COLLEGE of AMERICAN PATHOLOGISTS

Protocol for the Examination of Specimens From Patients With Carcinoma of the Urethra

Protocol applies to invasive carcinomas and carcinoma in situ.

Based on AJCC/UICC TNM, 7th edition
Protocol web posting date: October 2013

Procedures

- Urethral Biopsy, Transurethral Resection Specimen
- Urethrectomy (Partial, Total)
  - With Radical Cystoprostatectomy
  - With Radical Cystectomy
  - With Penectomy
  - With Pelvic Exenteration

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The College of American Pathologists offers these protocols to assist pathologists in providing clinically useful and relevant information when reporting results of surgical specimen examinations of surgical specimens. The College regards the reporting elements in the "Surgical Pathology Cancer Case Summary" portion of the protocols as essential elements of the pathology report. However, the manner in which these elements are reported is at the discretion of each specific pathologist, taking into account clinician preferences, institutional policies, and individual practice.

The College developed these protocols as an educational tool to assist pathologists in the useful reporting of relevant information. It did not issue the protocols for use in litigation, reimbursement, or other contexts. Nevertheless, the College recognizes that the protocols might be used by hospitals, attorneys, payers, and others. Indeed, effective January 1, 2004, the Commission on Cancer of the American College of Surgeons mandated the use of the required data elements of the protocols as part of its Cancer Program Standards for Approved Cancer Programs. Therefore, it becomes even more important for pathologists to familiarize themselves with these documents. At the same time, the College cautions that use of the protocols other than for their intended educational purpose may involve additional considerations that are beyond the scope of this document.

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CAP Urethra Protocol Revision History

Version Code
The definition of the version code can be found at www.cap.org/cancerprotocols.

Version: Urethra 3.2.1.0

Summary of Changes
The following changes have been made since the June 2012 release.

Biopsy

Tumor Type
A reporting element for tumor type was added, as follows:

+ Tumor Type
+ ___ Invasive carcinoma
+ ___ Noninvasive carcinoma
+ ___ Carcinoma in situ

Total Urethrectomy; Cystectomy, Cystoprostatectomy; Anterior Exenteration

Tumor Type
A reporting element for tumor type was added, as follows:

Tumor Type
___ Invasive carcinoma
___ Noninvasive carcinoma
___ Carcinoma in situ

Surgical Pathology Cancer Case Summary

Protocol web posting date: October 2013

URETHRA: Biopsy (Note A)

Note: Use of case summary for biopsy specimens is optional.

Select a single response unless otherwise indicated.

+ Specimen
+ ___ Urethra
+ ___ Other (specify): _____
+ ___ Not specified

+ Tumor Site (select all that apply)

+ Male
+ ___ Penile
+ ___ Bulbomembranous
+ ___ Prostatic
+ ___ Cannot be determined

+ Female
+ ___ Anterior
+ ___ Posterior
+ ___ Cannot be determined

+ Tumor Type
+ ___ Invasive carcinoma
+ ___ Noninvasive carcinoma
+ ___ Carcinoma in situ

+ Histologic Type (Note B)
+ ___ Squamous cell carcinoma, typical
+ ___ Squamous cell carcinoma, variant histology (specify): _____
+ ___ Urothelial (transitional cell) carcinoma
+ ___ Urothelial (transitional cell) carcinoma with squamous differentiation
+ ___ Urothelial (transitional cell) carcinoma with glandular differentiation
+ ___ Urothelial (transitional cell) carcinoma with variant histology (specify): _____
+ ___ Adenocarcinoma, typical
+ ___ Adenocarcinoma, variant histology (specify): _____
+ ___ Small cell carcinoma
+ ___ Undifferentiated carcinoma (specify): _____
+ ___ Mixed cell type (specify): _____
+ ___ Other (specify): _____
+ ___ Carcinoma, type cannot be determined

+ Associated Epithelial Lesions (select all that apply) (Note C)
+ ___ None identified
+ ___ Condyloma
+ ___ Squamous dysplasia (low, intermediate, high grade)
+ ___ Urothelial (transitional cell) papilloma
+ ___ Urothelial (transitional cell) papilloma, inverted type
+ ___ Papillary urothelial (transitional cell) neoplasm, low malignant potential
+ ___ Cannot be determined

