Prostate Gland

Protocol applies to invasive carcinomas of the prostate gland.

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

Procedures

- Needle Biopsy
- Transurethral Prostatic Resection
- Suprapubic or Retropubic Enucleation (Subtotal Prostatectomy)
- Radical Prostatectomy

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Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2004
Applies to invasive carcinomas only
Based on AJCC/UICC TNM, 6th edition

PROSTATE GLAND: Needle Biopsy, Transurethral Prostatic Resection (TUR), Enucleation Specimen

Patient name:
Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC

Specimen Type
___ Needle biopsy
___ Transurethral prostatic resection
*Weight: ___ g
___ Enucleation
*Weight: ___ g
___Other (specify): _____
___Not specified

MICROSCOPIC

Histologic Type
___ Cannot be determined
___ Adenocarcinoma (conventional, not otherwise specified)
___ Prostatic duct adenocarcinoma
___ Mucinous (colloid) adenocarcinoma
___ Signet-ring cell carcinoma
___ Adenosquamous carcinoma
___ Small cell carcinoma
___ Sarcomatoid carcinoma
___ Other (specify): _____
___ Undifferentiated carcinoma, not otherwise specified

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

Histologic Grade
Gleason Pattern:
(if 3 patterns present, use most predominant pattern and worst pattern of remaining 2)

___ Not applicable
___ Cannot be determined

Primary Pattern
___ Grade 1
___ Grade 2
___ Grade 3
___ Grade 4
___ Grade 5

Secondary Pattern
___ Grade 1
___ Grade 2
___ Grade 3
___ Grade 4
___ Grade 5

Total Gleason Score: ____

Tumor Quantitation: Needle Biopsy Specimens
Proportion (percent) of prostatic tissue involved by tumor: ____%
and/or
Total linear millimeters of carcinoma/length of core(s): ___/___ mm
and/or
Other quantitation (specify): _____
*Number cores positive/total number cores: ____/____

Tumor Quantitation: TUR Specimens
Proportion (percent) of prostatic tissue involved by tumor: ___%
___ Tumor incidental histologic finding in no more than 5% of tissue resected
___ Tumor incidental histologic finding in more than 5% of tissue resected
*Number of positive chips/total chips: ____/____

Tumor Quantitation: Enucleation Specimens
Proportion (percent) of prostatic tissue involved by tumor: ____%
*Tumor size (dominant nodule, if present):
*Greatest dimension: ___ cm
*Additional dimensions: ___ x ___ cm

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Periprostatic Fat Invasion (document if identified)
*___ Not identified
___ Present

Seminal Vesicle Invasion (document if identified)
*___ Not identified
___ Present

***Perineural Invasion**
*___ Not identified
*___ Present

***Lymphatic (Small Vessel) Invasion (L)**
*___ Absent
*___ Present
*___ Indeterminate

***Additional Pathologic Findings (check all that apply)**
*___ None identified
*___ High-grade prostatic intraepithelial neoplasia (PIN)
*___ Atypical adenomatous hyperplasia
*___ Benign prostatic hyperplasia
*___ Inflammation (specify type): _____
*___ Other (specify): _____

***Comment(s)**

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Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2004
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PROSTATE GLAND: Radical Prostatectomy

Patient name:
Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC (rarely applicable; see Microscopic)

MICROSCOPIC

Histologic Type
___ Cannot be determined
___ Adenocarcinoma (conventional, not otherwise specified)
___ Prostatic duct adenocarcinoma
___ Mucinous (colloid) adenocarcinoma
___ Signet-ring cell carcinoma
___ Adenosquamous carcinoma
___ Small cell carcinoma
___ Sarcomatoid carcinoma
___ Other (specify): _____
___ Undifferentiated carcinoma, not otherwise specified

Histologic Grade
Gleason Pattern:
(if 3 patterns are present, record the most predominant and second most common patterns; the tertiary pattern should be recorded if higher than primary and secondary patterns)

___ Not applicable
___ Cannot be determined

Primary Pattern
___ Grade 1
___ Grade 2
___ Grade 3
___ Grade 4
___ Grade 5

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Secondary Pattern
___ Grade 1
___ Grade 2
___ Grade 3
___ Grade 4
___ Grade 5

