Protocol for the Examination of Excision Specimens From Patients With Primary Carcinoma of the Uterine Cervix

Version: Uterine Cervix Excision 4.2.0.0 **Protocol Posting Date:** August 2019

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

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

Procedure	Description
Excision	
Tumor Type	**Description**
Carcinoma	
Carcinosarcoma	

The following should NOT be reported using this protocol:

Procedure
Resection (consider Uterine Cervix Resection protocol)
Cytologic specimens

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

Tumor Type
Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)
Sarcoma (consider Uterine Sarcoma protocol)

Authors
Uma Krishnamurti, MD, PhD*; Saeid Movahedi-Lankarani, MD*; Debra A. Bell, MD; George G. Birdsong, MD; Charles V. Biscotti, MD; Christopher N. Chapman Jr, MD; Blaise Clarke, MD; Christopher P. Crumm, MD; Farnaz Dadmanesh, MD; Bojana Djordjevic, MD; Alexandra N. Kalof, MD; Dina H. Kandil, MD; Veronica Klepeis, MD, PhD; Teri A. Longacre, MD; Alice Lytwn, MD; Catherine M. McLachlin, MD; Mariana J. Merino, MD; Anthony G. Montag, MD; Sharon L. Mount, MD; Marisa R. Nucci, MD; Christopher N. Otis, MD; Peter J. Rossi, MD; Cornelia Trimble, MD; Zhaolin Xu, MD

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

** Denotes primary author. All other contributing authors are listed alphabetically.*

Summary of Changes

Version 4.2.0.0
Resection and biopsy case summaries separated into discrete cancer protocols

The following was modified:
Stromal Invasion

Surgical Pathology Cancer Case Summary

Protocol posting date: August 2019

UTERINE CERVIX: Excision

Note: This case summary is recommended for reporting excision specimens, but is not required for accreditation purposes. Core data elements are bolded to help identify routinely reported elements.

Select a single response unless otherwise indicated.

Procedure (Note A)
___ Cold knife cone excision
___ Loop electrical excision procedure (LEEP)/large loop excision of the transformation zone (LLETZ)
___ Other (specify): _____
___ Not specified

Tumor Site (select all that apply) (Notes A, B, and C)
___ Left superior (anterior) quadrant (12 to 3 o'clock)
___ Left inferior (posterior) quadrant (3 to 6 o'clock)
___ Right inferior (posterior) quadrant (6 to 9 o'clock)
___ Right superior (anterior) quadrant (9 to 12 o'clock)
___ Other (specify): _____
___ Cannot be determined (explain): _____

Tumor Size (Note B)
Greatest dimension (centimeters): ___ cm
Additional dimensions (centimeters): ___ x ___ cm
___ Cannot be determined (explain): _____

Note: All dimensions are important; see definition for "superficially invasive squamous cell carcinoma" under T1a1/IA1.

Histologic Type (Note C)
___ Squamous cell carcinoma, NOS
___ Squamous cell carcinoma, keratinizing
___ Squamous cell carcinoma, nonkeratinizing
___ Squamous cell carcinoma, basaloid
___ Squamous cell carcinoma, verrucous
___ Squamous cell carcinoma, warty
___ Squamous cell carcinoma, papillary
___ Squamous cell carcinoma, lymphoepithelioma-like
___ Squamous cell carcinoma, squamotransitional
___ Endocervical adenocarcinoma, usual type
___ Mucinous carcinoma, NOS
___ Mucinous carcinoma, intestinal type
___ Mucinous carcinoma, signet-ring cell type
___ Mucinous carcinoma, gastric type
___ Villoglandular carcinoma
___ Endometrioid carcinoma
___ Clear cell carcinoma
___ Serous carcinoma
___ Mesonephric carcinoma
___ Adenocarcinoma admixed with neuroendocrine carcinoma
___ Adenosquamous carcinoma
___ Adenosquamous carcinoma, glassy cell variant
___ Adenoid cystic carcinoma

___ Adenoid basal carcinoma
___ Small cell neuroendocrine carcinoma
___ Large cell neuroendocrine carcinoma
___ Undifferentiated carcinoma
___ Carcinosarcoma
___ Other histologic type not listed (specify): _____
___ Carcinoma, type cannot be determined

Histologic Grade (Note D)
___ G1: Well differentiated
___ G2: Moderately differentiated
___ G3: Poorly differentiated
___ GX: Cannot be assessed
___ Not applicable

Stromal Invasion (Note B)

Depth of Stromal Invasion (millimeters):
___ Specify ___ mm
___ At least ___ mm
___ Cannot be determined (explain): _____

Depth of Stromal Invasion
__ Superficial one-third
__ Middle one-third
__ Deep one-third

Longitudinal Horizontal Extent/Length of Stromal Invasion (if applicable[#]) (millimeters): ___ mm
___ Cannot be determined (explain): _____

Circumferential Horizontal Extent/Width of Stromal Invasion (if applicable[#]) (millimeters): ___ mm
___ Cannot be determined (explain): _____

[#]*Not applicable in larger tumors that can be measured grossly.*

Margins (Note E)[#]

Endocervical Margin (select all that apply)
___ Cannot be assessed (explain): _____
___ Uninvolved by invasive carcinoma
    Distance of invasive carcinoma from margin (millimeters): ___ mm
    Specify location: _____
___ Involved by invasive carcinoma
    Specify location, if possible: _____
___ Uninvolved by intraepithelial neoplasia
___ Involved by high-grade squamous intraepithelial lesion (CIN 2-3)
    Specify location: _____
___ Involved by adenocarcinoma in situ (AIS)
    Specify location: _____

Ectocervical Margin (select all that apply)
___ Cannot be assessed (explain): _____
___ Uninvolved by invasive carcinoma
    Distance of invasive carcinoma from margin (millimeters): ___ mm
    Specify location: _____
___ Involved by invasive carcinoma

Specify location, if possible: _____
___ Uninvolved by intraepithelial neoplasia
___ Involved by high-grade squamous intraepithelial lesion (CIN 2-3)
Specify location: _____
___ Involved by adenocarcinoma in situ (AIS)
Specify location: _____

Deep Margin (select all that apply)
___ Cannot be assessed (explain): _____
___ Uninvolved by invasive carcinoma
Distance of invasive carcinoma from margin (millimeters): ___ mm
Specify location: _____
___ Involved by invasive carcinoma
Specify location, if possible: _____
___ Uninvolved by intraepithelial neoplasia
___ Involved by high-grade squamous intraepithelial lesion (CIN 2-3)
Specify location: _____
___ Involved by adenocarcinoma in situ (AIS)
Specify location: _____

 # Reporting high-grade squamous intraepithelial lesion (CIN 2-3) and/or AIS is not routinely reported if margin is involved by invasive carcinoma.

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

Additional Pathologic Findings (select all that apply)
___ None identified
___ Low-grade squamous intraepithelial lesion (CIN 1)
___ High-grade squamous intraepithelial lesion (CIN 2 or 3)
___ Inflammation
___ Other (specify): _____

Comment(s)

Explanatory Notes

A. Procedure

Specimen 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 (eg, stitch at 12 o'clock). The laterality of the specimen is in reference to the patient's perspective. Clock values refer to the cervix from the viewer's perspective (face on). However, specimens frequently are received without orientation. In these cases, the clock face orientation is designated by the pathologist and is arbitrary.

B. Tumor Size

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.

Tumor Size Measurement

Tumors should be measured in 3 dimensions in all cases, namely the depth of invasion and 2 measurements of horizontal extent (longitudinal/length and circumferential/width). Larger tumors are more accurately measured grossly, while smaller tumors and some larger tumors with a diffusely infiltrative pattern or with marked fibrosis are best measured microscopically. It is best to report only 1 set of tumor measurements based on a correlation of the gross and microscopic features to avoid confusion.

The depth of invasion is measured from its HSIL origin, that is, from the base of the epithelium either surface or glandular that is involved by HSIL to the deepest point of invasion. If the invasive focus or foci are not in continuity with the dysplastic epithelium, the depth of invasion should be measured from the deepest focus of tumor invasion to the base of the nearest dysplastic crypt or surface epithelium. If there is no obvious epithelial origin, the depth is measured from the deepest focus of tumor invasion to the base of the nearest surface epithelium, regardless of whether it is dysplastic or not. In situations where carcinomas are exclusively or predominantly exophytic, there may be little or no invasion of the underlying stroma. These should not be regarded as in situ lesions and the tumor thickness (from the surface of the tumor to the deepest point of invasion) should be measured in such cases. The depth of invasion below the level of the epithelial origin should not be provided in these cases as this may not truly reflect the biological potential of such tumors. If it is impossible to measure the depth of invasion, eg, in ulcerated tumors or in some adenocarcinomas, the tumor thickness may be measured instead, and this should be clearly stated on the pathology report along with an explanation for providing the thickness rather than the depth of invasion.

Horizontal extent: The longitudinal extent (length) of horizontal extent is measured in the superior-inferior plane (ie, from the endocervical to ectocervical aspects of the section), whereas the circumferential extent (width) is measured or calculated perpendicular to the longitudinal axis of the cervix. If the tumor involves only 1 block, the circumferential extent (width) will be 2.5 mm to 3 mm (thickness of 1 block). When more than 1 block is involved, it is the product of the number of consecutive blocks with tumor and thickness of a block.

