COLLEGE of AMERICAN PATHOLOGISTS

Protocol for the Examination of Specimens From Patients With Primary Sarcoma of the Uterus

Version: UterineSarcoma 4.1.0.0 **Protocol Posting Date:** August 2018
Includes pTNM requirements from the 8th Edition, AJCC Staging Manual, and 2015 FIGO Cancer Report

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

Procedure	Description
Resection	Includes total hysterectomy and supracervical hysterectomy
Tumor Type	**Description**
Sarcoma	Includes leiomyosarcoma, adenosarcoma, endometrial stromal sarcoma, and undifferentiated uterine/endometrial sarcoma

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

Procedure
Biopsy, myomectomy, or removal of tumor in fragments
Primary resection specimen with no residual cancer (eg, prior myomectomy)
Cytologic specimens

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

Tumor Type
Carcinoma (consider the Endometrium or Cervix protocols)
Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)

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

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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 (ie, 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 ie, all required elements must be in the synoptic portion of the report in the format defined above.

CAP Laboratory Accreditation Program Protocol Required Use Date: April 2019

CAP Uterine Sarcoma Protocol Summary of Changes

Version 4.1.0.0
The following data elements were modified:
Regional Lymph Nodes - Revised the format to clarify reporting involved and uninvolved nodes

Surgical Pathology Cancer Case Summary

Protocol posting date: August 2018

UTERUS:

Select a single response unless otherwise indicated.

Procedure (select all that apply)
___ Total hysterectomy and bilateral salpingo-oophorectomy
___ Radical hysterectomy
___ Simple hysterectomy
___ Supracervical hysterectomy
___ Bilateral salpingo-oophorectomy
___ Right salpingo-oophorectomy
___ Left salpingo-oophorectomy
___ Salpingo-oophorectomy, side not specified
___ Right oophorectomy
___ Left oophorectomy
___ Oophorectomy, side not specified
___ Bilateral salpingectomy
___ Right salpingectomy
___ Left salpingectomy
___ Salpingectomy, side not specified
___ Omentectomy
___ Peritoneal biopsies
___ Peritoneal washing
___ Other (specify): _____

Note: For information about lymph node sampling, please refer to the Regional Lymph Nodes section.

+ Hysterectomy Type
+ ___ Abdominal
+ ___ Vaginal
+ ___ Vaginal, laparoscopic-assisted
+ ___ Laparoscopic
+ ___ Laparoscopic, robotic-assisted
+ ___ Other (specify): _____
+ ___ Not specified

Specimen Integrity
___ Intact
___ Opened
___ Morcellated
___ Other (specify): _____

Tumor Size
Greatest dimension (centimeters): ___ cm
+ Additional dimensions (centimeters): ___ x ___ cm
___ Cannot be determined

Histologic Type (select all that apply) (Note A)
___ Leiomyosarcoma
___ Leiomyosarcoma, epithelioid type
___ Leiomyosarcoma, myxoid type
___ Endometrial stromal sarcoma, low grade[#]

___ Endometrial stromal sarcoma with smooth muscle differentiation, low grade
___ Endometrial stromal sarcoma with sex cord elements, low grade
___ Endometrial stromal sarcoma with glandular elements, low grade
___ Endometrial stromal sarcoma, high grade
___ Undifferentiated uterine/endometrial sarcoma
___ Adenosarcoma
___ Adenosarcoma with rhabdomyoblastic differentiation
___ Adenosarcoma with cartilaginous differentiation
___ Adenosarcoma with osseous differentiation
___ Adenosarcoma with other heterologous element (specify): _____
___ Adenosarcoma with sarcomatous overgrowth
___ Rhabdomyosarcoma
___ Malignant perivascular epithelioid cell tumor
___ Other histologic type not listed (specify): _____

