Imaging spectrum of the appearance of normal bone marrow on MRI

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Learning objectives

The aim of this educational exhibit is:

• To present the normal appearance of the vertebral and appendicular bone marrow on MRI, in relation to the normal composition and physiology of bone marrow.
• To present examples of focal and diffuse bone marrow variations.
• To highlight the importance of such knowledge by the general radiologist.
Background

The interpretation of bone marrow imaging poses a challenge to the radiologist in daily clinical practice. Whilst MRI remains an excellent non-invasive imaging modality for the evaluation of the bone marrow, knowledge of its varied appearances and the presence of normal variants is of utmost importance so as not to confuse the normal bone marrow with pathological patterns requiring further work-up.

The cellular and chemical composition of normal bone marrow varies with age, gender and other stimuli producing a wide spectrum of MR signal characteristics. This is further complicated by the presence of normal focal and diffuse variants which may mimic pathological processes. These range from common vertebral haemangiomas to diffuse red marrow hyperplasia which may be easily confused with processes such as diffuse marrow infiltration.

Overview on the composition, distribution and physiology of normal bone marrow:

Normal bone marrow is a markedly cellular connective tissue which occupies the medullary cavity [1]. It is embedded in a network of trabeculae and exists in two forms, the haematopoietically active red marrow and the inactive fatty yellow marrow, which differ in composition and distribution [2].

**Red marrow:** This consists of the richly vascular portion of the bone marrow [2]. At birth it is almost exclusively composed of haematopoietic cells, however, with growth there is a gradual increase in its proportion of fat with the result that by early adulthood its cellular composition consists of 60% hematopoietic cells and 40% fat cells. Its adult chemical composition consists of 40% fat, 40% water and 20% protein [3].

**Yellow marrow:** In contrast, yellow or fatty marrow is composed mainly of fat cells (95%) and contains approximately 80% fat, 15% water and 5% protein [3].

**Bone marrow conversion:** This physiological process consists of the gradual replacement of red marrow, which occupies most of the skeleton at birth, into fatty marrow. It starts distally during childhood within the appendicular skeleton and progresses centrally until, by the age of approximately 25 years, the adult pattern of marrow distribution is achieved [4,5]. Red marrow in adults is predominantly located in the axial skeleton and the proximal aspects of the femur and humerus whilst yellow marrow occupies mainly the appendicular skeleton [4].
**Bone marrow reconversion:** The reverse process of conversion may occur later as a physiological response to an increased haematopoetic demand. During this process yellow marrow is replaced by red marrow, whilst the already existing red marrow increases in its cellular component [4]. This may occur as a result of a number of medical and non-medical conditions, including smoking, long distance running, obesity, diabetes, anaemia of chronic disease and treatment with haemtopoetic growth factors [5].
Findings and procedure details

Normal MRI appearance of red and yellow bone marrow:

The appearance of normal bone marrow depends on the selected MR sequences as well as on the relative proportions of fat and water content within the bone marrow [3].

The excellent contrast differentiation between red and yellow marrow provided by the T1-weighted spin-echo (SE) sequence makes this the most important sequence in the imaging of bone marrow [4,6]. On this sequence yellow marrow is of high signal intensity similar to that of subcutaneous fat. On the other hand, whilst red marrow is of lower signal intensity due to its high water content, it is almost always hyperintense to skeletal muscle and intervertebral discs [1,2]. With the process of conversion there is an increase in the fat content of the bone marrow resulting in an increase in the T1 signal intensity.

Since T2-weighted SE sequences are limited in differentiating red and yellow marrow as they both appear somewhat hyperintense, fat-suppressed T2-weighted or STIR sequences are commonly used to accentuate signal intensity contrast [6]. On these sequences the red marrow remains slightly hyperintense to skeletal muscle whilst yellow marrow is hypointense [2]. This is particularly useful in identifying pathological lesions which on fat suppressed sequences usually exhibit higher signal intensities to that of red and yellow marrow [6].

Red marrow in children demonstrates significant enhancement following injection of intravenous gadolinium-containing contrast material. On the contrary, bone marrow enhancement is barely visible in adults [2,4]. In contrast, pathological lesions commonly enhance to a greater extent [6].

Normal distribution of vertebral and appendicular bone marrow:

Appendicular bone marrow:

The process of conversion within the individual long bones of the appendicular skeleton starts and proceeds in this order: the proximal and distal epiphyses, the diaphysis, the distal metaphysis and the proximal metaphysis Fig. 1 on page 20. In the adult appendicular skeleton, yellow marrow predominates within the long bone bones of the limbs with the exception of the proximal epiphyses of the femur and humerus which
contain residual red marrow Fig. 2 on page 20. In adults, bone marrow signal intensity on T1-weighted images is hyperintense to that of skeletal muscles [4].

