Protocol for the Examination of Resection Specimens From Patients With Soft Tissue Tumors

Version: 4.2.0.0
Protocol Posting Date: June 2024
CAP Laboratory Accreditation Program Protocol Required Use Date: March 2025
The changes included in this current protocol version affect accreditation requirements. The new deadline for implementing this protocol version is reflected in the above accreditation date.

For accreditation purposes, this protocol should be used for the following procedures and tumor types:

Procedure	Description
Resection	Includes specimens designated intralesional resection, excisional biopsy, marginal resection, wide resection, and radical resection
Tumor Type	**Description**
Soft tissue sarcomas	Includes soft tissue sarcomas for which pTNM staging is clinically relevant

This protocol is NOT required for accreditation purposes for the following:

Procedure
Biopsy (Consider the Soft Tissue Biopsy protocol)
Primary resection specimen with no residual or viable cancer (e.g., following neoadjuvant therapy)
Cytologic specimens
Tumor type
Soft tissue tumors that may recur locally but have either no or an extremely low risk of metastasis and malignant soft tissue tumors for which pTNM is not clinically relevant

The following tumor types should NOT be reported using this protocol:

Tumor Type
Carcinosarcoma / Metaplastic carcinoma / Sarcomatoid carcinoma (consider the appropriate site-specific carcinoma protocol)
Lymphoma / Leukemia (consider the Precursor and Mature Lymphoid Malignancies, Myeloid and Mixed / Ambiguous Lineage Neoplasms, or Plasma Cell Malignancies protocols)
Pediatric Ewing sarcoma (consider the Pediatric Ewing Sarcoma protocol)
Pediatric rhabdomyosarcoma (consider the Pediatric Rhabdomyosarcoma protocol)
Gastrointestinal stromal tumor (consider the Gastrointestinal Stromal Tumor protocol)
Uterine sarcoma (consider the Uterine Sarcoma protocol)
SMARCA4-deficient undifferentiated tumor (consider the Lung or Organ-Site-Specific protocol)

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Accreditation Requirements

This protocol can be utilized for a variety of procedures and tumor types for clinical care purposes. For accreditation purposes, only the definitive primary cancer resection specimen is required to have the core and conditional data elements reported in a synoptic format.

- Core data elements are required in reports to adequately describe appropriate malignancies. For accreditation purposes, essential data elements must be reported in all instances, even if the response is "not applicable" or "cannot be determined."
- Conditional data elements are only required to be reported if applicable as delineated in the protocol. For instance, the total number of lymph nodes examined must be reported, but only if nodes are present in the specimen.
- Optional data elements are identified with "+" and although not required for CAP accreditation purposes, may be considered for reporting as determined by local practice standards.

The use of this protocol is not required for recurrent tumors or for metastatic tumors that are resected at a different time than the primary tumor. Use of this protocol is also not required for pathology reviews performed at a second institution (i.e., secondary consultation, second opinion, or review of outside case at second institution).

Synoptic Reporting

All core and conditionally required data elements outlined on the surgical case summary from this cancer protocol must be displayed in synoptic report format. Synoptic format is defined as:

- Data element: followed by its answer (response), outline format without the paired Data element: Response format is NOT considered synoptic.
- The data element should be represented in the report as it is listed in the case summary. The response for any data element may be modified from those listed in the case summary, including "Cannot be determined" if appropriate.
- Each diagnostic parameter pair (Data element: Response) is listed on a separate line or in a tabular format to achieve visual separation. The following exceptions are allowed to be listed on one line:
    - Anatomic site or specimen, laterality, and procedure
    - Pathologic Stage Classification (pTNM) elements
    - Negative margins, as long as all negative margins are specifically enumerated where applicable
- The synoptic portion of the report can appear in the diagnosis section of the pathology report, at the end of the report or in a separate section, but all Data element: Responses must be listed together in one location

Organizations and pathologists may choose to list the required elements in any order, use additional methods in order to enhance or achieve visual separation, or add optional items within the synoptic report. The report may have required elements in a summary format elsewhere in the report IN ADDITION TO but not as replacement for the synoptic report i.e., all required elements must be in the synoptic portion of the report in the format defined above.

Summary of Changes

v 4.2.0.0

- Cover page update
- Updates to content and explanatory notes, including WHO Histologic Types
- pTNM Classification update
- LVI question update from optional to required (core) and “Lymphovascular Invasion” to “Lymphatic and / or Vascular Invasion
- Updated “MARGINS” section
- Addition of required (core) question response “Nodal Site(s) with Tumor (specify)”
- Addition of optional questions “Associated Syndrome”, “Radiologic Findings”, "Preresection Treatment", “Tumor Laterality” and “Tumor Extent and Depth of Invasion”
- SPECIAL STUDIES section update

Reporting Template

Protocol Posting Date: June 2024
Select a single response unless otherwise indicated.

CASE SUMMARY: (SOFT TISSUE: Resection)
Standard(s): AJCC-UICC 8
This checklist applies principally to soft tissue sarcomas in teenagers and adults. In general, pediatric sarcomas are treated under strict protocols that may differ significantly from the recommendations for adult type sarcomas.

CLINICAL

+Associated Syndrome
___ Li-Fraumeni syndrome
___ Neurofibromatosis type 1
___ Familial adenomatous polyposis
___ Other (specify): _____
___ Not specified

+Radiologic Findings
___ Specify: _____
___ Not available

+Preresection Treatment (select all that apply)
___ No known neoadjuvant therapy
___ Chemotherapy
___ Radiation therapy
___ Therapy administered, type not specified
___ Other (specify): _____
___ Not specified

SPECIMEN (Note A)

Procedure
___ Excisional biopsy
___ Intralesional resection
___ Marginal resection
___ Wide resection
___ Radical resection
___ Other (specify): _____
___ Not specified

TUMOR

Tumor Focality
___ Unifocal
___ Multifocal

___ Cannot be determined: _____

Tumor Site (Note B)
___ Head and neck (specify site, if known): _____
___ Trunk, extremities, joint / intra-articular (specify site, if known): _____
___ Abdominal visceral organs (specify site, if known): _____
___ Thoracic visceral organs (specify site, if known): _____
___ Retroperitoneum (specify site, if known): _____
___ Orbit (specify site, if known): _____
___ Not specified
___ Other (specify): _____

+Tumor Laterality
___ Left
___ Right
___ Central
___ Not specified
___ Cannot be determined

Tumor Size (Note C)
___ Greatest dimension in Centimeters (cm): _____ cm
+Additional Dimension in Centimeters (cm): ____ x ____ cm
+Radiological Greatest Dimension in Centimeters (cm): _____ cm
___ Cannot be determined (explain): _____