[#] *Low-grade endometrial stromal sarcoma is distinguished from benign endometrial stromal nodule by depth of myometrial invasion ≥3 mm, lymphovascular invasion, or ≥3 foci of myometrial invasion of any depth. Minor marginal irregularity in the form of tongues <3 mm is allowable for an endometrial stromal nodule. This protocol does not apply to endometrial stromal nodules.*

Histologic Grade (required only for adenosarcoma)
___ Low grade
___ High grade
___ With sarcomatous overgrowth
___ Cannot be assessed

Myometrial Invasion (required only for adenosarcoma)
___ Not identified
___ Present
    Depth of invasion (millimeters): ___ mm
    Myometrial thickness (millimeters): ___ mm
    Percentage of myometrial invasion: ____%

    OR, if exact percentage of invasion cannot be determined, state:
    ___ Depth of myometrial invasion cannot be determined (explain): _____
    ___ Myometrial thickness cannot be determined (explain): _____
    Percentage depth of myometrial invasion
    ___ Estimated less than 50% myometrial invasion
    ___ Estimated greater than or equal to 50% myometrial invasion
___ Cannot be determined (explain): _____

Other Tissue/ Organ Involvement (select all that apply)
Note: Any organ not selected is either not involved or was not submitted.
___ Not applicable
___ Not identified
___ Right ovary
___ Left ovary
___ Ovary (side not specified)
___ Right fallopian tube
___ Left fallopian tube
___ Fallopian tube (side not specified)
___ Vagina
___ Right parametrium
___ Left parametrium
___ Parametrium (side not specified)
___ Pelvic wall
___ Omentum

___ Other organs/tissue (specify): _____
___ Cannot be determined (explain):_____

Margins
___ Cannot be assessed
___ Uninvolved by sarcoma
+ Distance of sarcoma from closest margin: ___ mm
+ Specify closest margin: _____
___ Involved by sarcoma
Specify margin(s): _____

Lymphovascular Invasion
___ Not identified
___ Present
___ Cannot be determined

+ Peritoneal/Ascitic Fluid
+ ___ Not submitted/ unknown
+ ___ Negative for malignancy (normal/benign)
+ ___ Atypical and/or suspicious (explain): _____
+ ___ Malignant (positive for malignancy)
+ ___ Unsatisfactory/nondiagnostic (explain): _____
+ ___ Results pending

Regional Lymph Nodes

Note: Lymph nodes designated as pelvic (parametrial, obturator, internal iliac (hypogastric), external iliac, common iliac, sacral, presacral) and para-aortic are considered regional lymph nodes. Any other involved nodes should be categorized as metastases (pM1) and commented on in the distant metastasis section. Presence of isolated tumor cells no greater than 0.2 mm in regional lymph node(s) is considered N0(i+).

___ No lymph nodes submitted or found

Lymph Node Examination (required only if lymph nodes are present in the specimen)

___ All lymph nodes negative for tumor cells

___ Positive for tumor cells (select all that apply)
Number of Nodes with Metastasis (excludes isolated tumor cells): _____
Number of Nodes with Isolated Tumor Cells (0.2 mm or less) (if applicable): _____
Number cannot be determined (explain): _____

Note: Reporting the number of lymph nodes with isolated tumor cells is required only in the absence of metastasis greater than 0.2 mm in other lymph nodes.

+ Nodal Site(s) with Tumor Cells (specify): _____

Number of Lymph Nodes Examined: _____
___ Number cannot be determined (explain): _____
+ Specify Site(s): _____

Pathologic Stage Classification (pTNM, AJCC 8th Edition) (Note B)

Note: Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. Only the applicable T, N, or M category is required for reporting; their definitions need not be included in the report. The categories (with modifiers when applicable) can be listed on 1 line or more than 1 line.

