

“No News is Good News?” Non-Diagnostic CT-Guided Bone Biopsies in Paediatric Patients - A 10-year Multi-Centre Retrospective Review

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- INTRODUCTION -

CT-guided biopsy is a less invasive method compared to open biopsy or surgical resection to obtain pathological diagnosis of bone lesions. In adults, the non-diagnostic yield is about 30%. Around half of these non-diagnostic lesions are malignant upon further workup. In children, epidemiology of bone lesions differs. There are also paucity of studies investigating non-diagnostic CT-guided bone biopsies in the paediatric population.

- OBJECTIVES -

To determine the diagnostic yield of CT-guided bone biopsies in paediatric patients, and factors associated with non-diagnostic results. Final outcomes of non-diagnostic biopsies would also be evaluated.






- MATERIALS AND METHODS -

Study Design and Patient Selection

Retrospective study of the database of three tertiary referral hospitals for paediatric bone tumours in the period from December 2011 to March 2022.

Inclusion Criteria	Exclusion Criteria
Paediatric patients (≤ 21 years old) CT-guided bone biopsy performed	Bone lesion with known histopathological diagnosis Bone lesion not identifiable on CT Spondylodiscitis

Data Collection

	· Clinical · Demographics (e.g. age, sex), medical history (e.g. known malignancy), presenting symptoms
	· Radiological · Pre-biopsy CT assessment (e.g. lesion location, number, size, density, zone of transition, sclerotic margin, cortical destruction, periosteal reaction, extra-osseous soft tissue) Pre-procedural MRI categorisation of bone lesions – solid ($>90\%$ solid), mainly solid (50-90% solid), mainly cystic ($>50-90\%$ cystic), and cystic ($>90\%$ cystic)
	· Procedural · Biopsy needle model and gauge, number and length of tissue cores obtained, additional biopsy with forceps, types of anaesthesia administered, biopsy-related complications
	· Pathological · Histopathological results of CT-guided bone biopsy – benign diagnosis, malignant diagnosis, non-diagnostic (i.e. when no specific diagnosis could be established)
	· Follow-up · Post-biopsy management plan, additional histopathological results (e.g. repeated CT-guided biopsy, open biopsy, curettage, resection)*

* If an untreated non-diagnostic lesion was stable or smaller with >1 -year follow-up, it was considered benign clinically

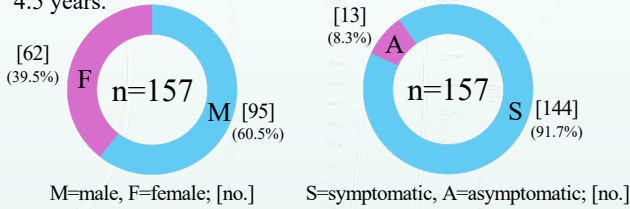
Statistical Analysis

Factors associated with non-diagnostic CT-guided bone biopsies were evaluated using Fischer's exact test for categorical data, Mann-Whitney U test for non-Gaussian continuous data, and unpaired t-test for Gaussian continuous data. P-value <0.05 was considered as statistically significant.

- RESULTS -

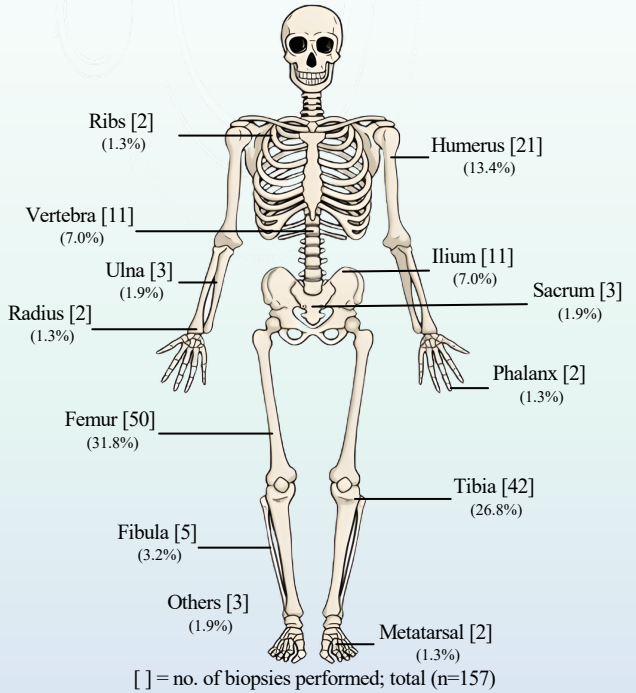
Demographics and Clinical Characteristics

A total of 157 CT-guided bone biopsies performed for 138 patients were included in this study. Age at biopsy was 13.9 ± 4.5 years.



