

Endometrium

**Protocol applies to all carcinomas
of the endometrium.**

*Protocol revision date: January 2005
Based on AJCC/UICC TNM, 6th edition
and FIGO 2001 Annual Report*

Procedures

- **Cytology** (No Accompanying Checklist)
- **Biopsy**
- **Curettage**
- **Hysterectomy**

Authors

Philip A. Branton, MD

Department of Pathology, Inova Fairfax Hospital, Falls Church, Virginia

William F. Moore, MD

Department of Pathology, USAF Medical Center, Keesler Air Force Base,
Mississippi

For the Members of the Cancer Committee, College of American Pathologists

Previous contributor: Steven G. Silverberg, MD

Summary of Changes to Checklist(s)

Protocol revision date: January 2005

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Surgical Pathology Cancer Case Summary (Checklist)

*Protocol revision date: January 2005
 Applies to invasive carcinomas only
 Based on AJCC/UICC TNM, 6th edition
 and FIGO 2001 Annual Report*

***ENDOMETRIUM: Biopsy**

(Note: Use of checklist for biopsy specimens is optional)

*Patient name:

*Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC**Specimen Type**

- * Biopsy
- * Curettage
- * Other (specify): _____
- * Not specified

MICROSCOPIC**Histologic Type**

- * Endometrioid adenocarcinoma, not otherwise characterized
- * Endometrioid adenocarcinoma, secretory (variant)
- * Endometrioid adenocarcinoma, ciliated cell (variant)
- * Endometrioid adenocarcinoma, with squamous metaplasia
- * Adenosquamous carcinoma
- * Serous adenocarcinoma
- * Clear cell adenocarcinoma
- * Mucinous adenocarcinoma
- * Squamous cell carcinoma
- * Mixed carcinoma (specify types and percentages): _____
- * Undifferentiated carcinoma
- * Other (specify): _____
- * Carcinoma, type cannot be determined

* Data elements **with asterisks** are **not required** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

***Histologic Grade (if applicable)**

(Grading system below applies primarily to endometrioid carcinoma)

- * Not applicable
- * GX: Cannot be assessed
- * G1: 5% or less nonsquamous solid growth
- * G2: 6% to 50% nonsquamous solid growth
- * G3: More than 50% nonsquamous solid growth
- * Other (specify): _____

***Additional Pathologic Findings (check all that apply)**

- * None identified
- * Hyperplasia
 - * Simple
 - * Complex (adenomatous)
- * Atypical hyperplasia
 - * Simple
 - * Complex (adenomatous)
- * Other (specify): _____

***Comment(s)**

Surgical Pathology Cancer Case Summary (Checklist)

*Protocol revision date: January 2005
 Applies to invasive carcinoma only
 Based on AJCC/UICC TNM, 6th edition
 and FIGO 2001 Annual Report*

ENDOMETRIUM: Hysterectomy, With or Without Other Organs or Tissues

Patient name:

Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC**Specimen Type**

- Hysterectomy
 Radical hysterectomy (includes parametria)
 Pelvic exenteration
 Other (specify): _____
 Not specified

***Tumor Site**

- *Specify location(s), if known: _____
 * Not specified

Tumor Size

- Greatest dimension: ____ cm
 *Additional dimensions: ____ x ____ cm
 Cannot be determined (see Comment)

Other Organs Present (check all that apply)

- None
 Right ovary
 Left ovary
 Right fallopian tube
 Left fallopian tube
 Urinary bladder
 Vagina
 Rectum
 Other(s) (specify): _____

* Data elements **with asterisks** are **not required** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

MICROSCOPIC**Histologic Type**

- Endometrioid adenocarcinoma, not otherwise characterized
- Endometrioid adenocarcinoma, secretory (variant)
- Endometrioid adenocarcinoma, ciliated cell (variant)
- Endometrioid adenocarcinoma, with squamous metaplasia
- Adenosquamous carcinoma
- Serous adenocarcinoma
- Clear cell adenocarcinoma
- Mucinous adenocarcinoma
- Squamous cell carcinoma
- Mixed carcinoma (specify types and percentages): _____
- Undifferentiated carcinoma
- Other (specify): _____
- Carcinoma, type cannot be determined

