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Clinical presentation and imaging of bone and soft-tissue sarcomas

■ ABSTRACT

The clinical presentation of bone and soft-tissue sarcomas is varied. Constitutional symptoms are rare, and although bone sarcomas tend to be painful while soft-tissue sarcomas usually are not, there are exceptions to this general rule. A high index of suspicion is required for any unexplained mass with indeterminate imaging findings. Choosing the right imaging modality is critical to the diagnosis and management of patients with suspected sarcoma, and referring clinicians have a multitude of imaging options. After discovery of a malignant-appearing bone lesion by radiography, further imaging is obtained for better characterization of the lesion (typically with magnetic resonance imaging [MRI]) and for staging (typically with computed tomography of the chest). In contrast, radiographs are rarely helpful for evaluation of soft-tissue lesions, which almost always require MRI assessment.

Sarcomas are rare neoplasms arising from connective tissue elements of the body. Approximately 80% arise in soft tissue, while the remainder originate in bone.¹ Soft-tissue sarcomas are tumors of the mesenchymal system, and about half develop in the extremities. Bone sarcomas are characterized by their location in bone and sometimes produce osteoid, or immature bone.

The most common types of soft-tissue sarcomas are malignant fibrous histiocytoma (although this term has lost favor with some pathologists) and liposarcoma.

The most common types of bone sarcomas are osteosarcoma (a sarcoma that makes osteoid or bone), Ewing sarcoma (composed of small round blue cells with a characteristic chromosomal translocation), and chondrosarcoma (a sarcoma that makes chondroid tissue, or cartilage).

■ EPIDEMIOLOGY AND PRIMARY BODY SITES

Approximately 10,600 new cases of soft-tissue sarcoma and 2,570 new cases of bone sarcoma were estimated to

have been diagnosed in the United States in 2009.^{2,3} For perspective, the annual incidence of soft-tissue sarcoma is approximately 5.5% that of breast cancer and approximately 5% that of lung cancer.³

Most sarcomas develop in the lower extremities, although the age groups at greatest risk vary among sarcoma types.⁴

Soft-tissue sarcomas develop most commonly in the thigh and occur primarily in adults.²

Osteosarcomas are the most common bone sarcoma and develop most frequently in 10- to 20-year-olds; their most common location is the distal femur.⁵⁻⁸ Metastatic osteosarcoma is found in approximately 20% of patients at the time of osteosarcoma diagnosis. Osteosarcomas mainly spread hematogenously, and the lungs are the most common initial site of metastases, being affected in up to 90% of patients with metastatic disease.⁹

Ewing sarcomas develop most often in the long bones of the extremities or bones of the pelvis. The large majority of cases develop in patients aged 10 to 15 years.⁵⁻⁸

Chondrosarcomas represent approximately 20% of all bone sarcomas and primarily affect older adults, with a peak incidence in the sixth decade of life.¹⁰

■ OVERVIEW OF PRESENTATION AND EVALUATION

Presentation is highly variable

The clinical presentation of patients with bone or soft-tissue sarcoma is highly variable. Patients often present with a mass, typically one that is increasing in size. In general, bone sarcomas are painful and soft-tissue sarcomas are not, but there are exceptions to this general rule. Constitutional symptoms are rare in patients with bone or soft-tissue sarcomas, but symptoms such as fever, malaise, and weight loss can be seen, especially in patients with Ewing sarcoma.¹¹

Delayed presentation and diagnosis are common

Particularly when a sarcoma is painless, patients sometimes do not seek medical attention until a suspicious mass becomes quite large. Certain tumors, such as synovial sarcoma, a high-grade soft-tissue sarcoma often seen in young adults, may present as a slowly growing or stable-appearing mass over several years. In one study of 33 children with synovial sarcoma, the mean duration of symptoms was 98

All authors reported that they have no financial interests or relationships that pose a potential conflict of interest with this article.

