CHS: an Overview of WHO Classification

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Chondrogenic tumours
- Subungual exostosis
- Bizarre parosteal osteochondromatous proliferation
- Periosteal chondroma
- Enchondroma
- Osteochondroma
- Chondroblastoma
- Chondromyxoid fibroma
- Osteochondromyxoma
- Synovial chondromatosis
- Central atypical cartilaginous tumour / chondrosarcoma, grade 1
- Secondary peripheral atypical cartilaginous tumour / chondrosarcoma, grade 1
- Central chondrosarcoma, grades 2 and 3
- Secondary peripheral chondrosarcoma, grades 2 and 3
- Periosteal chondrosarcoma
- Clear cell chondrosarcoma
- Mesenchymal chondrosarcoma
- Dedifferentiated chondrosarcoma

Osteogenic tumours
- Osteoma
- Osteoid osteoma
- Osteoblastoma
- Low-grade central osteosarcoma
- Osteosarcoma
- Parosteal osteosarcoma
- Periosteal osteosarcoma
- High-grade surface osteosarcoma
- Secondary osteosarcoma

Fibrogenic tumours
- Desmoplastic fibroma of bone
- Fibrosarcoma of bone

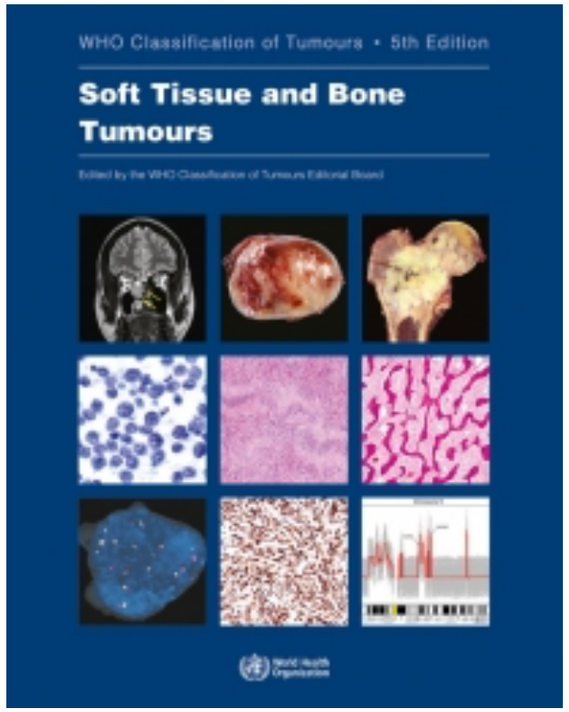
Vascular tumours of bone
- Haemangioma of bone
- Epithelioid haemangioma of bone
- Epithelioid haemangioendothelioma of bone
- Angiosarcoma of bone

Osteoclastic giant cell-rich tumours
- Aneurysmal bone cyst
- Giant cell tumour of bone
- Non-ossifying fibroma

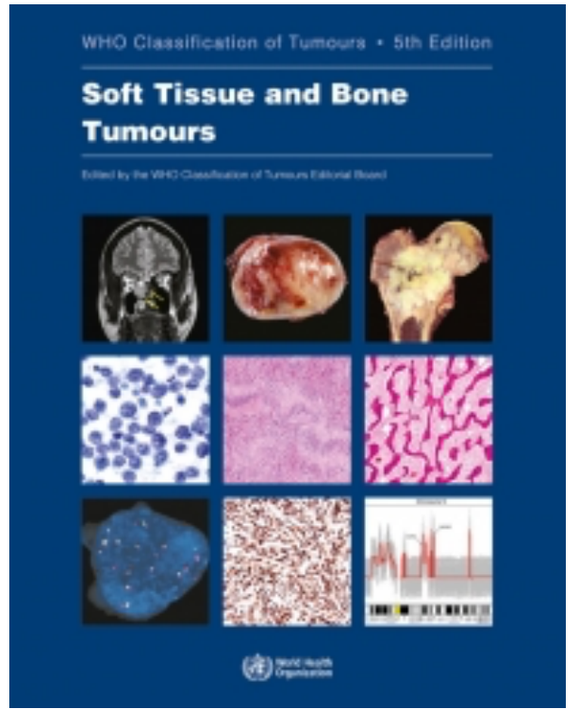
Notochordal tumours
- Benign notochordal cell tumour
- Conventional chordoma
- Dedifferentiated chordoma
- Poorly differentiated chordoma

Other mesenchymal tumours of bone
- Chondromesenchymal hamartoma of chest wall
- Osteofibrous dysplasia
- Adamantinoma of long bones
- Simple bone cyst
- Fibrocartilaginous mesenchymoma
- Fibrous dysplasia
- Lipoma and hibernoma of bone
- Leiomyosarcoma of bone
- Undifferentiated pleomorphic sarcoma
- Bone metastases

Haematopoietic neoplasms of bone
- Solitary plasmacytoma of bone
- Primary non-Hodgkin lymphoma of bone
- Langerhans cell histiocytosis
- Erdheim-Chester disease
- Rosai-Dorfman disease



58 different bone tumors!!!!



Chondrogenic tumours

- Subungual exostosis
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- Periosteal chondroma
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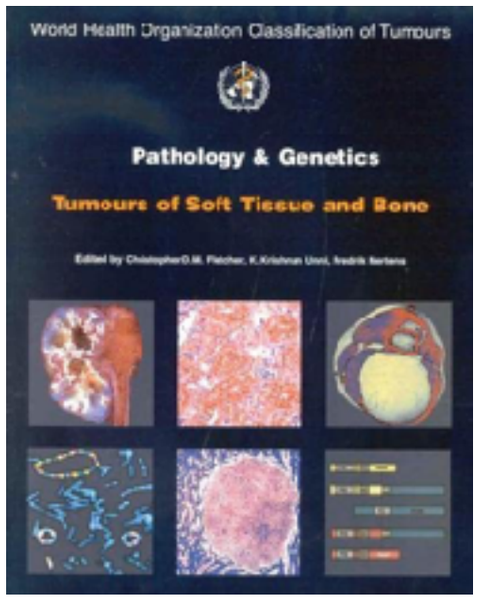
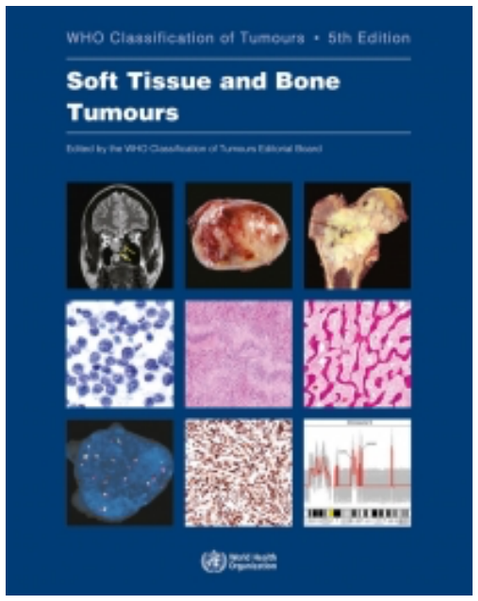
- Clear cell chondrosarcoma
- Mesenchymal chondrosarcoma
- Dedifferentiated chondrosarcoma

Kim and Lee, Cancers 2023

2013 WHO classification of chondrogenic bone tumors		
Benign	Intermediate	Malignant
Subungual exostosis	Chondroblastoma	Chondrosarcoma, grade 2
Bizarre parosteal chondromatous proliferation	Chondromyxoid fibroma	Chondrosarcoma, grade 3
Periosteal chondroma	Atypical cartilaginous tumor/Chondrosarcoma, grade 1	Clear cell chondrosarcoma
Enchondroma		Mesenchymal chondrosarcoma
Osteochondroma		Dedifferentiated chondrosarcoma
Osteochondromyxoma		
Synovial Chondromatosis		



2020 WHO classification of chondrogenic bone tumors		
Benign	Intermediate	Malignant
Subungual exostosis	Synovial Chondromatosis	Chondrosarcoma, grade 1
Bizarre parosteal chondromatous proliferation	Atypical cartilaginous tumor	Chondrosarcoma, grade 2
Periosteal chondroma		Chondrosarcoma, grade 3
Enchondroma		Clear cell chondrosarcoma
Osteochondroma		Mesenchymal chondrosarcoma
Chondroblastoma		Dedifferentiated chondrosarcoma
Chondromyxoid fibroma		
Osteochondromyxoma		



	Entity	Remarks
Conventional chondrosarcomas	Central atypical cartilaginous tumor (ACT)/chondrosarcoma grade 1 (CS1) Secondary peripheral ACT/CS1	De novo or secondary (possible precursor: enchondroma) Precursor: osteochondroma
	Central chondrosarcoma grades 2 and 3 (CS2,3)	De novo or secondary (possible precursor: enchondroma)
	Secondary peripheral CS2,3	Precursor: osteochondroma
Rare subtypes	Periosteal chondrosarcoma Dedifferentiated chondrosarcoma Mesenchymal chondrosarcoma Clear cell chondrosarcoma	Precursor: conventional chondrosarcoma

Chondrosarcoma (CS) Type	Molecular Features
Conventional central CS	IDH1/2 mutations COL2A1 mutations CDKN2A/B deletions
Conventional peripheral CS	EXT1/2 mutations
Conventional periosteal CS	Hedgehog pathway
Dedifferentiated CS	IDH1/2 mutations TP53 mutations PD-L1 expression
Mesenchymal CS	HEY1–NCOA2 fusion
Clear cell CS	No evidence of mutations