TNM Descriptors (required only if applicable) (select all that apply)
___ r (recurrent)
___ y (post-treatment)

For All Sarcomas Excluding Adenosarcoma (including Leiomyosarcoma, Endometrial Stromal Sarcoma, and Undifferentiated Endometrial Sarcoma/Uterine Sarcoma)

Primary Tumor (pT)
___ pTX: Primary tumor cannot be assessed
___ pT0: No evidence of primary tumor
___ pT1: Tumor is limited to the uterus
___ pT1a: Tumor 5 cm or less in greatest dimension
___ pT1b: Tumor more than 5 cm
___ pT2: Tumor extends beyond the uterus, within the pelvis
___ pT2a: Tumor involves adnexa
___ pT2b: Tumor involves other pelvic tissues
___ pT3: Tumor infiltrates abdominal tissues
___ pT3a: Tumor infiltrates abdominal tissues in one site
___ pT3b: Tumor infiltrates abdominal tissues in more than one site
___ pT4: Tumor invades bladder or rectum

For Adenosarcoma

Primary Tumor (pT)
___ pTX: Primary tumor cannot be assessed
___ pT0: No evidence of primary tumor
___ pT1: Tumor limited to the uterus
___ pT1a: Tumor limited to the endometrium/endocervix
___ pT1b: Tumor invades to less than half of the myometrium
___ pT1c: Tumor invades one half or more of the myometrium
___ pT2: Tumor extends beyond the uterus, but within the pelvis
___ pT2a: Tumor involves adnexa
___ pT2b: Tumor involves other pelvic tissues
___ pT3: Tumor infiltrates abdominal tissues
___ pT3a: Tumor infiltrates abdominal tissues in one site
___ pT3b: Tumor infiltrates abdominal tissues in more than one site
___ pT4: Tumor invades bladder and/or rectum

For All Sarcomas

Regional Lymph Nodes (pN)
___ pNX: Regional lymph nodes cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN0(i+): Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm
___ pN1: Regional lymph node metastasis

Distant Metastasis (pM) (required only if confirmed pathologically in this case)
___ pM1: Distant metastasis (excluding adnexa, pelvic and abdominal tissues)
Specify site(s), if known: _____

+ *For All Sarcomas Excluding Adenosarcoma (Including Leiomyosarcoma, Endometrial Stromal Sarcoma, and Undifferentiated Endometrial Sarcoma/Uterine Sarcoma)*

+ FIGO Stage (2015 FIGO Cancer Report)
+ ___ I: Tumor limited to uterus
+ ___ IA: Less than or equal to 5 cm

+ ___ IB: More than 5 cm
+ ___ II: Tumor extends beyond the uterus, within the pelvis
+ ___ IIA: Adnexal involvement
+ ___ IIB: Involvement of other pelvic tissues
+ ___ III: Tumor invades abdominal tissues (not just protruding into the abdomen)
+ ___ IIIA: 1 site
+ ___ IIIB: More than 1 site
+ ___ IIIC: Metastasis to pelvic and/or para-aortic lymph nodes
+ ___ IV: Tumor invades bladder and/or rectum and/or distant metastasis
+ ___ IVA: Tumor invades bladder and/or rectal mucosa
+ ___ IVB: Distant metastasis

+ *For Adenosarcoma*

+ FIGO Stage (2015 FIGO Cancer Report)
+ ___ I: Tumor limited to uterus
+ ___ IA: Tumor limited to endometrium/endocervix with no myometrial invasion
+ ___ IB: Less than or equal to half myometrial invasion
+ ___ IC: More than half myometrial invasion
+ ___ II: Tumor extends beyond the uterus, within the pelvis
+ ___ IIA: Adnexal involvement
+ ___ IIB: Tumor extends to extrauterine pelvic tissue
+ ___ III: Tumor invades abdominal tissues (not just protruding into the abdomen).
+ ___ IIIA: 1 site
+ ___ IIIB: More than 1 site
+ ___ IIIC: Metastasis to pelvic and/or para-aortic lymph nodes
+ ___ IV: Tumor invades bladder and/or rectum and/or distant metastasis
+ ___ IVA: Tumor invades bladder and/or rectal mucosa
+ ___ IVB: Distant metastasis

+ Ancillary Studies
+ Specify: _____
+ ____ Not performed

+ Comment(s)

Explanatory Notes

A. Histologic Type

Carcinosarcoma
Carcinosarcoma (malignant mixed Müllerian tumor) is excluded from the uterine sarcoma diagnostic category as it is considered in tumors of the endometrial epithelium.

