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ARTICLE

Primary bone tumors of adulthood

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Abstract

Imaging plays a crucial role in the evaluation of primary bone tumors in adults. Initial radiographic evaluation is indicated in all cases with suspected primary bone tumors. Radiographs are useful for providing the diagnosis, a short list of differential diagnosis or at least indicating the degree of aggressiveness of the lesion. More detailed information about the lesion, such as cortical destruction or local spread, can be obtained using cross-sectional imaging techniques such as computed tomography and magnetic resonance imaging. This article discusses the characteristic features of the more common primary bone tumors of adulthood, and also the pre-treatment evaluation and staging of these lesions using imaging techniques.

Keywords: *Bone malignancy; imaging; diagnosis; staging; radiography; magnetic resonance imaging.*

Introduction

The radiologist, together with a multi-disciplinary team including the orthopedic surgeon and oncologist, plays a crucial role in the evaluation of patients with primary bone tumors. The first task that a radiologist is often called upon to do is to provide a diagnosis or differential diagnosis of the lesion based on the radiographic findings. Further evaluation using other imaging techniques such as computed tomography (CT), magnetic resonance (MR) imaging and radionuclide bone scans can help determine the extent of local and distant tumor spread[1]. The stage of the tumor can thus be evaluated and help determine the subsequent management of the patient. The purpose of this article is to discuss the characteristic features of the more common primary bone tumors of adulthood, and to discuss the pre-treatment evaluation and staging of these lesions using imaging techniques.

Imaging techniques

Radiography

Radiographs provide information regarding the location, margins, matrix mineralization, periosteal reaction and aggressiveness of the lesion, and should be analyzed systematically[2,3]. This information, when interpreted together with the patient's clinical information such as age, lesion multiplicity and clinical presentation, provides a differential diagnosis of the lesion. Definitive diagnosis is provided through a biopsy. The information obtained from radiographs helps guide further investigation, if necessary.

CT

In the local evaluation of a primary bone tumor, CT is also useful in assessing cortical involvement and breakthrough. The presence or absence of intratumoral

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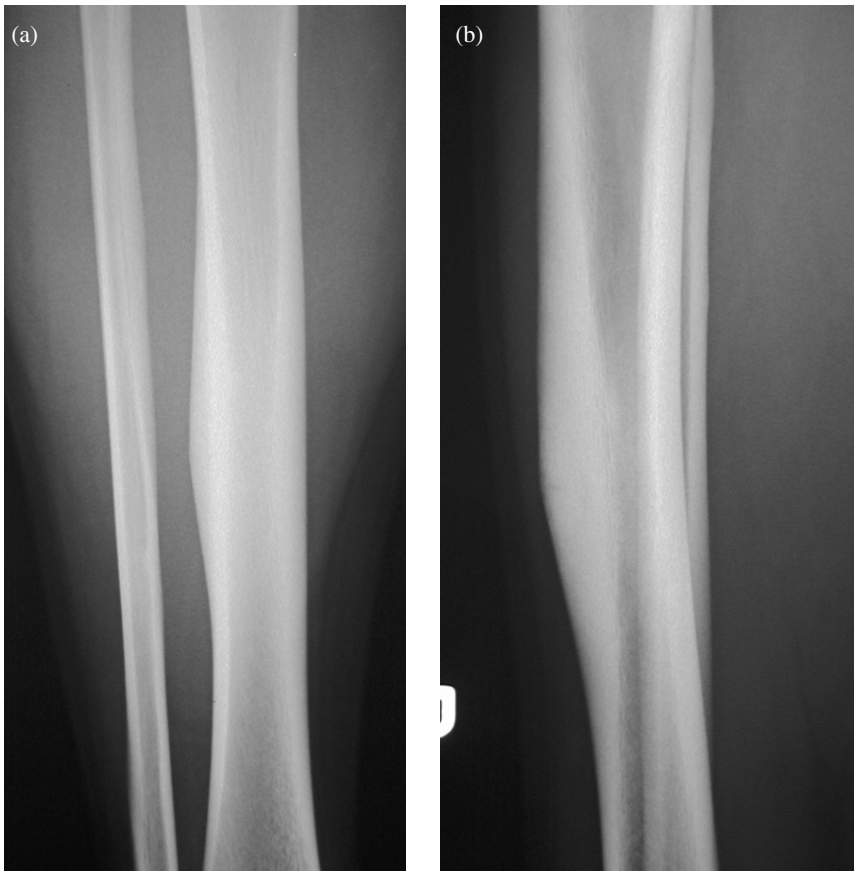

Figure 1 **Osteoid osteoma. (a) Anteroposterior and (b) lateral radiographs of the tibia show florid sclerosis and periosteal new bone formation around the lesion. The central nidus is barely visible.**

calcification or ossification can also be better seen. CT is particularly useful in providing information on tumors in complex-shaped bones such as the spine and pelvis which are not easily evaluated on radiographs[1]. CT is also superior to chest radiographs in evaluation for pulmonary metastases.

MR imaging

On MR imaging, most bone tumors have a similar appearance, being T1 hypointense and T2 hyperintense. If present, hemorrhage, necrosis and calcification/ossification may give the lesion a heterogeneous appearance. The main purpose of MR imaging in the evaluation of a primary malignant bone tumor is to assess the extent of tumor spread. MR imaging is able to detect tumor involvement of the adjacent muscle compartments, neurovascular structures and joints[1].

Bone scintigraphy

Primary bone tumors may metastasize to bones. Technetium (Tc)-99m-labeled diphosphonate scintigraphy is used in the pre-operative staging of bone tumors to evaluate for metastases and skip lesions. When an area of increased tracer uptake is noted on the bone scintiscans, radiographs of that region should be performed to rule out metastases.

Image-guided biopsy

Image-guided biopsy of primary bone tumors is an alternative to open biopsies and has the advantages of being cheaper and less invasive, with a lower complication rate, and has been shown to provide high diagnostic rates similar to open biopsy. Utilization of advanced imaging techniques such as CT and MR imaging aids with the direct site of needle biopsy by identification of high-yielding solid tumor tissue and low-yielding necrotic or hemorrhagic areas. It is important that the biopsy be performed by the most skilled available person working in consultation with the surgeon performing the definitive surgery at a center specializing in the treatment of bone tumors[1].

Specific tumors by age

20–30 years

Osteochondroma

An osteochondroma or exostosis is a cartilage-covered bony protuberance arising from a bone surface. These

lesions are usually discovered during childhood and adolescence but up to 20% are discovered after the age of 20 years. Osteochondromas occur in any bones that arise from enchondral ossification and usually present as non-tender slow growing lesions. Radiographically, osteochondromas appear as bony protuberances arising from the external surface of a long tubular bone. They commonly occur in the metaphyseal regions[4].

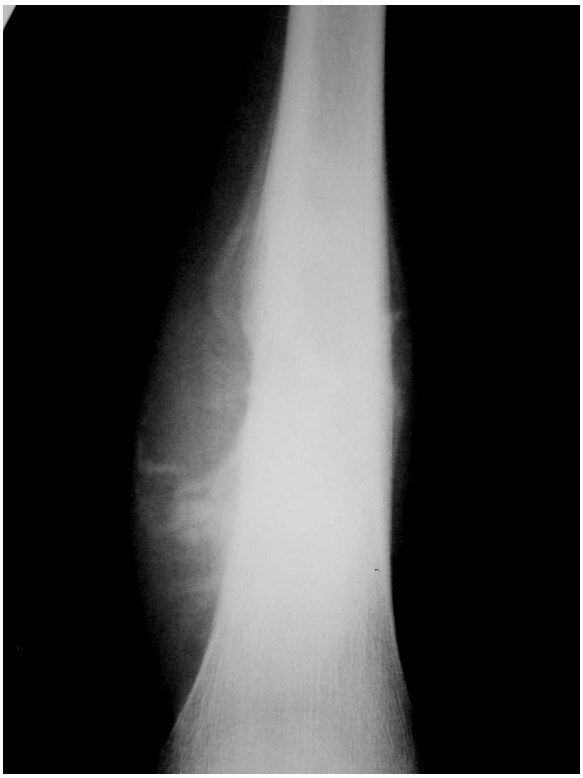

Figure 2 **Conventional osteosarcoma. Anteroposterior radiograph of the femur shows a predominantly osteosclerotic lesion of the distal diaphysis. There is cortical destruction and aggressive periosteal reaction.**

Diaphyseal aclasis is an autosomal dominant disease in which there are multiple exostoses. Clinically, patients present with bony swellings near the joints, short stature or pain due to pressure on adjacent nerve or malignant degeneration of an exostoses.

Enchondroma

Enchondromas are benign cartilage-forming tumors that arise within the medullary cavity of bone. These lesions are usually asymptomatic. Radiographically, they appear as medullary lesions with geographic margins, endosteal scalloping and calcifications[4]. Multiple enchondromas may be part of a syndrome and are predisposed to sarcomatous transformation.

Osteoid osteoma

Osteoid osteomas account for 12% of all benign bone lesions[3]. These lesions are benign osteoblastic lesions with a central area of vascular osteoid tissue and peripheral sclerotic bone (Fig. 1). Classically, a clinical history of pain, worse at night and relieved by aspirin, is elicited. Radiographically, a radiolucent cortically-based nidus measuring less than 2 cm in size with marked surrounding sclerosis is seen. CT can demonstrate these features, including the calcification seen within the nidus, better than other modalities. On MR imaging, the surrounding bone marrow reaction can obscure the nidus and suggest a more aggressive process[4].

Giant cell tumor

Giant cell tumor (GCT) is a locally aggressive tumor that is composed of connective tissue, stromal cells and giant cells. Pain and swelling are the most common presenting complaints. Radiographically, GCT typically involves the metaphysis and epiphyses and extends to the subarticular border. The lesion usually has geographic margins and is eccentrically situated with bony expansion, cortical thinning and erosion. Unlike other bone tumors, the solid portion of GCT may be low-to-intermediate signal on MR imaging due to the presence of hemosiderin, collagen or high cellularity[3].

Osteosarcoma

Osteosarcomas are the second most common primary bone tumors in adults, second to plasma cell myeloma[4]. Osteosarcomas may be classified according to the location of the tumor within the bone (central, intracortical, surface, periosteal, or parosteal), high- or low-grade, histological composition, number of foci and the status of the underlying bone. The most common tumor is conventional osteosarcoma which is usually seen in adolescents or young adults with males being more commonly affected than females.

Conventional osteosarcoma. Conventional osteosarcomas make up 75–85% of all osteosarcomas. These tumors are generally seen in the second and third decades of life. They are usually situated in the metaphyseal region of long bones. Radiographically, these lesions may appear sclerotic, lytic or have a mixed pattern. They typically appear as ill-defined, permeative, lucent medullary lesions. Periosteal reaction appearing as a ‘sunburst’ reaction or Codman’s triangle are also typical[4]. On MR imaging, the lesion is typically low in signal intensity on T1-weighted spin-echo sequences and high in signal intensity on T2-weighted spin-echo sequences. The viable areas show enhancement after the administration of gadolinium. Tumor extension into the surrounding soft tissue is a common occurrence (Fig. 2).

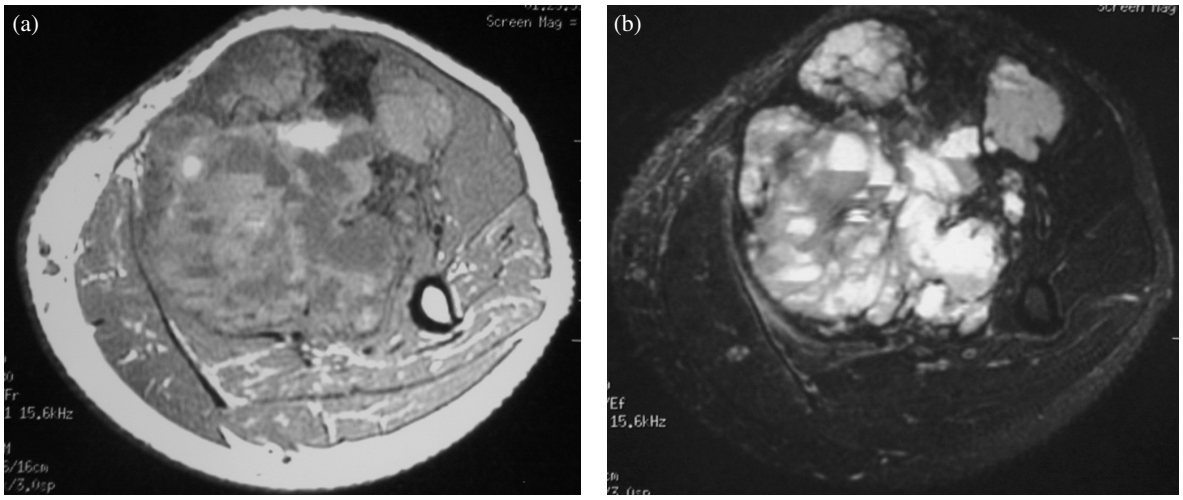

Figure 3 **Telangiectatic osteosarcoma. Axial (a) T1- and (b) T2-weighted MR images of the mid-tibia lesion shows multiple fluid–fluid levels within the large tumor mass. There is extensive soft tissue invasion with involvement of the major neurovascular structures and calf muscles.**

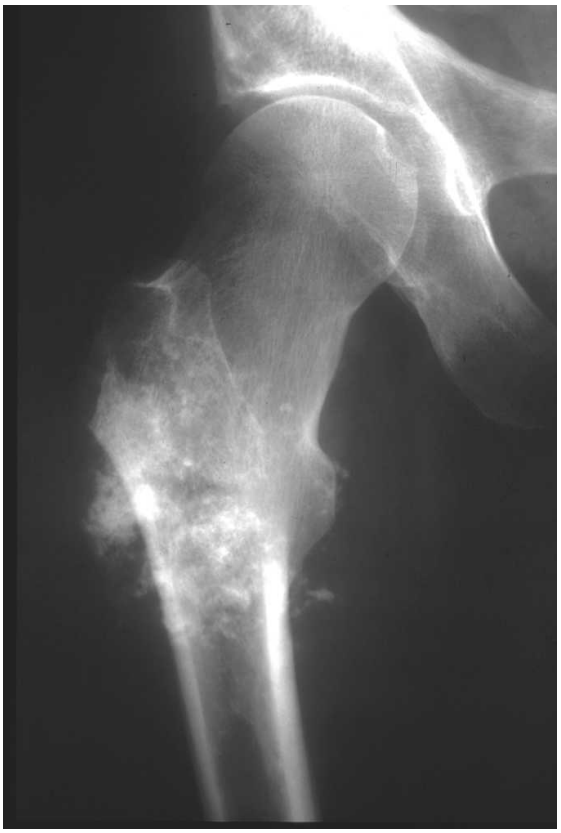

Figure 4 **Secondary chondrosarcoma developing in diaphyseal aclasis. Anteroposterior radiograph shows a destructive lesion arising from the upper femoral shaft. There is an associated large soft mass with numerous calcifications typical of cartilaginous origin. Note modeling deformity of the femoral neck due to diaphyseal aclasis.**

Histologically, osteoblastic, chondroblastic, and fibroblastic variants may be identified.

Telangiectatic osteosarcoma. Telangiectatic osteosarcomas account for 5% of all osteosarcomas[5]. Telangiectatic osteosarcomas are more aggressive than conventional osteosarcomas. They tend to occur within the metaphysis and diaphysis[4]. These lesions contain large cystic cavities filled with fresh and clotted blood which distinguish them from conventional osteosarcomas[4]. Radiographically, telangiectatic osteosarcomas may be predominantly osteolytic. Bone and cortical destruction, periosteal reaction and Codman's triangle are usually identified. MR imaging shows characteristic fluid–fluid levels due to layering of different blood products (Fig. 3).

Parosteal osteosarcoma. Parosteal osteosarcomas usually occur in the second to fifth decades of life. The parosteal osteosarcoma is the most common type of surface osteosarcoma and makes up 5% of all types of osteosarcomas. The most common site is in the metaphysis of long bones, with the femur being the most frequent site. Patients usually present with mild pain or limited range of motion due to interference with a joint. Radiographically, the lesion usually appears as a large, dense, ovoid or rounded mass. In the initial stages, the lesion is connected to the cortex of the underlying bone by a narrow stalk[5]. As the disease progresses, the stalk may broaden. However, the tumor may occasionally extend into the underlying medullary cavity. A thin radiolucent line separating the tumor from the underlying bone is a classical radiographic finding[4].

CT may be able to determine the local extent of the neoplasm but there may be difficulty in differentiating tumor invasion of the medullary cavity and reactive non-neoplastic loss of cancellous bone[4]. Radiolucent regions identified on CT within the dense tumor mass may be due to fibrous, cartilaginous, fatty or benign

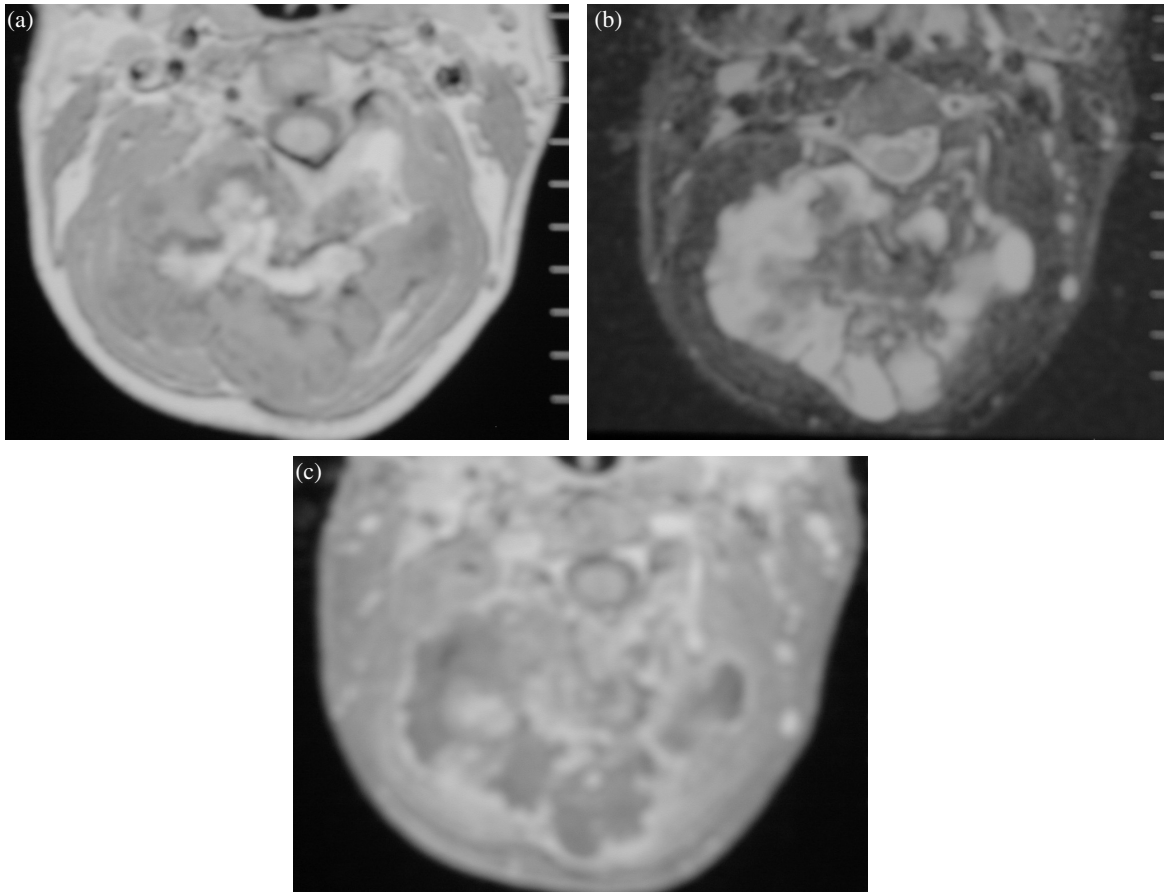

Figure 5 **MR imaging appearance of the cartilaginous component of an osteochondroma. Axial (a) T1-, (b) T2-and (c) enhanced fat-suppressed T1-weighted MR images of the mid cervical spine show a large lobulated tumor arising from the neural arch. The central fatty marrow containing stalk of the lesion is T1-hyperintense and T2-hypointense. The cartilage cap is T1-isointense, markedly T2-hyperintense and shows the typical rim and septal enhancement pattern. Scattered small areas that are hypointense on all sequences represent cartilage matrix calcification. The lesion compresses the adjacent muscles posteriorly but the spinal canal is unaffected.**

entrapped soft tissue, or dedifferentiated, high-grade areas of tumor. CT is also useful in demonstrating the radiolucent zone between the encircling tumor and the cortex. Parosteal osteosarcoma has a better prognosis compared to conventional osteosarcoma[5].

Adamantinoma

Adamantinoma is a rare, low-grade locally aggressive malignant tumor of epithelial origin. It typically occurs in the diaphysis of the tibia arising from cortex of the anterior mid-shaft. The tumor usually affects males in the fourth to fifth decades of life and females in the second to third decades of life[4]. Pathologically, adamantinomas appear as well-demarcated, gray-white, lobulated tumors with focal areas of hemorrhage and necrosis. Radiographically, the tumor appears as a lesion with mixed sclerotic and lytic areas, usually eccentrically situated within the affected bone. Well-defined margins are usually present and lesions may have a 'soap-bubble' appearance. Cortical thinning is present but periosteal reaction is usually absent. Extension of the lesion through the cortex and into the surrounding soft tissue may occur.

30–50 years

Chondrosarcoma

Chondrosarcoma is a cartilage-producing malignant bone tumor. Primary chondrosarcomas are lesions that arise de novo[6]. Most chondrosarcomas are secondary, arising from benign lesions such as osteochondromas or enchondromas. Patients with multiple hereditary exostoses, Ollier's disease (multiple enchondromatosis) and Maffucci's syndrome (multiple enchondromas and hemangiomas) are at much higher risk of developing chondrosarcoma which present in the third and fourth decades. De novo chondrosarcomas usually occur in the fifth or sixth decades of life and have a slight male predominance. Lesions arising from pre-existing enchon-

dromas have been classified as central chondrosarcomas and those that arise near the surface of the bone as peripheral chondrosarcomas which may arise from either pre-existing osteochondromas or the periosteum. Most lesions arise in the metaphysis, but extension into the epiphysis may occur after epiphyseal plate closure.

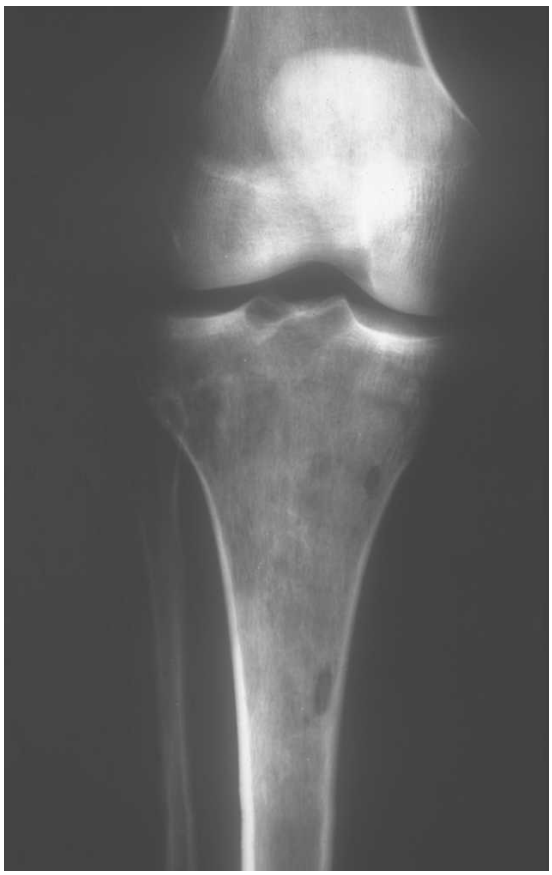

Figure 6 **Fibrosarcoma. Anteroposterior radiograph of the tibia shows multiple osteolytic lesions in the upper shaft. The borders are ill-defined and there is cortical destruction.**

Patients with fast growing high-grade tumors often complain of a painful swelling, while patients with low-grade tumors may complain of only mild pain and swelling. Rapid growth within an osteochondroma is a sign of malignant transformation. Pathologically, chondrosarcomas often appear as large grayish-white, lobulated masses with a firm consistency. Focal areas of calcification, mucoid degeneration or necrosis are often present. The borders of the tumor are often ill-defined and the true local extent may be difficult to determine on gross inspection of the sectioned tumor. Radiographically, tumoral calcification is an important characteristic feature of chondrosarcomas (Fig. 4). Low-grade tumoral calcification appears as calcific rings whilst high-grade tumors have an amorphous, punctate or scattered appearance. Central chondrosarcomas appear as elongated, expansile, multi-loculated osteolytic lesions. There is often associated periosteal reaction, cortical thickening and scalloping of the inner cortex. Soft tissue extension may be seen[6].

In peripheral osteosarcomas, a large cartilaginous cap associated with underlying irregular, scattered calcifications on radiographs is suggestive of malignancy. Amorphous areas of calcification adjacent to radiolucent areas and cortical bone destruction are also features of malignancy. CT provides further information regarding cortical erosion and the pattern of calcification. A cartilage cap measuring greater than 2 cm thick on MR imaging is a sign of malignant degeneration in an osteochondroma. The cartilaginous portions of the tumor have high signal intensity on T2-weighted spin-echo MR images. Enhancement following the intravenous administration of gadolinium on T1-weighted images is seen (Fig. 5). Low-grade chondrosarcomas have fibrovascular septa between lobules of hyaline cartilage. These septa are T2-hypointense and enhance markedly in a septal pattern following gadolinium administration[1].

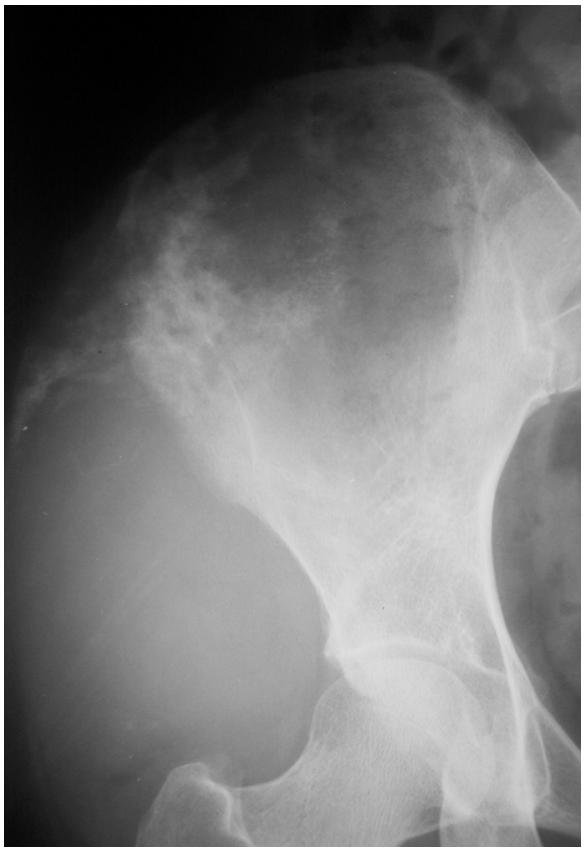

Figure 7 **Malignant fibrous histiocytoma. Anteroposterior radiograph of the ilium shows a large osteolytic lesion with extensive soft tissue involvement. Peripheral calcification is present.**

Fibrosarcoma

Fibrosarcoma is a malignant tumor characterized by the presence of fibrous tissue not associated with bone, cartilage or osteoid production[3,4]. Fibrosarcoma most

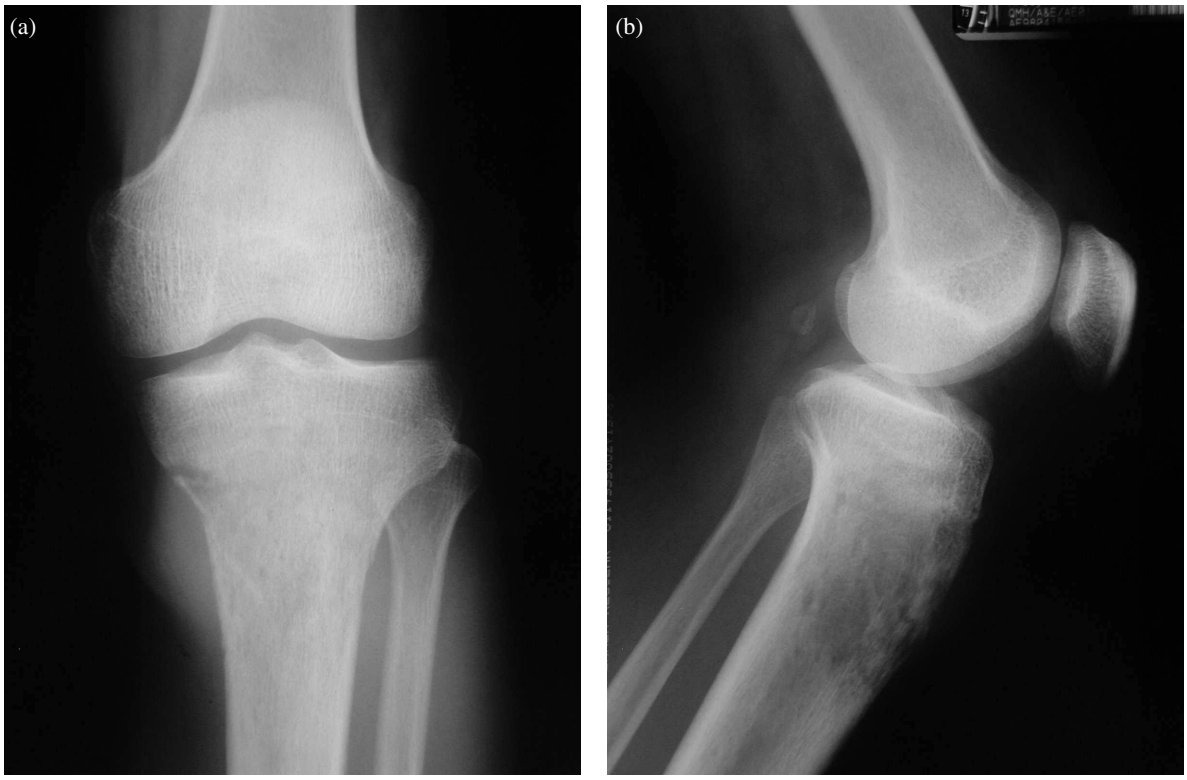

Figure 8 **Primary bone lymphoma. (a) Anteroposterior and (b) lateral radiographs of the tibia show an ill-defined osteolytic lesion in the upper shaft. Cortical destruction is seen.**

commonly occurs in the metaphysis or metadiaphysis of long bones, especially around the knee[7]. Epiphyseal extension may be seen. It presents in the fourth to sixth decades of life with no sexual predominance. Fibrosarcoma can arise as primary lesions or in areas of bone already affected by Paget's disease, fibrous dysplasia, bone infarct or chronic osteomyelitis. Presenting complaints include pain, swelling, limitation of motion and pathologic fractures.

Table 1 Components of the Enneking staging system

Grade (G)	
G0	Benign
G1	Low-grade malignant
G2	High-grade malignant
Site (T)	
T0	Benign intra-compartmental
T1	Aggressive intra-compartmental
T2	Extra-compartmental
Metastasis (M)	
M0	No metastasis
M1	Metastasis present

Adapted from [1].

Fibrosarcoma may occur in the medullary cavity or on the periosteum. Pathologically, the fibrosarcomas are brown to grayish-white in color and have a rubbery consistency. Some tumors may have hemorrhagic and necrotic foci and may appear encapsulated. Radiographically, fibrosarcomas are non-specific and usually appear as moth-eaten osteolytic lesions with ill-defined margins[7] (Fig. 6). Cortical destruction and soft tissue extension may be evident. Periosteal reaction is often absent.

Malignant fibrous histiocytoma

Primary osseous malignant fibrous histiocytoma occurs most commonly during the fifth to seventh decades of life. There is a slight male predominance. This lesion usually occurs in the metaphyseal or diaphyseal regions of the long bones. Malignant fibrous histiocytoma may occur in bones with prior insult such as radiation, surgery, fracture, avascular necrosis, Paget's disease or fibrous dysplasia. Clinically, patients present with acute or chronic pain, tenderness and swelling over the lesion. Pathologically, malignant fibrous histiocytoma appears as a lobulated, gray-white lesion with some hemorrhagic areas. The tumor is usually situated within the medullary cavity. Extension through the cortex and into the surrounding soft tissue is a common finding. Radiographically, malignant fibrous histiocytoma appears as an aggressive permeative lesion associated with a soft tissue mass with little periosteal reaction. Calcifications may be seen in the periphery of the mass[4] (Fig. 7).

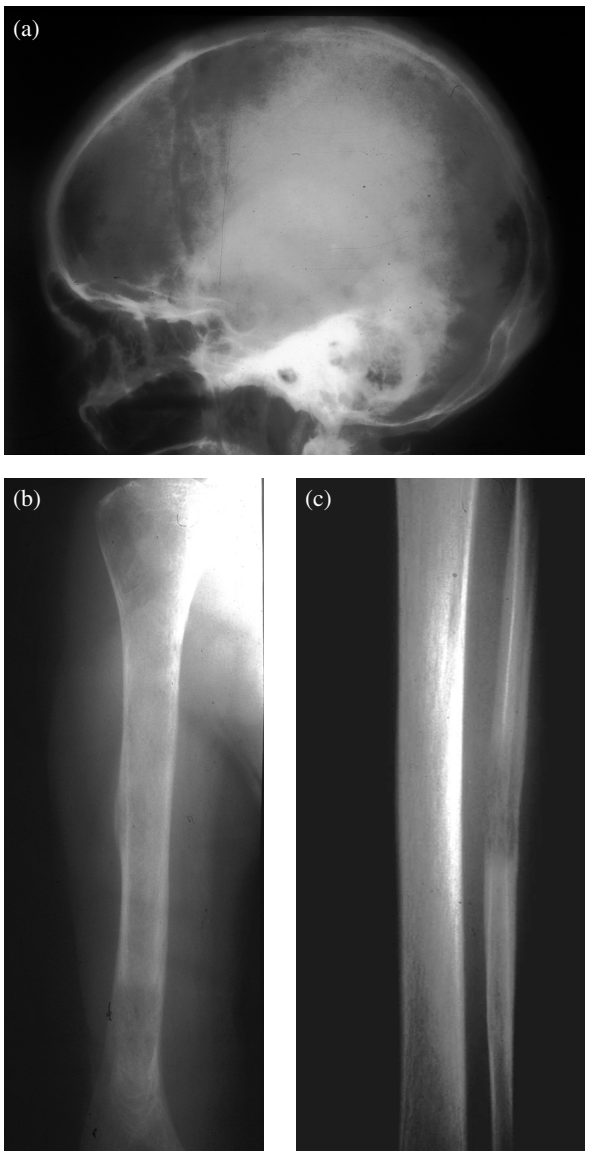

Figure 9 **Multiple myeloma. Radiographs of the (a) skull, (b) humerus and (c) fibula show multiple small punched-out osteolytic lesions.**

Lymphoma

Primary intraosseous lymphoma accounts for up to 5% of primary malignant bone tumors[8]. Non-Hodgkin's lymphoma makes up the majority of primary intraosseous lymphoma. Most cases occur between the fourth and sixth decades of life. Men are more commonly affected. Primary Hodgkin's lymphoma of the bone is very rare[8]. Clinically, patients present with pain or swelling over the site of involvement. Pathologically, primary non-Hodgkin's lymphoma of the bone appears as a gray-white infiltrative tumor. Radiographically, lymphoma of the bone may appear as a vague, mottled, permeative lesion in a long bone or may appear sclerotic[8] (Fig. 8). Diffuse sclerosis in a vertebra known as 'ivory vertebra' is a well-recognized entity. Cortical destruction is seen but overlying periosteal reaction is not a prominent feature. Radiographs often underestimate the size and extent of the lesion. MR imaging is useful in assessing bone marrow involvement.

>50 years

Multiple myeloma

Multiple myeloma is the most common primary malignancy of bone with an incidence of 3 per 100,000 in the USA. It is a disease of plasma cells with monoclonal proliferation of B cells resulting in marrow infiltration of the skeleton with the production of widespread osteolytic bone damage. Multiple myeloma may affect any bone with hematopoietic red marrow. Patients affected are usually over 50 years of age with the most common age group being between 60 and 65 years of age. Men are affected twice as often as women. Pain, especially of the lower back, is the most common presenting symptom but symptoms of anemia may also be present due to marrow failure.

There are four radiographic patterns of multiple myeloma. Radiographs may appear normal, or demonstrate diffuse demineralization, a single osteolytic lesion (plasmacytoma) or widespread lytic lesions (Fig. 9). These osteolytic lesions are well-defined punched-out lesions of varying sizes. It has been reported that multi-detector CT is able to detect more bone lesions than conventional radiography by assessing multi-planar reformations exclusively[9]. MR imaging may be of benefit in suspected cases because of its sensitivity in the detection of occult lesions. However, findings on MR imaging are not specific. Lesions appear as a foci of round low signal intensity on T1-weighted images, and high signal intensity on T2-weighted images. Enhancement occurs after gadolinium administration. Diffuse lesions appear as large areas of low signal intensity on T1-weighted images replacing normal fatty marrow. Radionuclide bone scans are falsely negative in up to 25% of patients.

Staging

Surgical staging of bone tumors

Enneking *et al.* developed a system for the staging of bone tumors based on the grade (G), anatomic location of the tumor (T), and the presence or absence of metastasis (M) (Table 1). This system has been adopted by the Musculoskeletal Tumor Society (MTS) and is also known as the MTS system.

Grade

The grade of the tumor is based on histologic, radiographic and clinical criteria[10]. Radiographic criteria are based on the Lodwick's radiographic grading system[2].