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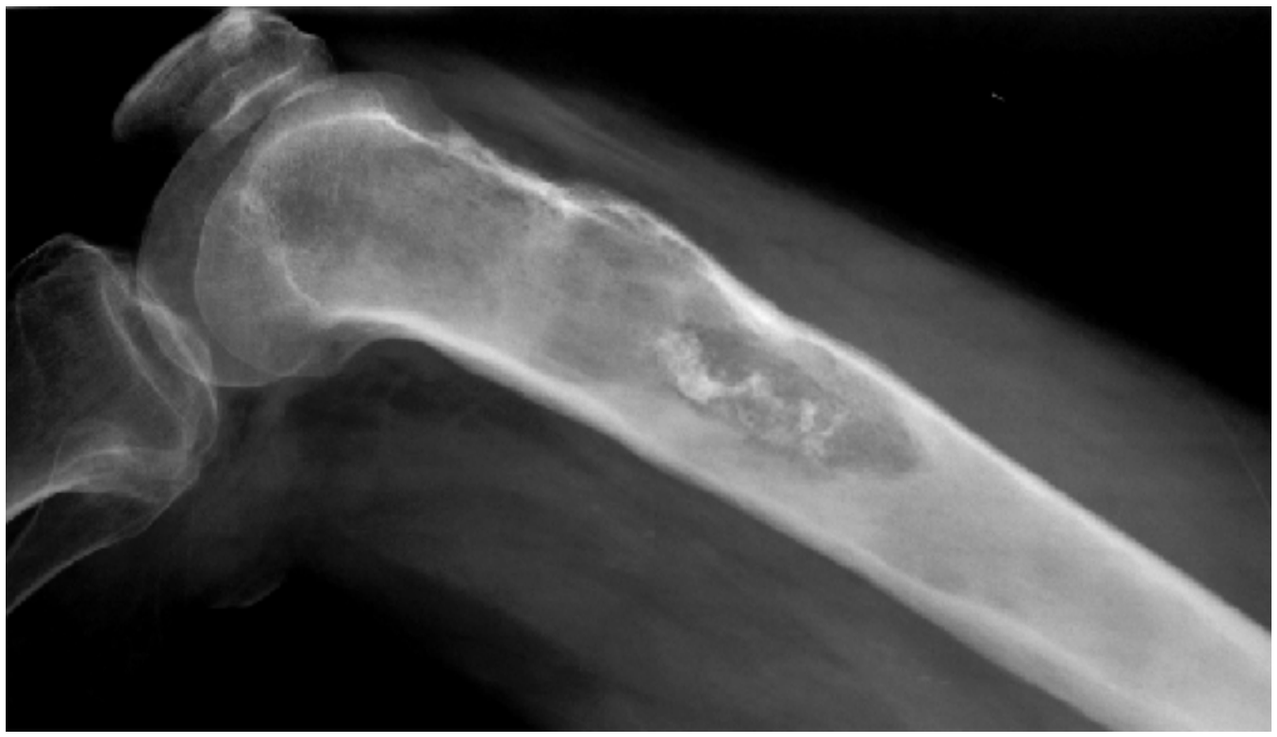

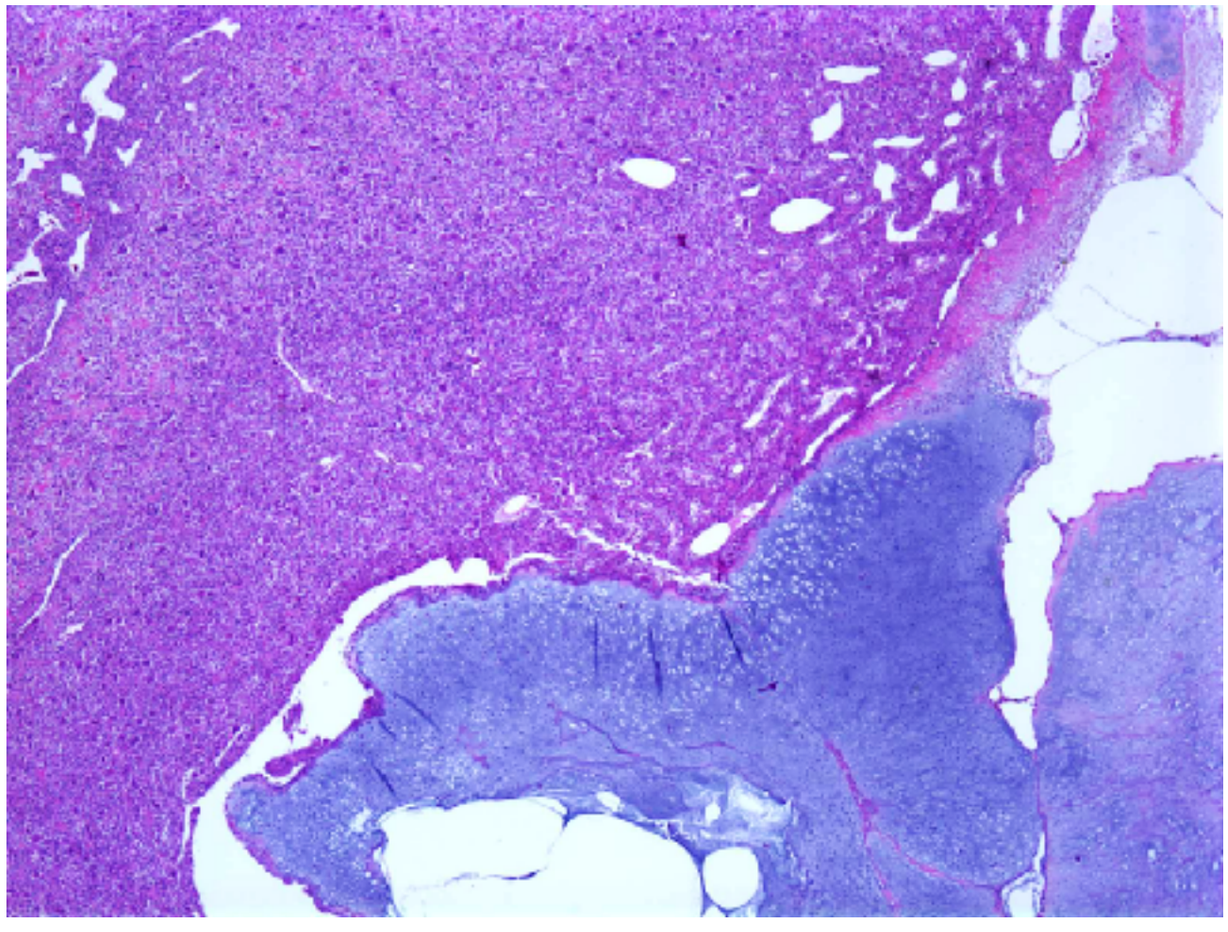

dedif/ted CHS

50-87%: IDH1 or *IDH2 mutations*
in both components
desirable diagnostic criterion! WHO 5th Ed.

