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Musculoskeletal Oncology



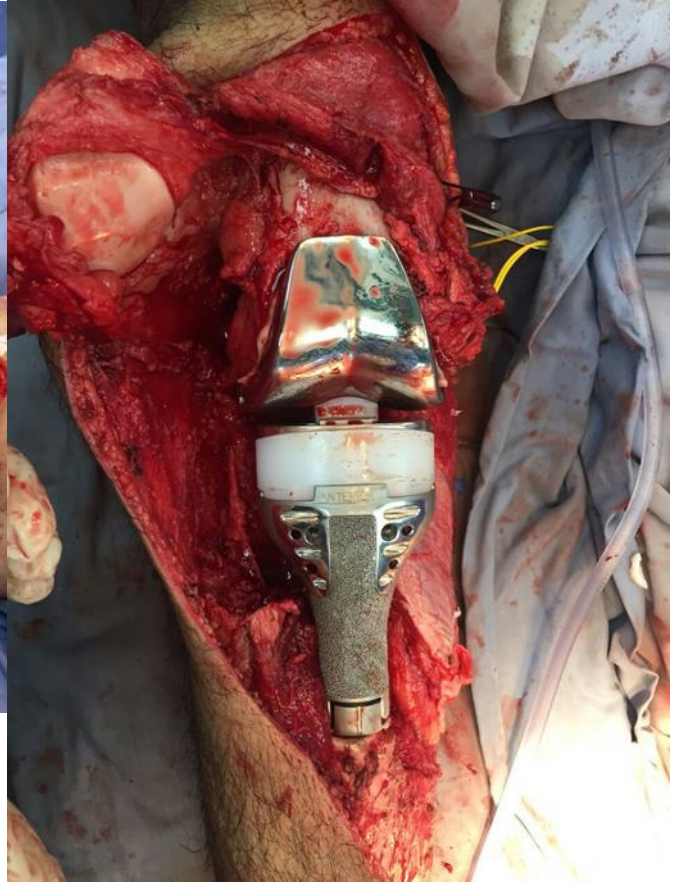
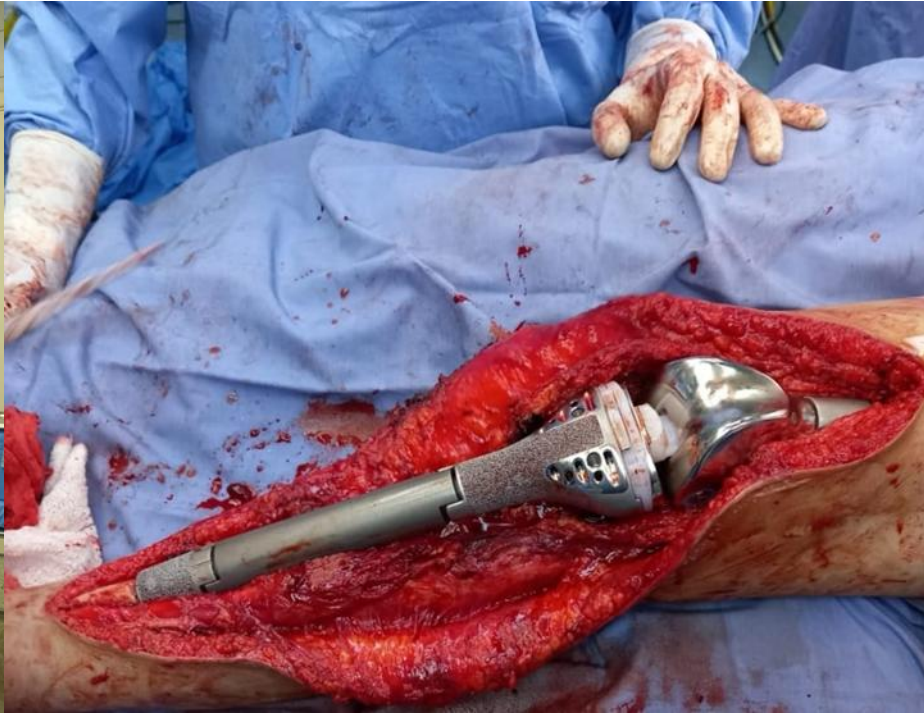
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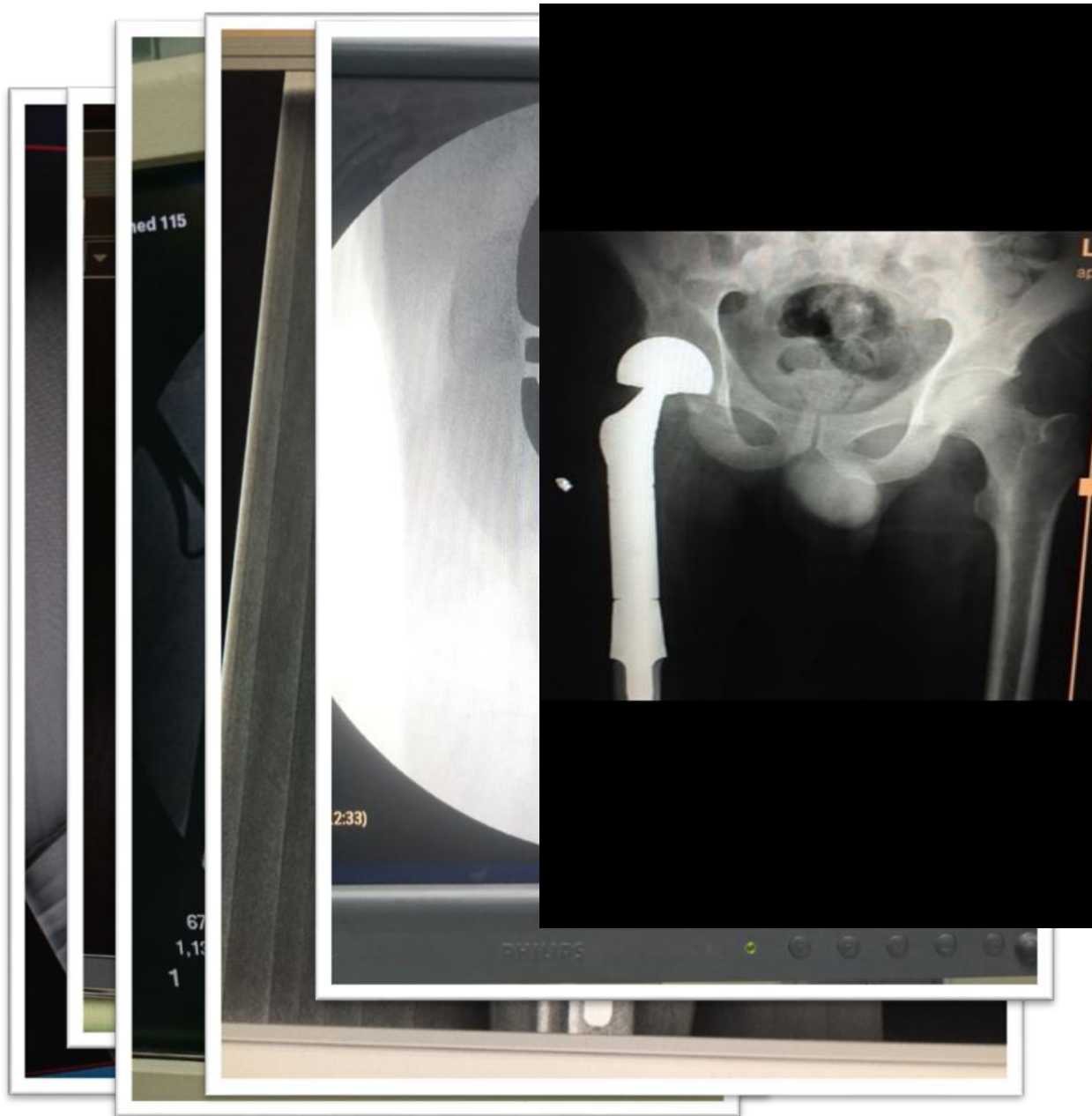
Overview

- Orthopedic oncology is a unique subspecialty within orthopedics. We see patients of all ages.
- We deal with problems involving the upper extremities, lower extremities, and pelvis.
- We see a variety of tumors, including benign and malignant primary bone tumors, benign and malignant soft tissue tumors, and metastatic tumors.
- We also see a variety of metabolic bone abnormalities, skeletal dysplasias, and genetic disorders.