Histologic Type# (Note D)
 # The list is derived from the World Health Organization (WHO) classification of soft tissue tumors, 5th edition, to include ONLY soft tissue tumors of intermediate (locally aggressive and rarely metastasizing) potential and malignant soft tissue tumors. Anatomical staging using the AJCC system 8th ed. is considered clinically relevant only for the entities listed as core (required) (see Note F).
___ Adipocytic tumors
___ Atypical spindle cell / pleomorphic lipomatous tumor
___ Atypical lipomatous tumor
___ Well-differentiated liposarcoma
___ Dedifferentiated liposarcoma
___ Myxoid liposarcoma
+Percentage of Hypercellular Areas (formerly known as round cells)
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined
___ Pleomorphic liposarcoma, NOS
___ Epithelioid pleomorphic liposarcoma
___ Myxoid pleomorphic liposarcoma
___ Fibroblastic / myofibroblastic / fibrohistiocytic tumors
___ Solitary fibrous tumor
___ Desmoid-type fibromatosis
___ Lipofibromatosis
___ Plexiform fibrohistiocytic tumor

___ Giant cell fibroblastoma
___ Dermatofibrosarcoma protuberans
___ Fibrosarcomatous dermatofibrosarcoma protuberans
___ Myxofibrosarcoma
___ Low-grade fibromyxoid sarcoma
___ Sclerosing epithelioid fibrosarcoma
___ Myofibroblastic sarcoma
___ Superficial CD34-positive fibroblastic tumor
___ Myxoinflammatory fibroblastic sarcoma
___ Histiocytic / giant cell rich tumors
___ Giant cell tumor of soft tissue
___ Langerhans cell sarcoma
___ True histiocytic sarcoma
___ Malignant tenosynovial giant cell tumor
___ Dendritic reticulum cell sarcoma
___ Interdigitating reticulum cell sarcoma
___ Fibroblastic reticulum cell sarcoma
___ Tyrosine kinase fusion tumors, RAS-MAP pathway (Note E)
___ NTRK 1/2/3 fusion tumor
___ BRAF fusion tumor
___ RET fusion tumor
___ RAF fusion tumor
___ ALK fusion tumor, NOS
___ Inflammatory myofibroblastic tumor
___ Epithelioid inflammatory myofibroblastic sarcoma
___ Infantile fibrosarcoma
___ Pericytic / myopericytic tumors
___ Glomus tumor, atypical / uncertain biologic potential
___ Glomus tumor, malignant
___ Vascular tumors
___ Kaposiform hemangioendothelioma
___ Papillary intralymphatic angioendothelioma
___ Retiform hemangioendothelioma
___ Composite hemangioendothelioma
___ Pseudomyogenic hemangioendothelioma
___ Kaposi sarcoma
___ Epithelioid hemangioendothelioma with WWTR1::CAMTA1 fusion
___ Epithelioid hemangioendothelioma with YAP1::TFE3 fusion
___ Epithelioid hemangioendothelioma, NOS
___ Epithelioid angiosarcoma
___ Radiation-associated angiosarcoma
___ Lymphedema-associated angiosarcoma
___ Angiosarcoma, NOS
___ Smooth muscle tumors
___ EBV-associated smooth muscle tumor
___ Leiomyosarcoma

___ Skeletal muscle tumors
- ___ Embryonal rhabdomyosarcoma
- ___ Alveolar rhabdomyosarcoma
- ___ Pleomorphic rhabdomyosarcoma
- ___ Spindle cell / sclerosing rhabdomyosarcoma, NOS
- ___ Congenital spindle cell rhabdomyosarcoma with VGLL2/NCOA2/CITED2 fusions
- ___ Spindle cell / sclerosing rhabdomyosarcoma with MYOD1 mutation
- ___ Spindle cell rhabdomyosarcoma with FUS/EWSR1::TFCP2 or MEIS1::NCOA2 rearrangements
- ___ Ectomesenchymoma

___ Peripheral nerve sheath tumors
- ___ Malignant peripheral nerve sheath tumor, NOS
- ___ Epithelioid malignant peripheral nerve sheath tumor
- ___ Malignant triton tumor
- ___ Melanotic malignant peripheral nerve sheath tumor
- ___ Malignant granular cell tumor
- ___ Malignant perineurioma

___ Chondro-osseous tumors
- ___ Extraskeletal osteosarcoma
- ___ Mesenchymal chondrosarcoma
- ___ Chondrosarcoma arising in synovial chondromatosis

___ Tumors of uncertain differentiation / additional round and spindle cell tumors
- ___ Hemosiderotic fibrolipomatous tumor
- ___ Pleomorphic hyalinizing angiectatic tumor
- ___ Atypical fibroxanthoma
- ___ Pleomorphic dermal sarcoma
- ___ Angiomatoid fibrous histiocytoma
- ___ Myoepithelioma
- ___ Mixed tumor, malignant
- ___ Myoepithelial carcinoma
- ___ Ossifying fibromyxoid tumor (Note F)
- ___ Phosphaturic mesenchymal tumor, malignant
- ___ Synovial sarcoma
- ___ Epithelioid sarcoma, distal classic type
- ___ Epithelioid sarcoma, proximal large cell type
- ___ Alveolar soft part sarcoma
- ___ Clear cell sarcoma of soft tissue
- ___ Extraskeletal myxoid chondrosarcoma
- ___ Extraskeletal Ewing sarcoma
- ___ Desmoplastic small round cell tumor (DSRCT)
- ___ Round cell sarcoma with EWSR1::non-ETS fusions
- ___ CIC-rearranged sarcoma
- ___ Sarcoma with BCOR genetic alterations
- ___ PEComa, NOS
- ___ PEComa, TSC2 mutated
- ___ PEComa, TFE3 rearranged
- ___ Intimal sarcoma

___ Extrarenal rhabdoid tumor
___ Undifferentiated sarcomas
  ___ Undifferentiated pleomorphic sarcoma
  ___ Undifferentiated sarcoma, NOS
___ Other histologic type not listed (specify): _____
___ Cannot be determined: _____
  +Histologic Type Comment: _____

Histologic Grade (French Federation of Cancer Centers Sarcoma Group [FNCLCC]) (Note G)
___ G1, total differentiation, mitotic count and necrosis score 2 or 3
___ G2, total differentiation, mitotic count and necrosis score 4 or 5
___ G3, total differentiation, mitotic count and necrosis score of 6, 7, or 8
___ GX, cannot be assessed: _____
___ Ungraded sarcoma / not applicable for this tumor type

Mitotic Rate (Note G)
___ Specify mitotic rate per mm2: _____ mitoses per mm2
___ Specify mitotic rate per 10 high-power fields (HPF): _____ mitoses per 10 high-power fields (HPF)
___ Cannot be determined (explain): _____

Necrosis (Notes G,H)
___ Not identified
___ Present
  Extent of Necrosis
  ___ Specify percentage: _____ %
  ___ Cannot be determined (explain): _____
___ Cannot be determined

