



Bone Tumors

May Parisien, M.D.

Columbia University, New York

CPMC



Classification

Secondary (metastases) (95%)

Primary (5%)



Secondary tumors

Malignancies originating from distant (primary) organs

- *most frequent: carcinomas/ malignant epithelial tumors of viscera*
- *rare: sarcomas /malignant mesenchymal tumors)*



Secondary Tumors of Bone ***Most frequent primaries***

Lung

Breast

Prostate

Gastro-intestinal

Kidney

Thyroid

In order of frequency from up to down and from your left to your right.



Secondary Tumors of Bone ***Mechanism of transport***

Paravertebral venous plexuses

- *retrograde access of tumor cells to bone*
- *bypass of porto-caval venous drainage*

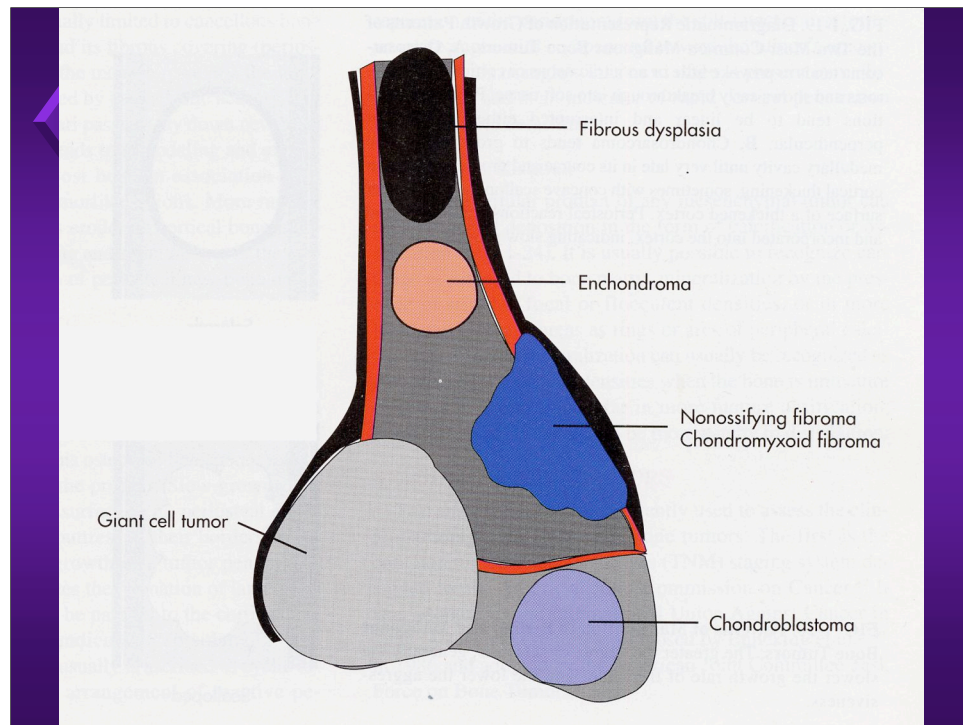
This mechanism explains the predilection of metastases for the axial skeleton (spine, pelvis) and adjacent proximal humerus and femur



Primary neoplasms of bone

***Definition:** tumors of **mesenchymal** origin arising in bone*

***Routes of spread:** hematogenous (lung, liver, bone)*



One of the characteristics of primary bone tumors is their predilection for certain bones and, within these bones, certain anatomic sites (diaphysis, metaphysis, epiphysis) and their central or excentric location.



Primary neoplasms of bone

Means of identification

Matrix morphology

Immunophenotypical markers

Clin/ radiologic correlation: a must!

In a primary tumor of bone, the mesenchymal cell produces a particular type of matrix in an attempt to imitate the original tissue. For example, bone tumors produce neoplastic osteoid, cartilage tumors neoplastic chondroid, fibrous tumors neoplastic fibrous matrix, etc... The morphologic features or immunohistochemical identification of this matrix, and the knowledge of the clinical/ radiographic presentation (location, location, location!) work together to facilitate the recognition of the tumor.



