

# Urinary Bladder, Ureter, and Renal Pelvis

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

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*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**

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## 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

**\*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): \_\_\_\_\_

**\*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)**

**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)

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**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): \_\_\_\_\_

**\*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: \_\_\_\_\_

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**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)**

- 8                   \* 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)

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**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): \_\_\_\_\_

**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): \_\_\_\_\_

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**\*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)**

**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)

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**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): \_\_\_\_\_

**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): \_\_\_\_\_

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\***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)**



## Background Documentation

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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<sup>1</sup> 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<sup>2</sup> 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.<sup>3-6</sup> 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.<sup>7-12</sup> 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<sup>#</sup>**

## 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<sup>##</sup>

- 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<sup>###</sup>
  - Small cell carcinoma
  - Large cell neuroendocrine carcinoma
  - Lymphoepithelioma-like carcinoma
  - Giant cell carcinoma
  - Not otherwise specified
- Metastatic Carcinoma

# Modified from Amin et al.<sup>7</sup>

## 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.<sup>12-16</sup> 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.<sup>7,9</sup> 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.<sup>12-14</sup> 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.<sup>12</sup> 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)<sup>12</sup> system and the older WHO (1973)<sup>14</sup> 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<sup>11</sup> differs only slightly from the WHO/ISUP (1998) system<sup>12</sup> 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<sup>#</sup>

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)<sup>#</sup>

Papillary Neoplasms

Papilloma

Inverted papilloma

Papillary neoplasm of low malignant potential

Papillary carcinoma, low-grade

Papillary carcinoma, high-grade<sup>###</sup>

Invasive Neoplasms

Lamina propria invasion

Muscularis propria (detrusor muscle) invasion

<sup>#</sup> May include cases formerly diagnosed as “mild dysplasia.”

<sup>##</sup> Includes cases with “severe dysplasia.”

<sup>###</sup> 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).<sup>17-19</sup> 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.<sup>20-22</sup> 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.<sup>12</sup> 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.<sup>23</sup> 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.<sup>24</sup> 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.<sup>25</sup>

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).<sup>26</sup>

### 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.<sup>17,18</sup>

By AJCC/UICC convention, the designation “T” refers to a primary tumor that has not been previously treated. The symbol “p” refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathologic staging is usually performed after surgical resection of the primary tumor. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumor has been completely removed. If a biopsied tumor is not resected for any reason (eg, when technically unfeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

**Primary Tumor (T): Urinary Bladder<sup>#</sup>** [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<sup>#</sup>** [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

<sup>#</sup> 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.<sup>19-22</sup> 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.<sup>7</sup>

#### **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.

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**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*. 4<sup>th</sup> ed. Berlin-Heidelberg, Germany: Springer-Verlag; 1997:311 (figure 399).  
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**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*. 4<sup>th</sup> ed. Berlin-Heidelberg, Germany: Springer-Verlag; 1997:304 (figure 387).  
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**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*. 4<sup>th</sup> ed. Berlin-Heidelberg, Germany: Springer-Verlag; 1997:304 (figure 388).  
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**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*. 4<sup>th</sup> ed. Berlin-Heidelberg, Germany: Springer-Verlag; 1997:305(figures 389-391).  
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