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

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

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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 MeasurementTumors 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 recommended1; 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

1. 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.