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Review Article

The Role of Biopsy Accuracy in the Treatment of Musculoskeletal Tumors

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Abstract

Background: The accurate treatment of Musculoskeletal (MSK) tumors necessitates appropriate timely biopsy of the mass of interest. With regards to malignant neoplasms biopsy plays a crucial role in the direction of treatment courses and patient outcome.

Methods: This is a retrospective single-center chart review of 924 biopsies from 2013-2023. Patients included were between 18-85 with MSK tumors that necessitated biopsy and subsequent surgical treatment. Biopsy and final resection histopathology reports were compared to determine the rate of accuracy for each biopsy type: excisional, incisional and needle (core/fine). Excisional biopsies were excluded. This left 687 biopsies to compare: 508 incisional and 168 core-needle biopsies of soft tissue and bone MSK tumors.

Results: Open biopsy had an overall accuracy rate of 98% with a 95% Confidence Interval (CI) of 97% to 99% and needle biopsy 88% (95% CI [82%, 92%]). Overall, 26 biopsies were not representative of the final resected tumor: eight incisional biopsies and 18 core-needle biopsies. The inaccuracy of these biopsies resulted in 14 patient's treatment to be changed. Three required meticulous surveillance due to a more aggressive nature of the tumor. One had an altered outcome due to over aggressive surgery. Nine required further biopsies.

Conclusion: This finding differs from previously conducted surveys on the biopsy of MSK tumors. The increased accuracy is due not only to dedicated MSK oncology tumor board specialists reviewing and often repeating the biopsies within the unit but also frequent consultation to MSK oncology units by community orthopaedic surgeons.

Keywords: Musculoskeletal; Biopsy; Tumors; Orthopaedic Surgeons

Introduction

In 1982 and again in 1996 orthopaedic physicians in conjunction with the Musculoskeletal Tumor Society (MSTS) polled colleagues to understand the biopsy, treatment and outcomes of patients with neoplasms of the bone and soft tissue [1-13]. In a surprising outcome, nearly 18.2% of patients reported had erroneous diagnoses that adversely affected their ultimate treatment outcome. In the space of 14 years between the two surveys the more concerning trend noted was no improvement in outcome. Since these studies with MSTS surgeons, considerable amount of research has been done on overall accuracy of each biopsy method with reported accuracy of percutaneous biopsy and incisional biopsy being reported up to 80%-97% and 91-97% respectively [1,3,4,7,9,14-16,23]. Accuracy alone however does not yield a true picture of the clinical utility of a biopsy and the impact upon patient outcomes of an inaccurate biopsy is still devastating [18,24].

Treatment of Musculoskeletal (MSK) neoplasms is dependent upon accurate diagnosis. To obtain an accurate diagnosis, biopsy is a required step. A successful biopsy depends greatly on an appropriate approach and method performed by a skilled orthopaedic Oncologist who will ultimately perform the final resection of the mass of interest or a skilled MSK Radiologist [22].

Obtaining adequate tissue volume and also use of a multidisciplinary team are essential to ensure an accurate diagnosis and ultimately the tailored treatment plan for each patient [6,20]. Understanding the effect of biopsy type and accuracy on the ultimate outcome of patients and why biopsy accuracy has increased so drastically is of particular interest to our team. To investigate similar outcomes, a study of tumor patients within the orthopaedic oncology unit at the University of Colorado Hospital (UCH) was conducted.

1. Which biopsy technique rendered the most accurate diagnosis?
2. Was the biopsy representative of the final excised tumor?
3. If the biopsy was not representative did the accuracy alter the way the patient was treated?
4. In the cases where the biopsy was not representative of the final excised tumor, did the inaccuracy of the biopsy alter the ultimate outcome of the patient?

Materials and Methods

This is a retrospective comparative study of 924 biopsies from 2013-2023 who were seen within the University of Colorado Department of Orthopaedics. All patients were diagnosed and treated within the orthopaedic oncology unit within the Department of Orthopaedics and consented to the use of their clinical data. Patients were followed for a maximum of 10 years or until their treatment follow-up ended at UCH. Patients included were between 18-85, seen within UCH orthopaedic oncology, with musculoskeletal tumors that necessitated biopsy and subsequent surgical resection.