Overview

- The oncology service operates throughout the body, including upper extremity, pelvis, and lower extremity.
- We rarely use a standard approach for our operations. We use a variety of methods for bony reconstructions, including PMMA, allograft bone, autograft bone, and oncology prosthesis. We use standard plates and rods, as well as specially designed plates and rods for any area of the body.
- We can use a variety of techniques for soft tissue reconstruction, including complex closures, negative pressure wound vacs, split thickness skin grafts, and rotation flaps.
- Some of our surgeries will require other surgical teams, including vascular for vascular reconstructions or large vascular injuries, microvascular for free flaps. We occasionally do combined cases with the general surgery and thoracic surgery services as well.





Approach to Musculoskeletal Oncology

- Introduction.
- Etiology of Musculoskeletal tumors.
- Epidemiology.
- Risk factors
- Evaluation of Musculoskeletal tumors.
- Imaging Studies.
- Lab studies.
- Biopsy.
- Staging system.

Introduction

- Tumors of musculoskeletal system are an extremely heterogeneous group of neoplasms
- Consist of over 200 benign types and 90 malignant types of neoplasms
- The incidence of benign to malignant disease is 200:1
- The musculoskeletal system tumors arise from embryonic mesoderm

Introduction

- Soft tissue sarcomas are rare. They account for less than 1% of all cases of [cancer](#). But there are dozens of different types, and they can happen in children and adults.
- About 13,000 people are diagnosed with one of these cancers every year.

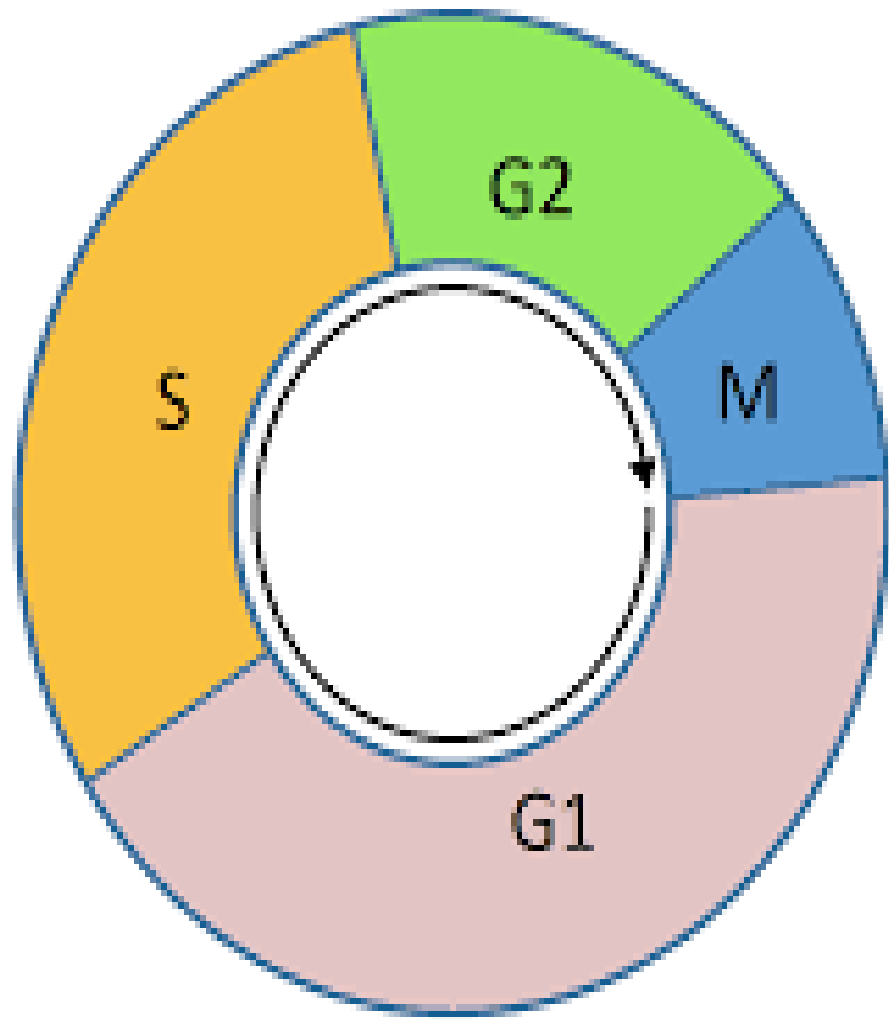
Etiology of Musculoskeletal tumors

- Tumorigenesis is a complex multiple step process by which healthy tissue progressively transforms from normal phenotype into abnormal colony of proliferating cells.
- Genetic abnormalities in oncogenes , tumor suppressor genes and other genes that directly and indirectly control proliferation

Cell cycle

- Four phases :
 - G1 : gap 1 majority of cell growth take place
 - S : DNA synthesis
 - G2 : gap 2
 - M : mitosis separation and cell division occur

- G0: the mature state



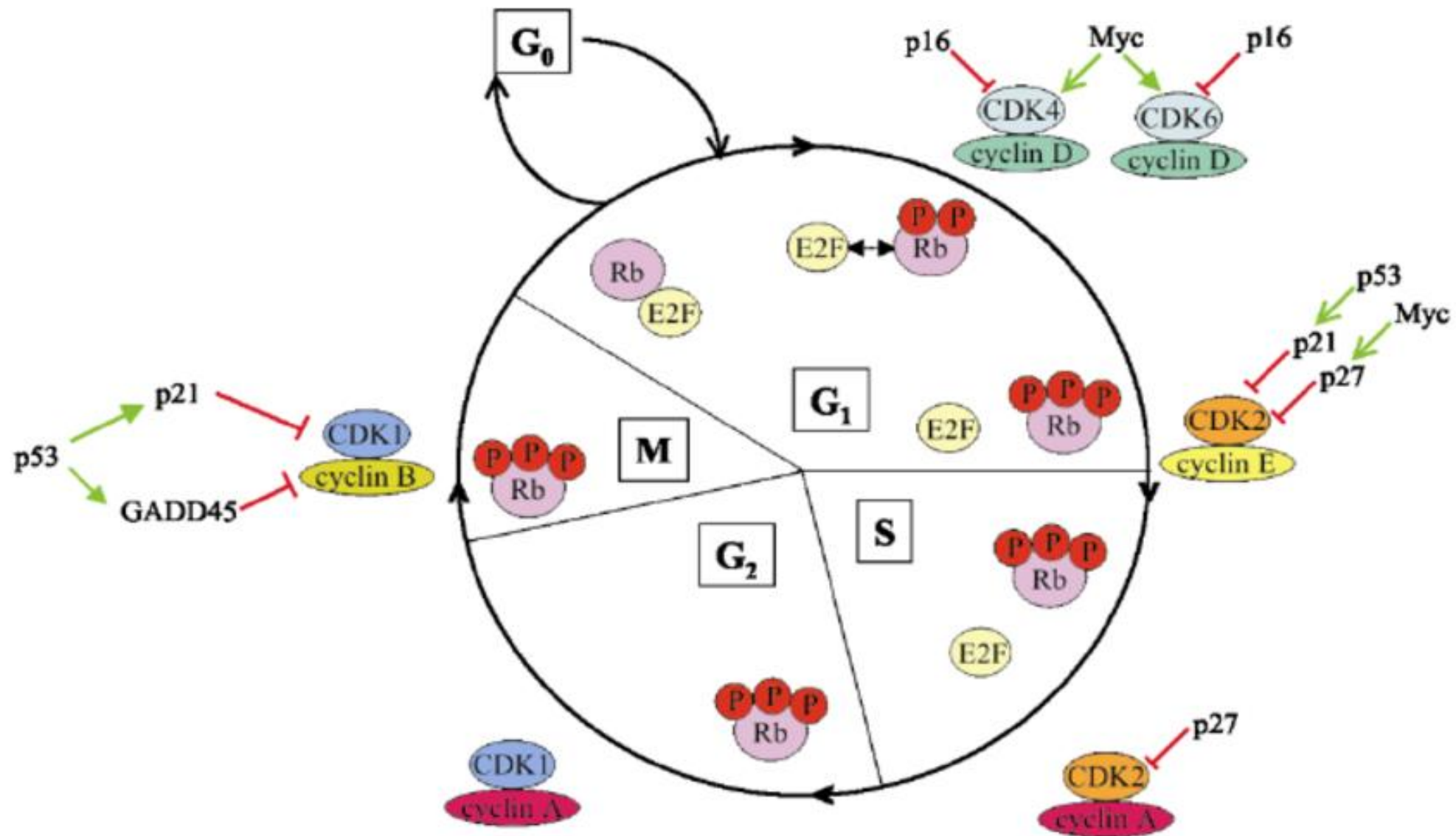
G1 - Growth

S - DNA synthesis

G2 - Growth and preparation for mitosis

M - Mitosis (cell division)

- The hallmark of neoplastic disease is factors affect the exit of the cell from G0 with entrance into G1.
- Inheritable genetics
- Environmental factors
 - Oncogenic viruses
 - Radiation
 - Chemical carcinogens



Epidemiology

- The American Cancer Society's estimates for cancer of the bones and joints for 2021 are:
 - About 3,610 new cases will be diagnosed
 - About 2,060 deaths from these cancers are expected
 - Primary cancers of bones account for less than 0.2% of all cancers.
- In adults, over 40% of primary bone cancers are chondrosarcomas. This is followed by osteosarcomas (28%), chordomas (10%), Ewing tumors (8%), and malignant fibrous histiocytoma/fibrosarcomas (4%). The remainder of cases are several rare types of bone cancers.

