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Diagnostic Imaging of Osteosarcoma

LEANNE L. SEEGER, M.D., RICHARD H. GOLD, M.D., AND VIJAY P. CHANDNANI, M.D.

The diagnosis, treatment planning, and follow-up evaluation of osteosarcoma rely heavily on a variety of imaging techniques. Plain roentgenography, radionuclide bone scanning, computed tomography, and magnetic resonance imaging play important roles in defining local tumor extent, detecting metastatic disease, and monitoring for recurrent tumor. Invasive studies such as angiography are now rarely necessary. In the future, newer imaging modalities, including positron emission tomography, can be expected to become important tools for evaluation of these tumors.

The diagnosis of osteosarcoma is usually founded on clinical history and plain roentgenographic findings and is confirmed with biopsy. Once the diagnosis has been established, decisions regarding medical and surgical management rely heavily on the results of a variety of imaging studies.

Radionuclide bone scanning with technetium 99m methylene diphosphonate (^{99m}Tc-MDP) assists in the detection of osseous metastatic lesions. Chest roentgenographs and computed tomography (CT) of the chest are useful tools for detecting pulmonary metastatic disease. CT and magnetic resonance imaging (MRI) are valuable methods of defining the osseous and soft-tissue extent of the tumor and determining their relationship to major neurovascular structures and adjacent joints. Comparison of images obtained

before and following preoperative chemotherapy may provide prognostic information by depicting tumor response to therapy. Following surgery, plain roentgenography, radionuclide bone scanning, and cross-sectional imaging may all be used to identify local recurrence and metastatic disease.

In this article, the authors discuss the preoperative and postoperative imaging evaluation of the patient with osteosarcoma. The concepts that are discussed reflect an ongoing collaborative effort between the sections of musculoskeletal radiology and oncologic orthopaedic surgery at the authors' institution.

PLAIN ROENTGENOGRAPHY

Whereas other imaging modalities may better depict the bone and soft-tissue extent of a lesion, plain roentgenography is the key imaging modality for its diagnosis. This is especially true for osteosarcoma.

Several classification systems of osteosarcoma have been proposed. The most common reflects the predominant type of tissue in the tumor as well as its location within the bone.[14] Primary osteosarcomas may be classified as intramedullary (central) or juxtacortical. The predominant histologic type may be reflected in its roentgenographic appearance. Since most osteosarcomas have a mixed histologic pattern, their roentgenographic appearance combines sclerotic and lytic changes. Some osteosarcomas are primarily composed of mineralized osteoid and are sclerotic (Fig. 1). For others, in which unmineralized cartilage, spindle cells, histio-

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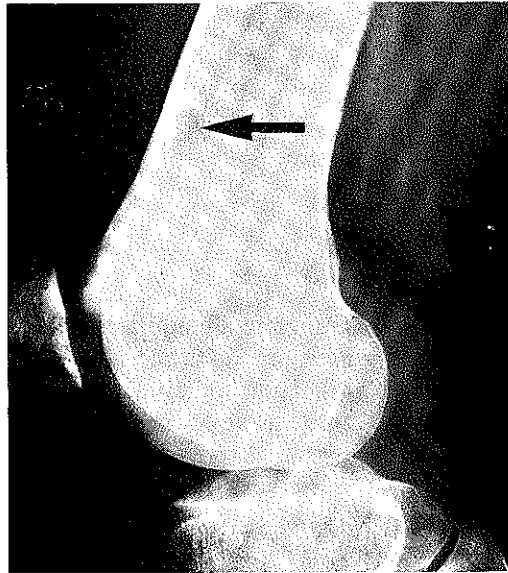
FIG. 1. Sclerotic osteosarcoma of the distal femur. The lesion contains a large amount of bone and osteoid and appears very dense roentgenographically. The arrow indicates the biopsy site.

cytes, or vascular tissue predominates, osteolysis is the rule (Fig. 2).