Data was gathered using UCH's electronic health record system Epic Systems Corporation (commonly known as Epic) and the records of UCH's Department of Pathology. Biopsies were categorized by type: excisional, incisional, core-needle and Fine-Needle Aspiration (FNA). Basic data regarding the site, location of the biopsy, staging, complications from either surgery, current status and surgical treatment were collected. Biopsies done within UCH occur in either interventional radiology by a MSK Radiologist or in the Operating Room (OR) by the unit orthopaedic Oncologist. If frozen section was utilized, the surgeon could choose within the same operative setting to close the wound after the biopsy and wait on final pathology or proceed with resection. A change in the biopsy method during the same operative setting can also occur if the primary method chosen does not yield sufficient tissue. All biopsy and resection samples were sent to the pathology department and reviewed by cytopathologists, clinical musculoskeletal pathologists and if necessary, consultation by specialist soft-tissue or bone experts. To determine if a biopsy was representative of the tumor, the histopathology reports of the biopsy and the final excision reports were compared. Of the 924 biopsies no biopsy was excluded due to technical reasons or non-diagnostic sampling. Excisional biopsies (427 total) were excluded because there was no opportunity to compare a biopsy to the final excision. This left 687 biopsies to compare: 508 incisional biopsies, 168 core-needle biopsies and 11 needle-biopsies.

A biopsy was deemed to be non-representative if the histopathological diagnosis from the biopsy and the diagnosis of the final resected tumor did not match. To determine if the treatment plan was altered the difference in the biopsy and final resection histopathology reports were compared to determine the extent to which they differed. If a report went from a benign to malignant finding or vice versa, was too degraded or not specific enough to determine a diagnosis or if the biopsy had to be repeated multiple times on the same lesion to obtain a final diagnosis, then these biopsies were considered to have changed the course of treatment for the patient. If the course of treatment was delayed or complications due to the inaccuracy of the biopsy occurred the ultimate outcome of the patient was negatively impacted. The incidence of consultation by an intramural panel of MSK pathologists or expert extramural consultation was also noted.

Data analysis was done using R software version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria.). For data summaries, numeric variables are reported as means and Standard Deviations (SD) and categorical data are reported as counts and relative percentages. When appropriate, independent t-tests are used for pairwise comparisons of means. For categorical data, chi-squared tests and Fisher's exact tests, dependent on sample size, are used to evaluate the differences in counts. 95% Confidence Intervals (CI) for certain measures are also reported. A statistical significance threshold is set at $p < 0.05$.

Results

Open biopsy had an overall accuracy rate of 98% (95% CI [97%, 99%]) and needle biopsy 88% (95% CI [82%, 92%], $p < 0.001$). 508 Incisional biopsies were performed and 179 total needle biopsies. Eight incisional biopsies were not representative of the final

excision which led to an accuracy rate of 98% (95% CI [97%, 99%]). Eighteen core-needle biopsies were not representative leading to an accuracy rate of 89% (95% CI [83%, 93%]). Three FNA biopsies were not representative yielding an accuracy rate of 73% (95% CI [39%, 93%]). The comparison of accuracy rates of each biopsy technique was statistically significant for all pairwise comparisons ($p<0.001$ for all tests).

Of the 687 biopsies performed from 2010-2023 at UCH 29 biopsies were non representative of their final resected tumor leading to an accuracy rate of 96% (95% CI [94%, 97%]). 191 biopsies were shown to be from metastatic disease, 194 from sarcomas, 119 from bone tumors, 181 from benign soft-tissue tumors. The most common benign findings were lipoma, giant cell tumor and fibromatosis respectively. The accuracy of finding metastatic disease was 98% (95% CI [95%, 100%]), sarcoma 92% (95% CI [87%,95%]), bone tumor 95% (95% CI [89%, 98%]) and a benign soft-tissue finding 98% (95% CI [94%, 99%]) ($p = 0.004$). The most common site biopsied were the femur and the soft tissue of the thigh or lower leg. Of the biopsies analyzed, 629 occurred at UCH and 58 at referring institutions. 24 of those occurring at UCH were not representative of their final excised tumor yielding an accuracy rate of 96% (95% CI [94%, 97%]) and 5 at referring institutions with an accuracy rate of 91% (95% CI [80%, 97%]) ($p = 0.089$). Of the 629 biopsies that occurred at UCH 604 biopsies occurred in the operating room with a dedicated orthopaedic Oncologist had an accuracy rate of 97% (95% CI [95%, 98%]) and 25 biopsies occurring in interventional radiology had an accuracy rate of 88% (95% CI [68%, 97%]) ($p = 0.065$).

