Protocol for the Examination of Radical Prostatectomy Specimens From Patients With Carcinoma of the Prostate Gland

Version: 4.3.0.0
Protocol Posting Date: September 2023
CAP Laboratory Accreditation Program Protocol Required Use Date: June 2024

The changes included in this current protocol version affect accreditation requirements. The new deadline for implementing this protocol version is reflected in the above accreditation date. For accreditation purposes, this protocol should be used for the following procedures AND tumor types:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostatectomy</td>
<td>Includes specimens designated radical prostatectomy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinoma</td>
<td>Includes all adenocarcinomas and histologic patterns and subtypes, neuroendocrine carcinomas, and other types.</td>
</tr>
</tbody>
</table>

This protocol is NOT required for accreditation purposes for the following:

<table>
<thead>
<tr>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transurethral resection of the prostate (TURP) and enucleation specimens (simple or subtotal prostatectomy) (consider Prostate TURP protocol)</td>
</tr>
<tr>
<td>Biopsy (consider the Prostate Biopsy protocol)</td>
</tr>
<tr>
<td>Primary resection specimen with no residual cancer (e.g., following neoadjuvant therapy)</td>
</tr>
<tr>
<td>Cytologic specimens</td>
</tr>
</tbody>
</table>

The following tumor types should NOT be reported using this protocol:

<table>
<thead>
<tr>
<th>Tumor Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urothelial carcinoma, including subtypes (consider the Urethra (prostatic urethra) protocol)</td>
</tr>
<tr>
<td>Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)</td>
</tr>
<tr>
<td>Sarcoma (consider the Soft Tissue protocol)</td>
</tr>
</tbody>
</table>

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With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.

* Denotes primary author.
Accreditation Requirements
This protocol can be utilized for a variety of procedures and tumor types for clinical care purposes. For accreditation purposes, only the definitive primary cancer resection specimen is required to have the core and conditional data elements reported in a synoptic format.

- **Core data elements** are required in reports to adequately describe appropriate malignancies. For accreditation purposes, essential data elements must be reported in all instances, even if the response is “not applicable” or “cannot be determined.”
- **Conditional data elements** are only required to be reported if applicable as delineated in the protocol. For instance, the total number of lymph nodes examined must be reported, but only if nodes are present in the specimen.
- **Optional data elements** are identified with “+” and although not required for CAP accreditation purposes, may be considered for reporting as determined by local practice standards.

The use of this protocol is not required for recurrent tumors or for metastatic tumors that are resected at a different time than the primary tumor. Use of this protocol is also not required for pathology reviews performed at a second institution (i.e., secondary consultation, second opinion, or review of outside case at second institution).

Synoptic Reporting
All core and conditionally required data elements outlined on the surgical case summary from this cancer protocol must be displayed in synoptic report format. Synoptic format is defined as:

- **Data element:** followed by its answer (response), outline format without the paired Data element: Response format is NOT considered synoptic.
- The data element should be represented in the report as it is listed in the case summary. The response for any data element may be modified from those listed in the case summary, including “Cannot be determined” if appropriate.
- Each diagnostic parameter pair (Data element: Response) is listed on a separate line or in a tabular format to achieve visual separation. The following exceptions are allowed to be listed on one line:
  - Anatomic site or specimen, laterality, and procedure
  - Pathologic Stage Classification (pTNM) elements
  - Negative margins, as long as all negative margins are specifically enumerated where applicable
- The synoptic portion of the report can appear in the diagnosis section of the pathology report, at the end of the report or in a separate section, but all Data element: Responses must be listed together in one location

Organizations and pathologists may choose to list the required elements in any order, use additional methods in order to enhance or achieve visual separation, or add optional items within the synoptic report. The report may have required elements in a summary format elsewhere in the report IN ADDITION TO but not as replacement for the synoptic report i.e., all required elements must be in the synoptic portion of the report in the format defined above.
Summary of Changes
v 4.3.0.0

- WHO 5th Edition update to content and Explanatory Notes
- pTNM Classification update to content and Explanatory Note
- LVI question update from “Lymphovascular Invasion” to “Lymphatic and/or Vascular Invasion”
- Update to “Minor Tertiary Pattern 5” questions, adding “Not identified” to the “Not applicable” answers
Reporting Template

Protocol Posting Date: September 2023
Select a single response unless otherwise indicated.

