

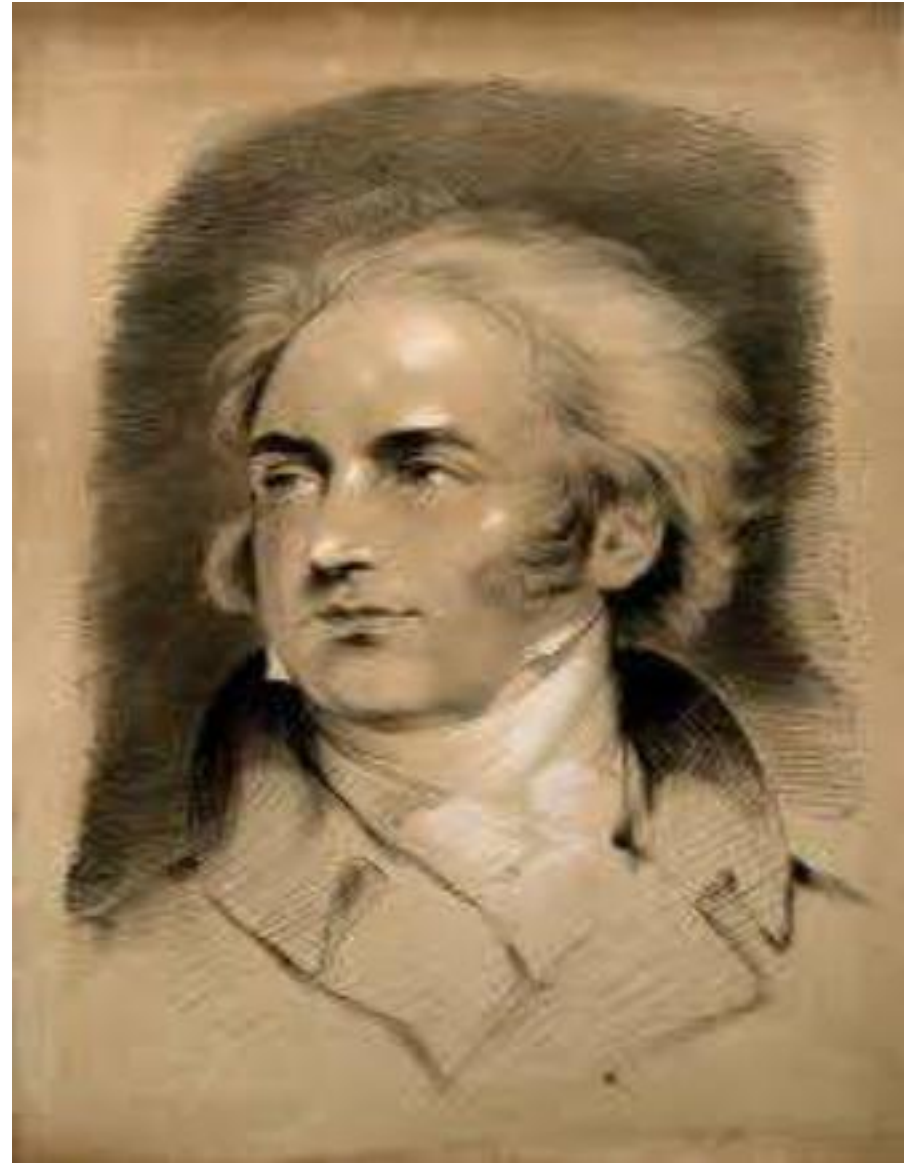
GIANT CELL TUMOR OF BONE

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HISTORY

- First described in 1818 by **Sir Astley Cooper**
- Described in detail in 1940 by **Jaffe and Lichenstein**



DEFINITION

- DISTINCT NEOPLASM ARISING FROM NON-BONE FORMING SUPPORTIVE CONNECTIVE TISSUE OF MARROW WITH NETWORK OF STROMAL CELLS REGULARLY INTERSPERSED WITH GIANT CELLS.

EPIDEMIOLOGY

- **5%** of all skeletal tumors in Caucasian population
- **20 %** of the benign tumors
- India -incidence - **30%** of all bone tumors.
- Occurs in skeletally mature individuals
- Most common - **3rd decade**

- < 2 % - open epiphysis
- < 10 % - older than 65 yrs
- GCT of hand and foot- younger age group, higher incidence of multicentricity
- Female predominance with ratio 1:1.5

SITE

- **Epiphyseo-metaphyseal region of long bones**
- Described from all bones **EXCEPT** middle ear bones
- Axial skeleton - 8%
- Upper Limb : Lower Limb = 1:3

- **55% AROUND THE KNEE(DISTAL FEMUR AND PROXIMAL TIBIA)**
- 10% in the distal radius
- 6% in the proximal humerus
- SPINE rarely involved (commoner in the sacrum)
- Distal tibia, proximal femur, proximal fibula
- Small bones of hand and feet
- Ribs
- In the head and neck region the maxilla and mandible are more commonly involved

MULTICENTRIC INVOLVEMENT

- Incidence-0.5-5%
- Simultaneous
- Hand – metaphyseal, abundant spindle cells
- **GOLTZ syndrome** = ocular defects, skeletal anomaly, multifocal GCT

CLINICAL FEATURES

- Generally symptomatic in > 97% of pts.
- Pain of variable severity that may be associated with a mass present from a few weeks to several months.
- Duration of symptoms - 1 to 18 months.
- Trauma or a pathological # may direct attention to the site of involvement & lead to discovery of tumor.
- 5 to 10% present with a pathological #

- Swelling at end of long bones with overlying skin stretched and shiny but no engorged veins
- Limitation of movement due to mechanical block
- Pathological fracture usually unicortical than a complete- EGG SHELL CRACKLING
- Neurological deficit if spine and sacrum involved
- Metastasis in 1-5 % cases, M/C SITE - LUNG IMPLANTS





