Uterine Cervix

Protocol applies to all invasive carcinomas of the cervix.

Protocol revision date: January 2004
Based on AJCC/UICC TNM, 6th edition
and FIGO 2001 Annual Report

Procedures

- **Cytology** (No Accompanying Checklist)
- **Incisional/Punch Biopsy** (No Accompanying Checklist)
- **Excisional/Cone Biopsy**
- **Hysterectomy**
- **Pelvic Exenteration**

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Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2004
Applies to invasive carcinomas only
Based on AJCC/UICC TNM, 6th edition
and FIGO 2001 Annual Report

UTERINE CERVIX: Cone Biopsy

Patient name:
Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC

Tumor Site
___ Right superior quadrant (12 to 3 o'clock)
___ Right inferior quadrant (3 to 6 o'clock)
___ Left inferior quadrant (6 to 9 o'clock)
___ Left superior quadrant (9 to 12 o'clock)
___ Not specified

MICROSCOPIC

***Tumor Size**
*Dimensions: ___ x ___ x ___ mm
*___ Cannot be determined (see Comment)

Note: all dimensions important; see definition for "microinvasive carcinoma" under T1a1/IA1

Histologic Type (check all that apply)
___ Squamous cell carcinoma
    *___ Keratinizing
    *___ Nonkeratinizing
    *___ Other (specify): _____
___ Adenocarcinoma
    *___ Mucinous
        *___ Endocervical type
        *___ Intestinal type
    *___ Endometrioid
    *___ Clear cell
    *___ Other (specify): _____
___ 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
___ Not applicable
___ GX: Cannot be assessed
___ G1: Well differentiated
___ G2: Moderately differentiated
___ G3: Poorly differentiated
___ G4: Undifferentiated

Stromal Invasion
Depth: ___ mm
Horizontal extent: ___ mm
___ Extent cannot be assessed

Margins (check all that apply)

___ Margins cannot be assessed (eg, obscuring electrocautery artifact)

Endocervical Margin
___ Uninvolved by invasive carcinoma
*Distance of carcinoma from margin: ___ mm
*Specify location, if possible: _____
___ Involved by invasive carcinoma
*Specify location, if possible: _____
*___ Focal
*___ Diffuse
*___ Uninvolved by intraepithelial neoplasia
*___ Involved by intraepithelial neoplasia
*Specify grade: _____

Exocervical Margin
___ Uninvolved by invasive carcinoma
*Distance of carcinoma from margin: ___ mm
*Specify location, if possible: _____
___ Involved by invasive carcinoma
*Specify location, if possible: _____
*___ Focal
*___ Diffuse
*___ Univolved by intraepithelial neoplasia
*___ Involved by intraepithelial neoplasia
*Specify grade: _____

Deep Margin
___ Uninvolved by invasive carcinoma
*Distance of carcinoma from margin: ___ mm
*Specify location, if possible: _____
___ Involved by invasive carcinoma
*Specify location, if possible: _____

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*___ Univolved by intraepithelial neoplasia
*___ Involved by intraepithelial neoplasia
*Specify grade: _____

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

*___None identified
*___ Koilocytosis
*___ Inflammation
*___ Other (specify): _____

***Comment(s)**

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Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2004
Applies to invasive carcinomas only
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and FIGO 2001 Annual Report

UTERINE CERVIX: Colpectomy, Hysterectomy, Pelvic Exenteration

Patient name:
Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC

Specimen Type
___ Colpectomy
___ Hysterectomy
___ Radical hysterectomy
___ Pelvic exenteration
___ Not specified

Tumor Site (check all that apply)
___ Right superior quadrant
___ Right inferior quadrant
___ Left superior quadrant
___ Left inferior quadrant
___ Not specified

Tumor Size
Greatest dimension: ___ cm
*Additional dimensions: ___ x ___ cm
___ Cannot be determined (see Comment)

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Other Organs Present
___ None
___ Right ovary
___ Left ovary
___ Right fallopian tube
___ Left fallopian tube
___ Uterine corpus
___ Vagina
___ Urinary bladder
___ Rectum
___ Other(s) (specify): _____

