Bone marrow: normal and pathologic aspects in MRI

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Learning objectives

MRI is the imaging modality of choice for the investigation of bone marrow disorders. Accurate interpretation of MR examinations of bone marrow requires an understanding of the anatomy, physiology, distribution, and conversion patterns of bone marrow. Technical factors of the MR examination are also important. Common pathophysiologic pathways allow a useful classification of bone marrow disorder.

we propose to attend this objectifs:

- Illustrate the different aspect of normal and pathologic bone marrow in mri.
- Propose a didactic approach for protocols of realisation and interpretation of mri exam suspected bone marrow pathologies.
- Illustrate some pitfalls in diagnosis of bone marrow lesion

Background

MRI is the imaging modality of choice for the investigation of bone marrow disorders. Accurate interpretation of MR examinations of bone marrow requires an understanding of the anatomy, physiology, distribution, and conversion patterns of bone marrow. Technical factors of the MR examination are also important. Common pathophysiologic pathways allow a useful classification of bone marrow disorder.

In order to interpret the appearances of marrow seen on MRI and to distinguish normal from abnormal, it is important to understand the normal components and composition of bone marrow, which vary greatly with age and anatomic location within the skeleton.

1. COMPONENTS AND COMPOSITION OF NORMAL BONE MARROW

Three basic marrow components are Trabeculae, Red marrow, Yellow marrow.

- **Trabeculae**: Serve as the architectural support for the marrow and as a mineral depot. Their number decreases with age.
- **Red Marrow**: considered as hematopoietically active bone marrow and is composed of hematopoietic cellular elements (red and white cells and platelets), supporting stroma (reticulum), and rich sinusoidal vascular supply. Red marrow contains approximately 40% water, 40% fat, and 20% protein. It increases if the demand for hematopoesis increases.
- **Yellow Marrow**: considered as hematopoietically inactive marrow. Contains smaller fraction of red marrow elements, larger fraction of fat cells, poor vascular supply and characterised by paucity of the reticulum. It contains approximately 15% water, 80% fat, and 5% protein. Increases with age.
These differences in chemical composition account for the appearance of red and yellow marrow on various MRI pulse sequences:

- **Yellow marrow** follows the signal intensity of subcutaneous fat, with relatively high signal on T1W images and low signal on STIR images.
- **Red marrow** follows the signal intensity of muscle and has an intermediate signal intensity on T1W images and STIR images.

### 2. Bone Marrow Conversion:

Amount and distribution of red and yellow marrow changes with the age as well as in response to physiologic stresses.

Normal conversion of red to yellow marrow occurs in a predictable and progressive manner.

At birth, nearly the entire osseous skeleton is composed of red marrow (fig. 2).

Conversion begins in the neonatal period and proceeds from the appendicular (distal to proximal extremities) and then to the axial skeleton in a bilateral symmetric fashion (fig. 3).

By the age of 25 years, the adult distribution of bone marrow is attained which is characterized by red marrow persisting in the axial skeleton, proximal humeri, and proximal femora. This pattern should not be mistaken for pathology.

In normal adult marrow, yellow marrow may reconvert to red marrow in the event of a functional demand for increased hematopoiesis. Benign conditions triggering reconversion include heavy smoking, long distance running, obesity, and middle age in women.

### 3. MR Techniques (Fig. 4)

Pulse sequence selection determines the MR appearance of normal bone marrow as well as the sensitivity and specificity for evaluating bone marrow disorders.

Vanel et al. have summarized three main factors that affect the signal intensity of bone marrow on MRI: the fat and water content of the marrow, the presence of bony trabeculae, and the use of contrast material. The MRI appearance of marrow is also dependent on the particular MR technique employed.

- **T1 weighted spin-echo images** (Fig. 1 and Fig 4) There is superb differentiation between red and yellow bone marrow on T1 weighted spin-echo images. On T1 weighted images the yellow marrow is hyperintense in signal intensity as contrasted with the relatively decreased signal intensity of red marrow. These differences in signal intensity are a direct reflection...
of the differences in fat/water content within red and yellow marrow. Both benign and malignant disorders of bone marrow have long T1 values which result in marrow signal intensity that is significantly decreased. The signal intensity of these lesions on T1 weighted spin-echo images is usually less than that of intervertebral discs in the spine and less than that of muscle in the extremities (fig. 1).

