Osteosarcoma and its Variants

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Osteosarcoma

- Definitions:
  - A mesenchymal malignancy (malignant spindle cells) that differentiates to produce osteoid/immature bone
  - Considered an osteosarcoma no matter how much osteoid is produced
  - Second most common primary malignant tumor of bone (first most common=multiple myeloma)
  - 15% of all biopsied primary bone tumors

Osteosarcoma

- Definitions:
  - Primary Osteosarcoma: arises from the bone in the absence of a benign precursor lesion or treatment
  - Secondary Osteosarcoma: arises from a precursor lesion to one that is metastatic from a primary osteosarcoma
  - Synchronous Osteosarcoma: Lesions that affect multiple bones discovered within 6 mos of each other
  - Metachronous Osteosarcoma: Lesions involving multiple bones discovered more than 6 mos apart

Osteosarcoma

- Definitions:
  - Intramedullary Osteosarcoma: Lesion arising within the medullary space of the bone (most common type)
  - Juxtacortical Osteosarcoma: Lesion arising on the surface of the bone in apposition to the cortex
  - Intracortical Osteosarcoma: Lesion arising from the cortex of the bone

Osteosarcoma Classification

- Intramedullary (75%)
  - Conventional
    - Osteoblastic (82%)
      - Mixed and Sclerosing
    - Chondroblastic (5%)
    - Fibroblastic (3-4%)
    - MFH-like (3-4%)
    - Osteoblastoma-like (.5%)
    - Giant Cell-rich (.5%)
    - Small-cell (1%)
    - Epithelioid (.5%)
  - Telangiectatic (3%)
  - Well-differentiated (low grade intraosseous; 4%-5%)
- Juxtacortical/Surface (7-10%)
  - Parosteal
  - Periosteal
  - High-grade surface
- Intracortical (.2%)
- Secondary (older population)
  - Pagets (67-90%); Post RT (6-22%); Bone infarct; Fibrous dysplasia; Metallic implant; Osteomyelitis
- OS with specific syndromes
  - Familial; Retinoblastoma; Rothmund-Thomson Syndrome; Multifocal; OI

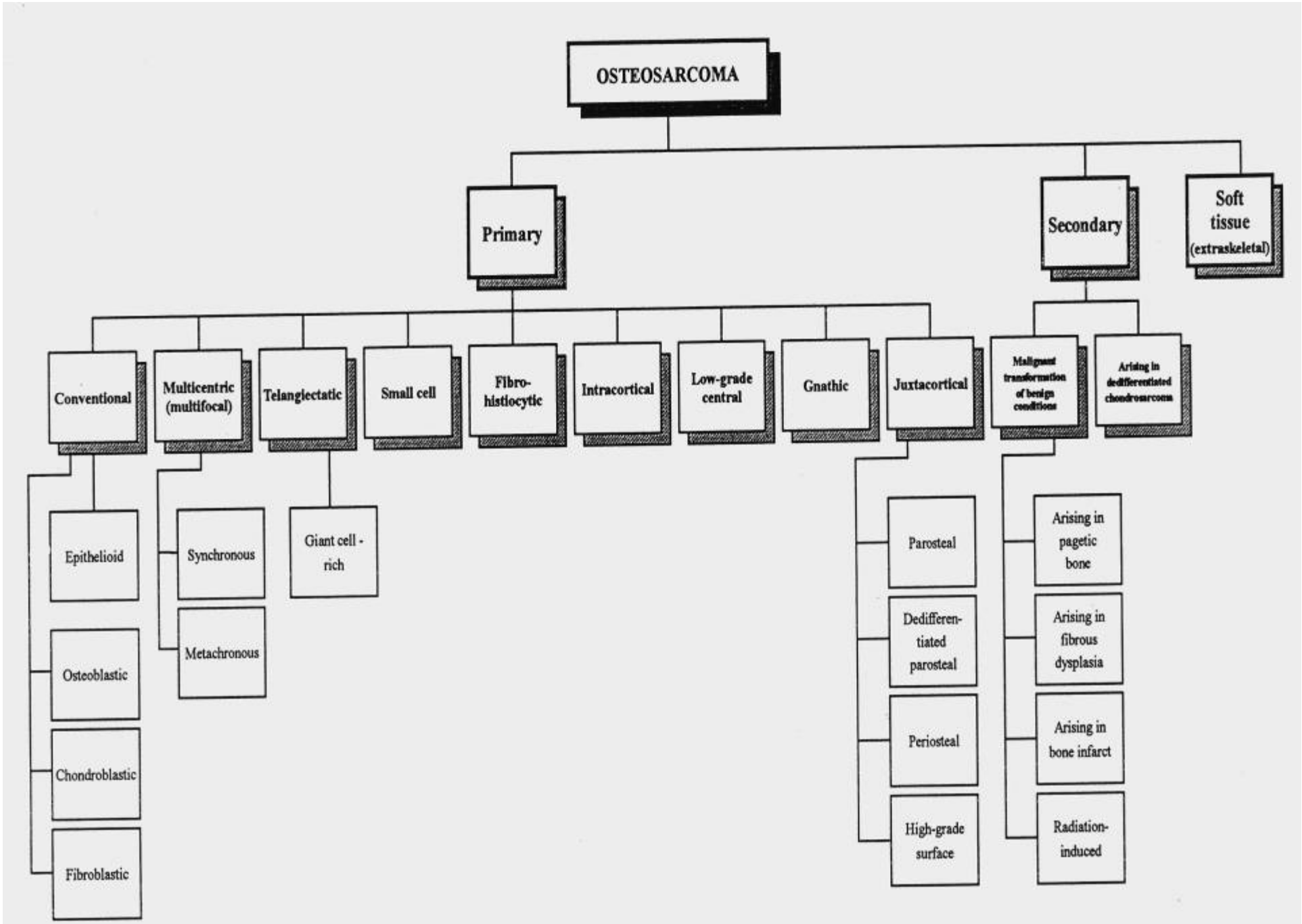
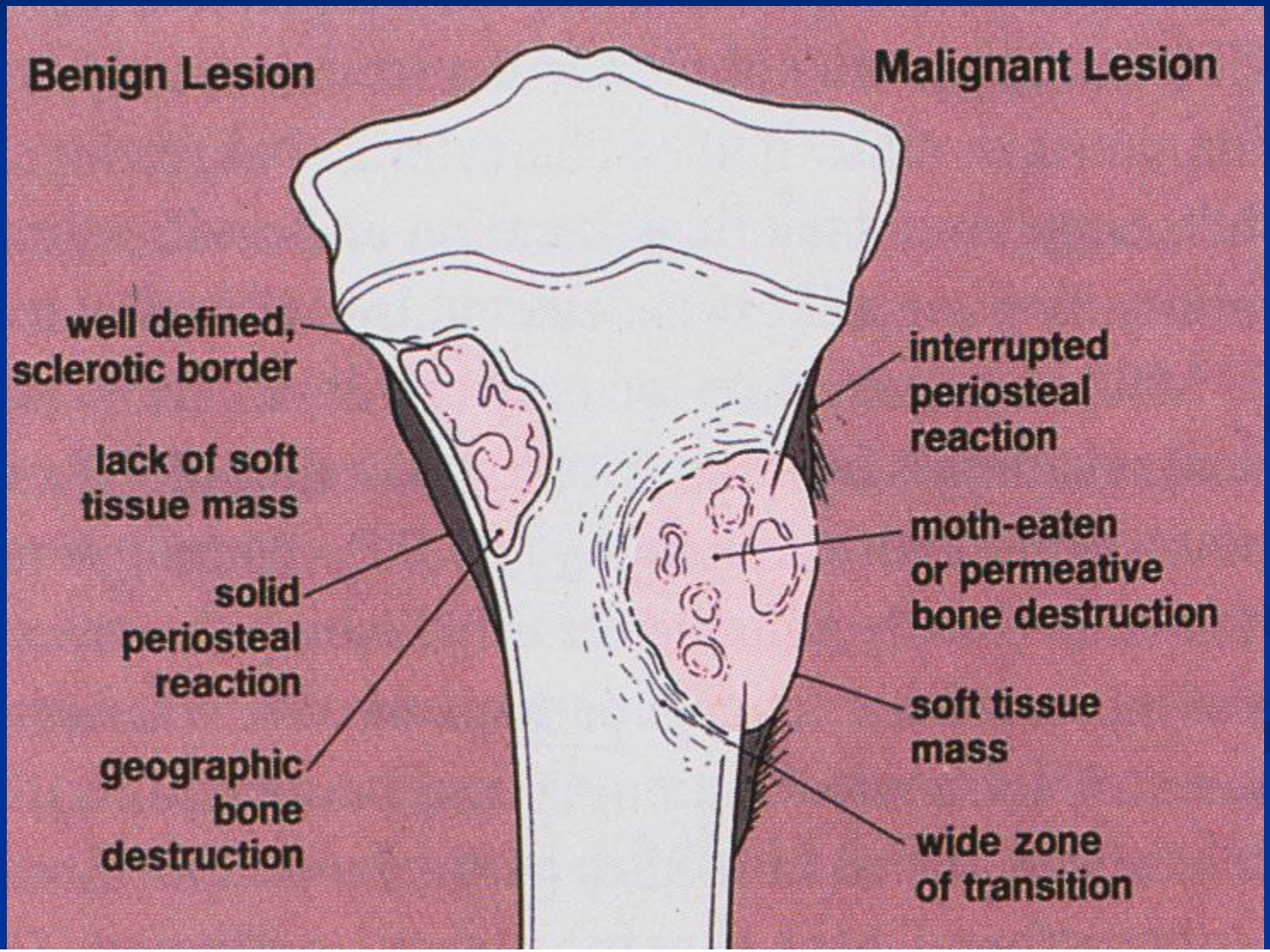


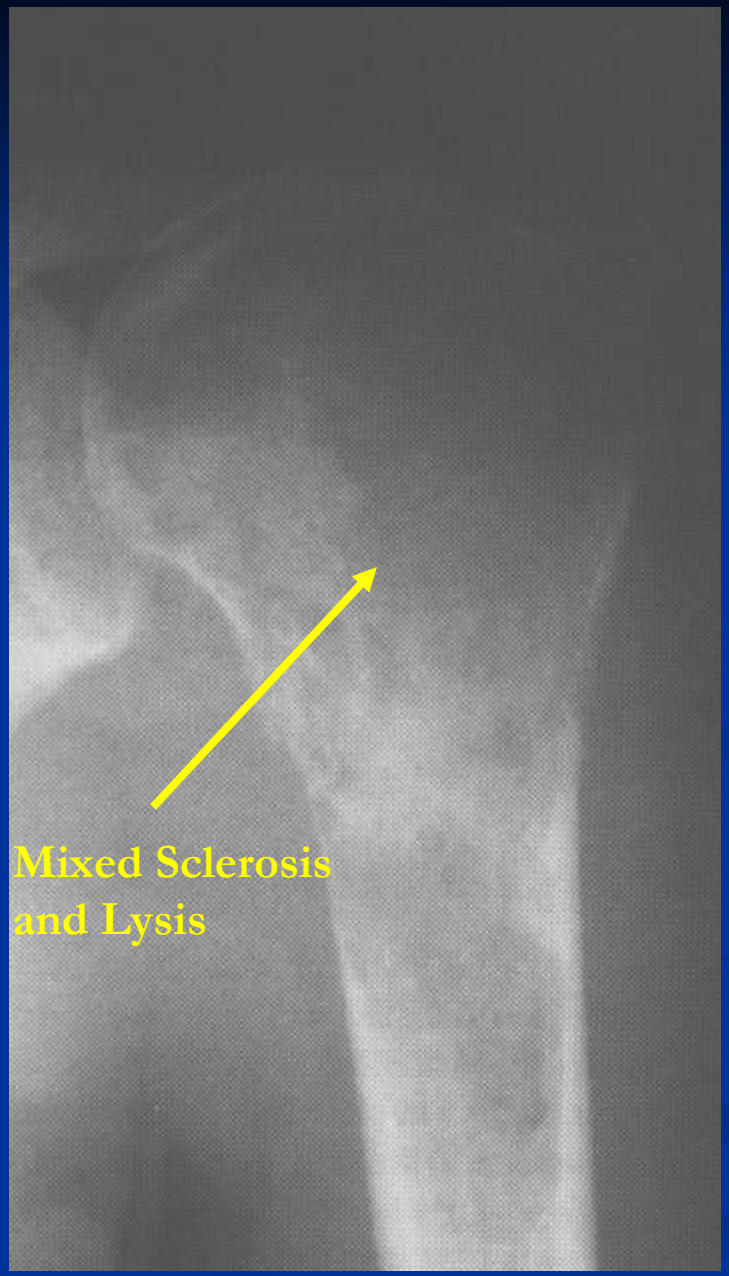
FIG. 55. Osteosarcoma and its subtypes.

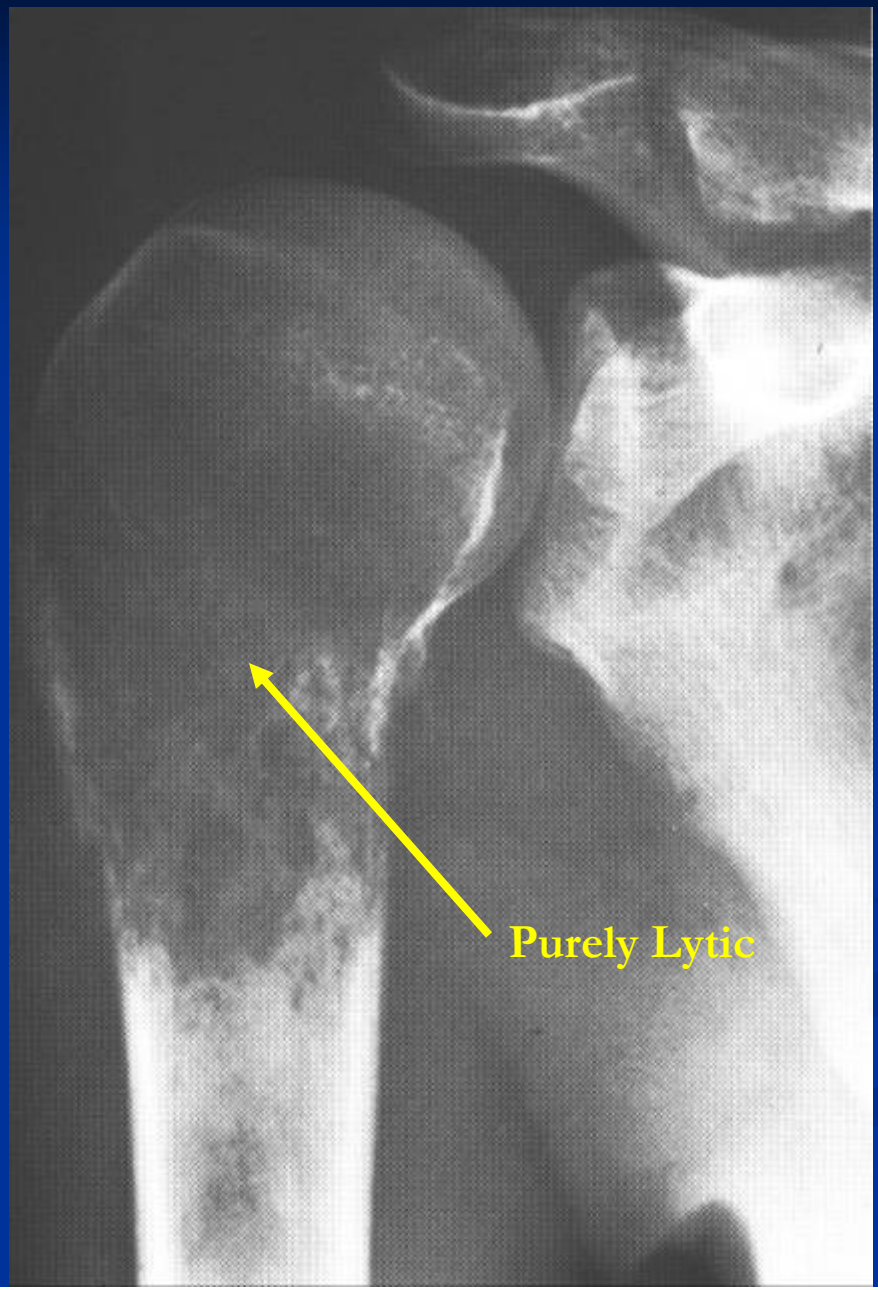
General Radiology

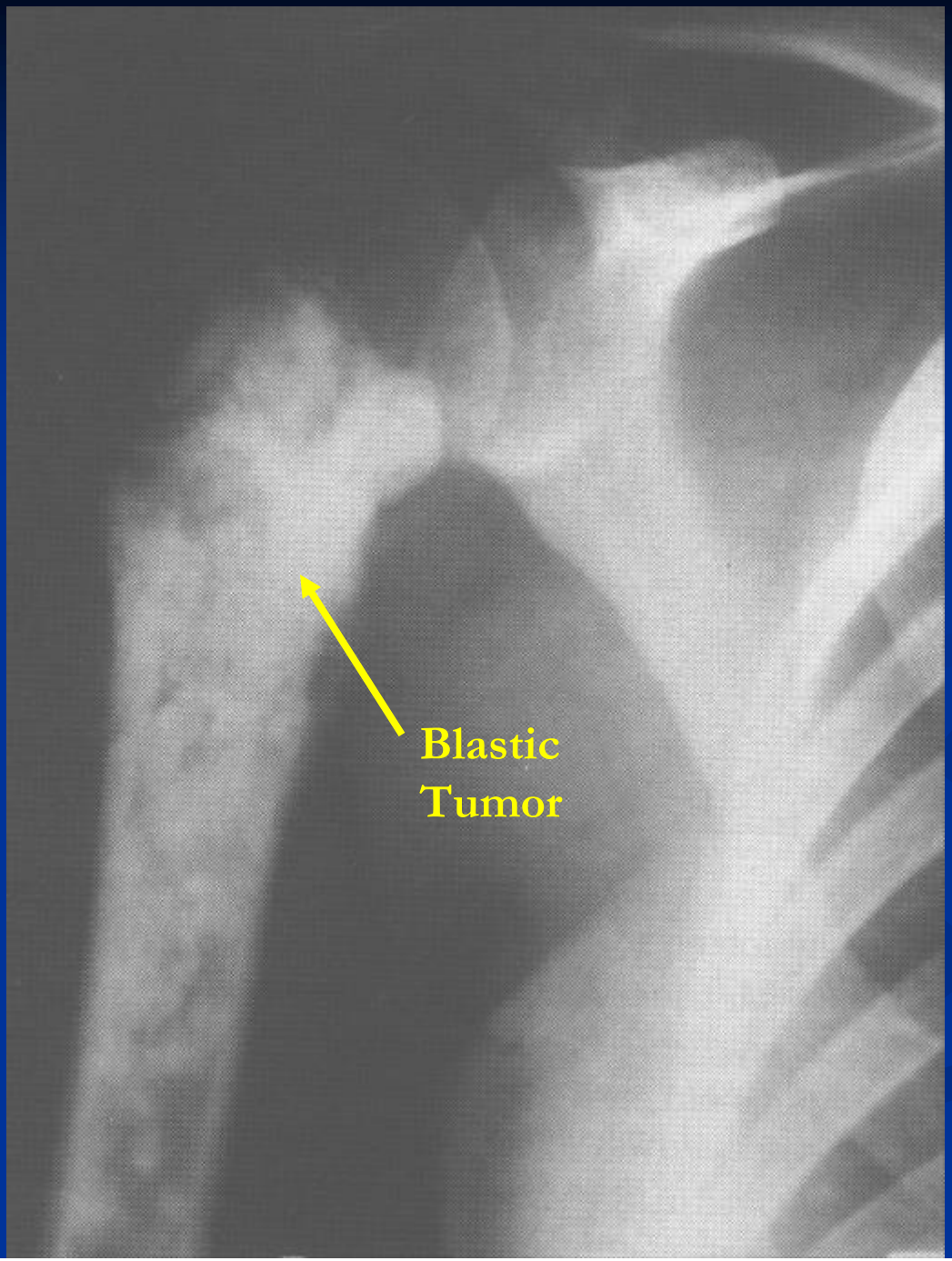


General Radiology: Plain Radiographic Presentation

- Osteoid/Ossification production on X-Ray
- Mixed Sclerotic and Lytic Lesion—Most common radiographic presentation
- Purely Lytic
- Purely Blastic