CASE SUMMARY: (PROSTATE GLAND: Radical Prostatectomy)
Standard(s): AJCC-UICC 8

SPECIMEN (Note A)

Procedure
___ Radical prostatectomy: _________________
___ Other (specify): _________________
___ Not specified

Prostate Size
+Prostate Weight in Grams (g): _________________ g
+Prostate Size in Centimeters (cm): _________________ cm
+Additional Prostate Dimension in Centimeters (cm): _________________ cm
+Additional Prostate Dimension in Centimeters (cm): _________________ cm

TUMOR

Histologic Type (Note B) (select all that apply)

Glandular
___ Acinar adenocarcinoma, conventional (usual)
___ Acinar adenocarcinoma, signet-ring-like cell
___ Acinar adenocarcinoma, pleomorphic giant cell
___ Acinar adenocarcinoma, sarcomatoid
___ Acinar adenocarcinoma, prostatic intraepithelial neoplasia-like
___ Intraductal carcinoma
___ Ductal adenocarcinoma

Squamous
___ Adenosquamous carcinoma
___ Squamous cell carcinoma
___ Basal cell (adenoid cystic) carcinoma

Neuroendocrine
___ Adenocarcinoma with neuroendocrine differentiation
___ Well-differentiated neuroendocrine tumor
___ Small cell neuroendocrine carcinoma
___ Large cell neuroendocrine carcinoma
___ Other histologic type not listed (specify): __________________
___ Carcinoma, type cannot be determined: __________________
+Histologic Type Comment: _________________

Histologic Grade (Note C)

Grade
___ Grade group 1 (Gleason Score 3 + 3 = 6)
___ Grade group 2 (Gleason Score 3 + 4 = 7)
___ Minor Tertiary Pattern 5 (less than 5%) (required only if applicable)
___ Not applicable / not identified
___ Present
**+Percentage of Pattern 4**
___ Less than or equal to 5%
___ 6 - 10%
___ 11 - 20%
___ 21 - 30%
___ 31 - 40%
___ Greater than 40%
___ Grade group 3 (Gleason Score 4 + 3 = 7)

**Minor Tertiary Pattern 5 (less than 5%)** (required only if applicable)
___ Not applicable / not identified
___ Present
**+Percentage of Pattern 4**
___ Less than 61%
___ 61 - 70%
___ 71 - 80%
___ 81 - 90%
___ Greater than 90%
___ Grade group 4 (Gleason Score 4 + 4 = 8)
___ Grade group 4 (Gleason Score 3 + 5 = 8)
___ Grade group 4 (Gleason Score 5 + 3 = 8)
___ Grade group 5 (Gleason Score 4 + 5 = 9)
___ Grade group 5 (Gleason Score 5 + 4 = 9)
___ Grade group 5 (Gleason Score 5 + 5 = 10)
___ Cannot be assessed: _________________
___ Not applicable: _________________

+If Gleason Score is Greater Than 7 Specify Percentage of Pattern 4: _________________ %

+If Gleason Score is Greater Than 7 Specify Percentage of Pattern 5: _________________ %

**Intraductal Carcinoma (IDC)** (Note D)
___ Not identified
___ Present
    **IDC Incorporated into Grade**
___ Yes
___ No
___ Cannot be determined

**Cribriform Glands** (applicable to Gleason score 7 or 8 cancer only)
___ Not applicable
___ Not identified
___ Present
___ Cannot be determined (explain): _________________

**Treatment Effect** (select all that apply)
___ No known presurgical therapy
___ Not identified
___ Radiation therapy effect present: __________________________
___ Hormonal therapy effect present: _________________________
___ Other therapy effect(s) present (specify): ___________________
___ Cannot be determined: ________________________________

TUMOR QUANTITATION (Note E)

