Chapter 2 Biopsy of Musculoskeletal Tumors

Jacob Bickels and Martin M. Malawer

BACKGROUND

- Biopsy is a fundamental step in the diagnosis of a musculoskeletal tumor. It should be regarded as the final diagnostic procedure, not as a mere shortcut to diagnosis.
- Biopsy should be preceded by careful clinical evaluation and analysis of the imaging studies.[2,4,7,8] Diagnosis of a musculoskeletal lesion is based on this triad of clinical, pathological, and imaging findings, and all three must coincide. Otherwise, the diagnosis should be questioned.[2,4]
- Most biopsies are technically simple to perform. Decisions regarding the indication for biopsy, the specific region of the lesion for biopsy, and the anatomic approach and biopsy technique, however, can make the difference between a successful biopsy and a catastrophe.
- A poorly performed biopsy can become an obstacle to proper diagnosis and may impede the performance of adequate tumor resection, as well as having a negative impact on patient survival.
- It has been shown that biopsies executed in a referring institution rather than in a specialized oncology center often are associated with unacceptably high rates of devastating complications, unnecessary amputations, and major errors in diagnosis.[5,6]

PATHOGENESIS

- Tumors arising in bone and soft tissues share characteristic patterns of biologic behavior, stemming from their common mesenchymal origin and anatomic environment. Those unique patterns form the basis of the staging system and current treatment strategies.
- Histologically, sarcomas are categorized as low, intermediate, or high grade based on tumor morphology, extent of pleomorphism, atypia, mitosis, and necrosis. Grading represents their biologic aggressiveness and correlates with the likelihood of metastases.
- Sarcomas form a solid mass that grows centrifugally, with the periphery of the lesion being the least mature part.

Pseudocapsules

- Unlike the true capsule that surrounds benign lesions, which is composed of compressed normal cells, sarcomas usually are enclosed by a reactive zone, or pseudocapsule. This consists of compressed tumor cells and a fibrovascular zone of reactive tissue with a variable inflammatory component that interacts with the surrounding normal tissues (**FIG 1A**).
- In addition, these cells may break through the pseudocapsule to form metastases ("skip metastases") within the same anatomic compartment in which the lesion is located. By definition, these are locoregional micrometastases that have not passed through the circulation (**FIG 1B–G**). This phenomenon may be responsible for local recurrences that develop in spite of apparently negative margins after a resection. Although low-grade sarcomas regularly interdigitate into the reactive zone, they rarely form tumor skip nodules beyond that area.

Compartmentalism

- Sarcomas respect anatomic borders. Local anatomy influences tumor growth by setting natural barriers to extension of the lesion. In general, sarcomas take the path of least resistance and initially grow within the anatomic compartment in which they arose.
- In a later stage the walls of that compartment (either the cortex of a bone or aponeurosis of a muscle) are violated, and the tumor breaks into a surrounding compartment (**FIG 2**).
- Most bone sarcomas are bicompartmental at the time of presentation; they destroy the overlying cortex and extend directly into the adjacent soft tissues (**FIG 3A–C**).
- Soft tissue sarcomas may arise between compartments (extracompartmental) or in an anatomic site that is not walled off by anatomic barriers such as the intermuscular or subcutaneous planes. In the latter case, they remain extracompartmental and only break into the adjacent compartment at a later stage (**FIG 3D,E**).
- Carcinomas, on the other hand, directly invade the surrounding tissues, irrespective of compartmental borders (**FIG 4A**).
- Unlike carcinomas, bone and soft tissue sarcomas disseminate almost exclusively through the blood. Hematogenous spread of extremity sarcomas is manifested in the early stages by pulmonary involvement and in later stages by bony involvement (**FIG 4B–D**).

DIAGNOSTIC STUDIES

- Biopsy of a musculoskeletal lesion should be performed only at the conclusion of staging, in which the imaging studies required to determine local tumor extension, its relation to adjacent anatomic structures, and presence of metastatic spread are performed. Data obtained from the staging process allow the surgeon to determine which region of the tumor represents the underlying pathology and to plan the surgical approach for the definitive resection.[1] When appropriately analyzed and combined with results of clinical evaluation, these data allow accurate diagnosis in most musculoskeletal lesions prior to biopsy. Thus, lesions that appear to be benign clinically and radiologically do not need biopsies.
- In contrast, benign-aggressive, malignant, and questionable lesions do require a biopsy for confirmation of the clinical diagnosis and for accurate classification before definitive treatment is initiated (**FIG 5**).
- A final reason for deferring biopsy until staging is completed is that biopsy superimposes both real and artificial radiologic changes at the biopsy site, and these can alter the interpretation of the imaging studies.

