Primary Tumour in Bone
Histopathology Reporting Guide
Biopsy Specimens

Family/Last name

Given name(s)

Date of birth DD – MM – YYYY

Patient identifiers

Date of request DD – MM – YYYY

Accession/Laboratory number

Elements in **black text** are CORE. Elements in **grey text** are NON-CORE.

☐ indicates multi-select values ◯ indicates single select values

SCOPE OF THIS DATASET

CLINICAL INFORMATION (select all that apply) (Note 1)

- ◯ Information not provided
- ☐ Pre-existing skeletal disease, *specify*
- ☐ Familial syndrome, *specify*
- ☐ Multifocal disease, *specify*
- ☐ Other (e.g., prior radiation therapy, implants, fracture), *specify*

IMAGING FINDINGS (Note 2)

Anatomical site

- ◯ Bone, not specified
- ◯ Bone, *specify*

Radiologic tumour dimensions

- ◯ Not provided

Maximum tumour dimension ____ mm

Additional dimensions ____ mm x ____ mm

- ◯ Cannot be assessed (e.g., multifocal/discontinuous tumour), *specify*

Tumour site (select all that apply)

- ☐ Epiphysis or apophysis
- ☐ Metaphysis
- ☐ Diaphysis
- ☐ Other, *specify*
- ☐ Not known

AND

- ☐ Cortex
- ☐ Medullary cavity
- ☐ Surface
- ☐ Not known

AND

- ☐ Tumour confined to bone
- ☐ Tumour involves joint
- ☐ Tumour extension into soft tissue
- ☐ Not known

Tumour laterality

- ◯ Left
- ◯ Right
- ◯ Not specified/Not applicable

Radiological differential diagnosis

- ◯ Not provided
- ◯ Provided, *describe*

OPERATIVE PROCEDURE (select all that apply) (Note 3)

- ◯ Not specified
- ☐ Core needle biopsy
  - Number of cores
- ☐ Open incisional biopsy
- ☐ Excisional biopsy/marginal excision
- ☐ Curettage
- ☐ Other, *specify*

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BIOPSY HANDLING (select all that apply) (Note 4)

- ◯ Not specified
- ☐ Formalin fixed paraffin embedded (FFPE)
- ☐ Fresh frozen, *specify if frozen section was performed*
- ☐ Decalcification, *specify type*

HISTOLOGICAL TUMOUR TYPE (Note 5)

(Value list based on the World Health Organization Classification of Soft Tissue and Bone Tumours (2020))

- ◯ Atypical cartilaginous tumour
- ◯ Central chondrosarcoma
- ◯ Peripheral chondrosarcoma
- ◯ Periosteal chondrosarcoma
- ◯ Clear cell chondrosarcoma
- ◯ Mesenchymal chondrosarcoma
- ◯ Dedifferentiated chondrosarcoma
- ◯ Low-grade central osteosarcoma
- ◯ Osteosarcoma (conventional, teleangiectatic, or small cell)
- ◯ Parosteal osteosarcoma
- ◯ Periosteal osteosarcoma
- ◯ High-grade surface osteosarcoma
- ◯ Secondary osteosarcoma
- ◯ Fibrosarcoma
- ◯ Epithelioid haemangioendothelioma
- ◯ Angiosarcoma
- ◯ Giant cell tumour of bone
- ◯ Giant cell tumour of bone, malignant
- ◯ Conventional chordoma (including chondroid)
- ◯ Poorly differentiated chordoma
- ◯ Dedifferentiated chordoma
- ◯ Adamantinoma of long bones
- ◯ Leiomyosarcoma of bone
- ◯ Undifferentiated pleomorphic sarcoma
- ◯ Ewing sarcoma
- ◯ Round cell sarcoma with *EWSR1*-non ETS fusions
- ◯ Sarcoma with *BCOR* genetic alterations
- ◯ Other, *specify*
- ◯ Indeterminate, *specify*

