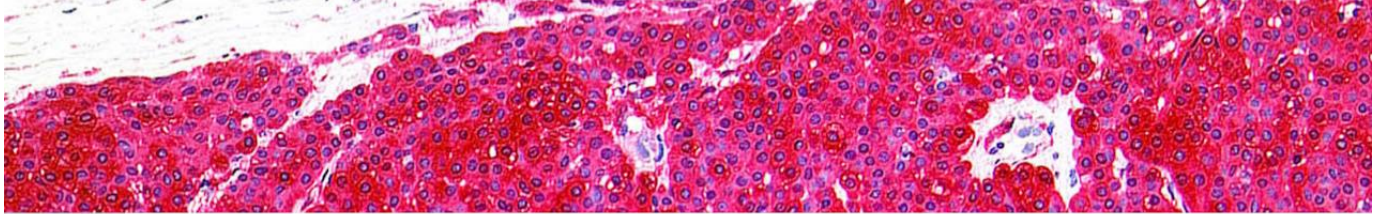


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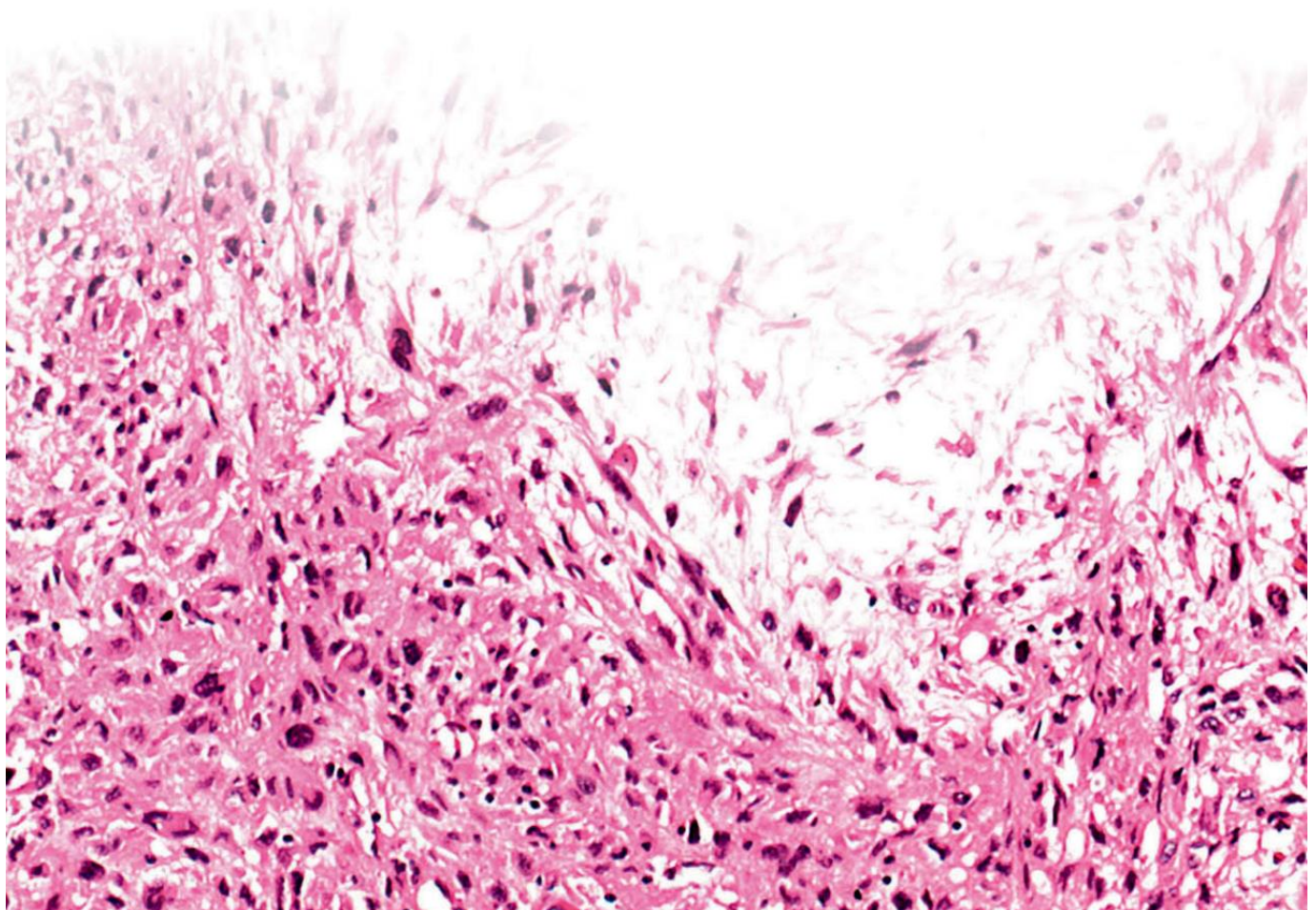
# Soft Tissue Introduction