Treatment Effect (for post-neoadjuvant treatment) (Note H)
___ No known presurgical therapy
___ Not identified
 # Therapy response is expressed as a percentage of total tumor area that is non-viable. (Note H)
___ Present (specify overall percentage of treatment effect)#: _____ %
  Select all that apply
  +___ Geographic necrosis
  +___ Fibrosis
  +___ Hyalinization
  +___ Hemorrhage
  +___ Cystic change
  +___ Histiocytic response
  +___ Inflammation
  +___ Other (specify): _____
___ Cannot be determined

+Tumor Extent and Depth of Invasion (Note F) (select all that apply)
___ Dermis
___ Subcutis
___ Deep fascia
___ Skeletal muscle, intramuscular
___ Skeletal muscle, intermuscular
___ Bone
___ Other (specify): _____

Lymphatic and / or Vascular Invasion (Note I)
___ Not identified
___ Present
___ Cannot be determined: _____

+Tumor Comment: _____

MARGINS (Note J)

Margin Status
___ All margins negative for tumor
Closest Margin(s) to Tumor
___ Specify closest margin(s): _____
___ Cannot be determined (explain): _____
Distance from Tumor to Closest Margin
Specify in Centimeters (cm)
___ Exact distance: _____ cm
___ Greater than: _____ cm
___ At least: _____ cm
___ Less than: _____ cm
___ Cannot be determined: _____
+Intact Fascial Envelope / Fibrous Pseudocapsule at Closest Margin
___ Present
___ Absent
___ Cannot be determined
___ Not applicable
+Other Close Margin(s) to Tumor (less than 0.5 cm)
___ Specify other close margin(s): _____
___ Cannot be determined (explain): _____
___ Not applicable
___ Tumor present at margin
Margin(s) Involved by Tumor
___ Specify involved margin(s): _____
___ Cannot be determined (explain): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____
___ Not applicable

+Margin Comment: _____

REGIONAL LYMPH NODES (Note K)

Regional Lymph Node Status
___ Not applicable (no regional lymph nodes submitted or found)
___ Regional lymph nodes present
___ All regional lymph nodes negative for tumor
___ Tumor present in regional lymph node(s)
Number of Lymph Nodes with Tumor
___ Exact number (specify): _____
___ At least (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____
Nodal Site(s) with Tumor (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____
Number of Lymph Nodes Examined
___ Exact number (specify): _____
___ At least (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Regional Lymph Node Comment: _____

DISTANT METASTASIS

Distant Site(s) Involved, if applicable (select all that apply)
___ Not applicable
___ Lung: _____
___ Other (specify): _____
___ Cannot be determined: _____

pTNM CLASSIFICATION (AJCC 8th Edition) (Note F)
Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. As per the AJCC (Chapter 1, 8th Ed.) it is the managing physician's responsibility to establish the final pathologic stage based upon all pertinent information, including but potentially not limited to this pathology report.

pTNM Classification (required only if applicable)
 # Regardless of the anatomic site, certain specific types of soft tissue neoplasms for which pTNM staging is not clinically relevant are excluded from the staging system. (Note F)
___ Not applicable (histologic type not appropriate for staging)#
___ Histologic type appropriate for staging
Modified Classification (required only if applicable) (select all that apply)
___ Not applicable
___ y (post-neoadjuvant therapy)
___ r (recurrence)

pT Category

___ Head and Neck

pT Category

___ pT not assigned (cannot be determined based on available pathological information)
___ pT1: Tumor less than or equal to 2 cm
___ pT2: Tumor greater than 2 cm to less than or equal to 4 cm
___ pT3: Tumor greater than 4 cm
pT4: Tumor with invasion of adjoining structures
___ pT4a: Tumor with orbital invasion, skull base / dural invasion, invasion of central compartment viscera, involvement of facial skeleton, or invasion of pterygoid muscles
___ pT4b: Tumor with brain parenchymal invasion, carotid artery encasement, prevertebral muscle invasion, or central nervous system involvement via perineural spread
___ pT4 (subcategory cannot be determined)

___ Trunk and Extremities

pT Category

___ pT not assigned (cannot be determined based on available pathological information)
___ pT0: No evidence of primary tumor
___ pT1: Tumor 5 cm or less in greatest dimension
___ pT2: Tumor more than 5 cm and less than or equal to 10 cm in greatest dimension
___ pT3: Tumor more than 10 cm and less than or equal to 15 cm in greatest dimension
___ pT4: Tumor more than 15 cm in greatest dimension

___ Abdomen and Thoracic Visceral Organs

pT Category

___ pT not assigned (cannot be determined based on available pathological information)
___ pT1: Organ confined
pT2: Tumor extension into tissue beyond organ
___ pT2a: Invades serosa or visceral peritoneum
___ pT2b: Extension beyond serosa (mesentery)
___ pT2 (subcategory cannot be determined)
 # Including other structures such as diaphragm, abdominal wall, or pelvic side wall
___ pT3: Invades another organ#
pT4: Multifocal involvement
___ pT4a: Multifocal (2 sites)
___ pT4b: Multifocal (3 - 5 sites)
___ pT4c: Multifocal (greater than 5 sites)
___ pT4 (subcategory cannot be determined)

___ Retroperitoneum#

 # Sarcomas arising within the peritoneal, pleural, or mediastinal cavities, but not from a specific visceral organ, may be staged in a manner similar to that of retroperitoneal sarcomas (Note B)

pT Category

___ pT not assigned (cannot be determined based on available pathological information)
___ pT0: No evidence of primary tumor
___ pT1: Tumor 5 cm or less in greatest dimension
___ pT2: Tumor more than 5 cm and less than or equal to 10 cm in greatest dimension
___ pT3: Tumor more than 10 cm and less than or equal to 15 cm in greatest dimension
___ pT4: Tumor more than 15 cm in greatest dimension

___ Orbit

pT Category
___ pT not assigned (cannot be determined based on available pathological information)
___ pT0: No evidence of primary tumor
___ pT1: Tumor less than or equal to 2 cm in greatest dimension
___ pT2: Tumor greater than 2 cm in greatest dimension without invasion of bony walls or globe
___ pT3: Tumor of any size with invasion of bony walls
___ pT4: Tumor of any size with invasion of globe or periorbital structures, including eyelid, conjunctiva, temporal fossa, nasal cavity, paranasal sinuses, and / or central nervous system

T Suffix (required only if applicable)
___ Not applicable
___ (m) multiple primary synchronous tumors in a single organ

pN Category
___ pN not assigned (no nodes submitted or found)
___ pN not assigned (cannot be determined based on available pathological information)
___ pN0: No regional lymph node metastasis
___ pN1: Regional lymph node metastasis

pM Category (required only if confirmed pathologically)
___ Not applicable - pM cannot be determined from the submitted specimen(s)
___ pM1: Distant metastasis

ADDITIONAL FINDINGS

+Additional Findings (specify): _____

SPECIAL STUDIES
The previously reported biopsy immunohistochemistry, cytogenetics, and molecular studies can be included in the resection report.