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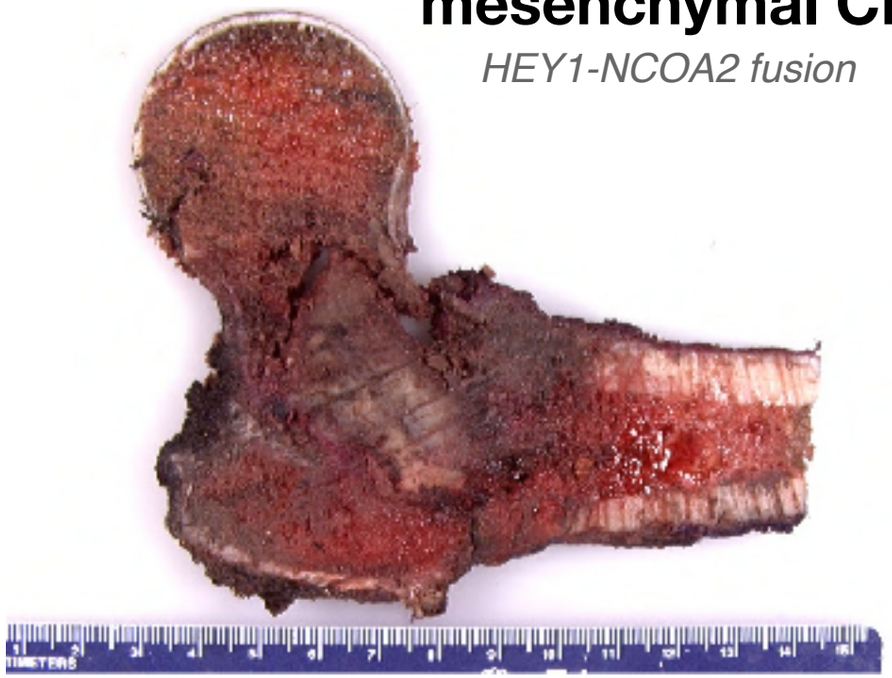
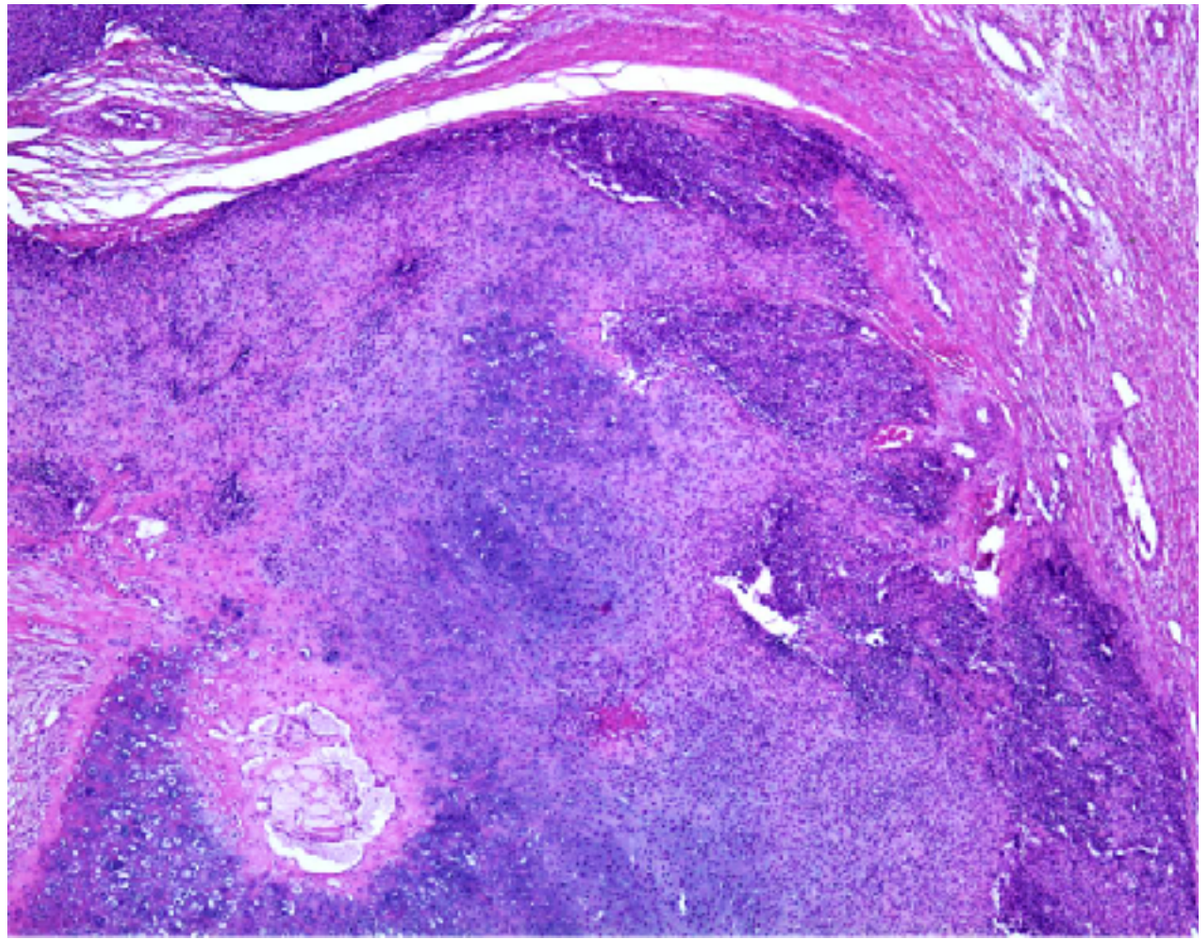
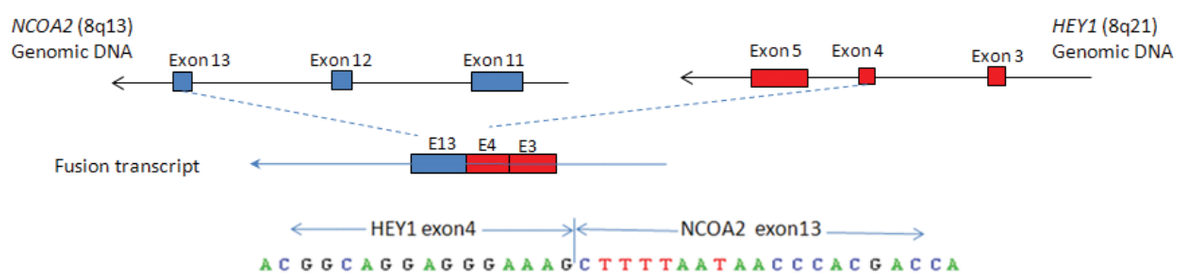
mesenchymal CHS

HEY1-NCOA2 fusion





HEY1 exon 4 to *NCOA2* exon 13 at the mRNA level
desirable diagnostic criterion! WHO 5th Ed.



Chromosomes Cancer. 2012 Feb;51(2):127-39

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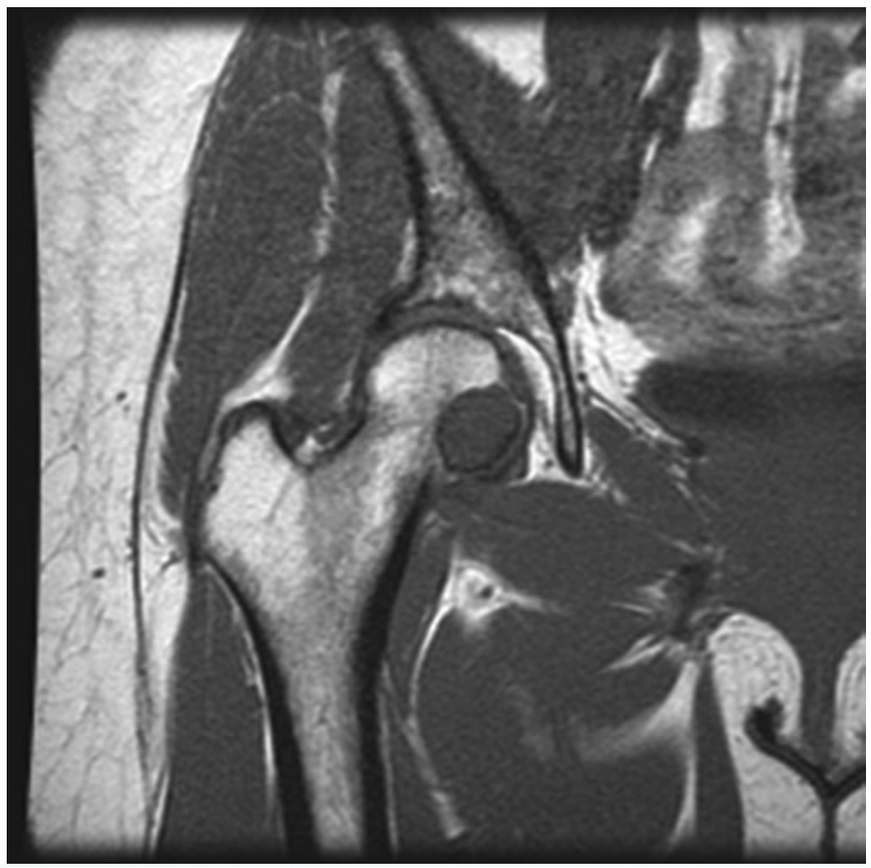
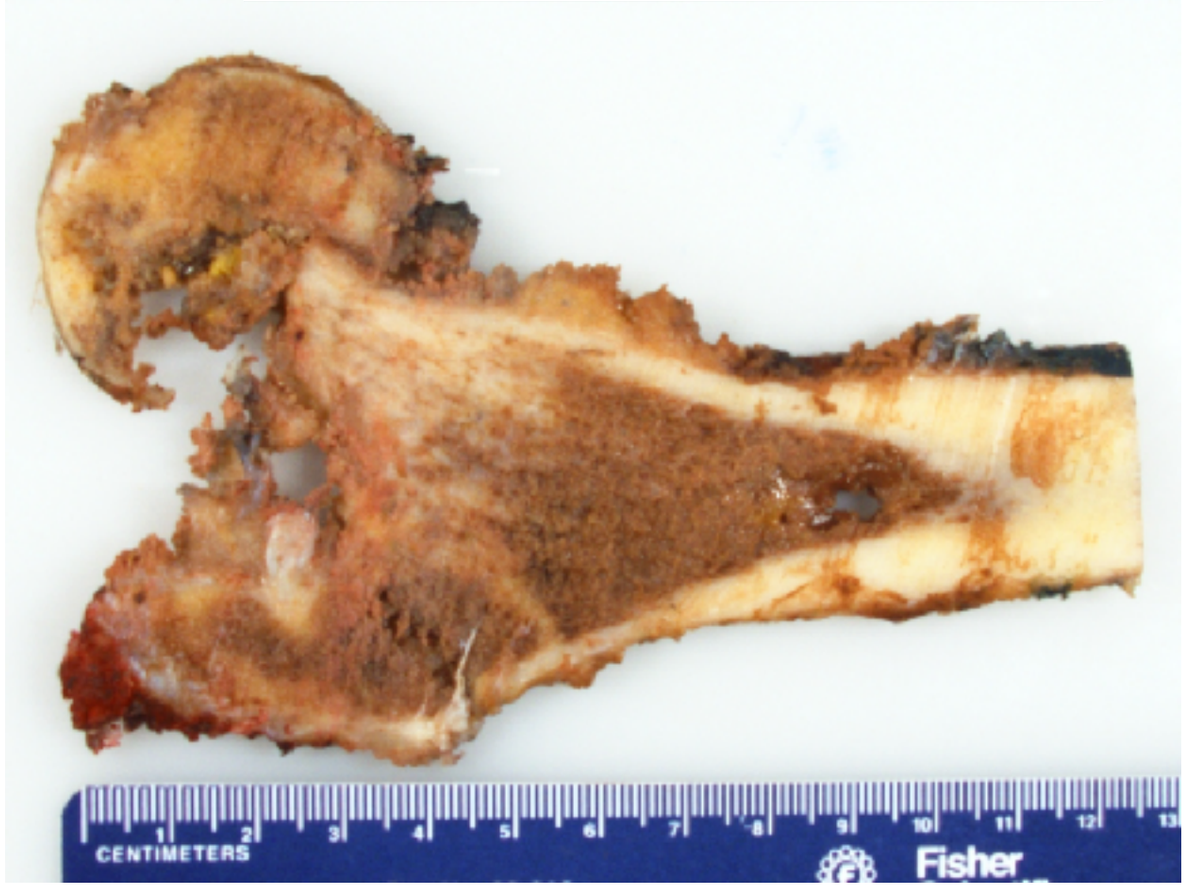
Clear Cell CHS





