Learning objectives

- Review of normal bone marrow signal and marrow reconversion in adults on magnetic resonance imaging (MRI).
- To illustrate characteristic MRI findings of serous atrophy of bone marrow (SABM) in adult patients.
- Summary of differential diagnoses of SABM.
- Discussion of diagnostic tips as well as ways to avoid imaging pitfalls.

Background

Imaging Appearance of Normal Bone Marrow

Bone marrow consists of [1, 2, 4]:

- Trabecular bone - Serves as architectural framework and site for mineral deposition.
- Red marrow - Haematopoietically active; produces red blood cells, white blood cells and platelets.
- Yellow marrow - Haematopoietically inactive.

The composition of red and yellow marrow determines the marrow signal on MRI [1, 2, 4]:

- Red marrow - Typically composed of 50% haematopoietic cells and 50% fat cells. **It is always of slightly higher signal intensity compared to normal intervertebral discs and muscle on T1-weighted (T1W) images. Pathology is likely when marrow signal becomes equal or lower than normal disc or muscle on T1W images.**
- Yellow marrow - Composed mainly of fat cells. It follows the signal intensity of subcutaneous fat on all MR sequences.

Distribution of red and yellow marrow varies with age, sex, hormonal and other factors. Normal physiological conversion of red to yellow marrow changes with age in a predictable and progressive manner [1, 2]:

- Infant skeleton, except for epiphyses and apophyses, is composed almost entirely of red marrow.
- Conversion of the whole skeleton begins distally: Hands and feet -> bones of forearms and lower legs -> humeri and femora -> axial skeleton.
• Conversion of individual long bone begins centrally: Diaphysis -> distal metaphysis -> proximal metaphysis.
• The normal conversion is complete by age 25. Residual red marrow is predominantly seen in the skull, vertebrae, ribs, sternum, pelvis and proximal portions of femora and humeri.

Reconversion of yellow to red marrow is the physiological response to increased haemopoietic requirements of the body [1, 2]:

• It begins in the axial skeleton (vertebrae and flat bones), followed by the limbs in a proximal to distal pattern - The reverse of normal physiological conversion.
• Some common causes include smoking, endurance sports, obesity, diabetes, chronic anaemia and treatment with hematopoietic growth factors.
• This phenomenon is not infrequently encountered. Its diversity in imaging appearances can be confused with pathologic findings and misleading during MRI interpretation.

MRI is the imaging modality of choice in the non-invasive investigation of bone marrow disorders [1, 2, 5, 6]. Sequences most commonly employed in routine clinical practice include:

• **T1W sequence:** Most important and sensitive sequence in the assessment of bone marrow. Validated sequence with reliable criterion for signal normality of red marrow.
• **Fat-suppressed sequences:** Commonly used sequences in musculoskeletal (MSK) MRI include chemical-selective T2-weighted fat-saturation (T2W FS) and short tau inversion recovery (STIR) sequences. These complement the T1W sequence and further increases sensitivity and specificity in the detection of marrow abnormality.
• Other less commonly employed sequences include DIXON-based fat-suppression, in- and out-of-phase gradient-recalled echo (GRE) and diffusion-weighted imaging (DWI) sequences.

**Serous Atrophy of Bone Marrow (SABM) [3, 4, 7-11]:**

• Also known as ‘gelatinous transformation of marrow’ and 'starvation marrow' - Patients with SABM are almost always cachectic.
• A rare marrow disorder that is histologically characterised by fat cell atrophy, loss of haematopoietic cells and extracellular deposition of gelatinous substances.
• The gelatinous substances were later identified as hyaluronic acid mucopolysaccharides.
• On histopathological examination, the gelatinous substances stain pink with Giemsa’s stain.
• It also stains strongly with alcian blue at pH 2.5.
• Almost exclusively seen in the adult population.
• A slight peak of incidence in young adults (patients in their 20s).
• Slight male preponderance was observed.
• SABM is not disease-specific: It is most commonly reported in malnourished patients related to anorexia nervosa and starvation. Other frequently associated conditions include chronic infection (e.g. tuberculosis and AIDS), malignancy, alcoholism and cytotoxic drugs.
• It is an indicator of severe or chronic illness.
• SABM is not thought to be a permanent condition, with reversal of SABM to normal marrow reported after clinical improvement of the underlying disorder.
• The deposition of gelatinous substances and subsequent alteration of marrow microenvironment is detrimental to haematopoiesis. However, the degree of cytopaenia does not correlate with the extent of SABM.
• Patients with SABM are frequently anaemic.
• Resultant leukopaenia also predisposes patient with SABM to infection.
• Patients with SABM are also at increased risk of fractures, in particular, of the lower limbs.
• This may be attributed to reduced biomechanical strength of bone due to change in bone marrow composition.