CT-Guided Bone Biopsy Sites

Biopsies were predominantly performed for lesions in the appendicular skeleton, especially the lower limbs.



Procedural Details

Biopsy system	
Co-axial needle (gauge), median [range]	13 [8-17]
Biopsy needle (gauge), median [range]	16 [13-18]
No. of biopsy passes, median [range]	4 [1-11]
No. of tissue cores obtained, median [range]	2 [1-10]
Length of tissue cores (cm), mean +/- SD	1.3 +/- 1.1
Additional biopsy with forceps, no. (%)	25 (15.9)
Procedure-related complications, no. (%)	0 (0)

MRI Assessment of Solid vs Cystic Bone Lesions

Ninety-four (59.9%) bone lesions had pre-procedural MRI available for evaluation. They were categorised into solid (n=50), mainly solid (n=19), mainly cystic (n=7) or cystic lesions (n=18). All cystic lesions were benign. Examples are shown below:

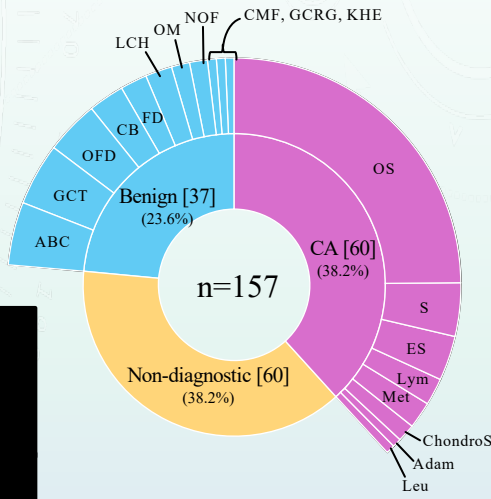
<p>Solid Bone lesion with >90% solid component</p>	<p>Left distal femur osteosarcoma</p>	<p>Mainly Cystic Bone lesion with >50-90% cystic component</p>
<p>Mainly Solid Bone lesion with 50-90% solid component</p>	<p>Right fibula telangiectatic osteosarcoma</p>	<p>Cystic Bone lesion with >90% cystic component</p>
	<p>Left talus chondroblastoma</p>	
	<p>Right humerus aneurysmal bone cyst</p>	<p>All Benign</p>

- RESULTS -

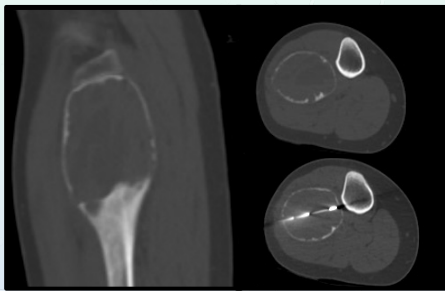
CT-Guided Bone Biopsy Histopathological Results

Nearly two-thirds (61.8%) of the CT-guided bone biopsies yielded a specific diagnosis. Malignant lesions (38.2%) were more common than benign lesions (23.6%), especially osteosarcomas (n=39). The other one-third were non-diagnostic (38.2%).

- Benign ·**
- Aneurysmal Bone Cyst [7]
 - Giant Cell Tumour [7]
 - OsteoFibrous Dysplasia [6]
 - ChondroBlastoma [4]
 - Fibrous Dysplasia [3]
 - Langerhan Cell Histiocytosis [3]
 - OsteoMyelitis [2]
 - Non-Ossifying Fibroma [2]
 - ChondroMyxoid Fibroma [1]
 - Giant Cell Reparative Granuloma [1]
 - Kaposiform HaemangioEndothelioma [1]



