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The *Journal of the American Osteopathic College of Radiology (JAOCR)* is designed to provide practical up-to-date reviews of critical topics in radiology for practicing radiologists and radiology trainees. Each quarterly issue covers a particular radiology subspecialty and is composed of high quality review articles and case reports that highlight differential diagnoses and important teaching points.

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In this Issue

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I am so excited to be a part of this noble academic enterprise, the *Journal of the American Osteopathic College of Radiology* (JAOCR). I am even more humbled to be invited to preside over its first musculoskeletal issue, namely because of the magnitude of the platform I have been given to reach out to radiologists everywhere.

When I was first approached about contributing to the Journal, I thought long and hard about a topic that would be interesting and challenging. In this issue, we present a two-part series reviewing MR imaging of bone marrow. Dr. Still professed over a century ago that before we can begin to understand what is abnormal we must first understand what is normal. Thus, part I of the series delves into normal marrow, its composition and normal pattern of maturation. The latter part of the first article and the entire second article are then devoted to discussing the various categories of marrow disease.

I am also delighted to present four noteworthy cases in our Case Report section which are written with emphasis on a gamut-based or differential diagnosis approach. We then round out the issue with three cases in the *At The Viewbox* section that I like to describe as “eye candy” for the radiologist.

I am thankful to the AOOCR for this wonderful opportunity. I wish to thank William O’Brien, D.O., for his warm and thoughtful invitation to write for the Journal which to any outside observer could have been interpreted as a Jedi mind trick, and for his expertise and advice in the critical review of the content in this issue. I want to extend my gratitude to Scot Campbell, M.D., for his diplomatic constructive criticism of both review articles, to Rebecca Kessler, D.O., for undertaking the more difficult half of the marrow review, and to Liem Mansfield, M.D., for contributing his educational material, valuable time, and sage experience. I also wish to thank all of the Case Report contributors, including Russ Chapin, M.D., Colin “I am the manager!” Strickland M.D., Matt Minor, M.D., David Shulman, M.D., and W. Banks ‘Honeytruck’ Petrey, M.D., for putting up with my incessant and entirely unnecessary pestering about deadlines. To my *At The Viewbox* contributors, you are the 180 degree refocusing pulse to my 90 degree RF pulse; without you this issue would dephase. Lastly, I would like to thank my wife Laura for supporting me in this consuming endeavor when she much rather would have preferred to allow our infant son to dismantle my computer as I typed.

Please enjoy this musculoskeletal issue of the *JAOCR*. We certainly enjoyed pooling our academic spirit to bring it to you.

*The views expressed in this material are those of the author, and do not reflect the official policy or position of the U.S. Government, the Department of Defense, or the Department of the Air Force.*
Magnetic Resonance Imaging of Bone Marrow: A Review – Part I

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Bone marrow is a complex organ containing undifferentiated cells from which the various constituents of blood originate. Under the control of hormones, cytokines and growth factors, normal marrow is susceptible to proliferation or suppression secondary to multiple influences, to include infection, medications, radiation, toxins, neoplasms, and nutritional deficiencies, among others.1 While histopathologic examination is the primary means for evaluating bone marrow, detection of marrow abnormality often occurs during medical imaging.

In part I of our review, the normal MRI appearance of bone marrow and its pattern of maturation from birth to adulthood will be discussed. We will then discuss disease processes characterized by marrow depletion, followed by a discussion of treatment-related marrow changes and marrow conditions which are not otherwise easily categorized. In part II of our review, bone marrow edema, myeloproliferative disease, marrow infiltration and replacement, and marrow ischemia will be covered in detail.

Normal Marrow

Normal bone marrow is composed of variable proportions of hematopoietic cells and fat. The proportion of each fluctuates over time depending on age and homeostatic requirements. These cells are set upon a framework of trabecular bone, perfused by a rich sinusoidal network of capillaries, and innervated by a neuroreticular complex of myelinated and unmyelinated neural fibers. The complex and dynamic process of bone remodeling is the result of a delicate balance of osteoblast and osteoclast activity. These processes are further supported by a cadre of reticuloendothelial cells, stromal cells, macrophages, lymphocytes, and plasma cells.2,3

The natural progression from birth to adulthood is a gradual shift from predominantly cellular or “red marrow,” to a mixture of predominantly fatty or “yellow marrow,” a process termed “marrow conversion.” With aging, there is a concomitant decline in the number of trabeculae. The shift toward predominantly fatty marrow follows a predictable pattern, occurring first in the appendicular skeleton followed by the axial skeleton. The process is usually completed by 25 years of age.

MRI evaluation of bone marrow exploits compositional differences between red and yellow marrow. Hematopoietically active red marrow contains 40% water, 40% fat, and 20% protein, while yellow marrow contains 15% water, 80% fat, and 5% protein.2 Because of the greater fat content, yellow marrow has hyperintense signal intensity on T1 and fast spin-echo T2-weighted sequences, intermediate signal on spin-echo T2 sequences, and signal drop out on fat suppressed sequences.4 While red marrow contains some fat, its higher cellular content results in relative hypointense signal compared to yellow marrow on T1 weighted images (but higher signal intensity than muscle), and intermediate to slightly hyperintense signal relative to yellow marrow on fluid sensitive MR sequences.4 Because MRI has such exquisite sensitivity in discerning the differences in marrow composition, the fatty component of marrow is often detected earlier in younger patients than would be expected by macroscopic histologic inspection.5,6

Marrow Conversion in the Appendicular Skeleton

The conversion of red to yellow marrow is a dynamic phenomenon that occurs in a predictable, orderly, symmetrical and centripetal pattern.2,4,7-11 Marrow conversion begins in the distal aspect of the extremities (hands and feet) and extends proximally to involve the long bones of the extremities. Within individual long bones, marrow
conversion follows a centrifugal pattern with replacement of red marrow by fatty marrow beginning in the shafts of long bones before progressing to the ends of bone. Marrow conversion in the long bones of the forearm and lower leg can lag slightly behind the femora and humeri.\textsuperscript{9,10} Many authors characterize the progression of marrow conversion into four distinct stages: infantile, childhood, adolescent, and adult patterns;\textsuperscript{2,4,8-11} however, variation has been observed with marrow conversion in the femur occurring earlier than expected in some subjects.\textsuperscript{12}

**Infantile marrow (newborn up to one year):**

Normal marrow in late fetal and early infant life is characterized by a high concentration of red marrow throughout the axial and appendicular skeleton. Thus, the diaphyses and metaphyses of long bones on MRI have low T\textsubscript{1} signal, while unossified epiphyses and apophyses composed predominantly of cartilage exhibit intermediate signal on T\textsubscript{1} weighted images (figs. 1 and 2).\textsuperscript{5,13} Later, when epiphyses and apophyses ossify, yellow marrow becomes evident within the ossification centers as areas of hyperintense T\textsubscript{1} signal.

![Figure 1](image1.png)

**Figure 1.** Schematic diagram of the infantile marrow (just after birth) showing global distribution of red marrow. (Red areas represent red marrow and black areas represent cartilage).

![Figure 2](image2.png)

**Figure 2.** Sagittal T\textsubscript{1} weighted image of the knee in a 18 day old male (A) shows hypointense red marrow in the proximal tibial (and distal femoral) metadiaphyses (white arrow) and intermediate signal (isointense to muscle) in the cartilaginous epiphyses (black arrow). Coronal T\textsubscript{1} weighted image of the pelvis in an 8 month old male (B) shows hypointense red marrow throughout the proximal femurs and pelvis.

**Childhood marrow (one year to 10 years):**

Near the end of the first year of life, marrow conversion begins in the phalanges of the hands and feet and is complete by 1 year of age. Additionally, marrow conversion in the femoral diaphyses commences by 12 months of age, sometimes seen as early as 3 months of age.\textsuperscript{10} After the first year of life, yellow marrow replaces red marrow in the diaphyses, while red marrow remains within the metaphyses. This results in relatively hyperintense signal in the diaphyses and low to intermediate signal intensity in the metaphyses on T\textsubscript{1} weighted sequences (figs. 3 and 4).\textsuperscript{2}

![Figure 3](image3.png)

**Figure 3.** Schematic diagram of childhood marrow (1-10 years) showing yellow marrow distributed in apophyses, epiphyses, and the diaphysis and red marrow situated in the proximal and distal metaphyses. (Red areas denote red marrow, yellow areas denote yellow marrow, and black areas denote cartilage).
Figure 4. Coronal T1 weighted image of the pelvis in a 20 month old male. Note hyperintense yellow marrow within the ossification centers of the femoral and tibial epiphyses (white arrows), intermediate to hypointense signal of the unossified cartilaginous epiphyses (black arrow), and the intermediate to low marrow signal of red marrow in the metaphyses (red arrow).

Adolescent marrow (10 years to 25 years):
In the second decade of life, continued conversion of predominantly red marrow to predominantly yellow marrow in the diaphyses of long bones is accompanied by recession of red marrow from the distal metaphyses. Thus, there is a slightly greater proportion of yellow marrow in the distal metaphyses, resulting in progressively increasing hyperintense signal on T1 weighted images (figs. 5 and 6).

Figure 5. Schematic diagram of adolescent marrow (10-20 years) showing recession of red marrow from the distal metaphysis and replacement of yellow marrow in the diaphysis and distal metaphysis. (Red areas denote regions of red marrow and yellow areas denote regions of yellow marrow).

Figure 6. Coronal T1 weighted image of the pelvis in an 18-year-old female. Note hyperintense yellow marrow within the femoral epiphyses and diaphyses (white arrows) and intermediate to low marrow signal of red marrow in the proximal femoral metaphysis.

Adult marrow (over 25 years):
By the middle of the third decade, the mature or adult pattern of marrow is achieved with yellow marrow predominating throughout the appendicular skeleton, except for the proximal metaphyses of the femora and humeri (figs. 7 and 8). In the proximal femur, marrow conversion has been further characterized by Ricci’s group who reported 4 distinct patterns with progressive loss of red marrow from the medial femoral neck, a phenomenon they proposed was related to mechanical stress. Eventually, complete recession of red marrow from the proximal femoral metaphyses develops later in life, occurring as early as 35 years of age in men and 55 years of age in women. This results in a near homogeneous hyperintense signal on T1 weighted images (fig. 8).

