

Diagnostic Approach for Musculoskeletal Tumors



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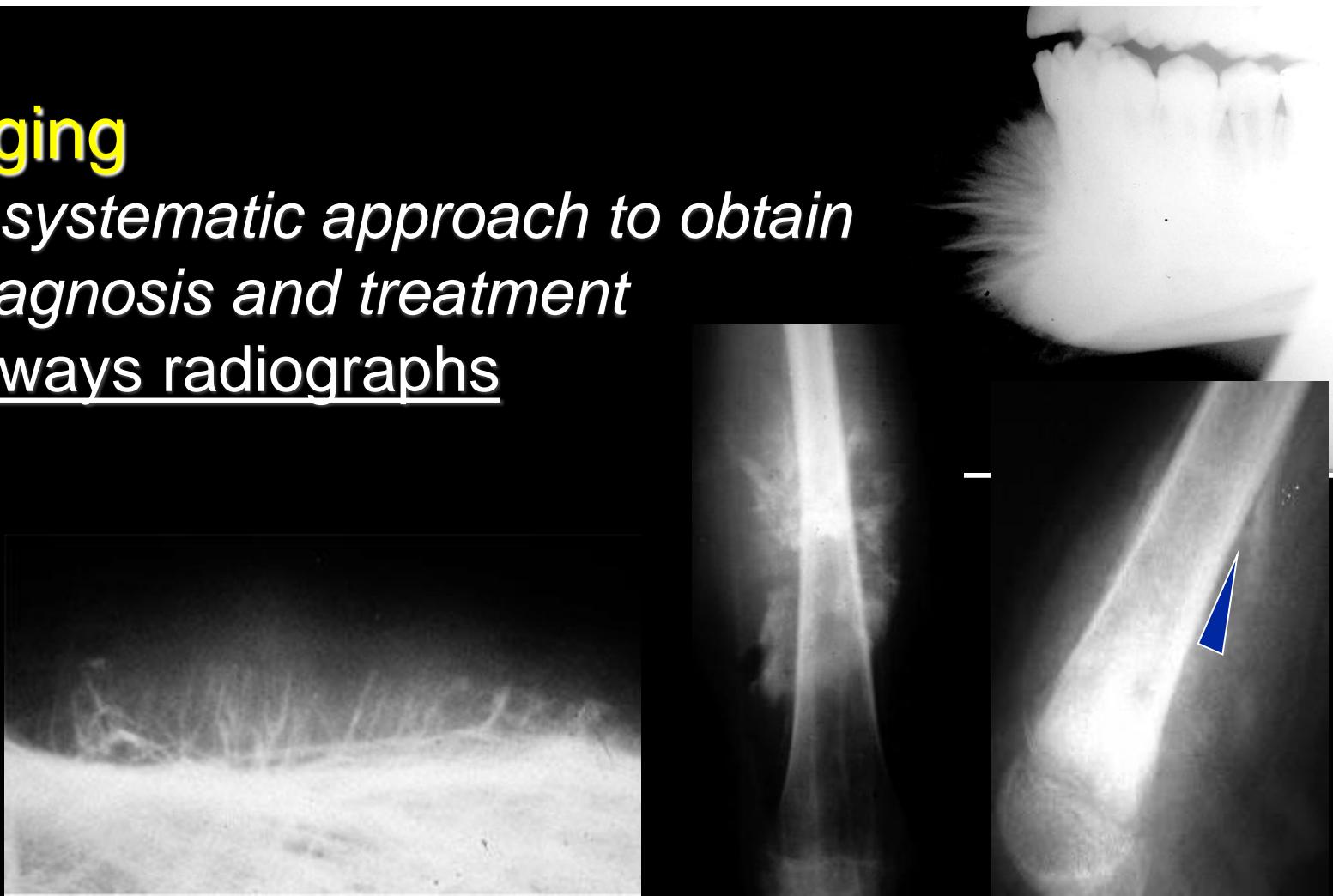


State-of-the-art approach for bone sarcomas

Andreas F. Mavrogenis · Andrea Angelini · Christos Vottis · Emanuela Palmerini ·
Eugenio Rimondi · Giuseppe Rossi · Panayiotis J. Papagelopoulos ·
Pietro Ruggieri

Staging

- *A systematic approach to obtain diagnosis and treatment*
- Always radiographs



Staging

- Paramount
- Especially in patients with a known history of cancer and solitary osteolytic lesions



Diagnosis and Management of Bone Sarcomas;
Rizzoli's Approach

Staging

- è History, age, trauma (>60%)
- è Family history (multiple hereditary exostosis)
- è Physical examination
- è Imaging studies



2. Biopsy
3. Treatment

Age

- Young

Benign

Osteomyelitis
EG

Malignant

Osteosarcoma
Ewing's tumors
Lymphoma
Leukemia



Ewing's sarc

- Adults

Benign

Enchondromas
Paget's disease
Bone infarct
Bone island
Hyperpara

Malignant

Metastases
Multiple myeloma
Lymphoma
Primary sarcomas
Secondary sarcomas



Chondrosarc

Clinical

- Pain
 - Most common symptom
Initially may be activity related
Progressive at rest and at night
 - Osteoid osteoma
- **Incidental radiographic finding**
- **Pathological fracture**
- **Mass**
 - Mostly in soft tissue tumors and sarcomas



Laboratory

Not very helpful

- Blood and urine tests

- Rarely lead to a diagnosis
- Useful in selected situations

Lymphoma

Myeloma

Paget's

Brown tumors

- CBC, ESR, CRP
- Liver enzymes
- Alkaline phosphatase
- Serum protein electrophoresis
- Bence Jones
- Prostate-specific antigen

Imaging

Local

- **Radiographs**

- CT

- If radiographs are normal
- Evaluation of matrix

- **MRI**

- Bone scan

-
- If radiographs are normal
 - Highly sensitive, not specific



Radiographs

Based on medical history, physical examination, and plain radiographs, the diagnosis of a bone tumor can be established in >80% of cases

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Imaging of bone tumors for the musculoskeletal oncologic surgeon

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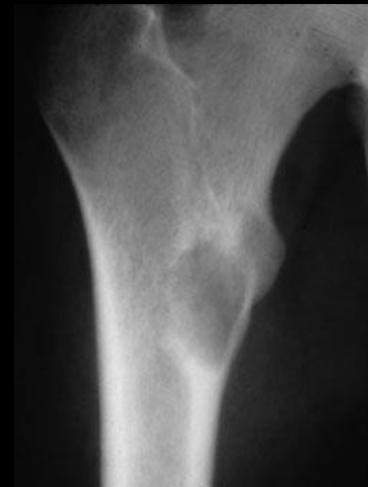
^c Department of Research, Istituto Ortopedico Rizzoli, Bologna, Italy

Radiographs

- Initial detection of a lesion or incidental finding
- How the tumor affects the bone is best appreciated on initial radiographs
- **Signs of benign**
- **Signs of malignancy**



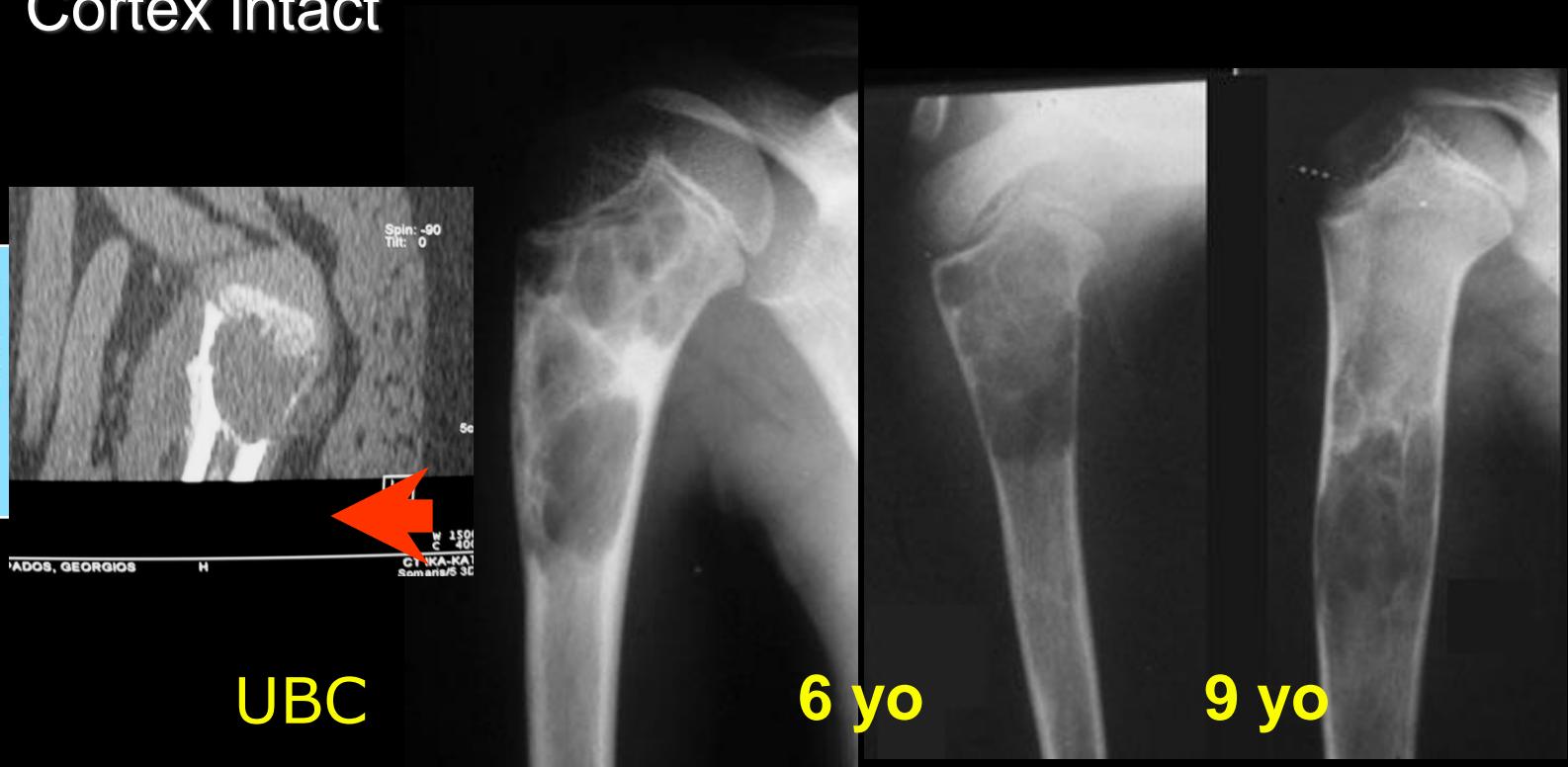
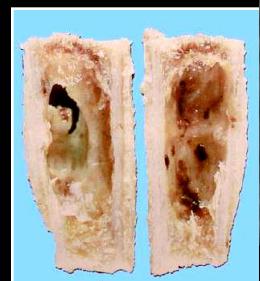
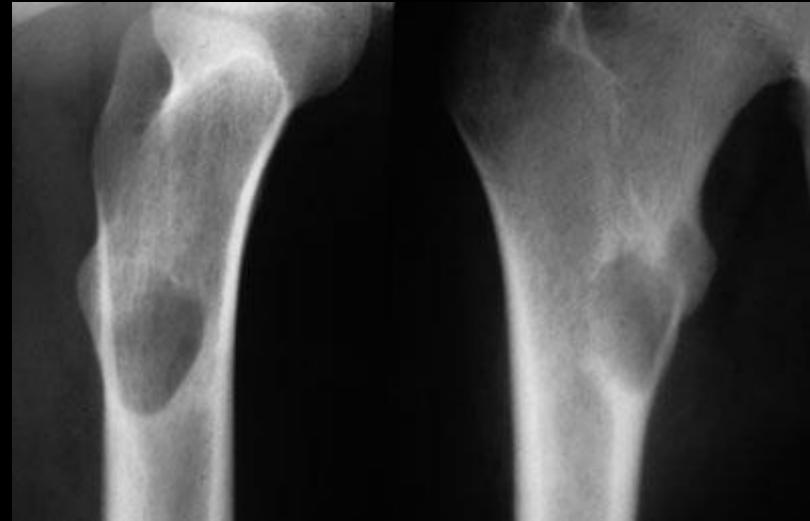
UBC



