Protocol for the Examination of Specimens from Patients with Carcinoma of the Ureter and Renal Pelvis

Protocol applies to invasive and in-situ carcinomas and/or associated epithelial lesions of the ureter and renal pelvis.

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Procedures
• Biopsy
• Nephroureterectomy or Ureterectomy

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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 (Checklist)” 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 checklist 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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Surgical Pathology Cancer Case Summary (Checklist)

Protocol web posting date: October 2009

URETER, RENAL PELVIS: Biopsy

Note: Use of checklist for biopsy specimens is optional.

Select a single response unless otherwise indicated.

***Specimen (Note A)**
*___ Renal pelvis
*___ Ureter
*___ Other (specify): _____
*___ Not specified

***Specimen Laterality**
*___ Left
*___ Right
*___ Not specified

***Histologic Type (Note B)**
*___ 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): _____
*___ Squamous cell carcinoma, typical
*___ Squamous cell carcinoma, 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
*___ Urothelial (transitional cell) papilloma (World Health Organization [WHO] / International Society of Urologic Pathology [ISUP], 1998; WHO 2004)
*___ Urothelial (transitional cell) papilloma, inverted type
*___ Papillary urothelial (transitional cell) neoplasm, low malignant potential (WHO/ISUP 1998; WHO 2004)
*___ Cannot be determined

* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

***Histologic Grade (Note C)**
*___ Not applicable
*___ Cannot be determined

*Urothelial Carcinoma (WHO/ISUP, 1998; WHO 2004)
*___ Low-grade
*___ High-grade
*___ Other (specify): _____

*Adenocarcinoma and Squamous Cell Carcinoma
*___ GX: Cannot be assessed
*___ G1: Well differentiated
*___ G2: Moderately differentiated
*___ G3: Poorly differentiated
*___ Other (specify): _____

***Tumor Configuration (select all that apply)**
*___ Papillary
*___ Solid/nodule
*___ Flat
*___ Ulcerated
*___ Indeterminate
*___ Other (specify): _____

***Adequacy of Material for Determining T Category (Note D)**
*___ Muscularis propria not identified
*___ Muscularis propria present
*___ Indeterminate

***Pathologic Staging (pTNM) (Note E)**

*TNM Descriptors (select all that apply)
*___ None
*___ m (multiple primary tumors)
*___ r (recurrent)
*___ y (post-treatment)

*Primary Tumor (pT)
*___ pTX: Cannot be assessed
*___ pT0: No evidence of primary tumor
*___ pTa: Noninvasive papillary carcinoma
*___ pTis: Flat carcinoma in situ
*___ pT1: Tumor invades subepithelial connective tissue (lamina propria)
*___ pT2: Tumor invades muscularis propria

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

*___ Urothelial carcinoma in situ
*___ Urothelial dysplasia (low-grade intraurothelial neoplasia)
*___ Inflammation/regenerative changes
*___ Therapy-related changes
*___ Cautery artifact
*___ Ureteritis or pyelitis cystica and/or glandularis
*___ Keratinizing squamous metaplasia
*___ Intestinal metaplasia
*___ Other (specify): _____

***Comment(s)**

Surgical Pathology Cancer Case Summary (Checklist)

Protocol web posting date: October 2009

RENAL PELVIS: Resection/Nephroureterectomy, Partial or Complete

Select a single response unless otherwise indicated.

Procedure (Note F)
___ Nephroureterectomy, partial
___ Nephroureterectomy, complete
___ Other (specify): _____
___ Not specified

Specimen Laterality
___ Right
___ Left
___ Not specified

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

Histologic Type (Note B)
___ 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): _____
___ Squamous cell carcinoma, typical
___ Squamous cell carcinoma, 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
___ Urothelial (transitional cell) papilloma (World Health Organization [WHO] / International Society of Urologic Pathology [ISUP], 1998; WHO 2004)
___ Urothelial (transitional cell) papilloma, inverted type
___ Papillary urothelial (transitional cell) neoplasm, low malignant potential (WHO/ISUP 1998; WHO 2004)
___ Cannot be determined

* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

Histologic Grade (Note C)
___ Not applicable
___ Cannot be determined

Urothelial Carcinoma (WHO/ISUP, 1998; WHO 2004)
___ Low-grade
___ High-grade
___ Other (specify): _____

