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SYMPOSIUM

The Biopsy

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Abstract

The biopsy of a musculoskeletal lesion is an important event, the outcome of which guides patient management and helps determine patient prognosis. The principles of biopsy include complete radiologic staging before the biopsy, thorough prebiopsy planning including consultation with the pathologist and radiologist, determining the most appropriate method of biopsy (fine needle, core needle, open surgical biopsy), placing the biopsy tract appropriately, and making sure the biopsy tract can be removed at the time of resection, avoiding contamination of uninvolved structures, avoiding transverse incisions, preventing pathologic fracture, handling biopsy tissue appropriately, and considering referral before biopsy. The common errors of biopsy include sampling errors, postbiopsy hematomas, the use of transverse incisions, tumor implantation, and the treatment of an unsuspected sarcoma with prophylactic fixation. Thoughtful prebiopsy planning and successful completion of the biopsy can result in an expedient and accurate diagnosis. If the treating physician lacks significant expertise in performing biopsy and management of patients with musculoskeletal lesions, then referral to a musculoskeletal oncologist before biopsy should be considered.

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The biopsy is a pivotal point in the management of musculoskeletal neoplasms.[1-12] It is a deceptively simple procedure, yet a cognitively complex event. If properly performed, the biopsy can yield an expedient and accurate diagnosis that guides patient management. If not planned and executed carefully, the biopsy can be the source of delay, frustration, misdiagnosis, and even result in significant patient morbidity. Because of this complexity, it is important that the biopsy be approached with much trepidation. Significant thought, planning, and care are needed to carry out biopsy of musculoskeletal neoplasms.

History

Two studies illustrate the complexity of the biopsy and related complications. The first study, published in 1982 by Mankin and associates,[13] looked at a multi-institutional group of patients and compared biopsies performed by the referring physician to those performed by the treating physicians, most of whom were orthopaedic oncologists. A larger number of complications and problems were found in the patients who underwent biopsy by the referring physicians. Major errors in diagnosis occurred in more than 18% of the patients, whereas the incidence of nonrepresentative or technically poor biopsies was more than 10%. A high rate of wound complications was seen. In 18% of the patients, optimum treatment was not achieved as a result of problems with the biopsy. More than 4% of the patients underwent otherwise unnecessary amputations, and prognosis and outcome were adversely affected in 8%. The authors concluded that biopsy-related problems occurred three to five times more frequently when the biopsy was performed at the referring institution as compared with a treatment center. Many educational activities followed this alarming study. More than a decade passed and the study was repeated and reported in 1996.[14] Unfortunately, the findings were similar in the second study. Errors and complications and changes in the course and outcome were 2 to 12 times greater when the biopsy was done in the referring institution rather than in a treatment center. Compared with treatment centers that routinely deal with musculoskeletal tumors, referring centers have a much higher rate of diagnostic error, poor technique, altered treatment plan, less than optimal outcome, and complications. The authors' recommendations were "... if the surgeon or the institution is not prepared to perform accurate diagnostic studies, or proceed with definitive treatment for these patients,

Table 1
Types of Biopsy

Biopsy Type	Tissue Yielded
Fine needle	Cells for cytology
True cut	Small tissue core
Craig, Jamshidi	Large core of tissue, bone biopsy
Incisional	Large samples (grams of tissue)

then the patients should be referred to a treating center before the biopsy."

Misdiagnosis, poorly planned and performed biopsy, and complications of biopsy are particularly a problem with soft-tissue tumors. In a recent study of approximately 300 patients with soft-tissue sarcomas, almost half of these patients had an excision or a generous biopsy before referral, most of the time without any staging studies. Of these, 65 patients in whom no mass had been found were referred to a treatment center for additional management.[12] Most had not undergone any preoperative staging studies. After referral, all patients had repeat resection and sarcoma was identified in 23 (35%). Of those 23 patients, 9 had a positive margin when the tumor was reexcised, yet nearly half of those patients had a local recurrence. This illustrates the frequency of poorly planned biopsy and the associated increase in morbidity. If sarcoma is suspected, particularly with soft-tissue tumors, it is important to perform an appropriate biopsy and consider a referral.[11,12]