Fig. 1: MRI of the right hip of a 4-year-old boy: A: Coronal T1W FSE image demonstrating hyperintense fatty marrow within the right femoral epiphyses. Red marrow within the femoral metaphysis and pelvic bones is of intermediate signal intensity. B: Coronal PD fat-saturated image shows fat suppression of the epiphyseal fatty marrow. The red marrow within the femoral metaphysis and pelvic bones retains high signal intensity.

References: Medical Imaging Department, Mater Dei Hospital - San Gwann/MT
Fig. 2: MRI of the left hip of a 57-year-old man: Coronal T1 FSE image (A) demonstrates a linear region of low signal intensity in the left proximal femoral metaphysis (red arrow). On the coronal PD fat saturated image (B) this remains of increased signal intensity (red marrow) whilst the surrounding bone marrow is suppressed. Findings are in keeping with persistent red marrow with the adult proximal femoral metaphysis.

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Vertebral bone marrow:

The axial skeleton at birth is also largely occupied by red marrow resulting in a homogenous T1-signal intensity equal or slightly lower to that of the intervertebral discs and skeletal muscle [3] Fig. 3 on page 21. During childhood, with the process of conversion, there is a continuous increase in the proportion of fat cells which starts centrally around the basivertebral venous plexus and progresses peripherally. This results in a gradual increase in signal intensity on T1-weighted images which is now typically higher than that of the intervertebral discs and skeletal muscle [3] Fig. 4 on page 22 Fig. 5 on page 22 Fig. 6 on page 23 Fig. 7 on page 24. Adult bone marrow on fat-saturated T2-weighted and STIR imaging produces an intermediate to moderately elevated signal intensity Fig. 8 on page 24. A common variant is that of an increased proportion of residual red marrow in the anterior portion of the vertebral body or near the endplates Fig. 7 on page 24 and a higher proportion of fat marrow in the region of the basi-vertebral vein [4].
Fig. 3: Sagittal T1W image of the spine demonstrating normal vertebral bone marrow in a 5-month-old girl. Vertebral bone marrow is of only slightly higher signal intensity than the adjacent intervertebral discs since this is still largely occupied by cellular red marrow.

**Fig. 4:** Sagittal T1W (A) and T2W (B) images of the spine demonstrating normal vertebral bone marrow in a 6-year-old boy. With growth there is gradual conversion of red to yellow marrow resulting in a progressive increase in T1 signal intensity of the vertebral bone marrow with respect to the intervertebral discs.


**Fig. 5:** Sagittal T1W (A), STIR (B) and T2W (C) images of the lower thoracic and lumbar spine demonstrating normal vertebral bone marrow in a 12-year-old girl. There is an increase in T1 in signal intensity of the vertebral bodies predominantly around the basivertebral veins.

**Fig. 6:** Sagittal T1W image of the lumbar spine of a 12 year old girl demonstrating increased signal intensity around the basivertebral venous plexus (red arrow) in keeping with fat conversion.

Fig. 7: Sagittal T1W (A), STIR (B) and T2W (C) images of the lumbar spine demonstrating normal vertebral bone marrow in a 35-year-old man. There is a further overall increase in the T1 and T2 signal intensity of the vertebral bone marrow. A closer look at the lumbar vertebral bodies demonstrates a subtle decrease in T1 and T2 signal intensity at their anterior aspects (red arrows). This is in keeping with a common variant of the distribution of bone marrow, that is, an increased proportion of residual cellular marrow in the anterior portion of the vertebral body.


Fig. 8: Sagittal T1W (A), STIR (B) and T2W (C) images of the lumbar spine demonstrating normal vertebral bone marrow in a 60-year-old man: In adulthood, vertebral bodies are now largely occupied by fatty marrow resulting in an overall higher T1 signal intensity of the bone marrow with respect to the intervertebral discs.