doi:10.3949/ccjm.77.s1.01

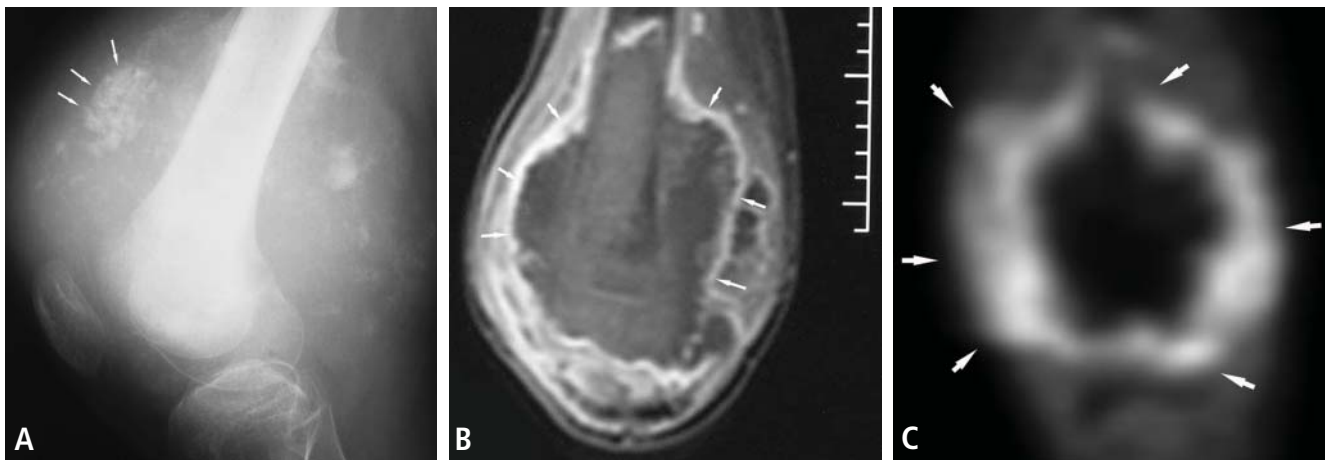


FIGURE 1. Imaging studies in a 14-year-old girl with a knee mass. **(A)** Lateral radiograph showing cloud-like osteoid mineralization (arrows) consistent with osteosarcoma. **(B)** Follow-up post-contrast T1-weighted MRI in the coronal plane shows evidence of significant tumor necrosis with enhancement confined to the tumor periphery (arrows), which correlates well with the absence of intratumoral metabolic activity centrally on a cross-sectional FDG-PET image **(C)**.

weeks (range, 2–364), the mean patient delay before a doctor was seen was 43 weeks (0–156), the mean doctor delay before a correct diagnosis was made was 50 weeks (0–362), and the mean number of doctors seen before referral was 3 (1–6).¹² For nearly half the patients in this study (15), the diagnosis was obtained only after unplanned excision, meaning that the surgeon did not expect a malignancy at the time of biopsy. Because delayed presentation is not uncommon in cases of bone or soft-tissue sarcoma, every patient with a mass with indeterminate imaging findings should be referred to or reviewed by an orthopedic or musculoskeletal oncologist.

Biopsy is gold standard for diagnosis

A comprehensive medical history and physical examination are essential at the initial presentation of patients with masses and/or pain suggestive of bone or soft-tissue sarcoma. Sarcoma simulators such as hematoma, metastatic disease, or infection can sometimes be ruled out by careful clinical examination, laboratory work-up, and appropriate imaging, but the gold standard for diagnosis is a biopsy. Moreover, an index of suspicion is required to rule out primary malignancy in any soft-tissue or bone lesion, and this index of suspicion will allow for referral or appropriate selection of the site for biopsy.

Biopsy considerations, as well as further detail on clinical presentation, are provided in the second and third articles in this supplement, which focus, respectively, on bone sarcoma and soft-tissue sarcoma. The remainder of this article reviews the use of imaging for the evaluation of suspected sarcomas, as imaging findings typically prompt or guide biopsy of a suspicious mass. Choosing the right imaging modality is critical to the diagnosis and management of patients with suspected sarcoma.

CONVENTIONAL IMAGING MODALITIES

Radiography. Despite recent advances in cross-sectional imaging with computed tomography (CT) and magnetic

resonance imaging (MRI), radiographs remain valuable for characterizing osseous lesions and enabling accurate differential diagnosis of benign and malignant tumors (**Figure 1**). Multiple lytic lesions in an adult older than 40 years almost always suggest metastases or multiple myeloma.¹³ Bone sarcomas are rare, and the most common cause of a solitary destructive lesion in an adult is metastasis.