MICROSCOPIC

Histologic Type (check all that apply)
___ Squamous cell carcinoma
    *___ Keratinizing
    *___ Nonkeratinizing
    *___ Other (specify): _____
___ Adenocarcinoma
    *___ Mucinous
        *___ Endocervical type
        *___ Intestinal type
    *___ Endometrioid
    *___ Clear cell
    *___ Other (specify): _____
___ Other (specify): _____
___ Carcinoma, type cannot be determined

Histologic Grade
___ Not applicable
___ GX: Cannot be assessed
___ G1: Well differentiated
___ G2: Moderately differentiated
___ G3: Poorly differentiated
___ G4: Undifferentiated

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Pathologic Staging (pTNM [FIGO])

Primary Tumor (pT)
___ pTX [--]: Cannot be assessed
___ pT0 [--]: No evidence of primary tumor
___ pTis [0]: Carcinoma in situ
pT1 [I]: Cervical carcinoma confined to uterus (extension to corpus should be disregarded)
___ pT1a [IA]: Invasive carcinoma diagnosed by microscopy only. All macroscopically visible lesions (even with superficial invasion) are pT1b/1B.
___ pT1a1 [IA1]: Stromal invasion 3.0 mm or less in depth and horizontal spread 7.0 mm or less ("microinvasive carcinoma")
___ pT1a2 [IA2]: Stromal invasion more than 3.0 mm but not more than 5.0 mm in depth and horizontal spread 7.0 mm or less
___ pT1b [IB]: Clinically visible lesion confined to the cervix or microscopic lesion greater than T1a2/IA2
___ pT1b1 [IB1]: Clinically visible lesion 4.0 cm or less in greatest dimension
___ pT1b2 [IB2]: Clinically visible lesion more than 4.0 cm in greatest dimension
pT2 [II]: Tumor invades beyond the uterus but not to pelvic wall or to lower third of vagina
___ pT2a [IIA]: Tumor without parametrial invasion
___ pT2b [IIB]: Tumor with parametrial invasion
pT3 [III]: Tumor extends to the pelvic wall and/or involves the lower third of the vagina and/or causes hydronephrosis or nonfunctioning kidney
___ pT3a [IIIA]: Tumor involves lower third of vagina, but not pelvic wall
___ pT3b [IIIB]: Tumor extends to pelvic wall and/or causes hydronephrosis or nonfunctioning kidney
___ pT4 [IVA]: Tumor invades the mucosa of bladder or rectum and/or extends beyond true pelvis (bullous edema is not sufficient evidence to classify a tumor as pT4)
___ pM1[IVB]: Distant metastasis

Regional Lymph Nodes (pN)
___ pNX: Cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: Regional lymph node metastasis
Specify: Number examined: ___
Number involved: ___

Distant Metastasis (pM)
___ pMX: Cannot be assessed
___ pM1 [IVB]: Distant metastasis
*Specify site(s), if known: _____

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Margins (check all that apply)
___ Cannot be assessed
___ Margins uninvolved by invasive carcinoma
Distance of tumor from closest margin: ___ mm
Specify margin , if possible: _____
___ Carcinoma in situ absent at distal margin
___ Carcinoma in situ present at distal margin
___ Margin(s) involved by invasive carcinoma
Specify location(s), if possible: _____
___ Not applicable

***Venous/Lymphatic (Large/Small Vessel) Invasion (V/L)**
*___ Absent
*___ Present
*___ Indeterminate

***Additional Pathologic Findings (check all that apply)**
*___ None identified
*___ Intraepithelial neoplasia (specify type and grade): _____
*___ Other (specify): _____