Comments

HISTOLOGICAL TUMOUR GRADE (Note 6)

- ◯ Not applicable
- ◯ Grade 1
- ◯ Grade 2
- ◯ Grade 3
- ◯ Cannot be assessed, *specify*

NECROSIS (Note 7)

- ◯ Cannot be assessed
- ◯ Not identified
- ◯ Present
  - %

LYMPHOVASCULAR INVASION (Note 8)

- ◯ Not identified
- ◯ Present
- ◯ Indeterminate

COEXISTENT PATHOLOGY[a] (Note 9)

- ◯ None identified
- ◯ Present, *specify*

[a] *Found at histological examination.*

ANCILLARY STUDIES (Note 10)

- ◯ Not performed
- ◯ Performed
  - ☐ Immunohistochemistry, *specify test(s) and result(s)*
  - ☐ Molecular findings, *specify test(s) and result(s)*
  - ☐ Other, *specify test(s) and result(s)*

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Definitions

CORE elements

CORE elements are those which are essential for the clinical management, staging or prognosis of the cancer. These elements will either have evidentiary support at Level III-2 or above (based on prognostic factors in the National Health and Medical Research Council (NHMRC) levels of evidence[1]). In rare circumstances, where level III-2 evidence is not available an element may be made a CORE element where there is unanimous agreement in the expert committee. An appropriate staging system e.g., Pathological TNM staging would normally be included as a CORE element.

The summation of all CORE elements is considered to be the minimum reporting standard for a specific cancer.

NON-CORE elements

NON-CORE elements are those which are unanimously agreed should be included in the dataset but are not supported by level III-2 evidence. These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.

Key information other than that which is essential for clinical management, staging or prognosis of the cancer such as macroscopic observations and interpretation, which are fundamental to the histological diagnosis and conclusion e.g., macroscopic tumour details, may be included as either CORE or NON-CORE elements by consensus of the Dataset Authoring Committee.

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Scope

The dataset has been developed for the pathology reporting of biopsy specimens of primary tumour in bone. Ewing sarcoma and related round cell sarcomas with primary bone presentation are also covered by this dataset. A separate dataset is available for reporting of resection specimens of primary tumour in bone. Some types of soft tissue sarcoma may on rare occasion arise primarily in bone and should be reported using the primary tumour in bone dataset, rather than the soft tissue sarcoma dataset.

If biopsies are taken from multiple tumour nodules at different sites, these should be documented separately.

Haematologic malignancies and metastatic specimens are excluded from this dataset.

The authors of this dataset can be accessed here.

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Note 1 – Clinical information (Non-core)

For accurate diagnosis of bone tumours, a multidisciplinary approach is imperative. It is the responsibility of the clinician or radiologist requesting the pathological examination of a specimen to

provide information to the pathologist that will have an impact on the diagnostic process or affect its interpretation. The use of a standard pathology requisition/request form including a checklist of important clinical information is strongly encouraged to help ensure that important clinical data is provided by the clinicians with the specimen.

It is also the responsibility of the pathologist to verify that all radiological and clinical information that is essential to make a diagnosis is available to guarantee that the final diagnosis is made within the appropriate clinical/imaging context. This often achieved through discussion at a multidisciplinary tumour board meeting.

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Note 2 – Imaging findings (Core)

