Diffusion-weighted, spectroscopy, and in- and out-of-phase imaging are expanding the role of MRI for characterizing musculoskeletal tumors.

Conventional Modalities and Novel, Emerging Imaging Techniques for Musculoskeletal Tumors

Meera Raghavan, MD

Background: Imaging of musculoskeletal tumors requires a multimodality approach and includes radiography, computed tomography (CT), and magnetic resonance imaging (MRI).

Methods: Topics related to primary bone and soft-tissue tumors are reviewed. The fundamental imaging principles are discussed as well as the applications of emerging imaging modalities.

Results: MRI is the preferred technique for the evaluation of musculoskeletal tumors, whereas other imaging modalities play a complementary role. Radiography is indicated as the first-line imaging modality in bone and soft-tissue tumors, whereas CT is the preferred modality for evaluating cortical osseous lesions or calcifications and in patients with contraindications to MRI. Positron emission tomography (PET)/CT and PET/MRI are helpful in identifying the glucose metabolism of the lesion. Ultrasonography is the most useful for biopsy guidance and can aid in differentiating cystic from solid masses and identifying vascularity. Novel modalities, such as diffusion-weighted imaging, spectroscopy, and habitat imaging, show promise in increasing diagnostic accuracy and affecting treatment strategies.

Conclusions: Conventional modalities and emerging, novel imaging techniques can provide noninvasive methods to diagnose and evaluate musculoskeletal tumors.

Introduction

The imaging evaluation of musculoskeletal tumors involves a multimodality approach. Each modality provides different diagnostic information. The patient's history, physical examination findings, and location of the abnormality will determine the type of imaging modality. The initial evaluation of bone and soft-tissue tumors is typically performed with plain radiography, followed by a cross-sectional modality such as computed tomography (CT) or magnetic resonance imaging (MRI). Nuclear medicine scintigraphy, ultrasonography, and positron emission tomography (PET) may also be performed in conjunction with or after the initial assessment. MRI is the technique of choice for the imaging assessment of soft-tissue tumors, whereas CT or MRI can be used to determine the extent of disease in bone tumors.

Novel techniques such as diffusion-weighted MRI, spectroscopy, and chemical shift are expanding the role of MRI in the characterization of musculoskeletal tumors. MRI-defined “habitats” in sarcoma provide another novel and evolving method to characterize and quantify features on MRI so as to provide prognostic and therapeutic information.
Conventional Modalities

Plain Radiography

Plain radiography remains the first-line choice of imaging modality for the initial evaluation of a bone lesion following clinical examination. Radiographs can be obtained quickly, easily, and at low cost. The differential diagnosis of many primary bone tumors is based on radiographic features. By combining radiographic features, such as lesion location, size, matrix, margin, and periosteal reaction, with patient age, sex, and clinical symptoms, the health care professional can effectively narrow the differential diagnosis to a small number of possibilities. The bone lesion can be classified as nonaggressive or aggressive from its radiographic appearance. A classic, nonaggressive bone lesion may not require subsequent imaging or treatment unless further anatomical information is required and surgical intervention is considered. Conversely, radiography can provide information about a lesion that helps determine appropriate further imaging with CT or MRI and useful clinical information about the potential fracture risk of the lesion. If multiple lesions are present on radiography, then the differential diagnosis will change to include other diagnoses such as metastatic disease or myeloma.

Radiographs are indicated in the workup of a soft-tissue mass. Radiographs should be inspected for tissue plane distortion, lucent areas — which might indicate fat — bony remodeling, and soft-tissue calcifications or mineralization. For example, a peripherally mineralized mass that arises following a clear history of trauma supports the diagnosis of myositis ossificans. Phleboliths in a soft-tissue mass support the diagnosis of a benign vascular lesion, whereas the presence of fat suggests a lipomatous mass.

The utility of radiographs alone in the evaluation of soft-tissue masses has been supplanted by MRI. Radiography does not obviate the need for cross-sectional evaluation and should be considered complementary to MRI and CT.

