32 Soft Tissue Tumors (Sarcomas)

Soft tissue tumors are among the most difficult neoplasms to diagnose. Often special studies (immunoperoxidase studies, EM, cytogenetics) are required for the appropriate classification of these tumors and for reliable separation from carcinomas, melanomas, and lymphomas.

RELEVANT CLINICAL HISTORY (IN ADDITION TO AGE AND GENDER)

See Table 32-1.

TABLE 32–1. RELEVANT CLINICAL HISTORY

HISTORY RELEVANT TO ALL SPECIMENS	HISTORY RELEVANT FOR SARCOMA SPECIMENS
Organ/tissue resected or biopsied	Location and depth of mass
Purpose of the procedure	Involvement of soft tissue or bone
Gross appearance of the organ/tissue/lesion sampled	Rate of growth (duration of lesion)
Any unusual features of the clinical presentation	Presenting symptoms and signs.
Any unusual features of the gross appearance	Preoperative therapy
Prior surgery/biopsies – results	Family history (e.g., Li-Fraumeni syndrome, familial retinoblastoma syndrome)
Prior malignancy	
Prior treatment (radiation therapy, chemotherapy, drug use that can change the histologic appearance of tissues)	
Compromised immune system	

BIOPSIES

Biopsies are usually performed to make decisions about the use of preoperative therapy and the extent of definitive surgery to obtain adequate margins. Either incisional or needle biopsies are used. It may not be possible to provide a specific diagnosis or grade based on very small specimens.

PROCESSING THE SPECIMEN

1. Relevant clinical history should be provided or obtained to establish a preoperative differential diagnosis (i.e., patient gender, age, location and depth of mass, involvement of soft tissue and/or bone, prior history of malignancies). The likely diagnosis will aid in deciding how to apportion limited amounts of lesional tissue.
2. Describe the specimen, including type (needle, incisional), size, color, necrosis or hemorrhage. Indicate what proportion of the specimen appears to be lesional and nonlesional (fibrous, fatty, etc.).
3. Very small or very heterogeneous (i.e., little tissue is available and viable tumor is difficult to identify grossly) specimens are fixed in formalin and submitted in entirety.

Larger specimens should be apportioned for special studies if lesional tissue can be identified. Also see Chapters 6 and 7.

In selected cases, a frozen section or cytologic preparation may be helpful to narrow the differential diagnosis to guide apportionment of limited tissue.

SPECIAL STUDIES

- **Formalin:** Formalin-fixed tissue remains the cornerstone of diagnosis. Make sure there are sufficient representative samples in formalin before submitting for special studies, which are listed below in order of importance.
- **EM:** Requires a small amount of tissue that can be examined by light microscopy as well as by EM. If the tumor is heterogeneous, submit multiple specimens paired with formalin sections. EM is useful for distinguishing carcinoma from sarcoma (intercellular junctions), melanoma (premelanosomes), and subtyping round cell sarcomas (e.g., rhabdomyosarcoma) and some spindle cell sarcomas (e.g., malignant peripheral nerve sheath tumors) (see in Chapter 7, "Electron Microscopy").
- **Frozen tissue:** One or more 1 cm^3 fragments are optimal. Smaller samples are acceptable if the specimen is limited. The tissue is cut into 0.2 cm fragments and stored at -70°C.The tissue can be used for molecular analysis (DNA, RNA, FISH, Southern blotting, PCR, RT-PCR). Frozen tissue may be required for some treatment protocols.
- **Cytogenetics:** It is helpful to save tissue for cytogenetics if sarcoma is suspected clinically and there is a sufficient sample. Cytogenetics is a very useful technique for classifying some tumors (see in Chapter 7, "Cytogenetics") but may require a large volume of tissue that cannot be examined histologically. The equivalent amount of two needle biopsies may be sufficient for highly cellular tumors, but 1 to 2 cm^3 of tumor is preferred.

LIPOMAS

Lipomas are common benign soft tissue tumors that are often removed for cosmetic reasons. However, malignancy must always be excluded. The likelihood of malignancy is increased if any of the following features are present:

- Large size (over 5 cm).
- Infiltration into surrounding tissues.
- Location in deep tissues or near the spermatic cord.
- History of recurrence.
- Unusual gross appearance – any appearance other than apparently normal fat (e.g., white or cream-colored, homogeneous, firm, fibrotic areas, attached tissues).