The LAST definition of superficial invasive squamous cell carcinoma (SISSCA) conforms to T1a1/ FIGO 1A1. The LAST consensus recommends SISCCA to include multifocal disease and that reporting include presence, number, and size of independent multifocal carcinoma, however, no LAST recommendation was made on the methodology to measure multifocal disease. Multifocal tumors should be defined as invasive foci separated by a tissue block within which there is no evidence of invasion or as invasive foci in the same tissue block that are more than 2 mm apart, or as invasive foci on different cervical lips. They recommend that multifocal tumors should be staged based on the largest focus.[1]

References

1. Day E, Duffy S, Bryson G, Syed S, Shanbhag S, Burton K, Lindsay R, Siddiqui N, Millan D: Multifocal FIGO Stage IA1 Squamous Carcinoma of the Cervix: Criteria for Identification, Staging, and its Good Clinical Outcome. *Int J Gynecol Pathol*. 2016 ;35(5):467-74.

C. Histologic Type

For consistency in reporting, the histologic classification proposed by the World Health Organization (WHO) is recommended[1]; 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/cervical intraepithelial neoplasia (SIL/CIN)
  - Low-grade squamous intraepithelial lesion [LSIL])/Mild dysplasia (CIN 1)
  - High-grade squamous intraepithelial lesion [HSIL]/Moderate dysplasia (CIN 2)
  - HSIL/Severe dysplasia (CIN 3)
  - HSIL/Carcinoma in situ (CIS)

Squamous cell carcinoma, NOS
Squamous cell carcinoma, keratinizing
Squamous cell carcinoma, non-keratinizing
Squamous cell carcinoma, basaloid
Squamous cell carcinoma, verrucous
Squamous cell carcinoma, warty
Squamous cell carcinoma, papillary
Squamous cell carcinoma, lymphoepithelioma-like
Squamous cell carcinoma, squamotransitional

Endocervical adenocarcinoma, usual type

Mucinous carcinoma, NOS
Mucinous carcinoma, intestinal type
Mucinous carcinoma, signet-ring cell type
Mucinous carcinoma, gastric type

Villoglandular carcinoma
Endometrioid carcinoma
Clear cell carcinoma
Serous carcinoma
Mesonephric carcinoma
Adenocarcinoma admixed with neuroendocrine carcinoma
Adenosquamous carcinoma
Adenosquamous carcinoma, glassy cell variant
Adenoid cystic carcinoma
Adenoid basal carcinoma
Small cell neuroendocrine carcinoma
Large cell neuroendocrine carcinoma
Undifferentiated carcinoma
Carcinosarcoma

References

2. Kurman RJ, Carcangiu ML, Harrington CS, Young RH, eds. *WHO Classification of Tumors of the Female Reproductive Organs.* Geneva, Switzerland: WHO Press; 2014.

D. 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.

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.[1-3]

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.

References

1. Kosary CL. FIGO stage, histology, histologic grade, age and race as prognostic factors in determining survival for cancers of the female gynecological system: an analysis of 1973-87 SEER cases of cancers of the endometrium, cervix, ovary, vulva, and vagina. *Semin Surg Oncol*. 1994;10:31-46.
2. Baalbergen A, -Ewing-Graham PC, Hop WC, Struijk P, Helmerhorst TJ. Prognostic factors in adenocarcinoma of the uterine cervix. *Gynecol Oncol*. 2004;92:262-267.
3. Takeda N, Sakuragi N, Takeda M, Okamoto K, Kuwabara M, Negishi H, Oikawa M, Yamamoto R, Yamada H, Fujimoto S Multivariate analysis of histopathologic prognostic factors for invasive cervical cancer treated with radical hysterectomy and systematic retroperitoneal lymphadenectomy. *Acta Obstet Gynecol Scand*. 2002;8:1144-1151.

E. Resection Margins

Margins can be involved, negative, or indeterminate for carcinoma. 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 and extent 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.

F. Lymphovascular Invasion

Many gynecologists feel that the presence of vascular/lymphatic vessel invasion is important because it may change the extent of their surgical treatment. Specifically, the Society of Gynecologic Oncology (SGO) differs with the International Federation of Gynecology and Obstetrics (FIGO) in the definition of early invasive carcinoma. The SGO defines such tumors as being invasive to a depth <3 mm, with a width of <7 mm, but most importantly lacking lymphovascular invasion. 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 (cannot be determined).[1]

References

1. Kodama J, Mizutani Y, Hongo A, Yoshinouchi M, Kudo T, Okuda H. Optimal surgery and diagnostic approach of stage IA2 squamous cell carcinoma of the cervix. *Eur J Gynecol Reprod Biol.* 2002;101(2):192-195.