Addis Ababa University

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Diagnostic accuracy of Core needle Biopsy of primary bone and soft tissue tumors with reference to final resection histopathology at Tikur anbessa specialized hospital. A retrospective cross-sectional study

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ADVISOR'S APPROVAL SHEET

This is to certify that the thesis entitled **"Diagnostic accuracy of core needle biopsy of primary bone and soft tissue tumors with reference to final resection histopathology at Tikur Anbessa specialized hospital. A retrospective cross-sectional study** "is submitted in partial fulfillment of the requirements for the Specialization Certificate in Orthopedics and trauma surgery to the department of orthopedics and Trauma surgery, Addis Ababa University college of health science and has been carried out by Dr. Dawit Getachew under my supervision. Therefore, I recommend that the student has fulfilled the requirements and hence hereby can submit the thesis to the Department.

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ABSTRACT

Background: Biopsy plays a crucial role in diagnosing musculoskeletal tumors. While open biopsy is traditionally seen as the gold standard, recent literature indicates that percutaneous core needle biopsy yields comparable results while offering benefits such as being less invasive, having fewer complications, and being faster and more cost-effective. This study aims to evaluate and compare the diagnostic accuracy and effectiveness of core needle biopsy against final surgical resection in musculoskeletal lesions.

Methods: This retrospective cross-sectional study, conducted from April 2022 to June 2024, identified and enrolled patients with primary bone or soft tissue tumors who underwent core needle biopsy (CNB) followed by tumor resection at the Orthopedics Department of Tikur Anbessa Specialized Hospital. The CNB results were evaluated for sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy.

RESULTS: A total of 87 patients were identified and enrolled in this study. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of the core needle biopsy (CNB) were 90%, 94.6%, 95.7%, and 87.5%, respectively. The overall diagnostic accuracy of CNB was 93.1%. A specific diagnosis was achieved in 80% of the cases (67 out of 87), and no complications were reported associated with the CNB procedure

Conclusion: Core needle biopsy is a reliable technique for differentiating benign and malignant as well as obtaining the final diagnosis of primary bone and soft tissue tumors, with a lower risk of complications. It may be confidently integrated into clinical practice as a substitute for the open incisional biopsy method.

Acknowledgement

I would like to express my sincere gratitude to my supervisors, Dr. Ermias Gizachew and Dr. Rahel Hailu, for their ongoing motivation and support. Your kindness and inspiration have had a profound impact on my career, and I will always be grateful for the significant role you have played in shaping my future. Additionally, I am thankful to the Orthopedics and Trauma Surgery Department at Tikur Anbessa Specialized Hospital for providing me with the educational opportunity to conduct this research, which will aid in furthering my career. I also appreciate , Professor Biruk Lambisso, for his willingness to support me throughout this research, starting from the development of the title.

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ABBREVIATIONS

AAU	Addis Ababa university
TASH	Tikur Anbessa specialized hospital
FNAC	Fine Needle Aspiration Cytology
PCNB	Percutaneous core needle biopsy
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
US	Ultrasonography
NICE	National Institute for Health and Clinical Excellence
WHO	World Health Organization
STS	Soft tissue sarcoma
UPS	Undifferentiated pleomorphic sarcoma
WLE	Wide local exicision
AKA	Above knee amputation
MBD	Metastatic bone disease

1. Introduction

1.1 Background

Soft-tissue sarcomas (STS) and bone sarcoma are rare malignancies of mesenchymal origin. Primary bone neoplasms accounts for only 0.2% of all human neoplasms and have a broad spectrum of morphology and biological behavior.(1)

Soft tissue sarcoma are heterogeneous tumors encompassing >80 histological subtypes and accounts approximately 1% of all malignancy in adults and 15-20% of pediatrics malignancy(2)

In Ethiopia there is increase in case number of musculoskeletal tumors from less than 10 cases per year to more than 100 cases in 2007 and 2008 each in Blacklion hospital. Soft tissue sarcoma is the leading musculoskeletal tumor accounting for 66.3%.(3)

The heterogeneity of tumor histology is associated with marked differences in their clinical course and response to conventional and targeted chemoradiotherapy, requiring refined treatment plans.

Management involves multidisciplinary approach including surgical resection with neoadjuvant and/or adjuvant chemoradiation protocols depending on histological classification and grade, tumor location, and size.

Therefore, correct histological classification is mandatory before the initiation of individualized treatment and early correct diagnosis helps for salvage of tumor affected limb and also increase patient prognosis(4)

Assessment consisting of clinical history and physical examination, followed by cross sectional imaging and tissue biopsy is recommended before initiation of treatment

(5)

In our hospital enlarging soft tissue mass associated with local pain and pathologic fracture are the most common presenting symptom of primary bone tumor. 10-29yrs of age are the most affected age group with primary bone tumors as well as distal femur and proximal tibia are the affected anatomical site. (6)

Biopsy is a procedure to remove a sample of tissue or cells for pathology examination. It is crucial step providing the basis for any further therapeutic strategy.

Types of biopsy procedure include fine-needle aspiration biopsy(FNAC), core needle biopsy (CNB), incisional biopsy and exicisional biopsy. All have their own advantage and disadvantage.
Excisional biopsy has almost no role in the diagnostic workup except for small superficial masses and if final histology turns sarcoma, it will not be therapeutic (7,8)
FNAC only provides cytology, not true histology so has limitations including the ability to determine tumor grade and the specific histologic subtype. So not recommended as primary diagnostic modality, though may be useful in confirming disease recurrence. (9)
In contrast to FNA biopsy, CNB provides a specimen for true histopathologic analysis. It is less invasive than open surgical biopsy. Sample is taken in relatively quick and easy manner, and these procedures can be carried out in the outpatient care.
Percutaneous CNB has advantages over open biopsies like cost effective performed as outpatient with local anesthesia, reduced and limited biopsy tract to be removed in case final surgery required.
Incisional biopsy is the traditional standard of care to establish definitive diagnosis. Although it can yield sufficient sample tissue, it is associated with disadvantages like spillage of tumor into adjacent compartments due to poor hemostasis or faulty biopsy site placement, complications of wound infection, and the usual requirement for hospitalization of the patient.(10,11)

Sub optimally performed incisional biopsy may compromise limb salvage surgery and have negative impact on overall survival of patients.
With increasing practice of limb salvage surgery, the less invasive biopsy techniques are being more acceptable. Open biopsy is reserved for inadequate or inconclusive percutaneous biopsy results.
Adequacy of quantity of tissue for pathologic diagnosis is the base for controversies for acceptance of percutaneous core needle biopsy. Limitations in diagnosis are due to tumor heterogeneity, poorly differentiated tumors, tumors with excessive reactive changes surrounding the tumor or excessive necrosis with in the tumor. (12)
In modern orthopedics minimally invasive core needle biopsy is becoming the first modality of biopsy study reserving open biopsy for inconclusive results though its accuracy rate vary from 66-98%. (13,14)
In our practice most of orthopedic surgeon take open biopsies with presumption that percutaneous biopsy doesn’t provide adequate tissue for histological diagnosis.