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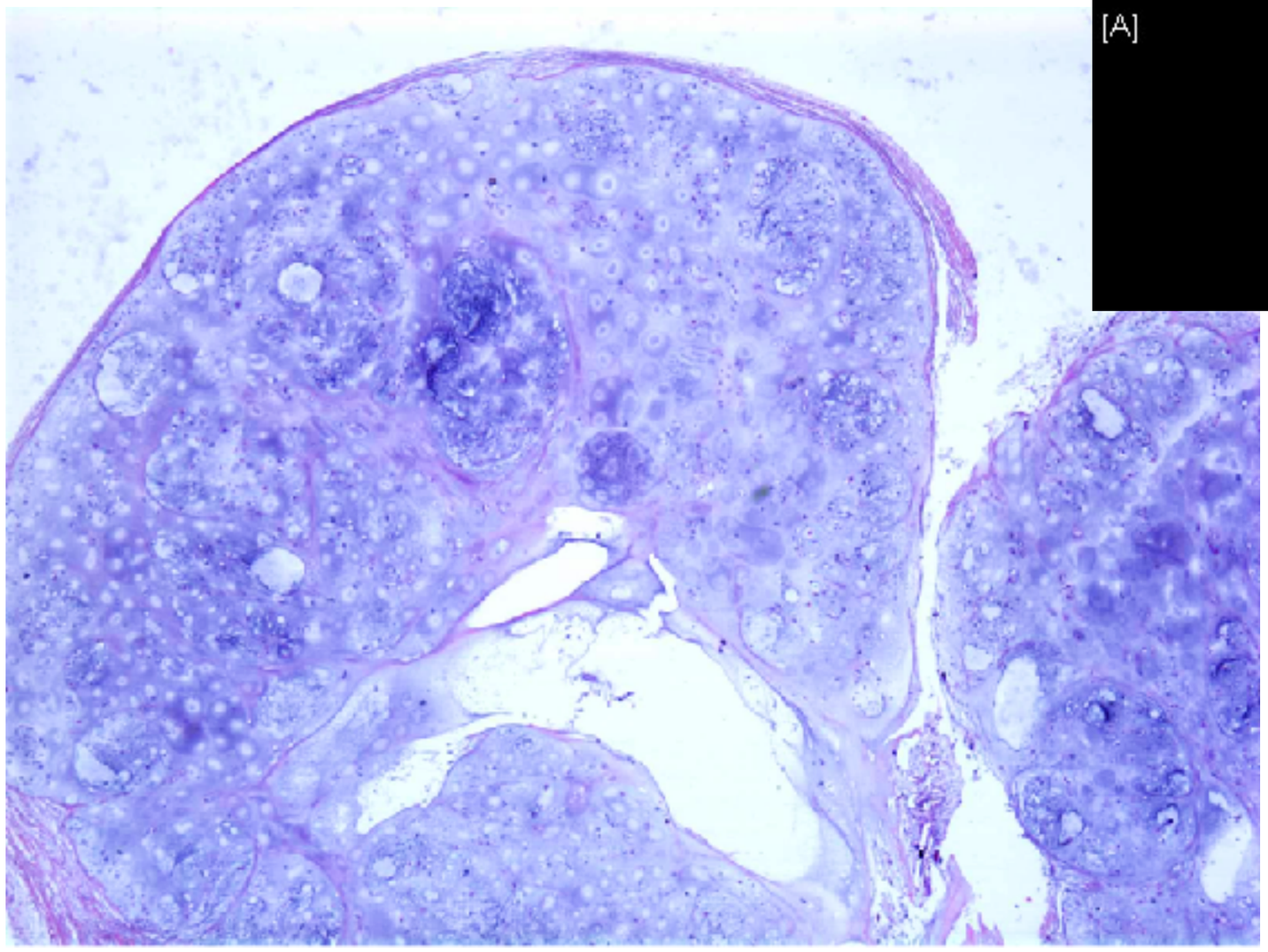
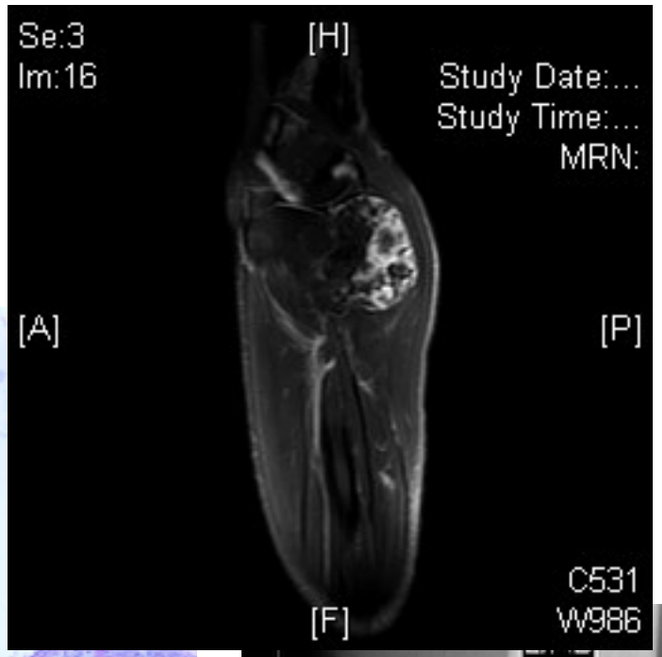
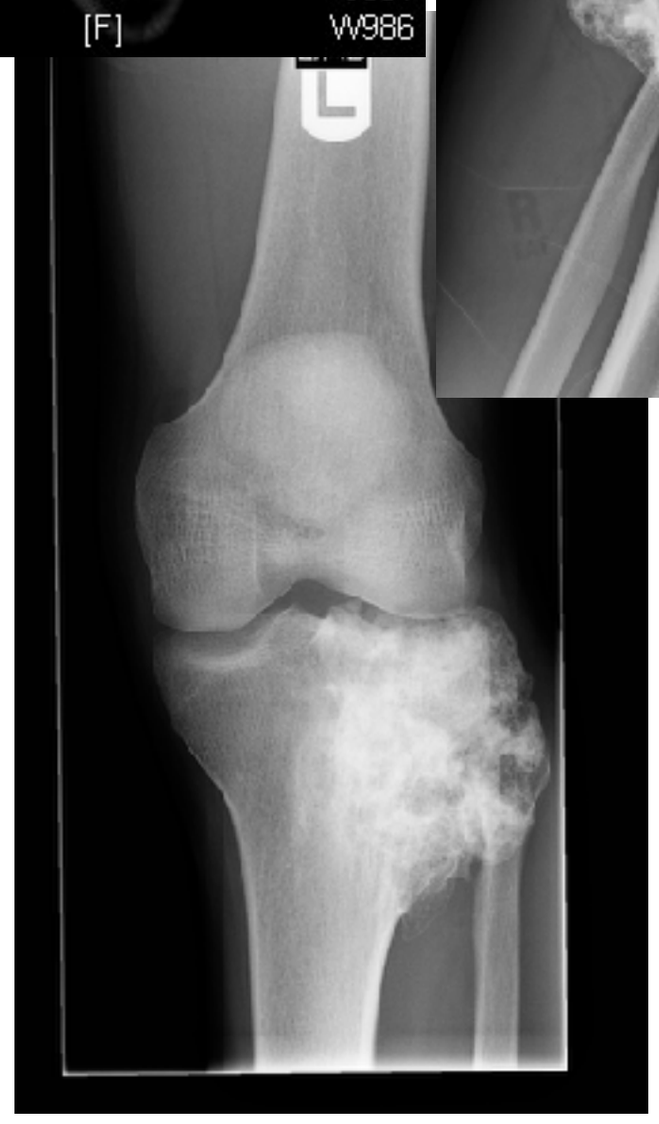
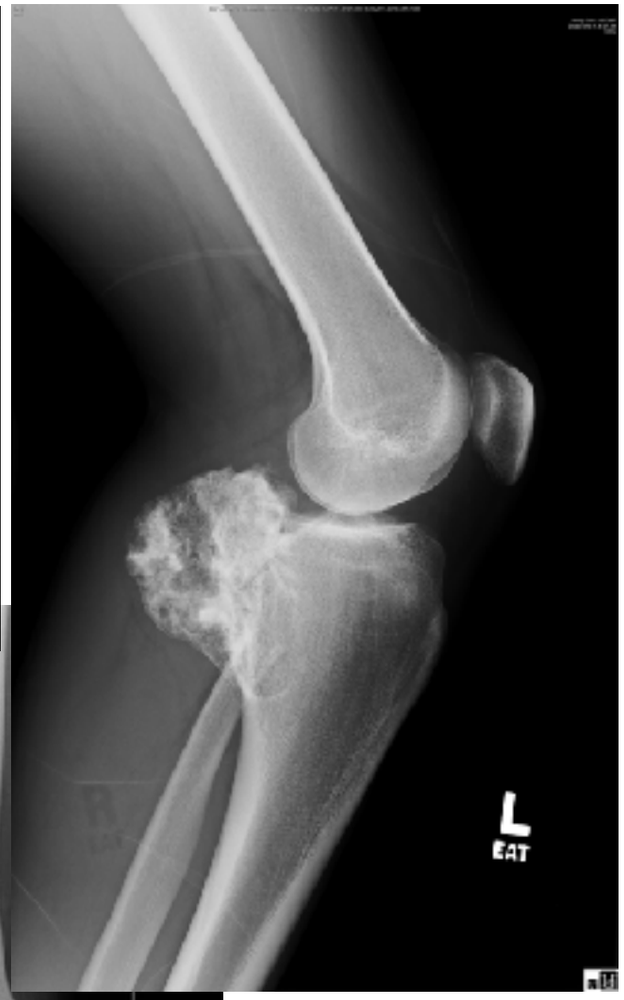
secondary peripheral CHS

