14 Bone and Joints

Bones are common surgical specimens that may be submitted after reconstructive or joint replacement surgery, as part of a larger soft tissue resection, to diagnose metabolic bone disease, or after resection of tumors primary to bone.

RELEVANT CLINICAL HISTORY (IN ADDITION TO AGE AND GENDER)

TABLE 14–1. RELEVANT CLINICAL HISTORY

HISTORY RELEVANT TO ALL SPECIMENS	HISTORY RELEVANT FOR BONE AND JOINT SPECIMENS
Clinical indication for the procedure	Reason for the procedure (e.g., degenerative joint disease, failed joint replacement, fracture, infection, malignancy, osteonecrosis, evaluation of metabolic bone disease)
Any unusual features of the clinical presentation	
Organs resected or biopsied (including location and number of lesions present)	
Gross appearance of the organ/tissue/lesions sampled as observed by the surgeon, if unusual	Joint disease (e.g., gout, rheumatoid arthritis)
Prior surgery or biopsies and the pathologic diagnoses	History of Paget disease of bone, bone infarction, or osteomyelitis
Prior malignancies (type, location, stage)	Family history of Ollier disease, Mafucci syndrome, Rothmund-Thomsom syndrome, etc.
Prior treatment (radiation therapy, chemotherapy, drug use that can change the histologic appearance of tissues)	
Immune system status	
Current or recent pregnancy	

TOTAL JOINT ARTHROPLASTY (HIPS AND KNEES)

Bone, cartilage, and adjacent soft tissues are removed during artificial joint replacements, usually performed to treat degenerative joint disease, but also performed in patients with rheumatoid arthritis, osteonecrosis, traumatic fractures, and pathologic fractures.

Clinically important unsuspected diseases may be found in "routine" specimens for degenerative joint disease (e.g., hemochromatosis, rheumatoid arthritis, gout, tumors, infection, osteonecrosis, Gaucher disease, and others). However, the incidence of such findings is small, ranging from <1% to 8% in different studies.[1-7]

The method of examining well-defined "routine" specimens (defined by therapeutic procedures for degenerative joint disease in patients without a history of malignancy [or risk factors for malignancy such as prior radiation], infection, or immunocompromise, and with normal gross findings) should be made jointly among pathologists and clinicians and, in accordance with Joint Commission standards,[8] should be part of a written hospital or laboratory policy (see also "Gross Examination"). Alternatives are gross examination by the surgeon, gross examination by both surgeon and pathologist, or gross and microscopic examination by the pathologist. Even if not all specimens are examined microscopically, this is always an option that can be requested by the surgeon.

PROCESSING THE SPECIMEN

1. Describe the number of fragments of bone (estimate if many), size in aggregate, range of sizes. Describe any recognizable portions of bone: femoral head (see next section), tibial plateau, femoral condyles.
2. Describe articular surface including color (usually white, black if ochronosis, brown/green if hemochromatosis), crystalline deposits (both gout and chondrocalcinosis will produce chalky white deposits), erosions or pits, or eburnation (= bone that is markedly thickened and smooth [like ivory] due to complete loss of the overlying cartilage - do not mistake eburnated bone for cartilage!). Describe subchondral cysts or osteophytes if present.
3. Describe the number of fragments of soft tissue (estimate if many), size in aggregate, range of sizes.
4. Describe the color and consistency of the soft tissue:
   - Normal = white/tan, delicate, villous
   - Hemochromatosis = brown/green
   - β2 microglobulin amyloidosis = tan/yellow, firm, and homogenous
   - Giant cell tumor, diffuse type (pigmented villonodular synovitis or PVNS) = red/brown and shaggy (delicate villi with small nodules may be appreciated if the tissue is floated in saline). Necrotic foci may appear yellow due to the presence of histiocytes.
   - Gout or chondrocalcinosis = chalk white crystalline material. See the separate section on "Synovium" for a more complete description and special processing of unusual specimens.
5. The bone is separated from the soft tissue. Submit one section of soft tissue including synovium if possible. Normal synovium will look like a thin delicate membrane. Fix the bone overnight in formalin and decalcify the following day. All decalcification procedures must be documented in the gross description.
6. Serially section through the decalcified bone to find the best diagnostic areas. One fragment of bone should include the junction of normal and abnormal cartilage and the other fragment should be from the periphery to include exostosis and/or pannus. The sections should be about 2 × 1 cm in size with the short axis perpendicular to the cartilage surface including 5 to 10 mm of subchondral bone.

If osteonecrosis is suspected, the entire specimen must be serially sectioned to look for the characteristic gross findings (see below). Submit sections to document the interface of normal and abnormal bone. Radiography of the specimen may be helpful to identify the area of necrotic bone.

SPECIAL STUDIES

Crystal Disease. Chalky white deposits in soft tissue may be due to urate crystals (gout) or calcium pyrophosphate dihydrate crystals (= calcium pyrophosphate dihydrate deposition disease [CPPD] = pseudogout = chondrocalcinosis). Tissue must be saved in absolute (100%) alcohol because these crystals are soluble in aqueous solutions. The tissue must be hand processed and stained with an anaqueous Wright stain. Crystals can also be visualized in tissue smears, frozen sections, or unstained sections.

Crystals sometimes survive routine processing in aqueous solutions but are lost in the final staining steps. Look for preserved crystals in tissue folds if present. An unstained slide may also be requested and examined under polarized light after deparaffinizing.