This study evaluates the diagnostic accuracy and effectiveness of core needle biopsy in primary musculoskeletal tumors

1.2 Statement of the Problem

Though open biopsies considered the gold standard traditionally recent studies suggest similar diagnostic accuracy for Core needle biopsy due to improved histopathologic procedures. (11) Recently image guided needle biopsy has increased its reliability and accuracy (15)
Guidelines suggest open biopsies should be planned in such a way that the biopsy tract can be safely removed at the time of definitive surgery to the risk of seeding and should be performed by sarcoma surgeon or in consultation with the managing surgeon (9)
Therefore, percutaneous biopsy has largely replaced open biopsy as preferred method for establishing histologic diagnosis.

In Ethiopia, most of orthopedic surgeons usually take open biopsies with the presumption that percutaneous biopsy does not provide adequate tissue for histopathologic diagnosis. Since April 2022 we established the first specialized musculoskeletal oncology unit in Tikur Anbessa specialized hospital department of Orthopedics and trauma surgery after the first ever abroad fellowship trained sarcoma surgeon joined the department.
It has been difficult to perform incisional biopsy in all cases in our setup due to surgical environment and man power.
Hence, we are using percutaneous core needle biopsy in discussion with musculoskeletal radiologists as first modality for histopathology diagnosis of bone and soft tissue tumors before any surgical or chemo-radiotherapy management.
To the best of my knowledge there is no single study on the reliability and diagnostic accuracy as well as effectiveness of percutaneous core needle biopsy on determining histopathology of bone and soft tissue tumors in our setup.
Therefore, there is a need to investigate and evaluate the reliability and diagnostic accuracy of core needle biopsy in musculoskeletal tumors.

1.3 Justification of the study

Most evidence show that percutaneous core needle biopsy has high diagnostic accuracy with insignificant complication rate. The complication with incisional biopsy especially inappropriately placed incisional site makes limb salvaging surgery challenging. (8)
Though accurately diagnosing musculoskeletal tumors can be challenging, early accurate diagnosis of histology is crucial for initiating treatment plan altering both prognosis and quality of life of the patients.
Histologic tumor grade is one of strongest predictor of metastatic risk and patient prognosis. (16)
Delay in diagnosis waiting for operative time with complication from open incisional biopsy leads to suboptimal patient outcome including delayed chemoradiotherapy.
The scarcity of trained sarcoma surgeon as well as operative time makes difficult to perform incisional biopsy in our setup in all patients.

Core needle biopsy which is performed as outpatient which can also be done by musculoskeletal radiologists is becoming a reliable first step to harvest representative and viable tissue specimen for accurate diagnosis reserving incisional biopsy for results not consistent with clinical and imaging findings.

Therefore, investigating diagnostic accuracy of core needle biopsy in bone and soft tissue tumors is essential for improving patient treatment planning and prognosis.

1.4 Significance of the study

Increased accuracy and reliability of CNB avoids morbidity of an open biopsy while obtaining adequate tissue to approach diagnostic accuracy of open technique.

The procedure can be performed in outpatient setting avoiding hospital admissions and anesthesia complications with timely diagnosis to guide treatments.
The histological grade plays significant role in predicating patient prognosis allowing better assessment which can guide treatment and patient counseling.
It also decreases referral to musculoskeletal sarcoma unit centers before tissue diagnosis helping referring center orthopedic surgeons to be selective in referring patients who needs limb salvaging reconstructive surgeries.
Less invasive procedures are also generally preferred by patients which can lead to higher acceptance with diagnostic recommendations.
The result of this study will replace the open biopsy techniques which is the usual practice in Ethiopia with timely diagnosis and treatment of bone and soft tissue tumors.

2. Literature Review

A biopsy is a critical prerequisite for the diagnosis and management of musculoskeletal tumors. Treatment decision and prognosis depends not only on benignity or malignancy of the tumor but also histological features and grade of the tumor. Immunohistochemistry and occasionally ultra-structural studies are necessary for specific diagnosis. Limited confidence in diagnosis with core needle biopsy arise from heterogeneity of the tumor with respect to grade or histology and insufficient sampling due to wide spread tumor necrosis (17,18)

Vincent crenn et al. reported in retrospective monocentric study which included 196 patients on efficiency and safety of percutaneous core needle biopsy in diagnosing primary bone tumors: diagnostic yield obtained in 84.7% after core needle biopsy allowing diagnosis and clear therapeutic strategy. Malignant tumor reported in 49.5% mostly osteosarcoma (13.8%), chondrosarcoma (13.8%), Ewing sarcoma (10.2%). The most common benign lesion was GCT (9.7%).
There was no diagnostic certainty in 15.3% (30 patients), 2 cases due to technical failure to harvest sufficient tissue sample, 28 cases due to necrotic tissue and nonspecific tissue.
Diagnostic accuracy calculated by comparing the core needle biopsy diagnosis with final surgical biopsy (67.8% (133 patients) operated patients) which showed 91.7 % accuracy and diagnostic discrepancy in 11 patients. From the 11 patients in 8 lack formal initial diagnosis in which second line

biopsy performed (5 open biopsy and 2 ct guided biopsy) and obtained final diagnosis (3 malignant and 4 benign). One undifferentiated pleomorphic sarcoma turned out to be osteosarcoma.
2 of the 5 malignant discrepancies were due to cartilaginous lesions suggesting chondral tumors require multidisciplinary approach for accurate diagnosis.
Complication with core needle observed in 1%(2 cases of hematoma) with no need of further treatment.(14)

A study conducted in developed countries like Germany retrospective study comparing percutaneus CNB (image guided either U/S or Ct scan) and open biopsy with final resection histopathology. The study included 77 patients(31 open biopsy, 46 CNB) and showed sensitivity of 96.9% for open biopsy and 88.8% for CNB with 100% specificity and PPV for both biopsy techniques. Compared to subsequent resection specimen the correct histopathologic diagnosis obtained in 93.9% of open biopsy and 84.2% of CNB. Insufficient sampling occurred in 7.6% of CNB of soft tissue tumor, for which with subsequent open biopsy correct diagnosis obtained . Three biospy specimens (1 obtained by open biopsy of bone lesion and 2 by CNB of soft tissue mass) diagnosed benign tumors but revealed malignant after final resection. The bone lesion initial diagnosis was enchondroma turned out to be low grade chondrosarcoma in final resection pathology. 2 lipomatous soft tissue masses were diagnosed as lipoma and final resection specimen showed low grade liposarcoma in both. All lesions with incorrect diagnosis of benign tumors were adequately treated with comlete resection according to sarcoma principle.
One open biopsy patient had impaired wound healing complication. Slightly superior result for CNB reported in malignant bone tumors relative to open biopsy. This may be due to relatively small number of cases included in the study.
CNB of soft tissue lesions revealed inferior result compared to open biopsy. This could be due to heterogenous tumors of soft tissue including liposarcoma, angiosarcoma and synovial sarcoma are amongst others potentially difficult to diagnose with CNB. Suggesting experienced orthopedic surgeon for indication of CNB in soft tissue masses regarding extent of necrosis, and location to avoid incorrect or deficient results (11)

comparative retrospective study on diagnostic accuracy of FNAC and CNB with respect to final resection histopathology done in Japan shows overall sensitivity, specificity, positive predictive value, and negative predictive value of FNAC were 78.4%, 94.2%, 92.6%, and 82.5%, respectively. The

diagnostic sensitivity, specificity, positive predictive value, and negative predictive value of CNB were 94.2%, 92.8%, 93.4%, and 93.6%, respectively. The diagnostic accuracy of FNAC and CNB was 86.6% and 93.5%, while the sampling error rate was 5.7% and 6.8% respectively. Most of the CNB discordant cases were adipose tumors. But this is not only a matter of technique, but also of the nature of the tumor itself, such as cell density or degree of nuclear atypia because distinction between lipomas and atypical lipomatous/well differentiated liposarcoma may be difficult to distinguish morpholoically even with open biopsy. For such histological types, additional immunohistological methods improve the accuracy rate.