Complete Tumor Staging Prior to Biopsy

Tumor staging should be completed before the biopsy is performed. Staging consists of imaging the primary tumor typically with plain radiographs, MRI, CT, and sometimes ultrasound. These staging studies determine the location of the lesion and any association with other structures (for example, the neurovascular bundle), and allow formulation of a differential diagnosis. In patients in whom there is the possibility of multicentric or metastatic disease, imaging surveys are needed. Bone scans, position emission tomography scans, skeletal surveys, chest CT (occasionally abdomen and pelvis CT scans as well) are used for surveillance. The particular studies to be performed are selected based on the differential developed after imaging the primary lesion. If the biopsy is done before the staging studies are complete, hematoma and inflammation caused by the biopsy complicates the interpretation of staging studies by introducing imaging artifacts. Thus, the imaging studies should be completed before biopsy.

Preoperative Consultation With the Pathologist and Radiologist

The knowledge provided by the radiologist and pathologist when evaluating musculoskeletal lesions is often invaluable. Radiologists with expertise in musculoskeletal diseases can help formulate a differential diagnosis and assist with selecting the most helpful staging studies. Often subtle imaging techniques are needed to best evaluate potential neoplasms. The addition of contrast to MRI and/or CT is often helpful. Sometimes the radiologist may even perform the biopsy under image guidance, and the orthopaedic surgeon should ensure that the biopsy tract is placed appropriately. Unfortunately, a common scenario is that the orthopaedic surgeon orders an MRI of an anatomic location such as the knee without communicating the concern about a bone or soft-tissue lesion. The MRI is then done according to the "knee protocol." The MRI focuses on the menisci and the ligamentous structures in the knee; no contrast is given, and the lesion is not well visualized. Careful communication with the radiologist can result in imaging studies that are more informative.

Consultation with the pathologist before the biopsy is of paramount importance to guide the type of biopsy needed and to appropriately handle the tissue obtained. The orthopaedic surgeon, radiologist, and pathologist together formulate the differential diagnosis by reviewing the history, physical examination, and radiographic information. The pathologist can determine the amount of tissue needed to narrow the differential diagnosis to a single diagnosis. The type of biopsy can then be selected. In general, small amounts of tissue are needed when the biopsy is confirmative of recurrent disease, when lesions are homogeneous, and when extensive pathologic evaluation is not necessary. Most general pathologists have little experience with the diagnosis of musculoskeletal lesions. Consultation before the biopsy will give them the opportunity to plan appropriate handling of the biopsy tissue.

Determine the Most Appropriate Method of Biopsy

The type of biopsy is chosen after the orthopaedic surgeon consults with the radiologist and pathologist. The types of biopsy are listed in order of increasing amounts of tissue obtained (Table 1).

Needle biopsies are appropriate when a small sample of tissue is likely to suffice to make the diagnosis.[1-4,7,8] Common clinical scenarios for which a needle biopsy is

appropriate include multiple myeloma, metastatic carcinoma, recurrence of a neoplasm, or other instances where a small sample is adequate. Needle biopsies are simple, cost effective, and efficient. If the needle biopsy does not yield the diagnosis then often the next step is to proceed with an open biopsy. Depending on the type of needle used, a needle biopsy can yield different amounts of tissue. A fine needle aspiration is a technique whereby a small gauge needle is hooked to a syringe, inserted into the lesion, and cells aspirated into the syringe. A suspension of cells is yielded and the pathologist evaluates the cytologic specimen. Fine needle aspirations require an experienced cytopathologist and lesions with relatively homogeneous tissue. Because of the small amount of tissue obtained, special studies such as immunohistochemistry, cytogenetics, or flow cytometry are not possible. True cut needle biopsies use a cutting needle that yields a core of tissue measuring about 1.0 by 0.1 cm. If multiple samples are obtained, then extensive studies of the tissue are possible. Craig and Jamshidi needles are used for bone biopsies. These needles yield samples of cortical and/or cancellous bone.