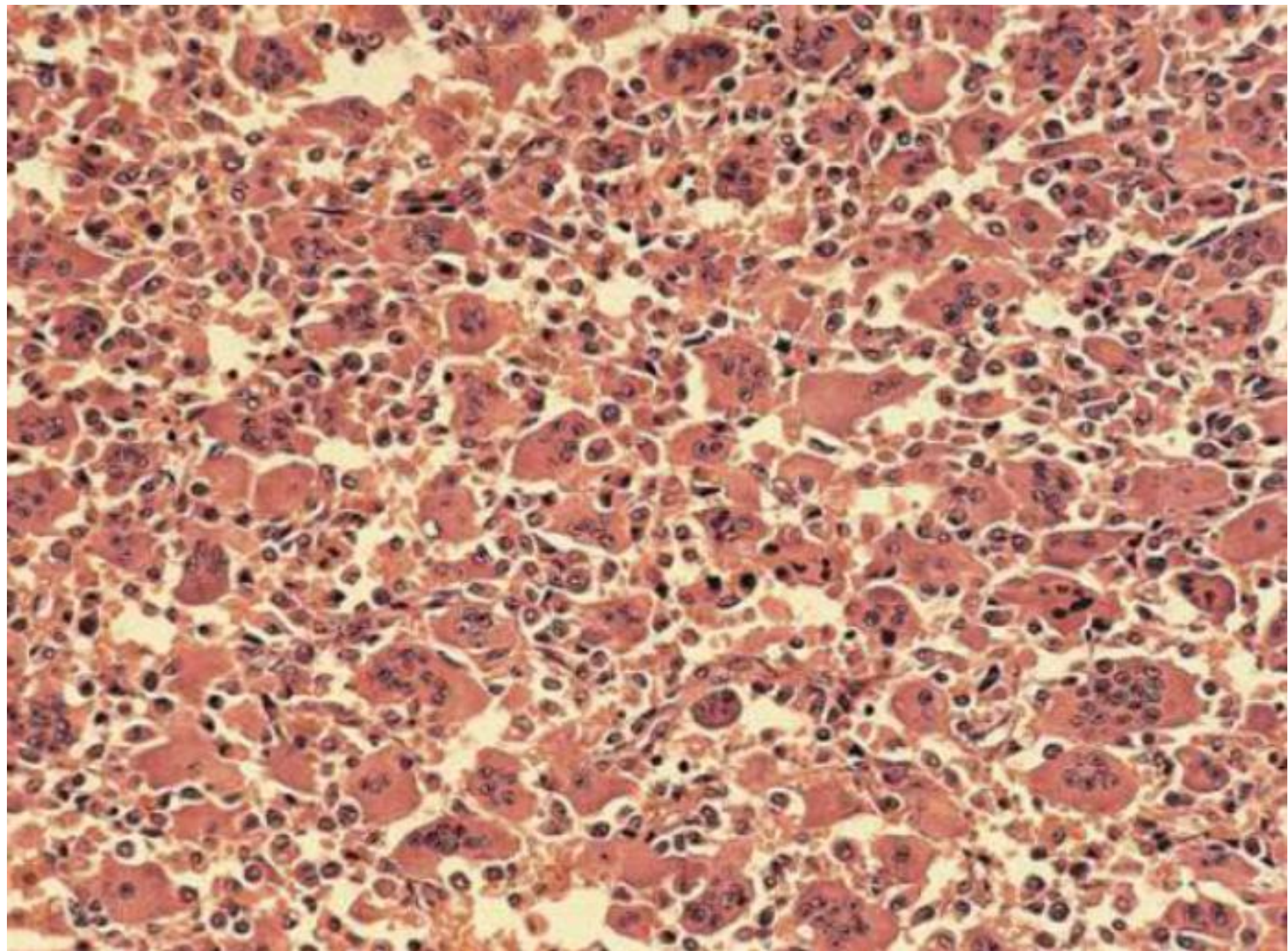
GROSS PATHOLOGY

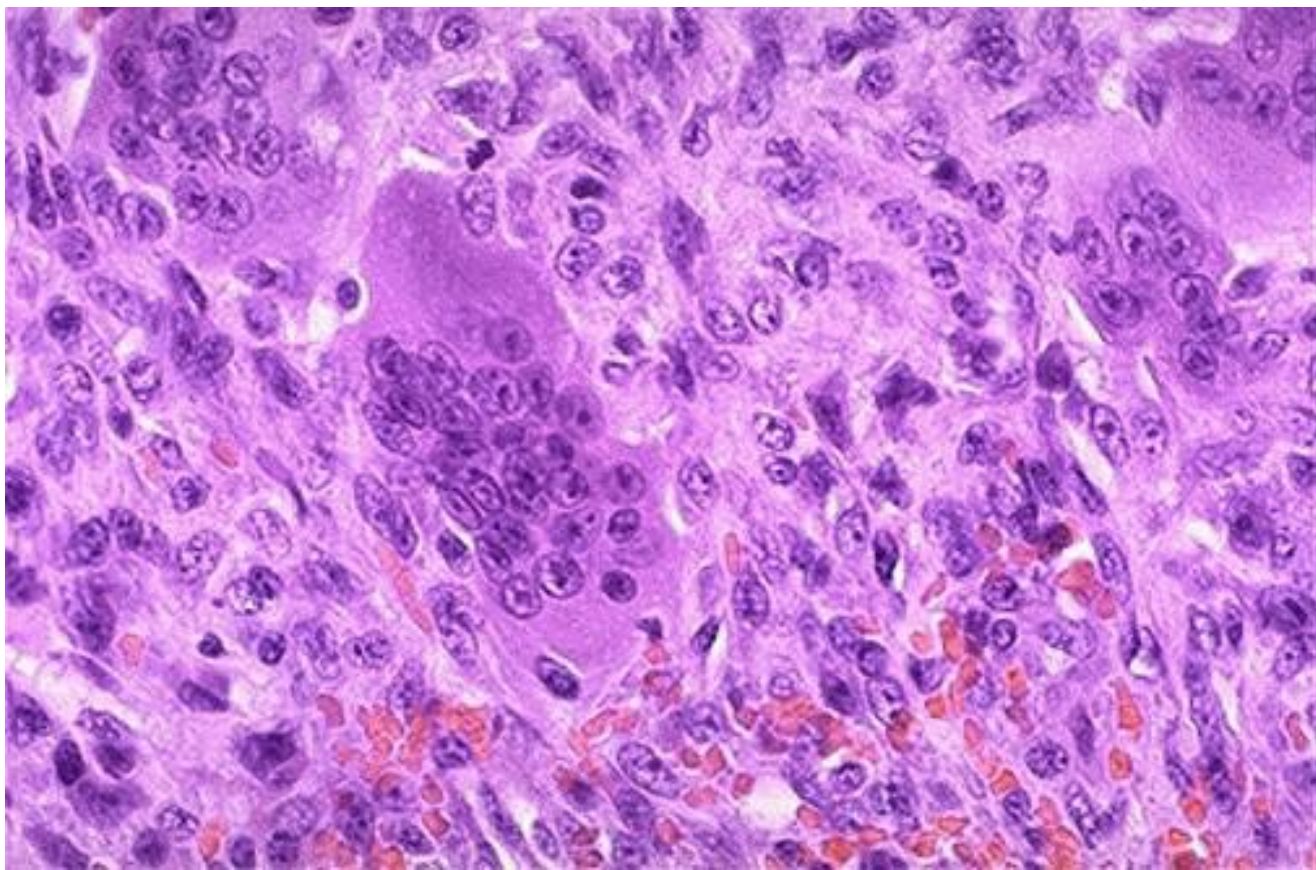
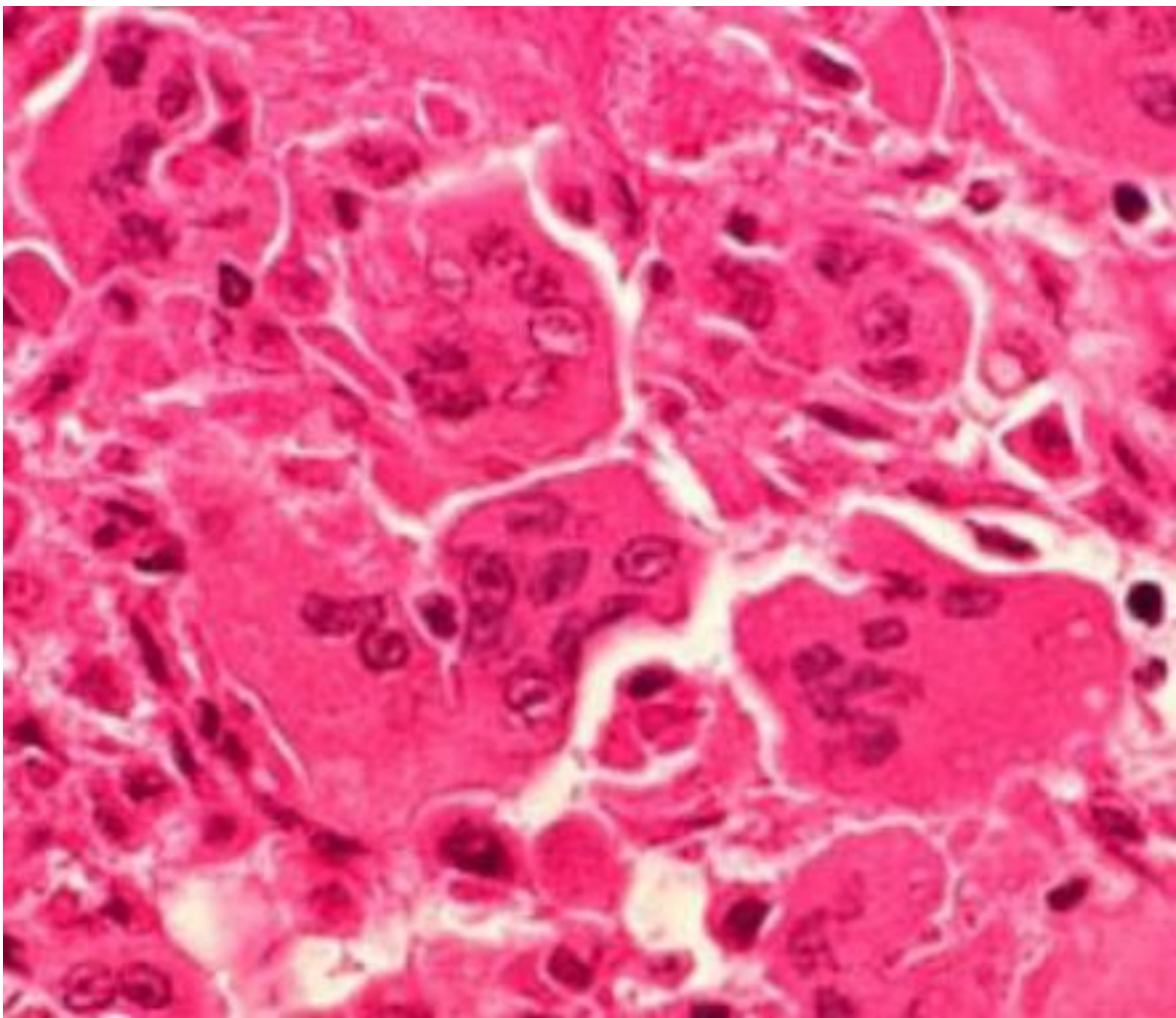
- End of bone is expanded.
- Eccentric lesion at the epiphyseometaphyseal region.
- Thin periosteum(shell of reactive bone)
- Fleshy reddish brown to yellow color, soft, friable mass.
- Cystic spaces seen
- Soft tissue extension of tumor may be present.



MICROSCOPIC APPEARANCE

- Round to polygonal mononuclear cells and multinucleate osteoclast like giant cells
- Giant cells – over 50 nuclei
- Giant cells uniformly scattered throughout.
- Mitoses numerous + intravascular extension ; but this don't indicate malignancy
- No correlation between histologic and biologic behavior





INVESTIGATIONS

- **BLOOD:**

- SERUM CALCIUM

- PHOSPHORUS

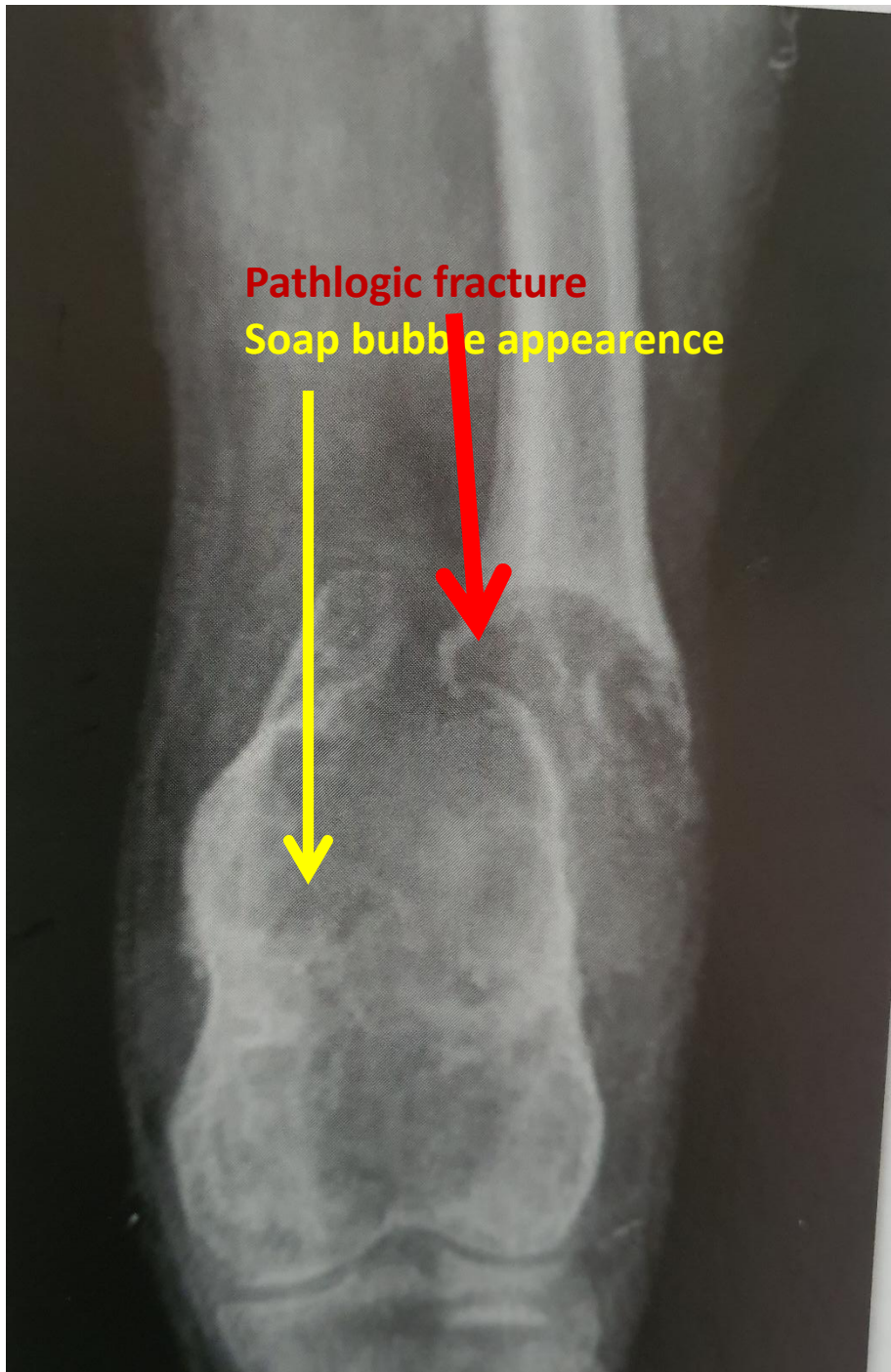
- ALKALINE PHOSPHATASE

} Normal

XRAY

- In long bones, a lytic lesion centered in epiphysis but involving metaphysis and extending at least in part close to adjacent subchondral bone
- Bulges beyond confines of cortex, varying degrees of resorption
- Thin shell of subperiosteal new bone

- Periosteal reactions if pathologic fracture present
- Margins of lesion well defined/ ill defined.
- No mineralized tumor matrix
- Multiple septae traverse interior –
loculated **“soap bubble” appearance.**



