With its exquisite contrast resolution and ability to differentiate hematopoietic and fatty marrow, MRI is an important technique for evaluating the bone marrow noninvasively [1–4]. The following discussion reviews the techniques of bone marrow MRI, normal anatomic and physiologic variants, and the MRI findings in common marrow disorders.

MRI of Bone Marrow

Normal Anatomy

The normal bone marrow has three primary components: osseous matrix, red marrow, and yellow marrow. The osseous components of the marrow are the trabeculae of cancellous bone, which provide the supporting framework for the red and yellow marrow elements. The red or cellular marrow is hematopoietically active, producing RBCs, WBCs, and platelet precursors. Hematopoietically inactive yellow marrow is composed of fat cells. These two types of marrow differ in their chemical composition. Recognition of these differences is important to understanding the MRI appearance of marrow. In infants and young children, red marrow consists of approximately 40% water, 40% fat, and 20% protein. As the individual ages, the fatty elements of hematopoietic marrow increase, and by age 70 years, red marrow is composed of approximately 60% fat, 30% water, and 10% protein. Yellow marrow contains approximately 80% fat, 15% water, and 5% protein [1–4].

MRI Techniques

MRI is performed most often to study a specific lesion(s), based on the results of other imaging or laboratory studies, or to evaluate focal pain or neurologic symptoms. In this instance, the study is limited to the skeletal site of interest. On some occasions, MRI is used to survey the whole body for marrow replacement or infiltration by neoplastic cells [5–12]. In these instances, the entire body is imaged from the vertex to the heels, usually with only coronal sequences acquired with three to six overlapping stations. The section thickness is chosen to ensure complete anterior-to-posterior coverage per station.

MRI Appearance of Normal Marrow

The MR appearance of the bone marrow depends on the pulse sequence selection and the relative amounts of cellularity, protein, water, and fat within the marrow. Spin-echo and fat-suppressed sequences have been most widely used to image bone marrow. The addition of other sequences will be influenced by the disease process and anatomic region being evaluated.

T1-weighted spin-echo sequences allow superb differentiation between red and yellow marrow. On T1-weighted images, hematopoietic marrow usually shows a
signal intensity equal to or slightly higher than that of muscle on both T1- and T2-weighted sequences (Fig. 1). In neonates, the signal intensity of hematopoietic marrow may be slightly lower than that of muscle on T1-weighted images, reflecting the larger percentage of cellular marrow. After the neonate period, signal intensity lower than normal muscle almost always indicates pathology.

Yellow marrow is isointense with subcutaneous marrow on T1-weighted spin-echo sequences (Fig. 1). On T2-weighted spin-echo sequences, the signal intensity of fatty marrow is usually higher than that of muscle and equal to or slightly lower than that of subcutaneous fat. Contrast differences between normal and pathologic marrow and between red and yellow marrow on T2-weighted images can be accentuated by using fat-suppressed sequences, either the fat-saturation technique or STIR images [13]. On these sequences, hematopoietic marrow shows intermediate signal intensity similar to that of muscle, whereas fatty marrow shows a signal intensity lower than that of muscle (Fig. 1). By comparison, most marrow pathology exhibits relatively high signal intensity, greater than that of red and yellow marrow, on fat-suppressed images.

The use of contrast-enhanced MRI can also improve lesion conspicuity. Normal marrow shows minimal enhancement after administration of gadolinium chelate agents. By comparison, many malignant neoplasms exhibit an increase in signal intensity that is greater than the increase shown by normal marrow and by benign lesions [14].

**Distribution of Normal Marrow**

The ability to recognize the normal variations in bone marrow distribution is important so that they are not interpreted as abnormal. Bone marrow is a dynamic organ that changes composition throughout life [3, 4, 15, 16] (Fig. 2). At birth, the marrow contains a predominance of hematopoietically active cells. Shortly after birth, an orderly and predictable conversion of hematopoietic to fatty marrow takes place, which begins in the appendicular or peripheral skeleton and progresses to the axial or central skeleton. Within individual long bones, marrow conversion occurs first in the diaphysis, then in the distal...
MRI of Bone Marrow

Metaphyses, and finally in the proximal metaphyses. The adult pattern of marrow distribution is reached by the middle of the third decade. At this time, red marrow is predominantly seen in the axial skeleton (skull, spine, sternum, flat bones) and the proximal ends of the humeri and femurs; yellow marrow predominates in the remainder of the long bones and the epiphyses and apophyses [15–22] (Fig. 3). Islands of red marrow can also be seen in the distal ends of the femurs in marathon runners and menstruating women.