Adenocarcinoma and Squamous Cell Carcinoma
___ GX: Cannot be assessed
___ G1: Well differentiated
___ G2: Moderately differentiated
___ G3: Poorly differentiated
___ Other (specify): _____

***Tumor Configuration (select all that apply)**
*___ Papillary
*___ Solid/nodule
*___ Flat
*___ Ulcerated
*___ Indeterminate
*___ Other (specify): _____

Margins (select all that apply) (Note G)
___ Cannot be assessed
___ Margins uninvolved by invasive carcinoma
    *Distance of invasive carcinoma from closest margin: ___ mm
    *Specify margin: _____
___ Margin(s) involved by invasive carcinoma
    Specify margin(s): _____
___ Margin(s) uninvolved by carcinoma in situ
___ Margin(s) involved by carcinoma in situ
    Specify margin(s): _____
___ Other(s) (specify): _____

***Lymph-Vascular Invasion (Note H)**
*___ Not identified
*___ Present
*___ Indeterminate

Pathologic Staging (pTNM) (Note E)

TNM Descriptors (required only if applicable) (select all that apply)
___ m (multiple)
___ r (recurrent)
___ y (post-treatment)

Primary Tumor (pT)
___ pTX: Cannot be assessed
___ pT0: No evidence of primary tumor
___ pTa: Papillary noninvasive carcinoma
___ pTis: Flat carcinoma in situ
___ pT1: Tumor invades subepithelial connective tissue (lamina propria)
___ pT2: Tumor invades muscularis propria
___ pT3: Tumor invades beyond muscularis into peripelvic fat or the renal parenchyma
___ pT4: Tumor invades adjacent organs, or through the kidney into the perinephric fat

Regional Lymph Nodes (pN)
___ pNX: Cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: Metastasis in a single regional lymph node, 2 cm or less in greatest dimension
___ pN2: Metastasis in a single regional lymph node, more than 2 cm but not more than 5 cm in greatest dimension, or multiple lymph nodes, none more than 5 cm in greatest dimension
___ pN3: Metastasis in a regional lymph node more than 5 cm in greatest dimension
Specify: Number examined: ___
Number involved (any size): ___

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

***Additional Pathologic Findings (select all that apply)**
*___ Urothelial carcinoma in situ
*___ Urothelial dysplasia (low-grade intraurothelial neoplasia)
*___ Inflammation/regenerative changes
*___ Therapy-related changes
*___ Pyelitis cystica and/or glandularis
*___ Keratinizing squamous metaplasia
*___ Intestinal metaplasia
*___ Lithiasis
*___ Other (specify): _____

***Comment(s)**

Surgical Pathology Cancer Case Summary (Checklist)

Protocol web posting date: October 2009

URETER: Resection

Select a single response unless otherwise indicated.

Procedure
___ Ureterectomy
___ Nephroureterectomy
___ Other (specify): _____
___ Not specified

Specimen Laterality
___ Right
___ Left
___ Not specified

Tumor Size
Greatest dimension: ___
*Additional dimensions: ___ x ___
___ Cannot be determined (see Comment)

Histologic Type (Note B)
___ 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): _____
___ Squamous cell carcinoma, typical
___ Squamous cell carcinoma, 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
___ Urothelial (transitional cell) papilloma (World Health Organization [WHO] / International Society of Urologic Pathology [ISUP], 1998; WHO 2004)
___ Urothelial (transitional cell) papilloma, inverted type
___ Papillary urothelial (transitional cell) neoplasm, low malignant potential (WHO/ISUP 1998; WHO 2004)
___ Cannot be determined

* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

Histologic Grade (Note C)
___ Not applicable
___ Cannot be determined

Urothelial Carcinoma (WHO/ISUP, 1998; WHO 2004)
___ Low-grade
___ High-grade
___ Other (specify): _____

Adenocarcinoma and Squamous Cell Carcinoma
___ GX: Cannot be assessed
___ G1: Well differentiated
___ G2: Moderately differentiated
___ G3: Poorly differentiated
___ Other (specify): _____

***Tumor Configuration (select all that apply)**
*___ Papillary
*___ Solid/nodule
*___ Ulcerated
*___ Flat
*___ Indeterminate
*___ Other (specify): _____