- **Short Time Inversion Recovery**: (Fig. 4) The clinical advantages of STIR are due to the following characteristics: (1) additive T1 and T2 contrast; (2) Marked fat suppression; (3) a two-fold increase in the magnetization range of spin-echo sequences. As a result, STIR images demonstrate extraordinarily high contrast, conspicuousness, and sensitivity for the depiction of most types of bone marrow pathology.

- **T2 weighted spin-echo images**: (Fig 4) Conventional T2 weighted spin-echo sequences demonstrate relatively low contrast between red marrow and yellow marrow. These problems are corrected by utilizing the very T2 weighted fast spin-echo images used in conjunction with fat saturation. The sensitivity of this sequence for detecting bone marrow pathology is similar to that of STIR imaging. Several practical advantages compared with STIR include: (1) significantly decreased imaging time; (2) improved signal-to-noise ratio. The major disadvantage of T2 weighted fast spin-echo with fat saturation is its dependence on excellent magnetic field homogeneity for adequate fat suppression.

- **Diffusion-weighted imaging (DWI)** can quantitatively assess the mobility of water molecules. Tumor in marrow generally appears hyperintense on DWI due to restricted diffusion. But, conflicting results have been reported: In a study of benign and pathologic spinal compression fractures using SSFP DWI, the author reported that all malignant compression fractures were hyperintense to normal marrow, whereas most benign compression fractures were hypointense to normal marrow. However, a subsequent study by Castillo et al. showed no advantage of DWI in the detection and characterization of vertebral metastases compared with T1-weighted imaging;

- **Post gadolinium injection sequences**: The commonly-employed gadolinium-based is T1 MR contrast agents (Fig. 4), it alters the local magnetic field by shortening relaxation times and thus selectively enhance the conspicuity of many lesions compared with neighboring tissues. The enhancement of normal marrow is greatest in young patients and those with lower marrow fat content. Strong enhancement in both routine and dynamic contrast studies is usually seen in different pathological processes, including infection, inflammation, and tumor, and thus is a nonspecific finding. Fat suppression imaging increases lesion conspicuity and detection of enhancement.
4. CLASSIFICATION OF BONE MARROW DISORDERS

MRI is ideally suited for evaluation of both diffuse and focal bone marrow disease. The bone marrow can be affected by a wide variety of pathologic processes, that may be divided in 5 groups according to common pathophysiological patterns: Marrow replacement, marrow infiltration, marrow depletion, marrow edema and marrow ischemia.

4.1. Marrow infiltrative disorders:

It is due proliferation of cells that normally exist in the marrow, and involve the marrow in a diffuse manner. It can be due to benign or malignant disorders. Examples of benign disorders are marrow reconversion, mastocytosis and Amyloidosis. Examples of malignant disorders are multiples myeloma, leukaemia, Myelofibrosis, Waldenstrom’s macroglobulinemia.

**Multiple Myeloma (MM):** (Fig. 5) Is the Most common primary bone tumor, when there is a Solitary lesion it is called plasmacytoma and more common is multiple form and called myeloma. different MRI patterns of MM may be seen: normal (low tumor burden), focal lesion, heterogeneous (variegated), homogenous (diffuse).

**Leukemia:** may be acute: diffuse skeletal involvement, or Chronic: (adults) involve areas of residual marrow in pelvis, spine, femurs. Involvement of the epiphyses/apophyses at any age reflects higher tumor burden

4.2. Marrow replacement disorders:

There is replacement of the normal fatty marrow cells by cells that do not normally exist. Marrow infiltration is the most often focal. MRI appearances include low T1 signal (equal or less than muscle or disc) and variable T2 signal (usually high, unless sclerotic). Marrow Replacement Disorders can be seen in benign diseases (Primary benign Bone tumors, Osteomyelitis) or in Malignant diseases (Metastasis, Lymphoma, Malignant Bone tumors, …).