Epidemiology

- In children and teenagers (those younger than 20 years), osteosarcoma (56%) and Ewing tumors (34%) are much more common than chondrosarcoma (6%).
- Chondrosarcomas develop most often in adults, with an average age at diagnosis of 51. Less than 5% of cases occur in patients younger than 20.
- Chordomas are also more common in adults. Less than 5% of cases occur in patients younger than 20.
- Both Osteosarcomas and Ewing tumors occur most often in children and teens.

Epidemiology

The vast majority of primary bone tumors are benign and since many are non-symptomatic they remain undetected or are detected only incidentally at radiographic examinations for other reasons. The true incidence of benign bone tumors have therefore been difficult to determine.

Primary bone malignancy Frequency (%)

Osteosarcoma	35.1
Chondrosarcoma	25.8
Ewing's sarcoma	16.0
Chordoma	8.4
Malignant fibrous histiocyoma	5.7
Angiosarcoma	1.4
Unspecied	1.2
Other	6.4

Classification of primary benign bone tumors peak age, and most common sites distribution

The histologic classification of bone tumors is based on cytologic findings (in particular cell type such as osteocyte/osteoblast, chondrocyte/chondroblast, osteoclast, etc.), architecture, and type of matrix produced by the tumor.

Histologic type	Peak age (years)	Most common sites
Cartilage tumors		
Osteochondroma	10–30	Distal femur, proximal tibia, proximal humerus, rarely from flat bone
Enchondroma	10–40	Hands, feet, long tubular bones
Periosteal chondroma	10–40	Proximal humerus, distal femur, hip region, and pelvis
Chondroblastoma	10–30	Distal femur, proximal tibia and humerus, calcaneus
Chondromyxoid bromoma	10–30	Proximal tibia, distal femur, pelvis, feet (metatarsal)

Osteogenic tumors		
Osteoid osteoma	5–25	Proximal femur, any long bones
Osteoblastoma	10–40	Spine, long tubular bones, jaws
Fibrogenic tumors		
Desmoplastic fibroma	10–30	Mandible, femur, pelvis
Fibrohistiocytic tumors		
Benign fibrous histiocytoma	20–60	Pelvis, femur
Giant cell tumor	20–45	Distal femur, proximal tibia, distal radius, sacrum

Vascular tumors		
Hemangioma (cavernous, capillary, epithelioid, etc.)	usually adults	Craniofacial bones, vertebrae Angiomatosis,
lymphangioma(tosis)	Often children	Highly variable
Glomus tumor	Usually adults	Hands, distal phalanx
Hemangiopericytoma	Usually adults	Pelvis
Epithelioid hemangioendothelioma	Adults	Long tubular bones, spine
Soft tissue type tumors		
Lipoma Schwannoma Leiomyoma	Adults	Femur, calcaneus Sacrum, mandible Mandible, tibia

**Classification of primary
malignant bone tumors, peak
age, and most common sites
distribution**

Histologic type	Peak age (years)	Most common sites
Chondrosarcoma		
Primary	50–80	Pelvis, proximal/distal femur, proximal humerus, ribs
Secondary	20–60	Ex osteochondroma(tosis): pelvis, hip and shoulder Dedifferentiated
chondrosarcoma	50–70	Pelvis, femur, humerus
Clear cell chondrosarcoma	25–60	Proximal femur, humerus
Mesenchymal chondrosarcoma	10–40	Jaws, ribs, pelvis, spine

Osteosarcoma		
Conventional	10–30	Distal femur, proximal tibia, hip and shoulder
Telangiectatic osteosarcoma	10–30	Femur, tibia, humerus Low-grade central
osteosarcoma	20–40	Distal femur, proximal tibia
Parosteal osteosarcoma	20–50	Posterior distal femur, proximal humerus
Periosteal osteosarcoma	10-30	Femur, tibia
High-grade surface	10–40	Distal femur, shoulder

Secondary osteosarcoma		
Paget's associated	50–90	Pelvis, hip and shoulder, craniofacial
Post-radiation	50–80	Pelvis, craniofacial, hip and shoulder, chest wall
Other conditions	40-70	Bones affected by FD, Bone infarcts, chronic osteomyelitis
Ewing's sarcoma, PNET	5–30	Pelvis, longbones of lower and upper extremities
Fibrosarcoma, MFH, spindle cell sarcoma	40-70	Knee, hip and shoulder regions, pelvis
Malignant giant cell tumor	20-60	Knee region, pelvis, shoulder

Histologic type	Peak age (years)	Most common sites
Angiosarcoma	20–70	Spine, pelvis, hip and shoulder
Adamantinoma	10-40	Tibia, rarely ulna, radius and fibula

Risk factors

- It's not clear what causes bone cancer, but doctors have found certain factors are associated with an increased risk, including:
 - Inherited genetic syndromes. Certain rare genetic syndromes passed through families increase the risk of bone cancer, including Li-Fraumeni syndrome and hereditary retinoblastoma.
 - Chemical exposure
 - Radiation therapy: Exposure to large doses of radiation, such as those given during radiation therapy for cancer, increases the risk of bone cancer in the future.
 - Weakened immune system: People with HIV sometimes develop Kaposi sarcoma, a type of soft tissue sarcoma that develops from the cells that line blood vessels or lymph vessels

Evaluation of Musculoskeletal tumors

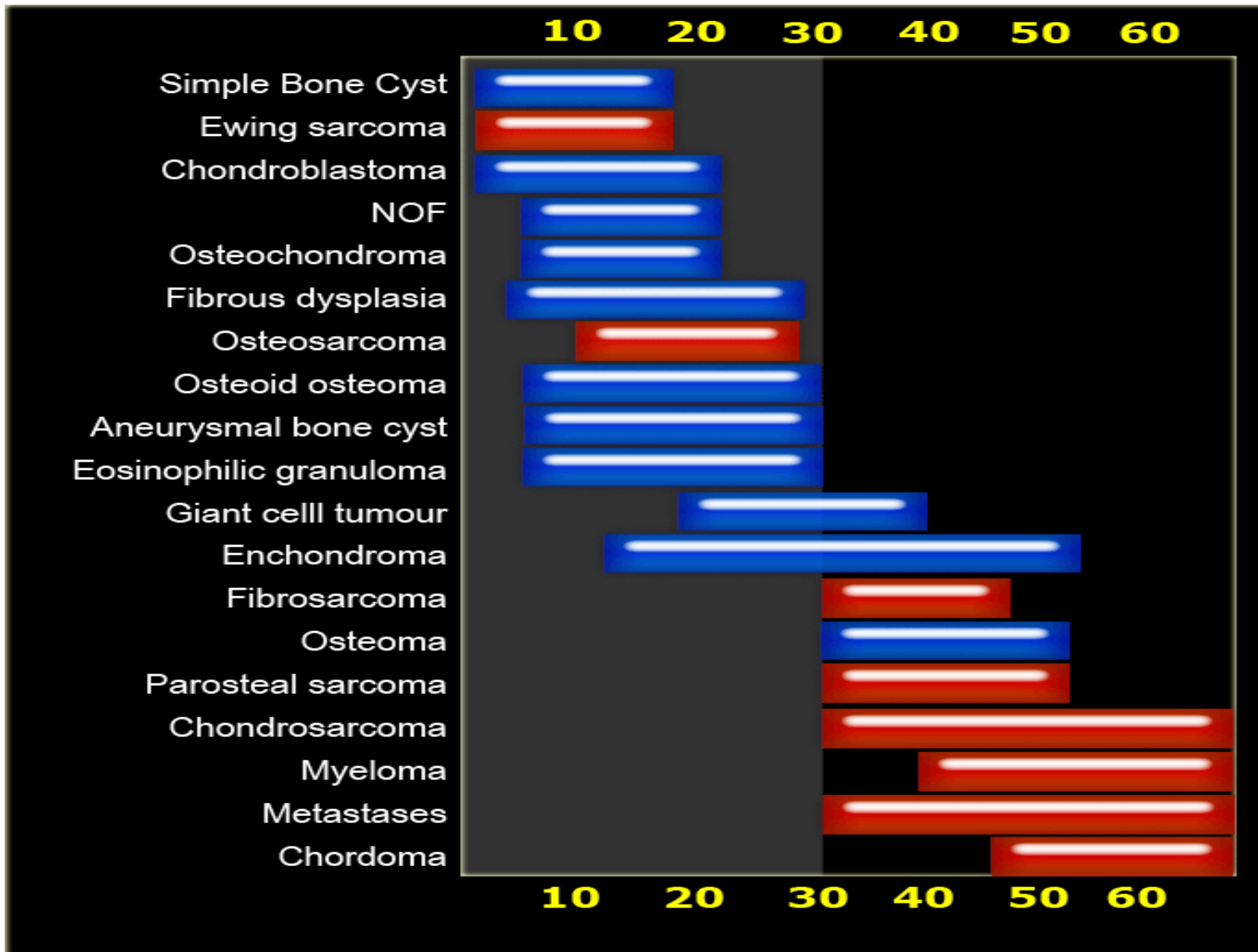
- History
- Physical examination
- Imaging studies
- Lab studies
- Biopsy