+ Histologic Grade (select all that apply) (Note C)
+ ___ Not applicable
+ ___ Cannot be determined
+ ___ Urothelial carcinoma
    + ___ Low-grade
    + ___ High-grade
    + ___ Other (specify): _____
+ ___ Squamous cell carcinoma or adenocarcinoma
    + ___ GX: Cannot be assessed
    + ___ G1: Well differentiated
    + ___ G2: Moderately differentiated
    + ___ G3: Poorly differentiated
    + ___ Other (specify): _____
+ ___ Other carcinoma
    + ___ Low-grade
    + ___ High-grade
    + ___ Other (specify): _____

+ Microscopic Tumor Extension (select all that apply) (Note D)
+ ___ Cannot be assessed
+ ___ No evidence of primary tumor
+ ___ Primary tumor (male and female) (excluding urothelial carcinoma of prostate)
    + ___ Noninvasive papillary, polypoid, or verrucous carcinoma
    + ___ Carcinoma in situ
    + ___ Tumor invades subepithelial connective tissue
    + ___ Tumor invades adjacent structures
        + ___ Corpus spongiosum
        + ___ Prostate
        + ___ Periurethral muscle
        + ___ Corpus cavernosum
        + ___ Beyond prostatic capsule
        + ___ Anterior vagina
        + ___ Bladder neck
        + ___ Other (specify): _____
+ ___ Urothelial (transitional cell) carcinoma of the prostate
    + ___ Carcinoma in situ, involvement of the prostatic urethra
    + ___ Carcinoma in situ, involvement of the prostatic ducts
    + ___ Tumor invades urethral subepithelial connective tissue
    + ___ Tumor invades adjacent structures
        + ___ Prostatic stroma
        + ___ Corpus spongiosum
        + ___ Periurethral muscle
        + ___ Corpus cavernosum

+ Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

+ ___ Beyond prostatic capsule
+ ___ Bladder neck (extraprostatic extension)
+ ___ Other (specify): _____

+ Tumor Configuration (select all that apply)

+ ___ Papillary
+ ___ Solid/nodule
+ ___ Flat
+ ___ Ulcerated
+ ___ Indeterminate
+ ___ Other (specify): _____

+ Pathologic Staging (pTNM) (Notes D and E)

+ Primary Tumor (pT) (male and female)
+ ___ pTX: Cannot be assessed
+ ___ pT0: No evidence of primary tumor
+ ___ pTa: Noninvasive carcinoma
+ ___ pTis: Carcinoma in situ
+ ___ pT1: Tumor invades subepithelial connective tissue
+ ___ pT2: Tumor invades any of the following: corpus spongiosum, prostate, periurethral muscle
+ ___ pT3: Tumor invades any of the following: corpus cavernosum, beyond prostatic capsule, anterior vagina, bladder neck

+ Primary Tumor (pT) (urothelial [transitional cell] carcinoma of the prostate)
+ ___ pTX: Cannot be assessed
+ ___ pT0: No evidence of primary tumor
+ ___ pTa: Noninvasive papillary, polypoid, or verrucous carcinoma
+ ___ pTis pu: Carcinoma in situ, involvement of prostatic urethra
+ ___ pTis pd: Carcinoma in situ, involvement of prostatic ducts
+ ___ pT1: Tumor invades subepithelial connective tissue (only applied to tumors invading from the urethral lumen)
+ ___ pT2: Tumor invades any of the following: prostatic stroma, corpus spongiosum, periurethral muscle
+ ___ pT3: Tumor invades any of the following: corpus cavernosum, beyond prostatic capsule, bladder neck (extraprostatic extension)

+ Additional Pathologic Findings (select all that apply)

+ ___ Keratinizing squamous metaplasia
+ ___ Urothelial dysplasia (low-grade intraurothelial neoplasia)
+ ___ Inflammation/regenerative changes
+ ___ Therapy-related changes
+ ___ Cautery artifact
+ ___ Urethritis cystica et glandularis
+ ___ Intestinal metaplasia
+ ___ Other (specify): _____

+ Comment(s)

Surgical Pathology Cancer Case Summary

Protocol web posting date: October 2013

URETHRA: Partial or Total Urethrectomy; Cystectomy, Cystoprostatectomy; Anterior Exenteration

Select a single response unless otherwise indicated.