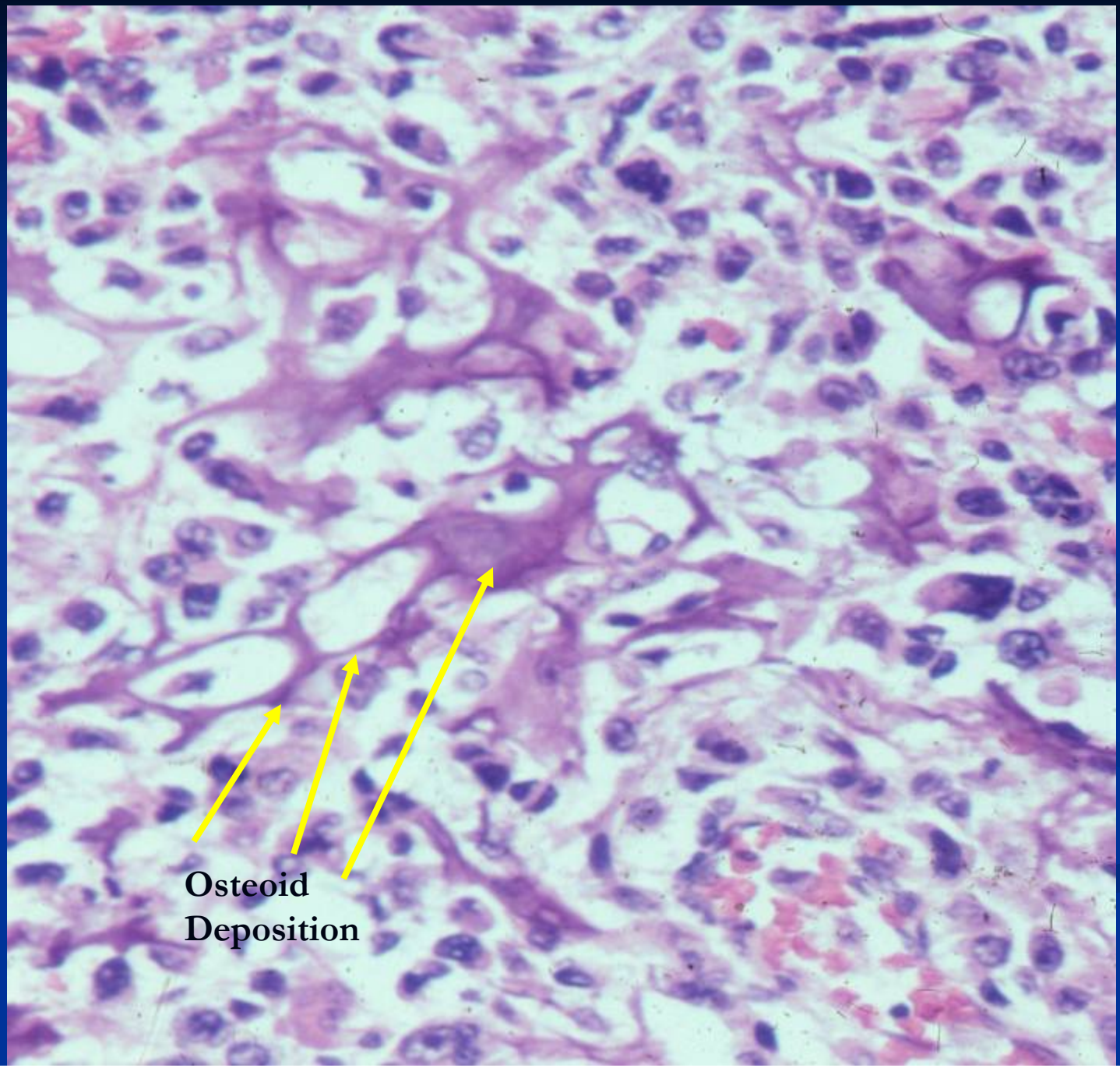

Mixed Sclerosis
and Lysis


Purely Lytic


Blastic
Tumor

Osteosarcoma

- General Pathology:
  - Osteoid and/or immature bone production by tumor cells
  - Malignant stromal cells
  - Graded on degree of anaplasia I-IV


Osteoid
Deposition

Osteosarcoma

- Primary, High Grade, Intramedullary (Conventional)
  - About 75% of all osteosarcomas
  - Ages: 15-25 years (rare <6y or >60y)
  - Sex: Male>Female 1.5-2:1
  - Sites:
    - Long Bones: 70%-80%
      - Distal Femur (40%; about twice as common as proximal tibia)
      - Proximal Tibia (20%)
      - Proximal Humerus (10-15%)
    - Axial Skeleton
      - Pelvis
      - Jaw

Osteosarcoma

- Sites:
  - Metaphysis: 90%
  - Diaphysis: 8-10%

Telangiectatic Osteosarcoma

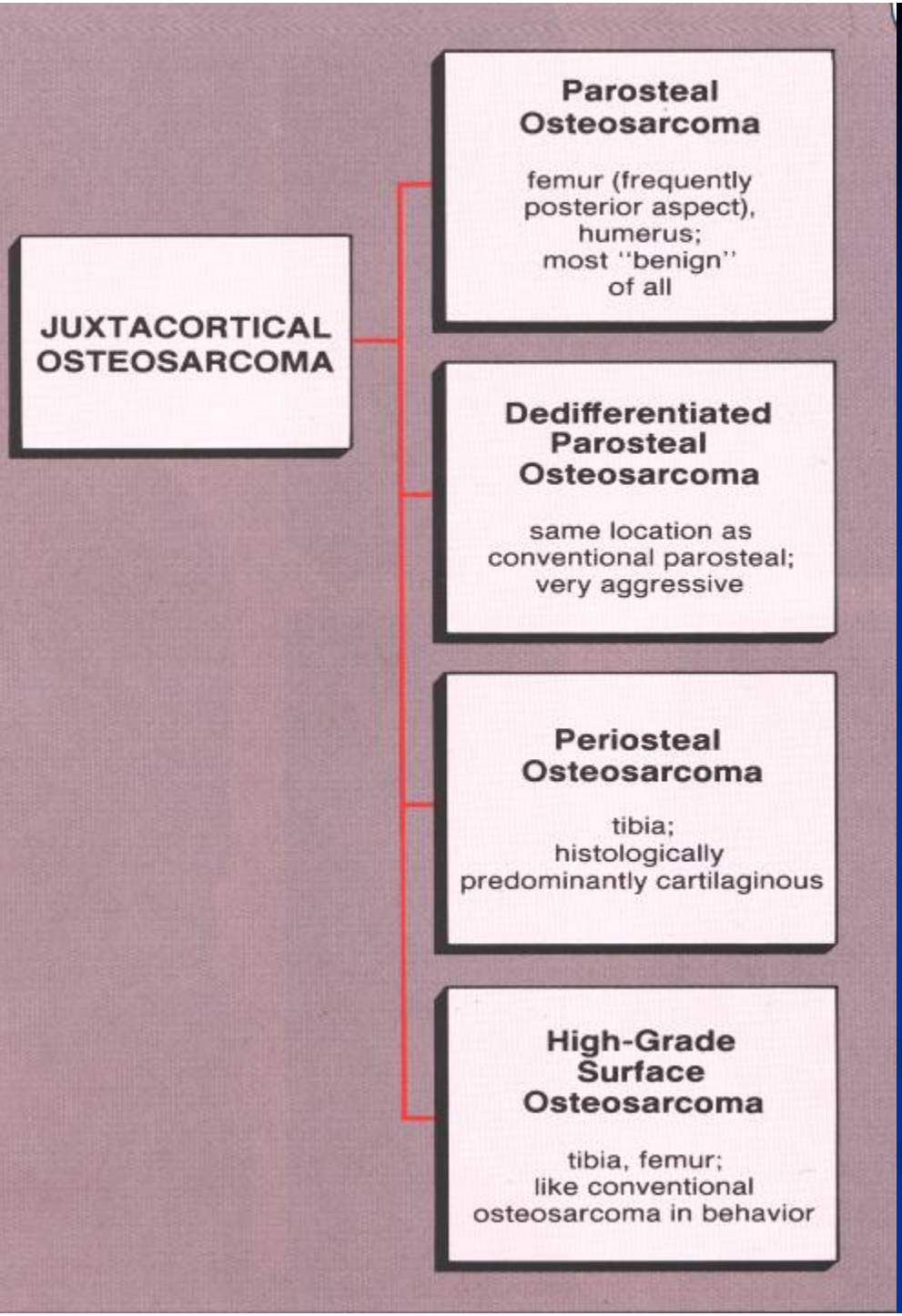
- Tumor largely composed of cystic cavities containing necrosis and hemorrhage
- ABC- like which can lead to a misdiagnosis on X-rays
- Sites: Similar to conventional
  - Distal femur, proximal tibia, proximal humerus
  - Metaphyseal (90%), diaphyseal (10%)

Telangiectatic Osteosarcoma

- Radiology:
  - Osteolytic and expansile on X-ray
  - Small areas of osteoid (more easily detected with CT)
  - Pathologic fracture (25%-30%)
  - MRI/CT: Fluid-fluid levels; soft tissue mass
  - Bone scan: Donut sign

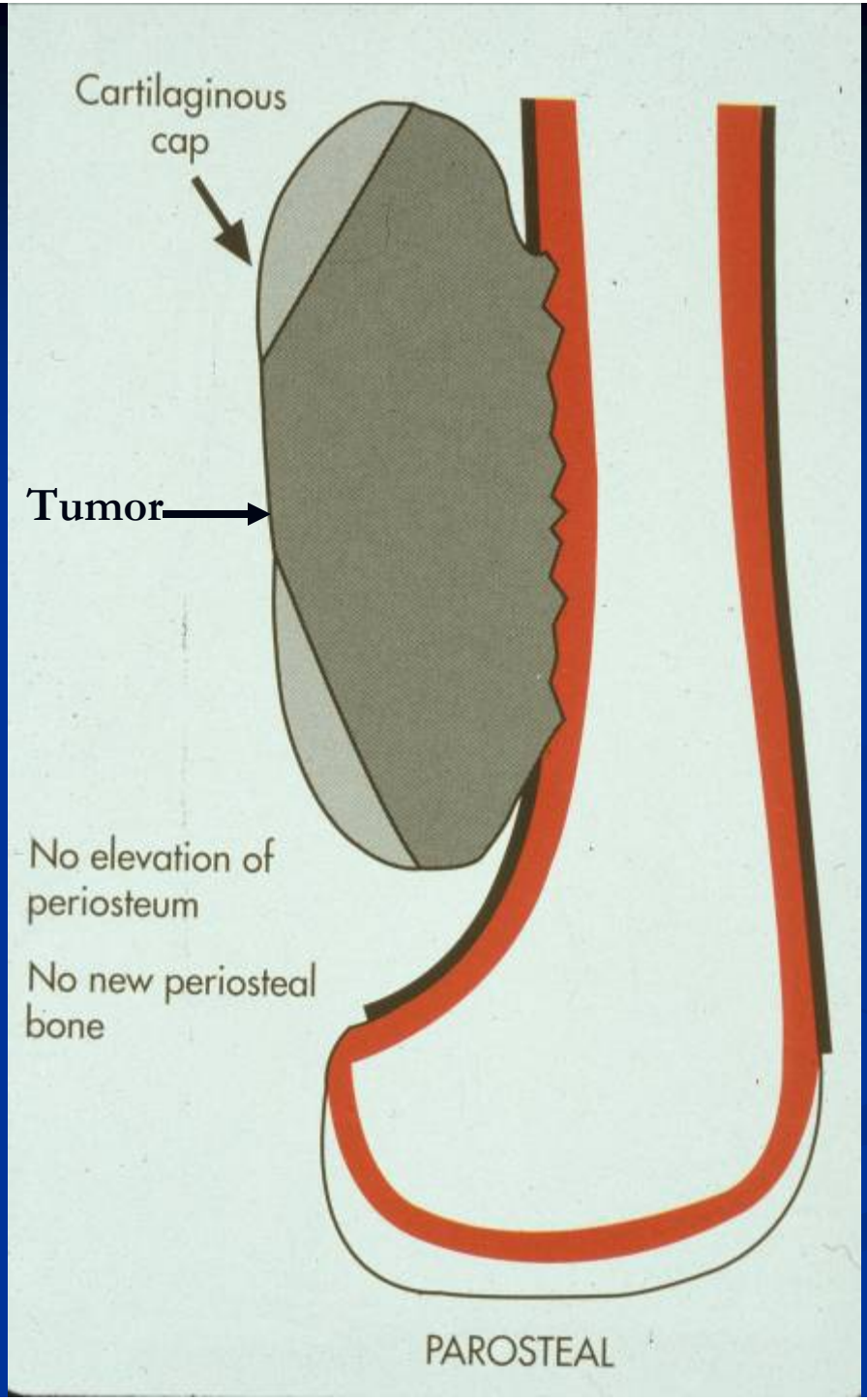
Juxtacortical Osteosarcoma

- Parosteal Osteosarcoma (65%)
- Periosteal Osteosarcoma (25%)
- High Grade Surface (10%)


JUXTACORTICAL OSTEOSARCOMA
Parosteal Osteosarcoma
femur (frequently posterior aspect), humerus; most "benign" of all
Dedifferentiated Parosteal Osteosarcoma
same location as conventional parosteal; very aggressive
Periosteal Osteosarcoma
tibia; histologically predominantly cartilaginous
High-Grade Surface Osteosarcoma
tibia, femur; like conventional osteosarcoma in behavior

Parosteal Osteosarcoma

- Origin: Arises from outer layer of periosteum
- Usually a low grade tumor with fibroblastic stroma and osteoid/woven bone
- Age: 20-30 yrs; usually about a decade older than conventional osteosarcoma
- Location:
  - Posterior distal femur metaphysis (65%)
  - Proximal humerus (15%); Tibia (10%); Fibula (3%)
- Clinical: painless mass in posterior distal thigh; may be present for several yrs; decreased ROM of adjacent joint
- Sex: Female>Male 2:1

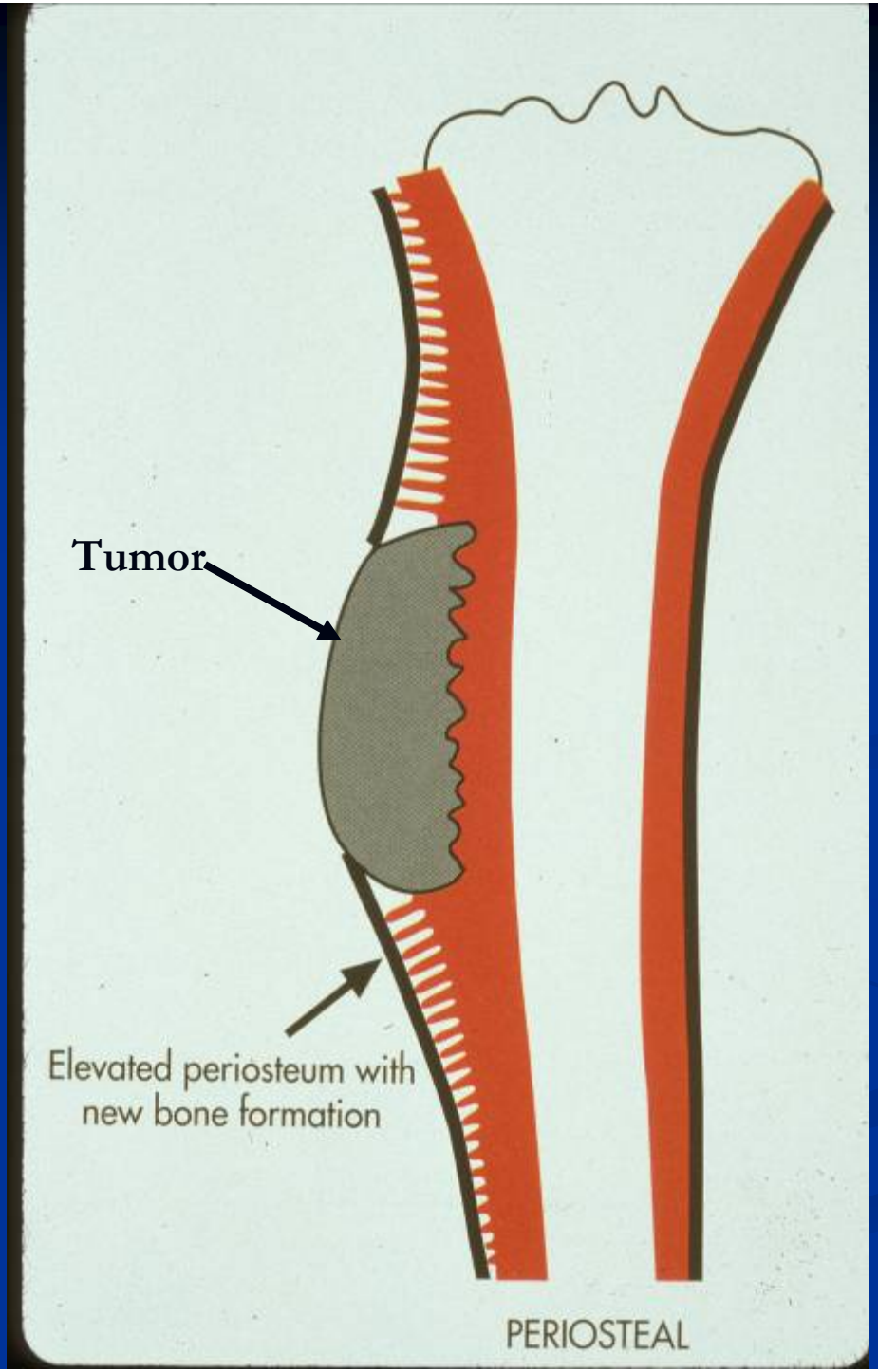

Cartilaginous cap
Tumor
No elevation of periosteum
No new periosteal bone
PAROSTEAL

Parosteal Osteosarcoma

- Radiology:
  - XR:
    - Lobulated and ossified exophytic mass (cauliflower-like) adjacent to the cortex with a lucent cleavage plane between lesion and the cortex
    - Radiodense centrally
    - Cortical thickening
    - Large tumors encircle the bone
    - Growth may obliterate cleavage plane between lesion and cortex and will appear to have broad attachment
    - Invasion of the medullary canal with long standing disease

Periosteal Osteosarcoma

- Low to intermediate grade bone forming sarcoma with predominant chondroblastic differentiation tumor (>90% of tumor); <2% of osteosarcomas
- Origin: Arises from the inner layer of the periosteum
- Age: 10-20 yrs; similar to conventional osteosarcoma
- Sex: Slight male predominance
- Location: Diaphysis of femur and tibia (>85%); ulna and humerus (10%)


Tumor
Elevated periosteum with new bone formation
PERIOSTEAL

Periosteal Osteosarcoma

- Radiology:
  - XR:
    - Diaphyseal lesion on surface of bone; medullary canal is uninvolved
    - Saucerized cortex with chondroblastic soft tissue mass
    - Cortical thickening at margins of erosion (40%)
    - May have Codman's triangle
    - Spiculated or sunburst periosteal reaction (elevates the periosteum)
    - Partial matrix mineralization may be seen consistent with chondroblastic nature
    - Rarely, intramedullary invasion

High Grade Surface Osteosarcoma

- High grade osteosarcoma that develops on the surface of the bone without any medullary involvement; very rare (<1% of osteosarcomas)
- Histology is the same as a conventional osteosarcoma with the same potential for mets
- Age: 2nd decade
- Sites: Femur (45%); Humerus (26%); Fibula (10%); arises usually on the metaphyseal surface

High Grade Surface Osteosarcoma

- Radiology:
  - Appearance similar to periosteal osteosarcoma but matrix mineralization is similar to conventional osteosarcoma with cloudlike opacities
  - Broad based lesion arising on surface
  - Codman's triangle; periosteal new bone
  - Cortical erosion/destruction but medullary cavity usually uninvolved

Low Grade Intramedullary Osteosarcoma

- Intramedullary low grade fibroblastic osteoid producing sarcoma characterized by benign cytologic features of spindle cells and maturity of tumor bone
- 1% of all osteosarcomas
- Age: peak— 3rd decade; individual cases in 2nd decade and 50s
- Sites: Metaphysis of femur and tibia most common