One common exception to the normal pattern of complete conversion is the epiphyses. The epiphyses are cartilaginous before they ossify. Cartilaginous epiphyses and apophyses exhibit signal intensity equal to that of muscle on T1-weighted images and equal to or slightly higher than that of fat on T2-weighted images. Once ossification has been present for 3 to 4 months, the epiphyses and apophyses exhibit high signal intensity on both T1- and T2-weighted images, reflecting their predominantly fatty marrow. How-
ever, islands of low-signal-intensity red marrow can be seen within the subchondral regions of the proximal humeral epiphyses on T1-weighted images in healthy adolescents and adults [23] (Fig. 4).

Age-related changes in marrow conversion have also been addressed in the axial skeleton. In the first decade of life, the vertebral marrow is predominantly hematopoietic and shows homogeneously low signal intensity except for high signal intensity around the basivertebral vein. With aging, the amount of hematopoietic marrow in the vertebral bodies progressively decreases, but even in adults the vertebral bodies contain abundant red marrow. The decline in red marrow is accompanied by an increase in fatty marrow (Fig. 5). In the first decade of life, the signal intensity of the vertebral bodies is often lower than that of the adjacent disk space. In individuals older than 10 years, the signal intensity of the vertebral marrow is higher than that of the adjacent disk. The conversion of red to yellow marrow in the vertebral bodies can occur in a diffuse or focal pattern [19].

An age-related pattern of red to yellow marrow conversion also occurs in the pelvis. Pelvic marrow is predominantly hematopoietic in the first two decades of life [17]. Red to yellow conversion begins in the acetabulum superiorly and medially. By the third decade, these areas usually contain mainly fatty marrow.

Pathologic Disorders

Disorders that affect marrow production can be divided into four categories: reconversion or hyperplasia, replacement disorders, depletion disorders, and myelofibrosis.

Marrow Reconversion (Myeloid Hyperplasia)

Marrow reconversion refers to the repopulating of yellow marrow by hematopoietic cells. Fatty marrow reconverts to red marrow where there is an increased demand for hematopoiesis and the hematopoietic capacity of existing red marrow stores is exceeded. Reconversion occurs in a pattern opposite that of physiologic marrow conversion, beginning in the vertebrae and flat bones of the pelvis and then progressing to the long bones of the extremities and ultimately to the hands and feet. In the individual long bones, marrow reconversion first occurs in the proximal metaphyses, followed by the distal metaphyses, and then the diaphyses. Reconversion occurs in the epiphyses and apophyses only when severe hematopoietic stress is present.

Causes of reconversion include severe chronic anemia (such as sickle cell disease, thalassemia, or hereditary spherocytosis), marrow replacement by neoplastic cells, treatment with granulocyte-macrophage colony-stimulating factor (GM-CSF) during chemotherapy, and circumstances in which an
increased oxygen requirement is present (e.g., rigorous athletics such as marathon running and high altitudes) [24–26]. Hyperplastic marrow has a signal intensity similar to skeletal muscle on T1- and T2-weighted spin-echo images (Fig. 6) and is slightly hyperintense to muscle on fat-suppressed images.

The signal characteristics of hematopoietic marrow on spin-echo images are not specific, and replacement disorders may have a similar appearance. Several criteria are helpful in distinguishing between red marrow and infiltrated marrow. First, reconversion follows the distribution of normal marrow and is usually a relatively symmetric process bilaterally. Most neoplastic processes have a random and asymmetric distribution. Second, the signal intensity of hematopoietic marrow is slightly greater than that of muscle on STIR images and fat-suppressed T2-weighted images, whereas the signal intensity of pathologic processes is usually much greater than that of muscle. Third, hematopoietic marrow does not cause cortical breakthrough or an adjacent soft-tissue mass. Finally, hematopoietic marrow tends to enhance less than pathologic marrow after gadolinium administration.

**Marrow Replacement Disorders**

Marrow can be replaced or infiltrated by a number of disorders, including leukemia, lymphoma, multiple myeloma, and metastases. Diseases such as leukemia, lymphoma, and multiple myeloma tend to originate in the hematopoietic marrow. Metastases localize in the red marrow because it has a richer blood supply than fatty marrow. In adult patients, the common sites for metastatic disease are the vertebrae (69%), pelvis (41%), proximal femoral metaphyses (25%), and skull (14%) [14].

On T1-weighted images, marrow infiltration causes abnormal marrow signal intensity that is lower than that of muscle. On T2-weighted images, the signal intensity increases, although the lesions can be difficult to identify on these images alone because of the poor contrast between normal and abnormal marrow. Lesion detection is improved on fat-suppressed images. On STIR and fat-saturated T2-weighted images, tumor infiltration typically produces a high signal intensity that is greater than that of red or yellow marrow, reflecting the high water content of the neoplastic cells (Fig. 7). Tumor infiltration may be focal.

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**Fig. 6**—Marrow reconversion in 21-year-old woman with sickle cell anemia and knee pain.  
**A,** Coronal T1-weighted image of knee shows low-signal-intensity reconverted hematopoietic marrow in metaphyses and even epiphyses. Foci of high signal intensity represent rest of fatty marrow. Normally, epiphyses and diaphyses in patient of this age would contain only fatty marrow. **B,** On T2-weighted image, hyperplastic red marrow has signal intensity slightly higher than that of muscle.
Metastases usually enhance after the administration of IV gadolinium chelate agents (Fig. 8). Exceptions include sclerotic metastases and treated lesions.

**Pitfalls in diagnosis of metastases**—The differential diagnosis in patients with neoplastic disorders and focal marrow abnormalities on MRI includes normal hematopoietic marrow, osteomyelitis, compression fractures, bone islands, and infarcts.

**Osteomyelitis**—Osteomyelitis is another cause of marrow infiltration. Infiltration of the marrow by inflammatory cells results in increased extracellular water or fluid, which causes decreased signal intensity on T1-weighted images and increased signal intensity on T2-weighted and fat-suppressed images (Fig. 9) and on contrast-enhanced images after the administration of gadolinium chelate agents [28]. Associated soft-tissue cellulitis or abscess, cortical destruction, and periosteal reaction are often noted by the time the MRI is performed.

**Osteoporotic fracture versus metastasis**—Distinguishing between an acute pathologic fracture of a vertebral body caused by tumor and a benign osteoporotic fracture is not an uncommon dilemma [14, 29]. Both lesions show low signal intensity on T1-weighted MR images and high signal intensity on fat-suppressed images. Features suggesting metastases include diffuse involvement of the vertebral body, involvement of the pedicle or posterior elements, multiple lesions, contrast enhancement of the abnormal area, and an associated soft-tissue mass (Fig. 10). Features suggesting osteoporotic fractures include involvement of only part of the vertebral body, a horizontal straight fracture line separating the nor-

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**Fig. 7**—Lymphoma. Coronal T1-weighted image through lower extremities of adolescent girl shows areas of bright signal intensity in femurs and tibiae in sites of tumor infiltration. Normal yellow marrow is nulled on STIR images.

**Fig. 8**—Metastatic breast cancer in 50-year-old woman. A, Sagittal T1-weighted image of lumbar spine shows low-signal-intensity tumor replacing multiple vertebral bodies. Normal fatty marrow is seen in remainder of spine. B, On sagittal T1-weighted image after gadolinium administration, metastatic disease exhibits high signal intensity, greater than muscle and fat.
Fig. 9—Staphylococcal osteomyelitis in 12-year-old boy.
A, Coronal T1-weighted image of left femur shows low-signal-intensity marrow in proximal metaphysis. 
B, Coronal T1-weighted image after gadolinium administration shows high-signal-intensity marrow. Also noted is increased signal intensity in soft tissues, representing spread of infection.

Fig. 10—Vertebral metastasis with pathologic fracture in 57-year-old man.
A, T1-weighted sagittal image shows low-signal-intensity marrow in proximal thoracic vertebral body (arrow).
B, Sagittal MR image after gadolinium administration shows diffuse enhancement of vertebral body and epidural extension.
normal marrow and abnormal marrow, and a thin paraspinal soft-tissue mass (Fig. 11). Follow-up MRI in 4 to 6 weeks can help establish the diagnosis. Tumor will remain unchanged or progress, whereas the hemorrhage associated with a benign fracture will usually resolve.

*Marrow infarction*- Medullary infarction can result from either malignant infiltration of the marrow with consequent elevation of intraosseous pressure or it can be secondary to chemotherapy or steroid administration. Infarction can also be seen in patients with sickle cell disease. Acute bone infarcts appear as regions of low signal intensity on T1-weighted images and high signal intensity on T2-weighted and fat-suppressed images. Chronic infarction usually appears as a focal lesion with central fatty marrow signal intensity and an adjacent hypointense rim, related to reactive or sclerotic bone formation.

**Myeloid Depletion**

Myeloid depletion refers to the loss of normal red marrow. Pathologically, the marrow is acellular or hypocellular, with yellow marrow filling the marrow space. Causes of myeloid depletion include viral infections, medications, and chemotherapy and radiation therapy, but in many instances, the cause is unknown. Aplastic or hypoplastic marrow shows diffusely high signal intensity on both T1- and T2-weighted images and low signal on fat-suppressed images [30, 31] (Fig. 12). The increase in fatty marrow is best appreciated in areas that normally contain a predominance of red marrow, such as the spine and pelvis.

Radiation is a cause of focal marrow depletion. Radiation-induced changes have been most often described in the spine [32–34]. Initial pathologic changes include edema, vascu-
lar congestion, and diminished hematopoiesis. The marrow subsequently is replaced by fat and fibrosis. These changes are usually complete by 3 months after the start of therapy. Alterations in marrow signal intensity can be observed as early as 2 weeks after initiation of treatment, especially on STIR images. The early pattern is that of low signal intensity on T1-weighted images and high signal intensity on T2-weighted and fat-suppressed sequences. The later pattern of fatty replacement usually appears as homogeneous high signal intensity within the radiation port on T1-weighted images. Fatty replacement also can be noted in nonradiated vertebral marrow adjacent to the radiation port in approximately 50% of patients. Decreased contrast enhancement of the nonirradiated bone marrow during and after the end of radiation has been reported on dynamic MRI and is thought to reflect the effect of radiation on the microvasculature of marrow [35]. Most patients have some degree of hematopoietic marrow recovery within 1 to 2 years after radiation therapy.

Chemotherapy also results in initial ablation of hematopoietic cells and marrow replacement by edema. Changes in the first few days after the administration of chemotherapy include decreased signal intensity on T1-weighted images and increased signal intensity on T2-weighted and fat-suppressed sequences. After the initial changes subside, the marrow may repopulate with normal elements or the cellular elements may be replaced by fat or a combination of fat and fibrosis.

**Myelofibrosis**

Myelofibrosis is characterized by replacement of normal marrow cells by fibrotic tissue. It usually is the result of radiation therapy or chemotherapy, but on occasion it can be a primary disorder. Fibrotic marrow usually produces low signal intensity on both T1- and T2-weighted images (Fig. 13). The signal intensity may be slightly higher than that of mus-
icle on fat-suppressed images.

Differential considerations for hypointense signal intensity include Gaucher’s disease and hemosiderosis. Gaucher’s disease is an autosomal recessive disease characterized by decreased levels of the enzyme glucocerebrosidase, leading to accumulation of glucocerebrosides within histiocytes in the monocyte-macrophage system. Marrow disease usually follows the distribution of recovered marrow and begins in the spine, pelvis, and proximal femoral metaphyses. Within the long bones, it progresses from a proximal to distal distribution. Epiphyseal marrow is rarely involved unless extensive disease is present [36].

Hemosiderin deposition can occur secondary to the breakdown of RBCs in hemolytic anemias or as a sequel of chronic blood transfusions [37]. The magnetic susceptibility effects of hemosiderin produce hypointense marrow on all pulse sequences. The marrow signal intensity is usually lower than that of normal hematopoietic marrow. Low signal intensity also can be seen in the liver and spleen.

**Conclusion**

MRI is a sensitive technique for evaluating bone marrow disorders noninvasively. During skeletal maturation, hematopoietic marrow is converted to fatty marrow. Knowledge of the normal conversion patterns is important if marrow pathology is to be identified. Alterations in bone marrow signal occur in a variety of disorders, including marrow hyperplasia, tumor infiltration, myeloid depletion, myelofibrosis, edema, and ischemia.

**REFERENCES**

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