GCTB

Radiographs

- Signs of benign
 - Well-defined margins
 - Peripheral sclerosis
 - Cortex intact



Radiographs

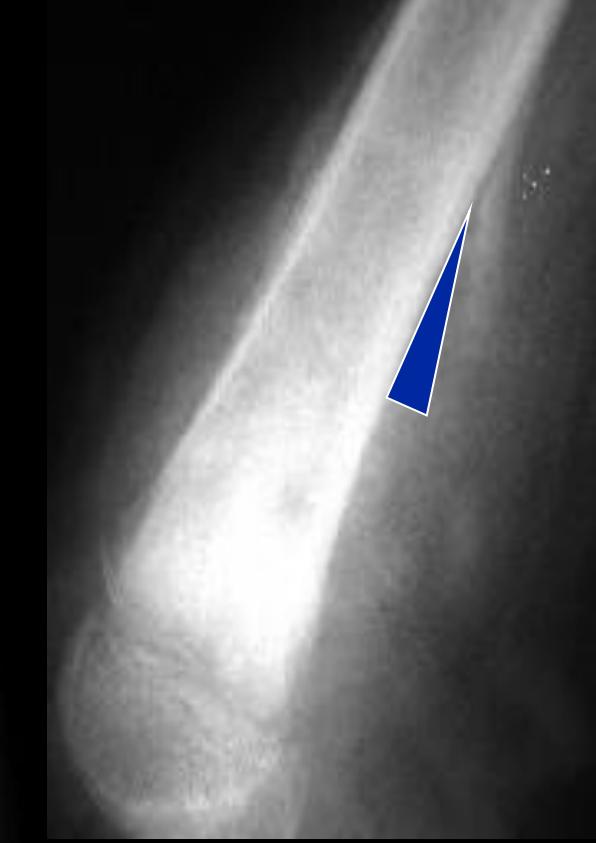
- Signs of malignancy
 - Irregular/unclear margins
 - Extensive osteolysis
 - Cortical erosion or breakage
 - Periosteal reaction
- Soft tissue extension



Sharpey's fibers



“Sunburst” pattern



Codman's triangle
Leukemia

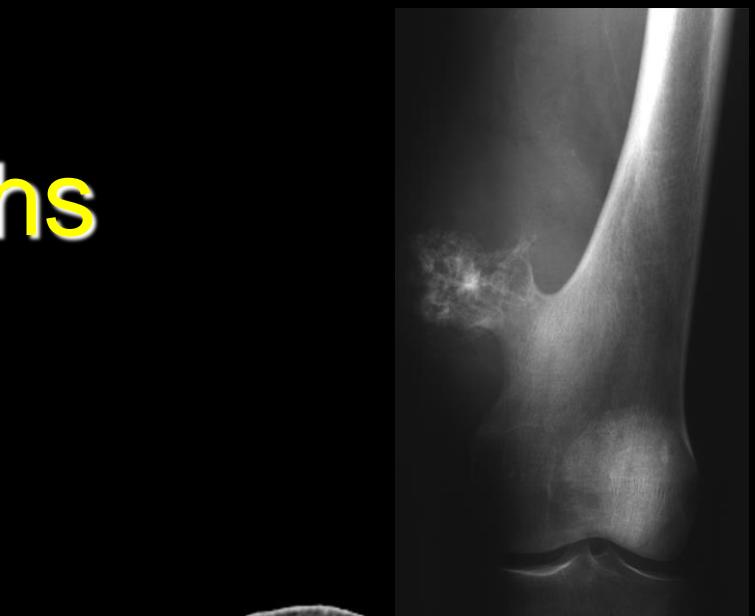
Osteosarcoma

Radiographs



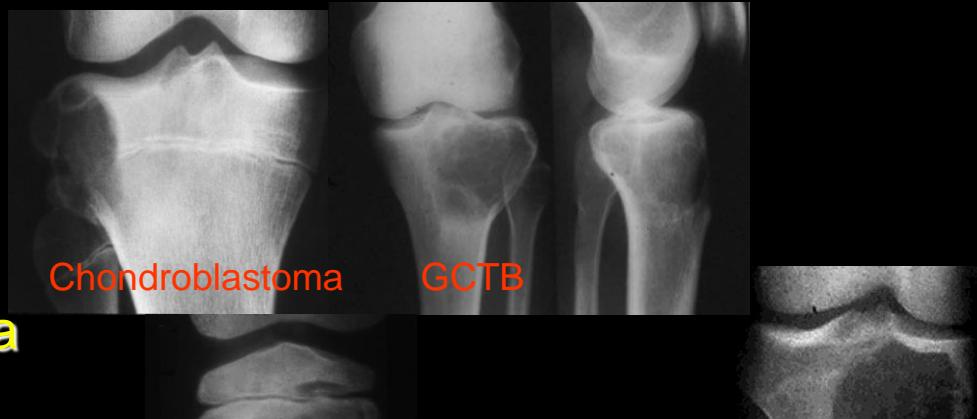
GCTB

Chondrosarcoma

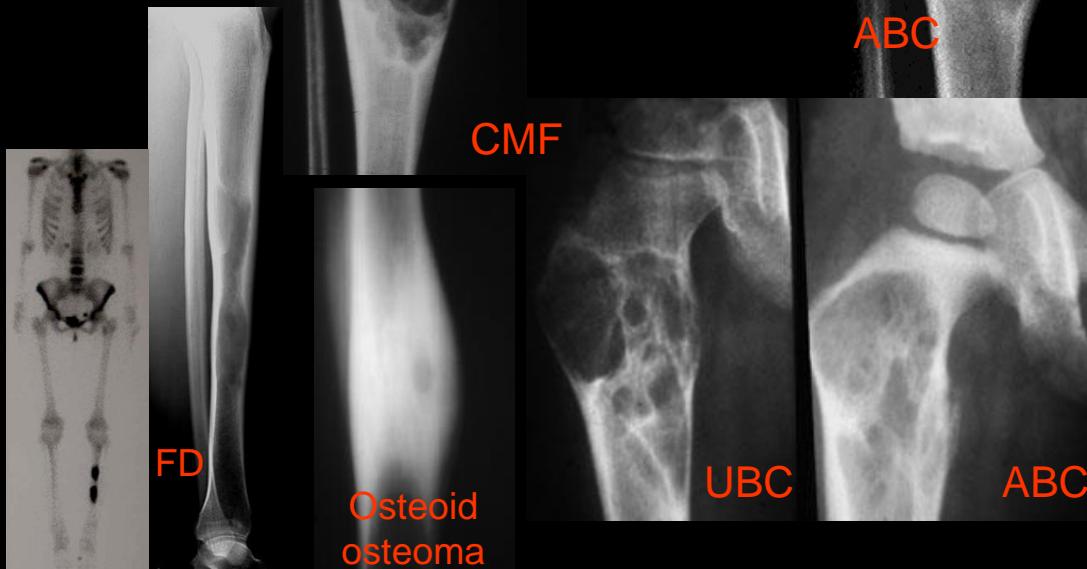


Radiographs – Bone topography

- Epiphysis
 - Chondroblastoma
 - GCTB
 - ABC
 - Clear cell chondrosarcoma



- Metaphysis
 - Cartilaginous tumors
 - Cysts
 - Histiocytic fibromas



- Diaphysis
 - Osteoid osteoma
 - FD
 - EG
 - Ewing's sarcoma

Diaphysis

Mirra JM, "Bone Tumors", 1989
"OFD progression to adamantinoma"
Czerniak B, Cancer, 1989
"Adamantinoma regression to OFD"