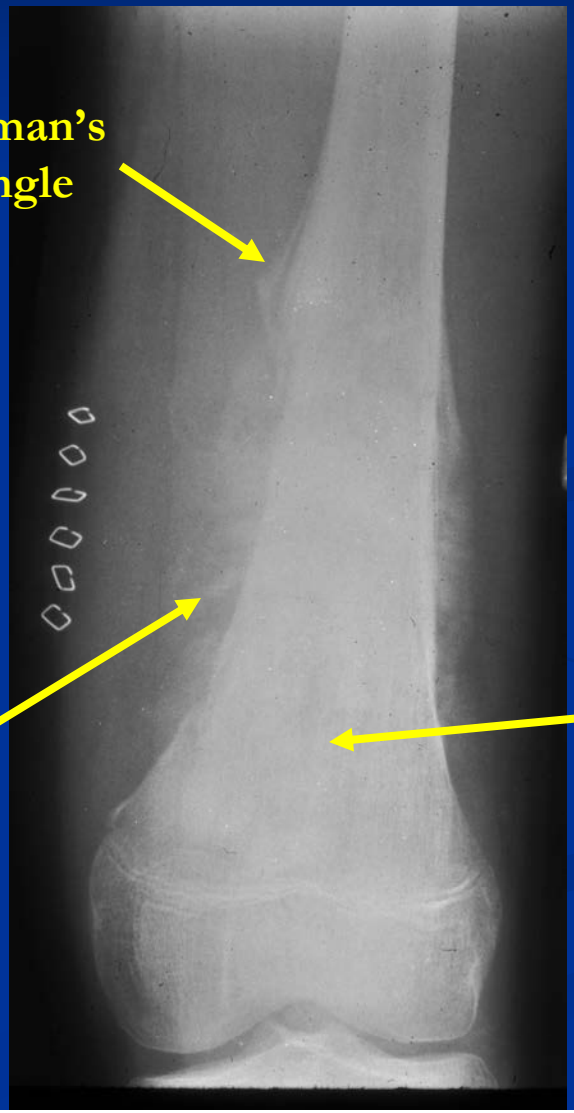
Low Grade Intramedullary

- Radiology:
  - XR:
    - Meta-epiphyseal
    - Central ossification/sclerosis with expansile remodeling
    - Ground glass density and internal trabeculation (simulates fibrous dysplasia)
    - Usually no soft tissue mass and not as aggressive appearing
    - Usually no periosteal reaction

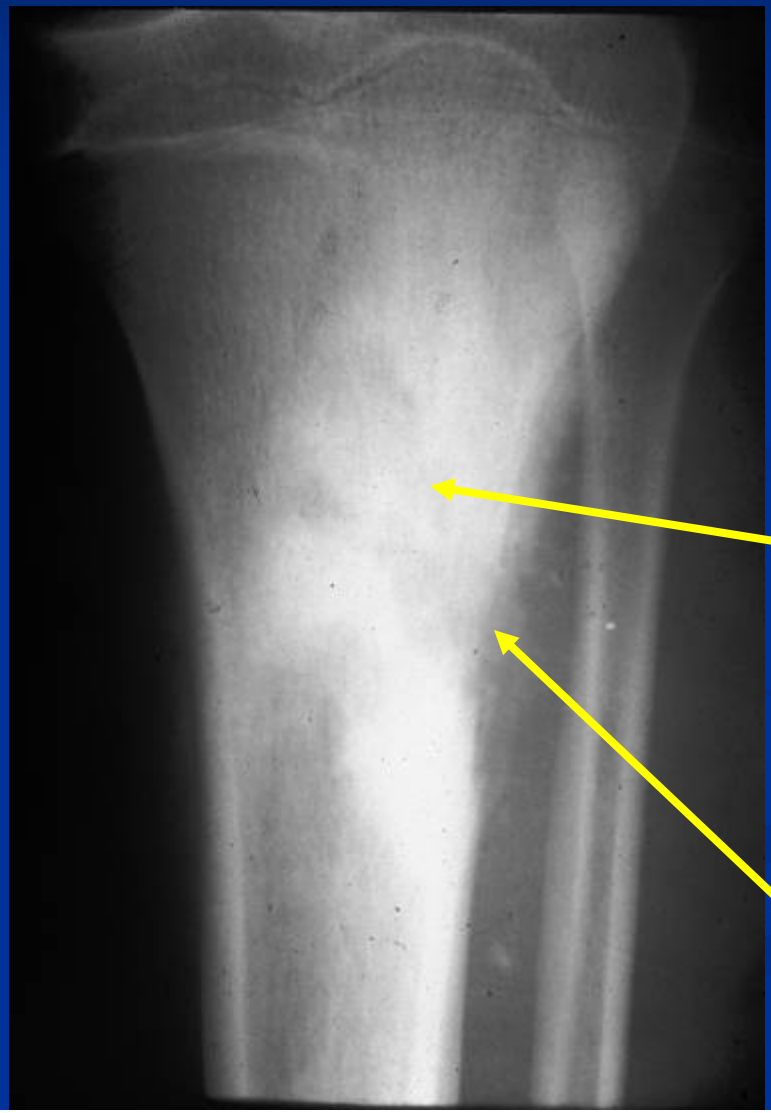
Intracortical Osteosarcoma

- High grade osteosarcoma confined to the cortex of a long bone
- Very rare; handful of cases
- Age: 10-30 yrs
- Sites: Diaphysis of femur or tibia
- Radiology:
  - Intracortical lucency with surrounding sclerosis of bone
  - No intramedullary or soft tissue involvement
  - Minimal or no periosteal reaction

Conventional Osteosarcoma of Distal Femur X-Ray

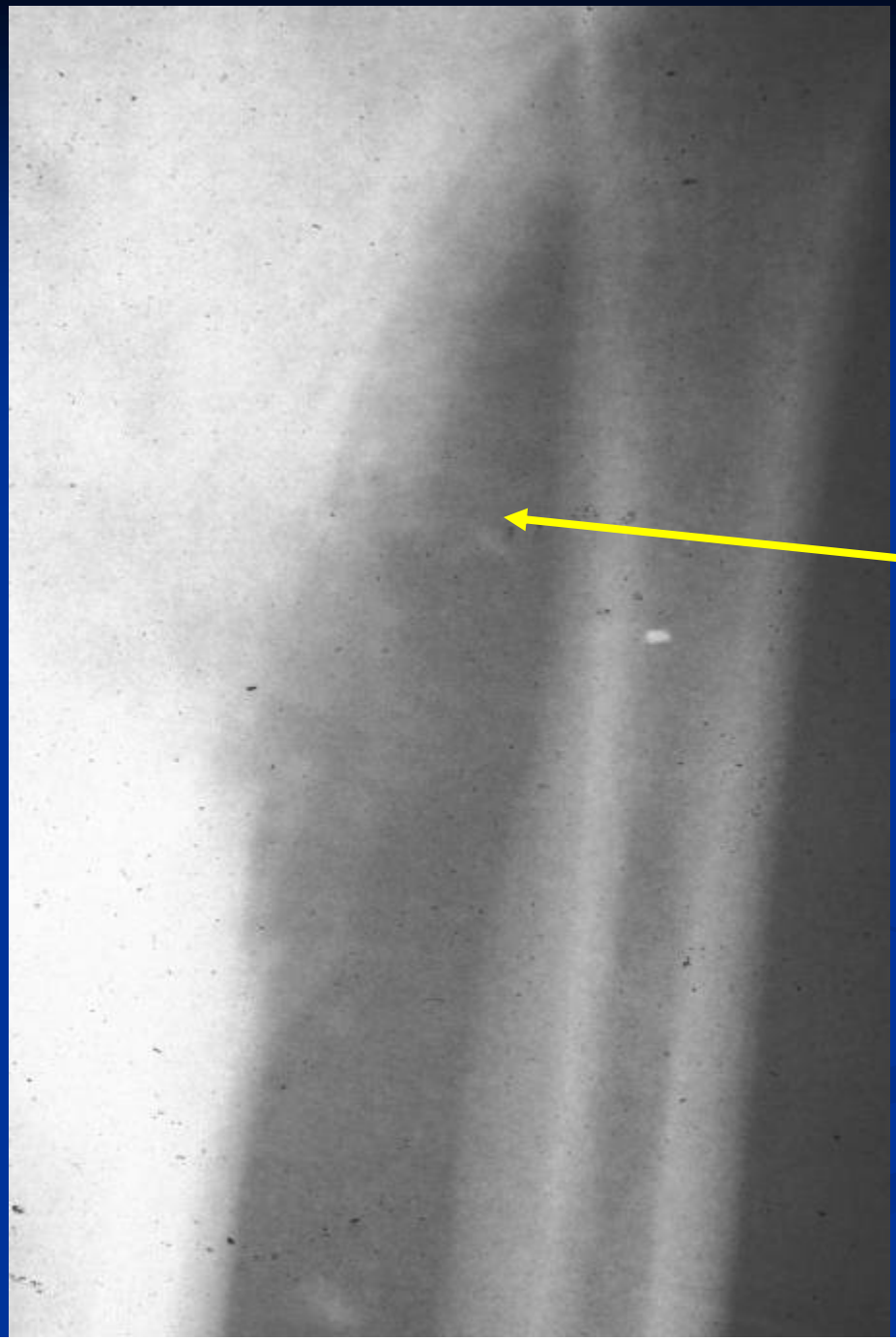


Conventional Osteosarcoma of Proximal Tibia



Permeative Lesion with Fluffy White Ossification (sclerosis)

Cortical Destruction

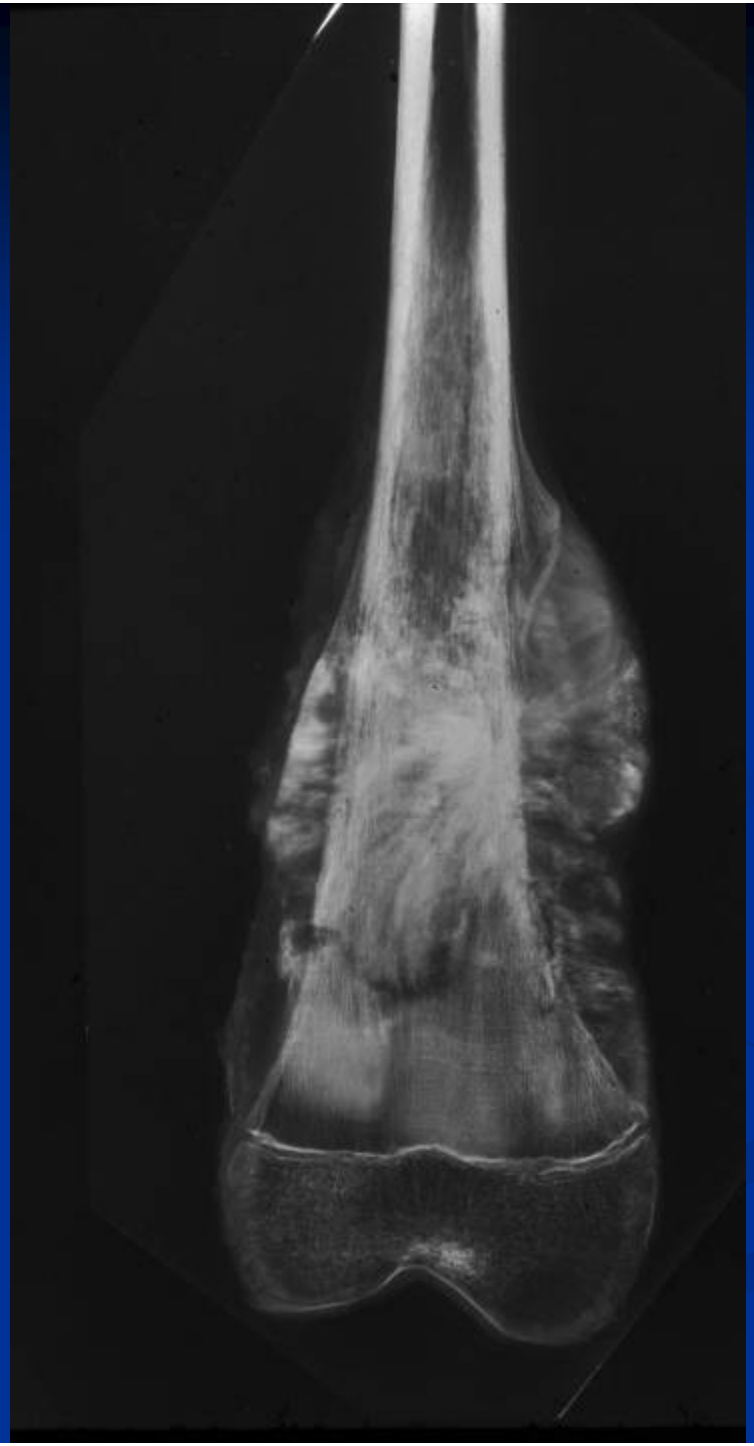


Cortical Destruction and Hair on End Periosteal Reaction

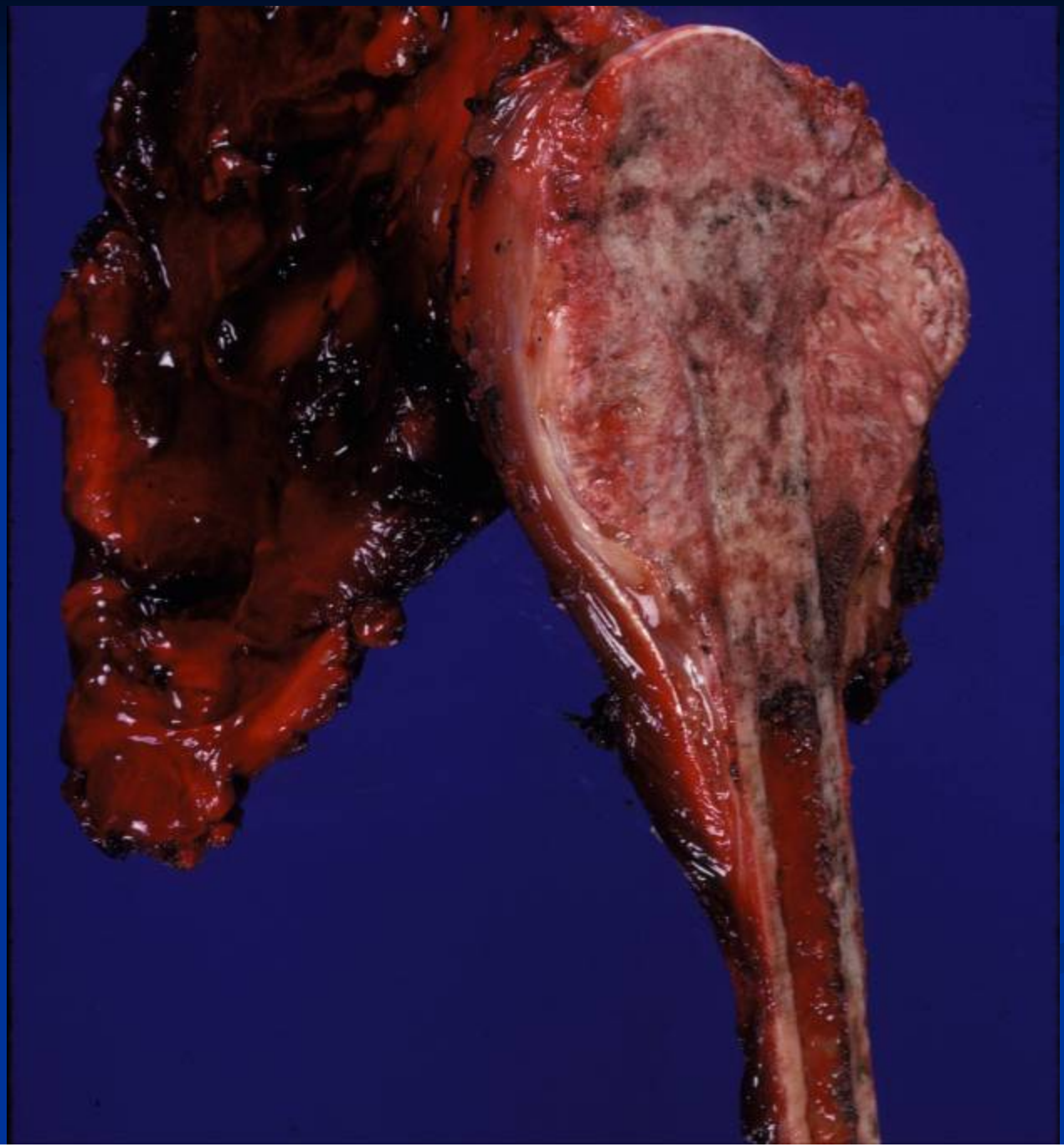
Osteosarcoma Conventional

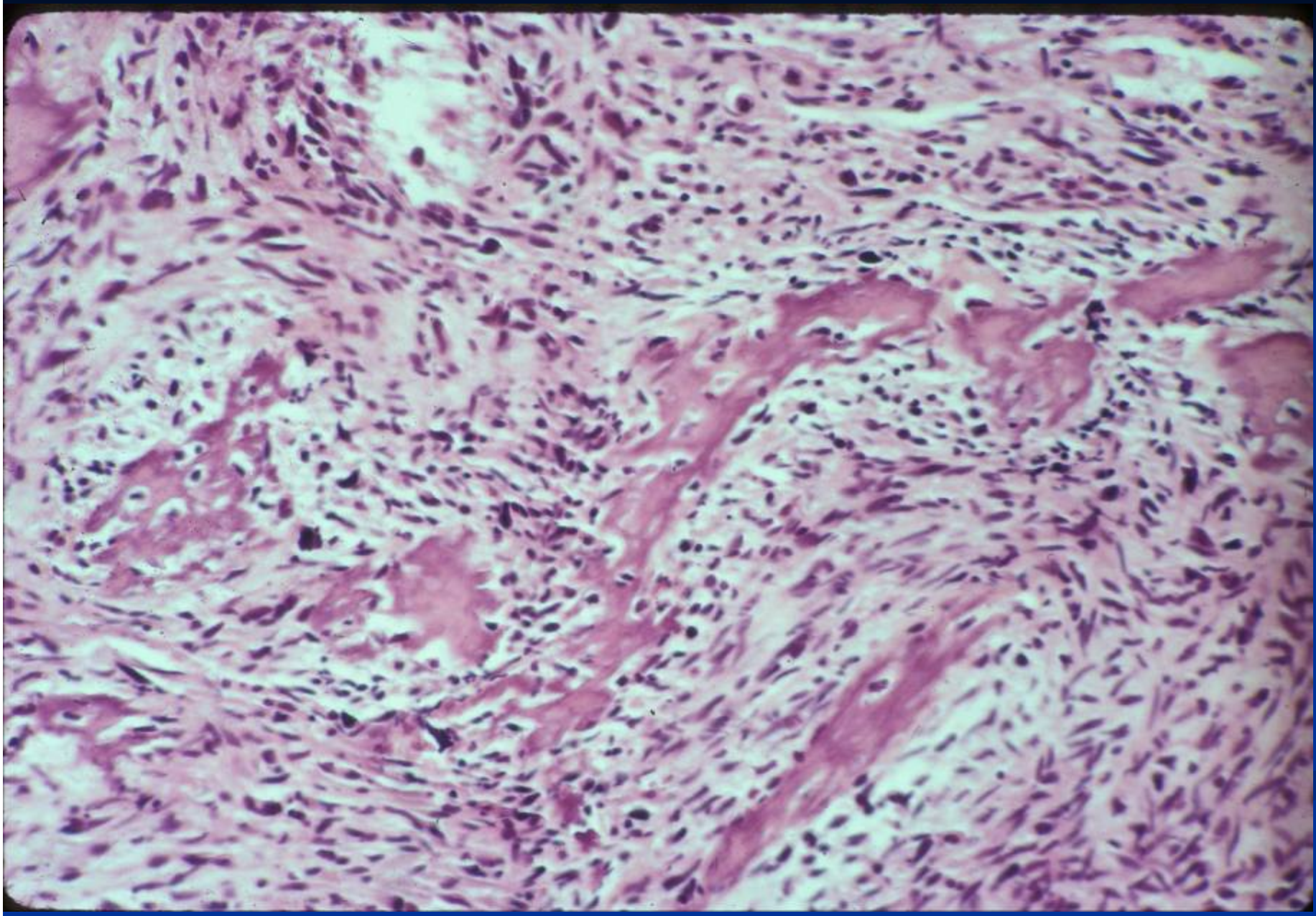
- Radiographic Differential Diagnosis:
  - Ewing sarcoma
  - Fibrosarcoma/MFH
  - Chondrosarcoma
  - Osteomyelitis
  - Osteoblastoma
  - Giant Cell Tumor