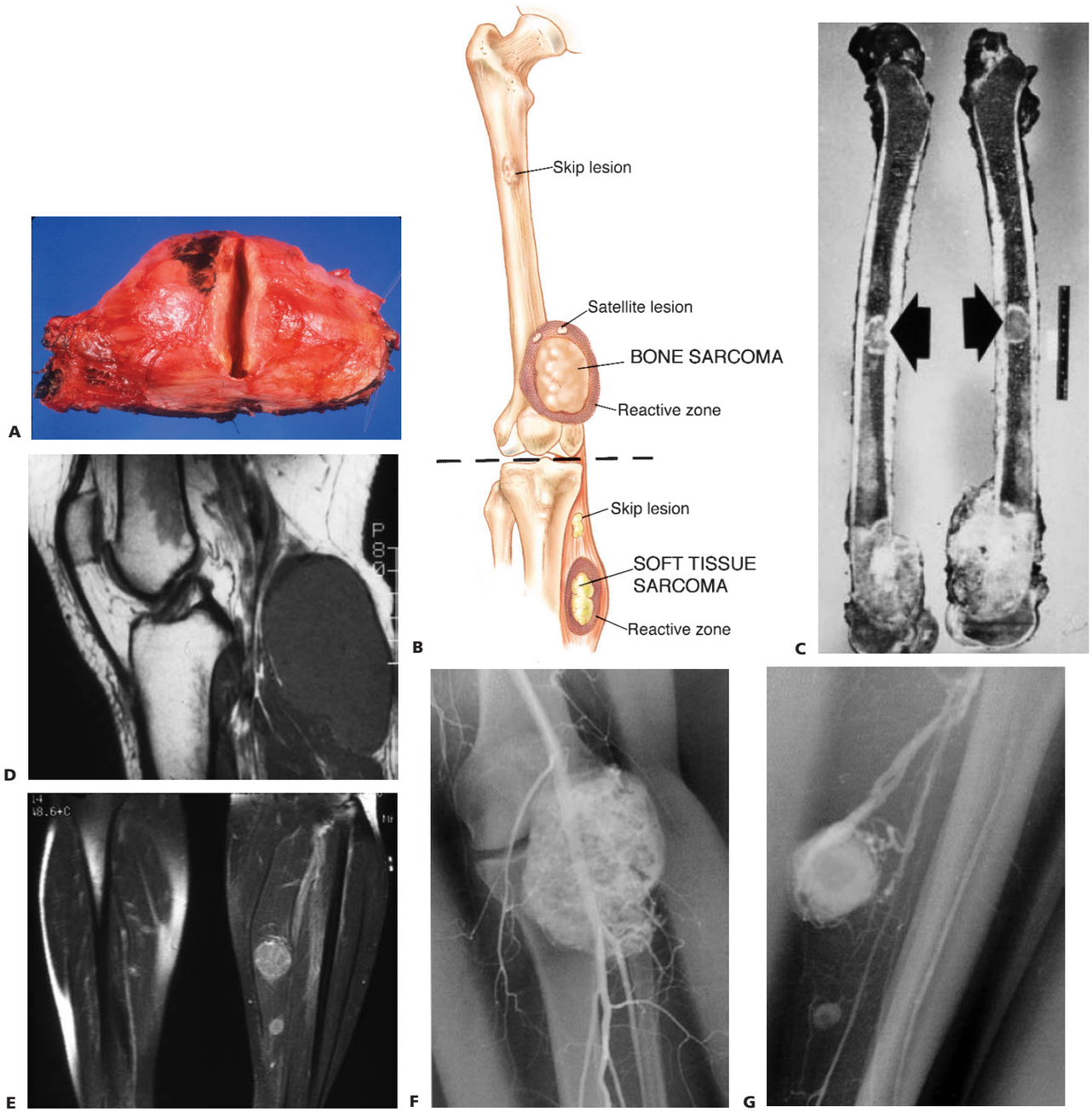


FIG 1 • A. A cut through a high-grade soft-tissue sarcoma showing its thin pseudocapsule, composed of compressed tumor cells, and a fibrovascular zone of reactive inflammatory response. **B.** Growth pattern of bone and soft tissue sarcomas. Sarcomas grow in a centripetal fashion, with the most immature part of the lesion at the growing edge. A reactive zone is formed between the tumor and the compressed surrounding normal tissues and may be invaded by tumor nodules that represent microextensions of the tumor (satellites) rather than a metastatic phenomenon. High-grade sarcomas may present with tumor nodules that grow outside the reactive zone ("skip" lesions) but within the same anatomic compartment in which the lesion is located. This finding is documented preoperatively in less than 5% of patients. **C.** High-grade sarcomas may break through the pseudocapsule to form "skip" metastases within the same anatomic compartment. Skip metastases (*arrows*) from an osteosarcoma of the distal femur. **D.** A 40-year-old woman presented with a rapidly enlarging mass that had developed in her calf. Physical examination revealed a deep-seated, firm mass, 10 cm in diameter, located at the proximal aspect of the calf. **E.** MRI demonstrated the primary lesion as well as two additional skip metastases in the substance of the soleus muscle. **F,G.** Angiograms of the lower extremity clearly show all three lesions. (**B:** Reprinted from Bickels J, Jelinek JS, Shmookler BM, et al. Biopsy of musculoskeletal tumors. Current concepts. Clin Orthop Relat Res 1999;368:212–219, with permission.)