Immunohistochemistry
___ Specify results: _____
___ Pending (specify): _____
___ Not performed: _____
___ Not applicable
___ Other (specify): _____

Cytogenetics
___ Specify results: _____
___ Pending (specify): _____
___ Not performed: _____
___ Not applicable
___ Other (specify): _____

Molecular Studies
___ Specify results: _____
___ Pending (specify): _____

___ Not performed: _____
___ Not applicable
___ Other (specify): _____

COMMENTS

Comment(s): _____

Explanatory Notes

A. Procedure/Tissue Processing

Fresh tissue versus formalin fixation

Ideally, tissue specimens from soft tissue tumors are received fresh/unfixed in the pathology laboratory, in case fresh tissue for ancillary studies, such as cytogenetics, needs to be collected. Although the ability to perform diagnostic molecular studies in formalin-fixed paraffin embedded tissue has substantially diminished the need to collect fresh tissue, frozen tissue may be needed to enter patients into treatment protocols.[1,2,3,4] Nevertheless, discretion should be used in triaging tissue from sarcomas. Adequate tissue should be submitted for conventional light microscopy and subsequent formalin-fixed immunostains, molecular-genetic studies before setting aside samples for cytogenetics or molecular analysis. Fresh tissue for special studies should be collected at the time the specimen is received. Tissue for microbiology cultures should go directly from the operating room to the microbiology laboratory.

Tissue Submission for Histologic Evaluation/Molecular Genetic Studies

Most tumors are sampled by 1 section per centimeter of the greatest dimension of the tumor, including heterogeneous areas and samples of necrosis as well as additional sampling of viable areas to have at least two blocks for H&E and additional studies. In cases with neoadjuvant therapy, some institutions prefer to submit a full cross section of the greatest surface area of tumor (longest plane) to be mapped and submitted to assess percent necrosis. If cystic hemorrhagic areas are present, this cross-sectional area of empty space can be added to the percent treatment effect. For large tumors, more than one section per cassette is acceptable. Occasionally, gross pathology can be misleading, and areas that appear to be grossly necrotic may actually be myxoid or edematous. When this happens, additional sections of these areas should be submitted for histologic examination. When estimates of gross necrosis exceed those of histologic necrosis, the greater percentage of necrosis should be recorded on the surgical pathology report. Tumors with greater areas of heterogeneity may need to be sampled more thoroughly.[5,6]

If snap frozen material is required for a clinical trial, approximately 1 cm^3 of fresh tissue (less is acceptable for small specimens, including core biopsies) should be cut into small, 0.2 cm fragments after reserving sufficient tissue for histologic examination. This frozen tissue should ideally be stored at minus seventy (-70°C) and can be shipped on dry ice to facilities that perform ancillary studies.

Definition of Procedures

The following is a list of guidelines to be used in defining what type of procedure has been performed.

Intralesional Resection

Leaving gross or microscopic tumor behind. Partial debulking or curettage are examples, or when microscopic tumor is left at the margin unintentionally in an attempted marginal resection.

Marginal Resection

Removing the tumor and its pseudocapsule with a relatively small amount of adjacent tissue. There is no gross tumor at the margin; however, there is a high likelihood that microscopic tumor is present. If microscopic disease is identified at the margin, then it is an intralesional resection. Note that occasionally a surgeon will perform an “excisional” biopsy, which effectively accomplishes the same outcome as a marginal resection.

Wide Resection
An intracompartmental resection. The tumor is removed with pseudocapsule and a cuff of normal tissue surrounding the neoplasm, but without the complete removal of an entire muscle group, compartment, or bone.

Radical Resection
The removal of an entire soft tissue compartment (for example, anterior compartment of the thigh, the quadriceps) or bone, or the excision of the adjacent muscle groups if the tumor is extracompartmental.

References

1. Ladanyi M, Bridge JA. Contribution of molecular genetic data to the classification of sarcomas. *Hum Pathol*. 2000;31(5):532-538.
2. Tomescu O, Barr FG. Chromosomal translocations in sarcomas: prospects for therapy. *Trends Mol Med*. 2001;7(12):554-559.
3. Jin L, Majerus J, Oliveira A. et al. Detection of fusion gene transcripts in fresh-frozen and formalin-fixed paraffin-embedded tissue sections of soft-tissue sarcomas after laser capture microdissection and rt-PCR, *Diagn Mol Pathol* . 2003 Dec;12(4):224-30.
4. Smith SM, Coleman J, Bridge JA et al. Molecular diagnostics in soft tissue sarcomas and gastrointestinal stromal tumors. *J Surg Oncol.* 2015 Apr;111(5):520-31.
5. Wang D, Harris J, Kraybill WG, et al: Pathologic Complete Response and Clinical Outcomes in Patients With Localized Soft Tissue Sarcoma Treated With Neoadjuvant Chemoradiotherapy or Radiotherapy: The NRG/RTOG 9514 and 0630 Nonrandomized Clinical Trials. *JAMA Oncol*. 9:646, 2023.
6. Pasquali S, Collini P, Romagosa C, et al: Histopathological response (HR) after neoadjuvant chemotherapy (ChT) for high-risk soft tissue sarcomas (STS): A planned analysis of the ISG-STS-1001 trial. *JCO*. 41:11511–11511, 2023.

B. Tumor Site
The 8th edition of the American Joint Committee on Cancer (AJCC) staging manual[1] places a great emphasis on the anatomic primary site of soft tissue sarcomas, due to implications for local recurrence and risk of metastatic disease. Separate staging systems have been developed for soft tissue sarcomas (STSs) of the extremities and trunk, retroperitoneum, head and neck, and visceral sites. For the first two sites, outcomes are well characterized, and good predictive models based on staging data are available. However, for the latter two anatomic sites, data are more limited, and the proposed staging systems are meant to be a starting point for refining risk assessment. Additionally, changes were made to the AJCC staging system for orbital sarcomas.[1]

<u>Head and Neck</u>
Includes STS arising in the neck (subcutaneous and deep structures, including neurovascular structures); oral cavity; upper aerodigestive tract, including laryngeal structures; pharyngeal areas; nasal cavity and paranasal sinuses; infratemporal fossa and masticator space; major salivary glands, thyroid and parathyroid glands; cervical esophagus and trachea; and peripheral and cranial nerves. Although these STSs are usually found at a smaller size than those arising in other anatomic sites, they often have a greater risk of local recurrence, and they usually present unique problems from an anatomic standpoint. Soft tissue sarcomas arising in the orbit have their own staging system (see below).