Intramedullary (central) osteosarcoma, the most common type, is generally located in the metaphysis of a long bone. Although early lesions may produce subtle roentgenographic changes,[6] most osteosarcomas are locally advanced at the time of diagnosis, and roentgenographic abnormalities are usually obvious. The findings most commonly include intramedullary osteolysis combined with osteosclerosis, reflecting the central origin of the tumor and its mixed histology. A disrupted cortex and an adjacent soft-tissue mass are also usually present. Additional roentgenographic features include typically delicate and interrupted periosteal new bone . in the form of a Codman's triangle or a perpendicular "sunburst" pattern.[2] Pathologic fractures may occasionally be present at the time of initial examination.[15]

Telangiectatic osteosarcoma, in which vascular tissue predominates, is an aggressive subtype of central osteosarcoma. This tumor has a distribution similar to conventional central osteosarcoma and is usually found in the metaphysis of a long bone. Its roentgenographic appearance differs from that of conventional osteosarcoma in that it is lytic, with little or no osteosclerosis, and only scant, if any, periosteal new bone.[3] It may appear multilocular, pseudocystic, and expansive. Because of its destructiveness, pathologic fractures are common. Roentgenographic differentiation of a telangiectatic osteosarcoma from a benign lesion such as a giant-cell tumor or an aneurysmal bone cyst may not be easy.[12]

Juxtacortical osteosarcoma is the designation applied to a group of tumors that arise on the surface of a bone. These can be further subdivided into parosteal, periosteal, and high-grade surface osteosarcomas.

Parosteal osteosarcoma occurs most commonly along the metaphyseal region of the posterior surface of the distal femur. Characteristic roentgenographic features include a large, sclerotic, longitudinally oriented oval mass with sessile attachment to the underlying cortex. At the site of attachment, the cortex may be thickened, and the surrounding tumor separated from it by a radiolucent
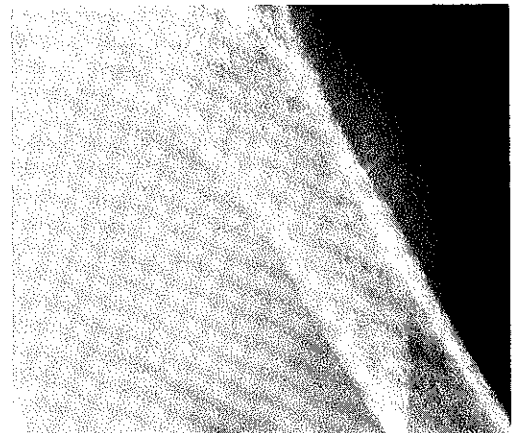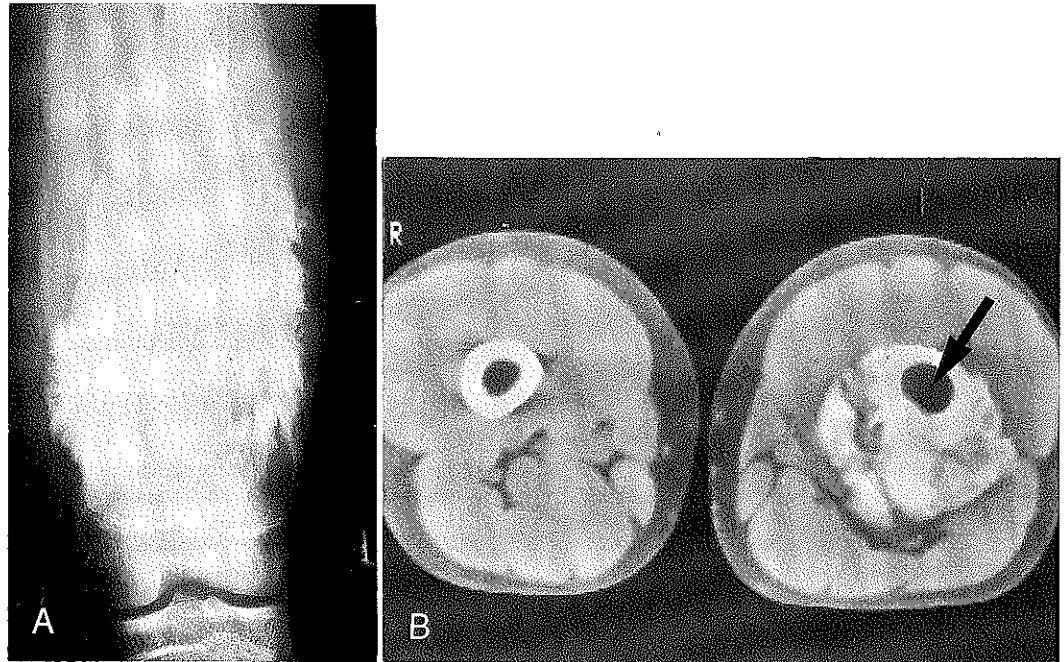

FIG. 2. Spindle cell predominant (fibroblastic) osteosarcoma of the proximal humerus. Anteroposterior (AP) roentgenograph reveals that the lesion is primarily lytic.