Specimen
___ Urethra
___ Other (specify): _____
___ Not specified

Procedure
___ Partial urethrectomy
___ Total urethrectomy
___ Urethrectomy with cystectomy
___ Urethrectomy with cystoprostatectomy
___ Urethrectomy with penectomy
___ Anterior exenteration
___ Other (specify): _____
___ Not specified

+ Tumor Site (select all that apply)

+ Male
+ ___ Penile
+ ___ Bulbomembranous
+ ___ Prostatic
+ ___ Cannot be determined

+ Female
+ ___ Anterior
+ ___ Posterior
+ ___ Cannot be determined

Tumor Size
Greatest dimension: ___ cm
+ Additional dimensions: __x___ cm
___ Cannot be determined (see Comment)

Tumor Type
___ Invasive carcinoma
___ Noninvasive carcinoma
___ Carcinoma in situ

Histologic Type (Note B)

___ Squamous cell carcinoma, typical
___ Squamous cell carcinoma, variant histology (specify): _____
___ Urothelial (transitional cell) carcinoma
___ Urothelial (transitional cell) carcinoma with squamous differentiation
___ Urothelial (transitional cell) carcinoma with glandular differentiation
___ Urothelial (transitional cell) carcinoma with variant histology (specify): _____
___ Adenocarcinoma, typical
___ Adenocarcinoma, variant histology (specify): _____
___ Small cell carcinoma
___ Undifferentiated carcinoma (specify): _____
___ Mixed cell type (specify): _____
___ Other (specify): _____
___ Carcinoma, type cannot be determined

+ Associated Epithelial Lesions (select all that apply) (Note C)

+ ___ None identified
+ ___ Condyloma
+ ___ Squamous dysplasia (low, intermediate, high grade)
+ ___ Urothelial (transitional cell) papilloma
+ ___ Urothelial (transitional cell) papilloma, inverted type
+ ___ Papillary urothelial (transitional cell) neoplasm, low malignant potential
+ ___ Cannot be determined

Histologic Grade (select all that apply) (Note C)

___ Not applicable
___ Cannot be determined
___ Urothelial carcinoma
    ___ Low-grade
    ___ High-grade
    ___ Other (specify): _____
___ Squamous cell carcinoma or adenocarcinoma
    ___ GX: Cannot be assessed
    ___ G1: Well differentiated
    ___ G2: Moderately differentiated
    ___ G3: Poorly differentiated
    ___ Other (specify): _____
___Other carcinoma
    ___ Low-grade
    ___ High-grade
    ___ Other (specify): _____

+ Tumor Configuration (select all that apply)

+ ___ Papillary
+ ___ Solid/nodule
+ ___ Flat
+ ___ Ulcerated
+ ___ Indeterminate
+ ___ Other (specify): _____

+ Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

Microscopic Tumor Extension (select all that apply) (Note D)

___ Cannot be assessed
___ No evidence of primary tumor
___ Primary tumor (male and female) (excluding urothelial carcinoma of prostate)
    ___ Noninvasive papillary, polypoid, or verrucous carcinoma
    ___ Carcinoma in situ
    ___ Tumor invades subepithelial connective tissue
    ___ Tumor invades adjacent structures
        ___ Corpus spongiosum
        ___ Prostate
        ___ Periurethral muscle
        ___ Corpus cavernosum
        ___ Beyond prostatic capsule
        ___ Anterior vagina
        ___ Bladder neck
        ___ Bladder wall
        ___ Rectum
        ___ Other (specify): _____
___ Urothelial (transitional cell) carcinoma of the prostate
    ___ Carcinoma in situ, involvement of the prostatic urethra
    ___ Carcinoma in situ, involvement of the prostatic ducts
    ___ Tumor invades urethral subepithelial connective tissue
    ___ Tumor invades adjacent structures
        ___ Prostatic stroma
        ___ Corpus spongiosum
        ___ Periurethral muscle
        ___ Corpus cavernosum
        ___ Beyond prostatic capsule
        ___ Bladder neck (extraprostatic extension)
        ___ Bladder wall
        ___ Rectum
        ___ Other (specify:) _____

Margins (select all that apply) (Notes F and G)