Adenosarcoma
According to World Health Organization (WHO) criteria, mitotic activity in the mesenchymal component in excess of 2 or more per 10 high-power fields (HPF) is required for a diagnosis of adenosarcoma, but others use a cut-off of 4 per 10 HPF.[1-5] However, given the multiple and well known problems associated with counting mitotic figures and the fact that the number of mitoses may be variable from area to area, in practice, if the characteristic leaf-like architecture of adenosarcoma is present with periglandular cuffing resulting in a cambium layer, a diagnosis of adenosarcoma should be strongly considered with mitotic counts <2 per 10 HPF or even in the absence of mitotic figures. In adenosarcomas without sarcomatous overgrowth, it is recommended to record on the pathology report whether the stromal component is morphologically “low grade” or “high grade.” Even though there are no studies showing that this is of prognostic significance, anecdotal evidence suggests that even a small focus of “high-grade” sarcoma may result in an adverse behavior. It is suggested that the parameter of nuclear atypia be used to distinguish between low grade and high grade neoplasms. In low-grade neoplasms, the atypia should be akin to that seen in low-grade endometrial stromal sarcoma. Sarcomatous overgrowth in adenosarcoma is defined as the presence of pure sarcoma, usually high grade and without an epithelial component, occupying at least 25% of the tumor.[6]

Adenosarcomas rarely exhibit lymphovascular invasion unless associated with deep myometrial invasion or sarcomatous overgrowth.

The depth of myometrial invasion is important in the substaging of stage I adenosarcomas (tumor confined to the uterus).[7] Stage IA tumors are limited to the endometrium or endocervix with no myometrial involvement, stage IB equates to less than or half of myometrial invasion, and stage 1C equates to more than one-half myometrial invasion. This staging system is similar to the 1988 FIGO staging system for carcinomas of the uterine corpus. Since low-grade endometrial stromal sarcoma (ESS) and leiomyosarcoma are predominantly myometrial-based lesions, myometrial invasion per se is not used in the staging of these neoplasms

In most adenosarcomas with a low-grade stromal component without sarcomatous overgrowth, the stromal element expresses estrogen receptor (ER), progesterone receptor (PgR), CD10, and WT1; is negative (“wild-type”) with p53; and exhibits a low MIB1 proliferation index.[2,4] Thus, the immunophenotype resembles that of low-grade endometrial stromal sarcoma. Smooth muscle actin and desmin may also be positive. In areas of high-grade sarcoma and of sarcomatous overgrowth, the mesenchymal component exhibits a higher MIB1 proliferation index and may be p53 positive/aberrant. There is usually loss of expression of the cell differentiation markers ER, PgR, and CD10, the immunophenotype being similar to that of an undifferentiated sarcoma. Rhabdomyosarcomatous elements in adenosarcomas express desmin and sometimes the skeletal muscle markers myogenin and myoD1. Sex cord-like elements may express inhibin and calretinin.

Endometrial Stromal Sarcoma
Low-grade endometrial stromal sarcoma, in contrast to endometrial stromal nodule, demonstrates myometrial invasion from the nodule or tumor mass of ≥3 mm, lymphovascular invasion, or ≥3 foci of myometrial invasion of any depth. About 60% of ESS have a translocation of the short arm of chromosome 7 and the long arm of chromosome 17 [t(7;17)], resulting in a fusion between 2 zinc finger genes (*JAZF1/JJAZ1*).[8] However, this is not specific to ESS and may be demonstrated in the benign variant known as ESN (endometrial stromal nodule).[9] Other rearrangements are a t(6;7), resulting in the *PHF1/JAZF1* fusion gene, and t(6;10), resulting in the *EPC1/PHF1* fusion.[2]