Osteofibrous dysplasia

Anterior tibia cortex

Bubble soap appearance

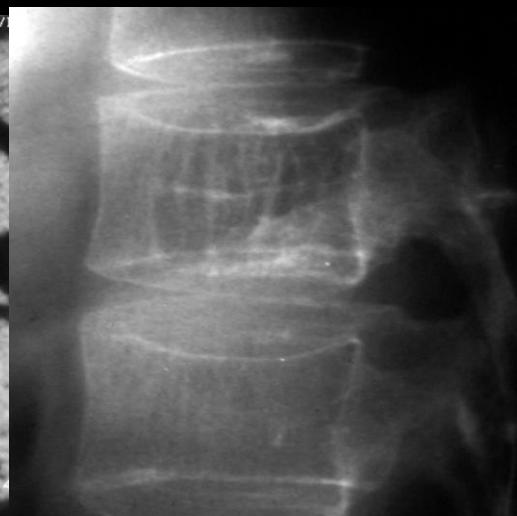
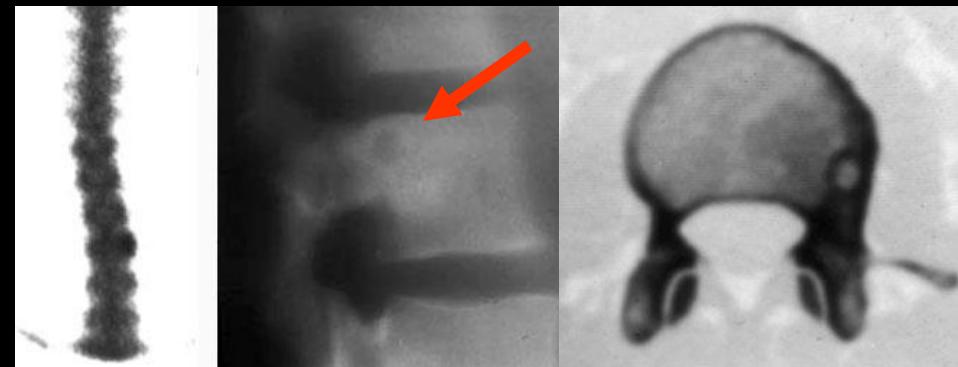
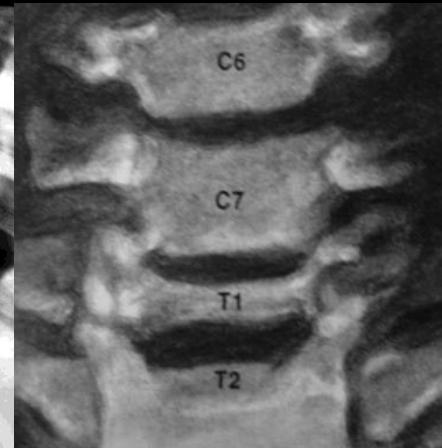
Adamantinoma

Imaging – Skeletal tomography

- Spine
 - EG
 - Hemangiomas, ABC, Osteoblastoma, Chordoma
- Flat bones
 - EG
- Hands
 - Chondromas
- Multifocal
 - FD
 - Encondromatosis
 - Osteocondromatosis
 - Hemangiomas
 - Infections

Radiographs

- Spine
- <30-yo
 - *Vertebral body*
EG
Hemangioma
 - *Posterior elements*
Osteoid osteoma
Osteoblastoma
ABC
- >40-yo
 - Metastases

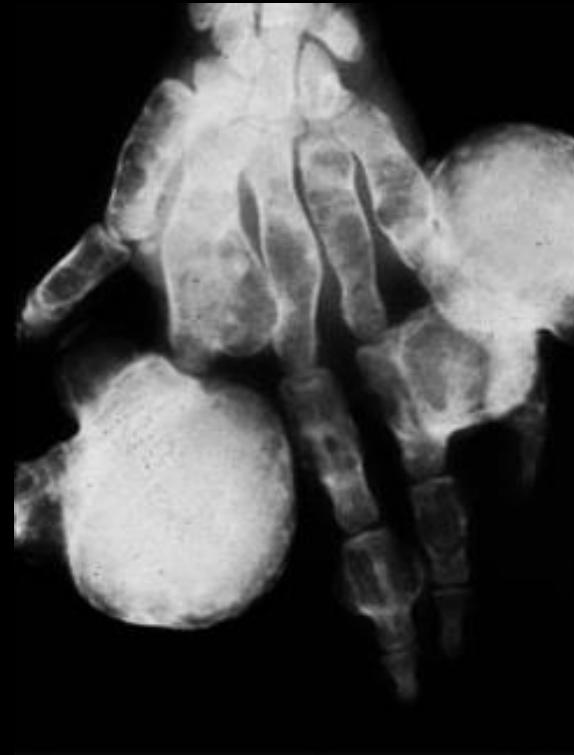


Radiographs

- Hand
 - Enchondromas
 - Epithelioid sarcoma
 - Synovial sarcoma



Enchondroma



Ollier's

Imaging

- Multiple lesions
 - **Histiocytosis**
 - **Enchondromatosis**
 - **Osteochondromatosis**
 - **FD**
 - **Vascular tumors**
 - **Infection**
 - **Hyperparathyroidism**



TBC



Chronic osteomyelitis



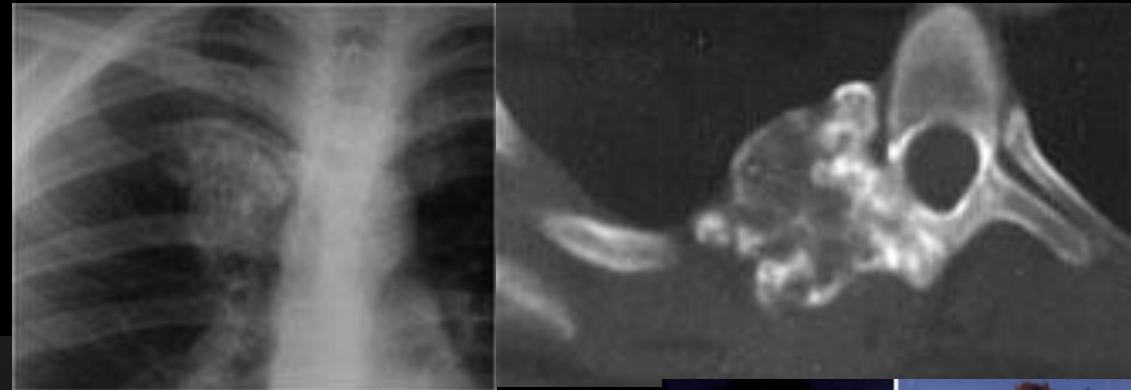
Multiple skeletal osteochondromas Bessel-Hagen disease

- Multiple Hereditary Exostoses, Hereditary Multiple Osteochondromas, Multiple Cartilaginous Exostoses.
- 1/50,000; 70-80% autosomal dominant; 20-30% *de novo* mutations (EXT1, EXT2, EXT3)



Multiple skeletal osteochondromas Bessel-Hagen disease

- Exostoses
- Deformities, LLD



Multiple skeletal osteochondromas Bessel-Hagen disease

- Malignant transformation
(chondrosarcoma)
 - up to 8.3%



Multiple chondromas

- Chondrodysplasias or
enchondromatoses
 - Ollier's disease
 - Maffucci's syndrome
- Most cases sporadic



Enchondromatoses

Ollier's disease

- 1/100,000 births
- Multiple enchondromas
 - **Hands** and feet
 - Palpable masses
 - Deformities, LLD
 - Bilateral involvement
 - Unilateral
predominance



Louis Léopold Ollier (1830–1900)

Enchondromatoses

Ollier's disease

- Increased risk of secondary chondrosarcoma
 - 25-40% by age 40 yrs



Enchondromatoses Maffucci's syndrome

- Rare (160 cases)
 - Multiple enchondromas
hands and long bones
 - Multiple hemangiomas
 - Lymphangiomas

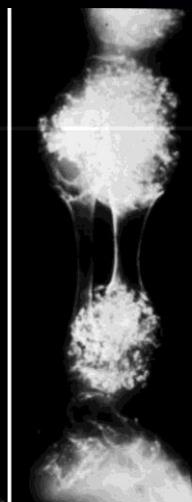


Angello Maffucci, 1881

Enchondromatoses Maffucci's syndrome

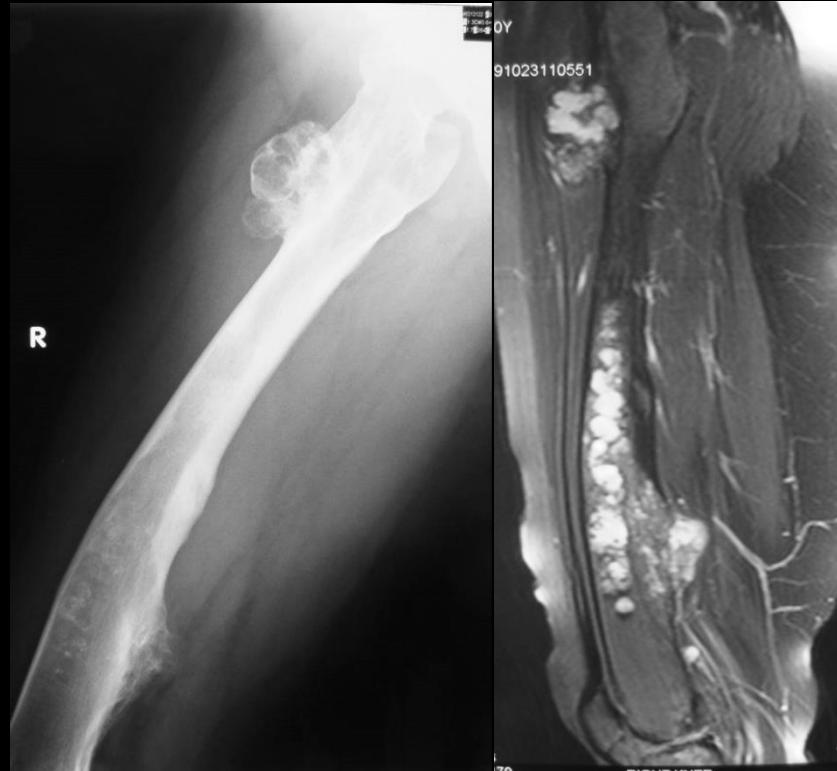
Cancer-prone syndrome (up to 100%)

- In enchondromas:
 - Chondrosarcoma
- In hemangiomas, lymphangiomas:
 - Angiosarcomas
 - Lymphangiosarcomas
- CNS, pancreatic,
d ovarian tumors



Metachondromatosis

- Multiple exostoses
- Multiple enchondromas
- Periarticular calcifications
- Frequent unilateral or bilateral Legg-Calvé-Perthes-like changes in the femoral heads
- Autosomal-dominant



Maroteaux P. La metachondromatose. Z Kinderheilkd. 1971;109:246-61.

