Urinary Bladder, Ureter, and Renal Pelvis

Protocol applies to all carcinomas of the urinary bladder, ureter, and renal pelvis.

Protocol revision date: January 2004
Based on AJCC/UICC TNM, 6th edition

Procedures

- **Bladder Biopsy, Transurethral Resection of Bladder Tumor (TURBT) Specimen**
- **Cystectomy (Partial, Total)**
  - **Radical Cystoprostatectomy**
  - **Pelvic Exenteration**
- **Nephroureterectomy or Ureterectomy**

Authors
Mahul B. Amin, MD
Department of Pathology, Emory University Hospital, Atlanta, Georgia
John R. Srigley, MD
Department of Laboratory Medicine, Credit Valley Hospital, Mississauga, Ontario, Canada
David J. Grignon, MD
Department of Pathology, Wayne State University School of Medicine, Detroit, Michigan
Victor E. Reuter, MD
Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York
Peter A. Humphrey, MD, PhD
Department of Pathology, Barnes-Jewish Hospital, St. Louis, Missouri
Michael B. Cohen, MD
Department of Pathology, University of Iowa Health Care, Iowa City, Iowa
M. Elizabeth H. Hammond, MD
Department of Pathology, LDS Hospital and University of Utah School of Medicine, Salt Lake City, Utah
For the Members of the Cancer Committee, College of American Pathologists

Previous contributors: Donald Earl Henson, MD

Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2004
Applies primarily to invasive carcinomas and/or associated epithelial lesions, including carcinoma in situ
Based on AJCC/UICC TNM, 6th edition

*URINARY BLADDER, URETER, RENAL PELVIS: Biopsy

(Note: Use of checklist for biopsy specimens is optional)

*Patient name:
*Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

***MACROSCOPIC**

***Specimen Type**
*___ Bladder biopsy
*___ Renal pelvis biopsy
*___ Ureter biopsy
*___ Other
*___ Transurethral specimen
*___ Other (specify): _____
*___ Not specified

***Laterality (Renal Pelvis and Ureter)**
*___ Left
*___ Right
*___ Not specified

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

***MICROSCOPIC**

*Histologic Type

*___ 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 (check all that apply)**

*___ None identified
*___ Urothelial (transitional cell) papilloma (World Health Organization [WHO] / International Society of Urologic Pathology [ISUP], 1998)
*___ Urothelial (transitional cell) papilloma, inverted type
*___ Papillary urothelial (transitional cell) neoplasm, low malignant potential (WHO/ISUP 1998)
*___ Cannot be determined

***Histologic Grade**

*___ Not applicable
*___ Cannot be determined

<u>*Urothelial Carcinoma (WHO/ISUP, 1998)</u>

*___ Low-grade
*___ High-grade
*___ Other (specify): _____

<u>*Adenocarcinoma and Squamous Carcinoma</u>

*___ GX: Cannot be assessed
*___ G1: Well differentiated
*___ G2: Moderately differentiated
*___ G3: Poorly differentiated
*___ Other (specify): _____

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

***Adequacy of Material for Determining T Category**
*___ Muscularis propria (detrusor muscle) absent
*___ Muscularis propria (detrusor muscle) present
*___ Indeterminate

***Pathologic Staging (pTNM)**

*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 (detrusor muscle)

***Additional Pathologic Findings (check all that apply)**
*___ Urothelial dysplasia (low-grade intraurothelial neoplasia)
*___ Inflammation/regenerative changes
*___ Therapy-related changes
*___ Cautery artifact
*___ Cystitis cystica glandularis
*___ Keratinizing squamous metaplasia
*___ Intestinal metaplasia
*___ Other (specify): _____

***Comment(s)**

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2004
Applies primarily to invasive carcinomas and/or associated epithelial lesions, including carcinoma in situ
Based on AJCC/UICC TNM, 6th edition

URINARY BLADDER: Cystectomy, Partial, Total, or Radical; Anterior Exenteration

Patient name:
Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC

Specimen Type
___ Partial cystectomy
___ Total cystectomy
___ Radical cystectomy
___ Radical cystoprostatectomy
___ Anterior exenteration
___ Other (specify): _____
___ Not specified

***Tumor Site (check all that apply)**
*___ Trigone
*___ Right lateral wall
*___ Left lateral wall
*___ Anterior wall
*___ Posterior wall
*___ Dome
*___ Other (specify): _____
*___ Not specified

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

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

MICROSCOPIC

Histologic Type

___ 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 (check all that apply)

___ None identified
___ Urothelial (transitional cell) papilloma (World Health Organization [WHO] / International Society of Urologic Pathology [ISUP], 1998)
___ Urothelial (transitional cell) papilloma, inverted type
___ Papillary urothelial (transitional cell) neoplasm, low malignant potential (WHO/ISUP 1998)
___ Cannot be determined

Histologic Grade

___ Not applicable
___ Cannot be determined

Urothelial Carcinoma (WHO/ISUP, 1998)