Histologic Grade (if applicable)

(Grading system below applies primarily to endometrioid carcinoma)

- Not applicable
- GX: Cannot be assessed
- G1: 5% or less nonsquamous solid growth
- G2: 6% to 50% nonsquamous solid growth
- G3: More than 50% nonsquamous solid growth
- Other (specify): _____

Myometrial Invasion

- No invasion
- Invasion present
 - Specify depth of invasion: ____ mm
 - Specify myometrial thickness: ____ mm

Pathologic Staging (pTNM [FIGO])Primary Tumor (pT)

- ___ pTX [--]: Primary tumor cannot be assessed
- ___ pT0 [--]: No evidence of primary tumor
- ___ pTis [0]: Carcinoma in situ
- pT1 [I]: Tumor confined to corpus uteri
- ___ pT1a [IA]: Tumor limited to endometrium
- ___ pT1b [IB]: Tumor invades less than one-half of the myometrium
- ___ pT1c [IC]: Tumor invades one-half or more of the myometrium
- pT2 [II]: Tumor invades cervix, but does not extend beyond uterus
- ___ pT2a [IIA]: Tumor limited to the glandular epithelium of the endocervix. There is no evidence of connective tissue stromal invasion.
- ___ pT2b [IIB]: Invasion of the stromal connective tissue of the cervix
- pT3 [III]: Local and/or regional spread as specified in T3a and T3b, and FIGO IIIA and IIIB
- ___ pT3a [IIIA]: Tumor involves serosa, parametria, and/or adnexa (direct extension or metastasis)
- * ___ pT3a [IIIA]: Tumor involves serosa and/or adnexa (direct extension or metastasis) and/or cancer cells in ascites or peritoneal washings
- ___ pT3b [IIIB]: Involvement of vagina (direct extension or metastasis), rectal or bladder wall (without mucosal involvement), or pelvic wall(s) (frozen pelvis)
- ___ pT4 [IVA]: Tumor invades bladder mucosa and/or bowel mucosa

Regional Lymph Nodes (pN)

- ___ pNX: Cannot be assessed
- ___ pN0: No regional lymph node metastasis
- ___ pN1 [IIIC]: Regional lymph node metastasis to the pelvic and/or para-aortic lymph nodes
- Specify: Number examined: ___
Number involved: ___

Distant Metastasis (pM)

- ___ pMX: Cannot be assessed
- ___ pM1 [IVB]: Distant metastasis (includes metastasis to abdominal lymph nodes other than para-aortic, and/or inguinal lymph nodes; excludes metastasis to vagina, pelvic serosa, or adnexa)
- *Specify site(s), if known: _____

Margins

- ___ Cannot be assessed
- ___ Uninvolved by invasive carcinoma
- *Distance of invasive carcinoma from closest margin: ___ mm
- *Specify margin: _____
- ___ Involved by invasive carcinoma
- Specify margin(s): _____

* Data elements **with asterisks** are **not required** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

Venous/Lymphatic (Large/Small Vessel) Invasion (V/L)

- Absent
- Present
- Indeterminate

***Additional Pathologic Findings (check all that apply)**

- * None identified
- * Hyperplasia
 - * Simple
 - * Complex (adenomatous)
- * Atypical hyperplasia
 - * Simple
 - * Complex (adenomatous)
- * Other (specify): _____

***Comment(s)**

* Data elements **with asterisks** are **not required** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

Background Documentation

Protocol revision date: January 2005

I. Cytologic Material

A. Clinical Information

1. Patient identification
 - a. Name
 - b. Identification number
 - c. Age (birth date)
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
 - a. Relevant history
 - (1) previous diagnosis, procedure, or treatment (Note **A**)
 - (2) menstrual history, including date of last normal period
 - (3) previous/current pregnancy history
 - (4) exogenous hormones, including type and duration
 - b. Relevant findings (eg, intraoperative, hysteroscopic, radiologic, laboratory)
 - c. Clinical diagnosis
 - d. Procedure
 - (1) cervical smear (see Uterine Cervix protocol for Bethesda 2001 terminology)
 - (2) vaginal pool aspiration
 - (3) endocervical or direct endometrial sampling (specify technique)
 - (4) peritoneal washing
 - (5) fine-needle aspiration (specify and describe site)
 - (6) scraping of diaphragmatic or peritoneal surface (specify if gross lesion present)