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## Gross Examination

## INTRODUCTION

## Overview

- Thorough but focused gross examination is vital component of overall evaluation and diagnostic work-up of soft tissue tumors
- Common errors (e.g., undersampling, inappropriate sampling, not inking margins) can severely hamper or preclude accurate diagnosis, pathologic staging, and subsequent clinical planning
- Review of patient clinical history and information prior to gross examination is strongly recommended

## CLINICAL FINDINGS

## History

- Review any available clinical notes or operative report
  - Note age of patient and clinical presentation of tumor
  - Note if patient has prior history of tumor in same anatomic location, nearby, or elsewhere
- Determine whether tumor has been previously biopsied or treated or if there is established diagnosis

## Imaging

- Review any pertinent radiographs, CT, or MR scans
  - Determine if tumor is homogeneous or heterogeneous
  - Identify any notable structures involved (e.g., large nerve trunk)
  - Determine whether radiologist favors benign or malignant process
- Note anatomic location (e.g., thigh, neck, retroperitoneum, finger)
- Note tissue plane (i.e., superficial/subcutaneous vs. deep/intramuscular)

## GROSSING PROCEDURE

## External Examination

- Specimen should be weighed and measured in 3 dimensions
- Describe external appearance and shape of mass

- Note any orientation provided by surgeon (e.g., stitches, strip of overlying skin, large nerves)
  - Skin is often excised to remove previous biopsy tract with rest of specimen
- Ink peripheral margins of specimen
  - Oriented tumors often require inking with up to 6 different colors
  - Unoriented tumors may be inked in 1 color

## Sectioning and Internal Evaluation

- Serially section ("bread loaf") mass in 1-cm thick sections, perpendicular to long axis of specimen
- Lay out all slabs of tumor and examine cut surfaces
- Describe appearance of cut surface and note areas of different coloration &/or texture
  - Common colors: Tan, white, gray, red, brown
  - Common textures: Firm/fibrous, fleshy, gelatinous/glistening, fatty
- Note any areas of hemorrhage &/or necrosis
  - Quantify necrosis (none,  $\leq 50\%$ , or  $> 50\%$ )
  - Highly necrotic tumors should be placed in formalin to fix and to minimize fragmentation
- Take representative fresh tissue for possible ancillary techniques or treatment protocols (may be snap frozen)

## Sampling

- Standard approach is to take 1 section per cm of greatest tumor dimension (margin sections counted separately)
  - e.g., 16-cm tumor gets 16 blocks with 1 tissue piece in each or 8 blocks with 2 tissue pieces in each
  - Fewer sections may be submitted for large tumors with diffuse homogeneous appearance
- Inked margins, specifically close ( $< 2$  cm) margins, should be sampled with perpendicular sections
- Sections should be taken from all distinctive areas (e.g., fibrous, gelatinous, fleshy, etc.)
  - Sections taken at interface between different areas can provide very useful histologic information
- Obviously necrotic areas should be minimally sampled
  - These areas often represent high-grade morphologies and are generally less useful diagnostically

External Examination

(Left) The gross appearance of a soft tissue tumor specimen varies depending on the type of surgery, but many tumors (especially sarcomas) are removed with at least a thin rim of surrounding soft tissue. If the tumor has been previously sampled by core biopsy, the biopsy tract and skin strip are often removed as well. (Right) Although known benign soft tissue tumors are often excised without orientation by the surgeon, sarcomas often arrive oriented by stitches and require inking, as depicted, for satisfactory margin evaluation.