***Comment(s)**

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Background Documentation

Protocol revision date: January 2004

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 cytologic and histologic diagnoses
      (2) hormones
      (3) pregnant/not pregnant
      (4) use of intrauterine device (IUD)
      (5) in utero diethylstilbestrol (DES) exposure
      (6) previous treatment (eg, radiation therapy, chemotherapy)
   b. Relevant findings (eg, pelvic examination, colposcopy)
   c. Procedure (eg, vaginal pool aspiration, endocervical aspiration, fine-needle aspiration [FNA])
   d. Type(s) or site(s) of specimen(s)

B. Macroscopic Examination

1. Specimen
   a. Unfixed/fixed (specify fixative)
   b. Number of slides received, if appropriate
   c. Other (eg, cytologic preparation from tissue)
   d. Results of intraprocedural consultation
2. Material submitted for microscopic evaluation (eg, smear, touch preparation)
3. Special studies (specify) (eg, immunocytochemistry)

C. Microscopic Evaluation (for complete Pap smear protocol, see Note **A**)

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

II. Incisional or Excisional Biopsy

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 cytologic and histologic diagnoses
      (2) hormones
      (3) pregnant/not pregnant
      (4) use of IUD
      (5) in utero DES exposure
      (6) previous treatment (eg, radiation therapy, chemotherapy)
   b. Procedure (eg, loop electrosurgical excision procedure [LEEP] conization, cervical biopsy, endocervical curettage)
   c. Operative findings
   d. Documentation of orientation of specimen by surgeon, if appropriate (Note **C**)
   e. Type(s) or site(s) of specimen(s)

B. Macroscopic Examination

1. Specimen (Note **C**)
   a. Unfixed/fixed (specify fixative)
   b. Number of pieces, size or size range
   c. Descriptive features
   d. Orientation, if designated by surgeon
   e. Results of intraoperative consultation
2. Tumor
   a. Dimensions, if appropriate
   b. Descriptive features
   c. Additional pathologic findings, if present
3. Tissue submitted for microscopic evaluation (Note **D**)
4. Frozen section tissue fragment(s) (unless saved for special studies)
5. Special studies (specify) (Note **B**)

C. Microscopic Evaluation

1. Tumor
   a. Histologic type (Note **E**)
   b. Histologic grade (optional if squamous; Note **F**)
   c. Extent of tumor (Note **G**)
      (1) noninvasive (intraepithelial)
         i. degree of severity (Note **E**)
      (2) invasive: note depth of invasion (Note **G**)
   d. Venous/lymphatic vessel invasion (Note **H**)
2. Resection margins (Note **I**)
3. Additional pathologic findings, if present (Note **J**)
4. Results/status of special studies (specify) (Note **B**)
5. Comments

a. Correlations 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 cytologic and histologic diagnoses
      (2) hormones
      (3) pregnant/not pregnant
      (4) use of IUD
      (5) in utero DES exposure
      (6) previous treatment (eg, radiation therapy, chemotherapy)
   b. Relevant findings (eg, on pelvic examination, on colposcopy)
   c. Clinical diagnosis
   d. Procedure (eg, hysterectomy, radical hysterectomy with bilateral lymphadenectomy)
   e. Operative findings
   f. Documentation of orientation of specimen by surgeon, if appropriate (Note **C**)
   g. Type(s) or site(s) of specimen(s)

B. Macroscopic Examination

1. Specimen
   a. Organ(s)/tissue(s) included
   b. Unfixed/fixed (specify fixative)
   c. Number of pieces
   d. Dimensions
   e. Orientation, if designated by surgeon
   f. Results of intraoperative consultation
2. Cervix
   a. Tumor, if present
      (1) location (eg, left, endocervix and ectocervix)
      (2) dimensions
      (3) extent (to other tissues and organs)
      (4) distance from all pertinent margins
      (5) descriptive features
   b. Additional pathologic findings, if present
3. Vagina
   a. Dimensions, including length of vaginal cuff
   b. Descriptive features
   c. Tumor, if present
      (1) dimensions

(2) descriptive features
(3) relation to cervical tumor
d. Additional pathologic findings, if present