Despite their utility for evaluating osseous lesions, radiographs have limited to no value in the evaluation of soft-tissue sarcomas but can demonstrate matrix mineralization and erosion or destruction of adjacent bone.

Angiography. In the past, angiography was frequently used to assess the vascularity of sarcomas preoperatively. Diagnostic angiography has been replaced by conventional MRI and magnetic resonance angiography, but some vascular sarcomas may require presurgical embolization to prevent excessive bleeding during surgery.

Radionuclide bone scans have long been a reliable tool for detecting multifocal or disseminated osseous lesions and remain the mainstay for evaluation of osseous metastases. They also are helpful in identifying skip lesions of osteosarcoma (ie, smaller discrete foci of osteosarcoma occurring in the same bone or on the opposing side of a joint).¹⁴ Advantages of this modality include whole-body scanning and low radiation at relatively low cost. Radionuclide bone scans demonstrate areas of bony repair and thus could be negative in purely lytic/destructive processes such as renal cell carcinoma metastases and multiple myeloma.

Chest radiographs are typically obtained in the initial stages of patient evaluation and are helpful in demonstrating large nodules or masses resulting from metastatic disease. In a patient with known sarcoma, a negative or equivocal chest radiograph should be followed by chest CT to definitively assess for metastasis.

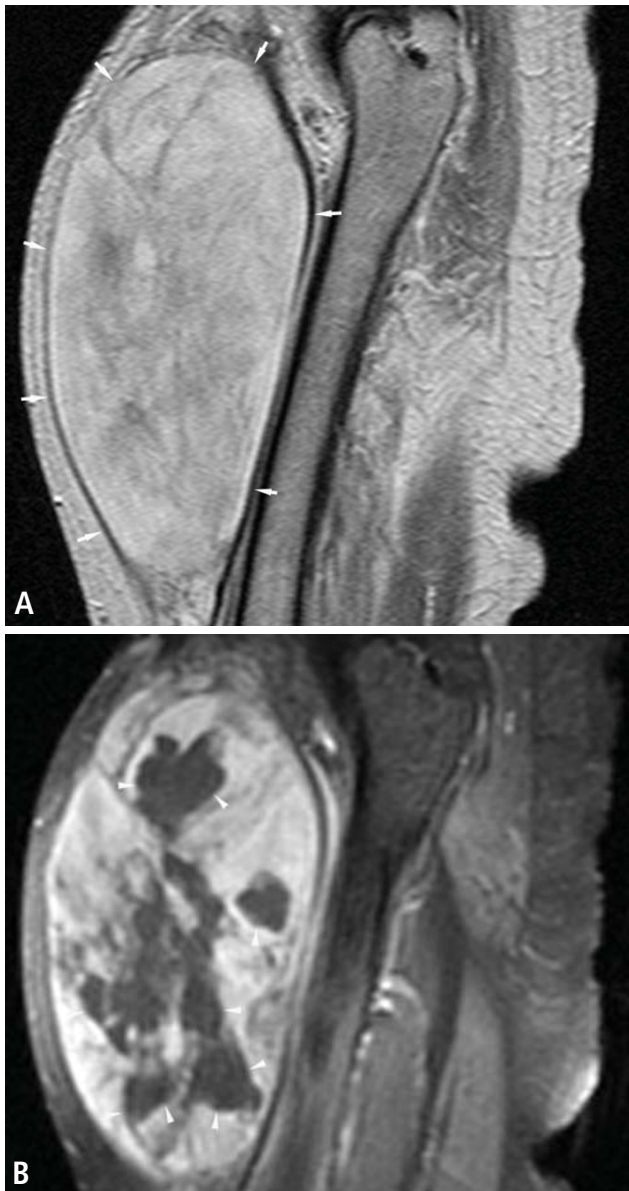


FIGURE 2. MRI findings highly suggestive of soft-tissue sarcoma in a 79-year-old man with a large anterior thigh mass. **(A)** T2-weighted image reveals a large mass with heterogeneous signal and surrounding pseudocapsule (arrows). **(B)** Post-contrast image shows pockets of absent enhancement (arrowheads) suggestive of necrosis.