Focal variations of bone marrow:

Fatty marrow islands: These foci of focal fatty replacement of red bone marrow are a fairly common occurrence, particularly in the older population [8]. They are the result of the slower and heterogeneous process of conversion which occurs during adulthood when compared to that which occurs in childhood. These lesions are characterized by the presence of focal areas of high T1 and T2 signal intensity. The high T1 signal intensity and corresponding low signal intensity on fat suppressed sequences confirms their fatty nature and clinical insignificance [9] Fig. 9 on page 25.
Fig. 9: Sagittal T1W FSE (A) and T2W FSE (B) images of the lumbar spine in a 60-year-old man show a heterogenous marrow signal which remains within normal limits. The heterogeneous pattern is the result of multiple nodules of fatty marrow (red arrows) which are of high T1 and T2 signal intensity.

References: Medical Imaging Department, Mater Dei Hospital - San Gwann/MT

Red marrow islands: The above mentioned heterogeneous process of conversion which occurs in adulthood may, less commonly, result in the presence of islands of red marrow. They are characterized by the presence of low signal intensity lesions in the spine or pelvis with typically the same MR signal characteristics of normal red bone marrow. Although they occur in a random fashion they tend to have a predilection for the subcortical aspects of the vertebral bodies. MRI features which can help identify their benign nature include: their presence in areas of relatively high cellularity, an elongated shape and ill-delineated margins, low signal intensity on T1-weighted images, central spot of high signal intensity on T1-weighted images, intermediate increase or no increase in signal intensity on T2-weighted, fat-suppressed and STIR images, no or minimal enhancement after injection of gadolinium. Stable appearances on follow-up MR imaging and normal appearances on CT and bone scans also confirm their benignity [2,4].

Enostosis: An enostosis (bone island) is a common benign hamartomatous bone lesion composed of layers of cortical bone embedded with the medullary cavity. These asymptomatic lesions usually measure between 2-10mm [2]. Although they may occur anywhere in the skeleton, they have a predilection for the pelvis, femur and spine [2, 11]. Although they almost always appear as low signal intensity lesions on all sequences, they
rarely demonstrate a peripheral rim of high signal intensity on STIR sequences which must be differentiated from sclerotic metastases [2] Fig. 10 on page 26 Fig. 11 on page 26.

Fig. 10: Sagittal T1W (A) and T2W (B) images of the lumbar spine demonstrate a 1 cm area of signal dropout in the L2 vertebral body. This is of low signal intensity on both T1 and T2 in keeping with a typical enostosis.

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**Fig. 11**: Plain radiograph (A) of the pelvis in a 58-year-old man with a history of prostate malignancy complaining of left hip pain demonstrates an incidental 34mm x 25mm sclerotic lesion in the right femoral neck with no associated fractures. Axial T1W (B), PD fat-saturated (C), STIR (D) and post-contrast T1W (E) images of the right pelvis demonstrate a well-defined lesion in the right femoral head. This is of low signal intensity on all sequences, with no evidence of contrast enhancement, and is not associated with any aggressive feature. Axial CT image (E) shows a sclerotic bone lesion with no evidence of cortical fractures or periosteal reaction. Further three phase bone scintigraphy of the pelvis and femora demonstrated no evidence of foci of abnormal uptake. Findings are consistent with an enostosis.

**References**: Medical Imaging Department, Mater Dei Hospital - San Gwann/MT

**Vertebral haemangiomas**: Vertebral haemangiomas are the commonest benign focal bone lesions within the spine [12]. They consist of multiple endothelial-lined and blood-filled vascular spaces embedded within a fatty stroma [4]. They are often multiple, slow growing and are most often asymptomatic. Only rarely do they present with pain resulting from neural compression secondary to collapse or extraosseous extension [13]. Asymptomatic haemangiomas are typically of high signal intensity on T1- and T2-weighted sequences and commonly demonstrate focal areas of low T1 and T2 signal intensity secondary to intervening thickened trabererculae [4,12] **Fig. 12** on page 27. Atypical haemangiomas may vary in appearance mimicking malignant lesions. They include those which are hypointense on T1- and hyperintense on T2-weighted images. CT can help differentiate haemangiomas from sinister lesions by demonstrating their prominent trabecular pattern and pathognomonic polka-dot sign [2] **Fig. 13** on page 28.
**Fig. 12**: Sagittal T1W (A) and T2W (B) images of the lumbar spine demonstrate a 2.2cm rounded lesion within the L4 vertebral body of high signal intensity on both sequences. Findings are in keeping with a typical vertebral haemangioma.