History

- The patient's age
- Duration of complaint
- Rate of growth
- Pain
- History of trauma
- Family history
- Systemic symptoms

The patient's age

- Certain tumors are relatively specific to particular age groups



Duration of complaint

- Benign lesions generally have been present for an extended period (years) while malignant tumors usually have been noticed for only weeks to months

Rate of growth

- Rapidly growing mass as in weeks to months is more likely to be malignant.
- Growth may be difficult to assess by the patient if it is deep seated
- Tip of the iceberg phenomenon

Pain

- Benign process usually asymptomatic or may cause secondary symptoms
- Most common presentation in malignant process is musculoskeletal pain :
 - Deep seated
 - Dull in nature
 - Intermittent
 - Related for activity
 - Increase at night
 - Progresses in intensity
 - Not relieved by NSAIDs

History of trauma

- Penetrating trauma
- Blunt trauma

Family history

Systemic symptoms

- In benign tumors there is no significant findings on the review system
- Fever, chills, night sweat, malaise, change in appetite, weight loss should alert the physician that an infectious or neoplastic process may be involved

Physical examination

- Inspection
- Palpation
- Specific systems examination

Mass examination

- Skin color
- Skin changes
- Location
- Size
- Tenderness
- Temperature
- Consistency
- Pulsation
- Joint range of motion
- Neurovascular exam
- Lymph nodes

Specific systems examination

- Thyroid
- Breasts
- Chest
- Liver
- Kidney
- Rectal (prostate & rectal tumours)

Imaging studies

- X-Ray
- U/S
- CT scan
- MRI
- Bone isotope scan
- PET scan

X-Ray

- Best modality for characterizing a bony lesion as benign or malignant.
- Many lesions have characteristic appearances that allow for accurate diagnosis.
- Provides the road map for further investigation and diagnosis.

X-Ray

X-Ray

- Bone involved
- Is the bone normal
- What part of bone
- Open or closed physis
- Mineralized matrix
- Cortical destruction
- Periosteal reaction Type
- Pattern of destruction(geographic, permeative, moth eaten)
- Margins
- Trabeculations
- Cortical erosion ,penetration, expansion
- Periosteal response/continuous or interrupted