B. Macroscopic Examination

1. Specimen
 - a. Unfixed/fixed (specify fixative)
 - b. Number of slides received, if appropriate
 - c. Quantity and appearance of fluid specimens, if appropriate
 - d. Other (eg, cytologic preparation from tissue)
 - e. Results of intraprocedural consultation
2. Material submitted for microscopic evaluation (eg, smear, cytocentrifuge, touch or filter preparation, cell block)
3. Special studies (specify) (eg, cytochemistry, immunocytochemistry, DNA analysis [specify type], morphometry, cytogenetic analysis)

C. Microscopic Evaluation

1. Adequacy of specimen (if unsatisfactory for evaluation, specify reason) (Note **B**)
2. Tumor, if present
 - a. Histologic type of tumor, if possible (Note **C**)
 - b. Other characteristics (eg, degree of differentiation)
3. Additional pathologic findings, if present
4. Results/status of special studies (specify)
5. Comments
 - a. Correlation with intraprocedural consultation, as appropriate
 - b. Correlation with other specimens, as appropriate
 - c. Correlation with clinical information, as appropriate

II. Biopsy and Curettage

A. Clinical Information

1. Patient identification
 - a. Name
 - b. Identification number
 - c. Age (birth date)
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
 - a. Relevant history
 - (1) previous diagnosis, procedure, or treatment (Note A)
 - (2) menstrual history, including date of last normal period
 - (3) previous/current pregnancy history
 - (4) exogenous hormones, including type and duration
 - b. Relevant findings (eg, intraoperative, hysteroscopic, radiologic, laboratory)
 - c. Clinical diagnosis
 - d. Procedure (eg, biopsy, fractional curettage, polypectomy)
 - e. Site of specimen (eg, endometrium, endocervix)

B. Macroscopic Examination

1. Specimen
 - a. Unfixed/fixed (specify fixative)
 - b. Size (if multiple pieces, aggregate dimensions or size range of pieces; distinguish tissue from blood, if possible)
 - c. Results of intraoperative consultation
2. Tumor, if discernible (eg, consistency or necrosis)
 - a. Dimensions
 - b. Other descriptive features
3. Tissue submitted for microscopic evaluation (Note D)
4. Special studies (specify) (eg, estrogen/progesterone receptors, immunohistochemistry, flow cytometry, morphometry, cytogenetic analysis)

C. Microscopic Examination

1. Adequacy of specimen (if inadequate for evaluation, specify reason) (Note E)
2. Tumor
 - a. Histologic type(s) (Note C)
 - b. Histologic grade (Note F)
 - c. Extent (proportion of specimen involved; or dimensions, if small and measurable)
3. Additional pathologic findings, if present
 - a. Hyperplasia (specify type) (Note C)
 - b. Metaplasia(s) (specify type[s])
 - c. Others(s)
4. Results/status of special studies (specify)
5. Comments
 - a. Correlation with intraoperative consultation, as appropriate
 - b. Correlation with other specimens, as appropriate
 - c. Correlation with clinical information, as appropriate

III. Hysterectomy

A. Clinical Information

1. Patient identification
 - a. Name
 - b. Identification number
 - c. Age (birth date)

2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
 - a. Relevant history
 - (1) previous diagnosis, procedure, or treatment (Note **A**)
 - (2) menstrual history, including date of last normal period
 - (3) previous/current pregnancy history
 - (4) exogenous hormones, including type and duration
 - b. Relevant findings (eg, intraoperative, hysteroscopic, radiologic, laboratory)
 - c. Clinical diagnosis
 - d. Procedure (eg, hysterectomy with bilateral salpingo-oophorectomy and pelvic lymph node sampling)