*Tertiary Pattern
*___ Grade 3
*___ Grade 4
*___ Grade 5

Total Gleason Score: ____

***Tumor Quantitation**
*Proportion (percent) of prostate involved by tumor: ____%
*Tumor size (dominant nodule, if present):
*Greatest dimension: ___ cm
*Additional dimensions: ___ x ___ cm

Pathologic Staging (pTNM)

Primary Tumor (pT)
___ Not identified
pT2: Organ confined
___ pT2a: Unilateral, involving one-half of 1 side ("lobe") or less
___ pT2b: Unilateral involving more than one-half of 1 side ("lobe") but not both sides ("lobes")
___ pT2c: Bilateral disease
pT3: Extraprostatic extension
___ pT3a: Extraprostatic extension
___ pT3b: Seminal vesicle invasion
___ pT4: Invasion of bladder and/or rectum

Regional Lymph Nodes (pN)
___ pNX: Cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: Metastasis in regional lymph node or nodes
Specify: Number examined: ___
Number involved: ___

Distant Metastasis (pM)
___ pMX: Distant metastasis cannot be assessed
pM1: Distant metastasis
___ pM1a: Distant metastasis, non-regional lymph node(s)
___ pM1b: Distant metastasis, bone(s)
___ pM1c: Distant metastasis, other site(s)

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

Note: When more than 1 site of metastasis is present, the most advanced category (pM1c) is used.

Margins (check all that apply)
___ Cannot be assessed
*___ Benign glands at surgical margin
___ Margins uninvolved by invasive carcinoma
___ Margin(s) involved by invasive carcinoma
*___ Unifocal
*___ Multifocal
___ Apical
___ Bladder neck
___ Anterior
___ Lateral
___ Postero-lateral (neurovascular bundle)
___ Posterior
___ Other(s) (specify): _____

Extraprostatic Extension (check all that apply)
___ Absent
___ Present
*___ Unifocal
*___ Multifocal
___ Indeterminate

Seminal Vesicle Invasion (invasion of muscular wall required)
___ Absent
___ Present
___ No seminal vesicle present

***Perineural Invasion**
*___ Absent
*___ Present

***Venous (Large Vessel) Invasion (V)**
*___ Absent
*___ Present
*___ Indeterminate

***Lymphatic (Small Vessel) Invasion (L)**
*___ Absent
*___ Present
*___ Indeterminate

***Additional Pathologic Findings (check all that apply)**
*___ None identified
*___ High-grade prostatic intraepithelial neoplasia (PIN)
*___ Inflammation (specify type): _____
*___ Atypical adenomatous hyperplasia
*___ Benign prostatic hyperplasia

* 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.

*___ Other (specify): _____

***Comment(s)**

Background Documentation

Protocol revision date: January 2004

I. Needle Biopsy

A. Clinical Information

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history (eg, urinary obstruction)
   b. Relevant findings (eg, digital rectal examination, prostate-specific antigen [PSA], ultrasound, magnetic resonance imaging [MRI])
   c. Clinical diagnosis (eg, carcinoma)
   d. Procedure (eg, thick-core [14-gauge] transrectal or transperineal biopsy, thin-core [18-gauge] image-guided gun biopsies [sextant, octant, etc])
   e. Specific site of needle biopsy (eg, peripheral zone, transition zone, apex, base)

B. Macroscopic Examination

1. Specimen
   a. Number of pieces
   b. Unfixed/fixed (specify fixative)
   c. Dimensions
   d. Orientation, if designated by surgeon
   e. Results of intraoperative consultation
2. Tissue submitted for microscopic examination (eg, all tissue), frozen section tissue fragment(s) (unless saved for special studies)
3. Special studies (specify) (eg, histochemistry, immunohistochemistry, morphometry, DNA analysis, cytogenetic analysis)