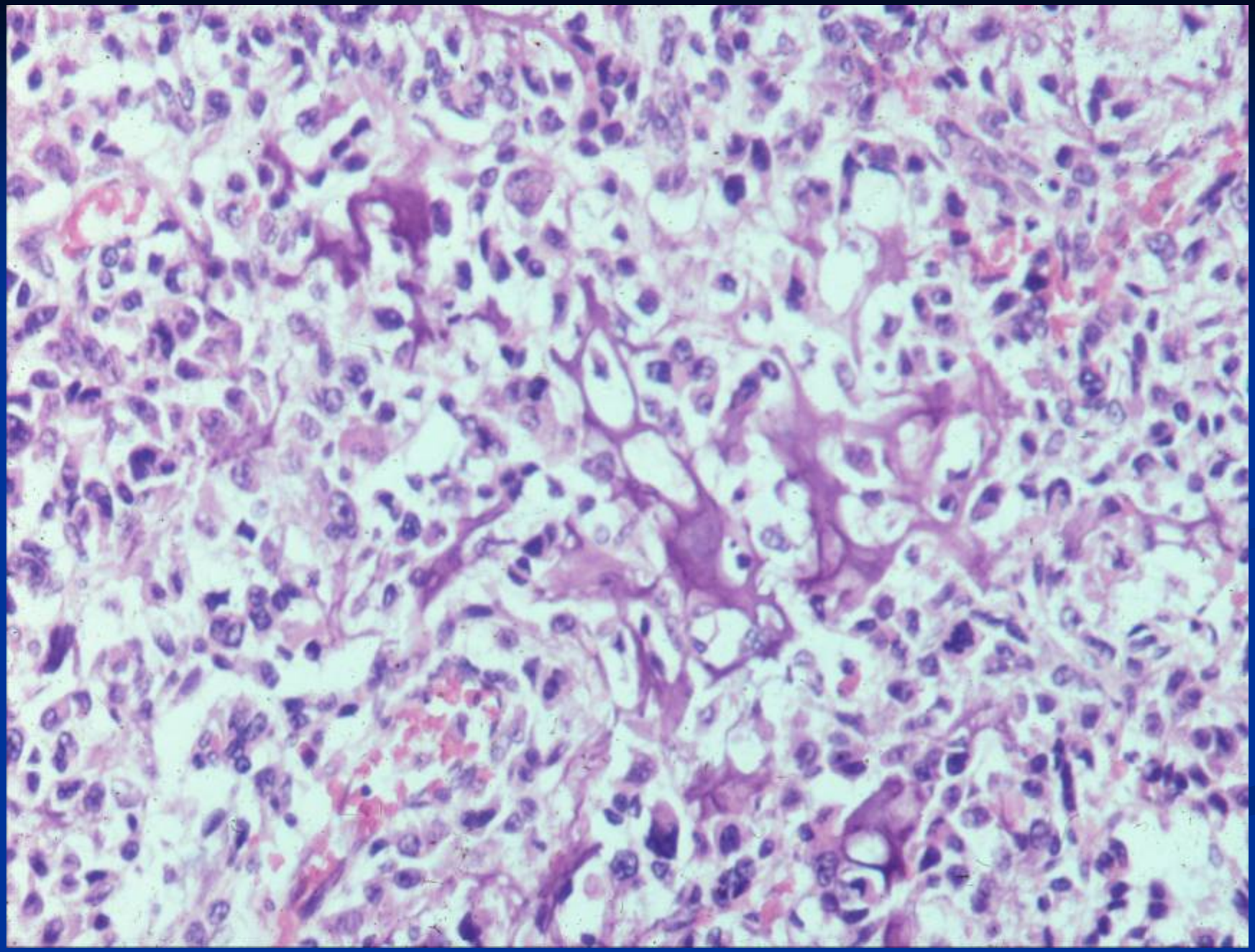
Examples of Conventional Osteosarcomas including Gross and Microscopic Pathology

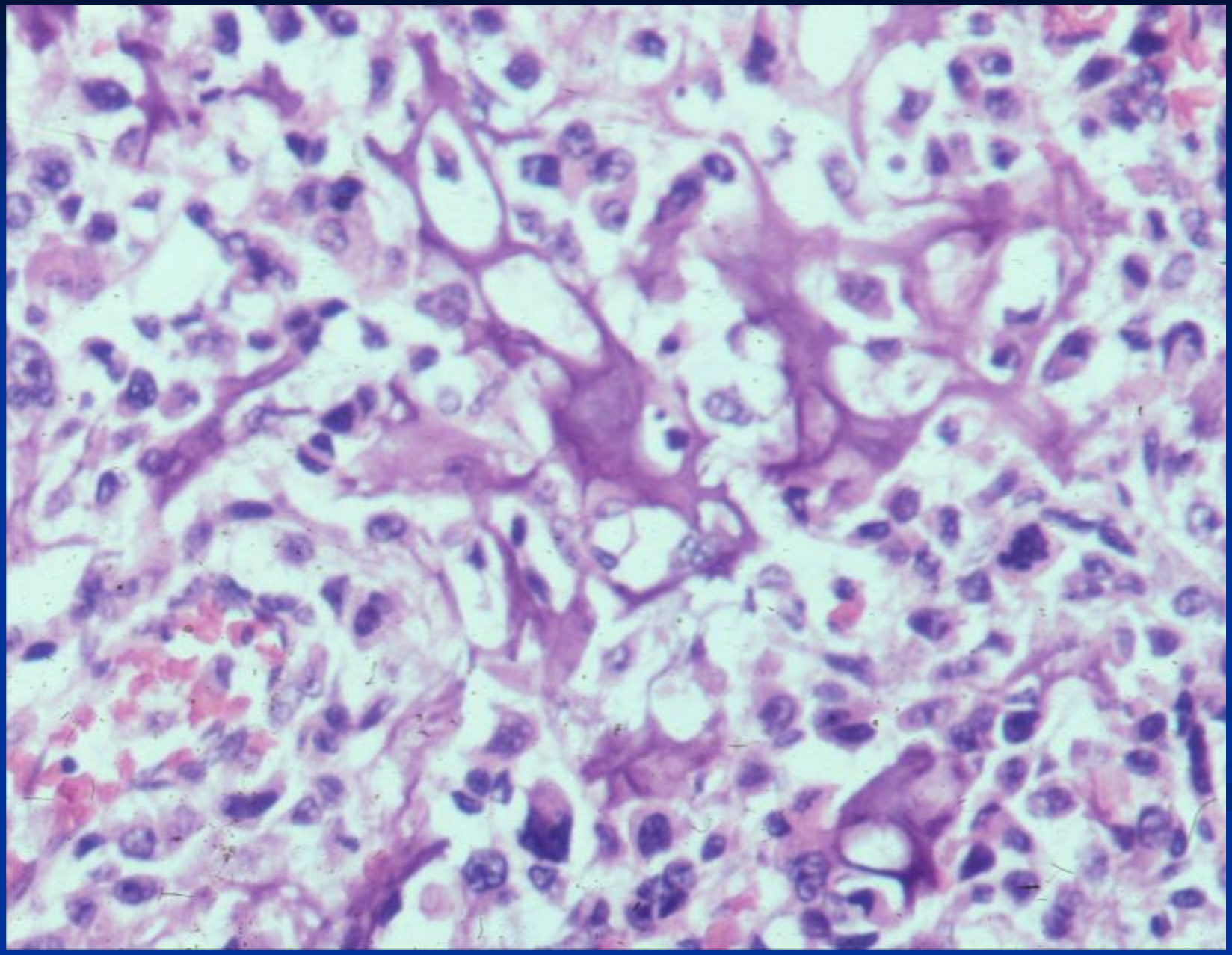


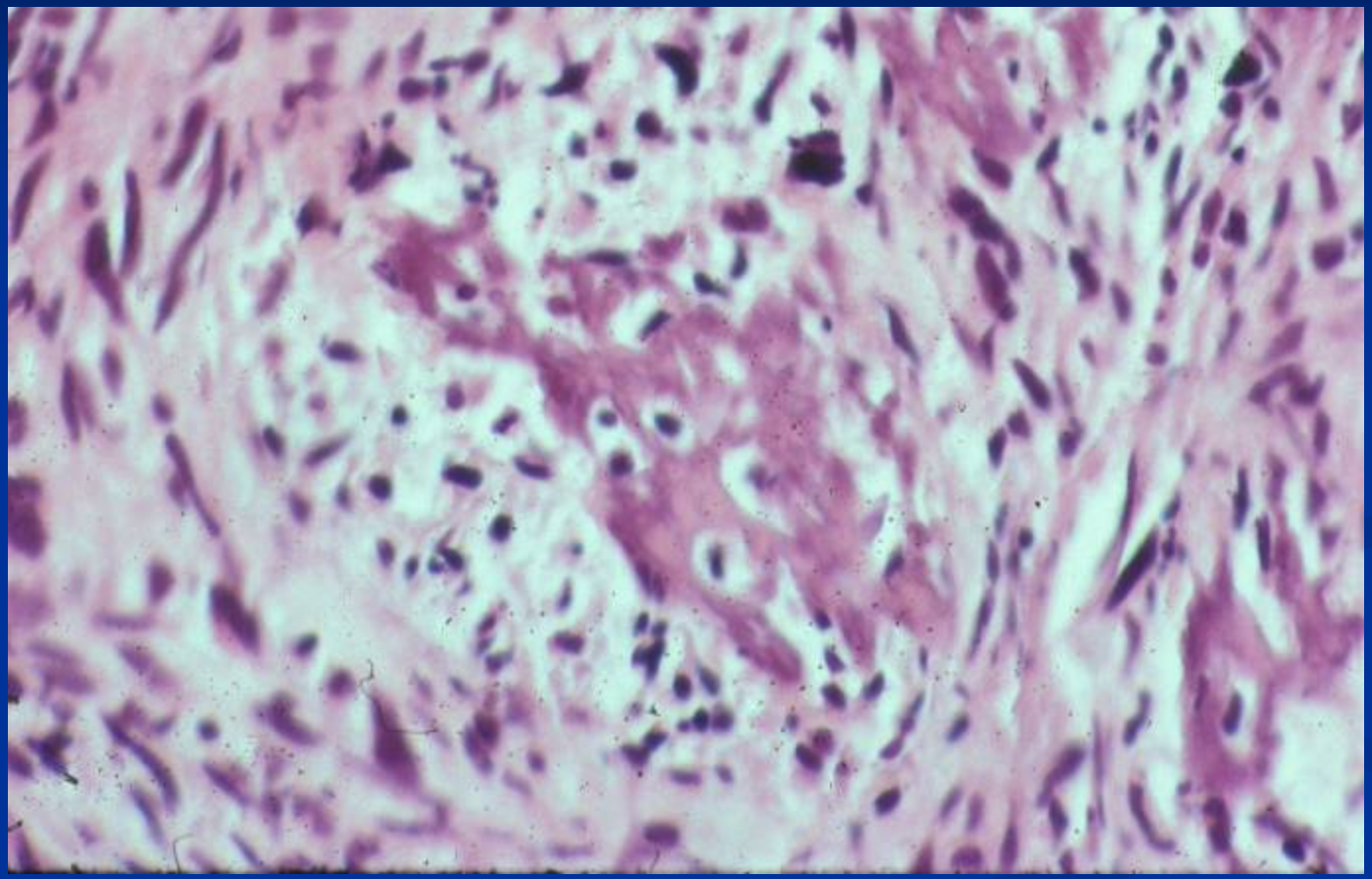

METRIC
2/11-73
3
4
5











Chondroblastic Subtype of a Conventional Osteosarcoma of Distal Tibia

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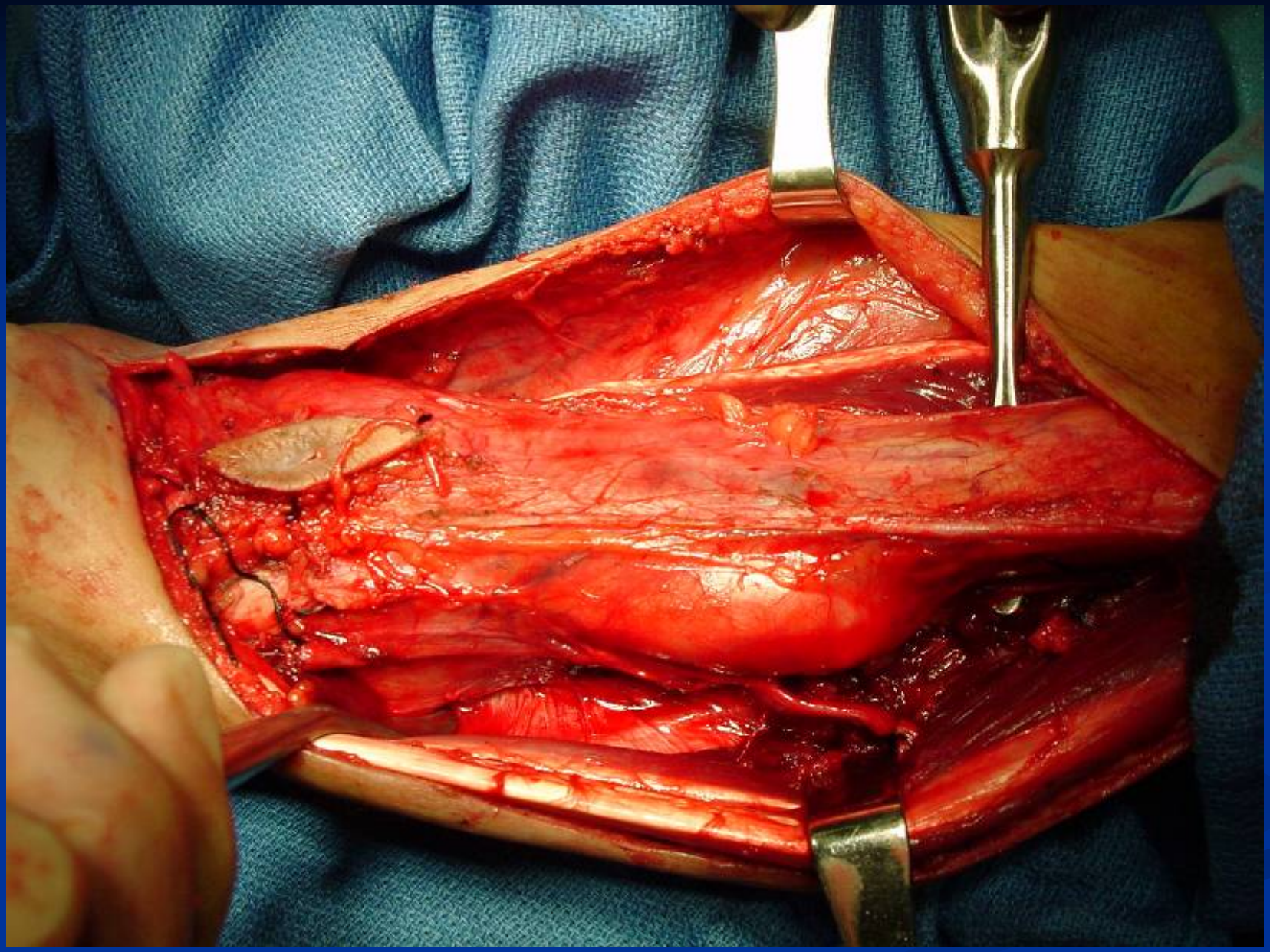
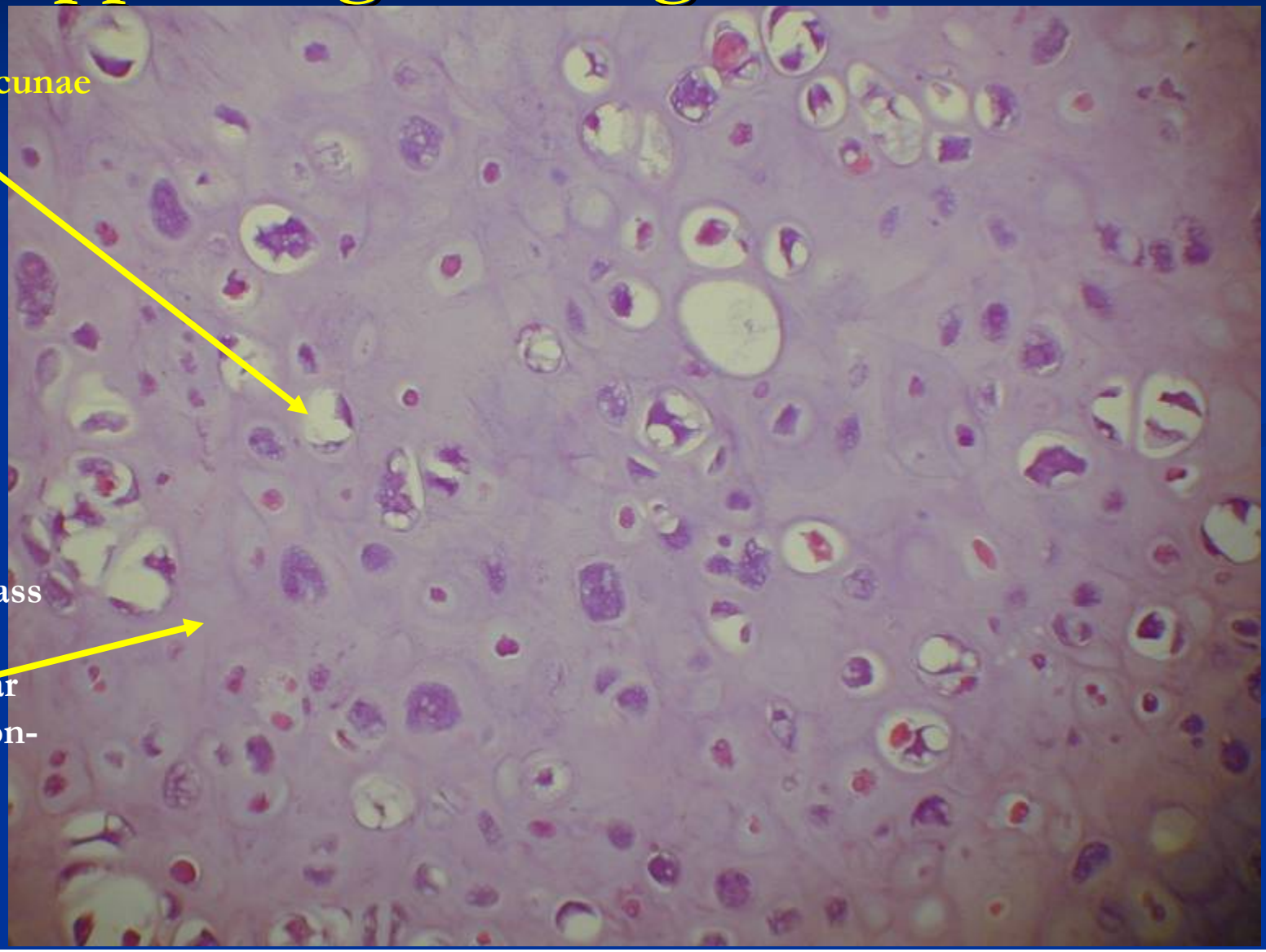
J