FIGS. 3A AND 3B. Large parosteal osteosarcoma of the left femur. (A) AP roentgenograph. (B) CT scan. Preservation of normal fatty marrow (arrow) indicates that the medullary cavity is spared.

plane. Ossification within the tumor begins at its base and extends to the periphery. This is in contradistinction to the zonal pattern of myositis ossificans, in which ossification begins at the periphery of the lesion and proceeds to its center. Plain roentgenography is often inadequate in ascertaining whether or not a parosteal osteosarcoma has invaded the medullary canal (Fig. 3).

Periosteal osteosarcoma is a rare subtype that occurs most commonly along the diaphysis of a long bone. Roentgenographically, it is limited to the cortex, which is thickened and irregular. Radiating, perpendicular, osseous spicules are often present, extending from the outermost portion of the cortex into the surrounding soft tissue. Involvement of the medullary cavity is rare.

Surface high-grade osteosarcoma has a roentgenographic appearance somewhat similar to periosteal osteosarcoma and is characterized by a broad base arising from the outer surface of the cortex.[17] However, the underlying cortex may be partially destroyed, and there may be osteosclerosis within the medullary space, signifying tumor extension.

Secondary osteosarcomas arise in association with an underlying bone abnormality. They may occur in pagetic or previously irradiated bone, or as a result of malignant transformation of a less malignant neoplasm (dedifferentiation). Roentgenographs usually disclose a mixed pattern of osteolysis and sclerosis, and an associated soft-tissue mass.

Plain roentgenography is the primary imaging modality for determining tumor response to preoperative chemotherapy (Fig. 4). High incidences of future recurrence and metastatic disease are associated with tumors that have not roentgenographically decreased in bulk and increased in matrix mineralization.

Plain roentgenography is also the imaging method most often used for the detection of recurrent tumor following surgery (Fig. 5). This is especially true for patients who have
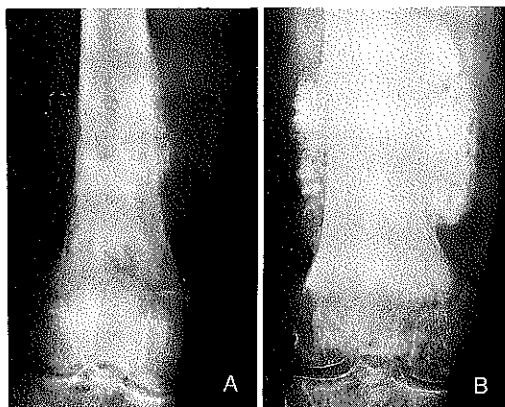
FIGS. 4A AND 4B. Osteosarcoma of the distal femoral diaphysis. (A) AP roentgenograph prior to chemotherapy. (B) Two and one-half months later, following chemotherapy. The soft-tissue mass has decreased in size and increased in mineralization, good prosnotic signs.

undergone limb salvage with an endoprosthesis, where metallic artifact may severely degrade the image quality of MRI and CT. Recurrent tumor generally features roentgenographic findings similar to those of the primary tumor, whether predominately sclerotic, lytic, or mixed.

RADIONUCLIDE IMAGING

^{99M}Tc-MDP BONE SCANNING

Once the diagnosis of osteosarcoma has been made, a diligent search for additional osseous lesions must be carried out. These lesions include bony metastases, the so-called skip lesions within the medullary cavity, and synchronous lesions in the case of multicentric osteosarcoma. Bone scanning with ^{99m}Tc-MDP is generally used for this purpose. This agent is adsorbed onto the surface of hydroxyapatite crystals of actively forming bone. Areas of increased uptake thus correspond to areas of accelerated bone turnover. Increased activity is, however, a nonspecific finding, and neoplastic, traumatic, inflammatory, and degenerative conditions usually

cannot be differentiated on the basis of scan appearance. For this reason, it is essential that the scan be interpreted with correlative roentgenographs to fully assess all areas of increased activity. Pulmonary metastases that produce osteoid may also be evident in bone scans (Fig. 6).

