

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

**Version:** Uterine Cervix Excision 4.3.0.0

**Protocol Posting Date:** February 2020

## 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 4.3.0.0

**The following data element was modified:**

Extent of Invasion

## Surgical Pathology Cancer Case Summary

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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. The “+” symbol is used to identify non-core subsections that may be combined with core data 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): \_\_\_\_\_

**Horizontal Extent of Stromal Invasion (millimeters)#**

- Not applicable
- Specify \_\_\_ mm
- Estimated as less than or equal to 7 mm  
**Specify Number of Block(s) Involved:** \_\_\_\_\_
- Estimated as greater than 7 mm  
**Specify Number of Block(s) Involved:** \_\_\_\_\_
- Cannot be determined

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

**Pattern of Invasion#**

- Pattern A
- Pattern B
- Pattern C

*#Silva System- applicable only to invasive endocervical adenocarcinomas*

**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

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### 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

According to the 2018 FIGO staging system for all stages the size of the primary tumor can be assessed by clinical evaluation (pre- or intraoperative), imaging, and/or pathological measurement.<sup>1</sup>

The depth of invasion is required for the sub-staging of Stage 1 carcinomas in the latest FIGO staging system (2018)<sup>1</sup> and in the latest AJCC system (2017)<sup>2</sup>. 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: It is only relevant to stage 1 tumors, and larger tumors can be reported as "not applicable". This is no longer used for sub-staging of Stage I carcinomas in the FIGO staging system 2018.<sup>1</sup> However, is still used in the latest AJCC system (2017)<sup>2</sup> and individual clinicians may request a horizontal extent for their practice.

The horizontal extent may be the longitudinal extent (length) measured in the superior-inferior plane (ie, from the endocervical to ectocervical aspects of the section), or it may be the circumferential extent (width) that is measured or calculated perpendicular to the longitudinal axis of the cervix. When a gross lesion is not identified, the accuracy of measuring the horizontal extent may be limited. If the extent is measured on a single glass slide, this may underestimate the true horizontal extent, because the tumor may involve multiple blocks and may have a greater "width" than "length". The thickness of sections of the cervix, which are often taken as "wedges" of a cone may be variable and may range from less than 1mm to greater than 3 mm. In addition, adding thicknesses of adjacent sections where the sections are taken as a cone are measuring the circumference rather than a linear "width". Estimates using a thickness of 2.5 mm to 3 mm may overestimate the true tumor extent.<sup>5</sup> The pathologist should report the maximum horizontal extent (when it on a single block) and where multiple blocks are involved, they should report the number of blocks involved and if it is estimated as less than or equal to 7mm or greater than 7 mm.

The LAST definition of superficial invasive squamous cell carcinoma (SISCCA) 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.<sup>4</sup>

#### Pattern of invasion

Accurately measuring the depth of stromal invasion can be challenging in some endocervical adenocarcinomas. The Silva system of classification<sup>5</sup> stratifies cases of invasive endocervical adenocarcinomas into three groups on the basis of the morphologic pattern of invasion and is predictive of the risk for LN metastasis. Briefly, Pattern A shows well-demarcated glands with rounded contours, frequently forming groups with no destructive stromal invasion, no single cells or cell detachment and no LVI. Complex intraglandular growth such as cribriform or papillary architecture is acceptable but there is no solid growth. Pattern B shows localized (limited, early) destructive stromal invasion. There are individual or small groups of tumor cells, separated from the rounded gland, in a focally desmoplastic or inflamed stroma. There is no solid growth and LVI is  $\pm$ . Pattern C shows diffuse destructive stromal invasion. There are diffusely infiltrative glands with associated extensive desmoplastic response. Growth pattern is confluent or solid and LVI is  $\pm$ . Pattern A cases were all stage I, had negative lymph nodes, and no recurrences. 23.8% of cases with pattern C had lymph node metastases, while pattern B tumors had metastatic lymph nodes rarely.

#### References

1. Bhatla N, Berek JS, Cuello Fredes M, et al. Revised FIGO staging for carcinoma of the cervix uteri. *Int J Gynaecol Obstet.* 2019;145(1):129-135.
2. Amin MB, Edge SB, Greene FL, et al, eds. *AJCC Cancer Staging Manual.* 8th ed. New York, NY: Springer; 2017.
3. McCluggage WG, Judge MJ, Alvarado-Cabrero I, et al. Data Set for the Reporting of Carcinomas of the Cervix: Recommendations From the International Collaboration on Cancer Reporting (ICCR). *Int J Gynecol Pathol.* 2018;37(3):205-228
4. 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.
5. Roma AA, Diaz De Vivar A, Silva EG et al. *Am J Surg Pathol* 2015; 39 (5); 667-672.

#### C. Histologic Type

For consistency in reporting, the histologic classification proposed by the World Health Organization (WHO) is recommended;<sup>1</sup> other classification systems may be used, however.

#### 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.<sup>1-3</sup>

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).<sup>1</sup>

#### 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.