TUMOR CLASSIFICATION AND BIOPSY PRINCIPLES

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https://www.youtube.com/watch?v=xwgyWthZSg8

Introduction :

- **Neoplasia :** It is defined as a mass of tissue formed as result of abnormal, excessive, uncoordinated, autonomous and purposeless proliferation of cells.

- Term Neoplasia includes both Benign and Malignant.

Benign lesion of bone :

- One that does not invade surrounding tissue or spread elsewhere in the body
- Limited capacity for recurrence
- Recurrence occur in a non destructive manner.
- Surgical resection is often curative

Wide variety of behaviors :

- **Latent or inactive** (e.g non-ossifying fibroma).
- **Active** with a higher risk of recurrence after treatment (e.g aneurysmal bone cyst).

Intermediate ***local aggressive*** lesions of bone :

- Can destroy bone and surrounding tissue (e.g osteoblastoma).
- Often re-occur and associated with an infiltrative and locally destructive locally pattern .
- Recurrence is frequent following limited surgical treatment .
- En bloc resection is required to completely remove the lesion .

Intermediate ***rarely metastasis*** lesions of bone:

- Often behave in similar way to local aggressive lesions but occasionally demonstrate the ability to spread distant sites .
- Risk of spread less than 2 % (e.g giant cell tumor).

Malignant tumors

- Truly aggressive with potential for both local extension and metastases to distant sites .
- The aggressiveness of tumor defined by histological grade :

1. ***Low grade tumor*** (e.g chordoma and parosteal osteosarcoma), Slow rate of growth and metastases less common , but can arise many years after initial diagnosis .
2. ***High grade tumors*** (e.g osteosarcoma and ewing sarcoma), very high risk of metastases and are locally invasive .

Contrasting Differences between Benign and Malignant Tumours

FEATURES	BENIGN (DIFFERENTIATED)	MALIGNANT (UNDIFFERENTIATED)
	MACROSCOPIC FEATURES	
Boundaries	Encapsulated or well circumscribed	Poorly circumscribed and irregular
Surrounding tissue	Often compressed	Usually invaded
Secondary Changes	Occur less often	Occur more often
	MICROSCOPIC FEATURES	
Pattern	Usually resemble tissue of origin	No resemblance
Nucleo – Cytoplasmic Ratio	Normal	Increased
Pleomorphism	Absent usually	Often present
Anisonucleosis	Absent	Generally present
Hyperchromatism	Absent	Often present
Growth Rate	Usually Slow	Rapid
Metastasis	Absent	Frequently Present

Routes of Metastasis :

- **Haematogenous Spread :** Most common spread in musculoskeletal tumours

- **Lymphatic Spread –** rare in musculoskeletal tumours.
    - Seen in Rhabdomyosarcoma, Synovial sarcoma, Malignant fibrous histiocytoma .

- **Direct Implantation :**
    - Through surgeons scalpel, needles, sutures, FNAC, diagnostic or excision biopsy

- **Spread through Cerebro Spinal Fluid :**
    - malignant tumours of ependyma and leptomeninges rarely spread through CSF to vertebrae.

Classification of Tumours

1. WHO Classification :

widely accepted and is based on histogenesis and histological criteria.

2. Classification **based on origin of tumours**

3. Classification **based on site of lesions.**

WHO HISTOLOGICAL CLASSIFICATION OF TUMORS

TABLE 12: Classification and differentiation of bone neoplasia

Broad tumor group	*Benign lesions*	*Aggressive lesions*	*Malignant lesions*
Tumor-like lesions/indefinite for neoplasia	• Unicameral (simple) bone cyst • Intraosseous ganglion and subchondral bone cyst	• Aneurysmal bone cyst	
Bone-forming lesions	• Osteoma • Osteoid osteoma • Bone island (enostosis)	• Osteoblastoma	• Osteosarcoma and related variants
Cartilage lesions	• Osteochondroma • Nora's lesion • Enchondroma • Benign chondroma • Subungual exostosis	• Chondroblastoma • Chondromyxoid fibroma • Multiple enchondromatosis	• Chondrosarcoma and related variants
Fibrous lesions		• Desmoplastic fibroma	• Fibrosarcoma
Giant cell lesions	• Giant cell tumor • Giant cell reparative granuloma	• Giant cell tumor	
Fibrohistiocytic lesions	• Benign fibrous histiocytoma (nonossifying fibroma)		• Malignant fibrous histiocytoma
Hematopoietic tumors			• Plasma cell myeloma • Malignant lymphoma
Vascular lesions	• Lymphangioma and hemangioma • Skeletal angiomatosis • Hemophilic pseudotumor • Vascular tumors in the immunocompromised • Glomus tumor	• Gorham's disease	• Hemangioendothelioma and epithelioid hemangioendothelioma • Angiosarcoma • Hemangiopericytoma
Miscellaneous mesenchymal lesions	• Fibrous dysplasia • Campanacci's disease (osteofibrous dysplasia) • Fibrocartilaginous mesenchymoma • Intraosseous lipoma • Intraosseous schwannoma	• ? Adamantinoma	• Adamantinoma • Chordoma • Ewing's sarcoma • Intraosseous liposarcoma • Leiomyosarcoma • Malignant mesenchymoma

SELECTED TUMORS CHANGED IN ICD-O CODE OR BIOLOGICAL POTENTIAL IN THE 2020 WHO CLASSIFICATION OF BONE TUMOR

Tumor Entities	2013 WHO Classification	2020 WHO Classification
Chondroblastoma	9230/1. Intermediate (rarely metastasizing) tumor	9230/0. Benign tumor
Chondromyxoid fibroma	9241/0. Intermediate (locally aggressive) tumor	9241/0. Benign tumor
Synovial chondromatosis	9220/0. Benign tumor	9220/1. Intermediate (locally aggressive) tumor
ACT/CS1	9222/1. Intermediate (locally aggressive) tumor	9222/1. ACT. Intermediate (locally aggressive) tumor 9222/3. CS1. Malignant tumor
Epithelioid hemangioma	9120/0. Intermediate (locally aggressive and rarely metastasizing) tumor	9120/0. Intermediate (locally aggressive) tumor
Aneurysmal bone cyst	9260/0. Intermediate (locally aggressive) tumor	9260/0. Benign tumor
OFD-like adamantinoma	9261/3. Malignant tumor	9261/1. Intermediate (locally aggressive) tumor
Pleomorphic sarcoma, undifferentiated	8830/3. Malignant tumor	8802/3. Malignant tumor
Langerhans cell histiocytosis	9752/1. Monostotic. Intermediate (locally aggressive) tumor 9753/1. Polystotic. Intermediate (locally aggressive) tumor	9751/1. Langerhans cell histiocytosis NOS. Intermediate (locally aggressive) tumor 9751/3. Langerhans cell histiocytosis, disseminated. Malignant tumor
Erdheim-Chester disease	9750/1. Intermediate (locally aggressive)	9749/3. Malignant tumor

SELECTED TUMOR REMOVED IN THE 2020 WHO CLASSIFICATION OF BONE TUMORS

Tumor Entities	2013 WHO Classification	2020 WHO Classification
Benign fibrous histiocytoma*	Fibrohistiocytic tumor	Removed
Giant cell lesion of the small bones†	Osteoclastic giant cell rich tumor	Removed
Leiomyoma	Myogenic tumor	Removed
Liposarcoma	Lipogenic tumor	Removed

Classification based on origin of tumours

1. **Primary Bone tumours :** Derived from bone

2. **Metastatic bone Tumours :** Due to Mets from :

–Breast	Lytic + **Blastic lesions**
-Kidney	Lytic
–Prostate	**Blastic**
- Adrenal	Lytic
–Thyroid	Lytic
- Intenstine	Lytic
- Lung, Liver	Lytic
- Urinary Bladder, Uterine Cervix	Lytic lesions

3. **Tumour Like Lesions :** Non neoplastic Conditions that resemble tumours. Eg : Solitary Bone cyst, Aneurysmal Bone cyst, Fibrous Dysplasia, Brown`s tumour.

Classification based on site of Origin

1. Epiphyseal

Osteoclastoma, Chondroblastoma

2. Metaphyseal

Osteioid osteoma, Osteochondroma,
Osteoblastoma, Bone cysts, Osteogenic Sarcoma

3. Diaphyseal

Ewing`s sarcoma, Multiple myeloma,

TABLE 4: Most common/representative location of focal bone lesion (anatomic bone region)

Epiphyseal lesions	*Metaphyseal lesions*	*Diaphyseal lesions*
Chondroblastoma Giant cell tumor (the tumor begins in metaphyseal region and progress to epiphysis settling below the articular cartilage)	Chondrosarcoma Giant cell tumor Aneurysmal bone cyst	Campanacci's disease or osteofibrous dysplasia
Clear cell chondrosarcoma	Fibrosarcoma	Ewing's tumor
Aneurysmal bone cyst	Osteochondroma	Osteoid osteoma
Langerhans cell histiocytosis*	Osteosarcoma	Osteoblastoma
	Malignant fibrous histiocytoma	(Metastatic disease, lymphoma/myeloma, eosinophilic granuloma, Paget's disease, unicameral bone cyst, hemangioma, fibrous dysplasia, enchondroma)*
	Nonossifying fibroma or metaphyseal cortical defect	
	(Metastatic disease, enchondroma, fibrous dysplasia, lymphoma/myeloma, Langerhans cell histiocytosis, hemangioma, Paget's disease, unicameral bone cyst)*	