Tumor Quantitation (select all that apply)
___ Via percentage
  Estimated Percentage of Prostate Involved by Tumor
  ___ Less than 1%
  ___ 1 - 5%
  ___ 6 - 10%
  ___ 11 - 20%
  ___ 21 - 30%
  ___ 31 - 40%
  ___ 41 - 50%
  ___ 51 - 60%
  ___ 61 - 70%
  ___ 71 - 80%
  ___ 81 - 90%
  ___ Greater than 90%
  ___ Cannot be determined (explain): ________________________

and/or
___ Via dimension
  Greatest Dimension of Dominant Nodule in Millimeters (mm): ____________ mm
  +Additional Dimension of Dominant Nodule in Millimeters (mm): __ x __ mm
  +Location of Dominant Nodule: _______________________

Extraprostatic Extension (EPE) (Note F)
___ Not identified
___ Present, focal
___ Present, nonfocal
___ Cannot be determined: __________________________

+Location of Extraprostatic Extension (select all that apply)
___ Right apical
___ Right bladder neck
___ Right anterior
___ Right lateral
___ Right posterolateral (neurovascular bundle)
___ Right posterior
___ Left apical
___ Left bladder neck
___ Left anterior
___ Left lateral
___ Left posterolateral (neurovascular bundle)
___ Left posterior
___ Other (specify): ______________________
___ Cannot be determined: ______________________
Urinary Bladder Neck Invasion (Note G)
____ Not identified
____ Present
____ Cannot be determined: ________________________

Seminal Vesicle Invasion (Note H)
____ Not identified
____ Present, right
____ Present, left
____ Present, bilateral
____ Present, laterality cannot be determined
____ No seminal vesicle present (Note H)

Lymphatic and / or Vascular Invasion (Note I)
____ Not identified
____ Present
____ Cannot be determined (explain): ________________________

+Perineural Invasion (Note J)
____ Not identified
____ Present: ________________________

MARGINS (Note K)

Margin Status
____ Cannot be assessed: ________________________
____ All margins negative for invasive carcinoma
____ Invasive carcinoma present at margin

+Linear Length of Margin(s) Involved by Carcinoma
____ Specify exact length in Millimeters (mm): ________________ mm
____ Less than 3 mm (limited)
____ Greater than or equal to 3 mm (non-limited)
____ Cannot be determined (explain): ________________________

+Focality of Margin Involvement
____ Unifocal
____ Multifocal

Margin(s) Involved by Invasive Carcinoma (select all that apply)
____ Right apical
____ Right bladder neck
____ Right anterior
____ Right lateral
____ Right posterolateral (neurovascular bundle)
____ Right posterior
____ Left apical
____ Left bladder neck
____ Left anterior
____ Left lateral
____ Left posterolateral (neurovascular bundle)
___ Left posterior
___ Other(s) (specify): _________________
___ Cannot be determined: _________________

**Margin Involvement by Invasive Carcinoma in Area of Extraprostatic Extension (EPE)**
___ Not identified
___ Present

**Margin(s) Involved by Invasive Carcinoma in Area of EPE:** _________________

**Gleason Pattern at Margin(s) Involved by Carcinoma (Note K) (select all that apply)**
___ Pattern 3
___ Pattern 4
___ Pattern 5

**Margin Comment:** _________________

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**REGIONAL LYMPH NODES**

**Regional Lymph Node Status**
___ Not applicable (no regional lymph nodes submitted or found)
___ Regional lymph nodes present
___ All regional lymph nodes negative for tumor
___ Tumor present in regional lymph node(s)

**Number of Lymph Nodes with Tumor**
___ Exact number (specify): _________________
___ At least (specify): _________________
___ Other (specify): _________________
___ Cannot be determined (explain): _________________