Figure 7. Schematic diagram of adult distribution of marrow (over 25 years) showing yellow marrow throughout the femur except for the proximal metaphysis. (Red areas denote red marrow and yellow areas denote yellow marrow).
Figure 8. Coronal T1 image in a 28-year-old male (A) shows areas of red marrow in the proximal femoral metaphyses (red arrows) and pelvis and fatty marrow in the epiphyses and trochanters (white arrows). Coronal T1 image in a 91-year-old male (B) shows diffuse yellow marrow.

Marrow Conversion in the Axial Skeleton
The axial skeleton includes the spine, ribs, sternum, skull, and pelvis. It serves as a repository of red marrow throughout life, with marrow conversion occurring much slower and to a lesser extent than in the appendicular skeleton.

In the spine, the pattern of marrow conversion often is less predictable. Ricci’s group described 4 patterns of marrow in the spine among varying age groups. In their study, the majority of subjects in the youngest group (ages less than 20) demonstrated a pattern of diffuse homogenously hypointense T1 signal within the vertebral bodies with linear hyperintense signal along the upper and lower margins of the basivertebral veins. Therefore, early in life, widespread red marrow results in lower signal intensity than adjacent intervertebral discs on T1 weighted images (Fig. 9).

In older groups of patients, Ricci noted variable distribution of the other 3 marrow patterns: (a) peripheral band-like and triangular areas of hyperintense signal adjacent to endplates and involving the anterior and posterior vertebral body corners; (b) punctate and/or patchy heterogeneous hyperintense signal; or (c) a combination of these two. These patterns varied from one region of the spine to another. Nevertheless, the expected pattern of marrow conversion in adulthood is from predominantly red marrow to a greater proportion of yellow marrow, resulting in hyperintense T1 marrow signal relative to adjacent intervertebral discs (Fig. 10).

Like the spine, the pattern of marrow conversion in the pelvis is less drastic than in the appendicular skeleton. Through the second decade of life, the pelvis is largely filled with red marrow, homogeneous until the age of 1. Over time, islands of yellow marrow arise in the acetabulum and anterior ilium. Ricci’s group reported 2 marrow patterns in the pelvis, both of which were marked by a predominant pattern of red marrow. One
pattern is seen in younger patients with small areas of yellow marrow in the acetabulum superior and medial to the hip joint; the second pattern is seen in older patients with additional areas of yellow marrow in the ilium and adjacent to the sacroiliac joints. While the majority of the literature on marrow conversion focuses on age related differences, the sacrum is one area where gender related differences were identified. Duda’s group found higher fat content in the sacral lateral masses in male subjects compared to females in a group of subjects 17-42 years old.

**Marrow Reconversion**

When the supply of blood cells is insufficient to maintain homeostasis, the body is able to upregulate blood cell production through marrow reconversion. Reconversion refers to red marrow proliferation or hyperplasia in areas where yellow marrow had become the dominant component. This pattern follows the reverse order as the pattern observed in marrow conversion. Specifically, resurgence of red marrow occurs in an overall centripetal manner, from the axial to the appendicular skeleton. The appearance of red marrow in individual long bones begins in the proximal metaphyses, followed by the distal metaphyses, and finally the diaphyses. The bones of the hands and feet are last to undergo marrow reconversion. Epiphyses may also be recruited for hematopoiesis, though usually only when the demand for blood cells is extreme.

Increased demand for blood cell production can result in hyperplasia as a physiologic response in patients with severe chronic anemia (sickle cell, thalassemia, hereditary spherocytosis), patients treated with granulocyte colony stimulating factor during chemotherapy, overweight female smokers, people living at high altitudes, and marathon runners (Figs 11, 12, 13). Unfortunately, marrow hyperplasia can also be seen in patients with underlying marrow replacement disease, such as lymphoma, leukemia, and metastases, which can confound the evaluation. Because of this, the MR characteristics of hyperplastic marrow can be difficult to differentiate from pathologic infiltration and vice versa.

![Figure 11](https://via.placeholder.com/150)

**Figure 11.** Sagittal T1 (A) and fat suppressed T2 (B) images show areas of red marrow in the distal femur in a 62 year old obese female nonsmoker (red arrows). Note the signal intensity of marrow is slightly hyperintense on T1 and T2 images compared to adjacent muscle.

![Figure 12](https://via.placeholder.com/150)

**Figure 12.** Sagittal T1 image of the foot/ankle (A) shows patchy areas of hypointense marrow reversion in a 22-year-old female with sickle cell anemia. Coronal T1 image of the pelvis (B) in the same patient reveals diffuse red marrow with the exception of fatty marrow within the epiphyses and trochanters. Crescentic regions of hypointense signal in the femoral heads is consistent with avascular necrosis.

![Figure 13](https://via.placeholder.com/150)

**Figure 13.** Coronal T1 (A) and T2 weighted with fat suppression (B) images of the pelvis show diffuse hypointense T1 and hyperintense T2 marrow reversion in a 37-year-old female treated with chemotherapy for breast cancer. Fatty marrow remains within the epiphyses and trochanters (white arrows).
A few useful discriminators favoring benign marrow hyperplasia include symmetric involvement, signal intensity of red marrow equal to that of normal muscle on STIR and fat suppressed T2 weighted images, and lack of aggressive features such as cortical destruction.\textsuperscript{14,20} Reconverted marrow will show intermediate signal on T1, T2, and STIR sequences in a nonconfluent patchy pattern.\textsuperscript{7,22}

In contrast, pathologic marrow infiltration tends to have hypointense T1 and hyperintense T2 signal relative to muscle.\textsuperscript{20} Therefore, T1 signal intensity less than or equal to that of muscle or intervertebral discs should prompt the radiologist to consider causes of abnormal marrow signal other than hematopoietic marrow.\textsuperscript{23} Because non-neoplastic hyperplastic marrow does not replace normal marrow elements (namely fat) as is expected with most neoplastic processes, opposed-phase imaging may have some utility in discriminating benign from pathologic marrow.\textsuperscript{7,24} Lastly, in those that are equivocal, short interval follow up with MRI or bone marrow biopsy are reasonable approaches.\textsuperscript{2,23}

**Marrow Depletion**

When the body fails to upregulate hematopoiesis to maintain homeostasis and the overall amount of red marrow elements becomes depressed, this is termed marrow depletion. Histologic evaluation of marrow depletion reveals hypocellular or acellular marrow on a background of diffuse fatty replacement, or predominantly yellow marrow. This pattern of abnormal marrow can be seen following treatment with chemotherapy or radiation, as well as with aplastic anemia of any cause. While diagnosis of marrow depletion is usually made with serological evaluation, medical imaging is useful for evaluation of recurrent disease or to evaluate response to therapy in the case of aplastic anemia.

**Aplastic Anemia:**

The earliest description of aplastic anemia was by Erlich in 1888 who published a case of a young pregnant woman who presented with bleeding, fever, and severe anemia. She was found to have marrow largely devoid of blood-forming elements at autopsy.\textsuperscript{25} Aplastic anemia is a relatively rare condition characterized by anemia with pancytopenia on peripheral smear (decreased circulating blood elements) and hypocellularity of the bone marrow (decreased progenitor cells). Aplastic anemia can be inherited (Fanconi anemia), acquired, or idiopathic. While the majority of cases are idiopathic, the list of acquired causes includes toxins (benzene), medications (Chloramphenicol, Carbamazepine, Phenytoin), infection (parvovirus and viral hepatitis), and radiation and chemotherapy treatment. Aplastic anemia has also been associated with connective tissue disease (systemic lupus erythematosus) and pregnancy.

On MRI, aplastic marrow tends to have diffusely hyperintense T1 signal because of predominantly fatty marrow. This is most conspicuous in areas typically dominated by red marrow, such as the spine and pelvis (Fig. 14). Occasionally, aplastic marrow can appear heterogeneous on T1 weighted sequences with areas of patchy low signal corresponding to foci of fibrosis. During treatment, myeloid elements may begin to return and T1 weighted images will show scattered small islands of hypointense signal corresponding to foci of resurgent red marrow.\textsuperscript{26} This appearance can be confused with areas of fibrosis, neoplasm, or myelodysplastic disease.

![Figure 14. Coronal T1 and STIR images in a 39-year-old female with aplastic anemia show diffuse fatty infiltration of the marrow with patchy areas of low T1 signal. Note the crescentic areas of low signal in the femoral epiphyses consistent with avascular necrosis.](image)

**Radiation:**

The medical uses of ionizing radiation include the treatment of various cancers, such as multiple...
myeloma and metastatic disease. An anticipated side effect of radiation therapy is marrow suppression. Myeloid elements, being the more sensitive component of marrow, are damaged and destroyed before fatty or yellow marrow. The degree of red marrow injury and its ability to replenish damaged cells is dependent upon radiation treatment dose, volume of marrow treated, and treatment frequency. Local irradiation with dose in the range of 3-45 Gy result in rapid bone marrow alteration which may persist up to 2 years. Regeneration of bone marrow is expected with local radiation doses below 30 Gy, while doses above 50 Gy will result in marrow ablation.

Following radiation, the earliest changes detected by MRI have been observed within 3 weeks, and as early as eight days. MRI demonstrates hyperintense signal on STIR images, which is thought to reflect bone marrow edema, hemorrhage, and possibly an influx of unirradiated cells. T1 weighted images in the first few days appear normal. The pattern of increased signal on STIR images decreases over time between the third and sixth week after treatment. At this point marrow signal on T1 weighted images increases, corresponding to predominantly fatty marrow. After the sixth week, the majority of affected patients will have hyperintense T1 signal (fatty marrow) that can last up to 2 years (Fig. 15). In the spine, two “late” patterns of marrow depletion following radiation have been described on T1 sequences: (a) homogeneous pattern of diffusely increased signal, and (b) “band” pattern with a peripheral region of intermediate signal intensity bordering a central zone of hyperintense signal. Irradiated marrow typically has a conspicuous appearance on T1 weighted images with hyperintense fatty marrow confined to the expected area of a radiation portal demarcated by a sharp line. Marrow changes outside the radiation portal have also been reported.