LESION LOCATION

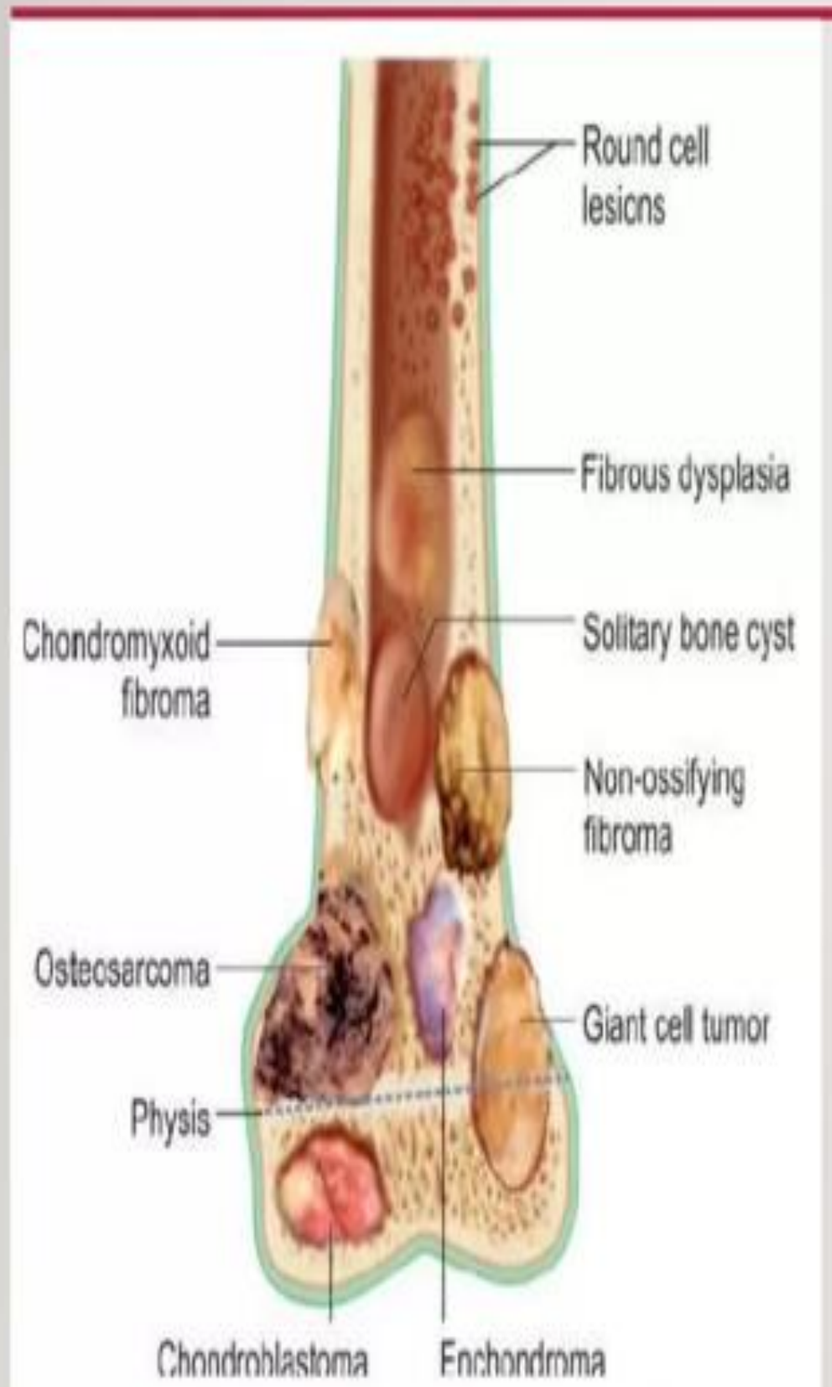


Fig. 4: Osseous location of various bone tumors

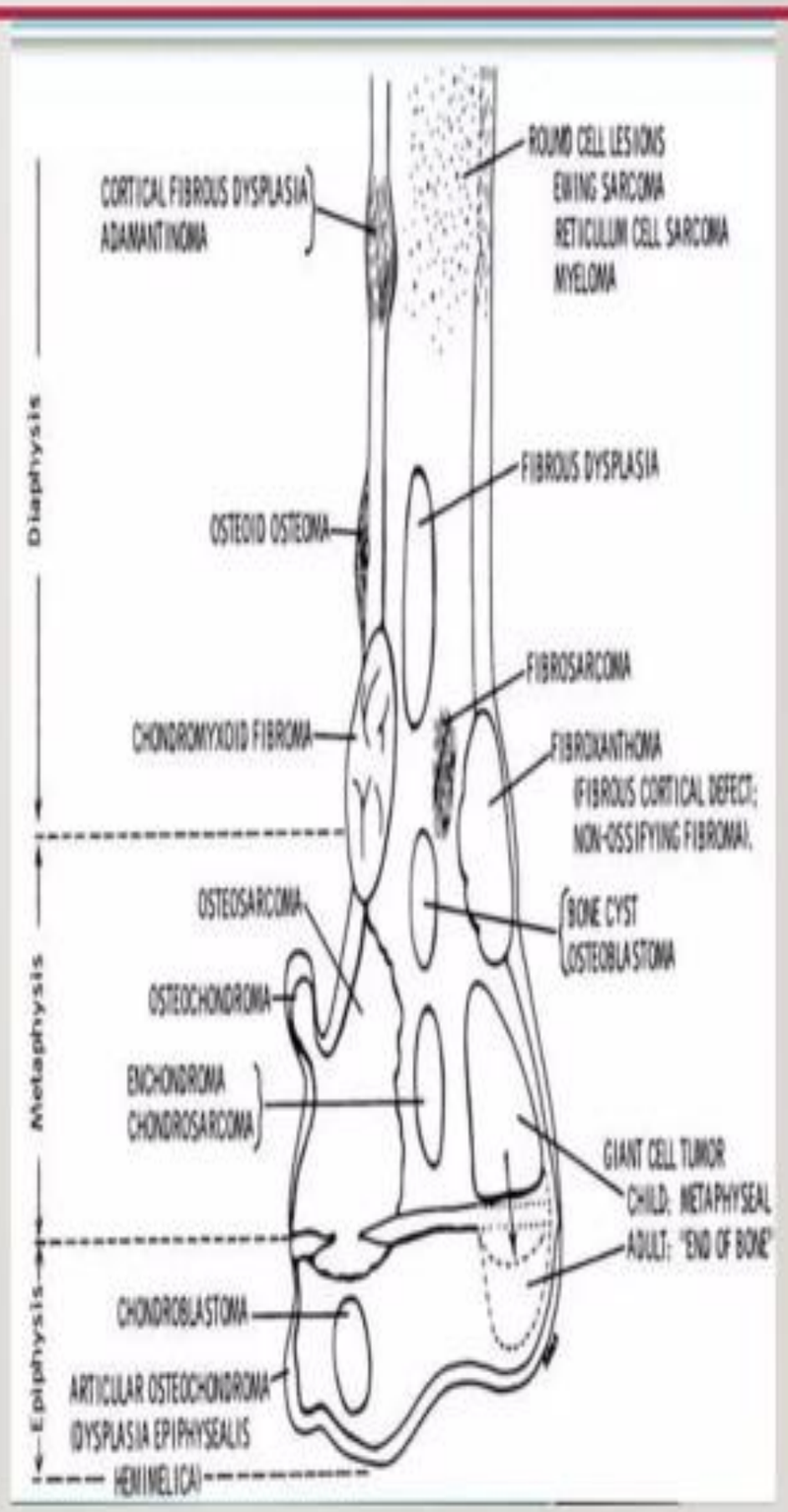


TABLE 8: Age at occurrence of various bone lesions

Age	*Type of lesion*	
	Malignant	*Benign*
Birth to 5 years	• Leukemia • Metastatic neuroblastoma • Metastatic rhabdomyosarcoma	Osteomyelitis Osteofibrous dysplasia
10–25 years	• Osteosarcoma • Ewing's tumor • Leukemia	Eosinophilic granuloma Osteomyelitis Enchondroma Fibrous dysplasia
40–80 years	• Metastatic bone disease • Myeloma • Lymphoma • Chondrosarcoma • Malignant fibrous histiocytoma • Paget's sarcoma • Postradiation sarcoma	Hyperparathyroidism Paget's disease Mastocytosis Enchondroma Bone infarct