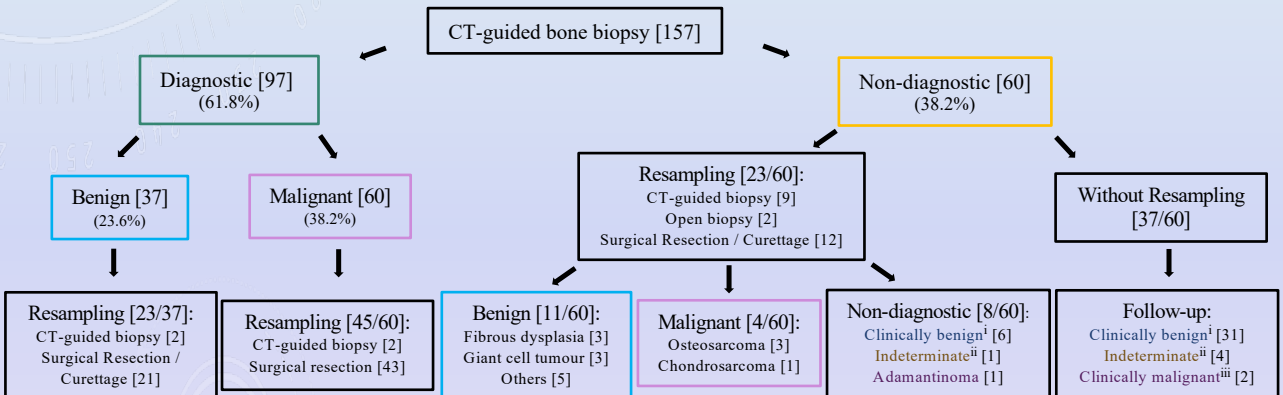
Left distal femur osteosarcoma



Right proximal fibula aneurysmal bone cyst

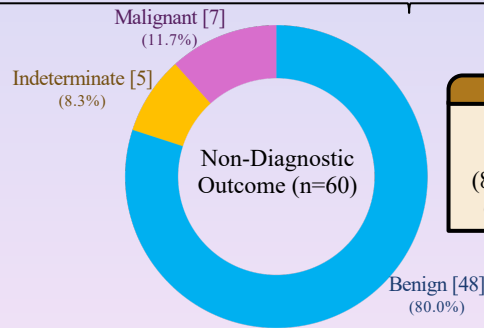
- Malignant ·**
- OsteoSarcoma [39]
 - Sarcoma [6]
 - Ewing's Sarcoma [5]
 - Lymphoma [3]
 - Metastasis [3]
 - ChondroSarcoma [2]
 - Adamantinoma [1]
 - Leukemia [1]

Follow-up on CT-Guided Bone Biopsies



ⁱ Clinically benign – bone lesions stable or resolved after >1-year follow-up
ⁱⁱ Indeterminate – patients lost to follow-up with <1-year follow-up
ⁱⁱⁱ Clinically malignant – history of metastatic cancer, with increased bone lesions

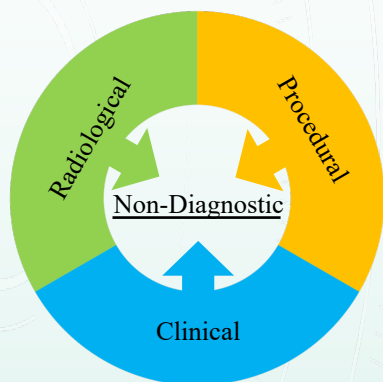
· Diagnostic ·
 For diagnostic CT-guided bone biopsies, **all** final pathological diagnoses in the repeated sampling remained the **same** compared to the initial results



· Non-Diagnostic ·
 For non-diagnostic CT-guided bone biopsies, **most** lesions (80.0%) were **benign** upon further evaluation or clinical follow-up

- RESULTS -

Factors associated with Non-Diagnostic Biopsy Results



· Clinical ·

Asymptomatic bone lesions



· Radiological ·

Small lesions
Cystic lesions
Lesions with non-aggressive features



· Procedural ·

Fewer tissue cores obtained
Shorter tissue cores obtained

- Comparison between Non-Diagnostic and Diagnostic CT-Guided Biopsies -

Parameter	Non-diagnostic lesion (n=60)	Diagnostic lesions (n=97)	p-value
Clinical			
Age (years), mean +/- SD	13.2 +/- 5.0	14.4 +/- 4.2	0.26
Male sex, no. (%)	31 (51.7)	64 (66.0)	0.09
Known malignancy, no. (%)	5 (8.3)	9 (9.3)	1.00
Symptomatic, no. (%)	51 (85.0)	93 (95.9)	0.03
Radiological			
Monostotic, no. (%)	52 (86.7)	80 (82.5)	0.65
Maximum lesion diameter (cm), mean +/- SD	5.1 +/- 3.6	6.8 +/- 4.2	0.004
Solid and cystic components (MRI)			
Solid, no. (%)	15/43 (34.9)	35/51 (68.6)	0.002
Mainly solid, no. (%)	11/43 (32.4)	8/51 (16.0)	0.30
Mainly cystic, no. (%)	3/43 (8.8)	4/51 (7.8)	1.00
Cystic, no. (%)	14/43 (41.2)	4/51 (7.8)	0.003
Density (CT)			
Lytic, no. (%)	38 (63.3)	45 (46.4)	0.049
Sclerotic, no. (%)	6 (10.0)	3 (3.1)	0.09
Mixed lytic and sclerotic, no. (%)	16 (26.7)	49 (50.5)	0.004
Narrow transition zone, no. (%)	49 (81.7)	32 (33.0)	<0.001
Sclerotic margin, no. (%)	28 (46.7)	17 (17.5)	<0.001
Cortical destruction, no. (%)	8 (13.3)	61 (62.9)	<0.001
Periosteal reaction, no. (%)	9 (15.0)	42 (43.3)	<0.001
Extra-osseous soft tissue mass, no. (%)	4 (6.7)	48 (49.5)	<0.001
Procedural			
Biopsy system			
Co-axial needle (gauge), median [range]	11 [9-16]	13 [8-17]	0.49
Biopsy needle (gauge), median [range]	16 [13-18]	16 [13-18]	0.56
No. of biopsy passes, median [range]	3 [1-8]	4 [1-11]	0.33
No. of tissue cores obtained, median [range]	1 [1-7]	3 [1-10]	0.02
Length of tissue cores (cm), mean +/- SD	1.1 +/- 1.3	1.4 +/- 0.9	0.01
Additional biopsy with forceps, no. (%)	11 (18.3)	14 (14.4)	0.51