Approximately 22% of patients undergoing hernia repair will also have an incidental cord lipoma. In the cited study by Montgomery and Buras[1], only 0.1% of hernia sac operations yielded an incidental liposarcoma. The two patients with liposarcoma were older than the average patient with cord lipoma (56 and 64 years versus 35 years) and the tumors were larger (13 and 10 cm versus 5.5 cm). Palpable cord tumors are more likely to be malignant.

Lipomas are usually enucleated without removal of the adjacent tissue. Thus, the lesion is often fragmented. There is no reason to ink these specimens, as the lesion is present at the margin and margins are irrelevant for the vast majority of benign lesions.

PROCESSING THE SPECIMEN

1. Record overall or aggregate measurements if fragmented. Thinly section through the specimen. Evaluate the specimen for tissues present (usually adipose tissue, occasionally muscle, all other tissues are rare).
2. Sample the lesion with one section per centimeter of greatest dimension, including all areas of varying appearance. Two fragments can be placed in one cassette.
3. It is helpful to send tissue for cytogenetics if any of the following features are present:
   - Subcutaneous lipomas >10 cm in size

- Lipomas in deep-seated locations (i.e., subfascial, intramuscular, intra-abdominal, retroperitoneal; including all clinically-evident cord lipomas)
- Lipomas with unusual gross appearance (e.g., creamy color, firm consistency)
- Request by surgeon.

RESECTIONS

Resections are often large and may include organs and limbs. It is usually advisable to discuss and orient large complicated resections with the surgeon at the time of resection and to identify all anatomic landmarks.

Types of resections:

- **Intralesional:** Gross tumor is left in the patient. These may be debulking procedures for palliation when complete resection is not possible (e.g., for sarcomas involving the abdominal cavity at multiple sites).
- **Marginal:** The tumor with its pseudocapsule is removed with a small amount of surrounding tissue. Tumor is generally microscopically present at the margin.
- **Wide:** This is an intracompartmental resection. The tumor is removed with a rim of at least 2 cm of normal tissue, but an entire compartment is not removed. The margin width may be less if there is a fascial plane.
- **Segmental/en bloc resection for bone:** The portion of involved bone is removed with a cuff of normal bone.
- **Radical:** An entire soft tissue compartment or bone is removed. This type of procedure includes amputations and disarticulations.

Margins are extremely important! Complete resection of the tumor with adequate width of margins or an uninvolved fascial plane, are important determinants of long-term outcome. Distance from the margin may determine the need for further surgery or postoperative radiation therapy.

PROCESSING THE SPECIMEN

1. Evaluate the outer surface of the specimen for structures present (muscle, bone, nerve, vessels, organs) and gross tumor involvement. Record measurements (outer dimensions, structures present). For very large retroperitoneal lesions, the weight may be requested by clinicians.
2. Selectively ink the outer margins if they appear closer than 2 cm, excluding skin if present. Avoid inking any nonmarginal tissue (e.g., soft tissue exposed by overlying retracted muscle). In general, margins more than 2 cm from the tumor need not be inked and those more than 5 cm from the tumor need not be sampled.
3. Serially section, leaving the sections attached at one side. Describe the lesion, including size in three dimensions (very important!), color, borders (infiltrating, pushing, satellite nodules), necrosis (percent of tumor involved) or hemorrhage, variation in gross appearance, involvement of adjacent structures (arising from a structure such as nerve, vessel, or muscularis propria), and location (skin, subcutaneous tissue, fascia, muscle, visceral).

   The closest gross distance from all margins and the type of tissue at each margin (e.g., fascial plane, periosteum, muscle, strands of soft tissue) are documented. Most specimens should have at least six margins evaluated (visualize the specimen as if it were a box with six sides).

   Complicated specimens will require a diagram documenting the location of the tumor and adjacent structures and the site of microscopic sections.

   If bone is included in the specimen, a specimen radiograph is performed to document the location of the bone(s) and areas of possible tumor involvement. See also Chapter 12.