Images for this section:
Fig. 1: MRI lumbar spine of a 20-year-old man on T1W, T2W and STIR sequences. Red marrow predominates in the vertebrae of a young person, accounting for intermediate T1-signal intensity (white *) that is lower than subcutaneous fat (red *), but higher than the adjacent normal intervertebral discs (arrow heads).

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Fig. 2: MRI lumbar spine of a 68-year-old man on T1W, T2W and STIR sequences. Following normal conversion of red to yellow marrow, the vertebrae show marrow signal intensities (blue *) that are equal to the subcutaneous fat (yellow *) on all MR sequences.

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Findings and procedure details

Appearance of SABM on MRI [3-5, 10]:

- First described by Vande Berg et al. in 1994 after pathologic correlation was performed in one of the patients with anorexia nervosa demonstrating fluid-like signal intensities in marrow spaces. Marrow biopsy revealed typical pathological findings of SABM.
- Focal or diffuse **marrow hypointensity on T1W images**, compared to muscle.
- Corresponding abnormal **marrow hyperintensity on fat-suppressed T2W / STIR images**, compared to muscle.
- SABM **does not show contrast enhancement**.
- There is **diminished subcutaneous fat**, which often exhibits signal intensities similar to that of SABM, particularly on fat-suppressed T2W / STIR images.
- There is no cortical erosion or associated soft tissue mass.
- The **distribution of SABM is unique**. Marrow reconversion and other replacement disorders typically begin at sites of red marrow (i.e. axial skeleton). SABM, in contrast, **typically begins in fatty marrow** (i.e. distal skeleton).

Differential Diagnoses for Diffuse or Multifocal Decreased Bone Marrow T1W Signal [5]:

Marrow infiltration / replacement:

- Benign: Marrow reconversion, haemosiderosis, amyloidosis, mastocytosis, Gaucher's disease.
- Malignant: Multiple myeloma, leukaemia, myelofibrosis, metastasis, lymphoma.

Systemic inflammatory processes:

- Sarcoidosis
- Gout
- Spondyloarthropathy

Challenges and Imaging Pitfalls [10]:

- No established diagnostic criterion for the diagnosis of SABM on MRI.
• SABM is *under-recognised* and may be *misinterpreted* as technical errors or imaging artefacts, leading to *misdiagnosis* and *unnecessary repeat imaging*. This is particularly true with chemical-selective T2W fat saturation imaging, where increased signal of bone marrow and subcutaneous tissues in SABM may be misinterpreted as technical failure of fat suppression, leading to repeat imaging using the same technique.

• Raised T2-signal of SABM may obscure concurrent fracture (Fig 3 & 4) or infection (Fig 7 & 8).

• Marrow abnormality of SABM may be mistaken for metastasis in patients with known malignancy.

**Overcoming Imaging Pitfalls:**

When marrow signal is abnormal and SABM is suspected:

- Always evaluate marrow signal on T1W sequence first, complemented by fat-suppressed T2W / STIR sequence (Fig 3 & 4).
- Assess the thickness and signal intensities of subcutaneous fat.
- **Perform alternate fat-suppressed techniques to exclude technical failure of fat suppression.** For example, if T2W FS has been performed, then perform STIR to confirm imaging findings. Unlike chemical-selective fat-saturation techniques, fat-suppression using the STIR sequence is robust as it is based on longitudinal magnetisation relaxation and less dependent on $B_0$ magnetic field homogeneity. Thus, the abnormal signal on STIR imaging is less likely due to artefacts from technical failure (Fig 3 & 4).
- Knowledge of the distribution of red and yellow bone marrow, familiarity with the appearance of red marrow reconversion and its relationship with age, concomitant diseases and presentation are essential.