Primary Tumors of Bone Classification

- ***Bone-forming***
- ***Cartilage-forming***
- *Fibrous tumors*
- *Tumors of unknown origin*



Bone-forming tumors

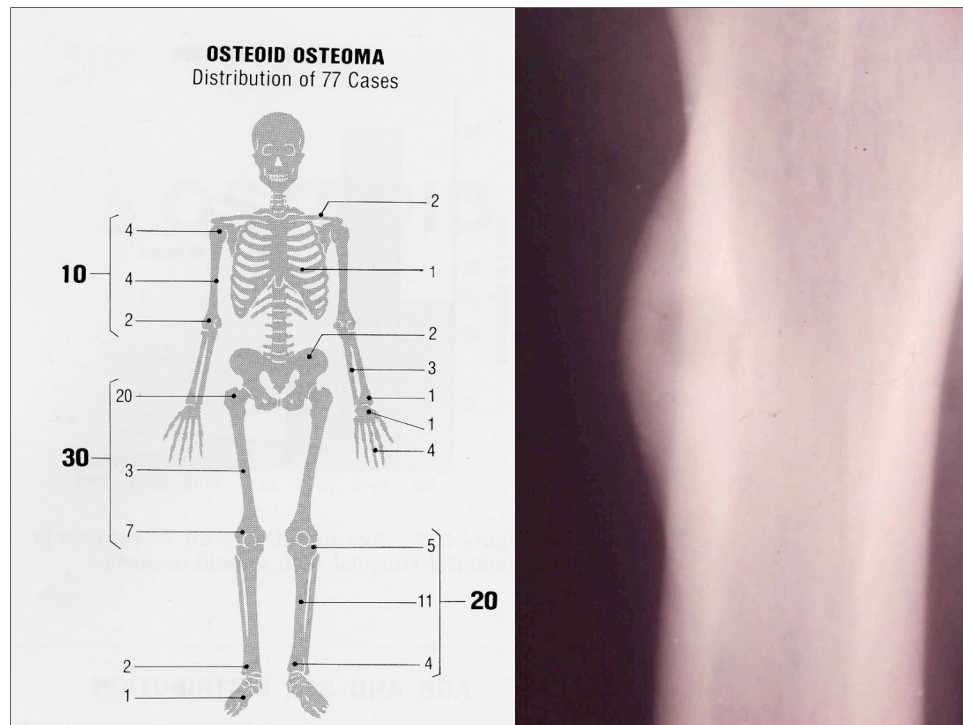
Benign

Osteoid osteoma

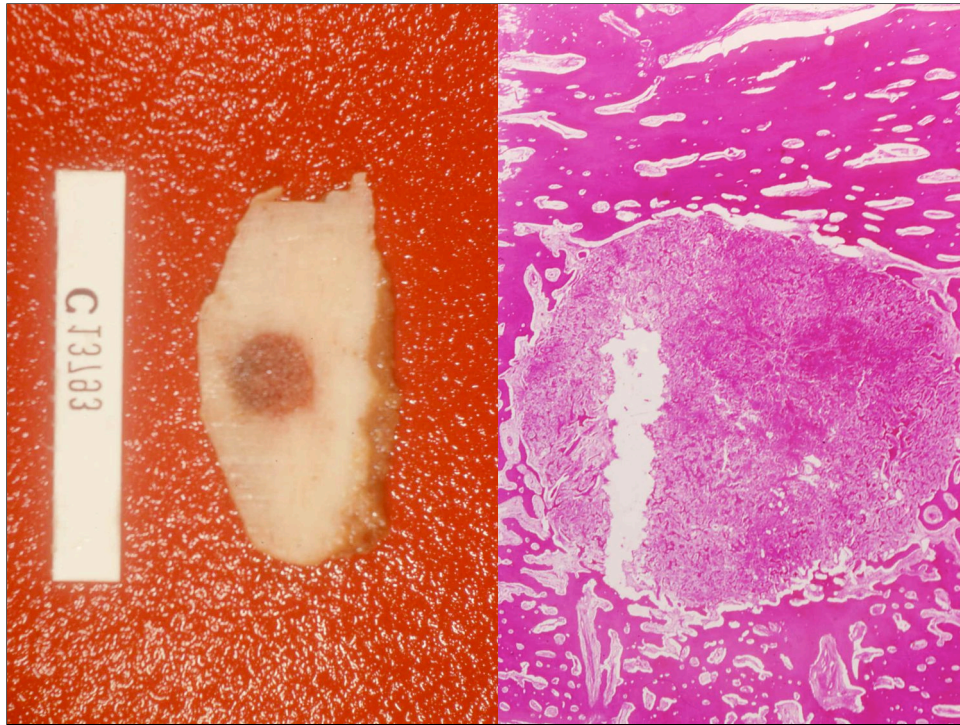
Osteoblastoma

Malignant

Osteosarcoma



This tumor predilects the lower extremities, particularly the femur, less frequently the tibia, with the single most common site being the neck of the femur. Pain, exacerbated at night, is the hallmark of this tumor and is dramatically relieved by aspirin.



Grossly and histologically, a small round defect of the bone “nidus” measuring no more than 1.5 cm represents the tumor. Cure is achieved when the nidus is completely removed.