^{201}THALLIUM

Thallium chloride (^{201}Tl) is a readily available radionuclide that acts as a potassium analog. This isotope has been extensively used for the detection of cardiac ischemia and infarction. More recently, there has been published data on the clinical usefulness of ^{201}Tl for evaluation of brain tumors. Although
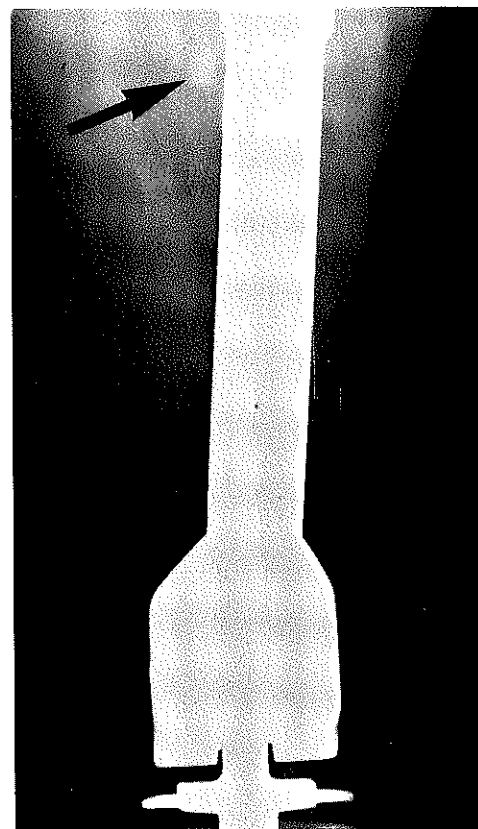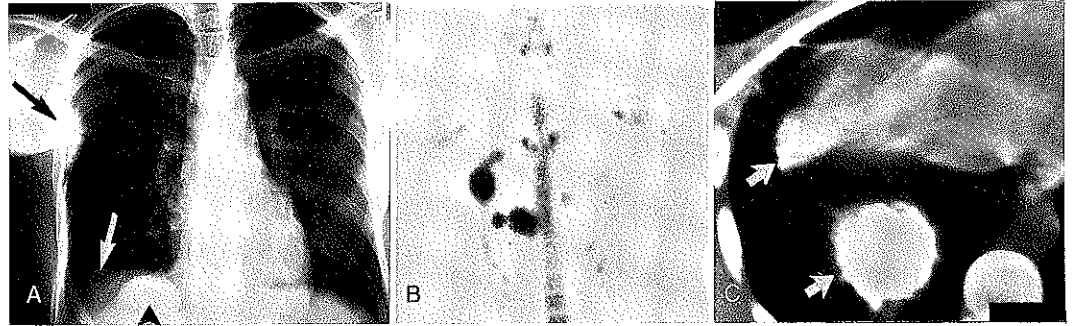

FIG. 5. Recurrent osteosarcoma. AP roentgenograph of the distal femur. Soft-tissue recurrence is present medially (arrow).

FIGS. 6A–6C. Ossified lung metastases of osteosarcoma, active on bone scan. (A) AP roentgenograph of the chest reveals expansile, sclerotic lesion of the right fifth rib laterally, representing osteosarcoma (black arrow). There is also a large, dense mass of ossification in the lung projected over the right hemidiaphragm (arrowhead), and a smaller one in the right lung base (white arrow). (B) ^{99m}Tc-MDP bone scan, AP projection. The primary rib lesion is evident laterally. The two foci of increased activity in the right lung base represent metastases. (C) CT scan through the lung base reveals both metastases (arrows).

there is, as yet, little published data regarding its usefulness in evaluating musculoskeletal tumors,[7] some centers have used ^{201}Tl to investigate tumor response to chemotherapy and detect tumor recurrence. Tumor uptake of the compound appears to be more related to sodium–potassium pump activity than to blood flow.[18] Although the initial results obtained using this radionuclide have been promising, this work is still considered experimental.

