Staging of Bone Tumors: A Review with Illustrative Examples

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OBJECTIVE. The radiologist plays an important role in the workup and staging of bone tumors. The purpose of this article is to review that role and to discuss recent changes to the primary malignant bone tumor staging system developed by the American Joint Committee on Cancer.

CONCLUSION. Knowledge of staging parameters for the diagnosis and management of bone tumors will help the radiologist to generate meaningful reports for the referring physician.

Keywords: bone cancer, musculoskeletal imaging, musculoskeletal system, oncologic imaging

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Two systems are currently used for staging malignant primary bone tumors: the Musculoskeletal Tumor Society (MSTS) system and the American Joint Committee on Cancer (AJCC) system. Recent revisions to the AJCC system have received little attention in the radiology literature. We review the importance of proper selection of the appropriate imaging techniques for the evaluation of a patient with a suspected benign or malignant bone tumor and describe the radiologist's role in staging primary bone neoplasms, emphasizing recent changes to the AJCC system.

The Initial Evaluation of a Bone Lesion

A patient may seek treatment for a bone lesion because it is painful, it is associated with a palpable mass, it is associated with a pathologic fracture, or it is discovered incidentally on an imaging study. The *Appropriateness Criteria* [1], established by the American College of Radiology, dictate that for the initial evaluation of a bone lesion, radiographs should be the first line of imaging (Table 1). Not only are radiographs relatively inexpensive, but the differential diagnosis of most primary bone tumors is generated based on features detected on radiographs [2, 3]. Such features suggest either benignity or malignancy and allow one to decide whether additional imaging examinations, if any, should be performed. The next imaging step generally depends on one of four clinical conditions: first, the radiograph shows normal findings, but the patient has persistent symptoms; second, the radiograph reveals abnormal findings and the clinician suspects metastatic disease or multiple myeloma on the basis of the patient's history, laboratory values, or both; third, the radiograph depicts abnormal findings, showing a nonaggressive-appearing tumor; or, fourth, the radiograph reveals abnormal findings, showing an aggressive-appearing primary bone tumor. An important role of the radiologist is to assist the clinician to ensure that imaging is performed in an appropriate manner.

Lytic bone lesions are often not detectable on standard radiographs until the tumor has resulted in 30–50% loss of mineralization [4]. If the radiograph shows normal or indeterminate findings, but the patient has persistent localized symptoms, additional imaging studies are frequently required. MRI is the preferred imaging technique in this setting [1]. It is the most sensitive technique for detecting marrow-based lesions, and the anatomic detail seen on MRI is superior to that of radionuclide studies [5]. In addition, MRI may offer a specific diagnosis other than that of a bone tumor (e.g., occult fracture, osteonecrosis), whereas this is often not possible with skeletal scintigraphy. If the patient's pain is not localized, then a nuclear medicine bone scan may be indicated as a screening test for evaluating the entire skeleton.

A lesion seen on a radiograph may represent a focus of metastatic disease from a known or unknown primary tumor, particularly in older patients. In the setting of a known primary tumor, radionuclide bone scanning is the primary imaging examina-

TABLE 1: Summary of Appropriate Radiologic Examination Procedures for Evaluation of Bone Tumors

Clinical Condition	Radiologic Examination Procedure and Appropriateness Rating			
	Routine Radiography	MRI	Nuclear Medicine Bone Scanning	CT
Screening, first study	9: Absolute requirement	1	1	1
Persistent symptoms, but radiograph negative		9: Contrast may be useful: depends on expertise and institutional preference	4: Good option if patient cannot have MRI; nonspecific (MRI more specific and sensitive)	3: If MRI not available; useful to evaluate cortex and trabecular pattern
Definitely benign on radiographs[a]		1	1	1
Clinically suspected osteoid osteoma	9: Necessary; follow up with CT if positive	6: CT is more useful but diagnosis can often be made with MRI; contrast may improve nidus identification	6: Very sensitive but nonspecific; good for localization if lesion is occult radiographically	9: Contrast not needed
Suspicious for malignant characteristics on radiographs		9: Contrast can provide more information; useful for vascularity and necrotic areas	3: Probably not indicated except to look for additional lesions	5: May be useful if MRI not available or possible; useful for evaluation of calcification, cortical breakthrough, and pathologic fractures

Note—Modified from the *American College of Radiology Appropriateness Criteria for Bone Tumors* [1]. The appropriateness rating ranges from 1 (least appropriate) to 9 (most appropriate).

[a]Additional studies (MRI or CT) may be needed if surgical intervention is contemplated and further anatomic information is required.

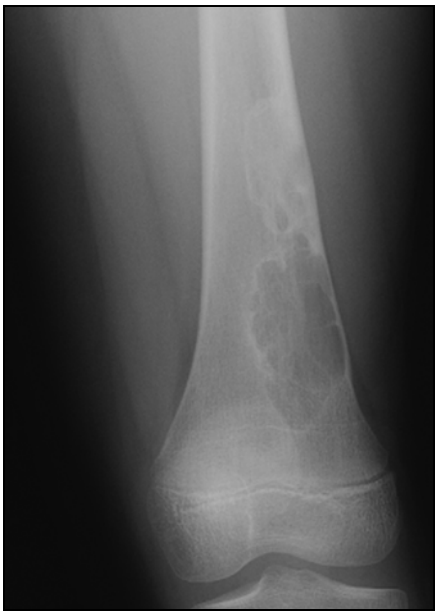


Fig. 1—11-year-old girl with fibroxanthoma (i.e., nonossifying fibroma). Note benign characteristics of lesion: narrow zone of transition, intact cortex, lack of periostitis, and lack of soft-tissue mass.

tion used to detect osseous metastases [6]. Patients presenting with a bone lesion on a radiograph who do not have a known primary tumor but are suspected of having metastatic disease based on data acquired through history and physical examination may also undergo bone scintigraphy to confirm whether there are multiple foci [7]. Additional imaging studies may be warranted in these cases to locate a primary tumor, including CT of the chest and abdomen, primarily to search for lung or renal carcinomas [8]. Mammography may be considered in women. Laboratory studies are also often performed, including a test to determine the prostate-specific antigen level in men. Protein electrophoresis is recommended to detect myeloma, in which case a radiographic skeletal survey is indicated for staging [9].

Solitary primary tumors and tumorlike lesions of bone are commonly encountered by radiologists. The radiologist should attempt to classify the lesion as either nonaggressive or aggressive on the basis of its radiographic characteristics. Nonaggressive characteristics include a narrow zone of transition between the lesion and the surrounding normal bone, an intact (although possibly thinned) cortex, mature periostitis, and lack of an associated soft-tissue mass [10] (Fig. 1). Such lesions are usually benign. If the radiograph shows a nonaggressive bone tumor, additional imaging studies may be required depending on the biologic behavior of the lesion suggested by the radiographic findings and the potential need for operative intervention. Chondroblastomas, for example, typically have a nonaggressive, benign appearance on radiographs; however, these le-

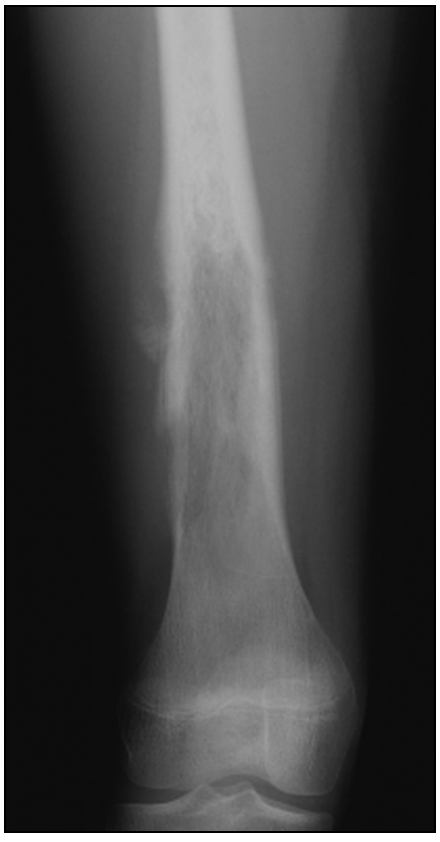


Fig. 2—12-year-old girl with osteosarcoma. Note malignant characteristics of lesion: wide zone of transition, aggressive periostitis, and soft-tissue extension.

sions show progressive growth and will need to be removed. MRI is usually the study of choice in these instances [11, 12] because it will often show marrow and soft-tissue involvement better than CT. CT remains of value, however, in assessing suspected cartilaginous neoplasms for the presence of intralesion mineralization and degree of cortical erosion. A staging system of benign bone tumors is described later in this article.

Radiographic characteristics of an aggressive bone lesion include a wide zone of transition between the tumor and the surrounding normal bone, cortical destruction, aggressive-appearing periosteal new bone formation (e.g., onionskin or sunburst appearance), and an associated soft-tissue mass (Fig. 2). Lesions with aggressive radiologic characteristics are often malignant, although certain benign entities, such as osteomyelitis and giant cell tumor, can also appear aggressive. These aggressive-appearing benign entities may be associated with additional radiographic or clinical features that will support the diagnosis of a nonmalignant lesion. For example, there is a good chance that a nonmineralized radiolucent metaepiphyseal lesion in a young adult that extends to the articular surface of the affected bone is a giant cell tumor, even if the margins of the lesion are poorly defined and there is limited cortical destruction. Similarly, an aggressive-appearing lesion with a central sequestrum in an IV drug abuser likely represents osteomyelitis. If there are no additional features to support benignity, however, then an aggressive-appearing lesion should be considered malignant until proven otherwise. If a malignant tumor is suspected, additional imaging is required. In most cases, MRI is the best imaging technique for local staging because it best shows features important for staging.

Although MRI is currently the best imaging technique for detecting marrow-based disease and for delineating the osseous and soft-tissue extent of a bone tumor, it is not as useful as conventional radiography for characterizing the aggressiveness of most bone lesions [1–3]; however, it may occasionally help with the histologic diagnosis in certain situations (e.g., aneurysmal bone cyst, intraosseous lipoma). CT may be preferred over MRI for the evaluation of cortical involvement or cortically based lesions, such as osteoid osteoma, periosteal reaction, matrix mineralization, and lesions in flat bones. Furthermore, MDCT, with its multiplanar capability, is a reasonable substitute for those patients who cannot undergo MRI and can provide exquisite 3D reformations for volumetric and preoperative assessment [13].

Staging of Primary Bone Tumors

Malignant Neoplasms

In 1980, Enneking et al. [14] described a system for staging bone sarcomas that was adopted by the MSTS. Staging with the Enneking system is based on three criteria. The first criterion is that of the extent of the tumor: The tumor is designated T1 if it remains confined to a single anatomic compartment (intracompartmental) and is designated T2 if it spreads into an additional compartment or compartments (extracompartmental). The second criterion is that of metastasis: The tumor is designated M0 if there are no metastases and is designated M1 if there are either regional or distant metastases. The third criterion is that of the grade of the tumor, which is a histologic assessment of cellular atypia and is related to the tumor's tendency to metastasize. The estimated metastatic risk of low-grade (G1) tumors is less than 25%, whereas that of high-grade (G2) tumors is greater than 25%. This staging system is summarized in Table 2.

TABLE 2: Enneking Staging System [14] for Primary Malignant Tumors of Bone

Stage	Tumor	Metastases	Grade
IA	T1	M0	G1
IB	T2	M0	G1
IIA	T1	M0	G2
IIB	T2	M0	G2
III	T1 or T2	M1	G1 or G2

Note—T1 = tumor is intracompartmental, T2 = tumor is extracompartmental, M0 = no regional or distant metastasis, M1 = regional or distant metastasis, G1 = low grade, G2 = high grade.

In 1983, the AJCC [15, 16] developed a slightly different system for the staging of malignant bone tumors. Until recently, staging with the AJCC system was based on the following four criteria: first, the extent of the primary tumor, either confined by bone cortex (T1) or extending through cortex (T2); second, the absence (N0) or presence (N1) of regional lymph node metastases; third, the absence (M0) or presence (M1) of distant metastases; and, fourth, the histologic grade of the tumor. Low-grade tumors were designated either G1 (well differentiated) or G2 (moderately differentiated), whereas high-grade tumors were designated either G3 (poorly differentiated) or G4 (undifferentiated). Low-grade lesions generally are associated with a better prognosis than high-grade lesions. This staging system is summarized in Table 3. Note that this system did not have a defined stage III.

The AJCC system was recently revised [17], and for cases diagnosed beginning January 1, 2003, the extent (T) of the tumor now reflects the size of the tumor rather than its transcortical extension. Tumors 8 cm or less in the greatest dimension are designated T1, whereas those greater than 8 cm are designated T2. Patients with small tumors generally have a better prognosis than those with large tumors. A new designation, T3, has been added to indicate skip metastases—that

TABLE 3: American Joint Committee on Cancer Staging System for Primary Malignant Tumors of Bone Before 2003 [16]

Stage	Tumor	Lymph Node	Metastases	Grade
IA	T1	N0	M0	G1 or G2
IB	T2	N0	M0	G1 or G2
IIA	T1	N0	M0	G3 or G4
IIB	T2	N0	M0	G3 or G4
III				Not defined
IVA	Any T	N1	M0	Any G
IVB	Any T	Any N	M1	Any G

Note—T1 = tumor confined to cortex, T2 = tumor extends beyond cortex; N0 = no regional lymph node metastasis, N1 = regional lymph node metastasis; M0 = no distant metastasis, M1 = distant metastasis; and G1 = well differentiated (low grade), G2 = moderately differentiated (low grade), G3 = poorly differentiated (high grade), G4 = undifferentiated (high grade).

TABLE 4: American Joint Committee on Cancer Staging System for Primary Malignant Tumors of Bone for Those Tumors Diagnosed on or After January 1, 2003 [17]

Stage	Tumor	Lymph Node	Metastases	Grade
IA	T1	N0	M0	G1 or G2
IB	T2	N0	M0	G1 or G2
IIA	T1	N0	M0	G3 or G4
IIB	T2	N0	M0	G3 or G4
III	T3	N0	M0	Any G
IVA	Any T	N0	M1a	Any G
IVB	Any T	N1	Any M	Any G
IVB	Any T	Any N	M1b	Any G

Note—Tx = primary tumor cannot be assessed, T0 = no evidence of primary tumor, T1 = tumor 8 cm or less in greatest dimension; T2 = tumor more than 8 cm in greatest dimension, T3 = discontinuous tumors in the primary bone; Nx = regional lymph nodes not assessed, N0 = no regional lymph node metastases, N1 = regional lymph node metastasis; Mx = distant metastasis cannot be assessed, M0 = no distant metastasis, M1 = distant metastasis, M1a = lung, M1b = other distant sites; and Gx = grade cannot be assessed, G1 = well differentiated (low grade), G2 = moderately differentiated (low grade), G3 = poorly differentiated high grade), G4 = undifferentiated (high grade).

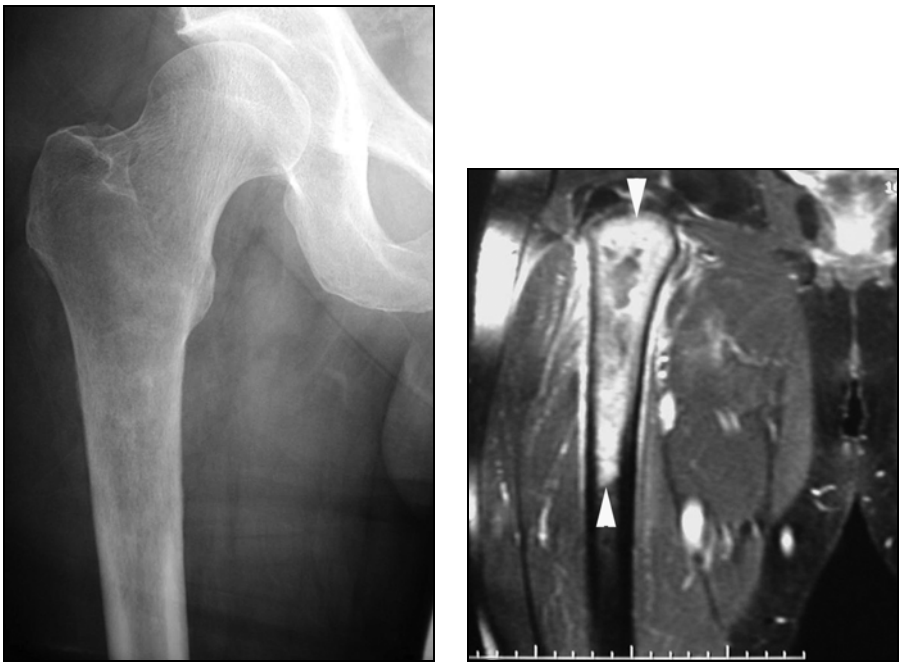


Fig. 3—58-year-old man with osteosarcoma.
A, Radiograph shows poorly defined radiolucency in proximal femoral diaphysis. Accurate measurement of lesion length is not possible.
B, Fat-suppressed T2-weighted coronal MR image of proximal femur better reveals extent of lesion (*arrowheads*), which is well over 8 cm in length. This finding would be classified as T2 using revised American Joint Committee on Cancer staging system [17].

is, discontinuous tumors in the primary bone site. Furthermore, M1 has been subdivided into M1a (lung-only metastases) and M1b (metastases to other distant sites, including distant lymph nodes). Lung-only metastases, particularly a solitary pulmonary metastasis, appear to convey a better prognosis than osseous or hepatic metastases. This new AJCC staging system is summarized in Table 4. Note that there is now a defined stage III, representing a tumor without regional nodal (N0) or distant (M0) metastases, but with a skip metastasis (T3) in the affected bone. For high-grade tumors such as osteosarcoma, a skip lesion portends a poor prognosis. Determining the effect on survival of multifocal low-grade lesions, such as low-grade chondrosarcomas or low-grade vascular tumors, has proven to be more difficult [18]. This AJCC staging system does not apply to primary malignant lymphoma of bone or multiple myeloma, but is used for all other primary malignant tumors of bone (e.g., osteosarcoma, Ewing's sarcoma).

In addition to providing assistance to the clinician to ensure that imaging is performed in an appropriate manner, the radiologist has a role in evaluating each of the parameters of the bone sarcoma staging systems. For example, when assessing the primary tumor (T), reporting the size of the neoplasm, particularly its greatest dimension, is important for staging using the revised AJCC system. As stated previously, MRI is best for evaluating tumor extent and therefore the size of the primary tumor [19–21], particularly if one cannot discern on radiographs whether the tumor is greater than 8 cm in greatest dimension (Fig. 3).

On the other hand, the Enneking system does not consider the actual size tumor size, but rather whether the tumor is intra- or extracompartmental. Intracompartmental tumors are those that are entirely intraosseous or parosseous without intraosseous or extrafascial extension (Figs. 4 and 5). Extracompartmental tumors are those that are intraosseous with soft-tissue extension or parosseous with intraosseous or extrafascial extension (Figs. 6 and 7). Identification of skip metastases is also important. Hence, we recommend that the MRI protocol contain at least one coronal or sagittal sequence with a large field of view that includes the entire affected bone to search for skip metastases (Fig. 8). We use STIR images for this purpose at our institution, but others prefer using T1-weighted images; we are unaware of any prospective study comparing the relative sensitivity and specificity of T1-weighted versus STIR images for the diagnosis of skip metastases.

We prefer MRI to bone scintigraphy for the evaluation of potential skip metastases

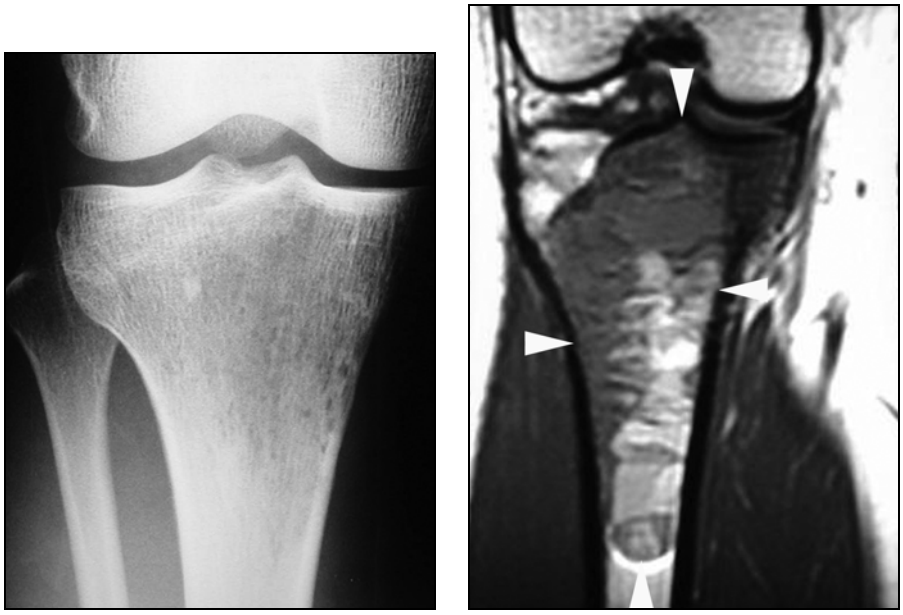


Fig. 4—24-year-old woman with telangiectatic osteosarcoma.
A, Radiograph shows poorly defined radiolucency in proximal tibia.
B, T1-weighted coronal MR image shows hemorrhagic tumor (*arrowheads*) in proximal tibia without soft-tissue extension, making it intracompartmental; it would be classified as T1 using Enneking staging system [14]. Tumor is greater than 8 cm in length and would be classified as T2 using revised American Joint Committee on Cancer staging system [17].

