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

Version: 4.1.0.0
Protocol Posting Date: June 2021

The use of this protocol is recommended for clinical care purposes but is not required for accreditation purposes.

This protocol may be used for the following procedures AND tumor types:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy</td>
<td></td>
</tr>
<tr>
<td>Tumor Type</td>
<td>Description</td>
</tr>
<tr>
<td>Soft tissue sarcomas</td>
<td>Includes soft tissue tumors of intermediate (locally aggressive and rarely metastasizing) potential and malignant soft tissue tumors.</td>
</tr>
</tbody>
</table>

The following should NOT be reported using this protocol:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resection (consider the Soft Tissue Resection protocol)</td>
<td></td>
</tr>
<tr>
<td>Cytologic specimens</td>
<td></td>
</tr>
<tr>
<td>Tumor type</td>
<td>Description</td>
</tr>
<tr>
<td>Soft tissue tumors that may recur locally but have either no or an extremely low risk of metastasis</td>
<td></td>
</tr>
<tr>
<td>Carcinosarcoma (consider the appropriate site-specific carcinoma protocol)</td>
<td></td>
</tr>
<tr>
<td>Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)</td>
<td></td>
</tr>
<tr>
<td>Pediatric Ewing sarcoma (consider the Ewing Sarcoma protocol)</td>
<td></td>
</tr>
<tr>
<td>Pediatric rhabdomyosarcoma (consider the Rhabdomyosarcoma protocol)</td>
<td></td>
</tr>
<tr>
<td>Kaposi sarcoma</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal stromal tumor (consider the Gastrointestinal Stromal Tumor protocol)</td>
<td></td>
</tr>
<tr>
<td>Uterine sarcoma (consider the Uterine Sarcoma protocol)</td>
<td></td>
</tr>
</tbody>
</table>

Authors
Javier A. Laurini*.

With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.

* Denotes primary author.
Accreditation Requirements
The use of this biopsy case summary is recommended for clinical care purposes, but is not required for accreditation purposes. The core and conditional data elements are routinely reported for biopsy specimens. Non-core data elements are included to allow for reporting information that may be of clinical value.

Summary of Changes

v 4.1.0.0

- General Reformatting
- New WHO 5th Edition Histological Updates
- Revised Margins Section
Reporting Template
Protocol Posting Date: June 2021
Select a single response unless otherwise indicated.

CASE SUMMARY: (SOFT TISSUE: Biopsy)
Standard(s): AJCC-UICC 8
The use of this template is recommended for reporting biopsy specimens, but is not required for accreditation purposes.

CLINICAL

+Prebiopsy Treatment (select all that apply)
___ No known prebiopsy therapy
___ Chemotherapy performed
___ Radiation therapy performed
___ Therapy performed, type not specified
___ Not specified

SPECIMEN (Note A)

Procedure
___ Core needle biopsy
___ Incisional biopsy
___ Excisional biopsy
___ Other (specify): _________________
___ Not specified

TUMOR

Tumor Site (Note B)
___ Head and neck (specify site, if known): _________________
___ Trunk and extremities (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

Histologic Type (World Health Organization [WHO] Classification of Soft Tissue Tumors) (Note C)
# The list is derived from the 2020 World Health Organization (WHO) classification of soft tissue tumors, edited to include ONLY soft tissue tumors of intermediate (locally aggressive and rarely metastasizing) potential and malignant soft tissue tumors for which anatomical staging using the AJCC system is considered to be clinically relevant.