   Lymph nodes are not usually resected along with soft tissue sarcomas and are rarely involved (other than in certain uncommon tumor types). However, any lymph nodes present in a resection specimen should be examined.
4. Pin the oriented specimen on wax and fix in an adequate volume of formalin for at least 10 to 12 hours to facilitate taking sections from the margins and the interface between normal and tumor tissue.

5. Submit tumor for special studies as indicated above. It is helpful to take tissue from all areas that have a different gross appearance (e.g., different consistencies or colors) and to match adjacent sections submitted for light microscopy and special studies. **Avoid necrotic areas when taking tissue for special studies.** If the specimen is a re-excision and gross tumor is not apparent, do not submit tissue for special studies.

   As a general rule, at least one section per centimeter of the tumor's greatest dimension should be examined including all areas of different gross appearance.

   Take sections to document the extent of necrosis in the absence of prior treatment.

   Perpendicular margins are taken to assess the distance of the tumor from each margin. If the margin is greater than 5 cm from the tumor, it need not be sampled except in cases of epithelioid sarcoma and angiosarcoma. Margin involvement by these two types of sarcoma may be difficult to evaluate grossly. En face blocks of margins are not recommended. If gross tumor is not apparent, the distance of the scar tissue/biopsy site to each margin is documented.

   If the patient has received neoadjuvant therapy, it is important to document the extent of response. An entire representative slice of the tumor should be sampled with the location of the blocks of tissue indicated on a diagram, photograph, or radiograph. This will allow an estimation of the percent of tumor that is necrotic or replaced by fibrous tissue or granulation tissue.

SPECIAL STUDIES

Tissue may be taken for special studies as described in Chapter 13. Frozen tissue may be required for some treatment protocols.

GROSS DIFFERENTIAL DIAGNOSIS

Sarcomas. In general, sarcomas grow as circumscribed white/tan fleshy masses, often with a pseudocapsule. The invasion into adjacent tissues may be subtle and not appreciated grossly. Some sarcomas have distinctive appearances (see below).

Lipomas. These tumors are well circumscribed or lobulated and have a thin delicate capsule. The tumor usually resembles normal adipose tissue. Lipomas are often enucleated and, thus, are often fragmented and the capsule cannot be appreciated.

Liposarcomas. Low-grade lipoma-like liposarcomas may be soft and resemble normal fat. However, these tumors are usually paler and have a more coarsely lobulated appearance. Higher grade liposarcomas are more likely to have firm solid areas as well as areas of necrosis.

Schwannoma. Circumscribed encapsulated mass consisting of tan/white to yellow firm tissue. It may be possible to identify an associated nerve.

Neurofibroma. Circumscribed mass with a thin capsule consisting of soft tan/white tissue. The nerve is incorporated into the lesion and may not be separately identified. In patients with neurofibromatosis, the lesions may be plexiform (multiple lesions along a nerve – "bag of worms").

Malignant Peripheral Nerve Sheath Tumor. Often infiltrative, and hemorrhage and necrosis may be present. These tumors sometimes arise from a nerve that may be identifiable entering one side of the tumor. Tumors arising in patients with neurofibromatosis may be plexiform (i.e., multiple finger-like projections of tumor in the surrounding tissue - "bag of worms" appearance).

Leiomyosarcomas. These tumors are often found in association with the smooth muscle from which they arise (e.g., a large vein or the myometrium). They often have a whorled appearance.

Gastrointestinal Stromal Tumors (GIST). These tumors are found throughout the gastrointestinal tract. They are composed of cells similar to Cajal cells of the smooth muscle lining, and are therefore found associated with smooth muscle. The gross appearance is similar to leiomyomas. 80% of GISTs have a mutation in the KIT tyrosine kinase gene. A smaller group (5% to 7%) have mutations in the KIT-homologous tyrosine kinase PDGFRA. About 10% to 15% of GISTs are negative

for KIT and PDGFRA mutations (termed "wild-type GISTs"). The type of mutation can be of prognostic importance and can correlate with response to different drugs. Sequence analysis may be requested at the time of diagnosis or for tumors negative for KIT by immunohistochemistry or tumors resistant to treatment. Resistance may be due to additional mutations in KIT or PDGFRA. Fixed tissue can be used.