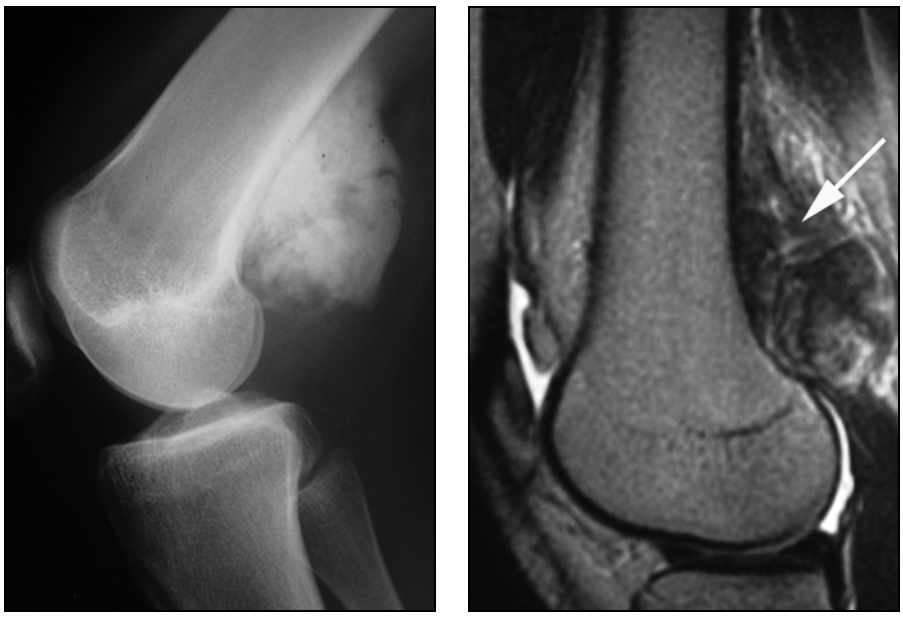


Fig. 5—20-year-old woman with parosteal osteosarcoma.
A, Radiograph shows ossified mass along posterior aspect of distal femoral metadiaphysis.
B, T2-weighted sagittal MR image shows low-signal-intensity mass (*arrow*) abutting posterior surface of distal femur. No intramedullary invasion is evident. This finding would be considered intracompartmental and classified as T1 using Enneking staging system [14].

because skip lesions that are close to the primary tumor may not be easily resolved with bone scintigraphy. The remaining MRI sequences should use a surface coil and the smallest field of view possible that includes the entire lesion; this provides optimal visualization of soft-tissue extension, including potential neurovascular and joint involvement. A sample MRI protocol for assessing the primary tumor, therefore, would include, first, a large field-of-view coronal or sagittal sequence covering the entire bone and, second, several additional sequences with a small field of view to cover the primary tumor in its entirety—for example, T1- and fat-suppressed T2-weighted sequences performed in the axial plane and T1- and fat-suppressed T2-weighted sequences performed in at least one orthogonal plane.

As a general rule, IV gadolinium administration is of limited value in the evaluation of primary bone tumors because the contrast between the tumor and normal marrow is sufficient without it [22–24]. Occasionally, however, gadolinium will allow one to better identify areas of solid tumor amid necrosis and hemorrhage, which is important for biopsy planning, and joint involvement. Some investigators have shown encouraging results using dynamic postgadolinium imaging to distinguish tumor from reactive edema after chemotherapy and residual tumor from nontumor tissue postoperatively [25–29]; however, this technique currently does not have a role in the initial staging of the tumor.

Lymphadenopathy accompanying primary bone sarcomas is rare, and a dedicated search for lymph node spread is thus rarely undertaken. However, after assessing the primary tumor using an MRI or CT examination, the radiologist should not forget to use the same study to search for any regional lymphadenopathy that would upstage the disease from N0 to N1. The lung is the most common site of distant metastasis from a primary bone sarcoma, and CT is currently the technique of choice for the detection of pulmonary metastases [15, 30] (Fig. 9). Bone metastases are uncommon at initial presentation of patients with primary bone sarcomas. However, the presence of osteosarcoma metastasis may affect treatment; therefore, skeletal scintigraphy is recommended for patients with osteosarcoma [31, 32] (Fig. 10). Identification of metastases would group the patient into stage III using the Enneking system and into stage IVa (lung-only metastases, M1a) or stage IVb (other distant metastases, M1b) us-

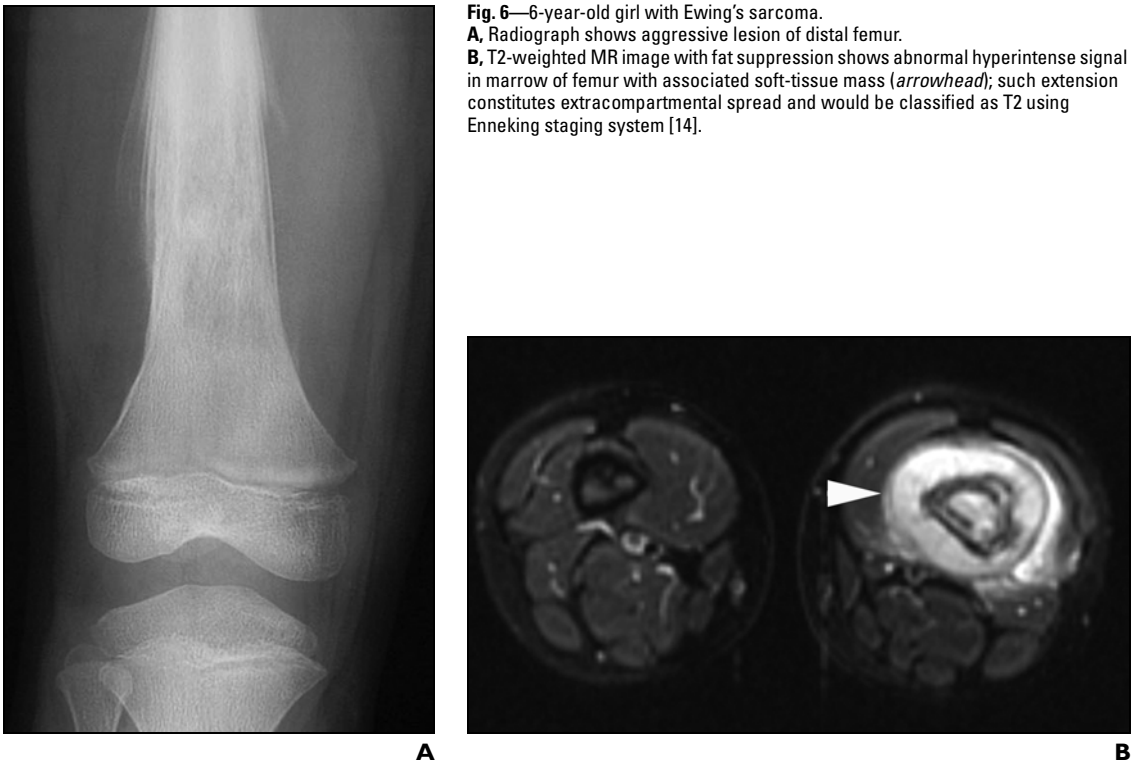


Fig. 6—6-year-old girl with Ewing's sarcoma.
A, Radiograph shows aggressive lesion of distal femur.
B, T2-weighted MR image with fat suppression shows abnormal hyperintense signal in marrow of femur with associated soft-tissue mass (*arrowhead*); such extension constitutes extracompartmental spread and would be classified as T2 using Enneking staging system [14].

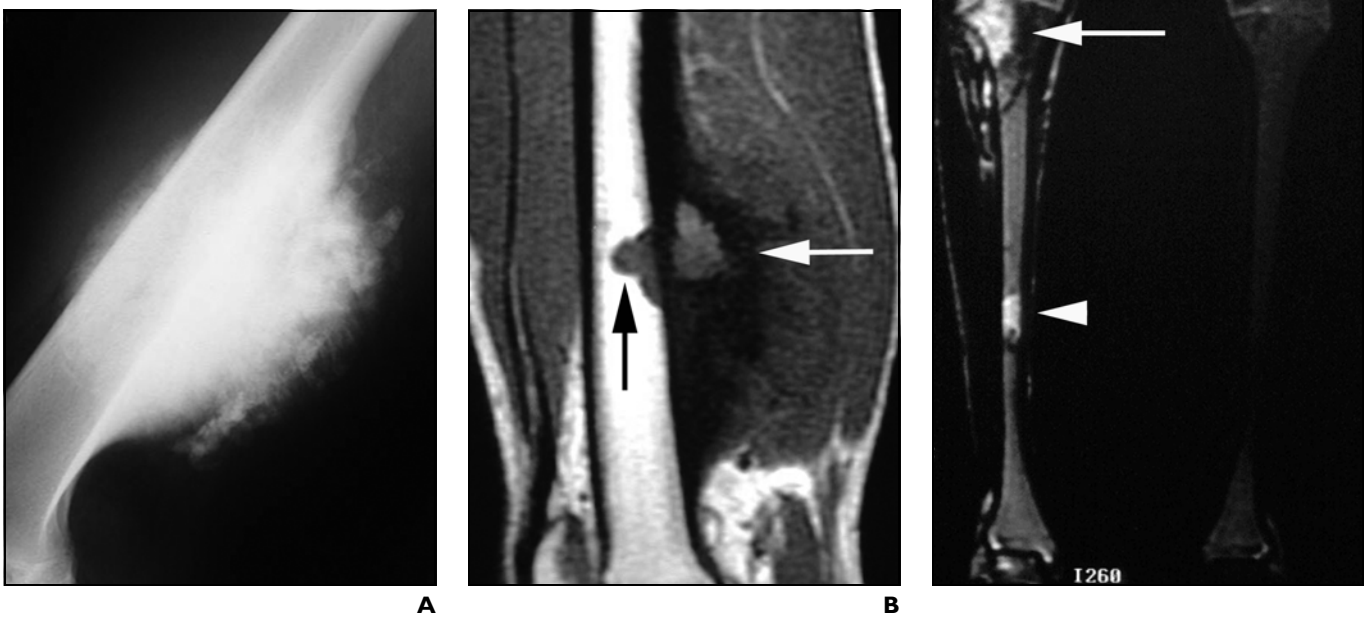
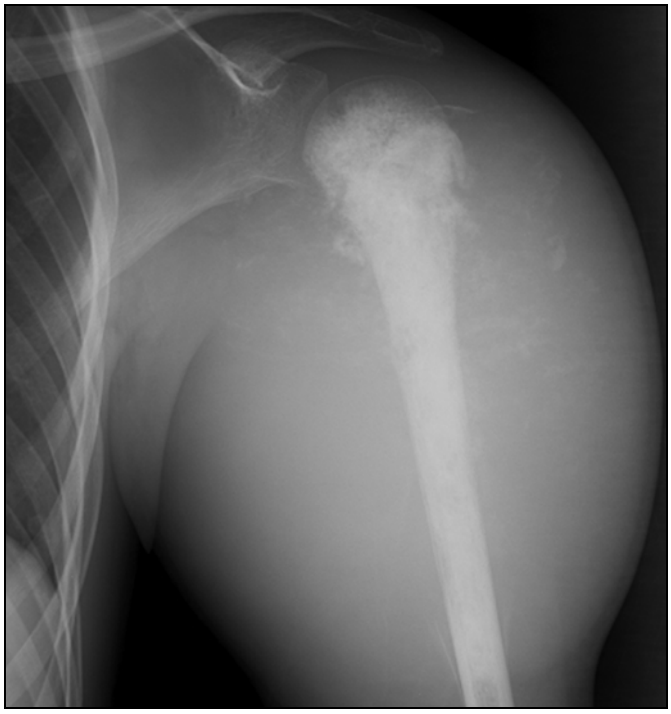


Fig. 7—16-year-old boy with parosteal osteosarcoma.
A, Radiograph shows ossified mass along distal femoral diaphysis.
B, T1-weighted sagittal MR image shows tumor abutting posterior surface of distal femur (*white arrow*) with extension into medullary cavity (*black arrow*); such extension constitutes extracompartmental spread and would be classified as T2 using Enneking staging system [14].

Fig. 8—16-year-old boy with osteosarcoma. Fat-suppressed T2-weighted coronal image with wide field of view shows primary tumor in proximal tibia (*arrow*). Note skip metastasis (*arrowhead*) in tibial diaphysis distally. This finding would be classified as T3 using revised American Joint Committee on Cancer staging system [17].



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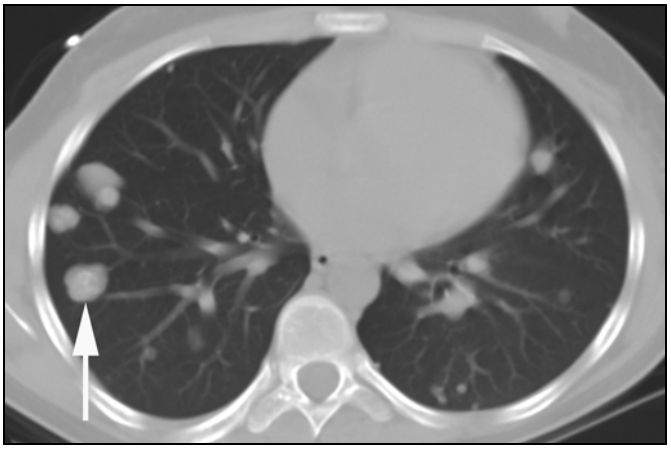

B

Fig. 9—17-year-old boy with metastatic osteosarcoma.
A, Arm radiograph shows osteosarcoma of proximal humerus with large soft-tissue mass.
B, Axial CT image through thorax shows multiple pulmonary metastases, some with mineralization (*arrow*).

ing the AJCC system. PET has yet to find a place in the algorithm of primary staging; however, it has shown promise in the evaluation of chemotherapy response and posttreatment evaluation for recurrence and residual tumor [33–35].

The radiologist also plays an important role in imaging-guided biopsies. Obtaining an adequate specimen for microscopic analysis completes the staging process and allows a histologic grade (G) to be assigned. The biopsy should be performed after all imaging studies that might otherwise become compromised by postbiopsy edema and hemorrhage have been obtained. The biopsy should be attempted only after consultation with the surgeon who plans to operate on the tumor because the biopsy track must be excised with the tumor and hence must not contaminate additional compartments, neurovascular structures, or areas that may be used for reconstruction.

Benign Neoplasms

Although not routinely used by radiologists, a staging system for benign bone tumors that is based on the biologic behavior of the tumors as suggested by the radiographic findings has been described by Enneking [36]. Stage 1 tumors are latent benign bone neoplasms that remain static or heal spontaneously. An example of such a lesion is a fibroxanthoma (nonossifying fibroma, Fig. 1). Further radiographic and clinical observation is usually not required, nor is treatment for lesions that are not at risk for or have not undergone fracture.

Stage 2 tumors are active benign bone tumors; their behavior shows progressive growth, but extension is limited by natural barriers. An example of such a lesion is a chondroblastoma (Fig. 11). These tumors are typically treated via curettage, and therefore additional imaging studies may be required preoperatively to assess the tumor extent. MRI is generally the preferred technique for assessing marrow extension, although CT may be warranted in certain instances as described earlier.

Stage 3 tumors are locally invasive benign bone tumors; their behavior shows progressive growth not limited by natural barriers. An example of such a lesion is a giant cell tumor (Fig. 12). These tumors are typically treated via extended curettage or marginal resection with or without adjuvant therapy, and therefore additional imaging is usually required preoperatively. MRI is generally the preferred technique for assessing osseous and soft-tissue extension.

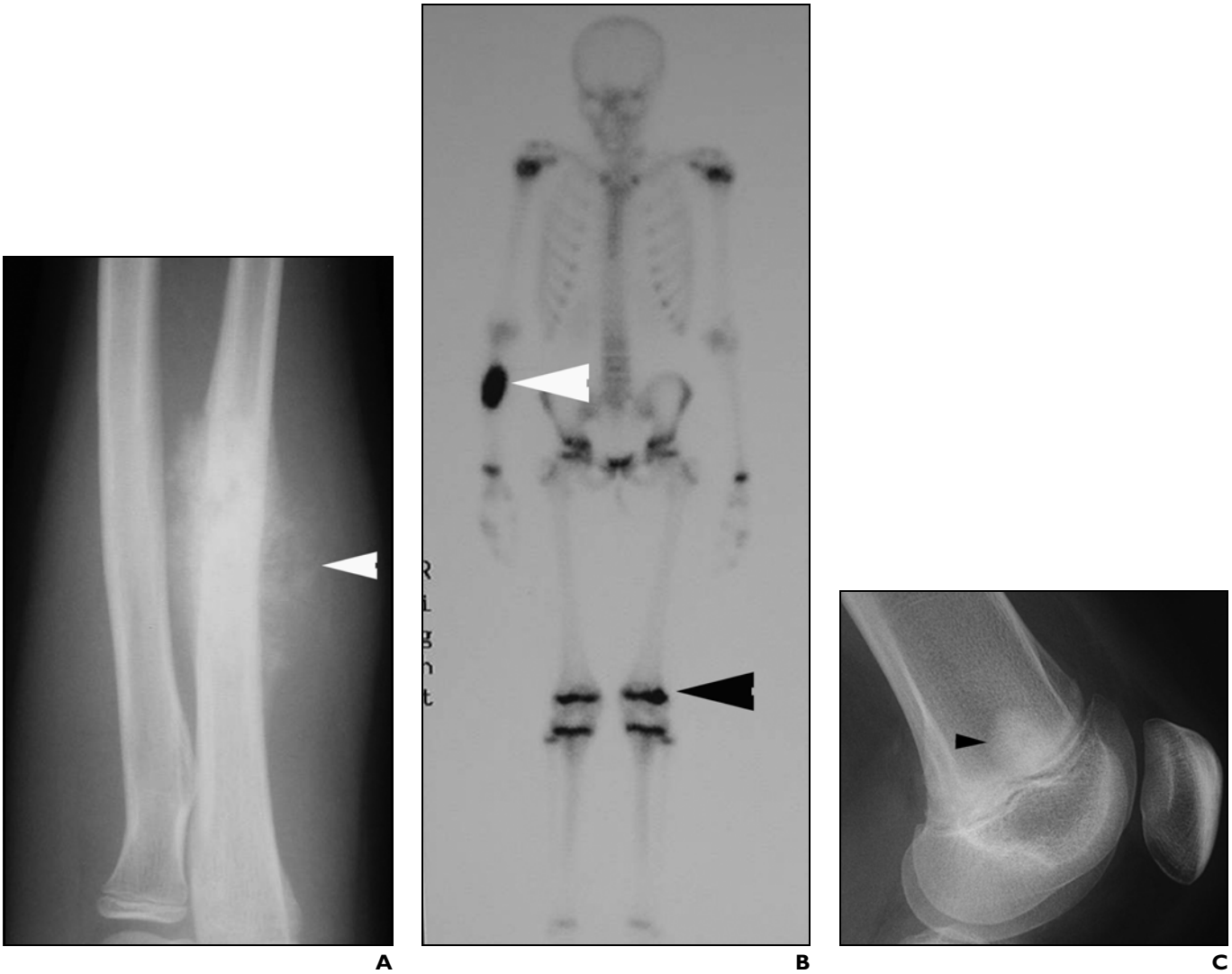

Fig. 10—11-year-old girl with metastatic osteosarcoma.
A, Forearm radiograph shows osteosarcoma of ulnar diaphysis (*arrowhead*).
B, Skeletal scintigram shows increased radiotracer activity in ulnar diaphysis (*white arrowhead*), corresponding to primary tumor, and increased activity in contralateral distal femur (*black arrowhead*) adjacent to physis.
C, Knee radiograph shows histologically confirmed osteosarcoma metastasis (*arrowhead*) in distal femoral metaphysis.

Conclusion

Proper selection of the appropriate imaging techniques for the evaluation of a patient with a suspected bone tumor is crucial for successful diagnosis and management; radiologists should work closely with the orthopedic oncologists for optimal management of patients with primary bone tumors. Recent changes to the AJCC staging system emphasize the importance of tumor size over transcortical extension. Transcompartmental extension, however, remains an important feature of the Enneking system. The new AJCC system also addresses skip metastases. These features, which are important for staging, should be evaluated by the radiologist and mentioned in his or her report. It is not necessary for most radiologists to be intimately familiar with the details of the two staging systems. In fact, if the radiologist is accustomed to producing complete and descriptive reports when evaluating bone tumors, then the recent changes to the AJCC system will probably not affect his or her dic-

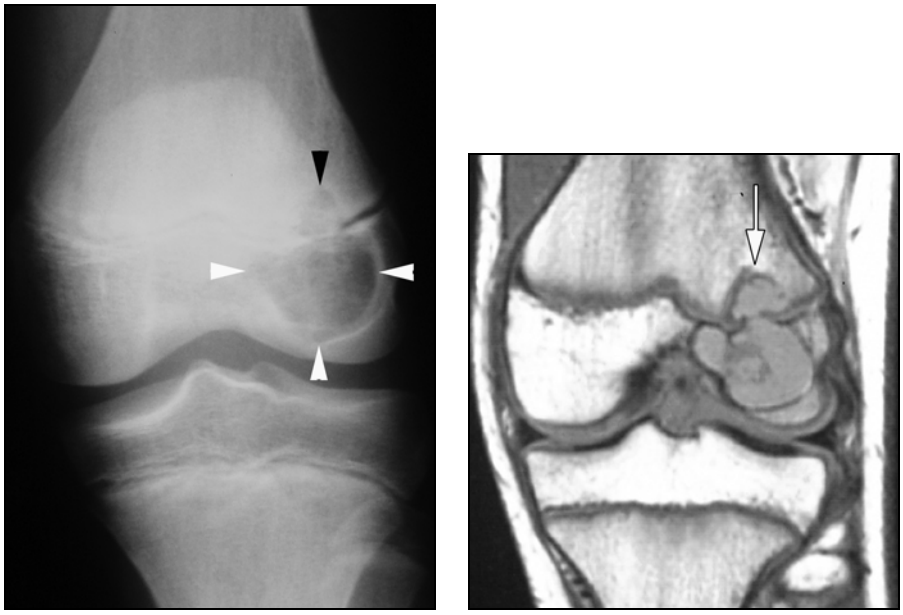

Fig. 11—12-year-old boy with chondroblastoma.
A, Knee radiograph shows radiolucent lesion with sclerotic margins (*white arrowheads*) in epiphysis of distal femur and with probable extension into metaphysis (*black arrowhead*).
B, T1-weighted coronal MR image of knee better depicts transphyseal extension of chondroblastoma (*arrow*).

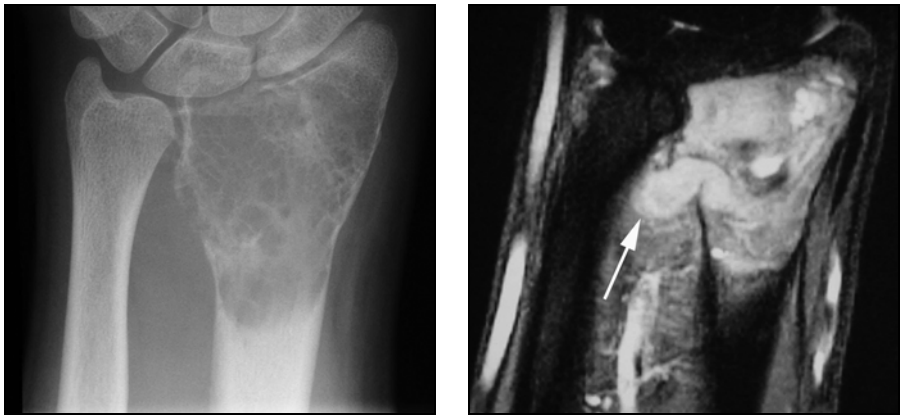

Fig. 12—50-year-old man with giant cell tumor of bone.
A, Wrist radiograph shows slightly expansile radiolucent lesion of distal radius extending to articular surface.
B, Fat-suppressed T1-weighted coronal MR image of wrist after IV administration of gadolinium chelate shows giant cell tumor with soft-tissue extension (*arrow*).

tations. All radiologists, however, should be aware that imaging factors heavily in the staging of bone tumors, and a basic knowledge of bone tumor staging parameters will help the radiologist produce meaningful reports.

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