POSITRON EMISSION TOMOGRAPHY (PET SCANNING)

Conventional radionuclide scanning utilizes compounds that emit gamma radiation. With positron emission tomography (PET scanning), cyclotron-produced positron-emitting isotopes are combined with compounds that trace physiologic or biochemical processes. The radionuclide activity in PET is therefore a reflection of physiology and biochemistry rather than anatomy, unlike conventional roentgenography, MRI, and CT. Although PET scanners are still limited in number and are used primarily for research, it is apparent that once this modality becomes widely available, it will make an enor-

mous impact on the evaluation of osteosarcoma.

By utilizing radioactive fluourine (^{18}F), bone metabolism can be measured. The use of [^{18}F] 2-fluoro-2-deoxy-D-glucose (FDG) allows measurement of glucose utilization. Normal tissue can be differentiated from inflammatory or neoplastic tissue because the pathologic tissues have a higher glycolytic rate and thus trap more FDG than normal tissue. Tumor response to chemotherapy can be similarly determined by an interval change in glucose metabolism. Recurrent tumor and metastatic disease can be identified as foci of increased metabolism.

PET does not depict the detail of anatomic relationships that can be visualized with MRI and CT. It is therefore unlikely that PET will replace conventional cross-sectional imaging for determining tumor extent and for planning surgery. PET will probably become the most useful modality for identifying metastatic disease, monitoring the response of tumor to chemotherapy, and detecting tumor recurrence.

ARTERIOGRAPHY

Before the advent of CT and MRI, arteriography offered a relatively simple and innocu-
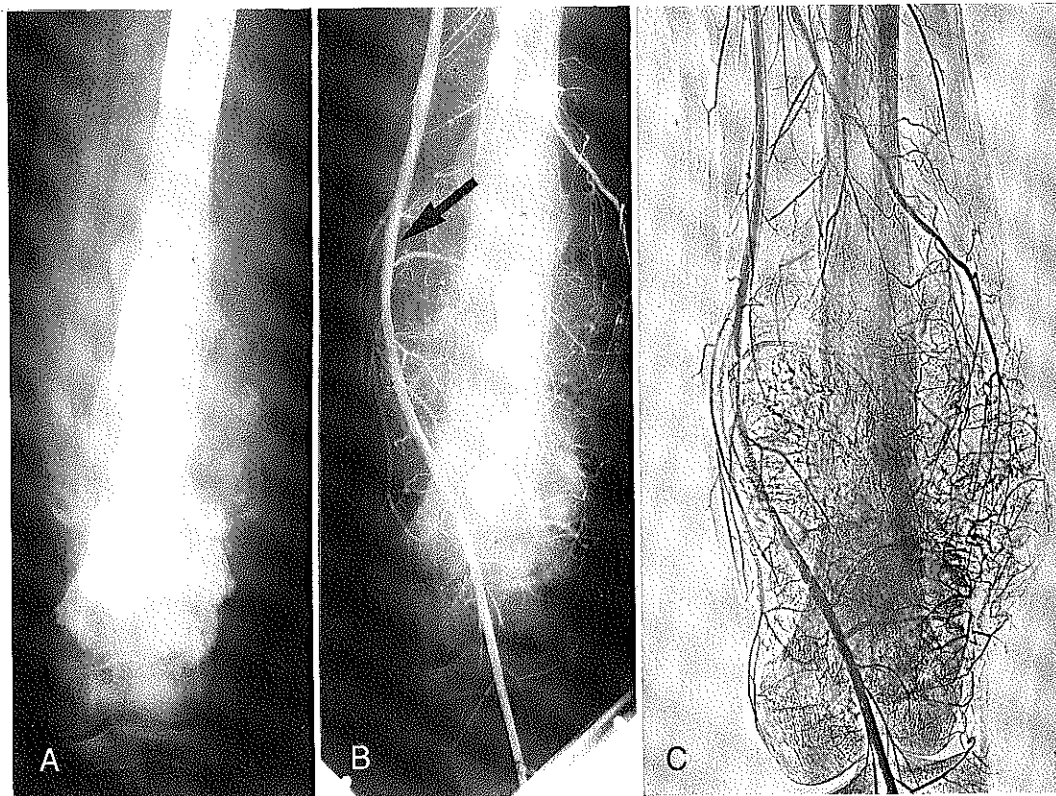
FIGS. 7A–7C. Arteriography of a locally advanced osteosarcoma of the femur. (A) AP scout roentgeno-graph. The tumor is characterized by increased density within the bone, cloud-like mineralization of extraosseous tumor masses, and Codman's triangles of periosteal new bone at the edges of the masses where they breach the cortex. (B) Arteriogram, mid-phase, showing displacement of the femoral artery by extraosseous tumor (arrow). (C) At a slightly later phase, tumor vessels are characterized by their irregular outline, failure to progressively diminish in caliber, and bizarre pathways. The exquisite detail results from the edge-enhancement effect of xeroradiography. (From Gold, R.: Radiographic evaluation of primary bone. In Vaeth, J. M. (ed.): Frontiers of Radiation Therapy and Oncology, vol. 10. Basel, Karger, 1975, pp. 82–107.