EXT1 or *EXT2* mutations









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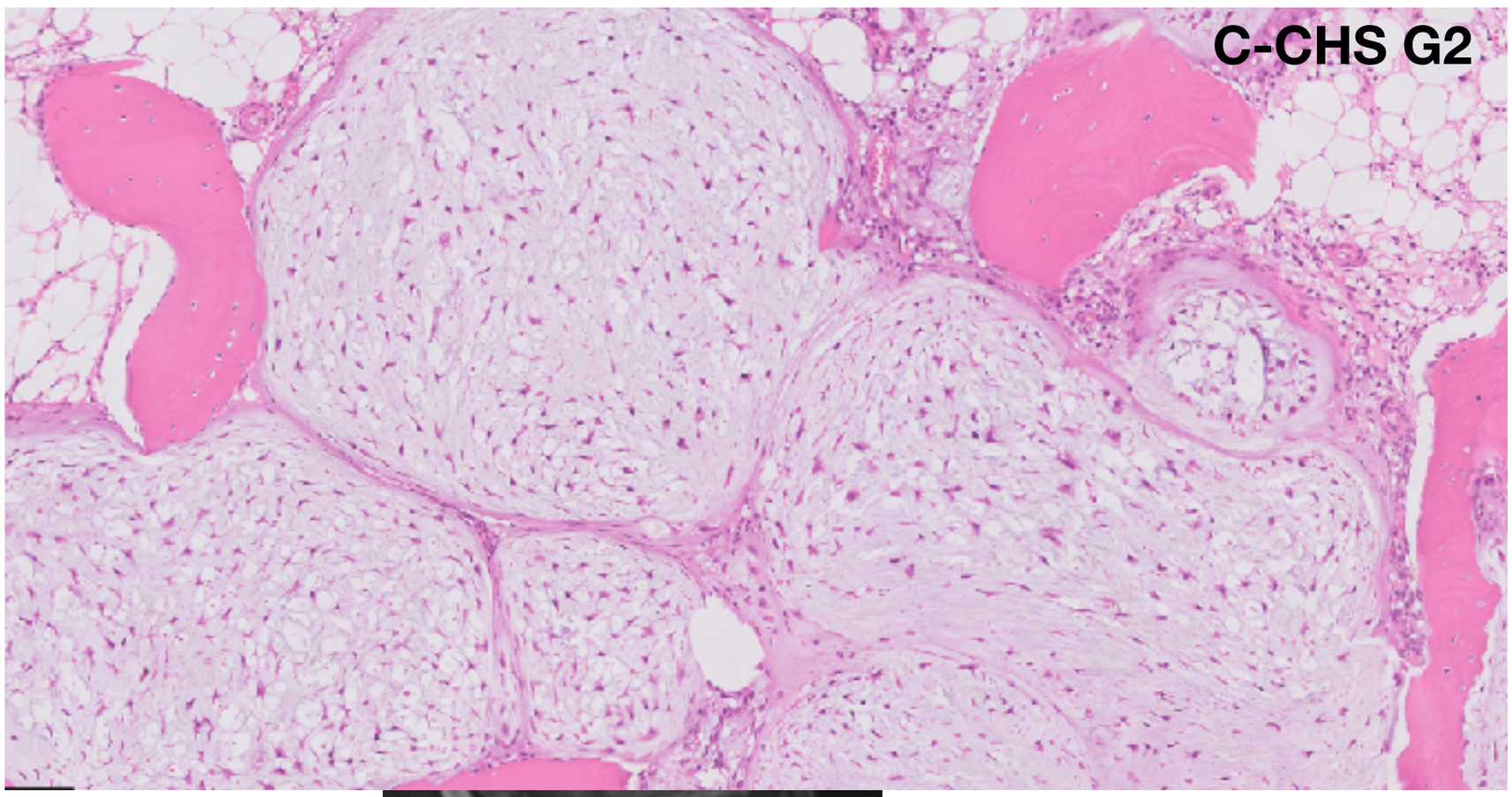