Image guided procedures had significantly lower sampling error rate compared to blind procedures (87.0% and 86.4% for FNAC, 94.9% and 90.8% for CNB). This highlights the effectiveness of image guidance in obtaining more accurate tissue samples. The study also found no significant difference in progression-free survival(PSF) and overall survival(OS) between true positive and false negative cases in patients with high grade malignant tumors.

This study showed high accuracy rate in both fine needle aspiration cytology and core needle biopsy. Image-guided procedure was useful for cases with no palpable mass. (10)

a prospective study done in India on core needle biopsy of bone lesion 136 patients included and definitive histopathologic diagnosis obtained in 89% of patients. 14 patients required two attempts and 2 patients required three attempts at needle biopsy In 15 patients the specimen was non diagnostic. Comparison with final histopathology done(64 patients) either based on operative excision specimen or clinical course of the patients. The CNB was inaccurate in 3.1% patients(2 of 64 patients). Hence, accuracy rate of the procedure is 96.9%. There was no correlation between inability to reach diagnosis on needle biopsy and either site of lesion or nature of the pathology. There was no complications following the needle biopsy.(12)

Retrospective analytic study on reliability of core needle biopsy in diagnosis of malignant bone tumors done at Ibrahim malik teaching hospital which included 152 core needle samples of benign and malignant bone tumors which had another documented biopsy result from definitive surgery with in the same study period. The most common anatomic site of bone tumor is distal femur 35.5%(54/152), less frequent anatomic site being scapula 2.6%(4/152).

Final diagnosis showed 71%(108 cases) malignant tumor, osteosarcoma(43.5%) being the most common. Benign tumors accounted 29%(44 cases), the most common being

osteochondroma(18.1%).There was no complication reported with hospital stay of 2-6hrs post procedure. The study shows sensitivity and specificity of core needle biopsy 96.2% and 93.1% respectively with 97.1% positive predictive value and 91.1% negative predictive value.
Core needle biopsy result matched final histological result in 95.3% representing diagnostic accuracy.
7 core needle biopsy didn't match with final diagnosis results, 4 considered non diagnostic(3 benign, 1 infection) but turned out to be malignant in final diagnosis.
3 cases considered malignant and turned out to be benign in final histology result. This diagnostic inaccuracy occurred during early step of building oncology unit which decreased lately due to improvement of learning curve. Another incriminated reason for mismatch is biopsy sample taken from fracture site of pathological fracture cases (19)

3. Research Objective

3.1 General objective

- ➔ To assess the diagnostic accuracy and effectiveness of core needle biopsy of bone and soft tissue tumors in comparison with final resection histopathology of definitive surgery specimen at Tikur anbessa specialized hospital in Addis Ababa, Ethiopia

3.2 specific objective

- ➔ To compare sensitivity and specificity of core needle biopsy of bone and soft tissue tumor with final histopathology result of surgically resected tumor sample
- ➔ To evaluate effectiveness of core needle biopsy in differentiating benign and malignant musculoskeletal tumors
- ➔ To determine the commonest MSK tumors diagnosed at TASH

4. Methods and Materials

4.1 Study area

The study will be conducted in Tikur Anbessa specialized hospital (TASH), Addis Ababa Ethiopia in Orthopedics and trauma surgery department.

TASH is a tertiary hospital located at the capital city of Ethiopia, Addis Ababa. Orthopedics and trauma surgery has its own 4 stair building with 110 beds for patients. There are 28 orthopedics specialists and subspecialists, 2 fellows and 58 residents and other supporting staffs. The department has 5 days per week outpatient clinics with annual visit of more than 11,000 patients. The operation theatre has 4 fully functional tables and elective surgeries done from Monday to Friday in 3 tables while 1 table is reserved for emergency procedures being active 24 hours a day 7 days a week.

The first musculoskeletal oncology unit in the country established in 2022 GC at TASH after the return of abroad fellowship trained sarcoma surgeon. Being the only musculoskeletal oncology surgeon in the country his outpatient clinic visited by hundreds of patients referred from all over the country.

4.2 Study period

This study will be conducted from july 1 to September 30, 2024

4.3 Study design

Diagnostic accuracy Cross sectional study design will be employed

4.4 Source population

patients who were admitted with musculoskeletal tumor diagnosis and operated from April 2022 to June 2024

4.5 Study population

All patients who were diagnosed with bone or soft tissue tumors with core needle biopsy and had final resection surgery during the study period and who fulfill the inclusion criteria.