Chemotherapy:

Similar to radiation, the goal of chemotherapy in the treatment of marrow disease is marrow ablation. Early after chemotherapy, marrow appears hypointense on T1 weighted images and hyperintense on fat-suppressed T2 and STIR images owing to marrow congestion. Over time, with destruction of the myeloid elements and increasing fatty deposition, the marrow will show hyperintense T1 signal. Failure to observe this pattern can provide a clue to the radiologist that there is treatment failure or disease relapse. If the chemotherapy regimen includes granulocyte-colony stimulating factor (G-CSF), fatty transformation can be delayed or reflect a pattern of marrow reconversion which can confound evaluation for disease relapse or treatment efficacy.

Figure 15. Sagittal T1 image of the sacrum in a 45-year-old female post radiation and chemotherapy for rectal carcinoma shows diffuse fatty marrow signal 8 months after radiation therapy.

Other Marrow Diseases

While the majority of marrow conditions fall within larger categories (marrow depletion, proliferation, replacement, infiltration, edema and ischemia), there are some conditions which are difficult to categorize but deserve mention among miscellaneous conditions.

Osteopetrosis:

Osteopetrosis is a hereditary skeletal dysplasia characterized by abnormal osteoclastic activity, resulting in a generalized pattern of diffusely increased bone density. Four distinct subtypes have been described: precocious or “infantile” (autosomal recessive and lethal), delayed (autosomal dominant and mild), intermediate (autosomal recessive), and tubular acidosis type
Abnormal osteoclastic activity affects bony remodeling such that there is poor cortical and medullary differentiation, leading to undertubularization, metaphyseal widening, and dense metaphyseal bands. Despite the increase in density, bones are structurally weak and prone to fracture. Classically, there is a “bone within a bone” appearance, which in the spine has been described as the “sandwich” vertebra sign. Abnormal remodeling of cranial nerve foramina can result in deafness and blindness.

On MRI, the typical appearance of osteopetrosis is that of diffuse sclerotic bone with diffusely hypointense signal on T1 and T2 weighted images (Fig. 16). This appearance is nonspecific and can be seen with hemosiderosis, diffuse blastic metastases, or fibrosis.

Figure 16. Coronal T1 (A) and STIR (B) MR images through the pelvis show marked cortical thickening with diffusely low signal on the T1 weighted image and narrowing of the marrow space, which contains relatively hyperintense red marrow on STIR (red arrow).

Paget Disease:

Paget disease is commonly seen in men over 40 years of age and of European descent. Hallmark radiographic features include bony expansion with trabecular and cortical thickening. While its cause is poorly understood, the disease is thought to be related to an imbalance of osteoclastic and osteoblastic activity. It is characterized by three phases of the disease: (a) purely lytic, (b) mixed lytic and blastic, and (c) purely blastic. While the diagnosis of Paget disease is typically made on the basis of the radiographic appearance, MRI can be useful in the evaluation for complications of Paget disease, to include osteomyelitis, sarcomatous degeneration, giant cell tumor formation (skull), and metastases to hypervascular Pagetic bone.

The MRI appearance is variable but thought to reflect the state of the marrow as it is influenced by the various phases of disease, which can occur simultaneously. Early disease without significant marrow disturbance will appear normal with the exception of decreased size of the marrow space due to cortical thickening. Between the lytic and mixed phases (which are considered the more active phases), the marrow space appears heterogeneous on T1 and T2 weighted images (Fig. 17). This is likely related to deposition of fibrovascular tissue, which appears hypointense on T1 but hyperintense on T2 weighted images because of granulation tissue and slow blood flow through vascular channels. Other foci of hyperintense signal on T1 are possibly related to areas of fatty filled marrow spaces. Unfortunately, the MRI appearance can be nonspecific and resemble that of infection or neoplasm.

Figure 17. Coronal T1 (A), coronal fat suppressed T2 (B), and axial proton density (C) weighted images of the pelvis in a 49-year-old man with Paget disease. Note the bony expansion and coarsened trabecular thickening of the left femur.
Gaucher Disease:
The most common of the lysosomal storage diseases, Gaucher disease is characterized by a deficiency of glucocerebrosidase, which results in abnormally high levels of glucocerebroside that is taken up by histiocytes (termed Gaucher cells). Proliferation of Gaucher cells ensues with accumulation of glycolipids throughout the reticuloendothelial system. Within the marrow, this ultimately leads to cellular necrosis, fibrous proliferation, and loss of spongy trabeculae. Expansion of the marrow space by lipid-laden Gaucher cells results in the Erlenmeyer flask deformity of the femora. Additionally, there is generalized osteoporosis with progressive weakening of subchondral bone, predisposing affected patients to fracture. Vertebral fractures may manifest as vertebra plana or an H-shaped vertebra, similar to that seen in sickle cell disease. Elsewhere, weakening of the bone and osteonecrosis can be a nonspecific finding indistinguishable from other causes of avascular necrosis.

On MRI, Gaucher disease is nonspecific with patchy heterogeneous hypointense signal on T1 and T2 weighted images, similar to that seen in marrow infiltrative disease. With osteonecrosis, there may be areas of hyperintense T2 signal acutely which later become hypointense when necrosis is chronic (Fig. 18).

Iron Storage Disease:
Deposition of iron in marrow occurs in conditions where there is increased breakdown of erythrocytes (such as sickle cell anemia or thalassemia), iron overload (as in those who are on chronic blood transfusion therapy), or when there is overall abnormal absorption (such as in primary hemochromatosis). Common to all is a diffuse pattern of marked hypointense marrow signal on both T1 and T2 weighted images with blooming artifact on T2 gradient echo imaging.

Serous Atrophy or Gelatinous Transformation:
In patients with profound loss of body fat stores, as in patients who have severe cachexia, anorexia nervosa, or acquired immunodeficiency syndrome, a phenomenon known as serous atrophy or gelatinous transformation of the bone marrow can occur. Histologic descriptions of the marrow in these patients show a gray-pink gelatinous or serous marrow that contains atrophied fat and hematopoietic cells set on a matrix rich in hyaluronic acid. This watery matrix results in marked hyperintense signal intensity on T2 weighted images with hypointense signal on T1 weighted images (Fig. 19). The process may be
focal or diffuse. Furthermore, the progression of disease mimics the pattern observed with normal marrow conversion, namely transformation begins in the hands and feet, followed by the long bones of the distal arms and legs, before finally affecting the spine and pelvis.

Summary

In conclusion, interpretation of marrow on MRI requires an understanding of the normal pattern of marrow maturation or conversion, as well as an understanding of how the hematopoietic and fatty constituents of marrow contribute to the normal MRI appearance. Knowledge of the normal appearance of marrow allows for recognition of pathologic marrow processes. In part I of this review, we discussed marrow conversion and reconversion, as well as disorders of marrow depletion and important but miscellaneous processes which are otherwise difficult to categorize. In part II of our review, additional marrow conditions such as bone marrow edema, infiltration, and replacement; myeloproliferative disease; and marrow ischemia will be discussed.

The views expressed in this material are those of the author, and do not reflect the official policy or position of the U.S. Government, the Department of Defense, or the Department of the Air Force.

References

In part I, the normal appearance, maturation pattern, benign reconversion and depletion states of bone marrow were reviewed, followed by a discussion of a collection of marrow conditions not easily categorized. In part II, we review bone marrow edema, myeloproliferative disease, marrow infiltration and replacement, and bone marrow ischemia with emphasis on their associated MR imaging characteristics. While MRI is exquisitely sensitive in the detection of marrow abnormalities, the imaging characteristics of bone marrow disease often are nonspecific with only subtle differences in distribution, signal intensity and enhancement. When findings are equivocal, attention to the location and pattern of bone marrow signal abnormality, along with the clinical history, can serve to differentiate several etiologies that secondarily affect bone marrow.

Anatomy

Within the medullary component of bone, there are trabeculae of cancellous bone providing structural support and mineral supply. Vascular supply arises from the nutrient artery, branching into an extensive sinusoidal system traversing the marrow, and ultimately draining into the central venous system, which also exits via the nutrient foramen. Nerve supply includes extensive sensory and sympathetic branches. The cellular elements of normal marrow include a dominant component of fat cells, in addition to erythrocyte and leukocyte precursor cells, and reticulum or stromal cells.

MR Imaging

T1 relaxation (spin-lattice relaxation) describes the rate at which protons, excited by the radiofrequency pulse into the transverse plane, release the absorbed energy into the surrounding tissues and regain longitudinal magnetization. One of the most important factors determining T1 relaxation times in normal tissues at clinically relevant field strengths is the tissue type. For example, the molecular structure of lipid contains many CH2 groups, which demonstrate efficient spin-lattice relaxation, resulting in high signal intensity on T1-weighted images. The presence or absence of marrow fat in the imaging pixel contributes significantly to its relative signal intensity. Disorders in which normal marrow is replaced by tumor (marrow replacement) would be expected to demonstrate lower T1 signal intensity than conditions in which a prominent component of marrow fat remains (marrow infiltration). T1 relaxation time is also affected by the relative ratio of bound to unbound water in the tissues. Consequently, a relative increase in interstitial water protons in the marrow would be expected to result in longer T1 relaxation times, as observed in the setting of marrow edema, fibrosis, or hemorrhage.

T2 relaxation time is affected by the mobility of the water protons. Longer T2 relaxation times may result from increased water content in the tissues, a relative increase in extracellular fluid, or more random tissue ultrastructure (e.g. trabeculae disrupted by fracture).

In the majority of cases, spin echo sequences with T1 weighting and T2 weighting are sufficient to evaluate the marrow. Fat suppression is commonly used with the T2 weighted images to enhance conspicuity of the marrow signal abnormality. Short inversion time inversion recovery (STIR) sequences can be used in place of fat suppressed T2 weighted imaging. STIR has the advantage of more homogeneous fat suppression, but suffers from relatively decreased signal to noise ratio compared to T2 weighted images. Intra-venous contrast is typically reserved for complicated cases, or cases in which infection is suspected. Some authors advocate the use of chemical shift imaging, in which similar contributions of fat and non-fat elements in the pixels causes signal decrease on out of phase
Alternative MR imaging techniques include diffusion weighting for differentiation of pathologic from benign vertebral compression fracture, MR spectroscopy for evaluation and characterization of tumors, magnetization transfer imaging with chemical exchange saturation transfer agents, or alternative contrast agents such as superparamagnetic nanoparticles. 