The inaccuracy of the biopsy resulted in 14 patients' course of treatment to be changed. Three patients required more aggressive treatment due to the biopsy. One patient had the final diagnosis changed after comparison with the resected tissue. Nine biopsies either contained an insufficient sample due to degraded tissue or there was inadequate tissue material to determine a definitive diagnosis and they required a second biopsy to achieve a definitive diagnosis thus delaying treatment. In one patient, the tumor was so undifferentiated that no diagnosis could be assigned to it.

Ultimately, two patients were negatively impacted by the inaccuracy of their biopsy. One patient ultimately diagnosed with multiple myeloma had a 6-month delay in their diagnosis after requiring three biopsies by two surgeons to obtain a correct diagnosis. The other patient diagnosed with an inflammatory myofibroblastic tumor was initially diagnosed with a more aggressive tumor type. Upon resection, the correct diagnosis was found but only after an aggressive resection that ultimately led to the development of an infection requiring debridement.

Of the non-representative findings all had a consult obtained on their final pathology, five of which were extramural specialist consultations. Out of 687 biopsies 24 developed a surgical complication. Eleven patients developed an infection. Eight patients had delayed wound healing or wound dehiscence. Four developed a hematoma or seroma that required further treatment to evacuate the hematoma. One patient had delayed bone healing after tumor resection. The rate of complication for incisional biopsy was 3.1% (95% CI [1.9%, 5.2%]), 4.2% (95% CI [1.8%, 8.7%]) for core-needle biopsy and 9.1% for FNA (one of eleven cases) (95% CI [0.48%, 43%]). One patient of the 14 whose treatment course was changed, developed a surgical complication. After the patient's resection surgery, an infection developed in the tumor prosthesis and needed revision surgery to correct.

Discussion

In the treatment and diagnosis of MSK tumors the balance between obtaining adequate tissue representation of the mass of interest, invasiveness and cost must be weighed. While open biopsy is the reference standard, core-needle biopsy alone and a combination of core-needle and FNA can yield acceptable accuracy rates. FNA alone is insufficient when diagnosing bone and soft tissue tumors as the cytologist can glean no information regarding tumor architecture and local environment which is often essential in diagnosing malignant MSK tumors. According to the literature, the incidence where a core-needle biopsy fails to yield a representative sample, open biopsy is used more often than repeating the core-needle biopsy [8]. Rate of repeat biopsy for percutaneous biopsy can be as high as 25% [11, 17]. Studies similar in nature to ours often vary in their definitions of accuracy and seldom report on the outcomes of patients with inaccurate biopsies. These studies often exclude non-diagnostic biopsies which can result in higher reported accuracy rates [18].

The limitation of this study is the single-center, non-randomized, comparative retrospective nature of this study. Due to the severity of some cases and the varying nature of treatment and pathogenesis this can lead to a selection bias. As this study included patients seen at a regional cancer center, this can also lead to a selection bias as more serious cases are often referred to

this institution. As a single-center study the comparison between the biopsy and final excision result is more consistent. However, due to the rarity of these cases and the heterogeneity of tumor types within this patient population this study is deemed worthwhile. In this study incisional biopsy is shown to be 98% accurate under the direction of an experienced orthopaedic surgeon. There is shown to be a statistically significant difference in the accuracy of each biopsy type, which occurs more often in soft tissue biopsies than in bone biopsies. In cases of cavitary bone lesions where the core needle technique was used the addition of curettage of the tumor wall was added which greatly improves the tissue yield. Even in cases where up to seven different core biopsies are taken in alternating directions this method can yield a non-representative sample.

The availability of advanced imaging technology including CT, MRI and ultrasound as well as the availability of frozen section add to the accuracy of biopsies. In the case of biopsy performed by an interventional Radiologist, which is often chosen as the first method and setting of biopsy for questionable lesions, performing a needle biopsy under guidance can be an effective method. However, even in such a setting the lack of information gleaned about the tumor tissue can be limited. In the case of biopsy in an operating room with or without frozen section, the orthopaedic Oncologist can use their clinical judgement in real time alongside the on-call pathologist to make assessments of a tumors malignancy or type. The benefit to accuracy rate is evident, (Fig. 1). The utilization of frozen section intraoperatively to determine whether a tumor is benign or malignant may lead to performing the final surgery during the same operative session. In 63% percent of cases the biopsy was reviewed by a panel of pathologists and in 14% of cases pathological consultation went to outside specialists. Discussion of cases at a multidisciplinary conference increases rates of accuracy and decreases negative patient outcomes due to inaccuracy.