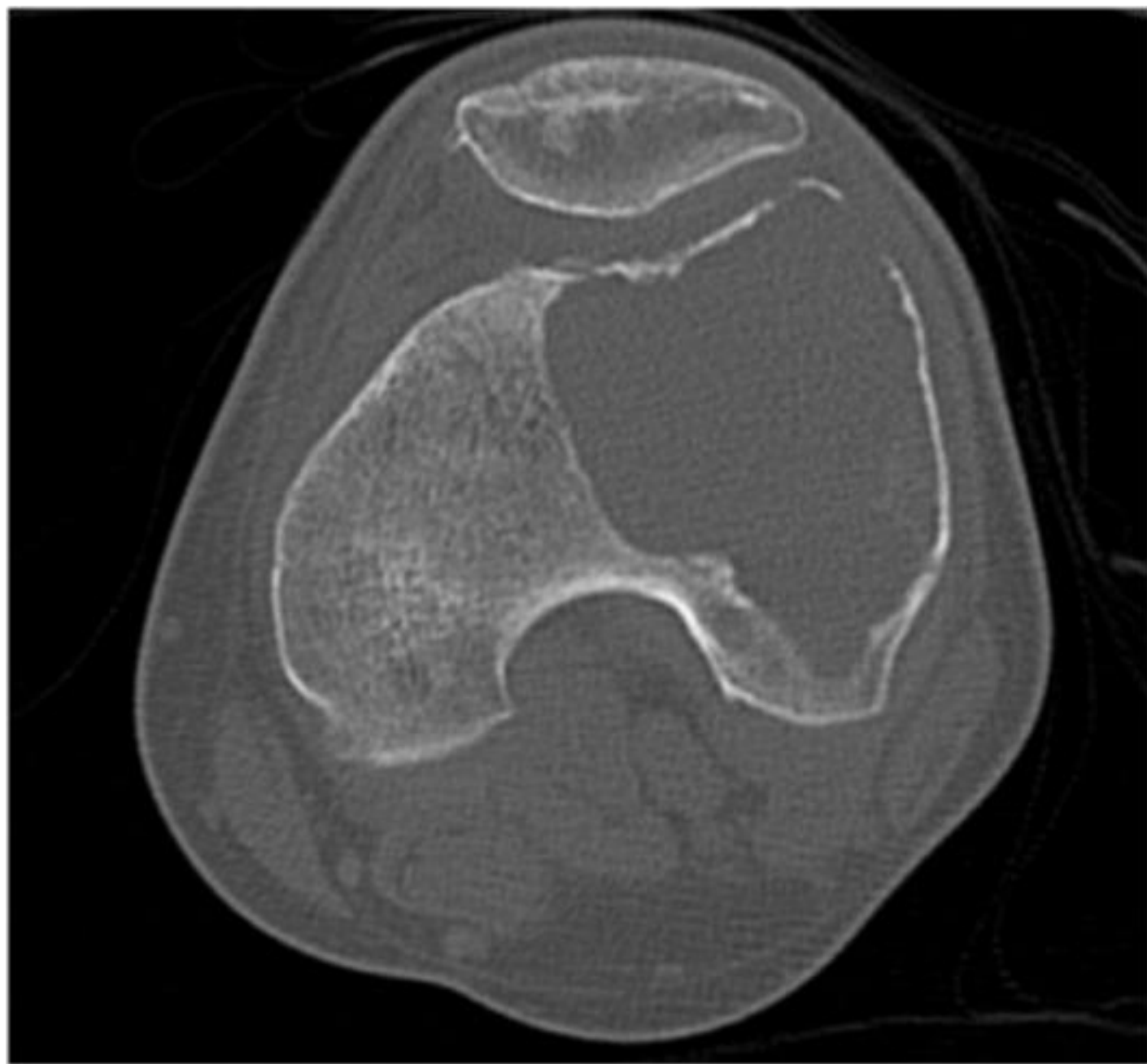
MRI

- Multiplanar imaging capabilities allow accurate tumor delineation.
- Low intensity - T1W
- High intensity - T2W
- Intramedullary tumor is best seen on T1W, while its extraosseous portion is best appreciated on T2W images.



CT

- Confirms integrity of cortex and outline tumor extent
- Sub cortical destruction
- Determining extraosseous extent and joint involvement
- Fluid levels may be seen secondary to an ABC component
- Soft tissue extension AND RELATIONSHIP CANT BE STUDIED.



ANGIOGRAPHY

- Not routinely done
- To assess relationship of major vessels to large tumors
- To know major feeding vessels to tumor

BONE SCAN

- GCT takes up increased uptake of technetium 99
- Does not correlate to grading or nature of tumor
- Useful when multicentric lesions suspected

BIOPSY

- Final diagnostic tool for GCT
- TYPES:

FNAC(22 GAUGE NEEDLE)

CORE NEEDLE BIOPSY(14 GAUGE NEEDLE)

OPEN INCISIONAL BIOPSY(Reliable,
pathologists to evaluate cellular morphologic features
and tissue architecture)

GRADING - Jaffe, Lichenstein and Portis(1940)

GRADE 2

- Boderline tumours
- Stromal cells are prominent and tightly packed
- Giant cells are less in number compared to grade 1 and their nuclei may show atypism
- Stromal cells show atypism
- Strong chance for recurrence and some may undergo malignant change

GRADING - Jaffe, Lichenstein and Portis(1940)

GRADE 1

- Conventional GCT
- Stroma- inconspicuous
- Giant cells dominate the field
- No atypism of stromal cells and are loosely arranged
- Stromal cells - predominantly spindle shaped

GRADING - Jaffe, Lichenstein and Portis(1940)

GRADE 3

- Sarcomatous type of stroma
- Frequently metastase
- Stromal cells abundant and closely compacted and present an irregular whorled arrangement
- Nuclei are unusually large, irregular and atypical
- Giant cells are few in number and atypical

Modified grading

Sannerkin et al(1980)

- Malignant GCT- with frank sarcomatous changes and full metastatic potential
- Borderline GCT- without sarcomatous changes but with abnormal mitoses or vascular permeation or both
- Conventional GCT- without features of any of the above two types

- ***No correlation exists between histological grading and clinical behavior of the tumour.***
- ***Hence grading not widely accepted.***

ENNEKING STAGING FOR GCT

STAGE 1-(10-15%)

- Patients asymptomatic
- Discovered incidentally
- May cause pathological fracture
- Has sclerotic rim on x-ray or CT
- Relatively inactive on bone scans
- Histologically benign

ENNEKING STAGING FOR GCT

STAGE 2-(70%)

- Symptomatic
- Often associated with pathologic fracture
- Has expanded cortex but no break through
- Is active on bone scans
- Histologically benign

ENNEKING STAGING FOR GCT

STAGE 3-(10-15%)

- Symptomatic
- Rapidly growing mass
- Has cortical perforation with accompanying soft tissue mass
- Activity on bone scan extends beyond the lesion in x ray
- Shows intense hypervascularity on angiogram
- Histologically benign

DIFFERENTIAL DIAGNOSIS

1. *ANEURYSMAL BONE CYST*
2. *GIANT CELL REPARATIVE GRANULOMA*
3. *CHONDROBLASTOMA*
4. *BROWN TUMOR*
5. *INTRA OSSEOUS GANGLION*
6. *BENIGN FIBROUS HISTEOCYTOMA*

- **BROWN TUMOR OF HYPERPARATHYROIDISM**

- Osteopenic
- Subperiosteal resorption
- Resorptive changes at distal phalanges
- Elevated Serum ALP, Serum Calcium
- Decreased Serum phosphorus

- **CHONDROBLASTOMA**

- Adolescent with open physis
- Multiple punctate calcifications
- Chicken wire appearance

- **ANEURYSMAL BONE CYST**

- Metaphysis(75%)
- Double density fluid-fluid level on CT/MRI

- **UNICAMERAL BONE CYST**

- Fallen fragment sign
- Below 20 yrs
- Metaphyseal lesion

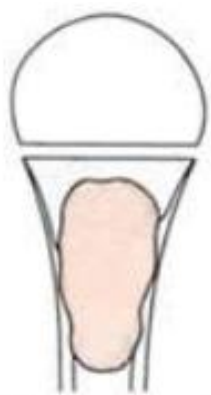
- **CHONDROMYXOID FIBROMA**

- 10 to 30 years
- Metaphyseal
- Pseudo trabeculations are denser and thicker

- **GIANT CELL RICH OSTEOSARCOMA**

- Metaphyseal
- Aggressive bone destruction
- Ill defined margin

EPIPHYSIOMETAPHYSEAL LESIONS AT A GLANCE



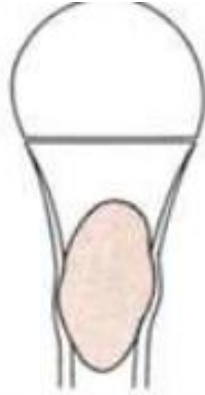
Solitary bone cyst
Upper limb
Metaphyseal
?Fracture



Aneurysmal bone cyst
Metaphyseal
Expanding
Eccentric



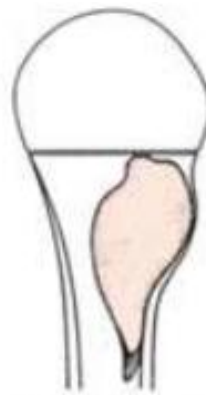
Fibrous cortical defect
Lower limb
Cortical lesion



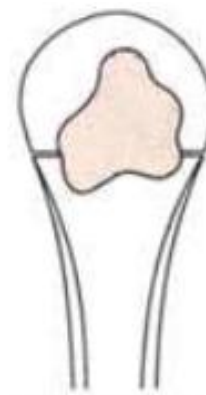
Fibrous dysplasia
Expanding
Ground glass



