

Prostate Gland

Protocol applies to invasive carcinomas of the prostate gland.

Protocol web posting date: July 2006
Protocol effective date: April 2007
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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The College of American Pathologists offers these protocols to assist pathologists in providing clinically useful and relevant information when reporting results of surgical specimen examinations of surgical specimens. The College regards the reporting elements in the "Surgical Pathology Cancer Case Summary (Checklist)" portion of the protocols as essential elements of the pathology report. However, the manner in which these elements are reported is at the discretion of each specific pathologist, taking into account clinician preferences, institutional policies, and individual practice.

The College developed these protocols as an educational tool to assist pathologists in the useful reporting of relevant information. It did not issue the protocols for use in litigation, reimbursement, or other contexts. Nevertheless, the College recognizes that the protocols might be used by hospitals, attorneys, payers, and others. Indeed, effective January 1, 2004, the Commission on Cancer of the American College of Surgeons mandated the use of the checklist elements of the protocols as part of its Cancer Program Standards for Approved Cancer Programs. Therefore, it becomes even more important for pathologists to familiarize themselves with the document. At the same time, the College cautions that use of the protocols other than for their intended educational purpose may involve additional considerations that are beyond the scope of this document.

Summary of Changes

Protocol web posting date: July 2006

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This is a significant update to the prostate protocol.

The checklist for biopsy specimens is separated from the checklist for transurethral prostatic resection (TUR) and enucleation specimens.

Extensive changes have been made in the section "Background Documentation."

Surgical Pathology Cancer Case Summary (Checklist)

Protocol web posting date: July 2006

Protocol effective date: April 2007

Applies to invasive carcinomas only

Based on AJCC/UICC TNM, 6th edition

PROSTATE GLAND: Needle Biopsy

Patient name:

Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC (rarely applicable; see “Microscopic”)

The Gleason scores (grades) and tumor extent measures should be documented for each positive specimen (container). In cases with multiple positive biopsies, there is no need to complete multiple copies of entire checklist. The essential information in each specimen could be conveyed with a simple diagnostic line such as, “Invasive adenocarcinoma; Gleason score 7(3,4); 1/2 cores positive; 20% tissue involvement; periprostatic fat invasion present.” A global (composite) Gleason score integrating all involved sites and an overall tumor extent measure reflecting all examined tissue may also be given but are considered optional.

MICROSCOPIC

Histologic Type

___ Cannot be determined

___ Adenocarcinoma (conventional, not otherwise specified)

___ Other (specify): _____

Histologic Grade (see Explanatory Note B)Gleason Pattern

(if 3 patterns present, use most predominant pattern and worst pattern of remaining 2)

- Not applicable
 Cannot be determined

Primary (Predominant) Pattern

- Grade 1
 Grade 2
 Grade 3
 Grade 4
 Grade 5

Secondary (Worst Remaining) Pattern

- Grade 1
 Grade 2
 Grade 3
 Grade 4
 Grade 5

Total Gleason Score: _____

Tumor Quantitation

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: ____/____

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

* 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.

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

- * None identified
- * High-grade prostatic intraepithelial neoplasia (PIN)
- * Atypical adenomatous hyperplasia (adenosis)
- * Inflammation (specify type): _____
- * Other (specify): _____

***Comment(s)**

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Surgical Pathology Cancer Case Summary (Checklist)*Protocol web posting date: July 2006**Protocol effective date: April 2007**Applies to invasive carcinomas only**Based on AJCC/UICC TNM, 6th edition***PROSTATE GLAND: Transurethral Prostatic Resection (TUR),
Enucleation Specimen**

Patient name:

Surgical pathology number:

Note: Check 1 response unless otherwise indicated.**MACROSCOPIC****Specimen Type** Transurethral prostatic resection

Weight: ___ g

 Enucleation

Weight: ___ g

 Other (specify): _____ Not specified**MICROSCOPIC****Histologic Type** Cannot be determined Adenocarcinoma (conventional, not otherwise specified) Other (specify): _____

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Histologic GradeGleason Pattern

(if 3 patterns present, use most predominant pattern and worst pattern of remaining 2)

- Not applicable
 Cannot be determined

Primary (Predominant) Pattern

- Grade 1
 Grade 2
 Grade 3
 Grade 4
 Grade 5

Secondary (Worst Remaining) Pattern

- Grade 1
 Grade 2
 Grade 3
 Grade 4
 Grade 5

Total Gleason Score: _____

Tumor Quantitation: TUR Specimens

Proportion (percent) of prostatic tissue involved by tumor: _____%

- Tumor incidental histologic finding in no more than 5% of tissue resected (cT1a)
 Tumor incidental histologic finding in more than 5% of tissue resected (cT1b)