B. Macroscopic Examination

1. Specimen
 - a. Organ(s)/tissue(s) included
 - b. Unfixed/fixed (specify fixative)
 - c. Number of pieces
 - d. Dimensions (3)
 - e. Orientation, if indicated by surgeon
 - f. Results of intraoperative consultation
2. Uterine tumor
 - a. Location (eg, fundus, cornu, isthmus)
 - b. Dimensions (3)
 - c. Descriptive characteristics (eg, exophytic, necrosis)
 - d. Distance from margins
 - e. Estimated extent of invasion (Note **G**)
3. Uninvolved uterus
 - a. Dimensions
 - b. Appearance of the following
 - (1) endometrium
 - (2) myometrium, including thickness
 - (3) serosa
 - (4) cervix
 - c. Additional pathologic findings, if present
4. Fallopian tube(s)
 - a. Tumor, if present
 - (1) dimensions
 - (2) location and relation to uterine tumor
 - b. Resection margins, as appropriate
 - c. Other pathologic findings, if present
5. Ovary(ies)
 - a. Tumor, if present (see Ovary protocol)
 - (1) dimensions
 - (2) location and relation to uterine tumor
 - b. Resection margins, as appropriate
 - c. Other pathologic findings, if present
6. Regional lymph nodes
 - a. Location, if specified by surgeon
 - b. Number at each location
 - c. Descriptive features of grossly involved nodes at each location
7. Other organs and tissues, including biopsy specimens with location specified by surgeon
 - a. Descriptive features

- b. Tumor, if present
 - (1) dimensions
 - (2) location and relation to uterine tumor
- c. Resection margins, as appropriate
- d. Other pathologic findings
- 8. Tissues submitted for microscopic evaluation
 - a. Carcinoma, including section(s) to demonstrate the following
 - (1) deepest invasion of myometrium (see Figure 1)

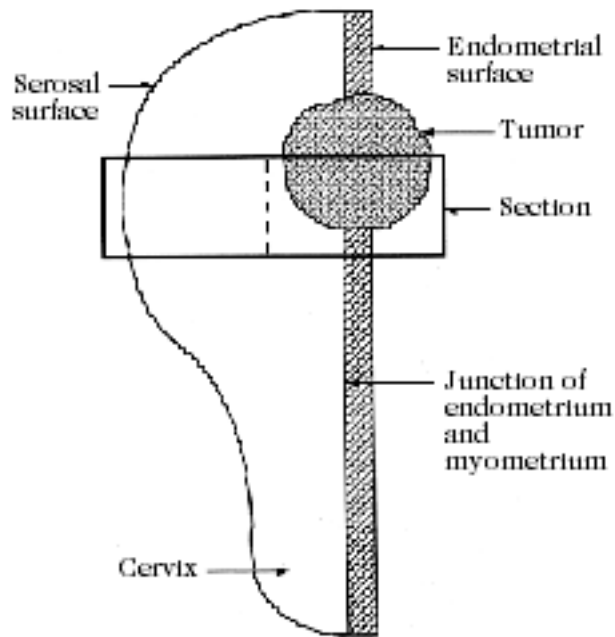


Figure 1. Sample section to demonstrate junction of tumor with adjacent benign endomyometrium and depth of myometrial invasion. If too large, the section may be submitted in 2 parts as indicated by the dotted line.

- (2) distance from serosa (if thickness of myometrium or depth of tumor is not known, extent may be specified as distance in millimeters from the serosa)
- (3) most inferior level of involvement
- (4) interface with adjacent uninvolved endometrium and myometrium
- b. Uninvolved endomyometrium
- c. Cervix, including endocervical and exocervical portions
- d. Resection margin, as appropriate
 - (1) cervical or vaginal
 - (2) parametrial
 - (3) other(s)
- e. Additional uterine lesions, if present
- f. Lymph nodes (at least 1 section of each)
- g. Staging biopsy specimens (1 section of each)
- h. Omentum (several sections if grossly negative; otherwise representative sampling)
- i. Frozen tissue fragment(s) (unless saved for special studies)
- j. Other organs and tissues
 - (1) tumor present, include sections adequate to demonstrate the following
 - i. histologic type and grade of tumor