Angiosarcomas. The tumor may subtly infiltrate the tissue, producing a grossly indistinct mass. Extensively involved areas are often very hemorrhagic.

MICROSCOPIC SECTIONS

- **Tumor:** The general rule of thumb is one cassette per cm of greatest dimension. Document all areas with different appearances, edges (e.g., capsule, infiltration), and involvement of any adjacent structures or organs.
  More extensive sampling is indicated for low-grade lesions, as the finding of a high-grade area would change stage and prognosis.
  If the tumor has not been treated, one section to document necrosis including an adjacent area of viable tumor is sufficient.
  If prior neoadjuvant therapy has been given, a complete representative cross section of tumor should be submitted with the location of the blocks of tissue recorded, in order to determine the extent of tumor response.
- **Margins:** Document all close margins with at least one cassette. If the tumor is very close to a margin (i.e., within 2 cm), multiple sections may be submitted. Take only perpendicular margins. If a margin is >5 cm from the tumor, and the tumor is not an angiosarcoma or an epithelioid sarcoma, the margin need not be submitted.
  Margins should be 1 to 2 cm or an uninvolved fascial plane for sarcomas.
- **Other structures:** Document any other anatomical structures present. Document any prior biopsy scars/sites.

PATHOLOGIC DIAGNOSTIC/PROGNOSTIC FEATURES SIGN-OUT CHECKLIST FOR SOFT TISSUE TUMORS

- **Procedure:** Needle core biopsy, intralesional resection, marginal resection, wide resection, radical resection, amputation
- **Tumor Site:** Location of tumor
- **Tumor Size:** Greatest dimension (other dimensions optional)
- **Extent of Tumor:** Superficial (dermal, subcutaneous/suprafascial), deep (fascial, subfascial, intramuscular, mediastinal, intra-abdominal, retroperitoneal, head and neck)
- **Histologic Type:** Liposarcoma, rhabdomyosarcoma, leiomyosarcoma, malignant peripheral nerve sheath tumor, numerous other types. The WHO Classification system is recommended.
- **Mitotic Rate:** Number of mitoses per 10 HPF (1 HPF = 0.1734 mm^2) in the most mitotically active area of the tumor. Count at least 50 HPF. If specific grading systems are used (see below) the mitotic count should be adjusted for the size of the HPF.
- **Necrosis:** Present or absent and extent (% of tumor)
- **Histologic Grade:** Some tumors are by definition high grade or low grade, and some cannot be graded. Other types can be divided into grades and this provides prognostic information (see below for the FNCLCC systems). Grading of malignant peripheral nerve sheath tumor, embryonal and alveolar rhabdomyosarcoma, angiosarcoma, extraskeletal myxoid chondrosarcoma, alveolar soft part sarcoma, clear cell sarcoma, and epithelioid sarcoma is not recommended.
- **Margins:** The distance to each margin should be recorded. Margins less than 2 cm should be specified as to location and distance. In re-excision specimens, the distance of scarring or granulation tissue from margins should also be measured. Margins bounded by a fascial plane or periosteum should be identified as a smaller distance may be adequate.
- **Lymph-Vascular Invasion:** Not identified, present. Rarely observed in sarcomas.
- **Tumor Margin Characteristics:** Circumscribed, focally infiltrative, diffusely infiltrative
- **Regional Lymph Nodes:** Rarely involved. Most common in alveolar rhabdomyosarcomas, angiosarcomas, epithelioid sarcomas, and clear cell sarcomas