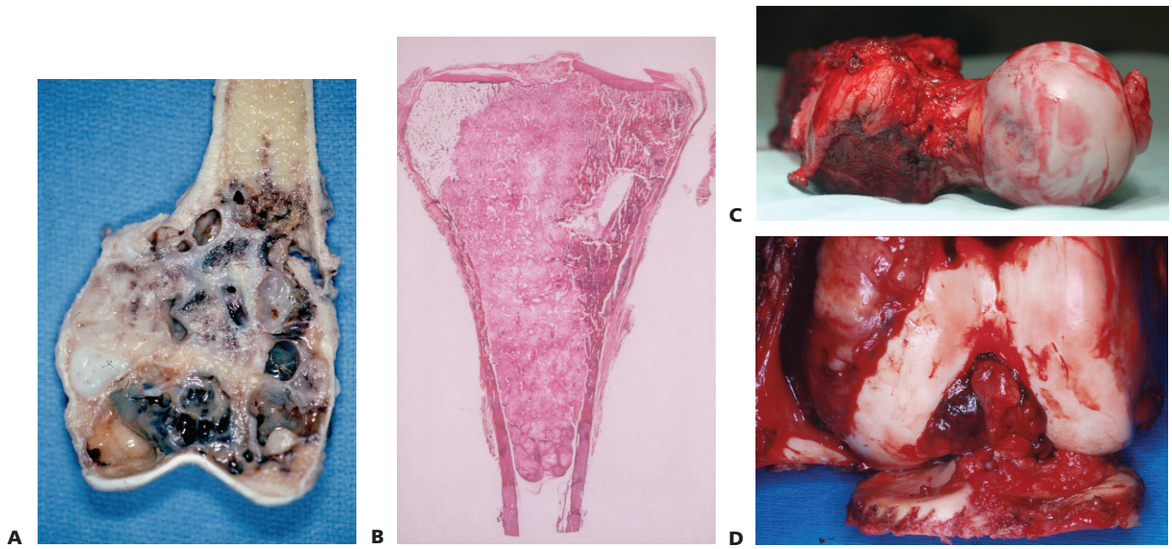


FIG 2 • High-grade osteosarcomas of the distal femur (**A**), proximal tibia (**B**), and proximal femur (**C**) showing tumor extension to the articular cartilage, which remains intact. This phenomenon allows intra-articular resection in most cases of juxta-articular sarcomas of bone. **D.** Extension of an osteosarcoma of the distal femur to the knee joint along the cruciate ligaments. The articular cartilage is intact. Knee joint extension of a high-grade sarcoma of the distal femur is a rare event, necessitating extra-articular resection (ie, en bloc resection of the distal femur, knee joint, and a component of the proximal tibia), as shown here.

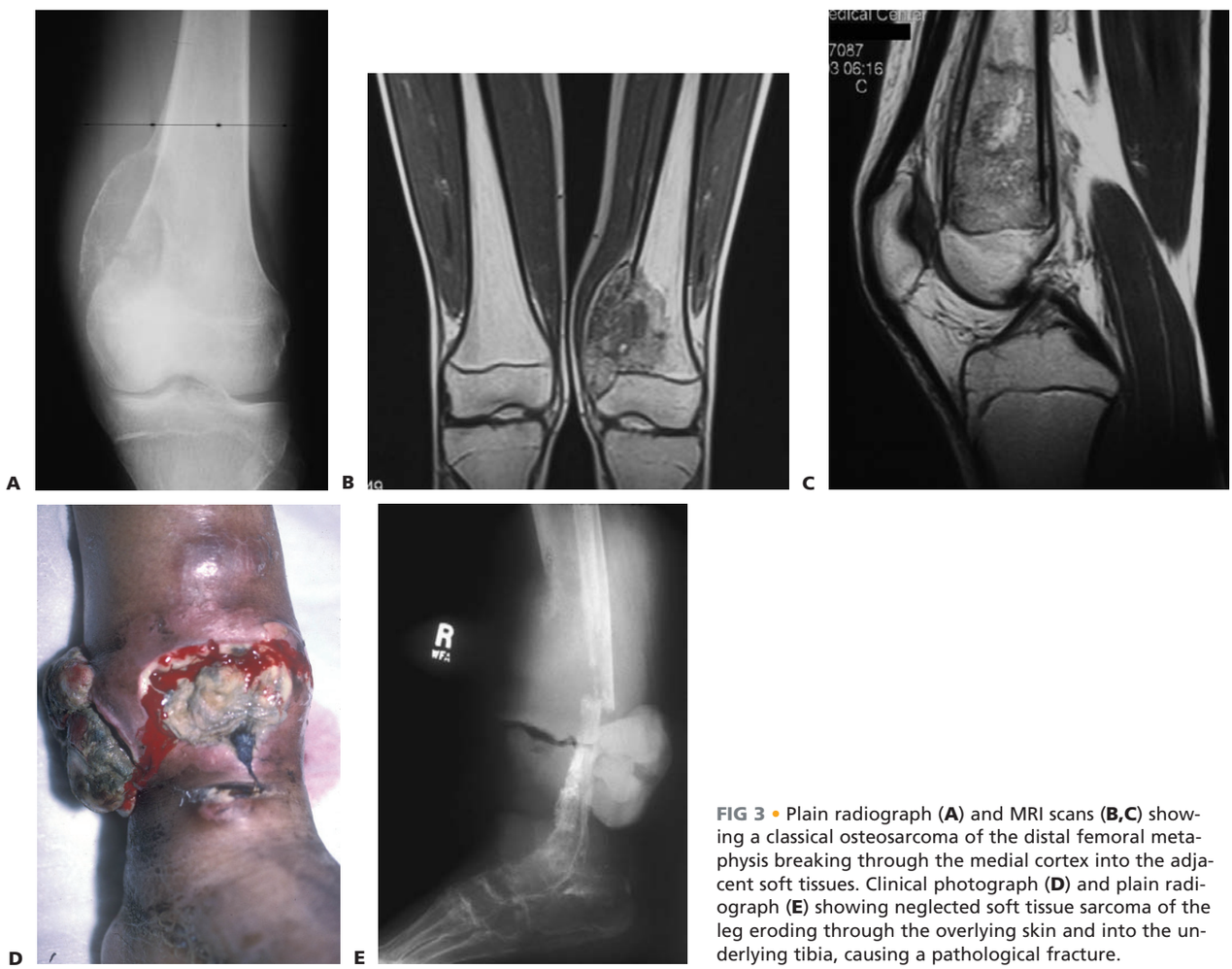


FIG 3 • Plain radiograph (**A**) and MRI scans (**B,C**) showing a classical osteosarcoma of the distal femoral metaphysis breaking through the medial cortex into the adjacent soft tissues. Clinical photograph (**D**) and plain radiograph (**E**) showing neglected soft tissue sarcoma of the leg eroding through the overlying skin and into the underlying tibia, causing a pathological fracture.