Sharp, Narrow Zone
Of Transition

Calcifications

Interrupted
Periosteal Rxn

Epiphysis

Metaphysis

Diaphysis

Geographic Bone
Destruction

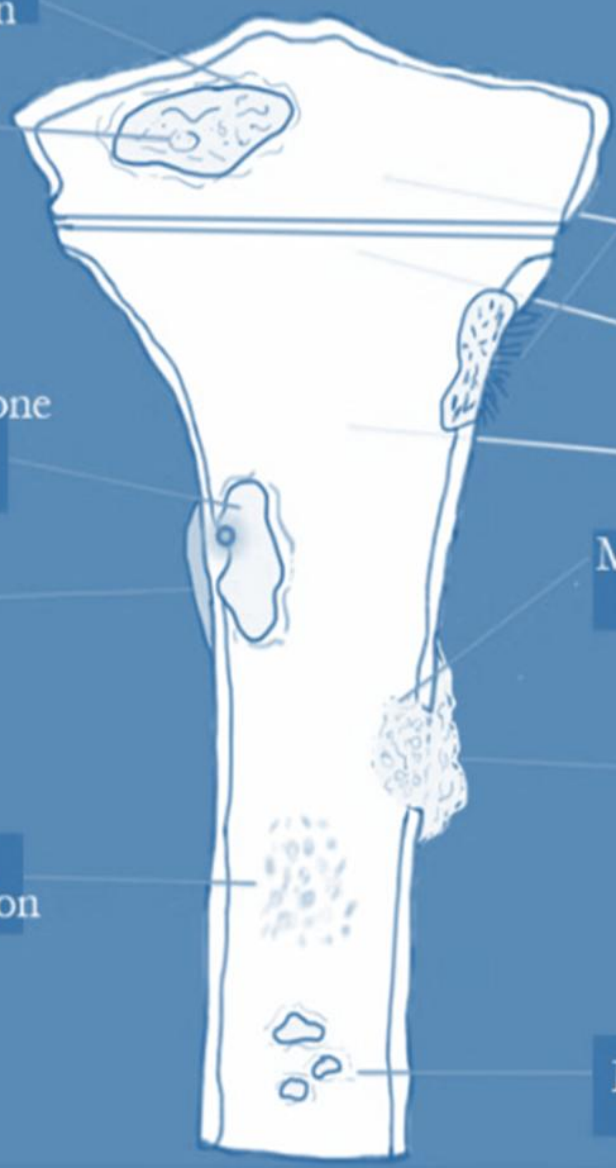
Moth Eaten Appearance

Solid Periosteal Rxn

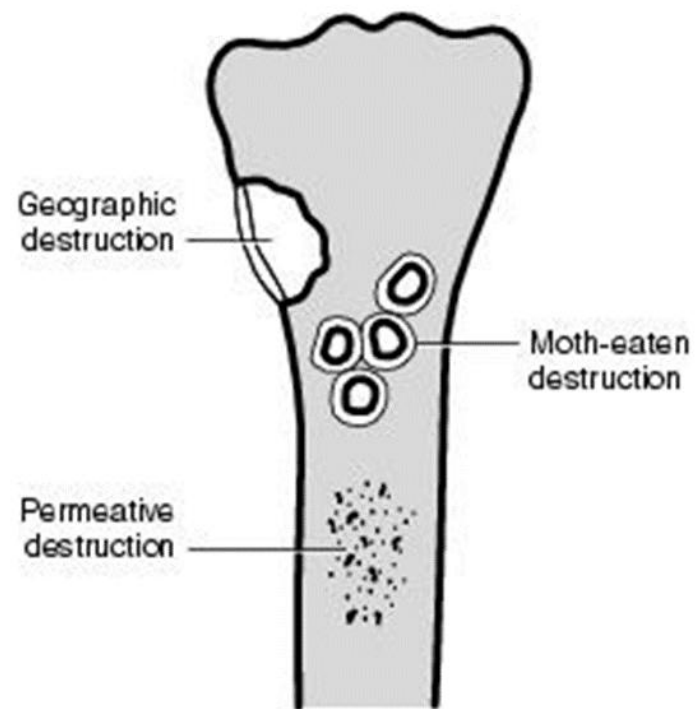
Soft Tissue Mass

Permeative
Bone Destruction

Multiplicity



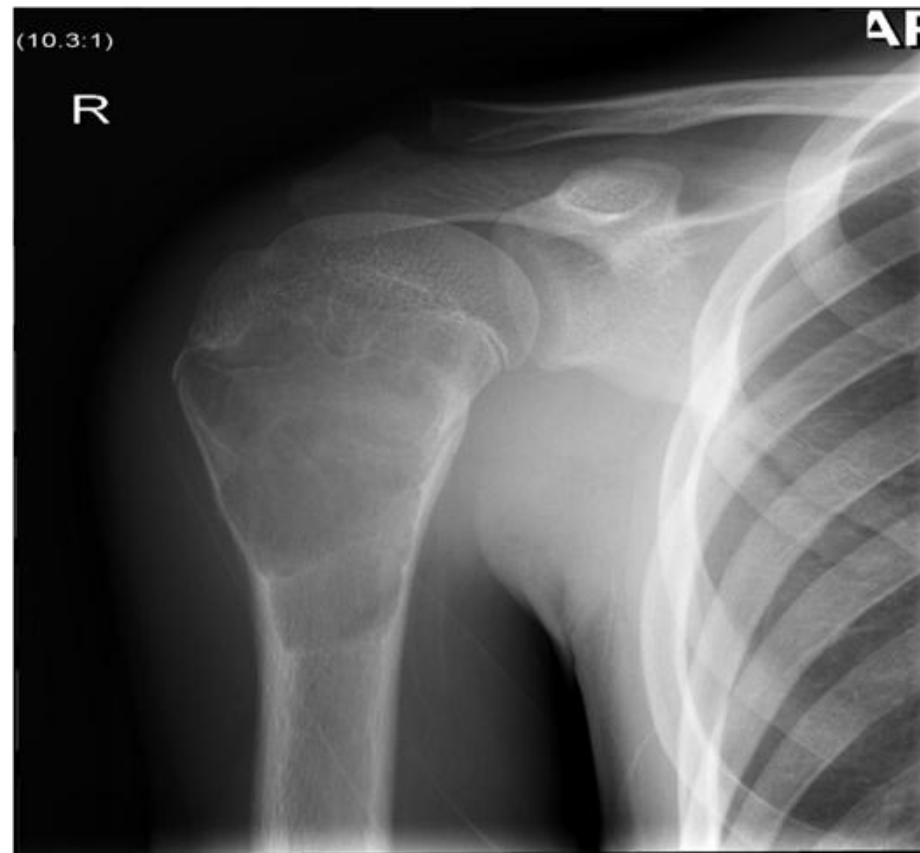
Types of bone destructions



Geographic lesion

- Slow growing
- Clearly demarcated borders
- Narrow zone of transmission
- +/- sclerotic rim
- Sclerotic margin=less aggressive
- Usually benign , exceptions
- (myeloma,mets,osteomyelitis)

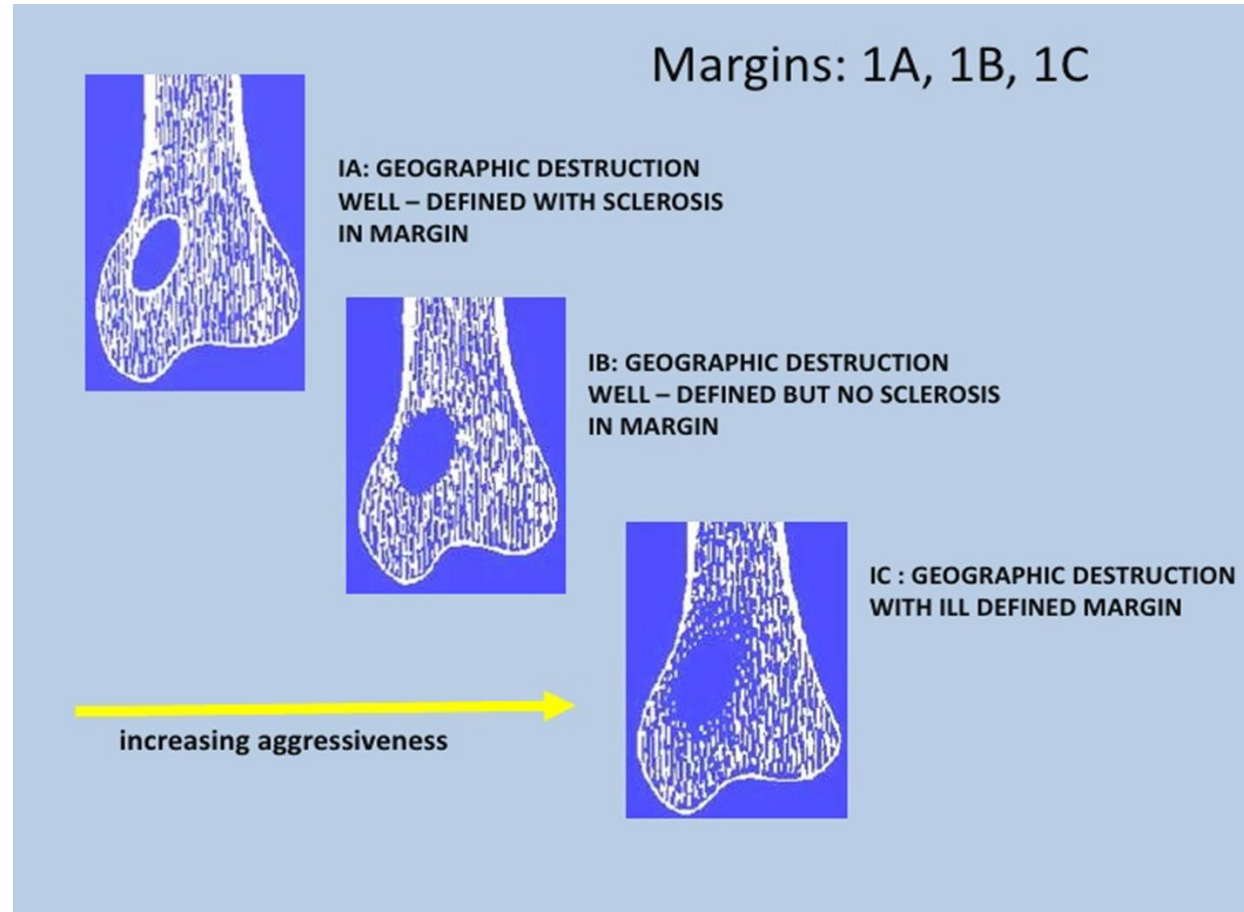
Geographic lesion



Geographic lesion

- Types of margins around lesionsactivity
 - IA (thick complete sclerotic margin)..... Inactive lesion
 - IB (thin and incomplete)..... Active lesion
 - IC (no sclerotic margin) ... Aggressive lesion

Geographic lesion



IA margin -NOF



IB margin - GCT



IC margin -GCT



Moth-eaten bone destruction

- More aggressive destruction
- Less well defined margins
- Larger zone of transmission
- Multiple punched out holes in bone
- e.g. : malignancy,OM,

Moth-eaten bone destruction



Permeative bone destruction

- Aggressive
- RAPID GROWTH POTENTIAL
- Poorly demarcation
- Cannot delineate where it begins and where it ends
- e.g. : ES,OS ,OM,osteoporosis



Visible tumor matrix

- Calcification....Cartilage
stippled,flocculent,rings and arcs
- Ossification....Osseous
solid, cloud-like ,ivory-like
- Must differentiate matrix from calcification due to necrotic tissue, callus or sclerotic response of non-neoplastic conditions .