Margins (select all that apply) (Note G)
___ Cannot be assessed
___ Margins uninvolved by invasive carcinoma
    *Distance of invasive carcinoma from closest margin: ___ mm
    *Specify margin(s): _____
___ Margin(s) involved by invasive carcinoma
    Specify margin(s): _____
___ Margins(s) involved by carcinoma in situ
___ Margin(s) uninvolved by carcinoma in situ
___ Other(s) (specify): _____

***Lymph-Vascular Invasion (Note H)**
*___ Not identified
*___ Present
*___ Indeterminate

Pathologic Staging (pTNM) (Note E)

TNM Descriptors (required only if applicable) (select all that apply)
___ m (multiple)
___ r (recurrent)
___ y (post-treatment)

Primary Tumor (pT)
___ pTX: Cannot be assessed
___ pT0: No evidence of primary tumor
___ pTa: Papillary noninvasive carcinoma
___ pTis: Carcinoma in situ
___ pT1: Tumor invades subepithelial connective tissue (lamina propria)
___ pT2: Tumor invades the muscularis propria
___ pT3: Tumor invades beyond muscularis propria into periureteric fat
___ pT4: Tumor invades adjacent organs

Regional Lymph Nodes (pN)
___ pNX: Cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: Metastasis in a single regional lymph node, 2 cm or less in greatest dimension
___ pN2: Metastasis in a single regional lymph node, more than 2 cm but not more than 5 cm in greatest dimension, or multiple lymph nodes, none more than 5 cm in greatest dimension
___ pN3: Metastasis in a regional lymph node more than 5 cm in greatest dimension
Specify: Number examined: ___
Number involved (any size): ___

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

***Additional Pathologic Findings (select all that apply)**
*___ Urothelial carcinoma in situ
*___ Urothelial dysplasia (low-grade intraurothelial neoplasia)
*___ Inflammation/regenerative changes
*___ Therapy-related changes
*___ Ureteritis cystica and/or glandularis
*___ Keratinizing squamous metaplasia
*___ Intestinal metaplasia
*___ Other (specify): _____

Pathologic Findings in Non-Neoplastic Kidney (select all that apply) (Note I)
___ Insufficient tissue (partial nephrectomy specimen with <5 mm of adjacent non-neoplastic kidney)
___ Significant pathologic alterations
___ None identified
___ Glomerular disease (type): _____
___ Tubulointerstitial disease (type): _____
___ Vascular disease (type): _____
___ Inflammation (type): _____
___ Other (specify): _____

***Comment(s)**

Explanatory Notes

A. History

A relevant history is important for interpretation of all upper urinary tract (renal pelvis and ureter) specimens. A history of renal stones, recent urinary tract procedures, infections, or obstruction can influence the interpretation of random biopsies obtained from patients with hematuria. Any neoplasms previously diagnosed should be specified, including the histologic type, primary site, and histologic grade. Primary tumors may be associated with hereditary non-polyposis colon cancer (HNPCC) syndrome (Lynch syndrome II). Renal pelvic tumors are more often seen in analgesic abusers, who often have analgesic nephropathy, including papillary necrosis. If prior therapy has been given, it should be described (systemic or intravesical chemotherapy, immunotherapy, radiation, etc). The method of collection and date also should be specified in urine cytology specimens. Cytologic specimens from the ureter or renal pelvis may be over-interpreted if their site of sampling is not stated.

B. Histologic Type

Like the urinary bladder, the vast majority (more than 95%) of carcinomas of the renal pelvis and ureter are urothelial in origin.[1-6] A working histologic classification encompassing the wide histologic diversity and histologic range within the different types of carcinomas of the urothelial tract is tabulated 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, either at the same time or over the clinical course of the disease. The full spectrum of invasive urothelial carcinoma and its variants as found in the urinary bladder may also be found in the upper tract. Of note, unusual histomorphological variants seem to be more common in the upper tract,[6] including carcinomas with micropapillary, lymphoepithelioma-like, sarcomatoid, squamous, clear cell, glandular, rhabdoid, signet-ring, and plasmacytoid features or areas. The distinction between a 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.