CROSS-SECTIONAL IMAGING WITH MRI AND CT

MRI preferred for evaluation of most masses

MRI is the examination of choice in the evaluation of soft-tissue masses in light of its superior contrast resolution and ability to demonstrate subtle changes in soft tissues.

Predicting the histology of most soft-tissue masses is difficult, with the exception of some benign vascular lesions (eg, hemangioma), ganglia, neurogenic lesions, and well-differentiated lipomatous lesions. Aggressive features of a soft-tissue neoplasm include size greater than 5 cm,¹⁵ deep

location, and absence of central enhancement, which is suggestive of necrosis (Figure 1). Yet one third of soft-tissue sarcomas are either superficial or smaller than 5 cm, which highlights the relative nonspecificity of these features.¹⁵

A pseudocapsule or capsule is commonly seen around a sarcoma in the soft tissues, producing well-defined margins on MRI that do not reflect benignity (Figure 2). MRI may show T2-weighted signal changes surrounding soft-tissue sarcomas. These abnormalities are considered to represent peritumoral edema. Tumor cells beyond the sarcoma margin were found within areas of peritumoral edema seen on preoperative MRI in 9 of a series of 15 cases.¹⁶ Hematomas and abscesses typically have marked edema of surrounding soft tissue (Figure 3) and no internal enhancement after contrast injection. If MRI features of a suspected hematoma are equivocal, a follow-up study is warranted to exclude hemorrhagic sarcoma.

Nowadays, CT of primary soft-tissue tumors is rarely performed. Rare exceptions are patients with a contraindication to MRI (eg, presence of cardiac pacemaker) or for detecting subtle matrix mineral, if it will alter management.

MRI is also the preferred modality in the evaluation of the majority of bone sarcomas, given its ability to accurately define the extent of marrow changes and soft-tissue involvement. MRI should be performed prior to a biopsy to prevent misinterpretation of biopsy-related signal changes in the surrounding tissues, which may negate the value of MRI in sarcoma staging.

Several distinct roles for CT

CT is better at detecting subtle matrix mineral and for establishing the presence or absence of a thin rim of cortex around expansive lesions or masses containing calcific densities—findings that may have a bearing on the differential diagnosis (Figure 4). Abdominal and chest CT remain particularly important tools in the staging process. CT is critical for evaluation of pulmonary nodules.

Chest CT should be obtained in all cases of known malignant neoplasms to evaluate for pulmonary nodules, masses, and lymphadenopathy. Despite the recent advances in MRI, CT remains the imaging modality of choice to evaluate the retroperitoneum, abdomen, and pelvis for masses, lymphadenopathy, or other signs of metastatic disease.

Post-treatment monitoring for recurrence

After definitive treatment, MRI remains the most sensitive imaging tool for diagnosing local recurrences of either bone or soft-tissue sarcomas. After surgery, hematomas or seromas often present as palpable soft-tissue masses and are easily diagnosed with contrast MRI (Figure 5). Baseline examination is critical for visualizing the postoperative distortion of tissues. The presence of metallic hardware in postsurgical patients is not an absolute contraindication, and artifacts may be minimized by new MRI techniques (Figure 6).¹⁷

ULTRASONOGRAPHY

Ultrasonography has a limited role in the initial diagnosis and follow-up of musculoskeletal tumors. Its main advan-