**Nodal Site(s) with Tumor (select all that apply)**
___ Hypogastric: _________________

**Laterality (select all that apply)**
___ Right
___ Left
___ Cannot be determined: _________________

**Obturator:** _________________

**Laterality (select all that apply)**
___ Right
___ Left
___ Cannot be determined: _________________

**Internal iliac:** _________________

**Laterality (select all that apply)**
___ Right
___ Left
___ Cannot be determined: _________________

**External iliac:** _________________

**Laterality (select all that apply)**
___ Right
___ Left
___ Cannot be determined: _________________

___ Iliac, NOS: _________________

**Laterality (select all that apply)**
___ Right
___ Left
___ Cannot be determined: _____________________

Pelvic, NOS: _____________________

+Laterality (select all that apply)
___ Right
___ Left
___ Cannot be determined: _____________________

Lateral sacral: _____________________

+Laterality (select all that apply)
___ Right
___ Left
___ Cannot be determined: _____________________

Presacral: _____________________

+Laterality (select all that apply)
___ Right
___ Left
___ Cannot be determined: _____________________

Promontory: _____________________

+Laterality (select all that apply)
___ Right
___ Left
___ Cannot be determined: _____________________

Sacral, NOS: _____________________

+Laterality (select all that apply)
___ Right
___ Left
___ Cannot be determined: _____________________

Other (specify): _____________________

+Size of Largest Nodal Metastatic Deposit
Specify in Centimeters (cm)
___ Exact size: _____________________ cm
___ At least (specify): _____________________ cm
___ Greater than: _____________________ cm
___ Less than: _____________________ cm
___ Other (specify): _____________________
___ Cannot be determined (explain): _____________________

+Nodal Site with Largest Metastatic Deposit (specify site): _____________________

+Size of Largest Lymph Node with Tumor
Specify in Centimeters (cm)
___ Exact size: _____________________ cm
___ At least (specify): _____________________ cm
___ Greater than: _____________________ cm
___ Less than: _____________________ cm
___ Other (specify): _____________________
___ Cannot be determined (explain): _____________________

+Largest Lymph Node with Tumor (specify site): _____________________

+Extranodal Extension
___ Not identified
Number of Lymph Nodes Examined

___ Present
___ Cannot be determined: _______________________
___ Other (specify): _______________________
___ Cannot be determined (explain): _______________________

Distant Metastasis

Distant Site(s) Involved, if applicable (select all that apply)
___ Not applicable
___ Nonregional lymph node(s): _______________________
___ Bone: _______________________
___ Other (specify): _______________________
___ Cannot be determined: _______________________

pTNM Classification (AJCC 8th Edition) (Note L)

Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. As per the AJCC (Chapter 1, 8th Ed.) it is the managing physician’s responsibility to establish the final pathologic stage based upon all pertinent information, including but potentially not limited to this pathology report.

Modified Classification (select all that apply)
___ Not applicable
___ y (post-neoadjuvant therapy)
___ r (recurrence)

pT Category#

# There is no pathologic T1 classification.
___ pT2: Organ confined
___ pT3: Extraprostatic extension
___ pT3a: Extraprostatic extension or microscopic invasion of bladder neck
___ pT3b: Tumor invades seminal vesicle(s)
___ pT3 (subcategory cannot be determined)
___ pT4: Tumor is fixed or invades adjacent structures other than seminal vesicles such as external sphincter, rectum, bladder, levator muscles, and / or pelvic wall

T Suffix (required only if applicable)
___ Not applicable
___ (m) multiple primary synchronous tumors in a single organ

pN Category
___ pN not assigned (no nodes submitted or found)
___ pN not assigned (cannot be determined based on available pathological information)
___ pN0: No positive regional nodes
___ pN1: Metastasis in regional nodes
pM Category (required only if confirmed pathologically)#
# When more than 1 site of metastasis is present, the most advanced category is used. M1c is most advanced.
___ Not applicable - pM cannot be determined from the submitted specimen(s)

pM1: Distant metastasis
___ pM1a: Nonregional lymph node(s)
___ pM1b: Bone(s)
___ pM1c: Other site(s) with or without bone disease
___ pM1 (subcategory cannot be determined)

ADDITIONAL FINDINGS

+Additional Findings (select all that apply)
___ None identified
___ Atypical intraductal proliferation (AIP)
___ High-grade prostatic intraepithelial neoplasia (PIN): _________________
___ Atypical adenomatous hyperplasia (adenosis)
___ Nodular prostatic hyperplasia
___ Inflammation (specify type): _________________
___ Other (specify): _________________