___ Low-grade
___ High-grade
___ Other (specify): _____

Adenocarcinoma and Squamous Carcinoma

___ GX: Cannot be assessed
___ G1: Well differentiated
___ G2: Moderately differentiated
___ G3: Poorly differentiated
___ Other (specify): _____

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

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

Pathologic Staging (pTNM)

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 (detrusor muscle)
___ pT2a: Tumor invades superficial muscle (inner half)
___ pT2b: Tumor invades deep muscle
pT3: Tumor invades perivesical tissue
___ pT3a: Microscopically
___ pT3b: Macroscopically (extravesicular mass)
pT4: Tumor invades any of the following: prostate, uterus, vagina, pelvic wall, abdominal wall
___ pT4a: Tumor invades prostate or uterus or vagina
___ pT4b: Tumor invades pelvic wall or abdominal wall

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)
___ pMX: Cannot be assessed
___ pM1: Distant metastasis
*Specify site(s), if known: _____

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

Margins (check all that apply)
___ 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 site(s): _____
___ Margin(s) uninvolved by carcinoma in situ
___ Margin(s) involved by carcinoma in situ
Specify site(s): _____

***Venous/Lymphatic (Large/Small Vessel) Invasion (V/L)**
*___ Absent
*___ Present
*___ Indeterminate

Direct Extension of Invasive Tumor (check all that apply)
___ None identified
___ Perivesical fat
___ Rectum
___ Prostatic stroma
___ Seminal vesicle (specify laterality): _____
___ Vagina
___ Uterus and adnexae
___ Pelvic sidewall (specify laterality): _____
___ Ureter (specify laterality): _____
___ Other (specify): _____

***Additional Pathologic Findings (check all that apply)**
*___ Urothelial dysplasia (low-grade intraurothelial neoplasia)
*___ Inflammation/regenerative changes
*___ Therapy-related changes
*___ Cystitis cystica glandularis
*___ Keratinizing squamous metaplasia
*___ Intestinal metaplasia
*___ Other (specify): _____

***Comment(s)**

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2004
Applies primarily to invasive carcinomas and/or associated epithelial lesions, including carcinoma in situ
Based on AJCC/UICC TNM, 6th edition

RENAL PELVIS: Resection/Nephroureterectomy, Partial or Complete

Patient name:
Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC

Specimen Type
___ Nephroureterectomy, partial
___ Nephroureterectomy, complete
___ Other (specify): _____
___ Not specified

Laterality
___ Right
___ Left
___ Not specified

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

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

MICROSCOPIC

Histologic Type

___ 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 (check all that apply)

___ None identified
___ Urothelial (transitional cell) papilloma (World Health Organization [WHO] / International Society of Urologic Pathology [ISUP], 1998)
___ Urothelial (transitional cell) papilloma, inverted type
___ Papillary urothelial (transitional cell) neoplasm, low malignant potential (WHO/ISUP 1998)
___ Cannot be determined

Histologic Grade

___ Not applicable
___ Cannot be determined

Urothelial Carcinoma (WHO/ISUP, 1998)

___ Low-grade
___ High-grade
___ Other (specify): _____

Adenocarcinoma and Squamous Carcinoma

___ GX: Cannot be assessed
___ G1: Well differentiated
___ G2: Moderately differentiated
___ G3: Poorly differentiated
___ Other (specify): _____

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

Pathologic Staging (pTNM)

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 muscle
___ 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)
___ pMX: Cannot be assessed
___ pM1: Distant metastasis
*Specify site(s), if known: _____

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

Margins (check all that apply)
___ 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 site(s): _____
___ Margin(s) uninvolved by carcinoma in situ
___ Margin(s) involved by carcinoma in situ
Specify site(s): _____
___ Other(s) (specify): _____

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

***Venous/Lymphatic (Large/Small Vessel) Invasion (V/L)**
*___ Absent
*___ Present
*___ Indeterminate

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

***Comment(s)**

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2004
Applies primarily to invasive carcinomas and/or associated epithelial lesions, including carcinoma in situ
Based on AJCC/UICC TNM, 6th edition

URETER: Resection

Patient name:
Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC

Specimen Type
___ Ureterectomy
___ Nephroureterectomy
___ Other (specify): _____
___ Not specified

Laterality
___ Right
___ Left
___ Not specified

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

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

MICROSCOPIC

Histologic Type

___ 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 (check all that apply)

___ None identified
___ Urothelial (transitional cell) papilloma (World Health Organization [WHO] / International Society of Urologic Pathology [ISUP], 1998)
___ Urothelial (transitional cell) papilloma, inverted type
___ Papillary urothelial (transitional cell) neoplasm, low malignant potential (WHO/ISUP 1998)
___ Cannot be determined

Histologic Grade

___ Not applicable
___ Cannot be determined

Urothelial Carcinoma (WHO/ISUP, 1998)

___ Low-grade
___ High-grade
___ Other (specify): _____

Adenocarcinoma and Squamous Carcinoma

___ GX: Cannot be assessed
___ G1: Well differentiated
___ G2: Moderately differentiated
___ G3: Poorly differentiated
___ Other (specify): _____