Classification of Neoplasms of the Ureter and Renal Pelvis, Including Urothelial (Transitional Cell) Carcinoma and Its Variants[#]

Urothelial (Transitional Cell) Neoplasia (World Health Organization [WHO] / International Society of Urologic Pathology [ISUP], 1998; WHO 2004)

- Benign
  - Urothelial papilloma
  - Inverted 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
- Squamous Cell Carcinoma
  - Typical
  - Variant
    - Verrucous carcinoma
    - Basaloid squamous cell carcinoma
    - Sarcomatoid carcinoma
- Adenocarcinoma
  - Histologic variants
    - Typical intestinal type
    - Mucinous (including colloid)
    - Signet-ring cell
    - Clear cell
    - Hepatoid
    - Mixture of above patterns – adenocarcinoma not otherwise specified (NOS)
- Tumors of Mixed Cell Types
- Undifferentiated Carcinoma[###]
  - Small cell carcinoma
  - Large cell neuroendocrine carcinoma
  - Lymphoepithelioma-like carcinoma
  - Giant cell carcinoma
  - Not otherwise specified
- Metastatic Carcinoma

[#] Modified from Amin et al.[7]

[##] Papillary tumors may be invasive or noninvasive.

[###] Refers to tumors that are undifferentiated by light microscopy.

C. Histologic Grade

The grading system is identical to that for urinary bladder neoplasms. Flat intraepithelial lesions and papillary and invasive lesions are graded separately. There has been significant controversy in the classification of these lesions. 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.[8] This system is utilized in the WHO 2004 "blue book"[1] and the 2004 AFIP Fascicle.[2] Urothelial carcinomas of the renal pelvis tend to more often be high-grade[3,9] compared to urinary bladder carcinomas.

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

Normal
- Normal[#]

Hyperplasia
- Flat hyperplasia
- Papillary 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
- Lamina propria invasion
- Muscularis propria invasion

[#] May include cases formerly diagnosed as "mild dysplasia."

[##] Includes cases with "severe dysplasia."

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

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

D. Extent of Invasion

Depth of invasion and pathologic stage are the most important prognostic indicators for patients with neoplasms of the upper urinary tract.[10,11] A critical role of the surgical pathologist is to diagnose the depth and extent of invasion into the subepithelial connective tissue/lamina propria (pT1), muscularis propria (pT2), or beyond (pT3 or pT4). The patterns of invasion are similar to the urinary bladder, except that for renal pelvis carcinoma, the type of tumor involvement of the kidney, when present, impacts stage. Also, it is important to note that the lamina propria is absent beneath the urothelium lining the renal papillae in the pelvis and is thin along the minor calyces.[12] As

in the urinary bladder, in papillary tumors, invasion occurs most often at the base of the tumor and very infrequently in the stalk. Tumor infiltrating the lamina propria is pT1 and, like the urinary bladder, there is no accepted approach for assessing depth of lamina propria invasion. However, pathologists are encouraged to provide some assessment as to the extent of lamina propria invasion (ie, focal versus extensive, or depth in millimeters, or by level – above, at, or below muscularis mucosae). Designation of a tumor as merely muscle invasive is inappropriate, but the type of muscle invasion, ie, muscularis mucosae (pT1 tumors) versus muscularis propria (pT2 tumors) invasion, needs to be clearly stated. Descriptive terminology, such as "urothelial carcinoma with muscle invasion, indeterminate for type of muscle invasion," may be used when it is not possible to be certain whether the type of muscle invaded by the tumor is hypertrophic muscularis mucosae or muscularis propria. For renal pelvic tumors, in-situ extension of carcinoma into renal collecting ducts and renal tubules does not affect stage, while carcinoma invading into the renal parenchyma is pT3. Renal pelvic carcinoma that invades through the kidney into perinephric fat is pT4. Patients with upper tract urothelial carcinoma often present at higher stage compared to patients with urinary bladder carcinoma.[3,9]

E. TNM and Stage Groupings

The TNM Staging System for carcinomas of the ureter and renal pelvis of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) is recommended and shown below.[13]

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) (Figure 1)

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.

