DETECTION OF BONE MARROW INVOLVEMENT IN HODGKIN'S DISEASE BY QUANTITATIVE MAGNETIC RESONANCE IMAGING TECHNIQUES

To the Editor:

In a recent issue of Blood (78:728, 1991) Hoane et al presented data illustrating the important role of magnetic resonance (MR) imaging in lymphoma. Published series comparing bone marrow biopsy with MR imaging for detecting bone marrow involvement in Hodgkin's disease (HD) have reported 15% to 40% of cases as being bone marrow biopsy negative and MR positive (see Table 1). These data suggest that unilateral and even bilateral bone marrow biopsy seriously underestimate the incidence of focal marrow involvement in HD. This obviously has important therapeutic implications when patients are being assessed for procedures such as autologous bone marrow transplantation (ABMT).

As Hoane et al stated, current standard MR techniques do not reliably detect focal deposits less than 5 mm in size. In addition, the interpretation of MR images is subjective, and depends on sometimes subtle alterations in signal intensity. In an attempt to improve the sensitivity and objectivity of MR imaging of marrow, we have developed and used quantitative MR techniques to study marrow in HD. Initial work with operator-controlled region of interest cursors placed in the lumbar vertebral marrow showed that marrow infiltration with HD was associated with an elevated marrow T1 relaxation time, and that focal deposits of lymphoma may be reflected as increased T1 variation. To address aspects of bone marrow heterogeneity and T1 variation further, pixel by pixel T1 mapping has been combined with image analysis techniques. TI maps are computed with use of a SUN 3/160 workstation (SUN Microsystems, California) from six spin echo images of a single midline sagittal slice of the lumbar vertebrae acquired with repetition times (TR) varying from 2,400 to 250 milliseconds.

| Table 1. Magnetic Resonance Imaging Studies of Bone Marrow in HD |
|------------------------|-----------------|-----------------|----------------|
| No. of Patients Studied | BM Positive (%) | MR Positive (%) | Reference     |
| 22*                    | 5               | 45              | Hoane et al'  |
| 20*                    | 10              | 30              | Smith et al'  |
| 38                     | 10              | 39              | Linden et al' |
| 13                     | 23              | 38              | Richards et al' |

Comparison of bone marrow biopsy positivity and MR positivity rate in published studies where patient numbers are greater than 10.

*Denotes studies where bilateral bone marrow biopsies were performed.
matrix size and field of view used in these studies give a pixel size of 0.94 mm². All MR imaging data were acquired with a 1.5 Tesla Signa system (GE Medical Systems). Total patient imaging time for the T1 data set was 40 minutes.

The boundaries of the lumbar vertebral bodies are identified semi-automatically (<5% operator interaction) from proton density (TR/TE 2400/25) MR images using line detection algorithms available on a Context Vision image analysis system (Struers Vision AB, Sweden). These masks are then used to isolate only those pixels that refer to the lumbar vertebral bone marrow. The T1 data are then displayed in histogram form, and the major moments of the histogram analyzed. From pooled T1 histogram data of control subjects, 5% and 95% probability limits are calculated and these limits used as thresholds for the patient data. The spatial distribution of T1 pixels below or above these limits can then be displayed in color on original gray scale images.3

This approach has been applied to 20 consecutive patients with refractory or relapsed HD being assessed before ABMT. Significant histogram abnormalities were detected in 4 of 18 patients with negative bone marrow biopsies, and in both patients with positive bone marrow biopsies. After thresholding to the 95% probability limit derived from studies of age-matched controls, abnormal areas of high T1 pixels could be identified in the lumbar vertebral bone marrow of these six patients. Serial studies showed normalization of the T1 histograms and the disappearance of the high T1 areas with therapy. Color display and quantification of abnormally high T1 pixels are particularly useful in patient follow-up, and provide accurate spatial information if biopsy is contemplated.

We believe quantitative MR imaging is a useful and complementary examination to bone marrow trephine in assessing bone marrow involvement in patients with high-grade non-Hodgkin's lymphoma and HD before procedures such as ABMT. Pixel by pixel relaxation time mapping combined with image analysis techniques provides an objective approach with improved spatial resolution and sensitivity, compared with the more conventional MR techniques.

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REFERENCES


RESPONSE

We are pleased that the letter of Drs Smith and Roberts supports our conclusion that magnetic resonance imaging (MRI) detects marrow involvement by lymphoma missed by bone marrow biopsy. While the development of quantitative techniques for MRI may provide additional information, quantitative T1 measurements are intrinsically nonspecific. It must be remembered that there are many things that can occur in the bone marrow that will prolong T1, with marrow edema, fibrosis, infection, or benign disorders such as Gaucher's disease, polycythemia rubra vera, and other causes of marrow hyperproliferation. Therefore, although quantitative T1 measurements may increase diagnostic sensitivity, there is a higher probability of false-positive diagnosis as well. Another consideration is the additional 40 minutes of imaging time.

For the present, we believe that the combined use of both qualitative MRI and marrow biopsy is the best and most practical method for determination of marrow involvement with malignant lymphoma.

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Detection of bone marrow involvement in Hodgkin's disease by quantitative magnetic resonance imaging techniques [letter; comment]

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