___ Cannot be assessed
___ Margin(s) involved by invasive carcinoma
    ___ Proximal mucosal margin
    ___ Distal mucosal margin
    ___ Deep soft tissue margin
    ___ Other margin(s) (specify)#: _____
___ Margins(s) involved by carcinoma in situ/noninvasive high-grade urothelial carcinoma
    ___ Proximal mucosal margin
    ___ Distal mucosal margin
    ___ Other margin(s) (specify)#: _____

+ Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

___ Margins uninvolved by invasive carcinoma/carcinoma in situ/noninvasive high-grade urothelial carcinoma
+ Distance of carcinoma from closest margin: ___ mm
+ Specify margin#: _____
+ Other significant changes at margin (specify margin)#: _____
+ ___ Low-grade dysplasia
+ ___ Noninvasive low-grade urothelial carcinoma

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

+ Lymph-Vascular Invasion (Note H)

+ ___ Not identified
+ ___ Present
+ ___ Indeterminate

Pathologic Staging (pTNM) (Notes D and E)

TNM Descriptors (required only if applicable) (select all that apply)
___ m (multiple primary tumors)
___ r (recurrent)
___ y (posttreatment)

Primary Tumor (pT) (male and female)
___ pTX: Cannot be assessed
___ pT0: No evidence of primary tumor
___ pTa: Noninvasive papillary, polypoid, or verrucous carcinoma
___ pTis: Carcinoma in situ
___ pT1: Tumor invades subepithelial connective tissue
___ pT2: Tumor invades any of the following: corpus spongiosum, prostate, periurethral muscle
___ pT3: Tumor invades any of the following: corpus cavernosum, beyond prostatic capsule, anterior vagina, bladder neck
___ pT4: Tumor invades other adjacent organs (invasion of the bladder)

Primary Tumor (pT) (urothelial [transitional cell] carcinoma of the prostate)
___ pTX: Cannot be assessed
___ pT0: No evidence of primary tumor
___ pTa: Noninvasive papillary, polypoid, or verrucous carcinoma
___ pTis pu: Carcinoma in situ, involvement of prostatic urethra
___ pTis pd: Carcinoma in situ, involvement of prostatic ducts
___ pT1: Tumor invades subepithelial connective tissue (only applied to tumors invading from the urethral lumen)#
___ pT2: Tumor invades any of the following: prostatic stroma, corpus spongiosum, periurethral muscle
___ pT3: Tumor invades any of the following: corpus cavernosum, beyond prostatic capsule, bladder neck (extraprostatic extension)
___ pT4: Tumor invades other adjacent organs (invasion of the bladder)

 # Tumors invading directly from prostatic ducts colonized by carcinoma in-situ are designated as at least pT2, regardless of depth or extent of invasion (ie, there is no pT1 category in that setting).

Regional Lymph Nodes (pN)
___ pNX: Cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: Metastasis in a single lymph node 2 cm or less in greatest dimension
___ pN2: Metastasis in a single lymph node more than 2 cm in greatest dimension, or in multiple nodes

___ No nodes submitted or found

Number of Lymph Nodes Examined
Specify: ____
___ Number cannot be determined (explain): _____

Number of Lymph Nodes Involved (any size)
Specify: ____
___ Number cannot be determined (explain): _____

Distant Metastasis (pM)
___ Not applicable
___ pM1: Distant metastasis
+ Specify site(s), if known: _____

+ Additional Pathologic Findings (select all that apply)

+ ___ Keratinizing squamous metaplasia
+ ___ Urothelial dysplasia (low-grade intraurothelial neoplasia)
+ ___ Inflammation/regenerative changes
+ ___ Therapy-related changes
+ ___ Urethritis cystica et glandularis
+ ___ Intestinal metaplasia
+ ___ Other (specify): _____

+ Comment(s)

Explanatory Notes

A. History

A relevant history is important for interpretation of urethral biopsies. A history of renal stones, recent urinary tract procedures, infections, obstruction, or prior therapy (intravesical or systemic chemotherapy, local radiation) can lead to reactive epithelial changes potentially mimicking malignancy. Any neoplasms previously diagnosed should be specified, including the histologic type, primary site, and histologic grade.