Recording anatomical site of the tumour is important as certain bone tumours have a preference for specific bones and do not occur in others, and there is a strong association between site and outcome. The latter is especially true for cartilaginous tumours, and as a consequence in the World Health Organization (WHO) Classification of Tumours, Soft Tissue and Bone Tumours, 5th edition, 2020,[2] a diagnosis of atypical cartilaginous tumours/chondrosarcoma grade 1, depends on whether the tumour is located in the appendicular or the axial skeleton, respectively. In the long and short tubular bones these tumours behave in a locally aggressive manner and do not metastasize, can be treated locally, and should not be classified as having full malignant potential. Therefore, the term 'atypical cartilaginous tumour' is used for these cartilaginous tumours in the appendicular skeleton (long and short tubular bones). In contrast, the term chondrosarcoma grade 1 is used for histologically similar tumours of the axial skeleton, including the pelvis, scapula and skull base (flat bones) – reflecting the poorer clinical outcome and the necessity of more aggressive treatment of these tumours at these sites. Note that in this dataset, the scapula and skull base are considered to be part of the axial skeleton. It should also be noted that the definition of axial versus appendicular is not universally accepted; while the 2020 WHO Classification[2] categorises the scapula and skull base as part of the axial skeleton, the Union for International Cancer Control (UICC)[3]/American Joint Committee on Cancer (AJCC)[4] TNM 8th editions include these with appendicular skeleton.

The size of the largest tumour nodule should be documented from imaging, preferably in three dimensions as this is important to evaluate the tumour volume. In cases where the radiological tumour dimensions cannot be assessed, such as for multifocal or discontinuous tumour, it is important to note this and record the relative volume of tumour if possible. If biopsies are taken from multiple tumour nodules at different sites, these should be documented separately.

It is important to know the exact tumour site within the bone; for intramedullary tumours and those arising primary at the surface of bone, the histological differential diagnosis will differ. Also, some tumours almost exclusively occur in the epiphysis of the bone (e.g., clear cell chondrosarcoma, giant cell tumour of bone), while others prefer the metaphysis (osteosarcoma) or diaphysis (Ewing sarcoma, adamantinoma). Moreover, primary soft tissue sarcomas may be in close proximity and even invade the bone, while primary bone sarcomas may have an extensive soft tissue component; in these cases, radiological information is required to decide whether the tumour originates primarily from bone or soft tissue.

It is important for the pathologist to be aware of the radiological differential diagnosis, and to be aware of previous radiological findings, if applicable. Correlation between the histology and imaging findings is critical in the diagnosis of bone tumours. For instance, aggressive features identified radiographically (permeative/moth-eaten growth, cortical destruction, soft tissue extension, periosteal

reaction) should be mentioned here, as well as multifocality, evidence of matrix deposition, presence of fluid-fluid levels etc. Ideally every case should be discussed in a multidisciplinary team or the pathologist should have access to the imaging findings, when evaluating a biopsy. For cartilaginous tumours for instance, the distinction between benign and low grade malignancy may depend solely on whether or not there is cortical destruction, which may be impossible to evaluate on biopsy or fragmented curettage specimens alone. Therefore, these diagnoses cannot be made without radiological correlation. The presence of fracture should always be documented as it may alter the morphological features and, in some instances, simulate aggressive features, such as host bone entrapment. As the histological alterations caused by the fracture change over time, it is important to know the time frame between fracture and biopsy. Finally, certain bone tumours (cartilaginous tumours, vascular tumours) tend to occur multifocally, and this information is also helpful for the pathologist. The histological diagnosis should always be correlated with the radiological diagnosis and one should always be cautious when there is a discrepancy between radiological and histological findings. Multidisciplinary discussion is essential and a repeat biopsy should be considered if differences of opinion are not resolved.

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Note 3 – Operative procedure (Core)

It is important to capture both the type and intent of the operative diagnostic procedure.

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Note 4 – Biopsy handling (Non-core)

Core needle biopsy is often performed under computerised tomography (CT) or ultrasound guidance, and preferably a minimum of three cores are submitted for diagnosis. A frozen section can be performed on a representative selection of cores or the tissue obtained at open biopsy, to evaluate whether the biopsy has yielded adequate tissue for diagnosis. Adequacy may also be determined by cytological rapid on-site evaluation (ROSE); the advantage of ROSE is that the biopsy core evaluated remains almost entirely intact, preserving tissue for other ancillary testing. Moreover, a provisional diagnosis can sometimes be given, and based on the results the remaining tissue can be triaged for further work-up. Bone tumours need decalcification before formalin fixed paraffin embedded (FFPE), which, depending on the type of decalcification used, may severely hamper the use of ancillary techniques. Decalcification should be done with solutions that preserve RNA and DNA, or a representative core should be kept frozen or embedded in paraffin without decalcification, to enable molecular testing. Acid-based decalcification should therefore be avoided if frozen tissue is unavailable.