Possible diagnosis based on the radiographic appearances, divided by age group

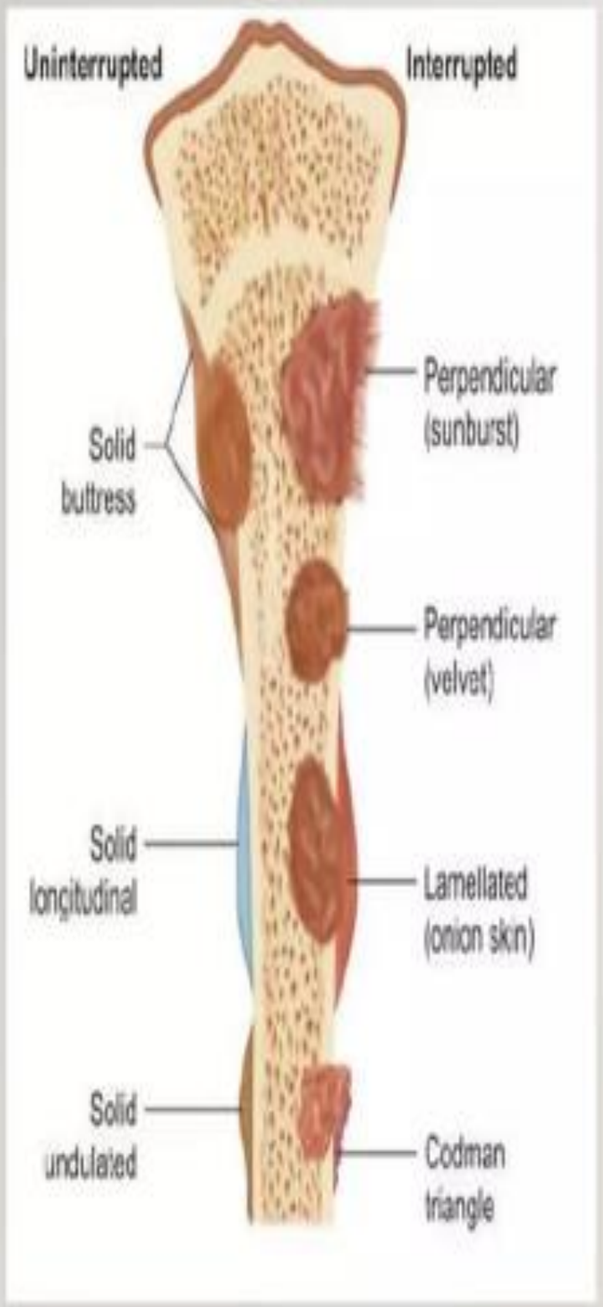
Age (years)	Well-circumscribed lesion	Ill-defined lesions	Sclerotic lesions
0–10	Eosinophilic granuloma Simple bone cyst	Eosinophilic granuloma Ewing's sarcoma Leukaemia	Osteosarcoma
10–20	Non-ossifying fibroma Osteoblastoma Fibrous dysplasia Eosinophilic granuloma Simple bone cyst Aneurysmal bone cyst Chondroblastoma Chondromyxoid fibroma	Ewing's sarcoma Eosinophilic granuloma Osteosarcoma	Osteosarcoma Fibrous dysplasia Eosinophilic granuloma Osteoid osteoma Osteoblastoma
20–40	Giant-cell tumour Enchondroma Low-grade chondrosarcoma Brown tumour Osteoblastoma	Giant-cell tumour	Enchondroma Bone island Parosteal osteosarcoma Burnt-out lesion: • Non-ossifying fibroma • Eosinophilic granuloma • Simple bone cyst • Aneurysmal bone cyst • Chondroblastoma
40+	Metastases Myeloma Geode	Metastases Myeloma High-grade chondrosarcoma	Metastases Bone island
All ages	Infection	Infection	Infection

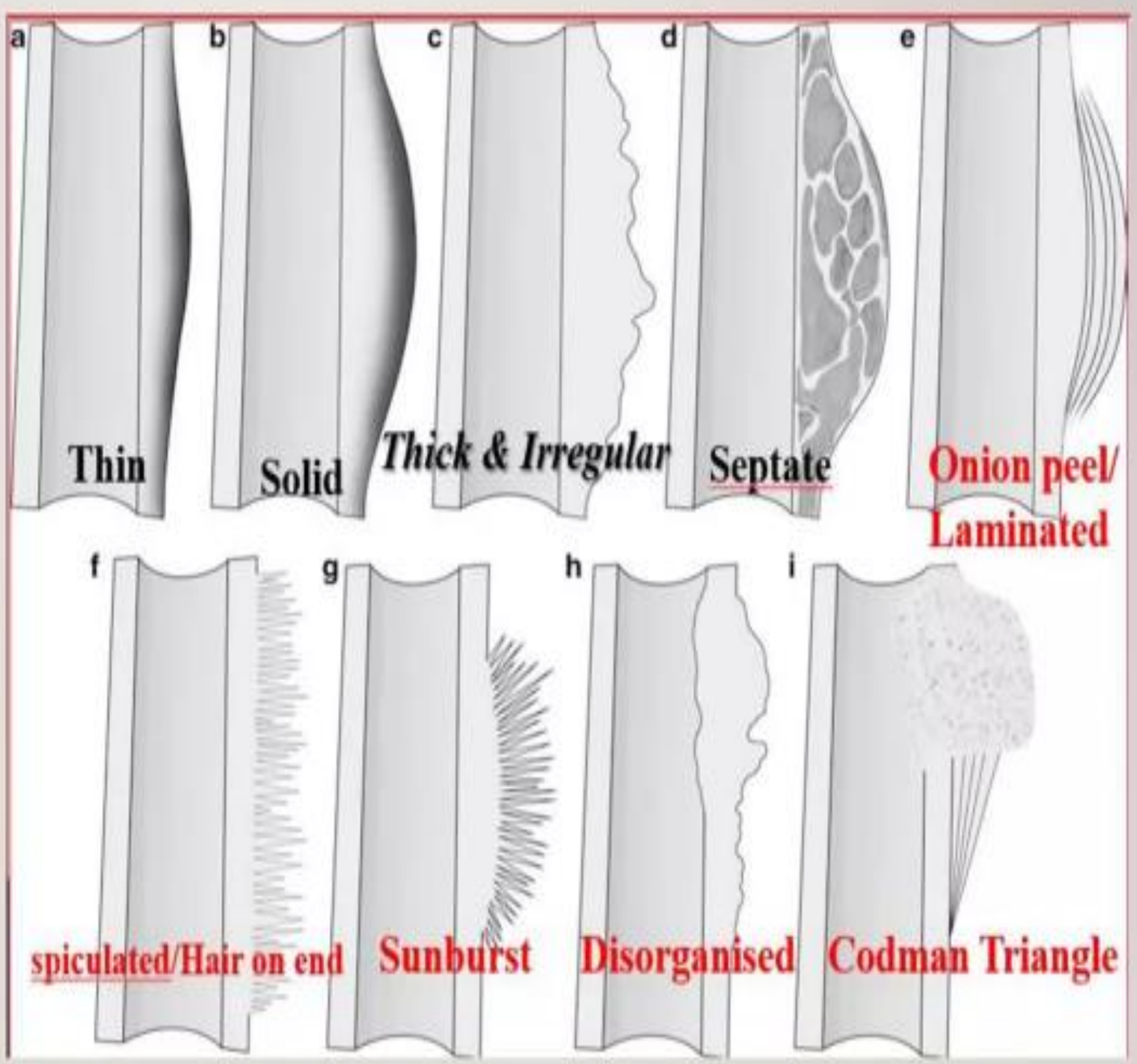
LESION DENSITY

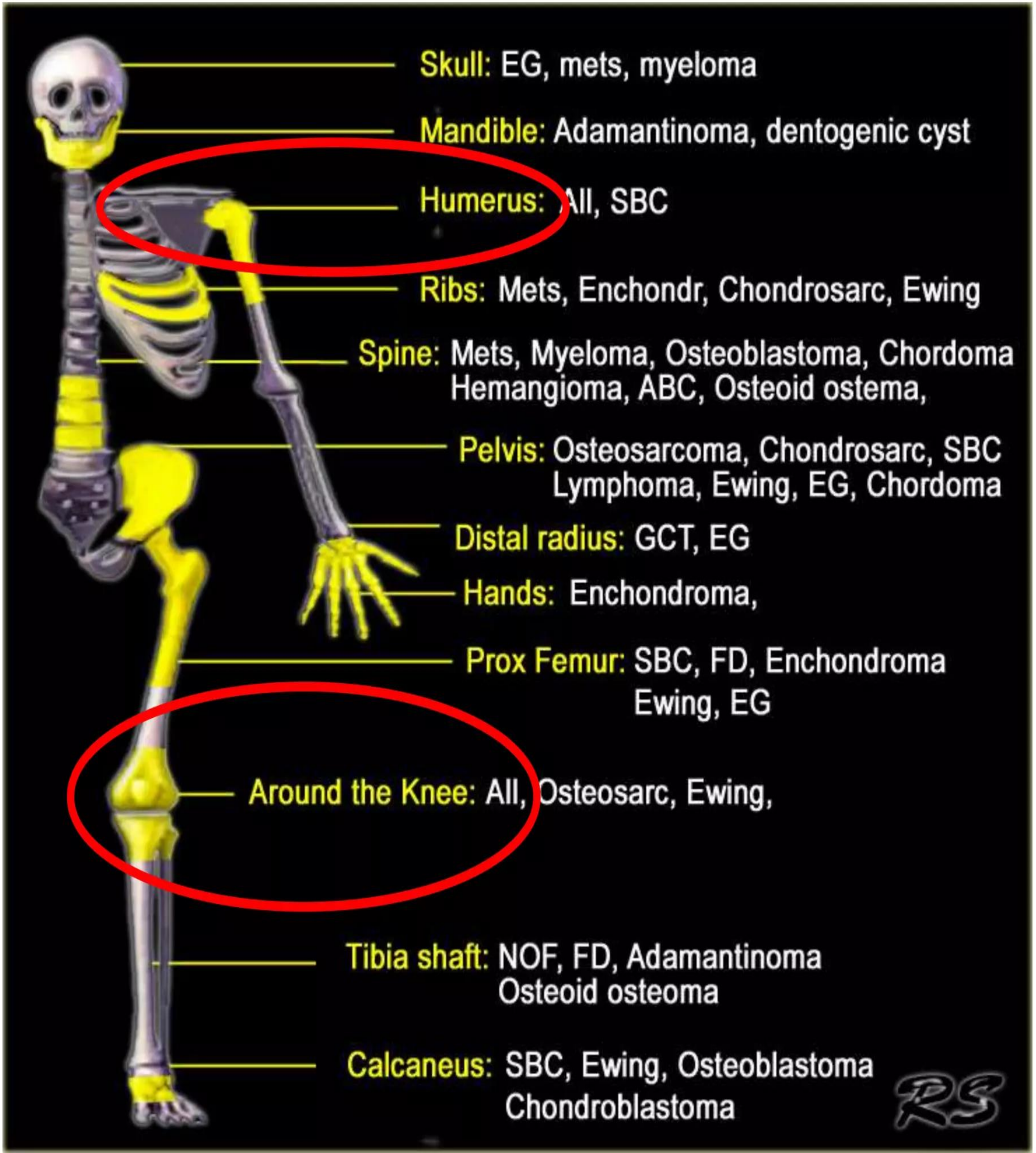
LUCENT LESIONS	SCLEROTIC LESIONS	MIXED
• Chondroblastoma • Giant cell tumor • ABC • Simple bone cyst • Fibrous dysplasia • Osteoblastoma in spine • NOF • Enchondroma • Brown tumor of hyperparathyroidism	• Bone island • Osteoid osteoma • Osteoblastoma • Osteosarcoma • Osteoblastic metastasis (Prostate & Breast) • Paget disease (Blastic phase)	• Fibrous dysplasia • Adamantinoma • Lymphoma • LCH • Metastasis