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

Pathologic Staging (pTNM)

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
___ pT3: Tumor invades beyond muscularis 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)
___ pMX: Cannot be assessed
___ pM1: Distant metastasis
*Specify site(s), if known: _____

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

Margins (check all that apply)
___ 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 site(s): _____
___ Margins(s) involved by carcinoma in situ
___ Margin(s) uninvolved by carcinoma in situ
___ Other(s) (specify): _____

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

***Venous/Lymphatic (Large/Small Vessel) Invasion (V/L)**
*___ Absent
*___ Present
*___ Indeterminate

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

***Comment(s)**

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

Background Documentation

Protocol revision date: January 2004

I. Bladder Biopsy, Transurethral Resection of Bladder Tumor (TURBT) Specimen

A. Clinical Information

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
   d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history (Note **A**)
   b. Relevant findings (eg, cystoscopic or imaging study findings)
   c. Clinical diagnosis
   d. Procedure (eg, TURBT, cold cup, electroresection biopsy, tumor removal [specify site])
   e. Anatomic site/type of specimen

B. Macroscopic Examination

1. Specimen
   a. Unfixed/fixed (specify type of fixative)
   b. Number of pieces
   c. Greatest dimension of single specimen
   d. Aggregate volume of multiple fragments
2. Results of intraoperative consultation, if appropriate
3. Tissue submitted for microscopic evaluation
   a. All or selected sample(s) (if selected, estimate percentage submitted)
   b. Frozen section tissue fragment(s) (unless saved for special studies)
4. Special studies (specify)

C. Microscopic Evaluation

1. Specimen
   a. Adequacy of specimen (if unsatisfactory for evaluation, specify reason)
   b. Layers of bladder (specify if present or absent)
      (1) urothelium
      (2) lamina propria (subepithelial connective tissue)
      (3) muscularis propria
2. Tumor
   a. Histologic type (Note **B**)
   b. Histologic grade (specify grading system and total number of grades, if applicable) (Note **C**)
   c. Site(s) of involvement (eg, trigone, dome)
   d. Pattern of growth
      (1) noninvasive (pure)
         i. papillary
         ii. flat carcinoma in situ (CIS)
         iii. papillary and flat CIS
      (2) invasive (pure)

(3) mixed, noninvasive and invasive
i. papillary and invasive
ii. flat CIS and invasive
iii. papillary and flat CIS and invasive
(4) indeterminate

e. Extent of invasion (specify invasion of layers listed)
(1) confined to epithelium (Note **D**)
(2) subepithelial connective tissue or lamina propria, including muscularis mucosae (Notes **D** and **E**)
(3) muscularis propria (Notes **D** and **E**)
(4) prostatic involvement (Note **E**)
i. urethral mucosa (flat in situ, papillary noninvasive, or invasive)
ii. restricted to prostatic ducts or acini (in situ)
iii. prostatic stromal invasion
iv. multiple patterns (urethral mucosa, prostatic ducts or acini, stromal)
v. indeterminate (state reason) (eg, tumor only, cautery artifact)

f. Venous/lymphatic vessel invasion (Note **F**)

3. Additional pathologic findings, if present
a. Urothelial carcinoma in situ (high-grade intraurothelial neoplasia) (focal/multifocal)
b. Urothelial dysplasia (low-grade intraurothelial neoplasia) (focal/multifocal)
c. Inflammation**/**regenerative changes
d. Therapy related
e. Thermocoagulation effect (Note **D**)
f. Other(s) (specify) (eg, cystitis cystica glandularis, keratinizing squamous metaplasia, intestinal metaplasia)
4. Results/status of special studies (specify) (eg, immunohistochemistry)
5. Comments
a. Correlation with intraoperative consultation, as appropriate
b. Correlation with other specimens, as appropriate
c. Correlation with clinical information, as appropriate

II. Cystectomy (Partial, Total), Radical Cystoprostatectomy, Pelvic Exenteration

A. Clinical Information

1. Patient identification
a. Name
b. Identification number
c. Age (birth date)
d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
a. Relevant history (eg, previous diagnosis, previous treatment) (Note **A**)
b. Relevant findings (eg, clinical findings, cystoscopic findings, radiologic studies)
c. Clinical diagnosis

d. Procedure
   (1) partial cystectomy
   (2) total cystectomy
   (3) cystoprostatectomy
   (4) pelvic exenteration
   (5) lymphadenectomy
e. Operative findings
f. Anatomic sites of specimen