Trunk and Extremities
Includes STS arising in extremities and trunk, including breast.

Abdomen and Thoracic Visceral Organs
Includes STS arising from hollow viscera, including esophagus, stomach, small intestine, colon and rectum, as well as solid viscera such as the liver, kidneys, lungs, and heart. Sarcomas arising within the peritoneal, pleural, or mediastinal cavities, but not from a specific visceral organ, may be staged in a manner similar to that of retroperitoneal sarcomas.

Retroperitoneum
Approximately 10% of STS arise in this complex anatomic compartment. Sarcomas arising within the peritoneal, pleural, or mediastinal cavities, but not from a specific visceral organ, may be staged in a manner similar to that of retroperitoneal sarcomas.

Orbit
The orbit is a cone-shaped cavity surrounded by 7 bones. Numerous anatomic structures that support the globe and periorbital tissues, including the optic nerve and its meninges, lacrimal gland, extraocular muscles, fascial connective tissue, orbital fat, cranial and autonomic vessels, and blood vessels, can be the site of origin for a wide variety of primary orbital sarcomas.

References

1. Amin MB, Edge SB, Greene FL, et al, eds. *AJCC Cancer Staging Manual*. 8th ed. New York, NY: Springer; 2017.

C. Tumor Size
In situations in which an accurate measurement of the excised primary tumor cannot be obtained (i.e., fragmented specimen), it is acceptable to use available imaging data (computed tomography [CT], magnetic resonance imaging [MRI], etc.) to assess tumor size for the purposes of determining the pT category.

D. Histologic Classification
Intraoperative Consultation
Histologic classification of soft tissue tumors is sufficiently complex that, in many cases, it is unreasonable to expect a precise classification of these tumors based on an intraoperative consultation. A complete understanding of the surgeon's treatment algorithm is recommended before rendering a frozen section diagnosis. Intraoperative consultation is useful in assessing if "lesional" tissue is present and in constructing a differential diagnosis that can direct the proper triage of tissue for flow cytometry (lymphoma), and molecular studies/cytogenetics. Tissue triage optimally is performed at the time of frozen section. In many cases, it is important that a portion of tissue be submitted for ancillary studies, even from fine-needle aspiration (FNA) and core needle biopsy specimens, after sufficient tissue has been submitted for histologic evaluation.

WHO Classification of Tumors
Classification of tumors should be made according to the World Health Organization (WHO) classification of soft tissue tumors, 5th Edition.[1] As part of the WHO classification system, soft tissue tumors are divided

into 4 categories: benign, intermediate (locally aggressive), intermediate (rarely metastasizing), and malignant.

The provided list of histologic types is derived from the World Health Organization (WHO) classification of soft tissue tumors, 5th Edition[1], edited to only include soft tissue tumors of intermediate potential, i.e., locally aggressive (including significant and problematic local recurrence and/or requiring oncologic management) and rarely metastasizing as well as malignant soft tissue tumors. The full reference contains information on additional soft tissue tumors. Table 1 lists the intermediate and malignant soft tissue tumors that demonstrate diagnostic molecular findings. Generally, the term well-differentiated liposarcoma has been used for groin/retroperitoneum and deep skeletal muscle tumors, due to their increased potential for de-differentiation, whereas atypical lipomatous tumor is preferred for superficial subcutaneous tumors with the same histology since these are generally cured by limited excision.

Table 1: Subset of Soft Tissue Tumors that Carry Diagnostic Molecular/Genetic Findings
Note: This list is not exhaustive. Only the most common molecular finding(s) is listed. Many molecular findings are not unique to a single entity.

Tumor	**Most common molecular genetic finding**
Atypical spindle cell/pleomorphic lipomatous tumor	*RB1* deletion
Atypical lipomatous tumor/well-differentiated liposarcoma	*MDM2* amplification
Dedifferentiated liposarcoma	*MDM2* amplification
Myxoid liposarcoma	*FUS/EWSR1::DDIT3* fusion
Solitary fibrous tumor	*NAB2::STAT6* fusion
Desmoid-type fibromatosis	*CTNNB1* or *APC* point mutation
Giant cell fibroblastoma	*COL1A1::PDGFB* fusion
Dermatofibrosarcoma protuberans	*COL1A1::PDGFB* fusion
Fibrosarcomatous dermatofibrosarcoma protuberans	*COL1A1::PDGFB* fusion
Inflammatory myofibroblastic tumor	*ALK* fusion (various partners)
Superficial CD34-positive fibroblastic tumor	*PRDM10* fusion (various partners)
Infantile fibrosarcoma	*ETV6::NTRK3* fusion
Low-grade fibromyxoid sarcoma	*FUS::CREB3L2* fusion
Sclerosing epithelioid fibrosarcoma	*EWSR1::CREB3L1* fusion
Malignant tenosynovial giant cell tumor	*CSF1* fusion
Pseudomyogenic hemangioendothelioma	*SERPINE1/ACTB::FOSB* fusion
Epithelioid hemangioendothelioma	*WWTR1::CAMTA1* fusion
	YAP1::TFE3 fusion
Angiosarcoma	*MYC* amplification (irradiation/lymphedema-associated angiosarcoma)
Malignant glomus tumor	*MIR143::NOTCH2* fusion *BRAF* mutation, *GLI1* fusion
EBV-associated smooth muscle tumor	EBER transcripts
Alveolar rhabdomyosarcoma	*PAX3/7::FOXO1* fusion
Spindle cell/sclerosing rhabdomyosarcoma	*VGLL2/NCOA2* fusion (various partners)
	MYOD1 mutation
	EWSR1/FUS::TFCP2, MEIS1::NCOA2
Malignant melanotic nerve sheath tumor	*PRKAR1A* mutation
Hemosiderotic fibrolipomatous tumor	*TGFBR3* and *OGA* (*MGEA5*) breakpoints
Myxoinflammatory fibroblastic sarcoma	*TGFBR3* and *OGA* (*MGEA5*) breakpoints; *BRAF* fusion, *VGLL3* amplification