SPECIAL STUDIES

+Ancillary Studies
___ Specify: _________________
   +Testing Performed on Block Number(s): _________________
___ Not performed

COMMENTS

Comment(s): _________________
Explanatory Notes

A. Submission of Tissue for Microscopic Evaluation in Radical Prostatectomy Specimens

A radical prostatectomy (RP) specimen can be submitted totally or partially in a systematic fashion.\textsuperscript{1,2,3} The prostate is measured in three dimensions, separately from the seminal vesicles and the ejaculatory ducts. Unless fresh tissue is harvested for research, the specimen must be fixed in buffered formalin for 18 to 24 hours to obtain optimal sections. The entire outer prostate must be inked using at least two different colors to identify laterality (right and left) and outer extent or margin of the specimen. Prostate regions are usually orientable histologically using histoanatomic landmarks except for laterality.\textsuperscript{4,5}

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 available, correlation with biopsies and location of MRI-targeted cancer(s) is helpful in identifying the significant tumor(s) location.

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.\textsuperscript{6} The anterior sampling detects the T1c cases arising in the transition zone and extending anteriorly.

The entire apical and bladder neck margins and the junction of each seminal vesicle with the prostate should also be submitted in a standardized fashion.\textsuperscript{1,4} Apical and bladder neck sections may be taken with radial (cone) or parallel (parasagittal) sections. The latter method has the advantage of yielding more uniform sections.

References


B. Histologic Type

This protocol applies to invasive adenocarcinomas and other carcinomas of the prostate gland.\textsuperscript{1} Carcinomas other than adenocarcinoma are exceptionally uncommon, accounting for less than 1% of prostatic tumors. Tumors such as neuroendocrine and squamous cell carcinomas may occur in pure form or are admixed with adenocarcinoma. This protocol does not apply to urothelial carcinoma.
References

C. Histologic Grade
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 hormonal ablation and radiation therapy. Readers are referred to the recommendations of three ISUP consensus conferences and the GUPS position paper dealing with the contemporary usage of the Gleason system in RP specimens (also see Figure 1).

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. If no secondary Gleason grade exists, the primary Gleason grade is doubled to determine a Gleason score. The primary and secondary grades should be reported in addition to the Gleason score, that is, Gleason score 7(3+4) or 7(4+3).

Figure 1. 2015 modified ISUP Gleason schematic diagram.

Tertiary Gleason patterns are common in RP specimens. A Gleason pattern 5 present as a minor tertiary (less than 5%) pattern should be recognized in the report. For instance, if the primary Gleason pattern is 3, the secondary pattern is 4, and there is less than 5% Gleason pattern 5, the report should
indicate a Gleason score of 7(3+4) with minor tertiary Gleason pattern 5. If Gleason pattern 5 is 5% or higher and constitutes the third most common pattern, it should be included as the secondary pattern, rather than as the minor tertiary pattern.

There are two manners of reporting grade for tumors with more than 95% Gleason pattern 3 and less than 5% (or minor secondary) Gleason pattern 4. One approach is to grade the tumor as 7(3+4) and report the small percentage of Gleason pattern 4. The second approach is to grade as 6(3+3) without including the less than 5% Gleason pattern 4 as the secondary pattern. If the latter grading approach is performed, it is recommended that a comment on the presence of the less than 5% Gleason pattern 4 should be made.

Gleason score should be assigned to the dominant nodule(s), if present. In some cases where a dominant nodule is not identified, grading is based on all carcinomatous foci. If more than one 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 (highest Gleason score or pT category, if not the largest) should be recorded. For instance, if there is a Gleason score 8(4+4) in the right peripheral zone and a separate smaller Gleason score 6(3+3) at the left peripheral zone, both scores should be reported, or, at least, the former score should be reported rather than these scores being averaged (also see Figure 2).

Figure 2. In multifocal tumors, the dominant tumor should be graded separately. In this case, the dominant tumor grade is Gleason score 4+4=8 (Grade group 4) and the two scores should not be averaged (as Gleason score 4+3=7).