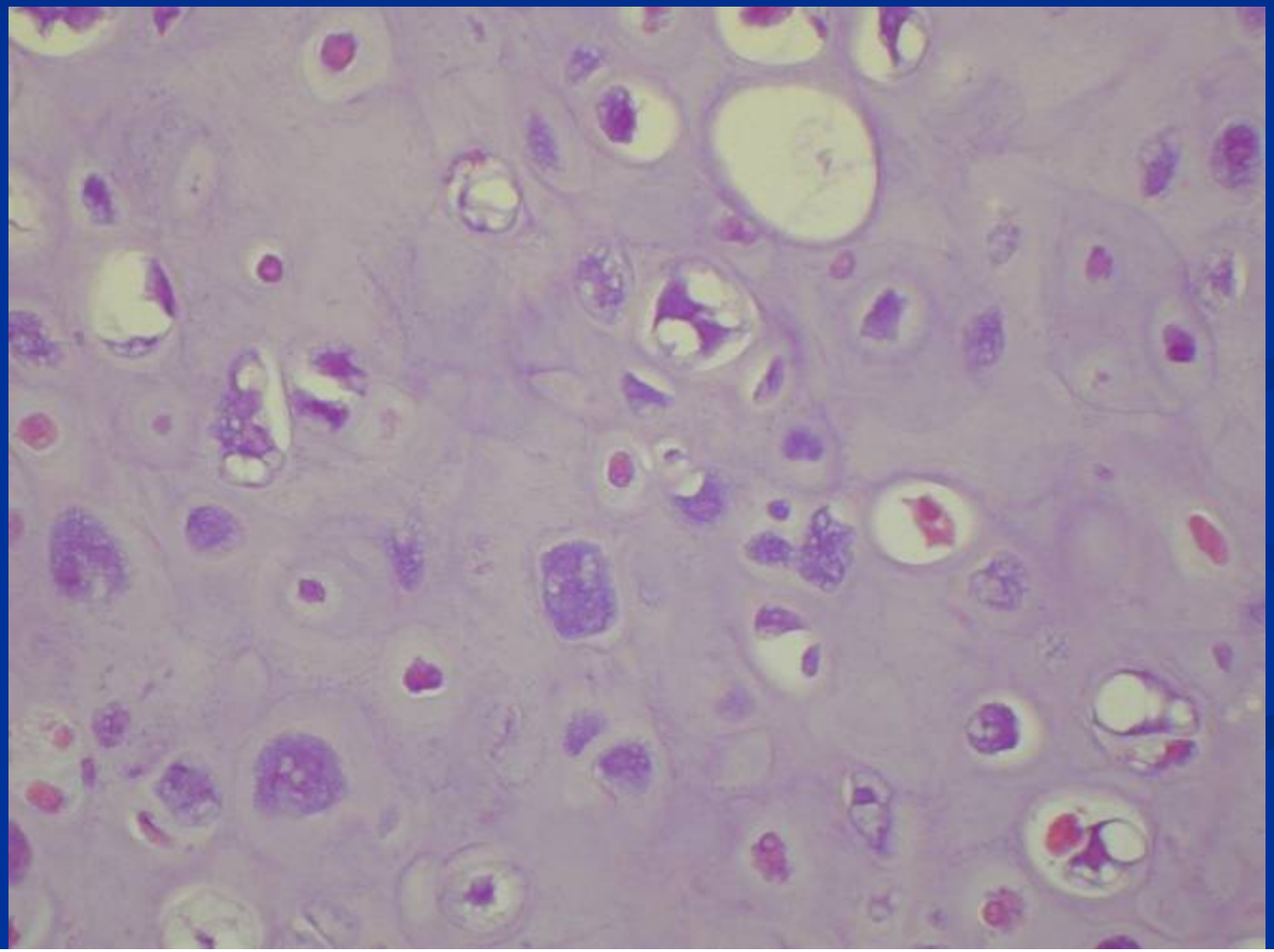

SPECIMEN
DATE


SPECIMEN S01-4534
DATE 3/16/01

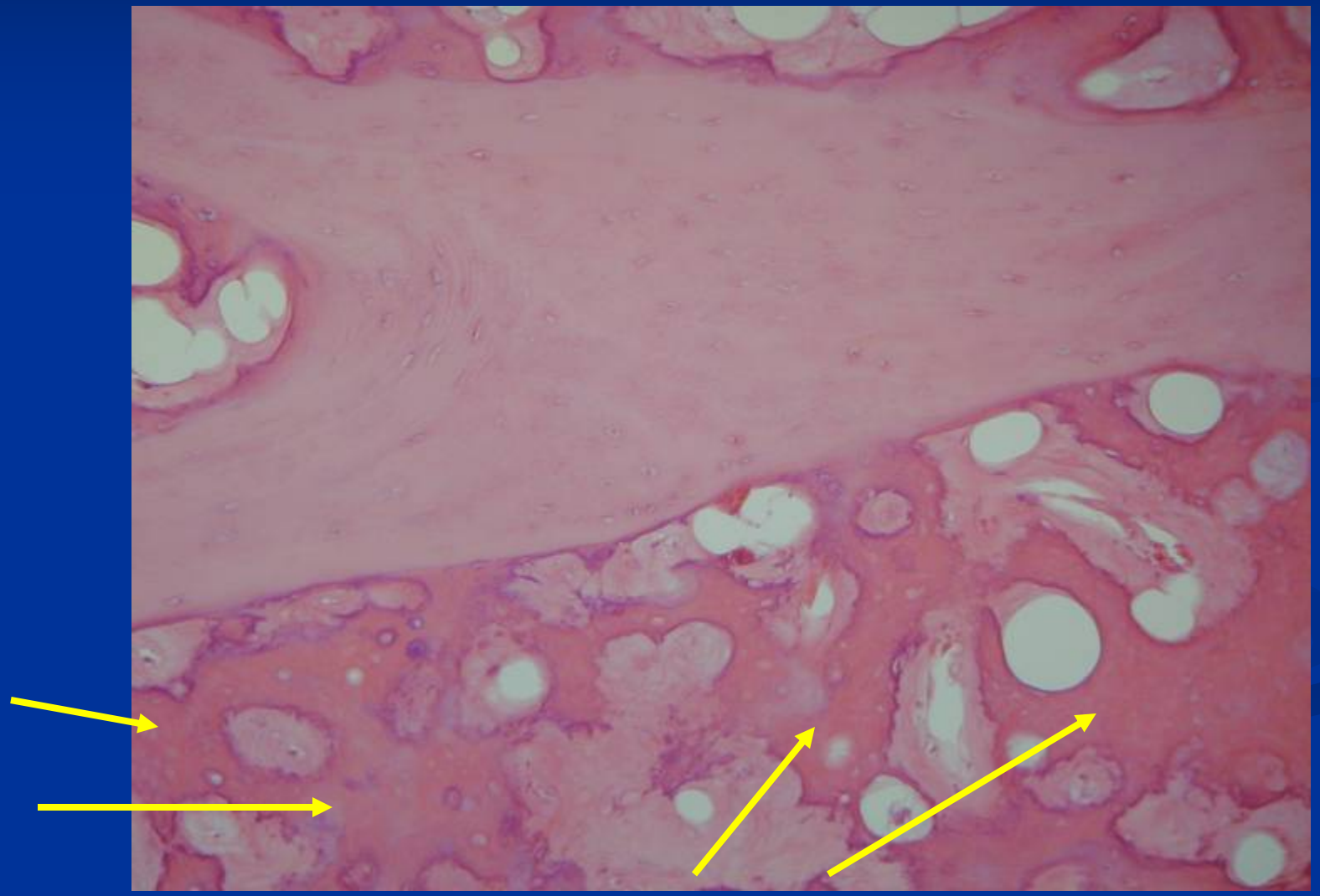
Microscopic Pathology—Malignant Appearing Cartilaginous Tissue



Hypercellular, Disorganized, Crowded Cells, Multinucleated Cells, Large Bizarre Nuclei



Bone Production Identified which Categorizes it as an Osteosarcoma



Osteosarcoma Conventional

- Pathologic Differential Diagnosis:
  - Osteoblastoma
  - Osteoid Osteoma
  - Giant Cell Tumor
  - Fracture Callus
  - Fibrosarcoma
  - Chondrosarcoma
  - MFH

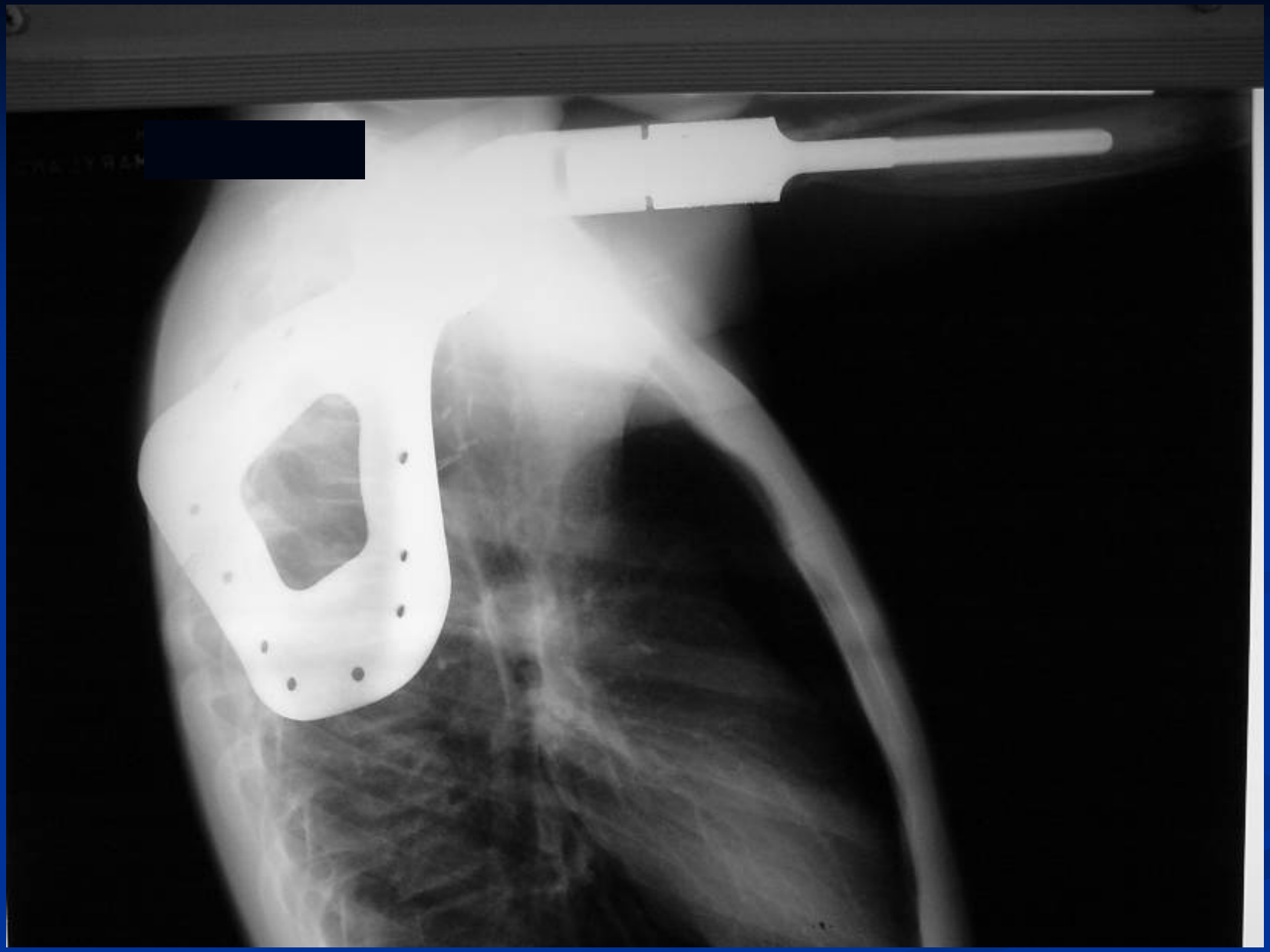
Osteosarcoma

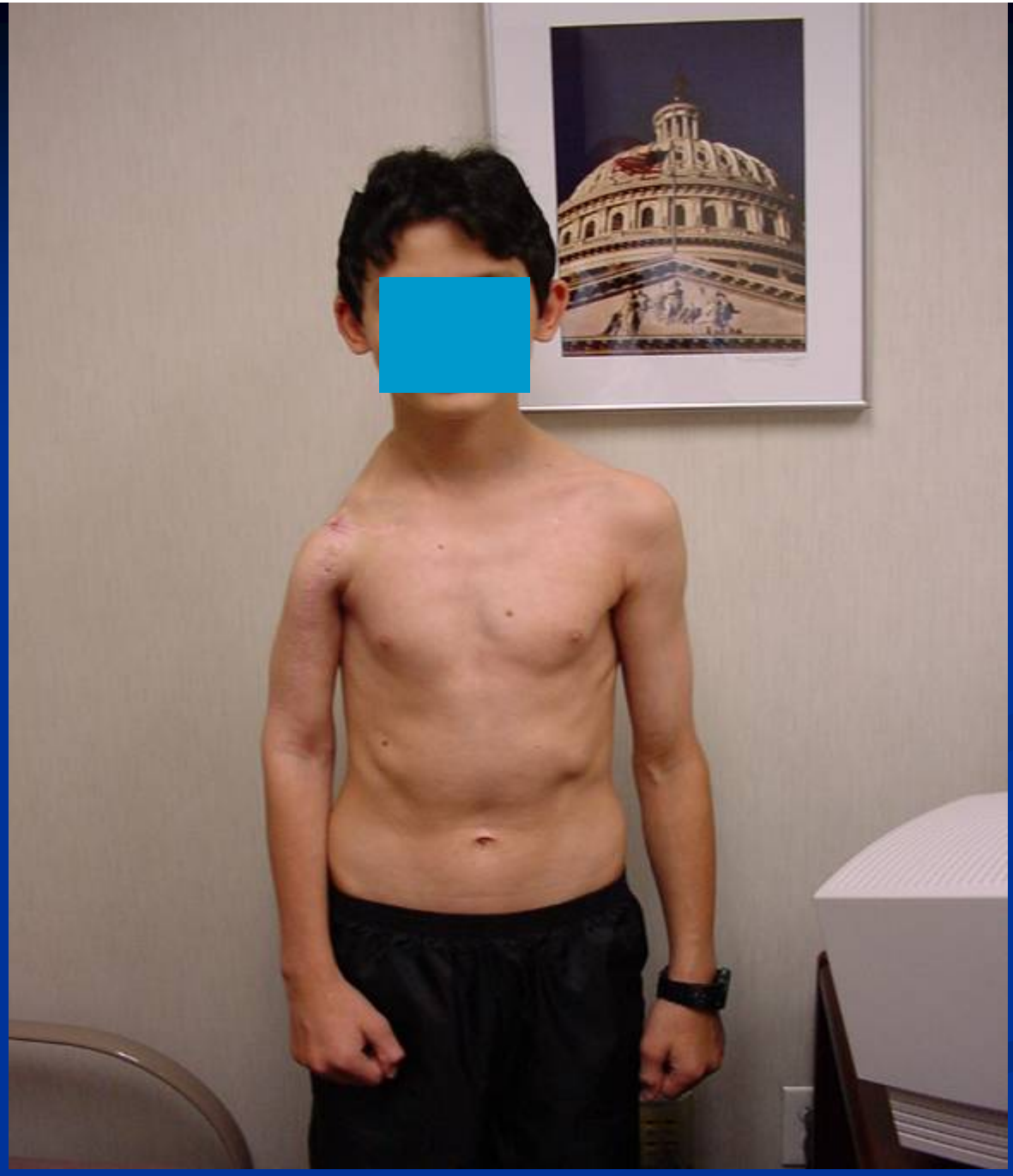
- Treatment:
  - Preoperative (induction) chemotherapy:
    - Adriamycin (doxorubicin)
    - Cisplatinum (cisplatin)
    - High Dose Methotrexate (HDMTX)
    - Ifosfamide/Etoposide in some regimens

    (2 cycles and then surgery)
  - Surgery:
    - Wide surgical resection /Limb Salvage(95% of extremity lesions)
    - Amputation (5% of extremity lesions)
  - Postoperative (adjuvant) chemotherapy:
    - Same regimen as preop; usually 4 cycles

Limb Salvage: Radical Resection of Distal Femur Osteosarcoma and Reconstruction with Distal Femur Tumor Prosthesis

Radical Resection of proximal Humerus Osteosarcoma with Metastasis to Scapula: Reconstruction with total Scapula Prosthetic Replacement



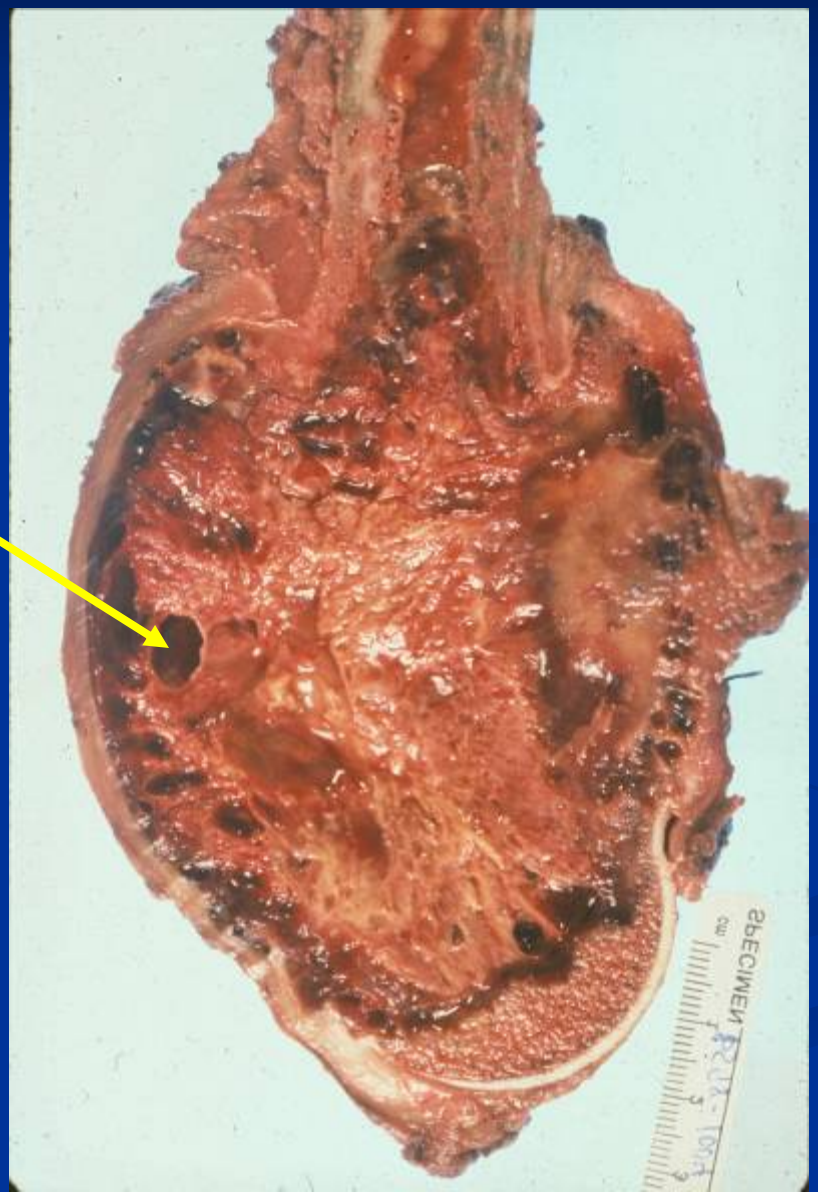


Telangiectatic Osteosarcoma of Distal Radius

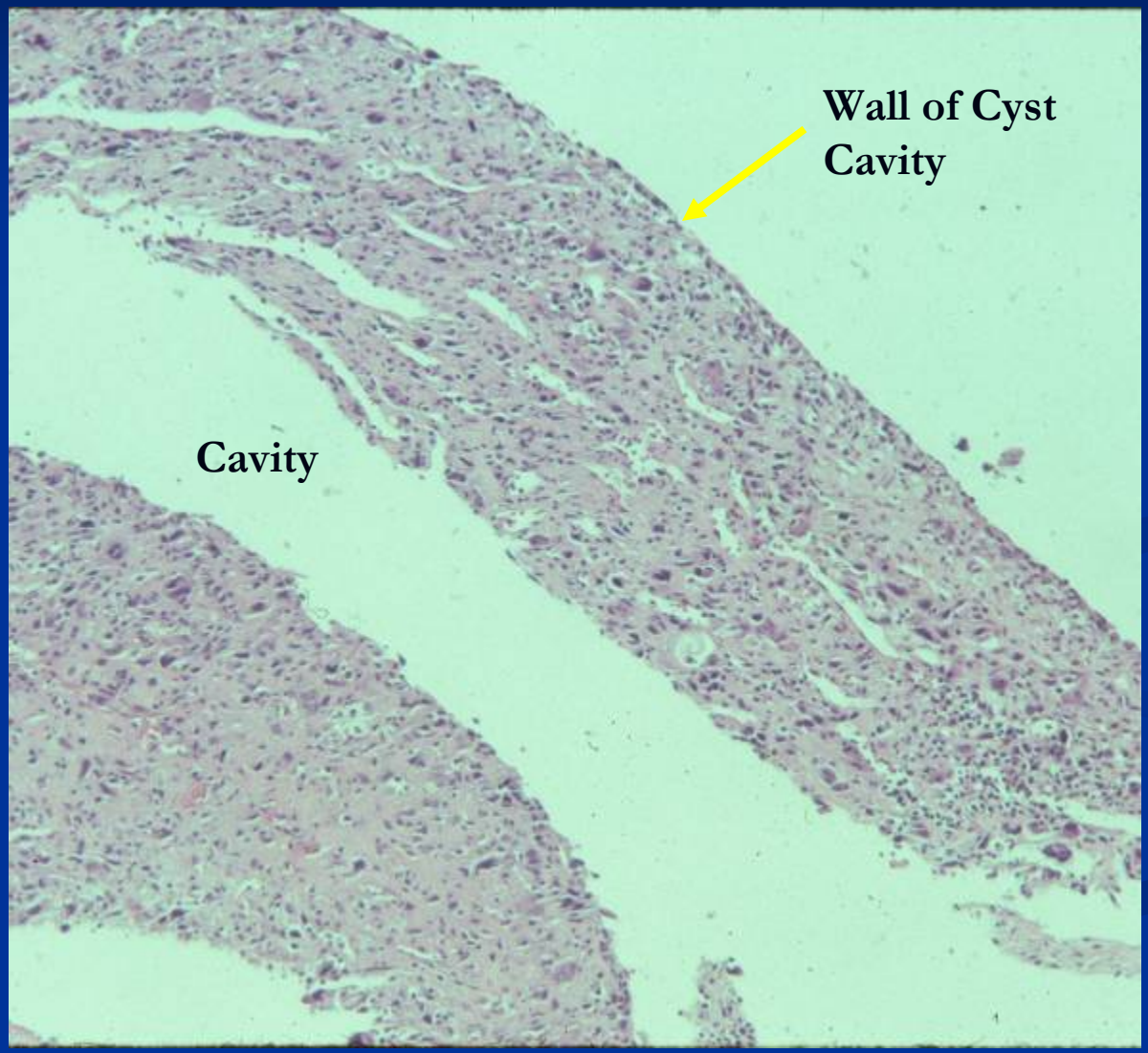
MRI Demonstrating Multiple fluid-Fluid Levels

