Biopsy and Staging of Musculoskeletal Neoplasms

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

- Bone / Soft tissue tumors (Primary)
  - Mesenchymally derived tumors (Mesodermal)
  - Benign or Malignant (Sarcoma)
  - Sarcoma = fleshy (Greek), fish flesh
  - Sarcoma—ability to metastasize systemically and invade locally
Classification

- Derived from primitive pluripotential mesenchymal cell
- Pluripotential mesenchymal cell can form
  - Bone
  - Cartilage
  - Fibrous Tissue
  - Lipogenic
  - Blood Vessels
  - Nervous tissue
  - Small Round Blue Cells
Classification

- Bone and soft tissue tumors are classified according to the predominant type of tissue (Pattern of Differentiation)
- Important to think in terms of these categories when evaluating
- Unique findings on imaging studies and pathology
- Specific types of tumors in each age group and anatomic site
<table>
<thead>
<tr>
<th>Histologic Type*</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematopoietic (41.4%)</td>
<td></td>
<td>Myeloma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reticulum cell sarcoma</td>
</tr>
<tr>
<td>Chondrogenic (20.9%)</td>
<td>Osteochondroma</td>
<td>Primary chondrosarcoma</td>
</tr>
<tr>
<td></td>
<td>Chondroma</td>
<td>Secondary chondrosarcoma</td>
</tr>
<tr>
<td></td>
<td>Chondroblastoma</td>
<td>Dedifferentiated chondrosarcoma</td>
</tr>
<tr>
<td></td>
<td>Chondromyxoid fibroma</td>
<td>Mesenchymal chondrosarcoma</td>
</tr>
<tr>
<td>Osteogenic (19.3%)</td>
<td>Osteoid osteoma</td>
<td>Osteosarcoma</td>
</tr>
<tr>
<td></td>
<td>Benign osteoblastoma</td>
<td>Parosteal osteogenic sarcoma</td>
</tr>
<tr>
<td>Unknown origin (9.8%)</td>
<td>Giant cell tumor</td>
<td>Ewing’s tumor</td>
</tr>
<tr>
<td></td>
<td>(Fibrous) histiocytoma</td>
<td>Malignant giant cell tumor</td>
</tr>
<tr>
<td>Fibrogenic (3.8%)</td>
<td>Fibroma</td>
<td>Adamantinoma</td>
</tr>
<tr>
<td></td>
<td>Desmoplastic fibroma</td>
<td>(Fibrous) histiocytoma</td>
</tr>
<tr>
<td>Notochordal (3.1%)</td>
<td></td>
<td>Fibrosarcoma</td>
</tr>
<tr>
<td>Vascular (1.6%)</td>
<td>Hemangioma</td>
<td>Chordoma</td>
</tr>
<tr>
<td>Lipogenic (&lt;0.5%)</td>
<td>Lipoma</td>
<td>Hemangiendothelioma</td>
</tr>
<tr>
<td>Neurogenic (&lt;0.5%)</td>
<td>Neurilemmoma</td>
<td>Hemangiopericytoma</td>
</tr>
</tbody>
</table>
Natural History

- **Benign**
  - Latent
  - Active
  - Aggressive

- **Malignant**
  - Low Grade
  - Intermediate
  - High Grade
Growth and Behavior

- Sarcomas grow locally in a centrifugal manner
- Form “Ball –Like” masses
- Periphery is least mature
- Benign aggressive and malignant tumors compress adjacent tissue into a pseudocapsular layer
- Pseudocapsular layer-microscopic extension of main tumor mass (satellite nodules)
Growth and Behavior

- **Pseudocapsule**: 2 zones
  - Compressed tumor cells
  - Fibrovascular zone of reactive tissue with an inflammatory component that interdigitates with normal tissue—contains satellite lesions
- **True capsule**—surrounds a benign lesion; composed of compressed normal cells and mature fibrous tissue
Growth and Behavior

- Surgical resection must include the pseudocapsule to ensure removal of the entire lesion.