TABLE 32-2. AJCC (7TH EDITION) CLASSIFICATION OF SOFT TISSUE SARCOMAS

Tumor	
TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor
T1	Tumor ≤5 cm in greatest dimension*
T1a	Superficial tumor
T1b	Deep tumor
T2	Tumor >5 cm in greatest dimension*
T2a	Superficial tumor
T2b	Deep tumor
*Superficial tumor is located exclusively above the superficial fascia without invasion of the fascia; deep tumor is located either exclusively beneath the superficial fascia, superficial to the fascia with invasion of or through the fascia, or both superficial yet beneath the fascia.	
Regional Lymph Nodes	
NX	Regional lymph nodes cannot be assessed.
N0	No regional lymph node metastasis
N1*	Regional lymph node metastasis
*Presence of positive nodes (N1) in M0 tumors is considered stage III.	
Distant Metastases	
M0	No distant metastasis
M1	Distant metastasis
Note: This classification system does not apply to inflammatory myofibroblastic tumor, infantile fibrosarcoma, Kaposi sarcoma, fibromatosis (desmoid tumor), mesothelioma, or sarcomas arising in tissues apart from soft tissue (e.g., parenchymal organs). There is a separate AJCC staging system for gastrointestinal stromal tumor. There is an alternative staging system for rhabdomyosarcoma of children and young adults (see CAP Protocol for the Examination of Specimens from Patients with Rhabdomyosarcoma, www.cap.org). 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.	

- **Preexisting Lesion:** If the tumor is a nerve-sheath neoplasm, state whether there is evidence of a preexisting benign lesion
- **Inflammatory Response:** Optional (no known relevance) – present or absent, extent, type
- **Treatment Effect:** If patient has received prior treatment: extent of tumor necrosis, percentage of viable tumor
- **Ancillary Studies:** Cytogenetics, molecular pathology, if appropriate
- **Distant Metastasis:** Present. If distant metastasis is not present on pathologic examination, the M category is a clinical classification.
- **AJCC Classification:** T, N, and M classifications should be provided, when possible (Table 32-2). 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/). 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.

PATHOLOGIC DIAGNOSTIC/PROGNOSTIC FEATURES SIGN-OUT CHECKLIST FOR PEDIATRIC RHABDOMYOSARCOMA AND RELATED NEOPLASMS

- **Procedure:** Excision (local, wide, or radical), compartectomy, amputation (type, neural, vascular, soft tissue margins), other (e.g., piecemeal, needle core biopsy, incisional biopsy)
- **Specimen Laterality:** Right, left, midline
- **Tumor Site:** Bladder/prostate, cranial parameningeal, extremity, genitourinary, head and neck (excluding parameningeal), orbit, other
- **Tumor Size:** Greatest dimension (other dimensions optional)
- **Tumor Depth:** Dermal, subcutaneous, subfascial, intramuscular, intra-abdominal, retroperitoneal, intracranial, organ based
- **Histologic Type:** Embryonal (botryoid, spindle cell, or not otherwise specified), alveolar (solid or not otherwise specified), mixed (give percentage of each type), undifferentiated
- **Anaplasia:** Not identified, focal (single or few scattered anaplastic cells), diffuse (clusters or sheets of anaplastic cells)
  - May be associated with any histologic type
  - Defined as large, lobate hyperchromatic nuclei (at least 3 times the size of neighboring nuclei) and atypical (obvious, multipolar) mitotic figures.
    Focal anaplasia (group I): A single or a few cells scattered amongst non-anaplastic cells
    Diffuse anaplasia (group II): Clusters or sheets of anaplastic cells present
- **Margins:** Cannot be assessed, uninvolved, distance from closest margin, involved margin (specify)
- **Regional Lymph Nodes:** Cannot be assessed, negative, metastases present (specify number of nodes examined and number with metastases)
- **Mitotic Rate:** Give number of mitoses per 10 HPF using a 40× objective in the most proliferative area.
- **Necrosis:** Absent, present (extent in %)
- **Distant Metastases:** Cannot be assessed, present (specify sites, if known)
- **Stage:** The Intergroup Rhabdomyosarcoma Study Postsurgical Clinical Grouping System or the Modified Site, Size, Metastasis Staging for Rhabdomyosarcoma may be used if sufficient information is available (Table 32.3).

This checklist incorporates information from the CAP Cancer Committee protocols for reporting on cancer specimens (see www.cap.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.