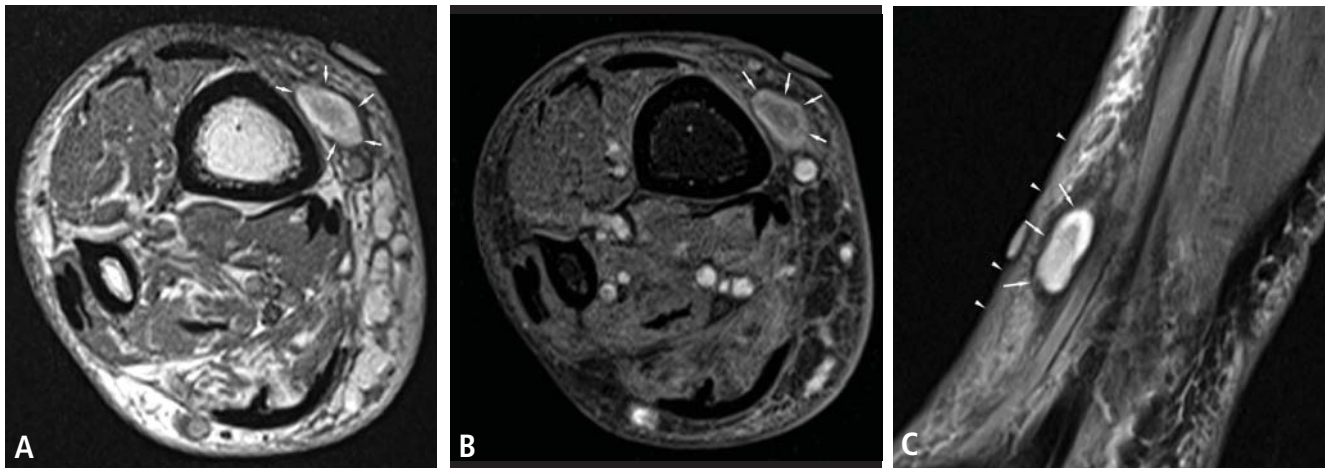


FIGURE 3. MRI findings in an 85-year-old man with a palpable right leg mass. **(A)** T1-weighted axial image shows a mass with increased signal (arrows) consistent with subacute blood products. **(B)** Post-contrast T1-weighted fat-suppressed axial image shows peripheral enhancement typical of a hematoma (arrows). **(C)** T2-weighted image in the sagittal plane demonstrates edema-like signal surrounding the hematoma (arrowheads).



FIGURE 4. CT of a 74-year-old man with a palpable mass along the sternum reveals a destructive mass with soft extension and chondroid-appearing calcifications (arrows) typical of a chondrosarcoma.

tages are a lack of ionizing radiation and dynamic imaging capabilities. Doppler ultrasonography allows direct visualization of tumor vascularity, which may be important for diagnosis and presurgical planning. Unfortunately, bone lesions cannot be evaluated with ultrasonography, owing to the inability of sound waves to penetrate the bony cortex. Poor sound wave penetration may prevent visualization of deep-seated lesions, such as retroperitoneal sarcomas.

Ultrasonography is best used for differentiating solid masses from cystic structures and can provide image guidance in solid tumor biopsy and cyst aspiration. It also may play a role in detecting suspected tumor recurrence in patients in whom artifact from implanted hardware precludes cross-sectional imaging, and it can be reliably used for following up unequivocal soft-tissue masses such as ganglia near joints.

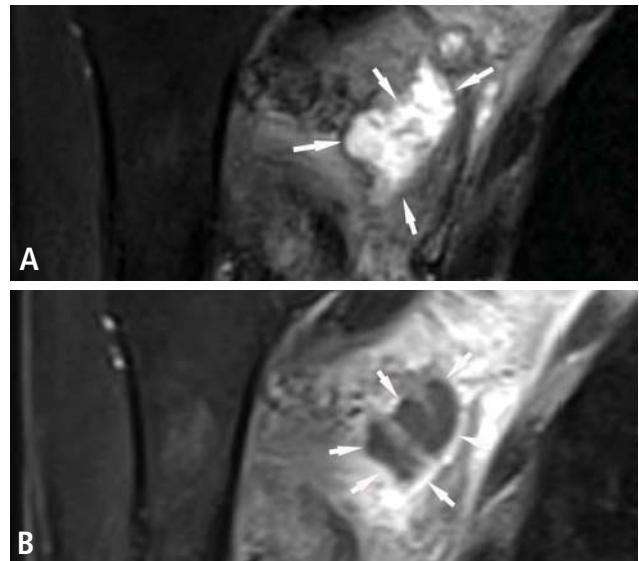


FIGURE 5. Follow-up MRIs in an 84-year-old man who had previously undergone surgical resection and radiation therapy for high-grade axillary sarcoma. **(A)** T2-weighted fat-saturated coronal image shows a mass-like structure with heterogeneous signal in the surgical bed (arrows). **(B)** Post-contrast image shows no internal enhancement typical of a postoperative hematoma or seroma. Note the diffuse surrounding edema and enhancement in the axillary area (arrows), which is related to the patient's prior radiation treatment.