AGGRESSIVE	NON AGGRESSIVE
➢Moth-eaten or permeative pattern of bone destruction. ➢Indistinct margins/wide zone of transition ➢Cortical breakthrough ➢Aggressive periosteal reaction -Laminated (onion skin) -Spiculated -Perpendicular -hair-on-end -Sunburst -Disorganized -Codman triangle	➢Geographic pattern of bone destruction ➢Well-defined margins /narrow zone of transition ➢Sclerotic margins ➢Intact cortex ➢Nonaggressive or no periosteal reaction – Thin – Solid – Thick, irregular – Septated

PERIOSTEAL REACTIONS





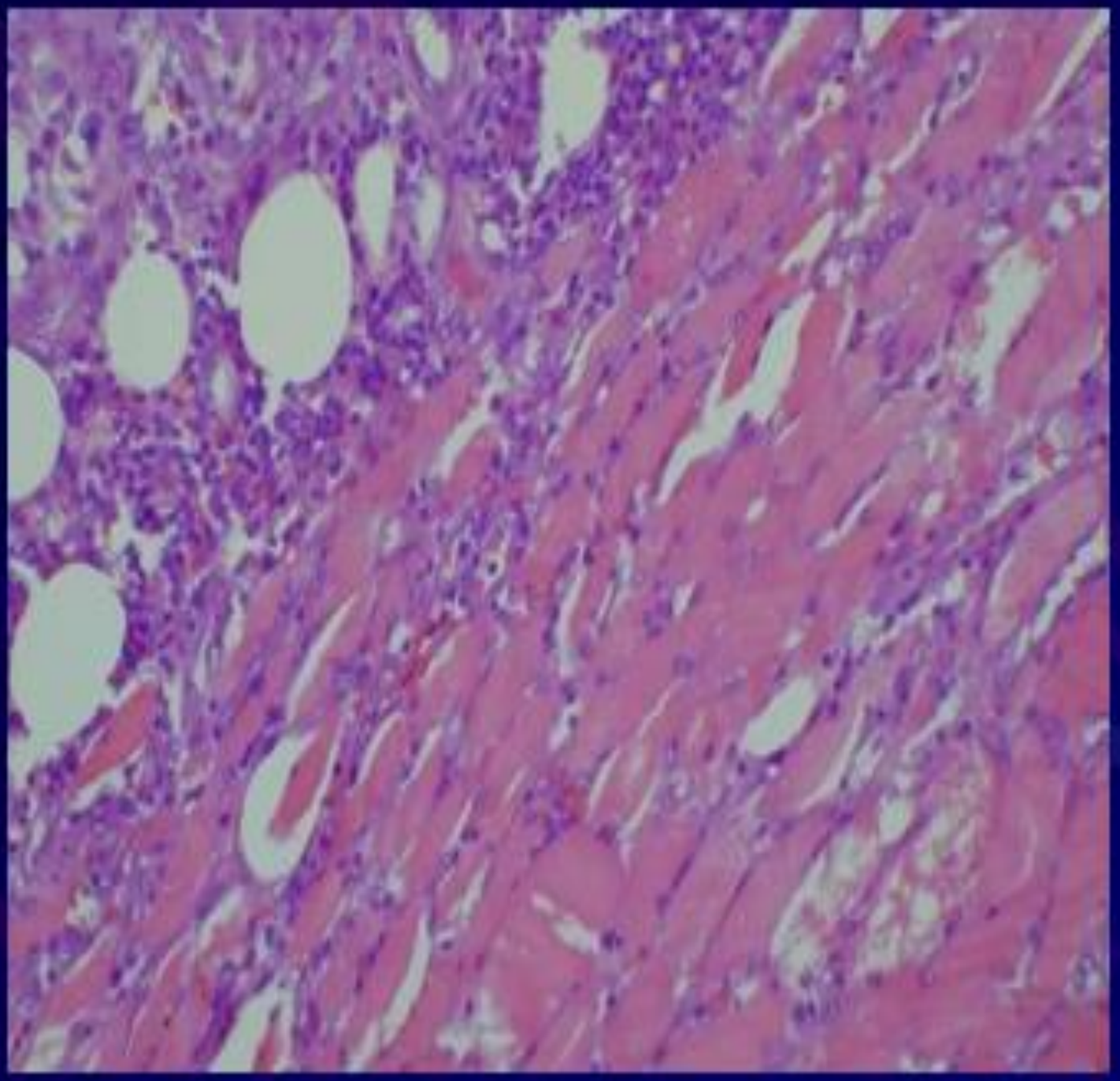

Skull: EG, mets, myeloma
Mandible: Adamantinoma, dentogenic cyst
Humerus: All, SBC
Ribs: Mets, Enchondr, Chondrosarc, Ewing
Spine: Mets, Myeloma, Osteoblastoma, Chordoma
Hemangioma, ABC, Osteoid ostema,
Pelvis: Osteosarcoma, Chondrosarc, SBC
Lymphoma, Ewing, EG, Chordoma
Distal radius: GCT, EG
Hands: Enchondroma,
Prox Femur: SBC, FD, Enchondroma
Ewing, EG
Around the Knee: All, Osteosarc, Ewing,
Tibia shaft: NOF, FD, Adamantinoma
Osteoid osteoma
Calcaneus: SBC, Ewing, Osteoblastoma
Chondroblastoma
RS

General Concepts in Tumour Terminology

- **True Capsule :**
    - Surrounds a benign lesion and is composed of compressed normal cells and mature fibrous tissue.

- **Pseudocapsule :**
    - Compressed tumour cells.
    - Fibrovascular zone of reactive tissue with an inflamamtory component that interdigitates with normal tissue and contains satellite lesions.

Reactive Zone or Pseudocapsule Tumor Compressing Muscle and Infiltrating between Muscle Fibers



- **Compartment :**

  It refers to bone or muscle of origin;

  – For Muscle, compartment is that within its Fascia.

  – For Bone :

    - **Intracompartmental** implies Bone tumour within the cortex

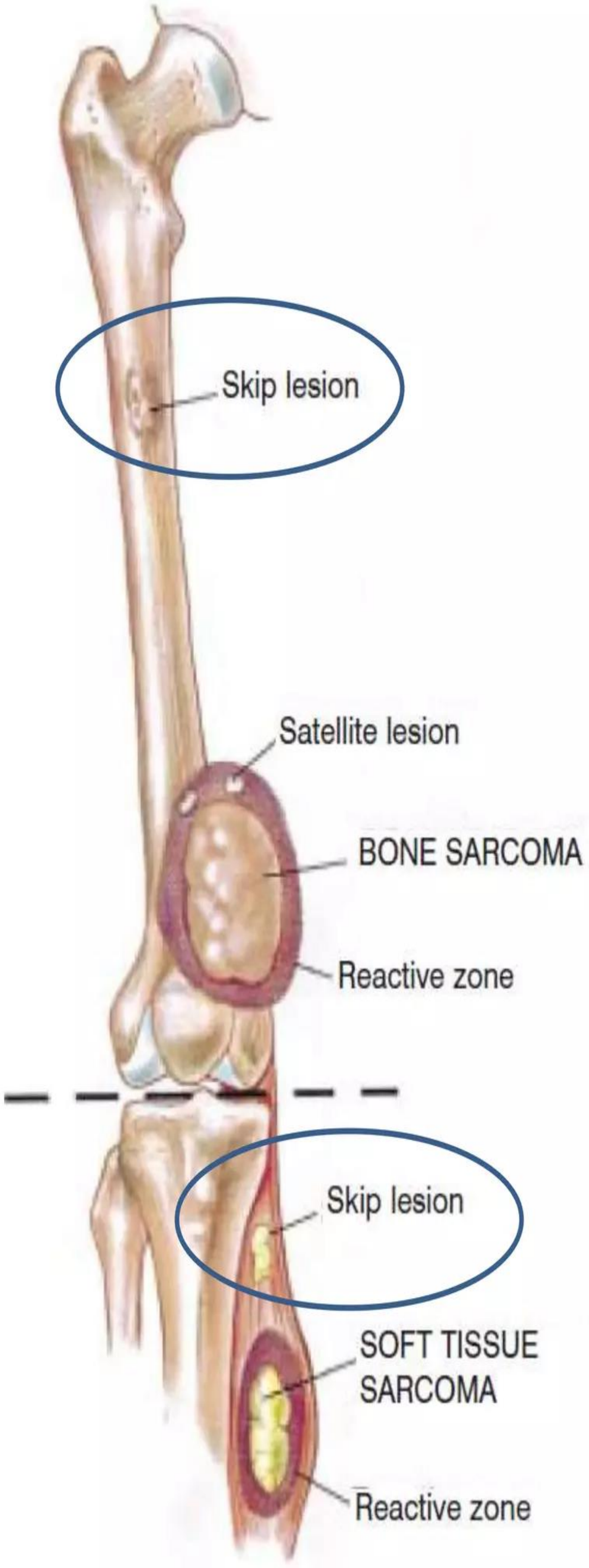
    - **Extracompartmental** implies a bone tumour that destroys the cortex and spreads in to the surrouding tissue.