Open surgical (incisional) biopsy is indicated when a tissue sample larger than what is obtained with needle biopsy is needed for diagnosis, following a nondiagnostic needle biopsy, and sometimes when the plan is to proceed with excision following biopsy. In an open incisional biopsy, the lesion is incised and a sample is taken. Typically a frozen section is obtained to confirm viability and adequacy of the sample. Occasionally excisional biopsies are performed whereby the entire lesion is removed. This is most frequently done with small lesions that are presumed to be benign based on patient history and clinical and radiographic findings. In these cases, it is important to be sure that, if the lesion is unexpectedly malignant, wide excision is still possible without functional compromise.

Prebiopsy Planning

Careful planning follows staging of the lesion and consultation with the pathologist and radiologist. Prebiopsy planning consists of appropriate biopsy tract placement, avoiding contamination of structures, ensuring the tract can be excised at the time of resection, avoiding transverse incisions, and preventing pathologic fracture. The principle is to avoid contamination of joints, the neurovascular structures, bone or any other uninvolved structures. The biopsy tract must be direct and avoid the neurovascular bundle. The biopsy tract needs to be placed so that it can be excised readily when a tumor proved to be malignant is resected. A common error is to place the biopsy tract through the tissue that will be used as a flap for coverage at the time of resection. For example, biopsy of a sarcoma of the iliac crest typically should be done without contaminating the gluteal muscles, the typical flap for coverage at the time of resection. Transverse incisions should be avoided because they are difficult to reexcise without increased morbidity and often require flap coverage. Biopsy of soft-tissue masses associated with bone tumors frequently can be done to avoid introducing a new stress riser by performing a bone biopsy. If it is necessary to enter the bone to do a biopsy, then the hole in the bone should be plugged with polymethylmethacrylate bone cement. Protected weight bearing can help prevent pathologic fracture.

Handle Biopsy Tissue Appropriately

Appropriate tissue handling is crucial to a successful biopsy. Prebiopsy consultation with the pathologist and careful selection of the method of biopsy are the first steps. The next step requires more communication and coordination between the surgeon and pathologist. After the biopsy specimen is obtained, it must be collected in the appropriate media and transported to the pathology department for processing. If a fine needle aspiration is performed the cytopathology technician typically will process the cell suspension as it is collected. If a core needle biopsy is collected, it can be processed immediately with a frozen section to ensure the specimen is adequate, or it can be preserved (usually in formalin) and processed later. For core needle biopsy or incisional biopsies the tissue should be delivered fresh, without preservatives, to the surgical pathology laboratory. The pathologists can then distribute the tissue into the appropriate media for routine and ancillary studies based on the differential diagnosis. A frozen section should be requested to assess tissue adequacy and viability.

Consider Referral Prior to Biopsy

The complexity of the biopsy process and the potential problems if the tumor proves to be malignant point toward referral before biopsy. Proper evaluation, planning, and coordination of the biopsy is time consuming and onerous to the general orthopaedic surgeon. If the radiologists and pathologists lack significant expertise, there is a significant risk of delay in diagnosis or even misdiagnosis. Studies on the hazards of biopsy conclude that it is prudent to refer patients with musculoskeletal neoplasms before biopsy.[13,14]

