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# Terrance D. Peabody Samer Attar *Editors*

# Orthopaedic Oncology

Primary and Metastatic Tumors of the Skeletal System

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# Orthopaedic Oncology

Primary and Metastatic Tumors of the Skeletal System



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## **Principles of Musculoskeletal Biopsy**

#### Raffi S. Avedian

#### Abstract

The appropriate treatment of any musculoskeletal tumor is based on a correct diagnosis. In some instances, a patient's history and imaging studies provide sufficient information to guide definitive treatment. However, in many cases, a biopsy may be necessary. A biopsy, although technically simple, must be conducted in a thoughtful manner in order to obtain an accurate tissue sample while avoiding complications. Some potential complications include inaccurate sampling, improperly placed incision that complicates future surgeries, and healthy tissue contamination that can add morbidity to the definitive surgery or preclude the chance of limb salvage. This chapter will review the considerations for planning and performing a biopsy of musculoskeletal tumors.

#### Keywords

Biopsy · Sarcoma · Soft tissue tumor · Limb salvage

#### 1 Introduction

The appropriate treatment of any musculoskeletal tumor is based on the knowledge of what the tumor is and its natural history. In some instances, a patient's history and imaging studies provide sufficient information to guide definitive treatment.

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However, in many cases, evaluation of a patient's history, physical exam, and imaging results in a differential diagnosis that requires further elucidation. This is especially true if the leading diagnosis is an aggressive tumor that would require treatment such as chemotherapy, radiation, or ablative surgery. As such, confirming the diagnosis with a biopsy prior to subjecting the patient to therapies with potentially morbid and permanent side effects is mandatory. Similarly, missing a diagnosis of an aggressive or malignant tumor may result in unnecessary morbidity or a lost opportunity for cure.

#### 2 Evaluation Prior to Biopsy

Prior to doing a biopsy, the clinician should perform a thorough history and physical exam and should scrutinize plain radiographs in the case of suspected bone pathology. In certain situations, the information obtained with this will be sufficient to yield a diagnosis or at least limit the differential to a benign etiology that may not need tissue sampling. This is often the case with incidentally noted bone tumors that are discovered when performing the workup for an unrelated problem (Fig. 1). When evaluating a soft-tissue mass, important aspects of the history include the duration of the mass, the rate of growth of the mass, and the presence of pain or any inciting events such as trauma. Findings that would be reassuring for a benign etiology include a several year history of a small mass without any growth. Also, tumors that are painful tend to be benign such as nerve sheath tumors or vascular malformations. Although there are no validated size criteria to indicate malignancy, most surgeons consider large masses or those greater than or equal to 3 cm to be concerning enough for malignancy to warrant further evaluation. The best radiological study for the evaluation of a soft tissue mass is an MRI with an intravenous contrast agent such as gadolinium [1]. Plain radiographs may be useful to rule out a bone tumor mimicking a soft tissue mass such as a prominent exostosis or to reveal phleboliths within a hemangioma.

#### **3 Biopsy Principles**

There are several biopsy techniques for sampling bone and soft tissue tumors. An important principle common to all techniques is that definitive treatment relies on a biopsy that is accurate and does not cause harm to a patient due to technical mistakes [2, 3]. Specifically, a poorly planned and executed biopsy may result in contamination of surrounding healthy tissue which may increase the risk of local recurrence and preclude the option of a limb-sparing surgery. The biopsy site will be contaminated with cancer cells and must be incorporated into and removed during the definitive cancer surgery. Therefore, thought must be given to where the surgical incision will be made. The biopsy ideally will be planned along this incision line (Fig. 2). In almost all cases, longitudinal incisions should be used as they can more easily be incorporated into the final surgery. Neurovascular bundles



**Fig. 1** Mortise oblique ankle radiograph of a 16 year old male who twisted his ankle while playing basketball and presented with anterior joint line pain. Physical exam was notable for tenderness over the anterolateral ankle but not over the lesion seen in the radiograph. Based on his history of an acute injury, exam findings suggesting an ankle sprain, and radiographs demonstrating a well-marginated lesion with a sclerotic border, a diagnosis of an ankle sprain with incidentally noted asymptomatic non-ossifying fibroma proximal to the ankle was made. A biopsy was not needed and follow-up radiographs ensured stability of the lesion