B. Macroscopic Examination

1. Specimen
   a. Organ(s)/tissue(s) included
   b. Unfixed/fixed (specify type of fixative)
   c. Opened/unopened
   d. External aspect (documentation of extent of resection)
   e. Size (3 dimensions) (specify for partial cystectomy)
   f. Note areas designated by surgeon
   g. Results of intraoperative consultation
2. Tumor
   a. Location (trigone, left/right/anterior/posterior wall, dome)
   b. Size (3 dimensions)
   c. Descriptive features (pattern of growth, gross appearance)
      (1) papillary (pure)
      (2) solid/nodular, flat, ulcerated
      (3) mixed
      (4) indeterminate
   d. Extent (depth of bladder wall) of invasion (Note **E**)
   e. Involvement of adjacent structures, if present (eg, prostate, vagina) (Note **G**)
   f. Relation to specimen margins (Note **H**)
3. Other pathologic findings, if present
   a. Mucosal abnormalities
   b. Other
4. Ureter(s)
5. Margins, as appropriate (Note **H**)
6. Regional lymph nodes
   a. Location (all nodes are designated contiguous unless specified by surgeon)
   b. Number
   c. Description (describe gross tumors)
7. Separately submitted lymph nodes
   a. Location (as specified by surgeon)
   b. Number
   c. Description (describe gross tumors)
8. Other submitted tissue
   a. Location (as specified by surgeon)
   b. Descriptive features
      (1) prostate
      (2) seminal vesicles
      (3) uterus
      (4) vagina
      (5) rectum
      (6) pelvic wall
      (7) urethra

(8) ureter(s)
(9) other(s) (specify)

9. Sections submitted for microscopic evaluation (Note **G**)
   a. Tumor
      (1) representative
      (2) tumor at point of deepest penetration of wall
      (3) interface of tumor with adjacent bladder wall
   b. Mucosa remote from cancer
   c. Areas with additional pathologic findings
   d. Margin(s) of resection
   e. Ureter(s)
   f. Penile/bulbomembranous urethra
   g. Prostatic urethra
   h. Prostate and seminal vesicles, representative
   i. Lymph nodes
   j. Pelvic wall
   k. Areas designated by surgeon
   l. Sections of other submitted tissues (specify) (eg, vagina, uterus, rectum)
   m. Frozen section tissue fragment(s) (unless saved for special studies)
10. Special studies (specify) (eg, immunohistochemistry, morphometry, DNA analysis [specify type], gross photograph [if obtained])

C. Microscopic Evaluation

1. Tumor
   a. Histologic type (Note **B**)
   b. Histologic grade (specify grading scheme and total number of grades, if applicable) (Note **C**)
   c. Site(s) (focal/multifocal)
   d. Pattern of growth
      (1) noninvasive (pure)
         i. papillary
         ii. flat CIS
         iii. papillary and flat CIS
      (2) invasive (pure)
      (3) mixed, noninvasive and invasive
         i. papillary and invasive
         ii. flat CIS and invasive
         iii. papillary and flat CIS and invasive
      (4) indeterminate
   e. Extent of invasion (specify each layer as involved or uninvolved by tumor) (Note **D**)
   f. Involvement of other tissue(s)/structure(s) (Notes **D** and **E**)
      (1) prostatic urethra (flat CIS, noninvasive papillary, or invasive)
      (2) prostate ducts and acini (without stromal invasion)
      (3) prostatic stroma
      (4) seminal vesicles
      (5) bulbomembranous or penile urethral mucosa
      (6) uterus
      (7) vagina
      (8) rectum
      (9) pelvic wall
      (10) abdominal wall

   g. Areas marked by surgeon
   h. Venous/lymphatic vessel invasion (Note **F**)
2. Margins (Note **H**)
   a. Ureters
   b. Urethral
   c. Paravesicular soft tissue (total cystectomy specimens)
   d. Pelvic soft tissue (pelvic exenteration specimens)
3. Additional pathologic findings, if present
   a. Urothelial carcinoma in situ (high-grade intraurothelial neoplasia) (focal/multifocal)
   b. Urothelial dysplasia (low-grade intraurothelial neoplasia) (focal/multifocal)
   c. Inflammation/regenerative changes
   d. Therapy related
   e. Other(s) (specify) (eg, cystitis cystica glandularis, keratinizing squamous metaplasia, intestinal metaplasia)
4. Regional lymph nodes (Note **E**)
   a. Site(s)/laterality
   b. Number
   c. Number involved by tumor
   d. Extranodal extension
   e. Size of metastasis
5. Separately submitted lymph nodes (report as specified)
   a. Total number examined, by site and laterality
   b. Number
   c. Number involved by tumor
   d. Extranodal extension
   e. Size of metastasis
6. Other submitted organ(s)/tissue(s)
   a. Prostate
      (1) invaded by bladder tumor
      (2) prostatic adenocarcinoma (see Prostate protocol[1] for details)
      (3) other pathologic features (eg, high-grade prostatic intraepithelial neoplasia, inflammation, hyperplasia)
   b. Other(s) (ureter/urethra/seminal vesicles/vagina/rectum)
      (1) invaded by bladder tumor
      (2) other tumors
      (3) other pathologic features (eg, inflammation, hyperplasia, CIS)
   c. Margins, as appropriate
7. Results/status of special studies (specify)
8. Distant metastasis (specify sites)
9. Comments
   a. Correlation with intraoperative consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