- Skip metastasis: High grade sarcomas have the ability to break through the pseudocapsule and metastasize within the same compartment.
Growth and Behavior

- High Grade Bone Sarcomas
  - Intraosseous Skip Mets---embolization of tumor cells within the marrow sinusoids
  - Transarticular Skip Mets---occur via periarticular venous anastomoses

- Clinical Incidence of Skip Mets<1%
- Very poor prognosis (0% cure)
Sarcomas have the ability to metastasize systemically—hematogenously (contradistinction to carcinomas—lymphatic spread primarily)

- Most common sites:
  - Lungs
  - Bones
  - Liver (primarily retroperitoneal soft tissue sarc)
Growth and Behavior

- Low Grade tumors—mets<5-10%
- High grade lesions—mets 60%-100%
- Some benign aggressive lesions can metastasize to the lungs, other bones (rare event)
  - Giant Cell Tumor
  - Chondroblastoma

- Multicentricity: Multiple bony sites at presentation (synchronous mets)
  - GCT, Osteosarcoma, Ewings
Reactive Zone or Pseudocapsule
Tumor Compressing Muscle and Infiltrating between Muscle Fibers
High Grade Sarcoma After Good Response to Chemotherapy: the Pseudocapsule is Converted to a True Fibrous Capsule
Local Growth of Sarcomas

- Local growth obeys fascial borders/compartamental borders
- Fascial borders resist tumor penetration
- Compartment refers to the bone or muscle of origin; muscle compartment surrounded by fascia (investing fascia on all sides—resists tumor penetration)
- When a bone tumor destroys the cortex and spreads into the surrounding soft tissue---extracompartamental
Growth and Behavior

- Bone Tumors that extend extracompartamental compress the surrounding muscles into a pseudocapsule
  (the fascia of the surrounding muscle usually contains the tumor and protects other muscles and structures)
  - Distal Femur: Vastus Intermedius
  - Proximal Tibia: Popliteus
  - Proximal Humerus: Subscapularis
  - Scapula: Rotator Cuff
Growth and Behavior

- **Soft Tissue Sarcomas**
  - Intramuscular---if extends beyond fascia---extracompartmental
  - Intermuscular---extracompartmental
GCT Proximal Tibia
Popliteus (Pseudocapsule)
LOCAL SPREAD OF HEMATOMA SECONDARY TO PATHOLOGICAL FRACTURE

- Osteotomy medial to coracoid process
- Infraspinatus
- Deltoid
- Fracture Hematoma
- Osteosarcoma of proximal humerus
- Coracobraclialis
- Body of scapular
- Serratus anterior
- Subscapularis
- Short head of biceps
- Axillary vessels and brachial plexus
- Pectoralis major
Staging

**Purpose**
- Determine tumor type
- Determine prognosis
- Guide treatment
- Compare results between study groups
- Delineate extent of local and distant disease
Staging Studies

- Plain Radiograph
- MRI
- CT scan
- Chest CT
- Bone Scan
Plain Radiographs

- Rate of tumor growth
- Tumor interaction with surrounding non-neoplastic tissue
- Internal composition of tumor
Plain Radiographs

- Bone involved
- Is involved bone normal?
- What part of the bone?
- Open or closed growth plate
- Epicenter of lesion (cortex or medullary canal)
- Tumor contour and zone of transition between tumor and host bone
Plain Radiographs

- Mineralized matrix?
- Cortical destruction?
- Periosteal reaction? What type
- Involvement of joint space?
- Tumor multifocal?
- Is tumor of uniform appearance or does it have several different components?
Mature Skeleton
(Growth Plate Closed)

- Intraosseous Ganglion
- Giant Cell Tumor
  Malignant Fibrous Histiocytoma
- Myeloma
- Cortical Metastasis
  (Lung, Breast)
- Adamantinoma
- Chondrosarcoma
- Metastasis
- Lymphoma
- Fibrosarcoma
- Osteoma
MALIGNANT

Lymphoma
Hodgkin
Myeloma
Ewing
Osteosarcoma
Chondrosarcoma
Metastasis

Exceptions:
Hemangioma
Langerhans-cell Granuloma
Fibrous Dysplasia

BENIGN

Osteoblastoma
Osteoid Osteoma
Aneurysmal Bone Cyst
Osteochondroma
Chondromyxoid Fibroma

Anterior

Posterior
### SIMPLIFIED RADIOLOGIC GRADING OF BONE TUMORS*

<table>
<thead>
<tr>
<th>Grade</th>
<th>Radiologic Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low grade, nonaggressive</td>
<td>Geographic destruction with sclerotic rim</td>
</tr>
<tr>
<td>Medium grade, moderately aggressive</td>
<td>Geographic destruction, no sclerotic rim, and/or cortex “expanded” more than 1 cm or completely penetrated</td>
</tr>
<tr>
<td>High grade, very aggressive</td>
<td>Moth-eaten and/or permeative destruction only</td>
</tr>
</tbody>
</table>
Intact cortex

Scalloped cortex

Complete cortical disruption

Dumbbell Configuration
Solid
Cloud-Like
Ivory-Like
Stippled
Flocculent
Rings and Arcs
Geographic
Permeative with Mineralization and Cortical Destruction
Permeative with Calcifications in a Ring and Arc-like Manner
Geographic Lesion
Permeative with Cortical Destruction and Soft Tissue Mass
Hair on End and Codman’s Triangle Periosteal Reactions
Geographic Lesion Intracortical Continuous Periosteal Reaction/Cortical Thickening
Geographic Lesion
Geographic Lesion
Permeative Lesion with Ossification, Cortical Destruction and Codman’s Triangle
MRI

- Evaluates entire bone and adjacent joint
- Best test for intraosseous extent and soft tissue extent
- Skip mets
- Proximity to vascular structures
- Occasionally helpful in diagnosis of bone or soft tissue tumors (experienced radiologist)
CT

- Good for evaluating cortical details and destruction
- Subtle cortical erosions (endosteal; periosteal)
- Calcifications / ossification
Fluid-Fluid Levels: Anuerysmal Bone Cyst Changes
Soft Tissue Extent and Fluid-Fluid Level
Bone Scan

- Whole body bone scan
- Sites of bony mets
- Active lesion??
Chest CT

- Presence of metastatic disease
Biopsy

- CT guided or Open
- Through one compartment
- Avoid neurovascular structures
- Biopsy soft tissue component
- Biopsy by surgeon who will perform procedure or by radiologist after communication with surgeon
- Tumors with necrosis and hemorrhage
Staging

Benign Staging System (Enneking)
Stage 1: Latent
   Grow slowly with growth of individual and then stop; tendency to heal spontaneously (ex. NOF; UBC)
Stage 2: Active
   Progressive growth
Stage 3: Aggressive
### Staging

**Malignant Bone Tumors**

**TNM Staging System (AJC)**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Grade</th>
<th>Tumor</th>
<th>Node</th>
<th>Mets</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>G1,2</td>
<td>T1</td>
<td>N 0</td>
<td>M 0</td>
</tr>
<tr>
<td>IB</td>
<td>G1,2</td>
<td>T2</td>
<td>N 0</td>
<td>M 0</td>
</tr>
<tr>
<td>IIA</td>
<td>G3,4</td>
<td>T1</td>
<td>N 0</td>
<td>M 0</td>
</tr>
<tr>
<td>IIB</td>
<td>G3,4</td>
<td>T2</td>
<td>N 0</td>
<td>M 0</td>
</tr>
<tr>
<td>III</td>
<td>Undefined for bone tumors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVA</td>
<td>Any G</td>
<td>Any T</td>
<td>N1</td>
<td>M 0</td>
</tr>
<tr>
<td>IVB</td>
<td>Any G</td>
<td>Any T</td>
<td>Any N</td>
<td>M 1</td>
</tr>
</tbody>
</table>
# Staging

**Enneking Staging System**

Malignant Bone Tumors

<table>
<thead>
<tr>
<th>Stage</th>
<th>Grade</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>G1</td>
<td>T1</td>
</tr>
<tr>
<td>IB</td>
<td>G1</td>
<td>T2</td>
</tr>
<tr>
<td>IIA</td>
<td>G2</td>
<td>T1</td>
</tr>
<tr>
<td>IIB</td>
<td>G2</td>
<td>T2</td>
</tr>
<tr>
<td>III</td>
<td>Mets</td>
<td>Mets</td>
</tr>
</tbody>
</table>