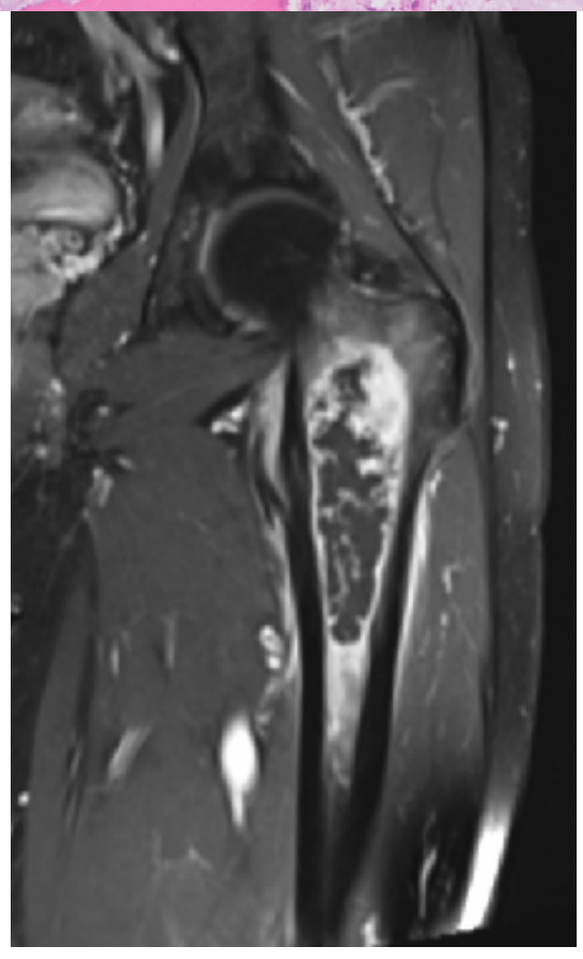
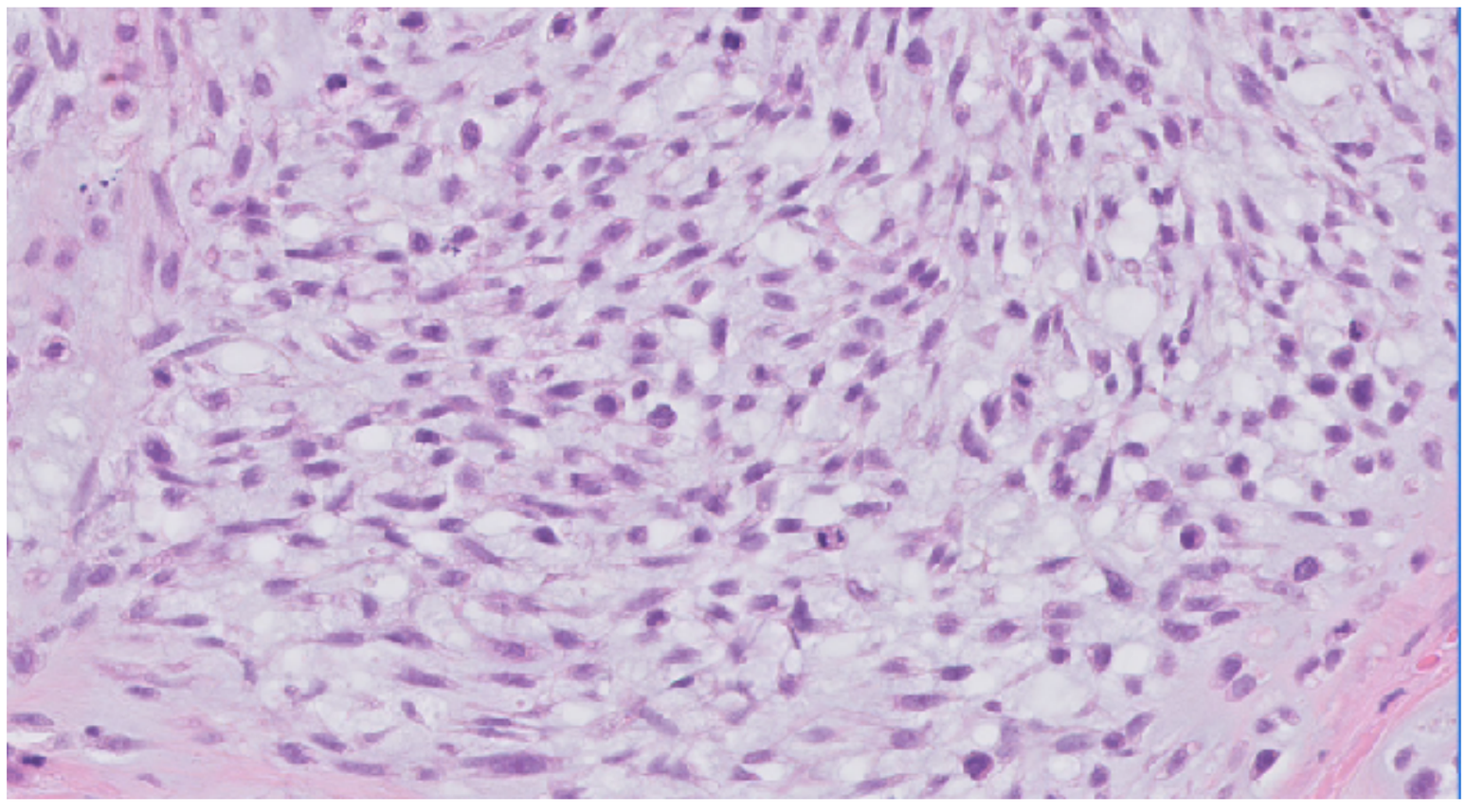
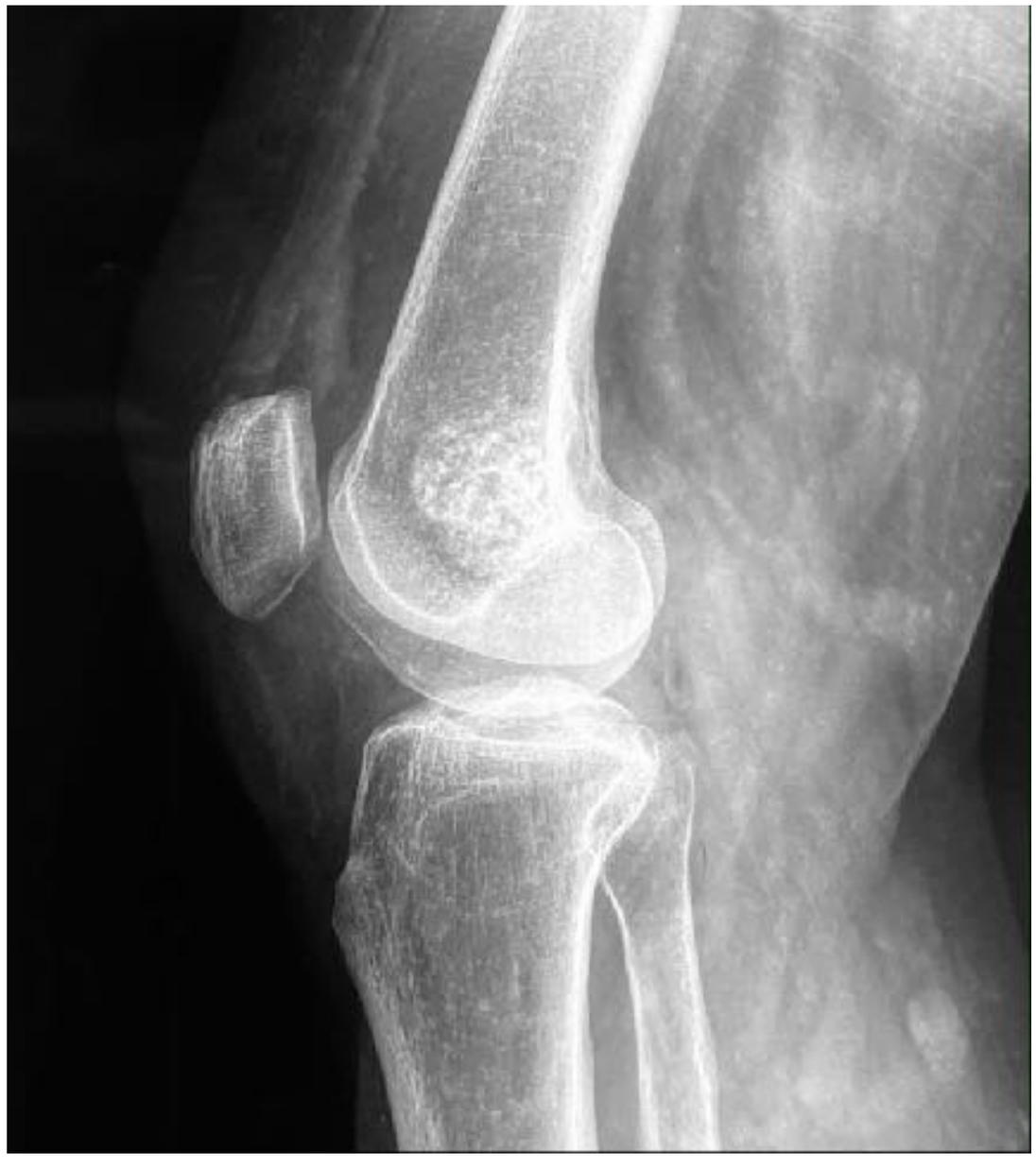
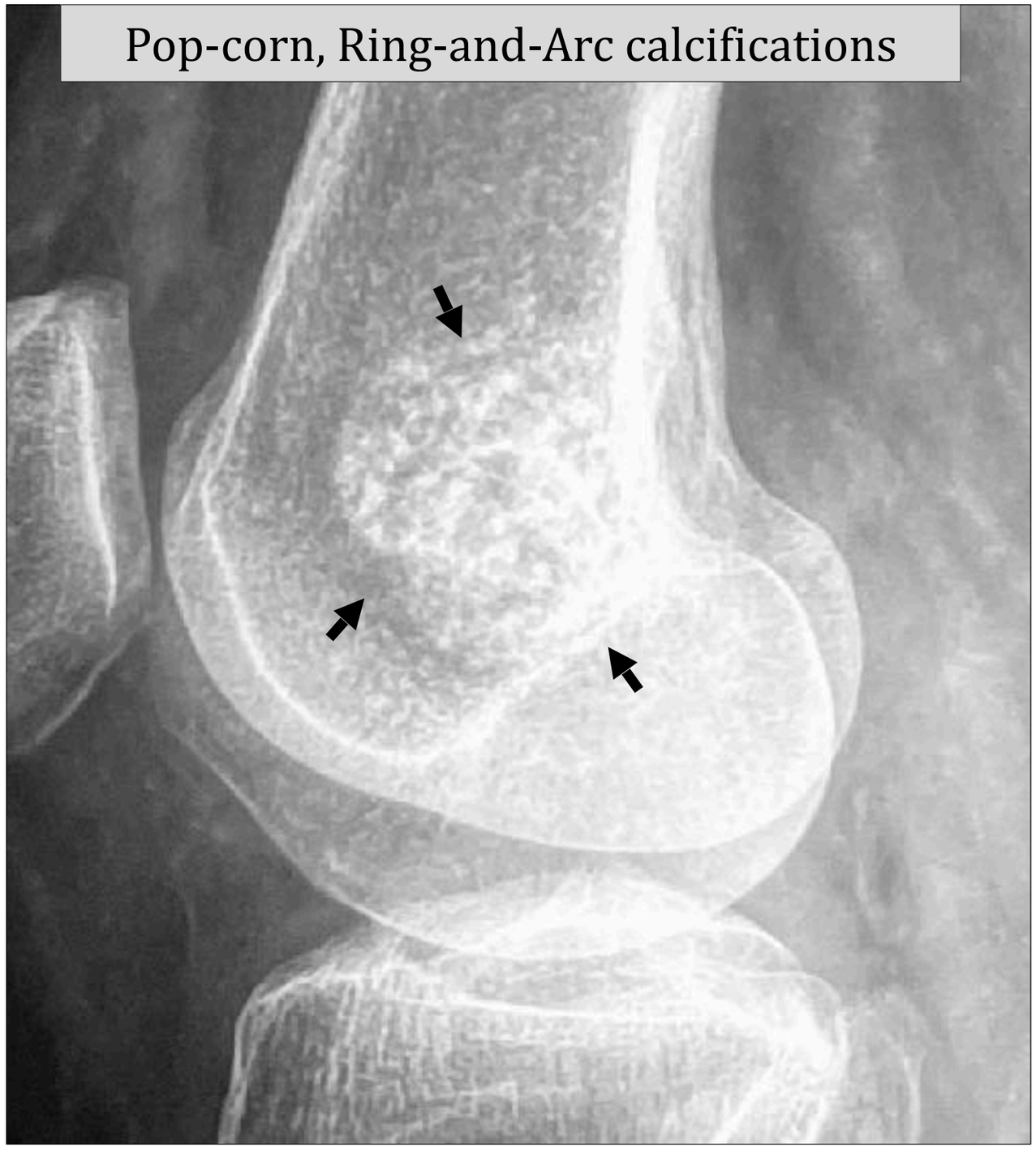