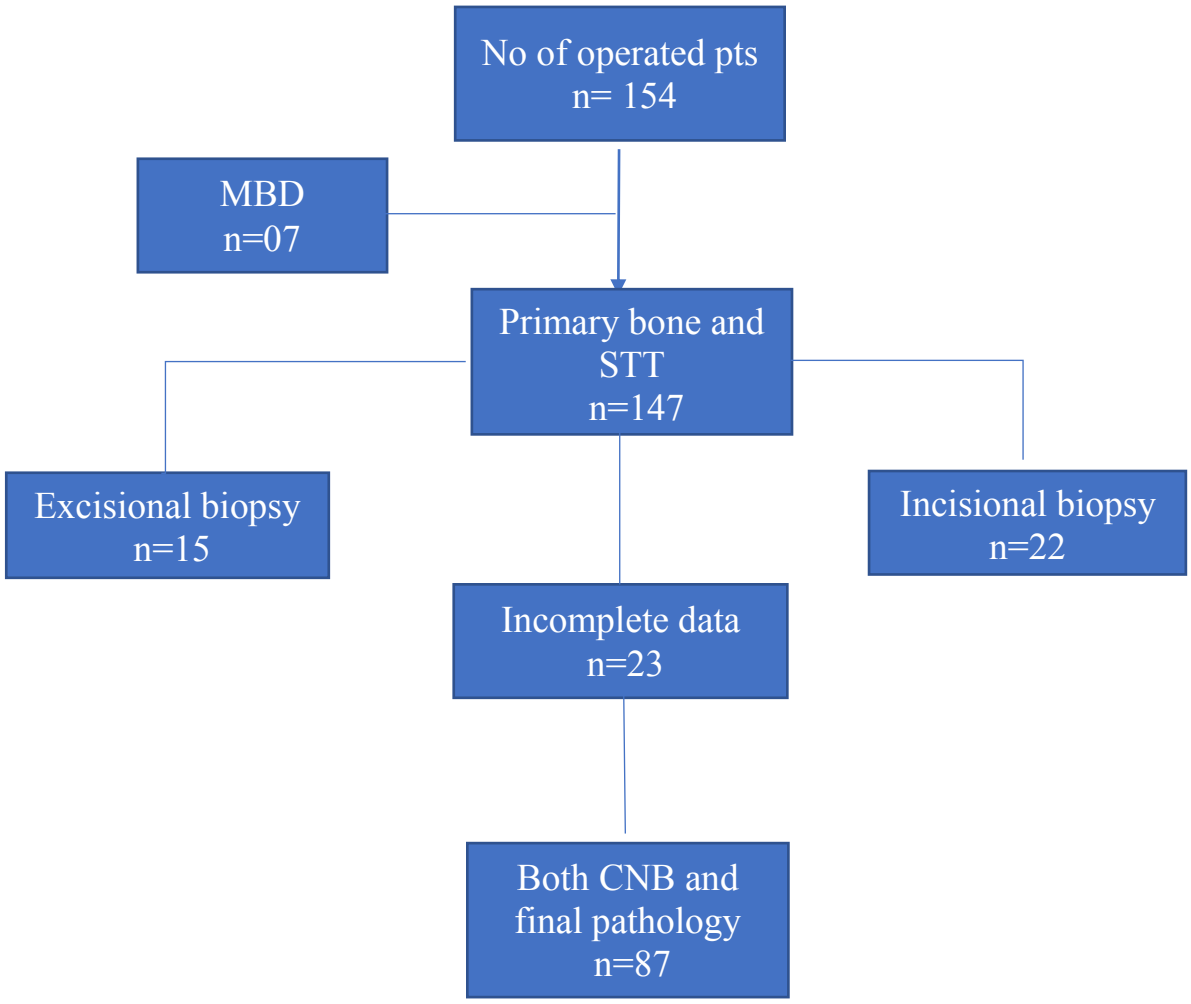


Figure 1: Flow chart of source population and study population, sampling technique. MBD: Metastatic bone disease, STT: soft tissue tumor

4.6 Inclusion Criteria

All patients who were diagnosed with primary bone or soft tissue tumors after core needle biopsy and had resection surgery and sent for final histopathology analysis

4.7 Exclusion criteria

Incomplete patients' data records

patients with secondary (metastatic tumors)

patients with excisional biopsy without core needle biopsy

patients with incisional biopsy without core needle biopsy

4.8 Sample size determination

All core needle biopsy results of bone and soft tissue tumors who had another documented biopsy result from definitive resection surgery with in April 2022 to June 2024 were included

4.9 Data Collection procedures and quality assurance

A checklist that consists of all the variables developed and used to collect the necessary data from operation logbook record, patient chart review and pathology unity electronic medical record of histopathology result.
Pathology results report reviewed for histopathologic diagnosis, grade (benign, low, intermediate or high grade) and specific tissue types.

Data collected from June to September. The collected data checked for its consistency and completeness before any attempt to enter code and analyze it.
Data consistence or validity checked, Cronbach alpha 0.78 which is acceptable.

4.10 Study variables

4.10.1 Dependent variables

Accuracy of core needle biopsy (accurate vs inaccurate)
Effectiveness of core needle biopsy (Benign vs Malignant)

4.10.2 Independent variables

Age
sex
anatomic site of tumor location
Bone tumor
soft tissue tumor

Benign

Malignant

4.11 Operational definition

The final surgical resection pathological diagnosis defined as 100% accurate on all accounts making the reference index. The pathological diagnosis of CNB and final resection tumor classified according to the WHO classification guideline of bone and soft tissue tumour.

Accurate core needle biopsy is results in agreement with subsequent pathologic examination of final surgical resection specimen results with respect to tumor histology and grade of the tumor.

Tumor grades considered to be high(grade3, grade 2), low(grade 1)

Inaccurate core needle biopsy is results that differ from final surgical specimen biopsy results in identifying malignancy, tumor grade or histologic features

Effective core needle biopsy is results accurate with respect to malignancy but not specific histologic features and can lead to appropriate treatment decision without open biopsy.

Ineffective needle biopsy is incorrect histologic results that could potentially lead to inappropriate treatment decisions and any core needle biopsy with inconclusive or non-diagnostic result that followed open biopsy. (10,17,18)

If lesions determined to be benign by both biopsy methods were designated as true negatives (TNs) and if a lesion was determined to be benign through CNB but turned out to be malignant final surgical excision, false negative (FN).

If both biopsies determined to be malignant designated as true positive (TPs) and if lesion was malignant with CNB but benign with final pathology, false positive (FP). (Walker JB et al.)

$$Sensitivity = \frac{TP}{TP + FN} * 100$$

$$Specificity = \frac{TN}{TN + FP} * 100$$

$$PPV = \frac{TP}{TP+FP} * 100$$

$$NPV = \frac{TN}{FN+TN} * 100$$

Overall accuracy rate was calculated by percentage of correctly classified instance

$$\frac{TP+TN}{TP+TN+FP+FN}$$

High level of specificity mean that we were likely to detect all benign masses as benign with CNB PPV shows all masses identified as malignant by CNB were identified as malignant in final pathology.

4.12 Procedure

All the core needle biopsy procedure was done by musculoskeletal radiologist or fellow on training. An informed consent was obtained in all cases prior to taking the patient for the procedure. Prior to CNB imagings of the lesion including CT and MRI reviewed by radiologist. The anatomical site of biopsy was chosen by future plan for definitive surgery. U/S was often used except for few patients with inaccessible area where CT-scan was used.

U/S pre-scan applied to detect location of tumour, optimal biopsy target with heterogenous lesion and NV bundle or vital organs to be avoided. 16-gauge core needle used guided by U/S after the site of the biopsy cleaned under aseptic technique and draped.

Local anaesthesia infiltrated and multiple tissue samples (4 or 5 on average) were taken to increase the diagnostic yield. The obtained tissue fixed with 10% formalin and labelled with the patient's name and MRN transferred to pathology unit with attached request form which includes pertinent history and physical examination. All specimen routinely stained with Haematoxylin and Eosin (H&E) staining.

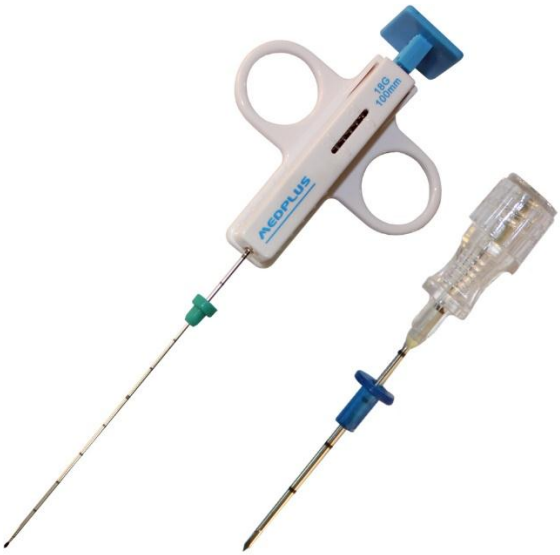


Figure 2: Core needle (semi-automatic core biopsy instrument)

