



MUSCULOSKELETAL TUMOR BIOPSY: I. CHOOSING THE APPROPRIATE METHOD

Albert J. Aboulafia, MD, FACS, and Joshua G. Schkrohowsky, BS

Biopsy is a key step in the overall management of patients with musculoskeletal lesions. The goal is more than simply removing tissue for diagnostic examination. Considerations for the ultimate management of the lesion must be taken into account.¹ Mankin and colleagues reported that there is a diagnosis error in 18% of biopsied patients, often resulting in alterations in the treatment plan.² A poorly planned biopsy can significantly compromise subsequent management and long-term outcomes.

Various options for performing a tissue biopsy are available, including the use of an open or closed procedure. Each technique has associated risks and benefits, and no one technique can be recommended for all patients. The ultimate choice of which biopsy procedure is most suited for an individual patient depends on the nature and location of the lesion as well as the experience of the institution's pathologists and surgeons.³ There are several important principles to remember when preparing for a biopsy and determining which technique is most appropriate.

1 **Pre-biopsy planning is as important as the biopsy itself.** The biopsy should not be performed until appropriate imaging of the lesion is completed (Figure 1).^{4,5} A focused differential diagnosis should be established on the basis of the clinical findings and imaging studies before proceeding to a biopsy.^{1,6,7} This information will help determine the most appropriate biopsy method to provide representative tissue with the fewest procedures and least morbidity.^{5,8} Careful review of appropriate pre-biopsy imaging studies will help in selecting the most appropriate site for biopsy with the least potential for contamination of uninvolved tissue planes.^{7,8} Managing the treatment of patients with musculoskeletal tumors is a multidisciplinary undertaking. At centers with expertise in musculoskeletal tumors, pathologists and radiologists are active members of the team and participate in the patient's care even prior to the biopsy.^{1,9-11} This is especially important in cases in which the lesion proves to be malignant. In a study addressing the hazards associated with biopsy, Mankin and colleagues reported that 19% of biopsies were problematic, directly resulting in a change of treatment plan; for 10% of biopsies, there was a substantial change in the patient's long-term outcome stemming from a problem with the biopsy itself.²

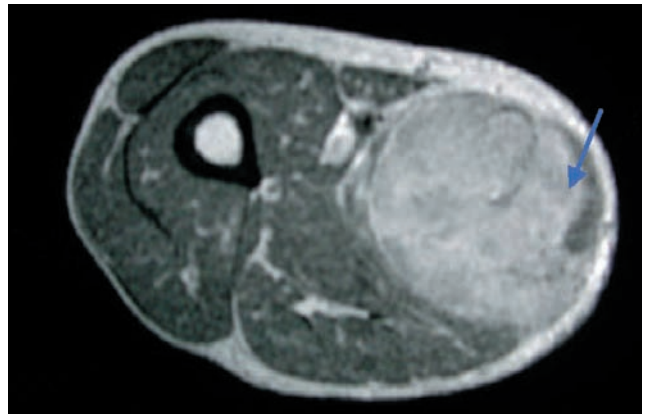


Figure 1. The magnetic resonance imaging (MRI) image shows a well-defined soft-tissue mass, deep to the fascia and larger than 5 cm, with signal characteristics that are not suggestive of a benign fat, neurogenic, or vascular tumor. The MRI characteristics suggest a sarcoma. The arrow indicates the most appropriate path for biopsy, avoiding the neurovascular bundle and not cross-contaminating compartments. In this case, a core biopsy revealed a high-grade soft-tissue sarcoma.

These findings have not changed significantly since Mankin and colleagues first reviewed the topic 11 years earlier.¹² In addition, Mankin and colleagues showed that the complication rates were significantly increased when biopsies were performed at a referring institution rather than at the treatment center.² In cases of suspected or potential malignancy, the biopsy should be performed by the physician who will perform the definitive resection.³



Dr. Aboulafia is Co-Director of Sarcoma Services, Cancer Institute, Sinai Hospital of Baltimore, and Assistant Professor, Department of Orthopaedic Surgery, University of Maryland, Baltimore, Maryland. Mr. Schkrohowsky is a 4th-year Medical Student, Johns Hopkins University School of Medicine, Baltimore, Maryland.



Address correspondence to Albert J. Aboulafia, MD, Orthopaedic Surgery and Oncology, Sinai Hospital of Baltimore, 2401 West Belvedere Ave, Baltimore, MD 21215-5271 (tel, 410-601-9266; fax, 410-601-4601; aaboulaf@lifebridgehealth.org).

2 When to obtain a fine-needle aspirate.

Fine-needle aspirate (FNA) is generally accepted in the work-up of metastatic disease and a variety of primary neoplasms.¹³

On the other hand, its use in the evaluation of musculoskeletal tumors varies from one country to another, from one institution to another within a country, and from one tumor type to another. In certain countries, particularly in Scandinavia, FNA has been used for more than 30 years as an important tool in the preoperative diagnosis of soft-tissue tumors and lesions of the bone.^{13,14} Differentiating between benign and malignant lesions by means of FNA is reported to be between 80% and 95% accurate.^{13,15,16} In the past, FNA has not received widespread acceptance within the United States because of concerns regarding precise subtyping and grading of the lesion and the procurement of adequate tissue.¹⁷ Several institutions have revisited the question, now stating that FNA is valuable in the initial diagnostic investigation and can correctly identify lesions as sarcomatous and often provide significant information toward determining the subtype and grade.¹³

FNA has many advantages in the primary work-up of soft-tissue sarcomas.⁴ It is relatively simple and quick and the most cost-effective tumor biopsy method because it can be performed in an outpatient setting under local anesthesia.^{4,18,19} Rapid-diagnostic confirmation may allow for further treatment planning during the initial clinic visit.^{18,19} FNA is performed using a 24-gauge needle, requiring no open wound and producing little bleeding.^{8,18} There is little or no risk of disrupting the tumor bed or subsequent contamination of the biopsy track.^{4,13,15,19} The surgeon can easily sample material from different parts of the tumor to diagnose heterogeneity and can usually obtain adequate sample for ancillary studies, such as immunohistochemistry, flow cytometry, cytogenetic analysis, and electron microscopy, by performing multiple passes.^{15,18,19} These ancillary studies can increase the specificity and sensitivity to nearly 95%.¹⁵ FNA is especially useful for evaluating clinically suspicious lymph nodes and evaluating a site for suspected local recurrence.^{3,8,20}

The main limitation to widespread use of FNA is the fact that few institutions have a cytopathologist comfortable or experienced enough in musculoskeletal tumors to make a definitive diagnosis.^{6,15,20} This is due to the overlapping cytologic features of many reactive and neoplastic lesions and to the lack of preservation of complex architecture in the biopsy sample.^{5,18,19} This technique also tends to under-grade sarcomas.^{13,21}

A definitive diagnosis must be based on a combination of the cytologic findings of the biopsy and the initial radiographic appearance (Figure 2A and B). In cases when FNA is inconclusive, a more definitive biopsy is needed to confirm the nature and grade of the lesion.²¹

3 When to perform core needle biopsy.

Core needle biopsy (CNB) is a more widely accepted biopsy method in the United States with an associated accuracy of diagnosis from 66% to 97%.²² It is important to note that the rates of altered treatment and outcome as a result of needle biopsy are considerably lower than those for open biopsy.² Like FNA, core needle biopsy has many of the same advantages that are associated with percutaneous biopsies, although these advantages are not quite as significant.⁶ CNB can be performed in an outpatient setting, under local anesthesia and is cost-effective when compared with open biopsy.^{6,8} No incision is required, thus significantly decreasing the risks for common biopsy complications.⁹ Like FNA, but unlike open biopsy procedures, CNB entails minimal trauma to the skin and so permits preoperative treatments such as radiation and/or chemotherapy to be initiated once the diagnosis is established.⁹

Unlike FNA, core biopsy preserves the structural architecture of the tissue sample and provides a larger quantity of tissue than FNA, making diagnosis and grading easier for general pathologists (Figure 3); this advantage accounts for its more widespread use.^{6,18} Inadequate tissue sampling, in quantity and representation, is still one of its greatest limitations, making it difficult to diagnose low-grade lesions.^{1,4} Multiple cores can be sampled to minimize this problem.⁵ An advantage of CNB is that it can be used to obtain samples of fibrocollagenous or bone lesions where FNA often fails.^{6,18} Core needle biopsy offers advantages over open biopsy, including the ability to direct the needle to various portions of the tumor so that various portions of a heterogeneous mass can be sampled. For deep lesions that are not palpable, CNB can be performed using fluoroscopic, ultrasound, or, most commonly, computed tomography assistance in

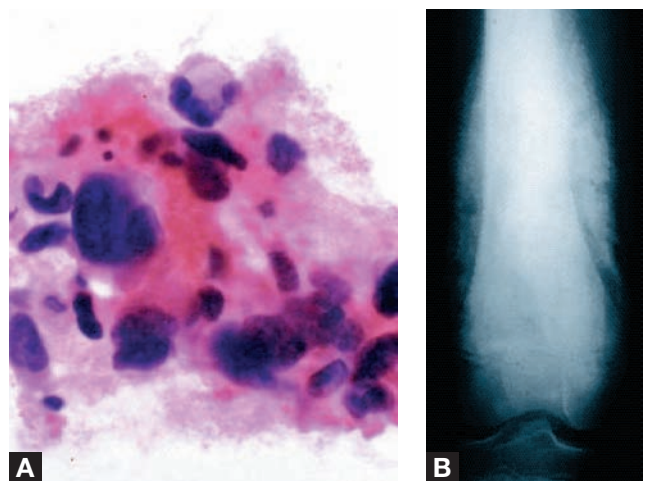


Figure 2. (A) The fine-needle aspirate (FNA) reveals a cluster of cells with marked nuclear atypia. The nuclei are enlarged, irregular, and hyperchromatic. This demonstrates a pleomorphic malignant neoplasm. (B) The FNA, in combination with the initial radiographic appearance, is diagnostic of osteosarcoma.



Figure 3. A typical gross appearance of a sarcoma biopsy specimen obtained using a True-Cut core needle biopsy technique. Multiple cores obtained at the time of biopsy minimize the risk of sampling error. Core needle biopsy preserves the structural architecture of the tumor.



Figure 4. An 18-year-old with osteosarcoma of the right proximal tibia, 3 months after incisional biopsy and following neoadjuvant chemotherapy, at the time of definitive limb-sparing resection. Line B represents the biopsy incision.

the radiology department by an experienced interventional radiologist.^{4,5,22-24} The surgeon should always review with the radiologist the planned surgical approach to ensure that the biopsy tract can be excised at the time of definitive surgery and that uninvolved tissue planes are not contaminated.^{10,22} It has been suggested that CNB can be used in addition to FNA or as follow-up to an undiagnostic FNA, thus greatly decreasing the need for open biopsy.^{18,21}

4 When to perform an open incisional biopsy. Open biopsy has long been considered the gold standard in obtaining tissue diagnosis, with a reported accuracy of 98% (Figure 4).^{4,22} An open biopsy may be either incisional or excisional.⁵ An open biopsy is most appropriate when the list of conditions in the differential diagnosis is long and varied.^{5,10} Open biopsy provides the great advantage of being able to visualize the mass, maximizing the likelihood of obtaining adequate tissue for diagnosis and ancillary studies.^{5,22} It should be performed in such a way as to ensure that representative tissue is obtained.¹⁰ As in the case of core needle biopsy, pre-biopsy imaging studies should be reviewed so that necrotic areas of the tumor are avoided.⁵ Frozen sections are sent at the time of open biopsy to confirm that adequate tissue has been obtained in order to avoid the need for repeated biopsies.^{4,9} Associated wound complications, including hematoma, infection, and possible tumor spillage, can interfere with definitive treatment and are the greatest disadvantages to open biopsy.²⁰ The increase in cost, over that of closed biopsies, and the associated risk of general anesthesia also can not be ignored.⁶



Figure 5. (A) The patient underwent excisional biopsy through a transverse incision for a suspected ganglion mass that proved to be a high-grade soft-tissue sarcoma. **(B)** Following wide local re-excision, soft-tissue reconstruction was necessary as a result of the poorly planned biopsy.

5 When to perform excisional biopsy. Excisional biopsy involves removal of a tumor without a prior biopsy. The main advantage of a successful excisional biopsy, indicating either a benign lesion or clear margins, is that there is no need for subsequent surgery.³ There is also minimal risk of tumor spillage if wide margins are undertaken, and this method also has the advantage of complete tissue sampling.³ Often an adequately radical excisional biopsy of a mass is not performed and the marginal resection leaves microscopic tumor behind (Figure 5A).^{6,25} In cases when the diagnosis of sarcoma is discovered, the patient needs to be referred for wide local reexcision (Figure 5B).^{6,25} The second operation requires a larger resection, or occasionally an amputation, that would not have otherwise been needed had the lesion not been excised.^{6,25} Noria and colleagues reported that at least 35% of patients who underwent an unplanned excision of a soft-tissue sarcoma had residual tumor cell as evident on histological examination at the repeat excision.²⁵

Although excisional biopsy may be indicated in select situations, it is associated with significant morbidity when used indiscriminately. Excisional biopsy is indicated in cases when the diagnosis of a benign lesion is

certain,^{8,9} for small subcutaneous lesions,⁹ or when the tumor type will not alter treatment. Other situations where it may be acceptable are those in which wide margins can be obtained without additional morbidity, such as complete removal of the proximal fibula.^{3,8,9} If these specific conditions do not apply, risks include gross tumor spillage and cross-contamination of tissue planes, in which case the possibility for limb salvage, if the mass is malignant, is significantly decreased.¹⁰

CONCLUSIONS

The type of biopsy method depends on the institution's ability, experience of the physicians, differential diagnosis, and tumor location. Regardless of which method is chosen, proper biopsy technique, such as preoperative planning, biopsy placement and orientation, and hemostasis, should be observed to avoid unnecessary complications and improve subsequent outcomes.

AUTHORS' DISCLOSURE STATEMENT & ACKNOWLEDGMENTS

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REFERENCES

- Dickinson IC, Duggal A, Choong PF. Biopsy of musculoskeletal tumours. *ANZ J Surg.* 2004;74:511-512.
- Mankin, HJ, Mankin CJ, Simon MA. The hazards of the biopsy, revisited. *J Bone Joint Surg Am.* 1996;78:656-663.
- Aboulafla AJ. Biopsy. *AAOS Instr Course Lect.* 1999;48:587-590.
- Lackman RD. Musculoskeletal oncology. In: Vaccaro AR, ed. *Orthopaedic Knowledge Update 5.* American Academy of Orthopaedic Surgeons; 2005:197-215.
- Bickels J, Jelinek JS, Shmookler BM, Neff RS, Malawer MM. Biopsy of musculoskeletal tumors. Current concepts. *Clin Orthop Relat Res.* 1999;368:212-9.
- Pollock RC, Stalley PD. Biopsy of musculoskeletal tumours—beware. *ANZ J Surg.* 2004;74:516-519.
- Sanders TG, Parsons TW. Radiographic imaging of musculoskeletal neoplasia. *Cancer Control.* 2001;8:221-231.
- Shives TC. Biopsy of soft-tissue tumors. *Clin Orthop.* 1993;289:32-35.
- Simon MA. Current concepts review: biopsy of musculoskeletal tumors. *J Bone Joint Surg.* 1982;64:1253-1257.
- Springfield DS, Rosenberg A. Biopsy: complicated and risky. *J Bone Joint Surg.* 1996;78:639-643.
- Hosalkar HS, Dormans JP. Limb sparing surgery for pediatric musculoskeletal tumors. *Pediatr Blood Cancer.* 2004;42:295-310.
- 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;64:1121-7.
- Jones C, Liu K, Hirschowitz S, Klipfel N, Layfield LJ. Concordance of histopathologic and cytologic grading in musculoskeletal sarcomas: can grades obtained from analysis of the fine-needle aspirates serve as the basis for therapeutic decisions? *Cancer.* 2002;96:83-91.
- Domanski HA, Akerman M. Fine-needle aspiration of primary osteosarcoma: a cytological-histological study. *Diagn Cytopathol.* 2005;32:269-75.
- Singh HK, Kilpatrick SE, Silverman JF. Fine needle aspiration biopsy of soft tissue sarcomas: utility and diagnostic challenges. *Adv Anat Pathol.* 2004;11:24-37.
- Wakely PE Jr, Kneisl JS. Soft tissue aspiration cytopathology. *Cancer.* 2000;90:292-8.
- Fletcher CDM, Kempton RL, Weiss SW. Recommendations for the reporting of soft tissue sarcomas. Association of Directors of Anatomic and Surgical Pathology. *Mod Pathol.* 1998;11:1257-1261.
- Domanski HA, Akerman M, Carlen B, et al. Core-needle biopsy performed by the cytopathologist. *Cancer.* 2005 May 25; [Epub ahead of print].
- Kilpatrick SE, Cappellari JO, Bos GD, Gold SH, Ward WG. Is fine-needle aspiration biopsy a practical alternative to open biopsy for the primary diagnosis of sarcoma? Experience with 140 patients. *Am J Clin Pathol.* 2001;115:59-68.
- 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.
- Laredo J. Percutaneous biopsy of primary soft tissue tumors. *Semin Musculoskelet Radiol.* 1999;3:139-144.
- Altuntas AO, Slavin J, Smith PJ, et al. Accuracy of computed tomography guided core needle biopsy of musculoskeletal tumours. *ANZ J Surg.* 2005;75:187-91.
- Torriani M, Etchebehere M, Amstalden E. Sonographically guided core needle biopsy of bone and soft tissue tumors. *J Ultrasound Med.* 2002;21:275-81.
- Koenig CW, Duda SH, Truebenbach J, et al. MR-guided biopsy of musculoskeletal lesions in a low-field system. *J Magn Reson Imaging.* 2001;13:761-8.
- Noria S, Davis A, Kandel R, et al. Residual disease following unplanned excision of soft-tissue sarcoma of an extremity. *J Bone Joint Surg Am.* 1996;78:650-5.