4. Uterine corpus
   a. Dimensions
   b. Descriptive features of endometrium, myometrium, and serosa
   c. Tumor, if present
      (1) dimensions
      (2) descriptive features
      (3) relation to cervical tumor
   d. Additional pathologic findings, if present
5. Parametria
   a. Amount (Note **K**)
   b. Tumor, if present
      (1) dimensions
      (2) descriptive features
      (3) relation to cervical tumor
   c. Additional pathologic findings, if present
6. Regional lymph nodes
   a. Number at each location, as specified by surgeon
   b. Number involved by tumor
   c. Dimensions of involved nodes
   d. Descriptive features
7. Additional organs and tissues
   a. Tumor, if present
      (1) dimensions
      (2) descriptive features
      (3) relation to cervical tumor
   b. Additional pathologic findings, if present
8. Tissue submitted for microscopic evaluation
   a. No macroscopic tumor, process cervix as a cone biopsy (Note **D**)
   b. Tumor
      (1) one section per centimeter of greatest tumor dimension
      (2) point of deepest invasion (full thickness through cervical wall, if possible)
      (3) interface with adjacent cervix
   c. Grossly uninvolved cervix
   d. Margins of resection
      (1) vagina
      (2) anterior cervix (bladder reflection)
      (3) posterior cervix/vagina (rectovaginal septum)
   e. Uterine corpus
   f. Parametria (right and left) (Note **K**)
   g. Area(s) of special interest marked by surgeon
   h. Lymph nodes (at least 1 section from each hemisected node)
   i. Ovaries and fallopian tubes
   j. Other organs and tissues
   k. Frozen section tissue fragment(s) (unless saved for special studies)
   l. Special studies (specify) (Note **B**)

C. Microscopic Evaluation

1. Tumor
   a. Histologic type (Note **E**)
   b. Histologic grade (optional if squamous) (Note **F**)
   c. Extent of invasion (Note **G**)
      (1) depth and width of invasion in cervix
      (2) extension to vagina, if present (specify extent and depth of invasion)
      (3) extension to corpus uteri, if present (specify extent and depth of invasion)
   d. Venous/lymphatic vessel invasion (Note **H**)
   e. Status of resection margins (Note **I**)
      (1) vaginal
      (2) anterior and posterior cervical
      (3) parametrial
   f. Additional pathologic findings, if present
   g. Results/status of special studies (specify) (Note **B**)
2. Comments
   a. Correlation with intraoperative consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

III. Pelvic Exenteration

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 cytologic and histologic diagnoses
      (2) hormones
      (3) pregnant/not pregnant
      (4) use of IUD
      (5) in utero DES exposure
      (6) previous treatment (eg, radiation therapy, chemotherapy)
   b. Relevant findings (eg, on pelvic examination, on colposcopy)
   c. Clinical diagnosis
   d. Procedure (eg, anterior pelvic exenteration, total pelvic exenteration)
   e. Operative findings
   f. Documentation of orientation of specimen by surgeon, if appropriate (Note **C**)
   g. Type(s) or site(s) of specimen(s)

B. Macroscopic Examination

1. Specimen
   a. Organs/tissues included
   b. Unfixed/fixed (specify fixative)
   c. Number of pieces

d. Dimensions
e. Orientation, if designated by surgeon
f. Results of intraoperarive consultation

2. Cervix
   a. Tumor, if present
      (1) location (eg, left, endocervix/ectocervix)
      (2) dimensions
      (3) extent (to other tissues and organs)
      (4) distance from all pertinent margins
      (5) descriptive features
   b. Additional pathologic findings, if present
3. Vagina
   a. Dimensions, including length of vaginal cuff
   b. Descriptive features
   c. Tumor, if present
      (1) dimensions
      (2) descriptive features
      (3) relation to primary tumor
   d. Additional pathologic findings, if present
4. Uterine corpus
   a. Dimensions
   b. Descriptive features of endometrium, myometrium, and serosa
   c. Tumor, if present
      (1) dimensions
      (2) descriptive features
      (3) relation to cervical tumor
   d. Additional pathologic findings, if present
5. Parametria
   a. Amount (Note **K**)
   b. Tumor, if present
      (1) dimensions
      (2) descriptive features
      (3) relation to cervical tumor
   c. Additional pathologic findings, if present
6. Ovaries
   a. Dimensions
   b. Descriptive features
   c. Tumor, if present
      (1) dimensions
      (2) descriptive features
      (3) relation to cervical tumor
   d. Additional pathologic findings, if present
7. Fallopian tubes
   a. Dimensions
   b. Descriptive features
   c. Tumor, if present
      (1) dimensions
      (2) descriptive features
      (3) relation to cervical tumor