Even though in the past endometrial stromal sarcomas were classified as low grade (LG) and high grade (HG) based on mitotic activity, the largest and most comprehensive review of these tumors by Chang and colleagues in

1990 showed that mitotic activity was not predictive of outcome in stage I tumors.[10] Thus, the diagnosis of HG-ESS was discouraged in those tumors that resemble proliferative-phase endometrial stroma but in which the mitotic index exceeded 10 per 10 HPF. Currently many expert gynecologic pathologists, without any proven basis outside of personal experience, make the diagnosis of HG-ESS when there is a transition from high-grade undifferentiated sarcoma to areas that can be recognized as conventional LG-ESS.[11] However, recently, a subset of cases previously diagnosed as HG-ESSs has been histologically and genetically defined by Lee et al[12,13] and Nucci et al (2007). In these tumors, the high-grade areas are characterized by cells with a round cell-epithelioid appearance and high-grade cytologic features, which often are associated with areas that have the appearance of the fibroblastic variant of low-grade conventional ESS.[12] These tumors have been shown to have a novel genetic fusion between *YWHAE* and *FAM22A/B* and harbor t(10;17)(q22;p13). The high-grade areas of the tumor express cyclin D1 but lose CD10, ER, and PgR expression (in contrast to the conventional low-grade areas) consistent with a high-grade sarcoma.[12] It is important to recognize these tumors as they have an intermediate prognosis between LG-ESS and undifferentiated uterine sarcoma (UUS), and appear not to respond to the usual treatment for low-grade ESS.

Low-grade ESS, high-grade ESS, and UUS all exist and should be separately diagnosed, although UUS should be a diagnosis of exclusion (leiomyosarcomas and other high-grade sarcomas, for example rhabdomyosarcoma, should be excluded). Molecular testing is diagnostically unnecessary in conventional ESS and in USS but is useful in confirming the diagnosis of HG-ESS in tumors with a round cell-epithelioid appearance that can be associated with areas that have the appearance of the fibroblastic variant of conventional LG-ESS.

Leiomyosarcoma

By definition, uterine leiomyosarcoma (LMS) is a highly malignant neoplasm with survival rates depending upon the extent of spread. For tumors confined to the uterine corpus, size plays a significant role in prognosis. Despite differences in survival rates, it is clear that stage is a significant factor related to outcome. Histologic grade, however, has not been consistently identified as a significant prognostic parameter.[14] The utility of grading uterine LMS is controversial, and no universally accepted grading system exists.[5] In 2011, Veras et al tried to characterize "low-grade uterine leiomyosarcomas" as a clinicopathological entity but came to the conclusion that this can be diagnosed only retrospectively at present.[15] Furthermore, when the Stanford criteria are strictly applied, all tumors classified as leiomyosarcomas should be regarded intrinsically as high grade.[15,16]

Conventional uterine LMS is a cellular tumor composed of fascicles of spindle-shaped cells exhibiting smooth muscle differentiation with moderate to severe pleomorphism. Usually coagulative tumor cell necrosis (CTCN) is present and mitoses exceed 10 to 15 per 10 HPF.[16] Two LMS subtypes included in the WHO classification deserve special attention as their pathologic features differ from those of ordinary spindle cell LMS. Epithelioid leiomyosarcoma (E-LMS) is composed predominantly of round or polygonal cells with eosinophilic to clear cytoplasm exhibiting nested, plexiform, or corded growth patterns. Nuclear atypia may be only mild and necrosis may be absent. Mitotic rate is generally greater than 3 per 10 HPF, and most tumors infiltrate adjacent myometrium. Myxoid leiomyosarcoma (M-LMS) may be grossly gelatinous, microscopically hypocellular with a predominant myxoid stroma, and often has a low mitotic rate. In the absence of severe cytologic atypia and high mitotic activity, both epithelioid and myxoid LMS are diagnosed as sarcomas based on their infiltrative borders.[14]