- **Skip Metastasis :**

  - A skip metastasis, is defined as a tumor nodule that is located within the same bone as the main tumor or on the opposing side of joint but not in continuity with it.

  - High grade sarcomas have the ability to break through the pseudo capsule and metastasize within the same compartment.

– MRI Scan better identifies them.



Intra Osseous Skip Mets :

Embolization of tumour cells within the marrow sinusoids.

Transarticular Skip Mets :

Occur via periarticular venous anastamosis – Very poor prognosis

Satellite lesion

Tumour nodule within reactive zone.

STAGING OF TUMOURS :

- ***STAGING*** is defined as extent of spread of tumour.
  - It is determined by clinical examination, Investigations and pathological studies.

  - Common staging systems are

1. ***ENNEKING `S STAGING SYSTEM***

2. ***AJCC SYSTEM***

3. ***TNM STAGING (Union International Cancer centre Geneva Staging System)***

GRADING and STAGING of TUMOURS

- To determine prognosis and choice of treatment.

GRADING :

- It is defined as macroscopic and microscopic degree of differentiation of tumour

- **BORDER`s GRADING :**
  - GRADE I : Well differentiated; <25% Anaplastic cells
  - GRADE II : Moderately Differentiated; 25-50% Anaplastic cells
  - GRADE III : Moderately differentiated; 50-75% Anaplastic cells
  - GRADE IV: Poorly differentiated; >75% Anaplastic cells

SURGICAL GRADE (G)

LOW GRADE(G1)	HIGH GRADE(G2)
➢**Clinically** : Indolent ➢**Histologically** : - Well differentiated - Few mitoses - Moderate cytologic atypia ➢**Radiologically** : Reactive new bone formation. ➢**Metastasis** : Low risk	➢**Clinically** : Marked activity ➢**Histologically** : - Poor differentiation - High cell/matrix ratio - High mitotic rate, necrosis and microvascular invasion. ➢**Radiologically** : Poorly marginated and have a permeated pattern. ➢**Metastasis** : High risk

ENNEKING'S STAGING FOR BENIGN TUMORS

Latent stage/stage 1	• Low biological activity • Well defined margin • Incidental finding(e.g. NOF)
Active stage/stage 2	• Symtomatic • Limited bone destruction • Pathological fracture (e.g. ABC)
Aggressive stage/stage 3	• Bone destruction/soft tissue extension • Aggressive • Don't respect natural barriers(e.g. GCT)

ENNEKING`s STAGING OF BENIGN TUMOURS

1. **Latent**—low biological activity; well marginated; often incidental findings (i.e., nonossifying fibroma)

2. **Active**—symptomatic; limited bone destruction; may present with pathological fracture (i.e., aneurysmal bone cyst)

3. **Aggressive**—aggressive; bone destruction/soft tissue extension; do not respect natural barriers (i.e., giant cell tumor)

ENNEKING STAGING FOR SARCOMA

Stage	Grade	Site	Metastasis
IA	Low (G1)	Intra-compartmental (T1)	None
IB	Low (G1)	Extra-compartmental (T2)	None
IIA	High (G2)	Intra-compartmental (T1)	None
IIB	High (G2)	Extra-compartmental (T2)	None
III	Any (G)	Any (T)	Regional or Distant Metastasis

American joint committee on cancer system bone sarcoma classification (AJCC Classification)

The AJCC system for bone sarcomas is based on tumor grade, size, and presence and location of metastases.

Stage	Grade	Size	Metastases
I-A	Low	≤8 cm	None
I-B	Low	>8 cm	None
II-A	High	≤8 cm	None
II-B	High	>8 cm	None
III	Any	Any	Skip metastasis
IV-A	Any	Any	Pulmonary metastases
IV-B	Any	Any	Nonpulmonary metastases

American Joint Committee on Cancer System for Staging Soft Tissue Sarcomas

STAGE	GRADE	SIZE	DEPTH	METASTASES
I	Low	Any	Any	None
II	High	5 cm	Any	None
	High	>5 cm	Superficial	None
III	High	>5 cm	Deep	None
IV	Any	Any	Any	Regional or distant

TNM STAGING (Union International Cancer centre Geneva Staging System)

- **T – Primary Tumour – T_0 to T_4**
  - In Situ lesion T_0 to largest and most extensive T_4 primary tumour

- **N – Nodal involvement – N_0 to N_3**
  - No lymph nodes involvement N_0 to wide spread nodal involvement N_3

- **M – Metastasis – M_0 to M_2**
  - No Metastasis M_0 to distant metastasis M_2

Definition of TNM

Primary Tumor (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor 2 cm or less in greatest dimension
T2	Tumor more than 2 cm, but not more than 5 cm, in greatest dimension
T3	Tumor more than 5 cm in greatest dimension
T4	Tumor invades deep extradermal structures (i.e., cartilage, skeletal muscle, or bone)

Note: In case of multiple simultaneous tumors, the tumor with the highest T category will be classified and the number of separate tumors will be indicated in parentheses, e.g., T2 (5)

Regional Lymph Nodes (N)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis

Distant Metastasis (M)

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Stage Grouping

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
	T3	N0	M0
Stage III	T4	N0	M0
	Any T	N1	M0
Stage IV	Any T	Any N	M1

BIOPSY PRINCIPLES

- **Indications** :
- aggressive bone or soft tissue lesions
- soft tissue lesions larger than 5cm, deep to fascia, or overlying bone/neurovascular structures
- unclear diagnosis in a symptomatic patient
- solitary bone lesions in a patient with history of carcinoma

WHEN A BIOPSY IS NOT INDICATED

- asymptomatic latent bone lesions or a symptomatic active bone lesions which appear entirely benign on imaging don't necessarily need a biopsy
- soft tissue lesion which are completely benign on MRI don't necessarily need a biopsy (e.g. lipoma, hemangioma)

TYPES OF BIOPSY

- **Fine Needle Aspiration** (FNA)
- provides cytologic (separated cellular) specimen
- does not provide adequate tissue samples for tumor architecture or mesenchymal stromal analysis
- frequently used for carcinoma
- not typically used for sarcoma

- **Core biopsy** (Tru-cut)
- allow for tumor structural examination
- can evaluate both the cytologic and stromal elements of the tumor
- frequently used for soft tissue sarcoma
- 85-95% accuracy in diagnosis

TYPES OF BIOPSY

- **Incisional biopsy**
- small surgical incision carefully placed to access tumor without contamination of critical structures
- overall lower rate of non-diagnostic biopsy results compared to core needle biopsy

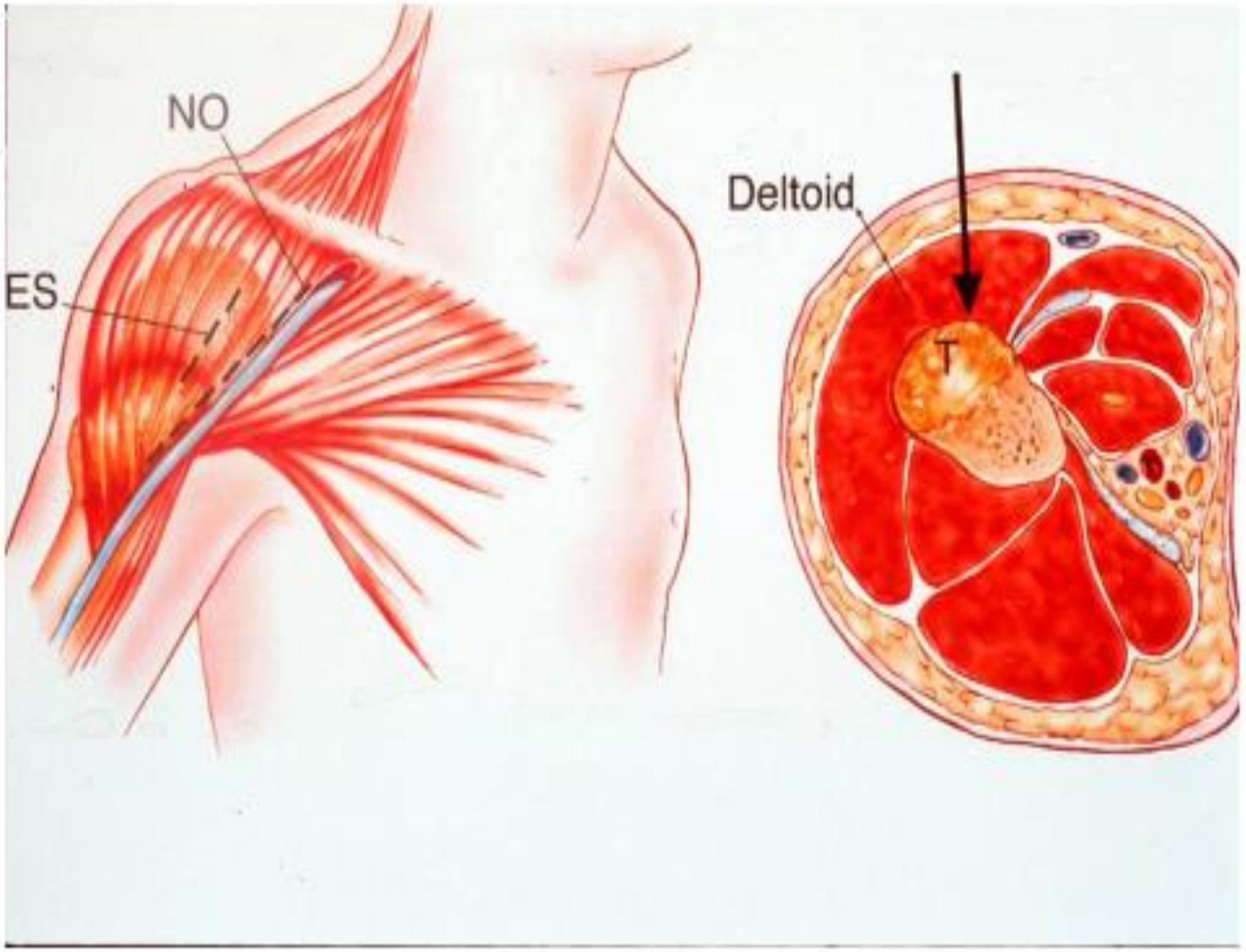
- **Excisional biopsy**
- select indications: small (<3cm), superficial (relatively to fascia) soft tissue masses