___ Adipocytic Tumors
   Intermediate (locally aggressive)
   ___ Atypical lipomatous tumor
   Malignant
   ___ 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
___ Epithelioid liposarcoma
___ Myxoid pleomorphic liposarcoma

___ Fibroblastic / Myofibroblastic Tumors

Intermediate (rarely metastasizing)
___ Fibrosarcomatous dermatofibrosarcoma protuberans
Malignant
___ Solitary fibrous tumor, malignant
___ Adult fibrosarcoma
___ Myxofibrosarcoma
___ Epithelioid Myxofibrosarcoma
___ Low grade fibromyxoid sarcoma
___ Sclerosing epithelioid fibrosarcoma

___ So-called Fibrohistiocytic Tumors

Malignant
___ Malignant tenosynovial giant cell tumor

___ Smooth Muscle Tumors
Malignant
___ Leiomyosarcoma

___ Pericytic (Perivascular) Tumors
Malignant
___ Malignant glomus tumor

___ Skeletal Muscle Tumors
Malignant
___ Embryonal rhabdomyosarcoma (including botryoid, anaplastic)
___ Alveolar rhabdomyosarcoma (including solid, anaplastic)
___ Pleomorphic rhabdomyosarcoma
___ Spindle cell / sclerosing rhabdomyosarcoma
___ Spindle cell / sclerosing rhabdomyosarcoma NOS
___ Congenital spindle cell rhabdomyosarcoma with VGLL2/NCOA2/CITED2 rearrangements
___ MYOD1-mutant spindle cell / sclerosing rhabdomyosarcoma
___ Intraosseous spindle cell rhabdomyosarcoma (with TFCP2/NCOA2 rearrangements)
___ Ectomesenchymoma

___ Vascular Tumors
Malignant
___ Epithelioid hemangioendothelioma with WWTR1-CAMTA1 fusion
___ Epithelioid hemangioendothelioma with YAP1-TFE3 fusion
___ Epithelioid hemangioendothelioma NOS

___ Peripheral Nerve Tumors
Malignant
___ Malignant peripheral nerve sheath tumor
___ Epithelioid malignant peripheral nerve sheath tumor
___ Malignant granular cell tumor
___ Malignant perineurioma
___ Chondro-osseous Tumors
    Malignant
    ___ Extraskeletal osteosarcoma

___ Tumors of Uncertain Differentiation
    Intermediate (rarely metastasizing)
    ___ Ossifying fibromyxoid tumor
    ___ Mixed tumor:
    ___ Mixed tumor NOS, malignant:
    ___ Myoepithelioma
    Malignant
    ___ Phosphaturic mesenchymal tumor, malignant
    ___ NTRK-rearranged spindle cell neoplasm
    ___ Synovial sarcoma, biphasic
    ___ Synovial sarcoma, spindle cell
    ___ Synovial sarcoma, poorly differentiated
    ___ Synovial sarcoma NOS
    ___ Epithelioid sarcoma, classic type
    ___ Epithelioid sarcoma, proximal or large cell type
    ___ Alveolar soft part sarcoma
    ___ Clear cell sarcoma of soft tissue
    ___ Extraskeletal myxoid chondrosarcoma
    ___ Ossifying fibromyxoid tumor, malignant
    ___ Myoepithelial carcinoma
    ___ Extraskeletal Ewing sarcoma
    ___ Round cell sarcoma with EWSR1-non ETS fusions
    ___ CIC-rearranged sarcoma
    ___ Sarcoma with BCOR genetic alterations

___ Undifferentiated / Unclassified Sarcomas
    ___ Undifferentiated spindle cell sarcoma
    ___ Undifferentiated pleomorphic sarcoma
    ___ Undifferentiated round cell 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 D)
___ Grade 1
___ Grade 2
___ Grade 3
___ Ungraded sarcoma
___ Cannot be assessed:

Mitotic Rate (Note D)
___ 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 (Note D)
___ Not identified
___ Present
   Extent of Necrosis
       ___ Specify percentage: _________________ %
       ___ Cannot be determined (explain): _________________
       ___ Cannot be determined

+Treatment Effect (Note E)
___ No known prebiopsy therapy
___ Not identified
___ Present
   Percentage of Viable Tumor (compared with pretreatment biopsy, if available)
       ___ Specify percentage: _________________ %
       ___ Cannot be determined (explain): _________________
       ___ Cannot be determined

+Lymphovascular Invasion (Note F)
___ Not identified
___ Present
___ Cannot be determined: _________________

+Tumor Comment: _________________

MARGINS (for excisional biopsies only) (Note G)

Margin Status
___ Not applicable
___ 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
           ___ Less than 2 cm
           ___ Other (specify): _________________
           ___ Cannot be determined:
   Other Close Margin(s) to Tumor (less than 2 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): _________________

+Margin Comment: _________________

ADDITIONAL FINDINGS

+Additional Findings (specify): _________________

SPECIAL STUDIES

Immunohistochemistry
___ Specify: _________________
___ Not performed: _________________
___ Not applicable

Cytogenetics
___ Specify: _________________
___ Not performed: _________________
___ Not applicable

Molecular Pathology
___ Specify: _________________
___ Not performed: _________________
___ Not applicable

COMMENTS

Comment(s): _________________
Explanatory Notes

A. Procedure / Tissue Processing

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.

Tissue Submission for Histologic Evaluation

One section per centimeter of maximum dimension is usually recommended, although fewer sections per centimeter are needed for very large tumors, especially if they are homogeneous. Tumors known to be high grade from a previous biopsy do not require as many sections as those that were previously diagnosed as low grade, as documentation of a high-grade component will change stage and prognosis in the latter case. Sections should be taken of grossly heterogeneous areas, and there is no need to submit more than 1 section of necrotic tumor (always with a transition to viable tumor). 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. In general, most tumors require 10 to 12 sections or fewer, excluding sections submitted to assess the status of surgical margins. Tumors with greater areas of heterogeneity may need to be sampled more thoroughly.

Although the ability to perform diagnostic molecular studies in formalin fixed paraffin embedded tissue has substantially diminished the need to collect fresh tissue on every case, frozen tissue may be needed to enter patients into treatment protocols. Nevertheless, discretion should be used in triaging tissue from sarcomas. Adequate tissue should be submitted for conventional light microscopy before setting aside samples for cytogenetics, electron microscopy, or molecular analysis. Fresh tissue for special studies should be collected at the time the specimen is received.

Molecular Studies

It may be important to snap freeze a small portion of tissue as availability of frozen tissue may be a requirement for patient enrollment into clinical trials. In general, 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, preserving sufficient tissue for histologic examination. This frozen tissue should ideally be stored at minus (-)70°C and can be shipped on dry ice to facilities that perform molecular analysis.

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


B. Tumor Site

The 8th edition of the American Joint Committee on Cancer (AJCC) staging manual 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.

Head and Neck

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 usually are 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**


**C. 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), electron microscopy, 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.

**Tumor Classification From Biopsies**

It is not always possible to classify soft tissue tumors precisely based on biopsy material, especially FNA and core needle biopsy specimens. Although pathologists should make every attempt to classify lesions in small biopsy specimens, on occasion stratification into very basic diagnostic categories, such as lymphoma, carcinoma, melanoma, and sarcoma, is all that is possible. In some cases, precise classification is only possible in open biopsies or resection specimens.

**WHO Classification of Tumors**

Classification of tumors should be made according to the 2020 World Health Organization (WHO) classification of soft tissue tumors. As part of the WHO classification, 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 2020 World Health Organization (WHO) classification of soft tissue tumors, edited to only include soft tissue tumors of intermediate (locally aggressive and rarely metastasizing) potential and malignant soft tissue tumors for which anatomical staging using the AJCC system is considered to be clinically relevant. The full reference contains information on additional soft tissue tumors.
D. Grading

Unlike with other organ systems, the 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, there is, however, no generally agreed-upon scheme for grading soft tissue tumors. The most widely used soft tissue grading systems are the French Federation of Cancer Centers Sarcoma Group (FNCLCC) and National Cancer Institute (NCI) systems. Both systems have 3 grades and are based on mitotic activity, necrosis, and differentiation, and are highly correlated with prognosis. 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. Other systems with 2 or 4 grades also have been used. The 8th edition of the AJCC Cancer Staging Manual 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 grades 2 to 3 (effectively low and high) 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 (ie, low and high grade) is encouraged. In many instances, the histologic type of sarcoma will readily permit this distinction (ie, Ewing sarcoma, pleomorphic liposarcoma), whereas in less obvious instances, the difficulty of assigning 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 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
Grade 2: 4 or 5
Grade 3: 6 to 8

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 (eg, well-differentiated liposarcoma, well-differentiated leiomyosarcoma)

Score 2: Sarcomas for which histologic typing is certain (eg, myxoid liposarcoma, myxofibrosarcoma)

Score 3: Embryonal sarcomas and undifferentiated sarcomas, synovial sarcomas and sarcomas of doubtful 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 1. Tumor Differentiation Score According to Histologic Type in the Updated Version of the French Federation of Cancer Centers Sarcoma Group System

<table>
<thead>
<tr>
<th>Tumor Differentiation</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atypical lipomatous tumor / Well-differentiated liposarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Well-differentiated leiomyosarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Malignant neurofibroma</td>
<td>1</td>
</tr>
<tr>
<td>Well-differentiated Fibrosarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Myxoid liposarcoma</td>
<td>2</td>
</tr>
<tr>
<td>Conventional leiomyosarcoma</td>
<td>2</td>
</tr>
<tr>
<td>Conventional fibrosarcoma</td>
<td>2</td>
</tr>
<tr>
<td>Myxofibrosarcoma</td>
<td>2</td>
</tr>
<tr>
<td>High-grade myxoid (round cell) liposarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Pleomorphic liposarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Dedifferentiated liposarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Pleomorphic Rhabdomyosarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Poorly differentiated / pleomorphic leiomyosarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Biphasic / monophasic / poorly differentiated Synovial sarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Mesenchymal chondrosarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Extraskeletal osteosarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Extraskeletal Ewing sarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Malignant rhabdoid tumor</td>
<td>3</td>
</tr>
<tr>
<td>Undifferentiated pleomorphic sarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Undifferentiated sarcoma, not otherwise specified</td>
<td>3</td>
</tr>
</tbody>
</table>

Note: 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. The case for grading malignant peripheral nerve sheath tumor is currently being debated.

Modified with permission from Coindre JM.

Mitosis Count: The count is made in the most mitotically active area, away from areas of necrosis, in either 10 consecutive high-power fields (HPF) (use the X40 objective) (1 HPF x 400 = 0.1734 mm²) or in the appropriate number of HPF to encompass 1 mm² based on each individual microscope. If the mitotic rate is close to the cutoff between mitotic scores, the count should be repeated.
Table 2. Mitotic Count Score equivalence

<table>
<thead>
<tr>
<th>Mitotic Score</th>
<th># mitosis / 10 HPF (1 HPF = 0.1734 mm²)</th>
<th># mitosis / 1 mm² (see table 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score 1</td>
<td>0 to 9 mitosis / 10 HPF</td>
<td>0 to 5 mitosis / 1 mm²</td>
</tr>
<tr>
<td>Score 2</td>
<td>10 to 19 mitosis / 10 HPF</td>
<td>6 to 11 mitosis / 1 mm²</td>
</tr>
<tr>
<td>Score 3</td>
<td>&gt; 19 mitosis / 10 HPF</td>
<td>&gt; 11 mitosis / 1 mm²</td>
</tr>
</tbody>
</table>

The area of 1 HPF originally used for mitotic count measured 0.1734 mm². However, the area of 1 HPF using most modern microscopes with wider 40x lenses will most likely be higher. Pathologists are encouraged to determine the field area of their 40x lenses 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.

An important change in the 5th Edition of the WHO Classification of Tumours series is the conversion of mitotic count from the traditional denominator of 10 HPFs to a defined area expressed in mm², as an attempt to standardize the area used for mitotic count. Table 3 shows the approximate number of fields required to encompass 1 mm² based on the field diameter and its corresponding area.

Table 3. Approximate number of fields per 1 mm² based on field diameter and its corresponding area

<table>
<thead>
<tr>
<th>Field diameter (mm)</th>
<th>Area (mm²)</th>
<th>Approximate number of fields per 1 mm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.40</td>
<td>0.126</td>
<td>8</td>
</tr>
<tr>
<td>0.41</td>
<td>0.132</td>
<td>8</td>
</tr>
<tr>
<td>0.42</td>
<td>0.138</td>
<td>7</td>
</tr>
<tr>
<td>0.43</td>
<td>0.145</td>
<td>7</td>
</tr>
<tr>
<td>0.44</td>
<td>0.152</td>
<td>7</td>
</tr>
<tr>
<td>0.45</td>
<td>0.159</td>
<td>6</td>
</tr>
<tr>
<td>0.46</td>
<td>0.166</td>
<td>6</td>
</tr>
<tr>
<td>0.47</td>
<td>0.173</td>
<td>6</td>
</tr>
<tr>
<td>0.48</td>
<td>0.181</td>
<td>6</td>
</tr>
<tr>
<td>0.49</td>
<td>0.188</td>
<td>5</td>
</tr>
<tr>
<td>0.50</td>
<td>0.196</td>
<td>5</td>
</tr>
<tr>
<td>0.51</td>
<td>0.204</td>
<td>5</td>
</tr>
<tr>
<td>0.52</td>
<td>0.212</td>
<td>5</td>
</tr>
<tr>
<td>0.53</td>
<td>0.221</td>
<td>5</td>
</tr>
<tr>
<td>0.54</td>
<td>0.229</td>
<td>4</td>
</tr>
<tr>
<td>0.55</td>
<td>0.237</td>
<td>4</td>
</tr>
<tr>
<td>0.56</td>
<td>0.246</td>
<td>4</td>
</tr>
<tr>
<td>0.57</td>
<td>0.255</td>
<td>4</td>
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<tr>
<td>0.58</td>
<td>0.264</td>
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</tr>
<tr>
<td>0.59</td>
<td>0.273</td>
<td>4</td>
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<tr>
<td>0.60</td>
<td>0.283</td>
<td>4</td>
</tr>
<tr>
<td>0.61</td>
<td>0.292</td>
<td>3</td>
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<tr>
<td>0.62</td>
<td>0.302</td>
<td>3</td>
</tr>
<tr>
<td>0.63</td>
<td>0.312</td>
<td>3</td>
</tr>
<tr>
<td>0.64</td>
<td>0.322</td>
<td>3</td>
</tr>
<tr>
<td>0.65</td>
<td>0.332</td>
<td>3</td>
</tr>
<tr>
<td>0.66</td>
<td>0.342</td>
<td>3</td>
</tr>
<tr>
<td>0.67</td>
<td>0.352</td>
<td>3</td>
</tr>
<tr>
<td>0.68</td>
<td>0.363</td>
<td>3</td>
</tr>
<tr>
<td>0.69</td>
<td>0.374</td>
<td>3</td>
</tr>
</tbody>
</table>
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. This means that FNCLCC grade 2 and grade 3 tumors are considered “high grade” for the purposes of stage grouping.

References


E. 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 viable. Nonliquefied 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. Nonsampled 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.

F. Lymphovascular Invasion

Lymphovascular invasion (LVI) indicates whether microscopic lymphovascular 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.

G. 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. We recommend specifying the location of all margins located less than 2 cm and the distance of the closest margin that is less than 2 cm from the tumor. Margins from soft tissue tumors should be taken as perpendicular sections, if possible. If bones are present in the specimen and are not involved by tumor, or the tumor is located more than 2 cm from the margin, the marrow can be scooped out and submitted as a margin.

References