Solid



Stippled



Cloud



Rings and Arcs



Ivory-Like



Flocculent

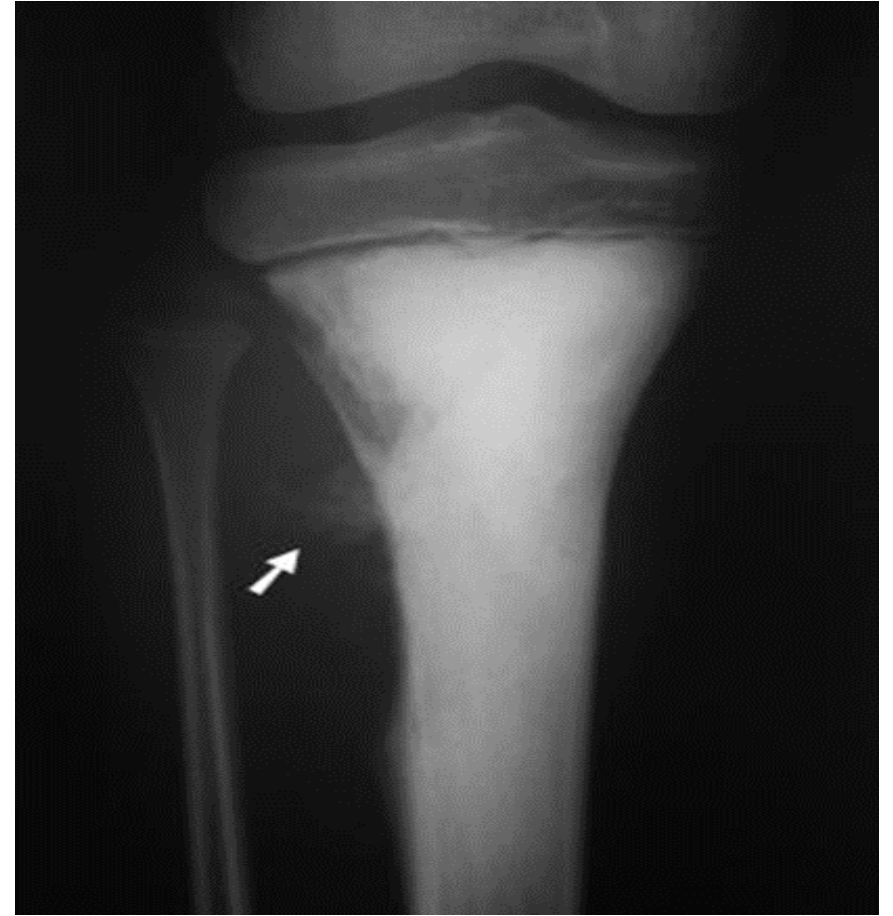
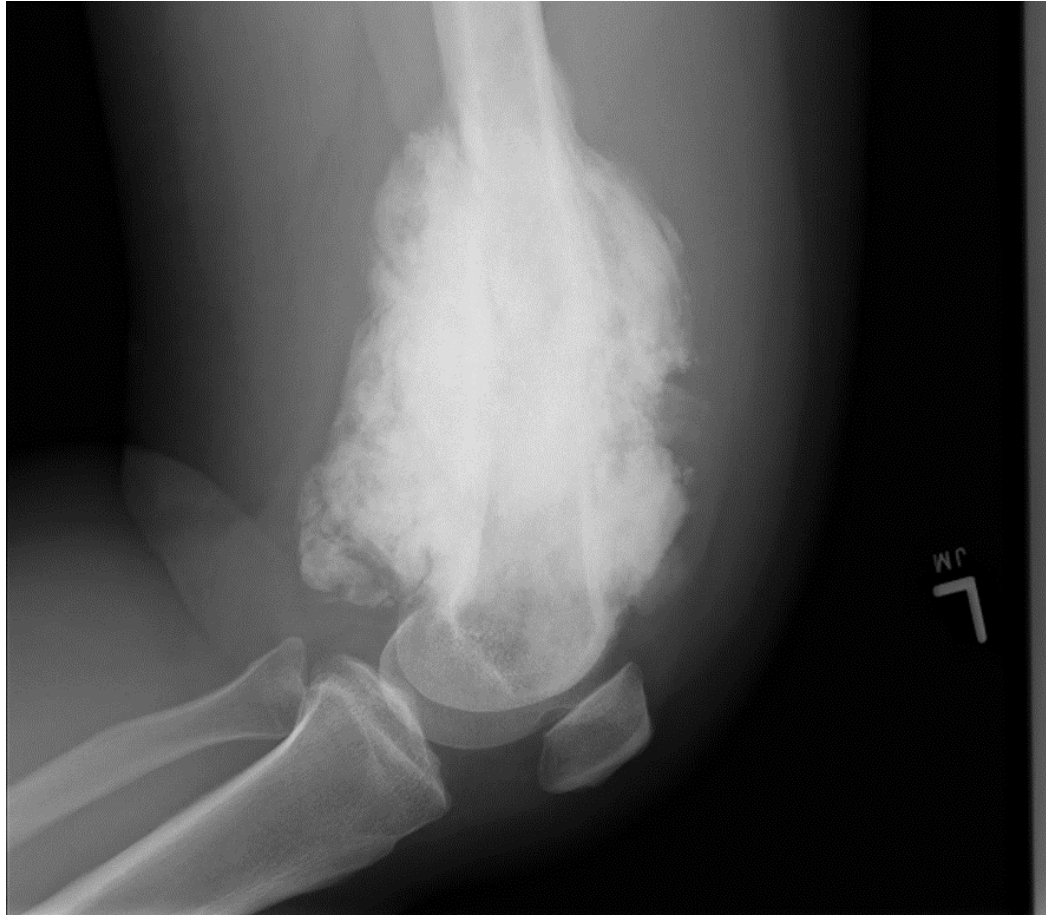
Calcifications

- Rings ,arcs ,flucculent,fleck like
 - Cartilage tumors
 - Cartilage Grows In lobular manner or ball like manner
 - Calcification occurs at periphery
 - If its complete circumferential >> RINGS
 - If partially around >>ARCS
-
- Enchondroma
 - Chondrosarcoma
 - Chondroblastoma
 - Chondromyxofibroma
 - osteochondroma



Ossification

- Cloud-like, fluffy, marble-like
 - Osteosarcomas
 - Osteoma
 - Osteoblastoma...rarely



Periostitis

- A periosteal reaction will occur whenever the periosteum is irritated.
- This may occur due to a malignant tumor, benign tumor, infection or trauma.
- There are two types of periosteal reaction, **Benign** or **Aggressive**.

Periostitis

- **Benign** processes such as a slow growing tumor will cause **thick, wavy, uniform** or dense periostitis. Since it is a low grade, chronic irritation, the periosteum has time to lay down thick new bone and remodel into a more normal appearing cortex.
- **Aggressive** processes such as a malignant tumor cause a periosteal reaction that is more acute and high-grade. The periosteum does not have time to consolidate. It appears **lamellated, “onion skinned”, amorphous or “sun-burst”**.

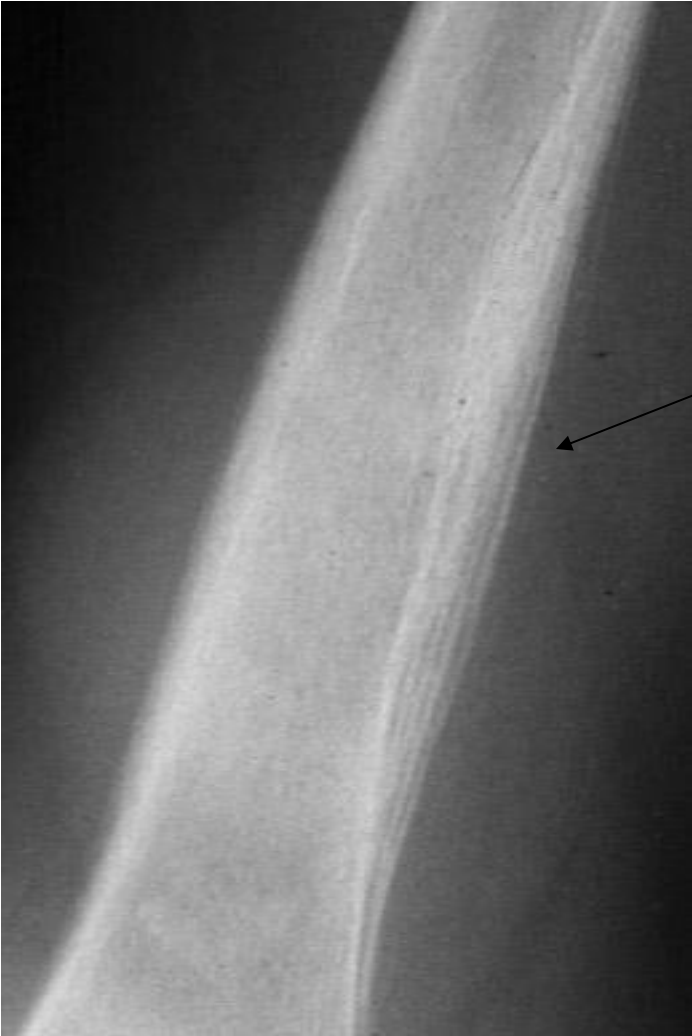
Periostitis

- When periostitis is seen the radiologist should therefore try to classify it into benign or aggressive.
- This classification also has its limitations.
- These limitations are similar to those seen with cortical destruction, such that benign processes such as **infection** or **eosinophilic granuloma** can cause an aggressive periostitis.

Periostitis

- However, seeing benign periostitis can be very helpful, because malignant lesions CAN NOT cause benign periostitis.