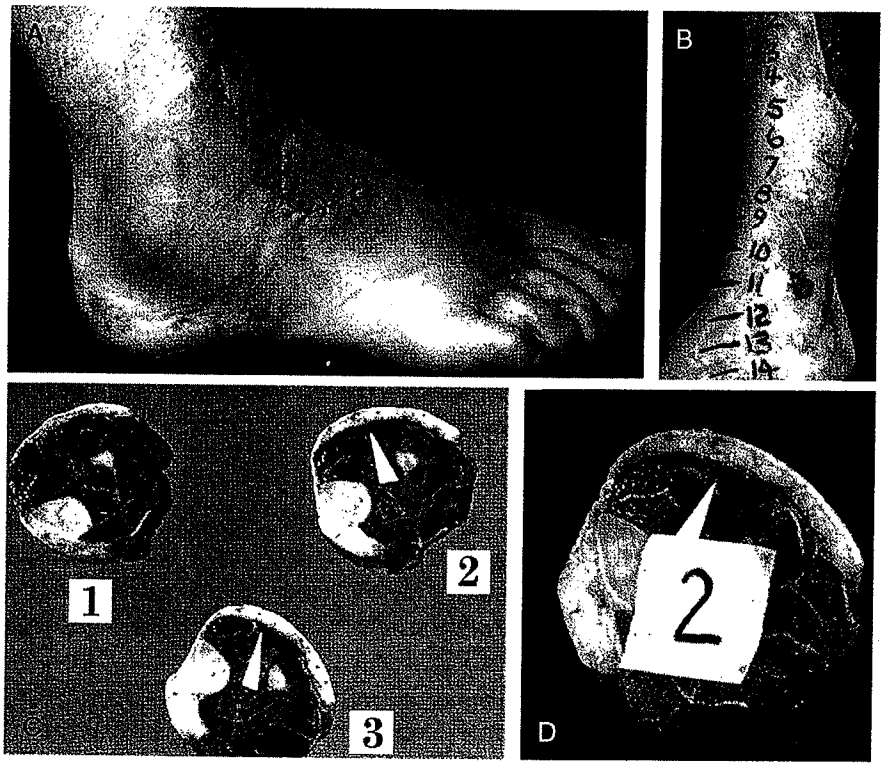

Figure 1 A, A clinical photograph of the foot of a patient who had a high-grade soft-tissue sarcoma. No preoperative imaging was performed. An incisional biopsy was performed and a large hematoma developed. The final diagnosis was high-grade sarcoma and an amputation was necessary. **B** through **D,** Serial sections of the amputation specimen at different levels were done to determine the extent of hematoma. Hematomas are common, and often, as in this patient, go much further than expected.

Errors and Complications Associated With Biopsy

Sampling Error

Sampling errors occur because the samples are insufficient, necrotic, unrepresentative, reactive, or otherwise unsuitable for diagnosis. Consultation with the pathologist before the biopsy can help facilitate obtaining a tissue sample that is sufficient to determine a diagnosis; the appropriate biopsy technique, tumor sampling, and tissue handling then can be planned. Pathologic evaluation of musculoskeletal tumor specimens is difficult because advanced techniques and significant experience are required to make the appropriate diagnosis. If a frozen section pathologic evaluation is to be done, the sample needs to be moist and fresh and promptly transported to the pathologic laboratory. If the sample is inadequate, additional samples can then be obtained during the same operation or, with needle biopsies, before the local anesthetic wears off. Further handling and processing of the samples should be under the direction of the pathologist. A common error is for the biopsy to be performed without consultation with the pathologist and the samples placed in formalin. When this is done, many of the complex diagnostic studies are then not possible. For example, cytogenetics studies require sterile tissue in culture media; flow cytometry is done on fresh tissue; and electron microscopy must be collected in specific media. If there is any chance that the lesion is related to an infectious process, then tissue should be taken for culture. Often aerobic, anaerobic, fungal, and acid-fast bacilli cultures are needed. The clinical and radiologic presentation of neoplasms and infections often overlap. Thus some surgeons go by the dictum "if you biopsy, culture, and if you culture, biopsy."

The pathologic interpretation of musculoskeletal tumors is a complex process. Because musculoskeletal neoplasms are rare, most pathologists have little training or experience in their evaluation. There are only about 10,700 new cases of bone and soft-tissue sarcoma per year in the United States.[15] Cancers of the lung (169,400), prostate (189,000), and breast (205,000) are far more common. Because of the relative inexperience of pathologists in the community setting, consideration for referral before biopsy should be entertained.

Hematoma

A hematoma caused by either a needle or an incisional biopsy can be a devastating complication resulting in distant spread of tumor. Hematomas can be prevented or minimized with careful technique. Major and minor vascular structures should be avoided. Often careful evaluation of the imaging and judicious technique can limit bleeding. When the biopsy must be done in proximity to vascular structures, sometimes image-guided biopsy is prudent to avoid perforation of the vessels. The use of a tourniquet is generally accepted with open surgical biopsies. The limb should not be exsanguinated because of the potential for embolic spread of tumor with pressurization. If a tourniquet is used, it should be deflated before closure and strict hemostasis should be obtained. If the bone is en-