Malignant Tumors of Bone ***Osteosarcomas***

Central

Low Grade

High Grade

Surface

Low Grade

High Grade



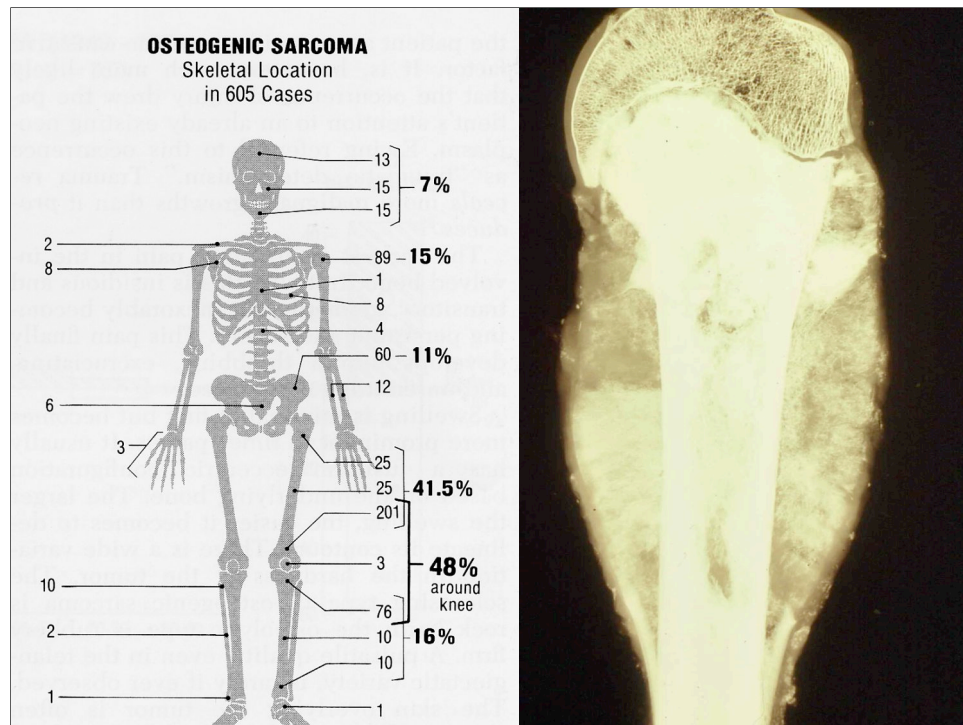
Osteosarcomas

Definition

Malignant neoplasm of bone

- *malignant mesenchymal cell*
- *malignant bone matrix*

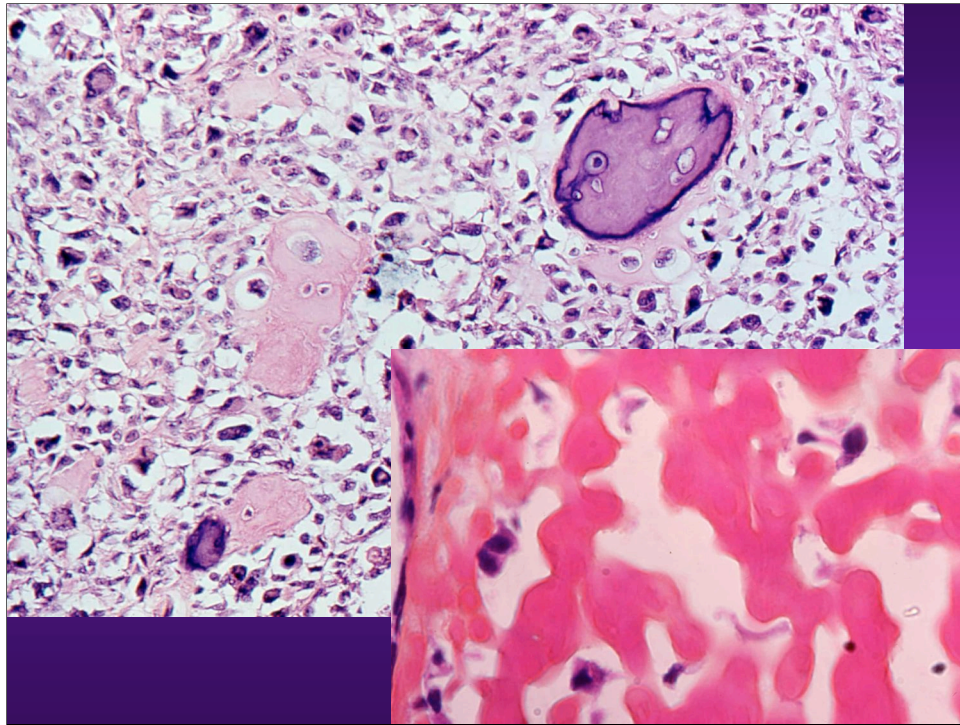
Recognition of osteosarcoma is based on the close relationship between the malignant mesenchymal cell and the malignant bone matrix “osteoid”, strongly suggesting the production of this matrix by the tumor cells.