There is recent inflation of Gleason score 7 tumors in RP specimens because of grading refinements and with more patients with Gleason score 6 cancers staying on active surveillance. Studies showed that Gleason score 7 (3+4 and 4+3) tumors are prognostically heterogeneous and can be further stratified prognostically by percentage and architectures of Gleason pattern 4. Among Gleason pattern 4 architectures, cribriform has been shown to be an independent predictor of poorer outcome in Gleason score 7 tumors. Both ISUP and GUPS recommend commenting on the presence of cribriform architecture in Gleason score 7 tumors. There are recent attempts to standardize the definition of cribriform pattern. ISUP defines cribriform patterns as a confluent sheet of contiguous malignant epithelial cells with multiple glandular lumina that are easily visible at low power (objective magnification x10) and with no intervening stroma or mucin separating individual or fused glandular structures. Until more evidence is accumulated, reporting the percentage of Gleason pattern 4 for Gleason score 7 tumors in RP specimen is recommended but not required.
The presence of treatment effects to cancer such as prior hormonal or radiation therapy effects should be reported and is important especially if Gleason grading is rendered not applicable. It should be recognized that in post-treatment settings, grading may still be applied for prostate cancers lacking treatment effects, particularly in new-onset (de novo) cancers.

Grade Group
It is recognized that contemporary Gleason scores can be grouped into five prognostic categories, Grade groups 1-5. This grade grouping has also been subsequently validated by other independent studies in surgical cohorts showing significant correlation with outcome. The new grade grouping has been endorsed by ISUP, GUPS and has been included in the 2016 WHO classification. The grade group is also referred to as ISUP grade or WHO grade in other publications. The Grade group should be reported in parallel with the Gleason score.

Table: Grade Groups

<table>
<thead>
<tr>
<th>Grade Group</th>
<th>Gleason Score</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Less than or equal to 6</td>
<td>Only individual discrete well-formed glands</td>
</tr>
<tr>
<td>2</td>
<td>3+4=7</td>
<td>Predominantly well-formed glands with lesser component of poorly formed/fused/cribriform glands</td>
</tr>
<tr>
<td>3</td>
<td>4+3=7</td>
<td>Predominantly poorly formed/fused/cribriform glands with lesser component (#) of well-formed glands</td>
</tr>
<tr>
<td>4</td>
<td>4+4=8</td>
<td>Only poorly formed/fused/cribriform glands</td>
</tr>
<tr>
<td></td>
<td>3+5=8</td>
<td>Predominantly well-formed glands and lesser component (##) lacking glands (or with necrosis)</td>
</tr>
<tr>
<td></td>
<td>5+3=8</td>
<td>Predominantly lacking glands (or with necrosis) and lesser component (##) of well-formed glands</td>
</tr>
<tr>
<td>5</td>
<td>9-10</td>
<td>Lack gland formation (or with necrosis) with or without poorly formed/fused/cribriform glands (#)</td>
</tr>
</tbody>
</table>

#For cases with greater than 95% poorly formed/fused/cribriform glands on a core or at radical prostatectomy, the component of less than 5% well-formed glands is not factored into the grade; should therefore be graded as grade group 4.
##Poorly formed/fused/cribriform glands can be a more minor component.

References


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**D. Intraductal Carcinoma (IDC)**

Intraductal carcinoma (IDC) identified in RP specimen is associated with higher Gleason score and stage and lower progression-free or cancer-specific survival.\(^{1,2,3,4}\) It is important to distinguish IDC from high-grade prostatic intraepithelial neoplasia (PIN) and atypical intraductal proliferation (AIP). Both ISUP and GUPS recommend that Gleason scores or grade groups should not be assigned to pure IDC, which is
exceedingly rare in RP specimens.\cite{6,7,8} However, grading invasive cancer with concomitant IDC is controversial. ISUP recommends incorporating IDC in determining the grade while GUPS recommends not to include IDC in determining the grade. It is recommended to specify which of these two approaches is applied when grading invasive cancer with concomitant IDC.

