



## Protocol for the Examination of Resection Specimens From Patients With Carcinoma of the Urethra and Periurethral Glands

**Version:** 4.1.0.0

**Protocol Posting Date:** June 2021

**CAP Laboratory Accreditation Program Protocol Required Use Date:** March 2022

The changes included in this current protocol version affect accreditation requirements. The new deadline for implementing this protocol version is reflected in the above accreditation date.

**For accreditation purposes, this protocol should be used for the following procedures AND tumor types:**

Procedure	Description
Resection	Includes specimens designated urethrectomy, radical cystectomy, radical cystoprostatectomy, penectomy, and pelvic exenteration
Tumor Type	Description
Carcinomas	Includes invasive carcinomas of the urinary tract, including urothelial carcinoma and its morphological variants (squamous cell carcinoma, adenocarcinoma, Müllerian carcinoma, neuroendocrine carcinoma, and sarcomatoid carcinoma) <sup>#</sup>

<sup>#</sup> This protocol is recommended for reporting noninvasive urothelial tumors (papillary and flat), but it is not required for accreditation purposes.

**This protocol is NOT required for accreditation purposes for the following:**

Procedure
Biopsy (consider the Urethra Biopsy protocol)
Transurethral resection <sup>#</sup>
Primary resection specimen with no residual cancer (eg, following neoadjuvant therapy)
Cytologic specimens

<sup>#</sup>Transurethral resection of a urethral tumor is NOT considered to be the definitive resection specimen, even though the entire cancer may be removed. A protocol is recommended for reporting such specimens for clinical care purposes, but this is not required for accreditation purposes.

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

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

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

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### **Accreditation Requirements**

This protocol can be utilized for a variety of procedures and tumor types for clinical care purposes. For accreditation purposes, only the definitive primary cancer resection specimen is required to have the core and conditional data elements reported in a synoptic format.

- Core data elements are required in reports to adequately describe appropriate malignancies. For accreditation purposes, essential data elements must be reported in all instances, even if the response is “not applicable” or “cannot be determined.”
- Conditional data elements are only required to be reported if applicable as delineated in the protocol. For instance, the total number of lymph nodes examined must be reported, but only if nodes are present in the specimen.
- Optional data elements are identified with “+” and although not required for CAP accreditation purposes, may be considered for reporting as determined by local practice standards.

The use of this protocol is not required for recurrent tumors or for metastatic tumors that are resected at a different time than the primary tumor. Use of this protocol is also not required for pathology reviews performed at a second institution (ie, secondary consultation, second opinion, or review of outside case at second institution).

### **Synoptic Reporting**

All core and conditionally required data elements outlined on the surgical case summary from this cancer protocol must be displayed in synoptic report format. Synoptic format is defined as:

- Data element: followed by its answer (response), outline format without the paired Data element: Response format is NOT considered synoptic.
- The data element should be represented in the report as it is listed in the case summary. The response for any data element may be modified from those listed in the case summary, including “Cannot be determined” if appropriate.
- Each diagnostic parameter pair (Data element: Response) is listed on a separate line or in a tabular format to achieve visual separation. The following exceptions are allowed to be listed on one line:
  - Anatomic site or specimen, laterality, and procedure
  - Pathologic Stage Classification (pTNM) elements
  - Negative margins, as long as all negative margins are specifically enumerated where applicable
- The synoptic portion of the report can appear in the diagnosis section of the pathology report, at the end of the report or in a separate section, but all Data element: Responses must be listed together in one location

Organizations and pathologists may choose to list the required elements in any order, use additional methods in order to enhance or achieve visual separation, or add optional items within the synoptic report. The report may have required elements in a summary format elsewhere in the report IN ADDITION TO but not as replacement for the synoptic report ie, all required elements must be in the synoptic portion of the report in the format defined above.