**Metastasis:** (Fig. 6) the common primaries are breast, lung and prostate. it Involve red marrow in spine, pelvis, proximal femur and humeri. the common aspect is of focal lesion with low T1 and high T2 and variable surrounding Edema.

**Lymphoma:** Primary lymphoma of bone rare and is more often from non Hodgkin lymphoma than Hodgkin lymphoma. it touch the appendicular skeleton in diaphyses of femur, tibia and humerus.

4.3 Marrow Depletion disorders:
These disorders are characterized by replacement of hematopoietic elements by fat cells. Involvement can be diffuse or regional in distribution. MRI appearances follow the signal intensity of fat. The 3 main causes include chemotherapy, radiation, and aplastic anemia.

**Chemotherapy**: It systemically destroys normal hematopoietic marrow and tumor cells. First week post chemotherapy, there is an edematous and hypocellular marrow. Then there is a progressive fat replacement of marrow (similar to untreated aplastic anemia).

**Radiation**: (fig 7 and Fig. 8) there may be acute and chronic induced changes. MR appearance of radiated marrow depends on phase in which it was imaged and dose: In the first 2 weeks, there are increased STIR with slight increase in T1. In the 3rd to 6th weeks: heterogeneous signal. After 6th weeks: there chronic changes of fat replacement that may have regeneration after 1 year if Dose < 30 Gy or irreversible changes if Dose >30-40 Gy.

**Aplastic Anemia**: May be caused by acquired diseases (infections, drugs, toxins) or congenital causes (Fanconi, TAR Sx, etc). The classic description is a diffuse fat replacement of marrow and foci of low T1 signal may represent residual islands of red marrow.

**4.4. Marrow Edema**: (Fig. 9, Fig. 10 and Fig. 11)

Bone marrow edema is usually focal. There is a nonspecific increase in water content within the bone marrow which manifests decreased signal intensity on T1 weighted spin-echo images, and markedly increased signal intensity on STIR images and T2 weighted fast spin-echo images with fat saturation. The finding of bone marrow edema is nonspecific, and can be seen as a result of trauma, infection, ischemia, reaction to adjacent neoplasia, or it may be idiopathic.

For example, the bone marrow edema seen on MR images of the hip (Fig. 9) may be secondary to transient or migratory osteoporosis, early osteonecrosis, or the bone marrow edema syndrome.

**4.5. Marrow Ischemia**: (Fig. 12 and Fig. 13)

This category of bone marrow disease encompasses both avascular necrosis of subchondral bone (Focal lesions in the epiphyses) and medullary bone infarcts (Metaphysis or diaphysis). Bone marrow ischemia favors fatty marrow over hematopoietic marrow. This is most likely due to the limited vascular supply of yellow marrow relative to red marrow.

**5. Potential Problems**: 


There are a number of potential problems encountered in the interpretation of bone marrow MR imaging.

The most common include recognition of normal variants.

There are also problems with Technical procedures such as the significant decrease in sensitivity for bone marrow pathology when intermediate weighted sequences are utilized in place of true T1 weighted spin-echo images. Also, it is important to obtain precontrast T1 weighted spin-echo images as post-gadolinium images alone, without the use of fat saturation, can cause yellow marrow to appear homogeneously high signal, completely obscuring lesions which are easily seen on pre-gadolinium images.

Problems can arise differentiating benign from malignant processes. Degenerative discogenic changes (Fig 13) within the spine on MRI are relatively common. These findings include a spectrum of marrow signal alteration adjacent to a degenerated disc including marrow edema, increased fatty marrow, or end plate sclerosis as they are classified by Modic.

One of the most common clinical problems is the distinction of benign osteoporotic compression fracture of the spine from pathologic compression fracture due to malignant processes. A vertebral body wedge compression fracture that demonstrates complete preservation of normal bone marrow signal intensity is consistent with a chronic benign compression fracture. Acute or subacute benign vertebral body compression fractures demonstrate marrow signal alteration in a regular pattern with smooth margins.