ous guide for the diagnosis and management of osteosarcoma. Arteriography was particularly useful for assessing possible involvement of major blood vessels and for determining the site for biopsy, since the area of greatest arteriographic abnormality usually represented the most malignant part of the tumor.[10,20] Serial analysis of the changing arteriographic features of tumors once played a role in the evaluation of their response to chemotherapy, but that role has now largely been assumed more accurately and noninvasively by CT and MRI.[5] Arteriography is still useful for accurate mapping of the blood supply of an osteosarcoma before intraarterial perfusion chemotherapy and, in rare situations, for the performance of transcatheter embolization to diminish exaggerated tumor vascularity before surgery.

Similarly, for the routine evaluation of the intramedullary and extraosseous extent of osteosarcoma, arteriography has largely been supplanted by CT and MRI. The latter modalities provide a more accurate and direct assessment of the extraosseous component of the tumor than is possible by analyzing the
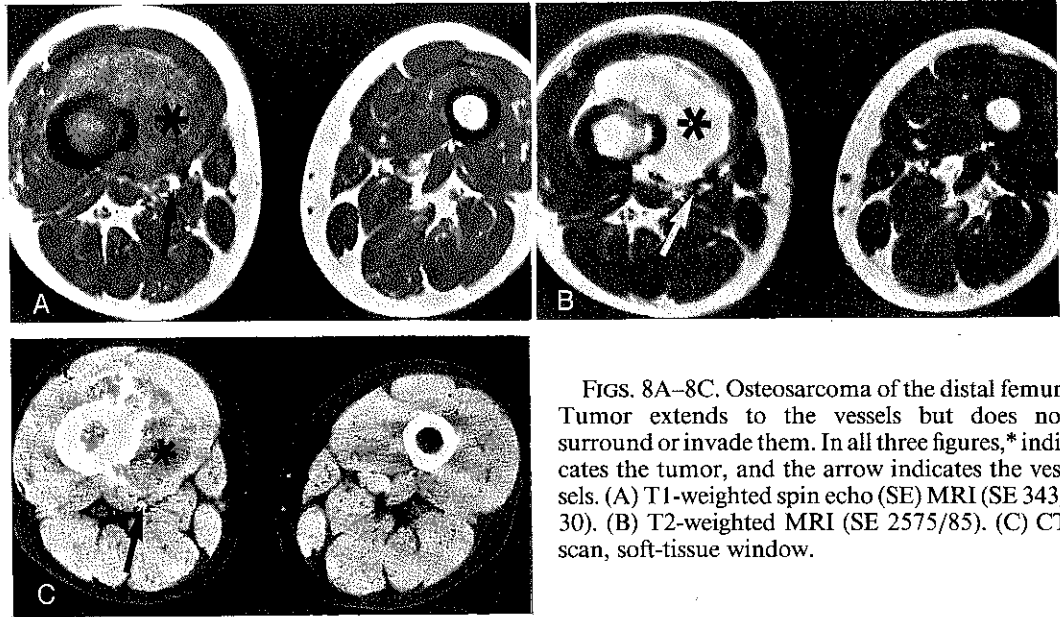
FIGS. 8A–8C. Osteosarcoma of the distal femur. Tumor extends to the vessels but does not surround or invade them. In all three figures,* indicates the tumor, and the arrow indicates the vessels. (A) T1-weighted spin echo (SE) MRI (SE 343/30). (B) T2-weighted MRI (SE 2575/85). (C) CT scan, soft-tissue window.