### **Summary of Changes**

#### **v 4.1.0.0**

- General Reformatting
- Revised Margins Section
- Revised Lymph Nodes Section
- Added Distant Metastasis Section
- Removed pTX and pNX Staging Classification

## Reporting Template

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**Protocol Posting Date: June 2021**

**Select a single response unless otherwise indicated.**

**CASE SUMMARY: (URETHRA: Resection)**

**Standard(s): AJCC-UICC 8**

### SPECIMEN

- Male anatomy  
 Female anatomy

### Procedure

- Partial urethrectomy  
 Total urethrectomy  
 Urethrectomy with cystectomy  
 Urethrectomy with cystoprostatectomy  
 Urethrectomy with penectomy  
 Anterior exenteration  
 Other (specify): \_\_\_\_\_  
 Not specified

### TUMOR

#### +Tumor Site (select all that apply)

*Male*

- Penile urethra  
 Bulbomembranous urethra  
 Prostatic urethra

*Female*

- Anterior urethra  
 Posterior urethra

*Other*

- Urethra, not otherwise specified: \_\_\_\_\_

#### Histologic Type (Note [A](#)) (select all that apply)

*Urothelial*

- Papillary urothelial carcinoma, noninvasive  
 Papillary urothelial carcinoma, invasive  
 Urothelial carcinoma in situ  
 Urothelial carcinoma, invasive  
 Urothelial carcinoma, nested (including large nested) variant  
 Urothelial carcinoma, microcystic variant  
 Urothelial carcinoma, micropapillary variant  
 Urothelial carcinoma, lymphoepithelioma-like variant  
 Urothelial carcinoma, plasmacytoid / signet ring / diffuse variant  
 Urothelial carcinoma, sarcomatoid variant  
 Urothelial carcinoma, giant cell variant  
 Urothelial carcinoma, poorly differentiated variant  
 Urothelial carcinoma, lipid-rich variant  
 Urothelial carcinoma, clear cell variant

Urothelial carcinoma with squamous differentiation

**+Percentage of Squamous Differentiation**

Specify percentage: \_\_\_\_\_ %

Other (specify): \_\_\_\_\_

Cannot be determined

Urothelial carcinoma with glandular differentiation

**+Percentage of Glandular Differentiation**

Specify percentage: \_\_\_\_\_ %

Other (specify): \_\_\_\_\_

Cannot be determined

Urothelial carcinoma with trophoblastic differentiation

**+Percentage of Trophoblastic Differentiation**

Specify percentage: \_\_\_\_\_ %

Other (specify): \_\_\_\_\_

Cannot be determined

Urothelial carcinoma with Müllerian differentiation

**+Percentage of Müllerian Differentiation**

Specify percentage: \_\_\_\_\_ %

Other (specify): \_\_\_\_\_

Cannot be determined

*Squamous*

Squamous cell carcinoma

Verrucous carcinoma

Squamous cell carcinoma in situ (no invasive carcinoma identified)

*Glandular*

Adenocarcinoma

Adenocarcinoma, enteric

Adenocarcinoma, mucinous

Adenocarcinoma, mixed

Adenocarcinoma in situ (no invasive carcinoma identified)

*Tumors of Müllerian Type*

Clear cell carcinoma

Endometrioid carcinoma

*Neuroendocrine Tumors*

Small cell neuroendocrine carcinoma

**+Percentage of Small Cell Neuroendocrine Component**

Specify percentage: \_\_\_\_\_ %

Other (specify): \_\_\_\_\_

Cannot be determined

Large cell neuroendocrine carcinoma

**+Percentage of Large Cell Neuroendocrine Component**

Specify percentage: \_\_\_\_\_ %

Other (specify): \_\_\_\_\_

Cannot be determined

Well-differentiated neuroendocrine carcinoma

**+Percentage of Well-differentiated Neuroendocrine Component**

Specify percentage: \_\_\_\_\_ %

Other (specify): \_\_\_\_\_

Cannot be determined

*Other*

Other histologic type not listed (specify): \_\_\_\_\_

**+Histologic Type Comment:** \_\_\_\_\_

**Histologic Grade (Note B)**

*For urothelial carcinoma, other variants, or divergent differentiation*

\_\_\_ Low-grade

\_\_\_ High-grade

*For squamous cell carcinoma or adenocarcinoma*

\_\_\_ G1, well-differentiated

\_\_\_ G2, moderately differentiated

\_\_\_ G3, poorly differentiated

\_\_\_ GX, cannot be assessed: \_\_\_\_\_

*Other*

\_\_\_ Other (specify): \_\_\_\_\_

\_\_\_ Cannot be assessed: \_\_\_\_\_

\_\_\_ Not applicable: \_\_\_\_\_

**+Tumor Size**

\_\_\_ Greatest dimension in Centimeters (cm): \_\_\_\_\_ cm

**+Additional Dimension in Centimeters (cm):** \_\_\_ x \_\_\_ cm

\_\_\_ Cannot be determined (explain): \_\_\_\_\_

**Tumor Extent (Note C)**

*Male*

\_\_\_ Carcinoma of penile and bulbomembranous urethra

\_\_\_ Noninvasive papillary urothelial carcinoma

\_\_\_ Carcinoma in situ

\_\_\_ Invades subepithelial connective tissue

\_\_\_ Invades adjacent structure(s)