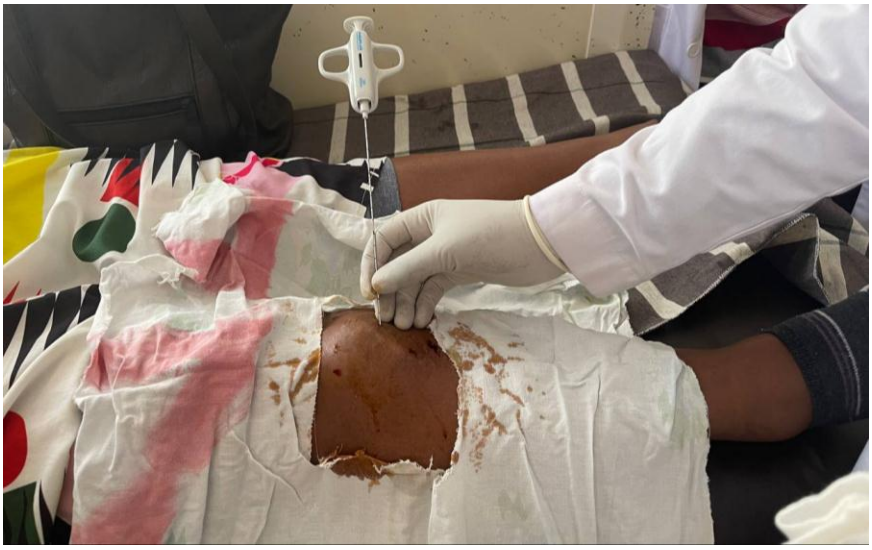


Figure 3: core needle biopsy being performed on a patient with left proximal leg soft tissue mass

Final surgical excision were performed by musculoskeletal oncology surgeon in operation theatre under General anaesthesia or spinal anaesthesia. Additional data including clinical and radiological information were available to aid the pathologists with diagnosis.

4.13 Data management and Analysis

Data collected were loaded onto Excel spreadsheet, coded and cleaned for statistical analysis software.

The data were analyzed SPSS Version 29.0 (SPSS Inc, Chicago, IL, USA).

Categorical group variables compared with chi-square exact test.

Discrete variables were calculated in percentages. Effectiveness determined by agreement in differentiating benign and malignant leading to treatment plan. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) were calculated for core needle biopsy. Results were compared against final resection pathology which is used as the reference standard.

A P-value less than 0.05 was considered statistically significant.

4.14 Ethical Considerations

The study conducted after obtaining permission and lettter of support from head of the department of orthopedics and Trauma after submission of the research proposal for approval.

Medical record number will be used for data collection and personal identifier of the pateients will not be used in the research report.

Access to the collected information were limited to the principal investigator and confidentiality maintained throughout the project.

5. Dissemination of Results

The findings of this study will be submitted and presented to the department of Orthopedics and trauma, pathology unit and Muskuloskeletal radiology unit of Addis Abeba university, Tikur anbessa specialized hospital, Addis Ababa, Ethiopia in the presence of all of all consultants and resident doctors.

The research paper will be sent to local and international journals for Publication of the study findings. Attempts will be made to share the findingds with other stakeholders through publication and through presentation at different conferences.

6. Results

Assessment included 87 patients, 59.8% (52) were male and 40.2% (35) were female. The age ranged 6-64 years with the median (IQR) age of 26.0(25,38) years. Bone tumor biopsy accounted 57.5%(n=50) and soft tissue tumors 42.5%(n=37)

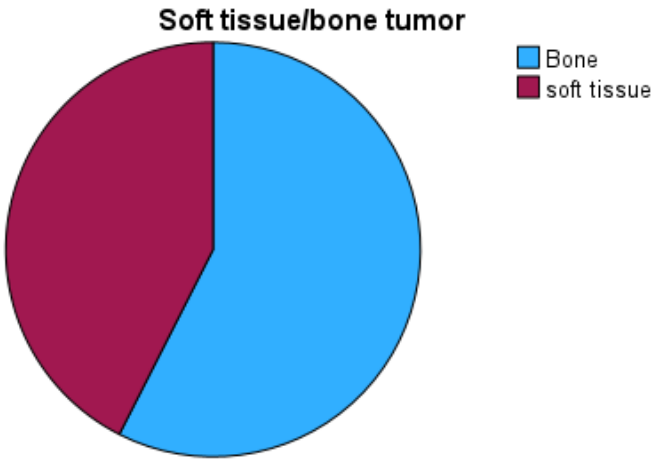


Figure 4: pie chart of bone and soft tissue tumor frequency

The most common anatomical location for soft tissue tumor biopsy was thigh followed by proximal arm. (Table 1)

Table 1: Anatomical site of soft tissue tumor biopsy(n=87)

Lesion location	No. of patients	Percent
distal arm	1	1.1
distal forearm	1	1.1
proximal arm	5	5.7
foot	2	2.3
knee	4	4.6
leg	2	2.3
distal thigh	8	9.2
proximal thigh	14	16.1

The most common anatomical location for bone tumour biopsy was proximal tibia 26% (14/50) followed by proximal humerus 24% (13/50) and distal femur 16%(8/50). (Table 2)

Table 2: Anatomical site of bone tumor biopsy(n=87)

Lesion location	No. of patients	percent
calcaneus	1	1.1%
distal femur	8	9.2%
distal humerus	2	2.3%
distal radius	2	2.3%
proximal femur	4	4.6%
proximal fibula	5	5.7%
proximal humerus	12	13.8%
proximal tibia	13	14.9%
radial head	1	1.1%
scapula	1	1.1%
Talus	1	1.1%

The most common encountered malignant bone tumor was osteosarcoma accounting 32% followed by Ewing sarcoma 6% and chondrosarcoma 6%.

The most common benign lesion was GCT 37% (14/37 lesions) followed by chondroblastoma 10.3% (9/37). (Table 3)

Table 3: Final histologic results in 50 patients with bone lesions(n=87)

Diagnosis	No. of patients	Percent
ABC	2	2.3
chondroblastoma	9	10.3
chondrosarcoma	3	3.4
CMF	1	1.1
Ewing sarcoma	3	3.4
GCT	14	16.1
osteosarcoma	16	18.4
solitary fibrous tumor	1	1.1
UPS	1	1.1

The most common encountered malignant soft tissue tumor was liposarcoma16% and benign tumor was atypical lipomatous tumor 10.8% (Table 4)

Table 4: Final histologic result in 37 patients of soft tissue lesion (n=87)

Diagnosis	No. of patients	Percent
ALT	4	4.6
Angiosarcoma	1	1.1
Chondrosarcoma	1	1.1
CMF	1	1.1
DFSP	1	1.1
epithelioid sarcoma	1	1.1
Fibromatosis	1	1.1
Fibrosarcoma	1	1.1
fibrous tumour	1	1.1
hibernoma myxoid variant	1	1.1
leiomyosarcoma	2	2.3
liposarcoma	6	6.9
myxofibrosarcoma	1	1.1
PVNS	2	2.3
RMS	3	3.4
schwannoma	1	1.1
solitary fibrous tumor	1	1.1
STS, NOS	2	2.3
synovial chondromatosis	1	1.1
synovial sarcoma	4	4.6
UPS	1	1.1

CNB showed sensitivity of 90% and specificity of 94.5% with PPV of 95.7 and NPV of 87.5 in detection nature of the tumor (Benign or malignant)

Overall effectiveness of CNB in differentiating between malignant and benign was identified in 93.1% with 95CI (86.2-97.7).

Five benign tumors (4 bone tumors and 1 soft tissue tumor) diagnosed with CNB turned out to be malignant in final resection pathology. one malignant tumor diagnosed with CNB turned out to be benign in final pathology and one tissue sample diagnosed mesenchymal neoplasm with no differentiation of nature of the tumor, turned out benign in final pathology.