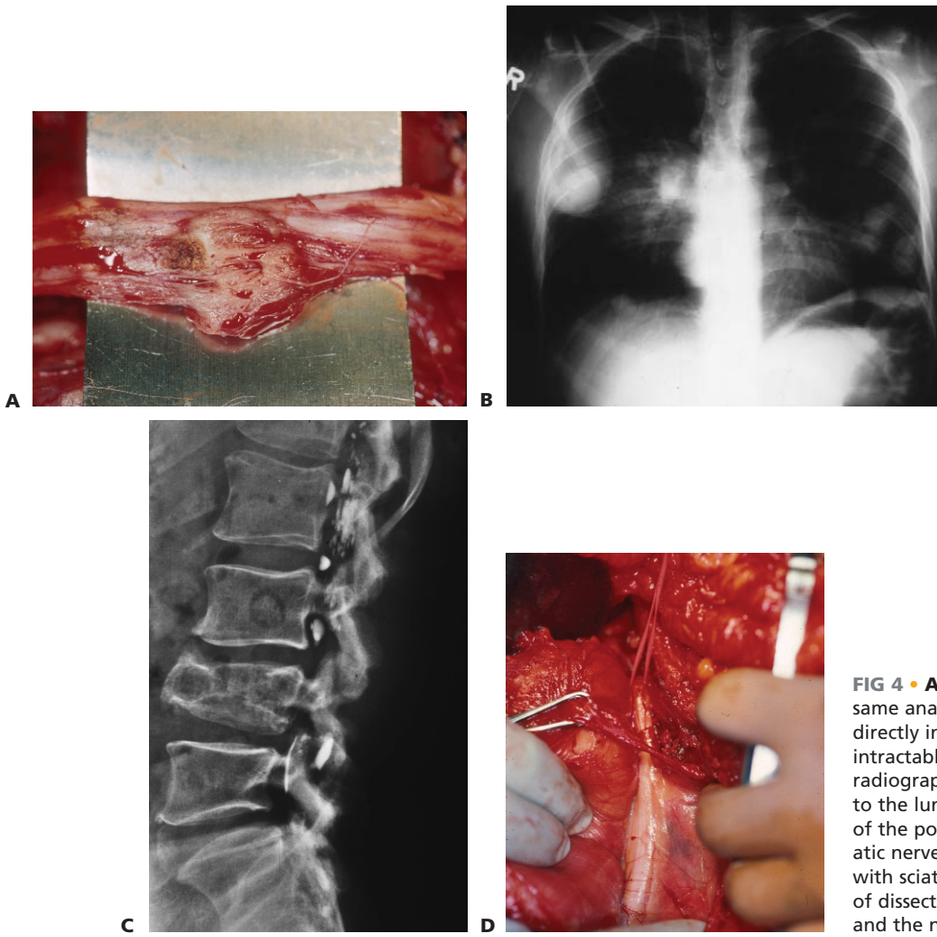


FIG 4 • **A.** Metastatic carcinoma at the same anatomic location penetrating directly into the nerve and causing an intractable, agonizing sciatic pain. Plain radiographs show metastatic osteosarcoma to the lungs (**B**) and L3 (**C**). **D.** Liposarcoma of the posterior thigh extending to the sciatic nerve. Although the patient presented with sciatic pain, there was a clear plane of dissection between the tumor capsule and the nerve.

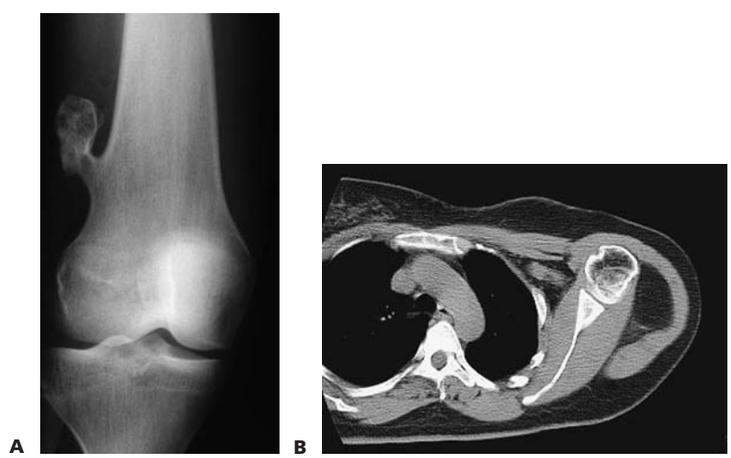


FIG 5 • Osteochondroma of the distal femur (**A**) and deep lipoma of the shoulder (**B**). These lesions have typical findings on clinical examination and classical appearance on imaging studies. Consequently, biopsy is not required for their diagnosis or for decision-making regarding their management.