Crystals can also be examined directly by smearing the unfixed crystals on a slide, or by suspending in absolute alcohol as necessary (remember that they will dissolve in water). If the crystals are viewed using a compensating first-order red filter under polarized light, uric acid can usually be distinguished from CPPD crystals. The crystals are aligned parallel to the line on the compensating filter. If not available in the pathology department, most rheumatologists will have such a microscope available for examination

of synovial fluids. Crystals will polarize in properly fixed and stained histologic sections, but positive and negative birefringence cannot be reliably performed on fixed tissue (see Chapter 9 for a description of polarization).[9,10]

- **Uric acid:** needle shaped, strong negative birefringence, bright yellow
- **CPPD crystals:** rhomboid, weakly positive birefringence, less bright and blue

Calcium oxalate crystals can be seen in bone, articular cartilage, and bone marrow in patients with primary (familial) oxalosis or secondary oxalosis (usually due to chronic renal failure). The crystals are needle shaped in radially arranged clusters and are both refractile and polarizable. They can dissolve in formalin, but only after several days. The type of crystal can be identified by chemical analysis, x-ray diffraction, or electron diffraction.

Metastasis. Determine from the clinical history whether there is a known primary malignancy. If not, additional studies may be warranted (e.g., snap freezing, EM, or immunohistochemistry). Remove as much soft tissue as possible to avoid exposing potential tumor to decalcification.

GROSS DIFFERENTIAL DIAGNOSIS

Degenerative Joint Disease. The cartilage surface shows fibrillation and loss over the center of the femoral head or over the tibial plateau. The exposed bone becomes thickened and smoothly polished ("eburnated" or "like ivory") and can be mistaken for a cartilage surface. Fractures through articular bone result in subchondral cysts and collapse of the bone. The femoral head is often flattened and misshapen. Osteophytes commonly form around the edge of the articular surface. The soft tissue is relatively unaffected and may be fibrotic.

Rheumatoid Arthritis. Patients usually undergo arthroplasty after significant secondary degenerative changes have occurred. Thus, most will show the changes of degenerative joint disease and features of rheumatoid arthritis may be subtle or absent. Findings characteristic of rheumatoid arthritis include an edematous hyperplastic synovium with growth over the cartilage surface to form a pannus.

Gout or CPPD. Chalky white crystalline deposits are present in soft tissue, cartilage, and sometimes erode bone. The synovium becomes fibrotic, thickened, and hyperplastic and forms a pannus overlying cartilage. It is usually not possible to distinguish gout from chondrocalcinosis grossly in mid-sized joints in which both are common. However, CPPD crystals may preferentially be found within the cartilage and uric acid crystals in periarticular soft tissue. Gout is much more common in small joints of the foot and hand. Neither commonly affects the hip. Usually joint replacement is performed after significant secondary degenerative changes have occurred (see above). Crystals should be saved in alcohol (see "Special Studies").

Osteonecrosis (Aseptic Necrosis, Avascular Necrosis). Osteonecrosis of bone is a common cause of joint disease (approximately 10% of joint replacements) and is often bilateral. Patients are younger than the typical patient with degenerative joint disease (averaging 55 vs. 67 years) and often have predisposing conditions such as steroid use, sickle cell disease, or alcoholism. The pathogenesis is poorly understood but is thought to result from ischemic infarction of subchondral bone.

There is a characteristic wedge-shaped area of pale yellow necrotic bone below the cartilage surface. A band of hyperemia is often present below this area. Usually the overlying cartilage will have separated away from the bone. The infarcted bone may collapse with distortion of the cartilage and resultant degenerative changes. Radiographs of bone slices can be helpful to look for areas of abnormal mineralization.

Metastatic Disease. A joint replacement is sometimes performed to repair a known or suspected pathologic fracture, generally within the femur. The metastatic tumor may be subtle and only apparent after histologic examination of numerous sections. The bone destruction observed radiologically is usually due to soluble factors produced by the tumor cells and not replacement of bone marrow by tumor per se. Therefore, in such cases histologic sampling of the fracture site is necessary to evaluate the presence of tumor. If a pathologic fracture is strongly suspected either clinically or grossly, and the primary site is unknown, consider taking tissue for special studies (e.g., snap freezing, EM). If possible, separate soft tissue and submit separately as decalcification adversely affects some antigens (e.g., ER and PR).

MICROSCOPIC SECTIONS

- **Soft tissue:** One section including any grossly recognizable synovium. If a metastatic deposit is suspected, submit as much soft material from the possible tumor and/or fracture site as possible that will not need decalcification.
- **Bone:** One section including the junction of normal and abnormal cartilage and one from the periphery.

If osteonecrosis is known or suspected, submit one to two sections of necrotic bone including interface with normal bone and the area below the detached cartilage.

- **Crystals:** If crystals are present, submit one section fixed in absolute alcohol for special anaqueous processing. Order 1 H&E, 1 anaqueous Wright stain, and one unstained slide.

SAMPLE DICTATION

Received fresh, labeled with the patient's name and unit number and "left total knee" are multiple fragments of bone (in aggregate 5 × 5 × 3 cm, largest 2 × 1 × 1 cm) and soft tissue (4 × 3 × 2 cm, largest 3.5 × 2 × 1 cm). The bone fragments include recognizable portions of the tibial plateau and femoral condyles. The articular surface is markedly roughened with areas of cartilage loss and eburnation of the bony surface. The soft tissue is tan/pink and includes fragments of meniscus. The bone is fixed and decalcified.

Cassette #1: bone with articular surface, 4 frags, RSS.
Cassette #2: soft tissue, 3 frags, RSS.

Specimens with Intact Femoral Heads

1. The femoral head is cut into thirds, parallel to the long axis, with the bone saw. The central section must be thin, approximately 0.5 cm in width.
2. Describe the femoral head including dimensions, shape (flattened, round), cartilage surface (smooth and glistening, erosions, pits, eburnation of bone surface, fibrillation of cartilage, pannus formation), detachment of cartilage (as in osteonecrosis), presence of exostoses. Describe the quality of the bone (osteoporotic, sclerotic, pale as in osteonecrosis) and subchondral cysts.
3. Describe the resection margin including surface (flat and smooth if surgical, jagged and with medullary hemorrhage if fracture), quality of adjacent bone (osteoporotic, sclerotic, or soft – may indicate metastatic tumor). If the fracture site is grossly or clinically suspicious for a pathologic fracture, save as much soft tissue from this site as possible in a cassette without bone (to avoid tissue alterations associated with decalcification) and consider taking tissue for special studies (see above).
4. Describe soft tissue (see description above) and submit one cassette including synovium if possible.
5. Fix the femoral head in formalin overnight and decalcify the following day.

MICROSCOPIC SECTIONS

- **Soft tissue:** One section including any grossly recognizable synovium.
- **Bone:** One section including the junction of normal and abnormal cartilage and one from the periphery.
- **Fracture site:** Two representative sections in one cassette from the fracture site. If sufficient soft tissue (i.e., possible tumor) is present, submit an additional cassette of nondecalcified tissue.

SAMPLE DICTATION - HIP REPLACEMENT FOR DEGENERATIVE JOINT DISEASE

Received fresh labeled with the patient's name and unit number and "left hip" is a 5 × 5 × 4 cm flattened femoral head and attached neck with a smooth resection margin. The articular surface is covered by irregularly surfaced cartilage with areas of cartilage loss and eburnation of the underlying bone. Multiple peripheral osteophytes are present. The bone is fixed and then decalcified. Also received are multiple fragments of pink/tan fibrous tissue measuring in aggregate 3 × 3 × 2 cm.

Cassette #1: Joint surface, 4 frags, RSS.
Cassette #2: Soft tissue, 3 frags, RSS.

SAMPLE DICTATION - HIP REPLACEMENT AFTER FRACTURE

Received fresh labeled with the patient's name and unit number and "right hip" is a 5 × 5 × 3 cm round femoral head with a smooth white cartilage surface. The femoral neck resection margin is irregular and hemorrhagic. There are multiple smaller fragments of irregular bone measuring in aggregate 3 × 3 × 1 cm. There are no areas of soft tissue within the bone. The bone trabeculae are markedly thinned. The bone is fixed and then decalcified. Also received are multiple fragments of pink/tan fibrous tissue measuring in aggregate 3 × 3 × 2 cm.

Cassette #1: Fracture site, 2 frags, RSS.
Cassette #2: Joint surface, 2 frags, RSS.
Cassette #3: Soft tissue, 3 frags, RSS.

SAMPLE DICTATION - HIP REPLACEMENT FOR AVASCULAR NECROSIS

Received fresh labeled with the patient's name and unit number and "right hip" is a 4.5 × 4 × 4 cm deformed flattened femoral head with a smooth resection margin. There is a wedge-shaped area of pale yellow bone immediately beneath the cartilage surface measuring 2 × 2 × 1 cm with a red/brown border. The overlying cartilage is intact but has pulled away from this area leaving a gap. The sliced section is radiographed. The bone is fixed and then decalcified. The remainder of the cartilage surface is smooth and unremarkable. Also received are multiple fragments of pink/tan fibrous tissue measuring in aggregate 3 × 2 × 2 cm.

Cassettes #1 - 2: Area of probable necrosis, 4 frags, RSS.
Cassette #3: Joint surface, 2 frags, RSS.
Cassette #4: Soft tissue, 3 frags, RSS.

Revision Total Joint Arthroplasty

About 5% of prosthetic joints fail, either from mechanical loosening or due to infection. It may be difficult to clinically distinguish between these two possibilities as the presentation may be similar and false positive and negative culture results are possible. Prosthetic joints that have failed mechanically may be removed and replaced in the same procedure. If infection is present, drainage or removal of the prosthesis may be indicated and replacement may be delayed until after treatment. The most common acute pathogens are *S. epidermidis* and *S. aureus* with gram-negative bacilli being more common in later infections. A frozen section evaluation of periarticular soft tissue may be requested if infection is suspected (see Chapter 6).

PROCESSING THE SPECIMEN

1. The specimen usually consists of small fragments of bone, fibrous soft tissue, and, often, fragments of bone cement. Bone cement is usually light brown, homogeneous in appearance, hard, and may be difficult to distinguish from bone. The soft tissue may be gray or black due to metallic debris.
2. Describe the number of fragments of bone (estimate if many), size in aggregate, range of sizes. However, bone may not be present.
3. Describe the number of fragments of soft tissue (estimate if many), size in aggregate, range of sizes, color, presence of necrosis. If infection is suspected clinically or by gross examination, and cultures have not yet been sent, send tissue for bacterial culture.
4. The explanted prosthesis is described including number of parts, hip or joint prosthesis, identification markings (e.g., serial numbers, brand names), and the presence of any marked abnormalities (e.g., broken metal components, erosions, ridges, or pits in the articular surfaces).
5. The bone is separated from the soft tissue. Submit one section of soft tissue, including synovium, if possible. Fix the bone overnight in formalin and decalcify the following day. All decalcification procedures must be documented in the gross description.

GROSS DIFFERENTIAL DIAGNOSIS

Detritic Synovitis. Occasionally, there will be an exuberant papillary proliferation of synovium with hemosiderin deposition in response to foreign material that grossly mimics pigmented villonodular synovitis (PVNS or giant cell tumor, diffuse type). However, unlike PVNS, there will be a history of an

artificial joint, foreign material is present, and the process is usually superficial and does not extend deeply into soft tissue.

Foreign Material from Implants. Numerous types of foreign material derived from the implant can be found around failed prostheses and include bone cement (with barium to make the material radiopaque), metal fragments, polyethylene, methylmethacrylate, silicone, and ceramic (see "Noncellular Material in Histologic Sections"). The tissue may be black due to deposits of oxidized metal.

Infection. The soft tissue from infected joints may be necrotic and purulent. Cultures should be sent either by the surgeon or the pathologist. Some infections may not be apparent grossly.

MICROSCOPIC SECTIONS

- **Soft tissue:** One section including any grossly recognizable synovium.
- **Bone:** One section.

SAMPLE DICTATION

Received fresh labeled with the patient's name and unit number and "left hip" are multiple fragments of soft tissue and bone. There are five bone fragments, measuring in aggregate 3 × 2 × 2 cm. No articular surfaces are present. The bone is fixed and decalcified prior to submission. There are approximately 20 fragments of tan/white fibrous soft tissue without recognizable synovium.

Also received is a joint prosthesis consisting of an acetabular component consisting of a white prosthetic socket (6 × 6 × 4 cm) inscribed with "ABDC" and femoral component consisting of a metallic ball attached to a stem (15 × 3 × 2 cm). A fragment of brown bone cement with a smooth outer surface is also present (4 × 2 × 2 cm).

Cassette #1: Bone, 4 frags, RSS.
Cassette #2: Soft tissue, 3 frags, RSS.

CORE BIOPSY FOR ASEPTIC (AVASCULAR) NECROSIS

Cores of bone may be submitted from patients with clinical and radiologic osteonecrosis. These cores are taken through the femoral head and into the area of necrosis in order to promote revascularization ("decompression"), and are generally used for treatment and not diagnosis. There should be an area of osteonecrosis at one edge of the biopsy. These core biopsies are fixed in formalin and then gently decalcified. If the specimen will not fit in a cassette in entirety, section the specimen longitudinally.

BIOPSY, METABOLIC BONE DISEASE

Needle or core bone biopsies are sometimes submitted from patients with metabolic bone disease (osteomalacia, osteoporosis, hyperparathyroidism, effects of long-term hemodialysis, etc) with a request for metabolic bone studies.

The evaluation of metabolic disease requires sectioning of nondecalcified bone, special stains, and morphometry. These techniques are generally performed by a specialty laboratory. The specialty laboratory will provide instructions for the fixation and transportation of these specimens.

CURETTINGS AND NEEDLE BIOPSIES, BONE TUMORS

Biopsies of bone lesions are occasionally performed for both benign and malignant lesions. See Chatper 6 for a description of how bone biopsies are processed for frozen sections. See Chapter 12 and below for larger specimens.

PROCESSING THE SPECIMEN

1. Determine the type of specimen: needle biopsy or curettings. Grossly examine for the presence of bone and soft tissue. Most cases have at least small foci of soft, non-calcified non-necrotic tissue that can be taken for special studies. However, if a definitive diagnosis of lesional tissue has not

been made intraoperatively, most of the tissue should be reserved for routine sections and tissue should not be taken for studies that will preclude examination of the tissue (e.g., cytogenetics). The clinical and radiologic differential diagnosis is helpful in guiding apportionment of tissue.

2. Fix the specimen in formalin for 2 to 4 hours depending on size.
3. After fixation, the bone is gently decalcified for 4 to 12 hours. In unusual cases including larger pieces of bone, it may be necessary to fix overnight, decalcify during the day (with periodic checks to see if the bone is soft), wash, fix again overnight, and decalcify again (up to four daily cycles) for optimal specimen preparation.

SPECIAL STUDIES

Most of these tumors are unusual and will warrant special studies. After lesional tissue has been taken for fomalin fixation, additional tissue can be taken for snap freezing, EM, and/or Zenker's fixation (which decalcifies while preserving cytologic detail).

If definite lesional tissue is present, then tissue can be submitted for **cytogenetics**. For example, Ewing's/PNET has a characteristic t(11;22) and extraskeletal myxoid chondrosarcoma has a characteristic t(9;22) (see Table 7-47). If no definitive lesional tissue is present, then all tissue should be examined histologically.

GROSS DIFFERENTIAL DIAGNOSIS

In general, gross examination of these small fragmented specimens is not helpful.

MICROSCOPIC SECTIONS

- **Tumor:** Entire specimen up to 10 cassettes. If little tissue is available (e.g., only one cassette is submitted), three levels are ordered.

SAMPLE DICTATION

Received fresh labeled with the patient's name and unit number and "femur lesion" are multiple irregular fragments of tan/brown tissue with minute areas of irregular bone, measuring in aggregate 1 × 1 × 0.5 cm (the largest fragment measuring 0.4 cm in size). Frozen section examination is performed on a representative section. Tissue is apportioned for snap freezing, electron microscopy, and cytogenetics. The remainder of the tissue is fixed in Zenker's fixative or fixed in formalin and then decalcified.

Cassette 1: Frozen section remnant, 1 frag, ESS.
Cassette 2: Tissue fixed in Zenker's, 3 frags, ESS.
Cassettes 3 - 9: Remainder of specimen in formalin and decalcified, mult frags, ESS.

BONE RESECTIONS FOR TUMORS

Bone resections may be performed for either benign (enchondromas, osteochondromas, osteoid osteomas, bone cysts, fibrous dysplasia, giant cell tumors) or malignant (most chondrosarcomas, some osteosarcomas) lesions.[11-13] The radiologic features of bone lesions are very helpful, and sometimes necessary, to distinguish benign from malignant tumors.

PROCESSING THE SPECIMEN

1. Determine the type of specimen (e.g., above-knee amputation, hip disarticulation, etc.). See the section on Chapter 12 for additional information.

Give the dimensions of each structure present including length and maximum circumference of limbs.

2. Radiograph the intact specimen. The radiograph provides diagnostic information and is helpful to guide the specimen dissection.
3. Incise the soft tissue in a plane that will demonstrate the greatest extent of the tumor. A band saw can be used to bisect the specimen. Gently brush away bone dust under running water and

photograph the specimen. It is useful at this point to make a diagram of the specimen to indicate where sections will be taken. For large specimens, an additional 0.5 cm parallel cut through bone should be made to produce a relatively thin cut section of the tumor. This section is also photographed if it yields additional information.

4. Describe the tumor including:
   - Size – three dimensions
   - Appearance – color, bone formation and/or cartilage formation
   - Necrosis – % of tumor (areas that appear necrotic may be myxoid or edematous)
   - Location – tissue compartment, region of bone (epiphysis, metaphysis, diaphysis, intramedullary, periosteal)
   - Relationship to surrounding structures (bone, vessels, nerves, muscle)
   - Erosion of cortex
   - Extension into soft tissue (compression or true invasion)
   - Extension through epiphyseal plate
   - Extension into or across joint space
   - Vascular involvement
   - Skip metastases
   - Distance from each margin.
5. Take soft tissue sections of margins, representative structures (e.g., vessels and nerves), and any areas of noncalcified tumor showing relationships to soft tissues. Tumor can be taken for special studies if not previously performed. Carefully search for lymph nodes and submit. Identify the prior biopsy site and sample this area to evaluate for soft tissue implants.
6. Fix the entire specimen in formalin. After overnight fixation, gently decalcify the sections with bone. The specimen must be checked every few hours in order to avoid overdecalcification which will adversely affect histologic examination.
7. Sections are taken to show the tumor, relationship to adjacent normal bone, invasion of contiguous structures (e.g., cortex, soft tissue, joint space), and margins. The location of sections taken is indicated on a diagram of the specimen. All areas of different radiologic appearance are sampled and correlated with the radiograph. For osteosarcomas and Ewing's sarcoma the extent of post therapy tumor necrosis is important to determine. An entire cross-section of these tumors is mapped out and submitted for histologic examination.

Bone dust can create artifacts that may be difficult to interpret. Orient the sections so that the portion cut by the histology laboratory will be opposite the side cut by the saw (e.g., ink one side and indicate the appropriate side to be sectioned).

SPECIAL STUDIES

Many of these tumors will be pretreated with radiation, chemotherapy, or both and will be predominantly necrotic. Special studies in general are not performed on such tumors. Cases with untreated tumors should have tissue sent for cytogenetic studies. Refer to Chapter 13.

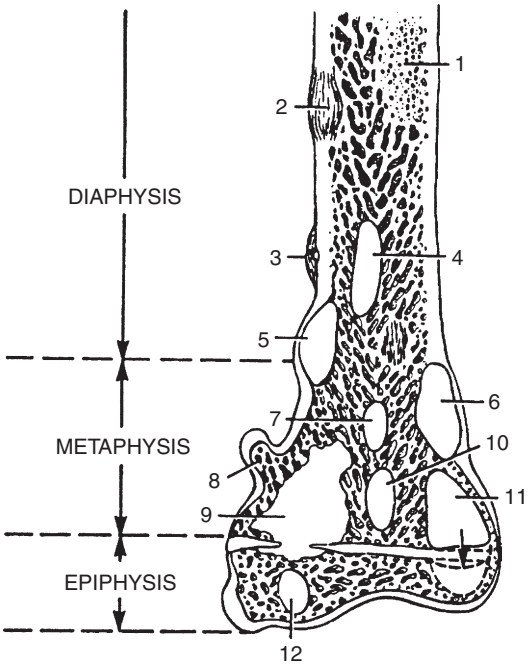
GROSS DIFFERENTIAL DIAGNOSIS

See Figure 14-1.

Ewing's Sarcoma/PNET. These tumors are generally treated with radiation and chemotherapy and not resected. Therefore, they will usually be diagnosed in biopsy specimens (see previous section). Grossly, the tumors are grayish white with indistinct borders and may have hemorrhage, cystic degeneration and necrosis. The adjacent bone is usually destroyed.

Osteoid Osteoma. The lesion is usually present in the cortex of a long bone and is less than 2 cm in size. Grossly, it may look like a bright red or pink nodule. Radiographs of the specimen can be helpful to demonstrate the characteristic central lucent zone with a rim of surrounding dense bone.

Fibrous Dysplasia. A fusiform expansion of the bone, with thinning of the cortex and replacement of the bone by firm white/gray gritty tissue. Cysts and cartilage may be present in the lesion. There may be a fracture site through the lesion.



1. Ewing's sarcoma, lymphoma, myeloma
2. Osseofibrous dysplasia, adamantinoma
3. Osteroid osteoma
4. Fibrous dysplasia
5. Chondromyxoid fibroma
6. Nonossifying fibroma
7. Bone cyst, osteoblastoma
8. Osteochondroma
9. Osteosarcoma
10. Enchondroma, chondrosarcoma
11. Giant cell tumor
12. Chondroblastoma

Figure 14–1. Most frequent locations of common osseous lesions. *(From Fechner RE, Mills SE: AFIP Atlast of Tumor Pathology: Tumors of the Bones and Joints, 3rd series, fascicle 8. Washington, DC, Armed Forces Institute of Pathology, 1993.)*

Aneurysmal Bone Cyst. A multiloculated cystic lesion, with cysts lined by soft brown fibrous tissue. The cysts may contain blood clots. The telangiectatic variant of osteosarcoma can mimic an aneurysmal bone cyst radiologically and clinically. Extensive sampling may be necessary to exclude this diagnosis.

Osteochondroma. A mushroom shaped subperiosteal projection or exostosis from the bone surface, usually juxta-articular. The bone merges with cortical bone and the medullary cavities are in continuity. The bone is covered by a thick cartilage cap.

Osteosarcoma. A destructive bone-forming tumor that often invades through the cortex and may invade into adjacent soft tissue. Lytic areas may be present. The tumor replaces the normal marrow space with firm tissue. Bone and/or cartilage may be present within the tumor mass.

Chondrosarcoma. Usually appears as a lobulated grayish white or blue tumor mass that often is calcified. The tumor may invade into or through normal bone. Areas of necrosis may be present.

Enchondroma. An intramedullary cartilagenous neoplasm consisting of multiple lobules of cartilage within bone.

Giant Cell Tumor. A well-defined lesion within the marrow space consisting of homogeneous tan/pink tissue. Hemorrhage and necrosis may be present.

Tumors after Treatment. Treated tumors may be predominantly necrotic or can be replaced by dense fibrous tissue. It may be difficult to find diagnostic areas.