*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

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 (adenosis)
- * Nodular prostatic hyperplasia
- * Inflammation (specify type): _____
- * Other (specify): _____

***Comment(s)**

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Surgical Pathology Cancer Case Summary (Checklist)

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PROSTATE GLAND: Radical Prostatectomy

Patient name:

Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC (rarely applicable; see “Background Documentation”)

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 GradeGleason 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 but does not get incorporated into the Gleason score)

- ___ 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

*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

Extraprostatic Extension (check all that apply)

- ___ Absent
 ___ Present
 * ___ Focal
 *Specify site(s): _____
 * ___ Nonfocal (established, extensive)
 *Specify site(s): _____
 ___ Indeterminate

Seminal Vesicle Invasion (invasion of muscular wall required)

- ___ Absent
 ___ Present
 ___ No seminal vesicle present

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

Pathologic Staging (pTNM)Primary Tumor (pT) 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 (see Explanatory Note J)*Note: Subdivision of pT2 disease is problematic and has not been proven to be of importance; hence, the subcategories pT2a,b,c are considered optional.*Regional Lymph Nodes (pN) pNX: Cannot be assessed pN0: No regional lymph node metastasis pN1: Metastasis in regional lymph node or nodesSpecify: 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)*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): _____***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 (adenosis)
- * Nodular prostatic hyperplasia
- * Other (specify): _____

***Comment(s)**

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

Background Documentation

Protocol web posting date: July 2006

Protocol effective date: April 2007

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, prior therapy, 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) and number of cores submitted per container

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)

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 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, prior therapy, 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 g or less, submit entirely
 - c. Specimen more than 12 g, submit at least 12 g (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 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
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. Perineural invasion (Note **E**)
 - f. Venous/lymphatic vessel invasion
2. Margins (Note **H**)

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
 - (3) laparoscopic procedure
 - 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) 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 systematic sampling of prostate when tumor not grossly identified (Note **G**)
 - c. Blocks to determine extent of invasion (Note **I**)
 - (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)

C. Microscopic Evaluation

1. Tumor
 - a. Histologic type (Note **A**)
 - b. Gleason score with primary, secondary, and tertiary grades (Note **B**)
 - c. Location(s)
 - d. Extent of local invasion (Note **I**)
 - (1) extraprostatic extension
 - (2) seminal vesicle involvement
2. Margins (location and extent of margins involved with tumor) (Note **H**)
3. Regional lymph nodes
 - a. Number (specify location)
 - b. Number involved by tumor
 - (1) specify location, if possible
 - (2) size of metastatic deposit (optional)
 - (3) extracapsular extension, if present (optional)
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 specimens containing adenocarcinoma, with the exception of those showing treatment effects, usually in the setting of androgen withdrawal.²⁻⁵ Gleason score is an important parameter used in nomograms, such as the Partin tables, which guide individual treatment decisions.⁶ Readers are referred to the recommendations of a recent consensus conference dealing with the contemporary usage of the Gleason system.⁷ The Gleason score is the sum of the primary (most predominant in terms of surface area of involvement) 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, it is recommended that Gleason scores be assigned for each specimen (container). In addition, a global or composite score reflecting all specimens may be provided.

In needle biopsy specimens where there is a minor secondary component (<5% of tumor) and where the secondary component is of higher grade, the latter should be reported. For instance, a case showing >95% Gleason 3 and <5% Gleason 4 should be reported as Gleason score 7 (3,4 or 3+4). Conversely, if a minor secondary pattern is of lower grade, it need not be reported. For instance, where there is >95% Gleason score 4 and <5% Gleason 3, the score should be reported as Gleason 8 (4,4).

In needle biopsy specimens where more than 2 patterns are present, and the worst grade is neither the predominant nor the secondary grade, the predominant and highest

grade should be chosen to arrive at a score (eg, 75% grade 3, 20%-25% grade 4, <5% grade 5) is scored as 3+5=8.

Rules of grading similar to the above apply to transurethral resection and enucleation specimens.

Tertiary Gleason patterns are common in radical prostatectomy specimens. When Gleason pattern 5 is present as a tertiary pattern, its presence should be recognized in the report. For instance, in a situation where the primary Gleason grade is 3, the secondary is 4 and there is <5% Gleason 5, the report should indicate a Gleason score of 7 (3,4) with tertiary Gleason pattern 5.

