

Vagina

Protocol applies to all invasive carcinomas of the vagina.

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

Procedures

- **Cytology** (No Accompanying Checklist)
- **Biopsy**
- **Vaginectomy**
- **Radical Vaginectomy**

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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
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and FIGO 2001 Annual Report*

***VAGINA: 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**

* Incisional biopsy

* Other (specify): _____

* Not specified

***Tumor Site**

* Upper third

* Middle third

* Lower third

* Not specified

MICROSCOPIC**Histologic Type (check all that apply)**

* Squamous cell carcinoma

* Adenosquamous carcinoma

* Adenocarcinoma

* Mucinous

* Clear cell

* Not otherwise specified

* Other (specify): _____

* Carcinoma, type cannot be determined

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* 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
- * Other (specify): _____

***Extent of Invasion**

- * Cannot be assessed
- * Stromal invasion (specify if present)
- * Muscle invasion (specify if present)

***Margins**

- * Not applicable
- * Cannot be assessed
- * Uninvolved by tumor
- * Involved by tumor
Specify site: _____

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

- * None identified
- * Dysplasia
- * Condyloma acuminatum
- * Adenosis
- * Other (specify): _____

***Comment(s)**

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Surgical Pathology Cancer Case Summary (Checklist)

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VAGINA: Excisional Biopsy, Resection

Patient name:

Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC**Specimen Type**

- Excisional biopsy
 Partial vaginectomy
 Radical vaginectomy
 Other (specify): _____
 Not specified

Tumor Site (check all that apply)

- Upper third
 * Circumferential
 * Anterior
 * Posterior
 * Left lateral
 * Right lateral
 Middle third
 * Circumferential
 * Anterior
 * Posterior
 * Left lateral
 * Right lateral
 Lower third
 * Circumferential
 * Anterior
 * Posterior
 * Left lateral
 * Right lateral
 Not specified

Tumor Size

Greatest dimension: ___ cm

*Additional dimensions: ___ x ___ cm

 Cannot be determined (see Comment)

- 6 * 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 (check all that apply)**

- Squamous cell carcinoma
 Adenosquamous carcinoma
 Adenocarcinoma
 * Mucinous
 * Clear cell
 * Not otherwise specified
 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
 Other (specify): _____

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

- pTX [--]: Cannot be assessed
 pT0 [--]: No evidence of primary tumor
 pTis [0]: Carcinoma in situ
 pT1 [I]: Tumor confined to vagina
 pT2 [II]: Tumor invades paravaginal tissues but not to pelvic wall
 pT3 [III]: Tumor extends to pelvic wall
 pT4 [IVA]: Tumor invades mucosa of bladder or rectum and/or extends beyond true pelvis

Regional Lymph Nodes (pN)

- pNX: Cannot be assessed
 pN0: No regional lymph node metastasis
 pN1 [III]: Pelvic or inguinal lymph node metastasis (pT1-pT3)
 pN1 [IVA]: Pelvic or inguinal lymph node metastasis (pT4)
 pN1 [IVB]: Pelvic or inguinal lymph node metastasis (pT1-pT4, pM1)
 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 invasive carcinoma from closest margin: ___ mm
 - Specify margin, if possible: _____
 - Carcinoma in situ absent at margin
 - Carcinoma in situ present at margin
- Margin(s) involved by invasive carcinoma
 - Specify margin(s), if possible: _____

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

- * Absent
- * Present
- * Indeterminate

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

- * None identified
- * Dysplasia
- * Condyloma acuminatum
- * Adenosis
- * Other (specify): _____

***Comment(s)**

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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) pregnancy
 - (2) uterine bleeding pattern, if abnormal
 - (3) discharge per vagina
 - (4) previous therapy (eg, hormonal, radiation, chemotherapy)
 - (5) prenatal exposure to diethylstilbestrol (DES) or related synthetic drugs (Note **A**)
 - (6) previous tumors and operations of possible relevance (Note **B**)
 - b. Relevant findings (eg, radiologic studies, laboratory data) (Note **C**)
 - c. Clinical diagnosis
 - d. Operative findings
 - e. Procedure (eg, vaginal pool aspiration, scraping of vaginal surface, fine-needle aspiration)
 - f. 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