PRINCIPLES OF THE OPEN INCISIONAL BIOPSY

- **Incision**
- use longitudinal incision in the extremities
- allows for extension of the incision for definitive management
- **Approach**
- do not expose neurovascular structures
- all tissue exposed during the biopsy is considered contaminated with tumor
- maintain meticulous hemostasis
- post-operative hematomas are considered contaminated with tumor
- release tourniquet prior to wound closure

PRINCIPLES OF THE OPEN INCISIONAL BIOPSY

- perform through the involved compartment of the tumor
- **Closure**
- if using a drain, bring drain out of the skin in line with surgical incision
- allows drain site to be removed with definitive surgical extensile incision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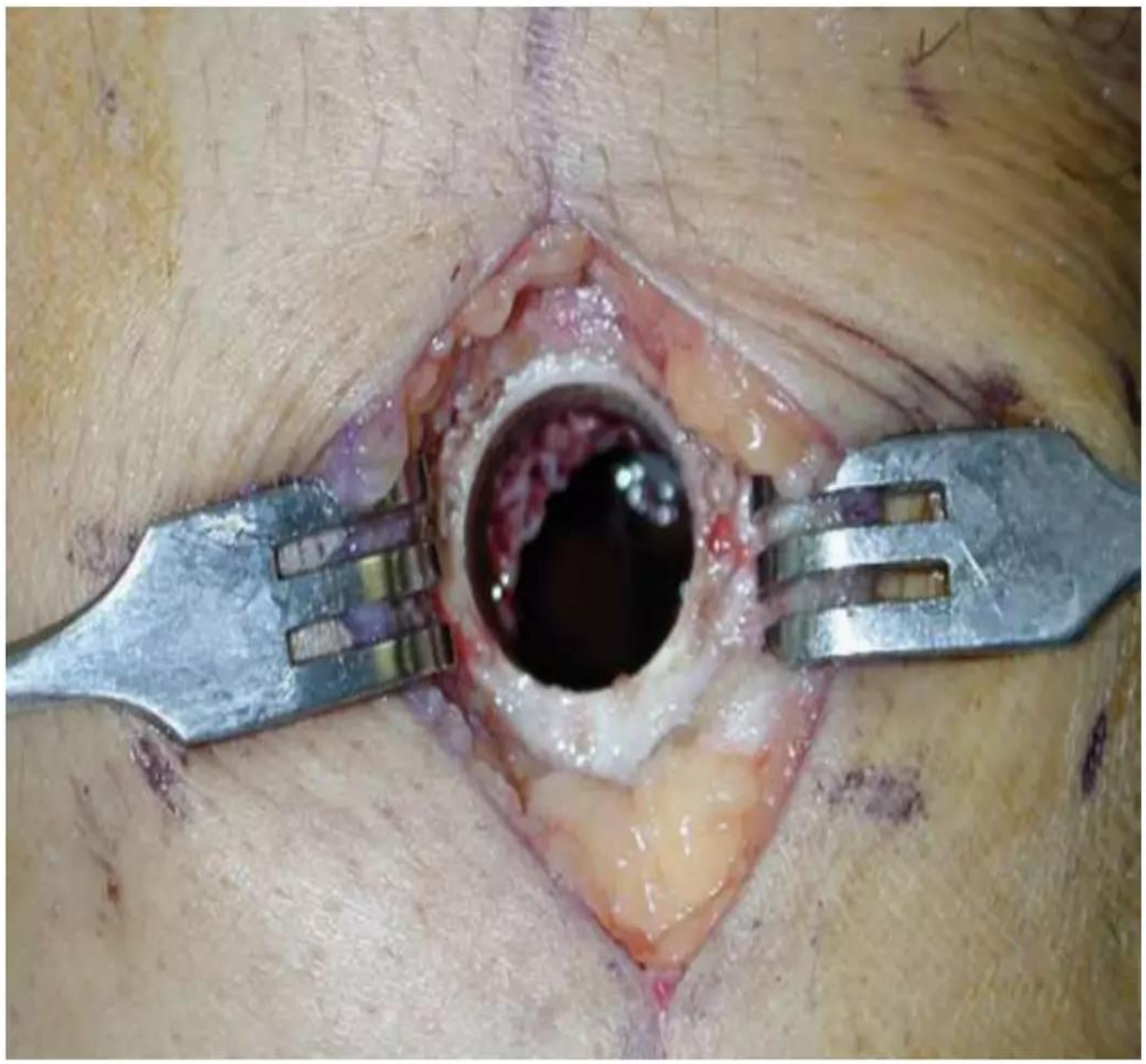
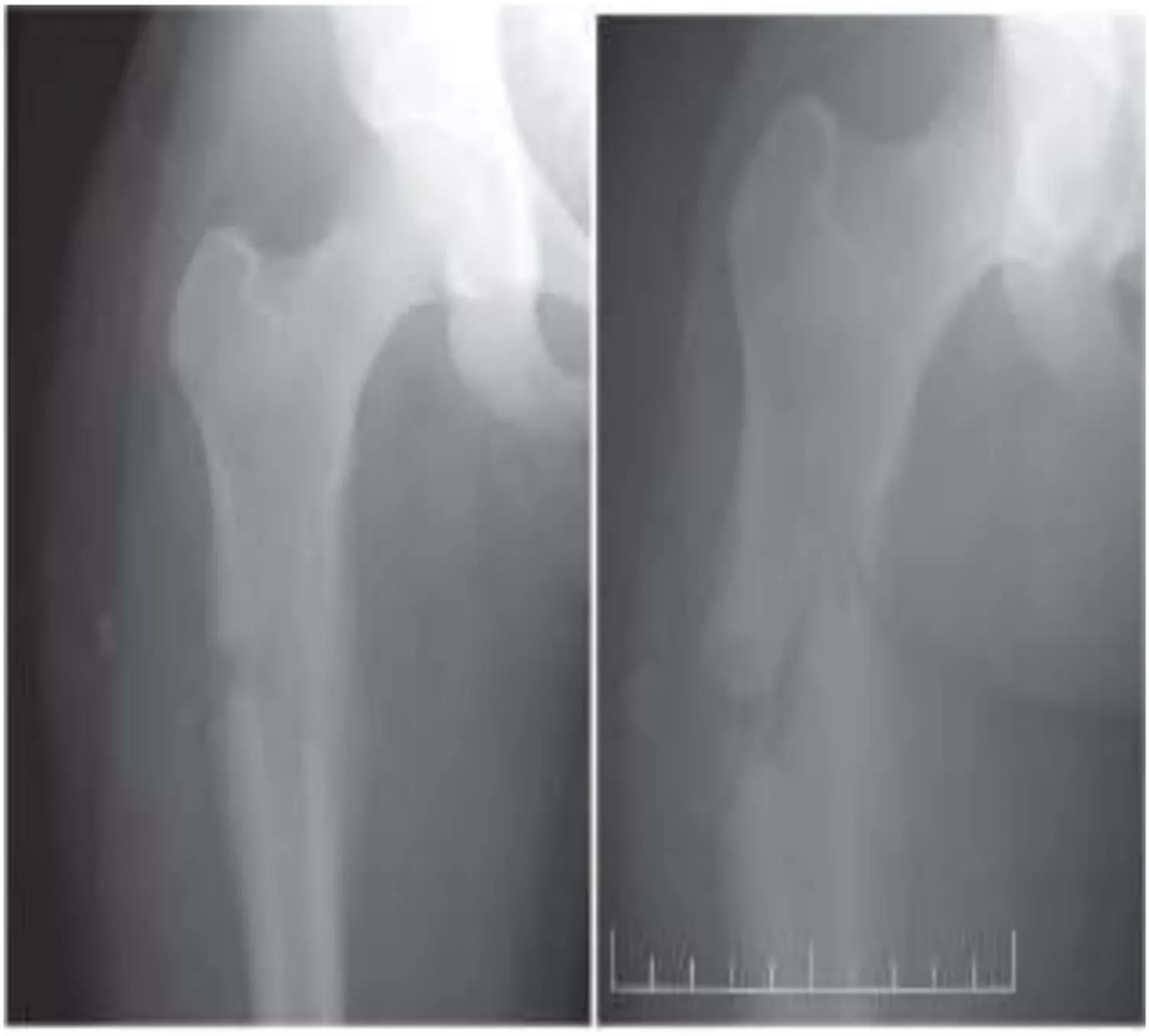