Periostitis



- Notice the “onion skin” appearance of this aggressive periostitis seen in Ewing’s sarcoma

Periostitis



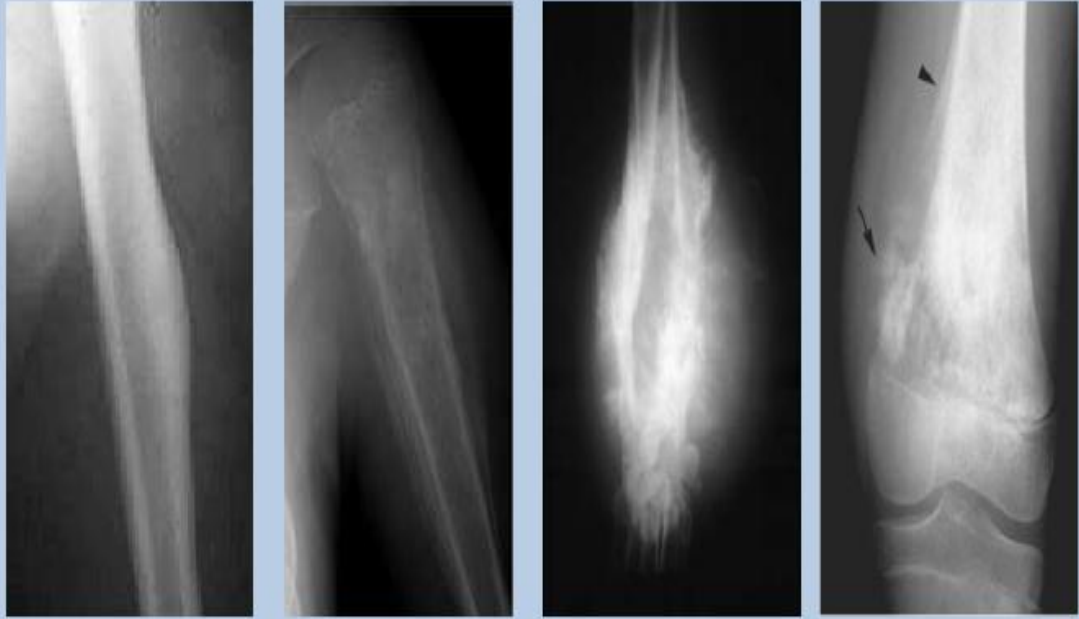
- Notice the “sunburst” pattern seen in this aggressive Osteosarcoma of the distal femur.

Periostitis



- Notice the “thick” periostitis seen in Eosinophilic Granuloma, a non-neoplastic proliferation of histiocytes. Remember, EG may also cause an aggressive periostitis

Periosteal Reactions



Solid

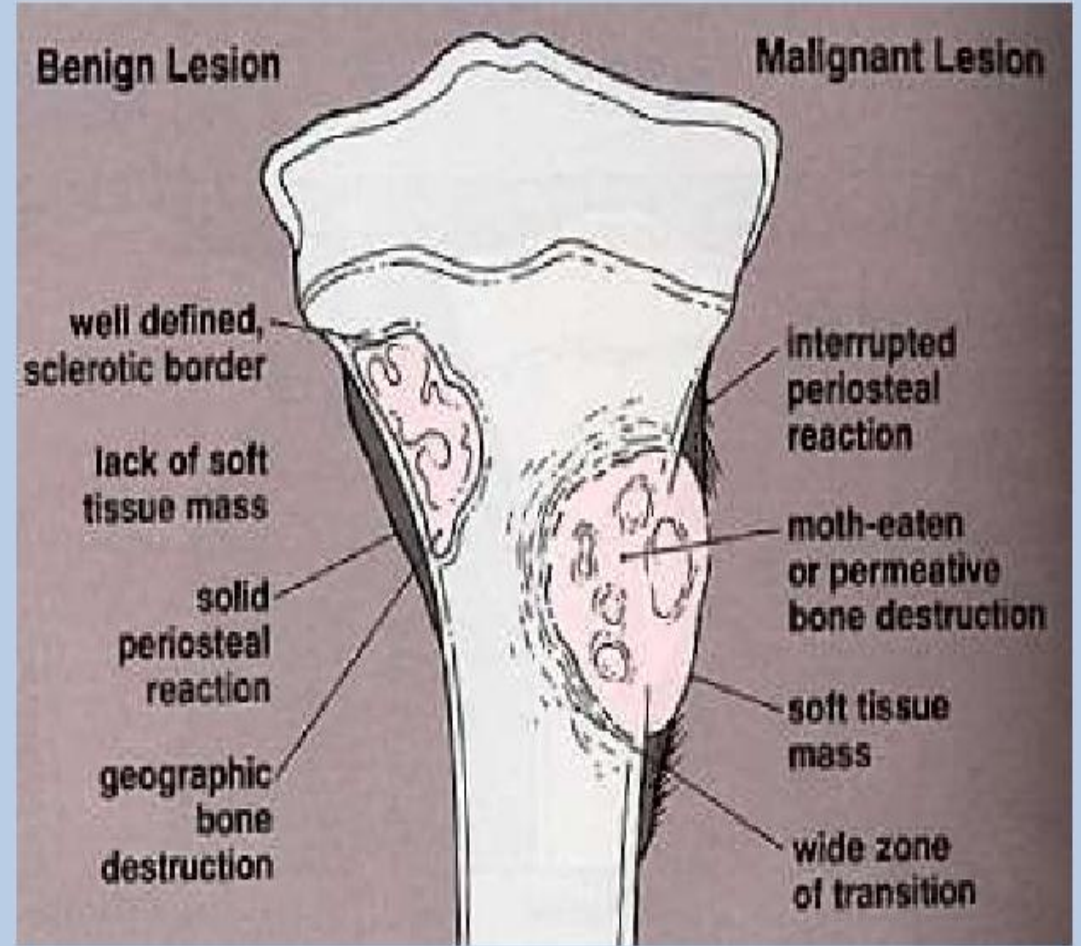
onion-peel

Sunburst

Codman's
triangle



Benign vs. Malignant



Orientation or Axis of lesion

- Lesions growing in the **long** axis of long bones are said to be **benign**.
- Lesions growing in a **circular** orientation are said to be **malignant**.
- **Poor** determinant of benign versus aggressive lesions.
- Too many exceptions to each to be useful.
- For example, Ewing's sarcoma, a malignant lesion, usually has its axis along the shaft of a long bone.

Zone of Transition

- Describes the border of the lesion with the normal bone.
- **Most reliable** plain film indicator for benign versus malignant lesions.
- **“Narrow”**, if it is so well defined that it can be drawn with a fine-point pen. A **benign** process should be considered as the most likely possibility.
- **“Wide”**, if it is imperceptible and can not be drawn at all. An aggressive process should be considered, although not necessarily a **malignant** lesion.

Zone of Transition



- **“Narrow”** Zone of Transition seen in a benign nonossifying fibroma. The margins of this lesion can be drawn with a fine-point pen.

Zone of Transition



- Permeative lesions seen in this primary lymphoma have a **“Wide”** Zone of Transition and are therefore aggressive. Notice also the pathologic fracture seen in the proximal humeral diaphysis

Summary of Radiographic Findings

- Cortical Destruction is less helpful than Periostitis in assessing whether a lesion is benign or aggressive on plain film.
- Axis of a lesion is not helpful.
- Zone of Transition is the most reliable plain film indicator of benign versus aggressive processes.
- If a lesion is aggressive, it is not necessarily malignant!

Summary of Radiographic Findings

- Types of bone destructions
 - Geographic
 - Moth-eaten bone destruction
 - Permeative bone destruction
- Tumor matrix
- periosteal reaction
- Orientation or Axis of lesion
- Zone of transition

CT scan

- Provides diagnostic information of bones and soft tissue in another plane.
- We use it for smaller lesions involving the cortex of the bone
- Mainstay for safe and accurate biopsy procedures
- Angiography
- For staging

MRI

- Imaging procedure of choice for determining the extent of a lesion, both in the skeleton and soft tissues.
- T1 weighted images best for looking at extent of marrow involvement and T2 more useful for evaluating cortical bone and soft tissue extent (NB - CT better for showing areas of calcification / ossification)
Best technique to identify hemorrhage/oedema/inflammation- eg prior biopsy
Oedema usually surrounds malignant lesions & is unusual around benign tumors
- If resection of a tumor is planned, MRI should be performed.