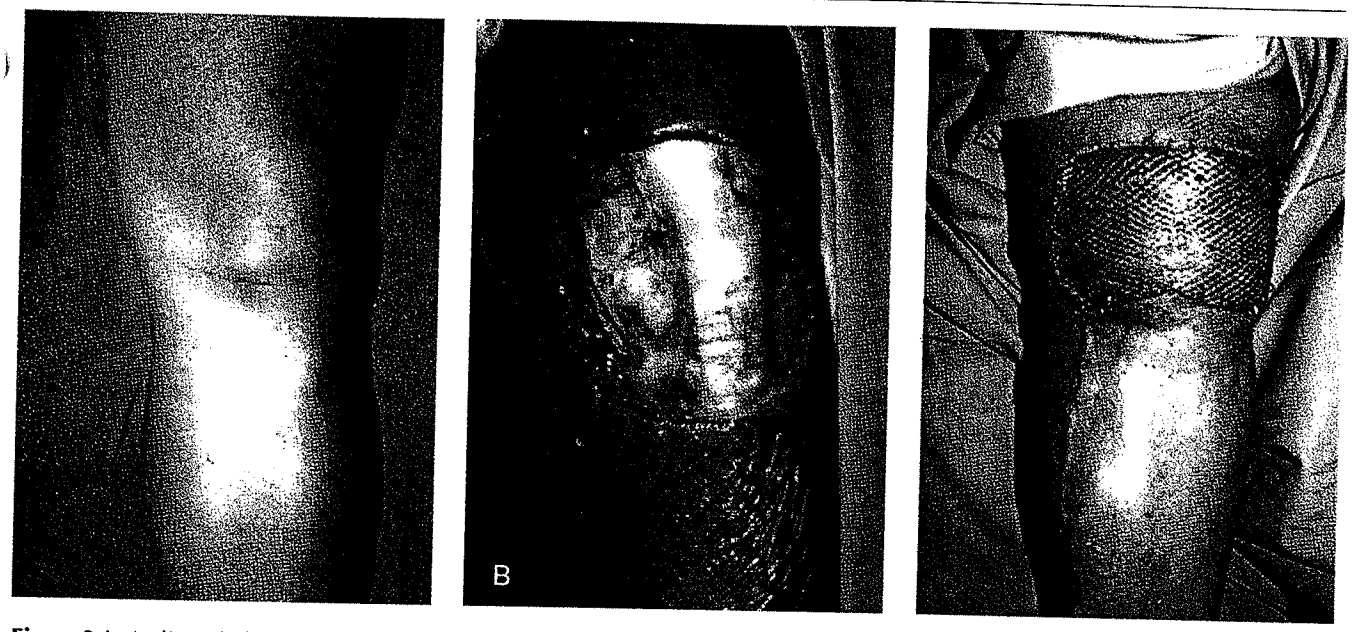

Figure 2 A, A clinical photograph of the knee of a patient with high-grade soft-tissue sarcoma, with no previous imaging and transverse incision just below the patella. **B,** A tumor bed reexcision was performed, leaving a large soft-tissue defect. **C,** A medial gastrocnemius fasciocutaneous flap and split-thickness skin graft were needed to obtain coverage.

tered, the entry hole should be plugged with bone cement. Coagulation aids such as thrombin and gel foam should be used as needed. Figure 1 illustrates a case where a large postoperative hematoma developed. An amputation was performed and the cut specimen shows the hematoma extended from the foot to the mid-calf area. Postoperative hematomas such as this are usually avoidable with careful technique.

Transverse Incision

Transverse biopsy incisions are typically done to place the incision along Langer's lines. The problem with transverse incisions arises at the time of resection, when the biopsy tract is removed. It is much easier to excise longitudinal incisions and do a primary closure than transverse incisions. If a transverse incision is done, often more invasive surgical techniques such as local flaps, skin grafts, and even free flaps are needed to provide soft-tissue coverage. Figure 2 shows a patient on whom a transverse biopsy incision was done. A gastrocnemius rotational flap and skin graft were needed for coverage. If a longitudinal biopsy incision or perhaps a needle biopsy had been done, the flap and skin graft might have been avoidable. Biopsy incisions on the extremities should be longitudinal and not transverse.

Implantation

Musculoskeletal tumors are very implantable and transfer of tumor to sites unaffected at the time of biopsy must be avoided. Figure 3 shows a distal radial lesion. An iliac crest bone graft was taken during the same procedure that the radial lesion was biopsied. The patient subsequently developed an iatrogenic giant cell tumor transplanted from the biopsy. Presumably the tumor was transplanted from the original location of the distal radius to the pelvis. Tumor implantation can be prevented by maintaining strict separation of instrumentation, gloves, and gowns between different surgical sites.

Unsuspected Sarcoma

Prophylactic fixation of a bone lesion performed under the false assumption that the lesion is not a sarcoma is a potentially devastating complication. Because the tumor is then extensively spread, amputation is often needed to control the local tumor. This scenario is usually seen when a patient has a solitary destructive bone lesion that occurs in the later decades of life. They may or may not have a remote history of carcinoma. Typically, minimal imaging is done preoperatively. The lesion is presumed to be a bone metastasis from a carcinoma and prophylactic internal fixation is performed. Tissue from the site of the prophylactic fixation is sent for evaluation and the surgeon is surprised when the presumed metastasis turns out to be a primary sarcoma. This error can be avoided by taking a careful history, doing a thorough physical examination, completing the staging studies before the surgery and, most importantly, by doing a biopsy of the lesion before

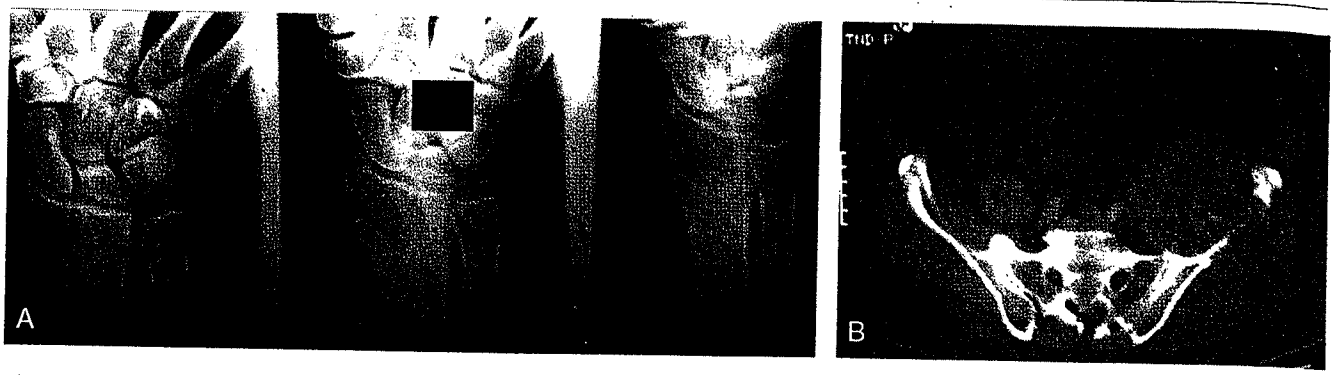

Figure 3 A 25-year-old woman had pain for 3 months. A bone scan showed increased uptake. The plain radiographs **(A)** show a radiolucent lesion of the distal radius. A biopsy revealed a giant cell tumor that was treated with curettage and autogenous iliac crest bone grafting. Six months later the patient developed low back and buttock pain. **B,** A CT scan at the site of the bone graft harvest site, showing the implanted giant cell tumor.

placing the prophylactic internal fixation. Because most metastatic lesions can be diagnosed with a limited sample size, a needle biopsy will often suffice. A frozen section should be done and the prophylactic fixation should not be inserted if the presumptive diagnosis of metastatic carcinoma is not confirmed. Adherence to these steps and principles will prevent the complication of contamination from the unsuspected sarcoma.

Summary

The biopsy is an important part of the diagnosis and management of patients with musculoskeletal lesions. Careful preoperative planning, consultation, and imaging are required to manage these patients successfully. Strict adherence to the principles presented and careful avoidance of the common errors will facilitate a successful biopsy outcome. Musculoskeletal oncologists deal with bone and soft-tissue tumors on a daily basis and are able to evaluate and treat these patients if they are referred. Early referral to a musculoskeletal oncologist is encouraged if the treating physician is not comfortable with the complexities of the differential diagnosis, workup, and treatment of musculoskeletal lesions.

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