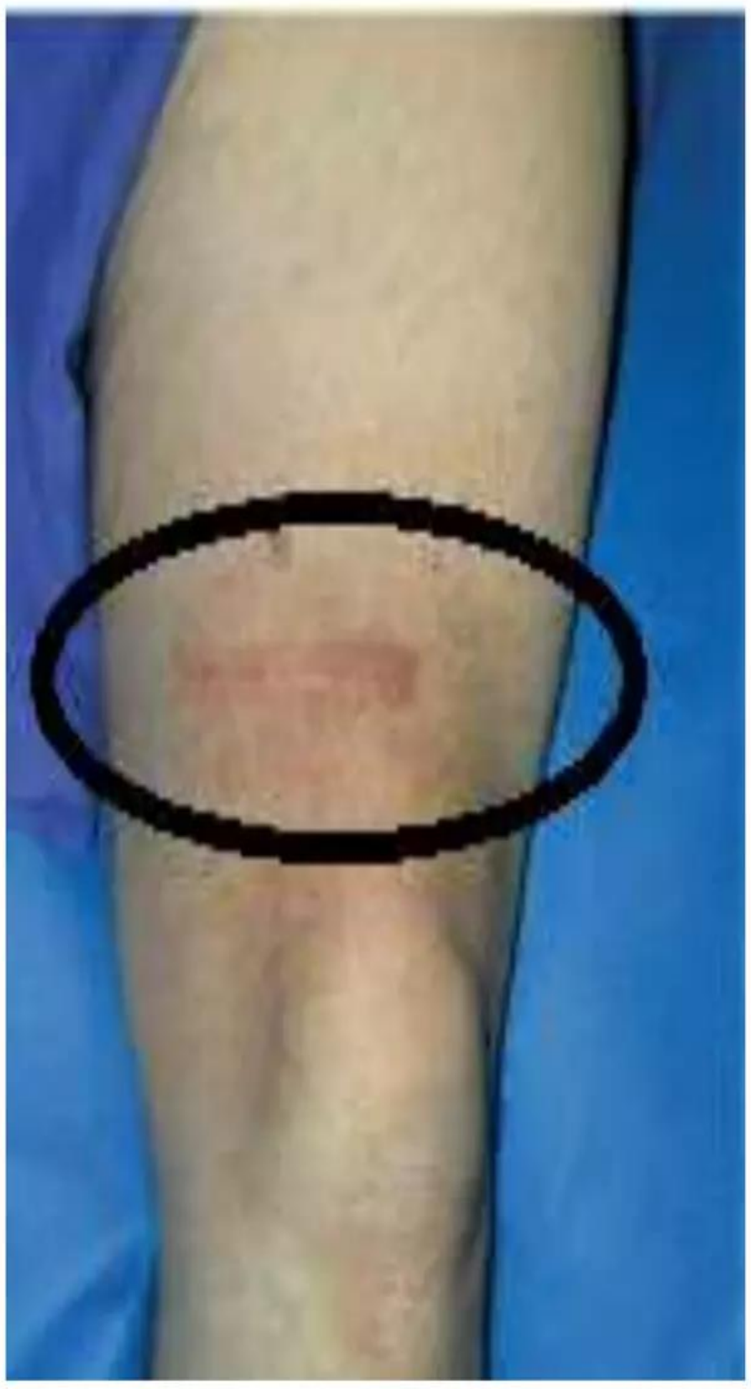
- If hole must be made in bone during biopsy, **defect should be round or oval to minimize stress concentration**, which otherwise could lead to pathological fracture.
- Torsional strength is not affected by length of defect. Always attempt to keep defects less than 10% of bone diameter.
- When biopsy size is greater than 20% of bone diameter, torsional strength decreases to 50%.