**Fig. 2** Intraoperative photograph showing the surgical resection of a distal femur osteosarcoma in a 15 year old girl. Notice how the biopsy site is in line with the main incision and is being incorporated into the tumor resection. A paddle of skin and subcutaneous tissue is kept on the biopsy site as a margin of safety to ensure all potentially contaminated tissue is removed. The smaller the biopsy the easier it is to remove

Fig. 3 A 70 year old woman underwent resection of a posterior thigh mass without prior imaging. The final diagnosis was a high grade pleomorphic sarcoma. The drain was placed 6 cm lateral to the surgical incision. A local recurrence occurred along the drain path as can be seen in this T1 fatsuppressed, contrastenhanced magnetic resonance image showing a mass between the surgical incision (arrow) and drain exit site (arrowhead)



**Fig. 4** Intraoperative photograph demonstrating the relationship of the principle incision (*arrow*), the drain site (*arrowhead*) and the local recurrence (*asterisk*) illustrating how an improperly placed drain site can lead to local recurrence



should not be dissected or manipulated, otherwise they may become contaminated and have to be resected later. The biopsy should be within a single muscle compartment rather than an intermuscular plane where multiple compartments are at risk for contamination. Skin and subcutaneous flaps should be kept to a minimum. Meticulous hemostasis should be obtained prior to closure to avoid hematomas or bleeding that can carry tumor cells to adjacent healthy tissues. If a drain is used it should exit in line and near the incision so the drain track and exit site can be resected easily during the definitive procedure (Figs. 3 and 4).

#### 4 Biopsy Techniques

Incisional biopsy (IB) has long been regarded as the gold standard for diagnosing musculoskeletal tumors. However, percutaneous procedures such as core needle biopsy (CNB) and fine needle aspiration (FNA) are cost-effective and reasonably accurate alternatives that have largely replaced open biopsy as the technique of choice for diagnosing soft tissue tumors in many orthopaedic oncology practices [4, 5]. The specific techniques for musculoskeletal biopsy include: FNA, CNB, IB and excisional biopsy.

The goal of an FNA is to obtain a sufficient quantity of cells to perform cytological analysis. The technique is relatively easy to perform but does not allow for evaluation of a tumor's histological characteristics such as architecture and matrix production [6].

A CNB is performed using a large diameter needle that is designed to capture a large enough piece of tissue that can be used for histological evaluation and ancillary studies such as cytogenetics [5].

Unlike FNA and CNB which are performed in the office, IB and excisional biopsy are surgical procedures that require anesthesia. An IB is performed by making a relatively small incision directly over the tumor and removing a sample of tissue. An excisional biopsy on the other hand is removal of the entire tumor by dissecting around its perimeter. The goal is to keep the tumor contained within its capsule and avoid spillage but no margin of healthy tissue is removed [7].

In a retrospective study comparing IB with CNB, Heslin et al. reported on accuracy results for 164 patients who presented to their institution with a soft tissue tumor. Sixty patients underwent CNB which had an accuracy of 95, 88 and 75 % for diagnosing malignancy, correct grade, and correct histology respectively. There was no statistical difference compared to forty-four patients who underwent IB which had an accuracy of 100, 95 and 88 % for the same variables. The authors did emphasize the significance of good technique and experience of the pathologist as important influences on the accuracy of any biopsy [8].

Yang and Damron conducted a prospective study of fifty patients comparing the accuracy of FNA with CNB. Each patient underwent a CNB that was immediately followed by a FNA. FNA achieved a diagnostic accuracy rate of 88 % for nature of lesion, 64 % for specific diagnosis, 78 % for histologic grading, and 74 % for histologic typing. CNB achieved an accuracy rate of 93 % for nature of lesions, 83 % for specific diagnosis, 83 % for histologic grading, and 90 % for histologic typing. Both biopsy methods had a higher diagnostic accuracy rate for high-grade tumors than for low-grade or benign lesions in determining the nature, specific diagnosis, and histologic grading [9].