displacement of opacified blood vessels and abnormal tumor vascularity with arteriography. CT and MRI also allow precise determination of gross involvement of the medullary cavity, providing essential information, such as the depiction of "skip metastases," which arteriography is unable to provide. Should MR imaging be unavailable, arteriography may help to assess vascular relationships that are unclear on CT.[11]

Osteosarcoma may exhibit one or more characteristic arteriographic signs (Fig. 7).[21] Pathologic or "tumor" vascularity, the most specific sign of malignancy, denotes vessels that pursue bizarre, irregular pathways, are ragged in outline, and fail to progressively diminish in caliber. Tumor vessels may terminate as small, scattered "tumor lakes" in which radiopaque contrast material pools. Other signs characteristic, but not specific, for malignancy include arteriovenous shunting (also found in some benign inflammatory processes), abrupt termination to an otherwise normal artery (because of its encasement by tumor), straight veins coursing at right angles to the normal flow of venous re-

turn, a myriad of small vessels encircling the periphery of an area of relatively avascular necrotic tissue, and diffuse staining of the tumor by the contrast material. Although some studies have indicated that tumors which respond to chemotherapy tend to exhibit a decrease in tumor vascularity and staining in comparison to pretreatment arteriograms,[13] others have shown that postchemotherapy arteriography cannot reliably predict the histologic response to therapy or the eventual outcome.[5]

CROSS-SECTIONAL IMAGING:
CT AND MRI

CT and MRI have made a profound impact on evaluation of the patient with osteosarcoma. In the extremities, these studies can accurately determine osseous and soft-tissue extent of tumor, and define the relationship of tumor to major neurovascular structures and adjacent joints (Figs. 8 and 9).[19] With primary pelvic tumors, CT or MRI may be used to identify infiltration into pelvic soft tissues, epidural space, sacral or sciatic
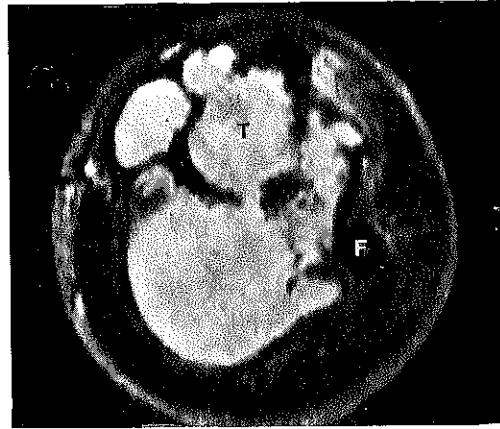
FIG. 9. Osteosarcoma of the proximal tibia. Axial MR image (SE 2000/85). The soft-tissue mass extensively invades muscle, engulfs and invades all major vessels, and crosses the interosseous membrane. T = tibia, F = fibula.

nerves, and sacroiliac joints. Findings in cross-sectional studies may therefore dictate the type of therapeutic surgical procedure appropriate for a given patient (limb salvage, amputation, disarticulation). Regardless of whether CT or MRI is used, it is important that the radiologist responsible for image acquisition have access to roentgenographs before scanning. This will allow imaging to be tailored to the size and location of the tumor, and will assure that maximum diagnostic information is obtained from each imaging study.

In spin echo T1-weighted MR images, intramedullary tumor appears as a region of low (black) to intermediate (grey) signal intensity that replaces the normal high (white) signal intensity of marrow fat. In T2-weighted images, tumor involvement of the soft tissues is evident as a mass of high signal intensity. In CT scans, marrow involvement by tumor is depicted as soft-tissue density replacing the normal low attenuation (black) marrow fat. The authors have found it useful to image the entire involved bone with CT or MRI. This allows demonstration of skip lesions that may or may not be active on a radionuclide bone scan, and provides reference

points for measurements that may assist in surgical planning and prosthesis manufacture (Fig. 10).

There have been several published reports comparing MRI and CT in the preoperative evaluation of osteosarcoma and other primary bone tumors.[1,4,8,16,22,23] Since these investigations addressed several different aspects of tumor imaging and used markedly different protocols, pooling of the data from the various series is difficult. There is fairly uniform agreement that MRI is superior to CT for determining tumor margins with respect to normal adjacent muscle, and CT is considered superior for the evaluation of subtle cortical changes and identification and characterization of mineralized tumor matrix. It is the experience of the authors that MRI and CT are usually comparable in their ability to determine intramedullary tumor extent at a clinically significant level. Any advantage of one imaging modality over the other relates primarily to roentgenographic

FIG. 10. T1-weighted MR image (SE 500/30) clearly shows intramedullary extent of tumor (arrows). From this image, measurements may be made that will assist in surgical planning and custom endoprosthesis manufacture.