Distinction between IDC and invasive cribriform or comedonecrosis patterns should be based on morphological examination. In the approach where IDC is not incorporated in grading, immunohistochemistry for basal cells can be used if the results will change the grade.\cite{7}

**References**


**E. Quantitation of Tumor**

Studies have shown that prostate cancer volume is predictive of biochemical recurrence and metastases. However, data are conflicting as to its independent prognostic significance.\cite{1,2,3,4,5} In subtotal and radical prostatectomy specimens, the percentage of tissue involved by tumor can be quantified by simple visual inspection.\cite{6} Additionally, 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 out of the total number of prostatic blocks submitted.

**References**


F. Extraprostatic Extension

Extraprostatic extension (EPE) is the preferred term for the presence of tumor beyond the confines of the prostate glands.\(^1\)\(^2\)\(^3\)\(^4\) EPE is a well-known adverse prognosticator and identification is important in RP specimen. Tumor admixed with fat or 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. EPE is uncommon in contemporary Gleason score 6 cancers, especially with small volume tumors.\(^5\)\(^6\)

EPE may also be reported when the tumor involves loose connective tissues or perineural spaces in the neurovascular bundles, even in the absence of periprostatic fat involvement.\(^3\) In certain locations, such as the anterior and apical 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. Tumor admixed with skeletal muscle elements at the apex or anterior fibromuscular stroma does not constitute EPE. In the distal apical perpendicular margin section, it is often difficult to identify EPE. 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. Since more than 50% of patients with EPE do not progress, descriptors of EPE (focal versus nonfocal) can be used to quantify its extent.\(^7\)\(^8\)\(^9\) Focal EPE equates with only a few neoplastic glands outside the prostate or a tumor involving less than 1 high-power field in 1 or 2 sections; nonfocal EPE is more extensively spread beyond the prostatic edge.\(^7\) The 5-year progression-free survival is 73% for focal EPE and 42% for non-focal EPE.

References


6. Kryvenko ON, Epstein JI. Definition of insignificant tumor volume of Gleason score 3 + 3 = 6 (Grade group 1) prostate cancer at radical prostatectomy – is it time to increase the threshold? J Urol. 2016;196:1664-1669.


**G. Urinary Bladder Neck Invasion**

Invasion of the urinary bladder neck is identified when neoplastic glands involve the thick intersecting smooth muscle bundles characteristic of the bladder neck region in the absence of associated benign prostate glandular tissue.\(^1\)\(^2\)\(^3\) This definition also applies to specimens separately submitted as “bladder neck” margin. Microscopic bladder neck involvement is a significant predictor of PSA recurrence similar to extraprostatic extension\(^3\)\(^4\)\(^5\) and is considered a criterion for category pT3a disease (AJCC 8th edition).\(^6\)

**References**


**H. Seminal Vesicle Invasion**

Seminal vesicle invasion is a significant adverse prognostic factor associated with increased risk of PSA recurrence and worse than EPE.\(^1\)\(^2\)\(^3\)\(^4\) There are several mechanisms of seminal vesicle invasion including: (1) direct invasion of the seminal vesicle from the base of the prostate; (2) EPE from prostate with subsequent invasion of seminal vesicle walls; (3) involvement along the ejaculatory duct into the seminal vesicle; and (4) discontinuous involvement, the latter which likely represents vascular spread.\(^4\) Seminal vesicle involvement is defined as tumor invasion of the muscular wall of seminal vesicle.

Only extraprostatic seminal vesicle involvement is included in the definition of seminal vesicle invasion (pT3b category).\(^5\)\(^6\) Intraprostatic seminal vesicle and ejaculatory duct can be difficult to differentiate, and involvement of these structures is not considered pT3b disease.

**References**


**I. Lymphatic and/or Vascular Invasion**

Lymphatic and/or Vascular Invasion (LVI) is an independent predictor of biochemical recurrence and progression and has been associated with metastasis and decreased survival after RP.1,2,3,4 LVI is characterized by tumor cells within an endothelial-lined space that is usually devoid of a muscular wall. LVI is reported in up to 21.5% of RP specimens. LVI can be confirmed by endothelial-associated markers, although this is not often necessary.