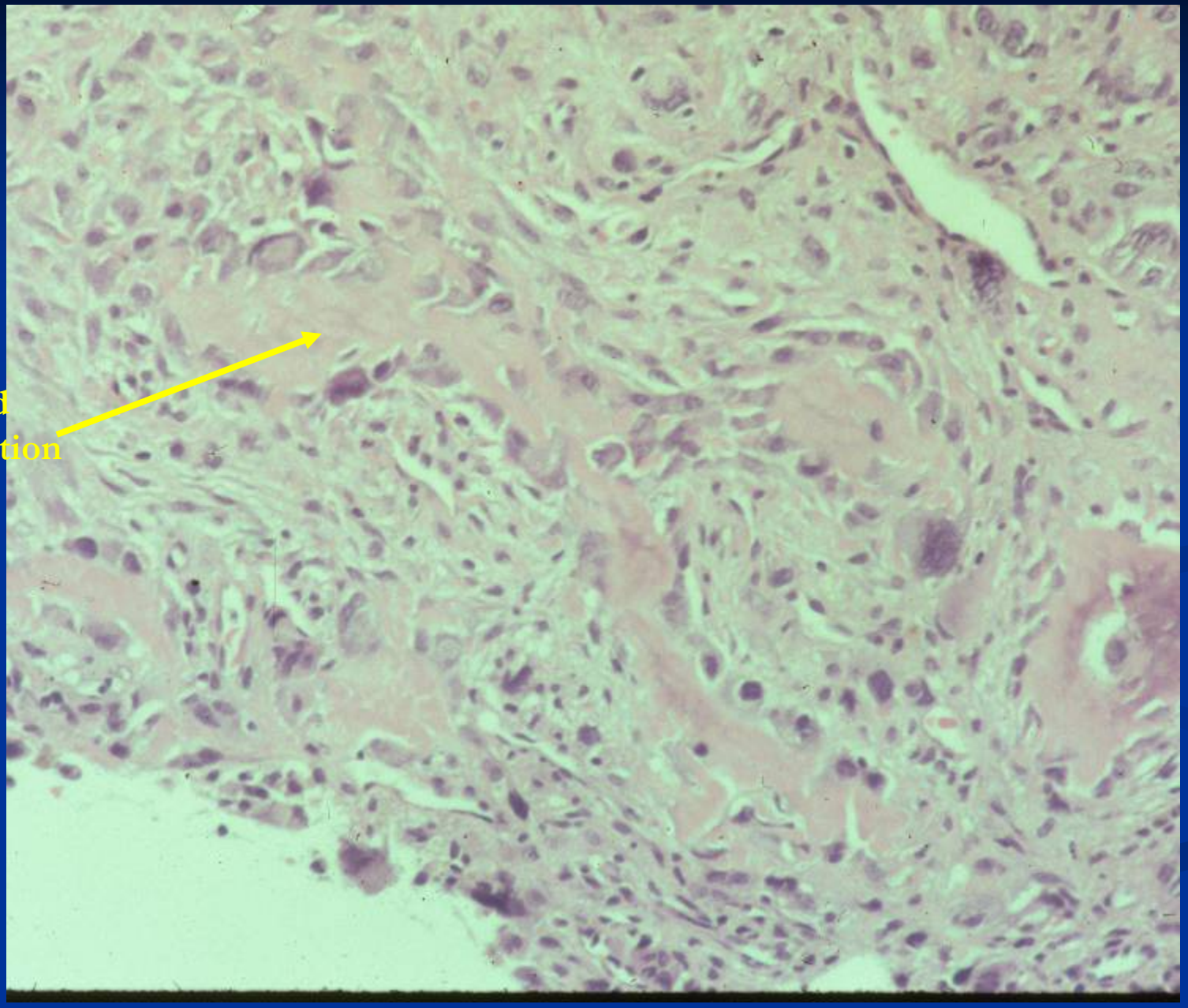
Gross Pathology: Telangiectatic Osteosarcoma

Multiple Cystic and Necrotic Spaces/Cavities



Microscopic Pathology




Osteoid
Production

Telangiectatic Osteosarcoma

- Radiographic Differential Dx:
  - Conventional osteosarcoma
  - Fibrosarcoma
  - MFH
  - Aneurysmal Bone Cyst

Telangiectatic Osteosarcoma

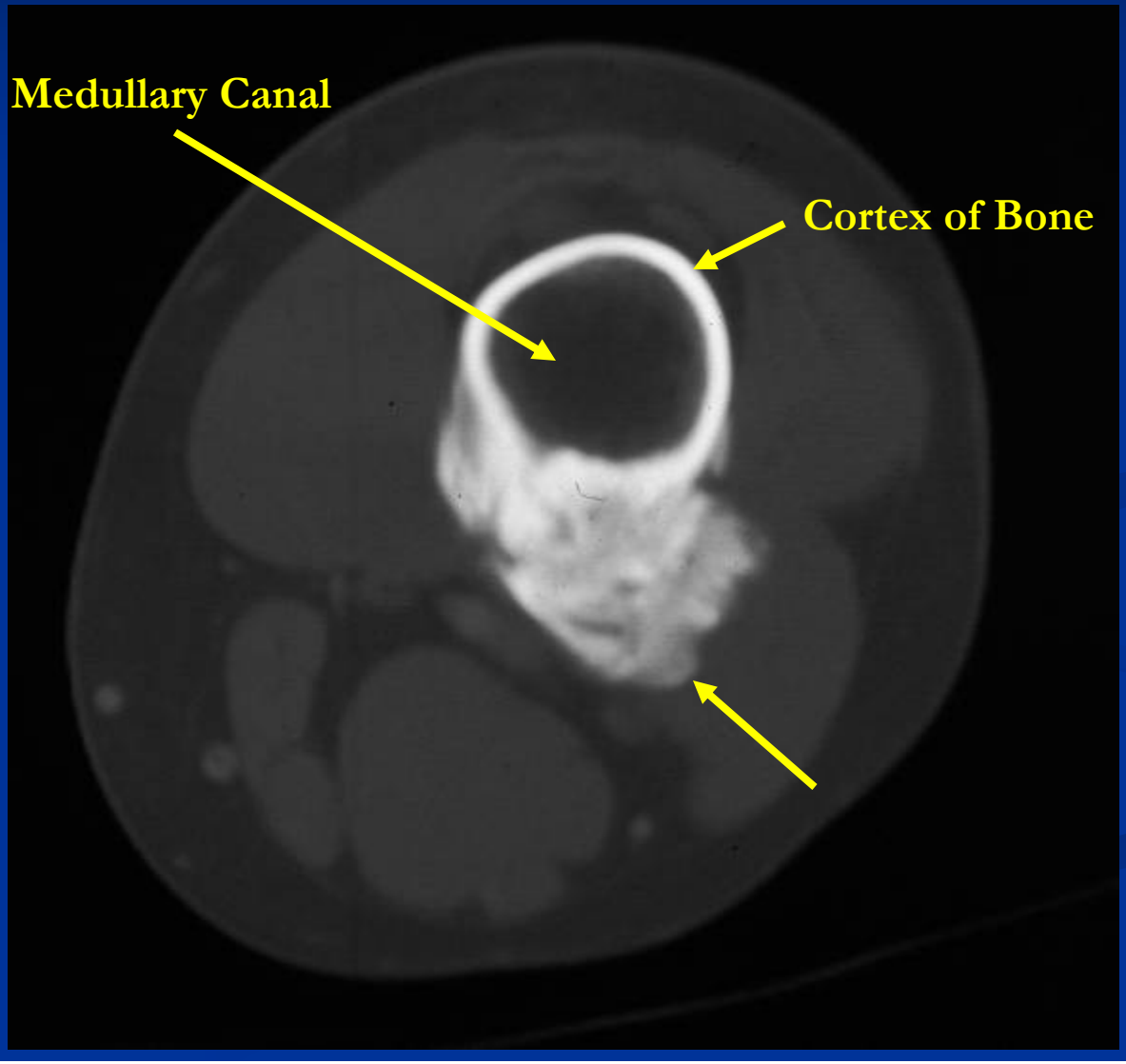
- Treatment and Prognosis same as conventional osteosarcoma

Parosteal Osteosarcoma

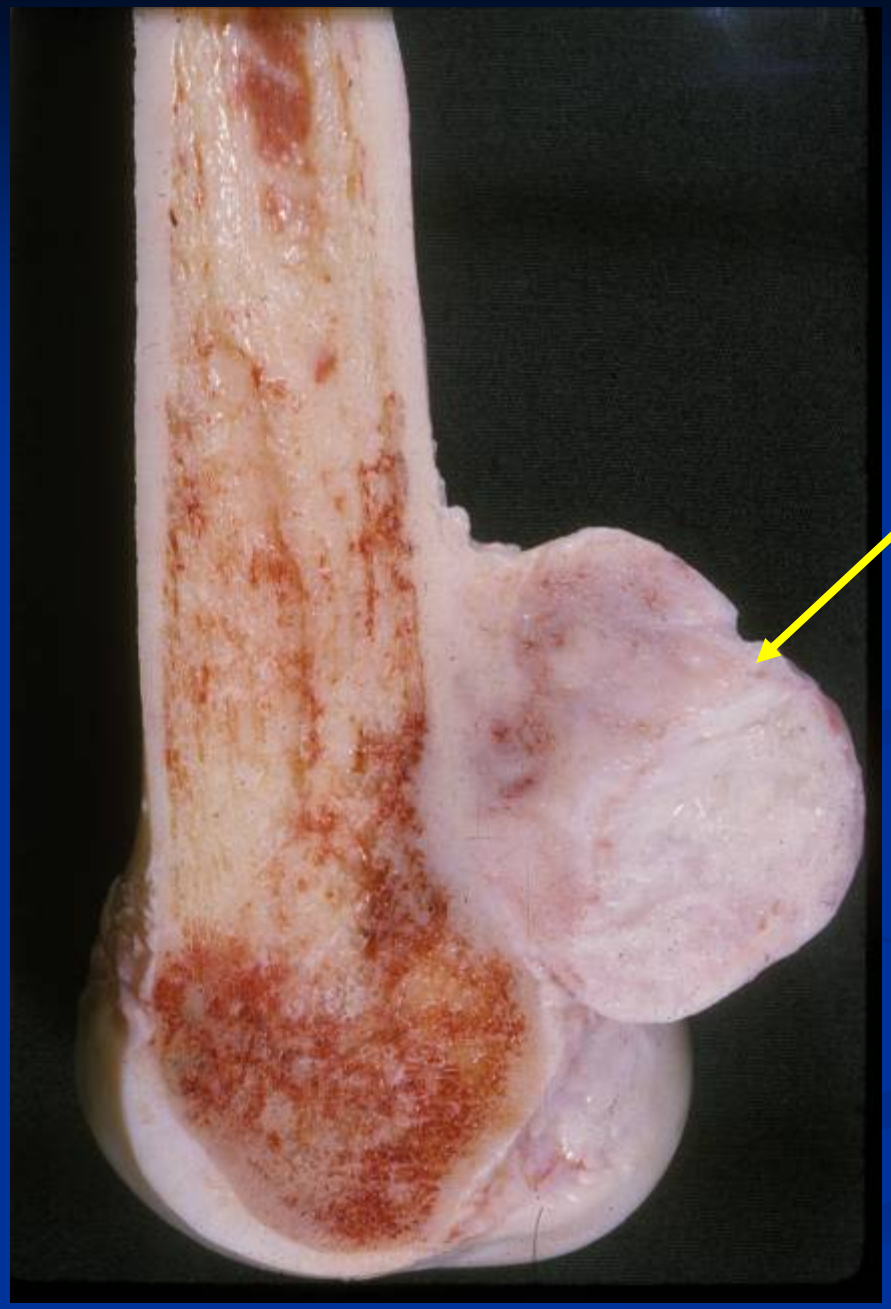
Parosteal Osteosarcoma

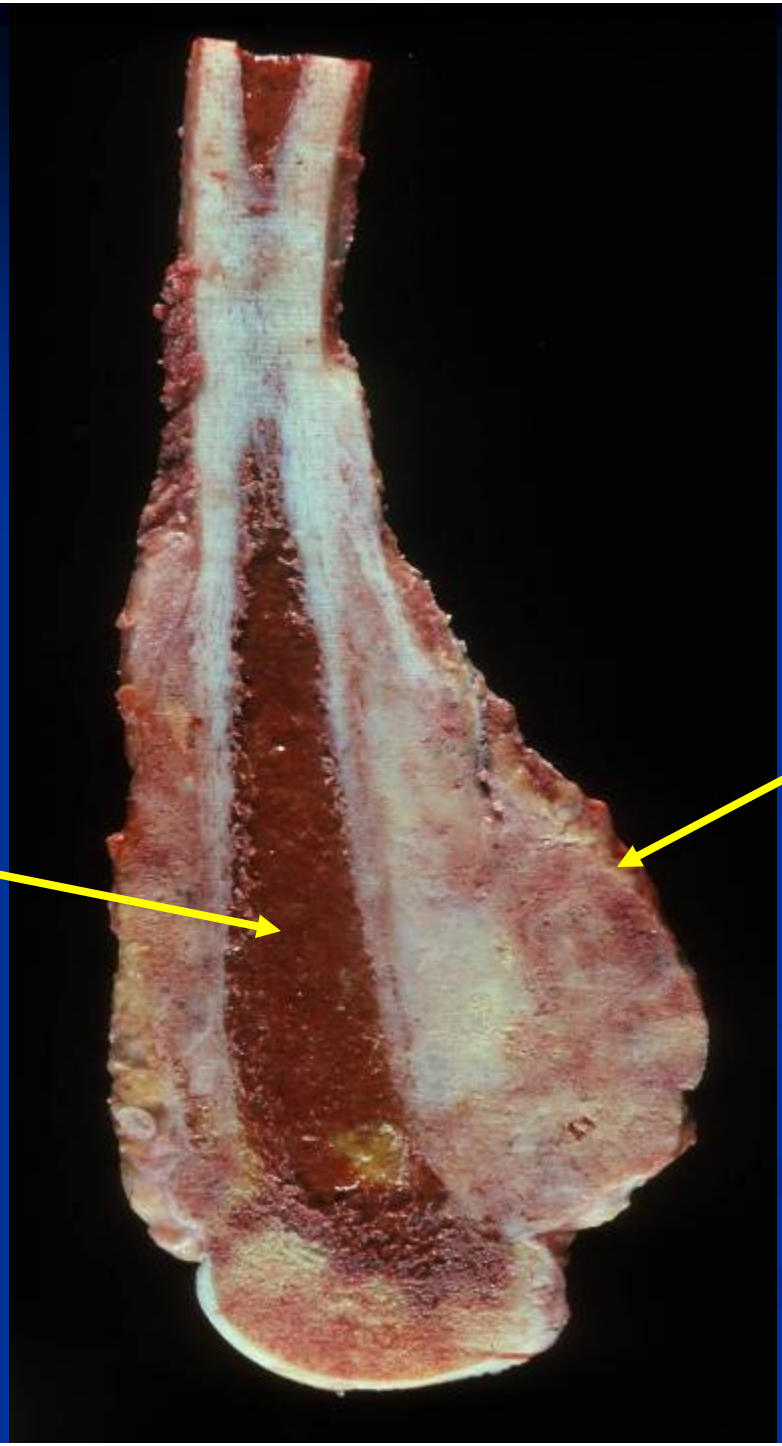
- Radiology:
  - MRI/CT:
    - Medullary invasion
    - Any areas that may be high grade
    - Local extent---circumference of femur
    - CT of chest for detecting pulmonary mets

CT Scan of Distal Femur Parosteal Osteosarcoma



Gross and Microscopic Pathology

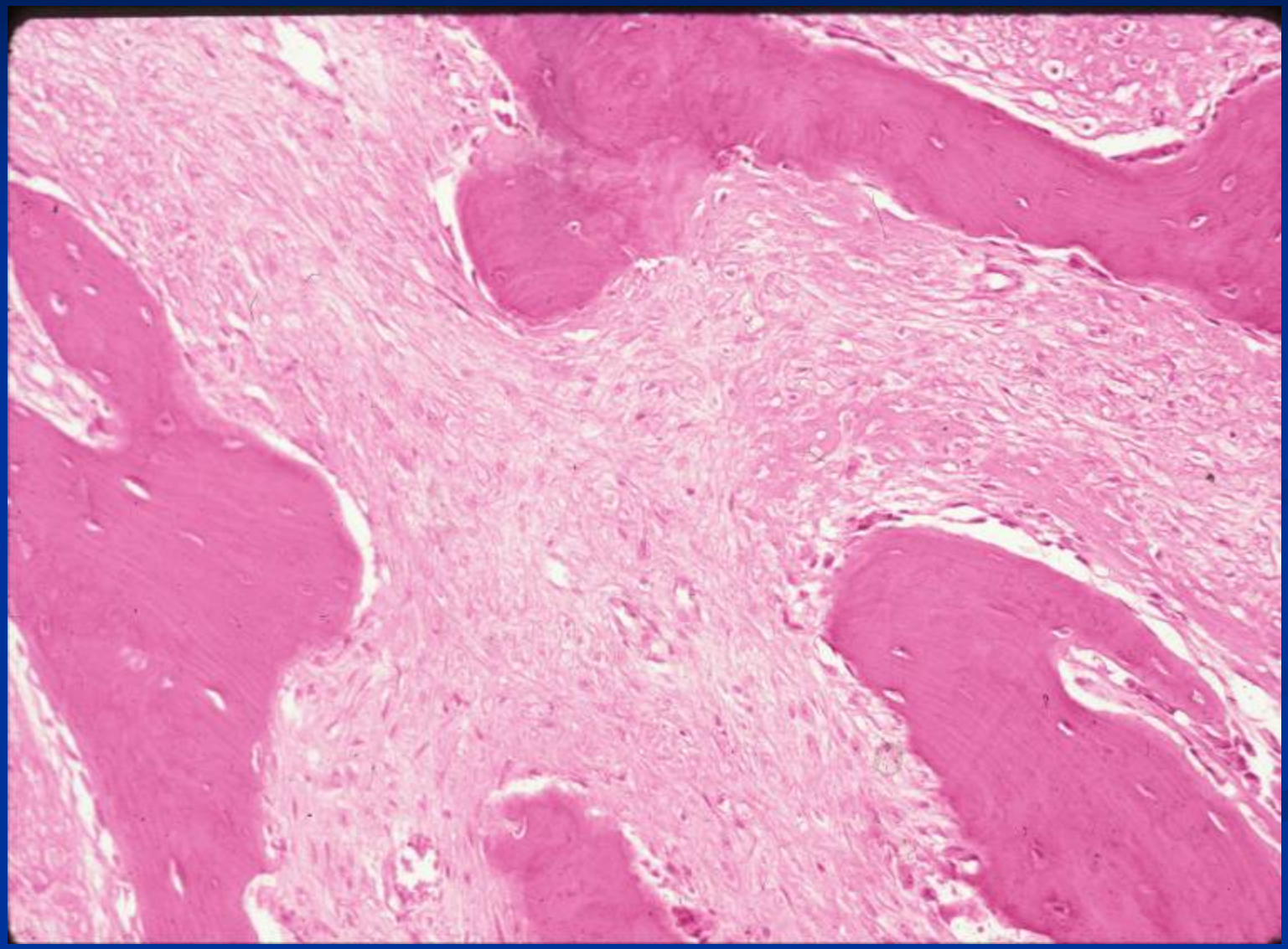

Tumor


Tumor on
Surface of Bone
Medullary
Canal of Bone

Pathology

- Microscopic pathology demonstrates a fibroblastic tumor that is producing bone and osteoid
- The islands of bone are interspersed amongst fibrous appearing tissue
- There is minimal nuclear atypia and a minimal number of mitotic figures
- The tumor is typically a low grade tumor


Bone Production



Parosteal Osteosarcoma

- Radiographic Differential Diagnosis:
  - Myositis ossificans
  - Periosteal osteosarcoma
  - Periosteal chondrosarcoma
  - High-grade surface osteosarcoma
  - Conventional osteosarcoma
  - Osteochondroma

Parosteal Osteosarcoma

- Pathologic Differential Diagnosis:
  - Osteochondroma
  - Myositis ossificans
  - High grade surface osteosarcoma
  - Periosteal osteosarcoma