   d. Additional pathologic findings, if present
8. Bladder (Note **L**)
   a. Dimensions
   b. Descriptive features
   c. Tumor, if present
      (1) dimensions
      (2) descriptive features
      (3) depth of invasion into bladder wall
      (4)relation to cervical tumor
   d. Additional pathologic findings, if present
9. Ureter
   a. Dimensions
   b. Descriptive features
   c. Tumor, if present
      (1) dimensions
      (2) descriptive features
      (3) relation to cervical tumor
   d. Additional pathologic findings, if present
10. Rectum (Note **L**)
   a. Dimensions
   b. Descriptive features
   c. Tumor, if present
      (1) dimensions
      (2) descriptive features
      (3) depth of invasion into rectal wall
      (4) relation to cervical tumor
   d. Additional pathologic findings, if present
11. Additional organs and tissues (specify)
   a. Dimensions
   b. Descriptive features
   c. Tumor, if present
      (1) dimensions
      (2) depth of invasion into rectal wall
      (3) relation to cervical tumor
   d. Additional pathologic findings, if present
12. Regional lymph nodes
   a. Number at each location as specified by surgeon
   b. Number involved by tumor
      (1) dimensions of involved nodes
      (2) descriptive features
13. Tissue submitted for microscopic evaluation
   a. No macroscopic tumor, process cervix as a cone biopsy (Note **D**)
   b. Tumor
      (1) one section per centimeter of greatest tumor dimension
      (2) at point of deepest invasion (full thickness through cervical wall, if possible)
      (3) at interface with adjacent cervix
   c. Grossly uninvolved cervix
   d. Margins of resection

(1) vagina
(2) anterior cervix (bladder reflection)
(3) posterior cervix/vagina (rectovaginal septum)
(4) parametria (right and left) (Note **K**)

e. Urinary bladder at site(s) of possible invasion
f. Rectum at site(s) of possible invasion
g. Other tissues at site(s) of possible invasion
h. Area(s) of special interest marked by surgeon
i. Lymph nodes (at least 1 section from each hemisected node)
j. Ovaries and fallopian tubes
k. Other organs and tissues
l. Frozen section tissue fragment(s) (unless saved for special studies)

14. Special studies (specify) (Note **B**)

C. Microscopic Evaluation (Note **E**)

1. Tumor
   a. Histologic type (Note **E**)
   b. Histologic grade (optional if squamous) (Note **F**)
   c. Extent of invasion (Note **G**)
      (1) into vagina (specify extent and depth of invasion)
      (2) into corpus uterus (specify extent and depth of invasion)
      (3) into parametria
      (4) into bladder (specify extent and depth of invasion)
      (5) into rectum (specify extent and depth of invasion)
      (6) other (eg, ovaries, fallopian tubes, ureter[s])
2. Venous/lymphatic vessel invasion (Note **H**)
3. Status of resection margins (Note **I**)
   a. Vaginal
   b. Anterior and posterior cervical
   c. Parametrial
4. Regional lymph nodes
   a. Number at each site
   b. Number involved by tumor at each site
5. Additional pathologic findings, if present
   a. Intraepithelial
   b. Therapy-related
   c. Other
6. Distance metastasis (specify site[s])
7. Results/status of special studies (specify)
8. 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. Cytology Diagnosis

The updated Bethesda System of cytologic classification[1] is strongly recommended for consistency in reporting of “Pap” smears and is shown below. Although other classification systems may be used, the Papanicalaou class designation system is

archaic and not recommended. The Bethesda System has been adopted by most cytology and pathology organizations for the classification of cytologic specimens from the female genital tract. According to this system, the terms “low-grade squamous intraepithelial lesion” (LSIL) and “high-grade squamous intraepithelial lesion” (HSIL) are used to encompass the spectrum of intraepithelial lesions otherwise classified as dysplasia-carcinoma in situ (CIN). Cellular changes characteristic of human papilloma virus (HPV), mild dysplasia, and a combination of both are classified as LSIL; and moderate (CIN 2) and severe dysplasia-carcinoma in situ (CIN 3) are classified as HSIL.

The Bethesda System 2001 Cervical/Vaginal Classification

Negative for Intraepithelial Lesion or Malignancy

Organisms

- *Trichomonas vaginalis*
- Fungal organisms morphologically consistent with *Candida* spp
- Shift in flora suggestive of bacterial vaginosis
- Bacteria morphologically consistent with *Actinomyces* spp
- Cellular changes associated with Herpes simplex virus

Other non-neoplastic findings (optional to report, list not inclusive)

- Reactive cellular changes associated with
  - inflammation (includes typical repair)
  - Intrauterine contraceptive device (IUD)
  - irradiation
- Glandular cells status post hysterectomy
- Atrophy

Other

- Endometrial cells (in a woman greater than or equal to 40 years of age; specify if *“negative for squamous intraepithelial lesion”)*

Epithelial Cell Abnormalities

Squamous Cell

- Atypical squamous cells
  - of undetermined significance (ASC-US)
  - cannot exclude HSIL (ASC-H)
- Low grade squamous intraepithelial lesion (LSIL)
  encompassing: HPV/mild dysplasia/CIN I
- High grade squamous intraepithelial lesion (HSIL)
  encompassing: moderate and severe dysplasia/ CIN2/CIN3/CIS
  - with features suspicious for invasion (if invasion suspected)
- Squamous cell carcinoma

Glandular Cell

- Atypical
  - endocervical cells (NOS or specify in comment)
  - endometrial cells (NOS or specify in comment)
  - glandular cells (NOS or specify in comment)
- Atypical

- endocervical cells, favor neoplastic
- glandular cells, favor neoplastic

• Endocervical Adenocarcinoma *in situ*
• Adenocarcinoma
- endocervical
- endometrial
- extrauterine
- not otherwise specified (NOS)

Other Malignant Neoplasms
Specify

B. Special Studies
Neither DNA ploidy measurements nor determinations of HPV type have been shown to be sufficiently and consistently predictive of the prognosis of cervical carcinoma to become standard practice. However, several studies show promise for so-called "reflex" HPV DNA testing, in which a sample is co-collected for possible HPV DNA testing at the time of the initial screening visit. The sample is tested for HPV only when conventional cytology results are "ASC-US." The utility of routine HPV typing in the management of precursor lesions remains to be clarified; women who are positive for high risk HPV DNA but show no evidence of dysplasia on colposcopic biopsy remain a particular management conundrum.[2]

C. Biopsy Orientation
If the specimen is the product of a cone biopsy or an excisional biopsy, it is desirable for the surgeon to orient the specimen to facilitate assessment of the resection margins.

D. Handling of Cone Biopsy
Cone specimens should have their margins inked and be step-sectioned with orientation by quadrant. For large, unfixed cervical cone specimens, the endocervical margin may be marked with ink and pinned on a cork board with the mucosa facing up. Three hours of fixation before cutting is optimal. The specimen should be sectioned entirely at 1- to 3-mm intervals. Each tissue section may be marked with India ink or a dye such as eosin in order to orient embedding and evaluation of margins. For optimal evaluation, the sections are placed into separate cassettes, which are numbered consecutively.

E. Histologic Type
For consistency in reporting, the histologic classification proposed by the World Health Organization (WHO) is recommended[3]; other classification systems may be used, however.