**References**


**J. Perineural Invasion**

Perineural invasion (PNI) is a common finding in radical prostatectomy.1,2 Most studies have shown that PNI is not an independent predictor of outcome in radical prostatectomy and reporting its presence is considered optional.

**References**


**K. Margins**

Margin positivity is a well-known significant adverse prognostic factor after RP.1 To properly evaluate surgical margins, the entire surface of the prostate should be inked. The apex should be carefully examined
because it is a common site of margin positivity. The apical and bladder neck surgical margins should be submitted entirely, preferably with a perpendicular sectioning technique.\textsuperscript{2,3,4} 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 EPE. Intraprostatic margins are positive in the setting of intraprostatic or capsular incision (so-called pT2+ disease; also see Figure 3).\textsuperscript{1,2,3,5,6} If the surgical margin finding is positive, the pathologist should state that explicitly, although this finding is not relied upon for pathologic staging. It is also important to indicate whether the positive margin is incisional or in an area of EPE.\textsuperscript{7,8,9} The latter has more adverse prognostic significance than the former.

**Figure 3.** Surgical incision can create stage pT2+ from either pT2 or pT3 disease.

Quantification of the extent of surgical margin positivity has been shown to correlate with outcome.\textsuperscript{8,10,11,12,13,14} Several studies have shown that a total length of 3 mm is a useful cut-off to stratify prognosis.\textsuperscript{8,10,12,13,14}

The location of positive margins varies and is most common at the apex, posterior, and posterolateral aspects of the prostate.\textsuperscript{13,15} Positive margin at posterolateral prostate may carry a higher risk for progression, however, location has not been shown to be an independent predictor of PSA recurrence. Multifocal positive margins have been suggested to be associated with increased risk of PSA recurrence.

Recent studies showed that the Gleason grade or score at a site of margin positivity independently correlated with PSA recurrence.\textsuperscript{12,16,17,18} The presence of any pattern 4 or 5 in tumor at a margin doubled the risk of PSA recurrence compared to only Gleason pattern 3 at margin. The Gleason grade or score at the positive margin may be similar or lower to that of the main tumor and it is recommended to be reported.
L. 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).1
By AJCC 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 (e.g., 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. Tumor confined to the prostate gland irrespective of amount and distribution is considered pT2. pT3a and pT3b are illustrated in Figure 4.1.

Figure 4. T3a is defined as a tumor with unilateral extraprostatic extension, as shown in A, or with bilateral extension, as shown in B. Microscopic extension into the bladder neck is also pT3a. T3b tumor invading the seminal vesicle. Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, III.1

Regional and Distant Lymph Nodes
Regional Lymph Nodes
The regional lymph nodes are the nodes of the true pelvis, which essentially are the pelvic nodes below the bifurcation of the common iliac arteries. They include the following groups:

- Pelvic, NOS
- Hypogastric
- Obturator
- Iliac (internal, external, or NOS)
- Sacral (lateral, presacral, promontory [Gerota’s], or NOS)

Laterality does not affect the N classification.

Distant Lymph Nodes
Distant lymph nodes lie outside the confines of the true pelvis. They can be imaged using ultrasound, computed tomography, magnetic resonance imaging, or lymphangiography. Although enlarged lymph nodes can occasionally be visualized on radiographic imaging, fewer patients are initially discovered with clinically evident metastatic disease. In lower risk patients, imaging tests have proven unhelpful. In lieu of imaging, risk tables are many times used to determine individual patient risk of nodal involvement prior to therapy. Involvement of distant lymph nodes is classified as M1a. The distant lymph nodes include the following:
Lymphatic and/or Vascular Invasion

Lymphatic and/or Vascular invasion (LVI) indicates whether microscopic lymph-vascular invasion is identified. LVI includes lymphatic invasion, vascular invasion, or lymphovascular invasion. By AJCC convention, LVI does not affect the T category indicating local extent of tumor unless specifically included in the definition of a T category.

References