**References**: Medical Imaging Department, Mater Dei Hospital - San Gwann/MT

**Fig. 13**: 53-year-old man who presented with a 2-month history of severe lower back pain radiating to the right lower limb, nocturnal pain and weight loss of 6kg
over 1 month. Sagittal T1W (A), T2W (B) and STIR (C) images of the lumbar spine demonstrate abnormal bone marrow signal occupying a large portion of the L3 vertebra (red arrow) which persists on fat suppression. There is no detectable abnormality on T1. Axial T2W image (D) demonstrates a polka dot appearance. Appearances were suggestive of an atypical haemangioma however metastatic disease could not be fully excluded. A CT trunk was recommended for assessment of possible primary disease. There was no evidence of underlying neoplastic disease. Axial (E) and sagittal (F) CT images of the lumbar spine on bone window demonstrate a benign trabeculation pattern within the L3 vertebra with no evidence of bone destruction (blue circles). Overall findings are consistent with that of a hemangioma.

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**Benign notochordal cell tumours (BNCT):** These notochordal remnants are usually found in the midline of the clivus however they may occur anywhere within the spine. Although there have been some reported cases of malignant transformation, these lesions are generally considered to be benign and are usually followed up radiologically [4, 14]. Typical findings on MRI which help distinguish these lesions from chordomas include: a slightly nodular intraosseous mass with no soft tissue component, low signal intensity on T1-weighted images and high signal intensity on T2-weighted images [14]. They do not usually enhance on contrast imaging although slight enhancement has been reported in a number of biopsy proven cases [4]. On CT they may appear as foci of subtle to marked sclerosis with no aggressive features [14] **Fig. 14** on page 29.

**Fig. 14:** Sagittal T1W (A), T2W (B) and T1W post Gadolinium (C) images of the cervical spine demonstrate a rounded lesion within the C6 vertebral body (red arrow) measuring 8mmx10mm of low signal intensity on T1 and high signal intensity on T2.
There is no evidence of contrast enhancement. Sagittal (D) and axial (E) CT images of the cervical spine demonstrate a focal area of faint sclerosis within the vertebral body of C6 (blue circles). This lesion appears to preserve the trabeculae and does not demonstrate any destructive features. A repeat MRI of the cervical spine 4 years later demonstrated unchanged appearances. Radiological features are benign and differential diagnosis includes a benign notochordal cell tumour.

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**Diffuse variations of bone marrow:**

**Diffuse haematopoetic bone marrow hyperplasia:** Red marrow hyperplasia is defined as the reconversion of yellow marrow into red marrow. Hyperplasia of hematopoietic marrow commences proximally in regions composed of predominantly red marrow and progresses distally to areas of fatty marrow. There are two main forms of red marrow hyperplasia: the primary idiopathic form and a secondary form. Idiopathic red marrow hyperplasia occurs as a response to various physiological stimuli, such as in middle-aged obese women, heavy smokers and in athletes. It is often incidentally discovered on routine knee MR exams and is characterized by symmetrical low T1 signal intensity within the femoral metaphyses [4] **Fig. 15** on page 30. A diffuse and more exaggerated form of red marrow hyperplasia may occur secondary to the use of hematopoetic growth factors in chemotherapeutic regimes or in chronic disorders associated with states of anaemia. This process, which may occur both in the appendicular skeleton and in the spine, demonstrates a signal intensity similar to that of red marrow. In the spine, the involved bone marrow is of low T1 signal intensity, at times lower than that of the intervertebral discs, whilst on fat saturated T2-weighted or STIR images a higher signal intensity to paravertebral muscles. On T2-weighted images low signal may be observed likely due to chronic hemosiderin deposition [2,4] **Fig. 16** on page 30.
**Fig. 15:** 31-year-old healthy lady complaining of medial right knee pain. Sagittal T1W (A) and coronal PD fat saturated (B) images of the right knee. The bone marrow of the femur, tibia and fibula, excluding the epihyseal regions, is diffusely hypointense on T1-weighted imaging and hyperintense on proton density imaging. Findings are in keeping with idiopathic diffuse hematopoietic bone marrow hyperplasia.

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**Fig. 16**: 49-year-old bodybuilder with a history of steroid and growth hormone abuse. Sagittal T1W(A) and T2W (B) images of the lumbar spine demonstrate abnormally low marrow signal throughout the lumbar spine in keeping with diffuse red marrow hyperplasia related to growth hormone abuse. A repeat MRI 3 years later demonstrated stable appearances.

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Conclusion

Whilst MRI remains the gold standard for the radiological evaluation of bone marrow, it is imperative that radiologists are familiar with the varied spectrum of normal appearances of the bone marrow on this imaging modality. Knowledge of these appearances can help distinguish focal and diffuse normal variants from pathological lesions which truly merit further investigation.
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