tesla was established (362–420 msec). No influence of age on spleen T_1 was detected. The range of T_1 values observed in males and females was similar, although the mean spleen T_1 for females was significantly longer than that for males.

The sensitivity of T_1 measurement for the detection of lymphoma in the spleen was poor, particularly for patients with Hodgkin's disease. In a minority of untreated patients, however, a spleen T_1 value outside the normal range may indicate the presence of lymphoma in the spleen. A significant decrease in spleen T_1 following treatment was observed in 9 patients who underwent serial scanning.

Accurate assessment of splenic involvement can be of great importance for the selection of appropriate treatment for patients with lymphoma. For example, mantle radiotherapy may be the treatment of choice for patients with localized supradiaphragmatic Hodgkin's disease (HD), but is clearly inappropriate in the presence of lymphoma in the spleen. At present laparotomy with splenectomy is the only accurate method for assessing such cases. Clinical examination of the spleen is frequently an unreliable guide to the presence or absence of lymphoma. Lymphomatous infiltration may occur in normal sized spleens (Goffinet *et al.*, 1973; Kadin *et al.*, 1971). Conversely, an enlarged spleen (particularly in patients with HD) does not always indicate the presence of lymphoma (Glatstein *et al.*, 1970; Sutcliffe *et al.*, 1976). CT scanning, radionuclide imaging and ultrasonography can help in the assessment of splenic size and may detect the presence of focal deposits, but the overall accuracy of each of these methods for detecting splenic lymphoma is poor (Best *et al.*, 1978; Milder *et al.*, 1973; Silverman *et al.*, 1972; Zornosa & Ginaldi, 1981).

This study has been undertaken to assess the accuracy of low field strength (0.08 Tesla) magnetic resonance imaging (MRI) with spin lattice relaxation time (T_1) measurement in the detection of splenic involvement by lymphoma.

Patients and methods

Volunteers and patients

Seventy nine healthy volunteers were examined to assess the normal appearance of the spleen on MRI and to establish the normal range of spleen T_1 . Their characteristics are shown in Table I.

Sixty two patients underwent MRI of the spleen. Nine patients were scanned on 2 occasions giving a total of 71 scans. The diagnosis and clinical status of these patients are shown in Table II.

Assessment of splenic involvement

Comparison of the results of MRI with histological assessment of the spleen was possible in 19 of the 62 patients. In 18 of these splenectomy was performed within 2 weeks of imaging (Table III). For these cases the size of the

spleen on MRI was compared with the weight measured following splenectomy. In one case histological assessment was made at autopsy.

Direct assessment of splenic involvement was not available in the other 43 patients. It is not possible to exclude the presence of splenic lymphoma in any of these cases. Twenty one of the patients were classified as having 'probable' splenic involvement based on the presence of at least one of the following features, each of which has been previously shown from laparotomy studies to be a strong indicator of the presence of splenic lymphoma (Aisenberg *et al.*, 1971; Goffinet *et al.*, 1973; Glatstein *et al.*, 1970; Stein *et al.*, 1976):

1. Biopsy proven hepatic lymphoma.
2. Bone marrow infiltration by lymphoma.
3. Moderate (>4 cm) splenomegaly in patients with non Hodgkin's lymphoma (NHL).
4. Gross (>10 cm) splenomegaly in patients with HD.

The remaining patients for whom direct histological assessment of the spleen was not available were classified as having 'possible' splenic involvement.

Scanning procedure

Axial images of the spleen were made in all patients and volunteers using a 'MD 800' resistive magnetic resonance imager operating at 0.08 Tesla (3.4 MHz). A standard pulse sequence with alternating saturation recovery and inversion recovery sequences with a repetition time of 1000 msec and an inversion time of 200 msec was used for all examinations. A calculated T_1 image is generated from a computed algorithm. The accuracy and reproducibility of T_1 measurements using this type of imager have been previously reported (Redpath, 1982; Richards *et al.*, 1988a). The homogeneity of the appearance of the spleen on T_1 images was assessed. Inhomogeneity was classified as either focal (with 'hot spots' of high T_1) or diffuse.