Pathological fractures

Children

- UBC (humerus, femur; 80% at presentation)
- NOF (femur, tibia)
- EG
- FD

Adults

- GCTB (5-10% at presentation)
- ABC
- Metastatic bone disease



Pathological fracture



Chondromas (solitary)

Pathological fracture



Metastatic bone disease (RCC)



**Metastatic bone disease
(breast cancer)**

Radiographs

- **Shape of the lesion**
- Some lesions tend to have a more spherical shape
 - GCT, osteosarcoma
- Other lesions tend to conform to the shape of the bone in which they arise
 - chondrosarcoma



Radiographs

- Margins of the lesion
- Provide most of the information regarding rate of growth
 - Static (solid, dense boundary)
 - Slow-growing (sharp demarcation, not dense)
 - Faster-growing (moth-eaten)
 - Fastest (permeative)

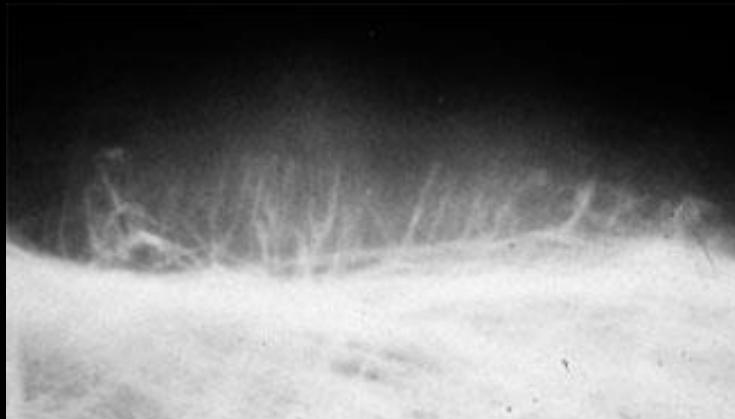
Radiology. 1980 Mar;134(3):577-83.

Determining growth rates of focal lesions of bone from radiographs.

Lodwick GS, Wilson AJ, Farrell C, Virtama P, Dittrich F.

Radiographs

- **Periosteal reaction** (biologic activity)
 - uninterrupted, smooth (slow-growing, benign lesion)
 - disrupted periosteal (bone sarcomas)
 - amorphous (thick)
 - laminated (“onion-skin”)
 - spiculated (“sunburst”)



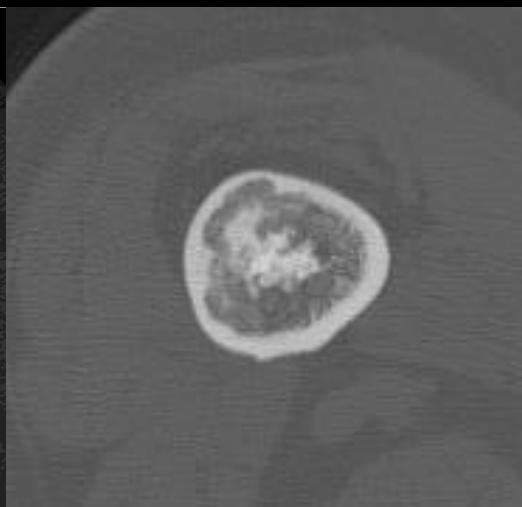
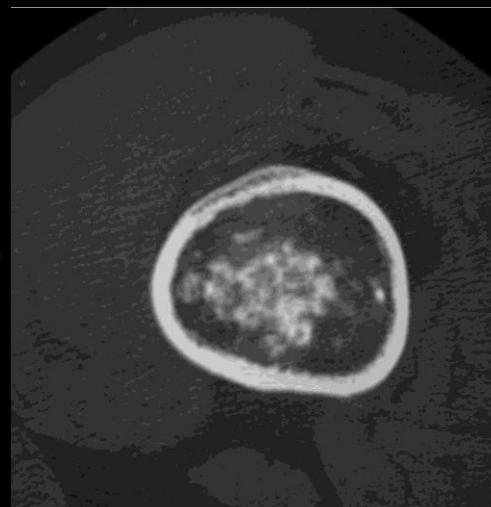
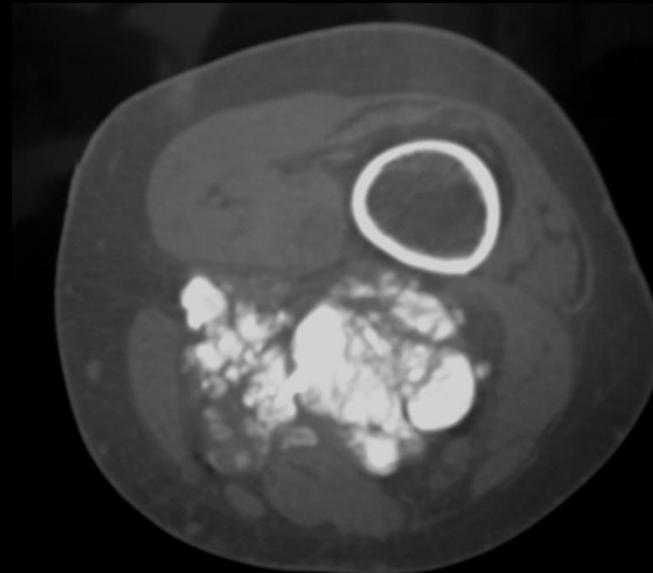
Radiographs (+/-CT)

- **Matrix mineralization**
 - Characterizes the intercellular material produced by the lesion
- Osteoblastic lesion
 - ossified matrix (ossification, dense lumps or clouds, fuzzy or sharp margins)
- Chondroblastic lesion
 - chondroid matrix (calcification, rings or arcs - enchondral ossification along lobules of cartilage)
- Ewing's sarcoma
 - matrix mineralization is absent



CT

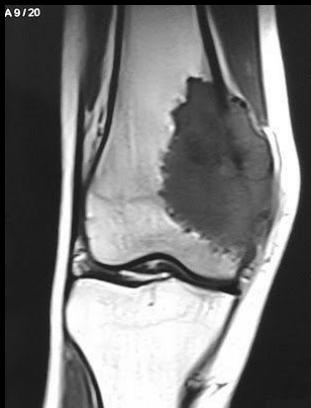
- Superior to Rx
 - evaluation of matrix
 - evaluation of path fx
- Superior to MRI
 - detection and characterization of cortical involvement
 - evaluation of occult pathological fractures



MR imaging

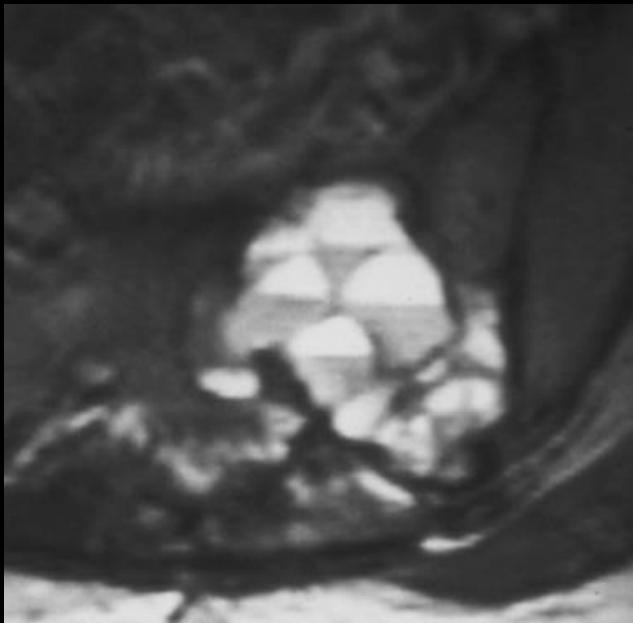
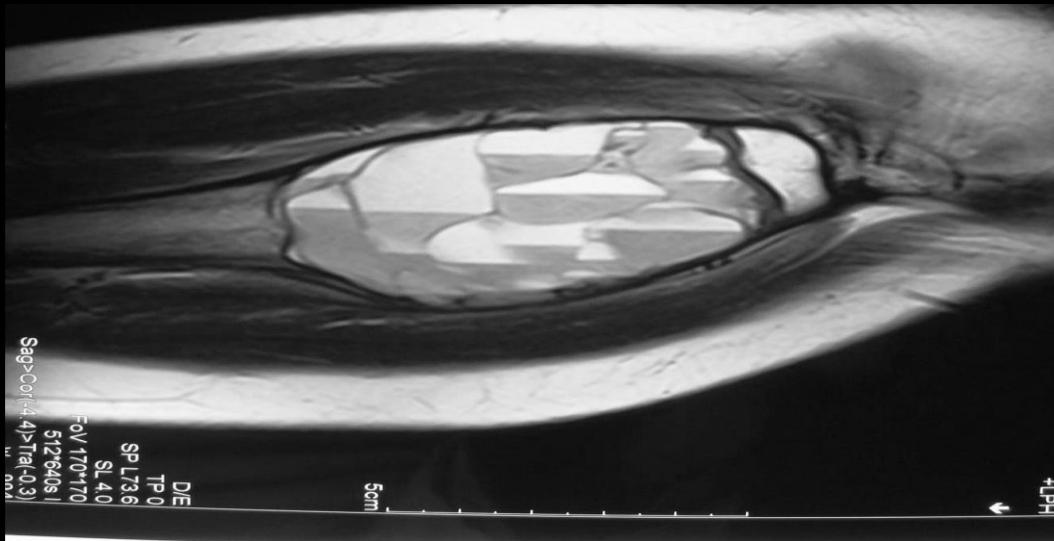
- Bone marrow edema
- Benign lesions – Large edema
 - osteoid osteoma,
osteoblastoma,
chondroblastoma, EG
- Malignant lesions
 - Minimal edema surrounding a large lesion
 - Large inflammatory response of surrounding soft tissues