1. Adequacy of specimen (if unsatisfactory for evaluation, specify reason)
2. Tumor, if present (Note **D**)
 - a. Histologic type, if possible (Note **E**)
 - b. Other characteristics, as pertinent
3. Additional cytologic 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**(Incisional or Excisional)****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) pregnancy
 - (2) uterine bleeding pattern, if abnormal
 - (3) discharge per vagina
 - (4) previous therapy (eg, hormonal, radiation, chemotherapy)
 - (5) prenatal exposure to diethylstilbestrol (DES) or related synthetic drugs (Note **A**)
 - (6) previous tumors and operations of possible relevance (Note **B**)
 - b. Relevant findings (eg, radiologic studies, laboratory data) (Note **C**)
 - c. Clinical diagnosis
 - d. Operative findings
 - e. Procedure (eg, excisional biopsy, needle biopsy)
 - f. Type(s) or site(s) of specimen(s) (eg, apex, anterior, posterior, lateral wall, upper, middle, lower third)

B. Macroscopic Examination

1. Specimen
 - a. Unfixed/fixed (specify fixative)
 - b. Number of pieces
 - c. Size or size range
 - d. Descriptive features
 - e. Orientation, if designated by surgeon
 - f. Results of intraoperative consultation
2. Tumor
 - a. Dimensions, if appropriate
 - b. Descriptive features
3. Margins, if pertinent
4. Other lesions, if present
5. Submit entire specimen for microscopic evaluation unless otherwise indicated
6. Special studies (specify)

C. Microscopic Evaluation

1. Tumor
 - a. Histologic type (Note **E**)
 - b. Histologic grade (Note **F**)
 - c. Extent, including resection margins, if pertinent
 - d. Other features of possible prognostic or therapeutic significance
2. Additional pathologic findings, if present (specify), and relation to tumor, if pertinent (Note **G**)
 - a. Dysplasia
 - b. Carcinoma in situ
 - c. Condyloma acuminatum
 - d. Adenosis
 - e. Other(s)
3. 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

III. Vaginectomy

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) pregnancy
 - (2) uterine bleeding pattern, if abnormal
 - (3) discharge per vagina
 - (4) previous therapy (eg, hormonal, radiation, chemotherapy)
 - (5) prenatal exposure to diethylstilbestrol (DES) or related synthetic drugs (Note **A**)
 - (6) previous tumors and operations of possible relevance (Note **B**)
 - b. Relevant findings (eg, radiologic studies, laboratory data) (Note **C**)
 - c. Clinical diagnosis
 - d. Operative findings
 - e. Procedure (eg, partial vaginectomy)
 - f. Type(s) or site(s) of specimens

B. Macroscopic Examination

1. Specimen
 - a. Organ/tissue(s) received
 - b. Fixed/unfixed (specify fixative)
 - c. Number of pieces
 - d. Size (length/circumference/thickness)
 - e. Orientation, if indicated by surgeon
 - f. Descriptive features (inner and outer surfaces, wall)
 - g. Results of intraoperative consultation
2. Tumor
 - a. Size
 - b. Descriptive features
3. Margins, if pertinent
4. Additional pathologic findings, if present
5. Tissue(s) submitted for microscopic evaluation
6. Special studies (specify) (eg, staining with Schiller's or Lugol's solution) (Note **H**)

C. Microscopic Examination

1. Tumor
 - a. Histologic type (Note **E**)
 - b. Histologic grade (Note **F**)
 - c. Extent of invasion (Note **I**)
 - d. Resection margins
 - e. Other features of possible prognostic or therapeutic significance

2. Additional pathologic findings, if present, and relation to tumor, if pertinent (Note J)
 - a. Dysplasia
 - b. Carcinoma in situ
 - c. Condyloma acuminatum
 - d. Adenosis
 - e. Other(s)
3. Results/status of special studies
4. Comments
 - a. Correlation with intraoperative consultation, as appropriate
 - b. Correlation with other specimens, as appropriate
 - c. Correlation with clinical information, as appropriate

IV. Radical Vaginectomy

(Hysterectomy, Unilateral or Bilateral Salpingo-Oophorectomy, Lymphadenectomy or Sentinel Lymph Node Biopsy, Removal of Other Organs and Tissues)