T_1 measurements were recorded from representative areas of the spleen using region of interest cursors measuring either 2 cm² or 4 cm². Measurements were made only from sections in which the margins of the spleen were clearly defined. Images taken through the upper and lower poles of the spleen had ill defined outlines and were therefore not measured in order to avoid partial volume effects. Similarly the region of interest cursors were not placed within 10 mm of the periphery of the spleen images. Areas of high T_1 immediately adjacent to the splenic hilum were assumed to

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be due to blood vessels and were excluded from the assessment of spleen T_1 . All other areas of high or low T_1 were included in the measurements. The number of measurements made on each subject ranged from 4 to 11 (median 7). The mean spleen T_1 for each subject was calculated from these values. The reproducibility of calculation of mean spleen T_1 was assessed by repeating the measurements on 20 of the scans after an interval of 3 months. The maximum difference observed in the estimation of mean spleen T_1 was 12 msec, representing a change of 3%. In 16 of the 20 cases the difference in the 2 measurements was 5 msec or less.

Results

Volunteers

In 54 of the 79 volunteers (68%) the spleen appeared homogeneous on the calculated T_1 images. In the other 25 cases inhomogeneity was detected. Ten had isolated focal 'hot spots' of high T_1 , one had a focal area of low T_1 , 12 had diffuse inhomogeneity of T_1 and a further 2 had both focal 'hot spots' and a background of diffuse inhomogeneity. The focal areas of high T_1 varied in size (from 1 cm² to 8 cm²), shape and location within the spleen. The presence of inhomogeneity was not related either to sex or age. The volunteer with the largest focal area of high T_1 was rescanned after an interval of 3 months, at which time the abnormality was not detectable. Because of the high incidence of inhomogeneity of normal spleens on calculated T_1 images this was considered to be a normal variant and was not used as a criterion of abnormality in patients with lymphoma.

Mean Spleen T_1 for the 79 volunteers ranged between 362 msec and 420 msec (mean 385 msec standard deviation 14 msec). The range of spleen T_1 for males (362–413 msec) and females (363–420 msec) was similar. The mean value for females (390 msec) was, however, significantly higher than that for males (379 msec) – $P < 0.001$. The influence of age on spleen T_1 was assessed separately for males and females. No effect was observed in either group. Eighteen of the 34 females under the age of 40 years were oral contraceptive users. The mean spleen T_1 for these 18 was 390 msec compared with 389 msec for the 16 who were not taking the pill ($P = 0.8$).

Patients with known splenic histology

Size on MRI compared with weight and histology (Table IV) Six patients had enlarged spleens on MRI. In 3 of

Table I Characteristics of volunteers

	Males	Females	Total
Age < 40 years	23	34	57
Age > 40 years	9	13	22
Total	32	47	79

Table II Characteristics of patients

	HD	NHL	Total
Treatment Status (at time of first scan)			
1. Previously untreated	23 (3)*	17 (5)	40 (8)
2. Post therapy	5	4	9
3. At relapse	8	5 (1)	13 (1)
Total	36 (3)	26 (6)	62 (9)

*Parentheses denote numbers of patients who also underwent follow up MRI of the spleen.

Table III Characteristics of patients undergoing splenectomy

N = 18		
Males	14	HD 14
Females	4	NHL 4
Age range 18–81 years (median 40 years)		
Indication for splenectomy		
	HD	NHL
Staging	9	0
Diagnostic	1	1
Post treatment re-evaluation	2	1
Therapeutic	2	2
(In an additional case the spleen was examined at autopsy).		

Table IV Results of splenectomy and MRI

Pt	Diagnosis	Treatment status	Splenectomy findings		MRI findings	
			Histology	Weight (g)	Size	T_1
1	HD	1	–	120	N	N
2	HD	1	–	60	N	N
3	HD	1	–	170	N	N
4	HD	1	–	140	N	N
5	HD	1	–	150	N	low
6	HD	1	–	100	N	N
7	HD	1	+	240	N	low
8	HD	1	–	75	N	N
9	HD	1	–	225	N	N
10	HD	1	+	485	+	N
11	HD	3	+	>2,000	+++	N
12	HD	3	+	230	N	low
13	HD	2	–	210	N	N
14	HD	2	–	85	N	low
15	NHL	1	+	>2,000	+++	high
16	NHL	1	+	450	+	N
17	NHL	1	+	>2,000	+++	high
18	NHL	2	–	80	N	N
19	HD	4	+	enlarged	+	low