WHO Histologic Classification of Cervical Carcinoma and Precursor Lesions
Epithelial Tumors and Related Lesions
Squamous lesions
Squamous intraepithelial lesions (dysplasia-carcinoma in situ; cervical intraepithelial neoplasia [CIN])
Mild dysplasia (CIN 1)

- Moderate dysplasia (CIN 2)
- Severe dysplasia (CIN 3)
- Carcinoma in situ (CIN 3)

Squamous cell carcinoma
- Keratinizing
- Nonkeratinizing
- Verrucous
- Warty (condylomatous)
- Papillary
- Lymphoepithelioma-like

Glandular lesions

Glandular intraepithelial lesions
- Dysplasia
- Adenocarcinoma in situ

Adenocarcinoma
- Mucinous
- Endocervical type
- Intestinal type
- Endometrioid
- Clear cell
- Serous
- Mesonephric

Other epithelial tumors
- Adenosquamous carcinoma
- Glassy cell carcinoma
- Adenoid cystic carcinoma
- Adenoid basal carcinoma
- Carcinoid tumor
- Small cell carcinoma
- Undifferentiated carcinoma

F. Histologic Grade

A wide variety of grading systems, including some that evaluate only the extent of cellular differentiation and others that assess additional features such as the appearance of the tumor margin, the extent of inflammatory cell infiltration, and vascular invasion, have been used for squamous cell carcinoma of the cervix. However, there is no consensus emerging from the literature that any of these systems are reproducible or that they provide useful prognostic information. Grading is considered optional at the present time.

For the grading of invasive squamous tumors, it is suggested that 3 grades be used:

GX Cannot be assessed
G1 Well differentiated
G2 Moderately differentiated
G3 Poorly differentiated

In contrast to squamous cell carcinoma, most authors who grade cervical adenocarcinoma on the basis of its architecture (glandular and papillary versus solid areas) and its nuclear features have found the grade to have prognostic value.

G1 Small component of solid growth and mild to moderate nuclear atypia
G2 Intermediate between grades 1 and 3
G3 Solid pattern with severe nuclear atypia

Tumors with no differentiation or minimal differentiation that is discernible only in rare, tiny foci (undifferentiated carcinomas by WHO classification) are categorized as grade 4.

G. Staging

The TNM staging system for cervical cancer endorsed by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC), and the parallel system formulated by the International Federation of Gynecology and Obstetrics (FIGO) are recommended as shown below.[4-6]

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.

TNM Classification and FIGO Staging System for Cervical Carcinoma
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	Cervical carcinoma confined to the uterus (extension to the corpus should be disregarded)
T1a	IA	Invasive carcinoma, diagnosed by microscopy only (all macroscopically visible lesions even those with superficial invasion are pT1b/Stage IB)

T1a1	IA1	Stromal invasion 3.0 mm or less in depth[#] and 7.0 mm or less in horizontal spread ("microinvasive carcinoma")
T1a2	IA2	Measured stromal invasion more than 3.0 mm in depth[#] and not more than 5.0 mm[#] with a horizontal spread 7.0 mm or less
T1b	IB	Clinically visible lesion confined to the cervix or microscopic lesion greater than T1a2/IA2
T1b1	IB1	Clinically visible lesion 4.0 cm or less in greatest dimension
T1b2	IB2	Clinically visible lesion more than 4.0 cm in greatest dimension
T2	II	Tumor invades beyond the uterus but not to pelvic wall or to lower third of vagina
T2a	IIA	Tumor without parametrial invasion
T2b	IIB	Tumor with parametrial invasion
T3	III	Tumor extends to the pelvic wall and/or involves the lower third of the vagina, and/or causes hydronephrosis or nonfunctioning kidney
T3a	IIIA	Tumor involves lower third of vagina, no extension to pelvic wall
T3b	IIIB	Tumor extends to pelvic wall and/or causes hydronephrosis or nonfunctioning kidney
T4[##]	IVA	Tumor invades the mucosa of bladder or rectum and/or extends beyond true pelvis[#]
M1	IVB	Distant metastasis

[#] The depth of invasion is measured from the base of the epithelium, either surface or glandular, from which it originates. The depth of invasion is defined as the measurement of the tumor from the epithelial-stromal junction of the adjacent most superficial epithelial papilla to the deepest point of invasion. Vascular space involvement, either venous or lymphatic, does not alter the staging.