SURGICAL MANAGEMENT

Preoperative Planning

- The questions that must be answered before performing a biopsy are:
  - What part of the lesion needs to be biopsied?
  - What is the safest anatomic route to that location?
- The position of the biopsy site within the lesion is of major significance, because soft tissue and bone sarcomas may have regional morphologic variations. As a result of that heterogeneity, when doing a needle biopsy, a considerable volume of tumoral tissue or multiple samples are required to establish a diagnosis.
- The term *sampling error* refers to an incorrect or inconclusive diagnosis that occurs because the biopsy specimen was taken from a region that does not represent the underlying primary disease.
- In contrast, carcinomas commonly are homogeneous, so a single core biopsy or needle aspirate is usually sufficient for diagnosis.
- The periphery of soft tissue sarcomas usually represents the underlying malignancy authentically, and it should be the target of biopsy. Performing a biopsy on a sample taken from the center of this type of lesion may result in ambiguous findings, because these sites may contain mostly necrotic tissue and blood.
- Similarly, the extraosseous component of a malignant bone tumor is as representative of the tumor as is the bony component, and it should be biopsied if present. Violating the cortex of a bone that harbors a malignant tumor predisposes the patient to a pathologic fracture, and is acceptable only if there is no extraosseous extension of the tumor.
- In planning the definitive surgery, it must be assumed that the biopsy tract is contaminated with tumor cells and, therefore, it should be resected with the same safety margins (ie, wide margins) as the primary tumor (**FIG 6A**). For these reasons, the surgeon performing the biopsy must be familiar with the planned surgical technique, whether it is limb-sparing surgery or amputation.
- The biopsy incision or the needle puncture hole and the tract to the tumor must be made within the planned surgical incision site so that they will be included within the surgical specimen (**FIG 6B–F**).

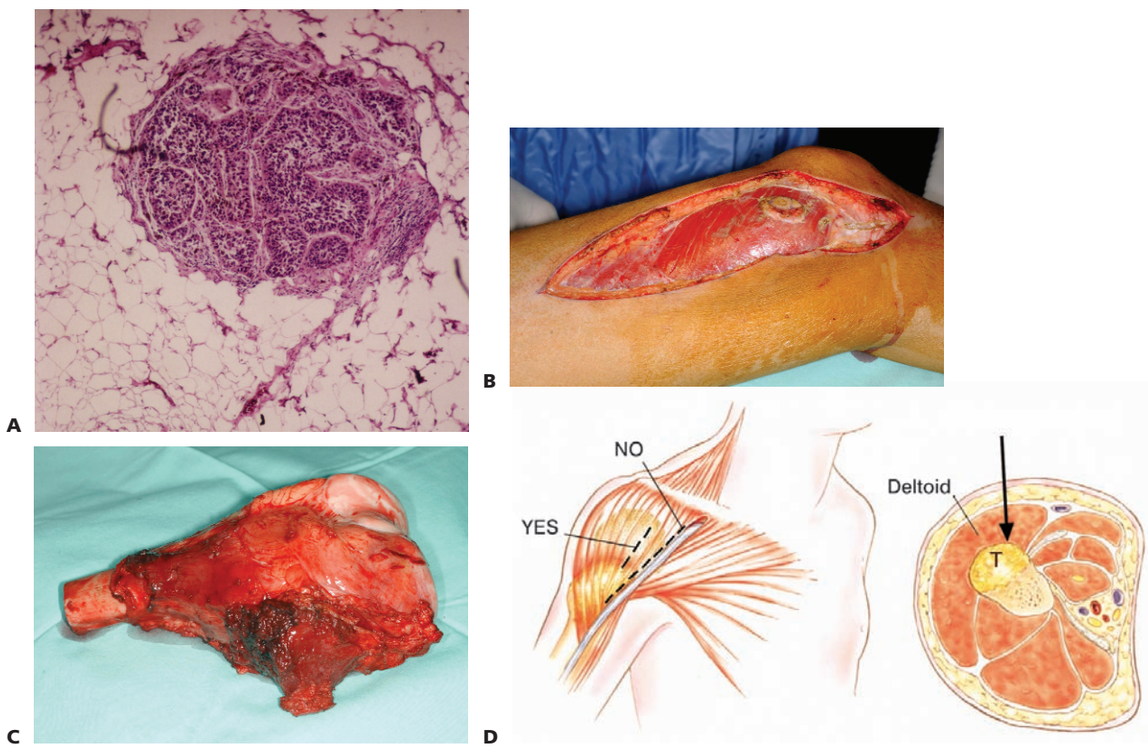


FIG 6 • **A.** Pathological evaluation of a biopsy tract, resected en bloc with metastatic melanoma of the distal humerus, showing a viable tumor focus. **B.** The needle biopsy entry site and tract to the osteosarcoma shown in Fig 3A–C are removed en bloc with the tumor. **C.** The surgical specimen. **D.** Planned biopsy incision around the proximal humerus. Because most primary bone sarcomas extend into the surrounding soft tissues, the overlying muscle should be removed en bloc with the tumor. In this case, the deltoid muscle should be removed with the tumor, and the biopsy tract should be included within the surgical specimen, indicating the choice of a transdeltoid approach through the anterior third of the muscle. The traditional deltopectoral approach for such a biopsy would necessitate a wider resection of the pectoralis major muscle, compromise its subsequent use for soft tissue reconstruction, and possibly contaminate the main neurovascular bundle of the upper extremity. *(continued)*