Pleomorphic hyalinizing angiectatic tumor of soft part	*OGA (MGEA5), TGFBR3* breakpoints
Phosphaturic mesenchymal tumor	*FN1::FGFR1* fusion
Angiomatoid fibrous histiocytoma	*EWSR1/FUS::ATF1/CREB1* fusion
Ossifying fibromyxoid tumor	*PHF1* fusion (various partners)
Myoepithelial carcinoma	*EWSR1/FUS::POU5F1/PBX1, PLAG1* fusion (various partners)
NTRK-fusion tumor	*NTRK1/2/3* fusion (various partners)
ALK-fusion tumor including inflammatory myofibroblastic tumor and epithelioid inflammatory myofibroblastic tumor	*ALK* (various partners)
BRAF-fusion tumor	*BRAF* (various partners with second fusion)
Synovial sarcoma	*SS18::SSX1/2/4* fusion
Epithelioid sarcoma	*SMARCB1* deletion
Alveolar soft part sarcoma	*ASPSCR1::TFE3* fusion
Clear cell sarcoma of soft tissue	*EWSR1::ATF1/CREB1* fusion
Extraskeletal myxoid chondrosarcoma	*EWSR1/TAF15::NR4A3* fusion
Mesenchymal chondrosarcoma	*HEY1::NCOA2* fusion
Desmoplastic small round cell tumor	*EWSR1::WT1* fusion
Extrarenal rhabdoid tumor	*SMARCB1* deletion
PEComa	*TSC2* mutation, *TFE3* fusion (various partners)
Ewing sarcoma	*EWSR1/FUS::FLI1/ERG* fusion
Round cell sarcoma with *EWSR1::non-ETS fusion*	*EWSR1::PATZ1, FUS/EWSR1::NFATC2*
CIC-rearranged sarcoma	*CIC::DUX4* fusion
BCOR altered sarcoma	*BCOR::CCNB3* fusion *BCOR* ITD (infants)
Epithelioid malignant peripheral nerve sheath tumor	*SMARCB1* deletion

Histologic Classification of Treated Lesions

Because of extensive treatment effects, such as necrosis, fibrosis, and chemotherapy-induced and radiation-induced pleomorphism, it may not be possible to classify some lesions that were either never biopsied or where the biopsy was insufficient for a precise diagnosis. In problematic cases, the grade of the pretreatment specimen (if available) should take precedence.

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E. Tyrosine Kinase Fusion Sarcomas

While fusions involving the *RAS::MAPK* pathway are rare in mesenchymal tumors, these tumors have driver alterations in genes that encode tyrosine kinases and may respond to therapy targeting *NTRK, ALK, BRAF, RET, RAF, FGFR1, or ABL1*, etc. Notably, *NTRK* tumors fused with *KANK1* or *TPR* have been demonstrated to exhibit higher-grade appearance, including spindled and pleomorphic characteristics, accompanied by necrosis and mitoses, leading to unfavorable outcomes. Consequently, it is advisable to conduct comprehensive RNA-based Next-Generation Sequencing (NGS) for fusions, particularly in spindled pleomorphic tumors occurring in individuals under 50 years old, especially those in soft tissue or intraosseous locations. This recommendation is especially pertinent with tumors that have variable ovoid spindled to epithelioid morphology, variable collagenous to myxoid stroma, variable gaping

to staghorn vasculature, and specifically focal CD34 and/or focal S100 protein, without any staining for SOX10. In these tumors, BRAF, ALK, or panTrk or no specific immunostaining is identified.[1,2,3,4,5,6,7,8,9,10]

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F. pTNM Classification

The TNM staging system for soft tissue tumors of the AJCC and UICC is recommended.[1,2] The staging system applies to all soft tissue sarcomas for which pTNM staging is clinically relevant, based on recommendations of the WHO Classification of Soft Tissue and Bone Tumors (5th Edition) and the AJCC Staging Manual (8th Edition). These tumors are listed in the table below.

Table 2. List of malignant soft tissue tumors for which pathological staging using the AJCC system is considered to be clinically relevant

Dedifferentiated liposarcoma
Myxoid liposarcoma
Pleomorphic liposarcoma
Myxoid pleomorphic liposarcoma
Fibrosarcomatous dermatofibrosarcoma protuberans
Myxofibrosarcoma
Low-grade fibromyxoid sarcoma
Sclerosing epithelioid fibrosarcoma
Epithelioid hemangioendothelioma (see note below)
Leiomyosarcoma
Rhabdomyosarcoma (see note below)
Ectomesenchymoma
Extraskeletal osteosarcoma
Mesenchymal chondrosarcoma
Malignant tyrosine kinase fusion sarcoma
Synovial sarcoma
Epithelioid sarcoma
Alveolar soft part sarcoma
Clear cell sarcoma of soft tissue
Extraskeletal myxoid chondrosarcoma
Undifferentiated sarcoma
Ewing sarcoma
Round cell sarcoma with *EWSR1*::non-ETS fusions
CIC-rearranged sarcoma
Sarcoma with *BCOR* genetic alterations

The AJCC staging criteria serve as a crucial metric for prognostic stratification across various cancer types. However, the complexity of soft tissue sarcomas, encompassing over 50 distinct tumor types, presents challenges in establishing a uniform stage classification. While it is impractical to devise a staging system for each histology, shared characteristics among sarcomas offer some capacity to stratify prognosis at a group level. Despite this, pathological staging proves ineffective or inapplicable for certain subtypes of sarcomas. Examples include

1. Tumors best classified using risk stratification systems such as solitary fibrous tumor (Table 3), gastrointestinal stromal tumor (see GIST protocol), ossifying fibromyxoid tumor, and glomus tumor
2. Multifocal tumors such as epithelioid hemangioendothelioma of abdominal and thoracic cavities
3. Tumors that do not share the same behavior and natural history of other sarcomas, such as Kaposi sarcoma, angiosarcoma, head and neck embryonal and alveolar rhabdomyosarcoma, infantile fibrosarcoma, dura and brain sarcoma, desmoplastic small round cell tumor, PEComa, and retroperitoneal leiomyosarcoma
4. Locally aggressive soft tissue neoplasms, which may recur locally but have either no risk of metastatic disease or an extremely low risk of metastasis such as desmoid tumor, dermatofibrosarcoma protuberans, kaposiform hemmangioendothelioma, atypical fibroxanthoma, angiomatoid fibrous histiocytoma, pleomorphic hyalinizing angiectatic tumor, atypical lipomatous

tumor, inflammatory myofibroblastic tumor, low-grade myofibroblastic sarcoma and myxoinflammatory fibroblastic sarcoma

5. Emerging and rare entities with insufficient evidence for stage categorization (see also Note E)

Table 3. Risk stratification for solitary fibrous tumor[3]

Risk factor	Score
Age	
<55	0
>55	1
Tumor size (cm)	
<5	0
5 to <10	1
10 to <15	2
≥15	3
Mitotic count (/10 high-power fields)	
0	0
1-3	1
≥4	2
Tumor necrosis	
<10%	0
≥10%	1
Risk class	**Total score**
Low	0-3
Intermediate	4-5
High	6-7

Pathologic (pTNM) staging consists of the removal and pathologic evaluation of the primary tumor and clinical/radiologic evaluation for regional and distant metastases. In circumstances where it is not possible to obtain accurate measurements of the excised primary sarcoma specimen, it is acceptable to use radiologic assessment of tumor size to assign a pT category. In examining the primary tumor, the pathologist should subclassify the lesion and assign a histopathologic grade.