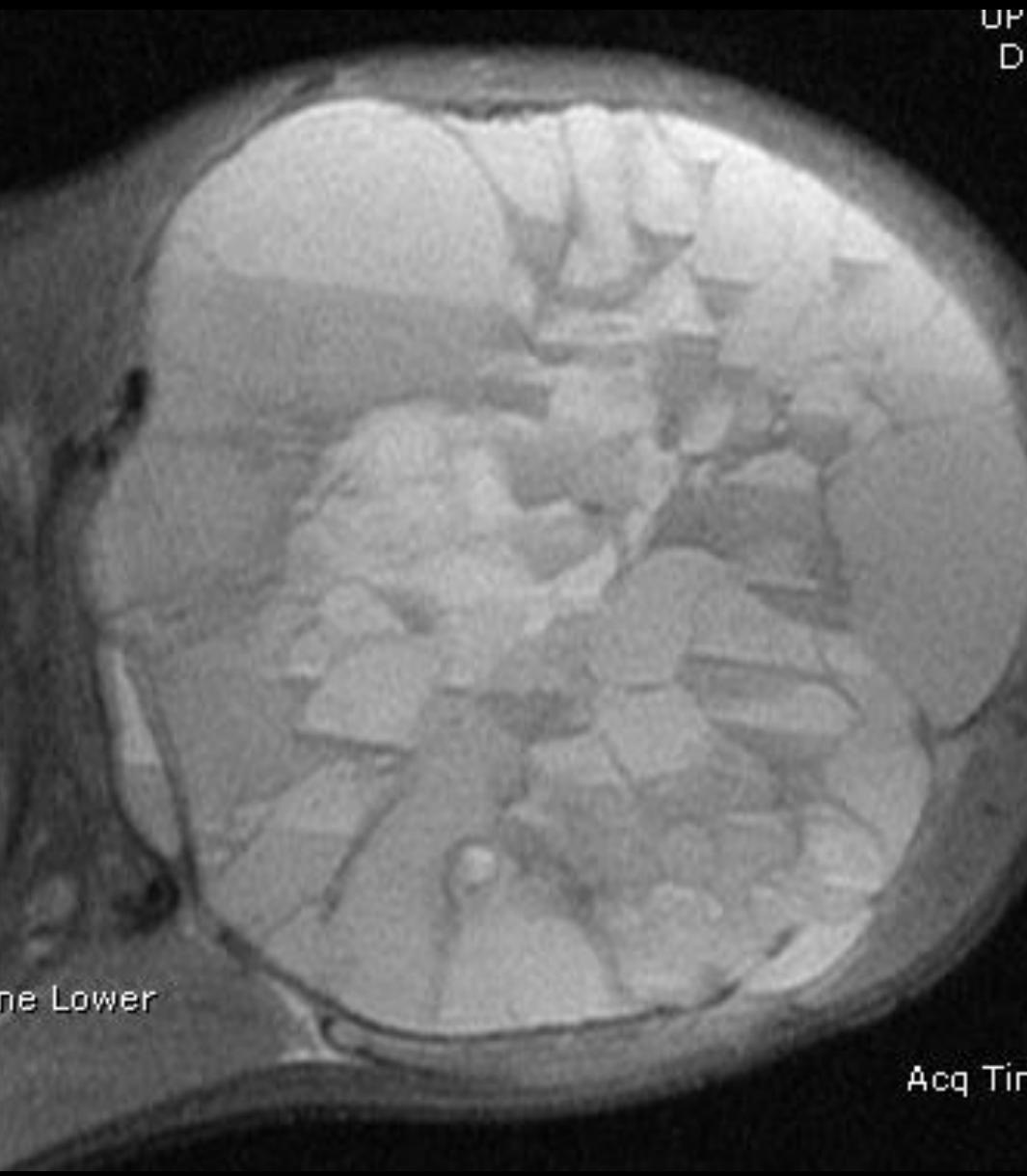


MR imaging

- Fluid-fluid levels
 - ABC
 - GCTB
 - Ewing's sarcoma
 - Telangiectatic OGS



ne Lower



UP
Do

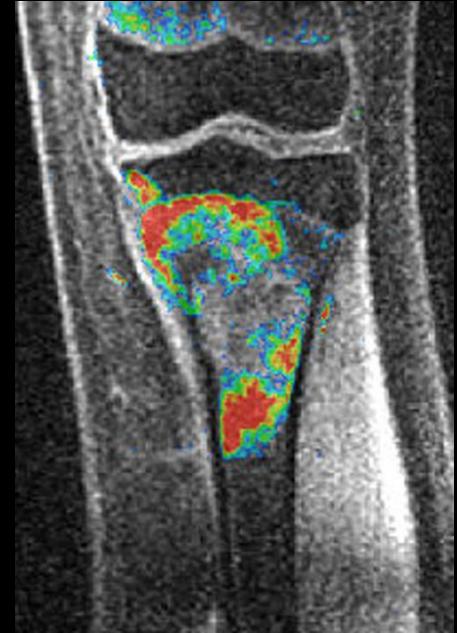
Acq Tin



cm

MR imaging

- Does not provide sufficient information on degree of tumor viability
 - signal intensity changes do not distinguish between viable tumor, tumor necrosis, and edema, even after administration of intra-venous gadolinium
- **Dynamic MRI**
 - rapid uptake: viable tumor
 - edema: takes gadolinium at a slower rate



Imaging

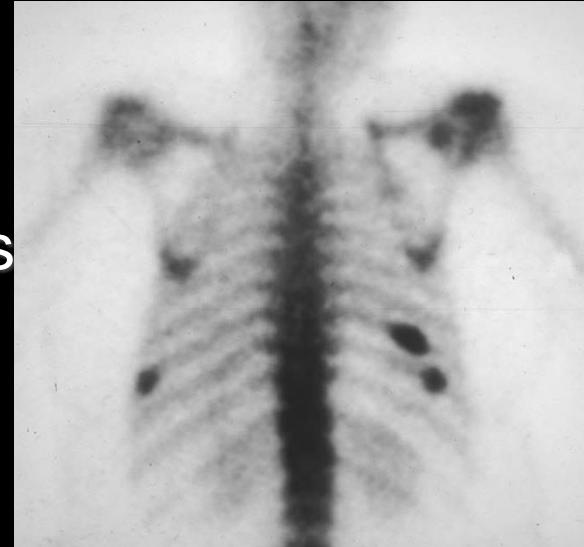
Systemic

- Chest CT
- Bone scan
- Abdomen/
retroperitoneal CT
- PET/CT



Bone scan

- Highly sensitive
- Dynamic images (aggressiveness)
- Delayed-phase images (non-specific)
- False negative “cold” scan
 - plasmacytoma, multiple myeloma, and occasionally in chordoma



FDG-PET

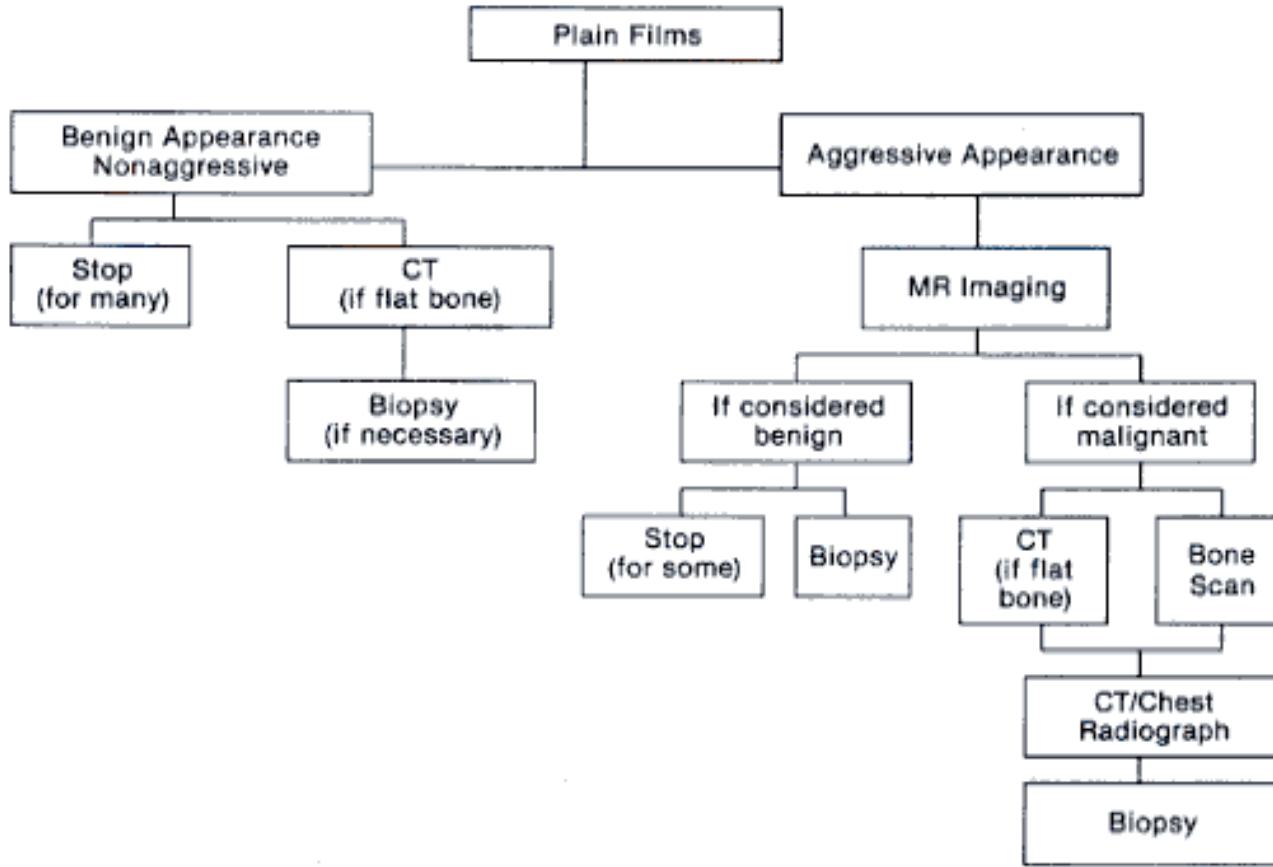
- It quantifies the **biologic activity of tissue**
- It does not quantify morphologic abnormality
- It correlates with the cellularity, mitotic activity, and over-expression of p53 in bone sarcomas
 - May have prognostic value in sarcoma