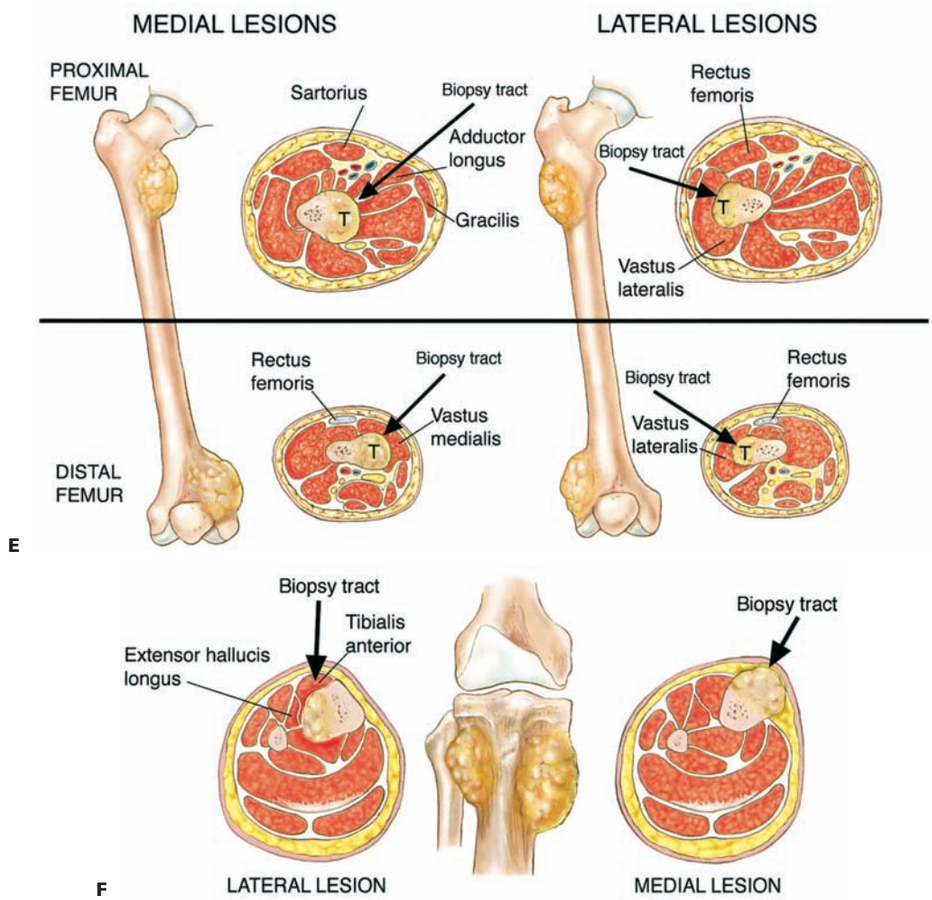


FIG 6 • *(continued)* **E.** Biopsy tracts around the proximal and distal femur; a distinction is made between lateral and medial lesions. **F.** Biopsy tracts around the proximal tibia; a distinction is made between lateral and medial lesions. (**D–F:** Reprinted from Bickels J, Jelinek JS, Shmookler BM, et al. Biopsy of musculoskeletal tumors. Current concepts. Clin Orthop Relat Res 1999;368:212–219, with permission.)