### Bone Marrow Edema

In the setting of injury, arthrosis, adjacent tendinosis, nearby neoplasia, reflex sympathetic dystrophy, and a variety of other causes, the bone marrow demonstrates relatively hyperintense T2 and hypointense T1 signal. This is commonly referred to as a bone marrow edema pattern, although the mechanism and histological composition of bone marrow “edema” may vary depending upon the inciting disease or process. It is postulated that there is an increase in interstitial water content, and that hyperperfusion contributes to its formation.

A bone marrow edema pattern will typically show poorly defined margins, and faint marrow signal abnormality relative to adjacent muscle on T1 weighted images. The signal intensity of the marrow abnormality alone is generally not specific for a disease process. However, the location and distribution of marrow abnormality can often provide a clue to both etiology and, if related to trauma, the mechanism of injury. For example, when a marrow edema pattern is present at the sulcus terminalis of the lateral femoral condyle and at the posterior margin of the lateral tibial plateau, the pattern can be recognized as resulting from a pivot-shift mechanism (Fig. 1). The radiologist may then look for the associated soft tissue injuries, including anterior cruciate ligament tear, and often medial collateral ligament tear.

Another example of a characteristic bone marrow edema pattern in the knee is the posterolateral corner injury (Fig. 2). It is characterized by hyperextension with a varus directed force leading to contusion and/or fracture of the anteromedial tibia and femoral condyle, as well as injury to the lateral collateral ligament, popliteus tendon, and arcuate ligament complex. Associated avulsion of the proximal fibula may be present. This injury is commonly associated with anterior cruciate ligament tear, and may involve stretch injury of the common peroneal nerve. It is critically important to recognize this specific injury pattern because of inherent instability which requires timely surgical intervention.

Lastly, when the radiologist identifies bone marrow edema pattern involving the medial border of the patella and the lateral border of the lateral femoral condyle, a patellar dislocation-relocation injury has occurred (Fig. 3). Additional patterns of marrow edema within the knee, and corresponding mechanisms of injury are detailed in Table 1.

Abnormal marrow signal intensity isolated to the subchondral bone can be seen in a number of conditions, including underlying joint disease such as degenerative arthritis or rheumatoid arthritis, osteochondral lesion, contusion, insufficiency fracture, avascular necrosis, infection and neoplasm. In osteoarthritis, signal abnormality within the subchondral bone may result from a combination of subchondral cyst formation, fibrosis, hyperemia, necrosis, and bone marrow edema. With insufficiency fracture of the knee, a condition previously called spontaneous osteonecrosis of the knee (SONK), there is signal abnormality in the region of the insufficiency fracture (Fig. 4). While somewhat controversial, a pattern of bone marrow edema involving the hip can be seen. Previously thought to represent unique entities, such diagnoses as “transient osteoporosis,” “regional...
migratory osteoporosis”, and “bone marrow edema syndrome” are now thought to represent a spectrum of disease related to underlying insufficiency or stress fracture (Fig. 5). Additional diseases that may affect the subchondral marrow are listed in Table 2.

**Figure 2.** Coronal (A) and sagittal (B) fat suppressed T2 images of the left knee in a 28-year-old male show bone marrow contusion of the anteromedial aspect of medial femoral condyle and tibial plateau. Coronal proton density weighted image of the left knee (C) shows disruption of the lateral collateral ligament.

**Figure 3.** Coronal T2 images of the left knee in a 20-year-old female with marrow contusions involving the lateral femoral condyle (A) and medial patella (B), consistent with lateral patellar dislocation and relocation injury.

**Figure 4.** Coronal proton density (A) and fat suppressed T2 (B) weighted images of the right knee in a 77-year-old male show insufficiency fracture involving the mesial medial femoral condyle.

**Table 1 – Complex Knee injuries and bone marrow contusions**

<table>
<thead>
<tr>
<th>Bone Contusion or Fracture Locations</th>
<th>Mechanism of injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior femur and tibia</td>
<td>Pure hyperextension (kicking)</td>
</tr>
<tr>
<td>Anteromedial tibia and femur, posterolateral corner, proximal fibula avulsion</td>
<td>Hyperextension with varus (posterolateral corner injury)</td>
</tr>
<tr>
<td>Anterolateral tibia and femur, posteromedial tibial avulsion</td>
<td>Hyperextension with valgus</td>
</tr>
<tr>
<td>Lateral tibia and femur</td>
<td>Pure valgus</td>
</tr>
<tr>
<td>Medial tibia and femur</td>
<td>Pure varus</td>
</tr>
<tr>
<td>Lateral femur and posterolateral tibia, posteromedial tibia and femur avulsion or contrecoup lesion</td>
<td>Flexion with valgus and external rotation</td>
</tr>
<tr>
<td>Lateral femur, posterolateral tibia, posterolateral tibia and fibular head avulsions</td>
<td>Flexion with varus and internal rotation</td>
</tr>
<tr>
<td>Medial patella, lateral condyle</td>
<td>Patellar dislocation</td>
</tr>
<tr>
<td>Directly at trauma site</td>
<td>Direct trauma</td>
</tr>
<tr>
<td>None, unless severe force or axial load</td>
<td>Flexion with posterior tibial translation</td>
</tr>
</tbody>
</table>

**Table 2 - Joint diseases which secondarily affect adjacent subchondral bone (23)**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septic arthritis</td>
<td>Amyloid arthropathy</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>Hemophilic arthropathy</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
<td>Pigmented villonodular synovitis</td>
</tr>
<tr>
<td>Gout</td>
<td>Neuropathic arthropathy</td>
</tr>
<tr>
<td>Milwaukee shoulder</td>
<td>Foreign body synovitis</td>
</tr>
<tr>
<td>Rapidly destructive articular disease</td>
<td>Primary synovial osteochondromatosis</td>
</tr>
</tbody>
</table>
Figure 5. Coronal STIR image (A) demonstrates hyperintense signal throughout the left femoral head, neck and intertrochanteric region. Coronal STIR image acquired at a later date (B) demonstrates complete resolution of signal abnormality in the left proximal femur with new hyperintensity in the right femoral head and neck with some extension into the proximal diaphysis.

A subtendinous, subligamentous and subphyseal location of marrow signal abnormality can also be useful in identifying potential etiologies. Subtendinous bone marrow edema is commonly associated with trauma (acute or chronic) such as tendon tear. However, tenosynovitis, hydroxyapatite deposition disease (HADD), and enthesitis are also common causes of subtendinous bone marrow edema. With HADD, deposition of hydroxyapatite crystal may occur within the tendon, bursa, or joint capsule, causing focal inflammation. This can be idiopathic or due to underlying systemic abnormality such as secondary hyperparathyroidism or renal osteodystrophy. Subligamentous bone marrow edema may be associated with disease of adjacent tendons or ligaments. Renal osteodystrophy has a predilection for bone resorption in both subligamentous and subphyseal locations. Lastly, subphyseal bone marrow edema can also be seen with focal physeal injury and rickets (Fig. 6).

Proliferative Disorders

Myeloproliferative disorders involve both benign and malignant diseases arising from proliferation of cells normally found in bone marrow. Marrow reconversion is considered a physiologic response to stress and was discussed in part I of our review. The subset of benign myeloproliferative diseases includes myelofibrosis, polycythemia vera, mastocytosis and myelodysplastic syndrome. The subset of malignant proliferative disorders includes leukemia and monoclonal. Monoclonal gammopathies are further subcategorized as either as aggressive (multiple myeloma, primary amyloidosis, Waldenstrom macroglobulinemia and lymphoproliferative disorder) or nonmyelomatous (monoclonal gammopathy of undetermined significance and borderline significance).

Multiple myeloma

Multiple myeloma (Fig. 7), amyloidosis and Waldenstrom macroglobulinemia are aggressive gammopathies with very similar MR features. While a useful discriminator in Waldenstrom macroglobulinemia is the presence of regional bone infarction, the appearance of these entities on MRI is quite variable. Marrow patterns may be normal, focal disease with hypointense T1 signal marrow lesions, marrow with diffuse heterogeneous or variegated signal, or marrow with diffuse homogeneous hypointense T1 signal. To complicate things further, any combination of these patterns can be found in patients with disease regression or progression.

Focal myelomatous lesions are often characterized by hypointense T1 signal intensity unless there is hemorrhage causing focal T1 hyperintensity. The T2 signal intensity of these lesions is highly variable. Unfortunately, the appearance of myeloma on MRI can be indistinguishable from metastatic disease. Occasionally, focal myeloma lesions can demonstrate a ‘mini-brain’ appearance on MRI with thick osseous struts radiating in from the outer margins of the lesion (resembling the sulci and gyri pattern of the brain), a feature which can help differentiate it from metastatic disease. Although MRI may be less helpful in determining a specific diagnosis, MRI proves most useful in the preprocedure planning for bone marrow biopsy, as well as evaluating disease progression and treatment response.
Figure 6. AP (A) and frog-leg lateral (B) views of the hips demonstrate a slipped physis on the right. Coronal T1 image (C) reveals widening of the affected right growth plate, as well as hypointense signal along the physis, most notable inferiorly. Coronal T2 weighted images (D and E) demonstrate hyperintense signal on either side of the physis, as well as a right-sided joint effusion.

Figure 7. Sagittal T1 (A) and T2 (B) MR images demonstrate heterogeneous bone marrow signal with subtle endplate deformities. Coronal T1 pre (C) and post (D) contrast images of the sacrum reveal an enhancing left sacral mass. Frontal skull radiograph (E) demonstrates numerous lytic calvarial lesions. Coronal FLAIR image of the brain (F) shows increased signal intensity associated with the calvarial lesions.
Leukemia

Leukemia is a disease characterized by proliferation of leukemic cells that replace normal marrow constituents. Both acute and chronic forms of leukemia commonly demonstrate diffuse marrow abnormality. Abnormal signal that extends into the epiphyses and apophyses may also represent red marrow hyperplasia due to replacement of red marrow by leukemia in the axial skeleton. On T1 weighted images, leukemic infiltrate has hypointense signal intensity (lower than disc or muscle). The T2 weighted signal is variable relating to the infiltrative nature of leukemic cells. More often than not, there is hyperintense signal relative to fat on T2 weighted and hyperintense signal relative to muscle on STIR images. Homogenous hypointense T1 signal may be difficult to appreciate in the setting of extensive bone marrow disease when no normal marrow is available for comparison. In this case, contrast enhanced imaging can help to show enhancement of abnormal bone marrow compared to adjacent discs. After the diagnosis has been made, MRI can be used to monitor for complications of leukemia such as osteomyelitis, hematoma and chloromas (solid tumors of granulocyte precursor cells occasional seen in acute leukemia). Serial MRI can also be used to monitor the status of disease remission and relapse.

