 Protocol for the Examination of Cystectomy Specimens From Patients With Carcinoma of the Urinary Bladder  

**Version:** Urinary Bladder Resection 4.0.2.0  
**Protocol Posting Date:** February 2020  
**CAP Laboratory Accreditation Program Protocol Required Use Date:** November 2020  

Includes pTNM requirements from the 8th Edition, AJCC Staging Manual

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

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystectomy</td>
<td>Includes specimens designated partial, total or radical cystectomy, radical cystoprostatectomy (for bladder cancer), and anterior exenterations</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinomas</td>
<td>Includes invasive carcinomas of the urinary tract, including urothelial carcinoma, its morphological variants, and other carcinoma (squamous cell carcinoma, adenocarcinoma, Müllerian carcinoma, neuroendocrine carcinoma, and sarcomatoid carcinoma)</td>
</tr>
</tbody>
</table>

### 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:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy, transurethral resection of the bladder tumor* (TURBT), or enucleations (consider Urinary Bladder Biopsy protocol)</td>
<td></td>
</tr>
<tr>
<td>Primary resection specimen with no residual cancer (e.g., following neoadjuvant therapy)</td>
<td></td>
</tr>
<tr>
<td>Cytologic specimens</td>
<td></td>
</tr>
</tbody>
</table>

* Transurethral resection of a bladder tumor is NOT considered to be the definitive resection specimen, even though the entire cancer may be removed.

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

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urachal Carcinoma</td>
<td></td>
</tr>
<tr>
<td>Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)</td>
<td></td>
</tr>
<tr>
<td>Sarcoma (consider the Soft Tissue protocol)</td>
<td></td>
</tr>
</tbody>
</table>

### Authors

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

* Denotes primary author. All other contributing authors are listed alphabetically.
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 i.e. all required elements must be in the synoptic portion of the report in the format defined above.

Summary of Changes

**Version 4.0.2.0**
Modified Histologic Type (Squamous cell carcinoma)
Surgical Pathology Cancer Case Summary

Protocol posting date: February 2020

URINARY BLADDER: Cystectomy and Anterior Exenteration

Select a single response unless otherwise indicated.

Procedure (Note A)
___ Partial cystectomy
___ Radical cystectomy (total cystectomy)
___ Radical cystoprostatectomy
___ Anterior exenteration
___ Other (specify): ____________________________
___ Cannot be determined

Tumor Site (select all that apply)
___ Trigone
___ Right lateral wall
___ Left lateral wall
___ Anterior wall
___ Posterior wall
___ Dome
___ Other (specify): ____________________________
___ Cannot be determined

Tumor Size
Greatest dimension (centimeters): ___ cm
+ Additional dimensions (centimeters): ___ x ___ cm
___ Cannot be determined (explain): ____________________________

Histologic Type (select all that apply) (Note B)

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
    + Specify percentage of squamous differentiation: _____%
___ Urothelial carcinoma with glandular differentiation
    + Specify percentage of glandular differentiation: _____%
___ Urothelial carcinoma with trophoblastic differentiation
    + Specify percentage of trophoblastic differentiation: _____%
___ Urothelial carcinoma with Müllerian differentiation

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.
+ Specify percentage of Müllerian differentiation: _____ %

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
   + Specify percentage of small cell neuroendocrine component: _____ %
___ Large cell neuroendocrine carcinoma
   + Specify percentage of large cell neuroendocrine component: _____ %
___ Well-differentiated neuroendocrine carcinoma
   + Specify percentage of well-differentiated neuroendocrine component: _____ %
___ Other histologic type not listed (specify): ____________________________

+ Associated Epithelial Lesions (select all that apply) (Note C)
  + ___ None identified
  + ___ Urothelial papilloma
  + ___ Urothelial papilloma, inverted type
  + ___ Papillary urothelial neoplasm, low malignant potential (PUNLMP)
  + ___ Urothelial proliferation of uncertain malignant potential
  + ___ Urothelial dysplasia
  + ___ Cannot be determined

Histologic Grade (Note C)

For urothelial carcinoma, other variants, or divergent differentiation
___ Low grade
___ High grade
___ Other (specify): ____________________________

For squamous cell carcinoma or adenocarcinoma
___ G1: Well differentiated
___ G2: Moderately differentiated
___ G3: Poorly differentiated
___ GX: Cannot be assessed
___ Other (specify): ____________________________
___ Not applicable
___ Cannot be assessed

+ Tumor Configuration (select all that apply)
  + ___ Papillary
+ ___ Solid/nodule
+ ___ Flat
+ ___ Ulcerated
+ ___ Cannot be determined
+ ___ Other (specify): ___________________________