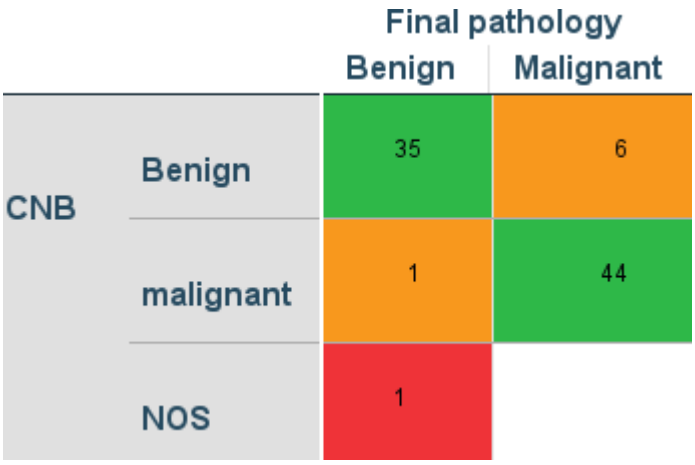


Figure 5: discordance of CNB and final pathology in diagnosing nature of the tumor (Benign vs Malignant), NOS; Not otherwise specified

Pathology result of CNB were matched with final resection histopathology in 80% (67/87) which represent the diagnostic accuracy.

Final resection pathology of bone tumor matched with CNB histopathology result in 86% (43/50) but in soft tissue tumors matched in 73% (27/37). (Table 5 and 6)

7 CNB histopathology result of bone tumour showed mismatch with final resection pathology. (Table 5)

Table 5: Mismatch of CNB and final pathology of bone tumors

No	Site of specimen	CNB diagnosis	Final pathology	Treatment
1	Calcaneus	Fibrous lesion	ABC	Intralesional curettage and bone graft
2	Distal femur	GCT	UPS	AKA
3	Proximal fibula	GCT	Synovial sarcoma	AKA
4	Proximal tibia	GCT	Osteosarcoma	AKA
5	Proximal femur	ABC	GCT	Girdlestone and extended curettage
6	Radial head	CMF	Atypical cartilaginous tumour/Chondrosarcoma	Extended curettage and bone graft
7	Proximal humerus	GCT	Chondroblastoma	Curettage and bone graft

Ten CNB histopathology results of soft tissue tumour showed mismatch with final pathology. (Table 6)

Table 6: Mismatch of CNB and final pathology of soft tissue tumors

No	Site of specimen	**CNB diagnosis**	**Final pathology**	**Rx**
1	Proximal thigh	RMS	UPS	WLE
2	Knee	Fibrosarcoma	Synovial sarcoma	AKA
3	Distal arm	UPS	Leiomyosarcoma	WLE
4	leg	Spindle cell lesion	Solitary fibrous tumour	WLE
5	Proximal thigh	UPS	Myxofibrosarcoma	WLE
6	distal thigh	Ewing sarcoma	RMS	Hip disarticulation
7	Proximal thigh	Ewing sarcoma	Synovial sarcoma	WLE
8	Distal thigh	Solitaryfibrous tumor	Synovial sarcoma	WLE
9	Distal thigh	Mesenchymal myxoid neoplasm	Hibernoma myxoid variant	WLE
10	Proximal thigh	Fibromyxoid sarcoma	Liposarcoma	WLE

Four patients of bone tumour diagnosed benign through CNB turned out be malignant in final resection pathology. 3 GCT of the bone turned out to be osteosarcoma, synovial sarcoma and UPS and one chondromyxoid fibroma (CMF) turned out to be low grade chondrosarcoma.

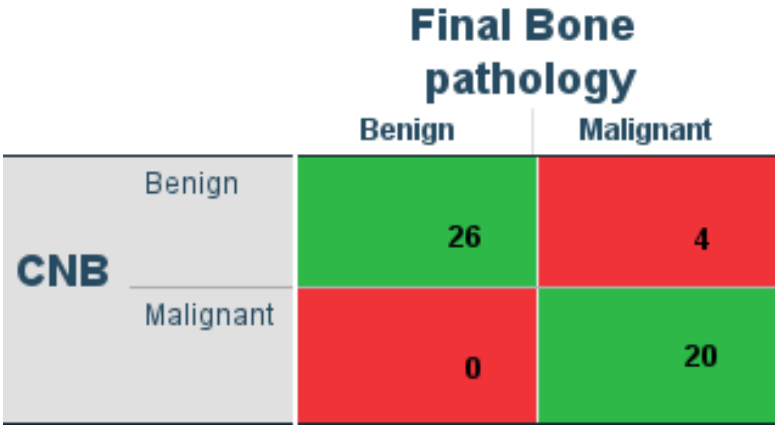


Figure 6: discordance of core needle biopsy of bone tumors with final resection histopathology in diagnosing nature of the tumor (Benign vs malignant)

Three soft tissue tumour sample of core needle biopsy was inadequate to reach definitive diagnosis (2 of the samples showed non-specific and necrotic tissue and one tissue sample showed inflammatory lesion).

One patient diagnosed malignant with CNB but turned out to be benign in final resection pathology. Another one patient diagnosed benign with CNB turned out to be malignant in final pathology. (figure 6)

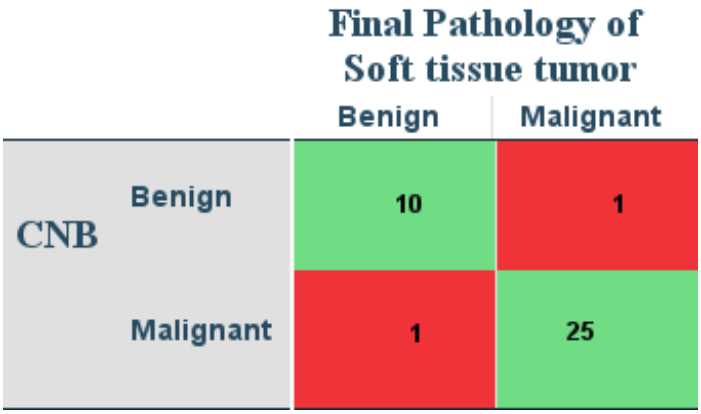
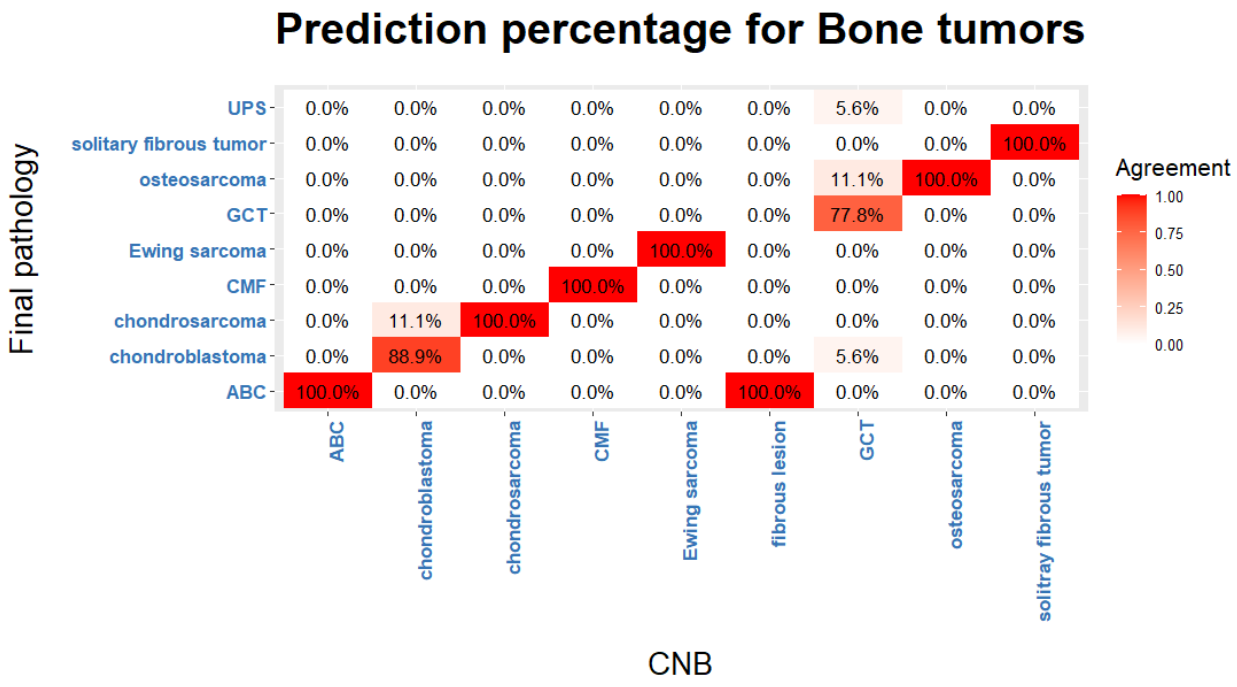