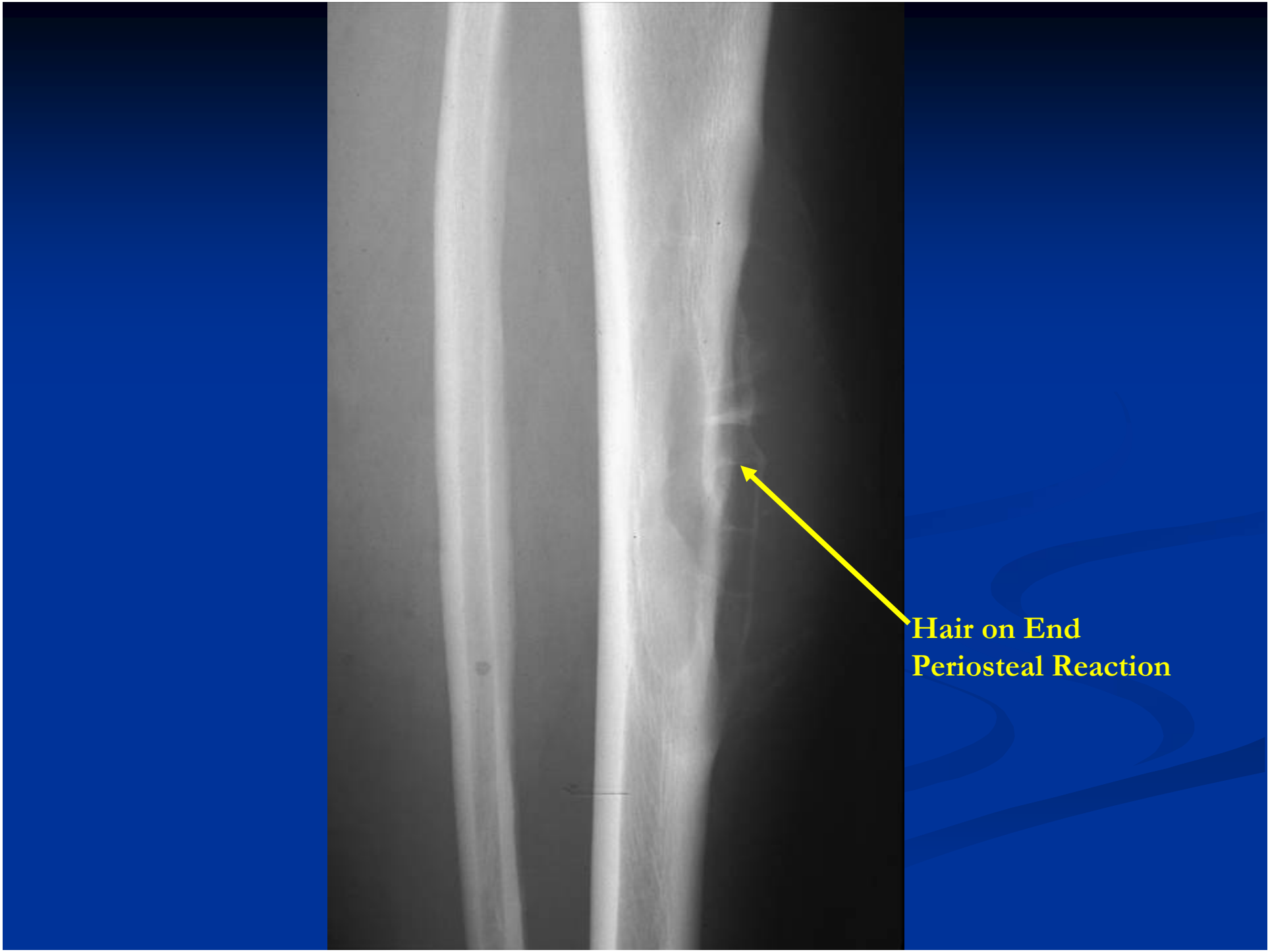
Parosteal Osteosarcoma

- Typically a parosteal osteosarcoma is a low grade type of tumor with little risk of metastasizing or spreading
- Most patients are cured with surgery alone. Chemotherapy is usually not used for treatment.
- Occasionally, parosteal osteosarcomas that are present for prolonged periods of time before being identified, can dedifferentiate and develop high grade areas. These higher grade variants have a higher likelihood of spreading and may be treated with chemotherapy in addition to surgery.

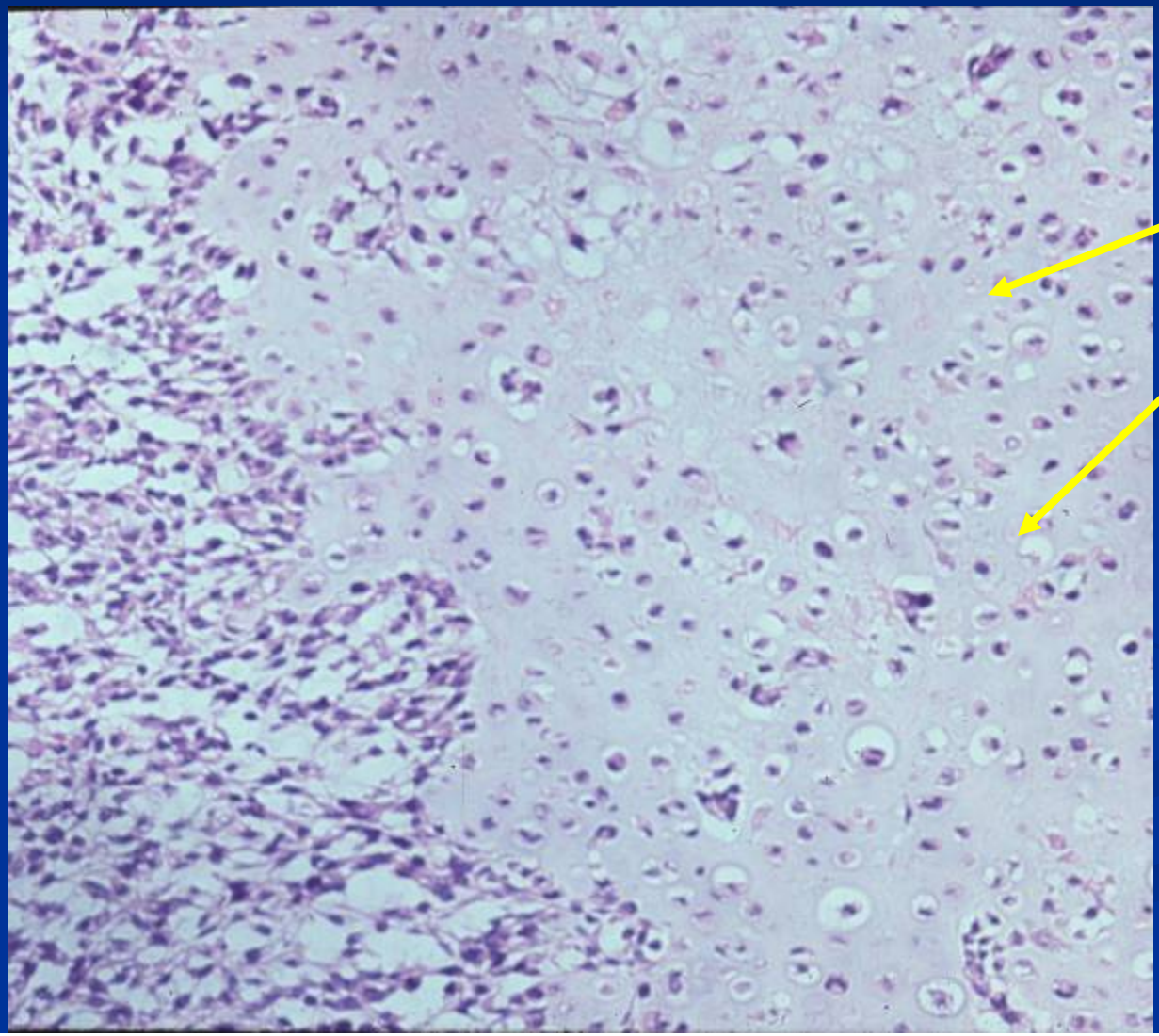
Parosteal Osteosarcoma

- Treatment:
  - Wide surgical resection and reconstruction
  - Chemotherapy only if grade 3 components or dedifferentiated components identified on biopsy or after resection (Same regimen as conventional)
  - Radiation: Not used in treatment of this tumor
- Prognosis:
  - 80-90% cure rate
  - Mets more common with medullary invasion and high grade components
  - Medullary invasion more common with high grade components

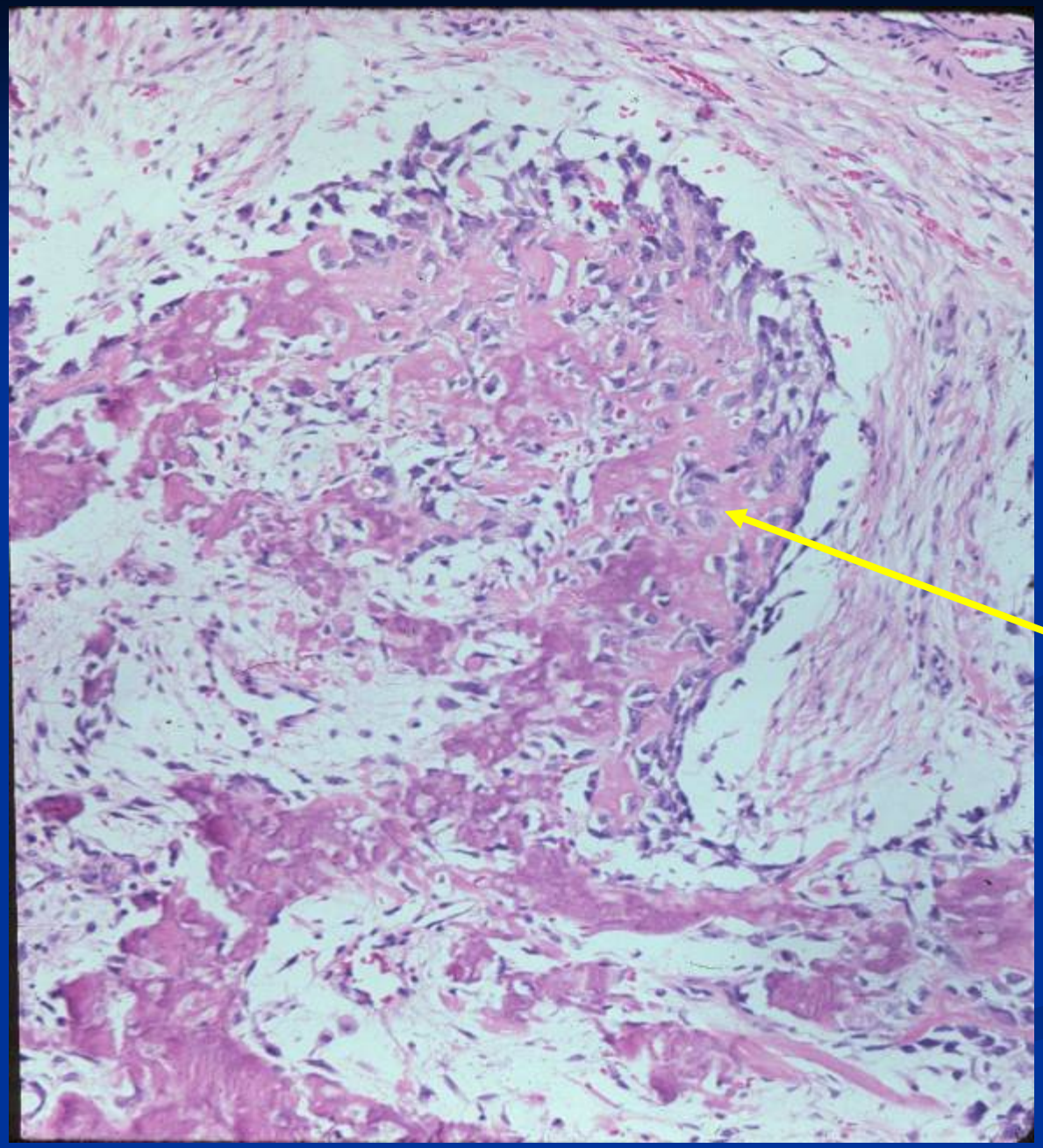
Periosteal Osteosarcoma of Tibia


Hair on End
Periosteal Reaction

Pathology: Primarily a Chondroblastic (Cartilaginous) Tumor with Bone (Osteoid) Production



Malignant Appearing Cartilage



Osteoid Production Identified in Various Areas of Tumor

Periosteal Osteosarcoma

- Radiographic Differential Diagnosis:
  - Parosteal osteosarcoma
  - High grade surface osteosarcoma
  - Periosteal chondrosarcoma
  - Myositis ossificans

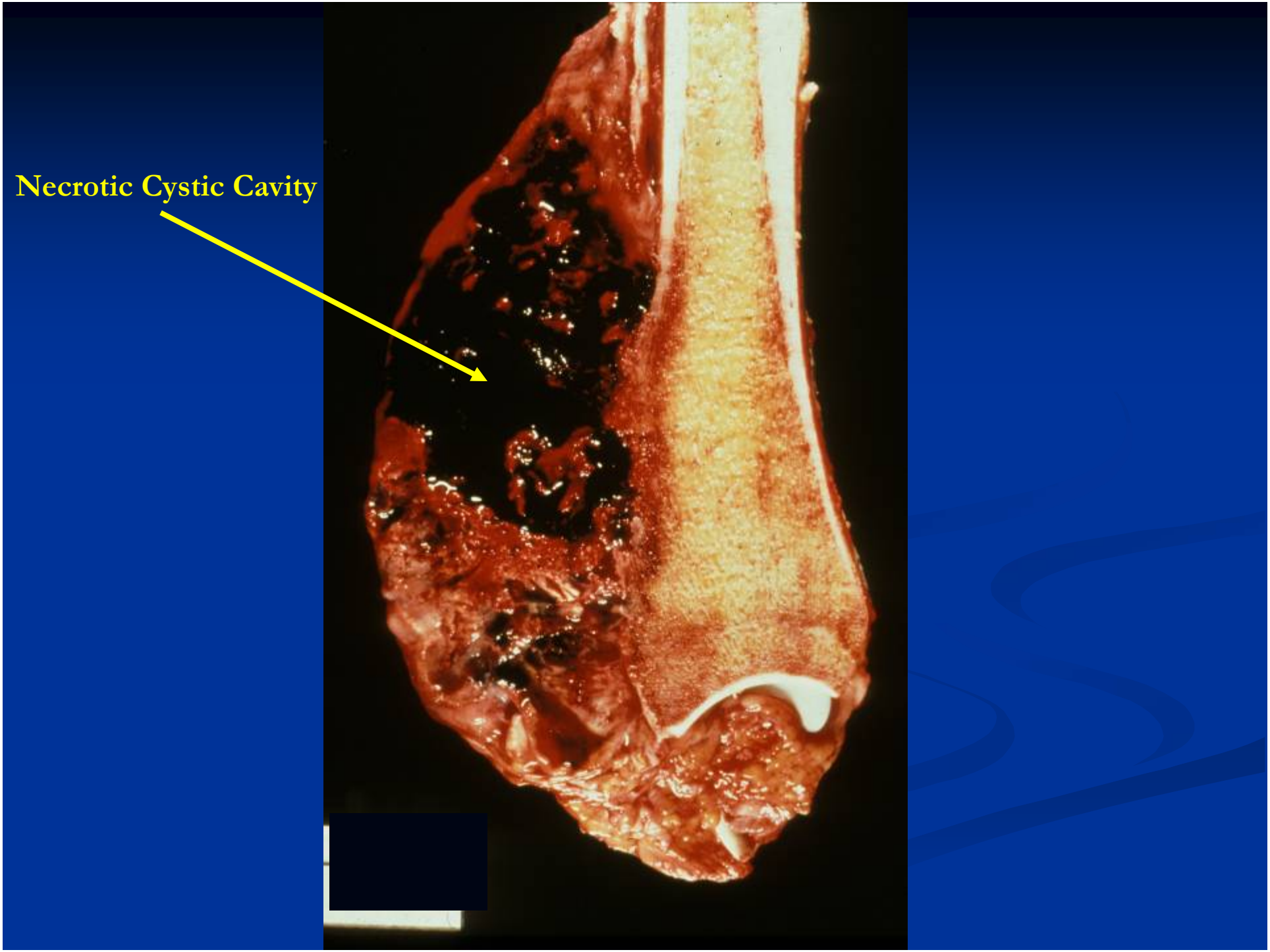
Periosteal Osteosarcoma

- Pathologic Differential Diagnosis:
  - Periosteal chondroma
  - Periosteal chondrosarcoma
  - High grade surface osteosarcoma
  - Conventional osteosarcoma with chondroblastic component

Periosteal Osteosarcoma

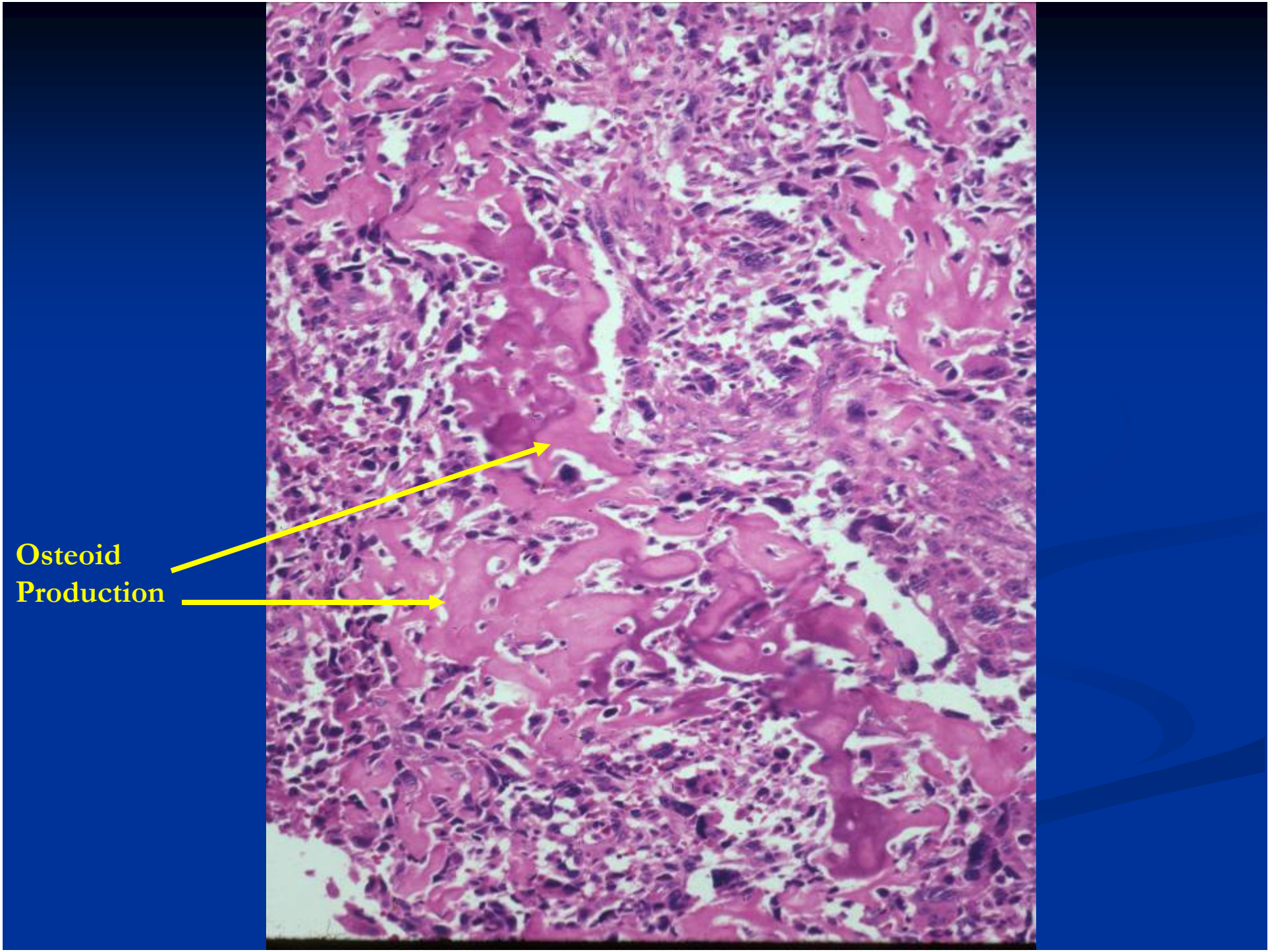
- Treatment:
  - En bloc resection and reconstruction
- Prognosis:
  - 15-25% metastatic rate to lungs
  - Role of chemotherapy is questionable