Frequently there is in a band-like pattern paralleling the involved vertebral body and plate. An underlying fracture line is frequently visible. The posterior height of the vertebral body is also frequently preserved.

Images for this section:
Fig. 1: frontal T1 weighted of the pelvic bone in 20 years old person showing red marrow (*) and yellow marrow (arrow)
Fig. 2: sagittal T2 (a) and T1 SE images in 13 days year old showing that the entire vertebra are composed of red marrow (low signal in T1 weighted sequence (a))
Fig. 3: Evolution of red and yellow marrow by the age

(a) (b) (c) (d)
**Fig. 4:** normal bone marrow in various pulse sequence: (a) T1 SE, (b) T2 SE, (c) STIR, (d) T1 with Fat Saturation and after injection of Gadolinium

**Fig. 5:** multiple myeloma: 75 years old man consulting for a backpain, biologie showing a monoclonal immunoglobulin G peak, MRI with T1 (a), T2 (b), STIR (c) and T1 FAT SAT GADO (d) showing a heterogeneous aspect of the bone marrow in the different pulse sequences
Fig. 6: Metastasis: 45 years old consulting for multiple bone pain, scintigraphy showing multiple intake. Mammography showing a spiculated mass ACR5 and MRI showing a heterogeneous aspect of the bone in different pulse sequences. Note that the lesions are better detected in STIR than in T2 sequence.

![Images of MRI scans](attachment:image1.png)

Fig. 7: Marrow depletion after radiotherapy (asterixis): 60 years old in female having a radiotherapy for spinal cord compression due to bone metastasis of rectal carcinoma.

![Image of MRI scan with asterixis](attachment:image2.png)
Fig. 8: Bone depletion after radiotherapy: 55 years old men followed since 2 years for undifferentiated nasopharyngeal carcinoma treated with radiotherapy consulting for paresthesia of the right upper limb. MRI: sagittal T1 (a), T2 (b) and T1 Gado (c): showing a hypersignal in all sequences of the upper cervical vertebra comparatively to the lower cervical vertebral in the exposed region to radiotherapy. note the presence of radiation myelopathy in the same region.
Fig. 9: Bone marrow oedema: 40 years old woman consulting for pain in right hip. Conventional radiography are normal. MRI showing oedema of the neck of femur: low signal in T1 (a), high signal in STIR (b, d)
Fig. 10: Bone marrow oedema: Stress fracture: 32 years old women having a low back pain 15 days after delivery. Coronal T1 (a, b) and STIR (c, d): low signal in T1, and in STIR there is a hypointense bandlike fracture line with surrounding bone edema.
Fig. 11: Sagittal T2 and T1 FS T1FS gado of the lumbar spine: Tuberculous spondilodicts of L3-L4 and spondylitis of T10, T12 and L1. The rear corners of L3 and L4 are affected associated to epidural enhancement and small somatic abscess.

Fig. 12: Marrow ischemia: osteonecrosis of proximal epiphysis of femura:
**Fig. 13:** Marrow ischemia: bone infarct:

**Fig. 14:** Degenerative discs changes type MODIC 2: high signal in T1 and T2
Imaging findings OR Procedure details

A 1.5 tesla MRI is used to perform exams.

Protocol included systematically a sagittal T1 and T2 spin echo acquisition completed according the results by sagittal gradient echo, sagittal and axial T1 post gadolinium injection.

Conclusion

Magnetic resonance imaging is an excellent noninvasive modality for evaluating bone marrow and detecting marrow lesions, as it provides information at the level of cellular and chemical composition, in addition to gross morphologic data. Knowledge of normal marrow components and composition and their variation, as well as of factors that alter MR signal intensity, is important for optimal interpretation of MR images. The signal intensity, morphology, and location of marrow findings on MRI can be used to provide more accurate diagnoses, to guide treatment, and to follow therapy-related changes.

Personal Information

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