Prostate Cancer Histopathology Reporting Guide
Transurethral Resection and Enucleation

Family/Last name

Given name(s)

Date of birth DD – MM – YYYY

Patient identifiers

Date of request DD – MM – YYYY

Accession/Laboratory number

Elements in **black text** are REQUIRED. Elements in **grey text** are RECOMMENDED.

CLINICAL INFORMATION (select all that apply) (Note 1)

- ○ Not provided
- ☐ Previous history of prostate cancer *(including the Gleason grade and score of previous specimens if known)*
- ☐ Previous biopsy, *specify date and where performed*
- ☐ Previous therapy, *specify*
- ☐ Other, *specify*

PRE-PROCEDURE SERUM PSA (Note 2) ng/mL

CLINICAL STAGE (Note 3)

OPERATIVE PROCEDURE (Note 4)

- ○ Not specified
- ○ Transurethral resection
- ○ Enucleation (suprapubic/simple/open prostatectomy)
- ○ Other, *specify*

SPECIMEN WEIGHT (Note 5) g

SPECIMEN DIMENSIONS (Note 6) *(Enucleation/suprapubic/open prostatectomy specimens only)*

mm x mm x mm

BLOCK IDENTIFICATION KEY (Note 7)
(List overleaf or separately with an indication of the nature and origin of all tissue blocks)

HISTOLOGICAL TUMOUR TYPE (select all that apply) (Note 8)

- ☐ Adenocarcinoma (Acinar, usual type)
- ☐ Other, *specify*

HISTOLOGICAL GRADE (Note 9)

Gleason score

Primary pattern/grade
○ 1 ○ 2 ○ 3 ○ 4 ○ 5

Secondary pattern/grade
○ 1 ○ 2 ○ 3 ○ 4 ○ 5

- ○ Indeterminate, *specify reason*

International Society of Urological Pathology (ISUP) Grade (Grade Group)

- ○ ISUP Grade (Grade Group) 1 (Gleason score ≤6)
- ○ ISUP Grade (Grade Group) 2 (Gleason score 3+4=7)
- ○ ISUP Grade (Grade Group) 3 (Gleason score 4+3=7)
- ○ ISUP Grade (Grade Group) 4 (Gleason score 8)
- ○ ISUP Grade (Grade Group) 5 (Gleason score 9-10)
- ○ Indeterminate, *specify reason*

Percentage Gleason pattern 4/5 *(applicable for Gleason scores ≥7)*

% ○ Not identified

PROSTATIC TISSUE INVOLVED BY TUMOUR (Note 10)
(Should be an estimate <5% and then 10% increments)

Prostatic tissue involved by tumour measured on the basis of area *(TURP or enucleation/suprapubic prostatectomy specimens)* %

OR

Prostatic tissue involved by tumour measured on the basis of number of chips *(TURP specimens only)* %

PERINEURAL INVASION (Note 11)

○ Not identified ○ Present

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SEMINAL VESICLE INVASION (Note 12)

◯ Not identified ◯ Present

LYMPHOVASCULAR INVASION (Note 13)

◯ Not identified ◯ Present

EXTRAPROSTATIC EXTENSION (Note 14)

◯ Not identified ◯ Present ◯ Indeterminate

INTRADUCTAL CARCINOMA OF PROSTATE (Note 15)

(If no intraductal carcinoma of prostate is present in any specimen, this need only be recorded once for the whole case)

◯ Not identified ◯ Present

COEXISTENT PATHOLOGY (Note 16)

◯ None identified

◯ Present, *specify*

Scope

The dataset has been developed for the examination of transurethral resection and enucleation (suprapubic/simple/open prostatectomy) specimens of the prostate. The elements and associated commentary apply to invasive carcinomas of the prostate gland. Urothelial carcinomas arising in the bladder or urethra are dealt with in a separate dataset

Note 1 - Clinical information (Recommended)

Reason/Evidentiary Support

It is the responsibility of the clinician requesting the pathological examination to provide information that will have an impact on the diagnostic process or affect its interpretation. The use of a standard pathology requisition/request form including a checklist of important clinical information is encouraged to help ensure that relevant clinical data is provided by the clinicians with the specimen. Generally, information about pathological findings in prior specimens or previous treatment aids interpretation of the microscopic findings and accurate pathological diagnosis.

Radiation and/or endocrine therapy for prostate cancer have a profound effect on the morphology of both cancer and benign prostatic tissue. Following irradiation, benign acinar epithelium shows nuclear enlargement and nucleolar prominence,[1] while basal cells may show cytological atypia, nuclear enlargement and nuclear smudging.[2] There may also be increased stromal fibrosis, which may resemble tumour-induced desmoplasia. These changes may persist for a considerable period, having been reported up to 72 months after treatment, and are more pronounced in patients who have undergone brachytherapy compared to those who have received external beam radiation therapy.[2,3] It is important to document any previous radiotherapy to help the pathologist to interpret changes accurately. Radiation may be associated with apparent upgrading of prostate cancer in prostatectomy specimens.[4]

Likewise, neoadjuvant androgen deprivation therapy (ADT) may induce morphological changes in both prostate cancer and benign tissue. Androgen blockade induces basal cell hyperplasia and cytoplasmic vacuolation in benign prostatic tissue, although this is unlikely to be confused with malignancy.[5] More significantly from a diagnostic point of view, neoadjuvant ADT may increase the risk of overlooking acinar adenocarcinoma on low power microscopic examination due to collapse of glandular lumina, cytoplasmic pallor and shrinking of nuclei.[6-8] The effect of androgen blockage on prostate cancer is variable and an apparent upgrading of the cancer has been reported in a number of studies.[4,5] As for needle core biopsies, in transurethral resection or enucleation specimens taken following either radiotherapy or androgen deprivation therapy, tumours that show significant treatment effect should not be graded.[9]

The Gleason score of prostate cancer in any previously submitted specimen should also be provided by the clinician as this allows assessment of any progression of the tumour towards a higher grade/ more undifferentiated state, which itself may be of prognostic significance.