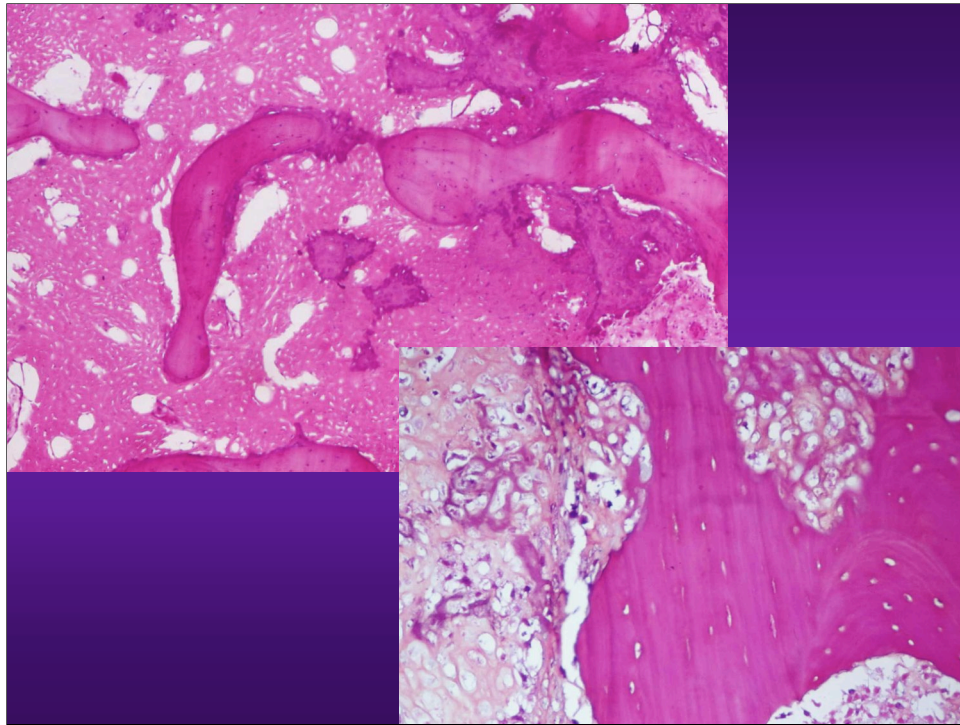
Most frequent sites are overwhelmingly the knee (distal femur, proximal tibia), followed by the proximal femur and proximal humerus. Within the bone, the metaphyseal location is characteristic of the tumor. Also characteristic of osteosarcoma is the frequency with which the tumor breaks out of the medullary canal to invade the soft tissues and form a soft tissue mass. Osteosarcoma is therefore “extracompartmental in the large majority of cases (stage IIB). The tumor typically does not breach the growth plate to enter the epiphysis until late in the disease. A typical genetic abnormality is a mutation of the Rb gene (13q14). Read about the hereditary germline or acquired mutation of Rb and retinoblastoma and the high risk of development of osteosarcoma. Other abnormalities are the amplification of MDM2 with inactivation of p53. A germline mutation of p53 allele leads to the Li-Fraumeni syndrome which carries a high risk of osteosarcoma. Osteosarcoma is generally a high-grade tumor and is lethal if not treated or poorly treated. In the past 30 years, the 5 years survival has climbed from 18% to 70% due to advances in the therapy (limb-salvage surgery+ multidrug chemotherapy), with marked improvement in the quality of life. (See last picture). Read about neoadjuvant chemotherapy.



The mandible is one of the sites (although less frequent) of involvement. Tumors at this site tend to have a better prognosis than those of the long bones.



Histological examples of osteosarcoma can be found in your website.
Tumor cells surrounded by strands of osteoid matrix.



This tumor typically infiltrates and replaces the bone marrow with a dramatic difference in structure between the host bone (lamellar, mature) and the tumor bone (immature), the latter deposited in fine strands forming lace-like or mesh-like patterns.



Osteosarcomas

Mesenchymal cell is multipotential

*Malignant osteoid **essential for**
recognition*

The mesenchymal cell is capable of producing different types of matrices. Regardless of what other type of matrix a malignant bone tumor forms (chondroid, fibrous, etc..), the presence of malignant osteoid positively identifies it as osteosarcoma.