Chondroma
Calcification



Chondromyxoid fibroma
Eccentric
Dense endosteal margin



Chondroblastoma
Epiphysis



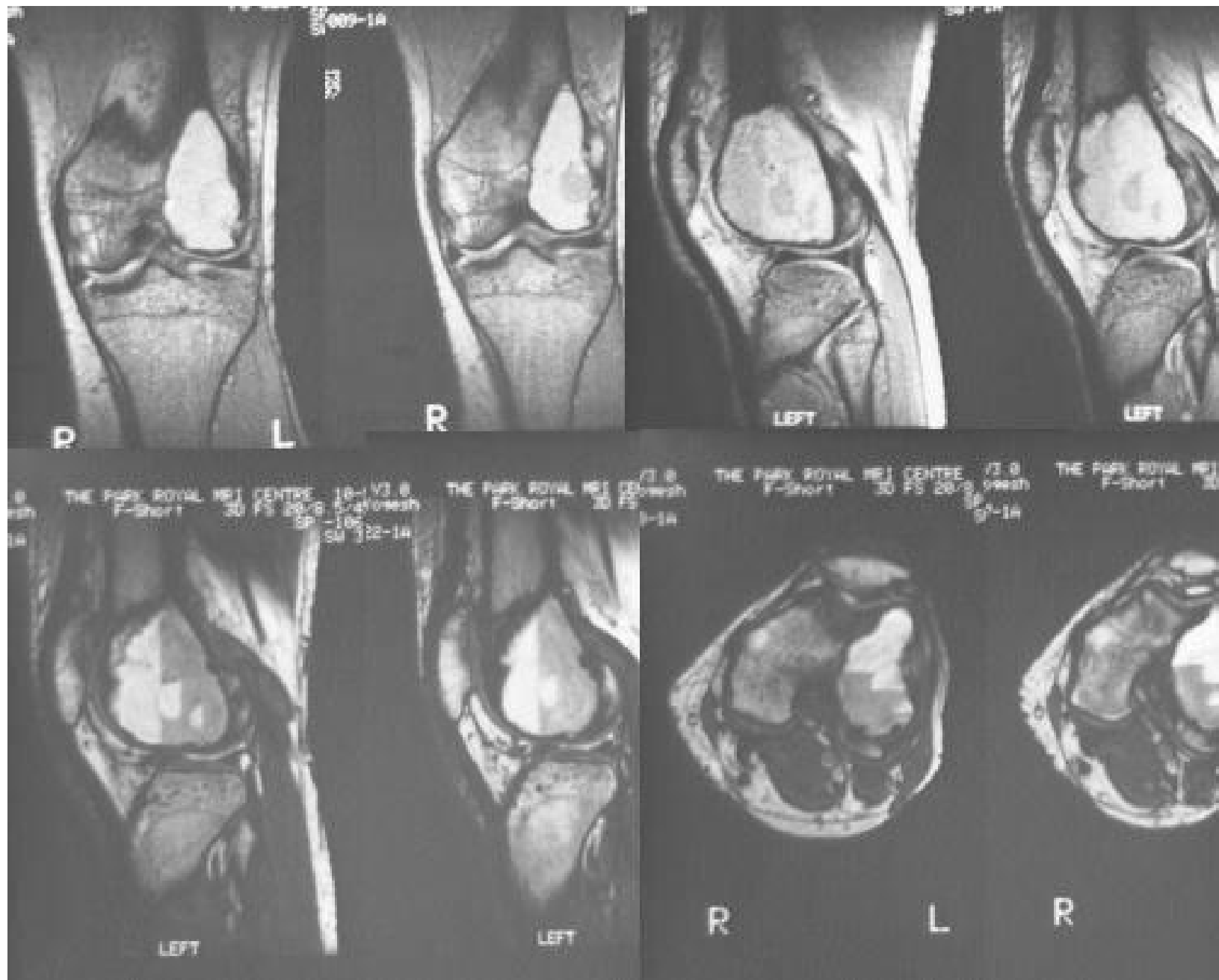
Giant cell tumour
Mature bone
Always extends to subarticular margin



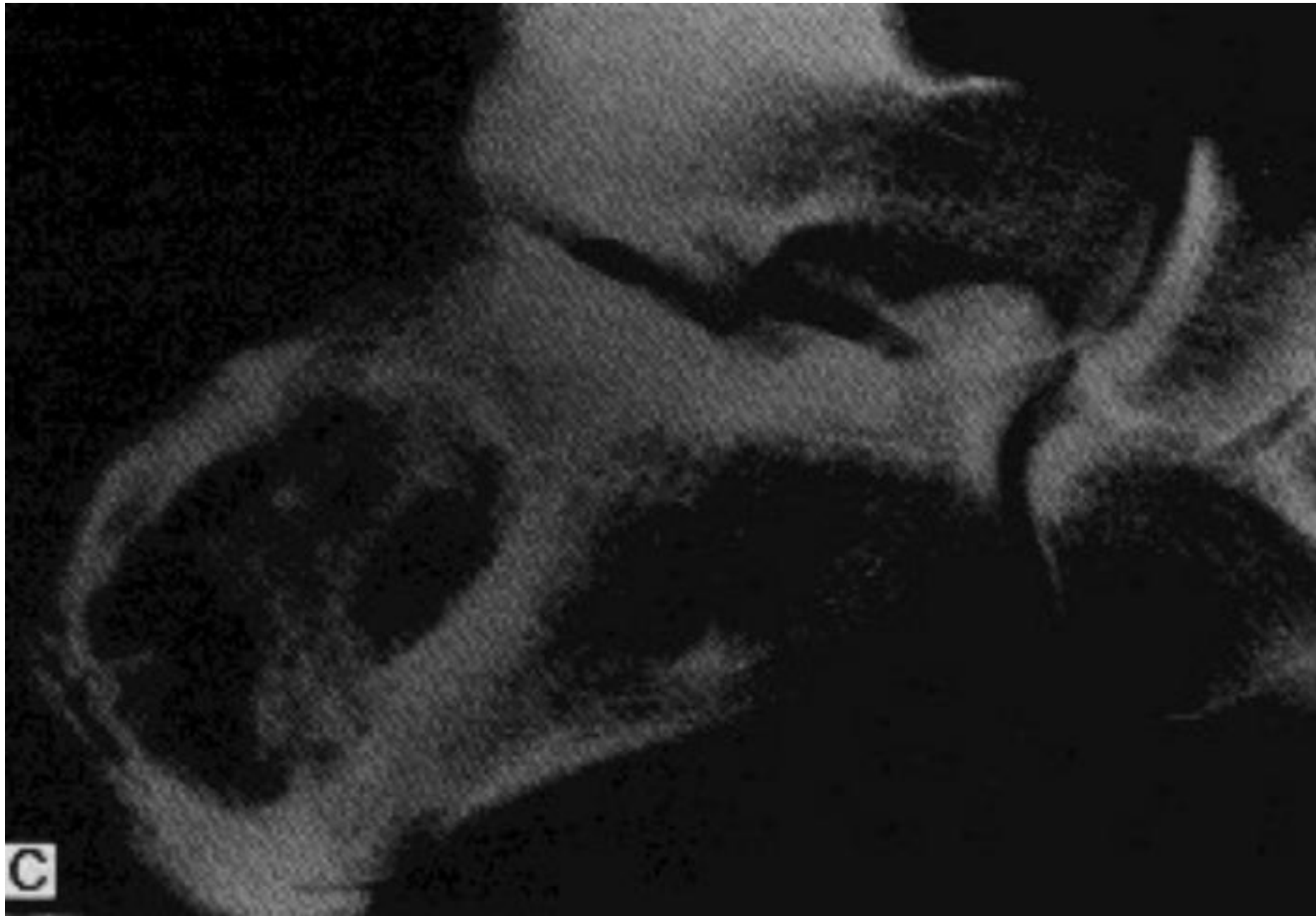
Brown tumour
Think of it!
Look for signs of HPT











TREATMENT

- Invasive and aggressive
- Commonly recurs, may become malignant after unsuccessful removal
- Recurrence - en bloc excision

Preop planning

- Malignancy should be ruled out
- 3 factors:
 1. Type of resection
 2. Use of adjuvant therapy
 3. Type of material to be used to fill defect

Treatment options

- SIMPLE CURETTAGE: Intralesional curettage alone
- EXTENDED CURETTAGE: curettage along with use of adjuvants to augment curettage
 - En bloc excision
 - Irradiation therapy
 - Embolization
 - Bisphosphonates
 - Amputation

INTRALESIONAL CURETTAGE

- Adequate exposure with large cortico cancellous window
- High power burr
- Pulsatile jet lavage
- Curettage alone has recurrence - 60 %

ADJUVANTS

- Eliminates microscopic disease and reduces recurrence
- Curettage and cementation causes a 2mm osteolytic lesion zone surrounding cement due to thermal injury
- HYDROGEN PEROXIDE
- PHENOL:
 - ❖ 12-50 % conc
 - ❖ Easily absorbed
 - ❖ Nephrotoxic
 - ❖ Soft tissue complication

✓ PMMA BONE CEMENT:

- ✓ Bone cement + Adriamycin + Methotrexate to reduce recurrence
- ✓ Heat of polymerization or direct toxicity of monomer
- ✓ Immediate structural support and early ambulation
- ✓ Radiographic detection of recurrence is easier
- ✓ Fear of long term degeneration of articular cartilage in sub chondral lesion in wt bearing stress.