<u>Ancillary Studies in the Differential Diagnosis</u>

Immunoreactivity for smooth muscle actin, muscle-specific actin, calponin, desmin, h-caldesmon, and heavy chain smooth muscle myosin are commonly seen in uterine LMS. Desmin expression may be focal.[17-19] Similarly, E-LMS and M-LMS may demonstrate lesser degrees of immunoreactivity for these markers. Cell cycle related markers Ki-67, p53, and p16 are usually overexpressed in LMS compared to leiomyoma.[20] Cytokeratins and EMA may be focally positive in LMS, especially in the epithelioid variant.

Undifferentiated Uterine/Endometrial Sarcoma

Undifferentiated uterine/endometrial sarcoma is a high-grade sarcoma that lacks specific differentiation. Histopathologically these tumors show marked cellular pleomorphism and abundant mitotic activity with atypical forms. They lack the typical growth pattern and vascularity of low-grade ESS and displace the myometrium in contrast to the infiltrative pattern of low-grade ESS. They often resemble the sarcomatous component of a carcinosarcoma. These sarcomas are most often aneuploid with an S-phase fraction greater than 10%, and are

negative for ER and PgR. Nucci et al proposed that high-grade ESS with the novel fusion gene *YWHAE-FAM22* should be distinguished from undifferentiated uterine/endometrial sarcoma.[18]

Other Tumor Types
Other differential diagnostic considerations included in spindle/sarcomatous lesions primary to the uterus include perivascular epithelioid cell tumor (PEComa) and rhabdomyosarcoma. PEComa belongs to a group of tumors characterized by both melanocytic and smooth muscle differentiation, and should be recognized separately from smooth muscle tumors.[21-23] Rhabdomyosarcoma is rare but is the most common uterine heterologous sarcoma.[24] Pleomorphic and embryonal subtypes are most frequent, while the alveolar and spindled variants are extremely rare.[25] Rhabdomyosarcomas are usually positive for desmin, muscle-specific actin, myogenin, Myo D1, and myoglobin, and negative for smooth muscle actin. Pleomorphic and alveolar subtypes have a worse prognosis than the embryonal subtype.[24]

B. Pathologic Stage Classification
The TNM staging system for uterine sarcoma endorsed by the American Joint Committee on Cancer (AJCC) and the parallel system formulated by the International Federation of Gynecology and Obstetrics (FIGO) are recommended, as shown below.[26]

According to AJCC/International Union Against Cancer (UICC) convention, the designation “T” refers to a primary tumor that has not been previously treated. The symbol “p” refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis. Single tumor cells or small clusters of cells not more than 0.2 mm in greatest diameter are classified as isolated tumor cells. These may be detected by routine histology or by immunohistochemical methods and are designated N0(i+). pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathologic staging is usually performed after surgical resection of the primary tumor. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumor has been completely removed. If a biopsied tumor is not resected for any reason (eg, when technically infeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

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

The “y” prefix indicates those cases in which classification is performed during or after initial multimodality therapy (ie, 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 before multimodality therapy (ie, 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.

The “a” prefix designates the stage determined at autopsy: aTNM.

Additional Descriptors

Residual Tumor (R)
Tumor remaining in a patient after therapy with curative intent (eg, surgical resection for cure) is categorized by a system known as R classification, shown below.

RX Presence of residual tumor cannot be assessed

R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor

For the surgeon, the R classification may be useful to indicate the known or assumed status of the completeness of a surgical excision. For the pathologist, the R classification is relevant to the status of the margins of a surgical resection specimen. That is, tumor involving the resection margin on pathologic examination may be assumed to correspond to residual tumor in the patient and may be classified as macroscopic or microscopic according to the findings at the specimen margin(s).