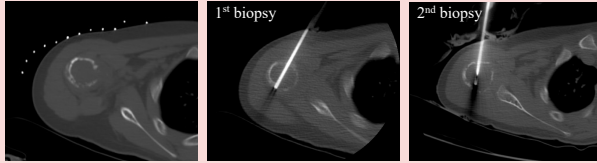
- DISCUSSION -

Malignant Lesions with Non-Diagnostic Biopsy Results

Though most bone lesions with non-diagnostic biopsy results were benign, seven (11.7%) were malignant. Details are as follow:

· Osteosarcomas (n=3) ·

They were large (>10cm) bone tumours with aggressive appearance, including wide zone of transition, extensive bone destruction and aggressive periosteal reactions. Repeated CT-guided biopsies were performed at different segments of the bone tumours by the same operators, which yielded osteosarcomas in the second attempts. Initial non-diagnostic results might be due to sampling of necrotic regions, which had reduced cellularity.



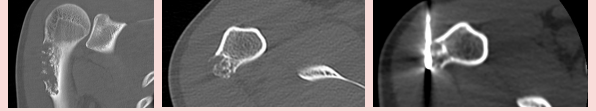
Right humerus osteosarcoma with initial non-diagnostic CT-guided biopsy

· Clinically Malignant / Metastases (n=2) ·

The patients had known malignancy (breast cancer and sarcomatous tumour) with lytic vertebral lesions. Although CT-guided bone biopsies were non-diagnostic, they were considered malignant / metastases clinically, as both patients developed more extensive bone lesions and multi-organ metastases in subsequent follow-up. Further tissue sampling was not performed as it did not affect management.

· Chondrosarcoma (n=1) ·

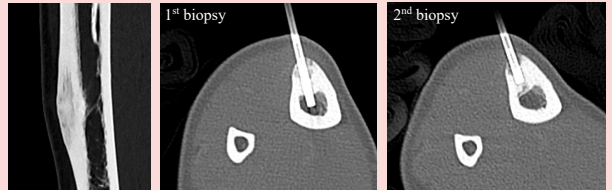
Core needle biopsies for cartilaginous tumours are prone to sampling error due to their heterogeneity. CT-guided biopsy for this case yielded cartilaginous tumour. Surgical resection was performed in view of the aggressive radiological appearance.



Right humerus chondrosarcoma confirmed after surgical resection

· Adamantinoma (n=1) ·

Osteofibrous dysplasia and adamantinoma are considered part of a disease spectrum. Differentiation is challenging both radiologically and pathologically. Despite repeated biopsies, a definitive diagnosis could not be obtained in this case. The diagnosis was obtained by surgical resection.



Right tibia adamantinoma confirmed after surgical resection

Limitations

As this study reviewed biopsies performed in different institutions, imaging protocol and interventional procedures were not standardised. Radiologists who performed the biopsies were also of varying experience.

- CONCLUSION -

01

About 1/3 (38.2%) of CT-guided bone biopsies in paediatric patients yielded non-diagnostic results. This is comparable to adults (~30%).

02

Bone lesions with non-aggressive features were associated with non-diagnostic results. Expected yield, risks and benefits should be considered before CT-guided bone biopsy.

03

Most (80.0%) non-diagnostic CT-guided bone biopsies in paediatric patients were benign, in contrast to adults (~50%). Watch and wait is a valid consideration.

04

However, tissue sampling is warranted when a non-diagnostic bone lesion demonstrates aggressive features inconsistent with a benign lesion.

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