Mastocytosis

Mastocytosis is a rare disorder of mast cell proliferation. It generally presents as a self-limited dermatologic disorder, urticaria pigmentosa. Rarely, a systemic form may present with involvement of internal organs and bone marrow. Osseous involvement usually affects the axial skeleton. On radiographs, nonspecific areas of lytic, sclerotic, or mixed lytic-sclerotic abnormality are seen in either a focal or diffuse distribution. MR imaging findings are generally nonspecific, ranging from normal to focal or diffuse heterogeneous signal within the bone marrow.

Marrow Infiltration and Replacement

Bone marrow may contain cellular areas (red marrow), or may be infiltrated by edema and inflammatory cells in the setting of osteomyelitis. At MRI, these processes may demonstrate similar signal intensity, which has been referred to as a “marrow infiltration” pattern. In the case of marrow with hematopoietic tissue, this terminology probably does not accurately reflect the histology, which may be better described as red marrow reconversion. On T1 weighted images, a marrow infiltration pattern is characterized by subtle to moderate decrease in signal intensity which remains relatively hyperintense compared to adjacent muscle or normal intervertebral disks. The margins of the marrow signal abnormality are typically poorly defined, and the signal intensity is often heterogeneous. The relative hyperintensity is attributed to the residual presence of marrow fat in the imaged tissue.

Osteomyelitis

Distinguishing between red marrow and osteomyelitis is generally straightforward. Red marrow is commonly diffuse and symmetric, with faint T1 and T2 signal abnormality. On the other hand, in osteomyelitis, infiltration by inflammatory cells and an increase in local extracellular fluid cause areas of hypointense signal on T1 weighted images and hyperintense signal on T2 weighted images (Fig. 8). The signal abnormality is often focal or confined to a geographic area. In addition, osteomyelitis which has formed a phlegmonous or abscess cavity may show the ‘penumbra sign’ on T1 weighted images. This is characterized by a central hypointense to intermediate T1 signal cavity surrounded by a discrete peripheral rim of relatively hypointense T1 signal. This decreased T1 signal represents adjacent reactive new bone formation and/or surrounding edema. Secondary findings of skin ulcer, cellulitis, abscess, sinus tract in the soft tissue or bone, foreign body, cortical destruction and periosteal reaction often improve specificity and help to delineate osteomyelitis from other entities.

Malignancies

Bone marrow may have regions in which normal marrow constituents are replaced by pathologic tissue, such as in the setting of malignancies with bone metastases. At MRI, replacement of normal marrow fat by tumor would be expected to
demonstrate a marked decrease in T1 signal intensity, with resultant similar signal intensity as adjacent muscle or normal intervertebral disks.\textsuperscript{1,9} Although this finding is helpful when present, its sensitivity in the setting of early disease or low tumor burden is not well established. Additionally, this finding is not adequately specific to distinguish between benign and malignant causes, or between primary and secondary disease.

In long bone fractures, MRI features that have been found to be useful in distinguishing pathologic fractures from stress fractures include a well-defined T1 signal abnormality, endosteal scalloping, adjacent muscle signal abnormality, and a soft tissue mass.\textsuperscript{36} When the marrow abnormality is diffuse enough such that no normal marrow is visible, it may not be obvious to the interpreting radiologist. It can be useful to observe the “flip-flop” pattern of hyperintense T2 signal intensity and hypointense T1 signal intensity in areas that typically have fatty marrow, such as the epiphyses of long bones.\textsuperscript{37} Additionally, when the bone marrow is diffusely replaced, complications such as pathologic fracture may not demonstrate a substantial change in marrow signal intensity, making diagnosis difficult.

The most common malignancies with a predilection for bone metastasis are breast, prostate, thyroid, lung, kidney, and pancreatic carcinomas. These account for more than 80% of primary tumors presenting with bony metastases.\textsuperscript{38} In general, metastases more commonly involve the axial skeleton (spine, pelvis, ribs and sternum), but disease may also involve the proximal femora and humeri. Peripheral disease involving hands and feet is less common, but when present often indicates underlying lung malignancy.\textsuperscript{39}

Metastases typically appear as multifocal lesions with hypointense signal on T1 weighted images (lower than disc or muscle) and hyperintense signal on T2 weighted images. Additionally, diffuse marrow involvement, in either a homogeneous or heterogeneous pattern can be seen.\textsuperscript{29} Metastatic lesions may demonstrate a ‘halo sign’, where tumor deposits have a peripheral rim of hyperintense T2 signal intensity.\textsuperscript{40,41} This most commonly occurs with prostate and some forms of breast metastases which often have lower T2 signal than other types of metastases because of their osteoblastic nature (Fig. 9). The halo sign may also be seen in aggressive primary bone tumors and osteomyelitis, though clinical history and radiographic findings should help to discriminate between these entities.\textsuperscript{41} Contrast enhanced studies may be useful to evaluate bone marrow abnormalities but are usually reserved for diffuse marrow abnormalities and cases in which noncontrast image findings are not.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure8.png}
\caption{Nuclear medicine bone scan image (A) in a 4-year-old boy with bacteremia demonstrates mild focal radiopharmaceutical uptake in the left femoral intertrochanteric region. No radiographic abnormality is seen (B). STIR (C) and T1 (D) weighted images angled through the left femur demonstrate hyperintense T2 and hypointense T1 signal in the region. Axial T1 pre (E) and post-contrast (F) images show enhancement of this region.}
\end{figure}
nonspecific. Generally, metastatic disease will enhance to a greater degree than normal hematopoietic marrow except for those with marrow hyperplasia or immature marrow as seen in children.\textsuperscript{31}

**Figure 9.** Sagittal T2 (A) and T1 (B) MR images in a patient with metastatic breast cancer demonstrate heterogeneous signal throughout the bone marrow with numerous hypointense lesions. A lesion within the L2 vertebral body demonstrates a halo sign with peripheral rim of increased T2 and T1 signal (arrows). There is a corresponding region of a faint rim sclerosis on CT (C). CT also demonstrates heterogeneous attenuation with foci of sclerosis throughout the spine, as well as a compression deformity at the superior L1 level.

In children, metastases and lymphoma tend to present with focal bone lesions; however, diffuse marrow infiltration can be seen with rhabdomyosarcoma and neuroblastoma.\textsuperscript{42} MRI is useful when bone pain and laboratory values suggest malignancy but other imaging studies fail to demonstrate lesions. MRI may also be used to determine extent of disease within marrow as well as involvement of surrounding structures. It may occasionally be used to follow response to therapy.\textsuperscript{29}

**Benign versus pathologic fracture**

An important use of MRI includes differentiating metastatic vertebral body fracture from osteoporotic or insufficiency fracture. Metastatic disease often shows diffuse involvement of the vertebral body with hypointense T1 signal, abnormal marrow signal extending into the pedicle and posterior elements, significant enhancement, multiplicity and adjacent enhancing soft tissue mass. On the other hand, MRI findings favoring osteoporotic compression fracture over pathologic fracture include a low signal intensity band in the vertebra, spared normal bone marrow within the vertebral body, retropulsion of a posterior bone fragment, and multiple compression fractures.\textsuperscript{43} Insufficiency fractures may demonstrate thin paraspinal soft tissue mass or hemorrhage; however, these lesions demonstrate little to no enhancement and improvement or resolution on follow-up imaging.\textsuperscript{32}

Sometimes, bone marrow edema from osteoporotic fracture is so extensive that no residual fat can be seen on T1 images. Some institutions use chemical shift or in and out-of-phase imaging to differentiate neoplasia from non-neoplastic entities by demonstrating coexistent fat and water in the region. Neoplasia often completely replaces the marrow fat and demonstrates no significant decrease in signal on out-of-phase images. This technique may be less useful in evaluating myeloproliferative and some infiltrative disorders that can present with a mixture of abnormal cells and normal marrow fat, leading to a false negative result.\textsuperscript{44} False positive results may occur in cases of marrow fibrosis with complete loss of marrow fat, mimicking neoplastic infiltration.\textsuperscript{45}

**Lymphoma**

Lymphomatous involvement of bone marrow on MRI is similar in appearance to metastatic disease
and is most commonly seen with non-Hodgkin lymphoma.\textsuperscript{46} When lymphoma involves the bone marrow, it is categorized as stage IV or extensive systemic disease.\textsuperscript{31} As with other infiltrative disorders, the extent of tumor burden correlates with MRI findings. Involved bone marrow may be normal when tumor burden is low. With more extensive disease, marrow abnormality can appear focal or diffuse with a pattern of involvement which may be patchy and heterogeneous or homogeneous. Lymphoma within marrow is characterized by hypointense T1 and T2 signal of involved portions of the bone marrow which enhance, a nonspecific pattern common to many of the infiltrative and replacement diseases. MRI may also show adjacent soft tissue mass without cortical destruction which is suggestive of but not diagnostic of lymphomatous involvement. Generally speaking, MRI is not typically used to definitively diagnose, stage or follow lymphoma but can be used to help direct bone marrow biopsy to aid in staging.\textsuperscript{31,46}

**Primary benign bone tumors**

Numerous primary benign bone tumors can be considered in the differential diagnosis of focal marrow replacement. Enchondroma is a benign chondroid lesion found in the marrow cavity originating from continued growth of displaced, benign cartilaginous rests from the growth plate. Enchondroma is usually lobular in appearance with nonmineralized portions of enchondroma demonstrating low to intermediate T1 signal and intermediate to high T2 signal. The mineralized and septated portions usually show hypointense signal in both T1 and T2 weighted sequences. Additionally, they may show peripheral or septal enhancement (Fig. 10). Occasionally enchondroma may demonstrate speckled areas of hyperintense T1 signal secondary to residual areas of fatty marrow; however, the MRI signal intensity and enhancement pattern are nonspecific and it may be difficult to separate enchondroma from a low-grade chondrosarcoma. Differentiating this benign process from chondrosarcoma is more often based on a few clinical and imaging findings: the size of the lesion, pain, the amount of endosteal scalloping (depth and extent of lesion), cortical destruction, bony remodeling and/or thickening, soft tissue mass, periosteal reaction and pathologic fracture.\textsuperscript{47}