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Note 5 – Histological tumour type (Core)

Histologic diagnosis is based on the WHO Classification of Tumours, Soft Tissue and Bone Tumours, 5th edition, 2020 (Table 1).[2] Many tumours of the bone are surgically assessed by biopsy. In some cases, the biopsy is suboptimally centred on the area(s) of interest or affected by the surgical process, leaving the pathologist with tissue that can be under-representative or misrepresentative of the lesion based

on the imaging studies. In a few instances, more sophisticated testing (e.g., molecular) may be required to achieve a full/correct diagnosis, but the small tissue size, tissue processing issues, or suboptimal targeting of biopsy materials may make this testing impossible. The pathologist should specify any, and all, limitations of the tissue in achieving optimal diagnosis. In addition, comments can be made in case the diagnosis on biopsy is not certain for reasons other than limitations of the material, or when there is still a differential diagnosis.

Table 1: World Health Organization classification of intermediate and malignant bone tumours and undifferentiated small round cell sarcomas.[2]

Descriptor	ICD-O codes[a]
Chondrogenic tumours	
Intermediate (locally aggressive)	
Atypical cartilaginous tumour	9222/1
Malignant	
Chondrosarcoma, grade 1	9222/3*
Chondrosarcoma, grade 2	9220/3
Chondrosarcoma, grade 3	9220/3
Periosteal chondrosarcoma	9221/3
Clear cell chondrosarcoma	9242/3
Mesenchymal chondrosarcoma	9240/3
Dedifferentiated chondrosarcoma	9243/3
Osteogenic tumours	
Malignant	
Low-grade central osteosarcoma	9187/3
Osteosarcoma	9180/3
Conventional osteosarcoma	
Telangiectatic osteosarcoma	
Small cell osteosarcoma	
Parosteal osteosarcoma	9192/3
Periosteal osteosarcoma	9193/3
High-grade surface osteosarcoma	9194/3
Secondary osteosarcoma	9184/3
Fibrogenic tumours	
Malignant	
Fibrosarcoma NOS	8810/3
Vascular tumours of bone	
Malignant	
Epithelioid haemangioendothelioma NOS	9133/3
Angiosarcoma	9120/3
Osteoclastic giant cell–rich tumours	
Intermediate (locally aggressive, rarely metastasizing)	
Giant cell tumour of bone	9250/1
Malignant	
Giant cell tumour of bone, malignant	9250/3

Descriptor	ICD-O codes[a]
Notochordal tumours	
Malignant	
Conventional chordoma	9370/3
Chondroid chordoma	
Poorly differentiated chordoma	9370/3
Dedifferentiated chordoma	9372/3
Other mesenchymal tumours of bone	
Malignant	
Adamantinoma of long bones	9261/3
Dedifferentiated adamantinoma	
Leiomyosarcoma NOS	8890/3
Pleomorphic sarcoma, undifferentiated	8802/3
Haematopoietic neoplasms of bone	
Plasmacytoma of bone	9731/3
Malignant lymphoma, non-Hodgkin, NOS	9591/3
Hodgkin disease NOS	9650/3
Diffuse large B-cell lymphoma NOS	9680/3
Follicular lymphoma NOS	9690/3
Marginal zone B-cell lymphoma NOS	9699/3
T-cell lymphoma NOS	9702/3
Anaplastic large cell lymphoma NOS	9714/3
Malignant lymphoma, lymphoblastic, NOS	9727/3
Burkitt lymphoma NOS	9687/3
Langerhans cell histiocytosis NOS	9751/1
Langerhans cell histiocytosis, disseminated	9751/3
Erdheim–Chester disease	9749/3
Rosai–Dorfman disease	
Undifferentiated small round cell	
Ewing sarcoma	9364/3
Round cell sarcoma with *EWSR1*–non-ETS fusions	9366/3*
CIC-rearranged sarcoma	9367/3*
Sarcoma with *BCOR* genetic alterations	9368/3*