Osteosarcoma ***Histologic types***

Osteoblastic

Chondroblastic

Fibroblastic

Telangiectatic

Small cell type

Giant cell rich

Osteoblastoma-like

Don't be alarmed. This is just to remind you that the mesenchymal cell is multipotential, hence there are different histologic subtypes of osteosarcoma. The most frequent is the osteoblastic type.



Cartilage-forming Tumors

Benign

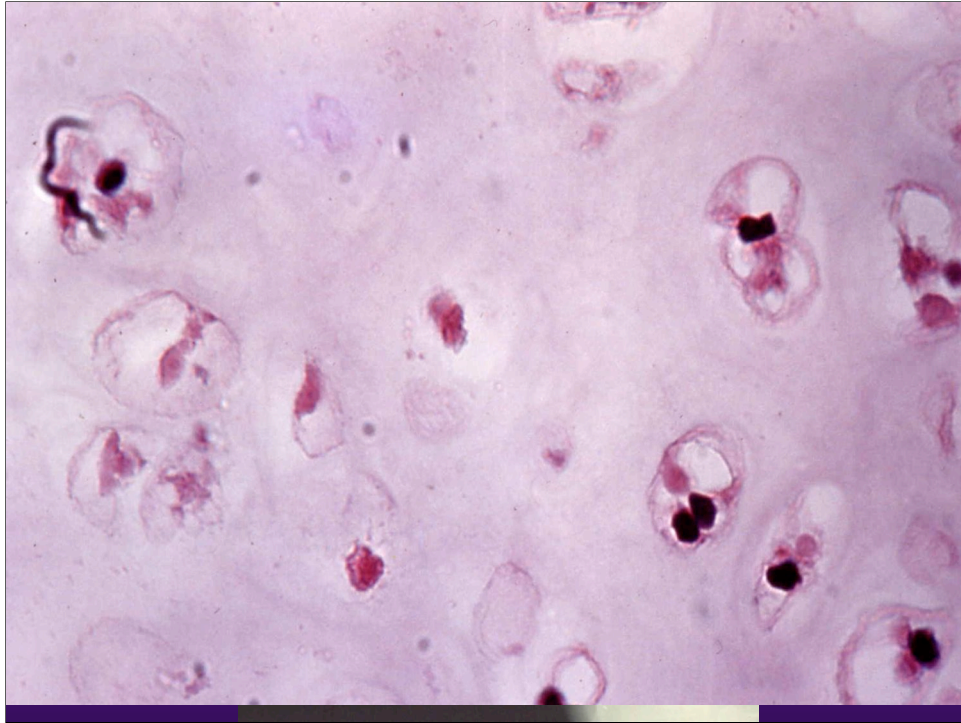
Chondroma

Malignant

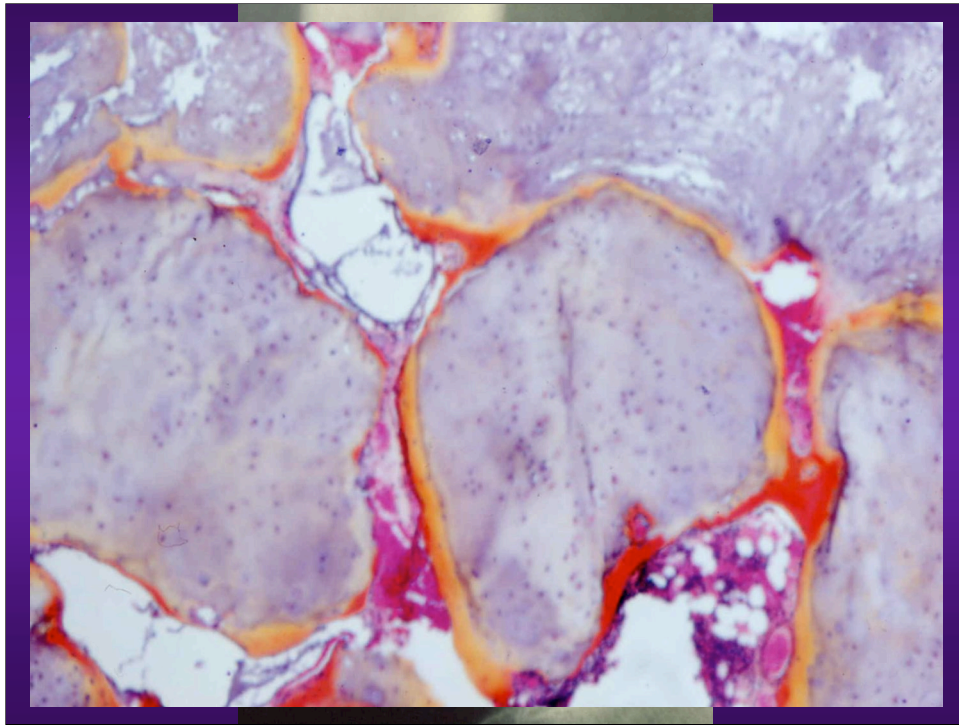
Chondrosarcoma

This table is oversimplified, and there are other histologic subtypes of benign and malignant cartilage-forming tumors. You are being spared for now!