III. Nephroureterectomy or Ureterectomy Specimen

A. Clinical Information

1. Patient identification
    a. Name
    b. Identification number
    c. Age (birth date)
    d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
    a. Relevant history (eg, previous diagnosis, previous treatment) (Note **A**)
    b. Relevant findings (eg, radiologic studies)
    c. Clinical diagnosis
    d. Procedure (specify anatomic site[s])
    e. Operative findings
    f. Anatomic site(s) of specimen
    g. Results of intraoperative consultation

B. Macroscopic Examination

1. Specimen
    a. Organ(s)/tissue(s) included
    b. Unfixed/fixed (specify type of fixative)
    c. External aspect (documentation of extent of resection)
    d. Size (3 dimensions) (specify if partial nephrectomy)
    e. Areas designated by surgeon
    f. Result of intraoperative consultation
2. Tumor
    a. Location (pelvi-calyceal system, ureter)
    b. Size (3 dimensions)
    c. Description (pattern of growth, gross appearance)
        (1) papillary (pure)
        (2) solid/nodule, flat, ulcerated
        (3) mixed
        (4) indeterminate
    d. Extent (depth) of invasion (Notes **D** and **E**)
3. Margins
    a. Ureteral margin (proximal and distal in ureterectomy specimen)
    b. Bladder cuff/renal pelvic margin
    c. Gerota's fascia/perinephric fat margin (in nephrectomy specimen)
    d. Hilar soft tissue
    e. Renal parenchyma (partial nephrectomy)
    f. Periureteral soft tissue radial margin (ureterectomy specimens)
4. Additional pathologic features, if present
    a. Mucosal abnormalities
    b. Other lesions (including of renal parenchyma)
5. Lymph nodes submitted as part of specimen
    a. Location (all nodes are designated contiguous unless otherwise specified by surgeon)
    b. Number
    c. Description (specify gross metastasis)

6. Separately submitted lymph nodes
   a. Location (as specified by surgeon)
   b. Number
   c. Description (specify gross metastasis)
7. Sections submitted for microscopic evaluation
   a. Tumor
      (1) representative
      (2) tumor at point of deepest penetration
      (3) interface of tumor with adjacent pelvis and kidney
   b. Mucosa of pelvis remote from cancer
   c. Areas with additional pathologic findings
   d. Margin(s) of resection
      (1) ureter (proximal and distal in ureterectomy specimens)
      (2) bladder cuff margin
      (3) Gerota's fascia (perinephric fat)
      (4) hilar soft tissue margin
      (5) renal parenchyma (partial nephrectomy)
   e. Areas designated by surgeon
   f. All lymph nodes
   g. Frozen section tissue fragment(s) (unless saved for special studies)
8. Special studies (specify type) (eg, immunohistochemistry, DNA analysis) and gross photography, if obtained

C. Microscopic Evaluation

1. Tumor
   a. Histologic type (Note **B**)
   b. Histologic grade (specify grading scheme and total number of grades, if applicable) (Note **C**)
   c. Pattern of growth
      (1) noninvasive (pure)
         i. papillary
         ii. flat CIS
         iii. papillary and flat CIS
      (2) invasive (pure)
      (3) mixed, noninvasive and invasive
         i. papillary and invasive
         ii. flat CIS and invasive
         iii. papillary and flat CIS and invasive
      (4) indeterminate
   d. Site(s)
   e. Extent of invasion (specify each layer as involved or uninvolved) (Notes **D** and **E**)
      (1) confined to epithelium
      (2) subepithelial connective tissue
      (3) muscularis propria
      (4) peripelvic connective tissue
      (5) renal parenchyma
      (6) beyond kidney in perinephric fat
   f. Venous/lymphatic vessel invasion (Note **F**)

2. Margins (Note **H**)
   a. Ureteral
   b. Bladder neck
   c. Gerota's fascia (perinephric fat margin)
   d. Hilar soft tissue
   e. Renal parenchyma (partial nephrectomy)
3. Additional pathologic findings, if present
   a. Urothelial carcinoma in situ (high-grade intraurothelial neoplasia) (focal/multifocal)
   b. Urothelial dysplasia (low-grade intraurothelial neoplasia) (focal/multifocal)
   c. Inflammation/regenerative changes
   d. Therapy related
   e. Renal epithelial neoplasm (see Kidney protocol[2] for details)
   f. Other(s) (specify) (eg, cystitis cystica glandularis, keratinizing squamous metaplasia, intestinal metaplasia)
4. Regional lymph nodes (Note **E**)
   a. Site(s)/laterality
   b. Number
   c. Number involved by tumor
   d. Extranodal extension
   e. Size of metastasis
5. Separately submitted lymph nodes (report as specified)
   a. Total number examined by site and laterality
   b. Number involved by tumor
   c. Extranodal extension
   d. Size of metastasis
6. Distant metastasis (specify sites)
7. Results/status of special studies (specify)
8. Comments
   a. Correlation with intraoperative consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

Explanatory Notes

A. History

A relevant history is important for interpretation of all bladder specimens.[3-6] A history of renal stones, recent urinary tract procedures, infections, or obstruction can influence the urinary cytologic interpretation or the interpretation of random biopsies obtained on patients with hematuria. Any neoplasms previously diagnosed should be specified, including the histologic type, primary site, and histologic grade. Primary tumors of the ureter may be associated with hereditary non-polyposis colon cancer (HNPCC) syndrome. 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

