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Original Article

Bone marrow cellularity MRI calculation and correlation with bone marrow biopsy☆,☆☆,★

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ABSTRACT

Purpose: To calculate bone marrow cellularity from MRI and correlate with bone marrow biopsy.
Methods: Twenty-seven lymphoma patients with staging bone marrow biopsies and lumbar MRI were reviewed. Cellularity was calculated from T1 signal intensity measurements=100 – {[(marrow – CSF)/(subcutaneous fat – CSF)] X 100}.
Results: The histologic cellularities demonstrated significant correlation with iliac bone MRI cellularity (r=0.59, P=.001). Cellularities increased from T11 to S1. Cellularity decreased with age=67.6 – (age X 0.36).
Conclusions: Marrow cellularity from MRI shows statistically significant correlation with biopsy and significant differences between vertebral levels and changes with age.

1. Introduction

Bone marrow cellularity has historically been assessed subjectively by visual examination of histological sections from iliac crest trephine biopsies. Histomorphometry (point counting) or computerized image analysis can lead to more reproducible measurements, although visual estimates show a reasonable correlation [1,2]. Bone marrow cellularity also depends on the site of biopsy, with lumbar vertebrae about 10% more cellular than the iliac crest [3].

An age-related decrease in percent cellularity has often been quoted to follow a rule of thumb of "100 minus the patient's age" [4]. However, a more recent study found no significant changes in cellularity during the first eighth decades of life and only reduced in the ninth and tenth decades [5]. Another study showed that in the pediatric age group, cellularity is highest under the age of 2 (~80%), decreases until age 5 (~60%) but, then, remains relatively stable into adulthood [6].

Part of the difficulty in determining normal ranges and age-related distributions for bone marrow cellularity is the invasive nature of a bone marrow biopsy, which precludes sampling from healthy controls and necessitates extrapolation from small studies of patients with disorders requiring biopsy for other reasons or from necropsy studies. Magnetic resonance imaging (MRI) offers a noninvasive assessment of bone marrow.

Several studies have focused on using MRI to estimate bone marrow cellularity or fat fraction. Early studies focused on specialized techniques such as proton spectroscopy or chemical-shift misregistration to separate the water and lipid peaks [7–10]. The Dixon method represents a refinement of the chemical shift imaging technique using multiecho in- and out-of-phase imaging to generate "pure water" and "pure fat" images for better quantitative assessment of marrow fat fraction and inverse cellularity [11–15]. Diffusion-weighted MRI has also been used to demonstrate a correlation between apparent diffusion coefficient values and bone marrow cellularity [16]. The problem with these techniques is that they require specialized sequences and postprocessing software that is not universally available or routinely performed as part of most MRI studies.

Other studies have shown that signal intensity (SI) ratios or indexes (relative to an internal reference) from T1-weighted (T1W) MRI sequences show a correlation with marrow cellularity [17–19]. The goal of this study was to develop a calculation of marrow cellularity from routinely acquired T1W magnetic resonance (MR) images with reasonable correlation with bone marrow biopsy histologic cellularities and to use this to assess age- and site-related changes.

2. Materials and methods

This retrospective study was approved by the institutional review board. Informed consent was waived.

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2.1. Subjects

Sixty-five patients with Hodgkin or non-Hodgkin lymphoma and available bone marrow biopsy specimens identified from a pathology database over a 5-year time period and MRI of the lumbar spine was retrospectively reviewed. The following exclusion criteria were applied:

- More than 6 months time interval between the MRI and the biopsy specimen dates
- Chemotherapy or corticosteroid therapy between MRI and biopsy dates
- Unavailable history to make this determination
- Technically inadequate MRI study or superimposed abnormalities that could interfere with reproducible measurements

Twenty-seven patients were included in this study after applying these exclusion criteria (age range: 22–85 years, mean: 56±17 years; 10 females, 17 males). On average, there was 35 days between the MRI and biopsy, with 12 of the 27 biopsies in this study done within 12 days or less. Eight of these 27 patients demonstrated involvement by lymphoma on the bone marrow biopsy specimens. These patients were included for the correlation analysis between the MRI and bone marrow biopsy cellularity estimates but were excluded for the analysis comparing marrow cellularity to the patient age.

2.2. MRI marrow cellularity measurements

Bone marrow cellularity was calculated from the mean SI measurements from T1W MR images (TR: 400–936; TE: 8.47–14.27; FA: 90; NEX: 2; FOV: 22×22 cm for axial and 30×30 cm for sagittal images). Measurements for the posterior iliac bones were taken from the axial T1 image at the L5/S1 level. Measurements for the T12 through S1 vertebral bodies were taken from a midsagittal T1 image. Regions of interests (ROIs) were placed at each of these levels and on areas of cerebrospinal fluid (CSF) and subcutaneous fat (Fig. 1). Bone marrow cellularity was calculated from these measurements by the following equation:

$$\text{Cellularity}(\%) = 100 - \{[(\text{Marrow} - \text{CSF})/(\text{Subcutaneous Fat} - \text{CSF})] \times 100\}$$

This equation was developed so that if the marrow SI was equal to that of CSF, the calculated cellularity would be 100%, and conversely, if the marrow SI was equal to that of the subcutaneous fat, the calculated cellularity would be 0%.