High Grade Surface Osteosarcoma of Distal Tibia


Necrotic Cystic Cavity

Pathology

- Microscopically, a high grade surface osteosarcoma looks the same as a conventional intramedullary osteosarcoma


Osteoid
Production

High Grade Surface Osteosarcoma

- Radiographic Differential Diagnosis:
  - Periosteal osteosarcoma
  - Parosteal osteosarcoma
  - Periosteal chondrosarcoma

High Grade Surface Osteosarcoma

- Pathologic Differential Diagnosis:
  - Myositis ossificans
  - Periosteal osteosarcoma
  - Conventional osteosarcoma with prominent soft tissue extension
  - Parosteal osteosarcoma

High Grade Surface Osteosarcoma

- Treatment and Prognosis:
  - Same as conventional osteosarcoma

Low Grade Intramedullary Osteosarcoma of Distal Femur

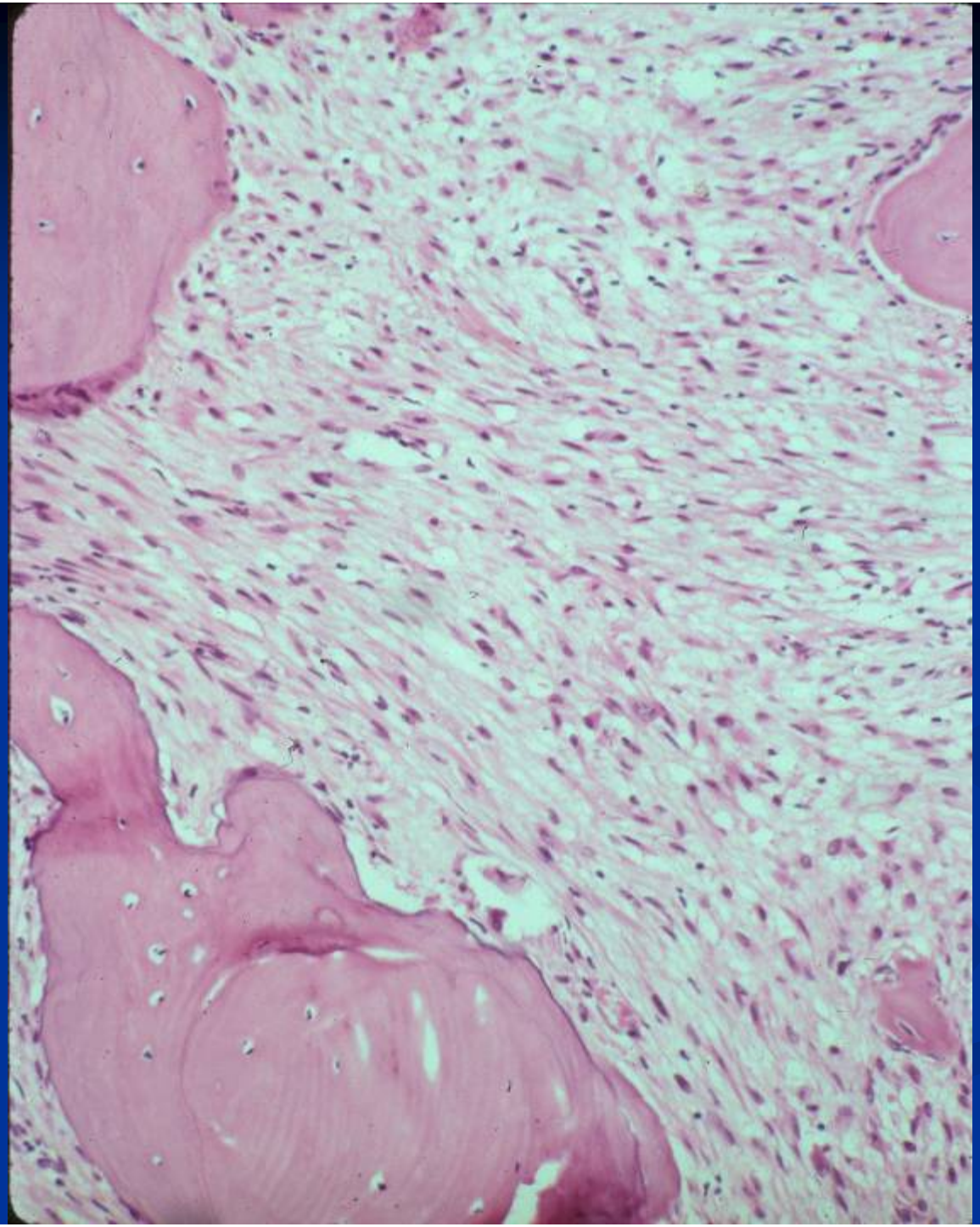
Ossification

Breaking through Cortex

Pathology

- Microscopically, low grade intramedullary osteosarcoma looks similar to a parosteal osteosarcoma
- Fibroblastic tumor producing bone (osteoid/immature bone)
- Minimal nuclear atypia, mildly hypercellular, minimal mitotic figures


Osteoid
Production



Low Grade Intramedullary

- Radiographic Differential Diagnosis:
  - Fibrous dysplasia
  - Giant cell tumor
  - Ordinary osteosarcoma
  - Fibrosarcoma
  - Malignant fibrous histiocytoma

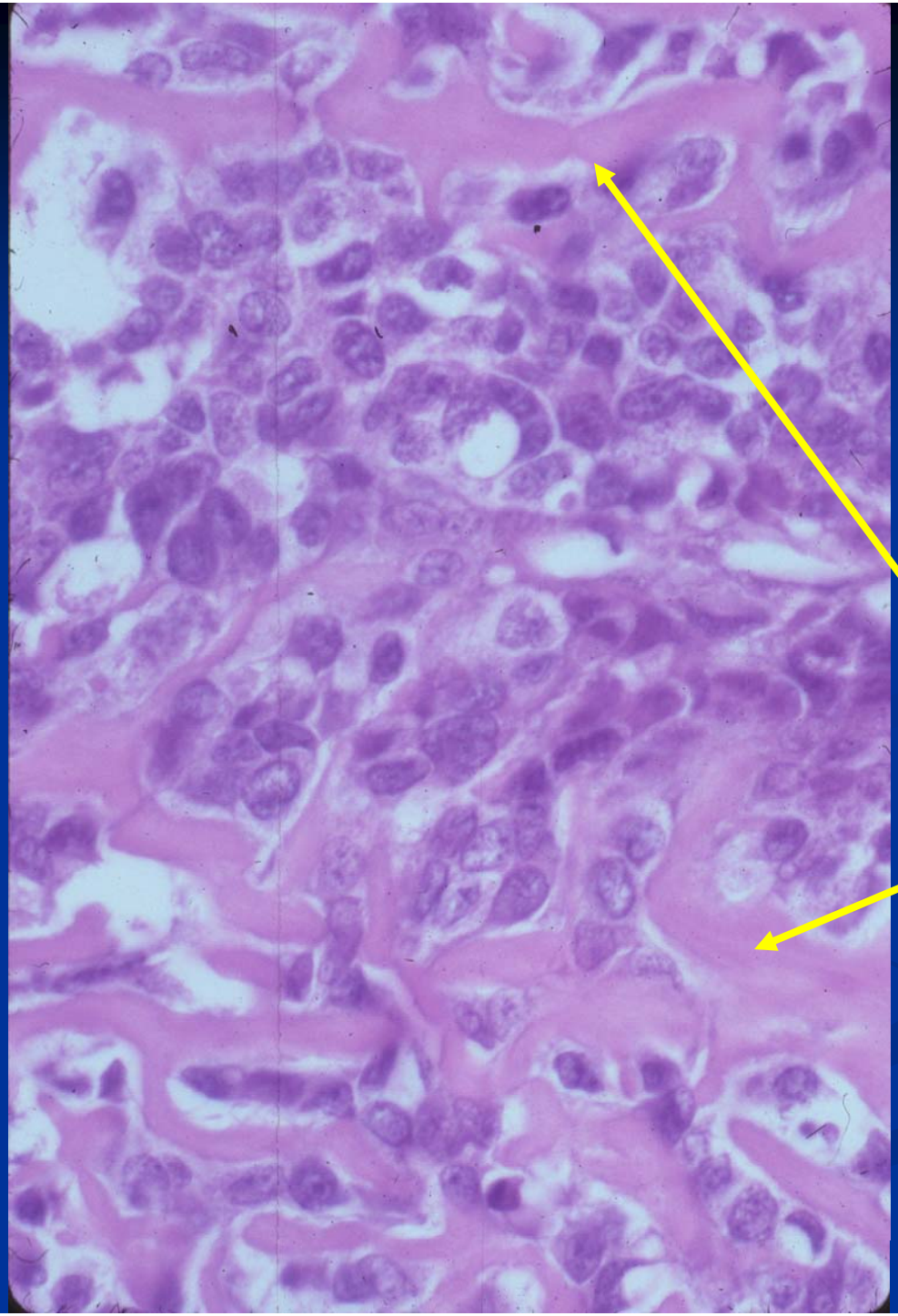
Low Grade Intramedullary

- Pathologic Differential Diagnosis:
  - Fibrous dysplasia
  - Osteofibrous dysplasia
  - Conventional osteosarcoma
  - Parosteal osteosarcoma

Low Grade Intramedullary

- Treatment:
  - Surgical resection and reconstruction
  - No chemotherapy unless dedifferentiation is present
- Prognosis:
  - 90% cure rate (<10% metastatic rate)

Intracortical Osteosarcoma


Osteoid
Production

Intracortical Osteosarcoma

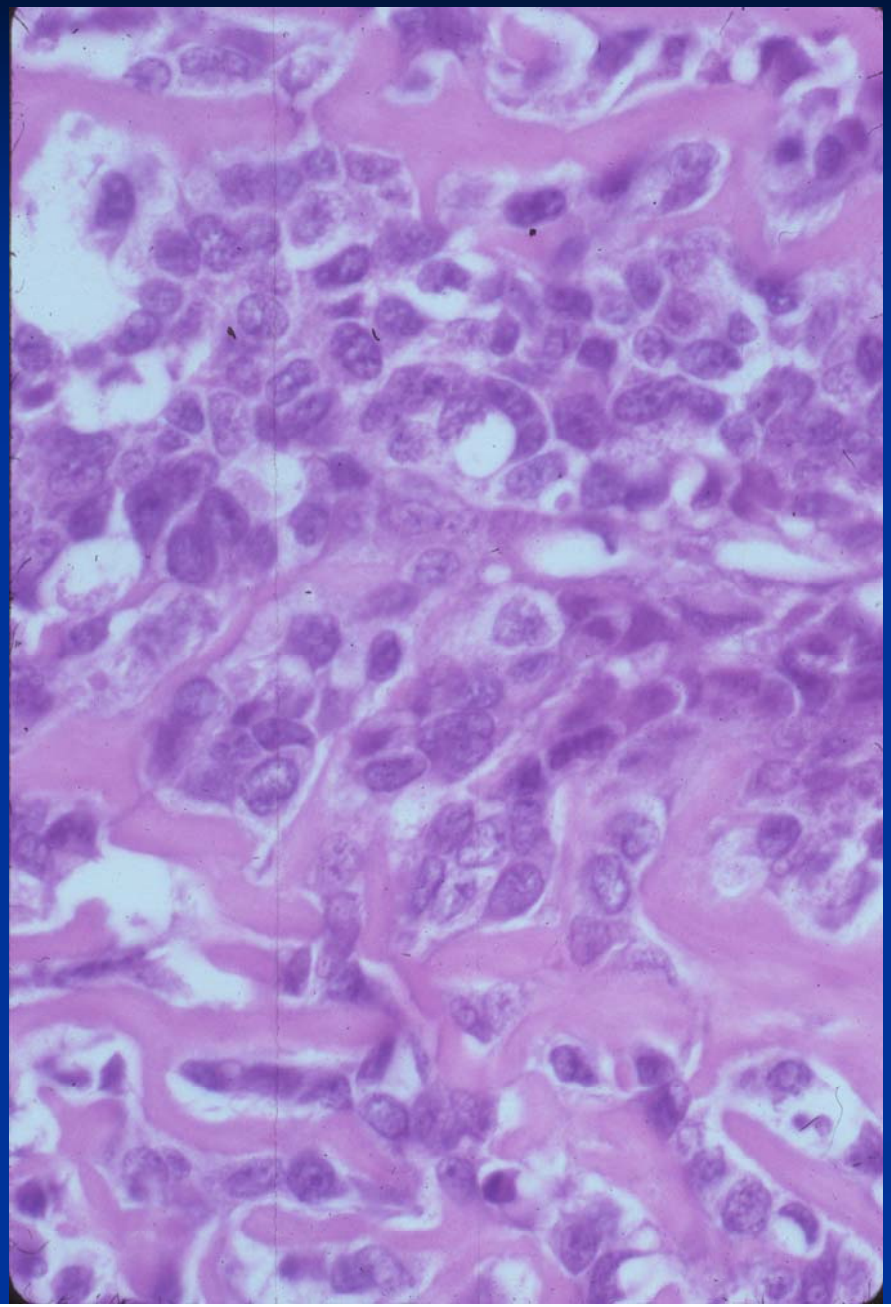
- Differential Diagnosis:
  - Stress fracture
  - Osteoid osteoma
  - Osteoblastoma
  - Intracortical abscess
  - Fibrous dysplasia
  - Nonossifying fibroma
  - Adamantinoma

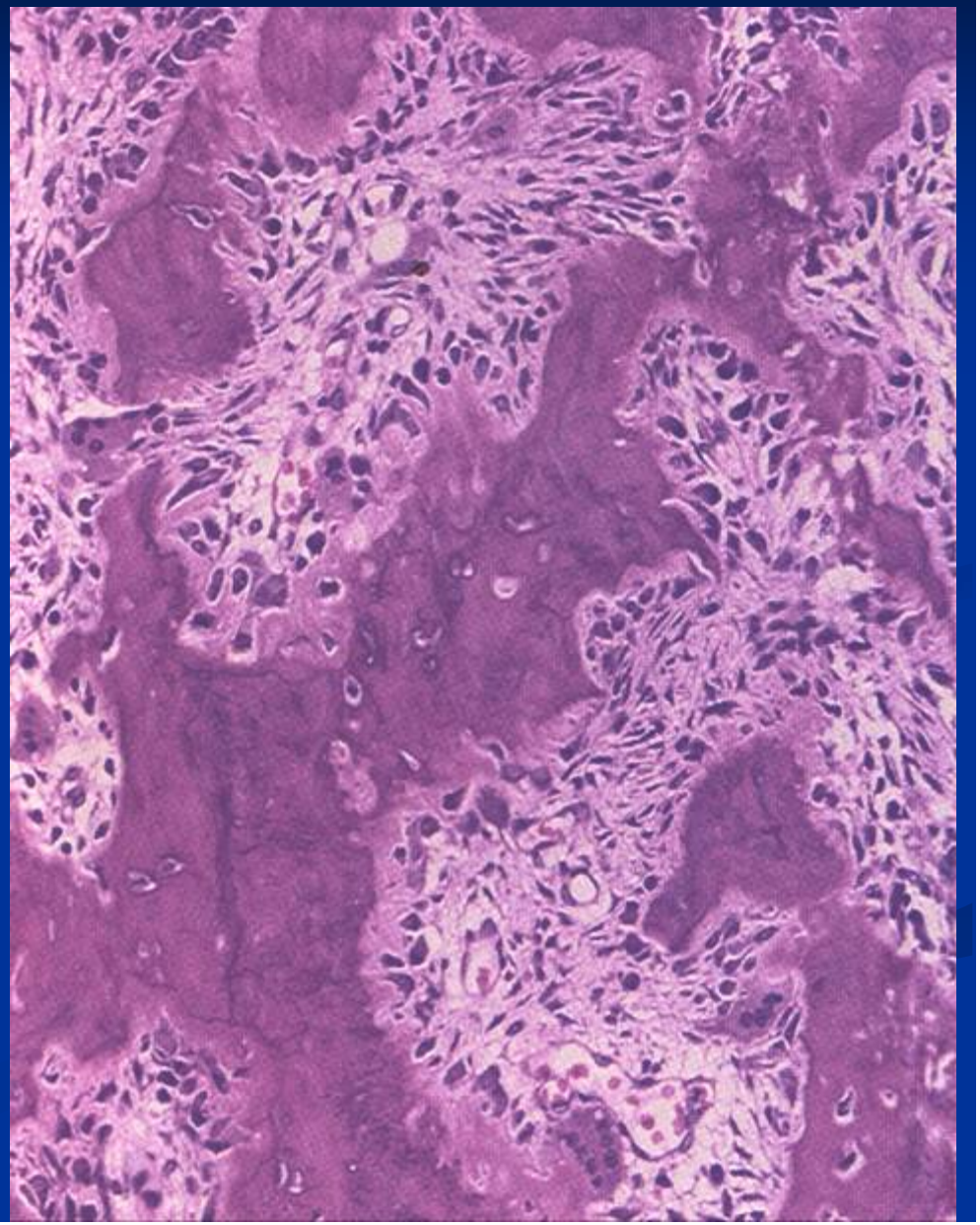
Intracortical Osteosarcoma

- Treatment:
  - En bloc resection
  - Chemotherapy

Osteosarcoma vs Osteoblastoma

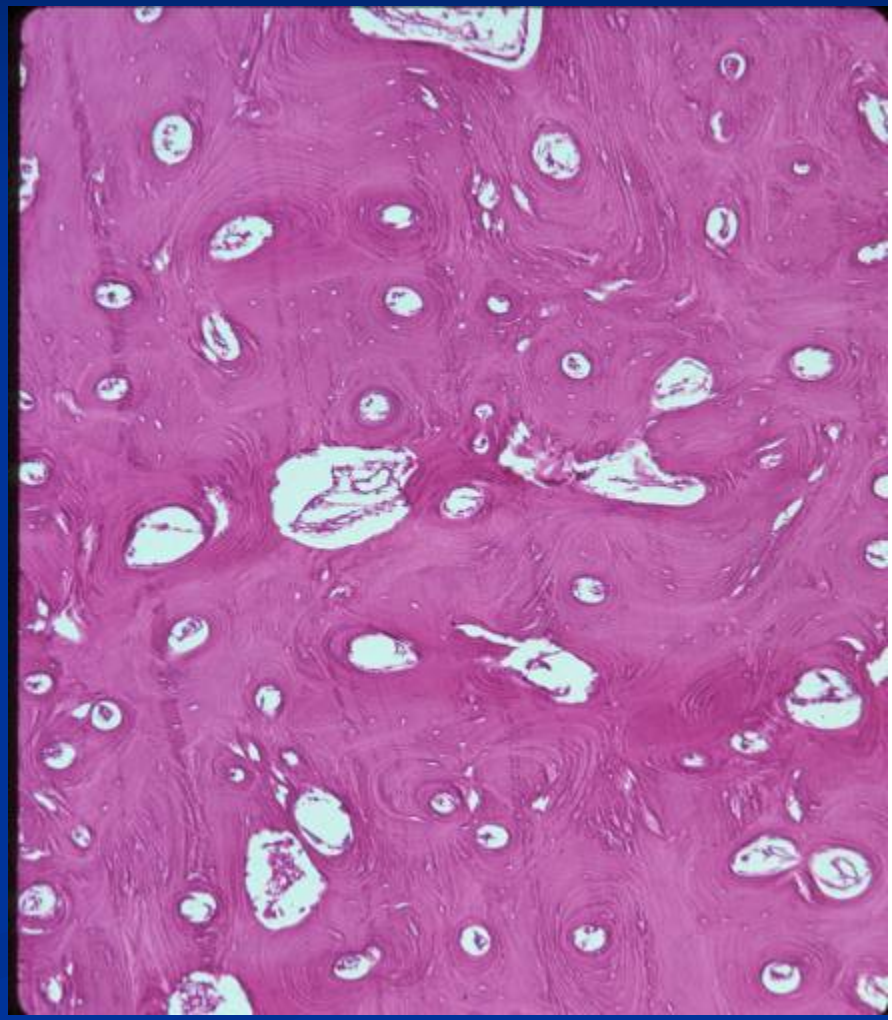
Osteosarcoma vs Osteoblastoma





Parosteal Osteosarcoma vs Osteoma

Parosteal Osteosarcoma vs Osteoma



Surface Lesions of Bone: Differential Diagnosis of Parosteal Osteosarcoma

Parosteal osteoma

Parosteal osteosarcoma

Sessile osteochondroma

Juxtacortical myositis ossificans

Periosteal osteoblastoma

Ossified parosteal (periosteal) lipoma

Melorheostosis (monostotic)