More recently, Pohlig et al. reviewed 77 patients who had undergone either core needle or IB for a suspected bone or soft tissue malignancy [10]. Sensitivity, specificity, PPV, NPV and diagnostic accuracy were 100 % for CNB in bone tumors. Sensitivity (95.5 %), NPV (91.7 %) and diagnostic accuracy (93.3 %) for open biopsy in bone tumors showed slightly inferior results without statistical significance (p > 0.05). In soft tissue tumors, favorable results were obtained in open biopsies compared to CNB with differences regarding sensitivity (100 vs. 81.8 %, p = 0.5), NPV (100 vs. 50 %, p = 0.09) and diagnostic accuracy (100 vs. 84.6 %, p = 0.19) without statistical significance. The overall diagnostic accuracy was 92.9 % for CNB and 98.0 % for open biopsy (p = 0.55). A specific diagnosis could be obtained in 84.2 and 93.9 %, respectively (p = 0.34).

Khoja et al. compared 103 core needle biopsies with 107 incisional biopsies to determine if grade established by one technique was more accurate in predicting metastasis and disease free survival [11]. They discovered that grade predicted by CNB was not predictive of metastasis or survival, but grade determined by IB was in fact predictive of both metastasis and disease free survival. The authors concluded that CNB is a convenient tool for making a diagnosis of a soft tissue tumor. However, IB is recommended if grade is to be used to guide treatment or counseling regarding prognosis.

In summary FNA, CNB and IB are acceptable techniques for performing a biopsy of a musculoskeletal tumor. Percutaneous biopsies such as FNA and CNB obviate the potential delays due to coordinating operating room, anesthesia, and surgeon availability, are technically easy to do, and are relatively low cost. However, they do not provide as much tissue as an IB and therefore may not be as accurate [4]. An important variable that is hard to quantify in the literature is the orthopaedic oncologist's technical and cognitive skill for choosing and performing a biopsy correctly and the pathologist's experience and skill at interpreting musculoskeletal neoplasms. Ultimately, it is the treating physician's responsibility to use appropriate judgment in combining the clinical, radiological, and pathological information to determine the most appropriate care for the patient.

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# Imaging Evaluation of Musculoskeletal Tumors

#### Nicholas Morley and Imran Omar

#### Abstract

In this chapter, we review different imaging modalities, including radiography, computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, and nuclear medicine scintigraphy, and their application to musculoskeletal neoplasm. Advantages and limitations of each modality are reviewed, and suggestions for imaging approach are provided.

#### Keywords

 $\begin{array}{l} \mbox{Radiology} \bullet \mbox{Medical Imaging} \bullet \mbox{X-ray} \bullet \mbox{Radiography} \bullet \mbox{Computed Tomography} \\ \mbox{(CT)} \bullet \mbox{Magnetic Resonance Imaging} \ \mbox{(MRI)} \bullet \mbox{Ultrasound} \bullet \mbox{Nuclear Medicine} \end{array}$ 

#### 1 Introduction

Imaging evaluation of musculoskeletal tumors often involves a combination of modalities, with each modality serving a specific function in workup. Initial evaluation is typically performed with plain radiography, followed by a more advanced imaging modality, such as computed tomography (CT), magnetic resonance imaging (MRI), nuclear medicine scintigraphy, or ultrasound. Advantages and limitations of each modality are reviewed in this chapter, along with suggestions for imaging approach.

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#### 2 Plain Radiography

Plain radiographs form the basis for initial imaging of suspected bone tumors. Radiography provides excellent resolution, allows for assessment of lesion characteristics, and is often more specific than MRI in generating a reasonable differential diagnosis. Radiography has been the optimal modality in distinguishing nonaggressive from aggressive osseous disease [1, 2]. It should be noted that imaging studies are often able to assess how aggressive a lesion is, but the determination of whether a lesion is benign or malignant is based on pathology. Benign lesions, such as osteomyelitis, may look quite aggressive. If a lesion is pathognomonic for a specific entity, a diagnosis can be made from radiographs alone. In many situations, however, a differential diagnosis is created, and further workup is performed by a combination of advanced imaging modalities [3, 4], and if necessary, tissue sampling. In cases where tissue sampling is necessary, percutaneous biopsy using imaging guidance has been shown to be safe and effective [5]. Soft tissue differentiation is limited at radiography, and evaluation of soft tissue masses primarily involves the identification of fatty or calcified components.