[##] Presence of bullous edema is not sufficient evidence to classify a tumor as T4. The lesion should be confirmed by biopsy.

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

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Regional lymph node metastasis

[#] Regional lymph nodes include paracervical, parametrial, hypogastric (obturator); common, internal and external iliac; presacral and sacral nodes. Metastasis to lymph nodes outside of the regional nodal group is classified as distant metastasis.

Distant Metastasis (M) (TNM Staging System)

MX Distant metastasis cannot be assessed
M0 No distant metastasis
M1 Distant metastasis (excludes peritoneal metastasis)[#]

[#] Classified as stage IVB in the FIGO Staging System.

TNM Stage Groupings

Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
Stage IA1	T1a1	N0	M0
Stage IA2	T1a2	N0	M0
Stage IB	T1b	N0	M0
Stage IB1	T1b1	N0	M0
Stage IB2	T1b2	N0	M0
Stage IIA	T2a	N0	M0
Stage IIB	T2b	N0	M0
Stage IIIA	T3a	N0	M0
Stage IIIB	T1	N1	M0
	T2	N1	M0
	T3a	N1	M0
	T3b	Any N	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 (ITC) are single cells or small clusters of cells not more than 0.2 mm in greatest dimension. Lymph nodes or distant sites with ITC found by either immunohistochemical (eg, cytokeratin) examination or nonmorphological/molecular techniques (eg, flow cytometry, DNA analysis, polymerase chain reaction [PCR] amplification of a specific tumor marker) should be so identified.[7] There is currently no guidance in the literature as to how these patients should be coded (in contradistinction to similar patients with breast carcinoma); until further studies are available, these patients should be coded as “N1,” with a comment noting how the cells were identified.

H. Venous/Lymphatic Vessel Invasion
Many gynecologists feel that the presence of vascular/lymphatic vessel invasion is important because it may change the extent of their surgical treatment. At times, it may be difficult to determine whether vascular/lymphatic vessel invasion is present; in such cases, its presence should be categorized as indeterminate.[8]

I. Resection Margins
Margins can be involved, negative, or indeterminate. If a margin is involved, whether endocervical, ectocervical, deep, or other, it should be specified. If indeterminate, the reason should be specified (eg, cautery artifact in electroexcision specimens may preclude evaluation of the status of the margin). The severity of a precursor lesion (eg, focal or diffuse) involving a resection margin of a cone should be specified.

If an invasive tumor approximates but does not directly involve a resection margin, the distance between the tumor and the margin should be measured in millimeters. If the tumor involves the uterine corpus, a determination of whether the cervix or corpus is the primary site should be made.

J. Absence of Tumor

If no tumor or precursor lesion is present in a cytology or biopsy specimen, the adequacy of the specimen (ie, its content of both glandular and squamous epithelium) should receive comment. The absence of tumor or precursor lesions in resections must always be documented.

K. Examination of Parametria

The parametria may be measured grossly, but their width varies according to the elasticity of the tissue. Careful microscopic examination of the parametria is important for evaluation of the lateral margins and/or soft tissue extension.

L. Examination of Bladder and Rectum

The extent of tumor involvement of the urinary bladder and rectum and the relation of the tumor to the cervical carcinoma should be described. To evaluate these features, the rectum and bladder should be opened, the specimen fixed, and sections taken perpendicular to the mucosa directly overlying the tumor in the cervix or vagina. A method that provides excellent orientation of the tumor to adjacent structures consists of inflation of the urinary bladder and rectum with formalin and fixation of the specimen for several hours. The entire specimen can then be hemisected through the neoplasm, and appropriate sections can be obtained.

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