Treatment Status: 1=previously untreated; 2=post treatment: in clinical remission; 3=relapse; 4=post mortem assessment of spleen. Size: N=normal; +=moderately enlarged; +++=massively enlarged. Spleen T_1 : N=normal; low=<362 msec; high=>420 msec. Histology: –=no lymphoma in spleen; +=lymphoma in spleen.

these the spleen appeared grossly enlarged. In each case the spleen weighed more than 2,000 g. In the other 3 cases the spleen appeared moderately enlarged on MRI. The weights for two of these were 450 g and 485 g. In the autopsy case the weight was not recorded but the spleen was described as enlarged. In the remaining 13 cases the spleen was normal in size on MRI and the weights ranged from 60–240 g.

Eight of the 19 patients had histological evidence of splenic lymphoma (5 out of 15 patients with HD, 3 out of 4 patients with NHL). All 6 cases in which the spleen was enlarged on MRI were histologically positive. The other 2 cases in which histological evidence of lymphoma was found weighed 230 and 240 g, but were considered to be of normal size on MRI.

T₁ measurements in patients with known spleen histology (Figure 1). Two of the 5 patients with HD in the spleen had normal spleen *T₁* (Figure 1, column 3). In one of these cases deposits of HD measuring up to 3 cm in diameter were found on histological examination of the spleen. Spleen *T₁* was below the normal range in the other 3 patients with HD in the spleen. Two of the 3 patients with low *T₁* had received previous chemotherapy and the other had recently undergone lymphography.

Two of the 3 patients with histologically proven NHL in the spleen had prolonged spleen *T₁* (Figure 1, column 4). In both cases the spleen was enlarged clinically and on MRI. The third had normal spleen *T₁*.

Histological examination of the spleen was negative for lymphoma in 11 of the 19 patients (Figure 1, columns 2 and 5). Nine of these had normal spleen *T₁*. The other 2 had low spleen *T₁*. Both of these patients had recently undergone lymphography. One had also recently completed chemotherapy. Histology of the spleen in this case showed hypocellular areas of fibrosis and the presence of fat vacuoles.

*Spleen *T₁* results from all patients (Figure 2).* The range of spleen *T₁* observed from all 71 examinations was 307–469 msec. Values outside the normal range were observed on 26 occasions, 13 being above the upper limit of normal (420 msec) and 13 below the lower limit of normal (362 msec). *T₁* measurements for patients with definite (i.e. histologically proven), 'probable' and 'possible' splenic involvement are shown in Figure 2. Results from scans taken during or after therapy are shown separately from those taken before treatment or at relapse.

Hodgkin's disease. Two out of 15 patients with definite or probable HD in the spleen had prolonged *T₁* (Figure 2, column 2). Both were scanned at the time of relapse. A further 7 patients in this group had normal *T₁*, while in the remaining 6 cases the *T₁* was below the normal range. Three of the patients with low values had neither received any treatment nor undergone lymphography. All 8 patients with possible (but not probable) splenic HD had normal *T₁* (Figure 2, column 3).

Figure 1 Spleen *T₁* in volunteers and patients with known splenic history.

*Results from one patient are shown twice (columns 2 and 7). This patient had recently received chemotherapy and was found to have HD in the spleen at autopsy.

Figure 2 Spleen *T₁*: Results from all patients.

Non Hodgkin's lymphoma. Nine out of 14 patients with definite or probable NHL in the spleen had prolonged spleen *T₁* (Figure 2, column 5). Values for the other 5 patients were normal (including one patient with definite NHL in the spleen). Two of the 8 patients classified as having possible rather than probable splenic involvement had prolonged *T₁* (Figure 2, column 6). No previously untreated patient with NHL had subnormal spleen *T₁*.

Effect of therapy. A total of 18 patients (9 HD, 9 NHL) were scanned during the course of chemotherapy or shortly after its completion. Seven of these (4 HD, 3 NHL) had *T₁* values below the normal range. Six of the 7 with low *T₁* had shown a good response to therapy. The other failed to respond and had HD in the spleen at autopsy.

Results for the 9 patients who were scanned before and after receiving treatment are shown in Figure 3. In each case the *T₁* decreased following therapy, including one patient who had only received radiotherapy to an area not involving the spleen. *T₁* values before and after treatment for the 8 patients who received systemic therapy were compared using a paired *t* test. The fall in *T₁* was highly significant ($P < 0.001$).

Discussion

The results of this study are disappointing. In contrast to our findings for the liver (Richards *et al.*, 1986), measurement of spleen *T₁* by low field strength MRI is an insensitive method for detecting involvement by lymphoma. The sensitivity was particularly poor in patients with HD, for whom the diagnosis of splenic involvement is clinically most important. Normal, high and low *T₁* values were observed in association with definite or probable HD in the spleen.

The sensitivity of *T₁* measurement was somewhat better in patients with NHL. Two out of 3 patients with proven NHL in the spleen and a further 7 out of 11 patients with probable splenic lymphoma had prolonged *T₁*. However, all 9 of these patients with abnormal *T₁* had splenomegaly, which in patients with NHL is itself a reasonable indicator of involvement (Goffinet *et al.*, 1973). *T₁* measurement therefore contributed little if anything to the overall assessment. In two other patients (both classified as having 'possible' involvement), prolonged spleen *T₁* was observed in the absence of splenomegaly. The presence of lymphoma in the spleen in one of these cases is doubtful, as spleen *T₁* returned to normal after the patient had been treated with radiotherapy to a distant site.

The poor sensitivity of *T₁* measurement for the detection

Figure 3 Spleen T_1 pre and post treatment.

of splenic lymphoma cannot be attributed simply to a failure to detect small tumour deposits. One patient had normal T_1 in the presence of large masses of HD in the spleen. Preliminary data indicate that lymphomatous node masses have T_1 similar to that of normal spleen (Richards, 1987a). If the T_1 of lymphoma in the spleen is similar to that in nodes, this would explain the difficulty in detecting splenic lymphoma either by T_1 measurement or visually on T_1 images.

A significant decrease in T_1 following therapy was observed in all patients examined before and after therapy. In some cases the post-treatment value was subnormal. While this might in part be due to successful treatment of

tumour in the spleen, it could also be due to effects of chemotherapy on normal spleen T_1 . Spleen T_1 has been reported to decrease in healthy animals exposed either to radiotherapy or to toxins (Bakker & Vriend, 1983; Ling & Foster, 1980). The fall in T_1 could be caused either by an accumulation of red blood cell debris (with a high paramagnetic iron content) or by a decrease in the water content of the spleen (Ling & Foster, 1980).

The relatively high incidence (32%) of inhomogeneity of spleen T_1 in healthy volunteers was unexpected. The presence of either focal areas of abnormal T_1 or of diffuse inhomogeneity on T_1 images from patients should not be interpreted as evidence of pathology. The inhomogeneity of splenic T_1 contrasts with the generally uniform appearance of other normal tissues on T_1 images made using the same scanner (Richards *et al.*, 1988a,b). The anatomical basis for either the focal or the diffuse inhomogeneity found on images of the spleen in volunteers is unknown. The single case in which a large 'hot spot' was detected on one scan but not on a similar image taken 3 months later makes it unlikely that this appearance was due to a fixed anatomical structure such as a blood vessel.

Although the mean T_1 of the spleen was significantly higher in females than in males the ranges of values observed in both sexes was similar. Consequently, a single normal range of T_1 can be used for assessing results of splenic T_1 made in patients. Spleen T_1 was not affected by age. This differs from our findings for either liver or bone marrow (Richards *et al.*, 1988a,b).

In conclusion, splenic T_1 and size measurement made by low field strength MRI are insensitive methods for detecting splenic involvement by lymphoma. In a minority of cases, however, the presence of a subnormal T_1 in previously untreated patients with HD or the presence of an elevated T_1 in a patient with either HD or NHL may indicate the presence of lymphoma in the spleen.

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