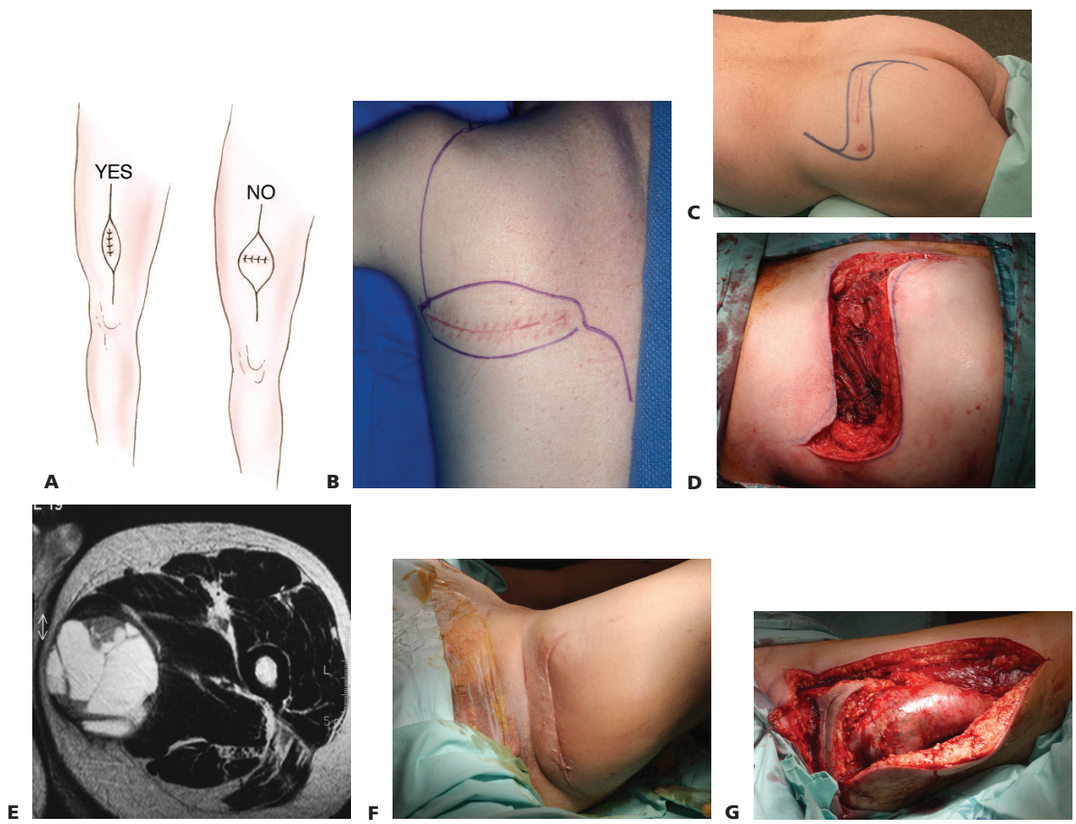
TECHNIQUES

BIOPSY TECHNIQUES

- A closed biopsy does not involve an incision. The specimen is obtained after skin puncture by a needle or trephine.
- An open biopsy, in contrast, does require an incision. It can be either "incisional," in which case only a representative specimen is removed from the lesion, or "excisional," in which case the lesion is completely removed.
- Open incisional biopsy remains the most reliable diagnostic technique to which all other biopsy modalities should be compared. It allows the pathologist to evaluate cellular morphologic features and tissue architecture from different sites of the lesion.
- Furthermore, it provides material for performing ancillary studies, such as immunohistochemistry, cytogenetics, molecular genetics, flow cytometry, and electron microscopy. These studies may help in the diagnosis and subclassification of bone and soft tissue tumors, and, therefore, guide the choice of definitive treatment.
- Open biopsies are criticized because of the increased risk of complications, which may include iatrogenic injury to blood vessels or nerves, complicated wound healing, wound infection, and tumor cell contamination along the biopsy tract and subsequent local recurrence. Furthermore, open biopsies are associated with considerably higher costs of hospitalization and operating room time.
- Refined techniques and accumulated experience with the interpretation of material obtained from needle biopsies as well as the use of CT-guided trephine biopsies have made possible the accurate diagnosis of most musculoskeletal lesions. Thus, guided needle biopsies have become the standard technique in most orthopaedic oncology centers.[9,10]
- When a needle biopsy does not make conclusive diagnosis possible, or when it is not compatible with the clinical or radiologic diagnoses that have already been made, the patient should be referred for to an open surgical biopsy rather than to repeated needle biopsy.

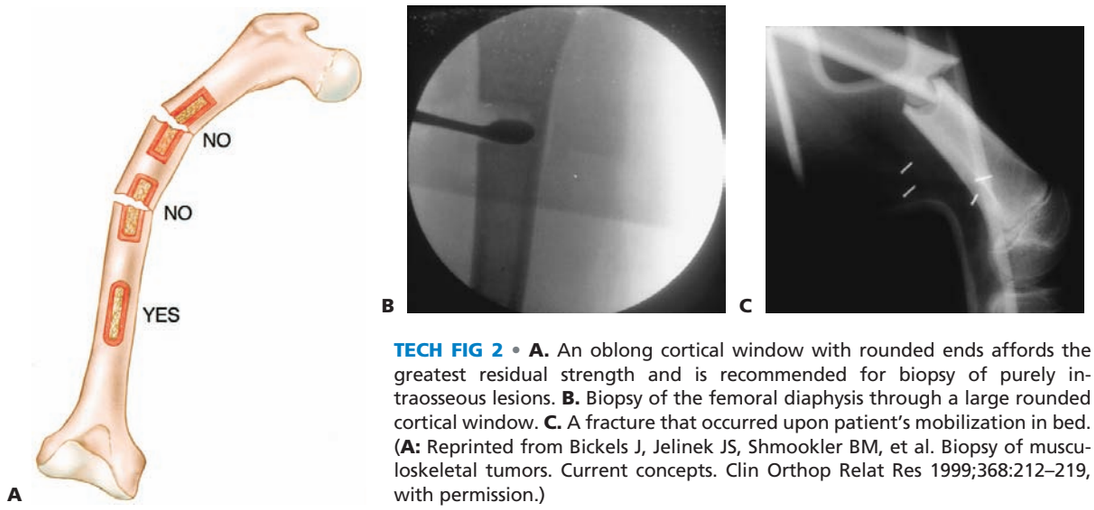
Guided Needle Biopsy

- After adequate planning of the biopsy tract, biopsy should be executed according to the following guidelines:
  - Use the smallest longitudinal incision compatible with obtaining an adequate specimen. Transverse incisions are contraindicated, because they will require a wider soft tissue resection at the time of definitive surgery (**TECH FIG 1**).
  - When a purely intraosseous bone lesion is being biopsied, make a cortical window, giving careful consideration to its shape. Clark et al[3] evaluated the impact of three types of biopsy hole shapes—rectangular hole with square corners, rectangular hole with rounded corners, and oblong hole with rounded ends—on the breaking strength of human femora. They found that an oblong hole with rounded ends afforded the greatest residual strength.[3] They also demonstrated that increasing the width of the hole caused a significant reduction in strength, but increasing the length did not. Therefore, when the biopsy specimen must be taken from the bone, a small circular hole should be made so that only minimal stress-risers are created. If a larger window is needed, an oblong shape should be used (**TECH FIG 2**).
  - Obtain enough tissue and use a knife or curette to avoid crushing or distorting the specimen's texture.
  - As a general rule, culture what you biopsy and biopsy what you culture.
  - Use *meticulous* hemostasis. Any hematoma around a tumor should be considered contaminated. A large hematoma may dissect the soft and subcutaneous tissues and contaminate the entire extremity, making limb-sparing surgery impossible.