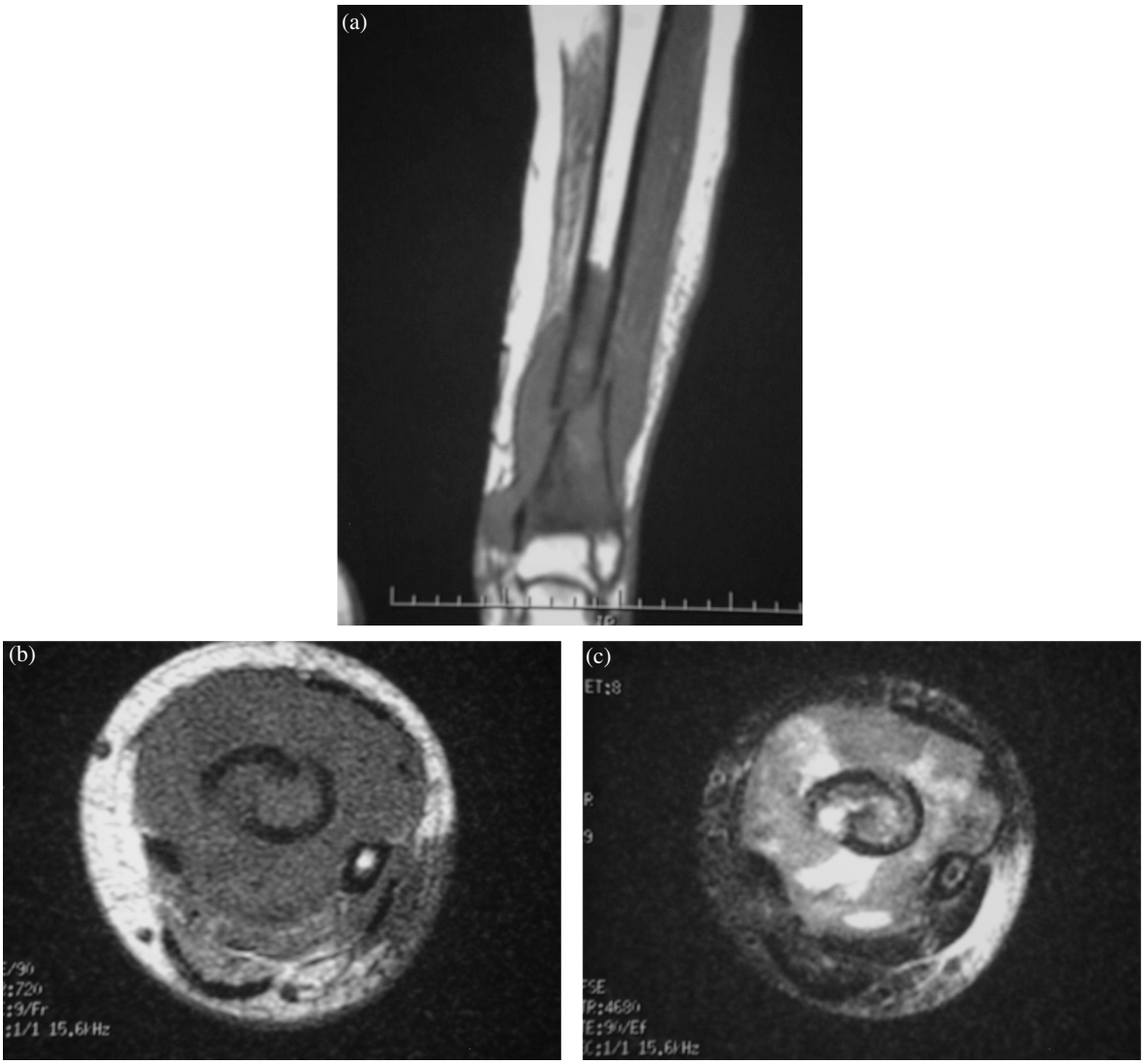

Figure 10 **MR in staging of osteosarcoma of the tibia. (a) Coronal T1-weighted MR image shows a pathological fracture through the distal tibial lesion. The superior-inferior medullary lesion extent and soft tissue component are well depicted. Axial (b) T1- and (c) T2-weighted MR images show not only lesion abutment upon the distal fibula but also extensive involvement of the adjacent muscles and neurovascular structures.**

Type I lesions are well-circumscribed lesions that can be classified by the appearance of the border as IA (sclerotic), IB (well-defined), or IC (poorly-defined). Type II lesions are moth-eaten lesions whilst Type III lesions preserve the bony outline but reveal numerous small, diffuse lytic lesions such as those seen in round cell tumors. Increasing radiographic grade generally correlates well with the aggressiveness of the lesion, although histologic evaluation of the lesion is essential in the definitive diagnosis of these lesions[10].

Clinical criteria include features such as growth rate, doubling time, size, temperature, biological markers, and symptoms such as pain and tenderness. Generally, the grade of a tumor follows the histologic grading but a higher surgical grade may be assigned to a tumor if it displays evidence of more aggressive radiographic features or clinical behavior[10].

Site

The anatomic location or site (T) of the tumor is classified according to whether the tumor is confined to its anatomic compartment of origin (intra-compartmental T1) or has extended beyond its natural barriers (extra-compartmental T2). For a tumor within bone, the natural barriers are the cortex and the articular cartilage (Figs. 3 and 10).

Metastasis

Tumors without metastasis are classified as M0. If metastasis is present, it is classified as M1.

Staging

Malignant tumors are classified into stages I–III (Table 2). Non-metastatic low-and high-grade tumors are classified as Stage I and Stage II lesions, respectively. Stage I and II lesions are further classified into subcategories A and B, depending on whether the tumor is intra- or extra-compartmental. Lesions with metastasis are classified as Stage III lesions. The Enneking staging system applies only to mesenchymal tumors and not tumors of round cell origin such as Ewing's sarcoma or lymphoma[10].

Table 2 Enneking staging system for malignant primary bone tumors

Stage	Grade	Site	Metastasis
IA	G1	T1	M0
IB	G1	T2	M0
IIA	G2	T1	M0
IIB	G2	T2	M0
III	G1-2	T1-2	M1

Adapted from [1].

Staging and limb salvage surgery

The staging of bone tumors is important because it determines the management of primary malignant bone tumors. Stage I tumors can generally be treated with wide excision and limb salvage surgery. Stage II lesions usually cannot be treated with a limb salvage operation alone, unless the tumor is responsive to chemotherapy. Stage III lesions that respond to adjuvant therapy can be treated with wide excision. Lesions that respond poorly to adjuvant therapy may be treated with palliative surgery[10].

Conclusion

The role of imaging in the pre-treatment evaluation of primary malignant bone tumors in adults is firstly to diagnose the lesion if possible on radiographs and secondly to stage the lesion by assessing the extent of local and distant spread of the disease process. The latter assessment can be performed using more advanced imaging techniques such as CT, radionuclide bone scans and MR imaging.

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