➤ CRYOSURGERY WITH LIQUID NITROGEN

- Create 1-2cm zone of tissue necrosis
- Local complications- thermal shock, dehydration, wound healing problems
- Not easily available and costly
- Storage difficulties

Reconstruction of residual defect

- **BONE GRAFTING**
 - Autogenous
 - Allograft
 - Artificial bone graft substitutes
 - Demineralized bone matrix
- **BONE CEMENT**

BONE GRAFT

- ADV
 - Remodeling along stress lines
 - Permanent reconstruction
 - Restores bone stock
 - Restores normal biomechanics at joint surface
- DISADV
 - Less quantity
 - Donor site morbidity
 - Allograft expensive
 - Recurrence difficult to distinguish from graft resorption

Sandwich technique

- Indicated in subarticular lesions where the amount of residual subchondral bone after an extended curettage is less than 1 cm.
- The cavity is reconstructed in layers.
- A mixture of morcellized auto and allograft (about 1 cm thick) is packed adjacent to subarticular surface.
- A layer of gelfoam is layered over this to reduce heat damage to graft and the remaining cavity is packed with cement

Minimal residual subchondral bone



En bloc resection and subsequent reconstruction/arthrodesis

- Initial procedure of choice in more aggressive tumors
- 2cm of normal tissue excised
- Defects filled with cancellous bone grafts , freeze dried allografts or prosthesis
- Low recurrence rate

Indications are;

1. Stage 3 lesions
2. Recurrence
3. Large defects are expected
4. Joint surface destroyed or cannot be salvaged
5. Certain bones which can be sacrificed such as:
 1. Lower end of ulna
 2. Upper end of fibula

Reconstruction options

BIOLOGIC

- Autograft Arthrodesis
- Live Microvascular Fibular Graft
- Osteo-articular Allografts
- Ilizarov Method

ENDOPROSTHETIC JOINT REPLACEMENT

- Custom Mega Prosthesis

ROLE OF CHEMOTHERAPY AND RADIOTHERAPY

- No recognised effective chemotherapeutic agents available for GCT.
- Literature documents a close association of secondary sarcomatous transformation in the region of GCT treated by radiation therapy.
- In the rare unresectable primary or secondary lesions with a clear cut diagnosis, high voltage irradiation therapy has a place in their management

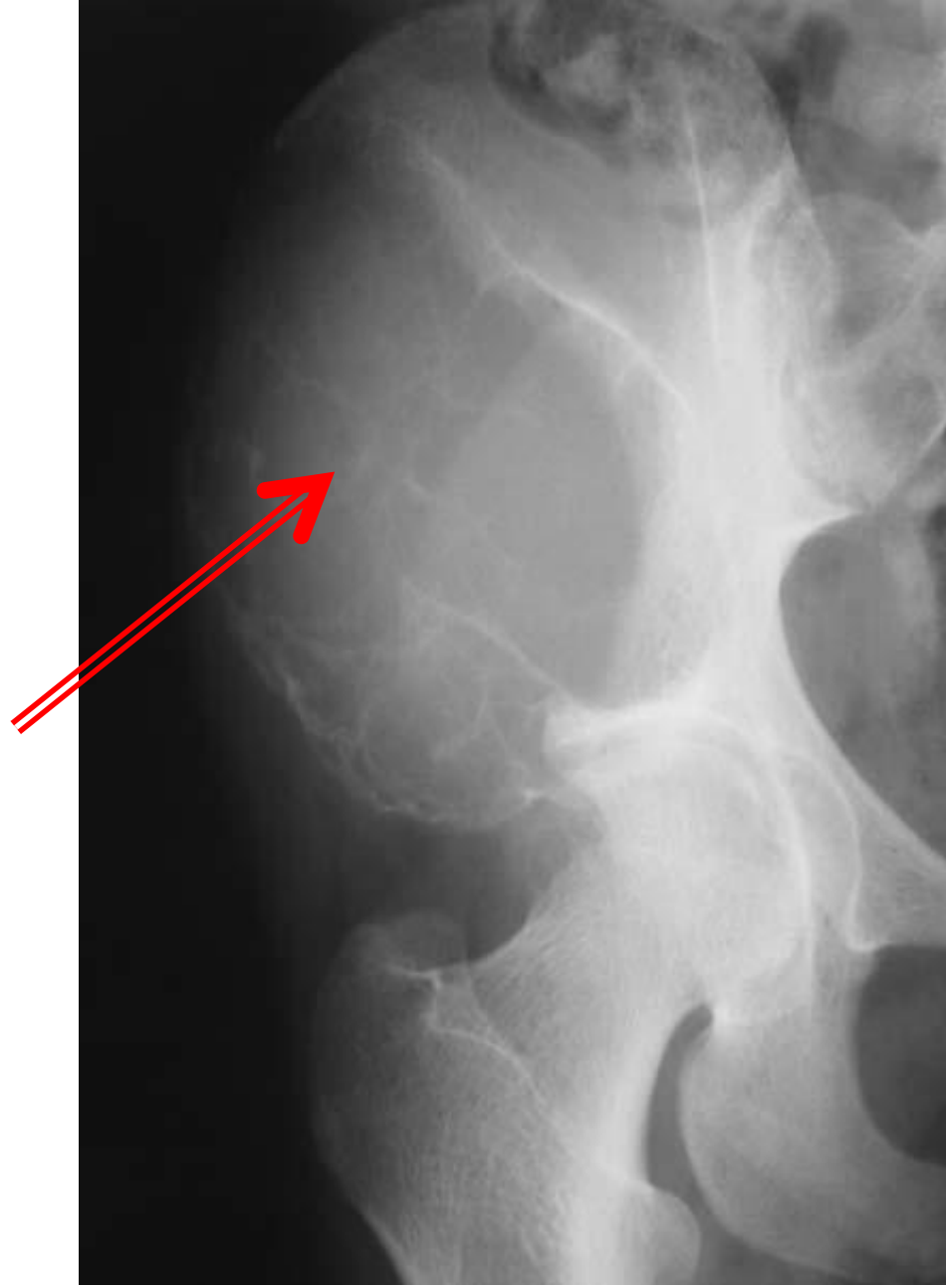
Radiotherapy

- When complete excision or curettage not possible
- Aggressive, multiple /recurrent tumor
- Lesions of spine and sacrum
- Dosage- 1500 to 5000 rads for 5 to 6 weeks using mega voltage therapy cobalt 62
- Induces malignant change if it is given to benign lesion

- In lesions involving axial skeleton, with the exception of the sacrum, it is felt that excision with stabilization of spine as dictated by resection & biologic reconstruction of anterior column, followed by reduced levels of irradiation based on assumption that you are dealing with microscopic residual tumor only, would offer the patient the best chance of long term local control.

EMBOLISATION

- Trans-catheter embolisation of blood supply of certain unresectable tumors like sacrum and pelvis.
- Brings down size of tumor and provides pain relief
- Re-embolization needed at monthly intervals
- Tumors in these areas amenable to surgical resection also benefit by preoperative embolisation in an attempt to reduce the amount of intraoperative blood loss.



After embolisation and curettage of the tumour followed by reconstruction with PMMA cement and screws.



Bisphosphonates

- Recently researchers have demonstrated the efficacy of bisphosphonates as an effective adjunctive modality in the management of large unresectable lesions.
- Pamidronate/zoledronate can be given
- Target osteoclast like giant cells
- Limit tumor progression

Newer Agents

- Osteoclast differentiation factor, receptor activator of nuclear factor kappa b(NF-kB) ligand (RANKL)
- A fully human monoclonal antibody to RANKL, denosumab - in unresectable GCT

Amputation

- Malignant tumor
- Fungation
- Recurrence after surgery and irradiation
- Deep seated associated infection
- Extensive destruction of bone
- Severe disability

Recurrence

- Most recurrences in the first 2 years
- Local recurrences appear to be related to surgical margin & are clinically characterized by pain radiologically by lysis of bone graft or adjacent cancellous bone.
- Following curettage & cementation an osteolytic zone caused by thermal injury measuring 2 mm surrounds the cement.

- This radiolucent zone is bordered by a thin outer sclerotic rim for about 6 months.
- Lysis or failed development of sclerotic rim between cement & cancellous bone may suggest recurrence.
- Soft tissue recurrence is visible on plain radiographs because of its tendency towards peripheral calcification.

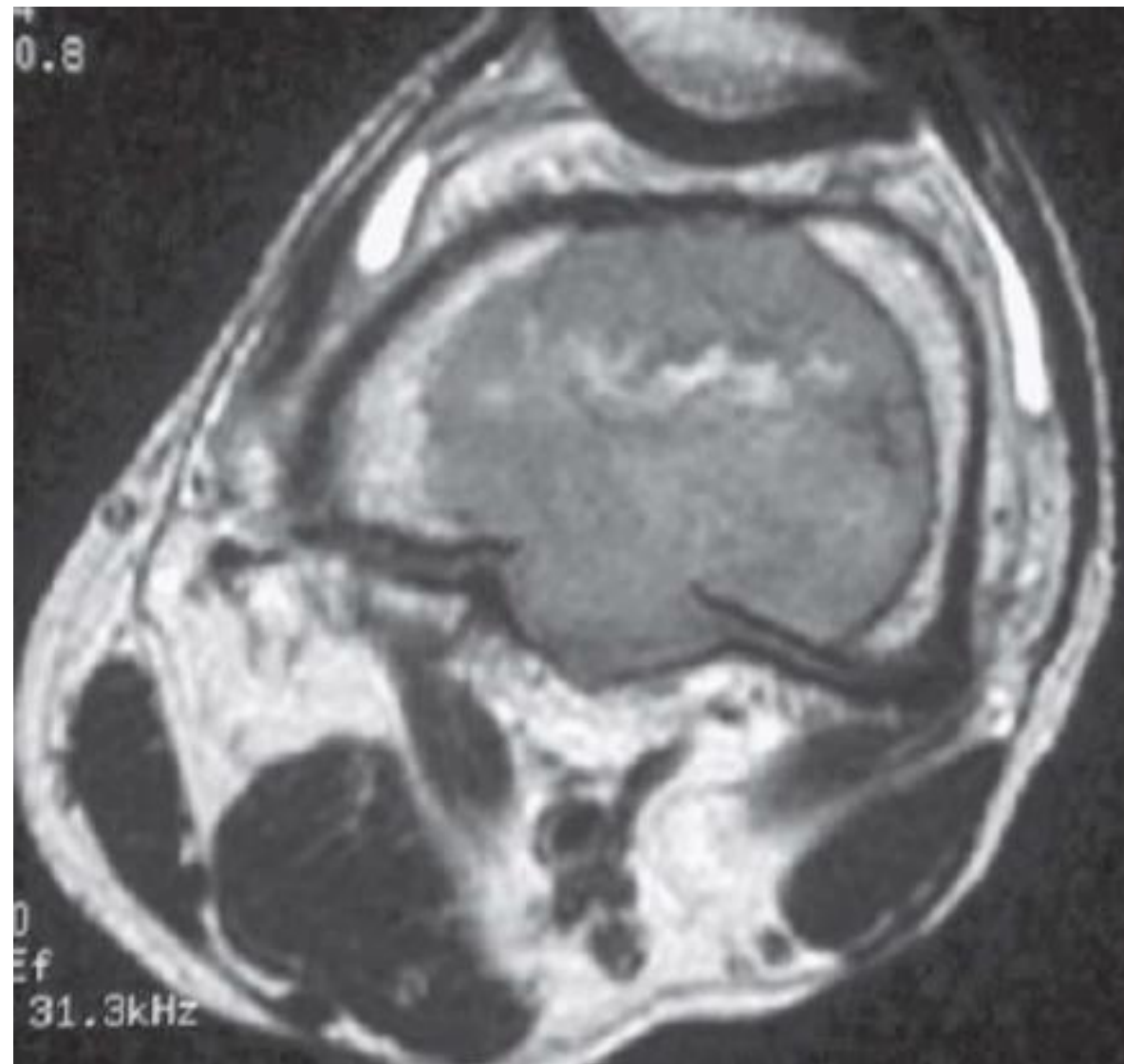
Metastasis

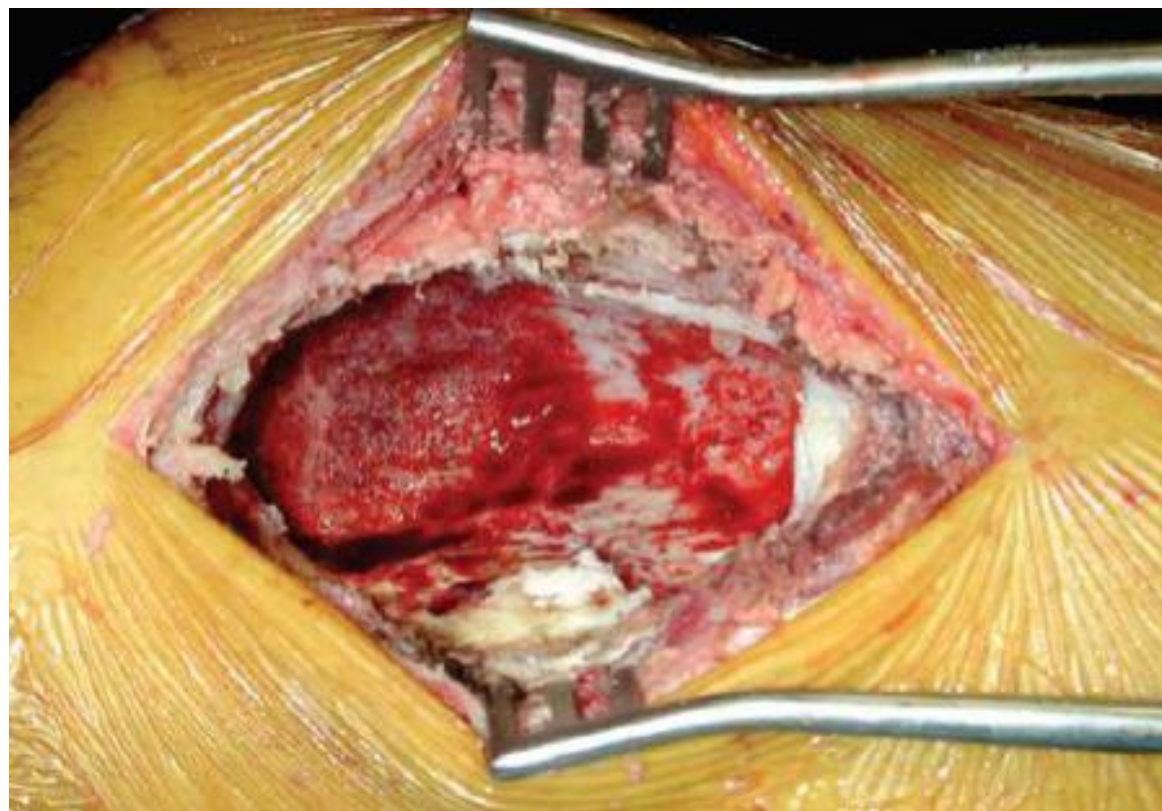
- Incidence - 1% to 6%.
- Metastatic lesions are histologically identical to primary lesions, showing no tendency to dedifferentiate.
- Majority of metastatic lesions are to **lung**.
- Mean interval between the onset of tumor & detection of lung metastases is about **4 to 5 yrs.**

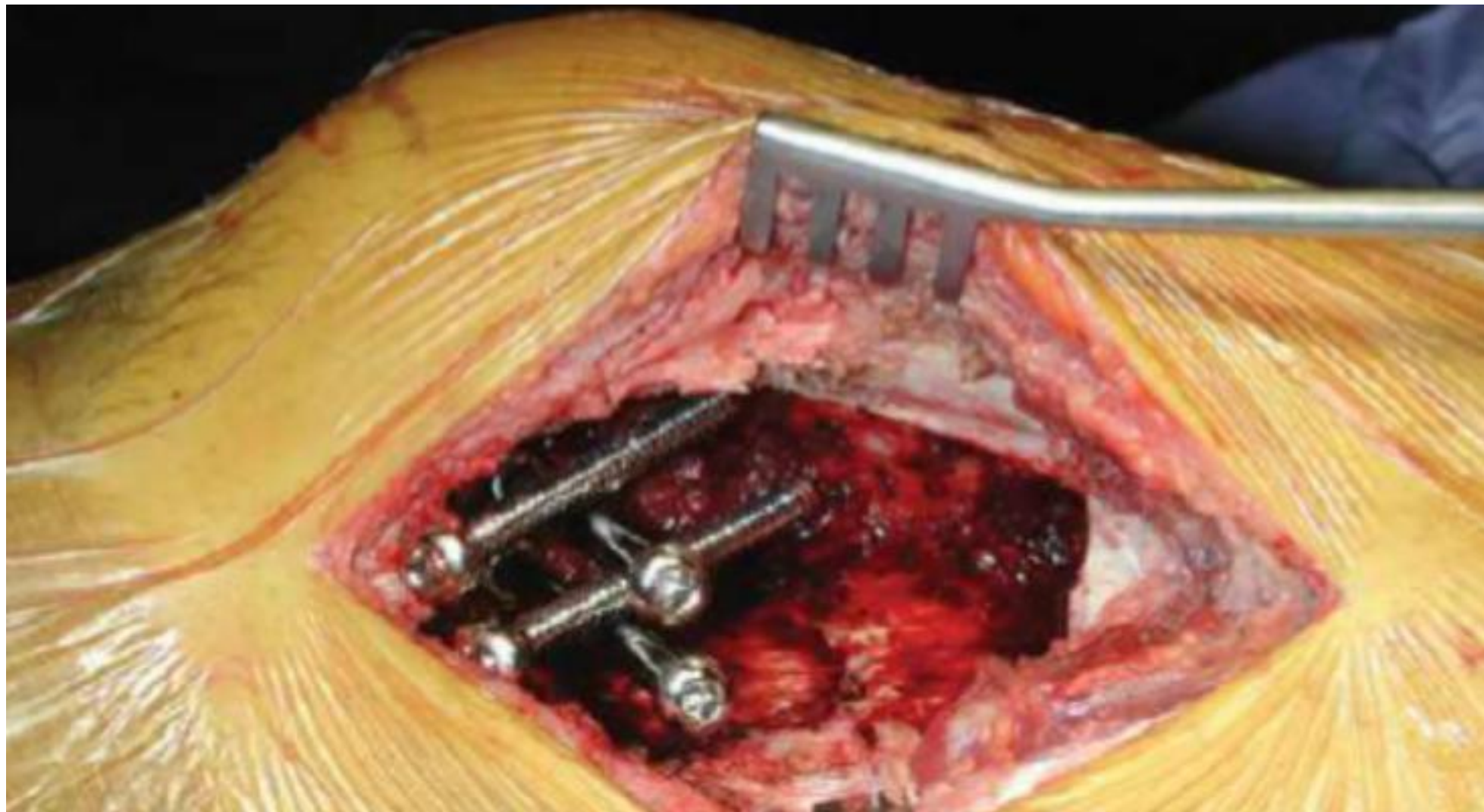
- Solitary metastasis to regional lymph nodes, mediastinum & pelvis have been reported, as has involvement of the scalp, bone & para-aortic nodes.
- Radiation & chemotherapy have limited success.
- Complete excision of metastatic lesions
- Steroids have been successfully used in the control of unresectable metastases.

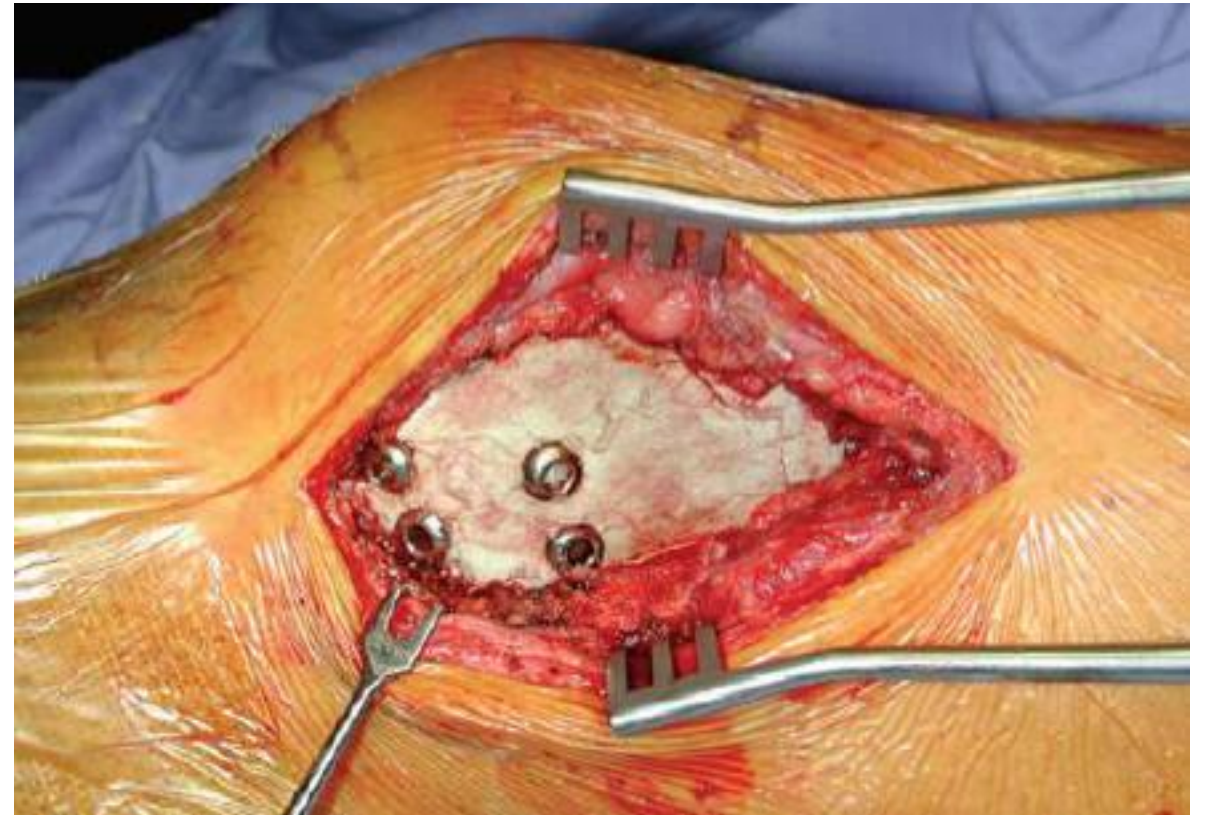
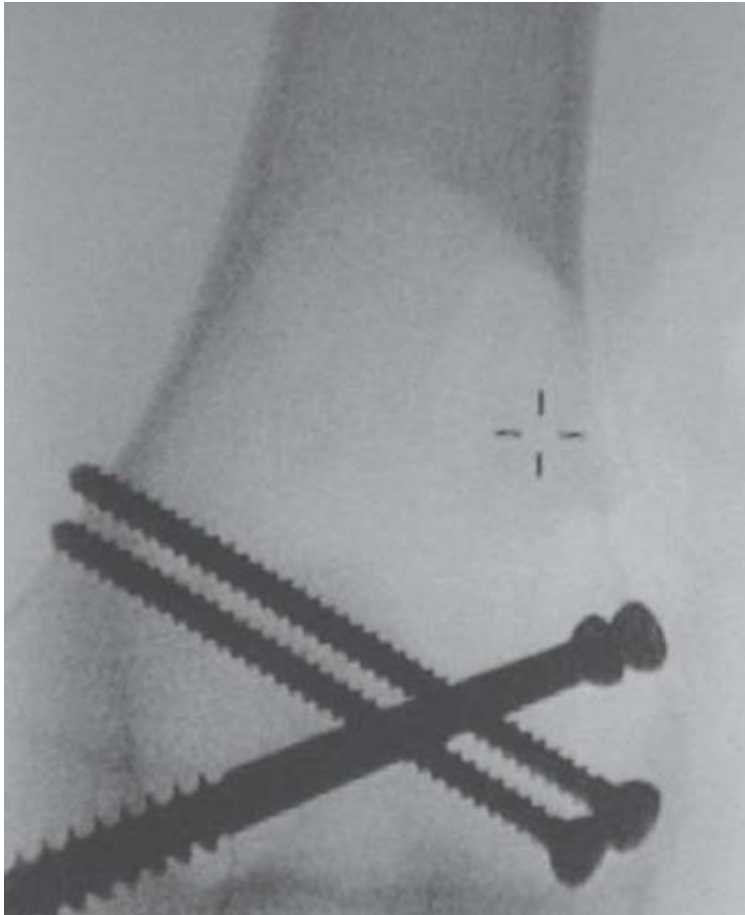
21 YR OLD MAN C/O LEFT KNEE PAIN













THANK YOU