GRADING OF SOFT TISSUE SARCOMAS

- **The Intergroup Rhabdomyosarcoma Study (IRS) post-surgical clinical grouping system:** If applicable, the appropriate stage group may be assigned by the pathologist (Table 32-3).
- **The Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading system for soft tissue sarcomas of adults (updated version):** Tables 32-4 and 32-5. Do not grade:
  - Treated tumors
  - Benign lesions
  - Bone sarcomas
  - Visceral sarcomas (uterine and gastrointestinal sarcomas)
  - Pediatric sarcomas
  - Dermatofibrosarcoma protuberans
  - Atypical fibroxanthoma
  - Fine needle or core biopsies (sampling error is likely to be high)

However, recurrent tumors should be graded.[3-5]

- **Gastrointestinal stromal tumor (GIST):** There are several suggested methods of dividing GIST into groups according to the risk of progression or metastasis. Most are based on the number of metastases and size (Tables 32-6 and 32-7).[6,7]

TABLE 32–3. THE INTERGROUP RHABDOMYOSARCOMA STUDY (IRS) POST-SURGICAL CLINICAL GROUPING SYSTEM

GROUP I	
A	Localized tumor, confined to site of origin, completely resected
B	Localized tumor, infiltrating beyond site of origin, completely resected
GROUP II	
A	Localized tumor, gross total resection, but with microscopic residual disease
B	Locally extensive tumor (spread to regional lymph nodes), completely resected
C	Locally extensive tumor (spread to regional lymph nodes), gross total resection, but with microscopic residual disease
GROUP III	
A	Localized or locally extensive tumor, gross residual disease after biopsy only
B	Localized or locally extensive tumor, gross residual disease after major resection (>50% debulking)
GROUP IV	
Any size primary tumor, with or without regional lymph node involvement, with distant metastases, without respect to surgical approach to primary tumor	

From CAP Protocol for the Examination of Specimens from Patients (Children and Young Adults) with Rhabdomyosarcoma (available at www.cap.org, Cancer Protocols and Checklists).

TABLE 32–4. THE FÉDÉRATION NATIONALE DES CENTRES DE LUTTE CONTRE LE CANCER (FNCLCC) GRADING SYSTEM FOR SOFT-TISSUE SARCOMAS OF ADULTS (UPDATED VERSION)

TUMOR DIFFERENTIATION[a]	FEATURES
Score 1	Sarcomas closely resembling normal, adult, mesenchymal tissue (e.g., well-differentiated liposarcoma)
Score 2	Sarcomas of certain histologic types (see Table 32-5)
Score 3	Synovial sarcomas, embryonal sarcomas, undifferentiated sarcomas, and sarcomas of doubtful tumor type (see Table 32-5)
MITOTIC COUNT[b]	
Score 1	0 to 9 mitoses per 10 HPF
Score 2	10 to 19 mitoses per 10 HPF
Score 3	20 or more mitoses per 10 HPF

Continued

TABLE 32–4. THE FÉDÉRATION NATIONALE DES CENTRES DE LUTTE CONTRE LE CANCER (FNCLCC) GRADING SYSTEM FOR SOFT-TISSUE SARCOMAS OF ADULTS (UPDATED VERSION)—cont'd	
TUMOR NECROSIS[c]	
Score 0	No tumor necrosis on any examined slides
Score 1	≤50% tumor necrosis over all the examined tumor surface
Score 2	>50% tumor necrosis over all the examined tumor surface

[a]The three scores are added together to determine the histologic grade:
Grade I: Total score = 2 or 3
Grade II: Total score = 4 or 5
Grade III: Total score = 6, 7, or 8
[b]**Mitotic count**: The count is made in most mitotically active areas in ten successive high power fields (defined as × 400 measuring 0.174 mm^2). This count is taken to establish the score. Ulcerated, necrotic, and hypocellular areas should not be counted. Only definitive mitotic figures (not pyknotic or apoptotic cells) should be counted.
[c]**Tumor necrosis:** The necrosis should appear spontaneous and not related to prior surgery or ulceration. Areas of hyalinization or hemorrhage are not scored.