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) pregnancy
 - (2) uterine bleeding pattern, if abnormal
 - (3) discharge per vagina
 - (4) previous therapy (eg, hormonal, radiation, chemotherapy)
 - (5) prenatal exposure to diethylstilbestrol (DES) or related synthetic drugs (Note A)
 - (6) previous tumors and operations of possible relevance (Note B)
 - b. Relevant findings (eg, radiologic studies, laboratory data) (Note C)
 - c. Clinical diagnosis
 - d. Operative findings
 - e. Procedure
 - f. Type(s) or site(s) of specimen(s)

B. Macroscopic Examination

1. Specimen
 - a. Organs/tissues received
 - b. Unfixed/fixed (specify fixative)
 - c. Measurements, if appropriate
 - d. Orientation, if indicated by surgeon
 - e. Results of intraoperative consultation
2. Vagina
 - a. Size (length, circumference, thickness)
 - b. Descriptive features (inner and outer surfaces, wall)
 - c. Tumor
 - (1) size
 - (2) descriptive features
 - d. Resection margins, if pertinent
 - e. Additional pathologic findings, if present

3. Uterine cervix
 - a. Descriptive features (Note **J**)
 - (1) appearance of ectocervix
 - (2) appearance of endocervix
 - b. Tumor, if present
 - (1) descriptive features
 - (2) size
 - (3) extent
 - (4) relation to vaginal tumor
 - c. Additional pathologic findings, if present (specify)
4. Uterine corpus
 - a. Descriptive features of endometrium, myometrium, and serosa
 - b. Tumor, if present
 - (1) measurements
 - (2) location
 - (3) relation to main tumor
 - c. Additional pathologic findings, if present (specify)
5. Fallopian tube(s) (Note **K**)
 - a. Descriptive features, including measurements
 - b. Tumor, if present
 - (1) measurements
 - (2) location
 - (3) relation to vaginal tumor
 - c. Additional pathologic findings, if present (specify)
6. Ovary or ovaries
 - a. Descriptive features
 - (1) outer surface
 - (2) sectioned surfaces
 - b. Dimensions
 - c. Tumor, if present
 - (1) measurements
 - (2) location
 - (3) relation to vaginal tumor
 - d. Additional pathologic findings, if present (specify)
7. Regional lymph nodes
 - a. Number and size range at each designated location
 - b. Tumor, if present
 - (1) size
 - (2) descriptive features
 - c. Additional pathologic findings, if present (specify)
8. Other organ (s) or tissue(s) removed
 - a. Type(s)
 - b. Dimensions
 - c. Descriptive features
 - d. Tumor, if present
 - (1) measurements
 - (2) location
 - (3) relation to vaginal tumor
 - e. Other features of possible prognostic or therapeutic significance
9. Tissues submitted for microscopic evaluation (specify)
10. Special studies (specify)

C. Microscopic Evaluation

1. Vagina
 - a. Tumor
 - (1) histologic type (Note **E**)
 - (2) histologic grade (Note **F**)
 - (3) extent of invasion (Note **I**)
 - (4) other features of possible prognostic or therapeutic significance
 - b. Status of resection margins
 - c. Additional pathologic findings, if present, and relation to tumor, if pertinent (Note **G**)
 - (1) dysplasia
 - (2) carcinoma in situ
 - (3) condyloma acuminatum
 - (4) adenosis
2. Uterine cervix (see Cervix protocol if second primary tumor is present)
 - a. Metastatic tumor, if present
 - (1) histologic type (Note **E**)
 - (2) histologic grade (Note **F**)
 - (3) extent of invasion
 - (4) location and relation to vaginal tumor
 - b. Additional pathologic findings, if present, and relation to tumor, if pertinent
 - (1) dysplasia
 - (2) carcinoma in situ
 - (3) condyloma acuminatum
3. Uterine corpus (see Endometrium protocol if separate primary tumor)
 - a. Metastatic tumor, if present
 - (1) histologic type (Note **E**)
 - (2) histologic grade (Note **F**)
 - (3) location and relation to vaginal tumor
 - b. Additional pathologic findings, if present, and relation to tumor, if pertinent
 - c. Portion uninvolved by tumor
4. Fallopian tube(s) (see Fallopian Tube protocol if separate primary)
 - a. Metastatic tumor, if present
 - (1) histologic type (Note **E**)
 - (2) histologic grade (Note **F**)
 - (3) location and relation to vaginal tumor
 - b. Additional pathologic findings, if present
5. Ovary/ovaries (see Ovary protocol if separate primary)
 - a. Metastatic tumor, if present
 - (1) histologic type (Note **E**)
 - (2) histologic grade (Note **F**)
 - (3) location and relation to vaginal tumor
 - b. Additional pathologic findings, if present
6. Regional lymph nodes (Note **I**)
 - a. Location, if designated
 - b. Tumor, if present
 - (1) histologic type, if different from vaginal tumor
 - (2) histologic grade, if different from vaginal tumor
 - c. Additional pathologic findings, if present

7. Other organ(s) or tissue(s) removed (see appropriate protocol for second primary)
 - a. Metastatic tumor, if present (Note I)
 - (1) location, distribution, and extent
 - (2) histologic type, if different from main tumor
 - (3) histologic grade, if different from main tumor
 - b. Resection margins, if applicable
 - c. Additional pathologic findings, if present
8. Results/status of special studies (specify)
9. 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. Prenatal DES Exposure

Prenatal exposure to diethylstilbestrol (DES) or related synthetic drugs were relatively common in the United States and other countries until 1971, when its relation to clear cell adenocarcinomas of the vagina and cervix led to proscription of these drugs by the Food and Drug Administration. From the 1970s to the turn of the 21st century, most patients with clear cell adenocarcinoma of the vagina had a history of DES exposure. As this cohort ages, the diagnosis has been less common, and most women with the diagnosis currently have no DES exposure history. A bimodal age peak for DES-related carcinoma has, however, been recently reported, and therefore a history of this type of prenatal drug exposure should alert the pathologist to the possible presence of those tumors and associated lesions.¹⁻⁴

B. Prior Tumors and Operations

A history of dysplasia, carcinoma in situ or invasive carcinoma of the cervix as well as knowledge of its microscopic features may be essential in the determination whether a subsequent vaginal tumor is a recurrent or new tumor. Also, a history of a carcinoma higher in the female genital tract may influence the interpretation of a neoplasm that is detected in a specimen from the vagina. Prior pathology slides and reports should be obtained and reviewed if a review is deemed essential by the clinician or pathologist for optimal pathologic evaluation of the present specimen.

C. Clinical Findings and DES Exposure

Naked-eye examination, colposcopy, and iodine staining of the cervix and vagina may disclose a variety of changes highly suspicious of prenatal diethylstilbestrol (DES) exposure, such as cervical hypoplasia, pseudopolyp, or coxcomb deformity, and vaginal adenosis or ridge, any of which should alert the pathologist to examine carefully for DES changes.¹⁻⁴

D. Bethesda Classification System of Cervical/Vaginal Cytology

For consistency in reporting, the cytologic classification proposed in The Bethesda System 2001 is recommended.⁵ Although this protocol does not preclude the use of other systems of classification, use of the Papanicolaou class designation system is strongly discouraged.

Cervical/Vaginal Cytology Classification (The Bethesda 2001 System)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)
 - irradiation
- Glandular cells status post hysterectomy
- Atrophy

OtherEpithelial 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/VAIN I
- High grade squamous intraepithelial lesion (HSIL)
 - encompassing: moderate and severe dysplasia/ VAIN2/VAIN3/VACIS
 - with features suspicious for invasion (if invasion suspected)
- Squamous cell carcinoma

Glandular Cell

- Atypical
 - glandular cells (NOS or specify in comment)
 - glandular cells, favor neoplastic
- Adenocarcinoma
 - not otherwise specified (NOS)

Other Malignant Neoplasms

- Specify

[#] Cellular changes of HPV cytopathic effect, previously termed “koilocytosis,” “koilocytotic atypia,” or “condylomatous atypia,” are included in the category of LSIL.

E Histologic Type

The World Health Organization (WHO) classification and nomenclature of vaginal tumors is recommended because of its wide acceptance.⁶

WHO Classification**Precancerous Lesions and Carcinomas of the Vagina (Modified)**

Squamous intraepithelial lesions	Vaginal intraepithelial neoplasia (VAIN)
Mild dysplasia	VAIN 1
Moderate dysplasia	VAIN 2
Severe dysplasia	VAIN 3
Carcinoma in situ	VAIN 3
Squamous cell carcinoma	
Keratinizing	
Nonkeratinizing	
Verrucous	
Warty (condylomatous)	
Atypical adenosis	
Adenocarcinoma	
Clear cell	
Endometrioid	
Mucinous	
Endocervical type	
Intestinal type	
Mesonephric	
Adenosquamous carcinoma	
Adenoid cystic carcinoma	
Adenoid basal carcinoma	
Carcinoid tumor	
Small cell carcinoma	
Undifferentiated carcinoma	

F. Histologic Grade

No specific grading system for vaginal cancers is recommended. For the sake of uniformity, however, it is suggested that 4 grades be used, as shown below, with grades 1 to 3 assigned to carcinomas showing squamous or glandular differentiation while grade 4 (undifferentiated) applied to tumors with no differentiation. Microinvasive carcinoma is not, currently, a recognized entity in the vagina, in contradistinction to the cervix, and the term is therefore not used. Superficially invasive tumors which invade 3 mm or less and which do not manifest lymphovascular invasion (LVI) have a low incidence of lymph node metastasis.⁷

Grade X	Cannot be assessed
Grade 1	Well differentiated
Grade 2	Moderately differentiated
Grade 3	Poorly differentiated
Grade 4	Undifferentiated

G. Other Lesions

Squamous dysplasia or carcinoma in situ, adenocarcinoma in situ, or atypical adenosis, particularly if such changes are at the resection margin, may increase the frequency of recurrent tumor.

H. Staining of Mucosal Surface

Schiller's or Lugol's solutions stain glycogenated epithelium brown. Therefore, they stain glycogenated squamous epithelium and well-glycogenated tumors. The stains are useful in identifying sites of non-staining vaginal adenosis or immature squamous metaplasia of adenosis in patients exposed to diethylstilbestrol (DES), which may not be detectable before staining.

I. TNM and FIGO Stage Groupings

The TNM staging system for vaginal cancer endorsed by the American Joint Committee on Cancer (AJCC) and the International Union against Cancer (UICC),^{8,9} and the parallel system formulated by the International Federation of Gynecology and Obstetrics (FIGO) are recommended.¹⁰

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 and FIGO Staging Systems for Vaginal 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	Tumor confined to vagina
T2	II	Tumor invades paravaginal tissues but not to pelvic wall [#]
T3	III	Tumor extends to pelvic wall
T4	IVA	Tumor invades mucosa of bladder or rectum and/or extends beyond the true pelvis (bullous edema is not sufficient to classify a tumor as T4)
(M1)	IVB	Distant metastasis (excludes peritoneal metastasis)

[#] Pelvic wall is defined as muscle, fascia, neurovascular structures, or skeletal portions of the bony pelvis.

Regional Lymph Nodes (N): TNM

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

Distant Metastasis (M): TNM

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Stage Groupings

AJCC/UICC TNM				FIGO
Stage 0	Tis	N0	M0	Stage 0
Stage I	T1	N0	M0	Stage I
Stage II	T2	N0	M0	Stage II
Stage III	T1	N1	M0	Stage III
	T2	N1	M0	
	T3	N0, N1	M0	
Stage IVA	T4	Any N	M0	Stage IVA
Stage IVB	Any T	Any N	M1	Stage IVB

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: 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 standard histologic examination, immunohistochemical stains (eg, 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 studies are available, they should be coded as “N1” with a comment noting how the cells were identified.

Sentinel Lymph Nodes

The sentinel lymph node is the first node to receive drainage from a primary tumor. There may be more than 1 sentinel node for some tumors. If a sentinel node contains metastatic tumor, it indicates that other more distant nodes may also contain metastatic disease. If sentinel nodes are negative, other regional nodes are less likely to contain metastasis.

J. Cervical Abnormalities

Ectropion (erosion, eversion) of the cervix, which is characterized by the appearance of glandular (columnar) epithelium outside the external os of the cervix, is seen in approximately 90% of women exposed to diethylstilbestrol (DES) in utero (but is often seen in non-exposed women as well). Approximately one-third of patients exposed to DES have 1 or more gross structural abnormalities of the cervix.¹⁻⁴

K. Fallopian Tubes

The fallopian tubes are abnormal in some women exposed to diethylstilbestrol (DES) in the form of hypoplasia or defects demonstrated on hysterosalpingographic examination.³

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