C. Microscopic Evaluation

1. Tumor
   a. Histologic type (Note A)
   b. Gleason score with primary and secondary grades (Note **B**)
   c. Quantitation of tumor (eg, proportion [percent] of prostatic tissue involved by neoplasm) (Note **C**)
   d. Local invasion (Note **D**)
      (1) periprostatic fat
      (2) seminal vesicle
   e. Perineural invasion (Note **E**)
   f. Venous/lymphatic (large/small) vessel invasion
2. Additional pathologic findings, if present
   a. High-grade prostatic intraepithelial neoplasia (PIN) (Note **F**)
   b. Therapy-related changes
   c. Other
3. Results/status of special studies (specify)

4. Comments, as appropriate, including correlation with intraprocedural consultation, results of other specimens, and clinical information

II. Transurethral Prostatic Resection

A. Clinical Information

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history (eg, urinary obstruction)
   b. Relevant findings (eg, digital rectal examination, prostate-specific antigen [PSA], ultrasound, magnetic resonance imaging [MRI])
   c. Clinical diagnosis (eg, carcinoma)
   d. Operative procedure (transurethral resection of prostate [TURP])
   e. Operative findings

B. Macroscopic Examination

1. Specimen
   a. Organ(s)/tissues(s) included
   b. Unfixed/fixed (specify fixative)
   c. Weight
   d. Descriptive features
   e. Results of intraoperative consultation
2. Tissue submitted for microscopic examination (Note **G**)
   a. All grossly suspicious chips (Note **G**)
   b. Specimen 12 grams or less, submit entirely
   c. Specimen more than 12 grams, submit at least 12 grams (about 6 to 8 cassettes)
   d. Frozen section tissue fragment(s) (unless saved for special studies)
3. Special studies (specify)

C. Microscopic Evaluation

1. Tumor
   a. Histologic type (Note **A**)
   b. Gleason score with primary and secondary grades (Note **B**)
   c. Quantitation of tumor (Note **C**)
   d. Local invasion (Note **D**)
      (1) periprostatic fat
      (2) seminal vesicle
   e. Perineural invasion (Note **E**)
   f. Venous/lymphatic (large/small) vessel invasion
2. Additional pathological findings, if present
   a. High-grade prostatic intraepithelial neoplasia (PIN) (Note **F**)
   b. Atypical adenomatous hyperplasia
   c. Therapy-related changes
   d. Other(s)
3. Results of special studies

4. Comments, as appropriate, including correlation with intraprocedural consultation, results of other specimens, and clinical information

III. Suprapubic or Retropubic Enucleation (Subtotal Prostatectomy)

A. Clinical Information

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history (eg, urinary obstruction)
   b. Relevant findings (eg, palpable mass, elevated prostate-specific antigen [PSA], imaging)
   c. Clinical diagnosis
   d. Procedure (eg, enucleation)
   e. Operative findings

B. Macroscopic Examination

1. Specimen
   a. Tissue(s)/organ(s) received
   b. Unfixed/fixed (specify fixative)
   c. Size (3 dimensions)
   d. Weight
   e. Descriptive features (eg, necrosis, nodular hyperplasia)
   f. Orientation, if indicated by surgeon
   g. Identification of margins, if indicated by surgeon
   h. Results of intraoperative consultation
2. Tumor (if identified)
   a. Location(s)
   b. Size(s)
   c. Descriptive features
   d. Extent of invasion (Note **H**)
3. Blocks submitted for microscopic evaluation
   a. Representative blocks (approximately 8 cassettes)[#]
   b. Tumor or areas suspicious for tumor, if identified
   c. Frozen section tissue fragment(s) (unless saved for special studies)

   [#] *Note: If an unsuspected carcinoma is found in tissue submitted and it involves 5% or less of the tissue examined, additional blocks should be submitted for microscopic analysis.*
4. Special studies (specify)