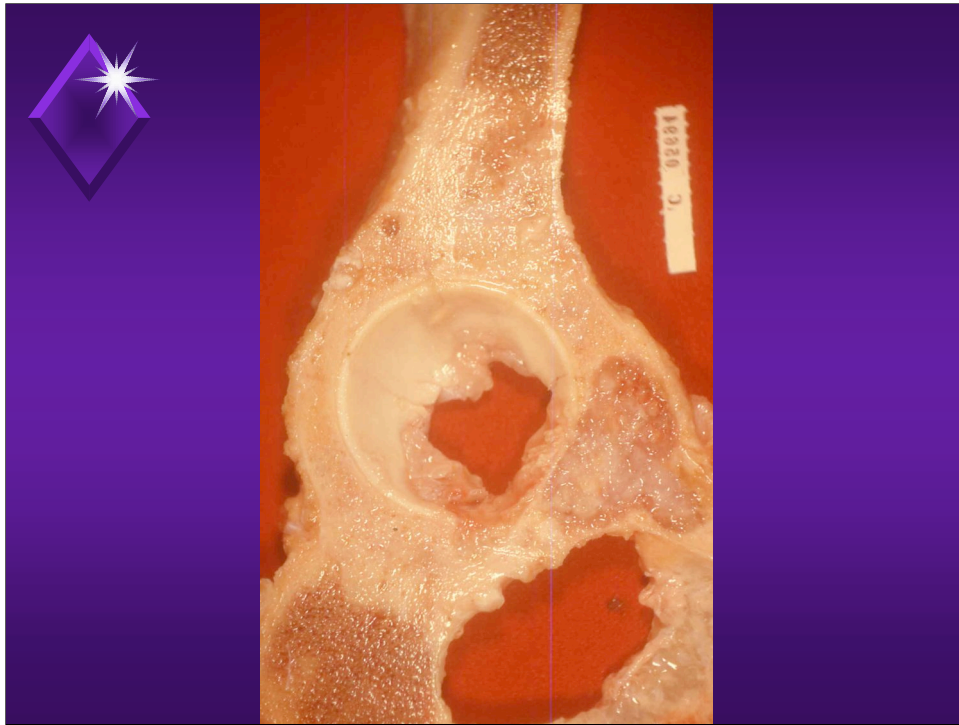
Chondromas or enchondromas are most often solitary. The multiple form is called Ollier's disease, and carries a high risk of malignant degeneration. In Ollier's disease, the chondromas tend to be unilateral and asymmetrical (the majority of lesions being on one side of the skeleton).



Cartilage-forming tumors are located in the acral (extremity) bones, the long bones, as well as in the axial skeleton. Their behavior is determined in great measure by their location (histologic characteristics are also important). Tumors of the hands and feet are benign in the great majority of cases, while those of the axial skeleton (spine, pelvis, sternum, rib, scapula) tend to be malignant. Tumors of the long bone may be benign or malignant. Benign tumors such as this lesion of the hand typically have cells with clear lacunar cytoplasm and small, dark, pin-point nuclei. These lesions may show mild degrees of atypia without this affecting their interpretation.