Figure 7:discordance of core needle biopsy of soft tissue tumors with final resection histopathology in diagnosing nature of the tumor (Benign vs malignant)

Table 7: Accuracy of CNB measured separately for bone and soft tissue tumours based on the final diagnosis

	Core needle biopsy	
	Bone tumour(n=50)	Soft tissue tumour(n=37)
Sensitivity	87%	96.2%
Specificity	100%	90.9%
PPV	100%	96.2%
NPV	90%	90.2%
Diagnostic accuracy	94%	97.3%

Cohen's Kappa value (0.84) showed strong level of agreement between core needle biopsy of bone tumors and final resection histopathology of bone tumors.

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Overall Statistics

               Accuracy : 0.88
                 95% CI : (0.7569, 0.9547)
    No Information Rate : 0.32
    P-Value [Acc > NIR] : 2.822e-16

                  Kappa : 0.8441
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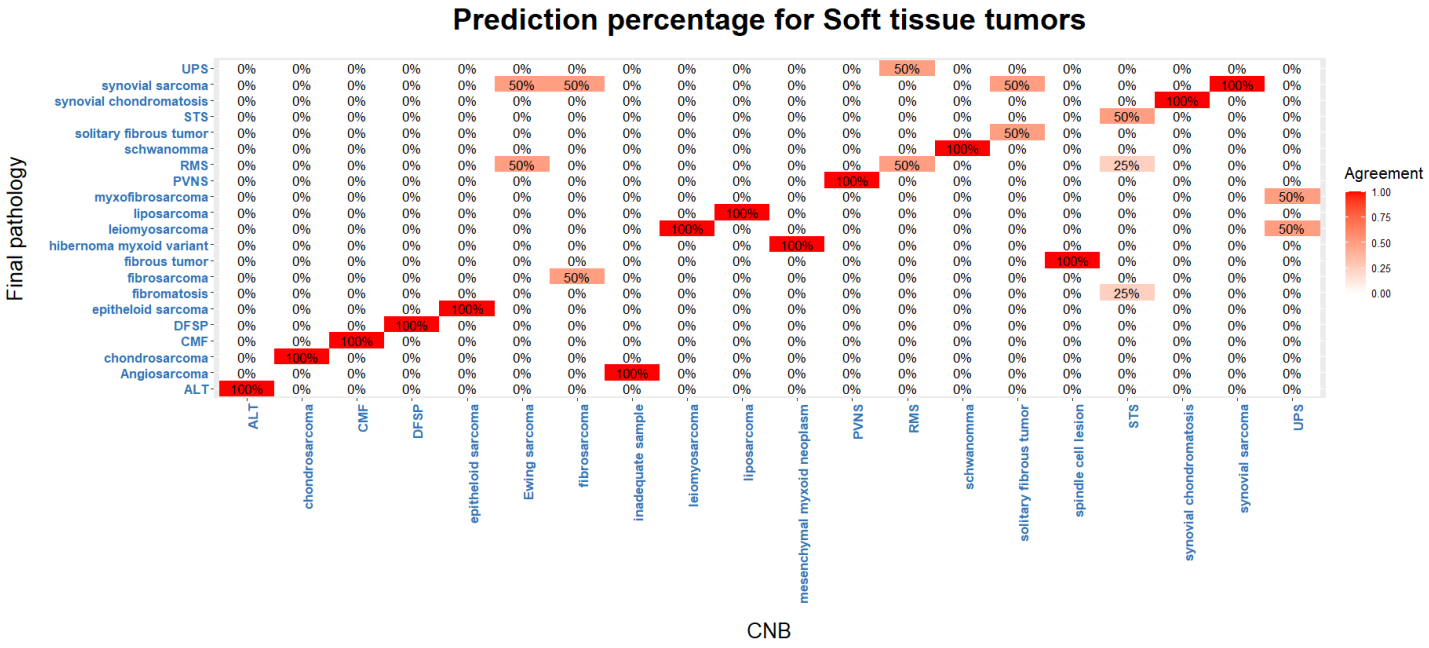
Figure 8: percentage of agreement between core needle biopsy and final resection pathology in bone tumors

Cohen's Kappa value (0.68) showed moderate level of agreement between core needle biopsy of soft tissue tumors and final resection histopathology of soft tissue tumors.

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Overall Statistics

               Accuracy : 0.7059
                 95% CI : (0.5252, 0.849)
    No Information Rate : 0.1765
    P-Value [Acc > NIR] : 1.71e-11