■ POSITRON EMISSION TOMOGRAPHY

Positron emission tomography (PET) is a functional imaging technique that allows evaluation of tumor or physiologic tissue metabolism *in vivo* with positron-emitting radionuclides. [¹⁸F]2-Deoxy-2-fluoro-D-glucose (FDG), the most commonly used radiolabeled tracer for PET imaging, demonstrates increased accumulation in several different types of benign and malignant neoplasms. PET/CT scanning of lesions offers a combination of concur-

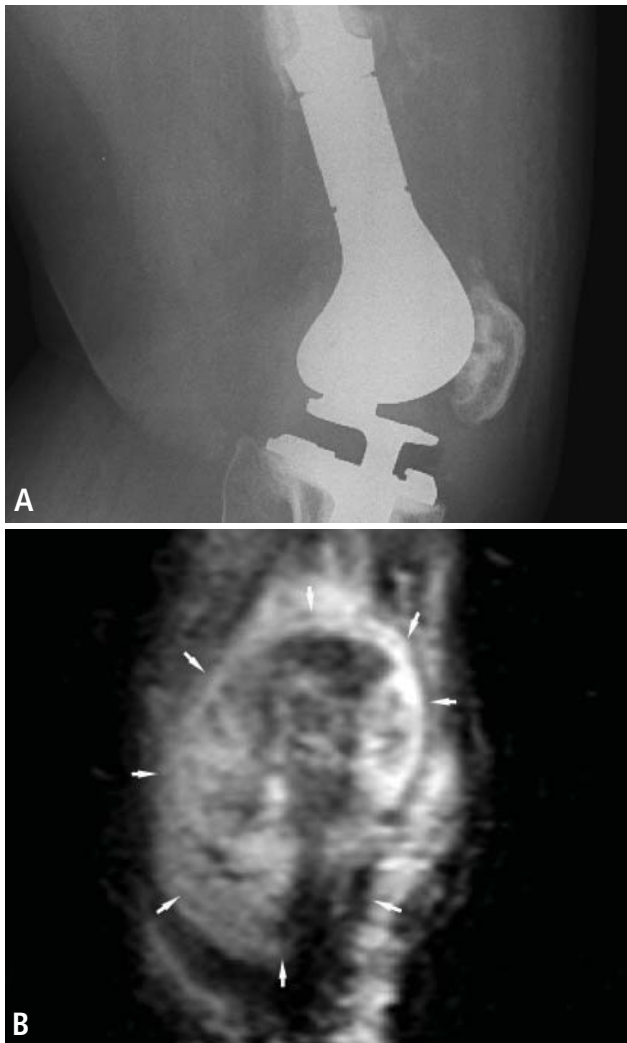


FIGURE 6. MRIs in a 36-year-old man presenting with an enlarging soft-tissue mass after a history of osteosarcoma resection 2 years earlier. **(A)** Lateral view of the knee shows surgical hardware and faint soft-tissue mineralization anteriorly. **(B)** Coronal short-tau inversion recovery (STIR) sequence demonstrates a large soft-tissue mass with heterogeneous signal (arrows) consistent with tumor recurrence.

rent anatomical and functional imaging findings (**Figure 7A**), and PET/CT scanner sales now account for more than 80% of the PET scanner market.¹⁸ In the setting of sarcoma, FDG-PET is useful for detection of local recurrence and metastatic disease¹⁹ as well as for evaluation of response to neoadjuvant chemotherapy.²⁰ Some initial studies have examined the ability of ¹⁸F-FDG-PET to differentiate between benign and malignant bone and soft-tissue tumors,²¹ which has been controversial because of the considerable number of false-positive and false-negative interpretations of lesions.¹⁹ In addition to benign tumors, non-neoplastic findings such as fractures (**Figure 7**), sarcoid, synovial chondromatosis, pigmented villonodular synovitis, and infection may demonstrate the