\_\_\_ Corpus spongiosum

\_\_\_ Periurethral muscle

\_\_\_ Corpus cavernosum

\_\_\_ Bladder wall

\_\_\_ Rectum

\_\_\_ Other (specify): \_\_\_\_\_

\_\_\_ Carcinoma of prostatic urethra

\_\_\_ Carcinoma in situ, involving prostatic urethra

\_\_\_ Carcinoma in situ, involving prostatic ducts

\_\_\_ Invades urethral subepithelial connective tissue immediately underlying the urothelium

\_\_\_ Invades prostatic stroma surrounding ducts either by direct extension from the urothelial surface or by invasion from prostatic ducts

\_\_\_ Invades periprostatic fat

\_\_\_ Invades adjacent structure(s)

\_\_\_ Extraprostatic invasion of the bladder wall

\_\_\_ Rectum

\_\_\_ Other (specify): \_\_\_\_\_

*Female*

\_\_\_ Noninvasive papillary urothelial carcinoma

\_\_\_ Carcinoma in situ

\_\_\_ Invades subepithelial connective tissue

\_\_\_ Invades adjacent structure(s)

\_\_\_ Periurethral muscle (fibromuscular and adipose tissue)

- Anterior vagina
- Bladder wall
- Rectum
- Other (specify): \_\_\_\_\_

*Other*

- Cannot be determined: \_\_\_\_\_
- No evidence of primary tumor

**+Lymphovascular Invasion (Note [D](#))**

- Not identified
- Present
- Cannot be determined: \_\_\_\_\_

**+Tumor Configuration (select all that apply)**

- Papillary
- Solid / nodule
- Flat
- Ulcerated
- Other (specify): \_\_\_\_\_
- Cannot be determined: \_\_\_\_\_

**+Tumor Comment:** \_\_\_\_\_

**MARGINS (Notes [E,F](#))**

**Margin Status for Invasive Carcinoma**

- All margins negative for invasive carcinoma

**+Closest Margin(s) to Invasive Carcinoma (select all that apply)**

- Proximal: \_\_\_\_\_
- Distal: \_\_\_\_\_
- Deep soft tissue: \_\_\_\_\_

*# If the specimen is received unoriented, precluding identification of margins as distal or proximal, it should be denoted here.*

- Other (specify)#: \_\_\_\_\_
- Cannot be determined (explain): \_\_\_\_\_

**+Distance from Invasive Carcinoma to Closest Margin**

*Specify in Millimeters (mm)*

- Exact distance: \_\_\_\_\_ mm
- Greater than: \_\_\_\_\_ mm
- At least: \_\_\_\_\_ mm
- Less than: \_\_\_\_\_ mm
- Less than 1 mm
- Other (specify): \_\_\_\_\_
- Cannot be determined: \_\_\_\_\_

- Invasive carcinoma present at margin

**Margin(s) Involved by Invasive Carcinoma (select all that apply)**

- Proximal: \_\_\_\_\_
- Distal: \_\_\_\_\_
- Deep Soft Tissue: \_\_\_\_\_

*# If the specimen is received unoriented, precluding identification of margins as distal or proximal, it should be denoted here.*

- Other (specify)#: \_\_\_\_\_
- Cannot be determined (explain): \_\_\_\_\_

- Other (specify): \_\_\_\_\_
- Cannot be determined (explain): \_\_\_\_\_
- Not applicable

**Margin Status for Carcinoma in Situ / Noninvasive Urothelial Carcinoma**

- All margins negative for carcinoma in situ / noninvasive urothelial carcinoma
- +Closest Margin(s) to Carcinoma in Situ / Noninvasive Urothelial Carcinoma (select all that apply)**

- Proximal: \_\_\_\_\_
- Distal: \_\_\_\_\_

*# If the specimen is received unoriented, precluding identification of margins as distal or proximal, it should be denoted here.*