- ii. relation to uterine tumor and resection margins, if appropriate
 - (2) tumor absent
 - i. routine sections
 - ii. sections through previous site of tumor, if discernible
 - (3) other pathologic lesions, as appropriate
- 9. Special studies (specify) (eg, DNA ploidy, hormone receptors, oncogene evaluation)

C. Microscopic Examination

1. Uterus
 - a. Tumor
 - (1) histologic type (Note **C**)
 - (2) histologic grade (Note **F**)
 - (3) extent of invasion (Note **G**)
 - (4) venous/lymphatic vessel invasion
 - b. Additional pathologic findings, if present
 - (1) hyperplasia and/or endometrial intraepithelial carcinoma (EIC) (particularly associated with serous carcinomas) (Note **C**)
 - (2) adenomyosis, with or without tumor (extension of tumor into adenomyosis is not considered true myometrial invasion, but is reported separately)
 - c. Margins
 - (1) cervical or vaginal
 - (2) parametrial
 - (3) other(s)
2. Regional lymph nodes
 - a. Number at each site (Note **G**)
 - b. Number involved by tumor at each site
 - c. Additional findings (eg, glandular inclusions)
3. Other organs and tissues, including staging biopsy specimens (specify)
 - a. Tumor, if present (Note **G**)
 - (1) histologic type, if different from main tumor
 - (2) histologic grade, if different from main tumor
 - (3) consistent with the following
 - i. direct extension
 - ii. metastasis
 - iii. separate primary tumor
 - (4) site
 - (5) extent
 - (6) relation to resection margins
 - b. Additional pathologic findings, if present
 - c. Results/status of special studies (specify)
4. Comments
 - a. Correlation with intraoperative consultation, as appropriate
 - b. Correlation with other specimens, as appropriate
 - c. Correlation with clinical information, as appropriate

Explanatory Notes

A. Previous Diagnoses

Slides of previous pertinent specimens should be made available to the pathologist if their review is deemed essential by the surgeon or pathologist for optimal interpretation of the present specimen.

B. Adequacy of Cytology Sample for Microscopic Evaluation

If a cytologic sample is procured by a transvaginal procedure other than direct endometrial sampling, the absence of endometrial cells does not signify specimen inadequacy.

C. Histologic Type

The World Health Organization (WHO) Histologic Classification of Endometrial Carcinoma and Hyperplasia¹ is shown as follows.

Carcinoma

- Endometrioid carcinoma
 - Adenocarcinoma
 - Secretory (variant)
 - Ciliated cell (variant)
 - Adenocarcinoma with squamous differentiation
(Adenocarcinoma with squamous metaplasia or morules
[so-called “Adenoacanthoma”])
- Adenosquamous carcinoma (both glandular and squamous components are malignant)
- Serous adenocarcinoma
- Clear cell adenocarcinoma
- Mucinous adenocarcinoma
- Squamous cell carcinoma
- Mixed carcinoma[#]
- Undifferentiated carcinoma

Hyperplasia

- Simple
- Complex (adenomatous)

Atypical Hyperplasia

- Simple
- Complex (adenomatous)

[#] A carcinoma (other than adenocarcinoma with squamous differentiation) in which 1 or more additional types of tumor account for at least 10% of the entire tumor. The diagnosis is optimally made on examination of a hysterectomy specimen, but if only a smaller specimen is available, any amount of a second tumor category suffices for the diagnosis. When a carcinoma is classified as “mixed,” the major and minor types and their relative proportions should be specified.

Criteria Defining Stromal Invasion²:

- (1) Irregular infiltration of glands associated with an altered fibroblastic stroma (desmoplastic response), or
- (2) Confluent glandular pattern (cribriform growth), or
- (3) Extensive papillary growth pattern (at least 4.2 mm in diameter).