In most radical prostatectomy specimens, a dominant nodule is not present, and the Gleason score is based on the tumor present in the entire gland. Where more than 1 separate tumor is clearly identified, the Gleason scores of individual tumors can be recorded separately, or, at the very least, a Gleason score of the dominant or most significant lesion should be recorded. For instance, if there is a large Gleason score 4 (2,2) transition zone tumor and a separate smaller Gleason score 8 (4,4) peripheral zone cancer, both scores should be reported, or, at the very least, the latter score should be reported rather than these scores being averaged.

C. Quantitation of Tumor

There are many methods of estimating the amount of tumor in prostatic specimens.⁸⁻¹⁷ 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 resections, the proportion (percent) of tissue involved by carcinoma, the number of positive chips and the ratio or percentage positive chips to total chips 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/or 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 suggested that, at the very least, the estimated 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.^{8,9} This observation should be noted since it indicates that the tumor is at least pT3a in the TNM system. 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.^{8,9,18} At times, especially in needle biopsy specimens, it is difficult to distinguish between seminal vesicle and ejaculatory duct tissue. It is important not to overinterpret ejaculatory duct as seminal vesicle since involvement of the former by tumor does not constitute pT3b disease. If there is doubt as to whether the involved tissue represents seminal vesicle or ejaculatory duct, then invasion of seminal vesicle should not be definitively diagnosed.

E. Perineural Invasion

Perineural invasion in core needle biopsies has been associated with extraprostatic extension in some correlative radical prostatectomy studies, although its exact prognostic

significance remains to be determined.^{9,19-22} 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 multivariate 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 isolated PIN should be reported in all biopsy specimens.⁹ The reporting of PIN in biopsies with carcinoma is considered optional but may be important, especially in the context of limited (minimal) adenocarcinoma. High-grade PIN in a biopsy without evidence of carcinoma is a 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 g or less should be submitted in their entirety, usually in 6 to 8 cassettes.^{26,27} For specimens greater than 12 g, the initial 12 g are submitted (6 to 8 cassettes), and 1 cassette for every additional 5 g 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 may be submitted for microscopic examination, especially in younger patients.

A radical prostatectomy specimen may be submitted in its entirety or partially sampled in a systematic fashion.^{28,29} For partial sampling in the setting of a grossly visible tumor, the tumor and associated periprostatic tissue and margins, along with the entire apical and bladder neck margins and the junction of each seminal vesicle with prostate proper, should be submitted. If there is no grossly visible tumor, a number of systematic sampling strategies may be used. One that yields excellent prognostic information involves submitting the posterior aspect of each transverse slice along with a mid anterior block from each side. The anterior sampling detects the T1c cases arising in the transition zone and extending anteriorly. The entire apical and bladder neck margins and junction of each seminal vesicle with prostate should also be submitted.

H. Margins

The entire surface of the prostate should be inked to evaluate the surgical margins.²⁸⁻³⁶ 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. When tumor is located very close to an inked surface but is not actually in contact with the ink, the margin is considered negative. Positive surgical margins should not be interpreted as extraprostatic extension. Intraprostatic margins are positive in the setting of capsular incision (so-called pT2+ disease).²⁸ 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).

I. Extraprostatic Extension

Extraprostatic extension (EPE) is the preferred term for the presence of tumor beyond the confines of the prostate gland.^{28,30,31} Tumor abutting on or admixed with fat constitutes extraprostatic extension. Tumor involving loose connective tissue in the plane of fat or beyond, even in the absence of direct contact between tumor and adipocytes, indicates EPE. Extraprostatic extension 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 (focal, nonfocal) may be used. The definition of focal versus nonfocal is subjective, but focal EPE equates with only a few neoplastic glands outside the prostate, and nonfocal EPE is more extensive spread beyond the prostatic edge. Focal or nonfocal EPE may involve 1 or more sites.

J. Apex and Bladder Neck

The apex should be carefully examined because it is a common site of margin positivity.²⁸⁻³¹ At the apex, tumor admixed with skeletal muscle elements does not constitute extraprostatic extension. The apical and bladder neck surgical margins should be submitted entirely, preferably with a perpendicular sectioning technique. Microscopic involvement of bladder neck muscle fibers in radical prostatectomy specimens should not be equated with a pT4 designation. The latter requires gross involvement of the bladder neck, generally with margin positivity. A recent study has shown that patients with microscopic bladder neck involvement have recurrence rates similar to patients with seminal vesicle involvement (pT3b).³⁷

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.^{38,39}

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 DescriptorsResidual 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.^{40,41} The assessment of ITCs in the context of prostatic adenocarcinoma is considered investigational and their biologic significance is unknown.

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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