TABLE 32–5. TUMOR DIFFERENTIATION SCORE – FNCLCC SYSTEM	
HISTOLOGIC TYPE	**SCORE**
Liposarcoma	
Well differentiated	1 (always Grade I)
Myxoid	2
Round cell	3
Pleomorphic	3 (always Grade III)
Dedifferentiated	3
Fibrosarcoma	2
Malignant triton tumor	3
Leiomyosarcoma	
Well differentiated	1
Conventional	2
Poorly differentiated/pleomorphic/epithelioid	3
Pleomorphic rhabdomyosarcoma	3
Chondrosarcoma	
Well differentiated	1
Myxoid	2
Mesenchymal	3 (always Grade III)

TABLE 32–5. TUMOR DIFFERENTIATION SCORE – FNCLCC SYSTEM—cont'd

HISTOLOGIC TYPE	SCORE
Extraskeletal osteosarcoma	3 (always Grade III)
Hemangiopericytoma	
Well differentiated malignant	2
Conventional malignant	3
Malignant fibrous histiocytoma (MFH)	
Myxofibrosarcoma (myxoid MFH)	2
Typical storiform MFH (sarcoma, not otherwise specified)	2
Pleomorphic type (patternless pleomorphic sarcoma)	3
Giant-cell and inflammatory MFH (pleomorphic sarcoma, not otherwise specified with giant cells or inflammatory cells)	3
Ewing sarcoma/PNET	3 (always Grade III)
Malignant rhabdoid tumor	3
Synovial sarcoma	
Biphasic or monophasic synovial sarcoma	3
Poorly differentiated synovial sarcoma	3
Undifferentiated sarcoma	3

TABLE 32–6. RISK STRATIFICATION OF PRIMARY GIST BY MITOTIC INDEX, SIZE, AND SITE

TUMOR PARAMETERS		RISK OF PROGRESSIVE DISEASE (%)[a]			
MITOTIC INDEX	SIZE	GASTRIC	DUODENUM	JEJUNUM/ILEUM	RECTUM
≤5 per 50 HPF	≤2 cm	None (0%)	None (0%)	None (0%)	None (0%)
	>2 but ≤5 cm	Very low (1.9%)	Low (4.3%)	Low (8.3%)	Low (8.5%)
	>5 but ≤10 cm	Low (3.6%)	Moderate (24%)	Insufficient data	Insufficient data
	>10 cm	Moderate (10%)	High (52%)	High (34%)	High (57%)
>5 per 50 HPF	≤2 cm	None[b]	High[b]	Insufficient data	High (54%)
	>2 but ≤5 cm	Moderate (16%)	High (73%)	High (50%)	High (52%)
	>5 but ≤10 cm	High (55%)	High (85%)	Insufficient data	Insufficient data
	>10 cm	High (86%)	High (90%)	High (86%)	High (71%)

[a]Defined as metastasis or tumor-related death.
[b]Risk assessment based on small numbers of cases.
Adapted from Miettinen M, Lasota J, Gastrointestinal stromal tumors: pathology and prognosis at different sites, Semin Diagn Pathol 23:70-83, 2006.

TABLE 32-7. AJCC (7TH EDITION) CLASSIFICATION OF GASTROINTESTINAL STROMAL TUMORS

Tumor	
TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor
T1	Tumor 2 cm or less
T2	Tumor more than 2 cm but not more than 5 cm
T3	Tumor more than 5 cm but not more than 10 cm
T4	Tumor more than 10 cm in greatest dimension
Regional Lymph Nodes	
NX	Regional lymph nodes cannot be assessed.
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
Distant Metastases	
M0	No distant metastasis
M1	Distant metastasis

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ABDOMINAL FAT PAD BIOPSY FOR THE DIAGNOSIS OF AMYLOIDOSIS

There are several methods of sampling tissues to establish the diagnosis of systemic amyloidosis. Rectal biopsies are reported to be the most sensitive (97%) followed by fine needle aspiration of the abdominal fat pad (75%), oral biopsy (64%), and biopsy of the abdominal fat pad (50%). These latter biopsies can be either excisional or by core biopsy.

The tissue can be fixed in formalin and stained with Congo Red. Both false positive and false negative results have been reported. If there is sufficient tissue, some can be saved for EM, which may be helpful in confirming a diagnosis. Immunohistochemical studies can be used to identify subtypes of amyloid.

The abdominal fat pad biopsy technique is not helpful in the evaluation of dialysis patients with β-2 microglobulin amyloidosis as this type of amyloid is preferentially found near joints.

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