Endometrial Intraepithelial Neoplasia

In part arising from poor agreement in the diagnosis of atypical hyperplasia of the endometrium under WHO criteria,³ new diagnostic terminology, “Endometrial Intraepithelial Neoplasia” or EIN, has been proposed. EIN describes a clonal expansion of pre-malignant endometrial glands with endometrioid features, but without invasion. Since clonality determination of endometrial proliferations is not routinely performed in most laboratories, light microscopic guidelines are proposed and are 4-fold.⁴ The lesion must: (1) display architecturally crowded glands whose Volume Percentage Stroma

(VPS) is less than 55%; (2) measure at least 1 to 2 mm in diameter; (3) display altered/demarcated cytology from the background endometrial glands; and (4) not be part of a benign mimic with focal glandular crowding (such as a polyp). It remains to be seen whether the concept of EIN will be adopted into the vernacular of pathology practice, as ideally, such precise assessments of gland-stroma alteration would require morphometric analysis, which is not routinely available in most laboratories.⁵

D. Tissue Submitted for Microscopic Evaluation

All biopsy or curettage tissue is generally submitted, often in an embedding bag. The blood may be removed before submission either with a clean forceps or by gentle washing in saline solution.

E. Adequacy of Biopsy/Curettage Material

It should be noted that adequacy varies both with the procedure (eg, more tissue is expected from a curettage than an outpatient biopsy) and with the diagnosis (eg, atrophic endometrium generally yields scanty specimens, even at curettage). If the tissue obtained is not representative of functioning endometrium (eg, endocervix, lower uterine segment, or surface endometrium only), this fact should be specified.

F. Histologic Grading

The glandular component of all endometrioid carcinomas is graded as follows.¹

Grade X	Cannot be assessed
Grade 1	5% or less nonsquamous solid growth pattern
Grade 2	6% to 50% nonsquamous solid growth pattern
Grade 3	More than 50% nonsquamous solid growth pattern

Notable nuclear atypia inappropriately severe for the architectural grade of the tumor raises the grade of otherwise grade 1 tumors by 1 level.

Comment: Serous, clear cell, and undifferentiated carcinomas are generally considered to be high-grade and need not be graded. No universally accepted criteria exist for grading of mucinous adenocarcinomas, but if graded by the same criteria listed above for endometrioid adenocarcinomas, they are almost all grade 1. The squamous component of endometrioid adenocarcinoma with squamous differentiation generally is not graded.

G. TNM and FIGO Staging of Endometrial Carcinoma

The TNM staging system for endometrial cancer endorsed by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC),⁶⁻⁸ and the parallel system formulated by the International Federation of Gynecology and Obstetrics (FIGO)⁹ are recommended, as shown below.

By AJCC/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, and 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 unfeasible) 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.

Primary Tumor (T)

TNM Category	FIGO Stage	Definition
TX	(--)	Primary tumor cannot be assessed
T0	(--)	No evidence of primary tumor
Tis	0	Carcinoma in situ
T1	I	Tumor confined to corpus uteri
T1a	IA	Tumor limited to endometrium
T1b	IB	Tumor invades less than one-half of the myometrium
T1c	IC	Tumor invades one-half or more of the myometrium
T2	II	Tumor invades cervix but does not extend beyond uterus
T2a	IIA	Tumor limited to the glandular epithelium of the endocervix. There is no evidence of connective tissue stromal invasion
T2b	IIB	Invasion of the stromal connective tissue of the cervix
T3	III	Local and/or regional spread as specified in T3a and T3b, and in FIGO IIIA and IIIB
T3a	IIIA	Tumor involves serosa, and/or adnexa (direct extension or metastasis) and/or cancer cells in ascites or peritoneal washings
T3b	IIIB	Involvement of vagina (direct extension or metastasis), rectal or bladder wall (without mucosal involvement), or pelvic wall(s) (frozen pelvis)
T4 [#]	IVA	Tumor invades bladder mucosa [#] and/or bowel mucosa [#]

[#] Presence of bullous edema is not sufficient evidence to classify a tumor as T4.

