Osteosarcoma and its Variants

James C. Wittig, MD
Associate Professor of Orthopedic Oncology
Chief, Orthopedic Oncology
Mount Sinai Medical Center
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**

- **Benign Lesion**
  - well defined, sclerotic border
  - lack of soft tissue mass
  - solid periosteal reaction
  - geographic bone destruction

- **Malignant Lesion**
  - interrupted periosteal reaction
  - moth-eaten or permeative bone destruction
  - soft tissue mass
  - wide zone of transition
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
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 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: 2\textsuperscript{nd} 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

- Codman’s Triangle
- Permeative Lesion
- Ossification in Soft Tissue Component
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
Chondroblastic Subtype of a Conventional Osteosarcoma of Distal Tibia
Microscopic Pathology—Malignant Appearing Cartilaginous Tissue

- Cells in Lacunae
- Ground Glass Matrix—Intercellular Matrix (Non-cellular Substance)
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 Levels
Gross Pathology: Telangiectatic Osteosarcoma

Multiple Cystic and Necrotic Spaces/Cavities
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 on Surface of Bone

Medullary Canal of Bone

Tumor on Surface 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.
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
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

Ossification in Tumor
Necrotic Cystic Cavity
Microscopically, a high grade surface osteosarcoma looks the same as a conventional intramedullary osteosarcoma.
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
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
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
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)