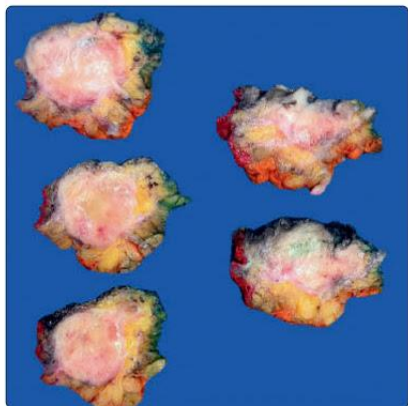


Specimen Inking

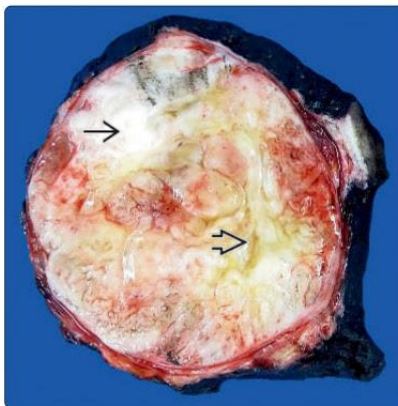




## Gross Examination

Serial Sectioning

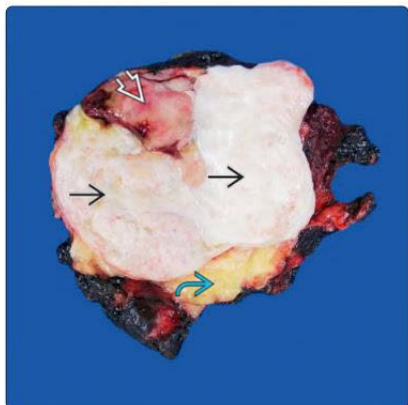


Evaluation of Cut Surface

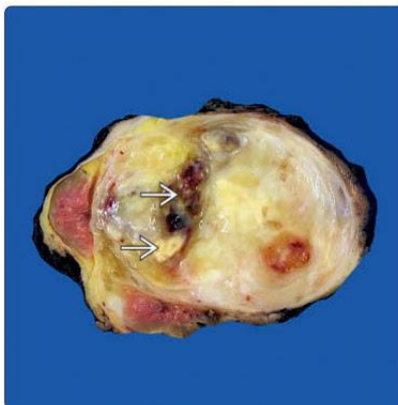






(Left) After external examination and inking of the soft tissue tumor specimen, it should be serially sectioned in ~ 1-cm slices. After all sections are laid out, the margins should be assessed and sampled, and the appearance of the cut surfaces should be evaluated with any variations noted. (Right) The cut surface of a soft tissue tumor may show a variety of appearances (e.g., fibrous , fleshy, fatty, gelatinous , and all distinctive areas should be noted and sampled. Transition areas should be particularly targeted.

Evaluation of Cut Surface

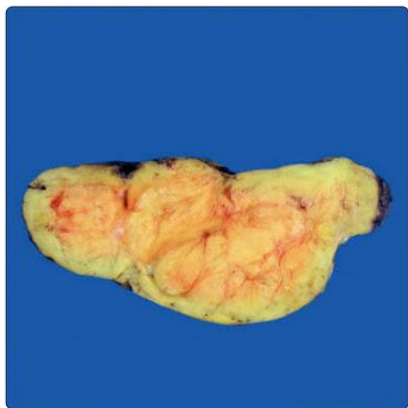


Documentation of Necrosis

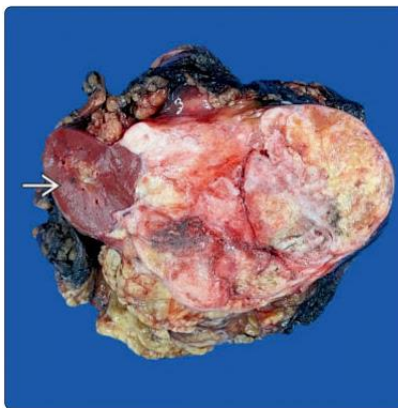



(Left) Gross photo of a dedifferentiated liposarcoma shows a mixture of fibrous , and fleshy  areas representing the high-grade component. The minimal, well-differentiated component  may be easily mistaken for normal fat and ignored. (Right) It is important to assess and document the amount of necrosis  present during gross examination, as it may be useful in subsequent grading of the tumor. Of note, sometimes nonnecrotic, degenerative, edematous, or myxoid areas may be mistaken for necrosis grossly.

Large Homogeneous Tumors



En Bloc Radical Resection Specimen



(Left) Some larger soft tissue tumors show a similar homogeneous cut surface on all gross slices without areas of variation, as is seen in this gross photo of a lipoma. The "1 section per cm" rule may be relaxed in this situation. (Right) Soft tissue tumors that arise in body cavities (particularly the retroperitoneum) can grow to incredible sizes and may require radical surgical resection and debulking. This gross photo shows a dedifferentiated liposarcoma with renal  involvement.