C. Microscopic Evaluation

1. Tumor
   a. Histologic type (Note **A**)
   b. Gleason score with primary and secondary grades (Note **B**)
   c. Quantitation of tumor
      (1) size of tumor(s) (2 or more dimensions)
      (2) proportion (percent) of specimen involved by tumor

   d. Location of tumor(s)
   e. Local invasion (Note **H**)
   f. Perineural invasion (Note **E**)
   g. Venous/lymphatic (large/small) vessel invasion
2. Margins (Note **I**)
3. Additional pathologic findings, if present
   a. High-grade prostatic intraepithelial neoplasia (PIN) (Note **E**)
   b. Atypical adenomatous hyperplasia
   c. Therapy-related changes
   d. Other(s)
4. Results/status of special studies (specify)
5. Comments, as appropriate, including correlation with intraprocedural consultation, results of other specimens, and clinical information

IV. Radical Prostatectomy

A. Clinical Information

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
2. Responsible physician(s)
3. Date of procedure
4. Clinical information
   a. Relevant history (previous diagnosis, treatment, includes prostate-specific antigen [PSA], imaging)
   b. Relevant findings
   c. Procedure
      (1) perineal procedure
      (2) retropubic procedure
         i. nerve sparing
         ii. standard radical
   d. Operative findings
   e. Anatomic site(s) of specimen(s)

B. Macroscopic Examination

1. Specimen
   a. Organ(s)/tissues included
   b. Unfixed/fixed (specify fixative)
   c. Opened/unopened
   d. Orientation, if indicated by surgeon
   e. Structures included in specimen
      (1) prostate
      (2) seminal vesicles
      (3) segments of vasa deferentia
      (4) bladder neck
      (5) urethra
      (6) other(s) (specify)
   f. Size (3 dimensions)
   g. Weight
   h. Obstruction of urethra (partial/complete)

   i. Descriptive features (eg, necrosis, nodular hyperplasia)
   j. Results of intraoperative consultation
2. Tumor, if identified
   a. Location(s)
   b. Size(s)
   c. Descriptive features
   d. Extent of local invasion
3. Regional lymph nodes
   a. Location
   b. Number (each location, if possible)
4. Blocks submitted for microscopic evaluation (include diagrams, if appropriate) (Note **G**)
   a. Tumor(s) (each grossly recognizable tumor)
   b. Blocks from other anatomic locations within the prostate (to evaluate for multicentricity) or representative blocks of prostate when tumor not grossly identified
   c. Blocks to determine extent of invasion (Note **H**)
      (1) prostatic capsule and periprostatic tissue adjacent to each tumor including inked margins
      (2) seminal vesicles
      (3) periprostatic tissue at bases of seminal vesicles
   d. Apex (Note **J**)
   e. Vesical neck margin (Note **J**)
   f. All lymph nodes
   g. Frozen section tissue fragment(s) (unless saved for special studies)
   h. Other tissues (specify)
5. Special studies (specify) (eg, immunohistochemistry, ploidy analysis, S-phase fraction)

C. Microscopic Evaluation

1. Tumor
   a. Histologic type (Note **A**)
   b. Gleason score with primary and secondary grades (Note **B**)
   c. Location(s)
   d. Extent of local invasion (Note **H**)
      (1) extraprostatic extension
      (2) seminal vesicle involvement
2. Margins (location and extent of margins involved with tumor) (Note **I**)
3. Regional lymph nodes
   a. Number (specify location)
   b. Number involved by tumor
      (1) specify location, if possible
      (2) size of metastatic deposit
      (3) extracapsular extension, if present
4. Additional pathologic findings, if present
   a. High-grade prostatic intraepithelial neoplasia (PIN)
   b. Therapy-related changes
   c. Other(s)
5. Metastasis to other organ(s) or structure(s) (specific sites)
6. Other tissue(s)/organ(s)

7. Results/status of special studies (specify)
8. Comments, as appropriate, including correlation with intraprocedural consultation, results of other specimens, and clinical information

Explanatory Notes

A. Histologic Type

This protocol applies only to carcinomas of the prostate gland. The histologic classification of prostate carcinoma is recommended and shown below.[1] However, this protocol does not preclude the use of other systems of classification or histologic types. Mixtures of different histologic types should be indicated.

Histologic Classification of Carcinoma of the Prostate

Adenocarcinoma (conventional, not otherwise specified)
Special variants of adenocarcinoma and other carcinomas
- Prostatic duct adenocarcinoma
- Mucinous (colloid) adenocarcinoma
- Signet-ring cell carcinoma
- Adenosquamous carcinoma
- Squamous cell carcinoma[#]
- Basaloid and adenoid cystic carcinoma[#]
- Urothelial (transitional cell) carcinoma[#]
- Small cell carcinoma
- Sarcomatoid carcinoma
- Lymphoepithelioma-like carcinoma[#]
- Undifferentiated carcinoma, not otherwise specified

[#] This protocol does not apply to these carcinomas.

B. Gleason Score

The Gleason grading system is recommended for use in all prostatic cancer specimens.[2-6] The Gleason score is the sum of the primary (most predominant) Gleason grade and the secondary (second most predominant) Gleason grade. Where no secondary Gleason grade exists, the primary Gleason grade is doubled to arrive at a Gleason score. The primary and secondary grades should be reported in addition to the Gleason score, eg, Gleason score 7(3,4) or 7(3+4). In needle biopsy specimens in which more than 2 patterns are present and the worst grade is neither the predominant nor the secondary grade, the predominant and the highest grade should be chosen to arrive at a score (eg, 60% grade 3, 30% grade 2, 10% grade 4 is scored as 3+4=7). When multiple needle biopsy specimens are submitted and they have differing Gleason scores, an overall (composite) Gleason score for the case should be clearly reported in a note.

In radical prostatectomy specimens, in which more than 1 separate tumor is identified, the Gleason scores of the individual tumors may be reported separately or, at the very least, the Gleason score of the most significant lesion should be recorded. For instance, if there is a large Gleason score 5 transition zone cancer and a separate smaller Gleason score 7 peripheral zone cancer, both scores or the latter score should be reported rather than the scores being averaged. At the very least, there should be

some indication of the presence of Gleason pattern 4 accounting for the Gleason score 7 tumor.

Another grading system may be used according to institutional preference (eg, World Health Organization [WHO], MD Anderson), but the Gleason score must be included to facilitate comparison of data.

Gleason Grades (Patterns)

Grade 1	Single, separate, closely packed acini
Grade 2	Single acini, more loosely arranged, less uniform
Grade 3	Single acini of variable size, and separation, cribriform and papillary patterns
Grade 4	Irregular masses of acini and fused epithelium, can show clear cells
Grade 5	Anaplastic carcinoma

C. Quantitation of Tumor

There are many methods of estimating the amount of tumor in prostatic specimens.[7-16] In core biopsies, the absolute number or percentage of cores involved, the linear extent of involvement in millimeters, and the proportion (percent) of surface area of prostatic tissue involved may be used. In transurethral resectates, the proportion (percent) of tissue involved by carcinoma and the number of positive chips (foci) may be used. In subtotal and radical prostatectomy specimens, the percentage of tissue involved by tumor can also be "eyeballed." Additionally, in these latter specimens, it may be possible to measure a dominant tumor nodule in at least 2 dimensions and to indicate the number of blocks involved by tumor over the total number of prostatic blocks submitted.

For the purpose of this protocol, it is recommended that, at the very least, the proportion (percent) of prostatic tissue involved by tumor be included for all specimens.

D. Local Invasion in Needle Biopsies

Occasionally in needle biopsies, periprostatic fat is present and involved by tumor.[7-9] This observation should be noted since it indicates that the tumor is at least stage pT3a. Furthermore, if seminal vesicle tissue is present (either unintentionally or intentionally, as in a directed biopsy) and involved by tumor, this should be reported since it indicates that the tumor is at least pT3b. Seminal vesicle invasion is defined by involvement of the muscular wall.[7-9,17] At times, especially in needle biopsy specimens, it is difficult to distinguish between seminal vesicle and ejaculatory duct-type tissue. It is important not to over-interpret ejaculatory duct as seminal vesicle-type tissue. Ejaculatory duct epithelium is generally surrounded by loose fibrous connective tissue with abundant blood vessels, whereas the seminal vesicle epithelium is surrounded by smooth muscle bundles constituting its wall.

E. Perineural Invasion

Perineural invasion on core needle biopsies has been associated with a high risk of extraprostatic extension in some studies, although the exact prognostic significance remains to be determined.[18-21] Perineural invasion has also been found to be an independent risk factor for predicting an adverse outcome in patients treated with

external beam radiation. The value of perineural invasion as an independent prognostic factor, however, has been questioned in a multi-variate analysis.[22]

F. Prostatic Intraepithelial Neoplasia (PIN)

The diagnostic term prostatic intraepithelial neoplasia (PIN), unless qualified, refers to high-grade PIN.[23] Generally, low-grade PIN is not reported. The presence of PIN should be reported in all biopsy specimens including those with carcinoma.[9] High-grade PIN in a biopsy without evidence of carcinoma is a significant risk factor for the presence of carcinoma on subsequent biopsies.[24,25] The reporting of high-grade PIN in prostatectomy specimens is optional.

G. Submission of Tissue for Microscopic Evaluation in Transurethral Resection and Radical Prostatectomy Specimens

Specimens weighing 12 grams or less should be submitted in their entirety, usually in 6 to 8 cassettes.[26,27] For specimens greater than 12 grams, the initial 12 grams are submitted (6 to 8 cassettes), and 1 cassette for every additional 5 grams may be submitted.

In general, random chips are submitted; however, if some chips are firmer or have a yellow or orange-yellow appearance, they should be preferentially submitted.

If an unsuspected carcinoma is found in tissue submitted and it involves 5% or less of the tissue examined, the remaining tissue is generally submitted for microscopic examination.

In radical prostatectomy specimens with no grossly visible tumor, the specimen may be submitted in its entirety or partially sampled in a systematic fashion. One method of partial sampling involves submitting the entire apical segment and bladder neck along with alternating posterior transverse sections. Two or three random blocks demonstrating the anterior surface are also submitted along with samples of each seminal vesicle, including their juncture with prostate proper.

H. Extraprostatic Extension

Extraprostatic extension (EPE) is the preferred term for the presence of tumor beyond the confines of the prostate gland.[8,28] Tumor abutting on or admixed with fat constitutes extraprostatic extension. EPE also may be reported when tumor involves perineural spaces in the neurovascular bundles, even in the absence of periprostatic fat involvement. In certain locations, such as the anterior prostate and bladder neck regions, there is a paucity of fat, and in these locations EPE is determined when the tumor extends beyond the confines of the normal glandular prostate. Sometimes there is a distinct bulging tumor nodule, which may be associated with a desmoplastic stromal reaction. The specific location(s) and the number of sites (blocks) of EPE are useful to report. Descriptors of EPE (unifocal, multifocal, established, extensive, linear millimeters) may be used.

I. Margins

The entire surface of the prostate should be inked to evaluate the surgical margins.[29-36] Usually, surgical margins should be designated as “negative” if tumor is not present at the inked margin and as “positive” if tumor cells touch the ink at the margin. Tumor that

is located very close to an inked surface, but is not actually in contact with ink is considered a negative margin. Positive surgical margins should not be interpreted as extraprostatic extension. If the surgical margin is positive, the pathologist should state this explicitly, although this finding is not relied upon for pathologic staging. The specific locations of the positive margins are useful to report, and there should be some indication of the extent of margin positivity (eg, unifocal versus multifocal, number of positive sites [blocks], linear extent in millimeters).

J. Apex and Bladder Neck

The apex should be closely examined because of its unusual susceptibility to positive margins.[29-31] At the apex, tumor admixed with skeletal muscle elements does not constitute extraprostatic extension. The apical and bladder neck surgical margins should be sectioned entirely, preferably with a perpendicular orientation. Microscopic involvement of bladder neck muscle fibers in radical prostatectomy specimens should not be equated with a pT4 designation. The latter generally requires gross involvement of the bladder neck.

K. TNM and Stage Groupings

The protocol recommends the use of the TNM Staging System for carcinoma of the prostate of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC), as shown below.[37,38]

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): Clinical Classification

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Clinically inapparent tumor neither palpable nor visible by imaging
T1a	Tumor incidental histologic finding in 5% or less of tissue resected
T1b	Tumor incidental histologic finding in more than 5% of tissue resected
T1c	Tumor identified by needle biopsy (eg, because of elevated PSA)
T2	Tumor confined within prostate[#]
T2a	Tumor involves one-half of 1 lobe or less
T2b	Tumor involves more than one-half of 1 lobe but not both lobes

T2c Tumor involves both lobes
T3 Tumor extends through the prostate capsule[##]
T3a Extracapsular extension (unilateral or bilateral)
T3b Tumor invades seminal vesicle(s)
T4 Tumor is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, and/or pelvic wall

[#] Tumor found in one or both lobes by needle biopsy, but not palpable or reliably visible by imaging, is classified as T1c.

[##] Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is classified not as T3 but as T2.

Primary Tumor (pT): Pathologic Classification
pT2[#] Organ confined
pT2a Unilateral, involving one-half of 1 lobe or less
pT2b Unilateral involving more than one-half of 1 lobe but not both lobes
pT2c Bilateral disease
pT3 Extraprostatic extension
pT3a Extraprostatic extension[##]
pT3b Seminal vesicle invasion
pT4 Invasion of bladder and/or rectum

[#] There is no pathologic T1 classification.

[##] Positive surgical margin should be indicated by an R1 descriptor (residual microscopic disease).

Regional Lymph Nodes (N)
NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in regional lymph node or nodes

Distant Metastasis[#] (M)
MX Distant metastasis cannot be assessed
M0 No distant metastasis
M1 Distant metastasis
M1a Non-regional lymph node(s)
M1b Bone(s)
M1c Other site(s)

[#] When more than 1 site of metastasis is present, the most advanced category (pM1c) is used.

Stage Groupings (TNM)				**Grade**
Stage I	T1a	N0	M0	G1
Stage II	T1a	N0	M0	G2, G3-4
	T1b	N0	M0	Any G
	T1c	N0	M0	Any G

	T1	N0	M0	Any G
	T2	N0	M0	Any G
Stage III	T3	N0	M0	Any G
Stage IV	T4	N0	M0	Any G
	Any T	N1	M0	Any G
	Any T	Any N	M1	Any G

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).

Vessel Invasion
By AJCC/UICC convention, vessel invasion (lymphatic or venous) does not affect the T category indicating local extent of tumor unless specifically included in the definition of

a T category. In all other cases, lymphatic and venous invasion by tumor are coded separately as follows.

Lymphatic Vessel Invasion (L)
LX Lymphatic vessel invasion cannot be assessed
L0 No lymphatic vessel invasion
L1 Lymphatic vessel invasion

Venous (Large Vessel) Invasion (V)
VX Venous invasion cannot be assessed
V0 No venous invasion
V1 Microscopic venous invasion
V2 Macroscopic venous invasion

Regional Lymph Nodes (pN0): Isolated Tumor Cells
Isolated tumor cells (ITCs) are single cells or small clusters of cells not more than 0.2 mm in greatest dimension. Lymph nodes or distant sites with ITCs found by either histologic examination, immunohistochemistry, or nonmorphologic techniques (eg, flow cytometry, DNA analysis, polymerase chain reaction [PCR] amplification of a specific tumor marker) should be classified as N0 or M0, respectively. Specific denotation of the assigned N category is suggested as follows for cases in which ITCs are the only evidence of possible metastatic disease.[39,40]

pN0	No regional lymph node metastasis histologically, no examination for isolated tumor cells (ITCs)
pN0(i-)	No regional lymph node metastasis histologically, negative morphologic (any morphologic technique, including hematoxylin-eosin and immunohistochemistry) findings for ITCs
pN0(i+)	No regional lymph node metastasis histologically, positive morphologic (any morphologic technique, including hematoxylin-eosin and immunohistochemistry) findings for ITCs
pN0(mol-)	No regional lymph node metastasis histologically, negative nonmorphologic (molecular) findings for ITCs
pN0(mol+)	No regional lymph node metastasis histologically, positive nonmorphologic (molecular) findings for ITCs

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