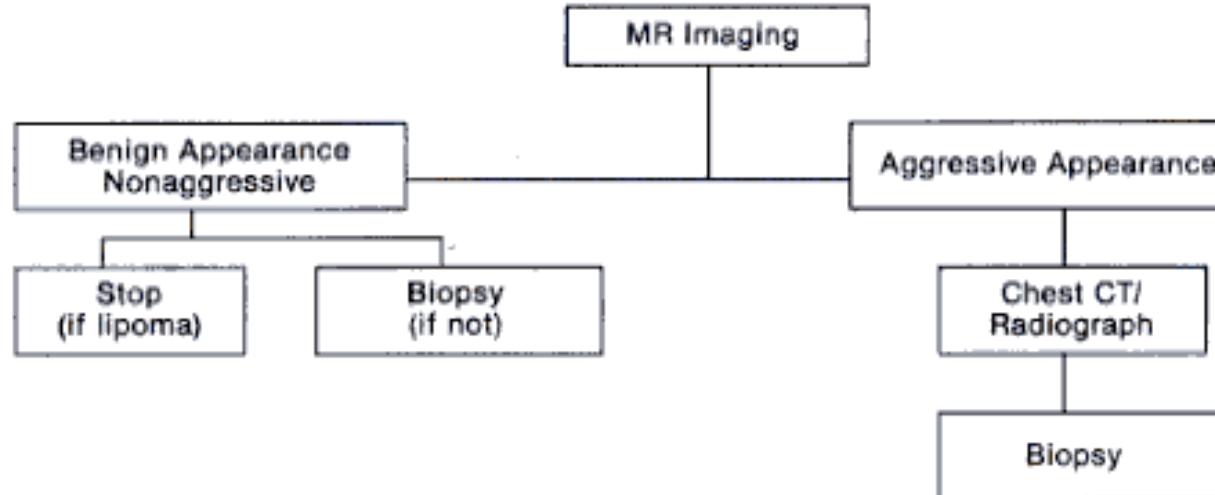
Biopsy

- Is a biopsy necessary?
- A narrow differential
 - to monitor the lesion radiographically over time or to proceed directly with appropriate treatment
- A broad differential and/or a precise diagnosis is critical
 - biopsy

BONE TUMORS



SOFT TISSUE TUMORS



Biopsy

- The last step
- Obtain cultures



How Should Musculoskeletal Biopsies Be Performed?

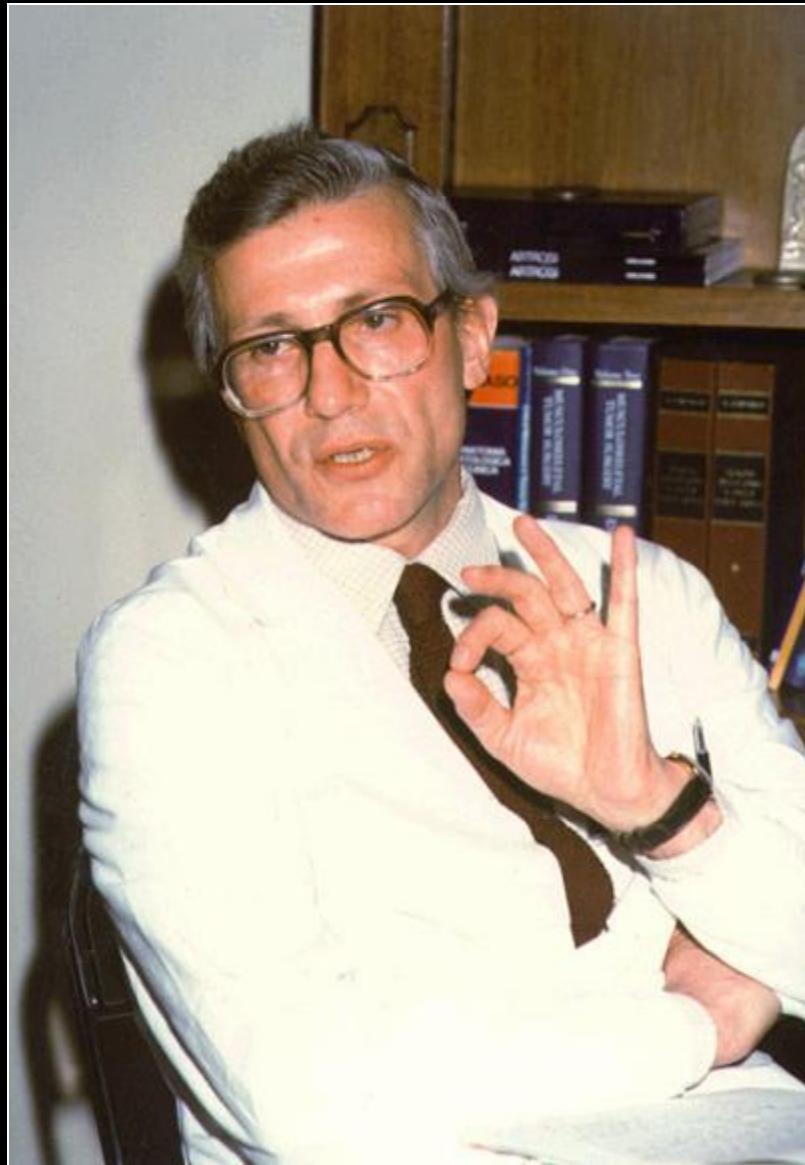
Andreas F. Mavrogenis, MD; Andrea Angelini, MD; Costantino Errani, MD; Eugenio Rimondi, MD

The principles of biopsy

Andreas F. Mavrogenis

CT-guided Biopsy for Musculoskeletal Lesions

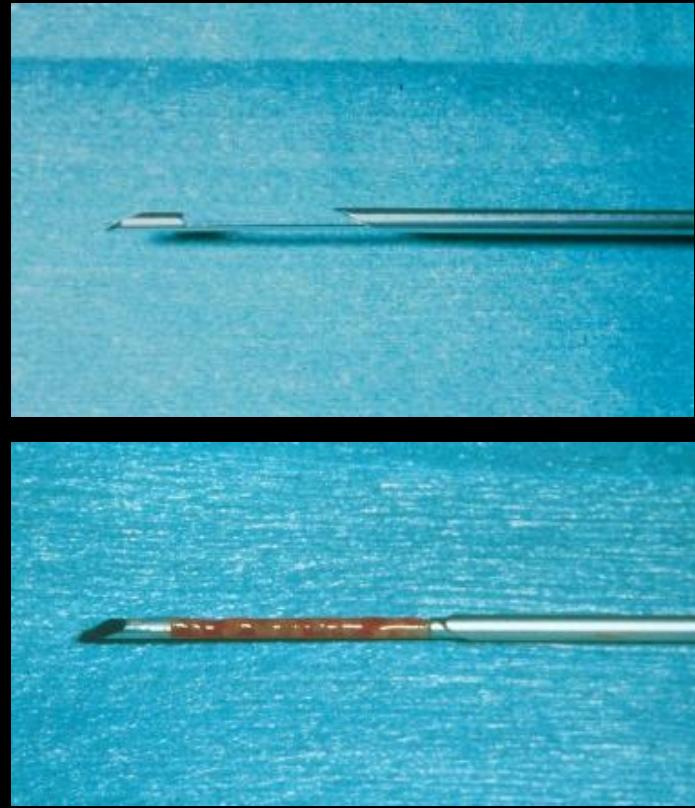
Andreas F. Mavrogenis, MD; Eugenio Rimondi, MD; Giuseppe Rossi, MD; Teresa Calabò, MD; Pietro Ruggieri, MD



..... biopsy is an important surgical procedure and it should be performed by an experienced surgeon, while definitive surgery can also be performed by the young orthopaedic surgeon!

Closed biopsy

- **The gold standard**
 - Safe (minimally invasive)
 - High accuracy (68%-97%)
 - **No difference with open biopsy**
 - Cost effective (office procedure)
 - Rare complications (<11%)

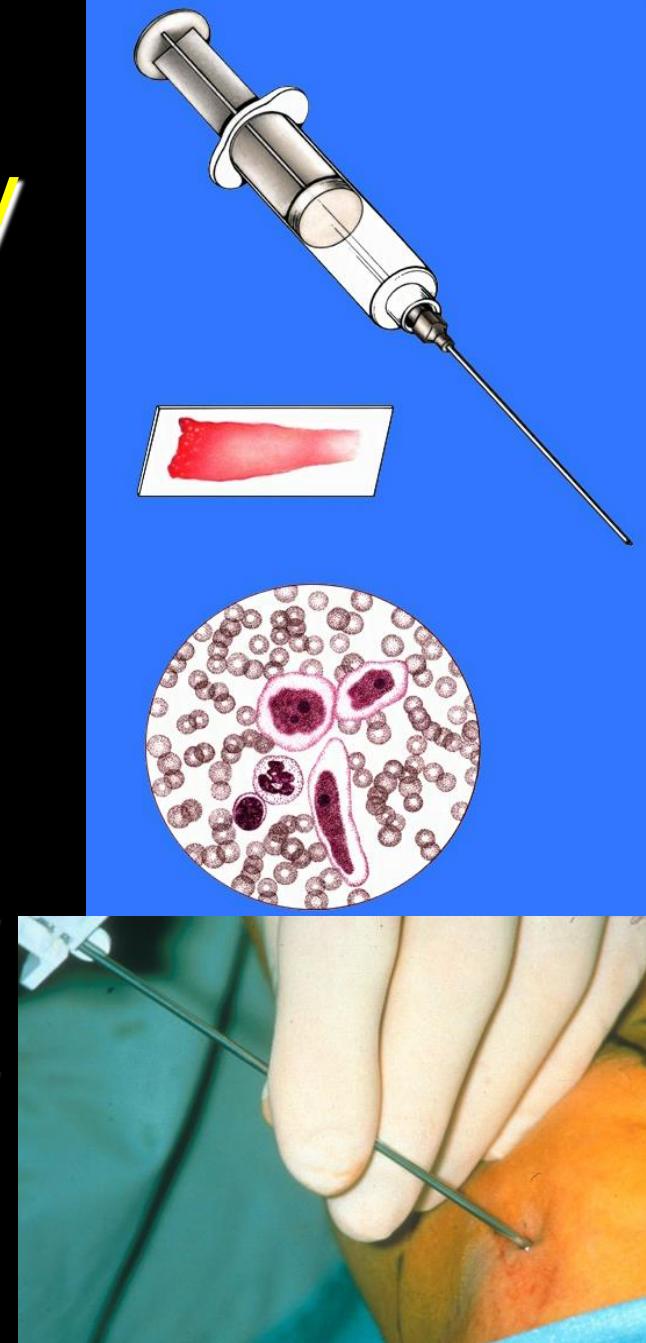


Adams et al, CORR. 2010
Le et al, Semin Intervent Radiol. 2010
Rimondi E, et al, Eur Radiol, 2011
Pohlig et al, Eur J Med Res. 2012

Closed biopsy

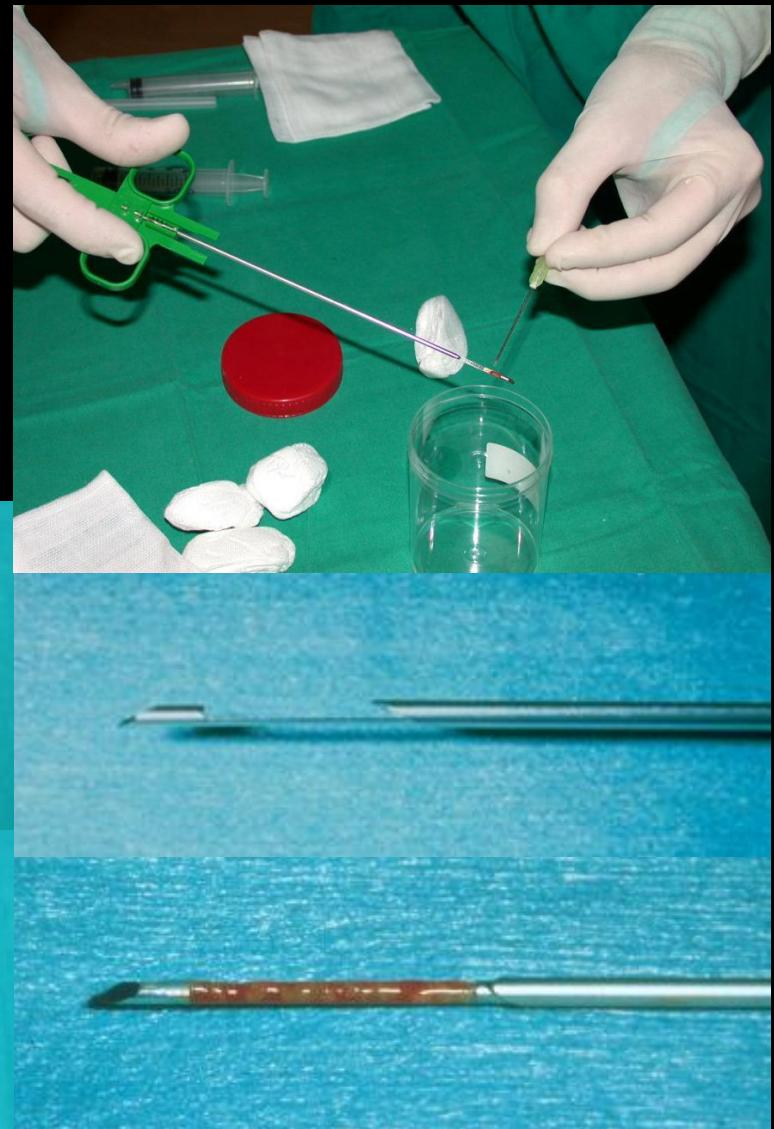
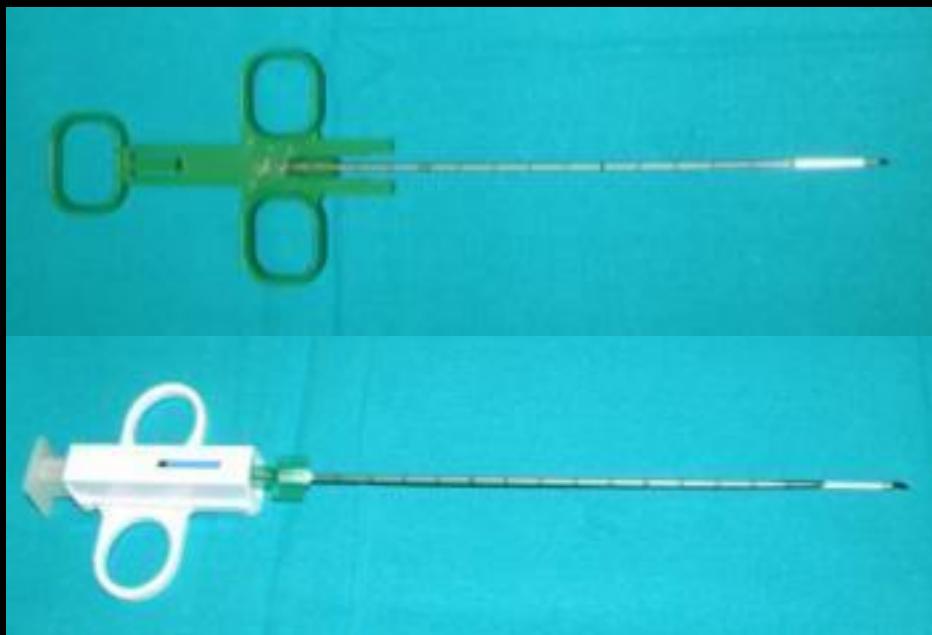
- **FNA**

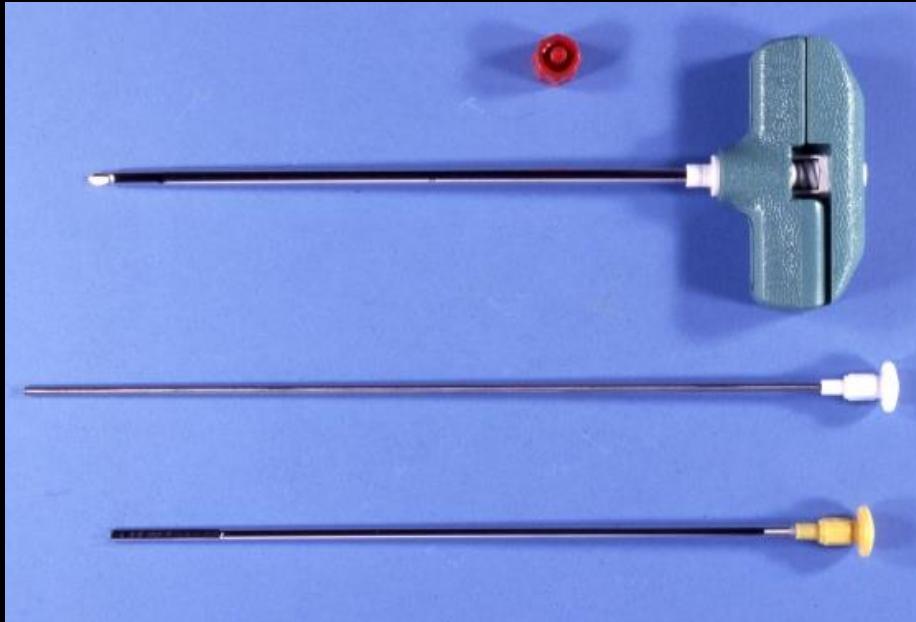
- High rate of false negative results
- Tissue architecture cannot be evaluated
- Cytology samples are not always adequate for cytogenetic, molecular, or immunohisto studies
- Recommended for documentation of metastases and local or distant tumor recurrence where the cytology findings can be compared with the prior histology



Closed biopsy

- Core, TruCut®, Jamshidi, others...

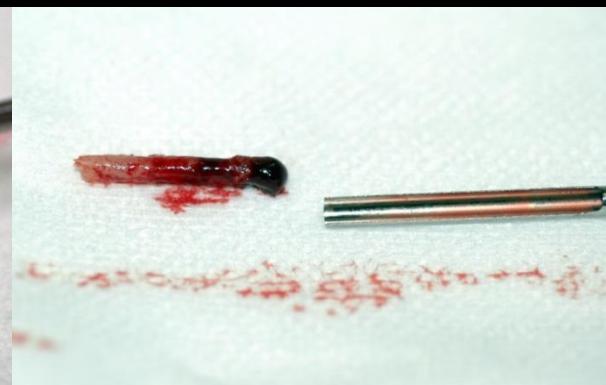






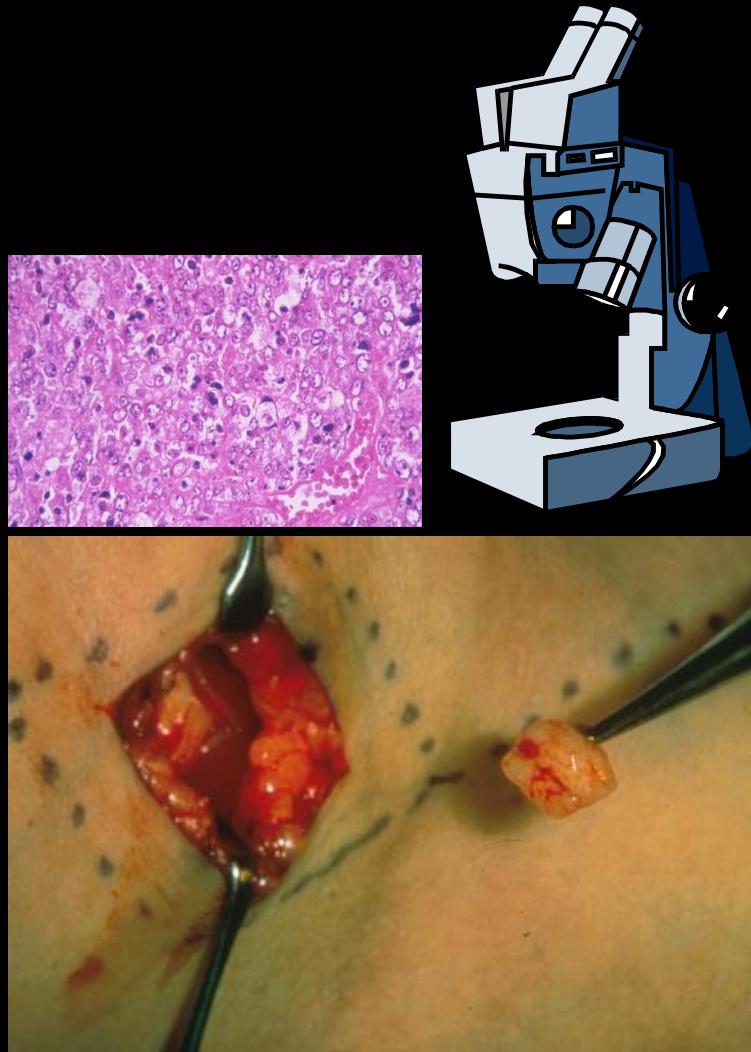
Closed Biopsy

- Non-guided (free hand)
- Guided
 - Fluoroscopy
 - US
 - CT
 - MRI
 - PET-CT



Open biopsy

- **Indications**
 - When adequate tissue sample cannot be obtained with closed biopsy
 - When accurate histological diagnosis and grading is required to decide for preoperative chemotherapy or radiation therapy
 - When closed biopsy does not correlate with the clinical presentation and imaging



CLASSIFICATION OF PRIMARY TUMORS OF BONE

LOUIS LICHTENSTEIN, M.D.

CANCER March 1951

**BENIGN TUMORS
OF BONE**

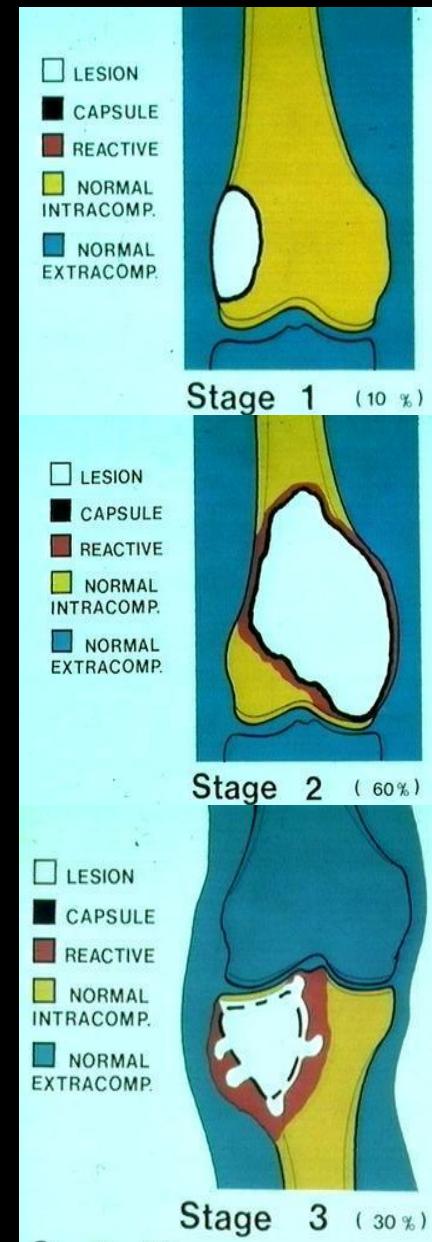
		MALIGNANT COUNTERPART (IF ANY)	MALIGNANT TUMORS OF BONE (ARISING THROUGH MALIGNANT CHANGE OR INDEPENDENTLY)
OF CARTILAGE-CELL OR CARTILAGE-FORMING CON- NECTIVE-TISSUE DERIVATION	PERIPHERAL CENTRAL	{ OSTEOCARTILAGENOUS EXOSTOSIS (MULTIPLE EXOSTOSIS) ENCHONDROMA (SKELETAL ENCHONDROMATOSIS) BENIGN CHONDOBLASTOMA CHONDROMYXOID FIBROMA	PERIPHERAL CHONDROSARCOMA CENTRAL CHONDROSARCOMA } CHONDROSARCOMA (NOT KNOWN) (NOT KNOWN)
OF OSTEOBLASTIC DERIVATION		{ OSTEOMA OSTEOID-OSTEOMA OSTEOGENIC FIBROMA OTHER OSTEOID-TISSUE-FORMING TUMORS (OSTEOGENIC SARCOMA)	(NOT KNOWN) (NOT KNOWN) (NOT KNOWN) OSTEOPETROUS SARCOMA
OF NONOSTEOBLASTIC CON- NECTIVE-TISSUE DERIVATION		{ NONOSTEOGENIC FIBROMA LEAST-AGGRESSIVE GIANT-CELL TUMORS—MORE AGGRESSIVE & MALIGNANT GIANT-CELL TUMORS—FRANKLY MALIGNANT GIANT-CELL TUMORS	(NOT KNOWN) FIBROSARCOMA GIANT-CELL TUMORS—FRANKLY MALIGNANT GIANT-CELL TUMORS
OF MESENCHYMAL CON- NECTIVE-TISSUE ORIGIN		-----	EWING'S SARCOMA
OF HEMATOPOIETIC ORIGIN		-----	{ MULTIPLE MYELOMA CHRONIC MYELOID LEUKEMIA ACUTE LEUKEMIAS MALIGNANT LYMPHOMA } RETICULUM-CELL SARCOMA "LYMPHOSARCOMA" HODGKIN'S DISEASE
OF NERVE ORIGIN		{ NEUROFIBROMA NEURILEMOMA	(MALIGNANT SCHWANNOMA)
OF VASCULAR ORIGIN		{ HEMANGIOMA HEMANGIOPERICYTOMA (GLOMUS)	(HEMANGIOENDOTHELIOMA) HEMANGIOENDOTHELIOMA
OF FAT-CELL ORIGIN		-----	LIPOSARCOMA (?)
OF NOTOCHORDAL DERIVATION		-----	CHORDOMA
OF ADAMANTINE OR POSSIBLY BASAL-CELL DERIVATION		-----	SO-CALLED ADAMANTINOMA



Enneking's Classification

Benign

- Stage 1: Latent, inactive
G0, T0, M0
 - (capsule, cortex intact, intracompartmental)
- Stage 2: Active
G0, T1, M0
 - (no capsule, cortex focally broken, intracompartmental)
- Stage 3: Aggressive
G0, T1-2, M0-1
 - (no capsule, cortex broken, extracompartmental)



Enneking WF, Spanier SS, Goodman MA,
CORR 1980



Enneking's Classification Malignant

- Stage I: Low grade
G1, M0
- Stage II: High grade
G2, M0
- Stage III: Any grade
M1

A: intracompartmental
B: extracompartmental



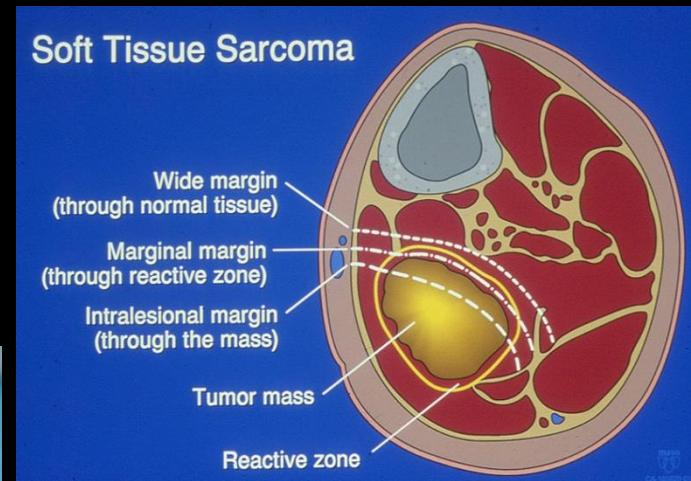
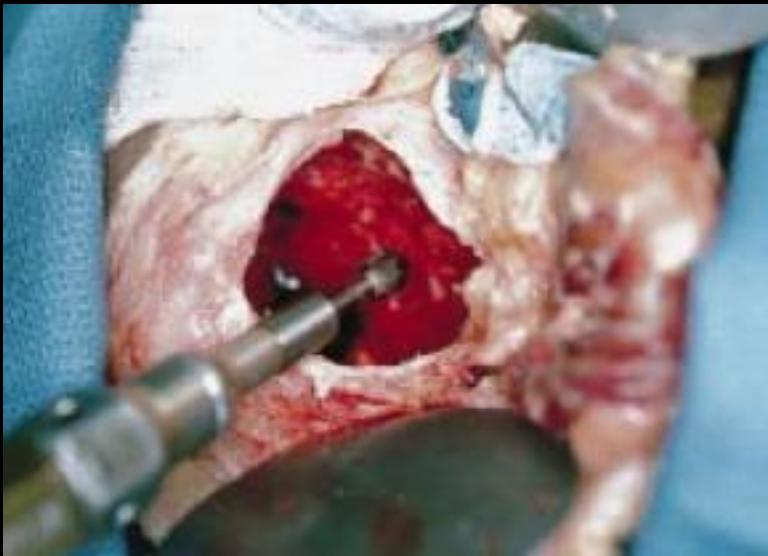
Editorial

Recent Developments in the Surgical Treatment of Bone Tumors and Their Impact on Quality of Life

Andreas F. Mavrogenis,¹ Ulrich Lenze,² Hans Rechl,²
G. Douglas Letson,^{3,4} and Pietro Ruggieri¹



The Management



Conclusion

Approach – Staging

- History – Clinical examination
- Imaging
 - Rx, MRI, bone scan, CT
- Laboratory
 - ALP, serum electrophoresis, PSA
- Biopsy
 - Closed, guided
- Classification
 - Histological, Surgical



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