**Tumor Extension (select all that apply) (Note D)**
___ No evidence of primary tumor
___ Noninvasive papillary carcinoma
___ Urothelial carcinoma in situ
___ Tumor invades lamina propria (subepithelial connective tissue)
___ Tumor invades muscularis propria
   ___ Tumor invades superficial muscularis propria (inner half)
   ___ Tumor invades deep muscularis propria (outer half)
___ Tumor invades perivesical soft tissue
   ___ Microscopically
   ___ Macroscopically (extravesical mass)
___ Tumor invades adjacent structures#
   ___ Prostate (transmural invasion from the bladder tumor)##
   ___ Seminal vesicles
   ___ Uterus
   ___ Vagina
   ___ Adnexae
   ___ Pelvis wall
   ___ Abdominal wall
   ___ Rectum
   ___ Other (specify): ___________________________
___ Cannot be assessed

* Note: Use the Urethral protocol for tumors that involve the urethral mucosa without invasion, tumors that involve the urethral mucosa with invasion of subepithelial connective tissue/prostate stroma, or tumors that involve prostatic ducts and acini with or without stromal invasion.

## See Note D, Figure 1.

**Margins (select all that apply) (Note E)**
___ Cannot be assessed
___ Uninvolved by invasive carcinoma and carcinoma in situ/ noninvasive urothelial carcinoma
___ Uninvolved by invasive carcinoma
___ Involved by invasive carcinoma
   ___ Right ureteral margin
   ___ Left ureteral margin
   ___ Urethral margin
   ___ Soft tissue margin
   ___ Other margin(s) (specify): ___________________________
___ Involved by carcinoma in situ/noninvasive high-grade urothelial carcinoma
   ___ Right ureteral margin
   ___ Left ureteral margin
   ___ Urethral margin
   ___ Soft tissue margin
   ___ Other margin(s) (specify): ___________________________
___ Involved by noninvasive low-grade urothelial carcinoma/urothelial dysplasia
   ___ Right ureteral margin
   ___ Left ureteral margin
   ___ Urethral margin
   ___ Soft tissue margin
   ___ Other margin(s) (specify): ___________________________

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.
* Note: For partial cystectomies, if the specimen is received unoriented precluding identification of specific margins, it should be denoted here.

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

**Regional Lymph Nodes**
- No lymph nodes submitted or found

*Lymph Node Examination (required only if lymph nodes are present in the specimen)*

**Number of Lymph Nodes Involved:** ____

*Lymph Node Metastasis*
- Size of Largest Metastatic Deposit (centimeters): ___ cm
- Specify Site: _________
- Size of Largest Lymph Node Involved (centimeters): ___ cm
- Specify Site: _________
- Extranodal Extension
- Not identified
- Present
- Cannot be determined

**Number of Lymph Nodes Examined:** ____

**Pathologic Stage Classification (pTNM, AJCC 8th Edition) (Note G)**
*Note: Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. Only the applicable T, N, or M category is required for reporting; their definitions need not be included in the report. The categories (with modifiers when applicable) can be listed on 1 line or more than 1 line.*

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

**Primary Tumor (pT)**
- pTX: Primary tumor cannot be assessed
- pT0: No evidence of primary tumor
- pTa: Noninvasive papillary carcinoma
- pTis: Urothelial carcinoma in situ: “flat tumor”
- pT1: Tumor invades lamina propria (subepithelial connective tissue)
- pT2: Tumor invades muscularis propria
- pT2a: Tumor invades superficial muscularis propria (inner half)
- pT2b: Tumor invades deep muscularis propria (outer half)
- pT3: Tumor invades perivesical soft tissue
- pT3a: Tumor invades perivesical soft tissue microscopically
- pT3b: Tumor invades perivesical soft tissue macroscopically (extravesical mass)
- pT4: Extravesical tumor directly invades any of the following: prostatic stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall
- pT4a: Extravesical tumor invades directly into prostatic stroma, uterus, or vagina
- pT4b: Extravesical tumor invades pelvic wall, abdominal wall

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.
Regional Lymph Nodes (pN)
  ___ pNX: Lymph nodes cannot be assessed
  ___ pN0: No lymph node metastasis
  ___ pN1: Single regional lymph node metastasis in the true pelvis (perivesical, obturator, internal and external iliac or sacral lymph node)
  ___ pN2: Multiple regional lymph node metastasis in the true pelvis (perivesical, obturator, internal and external iliac or sacral lymph node metastasis)
  ___ pN3: Lymph node metastasis to the common iliac lymph nodes