                  Kappa : 0.6822
```

Figure 9: percentage of agreement between core needle biopsy and final resection pathology of soft tissue tumor

We found no relationship (p =0.89) between anatomical site and nature of the tumor (Benign vs malignant) in affecting the diagnostic yield.

There were no recorded complications like infection, hematoma, inadvertent neurovascular injury or bleeding with all core needle biopsy procedures.

7. DISCUSSION

In our study Bone tumor is more commonly biopsied than soft tissue tumors which accounts 57.5% (50/87). Literatures show soft tissue sarcoma diagnosis predominate over bone sarcoma with 4:1 incidence ratio. (Vodanovich DA et al)

A study done in our hospital by Wamisho BL et al. also showed soft tissue sarcoma are more common than bone tumor accounting 66.3%, but in our study the number of CNB in soft tissue tumors were lower than bone tumors. This is due to most patients with soft tissue tumor referred to our hospital with incisional biopsy result or excisional biopsy was done but referred for a reason of recurrence. Excisional biopsy was also done for superficial masses like ganglion cysts and lipoma without initial biopsy.

Similar study which was done in Germany also showed bone tumor biopsied more than soft tissue tumor accounting 62.3%.

The most common anatomical site of bone biopsy in this study was proximal tibia proximal humerus and distal femur accounting 26%, 24% and 16% respectively

Previous studies in the reviewed literature show proximal tibia and distal femur are the most common biopsied area of bone lesions. A study done in Sudan by Elbahri HM showed proximal tibia (25.6%) and distal femur (35.5%) were the most common biopsied bone lesion

The most common biopsied anatomical site of soft tissue tumor was thigh (proximal or distal) accounting 59.5% (22/37 patients). This could be due to the common site of soft tissue sarcoma is the lower limb specifically the thigh accounting 44% of all extremity soft tissue sarcomas. (Vodanovich DA et al.)

Osteosarcoma (32%), Ewing sarcoma (6%) and chondrosarcoma (6%) are the most common encountered malignant tumors. Previous study done in our hospital by Weyessa TG et al showed osteosarcoma, Ewing sarcoma and chondrosarcoma are the most common malignant bone tumors accounting 62%, 15.2% and 11.3% respectively. Similar study done in Sudan also shows osteosarcoma the most common malignant bone tumor. (Elbahir et al)

The most common benign bone tumor was GCT accounting 37% followed by chondroblastoma10.3%. similar studies show osteochondroma and GCT being the commonest, in our study most of symptomatic osteochondroma cases were diagnosed with clinical and imaging assessment without needle biopsy. (Weyessa TG et al)

The most common encountered malignant soft tissue tumor was liposarcoma16% and benign tumor was atypical lipomatous tumor 10.8%

CNB showed sensitivity, specificity, PPV and NPV in detection nature of the tumor 90%, 94.5%,95.7%,87.5% respectively with overall 93.1% effectiveness in differentiating between malignant and benign tumors. 95.7% of specificity mean that we were likely to detect all benign tumors as benign with CNB in 95.7% of the samples.

80% of pathology result of CNB in specific diagnosis were matched with final resection histopathological specific diagnosis which represent the diagnostic accuracy. Similar study which was done in Germany by pohlig et al showed sensitivity, specificity, PPV, and NPV of 88.8%, 100%, 100%, 83.3% respectively. With diagnostic accuracy of 92.9% and agreement in specific diagnosis of 84.2%.

Seven CNB result of bone tumor showed mismatch with final resection histopathology of which 4 patients diagnosed benign through CNB turned out be malignant in final pathology.

3 GCT of bone diagnosed with CNB turned out to be osteosarcoma, synovial sarcoma and UPS in final pathology. But for there was major discrepancy with clinical and image diagnosis after MDT discussion, considered malignant bone tumour and above knee amputation (AKA) was done. One chondromyxoid fibroma (CMF) with CNB turned out to be atypical cartilaginous tumour/low grade chondrosarcoma for which intralesional curettage and bone graft was done. Literatures indicate surgical intralesional curettage is sufficient for low grade chondrosarcoma unlike other chondrosarcomas. (Suster et al)

Hence all discordant cases were managed according to sarcoma principle emphasizing the importance of clinical evaluation, imaging correlation and MDT discussion in tumour management.

One benign soft tissue tumour with core needle biopsy turned out to be malignant in final resection pathology. CNB showed acute on chronic inflammatory lesion suggesting inadequate sample for definitive diagnosis. Open incisional biopsy was done and showed chronic inflammatory lesion and suggested the sample was not representative. After MDT discussion WLE was done and final resection pathology showed malignant vascular tumour with Angiosarcoma top differential suggesting IHC for confirmation. The diagnosis of some soft tissue lesions is difficult even with complete resection and require ancillary testing

One malignant soft tissue tumour with CNB turned out to be benign in final resection pathology. CNB showed low grade soft tissue sarcoma and after MDT sarcoma discussion for the discrepancy with clinical and radiological imaging open incisional biopsy was done and indicated benign spindle cell lesion fibromatosis. Final resection pathology confirmed fibromatosis.

One patient with proximal thigh mass CNB was done and diagnosed with Mesenchymal myxoid neoplasm, with no specified nature of the tumour (Benign or malignant) or specific histopathology. After MDT discussion on the clinical and imaging of the soft tissue mass, WLE was done and final resection pathology showed hibernoma myxoid variant.

Similar published literatures show comparable diagnostic accuracy and effectiveness of core needle biopsy in diagnosing primary bone and soft tissue tumors.

Table 8: Results of some published literature regarding reliability of core needle biopsy.

cases	Author et al	Year	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Effectiveness (%)	Accuracy (%)
152	Elbahri	2020	96.2	93.1	97.1	91.1	95.3%	
77	Pohlig	2012	88.8	100	100	83.3	92.9	84.2
69	Walker	2018	87.1	100	100	90.5	94.2	87
87	our study	2024	90	94.6	95.7	87.5	93.1	80

The correct histopathological diagnosis compared to resection specimen was obtained in 86% of bone tumors and 73% of soft tissue tumor, confirming comparable result with previously published results. Our result showed lower specific diagnosis of CNB in soft tissue tumor than in bone tumors. To prevent lower diagnostic accuracy, McCarthy proposed a full discussion between orthopedic surgeons, radiologist and pathologists to identify suitable tumor region prior to CNB procedures.

Overall effectiveness of CNB in diagnosing nature of bone and soft tissue tumor is 94% and 97 % which is effective in suggesting surgical plan of management. (pohlig et al)

8. Strength and limitation

To the best of my knowledge this is novel study in our country which can provide valuable clinical information regarding core needle biopsy.

Standardized core needle biopsy procedure which is performed by musculoskeletal radiologist or fellow on training and final resection procedures performed by single musculoskeletal sarcoma surgeon.

Our study also has several limitations. Due to retrospective design of study, it was not possible to find out the presence of minor complications like hematoma and superficial infections. Pathology report is one limitation to the study. We were unable to compare grading of the biopsy samples because grading was not performed in every case. Unable to compare no of core needles to establish the standard number of core needles for it was not recorded in majority of patients. Report also done by general anatomic pathologists and not sarcoma specialists. Multiple pathologists were involved in the interpretation and analysis of specimen.

Confirmatory tests are lacking and ambiguous cases couldn't be conclusively diagnosed.
Diagnostic standard based on final surgical resection pathology, possibly wrong diagnosis could influence our result.

9. CONCLUSION

CNB is safe, fast and effective in diagnosing bone and soft tissue tumours with fewer complication. Open biopsy must be reserved for inconclusive and discordant results with clinical and radiological diagnosis. Moderately lower results were found in soft tissue tumour hence, indication for CNB especially in soft tissue tumours must be made with respect to suspected entity, extent of necrosis and location, to avoid incorrect or deficient results. Some soft tissue lesions are difficult to reach to specific histopathology even with complete resection biopsy and require ancillary testing like immunohistochemistry.

MDT approach including pathologists, radiologist, oncologist and musculoskeletal sarcoma surgeon in diagnosing and treating bone and soft tissue tumours is crucial.

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11. ANNEXES

A: DATA COLLECTION SHEET

Patient MRN	
Age	
Sex Male Female	
Anatomical site of lesion location	
Primary lesion Bone Soft tissue	
Nature of the lesion with CNB Benign Malignant	
Nature of the lesion with final pathology Benign Malignant	
CNB pathology result	
Final resection pathology result	
Complications of CNB	