Protocol for the Examination of Specimens from Patients with Primary Carcinoma of the Urinary Bladder

Protocol applies to invasive carcinomas of the urinary tract, including urothelial carcinoma, its morphological variants, and other carcinomas (squamous cell carcinoma, adenocarcinoma, Müllerian carcinoma, neuroendocrine carcinoma, and sarcomatoid carcinoma). This protocol does not include urachal carcinoma, lymphoma, or sarcoma.

Based on:

AJCC Cancer Staging Manual, Eighth Edition pTNM requirements
CAP Cancer Protocols: Bladder_4.1.0.0, Bladder.Bx.TURBT_4.1.0.0
CAP Protocol Web Posting Date: June 2021
AAPA Macroscopic Examination Template Edition 3.0
AAPA Web Posting Date: December 2022

Revision History:

1st Edition – April 2017
2nd Edition – October 2018

Summary of Changes:

This protocol has been updated to the 8th Edition AJCC Cancer Staging Manual and the current version of the CAP Cancer Protocols Bladder_4.1.0.0 and Bladder.Bx.TURBT_4.1.0.0.

This is a major revision to the protocol. Extensive changes have been made throughout the document.

Procedures Covered in this Protocol:

- Biopsy
- Transurethral resection of bladder tumor
- Cystectomy
  - Partial cystectomy
  - Total or radical cystectomy
  - Radical cystoprostatectomy
  - Anterior exenteration

Authors:
Mari Kiedysz, PA (ASCP)CM*, Patrice Brown, PA(ASCP)CM, Lainee Bulawa, PA(ASCP)CM, Eleni Constantopoulos, PA(ASCP)CM, Heather Gaburo, PA(ASCP)CM, Courtney Hyland, PA(ASCP)CM, Monica Kendall, PA(ASCP)CM, Darryl Kinnear, PA(ASCP)CM, Alysha Martini, PA(ASCP)CM, Erika Paulsen, PA(ASCP)CM, Molly Person, PA(ASCP)CM, Erica Reed, PA(ASCP)CM, Dennis Strenk, PA(ASCP)CM, Constance Thorpe, PA(ASCP)CM, Jon Wagner, PA(ASCP)CM

*Denotes primary author. All other contributing authors are listed alphabetically.

Previous Lead Contributor:
Anthony Cerullo, PA(ASCP)CM

Art Director:
Jesse McCoy, BFA, MHS, PA(ASCP)CM

Photograph Curator:
Lainee Bulawa, MS, PA(ASCP)CM

Illustrator:
Tami Tolpa

Structured Macroscopic Report
Carcinoma of the Urinary Bladder

Procedure
____ Biopsy
____ Transurethral resection of bladder *(TURBT)*
____ Partial cystectomy
____ Radical cystectomy *(total cystectomy)*
____ Radical cystoprostatectomy
____ Anterior exenteration
____ Other *(specify)*: _____

Nature of Specimen Received
____ Fresh
+____ Frozen section *(intraoperative consultation)*
+____ Tissue collected for ancillary diagnostic studies *(specify test)*: _____
____ In fixative
Fixative type: _____
+ Cold ischemic time: _____
+ Fixation time *(specify if for entire specimen or specific components):* _____
____ Other transport media *(specify)*: _____

Specimen Orientation
____ Specimen oriented
____ Oriented by surgeon *(specify)*: _____
____ Oriented based on anatomic landmarks
____ Not oriented

Specimen Integrity
____ Intact
____ Disrupted / fragmented
____ Other *(specify)*: _____

Ink Key
____ Ink applied *(provide anatomic site and color applied)*:
____ Right perivesical soft tissue and fat margin
____ Left perivesical soft tissue and fat margin
+____ Transmural excision margin *(partial cystectomy)*
+____ Right prostate margin
+____ Left prostate margin
+____ Anterior prostate staple margin *(dorsal vein complex margin)*
+____ Vaginal wall margin
+____ Posterior cervical amputation margin
+____ Anterior uterine serosa
+____ Posterior uterine serosa
+____ Mesorectum

Overall Dimensions *(cm)*
___ x ___ x ___ cm

Specimen Anatomical Components and Size in Three Dimensions *(if applicable, list specimen components)*
____ Bladder: ___ x ___ x ___ cm
____ Right ureter: ___ cm *(length)* x ___ cm *(diameter)*
____ Left ureter: ___ cm *(length)* x ___ cm *(diameter)*

Additional Structures Identified and Measurements *(if applicable, list additional structures identified)*

+____ Prostate: ___ cm *(right to left)* x
___ cm *(superior to inferior)* x
___ cm *(anterior to posterior)*
+____ Right seminal vesicle: ___ x ___ x ___ cm
+____ Left seminal vesicle: ___ x ___ x ___ cm
+____ Right vas deferens: ___ cm *(length)* x ___ cm *(diameter)*
+____ Left vas deferens: ___ cm *(length)* x ___ cm *(diameter)*
+____ Urethra: ___ cm *(length)* x ___ cm *(diameter)*
+____ Vaginal wall: ___ cm *(length)* x ___ cm *(width)* x ___ cm *(thickness)*
+____ Vulva: ___ cm *(length)* x ___ cm *(width)* x ___ cm *(excisional depth)*
+____ Uterus: ___ cm *(superior to inferior)* x
___ cm *(cornu to cornu)* x
___ cm *(anterior to posterior)*
+____ Right ovary: ___ x ___ x ___ cm
+____ Left ovary: ___ x ___ x ___ cm
+____ Right fallopian tube: ___ x ___ x ___ cm
+____ Left fallopian tube: ___ x ___ x ___ cm
+____ Rectum / colon: ___ cm *(length)* x ___ cm *(circumference)*
+____ Anus: ___ cm *(length)* x ___ cm *(circumference)*

Macroscopic Tumor

____ Not identified
____ Present

Tumor Focality

____ Unifocal
____ Multifocal
Number of tumors: ___
____ Indeterminate *(explain)*: _____

Tumor Site*(s)*

____ Right lateral wall
____ Left lateral wall
____ Trigone
____ Anterior wall
____ Posterior wall
____ Dome
____ Other
____ Not specified

Macroscopic Tumor Size *(of each if multifocal)*

Greatest dimension: ___ cm
+Additional dimensions: ___ x ___ cm
____ Indeterminate *(explain)*: _____

+**Macroscopic Appearance of Tumor**

+Color: _____	Homogeneous	Variegated		
+Consistency:	Firm	Soft	Ulcerated	Other: _____
+Shape:	Flat	Papillary	Other: _____	
+Hemorrhage:	Yes	No		
+Necrosis:	Yes	No		

Macroscopic Extent of Tumor *(involvement of adjacent structures)*

____ Tumor confined to epithelium

____ Tumor invades lamina propria
____ Tumor invades muscularis propria
____ Tumor invades perivesical soft tissue
____ Tumor invades adjacent structures
Male:
____ Prostate *(transmural invasion)* *
____ Seminal vesicles
Female:
____ Uterus
____ Vagina
____ Adnexae
____ Vulva
Male / Female:
____ Pelvic wall
____ Abdominal wall
____ Rectum
____ Other *(specify)*: _____

**Transmural invasion of the prostate is defined as extension of the bladder tumor through the bladder wall into the prostate gland or extension through the bladder wall into the perivesical soft tissue or fat then into the prostate gland stroma. This differs from the 'transurethral mucosal route,' which is the extension of the bladder tumor via the prostatic urethral mucosa prostate glands with subsequent invasion of the prostate gland.*

Macroscopic Margin Involvement
____ Margin*(s)* uninvolved by macroscopic tumor
Distance of tumor to closest perivesical soft tissue margin: ___ cm
Specify margin, if oriented: _____
Distance of tumor to right ureteral margin: ___ cm
Distance of tumor to left ureteral margin: ___ cm
Distance of tumor to urethral margin: ___ cm
Other margin*(s) (specify)*: _____
____ Margin*(s)* involved by macroscopic tumor
Specify margin*(s)*, if possible: _____
____ Indeterminate *(explain)*: _____

+**Macroscopic Appearance of Uninvolved Tissue / Organ*(s)***
____ Bladder mucosa

+Color: _____	Pink-tan	Glistening	Dull
+Consistency:	Trabecular	Smooth	Rough
+Hemorrhage:	Yes	No	
+Necrosis:	Yes	No	

____ Ureteral mucosa

+Color: _____	Pink-tan	Glistening	Dull
+Consistency:	Smooth	Rough	
+Hemorrhage:	Yes	No	
+Necrosis:	Yes	No	

____ Urethral mucosa

+Color: _____	Pink-tan	Glistening	Dull
+Consistency:	Smooth	Rough	
+Hemorrhage:	Yes	No	
+Necrosis:	Yes	No	

+____ Prostate

+Color: _____	Homogeneous	Pink-tan	Yellow-tan
+Consistency:	Nodular	Granular	

+____ Vaginal Wall

+Color: _____	Pink-tan	Glistening	Dull
+Consistency:	Smooth	Firm	Rough

Lymph Node Examination

____ No lymph nodes submitted or macroscopically identified

____ Number of lymph nodes sectioned and macroscopically examined: ___

Number of lymph nodes macroscopically suspected to be involved by tumor: ___

Size of lymph nodes in three dimensions: ___ x ___ x ___ cm or range in size ___ -___ cm

Specify site*(s)* if known: _____

Number of lymph nodes cannot be determined *(explain)*: _____

+Macroscopic Extranodal Extension *(ENE)*

+____ Not identified

+____ Present

+____ Indeterminate

+____ **Tissue Submitted for Research** *(specify, if possible)*: _____

(+) Data elements preceded by this symbol are optional elements which may be clinically important but are not yet validated or regularly used in patient management.

Recommended Block Allocation Key

Partial Cystectomy

A1-3: * Mass with greatest depth of invasion with serosa, full thickness
A4: * Mass with adjacent mucosa
A5: Mass with closest transmural excision margin
A6: Unremarkable bladder

Radical Cystectomy

A1-3: * Mass with greatest depth of invasion with serosa or perivesical soft tissue margin (specify which margin), full thickness
A4: * Mass with adjacent mucosa
A5: Anterior bladder wall
A6: Posterior bladder wall
A7: Dome wall
A8: Right lateral wall
A9: Left lateral wall
A10: Right ureteral orifice with ureterovesicular junction
A11: Left ureteral orifice with ureterovesicular junction
A12: Trigone with urethra
A13: Right ureter margin, *en face*
A14: Left ureter margin, *en face*
A15: Urethral margin, perpendicular
A15: Right perivesical soft tissue margin, perpendicular
A16: Left perivesical soft tissue margin, perpendicular
A17: Lymph nodes (or perivesical fat)

Cystoprostatectomy

A1-3: * Mass with greatest depth of invasion with serosa or perivesical soft tissue margin (specify which margin), full thickness
A4: * Mass with adjacent mucosa
A5: Anterior bladder wall
A6: Posterior bladder wall
A7: Dome wall
A8: Right lateral wall
A9: Left lateral wall
A10: Right ureteral orifice with ureterovesicular junction
A11: Left ureteral orifice with ureterovesicular junction
A12: Trigone with urethra
A13: Right ureter margin, shave
A14: Left ureter margin, shave
A15: Right perivesical soft tissue margin, perpendicular
A16: Left perivesical soft tissue margin, perpendicular
A17: Lymph nodes (or perivesical fat)
A18: Prostatic urethral margin, perpendicular
A19: Transmural invasion of mass into prostate (if present)
A20-22: Representative right posterior prostate, submitted base to apex
A23-26: Representative left posterior prostate, submitted base to apex
A27: Right seminal vesicle base and right vas deferens margin, *en face*
A28: Left seminal vesicle base and left vas deferens margin, *en face*

Anterior Exenteration

A1-3: * Mass with greatest depth of invasion with serosa or perivesical soft tissue margin (specify which margin), full thickness
A4: * Mass with adjacent mucosa
A5: Anterior bladder wall
A6: Posterior bladder wall
A7: Dome wall
A8: Right lateral wall
A9: Left lateral wall
A10: Right ureteral orifice with ureterovesicular junction
A11: Left ureteral orifice with ureterovesicular junction
A12: Trigone with urethra
A13: Right ureter margin, *en face*
A14: Left ureter margin, *en face*
A15: Right perivesical soft tissue margin, perpendicular
A16: Left perivesical soft tissue margin, perpendicular
A17: Lymph nodes (or perivesical fat)
A18: Urethral margin, perpendicular
A19: Anterior vaginal wall
A20: Cervix, ____ (location)
A21-22: Endomyometrium of uterus
A23: Right fallopian tube, with entire fimbria
A24: Right ovary
A25: Left fallopian tube, with entire fimbria
A26: Left ovary

Additional sections for Male and Female Pelvic Exenteration

A27-29: Rectum (normal or with mass extension) and proximal / distal margins, *en face* / perpendicular
A30: Abdominal wall (normal of with mass extension)
A31: Pelvic wall (normal or with mass extension)

Sections containing the various attached organs should show any direct involvement of the tumor into that organ if present. If there is no involvement, a section of unremarkable organ is submitted.

* Total cassette number of mass is dependent on the extent of invasion of the mass as well as organs and tissues involved (in order to show relationships).

References:

1. Panner GP, Zhou M, Srigley JR, et al. Protocol for the Examination of Cystectomy Specimens from Patients with Carcinoma of the Urinary Bladder. *CAP Cancer Protocol Urinary Bladder Resection 4.0.2.0.* 2020. www.cap.org/cancerprotocols.

2. Lester SC. *Manual of surgical pathology,* 3rd ed. Philadelphia: Saunders/Elsevier; 2010.

3. Oliva IV, Smith SL, Chen Z, Osunkoya AO. Urothelial Carcinoma of the Bladder with Transmural and Direct Prostatic Stromal Invasion; Does Extent of Stroma Invasion Significantly Impact Patient Outcome? *Human Pathology* 2011;42:51-56.

Specimen Handling / Dissection Guidelines

Bladder Biopsy

- Measure the aggregate of tissue in three dimensions.
- Submit entirely.

Transurethral Resection of Bladder Tumor (TURBT)

- Weigh and measure (three dimensions) the aggregate of tissue.
- Submit entirely.

Partial Cystectomy

- Measure the specimen in three dimensions.
- Note the integrity of the serosa. Mention if there is any attached perivesical soft tissue.
- There will not be inherent anatomical orientation in the majority of specimens. Pay attention to surgeon provided orienting sutures.
- Ink the transmural resection margin - one color if the specimen is unoriented and additional colors as needed for oriented specimens.
- Describe and measure the mass. Section through the tumor to assess the third dimension and note any gross invasion into or through the muscularis propria.
    - If the tumor has been treated, the entire tumor bed / scar / ulceration should be submitted.
- Measure the distance of the tumor to the serosa and to any present perivesical soft tissue margins.
- Measure the tumor to the transmural excision margin.
- Sections of the mass are taken as full thickness to show the depth of tumor invasion.
- If the mass is within 1 cm to the transmural excision margin, a perpendicular section with the mass to the margin should be taken.
- If the mass is further away, the transmural excision margin can be taken as an *en face* section at the site where the margin is the closest to the mass.
- Describe the remainder of the bladder mucosa and measure the wall thickness.
- Submit representative sections from uninvolved bladder.

Cystectomy

- Orient the specimen and identify the ureters, entering the bladder posterolaterally.
- Assess the integrity of the perivesical soft tissue and fat, noting any defects and their locations. Comment on how much perivesical fat is present (minimal, moderate, abundant) and give a thickness measurement.
- Measure bladder in three dimensions and the urethra and ureters in two dimensions.
- Differentially ink the perivesical soft tissue and fat margins based on your institution's preferences. Suggestion: right perivesical margin one color and the left perivesical margin a second.
- If the bladder is received intact, perfuse the specimen with formalin overnight using a syringe and placing it through the urethra to inject formalin into the bladder; gauze can be placed in the distal urethra to retain the formalin.
- If the bladder has been previously opened, pin out the specimen on a paraffin board and fix in formalin overnight.
- To open the bladder, cut anteriorly through the urethra into the bladder. Advance the cuts right and left in a 'Y'- incision fashion and flip the anterior wall upwards.

- Locate, describe, and measure the mass. Make serial sections through the tumor to assess the third dimension and note any gross invasion into or through the muscularis propria.
    - If the tumor has been treated, the entire tumor bed / scar / ulceration should be submitted.
- Measure the distance of the tumor to deep perivesical soft tissue margin. Be specific whether it is the soft tissue margin or serosa.
- Measure distance to urethral margin, right ureter margin and left ureter margin.
- Describe the remainder of the bladder mucosa and measure the wall thickness.
- Describe the urethral mucosa and assess for addition lesions.
- Shave the ureter margins; submit separately.
- Open the ureters longitudinally and assess the urothelium for additional lesions.
- Section through the perivesical fat for lymph nodes. Submit one section from each macroscopically positive lymph node. All macroscopically negative lymph nodes should be entirely submitted.

Cystoprostatectomy

- Orient the specimen and identify the ureters, entering the bladder posterolaterally. ***(Figures 1A and 1B)***

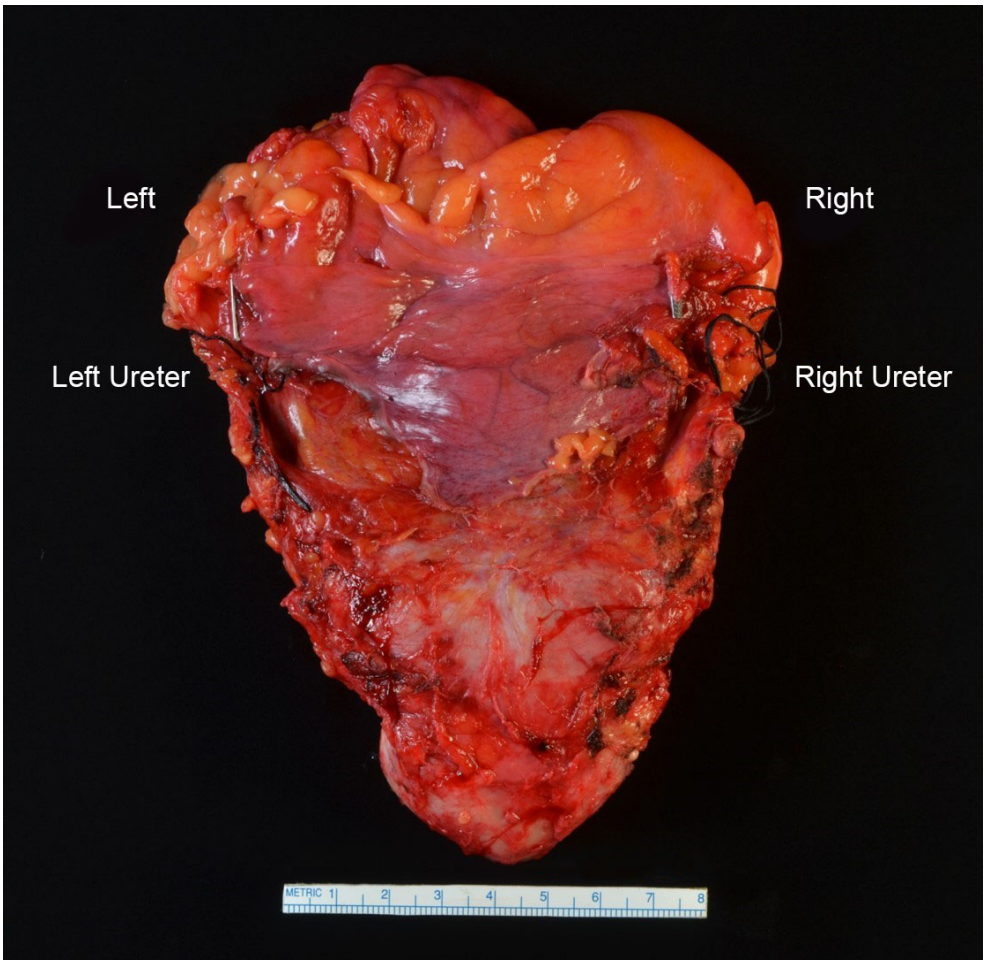

Figure 1A: Posterior Cystoprostatectomy Anatomy.
Photograph courtesy of E. Heidi Cheek-Norgan, PA(ASCP)^{CM}, Mayo Clinic, Rochester, MN.

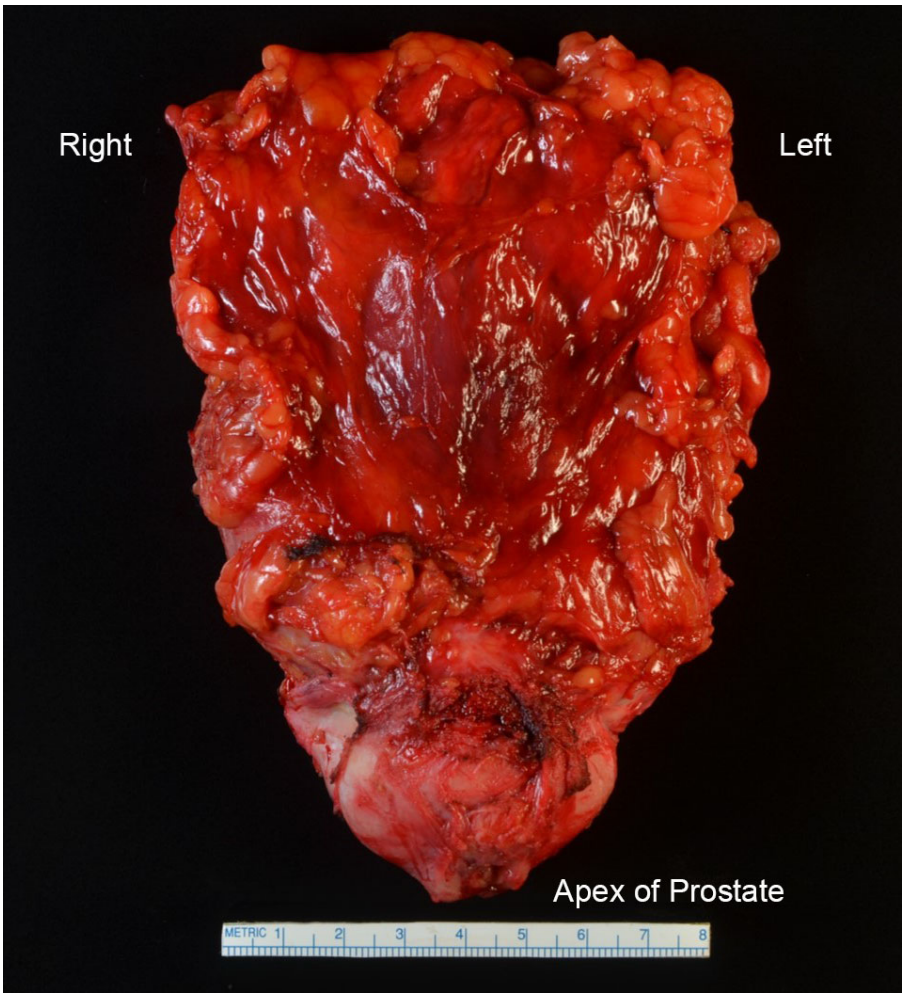

Figure 1B: Anterior Cystoprostatectomy Anatomy.
Photograph courtesy of E. Heidi Cheek-Norgan, PA(ASCP)^{CM}, Mayo Clinic, Rochester, MN.

- Assess the integrity of the perivesical soft tissue and fat, noting any defects and their locations. Comment on how much perivesical fat is present (minimal, moderate, abundant) and give a thickness measurement.
- Measure bladder in three dimensions and the ureters in two dimensions.
- Identify and measure additional structures: prostate, seminal vesicles, vas deferentia.
- Differentially ink based on your institution's preferences. Suggestions are as follows:
    - Right perivesical margin
    - Left perivesical margin
    - Right prostate
    - Left prostate
    - Anterior prostate, staple margin, if present
- If the bladder is received intact, perfuse the specimen with formalin overnight using a syringe and placing it through the urethra to inject formalin into the bladder; gauze can be placed in the distal urethra to retain the formalin.
- If the bladder has been previously opened, pin out the specimen on a paraffin board and fix in formalin overnight.

- To open the bladder, cut anteriorly through the prostatic urethra into the bladder. Advance the cuts right and left in a 'Y'- incision fashion and flip the anterior wall upwards. ***(Figure 2)***

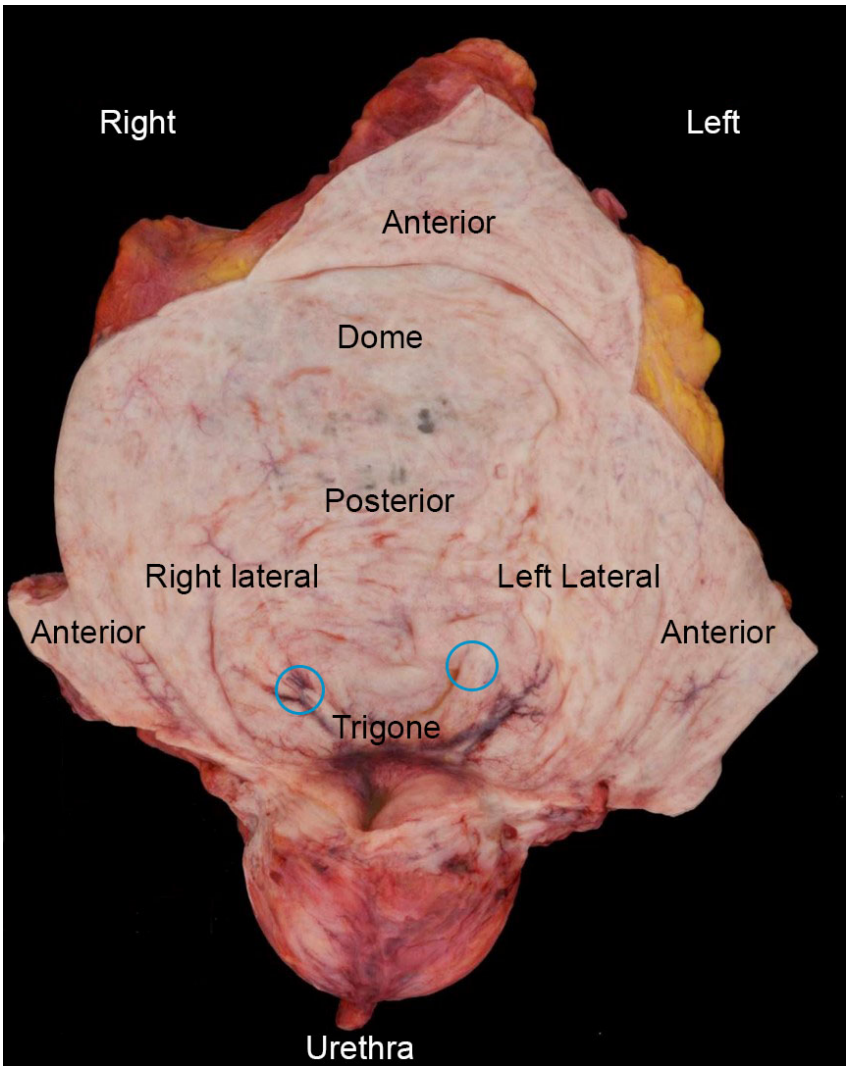

Figure 2: Open Cystoprostatectomy.
Photograph courtesy of E. Heidi Cheek-Norgan, PA(ASCP)^{CM}, Mayo Clinic, Rochester, MN.

- Locate, describe, and measure the mass. Section through the tumor to assess the third dimension and note any gross invasion into or through the muscularis propria.
    - If the tumor has been treated, the entire tumor bed / scar / ulceration should be submitted.
- Measure the distance of the tumor to deep perivesical soft tissue margin. Be specific whether it is the soft tissue margin or serosa.
- Measure distance to urethral margin, right ureter margin and left ureter margin.
- Describe the remainder of the bladder mucosa and measure the wall thickness.
- Shave ureter margins; submit separately.
- Open the ureters longitudinally, assess the urothelium for additional lesions.
- Serially section the prostate at the posterior aspect, from base to apex at 3-4 mm intervals.

- Measure the tumor to the prostate and state whether or not there is prostatic stromal involvement. If it is involving the prostate, measure the tumor distance to the closest prostatic margin.
- Describe the prostatic urethra (assess for additional tumors or involvement from the primary mass) and the prostatic parenchyma (paying special attention to any incidental prostate primary tumors).
- Shave the apical prostate margin; bisect into right and left halves; perpendicularly section each half and entirely submit.
- Submit sections of any transmural invasion of the tumor into the prostate. If unremarkable, submit posterior parenchyma from right and left lobes.
- Submit the base of the seminal vesicles and vas deferentia margins.
- Section through the perivesical fat for lymph nodes. Submit one section from each macroscopically positive lymph node. All macroscopically negative lymph nodes should be entirely submitted.

- **Anterior Exenteration**
  - Orient the specimen and identify the ureters, entering the bladder posterolaterally.
  - Assess the integrity of the perivesical soft tissue and fat, noting any defects and their locations. Comment on how much perivesical fat is present (minimal, moderate, abundant) and give a thickness measurement.
  - Measure bladder in three dimensions and the urethra and ureters in two dimensions.
  - Identify and measure additional structures: vagina, vulva, uterus, cervix, pelvic wall, abdominal wall, etc.
  - Differentially ink based on your institution's preferences. Suggestions are as follows:
    - Right perivesical margin
    - Left perivesical margin
    - Right urethral soft tissue margin
    - Left urethral soft tissue margin
    - Right vaginal wall
    - Left vaginal wall
    - Distal vaginal margin
    - Right vulvar / perineum skin
    - Left vulvar / perineum skin
    - Cervical amputation site
  - If the bladder is received intact, perfuse the specimen with formalin overnight using a syringe and placing it through the urethra to inject formalin into the bladder; gauze can be placed in the distal urethra to retain the formalin.
  - If the bladder has been previously opened, pin out the specimen on a paraffin board and fix in formalin overnight.
  - If uterus and cervix are present, bisect them coronally to allow for better fixation.
  - To open the bladder, cut anteriorly through the urethra into the bladder. Advance the cuts right and left in a 'Y'- incision fashion and flip the anterior wall upwards.
  - Locate, describe, and measure the mass. Section through the tumor to assess the third dimension and note any gross invasion into or through the muscularis propria.
    - If the tumor has been treated, the entire tumor bed / scar / ulceration should be submitted.
  - Measure the distance of the tumor to deep perivesical soft tissue margin. Be specific whether it is the soft tissue margin or serosa.
  - Measure distance to urethral margin, right ureter margin and left ureter margin.
  - Describe the remainder of the bladder mucosa and measure the wall thickness.
  - Describe the urethral mucosa and note any additional lesions.

- Shave ureter margins; submit separately.
- Open the ureters longitudinally, assess the urothelium for additional lesions.
- Measure the tumor to the vaginal wall mucosa, the closest vaginal margin, cervix, and vulva. State whether or not the tumor is involving the attached organs. If there is involvement, take a section depicting the relationship.
- Describe the unremarkable parenchyma of the organs present. One section of each present organ should be taken.
- Section through the perivesical fat to find lymph nodes. Submit one section from each macroscopically positive lymph node. All macroscopically negative lymph nodes should be entirely submitted.

Urinary Bladder Carcinoma

Introduction

Bladder carcinoma is one of the more common cancers in the United States; specifically, urothelial carcinoma of the bladder represents the vast majority of these cases (approximately 95%) verses other histologic types. The urothelial cells of the bladder become neoplastic and involve / invade the basement membrane, lamina propria, or deeper into the bladder wall. In the US, the incidence is higher in males over the age of 55 verses females and ranks 4th in most common cancers in males. The 5-year survival rate varies depending on extent of disease: 51% for in situ carcinoma, 34% for localized disease, 7% for regional disease, and 5% for distant disease. In developing countries, squamous cell carcinoma of the bladder is more prevalent than urothelial cell. Worldwide, bladder cancer is the 7th most common cancer. Other types of bladder cancer include adenocarcinoma, sarcomatoid carcinoma, Müllerian carcinoma, and neuroendocrine carcinoma.

Epidemiology

Increased risk of bladder carcinoma has been seen with smoking, schistosomiasis, and exposure to industrial chemicals (phenacetin and dyes). Smoking is the most important risk factor in the US. Additionally, in the US, industrial chemicals are an occupational hazard for painters, machinists, hairdressers, etc. Carcinogenesis is thought to be related to the increased exposure to these toxins in the bladder, as urine is stored for relatively prolonged periods of time. This theory is supported by the higher incidence of urothelial carcinoma within the bladder verses the remainder of the urinary tract organs. In developing countries, schistosomiasis infection is the leading cause of squamous cell carcinoma of the bladder as the parasite causes inflammation, chronic irritation, squamous metaplasia, dysplasia, and subsequent carcinoma. In addition to the contribution of environmental factors listed above, genetic alterations and deletions have been identified in urothelial tumors.

For urothelial cell carcinoma, there are two distinct pathways of describing the morphology and development of the tumor:

1) Low grade lesions
    - Arise from hyperplasia (papillary precursor lesion)
    - Associated with loss of tumor suppressor genes on chromosome 9, activating mutations of FGRF3, PIK3CA and inactivating STAG2
    - Superficial, papillary lesion
    - Low malignant potential, usually pT1
2) High grade lesions
    - Arise from dysplasia / carcinoma in situ (flat precursor lesion)
    - Associated with mutations in tumor suppressor genes TP53, RB, and PTEN
    - Invasive tumors
    - Higher malignant potential, usually pT2-T4

Clinical Presentation

Clinically, bladder cancers initially present with painless hematuria and may progress to gross hematuria with advanced stage; secondary symptoms include frequency, urgency, and dysuria. If the tumor has grown large enough to obstruct the ureteral orifice, pyelonephritis or hydronephrosis can occur. The diagnosis is primarily made via cystoscopy but can also be diagnosed with urine cytology; computed tomography (CT) or ultrasound may also be used to identify a bladder mass (see imaging considerations below).

Imaging Considerations

When clinically presenting with the symptoms of bladder cancer or when tumor is seen on cystoscopy, computed tomography (CT) or magnetic resonance imaging (MRI) of the pelvis is used to confirm the location of tumor, identify any secondary lesions, and assess local extent of the disease. This is done prior to biopsy, as biopsy procedures may cause inflammation and scarring, which can obscure imaging. Visualization of the remainder of the urinary tract can be done with MR or CT urography; MRU is favored over CTU due to its increased ability to denote the bladder wall layers, which allows for clinical tumor stage to be determined as well as being safer for patients that cannot receive intravenous contrast. Additionally, both CT and MRI can identify regional lymph node involvement.

Depending on the tumor stage and additional symptoms, the clinician may order positron emission tomography (PET), MRI, or CT to identify distant metastasis within the retroperitoneal lymph nodes, lung, liver, brain, or bone. Additionally, the clinician may request molecular testing for a patient with metastatic disease at the time of diagnosis; testing will help the clinician determine treatment.

Pertinent Anatomy

The urinary bladder sits within the pelvis superior to the prostate in males and anterior to the uterus in females. The dome of the bladder is covered by a smooth peritoneal surface, which extends anteriorly to the pelvic wall and posteriorly to the adjacent structures (rectum in males and uterus in females forming rectovesicular and vesicouterine pouches, respectively). The bladder has perivesical soft tissue and adipose tissue that is surgically dissected away from the pelvis and represents a true margin; the serosa is not a surgical resection margin. Within the macroscopic description and cassette summary, identify the location of the true perivesical soft tissue margin you are demonstrating with relation to the tumor.

The right and left ureters enter at the posterior aspect of the bladder. The urethra exits the bladder inferiorly. The ureteral orifices and urethral orifice form the trigone within the inferior aspect of the bladder.

The layers of the bladder wall consist of:

- Epithelium
  - Urothelium consists of stratified epithelium into three layers (apical, intermediate, and basal) in a full, distended bladder. Once the bladder is relaxed, the urothelium becomes 5 to 7 layers thick. Because of the stretching characteristic of this urothelium to transition between 3 layers and 5-7 layers, urothelium is also knows as transitional epithelium.
- Lamina propria:
  - Subepithelial connective tissue with elastic fibers, capillaries, lymphatics, nerve endings, interstitial cells of Cajal, etc.
  - Adipose tissue may be encountered within the lamina propria and muscular propria and should not be misinterpreted as perivesical fat in transurethral resection specimens.
- Muscularis propria
  - Detrusor muscle consists of three layers of smooth muscle cells: inner longitudinal, middle circular, and outer longitudinal.
- Serosa
  - Over the bladder dome, the thin layer of connective tissue covers the organ and is contiguous with the peritoneum of the abdomen and adjacent organs.
- Adventitia / Perivesical adipose tissue
  - Adventitia is the connective tissue outer boundary of the bladder where there is no serosa. The perivesicular adipose tissue extends from here and secures the bladder into the pelvic cavity.

- Extravesical extension (pT3)
    - Gross evaluation is critical in determining macroscopic extravesical extension of tumor and thus influencing pT3 substaging, as well as ensuring that all areas of prior bladder resections have been thoroughly sampled.
    - In cystoprostatectomy specimens, macroscopic evaluation is required to determine whether a urinary bladder carcinoma shows direct extravesical extension into the prostate and / or seminal vesicles.
    - In cystectomy specimens, it can be challenging to evaluate extravesical invasion as the boundary between the muscularis propria and its fat is not well demarcated from perivesical fat. This boundary can be distorted, obscured, or obliterated by fibrosis and inflammation associated with an infiltrating tumor.

Regional Lymph Nodes

- Pelvic, NOS, hypogastric, obturator, iliac (internal, external, or NOS) and sacral (lateral, presacral, promontory, or NOS).

Non-Regional Lymph Nodes Considered Metastatic Sites

- Aortic (paraaortic lumbar), common iliac, inguinal (deep or superficial), supraclavicular, cervical, scalene, retroperitoneal.

Macroscopic Features of Tumor

There are two morphologic patterns for urothelial carcinoma within the urinary bladder: papillary and flat. Both patterns have noninvasive and invasive counterparts. Generally, the papillary tumors are large, exophytic masses which are friable in consistency. If a transurethral resection of the tumor has occurred prior to the cystectomy, a flat, granular tumor bed or biopsy site will be seen. Flat tumors typically appear as hemorrhagic, granular, and flattened areas that contrast the tortuous folding pattern of the bladder urothelium. Because tumor staging is based on the extent of invasion of the tumor into the bladder wall and beyond into the adjacent structures, macroscopic invasion must be explicitly stated in the gross description of the tumor.

Treatment / Therapy Guidelines

When a lesion is identified (via cystoscopy), a transurethral resection of the bladder tumor (TURBT) will be done, and the procedure aims to include the muscularis propria. This will provide the initial diagnosis and the extent of the disease subsequently leading to the clinical staging* and grade of the tumor. In the event of carcinoma in situ and solid tumors, mapping bladder biopsies is done to assess the tumor field.

Low-grade tumors (cTa, cTis, and cT1), which are confined to the mucosa, submucosa, or lamina propria, are defined as non-muscle invasive bladder cancer. These tumors can be treated by transurethral resection immediately followed by intravesicular chemotherapy to inhibit tumor cell implantation and recurrence. Follow up surveillance consists of imaging, urine analysis and cystoscopy; the intervals are generally 3- to 6-months and the type of surveillance is dependent on the risk factors of the patient; low risk patients are surveyed via imaging and for intermediate and higher risk patients, urine analysis and cystoscopy are added. Approximately 31% - 78% of these patients experience reoccurrence. For cT1 patients, a second TURBT can be done as reassurance that the muscularis propria is not involved, which would upstage the patient. In the case of residual disease on the second TURBT, these patients are candidates for a cystectomy.

Large, invasive tumors are defined as muscle-invasive bladder cancers (cT2, cT3 and cT4), which involve the muscularis propria and beyond. They require a cystectomy or partial cystectomy (for dome tumors). Neoadjuvant therapy is considered for cT2, cT3, and cT4a patients to manage the extent of the disease when there is no suspicion of lymph node involvement. These patients have an increased survival rate (77 months verses 46 months) and lower rate of residual disease (15% verses 38%).

Following therapy, these patients will have a total cystectomy (partial cystectomy for a cT2 patient when the tumor is in an accessible location) and lymph node dissection. Adjuvant therapy can be used based on the pathologic tumor staging, lymph node status, and comorbidities. If a patient is cT4b and does not qualify for surgical intervention, systemic chemotherapy and radiation are used. If the patient responds well, a radical cystectomy may become an option again.

* At this point, staging is still referred to as “clinical” staging because it is based on an endoscopic biopsy, a bimanual examination under anesthesia, or imaging results. Once a cystectomy (partial or total) is completed, it is considered “pathologic” staging.

Prognosis and Prognostic Features

Tumor stage and grade are the most important prognostic factors with supplemental information drawn from pathologic, clinical, and molecular characteristics of the tumor. Micropapillary tumor growth pattern and lymphovascular invasion have been noted in worse prognoses. Tumors that are multifocal, large and / or have carcinoma in situ components are adverse prognostic factors as well.

Regional lymph node involvement has a negative impact on recurrence and long-term survival; these lymph nodes include the obturator, external / internal iliac, perivesical, pelvic, sacral (primary) and common iliac (secondary). The total number of lymph nodes resected is associated with better outcomes, whether or not, they are positive.

Metastatic Sites

The most common distant sites for primary bladder carcinoma metastasis are retroperitoneal lymph nodes, lung, bone, and liver. Direct extension into adjacent pelvic wall, abdominal wall or local organs does not constitute metastasis. Lymph node involvement beyond the common iliac nodes (e.g., paracaval or intra-aortocaval) is considered metastatic disease (M1a).

References:

1. Amin MB, Edge SB, Greene FL, Byrd DR, et al. (Eds.) *AJCC Cancer Staging Manual,* 8th ed. New York, NY: Springer; 2017.

2. Bolla SR, Odeluga N, Jetti R. Histology, Bladder. [Updated 2020 Apr 15]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK540963/

3. Eble JN, Sauter G, Epstein JI, Sesterhenn IA. *Pathology and Genetics of Tumors of the Urinary System and Male Genital Organs.* World Health Organization Classification of Tumors. Lyon: IARDPress:2004.

4. Flaig TW. NCCN Guideline Updates: Management of Muscle-Invasive Bladder Cancer. *J Natl Compr Canc Netw.* 2019;17(5.5):591-593.

5. Flaig TW, Spiess PE, Agarwal N, et al. NCCN Clinical Practice Guidelines in Oncology: Bladder Cancer, Version 3.2020. *J Natl Compr Canc Netw*. 2020;18(3):329-354.

6. Flaig TW, Spiess PE, Agarwal N, et al. NCCN Guidelines Insights: Bladder Cancer, Version 5.2018. *J Natl Compr Canc Netw*. 2018;16(9):1041-1053. doi:10.6004/jnccn.2018.0072

7. Kaseb H, Aeddula NR. Cancer, Bladder. [Updated 2019 Jul 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK536923/

8. Kumar V, Abbas AK, Faust N, Aster JC, et al. *Robbins and Cotran Pathologic Basis of Disease,* 8th Ed. Philadelphia PA: Saunders/Elsevier; 2010.

9. Lester SC. *Manual of surgical pathology,* 3rd ed. Philadelphia, PA: Saunders/Elsevier; 2010.

10. Panner GP, Zhou M, Srigley JR, et al. Protocol for the Examination of Cystectomy Specimens from Patients with Carcinoma of the Urinary Bladder. *CAP Cancer Protocol Urinary Bladder Resection 4.0.2.0.* 2020.

11. Panner GP, Zhou M, Srigley JR, et al. Protocol for the Examination of Biopsy and Transurethral Resection of Bladder Tumor (TURBT) Specimens from Patients with Carcinoma of the Urinary Bladder. *CAP Cancer Protocol Urinary Bladdery Biopsy/TURBT 4.0.2.0.* 2020.

12. Pfeifer JD, Dehner LP, Humphrey P. *Washington Manual of Surgical Pathology*. New York: Wolters Kluwer Medical; 2020.

13. SEER Cancer Stat Facts: Bladder Cancer. National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/statfacts/html/urinb.html

14. Spiess PE, Agarwal N, Bangs, R, et al. NCCN Clinical Practice Guidelines in Oncology: Bladder Cancer, Version 5.2017. *J Natl Compr Canc Netw*. 2017;15(10)1240-1267.

15. Zarei S, Frank I, Boorjian SA, Thompson H, et al. Prognostic Significance of Measured Depth of Invasion of Urothelial Carcinoma of the Bladder Compared to the 2010 American Joint Committee on Cancer pT2 and pT3 Classifications. *The Journal of Urology.* 2012;188(5):1706-1711.

APPENDIX I
TNM Criteria for Urinary Bladder Tumors

Definition of Primary Tumor (pT) ***(Figure 3, page 21)***

pT Category	pT Criteria
pT0	No evidence of primary tumor
pTa	Non-invasive papillary carcinoma
pTis	Urothelial carcinoma *in situ*: "flat tumor"
pT1	Tumor invades lamina propria (subepithelial connective tissue)
pT2	Tumor invades muscularis propria
pT2a	Tumor invades superficial muscularis propria (inner half)
pT2b	Tumor invades deep muscularis propria (outer half)
pT3	Tumor invades perivesical soft tissue
pT3a	Microscopically
pT3b	Macroscopically (extravesical mass)
pT4	Extravesical tumor directly invades any of the following: prostatic stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall*
pT4a	Extravesical tumor invades directly into prostatic stroma, seminal vesicles, uterus, vagina
pT4b	Extravesical tumor invades pelvic wall, abdominal wall

Used with permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging System (2020).

*Note: T4 Criteria - Depending on the extent of resection, it may only be possible to determine this stage clinically by imaging techniques.

Definition of Regional Lymph Node (pN)

pN Category	pN Criteria
pN0	No lymph node metastasis
pN1	Single regional lymph node metastasis in the true pelvis (perivesical, obturator, internal and external iliac, or sacral lymph node)
pN2	Multiple regional lymph node metastases in the true pelvis (perivesical, obturator, internal and external iliac, or sacral lymph node metastasis)
pN3	Lymph node metastasis to the common iliac lymph nodes

Used with permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging System (2020).

Definition of Distant Metastasis (pM) (required only if confirmed pathologically)

pM Category	pM Criteria
pM0	No distant metastasis
pM1	Distant metastasis
pM1a	Distant metastasis limited to lymph nodes beyond the common iliacs
pM1b	Non-lymph node distant metastases

Used with permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging System (2020).

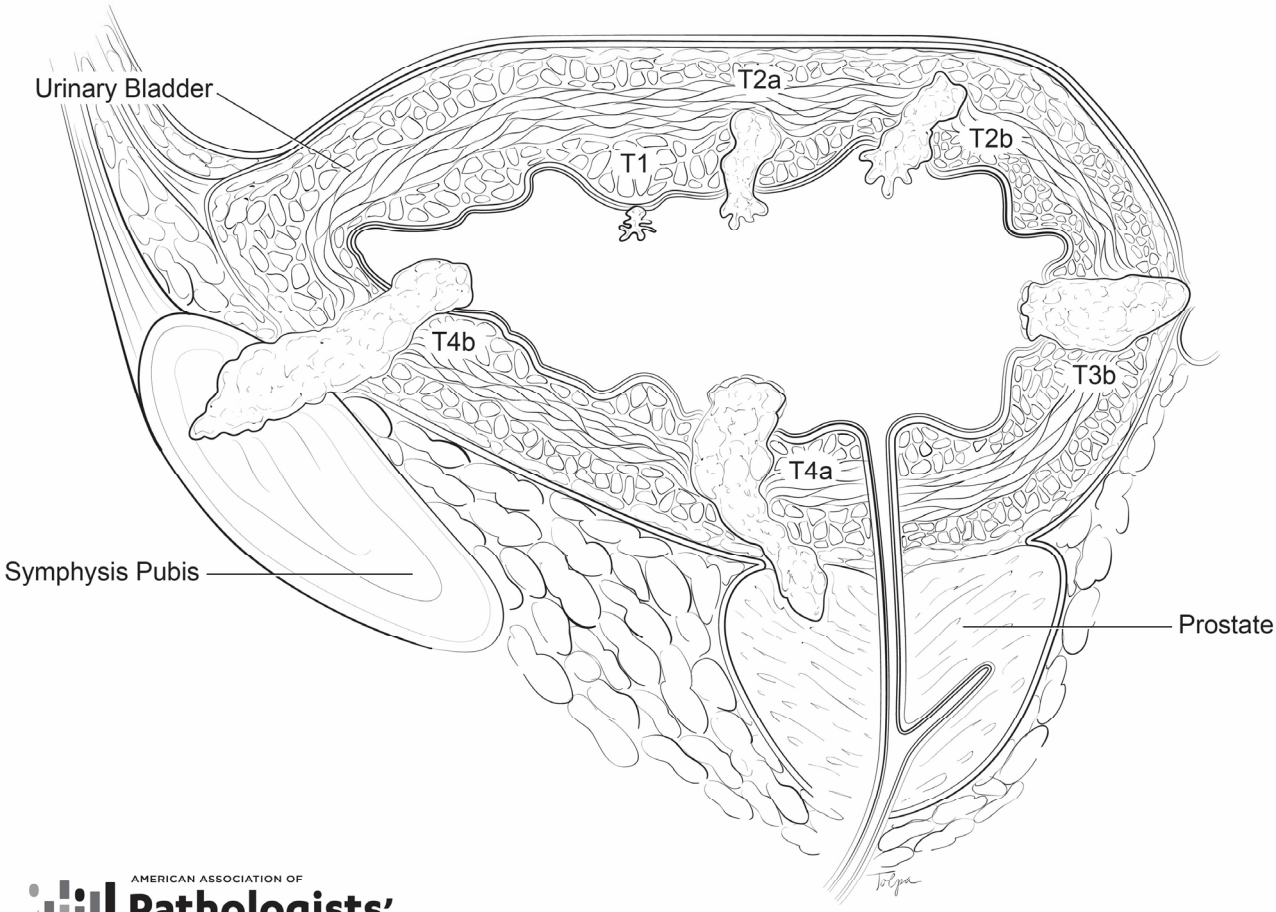

Figure 3: Urinary Bladder - T Criteria

T1: Tumor invades lamina propria (subepithelial connective tissue)
T2a: Tumor invades superficial muscularis propria (inner half)
T2b: Tumor invades deep muscularis propria (outer half)
T3b: Tumor invades perivesical soft tissue; macroscopically (extravesical mass)
T4a: Extravesical tumor invades directly into prostatic stroma, seminal vesicles, uterus, or vagina
T4b: Extravesical tumor invades pelvic wall, abdominal wall

TNM Descriptors:

cTNM: The "c" prefix is used when clinical staging is performed by the referring physician or when pathological assessment is not possible.

pT(m)NM: The "m" suffix is added within parentheses after the pT indicator and is used when there are multiple primary tumors within a single site.

ypTNM: The "y" prefix is used when neoadjuvant therapy has been performed.

rTNM: The "r" prefix is used when tumor recurrence is staged after a disease-free interval.

aTNM: The "a" prefix indicates when the stage is determined at autopsy.

Residual Tumor (R) Category

The absence or presence of residual tumor at the primary tumor site after treatment is denoted by the symbol R. The R categories for the primary tumor site are as follows:

R Category	R Definition
RX	Presence of residual tumor cannot be assessed
R0	No residual tumor
R1	Microscopic residual tumor
R2	Macroscopic residual tumor at the primary cancer site or regional nodal sites

Used with permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging System (2020).

APPENDIX II
Ancillary Testing

Molecular Considerations

The following molecular markers have been shown to be helpful prognostic indicators in bladder carcinoma:

- Alterations in p53, p21, p27, Cyclin E1 genes and retinoblastoma (pRb) tumor suppressor gene.
- Alterations in the apoptosis pathway genes, including CD95, Bcl-2, Caspase-3 and Survivin.
- Increased angiogenesis indicated by microvessel density, elevated vascular endothelium growth factor (VEGF) and decreased Thrombospondin-1 activity.
- Overexpression of tyrosine-kinase receptors that affect signaling of many growth factors including epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), and HER2/neu have been identified as prognostically relevant alterations in bladder cancer.

Muscle-invasive bladder cancers form basal and luminal subtypes similar to those found in breast cancer. Basal bladder cancers share biomarkers with basal breast cancers and are characterized by p63 activation, squamous differentiation, and more aggressive disease at presentation. Luminal bladder cancers have features of active PPARγ and estrogen receptor transcription and are enriched with activating *FGFR3* mutations and potential FGFR inhibitor sensitivity.

FGFR3 is altered in 22.02% of bladder carcinoma patients and is tested via RT-PCR on FFPE tissue. Erdafitinib is an FDA approved and NCCN recommended biomarker-directed therapy for bladder carcinoma, in the setting of locally advanced or metastatic urothelial carcinoma that has susceptible *FGFR3* or *FGFR2* genetic alterations and that progressed during or following at least one line of prior platinum-containing chemotherapy.

ERBB2 (HER-2), MSH2, and MSH6 are the most frequent gene inclusion criteria for bladder carcinoma clinical trials, tested via IHC and FISH.

A cold ischemia time of 1 hour or less is recommended to meet the most current molecular testing needs for cancer patient specimens. It is recommended actual cold ischemia times or, at a minimum, deviations from the 1-hour recommendation are recorded in the pathology report.

Molecular tests, including solid tumor next generation sequencing (NGS), can be performed on FFPE tissue sections and fresh frozen tissue. Contact your reference laboratory for specific specimen requirements. For those tests that have multiple testing modalities, it is assumed that only one of these testing modalities would be used per case unless one test yields equivocal results.

Cytogenetic Considerations

Noninvasive bladder tumors frequently have alterations to chromosome 9, specifically 9q deletions. High-grade tumors are associated with loss of heterozygosity of chromosome 17p, 14q, 5q, and 3p.

Immunohistochemistry Considerations

Because of the importance of a patient's prognosis relative to bladder cancer, one should consider submitting dedicated sections for immunohistochemical analysis. These sections should be from viable tumor without hemorrhage or necrosis and be 1.0 cm and no more than 0.3 cm thick to assure appropriate tissue processing. Common urothelial-associated markers include GATA3, uroplakin II, p63, and HMWK.

These tests can be performed on formalin fixed paraffin embedded tissue sections. The macroscopic description should provide the fixative used. 10% neutral buffered formalin is the preferred fixative. It is recommended that the duration of fixation be provided as well.

References:

1. Compton C, Robb, JA, Anderson MW, et al. Preanalytics and Precision Pathology: Pathology Practices to Ensure Molecular Integrity of Cancer Patient Biospecimens for Precision Medicine. *Archives of Pathology & Laboratory Medicine*. 2019;143(11):1346-1363.

2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology - Bladder Cancer (5.2020). https://www.nccn.org/professionals/physician_gls/pdf/bladder_blocks.pdf. Accessed May 20, 2020.

3. Vanderbilt-Ingram Cancer Center. My Cancer Genome – Bladder Carcinoma. https://www.mycancergenome.org/content/disease/bladder-carcinoma/. Accessed May 25, 2020.

APPENDIX III
Frozen Section Considerations

Cystectomies may be submitted for frozen section / intraoperative consultation for ureteral and urethral margin status. At this time, the ureter margins are shaved and submitted separately for frozen section.

APPENDIX IV
Sample Narrative Macroscopic Description

Bladder Biopsy

Submitted *[fresh / in formalin]* in one container for gross and microscopic examination, labeled with the patient's name, [ ], medical record number, [ ], and "*[specimen designation,]*" is a ___ x ___ x ___ cm aggregate of multiple pink-tan soft tissue fragments. The specimen is filtered and entirely submitted in cassette A1.

Cold ischemic time: _____
Formalin fixation time: _____

Transurethral Resection of Bladder Tumor

Submitted *[fresh / in formalin]* in one container for gross and microscopic examination, labeled with the patient's name, [ ], medical record number, [ ], and "*[specimen designation,]*" is a ___ g, ___ x ___ x ___ cm aggregate of multiple fragments of pink-tan, cauterized tissue, and blood. The specimen is entirely submitted in cassettes A1-A_.

Cold ischemic time: _____
Formalin fixation time: _____

Partial Cystectomy

Submitted *[fresh / in formalin]* in one container for gross and microscopic examination, labeled with the patient's name, [ ], medical record number, [ ], and "*[specimen designation,]*" is a ___ x ___ x ___ cm portion of *[unoriented / oriented]* bladder *[oriented as follows: _____]*. There is overlying *[color, smooth / roughened / disrupted / hemorrhagic]* serosa and *[no]* attached perivesical soft tissue and adipose tissue. The specimen is inked as follows: transmural margin – *[color]*, soft tissue margin – *[color]*, surface defects – *[color]*.

The mucosa has a ___ x ___ x ___ cm *[color / hemorrhagic / papillary / flat]* mass. Sectioning through the mass shows a *[color / necrotic / texture]* cut surface and *[no invasion into / invasion into but not through / invasion into and through]* the muscularis propria. The mass *[abuts / is ___ cm from the serosa]*, *[abuts / is ___ cm from the soft tissue margin]*, and *[abuts / is ___ cm from the transmural margin]*.

The remainder of the bladder mucosa is *[color / texture]* with a normal folding pattern. The average wall thickness is ___ cm. *[There are no additional lesions. / Describe additional lesions – size, invasion, distance to first mass, distance to margin]*.

Cold ischemic time: _____
Formalin fixation time: _____

Representative sections are submitted as follows:

A1-A3:	Mass with greatest depth of invasion with serosa, full thickness
A4:	Mass with adjacent mucosa
A5:	Mass with closest transmural excision margin
A6:	Unremarkable bladder

Male, Cystoprostatectomy and Male Exenteration

Submitted *[fresh / in formalin]* in one container for gross and microscopic examination, labeled with the patient's name, [ ], medical record number, [ ], and "*[specimen designation,]*" is a / an *[previously opened / unopened]* cystoprostatectomy consisting of bladder (___ x ___ x ___ cm), attached right ureter (___ cm [length] x ___ cm [diameter]), left ureter (___ cm in [length] x ___ cm [diameter]), prostate (___ x ___ x ___ cm), right seminal vesicle (___ x ___ x ___ cm), right vas deferens (___ cm [length] x ___ cm [diameter]), left seminal vesicle (___ x ___ x ___ cm), and left vas deferens (___ cm [length] x ___ cm [diameter]). Sigmoid colon and rectum (___ cm [length] x ___ cm [circumference]) are attached posteriorly. There is attached abdominal / pelvic wall (___ x ___ x ___ cm). The bladder serosal surface is *[yellow, smooth, and unremarkable / note defects or implants]*. The perivesical soft tissue margin is roughened *[with / without disruptions].* The prostate has a *[pink-tan, smooth / disrupted]* external surface and the anterior surface has an overlying staple margin. The sigmoid colon / rectum has *[smooth / roughened]* serosa and an *[intact / disrupted]* mesorectum and pericolonic adipose tissue margin. The attached abdominal / pelvic wall is *[color / glistening with cauterized margins / roughened and hemorrhagic with cauterized margins.]*

The specimen is inked as follows: right bladder margin - *[color]*, left bladder margin - *[color]*, right prostate - *[color]*, left prostate - *[color]*, anterior prostate staple margin - *[color]*, mesorectum - *[color]*, pericolonic adipose tissue - *[color]*, abdominal / pelvic wall margin(s) - *[color]*, defects / disruptions - *[color]*.

The bladder is opened to show a ___ x ___ x ___ cm *[color / papillary / flat]* mass *[with hemorrhage / necrosis]* on the *[anterior / posterior / right / left / dome / trigone]* wall. The mass *[involves / is ___ cm from]* the right ureteral orifice, *[involves / is ___ cm from]* the left ureteral orifice, and *[involves / is ___ cm from]* the urethral orifice. The mass *[involves / is ____ cm from]* the right ureteral margin, *[involves / is ____ cm from]* the left ureteral margin, and *[involves / is ____ cm from]* the urethral margin.

Sectioning through the mass shows a *[color / texture]* cut surface and *[no invasion into / invasion into but not through / invasion into and through]* of the muscularis propria. The mass *[abuts / is ___ cm from the serosa]* and *[abuts / is ___ cm from the soft tissue margin]*.

The remainder of the bladder mucosa is *[color / texture]* with a normal folding pattern. The average wall thickness is ___ cm. The ureters are lined by pale tan, smooth urothelium. *[There are no additional lesions. / Describe additional lesions – size, invasion, distance to first mass, distance to margins]*.

The prostate is serially sectioned from base to apex to show tan-pink parenchyma. The mass *[invades into the prostatic stroma via the perivesical soft tissue or prostatic urethra / is ___ cm from the prostate]*. The prostatic urethra is *[patent / occluded]* and *[is lined by pale tan / hemorrhagic / roughened]* urothelium and is ___ cm from the mass. The mass *[involves / is ___ cm from]* the right / left seminal vesicles and the right / left vas deferens margins.

The mass *[involves / is ___ cm away]* from the sigmoid colon / rectum and is ____ cm away from the colonic margins. The mucosa is *[pink-tan / hemorrhagic / granular / unremarkable]* and the colonic wall thickness is ___ cm. There are *[#]* lymph nodes in the pericolonic adipose tissue and mesorectum (ranging from ___ -___ cm in greatest dimension). The mass *[involves / is ____ cm]* from the attached abdominal / pelvic wall and *[involves / is ____ cm]* from the margins.

Cold ischemic time: _____
Formalin fixation time: _____

Representative sections are submitted as follows:

A1-A3: Mass with greatest depth of invasion with perivesical soft tissue margin (specify which margin), full thickness

A4: Mass with adjacent mucosa
A5: Anterior bladder wall
A6: Posterior bladder wall
A7: Dome wall
A8: Right lateral wall
A9: Left lateral wall
A10: Right ureteral orifice with ureterovesicular junction
A11: Left ureteral orifice with ureterovesicular junction
A12: Trigone with urethra
A13: Right ureter margin, *en face*
A14: Left ureter margin, *en face*
A15: Right perivesicular soft tissue margin, perpendicular
A16: Left perivesicular soft tissue margin, perpendicular
A17: Lymph nodes (or perivesical fat)
A18: Prostatic urethral margin, perpendicular
A19: Transmural invasion of mass into prostate (if present)
A20-22: Representative right posterior prostate, submitted base to apex
A23-26: Representative left posterior prostate, submitted base to apex
A27: Right seminal vesicle base and right vas deferens margin, *en face*
A28: Left seminal vesicle base and left vas deferens margin, *en face*
A29-31: Rectum (normal or with mass extension) and proximal / distal margins
A32: Abdominal wall (normal or with mass extension)
A33: Pelvic wall (normal or with mass extension)

Female, Pelvic Exenteration

Submitted *[fresh / in formalin]* in one container for gross and microscopic examination, labeled with the patient's name, [ ], medical number, [ ], and "*[specimen designation,]*" is a / an *[previously opened / unopened]* cystectomy consisting of bladder (___ x ___ x ___ cm), attached right ureter (___ cm [length] x ___ cm [diameter]), left ureter (___ cm [length] x ___ cm [diameter]), attached uterine corpus (___ cm superior to inferior, ___ cm cornu to cornu, ___ cm anterior to posterior), attached cervix (___ cm [length], ___ cm [diameter]) and anterior vaginal wall (___ cm [length] x ___ cm [width] x ___ cm [thickness]). There is attached sigmoid colon and rectum (___ cm [length] x ___ cm [circumference]). There is attached abdominal / pelvic wall (___ x ___ x ___ cm).

The bladder serosa surface is *[yellow, smooth, and unremarkable / note defects or implants]*. The perivesical soft tissue margin is roughened *[with / without disruptions].* The sigmoid colon / rectum has *[smooth / roughened]* serosa and an *[intact / disrupted]* mesorectum and pericolonic adipose tissue margin. The attached abdominal / pelvic wall is *[color / glistening with cauterized margins / roughened and hemorrhagic with cauterized margins]*.

The specimen is inked as follows: right bladder margin - *[color],* left bladder margin - *[color]*, anterior uterine serosa / anterior cervical margin (if present) - *[color]*, posterior uterine serosa / posterior cervical margin - *[color]*, vaginal mucosal margin - *[color],* mesorectum - *[color]*, pericolonic adipose tissue - *[color]*, abdominal / pelvic wall margin(s) - *[color]*, defects / disruptions - *[color]*.

The bladder is opened to show a ___ x ___ x ___ cm *[color / papillary / flat]* mass *[with hemorrhage / necrosis]* on the *[anterior / posterior / right / left / dome / trigone]* wall. The mass *[involves / is ___ cm from]* the right ureteral orifice, *[involves / is ___ cm from]* the left ureteral orifice, and *[involves / is ___ cm from]* the urethral orifice. The mass *[involves / is ___ cm from]* the right ureteral margin, *[involves / is ___ cm from]* the left ureteral margin, and *[involves / is ___ cm from]* the urethral margin.

Sectioning through the mass shows a *[color / texture]* cut surface and *[no invasion into / invasion into but not through / invasion into and through]* the muscularis propria. The mass *[abuts / is ___ cm from the serosa]*, *[abuts / is ___ cm from the soft tissue margin].* The mass *[invades / is ___ cm from]* the

anterior vaginal wall, is ___ cm from the *[anatomic location]* vaginal margin and *[involves / is ___ cm from the]* posterior endometrium.

The remainder of the bladder mucosa is *[color / texture]* with a normal folding pattern. The average wall thickness is ___ cm. The ureters are lined by pale tan, smooth urothelium. *[There are no additional lesions. / Describe additional lesions – size, invasion, distance to first mass, distance to margins]*.

The vaginal mucosa is *[color / smooth / unremarkable / hemorrhagic / roughened]*. Bisecting the uterus shows a *[shape]* endometrial cavity (___ cm (length), ___ cm (cornu to cornu)) lined by *[color / glistening / roughened]* endometrium (___ cm in maximum thickness). The myometrium is *[color / smooth / trabecular]* and ___ cm in maximum thickness. The cervix bears a ___ cm *[linear / ovoid / irregular]* os and the ectocervical mucosa is *[color / smooth / roughened]*. The endocervical canal is *[patent / stenosed / occluded]* and lined by *[color, herringbone / hemorrhagic, granular]* mucosa.

Cold ischemic time: _____
Formalin fixation time: _____

Representative sections are submitted as follows:

A1-A3:	Mass with greatest depth of invasion with perivesicular soft tissue margin (specify which margin), full thickness
A4:	Mass with adjacent mucosa
A5:	Anterior bladder wall
A6:	Posterior bladder wall
A7:	Dome wall
A8:	Right lateral wall
A9:	Left lateral wall
A10:	Right ureteral orifice with ureterovesicular junction
A11:	Left ureteral orifice with ureterovesicular junction
A12:	Trigone with urethra
A13:	Right ureter margin, *en face*
A14:	Left ureter margin, *en face*
A15:	Right perivesicular soft tissue margin, perpendicular
A16:	Left perivesicular soft tissue margin, perpendicular
A17:	Lymph nodes (or perivesicular fat)
A18:	Urethral margin, perpendicular
A19:	Anterior vaginal wall
A20:	Cervix, ____ (location)
A21-22:	Endomyometrium of uterus
A23:	Right fallopian tube, with entire fimbria
A24:	Right ovary
A25:	Left fallopian tube, with entire fimbria
A26:	Left ovary
A27-29:	Rectum (normal or with mass extension) and proximal / distal margins
A30:	Abdominal wall (normal or with mass extension)
A31:	Pelvic wall (normal or with mass extension)