Distant Metastasis (pM) (required only if confirmed pathologically in this case)
  ___ pM: Distant metastasis
  ___ pM1a: Distant metastasis limited to lymph nodes beyond the common iliacs
  ___ pM1b: Non-lymph node distant metastases

Specify site(s), if known: ____________________________

+ Additional Pathologic Findings (select all that apply)
  + ___ Urothelial dysplasia
  + ___ Adenocarcinoma of prostate (use protocol for carcinoma of prostate)
  + ___ Inflammation/regenerative changes
  + ___ Therapy-related changes (specify): ____________________
  + ___ Cystitis cystica et glandularis
  + ___ Keratinizing squamous metaplasia
  + ___ Intestinal metaplasia
  + ___ Other (specify): ____________________________

+ Comment(s)
Explanatory Notes

A. Sections for Microscopic Evaluation

Bladder
Sections of bladder for microscopic evaluation for cystectomy specimens, several representative sections of the tumor, including the macroscopically deepest penetration, should be sampled. Submit several sections of the mucosa remote from the carcinoma, especially if abnormal, including the lateral wall(s), dome, and trigone. Submit one section of ureteral margin, unless submitted separately as frozen section specimens, and 1 section of urethral margin. If a long segment of the ureter(s) is present, then additional sections from the mid-portion may be necessary, as urothelial cancer often is multifocal.

Prostate and Prostatic Urethra
Prostatic urethral involvement should be carefully investigated in cystectomy specimens. Sections should include the prostatic urethra, including at the margin and with the surrounding prostatic parenchyma. Representative sections of the peripheral zone, central zone, and seminal vesicles should be included. Close gross examination may help target sampling of selective abnormal-appearing areas.

Lymph Nodes
Submit one section from each grossly positive lymph node. All other lymph nodes should be entirely submitted, as presence of nodal disease may be used as an indication for adjuvant therapy. Lymph nodes may be grossly or microscopically detected in the perivesical fat.

Other Tissues
Submit one or more sections of uterus (as indicated) and one or more sections of vagina, seminal vesicles, and other organs (as indicated). If the tumor grossly appears to invade the prostate, uterus, or vagina, sections should be targeted, such that the relationship of the infiltrating tumor in the bladder wall and the adjacent viscus is clearly demonstrable.

B. Histologic Type
The vast majority (more than 95%) of carcinomas of the urinary bladder, renal pelvis, and ureter are urothelial cell in origin. The most recent 2016 World Health Organization (WHO) classification of tumors of the urothelial tract, including urethra, urinary bladder, ureter, and renal pelvis, is provided in this note. Benign tumors are included in this classification because, within the same patient, a spectrum of differentiation from benign to malignant tumors may be seen in the bladder, either at the same time or over the clinical course of the disease. Also, clinicians stage most tumors irrespective of histologic grade. 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 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.

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:
C. Histologic Grade
Flat intraepithelial lesions and papillary and invasive lesions are graded separately.\textsuperscript{1-6} There has been significant controversy in the classification of these lesions. Flat lesions were graded as mild, moderate, and severe dysplasia and carcinoma in situ; or atypical hyperplasia and carcinoma in situ; or dysplasia and carcinoma in situ.\textsuperscript{9,10} Papillary lesions were classified as papillomas (grade 0) and transitional cell carcinomas, grades I, II and III; or as papillomas, low-grade and high-grade transitional cell carcinomas.\textsuperscript{4-6} 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.\textsuperscript{4} This system is adopted in the WHO 2004 classification\textsuperscript{1} and 2004 Armed Forces Institute of Pathology (AFIP) fascicle,\textsuperscript{3} and has been validated by many studies to be prognostically significant. The 2016 WHO system used essentially the same classification with minor modification.\textsuperscript{2} Other systems (that were being used previously) may still be used according to institutional preference. Tumor grade according to both the WHO/ISUP (1998)\textsuperscript{4} / WHO (2004)\textsuperscript{1} system and the older WHO (1973)\textsuperscript{6} system may be concurrently used.