*(based on biological behavior)*
# Grading

## Biological Behavior / Natural History

<table>
<thead>
<tr>
<th>Grade</th>
<th>Tumor Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>LG Chondrosarcoma</td>
</tr>
<tr>
<td></td>
<td>Chondrosarcoma</td>
</tr>
<tr>
<td></td>
<td>Secondary Chondrosarcoma</td>
</tr>
<tr>
<td></td>
<td>Parosteal Osteosarcoma</td>
</tr>
<tr>
<td></td>
<td>Adamantinoma</td>
</tr>
<tr>
<td>G2</td>
<td>High Grade Chondrosarcoma</td>
</tr>
<tr>
<td></td>
<td>Conventional Osteosarcoma</td>
</tr>
<tr>
<td></td>
<td>Ewing’s Sarcoma/PNET</td>
</tr>
<tr>
<td></td>
<td>MFH</td>
</tr>
<tr>
<td></td>
<td>Angiosarcoma</td>
</tr>
</tbody>
</table>
Staging

- Soft Tissue Sarcomas
- Important Prognostic Characteristics
  - Tumor Size (>5cm, worse prognosis)
  - Tumor Depth (Deep, worse prognosis)
  - Grade (High grade, worse prognosis)
  - Presence of Mets
# Staging

## Malignant Tumors

### TNM Staging System (AJC)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Grade</th>
<th>Tumor</th>
<th>Node</th>
<th>Mets</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>G1,2</td>
<td>T1a-b</td>
<td>N 0</td>
<td>M 0</td>
</tr>
<tr>
<td>IB</td>
<td>G1,2</td>
<td>T2a</td>
<td>N 0</td>
<td>M 0</td>
</tr>
<tr>
<td>IIA</td>
<td>G1,2</td>
<td>T2b</td>
<td>N 0</td>
<td>M 0</td>
</tr>
<tr>
<td>IIB</td>
<td>G3,4</td>
<td>T1a-b</td>
<td>N 0</td>
<td>M 0</td>
</tr>
<tr>
<td>IIC</td>
<td>G3-4</td>
<td>T2a</td>
<td>N 0</td>
<td>M 0</td>
</tr>
<tr>
<td>III</td>
<td>G3,4</td>
<td>T2b</td>
<td>N 0</td>
<td>M 0</td>
</tr>
<tr>
<td>IVA</td>
<td>Any G</td>
<td>Any T</td>
<td>N1</td>
<td>M 0</td>
</tr>
<tr>
<td>IVB</td>
<td>Any G</td>
<td>Any T</td>
<td>Any N</td>
<td>M 1</td>
</tr>
</tbody>
</table>
Grading

- Soft Tissue Sarcomas (Biological Behavior)
  - Tumors that are definitionally high grade
    - Ewing’s Sarcoma
    - PNET
    - Rhabdomyosarcoma
    - Angiosarcoma
    - Pleomorphic Liposarcoma
    - Soft Tissue Osteosarcoma
    - Mesenchymal Chondrosarcoma
Grading

Soft Tissue Sarcomas (Biological Behavior)

- Tumors that are definitionally low grade
  - Well Differentiated Liposarcoma
  - Dermatofibrosarcoma Protuberans
  - Infantile Fibrosarcoma
  - Angiomatoid MFH
Grading

- Soft Tissue Sarcomas
  - Tumors not gradable but which metastasize often
    - Alveolar soft part sarcoma
    - Clear cell sarcoma
    - Epitheloid sarcoma
    - Synovial sarcoma
    - Low grade fibromyxoid sarcoma
Grading

- Soft Tissue Sarcomas
  - Tumors of varying behavior— grading may be useful
    - Myxoid liposarcoma
    - Leiomyosarcoma
    - MPNST
    - Fibrosarcoma
    - Myxoid MFH
Grading

- Soft Tissue Sarcomas
  - Tumors of varying behavior—grading parameters not yet established
    - Hemangiopericytoma
    - Myxoid chondrosarcoma
    - Malignant granular cell tumor
    - Malignant mesenchymoma
Evaluating Response to Chemotherapy
Sarcoma of Biceps
Pseudocapsule after Chemotherapy