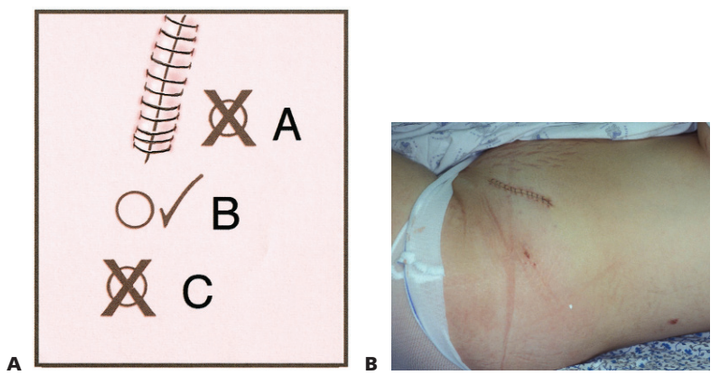


TECH FIG 1 • **A.** The smallest longitudinal incision that allows an adequate specimen to be obtained should be used. **B.** A transverse biopsy incision requires a longer and curved incision to allow its incorporation at the time of the definitive resection. These incisions often cross tension lines, compromise the blood supply to the myocutaneous flaps, and potentially contaminate a larger surgical field. As a result, postoperative radiation therapy, when indicated, is administered to a wider field. **C.** Open biopsy of a high-grade soft tissue sarcoma of the left buttock by means of a transverse incision. **D.** A long, curved incision was used at the time of the definitive surgery to allow adequate resection as well as subsequent closure of skin flaps. **E.** Axial T2-weighted MRI scan of the proximal thigh showing a high-grade soft tissue sarcoma of the adductor compartment. **F.** Open biopsy was done using a long transverse incision. **G.** Intersecting long incisions were required at the time of definitive surgery to remove the biopsy site en bloc with the tumor. All compartments of the thigh were grossly contaminated with tumoral tissue. (**A:** Reprinted from Bickels J, Jelinek JS, Shmookler BM, et al. Biopsy of musculoskeletal tumors. Current concepts. Clin Orthop Relat Res 1999;368:212–219, with permission.)

TECHNIQUES



TECH FIG 2 • **A.** An oblong cortical window with rounded ends affords the greatest residual strength and is recommended for biopsy of purely intraosseous lesions. **B.** Biopsy of the femoral diaphysis through a large rounded cortical window. **C.** A fracture that occurred upon patient's mobilization in bed. (**A:** Reprinted from Bickels J, Jelinek JS, Shmookler BM, et al. Biopsy of musculoskeletal tumors. Current concepts. Clin Orthop Relat Res 1999;368:212–219, with permission.)



TECH FIG 3 • **A.** A drain must be positioned in proximity to and parallel to the site planned for incision of the definitive procedure. **B.** Biopsy of the acetabulum for a high-grade osteosarcoma. The drain was positioned in the flank, causing considerable contamination of the ipsilateral pelvic girdle. (**A:** Reprinted from Bickels J, Jelinek JS, Shmookler BM, et al. Biopsy of musculoskeletal tumors. Current concepts. Clin Orthop Relat Res 1999;368:212–219, with permission.)

- A tourniquet rarely is indicated for an open biopsy, because bleeding vessels cannot be observed and adequate hemostasis is hard to achieve. If a tourniquet is used, the limb should not be exsanguinated by wrapping with an Esmarch bandage, because this may propel tumor cells to the proximal aspect of the extremity. To allow hemostasis, the tourniquet must be removed before wound closure
- Use drains if necessary. The port of entry must be in proximity with and a continuation of the skin incision, not at an angle to its sides (**TECH FIG 3**). The drain path is considered contaminated and must be excised with the surgical specimen. Guidelines regarding the excision of the draining tract are similar, therefore, to those that apply to the biopsy tract.

PEARLS AND PITFALLS

- Biopsy must be preceded by tumor staging.
- Plan site and tract according to the planned incision and tract of the definitive surgery.
- Use the smallest longitudinal incision possible for an open biopsy.
- The periphery of musculoskeletal tumors is preferable to a central site for biopsy.
- Obtain enough material and avoid crushing or distorting the specimen's texture.
- Culture what you biopsy and biopsy what you culture.
- Use meticulous hemostasis.
- When biopsy results do not match the results of clinical and radiologic evaluations, carefully reassess all three.
- Despite serious concerns regarding the potential of accelerated growth or metastatic dissemination of a malignant tumor after biopsy, there is no well-founded, objective evidence that biopsy promotes either adverse event. The real risk of open and needle biopsies is that they may spread tumor cells locally and facilitate local tumor recurrence when performed inadequately.

REFERENCES

1. Anderson MW, Temple HT, Dussault RG, et al. Compartmental anatomy: relevance to staging and biopsy of musculoskeletal tumors. AJR Am J Roentgenol 1999;173:1663–1671.
2. Bickels J, Jelinek JS, Shmookler BM, et al. Biopsy of musculoskeletal tumors. Current concepts. Clin Orthop Relat Res 2005;437: 201–208.
3. Clark CR, Morgan C, Sontegard DA, et al. The effect of biopsy hole shape and size on bone strength. J Bone Joint Surg Am 1977;59A: 213–217.
4. Jaffe HL. Introduction: problems of classification and diagnosis. In: Jaffe HL, ed. Tumors and Tumorous Conditions of the Bones and Joints. Philadelphia: Lea & Febiger, 1958:9–17.
5. Mankin HJ, Lange TA, Spanier SS. The hazards of biopsy in patients with malignant primary bone and soft tissue tumors. J Bone Joint Surg Am 1982;64A:1121–1127.
6. Mankin HJ, Mankin CJ, Simon MA. The hazards of biopsy, revisited. J Bone Joint Surg Am 1996;78A:656–663.
7. Peabody TD, Simon MA. Making the diagnosis: keys to a successful biopsy in children with bone and soft-tissue tumors. Orthop Clin North Am 1996;27:453–459.
8. Scarborough MT. The biopsy. Instr Course Lect 2004;53:639–644.
9. Yang YJ, Damron TA. Comparison of needle core biopsy and fine-needle aspiration for diagnostic accuracy in musculoskeletal lesions. Arch Pathol Lab Med 2004;128:759–764.
10. Yao L, Nelson SD, Seeger LL, et al. Primary musculoskeletal neoplasms: effectiveness of core-needle biopsy. Radiology 1999;212:682–686.