\textbf{2004 WHO / ISUP Consensus Classification for Urothelial Lesions}

\begin{itemize}
  \item Normal
    \begin{itemize}
      \item Normal\textsuperscript{#}
    \end{itemize}
  \item Hyperplasia
    \begin{itemize}
      \item Flat hyperplasia
      \item Papillary hyperplasia
    \end{itemize}
  \item Flat Lesions with Atypia
    \begin{itemize}
      \item Reactive (inflammatory) atypia
      \item Atypia of unknown significance
      \item Dysplasia (low-grade intraurothelial neoplasia)\textsuperscript{#}
      \item Carcinoma in situ (high-grade intraurothelial neoplasia)\textsuperscript{##}
    \end{itemize}
  \item Papillary Neoplasms
    \begin{itemize}
      \item Papilloma
      \item Inverted papilloma
      \item Papillary neoplasm of low malignant potential
      \item Papillary carcinoma, low-grade
      \item Papillary carcinoma, high-grade\textsuperscript{###}
    \end{itemize}
  \item Invasive Neoplasms
    \begin{itemize}
      \item Lamina propria invasion
      \item Muscularis propria (detrusor muscle) invasion
    \end{itemize}
\end{itemize}

\textsuperscript{#} May include cases formerly diagnosed as “mild dysplasia.”

\textsuperscript{##} Includes cases with “severe dysplasia.”

\textsuperscript{###} Option exists to add comment as to the presence of marked anaplasia.

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

Squamous carcinomas and adenocarcinomas may be graded as well-differentiated, moderately differentiated, and poorly differentiated.

References:


D. Extent of Invasion

A critical role of the surgical pathologist is to diagnose the depth and extent of invasion into the subepithelial connective tissue/lamina propria/submucosa (pT1), muscularis propria (pT2), or beyond (pT3 or pT4).1-3 In papillary tumors, invasion occurs most often at the base of the tumor and very infrequently in the stalk. In the urinary bladder, a tumor infiltrating the lamina propria (pT1) is sometimes overdiagnosed as vascular invasion; hence, caution should be exercised when diagnosing this feature, which in some cases may be supported by performing immunohistochemical studies for endothelial markers.4

Involvement of the prostate gland may occur in several different patterns. Tumors (flat carcinoma in situ, papillary or invasive carcinoma) can first spread along the prostatic urethral mucosa and prostate glands and subsequently invade prostatic stroma (transurethral mucosal route) (Figure 1, B). Tumors may also invade through the bladder wall and the base of the prostate directly into the prostate gland (Figure 1, A, straight arrow).11 Tumors can also invade into extravesical fat and then extend back into the prostate gland (Figure 1, B, curved arrow). The latter two routes are considered direct transmural invasion. The American Joint Committee on Cancer (AJCC) 8th edition staging manual defines direct extension of urinary bladder cancer into the prostate gland as T4 disease and excludes transurethral mucosal prostatic stroma invasion from the pT4a staging status. However, there is limited data on the best methodology to stage urothelial carcinoma that concurrently involves the urinary bladder and the prostatic urethra. In patients who have a large urinary bladder carcinoma that has invades through the full thickness of the bladder wall and thereby secondarily involves the prostatic stroma, a T4 stage should be assigned per urinary bladder staging. In other circumstances in which involvement by urothelial carcinoma is seen in both sites, separate urinary bladder and prostatic urethral staging should be assigned. Transmucosal route into prostatic stroma from a bladder cancer without transmural prostatic stromal invasion is now categorized as pT2 per urethral cancer staging, and the concomitant bladder proper cancer is given a separate stage category according to the bladder cancer staging.

References:

E. Margins
Resection margins, including those mentioned in Note A, should be carefully specified. Statements about deep soft tissue margins should specify whether peritoneal surfaces are involved by tumor. In cases of urachal adenocarcinoma in which partial cystectomy with excision of the urachal tract and umbilicus is performed, the margins of the urachal tract, ie, the soft tissue surrounding the urachus and the skin around the umbilical margin, should be specified.
F. Lymphovascular Invasion
Urothelial carcinoma may invade blood vessels or lymphatic channels. Lymphovascular invasion has been shown to be an independent predictor of recurrence and decreased overall survival. In suspicious cases, blood vessels can be highlighted by immunohistochemical staining for factor VIII-related antigen, CD31 or CD34. Staining will not resolve the problem of differentiating lymphatic versus artifactual space entrapment by tumor cells, and as mentioned, this is frequently seen in urothelial tumors invading the lamina propria. Retraction artifact is also prominent in the “micropapillary variant” of urothelial carcinoma.2

References:

G. TNM and Stage Groupings
The TNM Staging System for carcinomas of the urinary bladder of the AJCC is recommended.1 A cystoprostatectomy specimen may contain three separate primaries: carcinoma of the urinary bladder, carcinoma of the prostate and carcinoma of the urethra. Depending on the pathology in a given case, the number of protocols to be used in a cystoprostatectomy specimen will vary.

By AJCC 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) (Figure 2)
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.

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).

References: