Protocol for the Examination of TURP and Enucleation Specimens From Patients With Carcinoma of the Prostate Gland

Version: 4.2.0.0
Protocol Posting Date: September 2023
The use of this protocol is recommended for clinical care purposes but is not required for accreditation purposes.

This protocol may be used for the following procedures AND tumor types:

Procedure	Description
TURP and enucleation specimens	Includes specimens designated transurethral resection of the prostate (TURP), and enucleation specimens (simple or subtotal prostatectomy)
Tumor Type	**Description**
Carcinoma	Includes all adenocarcinomas and histologic patterns and subtypes, neuroendocrine carcinomas, and others

The following should NOT be reported using this protocol:

Procedure
Biopsy (consider Prostate Biopsy protocol)
Radical Prostatectomy (consider Prostate Radical Prostatectomy protocol)
Tumor Type
Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)
Sarcoma (consider the Soft Tissue protocol)

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With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.
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Accreditation Requirements
The use of this case summary is recommended for clinical care purposes but is not required for accreditation purposes. The core and conditional data elements are routinely reported. Non-core data elements are indicated with a plus sign (+) to allow for reporting information that may be of clinical value.

Summary of Changes

v 4.2.0.0

- WHO 5th Edition update to content and Explanatory Notes
- LVI question update from “Lymphovascular Invasion” to “Lymphatic and/or Vascular Invasion"

Reporting Template

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

CASE SUMMARY: (PROSTATE GLAND: Transurethral Prostatic Resection (TURP), Enucleation Specimen (Simple or Subtotal Prostatectomy))
This template is recommended for reporting TURP specimens, but is not required for accreditation purposes.

SPECIMEN

Procedure (Note A)
___ Transurethral resection of the prostate (TURP)
___ Enucleation (simple or subtotal prostatectomy)
___ Other (specify): _____
___ Not specified

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
___ Isolated 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
___ Not applicable: _____
___ Cannot be assessed: _____
___ Grade group 1 (Gleason Score 3 + 3 = 6)
___ Grade group 2 (Gleason Score 3 + 4 = 7)
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)
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)

+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 (explain): _____

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
___ For TURP Specimens
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): _____
+Number of Positive Chips: _____
+Total Number of Chips: _____

___ For Enucleation and Other Specimens
Greatest Dimension of Dominant Nodule in Millimeters (mm) (if present): _____ mm
+Additional Dimension of Dominant Nodule in Millimeters (mm): ____ x ____ mm
Specify Estimated Percentage of Prostatic Tissue Involved by Tumor: _____ %

Periprostatic Fat Invasion (report if identified in specimen)
___ Not identified
___ Present
___ Equivocal (explain): _____
___ Cannot be determined (explain): _____

Seminal Vesicle Invasion (report if identified in specimen)
___ Not identified
___ Present
___ Equivocal (explain): _____
___ Cannot be determined (explain): _____

+Lymphatic and / or Vascular Invasion
___ Not identified
___ Present
___ Cannot be determined: _____

+Perineural Invasion (Note F)
___ Not identified
___ Present

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): _____

COMMENTS

Comment(s): _____

Explanatory Notes

A. Submission of Tissue for Microscopic Evaluation in Transurethral Resection

Transurethral resection specimens that weigh 12 grams or less should be submitted in their entirety.[1] For specimens that weigh more than 12g, the initial 12g are submitted, and 1 cassette may be submitted for every additional 5 g of remaining tissue.[2]

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

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.[3] Involvement in 5% or less of the tissue is considered as T1a, whereas involvement in greater than 5% is considered as T1b.[4]

References

1. Humphrey PA, Walther PJ. Adenocarcinoma of the prostate, I: sampling considerations. *Am J Clin Pathol*. 1993;99:746-759.
2. Trpkov K, Thompson J, Kulaga A, Yilmaz A. How much tissue sampling is required when minimal prostate carcinoma is identified on transurethral resection? *Arch Path Lab Med.* 2008;132(8):1313-1316.
3. Paner GP, Magi-Galluzzi C, Amin MB, Srigley JR: Adenocarcinoma of the prostate. In: Amin MB, Grignon DJ, Srigley JR, Eble JN,eds. *Urological Pathology*. Philadelphia, PA: Lippincott William & Wilkins; 2014:559-673.
4. Amin MB, Edge SB, Greene FL, et al, eds. *AJCC Cancer Staging Manual.* 8th ed. New York, NY: Springer; 2017.

B. Histologic Type

This protocol applies to invasive adenocarcinomas and other carcinomas of the prostate gland.[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.
Some adenocarcinoma subtypes and unusual patterns have percentage cut-offs to render their diagnosis. Since examination of the entire tumor may not be amenable in TURP, a descriptive approach in their diagnosis should also be considered (e.g., adenocarcinoma with mucinous features, adenocarcinoma with signet ring-like cell features).

References

1. Amin MB, Kench JG, Rubin MA, et al. Tumours of the prostate. In: *WHO Classification of Tumours Editorial Board, eds. Urinary and Male Genital Tumours. WHO Classification of Tumours.* Geneva, Switzerland: WHO Press; 2022:193-234.

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 androgen deprivation and radiation therapy.[1,2,3,4,5,6,7,8,9] 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 (also see Figure 1).[4,5,6,7]

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 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(3+4). In TURP or enucleation specimens, Gleason score is the sum of the primary (most predominant) Gleason grade and highest Gleason grade.

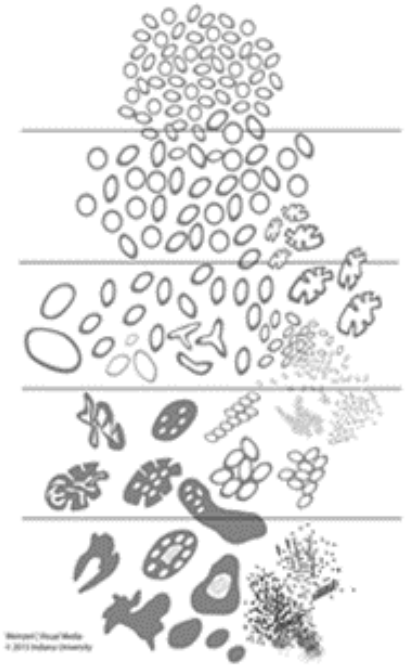

Figure 1. 2015 modified ISUP Gleason schematic diagram.[5]

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

In TURP 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 (e.g., 75% pattern 3, 20-25% pattern 4, less than 5% pattern 5 is scored as 3+5=8).

Another recommendation is that the percentage of pattern 4 should be reported in all Gleason score 7(3+4, 4+3) cases.[6,7,10,11,12] This measurement further stratifies Gleason score 7 and allows identification of cases with limited pattern 4 (e.g., <10%) or extensive pattern 4 (e.g., >80%).

It is now recognized that Gleason pattern 4 has four basic architectures in cribriform, fused, poorly-formed and glomeruloid glands.[12,13,14] Among these architectures, cribriform has been shown to be an independent predictor of poorer outcome particularly in Gleason score 7 tumors and its presence is now recommended to be reported in Gleason pattern 4 cancer. There are recent attempts to standardize the

definition of cribriform pattern.[15] 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.

The presence treatment effects to cancer should be reported and is important especially if Gleason grading is rendered not applicable.[3,4] 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.[16] This grade grouping has also been subsequently validated by other independent studies in surgical cohorts showing significant correlation with outcome.[17,18] The new grade grouping has been endorsed by ISUP, GUPS and in the 2016 WHO classification. The grade group is also referred to as ISUP grade or WHO grade in other publications.[1,5,6,7] The grade group should be reported in parallel with the Gleason score.

Table: Grade Groups

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

#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

1. Humphrey P, Amin MB, Berney D, Billis A, et al. Acinar adenocarcinoma. In: Moch H, Humphrey PA, Ulbright T, Reuter VE, eds. *Pathology and Genetics: Tumors of the Urinary System and Male Genital Organs. 4th edition. WHO Classification of Tumors.* Zurich, Switzerland: WHO Press; 2015:3-28.