Findings on radiography can also be used to tailor cross-sectional imaging. For example, if metal density is noted, then sequences that would normally be performed with fat saturation can be altered to short tau-inversion recovery imaging to mitigate artifacts. If tumor involvement of the adjacent bone is seen, then further cross-sectional evaluation can be performed with CT because it is more useful than other modalities in the evaluation of cortical bone. Results on radiography may also suggest that the process is articular or juxta-articular (eg, synovial chondromatosis, tumoral calcinosis); in that case, the imaging planes or sequences that optimize the specific joint can be performed.

Ultrasonography

Ultrasonography can be complementary to MRI or CT in the initial evaluation of soft-tissue masses. In general, it is widely available, portable, is associated with low cost, and can be performed without ionizing radiation. In particular, ultrasonography can be used for the initial evaluation of soft-tissue masses in patients with contraindications to MRI. Sonography can confirm the presence of the mass, characterizing it as solid or cystic, and assess its dynamic features such as compressibility and vascularity. Perhaps one of the most widely used applications of ultrasonography is imaging-guided intervention. Ultrasonography can be used to guide a minimally invasive technique to guide the placement of the needle during biopsy into an area of solid tissue.

In a prospective study of 358 patients, ultrasonograp-
Phy was found to be an effective tool for triaging patients with soft-tissue masses. Nearly 80% of lesions were characterized as benign based on ultrasonographic features; on further follow-up (clinical, MRI, or both), none of these patients had a malignant tumor. Of those lesions evaluated by MRI for suspicious or indeterminate findings on ultrasonography (large mass, deep-seated, painful solid components, or vascularity), fewer than 2% were histologically malignant at surgery. By contrast, a small study of soft-tissue tumors showed that 23% of the 43 patients studied were incorrectly diagnosed following initial findings on ultrasonography. A delay in diagnosis was observed (≤ 6 months) in 7 patients (5 with malignant tumors), and the most common error was interpreting a solid tumor as hematoma. These studies highlight the utility and pitfalls of ultrasonography. Although it is a useful tool in evaluating patients with soft-tissue masses and for use in guiding biopsy, ultrasonography is not routinely performed in clinical practice as an initial imaging study, nor does its use preclude the need for additional cross-sectional imaging evaluation.

Because of the inability of sound waves to penetrate bone, little role exists for ultrasonography in the evaluation of bone lesions.

**Nuclear Medicine**

Radionuclide skeletal scintigraphy uses technetium-labeled diphosphonates, which adsorb to the crystalline structure of hydroxyapatite. These tracers accumulate in areas of osteoblast activity, thus indicating areas of bone perfusion and bone turnover. Skeletal scintigraphy is a cost-effective, whole-body imaging modality for the evaluation of multifocal or disseminated osseous disease (Fig 4). Fludeoxyglucose F 18 (FDG) is the most commonly utilized radionuclide for PET. FDG-PET is a functional imaging technique that assesses tissue metabolism using radioisotopes that undergo positron emission de-
FDG is a glucose analogue transported into the cell; however, once it is phosphorylated, it does not undergo further metabolism and becomes trapped. Fluorine F 18 then decays, producing 2 coincident positrons that can be used to produce the image. Glucose metabolism can be quantified by measuring maximum standardized uptake value. A caveat to using PET/CT in musculoskeletal applications is the considerable overlap of standardized uptake values in benign and malignant soft-tissue and bone lesions. In addition, non-neoplastic conditions (e.g., inflammatory processes, trauma) can also result in abnormal uptake, mimicking malignancy and reducing the specificity of PET/CT. In clinical practice, CT is concurrently performed with PET for localizing the anatomical findings found on functional imaging.

PET/CT has been investigated for biopsy guidance, staging, and treatment response. Typically, MRI of the primary lesion is performed; therefore, PET/CT is used for the detection of metastatic disease. The lung is the predominant site of metastatic disease from soft-tissue sarcoma, and it is unclear how well PET can detect metastases not already identified by CT of the chest. In several studies on the initial staging of soft-tissue sarcoma in adults using PET/CT, fewer than 5% of patients were upstaged as a result of PET/CT, and few patients had the management of their disease changed as a result. In a study of pediatric patients, FDG PET/CT was equally effective in identifying primary tumors (100%) compared with conventional imaging (CT and MRI) and was superior in the identification of metastatic lymph nodes (25% vs 95%) and bone metastasis (57% vs 90%). PET/CT was also found to have diagnostic benefit in the detection of bone metastases in osteosarcoma and pediatric Ewing sarcoma, but it was less sensitive compared with conventional CT in the detection of lung nodules (Fig 5). This finding underscores the importance of CT of the chest in the staging workup of soft-tissue and bone sarcomas. The utility of PET/CT beyond diagnostic CT of the chest for the initial and subsequent follow up of sarcomas is unclear. However, it may have added value in certain sarcomas (rhabdomyosarcoma, clear cell, epithelioid) in which the pattern of spread includes nonpulmonary sites, such as bone, retroperitoneum, and lymph nodes.

Although the role of FDG-PET/CT is unclear in the initial diagnosis and staging of soft-tissue sarcoma, it can be used to assess therapeutic response early during treatment. Post-treatment changes measured by the FDG avidity of the tumor are an indicator of the effectiveness of the therapy. Earlier biochemical changes in a tumor can enable clinicians to evaluate therapeutic effectiveness earlier than conventional anatomical imaging. In particular, sarcomas are challenging because an increase in size often does not indicate poor response to therapy. Often, preoperative radiotherapy causes hemorrhage or necrosis leading to tumor enlargement. An increase in tumor size (≤ 20%) observed after radiotherapy but prior to surgery has not been associated with worse outcomes. PET/CT can also be used to guide biopsy. Soft-tissue sarcomas are often heterogenous on MRI, with areas of necrosis or myxoid components. If these areas are sampled, then the tumor may be inappropriately downgraded. PET/CT can assist in targeting hypermetabolic areas that can increase the diagnostic yield of sampling (Fig 6). However, the evidence for the use of PET for guidance during biopsy is based on a small number of studies, so.

Fig 5 A–C. — Utility of PET for evaluating osteosarcoma. Findings on (A) coronal and (B) axial PET demonstrate a large, peripherally avid tumor for fludeoxyglucose F 18 in the right hemithorax in a patient with primary osteosarcoma resected more than 7 years ago. (C) PET detected an area of avidity in the left rib (red arrow) corresponding to a spiculated, periosteal reaction. PET = positron emission tomography.

Fig 6A–B. — Utility of PET for evaluating osteosarcoma. Findings on (A) axial CT and (B) axial-fused PET/CT demonstrate a large, peripherally avid tumor for FDG in the right hemithorax in the patient from Fig 5. Primary osteosarcoma was resected more than 7 years ago. Note how FDG avidity follows the areas of ossific matrix seen on CT, thus suggesting the more metabolic regions and potential area for biopsy. The center of the mass is likely necrotic and non-FDG avid, so it would be of lower diagnostic yield if biopsy was performed. CT = computed tomography, FDG = fludeoxyglucose F 18, PET = positron emission tomography.
the routine use of PET to guide biopsy in real time is not routinely performed.26

More specifically, novel radiopharmaceuticals for use with PET, such as proliferation markers (fluorodeoxythymidine F 18), bone-seeking agents (sodium fluoride F 18), amino-acid tracers (methionine C 11, fluoroethyltyrosine F 18), or biomarkers of neoangiogenesis (galacto-RGD F 18), are not routinely used in clinical practice. However, they can potentially elucidate the underlying biological mechanisms of musculoskeletal tumors and, with future research, possibly contribute additional information to the grading, treatment monitoring, and post-therapy assessment.27

Applications for PET/MRI continue to grow in clinical practice.17 The literature on PET/MRI is not yet available for all tumors, but PET/MRI may be of benefit in staging and assessing treatment response in bone and soft-tissue sarcomas.17 In general, PET/MRI may be indicated in malignancies that require high soft-tissue contrast for visualization, and it will be of utility in the pediatric population because radiation exposure can be reduced.17,28

**Computed Tomography**

When the radiographic features of a bone lesion are indeterminate or aggressive, cross-sectional imaging is usually obtained. Because of its superior ability to visualize bony detail and evaluate cortical bone, CT is often the modality used to evaluate tumors located within the periosteal or cortical regions (eg, osteoid osteoma; Fig 7).3 CT can better demonstrate subtle mineralization or calcification that may not be appreciated on radiography.4 Evaluation of flat bones and small bones of the hands and feet are also better evaluated with CT (Fig 8).4 Due to the complex anatomy in the spine and pelvis, CT may also be a preferred modality or used in adjunct to MRI.4 CT may also be the most appropriate imaging modality for patients who are obese, patients with pacemakers, and when MRI is not feasible.1

Earlier literature comparing MRI and CT for the evaluation of bone tumors showed that MRI was superior for initial staging.4,29-31 Zimmer et al29 and Hogeboom et al30 studied features of bone tumors such as cortical destruction and involvement of marrow, soft tissue, joints, and neurovascular structure on CT and MRI.4 Both studies showed superiority of CT for evaluating cortical bone involvement, but MRI better demonstrated neuromuscular, and joint and compartmental involvement, as well as intramedullary extent.29,30 Both studies also favored MRI if both CT and MRI were available.29,30 One group demonstrated no statistical difference between CT and MRI in the evaluation of the extent of tumor involvement in 183 patients with primary bone tumors (Fig 9).14,31

CT is useful in evaluating mineralized matrix and bone changes related to soft-tissue sarcoma.32 It can

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Fig 7A–C. — CT evaluation of cortical lesions. (A) Radiography of the humerus and (B) coronal CT show a benign, smooth, continuous, solid, periosteal reaction along the medial cortex. (C) Axial CT demonstrates a cortical-based lucency in the cortex compatible with osteoid osteoma. The benign periosteal reaction was produced by inflammation caused by osteoid osteoma.

CT = computed tomography.

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Fig 8A–C. — CT evaluation of the small bones in the feet. (A) Oblique view of the foot shows a lucent lesion with a sclerotic center confirmed by (B) long-axis and (C) axial CT. CT demonstrates a lucent lesion consistent with osteoid osteoma as well as the calcified fibrovascular nidus, which is the inciting lesion. CT also shows the disruption of the cortical bone that was not observed on radiography. CT = computed tomography.

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Fig 9A–C. — (A) Lateral radiography of the tibia. (B) Sagittal T1-weighted MRI. (C) Sagittal-reconstruction CT in a boy aged 15 years with left tibial adamantinoma. Radiographs, CT, and MRI all show the eccentric, cortical-based location and extent of the lesion with an intact cortex. CT = computed tomography, MRI = magnetic resonance imaging.
be helpful in distinguishing soft-tissue sarcoma from myositis ossificans — a distinction that can be difficult on MRI, as both can have nonspecific features on T1- and T2-weighted imaging — because CT can delineate the zonal pattern of mineralization characteristic of myositis ossificans.32

**Magnetic Resonance Imaging**

Evaluation of bone tumors using MRI can help clinicians identify the extraosseous component, if present, and the compartmental location can be well evaluated — both are important factors in the preoperative evaluation. In addition, a diagnosis other than a tumor (eg, radiographically occult fracture, osteonecrosis) may be elucidated on MRI.33 It is important to remember that radiography plays an important and complementary role in the evaluation of bone tumors. Most bone lesions (malignant and benign) have high T1 and T2 relaxation times, producing nonspecific low T1 and high T2 signals.2 This fact makes the rendering of a particular histological diagnosis all the more difficult when evaluated in the absence of radiography. In-phase and out-of-phase (also known as opposed) imaging can be useful in the evaluation of bone lesions, particularly in delineating red marrow hyperplasia from metastatic disease.

In general, MRI has replaced CT as the imaging modality of choice in the evaluation of soft-tissue masses.1 Based on the findings of 133 soft-tissue tumors, one group found that MRI and contrast-enhanced CT were comparable when determining tumor size and involvement of surrounding structures.1,31 However, in clinical practice, MRI is the preferred imaging modality for the detection, evaluation, assessment, staging, and follow up of soft-tissue tumors.

The advantages of MRI include establishing a differential diagnosis of the lesion, precise compartmental localization, and assessment of neuromuscular and joint involvement. In addition, MRI can be used to visualize the entire compartment, which can demonstrate metastatic lymphadenopathy — seen only in certain sarcomas (Fig 10). MRI is excellent at delineating soft-tissue lesions, and a specific diagnosis can be obtained in many instances by evaluating lesion signal intensity, location, growth pattern, and other unique intrinsic properties.53 Unless a specific diagnosis can be made, the lesion should be considered indeterminate and then biopsied in close consultation with an orthopedic oncologist.

Unless it is contraindicated, contrast should be administered when evaluating soft-tissue tumors. Contrast enhancement delineates areas of necrosis within the lesion and allows differentiation of myxoid material from fluid foci (Fig 11). Myxoid tissue is a gelatinous material comprised of glycosaminoglycans, and it is commonly seen in soft-tissue sarcomas.54 Myxomatous stroma demonstrates mild enhancement, which is in contrast to cystic areas or necrosis that does not enhance.

Oftentimes, the degree of enhancement is visually equivocal. In these cases, subtraction sequences can be used. Precontrast, T1-weighted images are subtracted from the postcontrast T1-weighted sequences by software to yield areas of true enhancement (Fig 12). The utility of gadolinium in imaging bone tumors is controversial; nevertheless, the pattern and degree of contrast enhancement can be useful, particularly when evaluating for extraosseous extension.

**Important Features:** The location, size, and signal features of a lesion should be assessed. In general, heterogeneous signal is seen in sarcomas, including areas of mixed tissue, necrosis, or hemorrhage. If areas of intralesional fat or calcification are observed, or the mass is arising from a nerve, then the differential diagnosis can be appropriately narrowed as a lipomatous or nerve sheath tumor, respectively.

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**Fig 10A–B.** — MRI detection of lymphadenopathy. (A) Axial, post–contrast MRI of the thigh demonstrates a large, posterior, compartment mass with peripheral enhancement consistent with leiomyosarcoma proven by biopsy. (B) Axial MRI of the ipsilateral inguinal region demonstrates an enlarged, enhancing lymph node compatible with metastatic disease. With the exception of certain histological subtypes, nodal metastatic disease is not commonly seen in soft-tissue sarcomas. MRI = magnetic resonance imaging.

**Fig 11A–C.** — Heterogenous soft-tissue sarcoma. (A) Axial T1-weighted, (B) T2-weighted, and (C) post–contrast MRI of a thigh with malignant myxoid liposarcoma. High T2-signal areas throughout the mass represent myxoid stroma, a gelatinous material comprised of glycosaminoglycans, commonly seen in soft-tissue sarcoma. Myxomatous stroma demonstrates mild enhancement; this is in contrast to cystic areas or necrosis, neither of which enhance on MRI. MRI = magnetic resonance imaging.
presence of areas of low signal on multiple sequences can suggest the presence of fibrous tissue.

The high soft-tissue contrast of MRI enables the clinician to assess the relationship between the tumor and neurovascular bundle (Fig 13). If the contact between the tumor and the adjacent neurovascular structures exceeds 180 degrees, then encasement should be suspected.35

Direct osseous involvement by soft-tissue sarcoma rarely occurs, but the clinician should still evaluate for it because its presence has been shown to correlate with disease-related mortality.32,36 Osseous invasion of the medullary cavity can be assessed on MRI by signal changes in the normal fat-containing marrow (see Fig 13). Cortical involvement may be more difficult to detect on MRI due to the low signal of cortical bone on all sequences; in these cases, CT can be used as an adjunct imaging modality.

Typically, a rim of low signal surrounding the tumor can be seen in sarcomas. Malignant tumors push away normal tissue around them as they enlarge; therefore, sarcomas do not infiltrate the anatomical compartments and fascial borders until late in their course. Local growth of soft-tissue sarcoma occurs in a radial fashion, compressing surrounding fibrous connective tissue, which, in combination with associated inflammatory reaction, forms a “pseudocapsule” around the tumor (Fig 14).33,37

Another important feature to assess is the presence of peritumoral high T2 or fluid signal changes that can be seen in benign and malignant tumors.37 This may be due to the increased water content in the tissues, known as peritumoral edema (see Fig 14).38 Typically, areas of peritumoral edema enhance, and they have been attributed to microscopic tumors, inflammatory reactions, vascular congestion and hyperperfusion, or edema.38 In a study by White et al,38 malignant cells were histologically identified in tissue beyond the tumor margin in 10 out of 15 cases. Identification of malignant cells beyond the margin of the tumor necessitates treatment modifications, such as extension of the radiation field or repeated resection to reduce the risk of local recurrence.

In addition to the initial staging of primary soft-tissue and bone tumors, MRI is the preferred modality for the evaluation of locally recurrent disease.17,37 Surgical and radiation changes can produce abnormal signals related to fibrosis, edema, and metallic susceptibility artifact, thus making imaging...
interpretation complex. Postoperative fluid collections or seromas can complicate the detection of recurrent disease, which most often presents with enhancing nodules in the tumor bed (Fig 15). However, enhancing mural nodules within seromas may not necessarily represent recurrent disease and should be followed up. Another common finding is treatment-related changes of the bone marrow, which can be difficult to differentiate from tumor. T1-weighted sequences and chemical-shift MRI can be useful tools for delineating changes in bone marrow from neoplasms.

**Novel Techniques**

**Chemical Shift and In- and Out-of-Phase Magnetic Resonance Imaging**

In-phase and out-of-phase (opposed) MRI allows the clinician to detect the presence of fat in lesions, so this imaging modality may be useful for delineating whether a signal abnormality seen in the marrow is likely caused by red marrow hyperplasia or a marrow-replacing process. Normal yellow marrow has a high fat content with a hyperintense signal on non–fat-suppressed T1 sequences. Normal bone marrow is rich in both fat and water, but their relative amounts is the main factor affecting signal intensity of marrow on MRI. When both fat and water are present in the same voxel, this combination results in the suppression of signal intensity on out-of-phase imaging. Marrow-replacing processes result in a lower T1 signal and lack of suppression of signal intensity on out-of-phase imaging (Fig 16). Hematopoietic or red marrow can produce focal areas of decreased T1 signal, thus mimicking a marrow-replacing lesion. Red marrow also contains fat — albeit less when compared with yellow marrow — and, therefore, can be differentiated from true lesions by chemical shift MRI. A technique described by Costa et al involves drawing regions of interest of equal size over the abnormal areas on both the in-phase and out-of-phase imaging. The signal intensity ratio of the marrow on the out-of-phase and in-phase imaging is calculated. A signal intensity ratio below 0.80 is typical of a non-neoplastic process. A study by Zajick et al showed that a 20% decrease in signal intensity on the out-of-phase images from the in-phase images was a reliable feature for distinguishing benign from malignant bone marrow in the spine. Although using a signal intensity ratio higher than 0.80 has been proposed to identify neoplastic lesions, chemical shift MRI has not been consistently shown to differentiate malignant from benign tumors.

**Diffusion-Weighted Magnetic Resonance Imaging**

Diffusion-weighted is a noncontrast, functional MRI technique that has been investigated for the characterization of tumors throughout the body. The signal intensity of diffusion-weighted MRI relies on the Brownian motion, or the microscopic motion of water molecules within tissues. The apparent diffusion coefficient (ADC) is a quantitative measure of Brownian motion. In highly cellular environments, free diffusion of water restricted, resulting in low ADCs. Acellular tissue (ie, necrosis) allows free diffusion in all directions, resulting in high ADCs. Areas of restricted diffusion (ie, because of high cel-
lularity) have higher signal intensity on diffusion-weighted MRI but lower signal intensity on ADC maps (Fig 17).\textsuperscript{12,43} The ADC value for a specific region of interest is calculated by plotting the change in signal of the region as it varies with different diffusion gradient strengths (\textit{b} values).\textsuperscript{50}

Diffusion-weighted MRI has been used to better evaluate treatment response in patients with sarcoma receiving chemotherapy.\textsuperscript{13,49} However, the literature shows variable results in the ability of diffusion-weighted MRI to distinguish between benign and malignant soft-tissue masses.\textsuperscript{49,51} A study by Subhawong et al\textsuperscript{49} determined that a threshold mean ADC of 2.5 provided a 100\% specificity rate for predicting a cyst and ruling out a solid tumor. Demehri et al\textsuperscript{52} demonstrated the ability of a minimum ADC to differentiate benign from malignant peripheral nerve sheath tumors.

Few studies have examined the utility of diffusion-weighted MRI in the evaluation of bone lesions; however, a study by Ahlawat et al\textsuperscript{47} determined the minimum ADC threshold of 0.9 × 10\textsuperscript{-3} mm\textsuperscript{2}/second and 1.4 × 10\textsuperscript{-3} mm\textsuperscript{2}/second (mean ADC) for differentiating benign and malignant histology (see Fig 17). A study of patients with osteosarcoma suggests that change in ADC may be useful in assessing response to chemotherapy and can differentiate areas of granulation tissue and scarring from viable cellular tumor.\textsuperscript{50,53}

Although it is not routinely used, diffusion-weighted MRI is an unenhanced method that may provide helpful clinical information, and it can be used in situations in which intravenous contrast cannot be administered due to contraindications or patient refusal.

### Proton Magnetic Resonance Spectroscopy

Proton magnetic resonance spectroscopy is a technique used to characterize tumors based on their molecular properties; similar to diffusion-weighted MRI, it can be performed without intravenous contrast.\textsuperscript{54} The metabolic “footprint” of a lesion is determined based on the signal of water, lipids, and various metabolite content.\textsuperscript{53} Choline-containing compounds are constituents of cell membrane phospholipids and are a reflection of cell-membrane turnover. Therefore, the presence of a spectroscopic choline peak is suggestive of malignancy.\textsuperscript{54,56} The presence of a choline peak is supportive of malignancy, although some metabolically active benign tumors and abscesses may also have a choline peak.

Magnetic resonance spectroscopy is not widely used in clinical practice for musculoskeletal applications, but it shows promise in the noncontrast magnetic resonance evaluation of bone and soft-tissue lesions.

### Habitat Imaging

Several groups have been working on the quantitative evaluation of tumor subregions in the setting of soft-tissue sarcoma.\textsuperscript{57-61} Utilizing several computer-aided techniques, including clustering algorithms and texture-feature analyses, one group noninvasively evaluated tumor subregions, or “habitats,” to better elucidate the heterogeneity of soft-tissue sarcoma. T1-weighted, gadolinium-enhanced, and fluid-sensitive pretreatment MRI was analyzed in the extremities of patients with soft-tissue sarcoma.\textsuperscript{57} Segmentation based on the pixel signal intensity was performed, followed by an analysis within each distinctive subregion to predict metastatic disease and histological necrosis.\textsuperscript{57} From this analysis, habitat maps were derived based on combinations of pixel intensity combinations from the 2 sequences, demonstrating distinct, spatial intratumoral subregions (Fig 18). The yellow-color habitat map corresponds to a high T1, postcontrast/low, T2 signal (inferred as high vascularity and cellularity), which was both predictive and prognostic. The yellow subregion correlated with decreased overall survival (\textit{P} = .03) and, if present in more than 18\% of the tumor slice, is predictive for the development of metastatic or locally recurrent disease. Based on texture-feature analysis, pretreatment MRI predicted that the rate of metastatic development in patients with soft-tissue sarcoma was 72.4\%.\textsuperscript{41} Continued investigation into the change in habitats on pre- and post-treatment MRI is also being conducted.\textsuperscript{62} Habitat imaging is an evolving area of study that may be useful for more accurately assessing prognosis and tailoring personalized therapies.\textsuperscript{57}

### Conclusions

Progress has been made in the imaging evaluation of musculoskeletal tumors. Detecting lesions on mag-

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**Fig 17A–B.** — Diffusion-weighted magnetic resonance imaging in the evaluation of the lesion in Fig 16. The lesion shows high signal at (A) different \textit{b} values and (B) low signal on the apparent diffusion coefficients map, findings indicative of restricted diffusion. Restricted diffusion is caused by the restricted motion of water in a cellular environment and suggests that a lesion is malignant.

Images courtesy of Laura M. Fayad, MD, Johns Hopkins Medicine, Baltimore, Maryland.
Habitat imaging in a patient aged 48 years with high-grade, undifferentiated sarcoma in the left thigh. (A, D) Axial, contrast-enhanced, (B, E) T2-weighted, fat-suppressed, and (C, F) habit image color mapping obtained following computed tumor segmentation. Panels A to C show pre-treatment MRI. Panels D to F show post-treatment MRI. The color maps illustrate distinct, intratumoral subregions, or habitats, derived from pixel signal intensities. The degree of spatial heterogeneity within the tumor is better delineated on the habitat color map. Note the changes in distribution and size of the habitats between pre- and post-contrast color maps. The yellow subregion comprises more than 18% of the tumor pretreatment color map in panel C, thus inferring a poor prognosis. This patient had metastatic disease to the lungs and died less than 1 year after diagnosis. MRI = magnetic resonance imaging.

References


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