**Primary malignant bone tumors**

Primary malignant bone tumors that may involve bone marrow include osteosarcoma, Ewing and primary bone lymphoma. Osteosarcoma is the most common primary bone tumor in young adults. MRI is vital in the preoperative staging of osteosarcoma as it determines the extent of disease in the bone marrow, including skip lesions within an affected bone, adjacent soft tissue, joint or neurovascular involvement, and regions of viable tumor and matrix which can improve biopsy accuracy. Like the majority of replacement diseases, osteosarcoma...
MR Imaging of Bone Marrow – Part II, Kessler et al.

demonstrates nonspecific hypointense to intermediate signal on T1 weighted images and hyperintense signal on T2 weighted images. Regions of hypointense signal on both T1 and T2 weighted images are secondary to mineralized osseous matrix. Additional variability in appearance may be secondary to central hemorrhage or necrosis.48

Sarcoidosis and LCH

Non neoplastic systemic diseases may also affect bone marrow, most notably sarcoidosis and Langerhans cell histiocytosis. Sarcoidosis is an inflammatory disorder characterized by noncaseating granulomas that can be found anywhere throughout the body. Radiographs may be normal or demonstrate lacelike osteolysis and rarely osteosclerotic lesions. It usually involves the small bones and only rarely affects long bones or the axial skeleton. MRI findings may be variable with focal ill-defined or well circumscribed lesions, as well as patchy and confluent infiltration (Fig. 11).49 Langerhans cell histiocytosis (LCH) is a spectrum of disease with idiopathic proliferation of histiocytes and granulation formation that can have focal or systemic manifestations. Focal and diffuse forms most commonly present with osseous lesions. Disseminated disease may demonstrate generalized osteopenia. As with other marrow replacement disease, LCH demonstrates nonspecific signal abnormality, hypointense signal on T1 and hyperintense signal on T2-weighted images. Even though historically LCH has been diagnosed and followed with conventional radiography or scintigraphy, MRI may helpful in demonstrating bone marrow abnormality earlier in the disease process.50

Marrow Ischemia

Bone marrow ischemia can occur from microvascular occlusion or from increased intraosseous pressure. Other causes of osteonecrosis include chemotherapy, steroids, or recurrent malignancy which can involve marrow focally or diffusely. When bone marrow becomes ischemic, the hematopoietic cells are affected first, undergoing cell death often within the first 6-12 hours.51 The osteoclasts, osteocytes, and osteoblasts may survive up to 48 hours after the insult, and the fat cells may survive for 2-5 days.1,50 Subsequent to the insult and cell death, the tissue undergoes an inflammatory and reparative response characterized histologically by inflammatory cells, increased vascularity, fibroblastic tissue, and granulation tissue.1,51

MR imaging findings reflect these histologic alterations. Increased T2 signal intensity and decreased T1 signal intensity are present in acutely ischemic areas with associated edema (Figs. 12 and 13). A “double line sign” on MRI is a curvilinear region of low signal intensity on T2 weighted images in the region of necrotic bone, with an adjacent high signal intensity band which correlates with the tissue’s inflammatory and reparative response. Secondary fracture of the subchondral bone cortex demonstrates articular incongruity, a marrow edema pattern, and low signal intensity curvilinear regions correlating with trabecular fracture. MRI has been shown to be exquisitely sensitive for bone marrow ischemia, approaching 100%.1

Figure 11. Patient with known sarcoid. Whole body bone scan (A) reveals multifocal regions of increased osseous uptake. Focal uptake is seen within the right posterior calcaneus (B). Coronal T1 (C) and STIR (D) images demonstrate focal decreased and increased signal intensity within the posterior calcaneus, respectively.
Summary

MR imaging is useful in evaluating the bone marrow, with high sensitivity in diagnosing marrow disease. The T1 relaxation times within the marrow reflect the tissue types within the imaging voxels, particularly marrow fat, and are also affected by the relative amount of extracellular fluid present in the tissue. We have reviewed the MR imaging characteristics of a number of disease processes that affect the marrow, including marrow edema, proliferative disorders, infection, marrow replacement by tumor, and ischemia. When findings are equivocal, attention to the location and pattern of bone marrow signal abnormality, along with the clinical history, can serve to differentiate several etiologies that secondarily affect bone marrow. Future research may be useful to delineate MRI findings among these diseases with greater specificity.

The views expressed in this material are those of the author, and do not reflect the official policy or position of the U.S. Government, the Department of Defense, or the Department of the Air Force.

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Intramuscular Edema and Enhancement

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Case Presentation
A 21-year-old male presented with a 2 week history of increased proximal left leg swelling. He had a history of recent cervical spinal cord injury with tetraplegia, but no prior medical conditions. Erythrocyte sedimentation rate (ESR) was mildly elevated and he reported no fevers. White blood cell (WBC) count was normal. Lower extremity ultrasound was negative for DVT and initial radiographs showed only soft tissue swelling. MRI was performed (Fig. 1) and repeated 2 months later (Fig. 2).

Figure 1: Coronal T2-weighted STIR image of the pelvis and proximal thighs demonstrates left thigh swelling with diffuse high T2 signal and enlargement of the gluteus, iliopsoas, and quadriceps muscles. There is a small left hip joint effusion. A lesser amount of high T2 signal is present in the right gluteus and quadriceps muscles.

Figure 2: Follow-up axial T2-weighted STIR image (A) 2 months later demonstrates mild increased T2 signal in the left iliac bone with adjacent gluteus and iliacus muscle high signal. There is also high signal of the right gluteus and paraspinal muscles. A small amount of linear and lobular low T2 signal is present in the left iliacus muscle. Post contrast axial T1 image with fat suppression (B) more inferiorly demonstrates rim-enhancing areas anterior to the left hip displacing the left rectus femoris laterally and superficial to the right greater trochanter. Coronal T2 STIR image from the same exam shows left iliac bone and extensive muscular increased signal with laminar and lobular low T2 signal in the iliac fossa and anteromedial to the femur new from the prior exam.
Key clinical finding(s)
- Unilateral proximal leg swelling
- Paralysis with tetraplegia

Key imaging finding(s)
- Abnormal intramuscular signal and enhancement

Differential diagnoses
- Heterotopic ossification
- Pyogenic myositis
- Sarcoma

Discussion
The primary diagnostic considerations for intramuscular edema and enhancement include post-traumatic, infectious/inflammatory, and neoplastic etiologies. As the imaging appearance of these entities often overlap, clinical history and patient demographics are useful discriminators. In the setting of trauma, intramuscular edema and enhancement may be seen initially but should decrease or resolve over time, unless complicated by etiologies such as heterotopic ossification. Patients with myositis often present clinically with pain, fever, and elevated ESR and WBC. Localized erythema, skin ulcerations, or a sinus tract may occasionally be seen. Neoplastic processes typically present insidiously with chronic symptoms, unless complicated by pathologic fracture. In cases where imaging appearance and clinical history are not characteristic of a specific diagnosis, follow-up imaging or biopsy may be necessary.

Heterotopic Ossification: Heterotopic ossification (HO) is the formation of bone in soft tissue and is attributed to mesenchymal metaplasia. A history of local trauma is elicited in 60% of cases. Other risk factors include immobilization, paralysis, and burn injury. HO develops in >20% of spinal cord injury patients, most commonly around the hips, and is frequently bilateral. Patients may have fevers and an elevated ESR. Radiographs and CT are extremely helpful in demonstrating a zonal pattern of calcification with maturing bone over time. The soft tissue calcifications are initially observed between 4 weeks and 6 months after antecedent trauma, but may develop over many years. The MRI appearance of HO is non-specific and can be confused with inflammatory or infectious myositis and sarcoma. MRI will show extensive muscle edema becoming more mass like and decreasing in T2 signal over time. In those with spinal cord injury, there is a distinct predilection for occurrence anterior to the hip joint capsule and superficial to the greater trochanter with involvement of the iliopsoas and trochanteric bursae. Enhancement is diffuse or rim-like. Fluid-fluid levels, narrow edema, periostitis and reactive joint effusions have been described. Calcification will appear as areas of low T1 and T2 signal with fibrosis also contributing to low signal areas. In mature HO, the MRI appearance is the same as that of cortical bone with central fatty marrow.

Pyogenic Myositis: Initially described as a tropical disease, bacterial myositis with abscess is increasingly seen in HIV/immunocompromised patients. Diabetes, local trauma, and insect bites are also reported risk factors. Intramuscular involvement is often due to hematogenous spread from a distant infection; however, direct spread, as is seen with disc-osteomyelitis, is not uncommon. Patients often present with fever, erythema, elevated ESR, and elevated WBC. Localized erythema is commonly seen. Staphylococcus aureus is the cause in >75% of cases. MRI demonstrates muscle enlargement and diffuse increased T2 signal which may involve one or more muscles. Enhancement pattern is typically diffuse initially with rim-enhancement occurring in the setting of abscess formation. The quadriceps, gluteus, and iliopsoas are most commonly involved. Myonecrosis without infection can be seen with diabetes, sickle cell disease, and compartment syndrome.

Sarcoma: Ewing’s sarcoma is the second most common primary malignant bone tumor under age 30. Patients often present with fever and elevated ESR, in addition to pain and a mass. The pelvis is the second most common site of occurrence after the femur. There is a trend from (meta)diaphyseal long bone involvement to increasing flat bone involvement with increasing age. Lytic bone destruction is permeative often with a sclerotic component of reactive bone. Periosteal reaction is
spiculated or laminated/onion-skinned. A large soft tissue mass is frequently present with extensive increased T2 signal infiltrating the bone and adjacent muscle. Enhancement is avid and heterogeneous. When abundant, periosteal reaction will appear as laminar or spiculated low T2 signal locally. Differentiation from osteomyelitis is often difficult. Pretreatment soft tissue calcification is present in <10% of cases and is not extensive.5

Diagnosis
Heterotopic ossification (HO)

Summary
Primary diagnostic considerations for intramuscular edema and enhancement include post-traumatic, infectious/inflammatory, and neoplastic etiologies. As the imaging appearance of these entities overlap, clinical history is helpful. This case demonstrates characteristic as well as less common MRI findings of heterotopic ossification with expected evolution over time. Eliciting a history of trauma with spinal cord injury, in combination with the imaging findings, was useful in making the correct diagnosis in this case. At times, a specific diagnosis cannot be made initially, warranting follow-up imaging or biopsy as necessary.