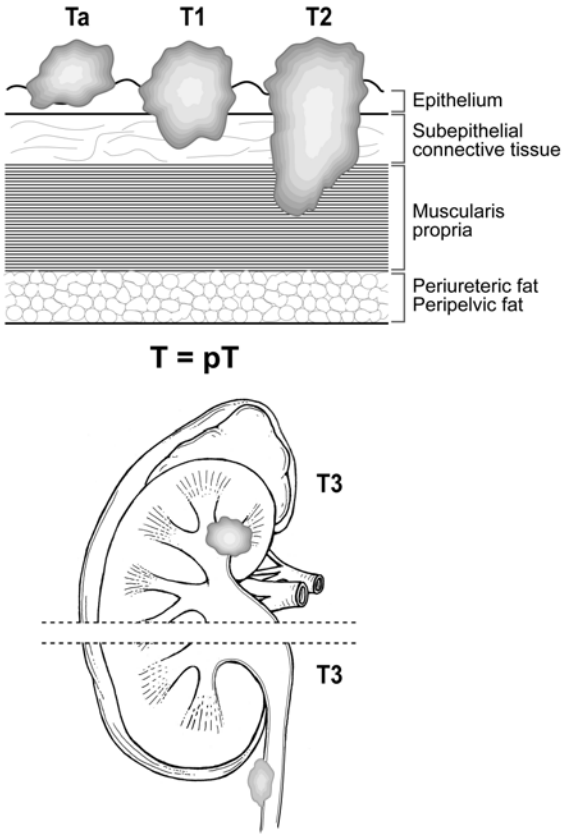

Figure 1. Depiction of pTa, pT1, pT2, and pT3.

Anatomic Stage/Prognostic Groups

Stage 0a	Ta	N0	M0[#]
Stage 0is	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
Stage IV	T4	N0	M0
	Any T	N1,2,3	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
Tissue samples include ureteroscopic biopsies, needle biopsies, segmental ureterctomy specimens, and radical nephroureterectomy with urinary bladder cuff resection specimens.

Ureteroscopic biopsies are entirely submitted. Since these are often minute in size, one approach to processing is to submit the biopsy sample for cytology cell block preparation.

Needle core biopsies of renal masses, including urothelial carcinoma involving the kidney, should be completely submitted.

Segmental ureterectomy is performed for tumors of the proximal or mid ureter. The length and diameter of the intact ureter is recorded, with a search for a mass by palpation and visual inspection. Proximal and distal cross-section margins are taken, and the outer aspect of the ureter is inked. The ureter is then opened longitudinally and assessed for mucosal abnormalities. After overnight fixation in 10% formalin, sections are taken to demonstrate the deepest invasion of any lesion(s). At least 1 section of uninvolved ureter should be submitted.

Radical nephroureterectomy with bladder cuff. Gross examination and sampling should document the relationship of tumor to adjacent renal parenchyma, peripelvic fat, nearest soft tissue margin, and ureter. Sections of grossly unremarkable kidney, pelvis, and ureter should be obtained. The important urothelial margin is the urinary bladder cuff, which can be sampled as shave sections.

Lymph Nodes
Regional lymph nodes are not always submitted or identified in cases of resection,[3] but evaluation of these nodes is important. Submit 1 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.

G. Margins
Resection margins, including those mentioned in Note **F**, should be carefully specified. Statements about deep soft tissue margins should specify whether peritoneal surfaces are involved by tumor. In renal pelvis, ureter, and nephroureterectomy specimens, the margins may include radial hilar soft tissue margin; bladder cuff; and ureteral, renal parenchymal, and Gerota's fascia margins, depending on the type of surgical specimen.

H. Lymph-Vascular Invasion
Urothelial carcinoma may invade blood vessels or lymphatic channels. This is an important prognostic factor in upper urinary tract urothelial carcinoma.[3,14,15] In suspicious cases, blood vessels can be highlighted by immunohistochemical staining for factor VIII-related antigen, CD31 or CD34. Staining can help resolve the problem of differentiating lymphatic versus artifactual space formation by tumor cells, a frequent finding seen in urothelial tumors invading the lamina propria. Retraction artifact is also prominent in the "micropapillary variant" of urothelial carcinoma.

I. Pathologic Findings in Non-Neoplastic Kidney
It is important to recognize that medical kidney diseases may be present in non-neoplastic renal tissue in nephrectomy and nephroureterectomy specimens.[16,17] Arterionephrosclerosis (or hypertensive nephropathy) and diabetic nephropathy are seen in approximately 30% and 20% of cases, respectively. Other medical renal diseases that have been identified include thrombotic microangiopathy, focal segmental glomerulosclerosis, and IgA nephropathy. The findings of greater than 20% global glomerulosclerosis or advanced diffuse diabetic glomerulosclerosis are predictive of significant decline in renal function 6 months after radical nephrectomy.[17] Evaluation for medical renal disease should be performed in each case; PAS and/or Jones methenamine silver stains should applied if necessary. Consultation with a nephropathologist should be pursued as needed.

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