# Grading and Staging

## GRADING AND STAGING SYSTEMS

### Grading System

- French FNCLCC system most commonly utilized

### Staging System

- TNM system (AJCC Cancer Staging Manual, 8th edition)

## HISTOLOGIC FEATURES EVALUATED IN GRADING (FNCLCC)

### Method

- Assign following 3 independent scores based upon particular histologic parameters
  - Differentiation
  - Mitotic rate
  - Necrosis
- 3 independent scores are totaled to determine histologic grade of sarcoma

### Degree of Cellular Differentiation

- Score 1: Sarcomas closely resembling normal, adult mesenchymal tissue
  - Well-differentiated examples of liposarcoma (LPS)
  - Leiomyosarcoma
  - Malignant peripheral nerve sheath tumor (MPNST)
  - Others
- Score 2: Sarcoma for which histologic typing is certain
  - Myxofibrosarcoma
  - Myxoid LPS (excluding cellular/round cell)
  - Conventional leiomyosarcoma
  - MPNST
  - Others
- Score 3: Embryonal or undifferentiated sarcomas, synovial sarcoma, or sarcoma of uncertain type
  - Dedifferentiated LPS
  - Pleomorphic LPS
  - High-grade myxoid LPS (formerly round cell LPS)
  - Most rhabdomyosarcoma
  - Ewing sarcoma
  - Mesenchymal chondrosarcoma
  - Extraskeletal osteosarcoma
  - Pleomorphic leiomyosarcoma
  - Pleomorphic MPNST
  - Undifferentiated pleomorphic sarcoma

### Mitotic Rate (Mitoses per 10 HPF)

- Score 1: 0-9
- Score 2: 10-19
- Score 3: > 19
  - Count total number in 10 successive HPF (40x objective) in most mitotically active areas
  - Avoid ulcerated, necrotic, or hypocellular areas

### Percentage of Microscopic Tumor Necrosis

- Score 0: No necrosis
- Score 1: Necrosis < 50% total tumor volume
- Score 2: Necrosis ≥ 50% total tumor volume
  - Tumor necrosis should be evaluated at macroscopic and microscopic levels

### Overall Histologic Grade

- Summation of 3 individual scores indicates grade
  - Grade 1 (low grade): Total score 2 or 3
  - Grade 2 (intermediate grade): Total score 4 or 5
  - Grade 3 (high grade): Total score 6, 7, or 8

### Limitations

- Grading schemata apply best to fully excised specimens that have not been preoperatively treated with neoadjuvant therapies
  - Only minimum grade can be applied to limited (biopsy) sample
  - Sarcomas treated preoperatively with chemotherapy &/or radiation cannot be accurately graded
- For some sarcomas, grade is automatically defined by histologic subtype
  - Always grade 1 (low grade)
    - Well-differentiated LPS
    - Conventional dermatofibrosarcoma protuberans
    - Infantile fibrosarcoma
  - Always grade 3 (high grade)
    - Ewing sarcoma
    - High-grade myxoid LPS (formerly round cell LPS)
    - Pleomorphic LPS
    - Dedifferentiated LPS
    - Extraskeletal osteosarcoma
    - Mesenchymal chondrosarcoma
    - Desmoplastic small round cell tumor
    - Extrarenal rhabdoid tumor
  - Not formally graded but often managed as high grade
    - Alveolar soft part sarcoma
    - Clear cell sarcoma
    - Epithelioid sarcoma
    - Extraskeletal myxoid chondrosarcoma
    - Angiosarcoma
    - Embryonal and alveolar rhabdomyosarcoma

### Additional Considerations

- Some mesenchymal neoplasms have unique criteria for histologic grading (or risk assessment) and do not routinely utilize FNCLCC system
  - Epithelioid hemangioendothelioma
  - Gastrointestinal stromal tumor
  - Solitary fibrous tumor
  - Ossifying fibromyxoid tumor
  - PEComa

## Grading and Staging

### Soft Tissue Sarcoma Staging (TNM System) for Trunk and Extremities

Pathologic Staging Category	Description
<b>Primary Tumor (T)</b>	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤ 5 cm in greatest dimension
T2	Tumor > 5 cm and ≤ 10 cm in greatest dimension
T3	Tumor > 10 cm and ≤ 15 cm in greatest dimension
T4	Tumor > 15 cm in greatest dimension
<b>Regional Lymph Nodes (N)</b>	
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
<b>Distant Metastasis (M)</b>	
M1	Distant metastasis [specify site(s), if known]

*All tables adapted from 8th edition AJCC Staging Forms (2018). Nx designation not used for soft tissue tumors.*

### Soft Tissue Sarcoma Staging (TNM System) for Retroperitoneum

Pathologic Staging Category	Description
<b>Primary Tumor (T)</b>	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤ 5 cm in greatest dimension
T2	Tumor > 5 cm and ≤ 10 cm in greatest dimension
T3	Tumor > 10 cm and ≤ 15 cm in greatest dimension
T4	Tumor > 15 cm in greatest dimension
<b>Regional Lymph Nodes (N)</b>	
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
<b>Distant Metastasis (M)</b>	
M1	Distant metastasis [specify site(s), if known]

### Soft Tissue Sarcoma Staging (TNM System) for Orbit

Pathologic Staging Category	Description
<b>Primary Tumor (T)</b>	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤ 2 cm in greatest dimension
T2	Tumor > 2 cm in greatest dimension without invasion of bony walls or globe
T3	Tumor of any size with invasion of bony walls
T4	Tumor of any size with invasion of globe or periorbital structures, including eyelid, conjunctiva, temporal fossa, nasal cavity, paranasal sinuses, &/or central nervous system
<b>Regional Lymph Nodes (N)</b>	
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
<b>Distant Metastasis (M)</b>	
M1	Distant metastasis [specify site(s), if known]

## Grading and Staging

### Soft Tissue Sarcoma Staging (TNM System) for Abdomen and Thoracic Organs

Pathologic Staging Category	Description
<b>Primary Tumor (T)</b>	
TX	Primary tumor cannot be assessed
T1	Tumor is organ confined
T2	Tumor extension into tissue beyond organ
T2a	Tumor invades serosa or visceral peritoneum
T2b	Tumor extends beyond serosa (mesentery)
T3	Tumor invades another organ
T4	Multifocal involvement
T4a	Multifocal (2 sites)
T4b	Multifocal (3-5 sites)
T4c	Multifocal (> 5 sites)
<b>Regional Lymph Nodes (N)</b>	
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
<b>Distant Metastasis (M)</b>	
M1	Distant metastasis [specify site(s), if known]

All tables adapted from 8th edition AJCC Staging Forms (2017).

### Soft Tissue Sarcoma Staging (pTNM System) for Head and Neck

Pathologic Staging Category	Description
<b>Primary Tumor (T)</b>	
TX	Primary tumor cannot be assessed
T1	Tumor ≤ 2 cm
T2	Tumor > 2 to ≤ 4 cm
T3	Tumor > 4 cm
T4	Tumor with invasion of adjoining structures
T4a	Tumor with orbital invasion, skull base/dural invasion, invasion of central compartment viscera, involvement of facial skeleton, or invasion of pterygoid muscles
T4b	Tumor with brain parenchymal invasion, carotid artery encasement, prevertebral muscle invasion, or central nervous system involvement via perineural spread
<b>Regional Lymph Nodes (N)</b>	
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
<b>Distant Metastasis (M)</b>	
M1	Distant metastasis [specify site(s), if known]

### Additional Descriptors (pTNM system)

Descriptor	Meaning
<b>Prefix</b>	
y	Tumor is being staged post therapy (i.e., neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation)
r	Tumor is recurrent (must follow documented disease-free interval)
<b>Suffix</b>	
m	Multiple primary tumors involving single site

Example: ypT3(m)N0 in pathologic stage T3 sarcoma, multifocal, treated with neoadjuvant therapy prior to resection.