References
Hemihypertrophy

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Case Presentation
A 54-year-old woman with a port wine stain since childhood presented with hypertrophy of the left lower extremity. She has been wearing compression stockings for painful swelling of the left lower extremity since childhood. In addition, she walks with a limp secondary to the left side of her pelvis "riding higher" than the right.

Figure: Axial fat suppressed T2 (A) and T1 (B) weighted images of the lower extremities demonstrate asymmetric enlargement of the left calf with lipomatous hypertrophy and prominent vasculature compared with the right.
Key clinical finding(s)
Cutaneous vascular nevus
Unilateral lower extremity hypertrophy

Key imaging finding(s)
Unilateral extremity lipomatous hypertrophy and vascular ectasia

Differential diagnoses
Klippel-Trénaunay Syndrome
Parke-Weber Syndrome
Neurofibromatosis
Maffucci Syndrome
Macrodystrophia lipomatosa
Proteus Syndrome

Discussion
Gigantism (focal or diffuse), macromelia, macrodactyly, and hemihypertrophy are all terms referring to enlargement of all or a part of the body. Specifically, hemihypertrophy is asymmetric enlargement or overgrowth of one side of the body with hypertrophy of the muscles, blood vessels, nerves, and bones. Enlargement of one portion of the body can be seen in a number of congenital and developmental conditions for which clinical history and physical exam will aid in the differential diagnosis.

Klippel-Trénaunay Syndrome:
First described in 1900, Klippel-Trénaunay Syndrome consists of three physical findings: cutaneous vascular nevus (capillary malformation), soft tissue or bony hypertrophy of the extremity, and varicose veins or venous malformations. A diagnosis of Klippel-Trénaunay requires two of the three findings. This rare anomaly only occurs in 1 of 20,000 to 40,000 live births. The cause of the disease is poorly understood.

Clinically, patients with Klippel-Trénaunay Syndrome have vascular abnormalities such as superficial pigmented hemangiomas (port-wine nevus or nevus flammeus), varicose veins, lymphangiomas, and a deficient deep venous system. Limb deformity is usually monomelic with local gigantism developing early in childhood and involving all or a portion of a limb. Asymmetry is variable and may be due to either soft-tissue (muscular or lipomatous) or osseous overgrowth. The vast majority of cases involve the lower limbs. On MRI, soft-tissue asymmetry can be appreciated with bilateral imaging of the extremities.

Venous anomalies have classically been imaged with CT venography and more recently with MRI. Abnormalities of the venous system range from simple ectasia of the superficial and deep system, including varicosities, to persistent fetal veins and large venous malformations. The presence of a sciatic vein has been well documented as a common finding in Klippel-Trénaunay Syndrome.

Parke-Weber Syndrome:
In 1907, Parke-Weber described a number of cases that involved the classic findings of Klippel-Trénaunay Syndrome with one important addition - arteriovenous fistulas. Over the years, many authors have simply combined these two syndromes into Klippel-Trénaunay-Weber Syndrome; however, the distinction between the two groups can be determined through arteriography.

Neurofibromatosis:
Neurofibromatosis type 1 (NF1) is the most common neurocutaneous disease. Also, known as von Recklinghausen disease, NF1 is characterized by neurofibromas, café au lait spots, gliomas, and skeletal dysplasia. Overgrowth of bone and soft tissue can result in elephantoid soft tissue hypertrophy of a part of or a whole extremity. Physical exam and clinical history are strong discriminators.

Maffucci Syndrome:
Maffucci Syndrome is a condition within the spectrum of multiple enchondromatosis characterized by enchondromatosis and soft tissue hemangiomias. The disease affects tubular bones, most commonly in the hands. Asymmetric nodular enlargement of the affected limb results in local gigantism. Radiographic examination will show pathognomonic phleboliths from the vascular lesions and multiple bony lytic lesions with a chondroid matrix, typical of enchondromas. The presence of enchondromas is a discerning feature.
Beckwith Weidemann Syndrome:
Beckwith Wiedemann Syndrome is an autosomal dominant disorder characterized by local gigantism, macrosomia, and hemihypertrophy. Associated anomalies include macroglossia, otic dysplasia, omphalocoele, cardiac anomalies, and organomegaly (kidney, liver, and spleen). There is a high risk for the development of neoplasia, including Wilms tumor, adrenocortical carcinoma, neuroblastoma, and hepatoblastoma, among others.

Macrodystrophia Lipomatosa:
Macrodystrophia lipomatosa is a developmental anomaly predominantly affecting fingers and toes characterized by overgrowth of all the tissues of mesenchymal origin, predominantly involving fibroadipose tissue. Its cause is unknown. Unilateral involvement is typical with overgrowth more pronounced distally. There is no gender predilection and the deformity can be seen at birth or early infancy, progressing until puberty. Other deformities such as syndactyly, clinodactyly and polydactyly can be associated with macrodystrophia lipomatosa.

Proteus Syndrome:
In 1960, Proteus syndrome was described, consisting of partial gigantism of the hands and/or feet, hemihypertrophy, pigmented nevi, subcutaneous ‘tumors,’ skull anomalies, accelerated growth, and visceral abnormalities. A hallmark of this syndrome is its mosaic pattern of involvement. Diagnostic criteria and guidelines include skeletal surveys; MRI evaluation of the abdomen, pelvis, and central nervous system; and CT evaluation of the chest. Recently, researchers determined that a variant of the AKT1 (protein encoding gene) is the cause of the Proteus syndrome.

Summary
Hemihypertrophy or unilateral asymmetric gigantism is a rare condition, which may arise from a variety of congenital and developmental conditions. Aside from known syndromes, the initial presenting symptom is often a limb length discrepancy. Clinical assessment, associated anomalies, and imaging findings help differentiate these rare conditions from one another. As seen with this case, MRI findings of venous abnormalities and limb hypertrophy are characteristic and readily evident in the setting of Klippel-Trénaunay Syndrome.

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References
Painful Forearm Mass

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Case Presentation
A 40-year-old woman presented with a painful mass on her forearm. She denied injury to the area or prior surgery at the site. She reported no additional lesions and stated that the mass arose over the past few weeks and has become painful to the touch. Physical examination revealed a non-compressible non-mobile nodular mass. There was no overlying skin discoloration or ulceration. Radiographs, ultrasound and MR images of the lesion were obtained. MR images are displayed (Fig.)

Figure: Axial T1 pre (A), T1 post with fat suppression (B), and T2 Fat-suppressed (C) images demonstrate an avidly enhancing mass at the superficial margin of the forearm musculature. Sagittal T1 post-contrast fat-suppressed image (D) demonstrates an enhancing fascial tail at the margin of the lesion.
Key clinical finding(s)
Painful non-mobile forearm mass
Rapid onset of symptoms

Key imaging finding(s)
Nodular enhancing mass on the surface of the forearm extensor musculature

Differential diagnoses
Nodular fasciitis
Malignant fibrous histiocytoma (or other sarcoma)
Fibromatosis

Discussion
A soft tissue mass is a relatively frequent presenting symptom with etiologies that range from the benign to the aggressive. Evaluation begins with a clinical history and physical examination, followed by imaging when the etiology is not readily apparent. Certain lesions such as lipomas have characteristic imaging features based upon which confident classification can be made by MRI. However, most lesions are not easily distinguished from one another and biopsy is necessary to exclude malignancy. The clinical features such as pain or redness, as well as patient demographics may narrow the differential diagnosis.

Nodular Fasciitis: Nodular fasciitis is a benign soft tissue lesion that is primarily inflammatory in nature and is likely the most common tumor-like lesion misdiagnosed as a sarcoma. Histological examination reveals evidence of rapid growth and increased mitotic activity. The upper extremity is the most common site of involvement, along with the head and neck in younger patients. The presentation of a painful forearm mass in a relatively young patient makes nodular fasciitis a leading consideration in this case.

Radiographs are typically noncontributory (as in this case) and additional imaging is necessary for characterization. Ultrasound is also nonspecific with the common appearance being that of a hypoechoic mass. Hyperemia may also be encountered as evidence of inflammation (obtained in the workup of this mass but not shown). MRI typically demonstrates a nodular mass that is isointense to muscle on T1-weighted images and hyperintense on T2-weighted images. Avid or peripheral enhancement is common. The presence of a linear fascial tail may be an important distinguishing feature in identifying the lesion and is well demonstrated in this case. Biopsy or excision is necessary to exclude a malignant lesion and lesions rarely recur. Recurrence should prompt a reevaluation of the lesion to confirm the diagnosis. Unlike radical excision approaches that are appropriate for sarcomas, a wide margin is not necessary and adjacent structures such as nerves may be spared.

Malignant Fibrous Histiocytoma: Malignant fibrous histiocytoma (MFH) is described as a pleomorphic sarcoma with multiple subtypes described by the World Health Organization (WHO) nomenclature. MFH is the most common soft tissue sarcoma of advanced age, though lesions have been described in younger patients as well. An important fact to consider is that the majority are deep lesions with only 5-10% being described in the subcutaneous tissue. Whenever an aggressive-appearing soft tissue mass is encountered, the diagnosis of MFH must be considered. Imaging features are nonspecific with variable appearances described on all MRI imaging sequences. The presence of a spontaneous hematoma may further confuse the imaging workup and in such cases it is critical to identify any solid nodular enhancing components of the tumor.

Fibromatosis: Fibromatoses arise from fascia or aponeuroses and are typically slow growing nodular lesions. Several common sites of involvement are well described in the literature and include the plantar and palmar regions of the extremities. Both superficial and deep types have been described. Fibromatoses demonstrate intermediate to low signal intensity on all MR imaging sequences. Chronic lesions demonstrate more collagen content and this characteristic likely accounts for the low signal intensity on MR imaging sequences. Regions of the lesion that are more cellular demonstrate relatively increased signal intensity on fluid sensitive sequences and are sites of probable recurrence after attempted resection. Surgical resection is the
primary treatment; however, recurrence is common. Following lesions closely with MRI before resection may demonstrate maturation of the fibromatosis (as evidenced by more collagenous regions with low signal intensity on MRI) and thus help to direct surgical intervention when the lesion is less cellular and less likely to recur.  