Complication rates often have little to do with biopsy type and more to do with the site biopsied or aggressive nature of the tumor. Highly malignant tumors often have a large necrotic component or undergo treatment prior to resection that will complicate wound healing. The average age of our patients with a malignant finding is greater and difficulty with slower healing can often be seen. There still exists in the literature a debate on the prevalence of tumor seeding of biopsy tracts. Some believe diminished risk of biopsy tract seeding is possible only with percutaneous biopsy [5,14]. However, it has been demonstrated that seeding is unlikely in either the case of open or percutaneous biopsy if the biopsy tract is excised en bloc. There is no association between tumor contamination and biopsy technique [2,10,19]. One notable exception being the case of retroperitoneal sarcoma [11]. Risks of any biopsy technique can be avoided if appropriate guidelines are adhered to, however the true cost vs benefit analysis must be determined [21-24]. Clinical judgement of an experienced orthopaedic oncological surgeon as part of a multidisciplinary team at the treatment center will ensure the best possible outcome and greatest accuracy in most cases.

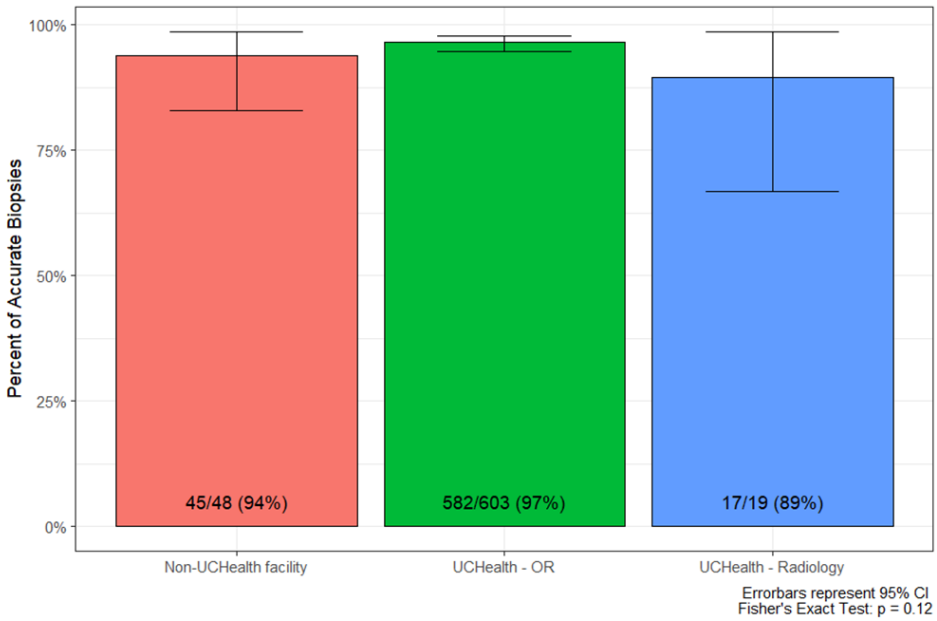

Figure 1: Comparison of accuracy rates within UCH and outside of UCH within this patient cohort. Outside of UCH refers to any initial biopsy that occurred outside of UCH which may or may not have been in an OR setting. Within UCH biopsies are broken down by those performed in the operating room by the orthopaedic surgeon and those performed in Interventional Radiology.

Conclusion

This finding differs from previously conducted surveys on the biopsy of MSK tumors. The increased accuracy is due not only to dedicated MSK oncology tumor board specialists reviewing and often repeating the biopsies within the unit but also frequent consultation to MSK oncology units by community orthopaedic surgeons.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethical Statement

The project did not meet the definition of human subject research under the preview of the IRB according to federal regulations and therefore was exempt.

Informed Consent Statement

Informed consent was obtained from all participants included in the study.

Authors' Contributions

All authors contributed equally to this paper.

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