MICROSCOPIC SECTIONS

- **Tumor:** At least 1 section per cm showing relationship to cortex, medulla, adjacent joint, soft tissue. Osteosarcomas and Ewing sarcoma cases that have been previously treated are blocked out in a complete cross section in order to evaluate the extent of necrosis. The location of blocks of tissue should be recorded on a diagram. Additional blocks are taken perpendicular to the cross section

to determine the extent of tumor in three dimensions. Blocks of tissue are also taken from areas that may be less susceptible to chemotherapy: soft tissue extension, tumor/nodal tissue interface, cortex, subcortical marrow, pericartilaginous regions, and areas surrounding hemorrhagic necrosis and ligaments.

Other types of tumors do not need to be mapped in such detail. At least one section per cm should be taken including all unusual appearing areas and satellite lesions.

- **Margins:** Usually will include both soft tissue and bone.
- **Normal structures:** Representative sections of all normal structures (e.g., major vessels, major nerve trunks).
- **Lymph nodes:** Submit all lymph nodes found (see Chapter 27).

SAMPLE DICTATION

Received fresh labeled with the patient's name, unit number, and "left distal femur" is an above-the-knee amputation with disarticulation of the knee (12 × 9 × 7 cm). The distal femur is 12 cm in length and surrounded by skeletal muscle. Centered within the metaphysis is a tan/yellow tumor (7.8 × 7 × 7 cm) that occupies the majority of the medullary cavity. The tumor appears to be entirely viable without gross areas of necrosis or hemorrhage. The tumor invades through the cortex medially, laterally, anteriorly, and posteriorly, and extends into soft tissue medially to form a soft tissue mass (2 × 1.8 × 0.4 cm). The tumor does not grossly involve the joint space. The tumor is located 3.5 cm from the proximal surgical resection margin, 0.4 cm from the posterior and lateral margins, and 0.1 cm from the anterior and medial margins. The tumor is 1 cm from the distal resection margin which consists of the grossly unremarkable cartilage surface of the distal femur. There is an attached skin ellipse over the anterior/medial portion of the specimen, measuring 9.3 × 1.1 cm, with a centrally located well-healed surgical scar measuring 7.5 cm. There is a hemorrhagic biopsy cavity (1 × 1 × 0.6 cm) located 4.5 cm deep to the skin surface and adjacent to the tumor. The femoral artery and accompanying nerves and vein are not present. The specimen is radiographed. A diagram is prepared with the location of sections marked. Sections containing bone are fixed and decalcified prior to submission.

Cassettes 1-15: Complete cross section of tumor including relationship to cortex, submitted from proximal to distal, 15 frags, RSS.
Cassette 16: Tumor and medial margin including soft tissue extension, 1 frag, RSS.
Cassette 17: Tumor and lateral margin, 1 frag, RSS.
Cassette 18: Tumor and posterior margin, 1 frag, RSS.
Cassette 19: Tumor and anterior margin, 1 frag, RSS.
Cassette 20: Bone at proximal margin, 1 frag, RSS.
Cassette 21: Bone and cartilage at distal margin, 1 frag, RSS.
Cassette 22: Soft tissue at proximal margin, 1 frag, RSS.
Cassette 23: Soft tissue at proximal margin, 1 frag, RSS.
Cassette 24: Skin with scar, 1 frag, RSS.
Cassette 25: Biopsy site, 1 frag, RSS.

PATHOLOGIC PROGNOSTIC/DIAGNOSTIC FEATURES SIGN-OUT CHECKLIST FOR BONE TUMORS

- **Specimen**: Bone involved
- **Procedure**: Core needle biopsy, curettage, excisional biopsy, intralesional resection, marginal resection, segmental/wide resection, radical resection
- **Tumor Location(s)**:
  - Epiphysis (articular cartilage to epiphyseal plate) or apophysis (a process on certain bones)
  - Metaphysis (epiphyseal plate to diaphysis)
  - Diaphysis (end of proximal metaphysis to beginning of distal metaphysis)
  - Cortical
  - Medullary cavity
  - Surface
  - Tumor involves joint
  - Tumor extension into soft tissue

TABLE 14-2. AJCC (7TH EDITION) CLASSIFICATION OF BONE TUMORS

Grade	GX	Grade cannot be assessed.
	G1	Well differentiated, low grade
	G2	Moderately differentiated, low grade
	G3	Poorly differentiated
	G4	Undifferentiated
Note: Ewing's sarcoma is classified as G4.		
Tumor	TX	Primary tumor cannot be assessed.
	T0	No evidence of primary tumor
	T1	Tumor 8 cm or less in greatest dimension
	T2	Tumor more than 8 cm in greatest dimension
	T3	Discontinuous tumors in the primary bone site
Regional Lymph Nodes	NX	Regional lymph nodes cannot be assessed.
	N0	No regional node metastasis
	N1	Regional node metastasis
Note: Because of the rarity of lymph node involvement in bone sarcomas, the designation NX may not be appropriate, and cases should be considered N0 unless clinical node involvement is clearly evident.		
Distant Metastasis	M0	No distant metastasis
	M1	Distant metastasis
	M1a	Lung
	M1b	Other distant sites

This system is used for all primary malignant tumors of bone except lymphoma and multiple myeloma.
Note: Primary malignant lymphoma and multiple myeloma are not included.
From the AJCC Cancer Staging Manual, Seventh Edition. New York, Springer-Verlag, 2009. Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois.

- **Tumor Size:** Greatest dimension (other dimensions optional), multifocal tumor/discontinuous tumor at primary site (skip metastasis)
- **Histologic Type**: The most important feature. Usually the diagnosis will have been established before definitive resection. The WHO Classification of bone tumors should be used.
- **Mitotic Rate:** Number of mitoses per 10 HPF (1 HPF = 0.1734 mm^2) The most proliferative area should be counted.
- **Necrosis**: Not identified, present (extent: %)
- **Histologic Grade**: See Tables 14-2 to 14-6 for grades of common bone tumors.
- **Margins**:
  - Bone, soft tissue, marrow, involvement and distance of tumor from margin
  - Neurovascular bundle at the margin: involved or not involved
  - Intralesional margin = positive margin
  - Marginal margin = < 2 cm of normal tissue at margin; less if the margin is fascia
  - Wide margin = > 2 cm of normal tissue at margins, less if bounded by fascia
- **Lymph-Vascular Invasion:** Not identified, present (present in 3% to 13% of osseous sarcomas)
- **Cystic Change:** Identified, not identified

TABLE 14–3. BONE TUMORS – GRADE	
Grade 1 (low grade)	Low-grade central osteosarcoma
	Parosteal osteosarcoma
	Adamantinoma
Grade 2	Periosteal osteosarcoma
Grade 3 (high grade)	Malignant giant cell tumor
	Ewing sarcoma/PNET
	Mesenchymal chondrosarcoma
	Dedifferentiated chondrosarcoma
	Conventional osteosarcoma
	Telangiectactic osteosarcoma
	Small cell osteosarcoma
	Secondary osteosarcoma
	High-grade surface osteosarcoma
Variable grade	Dedifferentiated chordoma
	Conventional chondrosarcoma of bone (grades 1 to 3)
	Soft-tissue type sarcomas (e.g., leiomyosarcoma)
See CAP protocol for tumors of bone (www.cap.org).	

TABLE 14–4. CHONDROSARCOMA – GRADE				
	Cellularity	**Nuclear Atypia**	**Mitoses**	**Other Features**
Grade 1 (low grade)	Hypocellular	Minimal	Minimal	Appearance similar to enchondroma
Grade 2 (intermediate grade)	More cellular	More atypia, greater hyperchromasia, increased nuclear size	Minimal	May have extensive myxoid stroma
Grade 3 (high grade)	Hypercellular	Pleomorphic nuclei	Prominent	
See CAP protocol for tumors of bone (www.cap.org).				

- **Hemorrhage:** Identified, not identified
- **Radiographic Findings**: Correlate with radiographic images
- **Treatment Effect**: No prior treatment, not identified, present. Report proportion of tumor that is necrotic or replaced by fibrous or granulation tissue (Tables 14–5 and 14–6 for osteosarcoma and Ewing sarcoma).
- **Ancillary Studies (if performed):** Immunohistochemistry, cytogenetics, molecular studies
- **Regional Lymph Node Metastasis**: Absent, present (number of nodes involved, number of nodes examined)
- **Distant Metastasis**: Present. If distant metastasis is not present on pathologic examination, the M category is a clinical classification.

TABLE 14–5. OSTEOSARCOMA – HISTOLOGIC RESPONSE GRADE TO TREATMENT	
I	No effect identified
IIA	Some necrosis, more than 50% viable tumor remaining
IIB	3% to 50% viable tumor remaining
III	Scattered foci, <3% viable tumor remaining*
IV	No viable tumor noted

*In some systems, 90% or 95% is used rather than 97%, which is the current standard of the Children's Oncology Group. Tumors that have 90% to 97% necrosis have a better prognosis.

TABLE 14–6. EWING SARCOMA – HISTOLOGIC RESPONSE GRADE TO TREATMENT	
Grade I	Macroscopic viable tumor
Grade II	Microscopic viable tumor
Grade III	No viable tumor

See CAP protocol for tumors of bone (www.cap.org).

- **AJCC Classification**: T, N, and M categories should be provided, when possible. M0 is conferred after clinical assessment; there is no pM0 category.

This checklist incorporates information from the CAP Cancer Committee protocols for reporting on cancer specimens (see www.cap.org/) and ADASP (see www.adasp.org). The underlined elements are considered to be scientifically validated or regularly used data elements that must be present in reports of cancer-directed surgical resection specimens from ACS CoC-approved cancer programs. The specific details of reporting the elements may vary among institutions.

INCIDENTAL RIBS

Portions of ribs are often removed to perform thoracotomies or nephrectomies. The rib is usually 2 to 5 cm long and is rarely of diagnostic importance. The most important missed histologic diagnosis on incidental ribs is multiple myeloma. The patients often survive for long periods of time, may have procedures performed not related to the disease (unlike, for example, acute leukemia), and the disease may not have been diagnosed clinically. Plasma cell dyscrasias can be diagnosed even on suboptimally fixed and decalcified tissue. Involvement by chronic lymphocytic leukemia is also occasionally found, but is usually clinically evident due to a high peripheral white blood count.

SPECIMEN PROCESSING

Ribs resected from patients without malignant disease and without other clinical indication for examination (e.g., a known hematologic disorder) do not necessarily require histologic examination. There are two methods for examining all other specimens.

Decalcification Method. This method should be used for all patients with a history of lymphoma or other hematologic disorder (treat as a diagnostic bone marrow biopsy; see Chapter 27); a history of a malignancy that frequently metastasizes to bone marrow (e.g., small cell lung carcinomas); or ribs with grossly evident or clinically suspected lesions.

1. The rib is described (measurements, color, gross identification as portion of rib) and fixed in formalin. Cartilage may be present at one end if near the costochondral junction. It will be homogeneously pale white, will cut easily with a razor blade, and will not be visible on x-ray.

2. If a gross lesion is present that is suspicious for metastatic disease, the specimen is radiographed, serially sectioned, and any soft tissue (i.e., potential tumor) removed prior to decalcification.
3. The remainder of the bone is gently decalcified. Grossly normal bones can be submitted as multiple sections in one cassette. If gross or radiographic lesions are present, submit them in a separate cassette. Do not submit grossly benign cartilage.

Rib Squeeze Method. The disadvantage of this method is that metastatic tumors and lymphomas may not be easily expressed from the bone marrow due to accompanying marrow fibrosis. However, often bone marrow involvement will have been investigated clinically before surgery is performed and the finding of malignancy in incidental ribs is very rare.