Examples of poorly performed biopsies

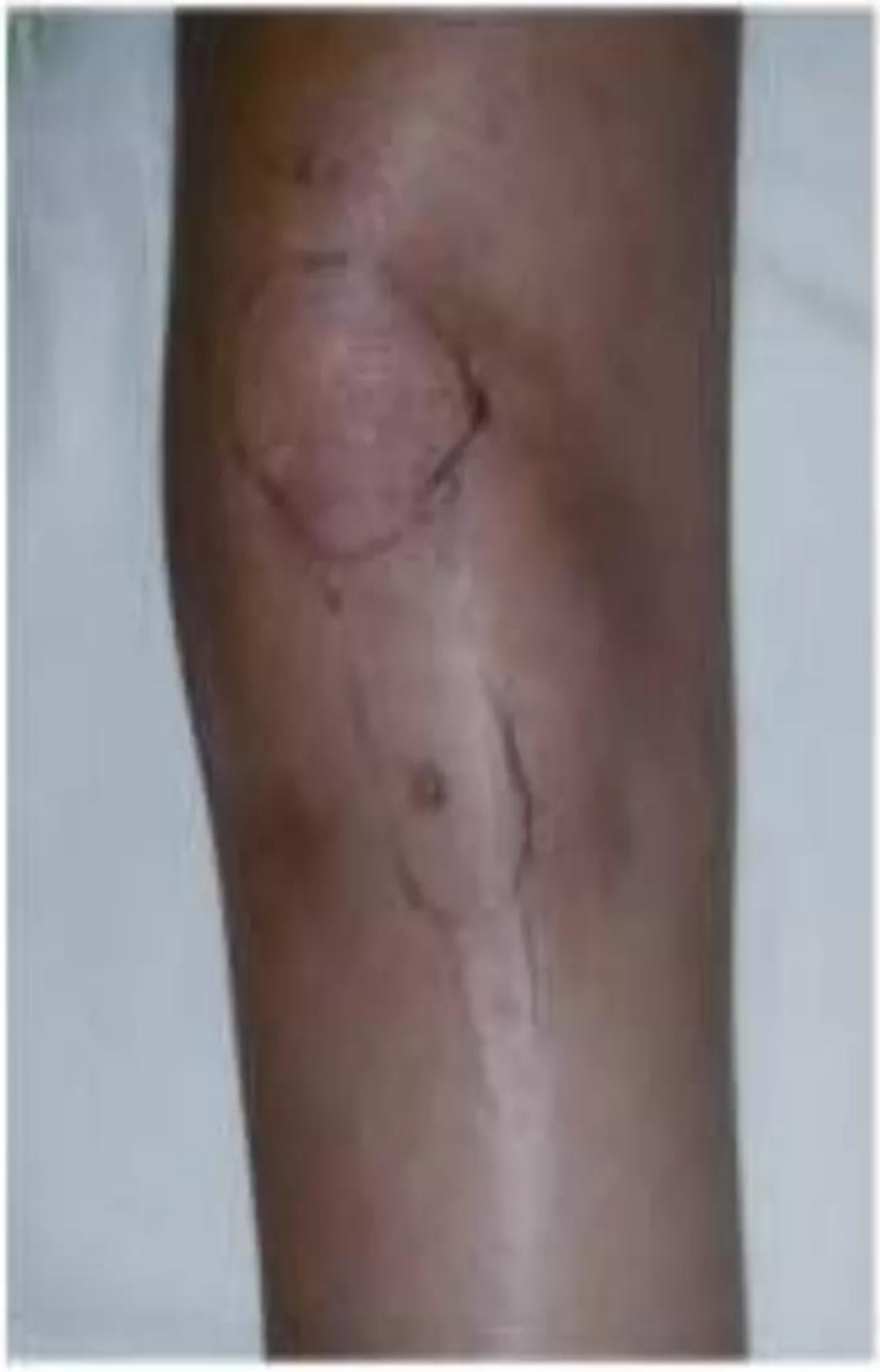


Biopsy resulted in irregular defect in bone, which led to pathological fracture

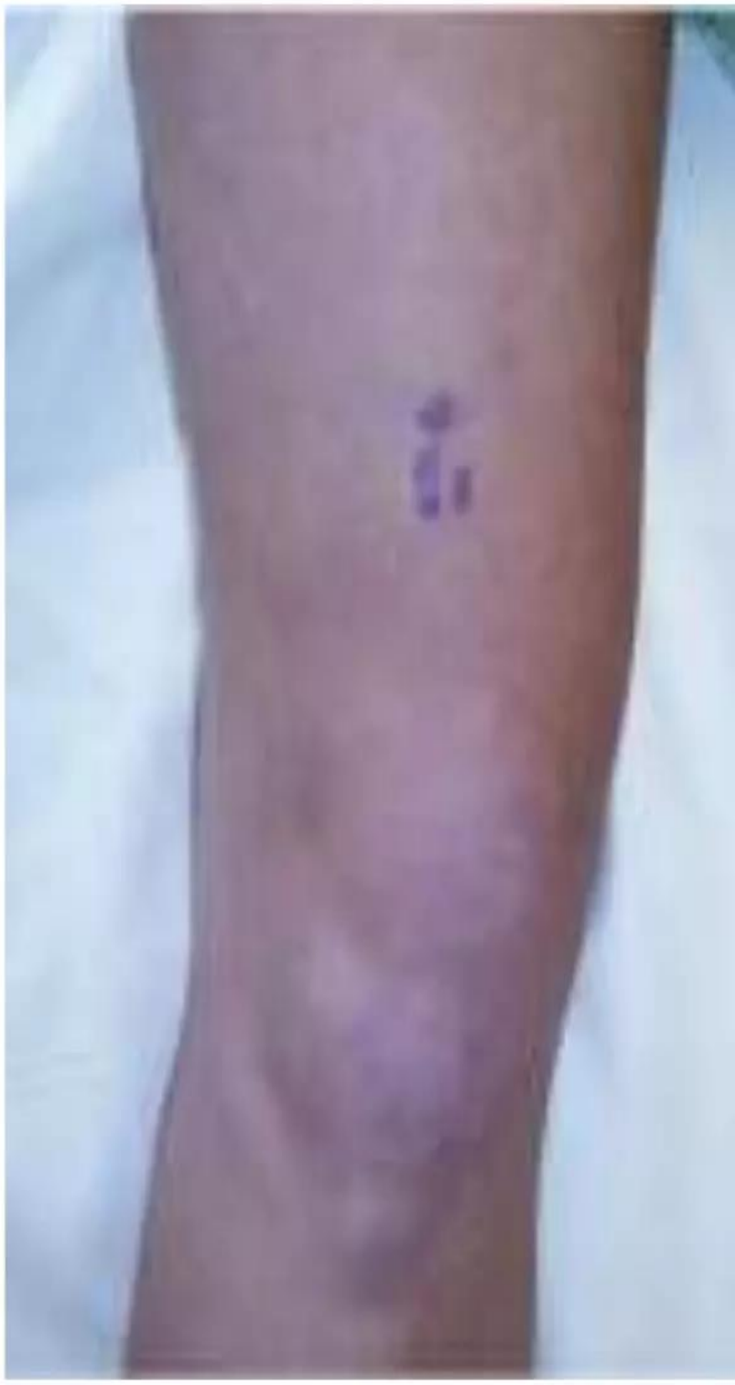
Examples of poorly performed biopsies



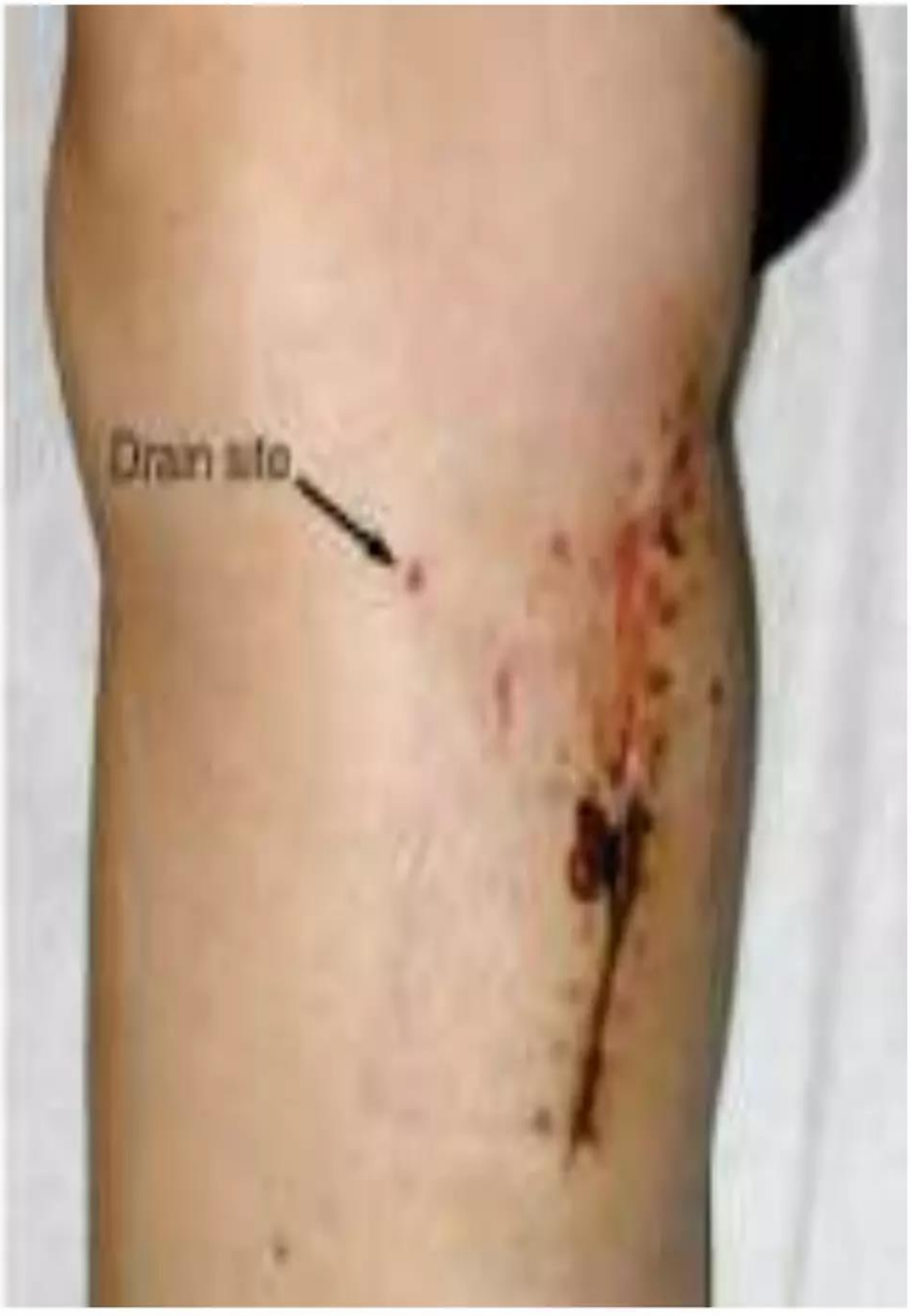
Transverse incisions should not be used



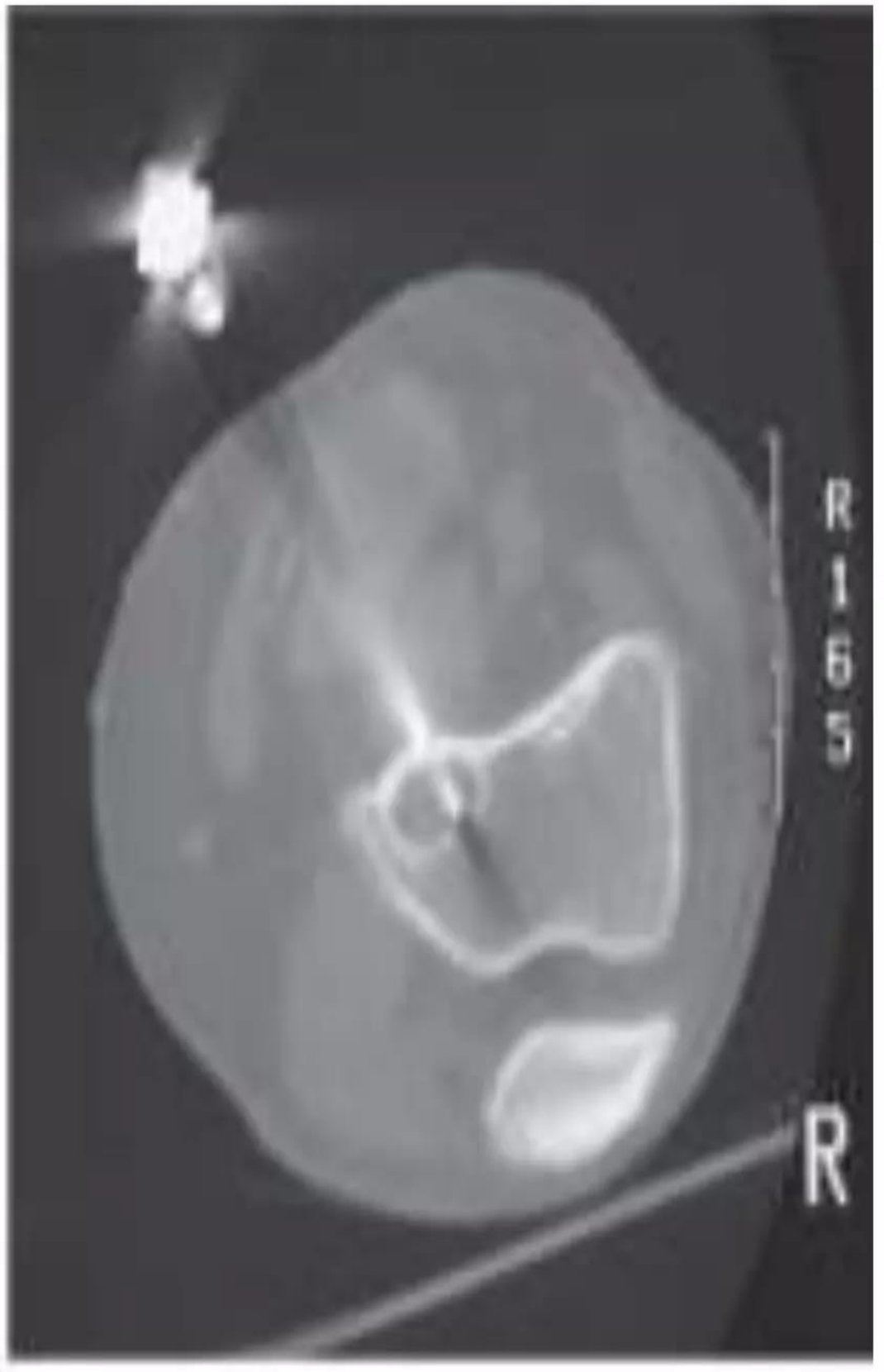
Needle biopsy track contaminated patellar tendon



Multiple needle tracks contaminate quadriceps tendon



Drain site was not placed in line with incision



Needle track placed posteriorly, location that would be extremely difficult to resect en bloc with tumor if it had proved to be sarcoma

- Biopsy should be done only after clinical, laboratory, and radiographic examinations are complete.

- Completion of the evaluation before biopsy aids in planning the placement of the biopsy incision, helps provide more information leading to a more accurate pathological diagnosis, and avoids artifacts on imaging studies.

- If the results of the evaluation suggest that a primary malignancy is in the differential diagnosis, Biopsy is not done unless it is possible to operate the case in the centre.


Thank You
For Your
Attention