**Diagnosis**

Nodular Fasciitis

**Summary**

Soft tissue masses are relatively common with a confident diagnosis possible in cases of lipoma and in a few select other lesions. Frequently however, benign and malignant lesions overlap in terms of presentation and imaging appearance. In such cases, biopsy and/or excision are necessary to exclude the presence of an aggressive lesion or malignant tumor. Knowledge of the more commonly encountered lesions is necessary to help guide treatment. In this case, the rapid onset of a painful nodule suggests a reactive or inflammatory lesion rather than a typically slow-growing fibromatosis or malignant fibrous histiocytoma. The age of the patient and location are also important clues to the ultimate diagnosis. Finally, the fascial tail demonstrated in this case helps to narrow the differential diagnosis as well. Excision confirmed the diagnosis and no further treatment was required.

**References**

Exophytic Osseous Growth

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Case Presentation:
A 31-year-old male presented to the emergency room with a one-day history of right hand pain after relatively minor trauma. The pain was exacerbated with movement. After further questioning, the patient reported an insidious onset of increase in size of the fifth digit, along with decreased range of motion. Physical examination revealed visible enlargement of the right fifth digit without erythema or hematoma. Conventional radiographic evaluation was performed in the emergency department.

Figure: Frontal radiograph of the right hand demonstrates a broad-based exophytic ossific mass extending dorsally and medially from the mid to distal cortex of the fifth proximal phalanx. The lesion measured 2.5 x 1.0 cm and demonstrated well-demarcated margins, mature trabeculated matrix, and lacked periostitis. There was no contiguity with the underlying marrow. No additional lesions were visualized.
**Key clinical findings(s)**
Right hand small finger enlargement

**Key imaging finding(s)**
Calcified/osseous exophytic mass

**Differential diagnoses**
Bizarre parosteal osteochondromatous proliferation (BPOP)
Osteochondroma
Parosteal osteosarcoma
Florid reactive periostitis

**Discussion**
Osseous exostosis is a relatively common radiologic finding seen in many different pathologies. Evaluation begins clinically with special attention given to the time course of symptoms. Radiologic examination becomes critical to distinguish between the many underlying causes. A key radiologic discriminating factor when evaluating exostosis is the presence or absence of disrupted osseous cortex; followed by structural changes involving the underlying medullary cavity. These diagnostic findings are essential in arriving at the appropriate diagnosis.

**Bizarre parosteal osteochondromatous proliferation (BPOP):**
BPOP (otherwise known as Nora’s lesion) is a rare, benign, exostotic osteochondromatous tumor of the hands and feet which pathologically is seen as part of a spectrum of reactive lesions.1 The cause is unknown, but is thought to be related to trauma. Nora’s lesion usually presents as a minimally painful pedunculated or sessile mass which grows slowly over months or years.2 Its size typically ranges from 0.4 to 3 cm in diameter.3 It most commonly affects patients in their thirties or forties without gender predilection.2 The tumor primarily affects bones of the hands and feet but can also be found in the mandible and long bones.4 Lesions originate from the periosteum of an intact underlying cortex.1 Pain is an infrequent symptom, and in rare instances, erythema or discoloration is seen in the overlying skin. Joint motions may be limited, depending on the location of the lesion.5

Conventional radiographs show parosteal calcification or bony masses with a typical mushroom-shape arising from the cortical surface of the underlying bone, usually involving the metaphysis. The lesion may be calcified or ossified with well-defined margins and broad-based attachment to the underlying bone without cortical disruption. There may be decreased mineralization of the cortex of the host bone, but no periosteal new bone formation. Cortical flaring at the junction with the lesion is not a feature of BPOP. The absence of continuity between the lesion and medullary cavity of the bone is a key radiographic finding that differentiates BPOP from osteochondromas. Evolution of the lesion can be seen radiographically with a first stage consisting of periosteal soft tissue swelling or mass, sometimes with tiny calcification; further along in the disease course, calcification becomes more prominent leading to complete ossification of the lesion.

**Osteochondroma:**
Osteochondroma is the most common cartilage containing tumor. Characteristically solitary, metaphyseal, and usually pointing away from the adjacent joint, it is found most commonly around the knee. While osteochondroma is one of the most common benign bone tumors, they are uncommon to arise in the distal extremities, a feature which distinguishes it from BPOP. The majority of cases occur in young patients less than 20 years old. Imaging of osteochondromas is fairly characteristic with normal marrow, cortex, and periosteum extending from parent bone into the exophytic lesion which has a cartilaginous cap. Histologically, osteochondromas do not display cytological atypia and show more regular alignment of chondrocytes, as opposed to the ‘bizarre’ appearance in BPOP. Patients with osteochondromas commonly suffer mechanical complications related to the exostosis. Occasionally, osteochondromas can degenerate into chondrosarcoma.

**Parosteal Osteosarcoma:**
Parosteal osteosarcoma is low grade osteosarcoma, arising along the surface of bone. The majority of
cases are seen between the ages of 20-50 and commonly present with pain and swelling, along with a mass. Parosteal osteosarcoma is most commonly seen along the posterior distal femoral metaphysis, but can involve the tibia and humerus as well. Parosteal osteosarcoma involving the hands and feet is rare. On imaging, parosteal osteosarcoma is observed to arise juxtacortically from the bone. The bulk of the mass extends into the soft tissues with smooth, lobulated margins and a characteristic cleavage plane between the tumor and the underlying bone with a “stuck-on” appearance. Parosteal osteosarcoma can dedifferentiate into a higher grade osteosarcoma.

**Florid reactive periostitis:**
Florid reactive periostitis is an entity that falls within the spectrum of diseases that includes BPOP and myositis ossificans. Like BPOP, there is usually a history of antecedent trauma. Florid reactive periostitis most commonly involves the hands, usually affecting a proximal or middle phalanx. On imaging, early florid reactive periostitis appears as an ossified or calcified soft tissue mass without underlying bony abnormality; later, its relationship with periosteum and cortex becomes more conspicuous. Histologically, islands of bone and hyaline cartilage are separated by a fibrous stroma, and focal osteoclastic remodeling of the bone is evident. Local excision is usually the definitive therapy; recurrence is uncommon.

**Diagnosis**
Bizarre parosteal osteochondromatous proliferation

**Summary**
Osseous exostosis is a relatively common finding which may be seen with a variety of conditions. A combination of clinical and imaging findings aid in narrowing the differential diagnosis and may even lead to a single diagnosis. In this case, the presence of a well-marginated mass arising from an intact underlying cortex was helpful in establishing the diagnosis of BPOP over the more common differentials discussed above. Although a rare entity, BPOP should be considered in the differential diagnosis of an exophytic osseous or chondromatous growth found in the hand.

**References**
1. Dhondt E, Oudenhoven L. Nora’s lesion, a distinct radiological entity? Skeletal Radiol 2006; 35:497-502
Patellar sleeve fracture:
This 11-year-old boy presented with left knee pain and inability to extend his knee following a football injury. Radiographs and subsequent MRI confirm a patellar sleeve fracture. A patellar sleeve fracture is an acute osteochondral injury, usually of the inferior pole. The extent of injury frequently is underestimated. In this boy, there is an avulsed bony fragment (arrows), a separated cartilaginous component (dashed arrow) and a large cartilaginous defect in the patella (star). Patellar sleeve fractures occur usually between 8-12 years of age, and result from a forceful contraction of the quadriceps muscles against resistance. On physical examination, there is lack of active extension and point tenderness over the lower patella. Lateral radiographs can show the bony fragment, soft tissue edema, and a joint effusion. Patella alta or a high-riding patella may be present. Radiographs may underestimate the degree of injury, as the bony fragment can be small or even absent, but the concomitant cartilaginous component can be large. MRI is helpful to depict the extent of cartilaginous injury and displacement, which in turn affects management. Nondisplaced fractures typically are treated conservatively whereas displaced fractures undergo surgical reduction. This child underwent internal fixation, as shown in the final radiograph.
Unicameral Bone Cyst with Fallen Fragment:

This 11-year-old male presented to the Emergency Department with severe pain and inability to use his right arm after falling during a soccer game. The figure shows a lytic lesion in the proximal metaphysis of the humerus in a skeletally immature patient with a narrow zone of transition. There is a “fallen fragment” (arrow) located dependently, which is characteristic of a pathological fracture through a unicameral bone cyst (UBC).

UBCs are benign, non-neoplastic bony lesions, also referred to as simple bone cysts. They occur in the metaphysis of long bones and are most common in the proximal humerus, followed by the proximal femur. The exact etiology of the lesions remains unclear. Lesions are most often detected incidentally on imaging. Occasionally, patients may present with a pathological fracture through the lesion as a result of weakening of the bone. UBCs typically heal when patients reach skeletal maturity. As such, physicians avoid treating these lesions whenever possible. The lesions often spontaneously resolve as a result of subsequent healing after fracture. Surgical treatment is sometimes necessary for larger lesions to prevent development or recurrence of a pathological fracture.

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Scheuermann disease:

Can you guess the cause of chronic back pain in this young adult? The T1 and T2 sagittal MR images demonstrate multiple levels of endplate irregularity (Schmorl nodes), anterior wedging of contiguous vertebral bodies, and focal increased thoracic kyphosis, along with disc desiccation and height loss. This constellation of findings is known as Scheuermann disease, which is a relatively common cause of chronic back pain in adolescents and young adults.

Scheuermann disease results from damage to the cartilaginous endplates in the skeletally immature spine. It is thought to be secondary to congenital weakening or repetitive trauma, which is common in young patients and athletes. The condition typically involves the thoracic spine and thoracolumbar junction. Pain is worsened by activity. The diagnosis of Scheuermann disease requires involvement of 3 contiguous levels. Diagnostic criteria include endplate irregularity or Schmorl nodes and at least 5 degrees of anterior wedging at each level. Secondary findings include limbus vertebrae, disc degeneration, scoliosis, and focal thoracic kyphosis (greater than 40 degrees is considered abnormal).

Treatment is typically conservative with analgesics, activity modification, physical therapy, and occasionally bracing. Surgical intervention is rare but may be necessary in severe cases with greater than 75 degrees of kyphosis, intractable pain, or neurologic deficit.

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