Definition of pT

Although size criteria currently vary by anatomic site, particular emphasis should be placed on providing size measurements. Size should be regarded as a continuous variable, with the centimeter cutoffs as arbitrary divisions that make it possible to characterize patient populations.

Depth

Due to the limited impact of depth on outcome and because the inherent inability to use depth in anatomic sites other than extremities and trunk, depth is no longer used in the 8th edition of the AJCC staging manual.[1] In previous staging systems, depth was evaluated relative to the investing fascia of the extremity and trunk. Superficial was defined as lack of any involvement of the superficial investing muscular fascia in extremity or trunk lesions. For staging, all retroperitoneal and visceral lesions were considered to be deep lesions. Tumor extent and depth of invasion for trunk and extremity tumors are included in this protocol as optional data elements.

Regional Lymph Nodes (pN)
Nodal involvement is rare in adult soft tissue sarcomas but, when present, has a very poor prognosis. In the absence of metastatic disease, N1 disease is classified as stage IIIB. When no lymph nodes are resected, the pathologic 'N' category is not assigned (pNX is not used for soft tissue tumors). Patients whose nodal status is not determined to be positive for tumor, either clinically or pathologically, should be designated as N0. NX should not be used.

Restaging of Recurrent Tumors
The same staging should be used when a patient requires restaging of sarcoma recurrence. Such reports should specify whether patients have primary lesions or lesions that were previously treated and have subsequently recurred. Reporting of possible etiologic factors, such as radiation exposure and inherited or genetic syndromes, is encouraged. Appropriate workup for recurrent sarcoma usually includes cross-sectional imaging (computed tomography [CT] scan or magnetic resonance imaging [MRI] scan) of the tumor, a CT scan of the chest, and a tissue biopsy to confirm diagnosis prior to initiation of therapy.

TNM Descriptors
For identification of special cases of TNM or pTNM classifications, the "m" suffix and the "y" and "r" prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The "m" suffix indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

The "y" prefix indicates those cases in which classification is performed during or following initial multimodality therapy (i.e., neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a "y" prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The "y" categorization is not an estimate of tumor prior to multimodality therapy (i.e., before initiation of neoadjuvant therapy).

The "r" prefix indicates a recurrent tumor when staged after a documented disease-free interval and is identified by the "r" prefix: rTNM.

T Category Considerations
Tumor size criteria vary by anatomic site.

N Category Considerations
Presence of positive nodes (N1), in the absence of metastatic disease, is considered stage IIIB.

M Category Considerations
pMX and pM0 (no distant metastasis) are no longer case summary options as the use of pMX provides no meaningful information to the clinician or cancer registrar and at times may create confusion in tumor staging.

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G. Grading

Unlike with other organ systems, the clinical staging of soft tissue sarcomas is largely determined by grade. Whilst nomograms assess multiple clinical and histologic parameters to calculate the probability of recurrence for a given patient,[1] there is, however, no generally agreed-upon scheme for grading soft tissue tumors.[2] The most widely used soft tissue grading systems are the French Federation of Cancer Centers Sarcoma Group (FNCLCC) and National Cancer Institute (NCI) systems.[3,4] Both systems have 3 grades and are based on mitotic activity, necrosis, and differentiation, and are highly correlated with prognosis.[5] However, in addition to these criteria, the NCI system requires the quantification of cellularity and pleomorphism for certain subtypes of sarcomas, which is difficult to determine objectively. The FNCLCC system is easier to use in our opinion, and it may be slightly better in predicting prognosis than the NCI system.[5] Other systems with 2 or 4 grades also have been used. The 8th edition of the AJCC Cancer Staging Manual[6] adopted the FNCLCC grading system. The revision of the American Joint Committee on Cancer (AJCC) staging system incorporates a 3-tiered grading system; however, grade 1 and separately grades 2 to 3 (effectively low and high, respectively) are used for stage grouping. Accurate grading requires an adequate sample of tissue, which is not always available from FNA or core needle biopsy specimens or in tumors previously treated with radiation or chemotherapy. However, given the importance of grade in staging and treatment, efforts to separate sarcomas on the basis of needle biopsies into at least 2 tiers (i.e., low and high-grade) is encouraged. In many instances, the histologic type of sarcoma will readily permit this distinction (i.e., Ewing sarcoma, pleomorphic liposarcoma), whereas in less obvious instances, the difficulty of assigning a grade should be noted. In general, multiple needle core biopsies exhibiting a high-grade sarcoma can be regarded as high-grade since the probability of subsequent downgrading is remote, but limited core biopsies of low-grade sarcoma may carry a risk of upgrading.

FNCLCC Grading

The FNCLCC grade is based on three parameters: differentiation, mitotic activity, and necrosis. Each of these parameters receives a score: differentiation (1 to 3), mitotic activity (1 to 3), and necrosis (0 to 2). The scores are summed to produce a grade.

Grade 1: 2 or 3 total score
Grade 2: 4 or 5 total score
Grade 3: 6 to 8 total score

Differentiation: Tumor differentiation is scored as follows (see Table 1).

Score 1: Sarcomas closely resembling normal, adult mesenchymal tissue and potentially difficult to distinguish from the counterpart benign tumor (e.g., well-differentiated liposarcoma, well-differentiated leiomyosarcoma)
Score 2: Sarcomas for which histologic typing is certain (e.g., myxoid liposarcoma, myxofibrosarcoma)

Score 3: Embryonal sarcomas and undifferentiated sarcomas, synovial sarcomas, and sarcomas of uncertain tumor type

Tumor differentiation is the most problematic aspect of the FNCLCC system. Its use is subjective and does not include every subtype of sarcoma. Nevertheless, it is an integral part of the system, and an attempt should be made to assign a differentiation score.

Table 4. Tumor Differentiation Score According to Histologic Type in the Updated Version of the French Federation of Cancer Centers Sarcoma Group System

Tumor Differentiation

Histologic Type	Score
Atypical lipomatous tumor/well-differentiated liposarcoma	1
Well-differentiated leiomyosarcoma	1
Myxoid liposarcoma	2
Conventional leiomyosarcoma	2
Myxofibrosarcoma	2
High-grade myxoid (round cell) liposarcoma	3
Pleomorphic liposarcoma	3
Dedifferentiated liposarcoma	3
Pleomorphic rhabdomyosarcoma	3
Poorly differentiated/pleomorphic leiomyosarcoma	3
Biphasic/monophasic/poorly differentiated synovial sarcoma	3
Mesenchymal chondrosarcoma	3
Extraskeletal osteosarcoma	3
Extraskeletal Ewing sarcoma	3
Malignant rhabdoid tumor	3
Undifferentiated pleomorphic sarcoma	3
Undifferentiated sarcoma, not otherwise specified	3