Radiographic evaluation is based on the classification system described by Lodwick, which classifies lesions based on four main groups of characteristics, including destruction of bone, proliferation of bone, mineralization of tumor matrix, and location, size and shape of the tumor [6].

Patterns of bone destruction include geographic, moth-eaten, or permeative. Geographic bone destruction involves loss of bone extending to the transition between tumor and structural bone. A thin sclerotic margin (type IA) is characteristically only seen with geographic lesions, although a geographic lesion can also have a clear nonsclerotic margin (type IB, the so-called "punched out" lesion), or a poorly defined margin, typical of local infiltration (type IC). Moth-eaten bone destruction (type II) is the creation of several smaller confluent holes within the bone. Permeative bone destruction (type III) involves many punctate holes with an ill-defined transition between the involved and uninvolved bone. Moth-eaten and permeative patterns are associated with more aggressive lesions. However, some malignant lesions such as fibrosarcoma and chondrosarcoma can arise within a benign lesion, and as such radiologic-pathologic apparent discordance can arise with an aggressive histology in a benign appearing radiographic lesion [7]. Of note, the fastest margin of tumor growth would be a radiographically invisible permeative lesion, as this involves the widest of margins.

In order for a radiolucent lesion to be appreciable at radiography, there must be destruction of either cortical or cancellous bone. Since the diaphysis of long bones is comprised of primarily cortical bone that envelops a thin internal margin of cancellous bone and the marrow in the central medullary cavity, lesions arising in the medullary space may not be visible at radiography. The term "endosteal scalloping" refers to a tumor that originates in the medullary canal, and as it grows, displaces, or replaces the internal cortical margin rather than the outer surfaces of the bone. This tends to have rounded margins, hence the scalloped appearance.

Endosteal scalloping is not by itself an aggressive finding and can be seen with benign lesions, but does suggest adjacent marrow replacement.

Proliferation of bone includes both encapsulated and unencapsulated patterns, with unencapsulated growth being more aggressive. This feature is particularly characterized by different patterns of periosteal reaction. Broadly speaking, periosteal reaction can be classified as continuous, interrupted, or complex, depending on its morphology. Continuous forms include both nonaggressive and aggressive morphologies, with the terms *smooth* and *continuous* representing examples of nonaggressive periosteal reaction. Interrupted or "*onion-skin*" representing examples of an aggressive reaction. Interrupted patterns include the Codman's angle or triangle, which is a focal periosteal elevation, and interrupted spiculated patterns. Complex patterns include a mix of various types [8].

Tumor matrix is reflective of the type of calcification or ossification, if any, that is present within the lesion. Osteoid matrix is often described as solid, cloud-like, or ivory-like, and when in an aggressive lesion can be associated with osteosarcoma. Chondroid matrix is classically described as stippled, flocculent, or "ring and arc" configuration, and when aggressive can be seen in the setting of chondrosarcoma [9]. Fibrous matrix, as seen in fibrous dysplasia, demonstrates a "ground glass" radiographic density as a result of small, abnormally arranged trabeculae of immature woven bone [10]. Many lesions of varying cell types do not show any type of internal matrix, and this is also the case with highly dedifferentiated osteoid or chondroid malignancies.

Location, size, and shape also play a role in the evaluation of a bone tumor. Generally speaking, malignancies tend to be larger and more spherical. Differential diagnosis is aided also by location, as some tumors originate in the diaphyseal, metaphyseal, or epiphyseal location. Age of the patient also aids in formation of a differential diagnosis, as different tumors tend to favor different age groups.

Once the lesion has been assessed radiographically, if there are aggressive features, further imaging evaluation is warranted. This is particularly true in the setting of cortical destruction or suspected extension into the adjacent soft tissues. The degree of soft tissue involvement is more accurately characterized by contrast enhanced CT or MRI [11], which allow better discrimination of the extent of disease. This is often not possible at plain radiography, as both tumor and adjacent normal soft tissues are of the same density and attenuate the X-ray to the same degree (Figs. 1, 2, 3, 4, 5 and 6).

#### 3 Computed Tomography

Computed tomography utilizes X-rays and complex computer algorithms to generate tomographic axial images, which can be reformatted in coronal and sagittal planes to aid interpretation. CT has many advantages over radiography, including allowing lesion characterization in complex regions of osseous overlap, such as the spine or pelvis, allowing determination of extent of soft tissue involvement, and in

**Fig. 1** Unicameral bone cyst. 18 year old man with a Lodwick type IA lesion, with a nonaggressive appearance. This does not require further evaluation



**Fig. 2** Nonossifying fibroma. Another lesion typifying a type IA lesion in this 21 year old man, with a nonaggressive appearance





**Fig. 3** a Dedifferentiated chondrosarcoma. 58 year old man with an aggressive lesion demonstrating ill-defined, permeative type III margins. Because of its dedifferentiation, no chondroid matrix is appreciable. There is a pathologic fracture of the lesser trochanter, a typical location for an underlying lesion. **b** Corresponding coronal T1-weighted MRI demonstrates replacement of the marrow by tumor

**Fig. 4** Osteosarcoma, high grade. This aggressive lesion in this 30 year old woman demonstrates aggressive interrupted lamellated periosteal reaction, with permeative margins and soft tissue extension



some cases, degree of intramedullary involvement. The relatively quick speed with which CT can be acquired is also of benefit in patients who are claustrophobic or unable to hold still, as motion artifact degrades all imaging. Limitations or drawbacks of CT include its inability in many cases to provide a specific histologic



**Fig. 5** Osteosarcoma. This aggressive lesion demonstrates periosteal reaction with a Codman's triangle of focal periosteal elevation in this 23 year old man. There is typical "cloud-like" osteoid matrix



**Fig. 6** a Multiple myeloma. 52 year old man with an ill defined right anterior iliac wing lesion, with a wide zone of transition. **b** MRI demonstrates better the extent of the lesion, showing that there is no adjacent soft tissue extension. This was subsequently biopsied and shown to be multiple myeloma

diagnosis of soft tissue tumors, and its associated radiation dose, which is particularly relevant for children and pregnant patients.

CT characterizes lesions based on their degree of attenuation of a focused X-ray beam. A specific volume of tissue is assigned a value representing this degree of attenuation, called a Hounsfield unit (HU), named for the inventor of CT, Sir Godfrey Hounsfield. Although not absolute, bone is typically +400 to +1000 HU, soft tissue +40 to +80, water 0, fat -60 to -100, and air is -1000 [12].

Although attenuation values can sometimes be helpful, such as in the setting of a lesion that contains fat or calcification, many times a lesion will be of soft tissue attenuation. This does not aid in providing a specific histologic diagnosis. Some tumors, such as osteosarcoma or chondrosarcoma, demonstrate internal matrix, which can allow for further characterization, although this information is often obtainable via radiography.

Patterns of osseous destruction seen on CT follow those seen on radiography. A slow growing process will demonstrate a narrow zone of transition and geographic margins, and more aggressive processes will have moth-eaten or permeative patterns of destruction. The endosteum is also well evaluated on CT, which can be scalloped or destroyed in the setting of tumor. The degree of marrow replacement is better evaluated on MRI, but an obvious soft tissue mass infiltrating the medullary cavity can be assessed on CT.

CT can also be helpful in identifying areas of reactive cortical destruction. CT allows direct visualization without overlying interfering attenuation from soft tissues. Cortical destruction can be assessed even in areas where several bones are in close proximity to one another or are of complex shape, such as in the spine or pelvis [13]. On X-rays, these areas of destruction can be obscured, as the three dimensional shape is flattened into two dimensions. Cortical destruction may be mistaken for overlap of other anatomic structures [14].

Extension of tumor into the adjacent soft tissues often accompanies aggressive osseous pathology, and CT can provide accurate assessment of the margins of extension. Addition of intravenous contrast can provide additional resolution between pathologic and uninvolved tissues. Despite these advantages with more well-encapsulated lesions, some tumors can be infiltrative, and the exact margin between tumor soft tissue and adjacent muscle may not be possible on CT. MRI may be advantageous in these patients as it offers superior soft tissue contrast when compared to CT, and as a result of its absence of ionizing radiation, has largely supplanted CT for the evaluation of soft tissue extent [15]. Intramedullary involvement is also better assessed on MRI [16], where subtle marrow infiltration may be detected by methods discussed below, but when grossly present may be detectable on CT by noting replacement of the marrow fat with soft tissue attenuation.

Despite the advantages of CT, in many cases, a specific histologic diagnosis of a soft tissue mass cannot be reached, and in these cases a differential diagnosis is generated. Further evaluation with MRI or tissue sampling is then performed.

Other potential limitations or drawbacks of CT include radiation dose, patient motion, and iodinated dye contrast allergy. Radiation dose associated with CT has received considerable media attention, and is particularly relevant for children and pregnant patients. Despite the attention it has received, the actual lifetime risk of developing fatal cancer from abdominopelvic CT has been the subject of a recent publication, and is by conservative estimate erring on the side of overestimation of at most 0.5 per 1,000 individuals. The risk of dying from pedestrian accident, for reference, is 1.6 per 1,000 individuals; from drowning, 0.9 per 1,000 individuals; and the risk of dving from lightning strike 0.013 per 1,000 individuals [17]. This is not to trivialize the possibility of radiation-induced cancer, but serves to provide a frame of reference of the likelihood to allow appropriate risk-benefit stratification. In general, a guiding principle with regards to medical imaging is to achieve the necessary diagnostic information using a radiation dose that is As Low As Reasonably Achieveable (ALARA). This can be done through both optimization of imaging protocols to include only the area of interest, and also by using techniques that do not involve ionizing radiation, such as ultrasound or MRI when appropriate. Additionally, newer generations of CT scanners have included features, such as dose modulation or iterative reconstruction, to marked reduce radiation exposures.

Patient motion degrades all imaging, regardless of modality. Although this can be a drawback on CT when a patient cannot hold still, CT is less susceptible to this limitation than is MRI, as imaging times are shorter. Sedation can be considered if the patient is a candidate when motion limits interpretation.

Iodinated contrast allergy is not uncommon. Severe anaphylaxis following contrast administration is rare, but can result in life-threatening complications that require immediate treatment [18]. Most reactions tend to be minor, and premedication regimens with steroids prior to contrast administration have been advocated. Of note, there is no specific cross-reactivity between allergy to iodinated contrast materials and allergy to gadolinium based contrast materials, so that a patient who has a history of severe allergic reaction to iodinated CT contrast material is often a candidate for contrast-enhanced MRI (Figs. 7, 8 and 9).

#### 4 Magnetic Resonance Imaging

Magnetic resonance imaging has traditionally been utilized for staging of bone lesions and as such has been extremely valuable in planning management, but the advent of more advanced pulse sequences allows for some increased lesion characterization as well. Conventional MRI sequences do not usually allow for lesion characterization, as both benign and malignant processes show increased relaxation times on both T1 and T2 sequences. Main strengths of MRI in bone tumor imaging include the ability to assess extent of marrow involvement, to determine the presence of discontinuous, or "skip" lesions within the same bone, and to determine the extent of any soft tissue component extending beyond the



**Fig. 7** a Osteoid osteoma. CT demonstrates focal cortical thickening with a central lucent nidus in this 19 year old man. b Under CT guidance, a radiofrequency ablation probe was directed to the nidus, providing relief of symptoms following ablation



**Fig. 8** Fibrous dysplasia. For complex locations such as the ribs, where there is osseous overlap with the adjacent scapula at radiography, CT is helpful in providing additional information. In this 37 year-old man, this lesion demonstrates the typical ground glass matrix of fibrous dysplasia, which was suggested at the initial CT examination. Biopsy was performed because of cortical breakthrough superiorly, and pathology confirmed fibrous dysplasia

cortex. For these reasons, continuous images extending from the joint above the lesion to the joint below are typically obtained. Additionally, MRI carries the advantage of absence of ionizing radiation. However, limitations of MRI include susceptibility artifact from metallic hardware, which is often placed in the surgical treatment of musculoskeletal tumors, and inability to safely image many patients with pacemakers or other metallic devices.

**Fig. 9** Osteosarcoma. CT of the same patient as in Fig. 5. The extent of soft tissue involvement is better assessed on CT



For evaluation of marrow infiltration, T1-weighted images are the workhorse sequence. Marrow conversion from red, hematopoietic marrow to yellow, fatty marrow in a normal patient occurs in a predictable distribution with advancing age. This can be appreciated on T1-weighted images as an increase in marrow signal correlating with increased fat content. When an area that should contain yellow marrow loses its bright signal, this may represent either marrow infiltration by a pathologic process or red marrow reconversion in response to increased hematopoietic needs. On T1 images, this can many times be differentiated by assessing the signal intensity with respect to muscle. Red marrow reconversion will typically be hyperintense to skeletal muscle, whereas a pathologic process typically will be isointense to hypointense.

Extent of disease involvement is assessed as areas of T1 hypointensity. This is evaluated both for the primary lesion, which is measured and reported, as well as for the presence of any concurrent lesions within the same bone. T1-weighted images can also suggest a diffuse pattern of marrow replacement, as is often seen in the setting of metastatic disease, myeloma or lymphoma.

Local infiltration of soft tissues adjacent to bone can usually be best characterized on T2-weighted images or T1-weighted images following the administration of intravenous contrast. T1-weighted images without IV contrast may demonstrate loss of fat planes or a demarcation between tumor and normal adjacent muscle if there is a difference in signal intensity, but these findings are often subtle, and small areas of involvement can be easily overlooked.

Pathological conditions are usually more conspicuous on fluid-sensitive sequences, such as T2-weighted imaging or with *short tau inversion recovery* (STIR), since the signal intensities of these areas are brighter than skeletal muscle. Additionally, fluid sensitive sequences are commonly performed with fat saturation. Decreasing the signal from fat further increases the conspicuity of abnormal fluid content within tissues. Thus, T2-weighted images increase the conspicuity of tumor infiltration. Chemically selective fat saturation sequences tend to have higher

spatial resolution but may suffer from areas of inhomogeneous fat suppression or may be more prone to other artifacts. On the other hand, STIR images demonstrate uniform fat suppression over larger fields of view but have poorer spatial resolution and may take longer to perform. T2-weighted images also increase the conspicuity of fluid-fluid levels. Although fluid–fluid levels are not specific, a lesion comprised of a higher percentage of fluid-fluid levels has a higher likelihood of being benign [19].

While the mainstay of MRI has been in assessing the extent of disease, the advent of advanced pulse sequences has allowed for some lesion characterization as well [20]. Chemical shift imaging, diffusion weighted imaging, and post-contrast imaging provide additional information for problem solving.

Chemical shift imaging is also called in and opposed phase imaging. The basic principle behind chemical shift imaging is that when water and fat molecules are located within the same sampled space and imaged while in phase, their signals will be additive, producing bright signal on the image. When imaged during the opposed phase, their signals will cancel one another out, resulting in a signal drop. Yellow marrow contains predominantly fat, and as such, will remain bright in signal on opposed phase imaging. Red marrow contains more hematopoietic elements, and as such is more cellular. With increased cellularity comes increased water content, although there is also usually some fatty marrow in these areas as well [21]. On opposed phase imaging, these signals then cancel, resulting in a signal drop.

Both marrow replacing processes and hematopoietic red marrow may be lower in signal intensity than fatty marrow on a T1-weighted image, and sometimes it can be difficult to distinguish between them simply by using comparison to internal references, such as muscle. This principle of chemical shift imaging can be applied to allow differentiation of an aggressive marrow replacing process from hematopoietic marrow. Marrow replacing processes are unlikely to spare the normal fatty marrow, and as a result, only cellular, water-heavy components are likely to remain. Thus, unlike with red marrow, there will be no signal drop on opposed phase imaging.

The role of diffusion-weighted imaging in the musculoskeletal system is less well defined. Diffusion-weighted sequences have been used extensively in the evaluation of stroke and many other intracranial processes, but have been less extensively studied with regard to bone tumors. Diffusion-weighted sequences are created based on Brownian motion at the microscopic level, and in tumor imaging, increased cellularity results in restricted diffusion. This is displayed on two sets of sequences. One of these is referred to by their *b value*, which is a representation of the diffusion weighting used to generate the image, and the other is called the *apparent diffusion coefficient*, or *ADC map*. Some authors have attempted to classify neoplastic versus normal marrow signal based on absolute ADC values [22]. However, the application of this technique for this usage is early, and absolute cutoffs may vary based on vendor and institution specific techniques used to generate the ADC map.