The advantage of this method is that it provides better histologic preservation of the bone marrow elements and does not delay the rib in processing. Thus, this is the preferred method with the exceptions noted above.

1. The rib is described as above.
2. The specimen must be fresh and unfixed. Use a bone saw to cut a portion about 2 cm in length with marrow present at both ends of the specimen. Use pliers to squeeze until marrow is expressed from both ends. Collect the marrow in formalin. If very little marrow can be expressed, the bone should be fixed and decalcified as described above. The remainder of the rib is cut longitudinally and examined for gross lesions. Submit any lesions seen. Document in the gross description that the bone was not decalcified.
3. The marrow should be wrapped in paper or placed in a specimen bag and submitted in one cassette.

MENISCUS

Menisci are usually removed because of traumatic tears that interfere with articular movement. Occasionally joint mice (= loose bodies) may be removed during the same type of procedure. These are fragments of free cartilage in the joint space and often become ossified. The meniscus can also be affected by CPPD and ochronosis (see gross differential diagnosis under "Synovium").

PROCESSING THE SPECIMEN

1. Describe the specimen including size, color (normally white and glistening), texture (smooth, fibrillated), and presence or absence of tears.
2. If chalky white deposits are present, a portion of the specimen is processed in absolute ethanol to preserve crystals (see also "Synovium").
3. Submit representative sections in one cassette.

SYNOVIUM

Synovium may be biopsied for diagnostic purposes (e.g., inflammatory arthritis) or removed for the treatment of disease (e.g., pigmented villonodular synovitis [giant cell tumor, diffuse type] or dialysis-related amyloidosis).

PROCESSING THE SPECIMEN

1. Record the aggregate dimensions, size range, and approximate number of fragments.
   Describe the color and consistency of the synovium (see descriptions under "Gross Differential Diagnosis").
   If infection is suspected and fresh tissue is received, confirm that cultures have been taken. If not, send sterile tissue to microbiology.
2. Submit up to two cassettes and order one level (H&E). Order special studies as indicated below for specific cases. If the specimen is a small biopsy, submit all the tissue and order three levels.

SPECIAL STUDIES

- **Crystal disease:** Chalky white deposits may be present in synovium and representative sections must be fixed in absolute alcohol. See "Total Joint Arthroplasty - Special Studies."

- **Amyloidosis:** All tissue can be fixed in formalin. Amyloid can be diagnosed using a Congo red stain and polarized light. Immunohistochemistry can be used to identify the type of amyloid present. Dialysis related amyloidosis of joints is due to β2 microglobulin.
- **Infection:** Fresh sterile tissue may be sent for culture.

GROSS DIFFERENTIAL DIAGNOSIS

Normal Synovium. Normal synovium is glistening white with delicate villous projections.

Gout or CPPD. Chalky white or crystalline deposits are present and must be fixed in absolute alcohol. See "Total Joint Arthroplasty - Special Studies" for information on how to process.

Giant Cell Tumor, Diffuse Type (Pigmented Villonodular Synovitis, PVNS). The synovium is a rusty red color due to extensive hemosiderin deposition. Coarse villi with occasional attached nodules are present. These areas become more apparent when floated in saline and can be photographed well in this manner. There may be an abundance of tissue with areas of fibrosis. Necrotic foci may appear yellow due to the presence of histiocytes.

Detritic Synovitis. Changes occurring around an artificial joint, which can appear very similar to PVNS (see "Revision Total Joint Arthroplasty").

Dialysis-Related Amyloidosis. There are characteristic yellow/tan plaques that may be superficial, run along tendons, or form large homogeneous nodules.

Synovial Chrondromatosis. Multiple small nodules of cartilage are present within the synovial tissue. The cartilage may need to be decalcified.

Hemochromatosis. The synovium can become hyperplastic and brown in color due to dense hemosiderin deposition. The appearance can mimic PVNS, but nodules are not present. The cartilage takes on a characteristic greenish-black appearance.

MICROSCOPIC SECTIONS

- **Synovium:** Up to two cassettes. If the biopsy is small (only enough tissue for one cassette), order three levels.

SAMPLE DICTATION

Received fresh labeled with the patient's name, unit number, and "synovium right knee" are multiple fragments of reddish brown soft tissue measuring in aggregate 5 × 4 × 1 cm. Delicate villous projections and small nodules are present.

Cassettes 1 and 2: mult frags, RSS.

CARPAL TUNNEL RELEASE (TENOSYNOVIUM)

Most patients present with idiopathic carpal tunnel syndrome, and only a small fraction of these patients will show evidence of amyloid on microscopic examination. However, in renal dialysis patients carpal tunnel syndrome is very common and β2 microglobulin amyloidosis is often present.

These specimens consist of synovium and soft tissue from around the tendons and nerves of the carpal tunnel that are removed during a carpal tunnel release procedure. The specimens may be processed in the same manner as synovium, but are examined with one level.

INTERVERTEBRAL DISC MATERIAL

These specimens are derived from operations on herniated discs and will consist of small fragments of bone, nucleus pulposus, annulus fibrosus, and ligamentum flavum. The specimen is fixed, decalcified, and one representative section is submitted.

The likelihood of finding a clinically significant unsuspected finding in a patient without a history of malignancy and/or suspected infection is very low (<1%).[14-18] However, if the patient has a significant history or an unusual presentation, important pathologic findings are reported in over half of cases. If an adequate clinical history is provided, it may not be necessary to examine all such specimens histologically. See "Gross Specimens" for a discussion of this issue.

Special cases:

- **Metastatic disease:** Any soft tissue is dissected away and submitted without decalcification. If the primary site is unknown, and there is sufficient tissue, then consideration should be given to saving tissue for special studies (e.g., frozen tissue or EM).
- **Infection:** Any soft tissue is dissected away and submitted without decalcification. If there is sufficient tissue, consideration should be given to sending tissue for cultures. Special stains may be helpful. Aspergillus can invade into cartilage without an inflammatory response and may not be detectable without fungal stains.

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