The vast majority (more than 95%) of carcinomas of the urinary bladder, renal pelvis, and ureter are urothelial or transitional cell in origin. 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 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.[7-12] 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 Urinary Bladder, Including Urothelial (Transitional Cell) Carcinoma and Its Variants[#]

- Urothelial (Transitional Cell) Neoplasia
  - Benign
    - Transitional papilloma (World Health Organization [WHO] / International Society of Urologic Pathology [ISUP], 1998; WHO, 1973, grade 0)
    - Inverted papilloma
  - Papillary urothelial neoplasm of low malignant potential (WHO/ISUP, 1998; WHO, 1973, grade I)
  - 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
  - Anatomic variants
    - Bladder mucosa
    - Urachal
    - With exstrophy
    - From endometriosis
  - 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, and when invasive may be microinvasive (invasive to a depth of 2 mm or less) or frankly invasive (like nonpapillary tumors).

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

C. Histologic Grade

Flat intraepithelial lesions and papillary and invasive lesions are graded separately.[12-16] Until recently, there was 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.[7,9] 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.[12-14] 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.[12] 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) [12] system and the older WHO (1973)[14] system, eg, papillary urothelial neoplasm of low malignant potential (WHO/ISUP, 1998)/transitional cell carcinoma, grade I (WHO, 1973), may be concurrently used.

The WHO (1999) classification of bladder tumors[11] differs only slightly from the WHO/ISUP (1998) system[12] in that carcinomas are graded on a I to III scale in the former and low-grade and high-grade in the latter. Most cases designated as grade II and III by the WHO (1999) system correspond to high-grade carcinomas in the WHO/ISUP (1998) Consensus Classification.

WHO/ISUP (1998) 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 (detrusor muscle) 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

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).[17-19] 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.[20-22] Although attempts at substaging bladder pT1 tumors have been made, the WHO/ISUP committee recommended that it is currently not necessary for the practice to be universally adopted.[12] Pathologists are, however, 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.[23] 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. A comment on thermocoagulation effect may be made, especially if its presence impedes diagnostic evaluation.[24] In transurethral resection of bladder tumor (TURBT) specimens invasive into muscularis propria, no attempt should be made to substage the depth of muscularis propria invasion. Since fat may be present in the lamina propria and muscularis propria, the presence of tumor in adipose tissue is not necessarily diagnostic of extravesical spread; this determination is reserved for cystectomy specimens.[25]

Involvement of the prostate gland may occur in several different patterns. The prostatic urethra may be involved (flat carcinoma in situ, papillary or invasive carcinoma), or the prostate gland may be involved. Involvement of the prostate gland may be evident as involvement of prostatic ducts and acini without stromal invasion (carcinoma in situ involving prostate glands), or as urothelial carcinoma involving prostatic stroma (either from prostatic urethral carcinoma, carcinoma extending directly through the bladder wall, or carcinoma involving prostatic ducts and acini additionally with stromal invasion).[26]

E. TNM and Stage Groupings

The TNM Staging System for carcinomas of the urinary bladder of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) is recommended and shown below.[17,18]

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): Urinary Bladder[#] [Figure 1]

TX Primary tumor cannot be assessed
T0 No evidence of primary tumor
Ta Papillary noninvasive carcinoma
Tis Carcinoma in situ: "flat tumor"
T1 Tumor invades subepithelial connective tissue
T2 Tumor invades muscle
T2a Tumor invades superficial muscle (inner half)
T2b Tumor invades deep muscle (outer half)
T3 Tumor invades perivesical tissue
T3a Microscopically
T3b Macroscopically (extravesicular mass)
T4 Tumor invades any of the following: prostate, uterus, vagina, pelvic wall, and abdominal wall
T4a Tumor invades prostate or uterus or vagina
T4b Tumor invades pelvic wall or abdominal wall

Primary Tumor (T): Renal Pelvis and Ureter[#] [Figures 2 through 4]

TX Primary tumor cannot be assessed
T0 No evidence of primary tumor
Ta Papillary noninvasive carcinoma
Tis Carcinoma in situ
T1 Tumor invades subepithelial connective tissue
T2 Tumor invades the muscularis
T3 For renal pelvis only: Tumor invades beyond muscularis into peripelvic fat or the renal parenchyma
T3 For ureter only: Tumor invades beyond muscularis into periureteric fat
T4 Tumor invades adjacent organs, or through the kidney into the perinephric fat

[#] 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.

Regional Lymph Nodes (N)

Regional lymph nodes are those within the true pelvis; all others are distant nodes.