## Grading and Staging

### Anatomic Stage/Prognostic Groups (Trunk and Extremities)

Stage	Tumor	Node	Metastasis	Grade (G)
Stage IA	T1	N0	M0	G1 or GX (low grade)
Stage IB	T2	N0	M0	G1 or GX (low grade)
	T3	N0	M0	G1 or GX (low grade)
	T4	N0	M0	G1 or GX (low grade)
Stage II	T1	N0	M0	G2 or G3 (high grade)
Stage IIIA	T2	N0	M0	G2 or G3 (high grade)
Stage IIIB	T3	N0	M0	G2 or G3 (high grade)
	T4	N0	M0	G2 or G3 (high grade)
Stage IV	Any T	N1	M0	Any G
	Any T	Any N	M1	Any G

*All tables adapted from 8th edition AJCC Staging Forms (2017). GX: Grade cannot be assessed; M0: No distant metastasis.*

### Anatomic Stage/Prognostic Groups (Retroperitoneum)

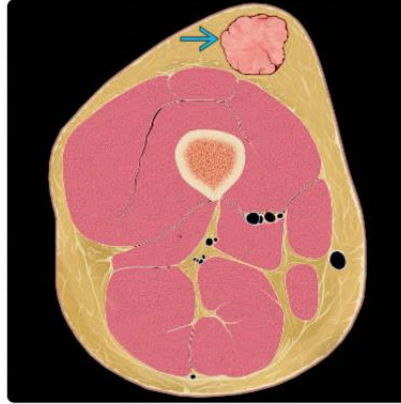
Stage	Tumor	Node	Metastasis	Grade (G)
Stage IA	T1	N0	M0	G1 or GX (low grade)
Stage IB	T2	N0	M0	G1 or GX (low grade)
	T3	N0	M0	G1 or GX (low grade)
	T4	N0	M0	G1 or GX (low grade)
Stage II	T1	N0	M0	G2 or G3 (high grade)
Stage IIIA	T2	N0	M0	G2 or G3 (high grade)
Stage IIIB	T3	N0	M0	G2 or G3 (high grade)
	T4	N0	M0	G2 or G3 (high grade)
Stage IV	Any T	N1	M0	Any G
	Any T	Any N	M1	Any G

*No formal stage groupings exist for head and neck, orbit, abdominal visceral organs, and thoracic visceral organ sites.*

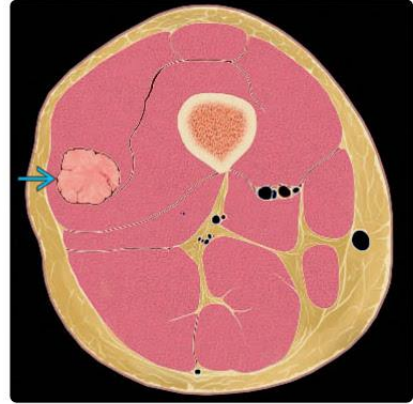
## Grading and Staging

(Left) Axial graphic of the thigh shows a T1 soft tissue sarcoma. By definition, these tumors are  $\leq 5$  cm in greatest dimension. The previous "a" and "b" designations used to denote superficial (T1a) and deep localization (T1b) are no longer utilized. (Right) Axial graphic of the thigh shows a T1 soft tissue sarcoma measuring  $< 5$  cm. Though once designated "pT1b" in previous staging schema due to its deep/subfascial involvement, this tumor would now be staged purely as T1.

T1 (TNM Staging)



T1 (TNM Staging)



(Left) Axial graphic of the thigh shows a T2 soft tissue sarcoma. By definition, these tumors measure 5-10 cm in greatest dimension. Localization above or below the fascia is no longer taken into account. (Right) Axial graphic of the thigh shows a T3 soft tissue sarcoma. By definition, these tumors measure 10-15 cm in greatest dimension. Although the tumor arises in the muscle, it does not affect the staging designation.

T2 (TNM Staging)

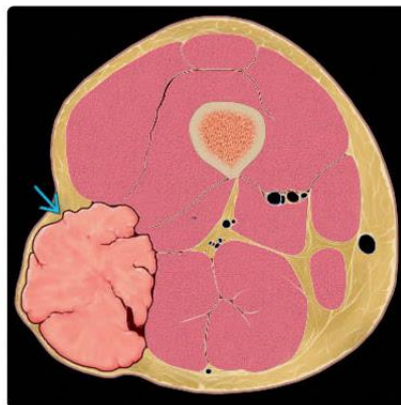


T3 (TNM Staging)

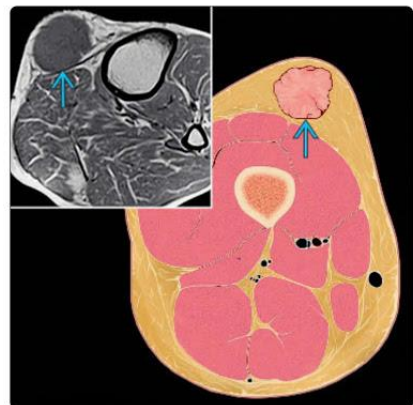


(Left) Axial graphic of the thigh shows a T4 soft tissue sarcoma. By definition, these tumors measure  $> 15$  cm in greatest dimension. (Right) Axial graphic and MR show an anatomic stage IA soft tissue sarcoma of the extremity. By definition, the tumor is  $< 5$  cm, histologically low grade, and no metastases (nodal or distant) are present. If this tumor were  $> 5$  cm, it would be grouped as IB.