2. Gleason DR, Mellinger GT, the Veterans Administration Cooperative Urological Research Group. Prediction of prognosis for prostate adenocarcinoma by combined histological grading and clinical staging. *J Urol.* 1974;111:58-64.
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6. Epstein JI, Amin MB, Fine SW, et al. The 2019 Genitourinary Pathology Society (GUPS) White Paper on Contemporary Grading of Prostate Cancer. *Arch Path Lab Med.* 2021;145:461-493.
7. van Leenders GJLH, van der Kwast TH, Grignon DJ, et al. The 2019 International Society of Urological Pathology (ISUP) Consensus Conference on Grading of Prostatic Carcinoma. *Am J Surg Pathol.* 2020;44:e87-e99.
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9. Paner GP, Gandhi J, Choy B, et al. Essential updates in grading, morphotyping, reporting and staging of prostate carcinoma for general surgical pathologists. *Arch Pathol Lab Med*. 2019;140:55-564.
10. Sauter G, Steurer S, Clauditz TS, et al. Clinical Utility of Quantitative Gleason Grading in Prostate Biopsies and Prostatectomy Specimens. *Eur Urol.* 2016;69:592-598.
11. Cole AI, Morgan TM, Spratt DE, et al. Prognostic value of percent Gleason grade 4 at prostate biopsy in predicting prostatectomy pathology and recurrence. *J Urol.* 2016;196:405-411.
12. Choy B, Pearce SM, Anderson BB, et al. Prognostic significance of percentages and architectural types of contemporary Gleason pattern 4 prostate cancer in radical prostatectomy. *Am J Surg Pathol*. 2016;40:1400-6.
13. Iczkowski KA, Torkko KC, Kotnis GR, et al. Digital quantification of five high-grade prostate cancer patterns, including the cribriform pattern, and their association with adverse outcome. *Am J Clin Pathol.* 2011;136:98-107.
14. Kweldam CF, Wildhagen MF, Steyerberg EW, et al. Cribriform growth is highly predictive for postoperative metastasis and disease-specific death in Gleason score 7 prostate cancer. *Mod Pathol.* 2015;28:457-464.
15. van der Kwast TH, van Leenders GJ, Berney DM, et al. ISUP consensus definition of cribriform prostate cancer. *Am J Surg Pathol.* 2021;45:1118-1126.
16. Pierorazio PM, Walsh PC, Partin AW, Epstein JI. Prognostic Gleason grade grouping: data based on the modified Gleason scoring system. *BJU Int*. 2013;111:753-760.
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18. Berney DM, Beltran L, Fisher G, et al. Validation of a contemporary prostate cancer grading system using prostate cancer death as outcome. *Br J Cancer.* 2016;114(10):1078-1083.

D. Intraductal Carcinoma (IDC)

Intraductal carcinoma (IDC) has independent prognostic significance and its reporting is recommended.[1,2,3,4,5] Intraductal carcinoma is uncommon in TURP specimens and when present it is

usually found within an invasive tumor. 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.[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.[7]

References

1. Guo CC and Epstein JI. Intraductal carcinoma of the prostate on needle biopsy: Histologic features and clinical significance. *Mod Pathol.* 2006;19(12):1528-1535.
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3. Zhou M. Intraductal carcinoma of the prostate: the whole story. *Pathology.* 2013;45(6):533-539.
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7. Epstein JI, Amin MB, Fine SW, et al. The 2019 Genitourinary Pathology Society (GUPS) White Paper on Contemporary Grading of Prostate Cancer. *Arch Path Lab Med.* 2021;145:461-493.
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E. Quantitation of Tumor

Studies have shown that prostate cancer volume is a prognostic factor, although the data on its independent prognostic significance is conflicting.[1,2,3,4,5]The designation of the percentage of cancer tissue in transurethral samples is important. When prostate cancer is discovered incidentally (i.e., discovered in specimens submitted for clinically benign disease, usually benign prostatic hyperplasia [BPH]), the percentage involvement is used to determine the clinical T1 substage, with less than or equal to 5% involvement being T1a and greater than 5% being T1b.[6] In TURP and enucleations specimens, the percentage of tissue involved by tumor can also be quantified by simple visual inspection.

References

1. Stamey T, McNeal J, Yemoto C, et al. Biological determinants of cancer progression in men with prostate cancer. *JAMA.* 1999;281:1395-1400.
2. Salomon L, Levrel O, Anastasiadis A, et al. Prognostic significance of tumor volume after radical prostatectomy: a multivariate analysis of pathological prognostic factors. *Eur Urol.* 2003;43:39-44.
3. Epstein JI. Prognostic significance of tumor volume in radical prostatectomy and needle biopsy. *J Urol.* 2011;187:790-7.

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5. Ito Y, Vertosick EA, Sjoberg DD, et al. In organ-confined prostate cancer, tumor quantitation not found to aid in prediction of biochemical recurrence. *Am J Surg Pathol.* 2019;43:1061-1065.
6. Amin MB, Edge SB, Greene FL, et al. eds. *AJCC Cancer Staging Manual.* 8th ed. New York, NY: Springer; 2017.

F. Perineural Invasion

Perineural invasion (PNI) in needle core biopsies has been associated with extraprostatic extension in some correlative radical prostatectomy studies. However, the significance of this finding as a predictor of stage and outcome is questionable in multivariate analysis.[1,2,3,4,5] Presence of perineural invasion may also be reported in TURP specimens.

References

1. O'Malley KJ, Pound CR, Walsh PC, Epstein JI, Partin AW. Influence of biopsy perineural invasion on long-term biochemical disease-free survival after radical prostatectomy. *Urology*. 2002;59:85-90.
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