For five randomly selected patients, the same examiner (G.M.) repeated the measurement five times at each level using variably placed and sized ROI. Intraclass correlation (ICC) used to assess intraobserver consistency for MRI measurements, with values of 0.7 or above, is considered acceptable.

2.3. Bone marrow biopsy cellularity measurements

Contemporaneous bone marrow biopsy specimens for each patient were assigned cellularity to the nearest 10% after consensus review by three hematopathologists using the point counting method.

2.4. MRI versus bone marrow cellularity correlation

Data normality was inspected using D'Agostino–Pearson, Shapiro–Wilk (SW), Kolmogorov–Smirnov (KS), Cramer–von Mises (CVM), Anderson–Darling (AD) tests, and histogram visualization. The statistical details of differences between these normality tests is beyond the scope of this paper, but each is designed to detect departures of a dataset from a normal Gaussian distribution due to either skewness, kurtosis, or both.

The Pearson correlation coefficient was used to assess the relationship between the data sets. Variation of bone marrow cellularity between measurement sites was tested using paired *t* test. The global mean difference as well as linear trend among vertebral levels was assessed using random effect model. Univariate linear regression was used to form a prediction equation for marrow cellularity from the MRI calculation using the measurement site having the strongest correlation with histologic cellularity. A univariate linear regression was also used to predict marrow cellularity from age, after excluding the eight cases with lymphomatous involvement of their marrow.

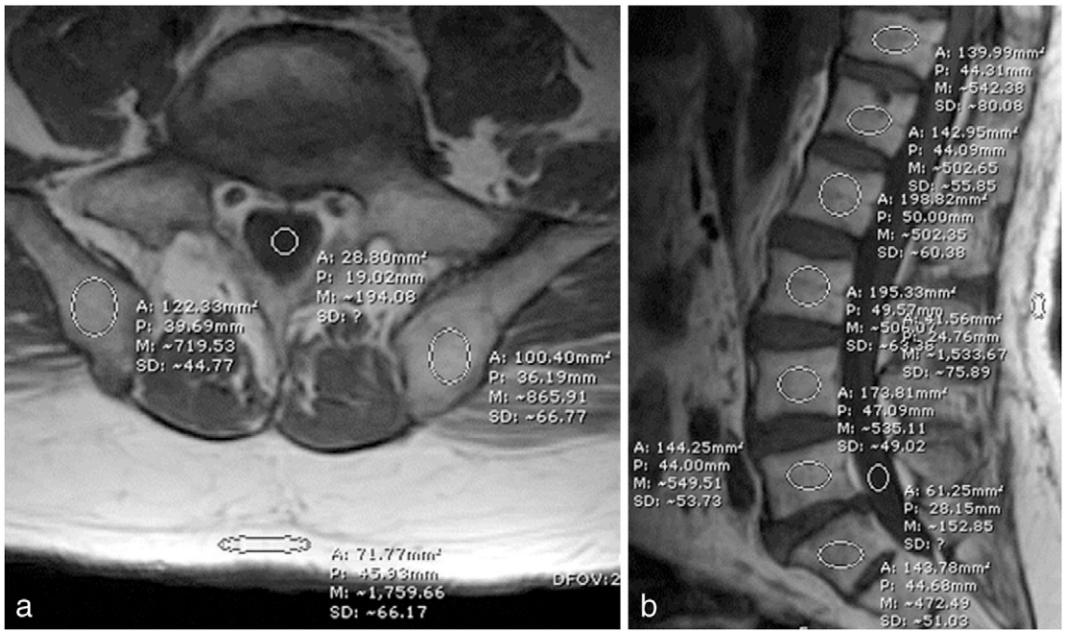

Fig. 1. A 56-year-old man with lymphoma without marrow involvement. Axial T1W MR image at the L5/S1 level (**a**) and midsagittal T1W MR image (**b**) demonstrate placement of ROI for CSF in the thecal sac, subcutaneous fat, and at each marrow level (right and left iliac bones on the axial image and T12 through S1 vertebral levels on the sagittal image) with corresponding mean SI measurements (M). The ROI area (A), path length (P), and standard deviation (SD) measurements were not used for the calculation of cellularity (%)=100 – {[(marrow – CSF)/(subcutaneous fat – CSF)] X 100}.