Bone isotope scan

- Diphosphonates labelled with Technetium 99 usually used in dose of 500 - 600 mBq
- Assess the degree of osteoblastic activity of a lesion
- It is an excellent modality to search skip lesions and occult bone involvement (staging)
- Gallium 67 has also been utilized

Lab studies

- FBC (leukaemic cells etc)
- ESR (often elevated)
- Biochemistry (Ca⁺⁺, PO₄, liver enzymes and Alkaline Phosphatase) -> mets
- Acid Phosphatase (prostate and increased with metastatic deposits)
- Thyroid function tests
- Parathyroid hormone level
- PSA
- Serum Protein Electrophoresis (Myeloma)
- Urinalysis

Tumors biopsy



Principles of bone Tumors biopsy

- Should know probable diagnosis and stage of tumor before biopsy as it is the last step in the staging of the patient
- Performed by the surgeon who will perform the definitive surgery (? biopsy -> frozen section -> definitive surgery during the same anesthetic)
- Biopsy tract orientation & location is critical - will need to be included in the definitive surgery if lesion is malignant.
- Meticulous hemostasis to avoid tracking hematomas
- Send samples for microbiological analysis
- Always culture your tumor and biopsy your infection

Open Biopsy

- Aim for excisional biopsy when possible esp. in benign lesions
Incisional biopsy preferable in malignant lesions
After consultation with the pathologist and radiologist
- Longitudinal incision
- Sharp dissection should proceed directly to the tumor, *through muscle* not between muscle planes
- Uninvolved anatomic compartments should not be exposed
- Avoid all major neurovascular structures to prevent contamination

Open Biopsy

- Excise block of reactive tissue, pseudo capsule, capsule, and block of tumor -> formalin +/- frozen section
- Windows in bone should be as small as possible and oval to avoid stress risers and pathological fracture
- Release tourniquet prior to closure -> hemostasis
- Close with a subcut. stitch
- Drains should come out through the wound or near to the wound in the same plane
- If proceed following biopsy -> new instruments and drapes to stop seeding

Needle Biopsy

- As for open biopsy
- Place the biopsy tract where it can be excised
- **Fine needle biopsy:**
 - relies on cytological interpretation by an experienced pathologist
 - accuracy = 65 to 95% (determined by the adequacy of the collected tissue sample)
 - does not allow for immunohistochemical analysis
- **Core needle biopsy:**
 - uses trocar cannula system, with a outer sleeve which closes over the trocar, capturing the sample of tissue
 - provides more tissue than fine needle and allows for immuno-histochemical analysis
 - accuracy = 75 to 95%
- Disadvantage of needle biopsy = tissue obtained may be from necrotic portion of tumor and therefore not suitable for diagnosis, or tissue may be reactive in nature and not representative of actual tumor. Frozen section may thus be beneficial.



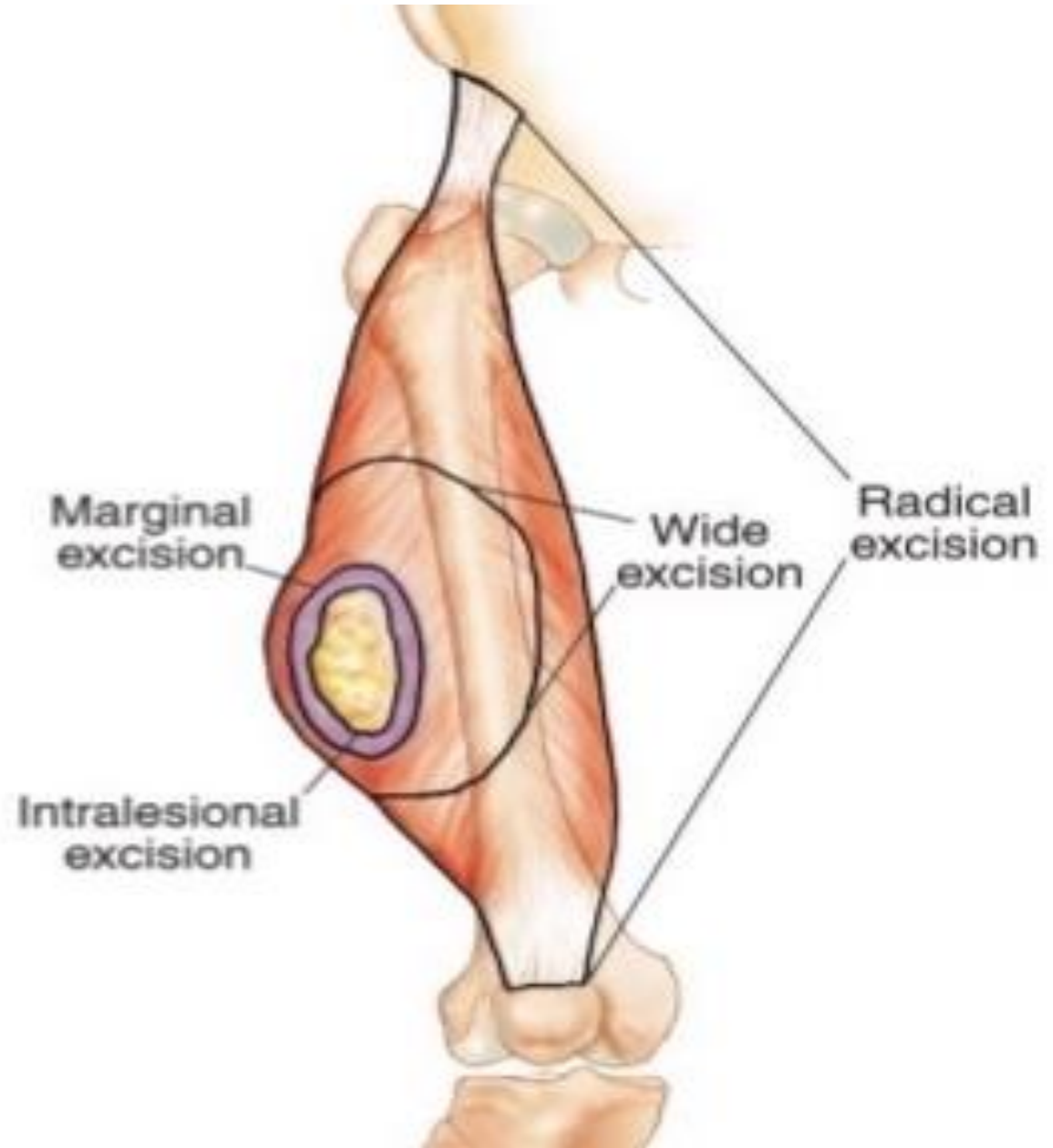
Surgical Margins

- ***Intra-lesional***
 - through the tumour
 - leaves macroscopic tumour
 - not therapeutic
- ***Marginal***
 - through pseudo-capsule of tumour / *reactive zone* (contains inflammatory cells, oedema, fibrous tissue, satellites of tumour cells)
 - controls non-invasive benign tumours
 - recurrence of malignant tumours = 25-50%

Surgical Margins

- **Wide**
 - around reactive zone, leaving a cuff of normal tissue
 - skip lesions left
 - recurrence of malignant tumours = < 10%
- **Radical**
 - removal of entire compartment or compartments
 - distant metastases left
- **Amputation**
 - should be thought of as a form of reconstruction where surgical control of the tumour precludes useful function

Surgical Margins



Staging system

- **Staging Musculo-skeletal Neoplasms ([Enneking](#)):**
 - Histological grade (G)
 - Site (T)
 - Metastases (M)

ENNEKING'S SURGICAL STAGES

STAGE	GRADE	SITE	METASTASES
1A 1B	Low(G1) Low(G1)	Intracompartmental(T1) Extracompartmental(T2)	None(M0) None(M0)
2A 2B	High(G2) High(G2)	Intracompartmental(T1) Extracompartmental(T2)	None(M0) None(M0)
3	Low(G1) or High(G2)	Intracompartmental(T1) or Extracompartmental(T2)	Yes (M1)

Grading

- G0 Histologically benign (well differentiated and low cell to matrix ratio)
- G1 Low grade malignant (few mitoses, moderate differentiation and local spread only); Have low risk of metastases
- G2 High grade malignancy (frequent mitoses, poorly differentiated); High risk of metastases

Site (anatomic setting of the lesion)

- T0 Intracapsular
- T1 Intracompartmental (eg cortical bone, joint capsule or fascia)
- T2 Extracompartmental (spreads beyond 'fascial' plane without longitudinal containment)

Metastasis (nodal or blood borne tumour spread)

- M0 No evidence of regional or distant metastases
- M1 Regional or distant metastases evident

Take Home Messages

- Orthopedic oncology is a unique subspecialty within orthopedics
- Tumors of musculoskeletal system are an extremely heterogeneous group of neoplasms arise from the embryonic mesoderm
- No clear risk factors that causes bone cancer
- Evaluation of Musculoskeletal tumors begins by history , physical examination and X-Rays
- Give you an idea of the diagnosis about 80%
- The biopsy has principles most be followed
- Always culture your tumor and biopsy your infection