Note: Tumors not included in the list, such as desmoplastic round cell tumor, alveolar rhabdomyosarcoma, and intimal sarcoma, are by definition high-grade. Other tumors such as alveolar soft part sarcoma, clear cell sarcoma, epithelioid sarcoma, extraskeletal myxoid chondrosarcoma, low-grade fibromyxoid sarcoma, and sclerosing epithelioid fibrosarcoma are not assigned FNCLCC grade but may demonstrate late metastasis.[4,7] Grade is not used for angiosarcoma, as deceptively bland angiosarcomas may behave poorly, thus all are considered clinically “high-grade”. The prognostic significance of FNCLCC grading in malignant peripheral nerve sheath tumor is unclear. Other tumors such as solitary fibrous tumors are best categorized by risk stratification parameters (see note F).
Modified with permission from Coindre JM.[3]

Mitosis Count:
The count is made in the most mitotically active area, away from areas of necrosis. Mitoses may be scored as either 10 consecutive high-power fields (HPF) (40X objective) or in an area of 1 mm^2. If whole slide digital pathology is used, 1 mm^2 is measured directly on the digital image. The mitotic count is converted to a score (Table 5). If the mitotic rate is close to the cutoff between mitotic scores, the count should be repeated.

The area of 1 HPF originally used for mitotic count measured 0.1734 mm^2. However, the area of 1 HPF using most modern microscopes with wider 40x lenses will be higher. Therefore, pathologists are encouraged to either correct for the area of their 40X objective or score mitoses per 1 mm^2.

1) To correct for the area of a 40X objective: determine the 40X field area (Table 6) and divide 0.1734 by the obtained field area to obtain a conversion factor. The number of mitotic figures in 10 HPF multiplied by the obtained conversion factor and rounded to the nearest whole number should be used for grading purposes.
2) To determine to number of 40X fields equivalent to 1 mm^2, consult Table 6.

Table 5. Mitotic Count Score Equivalence

Mitotic Score	# mitosis / 10 HPF (1 HPF= 0.1734 mm^2)	# mitosis /1 mm^2 (see table 6)
Score 1	0 to 9 mitosis / 10 HPF	0 to 5 mitosis / 1 mm^2
Score 2	10 to 19 mitosis / 10 HPF	6 to 11 mitosis / 1 mm^2
Score 3	> 19 mitosis / 10 HPF	> 11 mitosis / 1 mm^2

Table 6. Approximate number of fields per 1 mm^2 based on field diameter
Formula to calculate the area of one high-power field of a specific microscope = πr^2/*total magnification* = (½ field diameter)^2 x p/total magnification
Formula to calculate the field diameter = Objective Field Number/Objective Magnification

Field diameter (mm)	Area (mm^2)	Approximate number of fields per 1 mm^2
0.40	0.126	8
0.41	0.132	8
0.42	0.138	7
0.43	0.145	7
0.44	0.152	7
0.45	0.159	6
0.46	0.166	6
0.47	0.173	6
0.48	0.181	6
0.49	0.188	5
0.50	0.196	5
0.51	0.204	5
0.52	0.212	5
0.53	0.221	5
0.54	0.229	4
0.55	0.237	4
0.56	0.246	4
0.57	0.255	4
0.58	0.264	4
0.59	0.273	4
0.60	0.283	4
0.61	0.292	3
0.62	0.302	3

0.63	0.312	3
0.64	0.322	3
0.65	0.332	3
0.66	0.342	3
0.67	0.352	3
0.68	0.363	3
0.69	0.374	3

Tumor Necrosis: Evaluated on gross examination and validated with histologic sections.
Score 0: No tumor necrosis
Score 1: <50% tumor necrosis
Score 2: ≥50% tumor necrosis

TNM Grading
The 8th edition of the American Joint Committee on Cancer (AJCC) and International Union Against Cancer (UICC) staging system for soft tissue tumors recommends the FNCLCC 3-tiered system but effectively collapses into high-grade and low-grade.[6,8] This means that FNCLCC grade 2 and grade 3 tumors are considered "high-grade" for the purposes of stage grouping.

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H. Response to Chemotherapy/Radiation Therapy Effect
Although agreement has not been reached about measuring the effect of preoperative (neoadjuvant) chemotherapy/radiation therapy in soft tissue tumors, an attempt should be made to quantify these effects, especially in the research setting. Therapy response is expressed as a percentage of total tumor area that is non-viable. Adipocytic maturation, despite containing viable cells, is a distinct pattern of therapy response seen in myxoid liposarcoma and is of unclear significance.[1] Non-liquefied tumor tissue from a cross-section through the longest axis of the tumor should be sampled. At least 1 section of

necrotic tumor (always with a transition to viable tumor) should be sampled to verify the gross impression of necrosis. Non-sampled necrotic areas should be included in the estimate of necrosis and the percentage of tumor necrosis reported. The gross appearance can be misleading, and areas that appear grossly necrotic may actually be myxoid or edematous. Additional sections from these areas should be submitted for histologic examination. When estimates of gross necrosis exceed those of histologic necrosis, the greater percentage of necrosis should be recorded on the surgical pathology report.

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I. Lymphatic and/or Vascular Invasion

Lymphatic and/or Vascular Invasion (LVI) indicates whether microscopic lymphatic and/or vascular invasion is identified. LVI includes lymphatic invasion, vascular invasion, or lymphovascular invasion. By AJCC/UICC convention, LVI does not affect the T category indicating local extent of tumor unless specifically included in the definition of a T category.

J. Margins

The most important predictor of local recurrence is the status of surgical excision margins.[1] Therefore, detailed reporting of surgical margins is a critical role of the pathologist. It has been recommended that for all margins located less than 2 cm, the distance of the tumor from the margin be reported in centimeters.[2] However, there is a lack of agreement on this issue and more recent studies have demonstrated 1-5 mm margins or less are adequate for local control.[3,4,5] We recommend specifying the location of all margins located less than 0.5 cm and the distance of the closest margin that is less than 0.5 cm from the tumor. Margins from soft tissue tumors should be taken as perpendicular (radial) sections, if possible. If bones are present in the specimen and are not involved by tumor, or the tumor is located more than 0.5 cm from the margin, the marrow can be scooped out and submitted as a margin.

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K. Regional Lymph Nodes

With the exception of epithelioid sarcoma and clear cell sarcoma of soft parts, and rarely alveolar rhabdomyosarcoma, regional lymph node metastasis is uncommon in adult soft tissue sarcomas. Nodes are not sampled routinely, and it usually is not necessary to exhaustively search for nodes. When no lymph nodes are resected, the pathologic 'N' category is not assigned (pNX is not used for soft tissue tumors). When present, regional lymph node metastasis has prognostic importance and should be reported. For sarcomas arising in the trunk and extremities or retroperitoneum, the 8th edition of the AJCC Cancer Manual recommends that N1 M0 disease be regarded as stage IIIB rather than stage IV disease.[1]

References

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