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in a single lymph node, 2 cm or less in greatest dimension
N2 Metastasis in a single 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
N3 Metastasis in a lymph node more than 5 cm in greatest dimension

Distant Metastasis (M)

MX Distant metastasis cannot be assessed
M0 No distant metastasis
M1 Distant metastasis

TNM Stage Grouping: Bladder

Stage 0a	Ta	N0	M0
Stage 0is	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2a	N0	M0
	T2b	N0	M0
Stage III	T3a	N0	M0
	T3b	N0	M0
	T4a	N0	M0
Stage IV	T4b	N0	M0
	Any T	N1,2,3	M0
	Any T	Any N	M1

TNM Stage Grouping: Renal Pelvis and Ureter

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

TNM Descriptors

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

The “a” prefix designates the stage determined at autopsy: aTNM.

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. Venous/Lymphatic Vascular Invasion

Urothelial carcinoma may invade blood vessels or lymphatic channels. In suspicious cases, blood vessels can be highlighted by immunohistochemical staining for factor VIII-related antigen, CD31 or CD34.[19-22] 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.[7]

G. Sections for Microscopic Evaluation

Bladder

Sections of bladder for microscopic evaluation are as follows. In TURBT 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. If tumor is invasive into lamina propria in the initial sampling, additional sections (including possibly submitting the entire specimen) may be necessary to diagnose or rule out the possibility of muscularis propria invasion. In 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 1 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. Parenthetically, it must be noted that there is a higher incidence of prostatic adenocarcinoma in cystoprostatectomy specimens of bladder carcinoma. Close gross examination may help target sampling of selective abnormal-appearing areas.

Lymph Nodes

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. Lymph nodes may be grossly or microscopically detected in the perivesical fat.

Other Tissues
Submit 1 or more sections of uterus (as indicated) and 1 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.

H. Margins
Resection margins, including those mentioned in Note **G**, 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. 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.

References

1. Srigley JR, Amin MB, Humphrey PA, For the Members of the Cancer Committee, College of American Pathologists. *Prostate. Protocol Applies to Invasive Carcinomas of the Prostate Gland.* Northfield, Ill: College of American Pathologists; 2003. Available at: ftp://ftp.cap.org/cancerprotocols/prostate03_p.pdf. Accessed May 14, 2003.
2. Srigley JR, Amin MB, For the Members of the Cancer Committee, College of American Pathologists. *Kidney. Protocol Applies to All Invasive Carcinomas of Renal Tubular Origin. It Excludes Wilms Tumors and Tumors of Urothelial Origin.* Northfield, Ill: College of American Pathologists; 2003. Available at: ftp://ftp.cap.org/cancerprotocols/kidney03_p.pdf. Accessed May 14, 2003.
3. Murphy WM. Diseases of the urinary bladder, urethra, ureters and renal pelvis. In: Murphy WM, ed. *Urological Pathology*. 2nd ed. Philadelphia, Pa: WB Saunders Co; 1997:75-96.
4. Ro JY, Staerkel GA, Ayala AG. Cytologic and histologic features of superficial bladder cancer. *Urol Clin North Am.* 1992;19:435-453.
5. Grignon DJ. Neoplasms of the urinary bladder. In: Bostwick DG, Eble JN, eds. *Urologic Surgical Pathology.* St. Louis, Mo: Mosby Year Book, Inc; 1997:223-230.
6. Hughes JH, Raab SS, Cohen MB. The cytologic diagnosis of low-grade transitional cell carcinoma. *Am J Clin Pathol.* 2000;114(supp1):559-567.
7. Amin MB, Murphy WM, Reuter VE, et al. Controversies in the pathology of transitional cell carcinoma of the urinary bladder. Part I, Chapter 1. In: Rosen PP, Fechner RE, eds. *Reviews of Pathology.* Vol. 1. Chicago, Ill: ASCP Press; 1996:1-39.
8. Reuter VE, Melamed MR. The urothelial tract: renal pelvis, ureter, urinary bladder and urethra. In: Sternberg SS, Antonioli DA, Carter D, Mills SE, Oberman HR, eds. *Diagnostic Surgical Pathology.* 3rd ed. Philadelphia, Pa: Lippincott Williams and Wilkins; 1999:1853-93.
9. Amin MB, Young RH. Intraepithelial lesions of the urinary bladder with a discussion of the histogenesis of urothelial neoplasia. *Semin Diagn Pathol.* 1997;14(2):84-97.