T Category Considerations
It is important to note that in uterine sarcoma, as in cancer of other organs, the validity of T stage depends upon the adequacy and completeness of the surgical staging.

TNM Classification and FIGO Staging System for Leiomyosarcoma, Endometrial Stromal Sarcoma, and Undifferentiated Uterine Sarcoma

TNM Category	FIGO Stage	Definition
Primary Tumor		
pTX	[--]:	Primary tumor cannot be assessed
pT0	[--]:	No evidence of primary tumor
pT1	[I]:	Tumor is limited to the uterus
pT1a	[IA]:	Tumor is 5 cm or less (≤5 cm) in greatest dimension
pT1b	[IB]:	Tumor is greater than 5 cm (>5 cm) in greatest dimension
pT2	[II]:	Tumor extends beyond the uterus, but is within the pelvis (tumor extends to extrauterine pelvic tissue)
pT2a	[IIA]:	Tumor involves the adnexa
pT2b	[IIB]:	Tumor involves other pelvic tissue
pT3	[III]:	Tumor invades abdominal tissues (not just protruding into the abdomen)
pT3a	[IIIA]:	Tumor invades abdominal tissues at 1site
pT3b	[IIIB]:	Tumor invades abdominal tissues at more than 1 site
pT4	[IVA]:	Tumor invades bladder mucosa and/or rectum
Regional Lymph Nodes (pN)[#]		
pNX:		Cannot be assessed
pN0:		No regional lymph node metastasis
pN0(i+):		Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm
pN1	[IIIC]:	Regional lymph node metastasis to pelvic lymph nodes
Distant Metastasis (pM)		
pM0		No distant metastasis (no pathologic M0; use clinical M to complete stage group)
pM1	[IVB]:	Distant metastasis (excluding adnexa, pelvic and abdominal tissues)

[#] Regional lymph nodes include the pelvic, obturator, internal iliac (hypogastric), external iliac, common iliac, para-aortic, presacral, and parametrial lymph nodes.

Adenosarcoma

TNM Category	FIGO Stage	Definition
Primary Tumor		
pTX	[--]:	Primary tumor cannot be assessed
pT0	[--]:	No evidence of primary tumor

pT1	[I]:	Tumor is limited to the uterus
pT1a	[IA]:	Tumor is limited to the endometrium/endocervix without myometrial invasion
pT1b	[IB]:	Tumor invades less than or equal to 50% (≤50%) total myometrial thickness
pT1c	[IC]	Tumor invades greater than 50% (>50%) total myometrial thickness
pT2	[II]:	Tumor extends beyond the uterus, but is within the pelvis (tumor extends to extrauterine pelvic tissue)
pT2a	[IIA]:	Tumor involves the adnexa
pT2b	[IIB]:	Tumor involves other pelvic tissue
pT3	[III]:	Tumor invades abdominal tissues (not just protruding into the abdomen)
pT3a	[IIIA]:	Tumor invades abdominal tissues at one site
pT3b	[IIIB]:	Tumor invades abdominal tissues at more than one site
pT4	[IVA]:	Tumor invades bladder mucosa and/or rectum

Regional Lymph Nodes (pN)[#]

pNX:		Cannot be assessed
pN0:		No regional lymph node metastasis
pN1	[IIIC]:	Regional lymph node metastasis to pelvic lymph nodes

[#] Regional lymph nodes include the pelvic, obturator, internal iliac (hypogastric), external iliac, common iliac, para-aortic, presacral, and parametrial lymph nodes.

Distant Metastasis (pM)

pM0		No distant metastasis (no pathologic M0; use clinical M to complete stage group)
pM1	[IVB]:	Distant metastasis (excluding adnexa, pelvic and abdominal tissues)

References

1. Clement PB, Scully RE. Mullerian adenosarcoma of the uterus: a clinicopathologic analysis of 100 cases with a review of the literature. *Hum Pathol.* 1990;21:363-381.
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