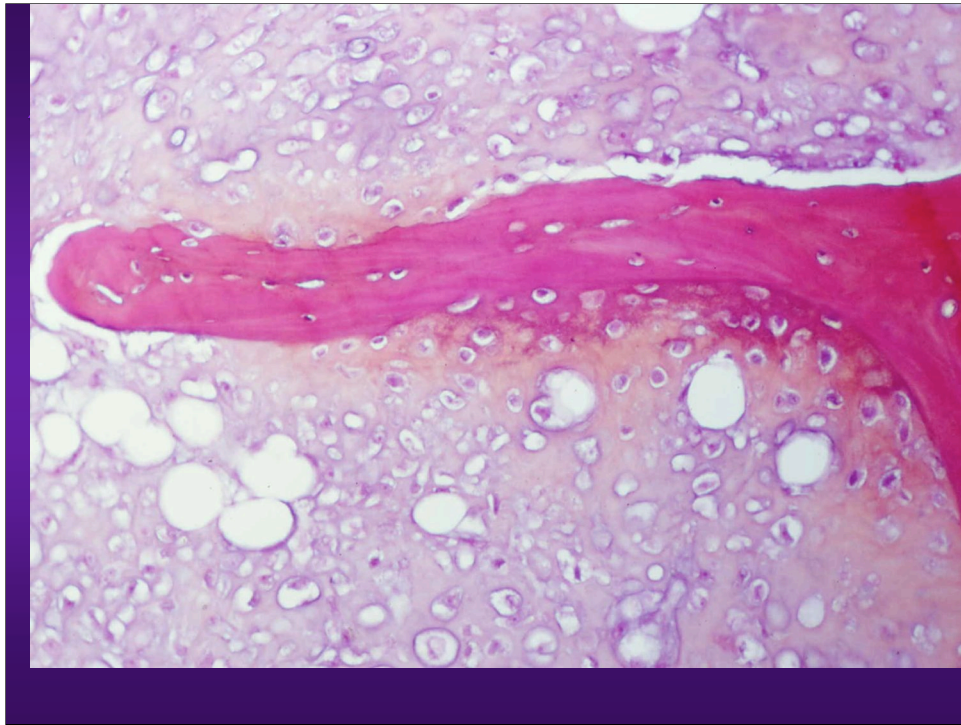
Lesions of the long bones particularly the distal femur frequently present as radio-opaque lesions showing tipped or fluffy calcifications (popcorn calcifications). This appearance is due to the fact that the cartilage lobules which comprise the lesion are surrounded by a thin rim of bone matrix which becomes calcified.



Malignant tumors predilect the pelvis (innominate bone, acetabular and pubic rami). Grossly, the tumor often appears gray, translucent, lobulated or gelatinous (reminiscent of “tapioca pudding”).

Chondrosarcomas can be of low-, intermediate or high-grade. Most are grades 1 and 2 and have high risks of local recurrence. The grade 1 tumors rarely metastasize, and grade 2 tumors show a moderate rates of metastasis. In contrast, high rates of metastases are associated with grade 3 tumors.

Chondrosarcomas are typically slow-growing tumors, but can transform into very high-grade tumors and follow a more rapid course (de-differentiation).



Microscopically, the cartilage infiltrates the bone marrow, typically entrapping the pre-existing trabeculae. This is the single most important sign of malignancy.



Tumors of fibroblastic origin

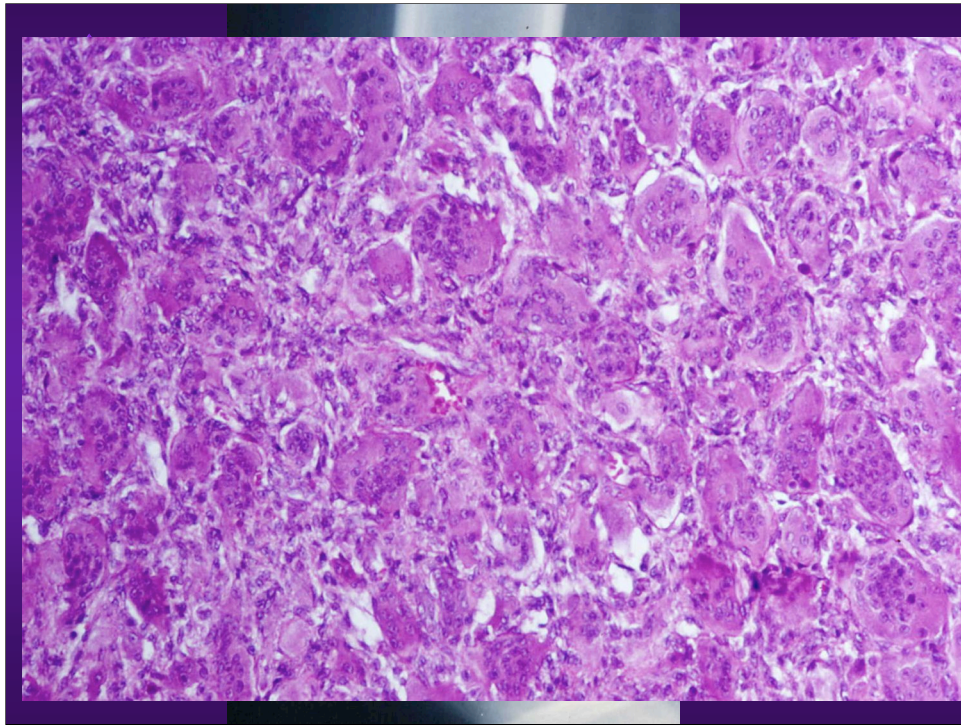
- ***Benign*** ***Non-ossifying fibroma***
- ***Malignant*** ***.Fibrosarcoma***
 .Malignant fibrous
 histiocyoma

In the interest of time, we will not be presenting microscopic images of this group. In this category, non-ossifying fibroma, a benign prototype, is not a true neoplasm but a dysplasia which resembles- and enters into the differential diagnosis of bone tumors. This is a very frequent lesion which affects young individuals (1st decade). In the malignant group, malignant fibrous histiocyoma is the most frequent, while fibrosarcoma is a fairly rare bone tumor.