When complications (fracture or infection) and malignancy is suspected:

- Correlation with other imaging modalities, such as radiograph or computed tomography (CT), may help to detect fracture and established osteomyelitis (Fig 7).
- Bony cortical changes and soft tissue mass are not typically found in SABM and if present warrants further evaluation for other underlying or associated conditions such as infection, metastatic disease, fractures, etc.
- Administration of intravenous contrast may help to exclude SABM or to detect bony metastasis on background of SABM.
- In difficult cases, histological correlation through bone marrow biopsy or aspiration may be required.

**Images for this section:**
Fig. 3: Selected images from MRI left knee of a 30-year-old man with poorly controlled diabetes. He presented following a fall and was unable to weight-bear on his left leg. (LEFT) The T1W image shows the marrow signal of tibia and fibula to be only slightly more hyperintense to the adjacent muscle, indicating marrow abnormality. The thin subcutaneous fat plane also shows abnormally low signal intensity on T1W image. Note the isointense signal of subcutaneous fat to muscle. Fat suppression was not employed on this T1W sequence. (RIGHT) Upon cursory assessment, one might conclude that there is failure of fat suppression on the sagittal T2W FS as the marrow and subcutaneous fat show abnormally high signal intensity that is almost isointense to the suprapatellar effusion (*). This illustrates the importance of evaluating marrow signal on T1W image. Note the acute fracture of the tibial plateau.

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Fig. 4: In the same patient as in Fig. 3, STIR sequence was also performed to demonstrate that the abnormal high T2W signal intensities of marrow and subcutaneous fat are persistent and not due to failure of chemical-selective T2W fat-saturation.

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Fig. 5: Selected images from MRI right calf of a 54-year-old man with medical history of alcoholism, alcohol-induced pancreatitis and poorly controlled diabetes. He was a chronic smoker with history of treated tonsillar carcinoma. He presented with right lower limb cellulitis. (LEFT) SABM is thought to begin as small foci that eventually coalesce to become more diffuse. This may produce areas of heterogeneously low marrow signal intensity on T1W imaging. (RIGHT) There is correspondingly raised marrow signal on the STIR image. Paucity and abnormal signal intensity of subcutaneous fat (*) are further supporting evidence of underlying SABM.

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**Fig. 6:** Large FOV Coronal STIR image of the same patient in Fig 5 reveals diffusely raised marrow signal in both lower limbs, including the partially imaged talar and calcaneal bones. Bilateral and symmetric involvement suggests an underlying systemic disorder.

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**Fig. 7:** Selected right foot radiograph and images from MRI right foot of an 82-year-old bed-bound male patient who presented with a chronic heel ulcer. He also suffered from ischaemic heart disease. (LEFT) Oblique left foot radiograph reveals irregular bony erosion at the calcaneal tuberosity (black arrowheads), which was suspicious for osteomyelitis. (MIDDLE and RIGHT) Selected axial T1W images of the foot show signal abnormalities of the marrow and thin subcutaneous fat plane that are suggestive of SABM. MRI confirmed the presence of bony erosion at the calcaneal tuberosity (black arrow).

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Fig. 8: There are abnormally raised signal intensities of the marrow and subcutaneous fat on sagittal STIR image of the same patient in Fig 7. The known bony erosion at the calcaneal tuberosity is less conspicuous (white arrowhead). Expected marrow oedema related to acute osteomyelitis is obscured by the generalised abnormal marrow signal of SABM. This illustrates the complementary role of other imaging modalities to aid detection of established osteomyelitis in the setting of SABM.

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Conclusion

- Knowledge of normal distribution of red and yellow bone marrow, as well as red marrow reconversion, is essential.
- Radiologists should be cognizant of SABM and its imaging findings, allowing for correct diagnosis and avoid unnecessary repeat imaging.
- Employing robust fat-suppression techniques is useful in distinguishing SABM from technical errors and imaging artefacts.
- SABM may obscure concurrent infection, fracture or neoplasm. Contrast-enhanced MRI or correlation with other imaging modalities may be helpful.
- Final definitive diagnosis in difficult cases may require histological correlation with bone marrow aspiration or biopsy.

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References