B. Histologic Type

Carcinomas of the urethra vary in histologic type, depending on type of epithelium lining the urethra in a given anatomic location.[1-4] In women, squamous cell carcinoma is the most common histologic subtype (approximately 75%) and is most common in the anterior urethra (distal third). Urothelial (transitional cell) 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.[5] 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 (transitional cell) 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.[4] The distinction between urothelial carcinoma with aberrant squamous or glandular differentiation and a primary squamous cell carcinoma or adenocarcinoma is rather arbitrary. Most authorities require a pure histology of squamous cell carcinoma or adenocarcinoma 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 aberrant differentiation.[6]

Classification of Neoplasms of the Urethra

- Squamous Cell Carcinoma
  - Typical
  - Variant
    - Verrucous carcinoma
    - Basaloid squamous cell carcinoma
    - Sarcomatoid carcinoma
- Urothelial (Transitional Cell) Neoplasia
  - Benign
    - Urothelial (transitional cell) papilloma
    - Inverted urothelial (transitional cell) papilloma
  - Papillary urothelial neoplasm of low malignant potential
  - Malignant
    - Papillary
      - Typical, noninvasive
      - Typical, with invasion
        - Variant
          - With squamous or glandular differentiation
      - Micropapillary
    - Nonpapillary
      - Carcinoma in situ
      - Invasive carcinoma
        - Variants containing or exhibiting
          - Deceptively benign features
            - Nested pattern (resembling von Brunn's nests)

- Small tubular pattern
- Microcystic pattern
- Inverted pattern
- Squamous differentiation
- Glandular differentiation
- Micropapillary histology
- Sarcomatoid foci ("sarcomatoid carcinoma")
- Urothelial carcinoma with unusual cytoplasmic features
  - Clear cell
  - Plasmacytoid
- Urothelial carcinoma with syncytiotrophoblasts
- Unusual stromal reactions
  - Pseudosarcomatous stroma
  - Stromal osseous or cartilaginous metaplasia
  - Osteoclast-type giant cells
  - With prominent lymphoid infiltrate

Adenocarcinoma
- Non-clear cell
  - Mucinous (including colloid)
  - Signet-ring cell
  - Adenocarcinoma not otherwise specified (NOS)
- Clear cell

Tumors of Mixed Cell Types
Undifferentiated Carcinoma
Non-urethral Carcinoma From Adjacent Anatomic Site (Direct Extension)

C. 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[7] and has been adopted in the latest WHO classification (2004).[6,8] Other systems (that were being used previously) may still be used according to institutional preference. Until the WHO/ISUP system is clinically and prognostically validated, tumor grade according to both the WHO/ISUP (1998) system and the older WHO (1973) system may be concurrently used.[9]

WHO/ISUP (1998) - WHO (2004) Consensus Classification for Urothelial (Transitional Cell) Lesions

Normal
- Normal

Hyperplasia
- Flat hyperplasia

Flat Lesions with Atypia
- Reactive (inflammatory) atypia
- Atypia of unknown significance
- Dysplasia (low-grade intraurothelial neoplasia)
- Carcinoma in situ (high-grade intraurothelial neoplasia)

Papillary Neoplasms
- Papilloma

Inverted papilloma
Papillary neoplasm of low malignant potential
Papillary carcinoma, low-grade
Papillary carcinoma, high-grade#
Invasive Neoplasms

Option exists to add comment as to the presence of marked anaplasia.

D. Extent of Invasion

A critical role of the surgical pathologist is to diagnose the depth/extent of invasion into the tissues surrounding the urethra.[10] The surrounding anatomic structures vary by 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.[10] In papillary urothelial tumors, invasion occurs most often at the base of the tumor and less frequently in the stalk.

E. TNM and Stage Groupings

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 and shown below.[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.

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 Stage Groupings

Stage 0a	Ta	N0	M0#
Stage 0is	Tis	N0	M0
	Tis pu	N0	M0
	Tis pd	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1	N1	M0
	T2	N1	M0
	T3	N0	M0

	T3	N1	M0
Stage IV	T4	N0	M0
	T4	N1	M0
	Any T	N2	M0
	Any T	Any N	M1

M0 is defined as no distant metastasis.

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.

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).

F. 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.

G. Margins

Resection margins, including those mentioned in Note **F**, 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.

H. Venous/Lymphatic Vascular 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.[11,12] Retraction artifact is prominent in invasive urothelial carcinoma, particularly the micropapillary variant, and should be distinguished from vascular space invasion.[13]

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