10. Eble JN, Young RH. Carcinoma of the urinary bladder: a review of its diverse morphology. *Semin Diagn Pathol.* 1997;14(2):98-108.
11. Mostofi FK, Davis CJ, Sesterhenn IA. Histologic typing of urinary bladder tumors. In: *World Health Organization International Histologic Classification of Tumours.* 2nd ed. Heidelberg, Germany: Springer-Verlag, Berlin; 1999.
12. 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;22:1435-1448.
13. Murphy WM, Beckwith JB, Farrow GM. Tumors of the kidney, bladder, and related urinary structures. In: *Atlas of Tumor Pathology*. 3rd series. Fascicle 11. Washington, DC: Armed Forces Institute of Pathology; 1994.
14. Mostofi FK. Histological typing of urinary bladder tumours. In: *WHO Histological Classification of Tumours. No. 10.* Geneva, Switzerland: World Health Organization; 1973.
15. Bergkvist A, Ljungqvist A, Moberger G. Classification of bladder tumors based on the cellular pattern. *Acta Chir Scand*. 1965;130:371-378.
16. Friedell GH, Bell JR, Burney SW, Soto EA, Tiltman AJ. Histopathology and classification of urinary bladder carcinoma. *Urol Clin North Am*. 1976;3:265-227.
17. Greene FL, Page DL, Fleming ID, et al, eds. *AJCC Cancer Staging Manual.* 6th ed. New York: Springer; 2002.
18. Sobin LH, Wittekind C. *UICC TNM Classification of Malignant Tumours.* 6th ed. New York: Wiley-Liss; 2002.
19. Jimenez RE, Keane TE, Hardy HT, Amin MB. pT1 urothelial carcinoma of the bladder: criteria for diagnosis, pitfalls, and clinical implications. *Adv Anat Pathol.* 2000;7(1):13-25.
20. Amin MB, Murphy WM, Reuter VE, et al. Controversies in the pathology of transitional cell carcinoma of the urinary bladder. Part II, Chapter 5. In: Rosen PP, Fechner RE, eds. *Reviews of Pathology.* Vol. 2. Chicago, Ill: ASCP Press; 1997:71-110.
21. Larsen MP, Steinberg GD, Brendler CB, Epstein JI. Use of Ulex europaeus agglutinin I (UEAI) to distinguish vascular and “pseudovascular” invasion in transitional cell carcinoma of bladder with lamina propria invasion. *Mod Pathol.* 1990;3:83-88.
22. Ramani P, Birch BR, Harland SJ, Parkinson MC. Evaluation of endothelial markers in detecting blood and lymphatic channel invasion in pT1 transitional carcinoma of bladder. *Histopathology.* 1991;19:551-554.
23. Ro JY, Ayala AG, El-Naggar A. Muscularis mucosa of urinary bladder: importance for staging and treatment. *Am J Surg Pathol*. 1983;136:265-271.
24. Murphy WM. ASCP survey on pathology examination of the urinary bladder. *Am J Clin Pathol*. 1994;102:715-723.
25. Philip AT, Amin MB, Tamboli P, Lee TJ, Hill CE, Ro JY. Intravesical adipose tissue: a quantitative study of its presence and location with implications for therapy and prognosis. *Am J Surg Pathol.* 2000;24:1286-1290.
26. Mahadevia PS, Koss LG, Tar IJ. Prostatic involvement in bladder cancer. *Cancer.* 1986;58:2096-2102.

QuickTime™ and a
Photo - JPEG decompressor
are needed to see this picture.

Figure 1. Schematic depiction of pathologic stage (TNM, 1997; and TNM, 2002) for carcinomas of the urinary bladder.
From: Hermanek P, Hutter RVP, Sobin LH, Wagner G, Wittekind C, eds. *UICC TNM Atlas: Illustrated Guide to the TNM/pTNM Classification of Malignant Tumors.* 4th ed. Berlin-Heidelberg, Germany: Springer-Verlag; 1997:311(figure 399).
Reproduced with permission.

QuickTime™ and a
Photo - JPEG decompressor
are needed to see this picture.

Figure 2. Schematic depiction of pathologic stage (TNM, 1997; and TNM, 2002) pTa, pT1 and pT2 carcinomas of the renal pelvis and ureter.
From: Hermanek P, Hutter RVP, Sobin LH, Wagner G, Wittekind C, eds. *UICC TNM Atlas: Illustrated Guide to the TNM/pTNM Classification of Malignant Tumors.* 4th ed. Berlin-Heidelberg, Germany: Springer-Verlag; 1997:304(figure 387).
Reproduced with permission.

QuickTime™ and a
Photo - JPEG decompressor
are needed to see this picture.

Figure 3. Schematic depiction of pathologic stage (TNM, 1997; and TNM, 2002) pT3 carcinomas of the renal pelvis and ureter.
From: Hermanek P, Hutter RVP, Sobin LH, Wagner G, Wittekind C, eds. *UICC TNM Atlas: Illustrated Guide to the TNM/pTNM Classification of Malignant Tumors.* 4th ed. Berlin-Heidelberg, Germany: Springer-Verlag; 1997:304(figure 388).
Reproduced with permission.

QuickTime™ and a
Photo - JPEG decompressor
are needed to see this picture.

Figure 4. Schematic depiction of pathologic stage (TNM, 1997; and TNM, 2002) pT4 carcinomas of the renal pelvis and ureter.
4A. Involvement of a vertebral body.
4B. Involvement of major blood vessel and direct extension into the bladder.
4C. Extension into perinephric fat through the kidney.
From: Hermanek P, Hutter RVP, Sobin LH, Wagner G, Wittekind C, eds. *UICC TNM Atlas: Illustrated Guide to the TNM/pTNM Classification of Malignant Tumors.* 4th ed. Berlin-Heidelberg, Germany: Springer-Verlag; 1997:305(figures 389-391). Reproduced with permission.