[a] These morphology codes are from the International Classification of Diseases for Oncology, third edition, second revision (ICD-O-3.2).[5] Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; /3 for malignant tumours, primary site; and /6 for malignant tumours, metastatic site.

* Codes marked with an asterisk were approved by the International Agency for Research on Cancer/WHO Committee for ICD-O at its meeting in January 2020. Incorporates all relevant changes from the 5th Edition Corrigenda October 2020.

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Note 6 – Histological tumour grade (Core)

In bone sarcomas, the histotype mostly determines grade, as indicated in the list below (based on the 2020 WHO Classification[2]), with only a very few exceptions.

Bone sarcomas in which grade is determined by histotype:

Grade 1 (low grade):

- Low grade intramedullary osteosarcoma
- Parosteal osteosarcoma
- Clear cell chondrosarcoma

Grade 2 (intermediate grade):

- Periosteal osteosarcoma

Grade 3 (high grade):

- Osteosarcoma (conventional, telangiectatic, small cell, secondary, high grade surface)
- Undifferentiated high grade pleomorphic sarcoma
- Ewing sarcoma and BCOR rearranged sarcoma
- Dedifferentiated chondrosarcoma
- Mesenchymal chondrosarcoma
- Dedifferentiated chordoma
- Poorly differentiated chordoma
- Angiosarcoma

Variable:

- Conventional chondrosarcoma (Grade 1-3 according to Evans)[2,6]
- Leiomyosarcoma of bone (Grade 1-3, no established grading system)
- Low and high grade malignancy may occur in giant cell tumour of bone

Not applicable:

- Adamantinoma and conventional chordoma.

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Note 7 – Necrosis (Non-core)

Necrosis in biopsy specimens where the patient has not received neoadjuvant treatment should be documented, especially if necrosis is abundant hampering microscopic evaluation of the tumour.

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Note 8 – Lymphovascular invasion (Non-core)

Lymphovascular invasion (LVI) is extremely rare in bone tumours. However, it is important to report if present.

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Note 9 – Coexistent pathology (Non-core)

If present, the pathologist should report other abnormalities that are relevant for the diagnosis and any other significant pathologic finding, even if not directly relevant or unrelated. For instance, the presence of precursor lesions for chondrosarcoma, such as multiple enchondromas, osteochondroma, or synovial chondromatosis, should be documented. Paget disease and osteonecrosis or bone infarction may be seen in addition to a secondary sarcoma. The presence of a pathologic fracture may influence the histological evaluation and should be documented. Other unrelated findings may include vasculitis, infection, coexistent chronic lymphocytic leukaemia (CLL) or incidental/unexpected metastatic carcinoma in the same specimen.

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Note 10 – Ancillary studies (Core)

All immunohistochemical stainings and molecular tests that contributed to the diagnosis should be documented. For instance, for Ewing sarcoma and other round cell sarcomas, lymphoma, adamantinoma and chordoma, these ancillary studies (immunohistochemical and/or molecular) are critical.

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References

1 Merlin T, Weston A and Tooher R (2009). Extending an evidence hierarchy to include topics other than treatment: revising the Australian 'levels of evidence'. *BMC Med Res Methodol* 9:34.

2 WHO Classification of Tumours Editorial Board (2020). *Soft Tissue and Bone Tumours. WHO Classification of Tumours, 5th Edition, Volume 3*. IARC Publications, Lyon.

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