C-CHS G2




C-CHS G3

Where the shoe pinches…





Distinction between Enchondromas and ACT/G1 CHS

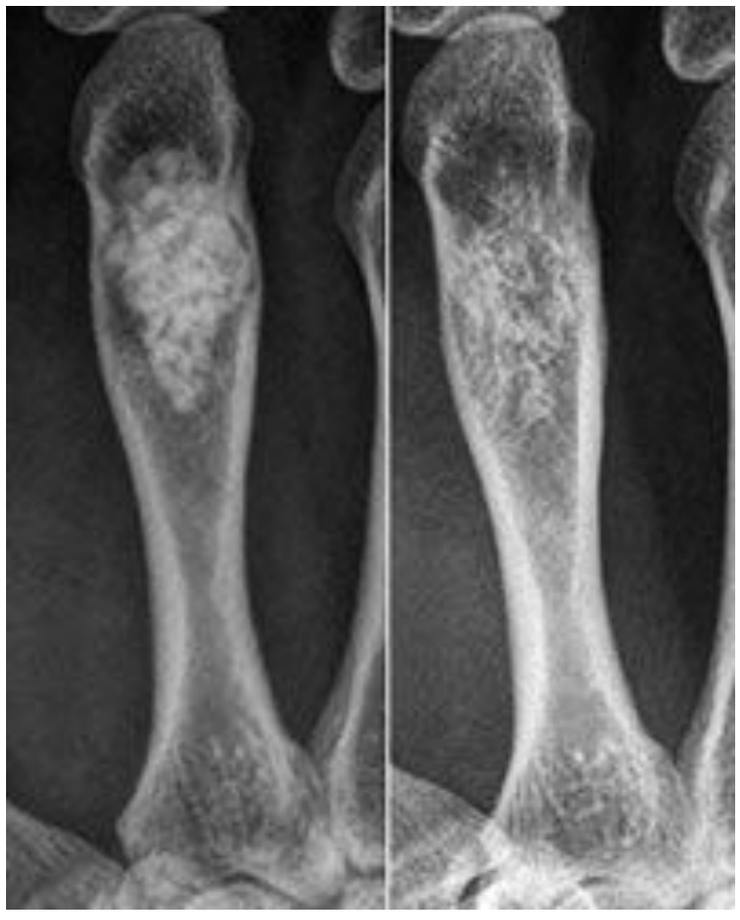
- Radiology many times does not help
- There are no reliable biomarkers
- The Dx is primarily based upon histopathology
- Tumor board is required