Regional Lymph Nodes (N)[#]: TNM Staging System

NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1	IIIC	Regional lymph node metastasis to pelvic and/or para-aortic lymph nodes

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

Distant Metastasis (M): TNM Staging System

MX		Distant metastasis cannot be assessed
M0		No distant metastasis
M1	IVB	Distant metastasis (includes metastasis to abdominal lymph nodes other than para-aortic, and/or inguinal lymph nodes; excludes metastasis to vagina, pelvic serosa, or adnexa)

TNM Stage Groupings

Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage IC	T1c	N0	M0
Stage IIA	T2a	N0	M0
Stage IIB	T2b	N0	M0
Stage IIIA	T3a	N0	M0
Stage IIIB	T3b	N0	M0
Stage IIIC	T1	N1	M0
	T2	N1	M0
	T3a,b	N1	M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	Any N	M1

TNM Descriptors

For identification of special cases of TNM or pTNM classifications, the “m” suffix and “y,” “r,” and “a” 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 (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 prior to 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).

Vessel Invasion

By AJCC/UICC convention, vessel invasion (lymphatic or venous) does not affect the T category indicating local extent of tumor unless specifically included in the definition of a T category. In all other cases, lymphatic and venous invasion by tumor are coded separately as follows.

Lymphatic Vessel Invasion (L)

LX Lymphatic vessel invasion cannot be assessed
 L0 No lymphatic vessel invasion
 L1 Lymphatic vessel invasion

Venous Invasion (V)

VX Venous invasion cannot be assessed
 V0 No venous invasion
 V1 Microscopic venous invasion
 V2 Macroscopic venous invasion

Regional Lymph Nodes (pN0): Isolated Tumor Cells

Isolated tumor cells (ITCs) are single cells or small clusters of cells not more than 0.2 mm in greatest dimension. Lymph nodes or distant sites with ITCs found by either histologic examination (eg, immunohistochemical evaluation for cytokeratin) or nonmorphological techniques (eg, flow cytometry, DNA analysis, polymerase chain reaction [PCR] amplification of a specific tumor marker) should be so identified. There is currently no guidance in the literature as to how these patients should be coded; until further data are available, they should be coded as “N1” with a comment noting how the cells were identified.

References

1. Scully RE, Bonfiglio TA, Kurman RJ, Silverberg SG, Wilkinson EJ. Histological typing of female genital tract tumours. In: *World Health Organization: International Histological Classification of Tumours*. New York: Springer-Verlag; 1994.
2. Kurman RJ, Norris HJ. Evaluation of criteria for distinguishing atypical endometrial hyperplasia from well-differentiated carcinoma. *Cancer*. 1982;2547-2559.
3. Kendall BS, Ronnett BM, Isacson D, et al. Reproducibility of the diagnosis of endometrial hyperplasia, atypical hyperplasia, and well-differentiated carcinoma. *Am J Surg Pathol*. 1998;22(8):1012-1019.
4. Mutter GL. International Society of Gynecological Pathologists Symposium on Endometrial Hyperplasia, I: histopathology of genetically defined endometrial precancers. *Int J Gynecol Pathol*. 2000;19(4):301-309.
5. Zaino RJ. International Society of Gynecological Pathologists Symposium on Endometrial Hyperplasia, III: endometrial hyperplasia - is it time for a quantum leap to a new classification? *Int J Gynecol Pathol*. 2000;19(4):314-321.
6. Greene FL, Page DL, Fleming ID, et al, eds. *AJCC Cancer Staging Manual*. 6th ed. New York: Springer; 2002.
7. Sobin LH, Wittekind C. *UICC TNM Classification of Malignant Tumours*. 6th ed. New York: Wiley-Liss; 2002.
8. Wittekind C, Henson DE, Hutter RVP, Sobin LH, eds. *TNM Supplement. A Commentary on Uniform Use*. 2nd ed. New York: Wiley-Liss; 2001.
9. Creasman W, Odicino F, Maisonneuve P, et al. Carcinoma of the corpus uteri: FIGO Annual Report. *J Epidemiol Biostat*. 2001;6:45-86.