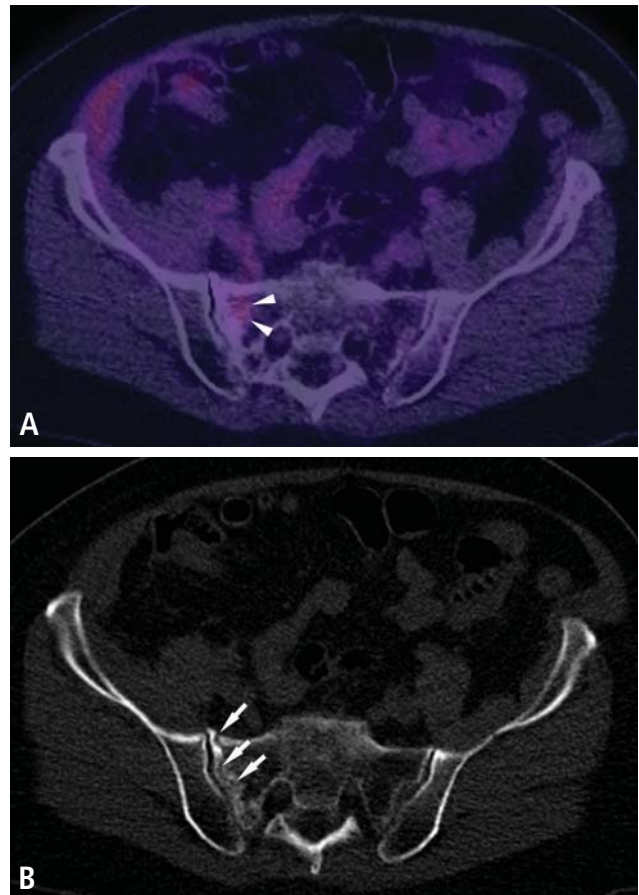


FIGURE 7. **(A)** PET/CT scan in a 67-year-old man with a history of spindle-cell sarcoma of the groin showing increased metabolic activity in the right sacral area (arrowheads) suspicious for metastasis. **(B)** CT scan in bone windows from the same examination reveals an insufficiency-type fracture (arrows) with no evidence of a destructive tumor.

maximum standardized uptake value (SUV_{max}) levels that are characteristic of malignant tumors.¹⁹

IMAGING-GUIDED INTERVENTIONS

Percutaneous imaging-guided procedures have increasingly replaced open surgical biopsies for bone and soft-tissue tumors. CT guidance is commonly used for percutaneous biopsy, whereas ultrasonographic guidance is sometimes used for superficial soft-tissue lesions. Although the shortest and most direct approach is desirable, this may not be possible in all cases due to the presence of nearby vital structures or the risk of contamination. Seeding of malignant cells along the biopsy tract is a well-known possible complication of image-guided biopsies, and en bloc resection of the needle tract is typically performed at the definitive surgery.

Knowledge of compartmental anatomy is paramount in planning the approach for these biopsies, and consultation with the referring orthopedic surgeon is recommended for optimal management. Expert histopathological interpretation of bone and soft-tissue specimens is essential for the

efficacy and high success rates of percutaneous imaging-guided biopsies. Such expertise is integral to the broader interdisciplinary collaboration that is needed to arrive at the most plausible diagnosis, especially in the setting of uncommon or atypical neoplasms.

Currently, MRI-guided interventions are in the initial stage of evolution and could provide valuable guidance for subtle marrow or soft-tissue lesions visible on MRI but not well seen on CT.²² In the future, MRI could play an increasingly important role in imaging-guided procedures because of its lack of ionizing radiation and its ability to demonstrate subtle soft-tissue and bone marrow changes. Imaging-guided therapeutics are growing in their applications in musculoskeletal oncology. CT-guided radiofrequency ablation and cryoablation have been used in the treatment of a variety of tumors²³ as well as in the palliation of metastatic bone pain.²⁴

SUMMARY AND CONCLUSION

Bone and soft-tissue sarcomas are rare neoplasms with variable clinical presentations. A high index of suspicion is required for any unexplained mass with indeterminate imaging findings. Recent advances in imaging technology, including cross-sectional MRI and CT, have significantly refined the diagnosis and management of bone and soft-tissue sarcomas. When faced with a possible sarcoma, the clinician's selection of imaging modalities has a direct impact on diagnosis, staging, and patient management.

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