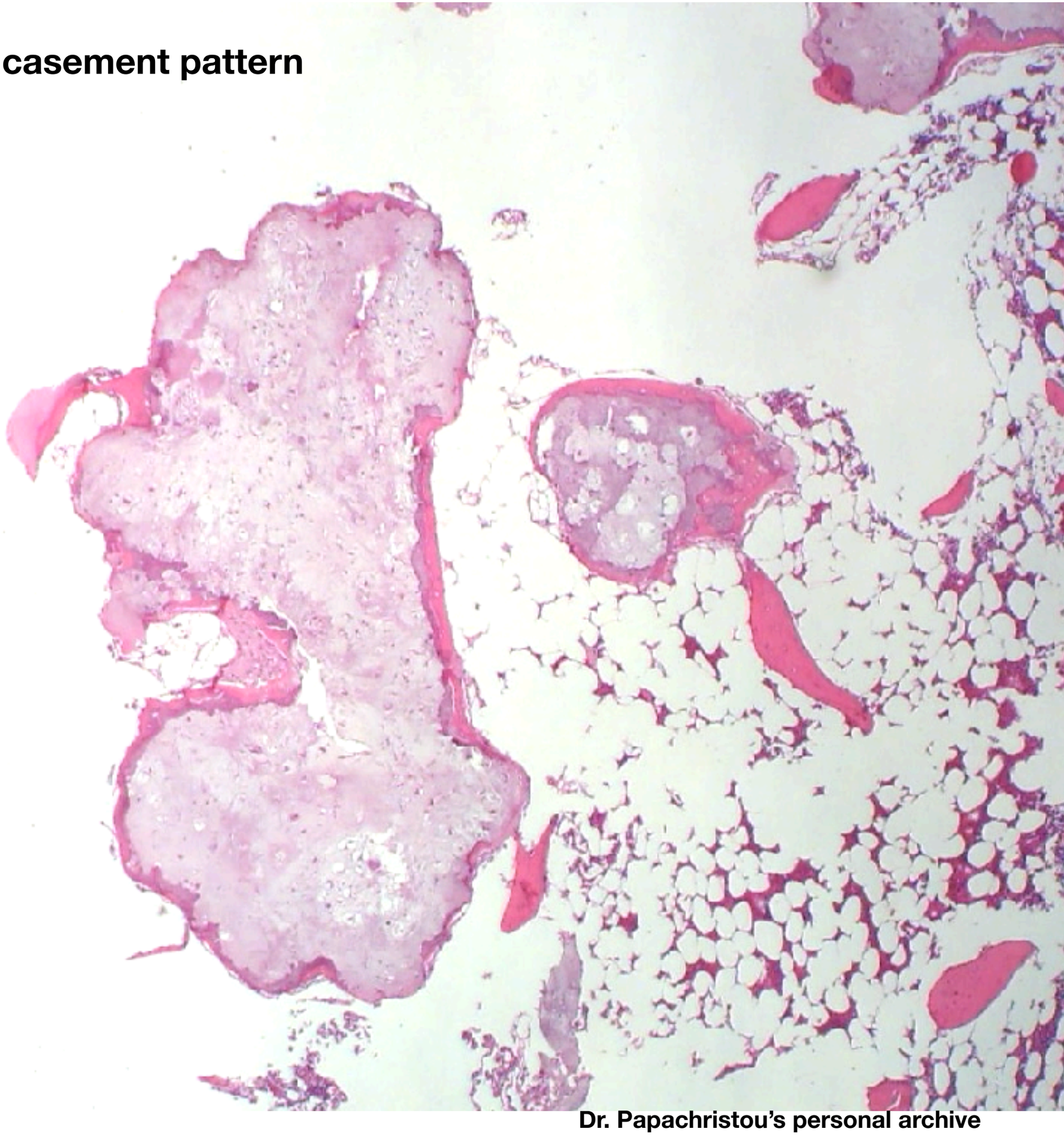
cartilaginous lesions patterns

A. BM islands pattern
B. Encasement
C. Permeation pattern
D. Cells and ECM

BM islands - Encasement pattern

Pop-corn, Ring-and -Arc calcifications





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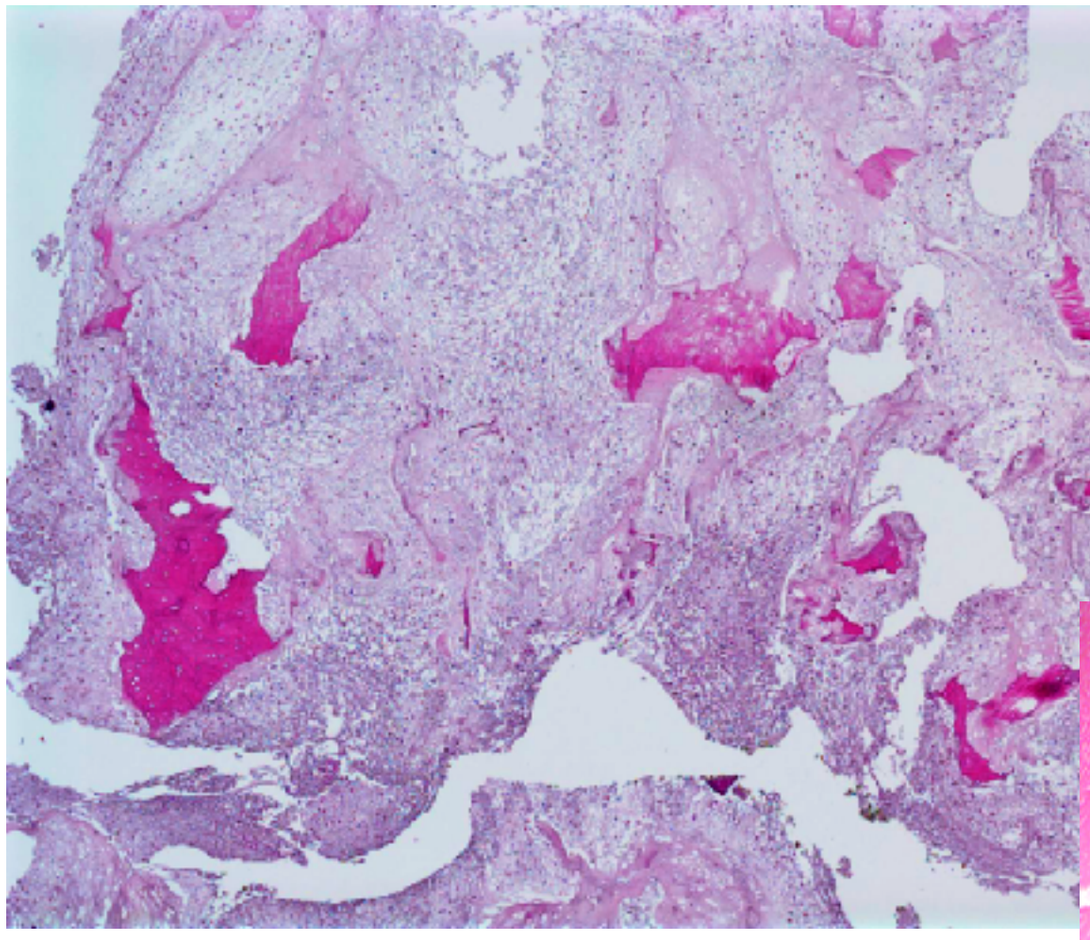
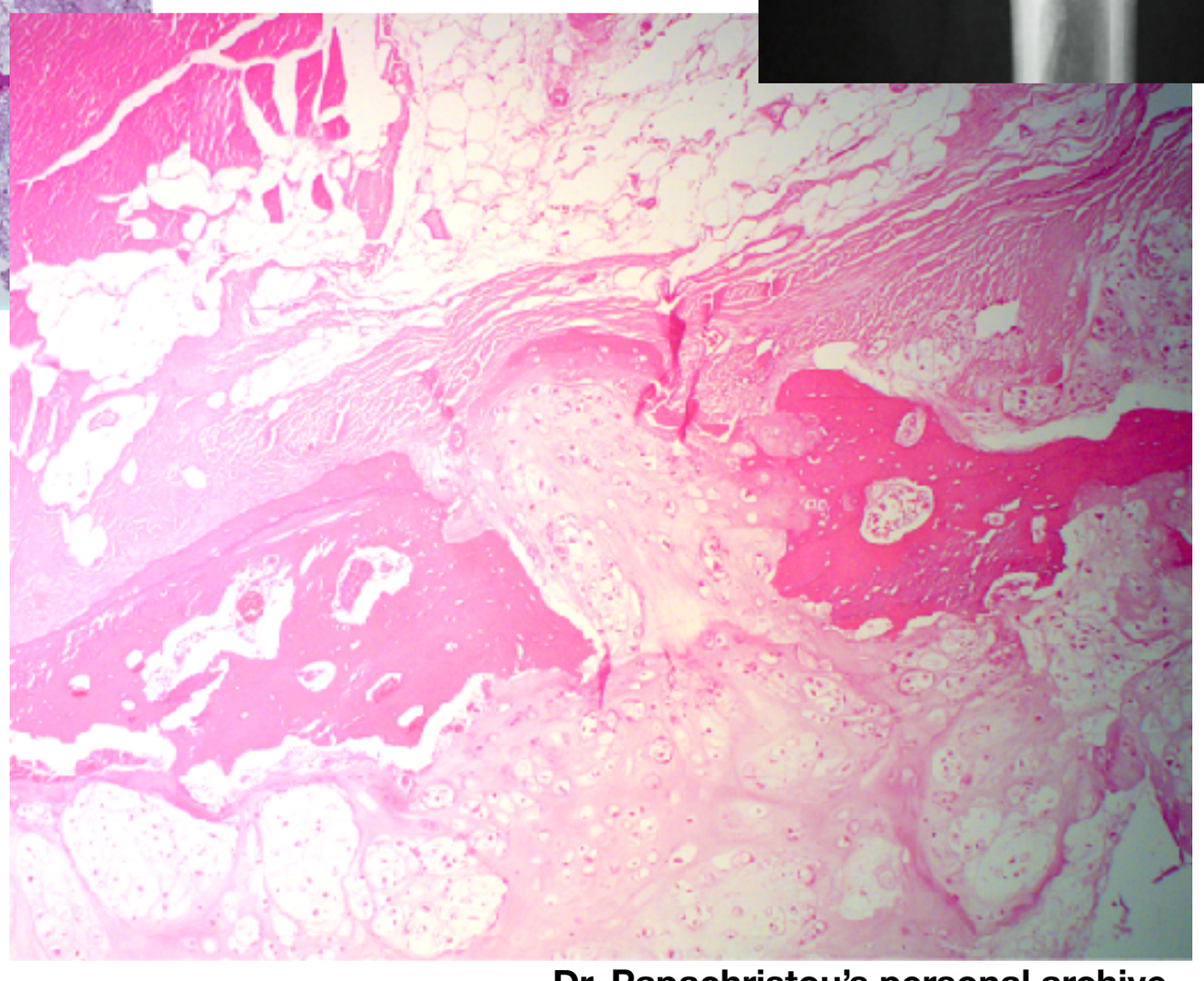
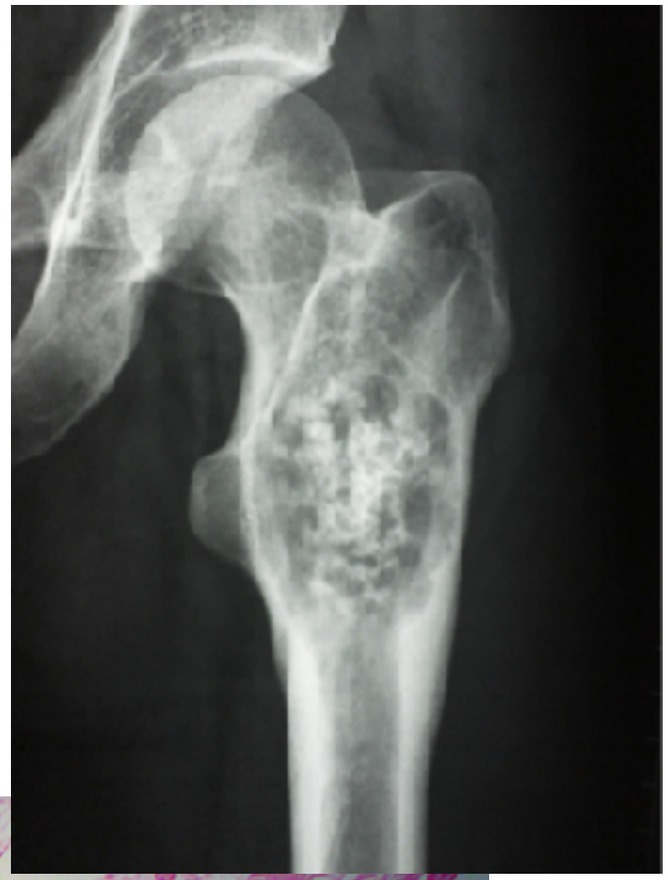
Enchondroma

Permeation pattern







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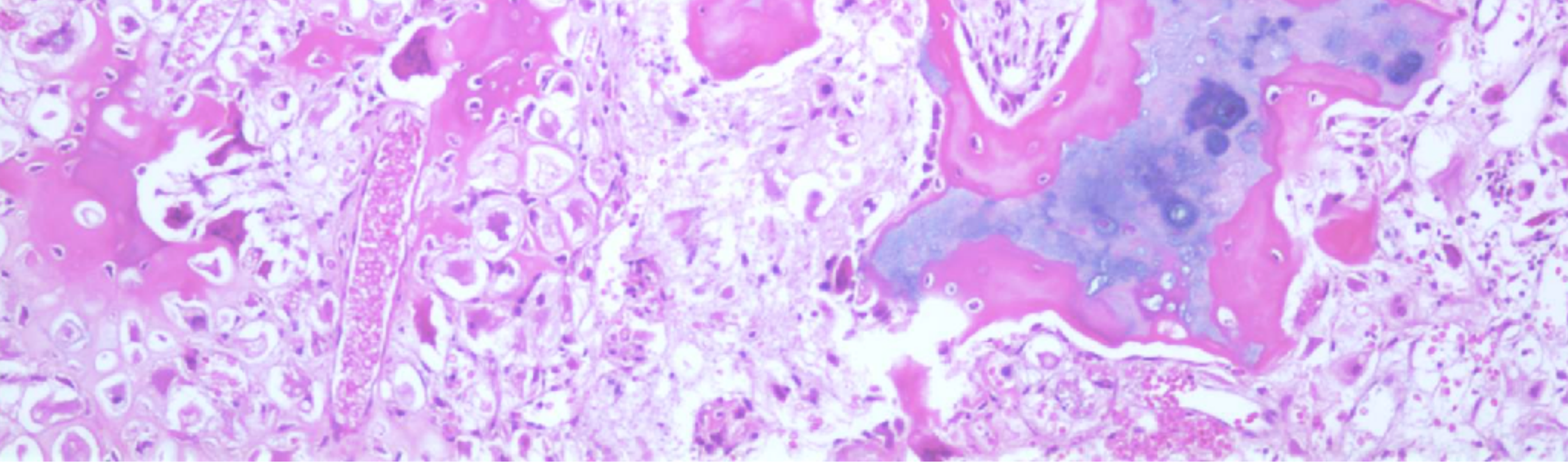
Conclusions

- Chondrosarcomas are a **heterogeneous group** of malignant bone tumors
- Their common feature is the production of "**some form of cartilage**"
- They develop almost exclusively is bones that follow **endochondral ossification**
- Dx is based primarily on **histology** in correlation with Rx and clinical data
- **Location** matters
- IHC or molecular genetics are **not really** helpful as regards DX
- The **distinction** between enchondroma and CSG1/ACT can be very challenging, esp. in curettage material
- How do we treat and follow **ACT**?
- **More data** are needed esp. towards Tx



Thank you!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