T4 (TNM Staging)

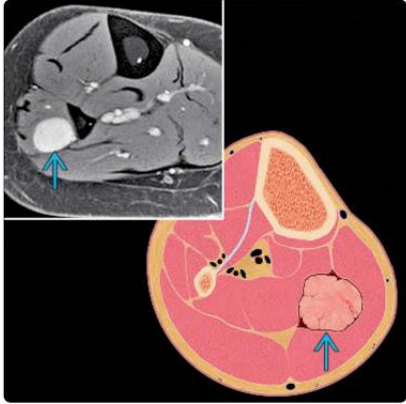


Anatomic/Prognosis Stage IA Group



## Grading and Staging

Anatomic/Prognosis Stage II Group



Anatomic/Prognosis Stage IIIB Group

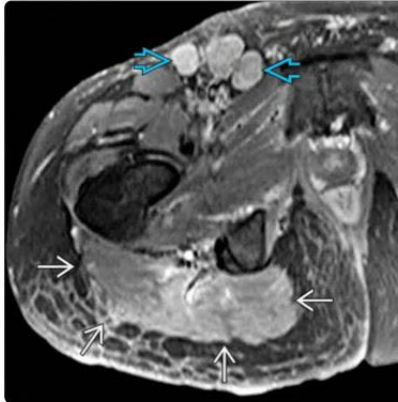


(Left) Axial graphic and MR of the extremity show a stage II soft tissue sarcoma. These lesions are G2 or G3 (high grade) and all measure < 5 cm in greatest dimension. No metastases are present. (Right) Axial graphic and MR of the extremity show a stage IIIB soft tissue sarcoma. These tumors are G2 or G3 (high grade), and all measure > 10 cm in greatest dimension. No nodal metastases are present. If this same tumor measured between 5-10 cm, it would be grouped as IIIA.

Anatomic/Prognosis Stage IV Group

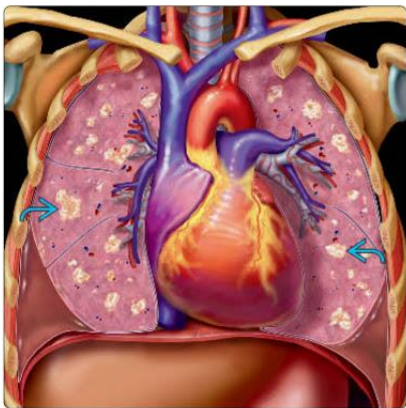


Anatomic/Prognosis Stage III Group

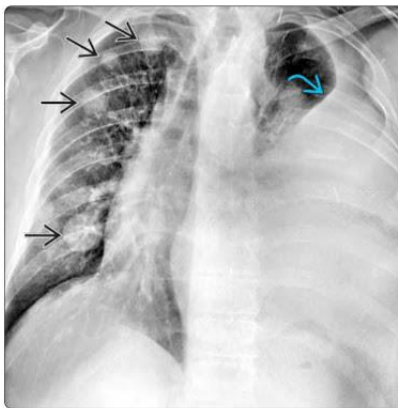


(Left) Axial graphic through the low pelvis shows inguinal adenopathy. The presence of involved lymph nodes, though uncommon in sarcoma, makes this stage IV disease. The primary tumor can be any size or histologic grade. (Right) Axial MR with contrast shows an abnormal gluteus maximus muscle, which was infiltrated with tumor. Note the prominent inguinal adenopathy, making this a stage IV sarcoma.

Anatomic/Prognosis Stage IV Group



Anatomic/Prognosis Stage IV Group



(Left) Coronal graphic through the lungs demonstrates multiple bilateral pulmonary metastases from a soft tissue sarcoma. The presence of distant metastases makes this stage IV disease. In this setting, the size and histologic grade of the primary tumor are irrelevant. (Right) This chest radiograph in a patient with a malignant nerve sheath tumor shows multiple pulmonary metastases and a large malignant effusion filling the left hemithorax.