FIGS. 11A–11C. Parosteal osteosarcoma of the distal femur. Because the lesion is primarily sclerotic, it is better demonstrated with CT than MRI. (A) CT scan, soft-tissue window. (B) T1-weighted MR scan (SE 650/22). (C) T2-weighted MR scan (SE 2000/85).

features of the tumor and its location. In general, CT will define better the margins of neoplasms that are highly sclerotic, and MRI may be preferable for those that are osteolytic (Fig. 11).

When CT is used for imaging pelvic tumors, it is extremely important to determine if the lesion is roentgenographically sclerotic or lytic before scanning. If the tumor is lytic, both oral and intravenous contrast should be used. If it is sclerotic, the contrast agents may interfere with the determination of intrapelvic tumor extent.

Comparison of imaging studies obtained before and at the completion of chemotherapy, but before surgical intervention, may provide prognostic information regarding tumor response (Fig. 12). Whereas CT is preferred for identifying changes in tumor mineralization, MRI can usually provide similar information, especially when the scan is read in conjunction with prechemotherapy and postchemotherapy roentgenographs. Either method will show a change in tumor size.

Either MRI or CT may be used in the postoperative evaluation of the patient who has
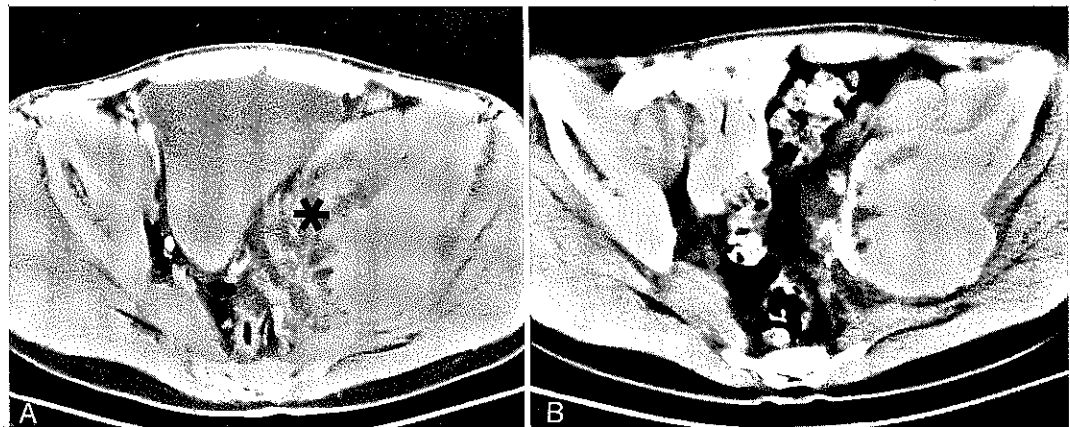
FIGS. 12A AND 12B. Osteosarcoma of the ilium. CT scan, soft-tissue window. (A) Prior to chemotherapy. The soft-tissue mass (*) is poorly ossified, and its margins are difficult to ascertain. (B) One and one-half months later, and following chemotherapy, the tumor has decreased in bulk and increased in mineralization. Note that oral contrast was given for both scans. Near the margins of the soft-tissue mass, it is impossible to differentiate contrast-filled loops of bowel from sclerotic tumor.

been treated with amputation, hemipelvectomy, or local resection for osteosarcoma. The choice of which method to use should be dictated by the amount of tumor mineralization and tumor location. As in the preoperative setting, MRI is preferable for evaluating lytic lesions, and CT for the depiction of subtle tumor mineralization. In patients who have undergone placement of an endoprosthesis, metal artifact in CT and MRI may, at times, be severe. The severity will depend on the type of metal in the prosthesis.[9] The artifact is less with magnets of lower field strength. Cross-sectional imaging is also useful in evaluating postoperative complications such as hematoma, infection, and seroma.

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