Tumors of unknown origin

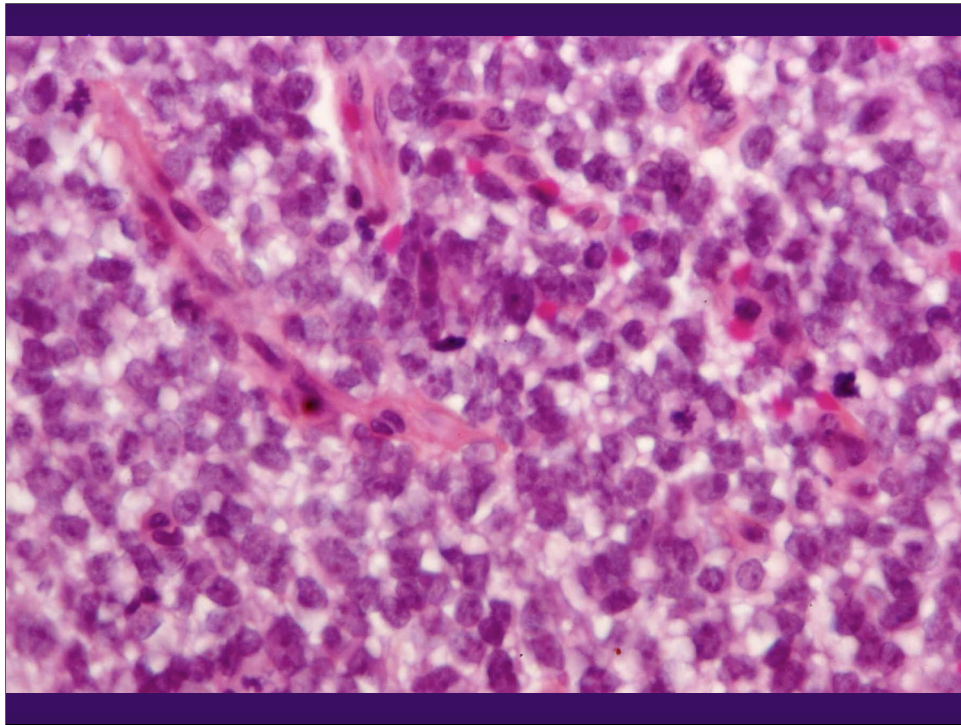
- ◆ ***Giant cell tumor of bone***
- ◆ ***Ewing Sarcoma***



This tumor characteristically affects patient above 20 years and is most frequently located around the knee (distal femur, proximal tibia) and at the distal radius. It typically involves the epiphysis of long bones, appearing as a large radiolucency. This tumor can be locally aggressive and is best treated by complete curettage or resection. 10% are frank sarcomas, capable of metastases.



Ewing sarcoma affects young subjects (1st and 2nd decades) and tends to affect the pelvis and the long bones of the lower limbs. In the long bones, the tumor may occupy a segment of the bone or may involve the entire length of the bone. It is located in the medullary compartment, extensively replaces the bone marrow, infiltrates the cortex and frequently breaks out of the bone to form a soft tissue mass. This particular tumor involves diffusely the humerus. Note the gnawed appearance of the cortex and the soft tissue mass. An important fact to remember is that Ewing sarcoma is extremely rare in black subjects.



Histologically, this tumor must be distinguished from the other “small round cell tumors” of bone. Genetic abnormalities include a reciprocal translocation [t(11;22) (q24;q12) with fusion of FLI-1 and EWS genes and a resulting EWS-FLI-1 chimeric protein, a transcription factor that stimulates cell proliferation.



A young lady treated by neoadjuvant chemotherapy (before and after ablation of the tumor). A limb-salvage procedure was performed (as opposed to an amputation). This involves the resection of the segment of long bone harboring the tumor (en bloc resection) and its replacement by a segment of cadaver bone of the same size (intercalary allograft) which is secured with the proper hardware. The patient survives with better quality of life.

CLASS OF 2009, THANK YOU AND GOOD LUCK!