- Other (specify)#: \_\_\_\_\_
- Cannot be determined (explain): \_\_\_\_\_

**+Distance from Carcinoma in Situ / Noninvasive Urothelial Carcinoma to Closest Margin**

*Specify in Millimeters (mm)*

- Exact distance: \_\_\_\_\_ mm
- Greater than: \_\_\_\_\_ mm
- At least: \_\_\_\_\_ mm
- Less than: \_\_\_\_\_ mm
- Less than 1 mm
- Other (specify): \_\_\_\_\_
- Cannot be determined: \_\_\_\_\_

- Carcinoma in situ / noninvasive urothelial carcinoma present at margin

**Margin(s) Involved by Carcinoma in Situ / Noninvasive Urothelial Carcinoma (select all that apply)**

- Proximal: \_\_\_\_\_
- Distal: \_\_\_\_\_

*# If the specimen is received unoriented, precluding identification of margins as distal or proximal, it should be denoted here.*

- Other (specify)#: \_\_\_\_\_
- Cannot be determined (explain): \_\_\_\_\_

- Other (specify): \_\_\_\_\_
- Cannot be determined (explain): \_\_\_\_\_
- Not applicable

**+Margin Comment:** \_\_\_\_\_

**REGIONAL LYMPH NODES**

**Regional Lymph Node Status**

- Not applicable (no regional lymph nodes submitted or found)
- Regional lymph nodes present
  - All regional lymph nodes negative for tumor
  - Tumor present in regional lymph node(s)

**Number of Lymph Nodes with Tumor**

- Exact number (specify): \_\_\_\_\_
- At least (specify): \_\_\_\_\_
- Other (specify): \_\_\_\_\_
- Cannot be determined (explain): \_\_\_\_\_

**+Size of Largest Nodal Metastatic Deposit**

*Specify in Centimeters (cm)*

- Exact size: \_\_\_\_\_ cm
- At least: \_\_\_\_\_ cm
- Greater than: \_\_\_\_\_ cm
- Less than: \_\_\_\_\_ cm
- Other (specify): \_\_\_\_\_
- Cannot be determined (explain): \_\_\_\_\_

**+Nodal Site with Largest Metastatic Deposit (specify site):** \_\_\_\_\_

**+Size of Largest Lymph Node with Tumor**

*Specify in Centimeters (cm)*

- Exact size: \_\_\_\_\_ cm
- At least: \_\_\_\_\_ cm
- Greater than: \_\_\_\_\_ cm
- Less than: \_\_\_\_\_ cm
- Other (specify): \_\_\_\_\_
- Cannot be determined (explain): \_\_\_\_\_

**+Largest Lymph Node with Tumor (specify site):** \_\_\_\_\_

**+Extranodal Extension (ENE)**

- Not identified
- Present
- Cannot be determined: \_\_\_\_\_
- Other (specify): \_\_\_\_\_
- Cannot be determined (explain): \_\_\_\_\_

**Number of Lymph Nodes Examined**

- Exact number (specify): \_\_\_\_\_
- At least (specify): \_\_\_\_\_
- Other (specify): \_\_\_\_\_
- Cannot be determined (explain): \_\_\_\_\_

**+Regional Lymph Node Comment:** \_\_\_\_\_

**DISTANT METASTASIS**

**Distant Site(s) Involved, if applicable**

- Not applicable
- Specify site(s): \_\_\_\_\_
- Cannot be determined: \_\_\_\_\_



**PATHOLOGIC STAGE CLASSIFICATION (pTNM, AJCC 8th Edition) (Note [G](#))**

*Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. As per the AJCC (Chapter 1, 8th Ed.) it is the managing physician's responsibility to establish the final pathologic stage based upon all pertinent information, including but potentially not limited to this pathology report.*

**TNM Descriptors (select all that apply)**

- Not applicable: \_\_\_\_\_
- m (multiple primary tumors)
- r (recurrent)
- y (post-treatment)

**pT Category**

For the Male Penile Urethra and Female Urethra

**pT Category**

- pT not assigned (cannot be determined based on available pathological information)
- pT0: No evidence of primary tumor
- pTa: Non-invasive papillary carcinoma
- pTis: Carcinoma \*in situ\*
- pT1: Tumor invades subepithelial connective tissue
- pT2: Tumor invades any of the following: corpus spongiosum, periurethral muscle
- pT3: Tumor invades any of the following: corpus cavernosum, anterior vagina
- pT4: Tumor invades other adjacent organs (invasion of the bladder)

For the Prostatic Urethra

**pT Category**

- pT not assigned (cannot be determined based on available pathological information)
- pT0: No evidence of primary tumor
- pTa: Non-invasive papillary carcinoma
- pTis: Carcinoma \*in situ\* involving the prostatic urethra or periurethral or prostatic ducts without stromal invasion
- pT1: Tumor invades urethral subepithelial connective tissue immediately underlying the urothelium
- pT2: Tumor invades the prostatic stroma surrounding ducts either by direct extension from the urothelial surface or by invasion from prostatic ducts
- pT3: Tumor invades the periprostatic fat
- pT4: Tumor invades other adjacent organs (e.g., extraprostatic invasion of the bladder wall, rectal wall)

**pN Category**

- pN not assigned (no nodes submitted or found)
- pN not assigned (cannot be determined based on available pathological information)
- pN0: No regional lymph node metastasis
- pN1: Single regional lymph node metastasis in the inguinal region or true pelvis [perivesical, obturator, internal (hypogastric) and external iliac], or presacral lymph node
- pN2: Multiple regional lymph node metastasis in the inguinal region or true pelvis (perivesical, hypogastric, obturator, internal and external iliac, or presacral lymph node)

**pM Category (required only if confirmed pathologically)**

- Not applicable - pM cannot be determined from the submitted specimen(s)
- pM1: Distant metastasis

**ADDITIONAL FINDINGS**

**+Associated Epithelial Lesions (Note B) (select all that apply)**

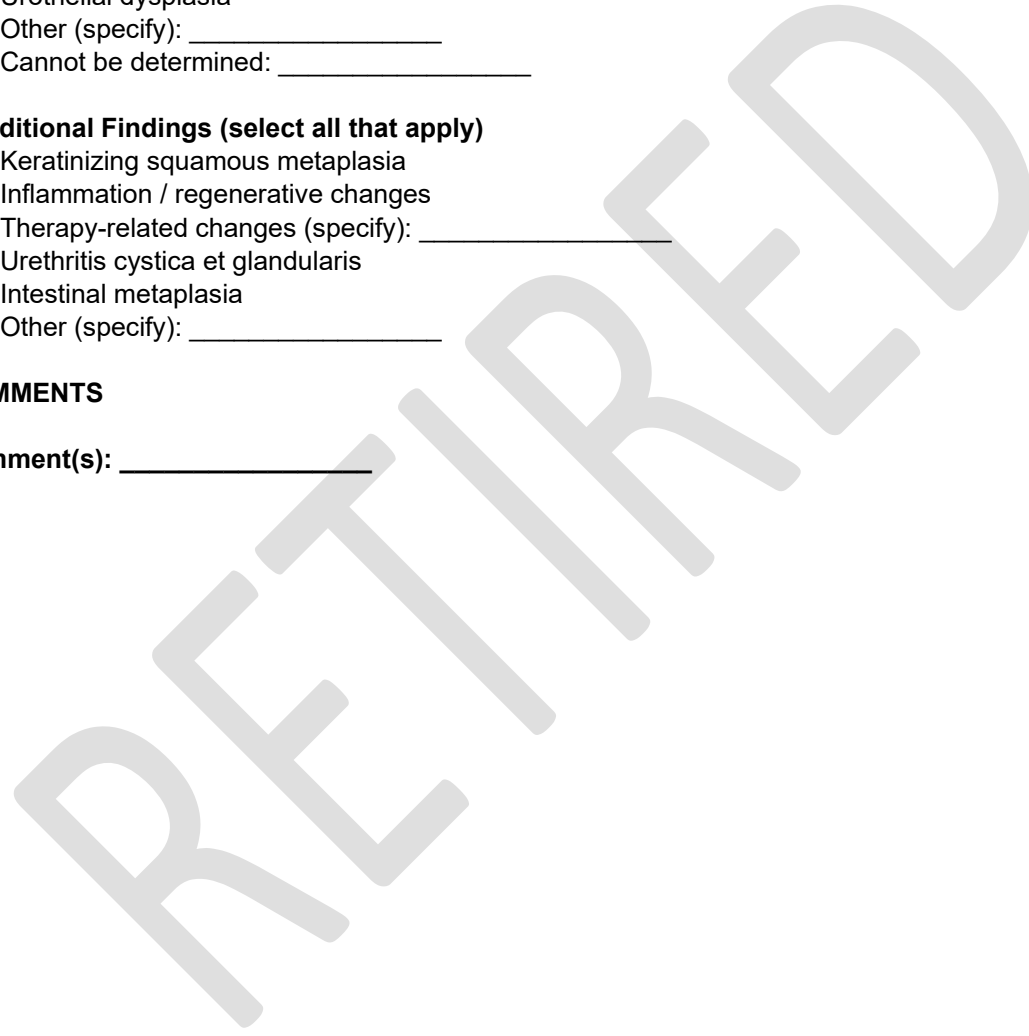
- None identified
- Condyloma
- Squamous dysplasia (low, intermediate, high grade)
- Urothelial papilloma
- Urothelial papilloma, inverted type
- Papillary urothelial neoplasm, low malignant potential (PUNLMP)
- Urothelial proliferation of uncertain malignant potential
- Urothelial dysplasia
- Other (specify): \_\_\_\_\_
- Cannot be determined: \_\_\_\_\_

**+Additional Findings (select all that apply)**

- Keratinizing squamous metaplasia
- Inflammation / regenerative changes
- Therapy-related changes (specify): \_\_\_\_\_
- Urethritis cystica et glandularis
- Intestinal metaplasia
- Other (specify): \_\_\_\_\_

**COMMENTS**

Comment(s): \_\_\_\_\_



## Explanatory Notes

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### A. Histologic Type

Carcinomas of the urethra vary in histologic type, depending on type of epithelium lining the urethra in a given anatomic location.<sup>1,2,3,4</sup> In women, squamous cell carcinoma is the most common histologic subtype (approximately 75%) and is most common in the anterior urethra (distal third). Urothelial carcinoma is next in frequency, followed by adenocarcinoma (approximately 10% to 15% each). Clear cell adenocarcinomas comprise a significant proportion of adenocarcinomas in women but are quite rare in men.<sup>5</sup> In the male, most tumors involve the bulbomembranous urethra, followed by penile urethra and prostatic urethra. Most carcinomas of the male urethra (80%) are squamous cell carcinoma, followed by urothelial origin. As in women, urothelial carcinomas are typically more proximal. Primary urethral adenocarcinomas are rare in men. Adenocarcinomas may rarely arise from the periurethral Skene's (female) or Littre's (male) glands.<sup>4</sup> The distinction between a urothelial carcinoma with divergent squamous, glandular, or Müllerian differentiation and a pure squamous cell carcinoma, adenocarcinoma or Müllerian is rather arbitrary. Most authorities, including the 2016 World Health Organization (WHO) classification, require a pure histology of squamous cell carcinoma, adenocarcinoma, or Müllerian to designate a tumor as such, all others with recognizable papillary, invasive, or flat carcinoma in situ (CIS) urothelial component being considered as urothelial carcinoma with divergent differentiation. A malignant neoplasm with small cell neuroendocrine carcinoma component arising in the urinary tract is designated as small cell carcinoma.<sup>6</sup>

### 2016 WHO Classification of Tumors of the Urothelial Tract

#### Urothelial tumors

##### Infiltrating urothelial carcinoma

- Nested, including large nested
- Microcystic
- Micropapillary
- Lymphoepithelioma-like
- Plasmacytoid/signet ring cell/diffuse
- Sarcomatoid
- Giant cell
- Poorly differentiated

##### Noninvasive urothelial lesions

- Urothelial carcinoma in situ
- Noninvasive papillary urothelial carcinoma, low grade
- Noninvasive papillary urothelial carcinoma, high grade
- Papillary urothelial neoplasm of low malignant potential
- Urothelial papilloma
- Inverted urothelial papilloma

Urothelial proliferation of uncertain malignant potential

Urothelial dysplasia

### **Squamous cell neoplasms**

Squamous cell carcinoma

Verrucous carcinoma

Squamous cell papilloma

### **Glandular neoplasms**

Adenocarcinoma, NOS

Enteric

Mucinous

Mixed

Villous adenoma

Urachal carcinoma

### **Tumors of Mullerian type**

Clear cell carcinoma

Endometrioid carcinoma

### **Neuroendocrine tumors**

Small cell neuroendocrine carcinoma

Large cell neuroendocrine carcinoma

Well differentiated neuroendocrine tumor

Paraganglioma

### **References**

1. Amin MB, Young RH. Primary carcinomas of the urethra. *Semin Diag Pathol.* 1997;14(2):147-160.
2. Reuter V.E. Urethra. In: Bostwick DG, Eble JN, eds. *Urologic Surgical Pathology.* St. Louis, MO: Mosby Year Book, Inc; 1997:223-230.
3. Reuter VE. The urothelial tract: renal pelvis, ureter, urinary bladder and urethra. In: Mills SE, Carter D, Greenson JK, Oberman HA, Reuter VE, Stoler MH, eds. *Sternberg's Diagnostic Surgical Pathology.* 4th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2004:2035-2081.
4. Murphy WM, Grignon DJ, Perlman EJ. Tumors of the kidney, bladder, and related urinary structures. In: *Atlas of Tumor Pathology.* 4th series. Fascicle 1. Washington, DC: American Registry of Pathology; 2004.
5. Oliva E, Young RH. Clear cell adenocarcinoma of the urethra: a clinicopathologic analysis of 19 cases. *Mod Pathol.* 1996;9:513-520.
6. Lopez-Beltran A, Sauter G, Gasser T, et al. Infiltrating urothelial carcinoma. In: Eble JN, Sauter G, Epstein JI, Sesterhenn IA, eds. *World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs.* Lyon, France: IARC Press; 2004:97.

## B. Histologic Grade

Squamous cell carcinoma and adenocarcinoma are graded on a 3-tiered system as well differentiated (grade 1), moderately differentiated (grade 2), or poorly differentiated (grade 3).

For urothelial neoplasia, flat intraepithelial lesions and papillary and invasive lesions are graded separately. Due to variable classification systems and the need for a universally acceptable system, the World Health Organization/International Society of Urological Pathology (WHO/ISUP) consensus classification was proposed and has been adopted in the 2016 WHO classification<sup>1,2</sup> and has been validated by many studies to be prognostically significant. Other systems (that were being used previously) may still be used according to institutional preferences. Tumor grade according to both the WHO/ISUP (1998) system and the older WHO (1973) system may be concurrently used.<sup>3,4</sup>

Flat and papillary urothelial hyperplasia has been renamed as “urothelial proliferation of uncertain malignant potential” in the 2016 WHO classification.

### References

1. Moch H, Humphrey PA, Ulbright TM, Reuter VE. *WHO Classification of Tumours of the Urinary System and Male Genital Organs*. Geneva, Switzerland: WHO Press; 2016.
2. Sauter G, Algaba F, Amin MB, et al. Non-invasive urothelial tumours. In: Eble JN, Sauter G, Epstein JI, Sesterhenn IA, eds. *World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs*. Lyon, France: IARC Press; 2004:110.
3. Epstein JI, Amin MB, Reuter VR, Mostofi FK, the Bladder Consensus Conference Committee. The World Health Organization/ International Society of Urological Pathology Consensus classification of urothelial (transitional cell) neoplasms of the urinary bladder. *Am J Surg Pathol*. 1998;22(12):1435-1448.
4. Mostofi FK. Histological typing of urinary bladder tumours. In: *WHO Histological Classification of Tumours*. No. 10. Geneva, Switzerland: World Health Organization; 1973.

## C. Extent of Invasion

A critical role of the surgical pathologist is to diagnose the depth/extent of invasion into the tissues surrounding the urethra.<sup>1</sup> The surrounding anatomic structures vary by gender and location within the urethra but include the subepithelial connective tissue, corpus spongiosum, corpus cavernosum, prostate, periurethral muscle, extraprostatic soft tissue, anterior vagina, bladder neck, or other adjacent organs. In the prostatic urethra, invasion may arise from a tumor lining the urethral lumen or from carcinoma in situ colonizing prostatic ducts. The pT1 designation should only be applied to superficial invasion arising from the urethral lining; invasion arising from the prostatic ducts is designated as at least pT2.<sup>2</sup> In papillary urothelial tumors, invasion occurs most often at the base of the tumor and less frequently in the stalk.

### References

1. Mostofi FK. Histological typing of urinary bladder tumours. In: *WHO Histological Classification of Tumours*. No. 10. Geneva, Switzerland: World Health Organization; 1973.
2. Amin MB, Edge SB, Greene FL, et al., eds. *AJCC Cancer Staging Manual*. 8th ed. New York, NY: Springer; 2017

## D. Lymphovascular Invasion

Urethral carcinomas may invade blood vessels or lymphatic channels. In suspicious cases, surrounding endothelial cells can be highlighted by immunohistochemical staining for CD31 or CD34 and lymphatic vessel invasion by D2-40.<sup>1,2</sup> Retraction artifact is prominent in invasive urothelial carcinoma, particularly the micropapillary variant, and should be distinguished from vascular space invasion.<sup>3</sup>

## References

1. Ramani P, Birch BR, Harland SJ, et al. Evaluation of endothelial markers in detecting blood and lymphatic channel invasion in pT1 transitional carcinoma of bladder. *Histopathology*. 1991;19(6):551-554.
2. Acs G, Dumoff KL, Solin LJ, et al. Extensive retraction artifact correlates with lymphatic invasion and nodal metastasis and predicts poor outcome in early stage breast carcinoma. *Am J Surg Pathol*. 2007;31(1):129-140.
3. Amin MB, Ro JY, el-Sharkawy T, et al. Micropapillary variant of transitional cell carcinoma of the urinary bladder: histologic pattern resembling ovarian papillary serous carcinoma. *Am J Surg Pathol*. 1994;18(12):1224-1232.

## E. Sections for Microscopic Evaluation

### Urethra

In transurethral specimens, submit 1 section per centimeter of tumor diameter (up to 10 cassettes). If the tumor is noninvasive by the initial sampling, additional submission of tissue (including possibly submitting all tissue) is necessary to diagnose or rule out the presence of invasion. In urethrectomy specimens, submit 1 section per centimeter of tumor, including the macroscopically deepest penetration. Documentation of tumor in relation to surrounding anatomic structures (such as corpus spongiosum, corpus cavernosum, prostate, periurethral muscle, vagina, and bladder) is critical to proper staging. The distal and proximal urethral margins should be submitted (or distal urethra and bilateral ureteral margins if bladder is included), if not evaluated intraoperatively by frozen section. These margins are typically submitted en face in order to see the entire urothelial lining; however, if the tumor is grossly in close proximity to the margin, a perpendicular section showing relationship to ink may be more appropriate. The surrounding radial soft tissue margins should also be submitted, guided by the closest approximation of the tumor to ink by gross evaluation.

### Lymph Nodes

Submit 1 section from each grossly positive lymph node. The size of grossly positive lymph nodes should be carefully recorded, especially if only representative sections are submitted that do not account for the largest dimension. All other lymph nodes should be entirely submitted, as presence of nodal disease may be used as an indication for adjuvant therapy.

### Other Tissues

Submit 1 or more sections of other organs included in the resection. If the tumor grossly appears to invade the prostate, uterus, bladder, or vagina, sections should be targeted, such that the relationship of the infiltrating tumor in the urethra and the adjacent viscus is clearly demonstrable. Submit several sections of the urinary bladder mucosa remote from the carcinoma, especially if abnormal, including the lateral wall(s), dome, and trigone, because urothelial neoplasia is frequently multifocal. One section from each ureteral margin should be submitted if not evaluated by frozen section. Representative sections of the peripheral zone, central zone, and seminal vesicles should be included because concomitant prostatic adenocarcinoma is not uncommon. The gross examination may help target sampling of selective abnormal-appearing areas.

## F. Margins

Resection margins, including those mentioned in Note D, should be carefully specified. Whether the margin is submitted en face or perpendicular to the inked surface should be clearly stated in the block summary.

### **G. Pathologic Stage Classification**

The TNM Staging System for carcinomas of the urethra of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) is recommended.<sup>1</sup>

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.

#### **Primary Tumor (T)**

The suffix “m” should be added to the appropriate T category to indicate multiple tumors. The suffix “is” may be added to any T to indicate the presence of associated carcinoma in situ.

#### **TNM Descriptors**

For identification of special cases of TNM or pTNM classifications, the “m” suffix and “y” and “r” 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.

#### **References**

1. Amin MB, Edge SB, Greene FL, et al., eds. *AJCC Cancer Staging Manual*. 8th ed. New York, NY: Springer; 2017