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Note 2 - Pre-procedure serum PSA (Recommended)

Reason/Evidentiary Support

The clinician requesting the pathological examination should provide information on the pre-transurethral resection/enucleation serum prostate-specific antigen (PSA) level, if measured. The use of a standard pathology requisition/request form including a checklist of important clinical information is strongly encouraged to help ensure that relevant clinical data is provided by the clinicians with the specimen and its use.

If the patient is on 5-alpha-reductase inhibitor medications, such as finasteride or dutasteride, this should be recorded as it may lower serum PSA levels and affect interpretation of serum PSA values for detecting prostate cancer.[10-13]

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Note 3 - Clinical stage (Recommended)

Reason/Evidentiary Support

In the large majority of cases these procedures are performed for the relief of benign prostatic hyperplasia when it is not anticipated that there will be a cancer present and clinical stage is not applicable; if cancer is found on microscopic examination in this situation it will be assigned to category T1. In the small number of cases in which it is known that there is cancer present, a transurethral resection of the prostate may be done to relieve an obstruction where a patient is not amenable to other procedures. In these cases, the clinical stage may be more relevant.

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Note 4 - Operative procedure (Required)

Reason/Evidentiary Support

Information regarding the nature of the surgical procedure undertaken is generally regarded as a required item in International Collaboration on Cancer Reporting (ICCR) datasets since it allows the morphological findings to be placed in context.

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Note 5 - Specimen weight (Required)

Reason/Evidentiary Support

The specimen weight is the best estimate of the amount of tissue resected and received by the pathology laboratory for examination and current histological sampling guidelines are based on this parameter.[14] The specimen may be weighed in either the operating theatre or in the pathology laboratory.

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Note 6 - Specimen dimensions (Recommended)

Reason/Evidentiary Support

Information regarding the size of the specimen received is generally regarded as either a recommended or required item in ICCR datasets, since it documents the tissue actually received by the pathology laboratory and upon which the diagnostic and prognostic information is based. Enucleation (suprapubic/simple/open prostatectomy specimens) are often received in pieces and only the largest piece or pieces need to be measured.

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Note 7 - Block identification key (Recommended)

Reason/Evidentiary Support

Information regarding the nature of the surgical procedure undertaken is generally regarded as a recommended item in ICCR datasets since it facilitates internal and external case review. Although a reviewer does not need information about the origin of each block in a transurethral resection specimen in order to provide an informed specialist opinion, such data may be more useful in enucleation specimens. Moreover, recording the origin/designation of tissue blocks facilitates retrieval of blocks, for example for further immunohistochemical or molecular analysis, research studies or clinical trials.

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Note 8 - Histological tumour type (Required)

Reason/Evidentiary Support

The vast majority (>95%) of prostate cancers are acinar adenocarcinomas.[15] Other types of carcinoma are rarer but must be recorded if present, since some variants, such as ductal adenocarcinoma, small cell carcinoma, sarcomatoid carcinoma and urothelial-type adenocarcinoma,

have a significantly poorer prognosis.[15-21] The tumour type should be assigned in line with the 2016 World Health Organisation (WHO) classification and mixtures of different types should be indicated.[15] Subtypes of prostate carcinoma are often identified in combination with acinar type and in such cases the tumour type should be classified according to the subtype.

WHO classification of tumours of the prostate[a][15]

Descriptor	ICD-O codes
Epithelial tumours	
Glandular neoplasms	
Acinar adenocarcinoma	8140/3
Atrophic	
Pseudohyperplastic	
Microcystic	
Foamy gland	
Mucinous (colloid)	8480/3
Signet ring-like cell	8490/3
Pleomorphic giant cell	
Sarcomatoid	8572/3
Prostatic intraepithelial neoplasia, high-grade	8148/2
Intraductal carcinoma	8500/2
Ductal adenocarcinoma	8500/3
Cribiform	8201/3
Papillary	8260/3
Solid	8230/3
Urothelial carcinoma	8120/3
Squamous neoplasms	
Adenosquamous carcinoma	8560/3
Squamous cell carcinoma	8070/3
Basal cell carcinoma	8147/3
Neuroendocrine tumours	
Adenocarcinoma with neuroendocrine differentiation	8574/3
Well-differentiated neuroendocrine tumour	8240/3
Small cell neuroendocrine carcinoma	8041/3
Large cell neuroendocrine carcinoma	8013/3

a The morphology codes are from the International Classification of Diseases for Oncology (ICD-O). Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours.

Urothelial carcinomas arising in the bladder or urethra are dealt with in separate datasets; however, those rare urothelial carcinomas arising within the prostate are included in this dataset.

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Note 9 - Histological grade (Required and Recommended)

Reason/Evidentiary Support

Prostate cancer in transurethral resection specimens is graded according to similar principles as in needle core biopsies since, like needle biopsies, transurethral resection of the prostate (TURP) does not sample the entire tumour. Since transurethral resection of the prostate mainly samples the transition zone, cancers arising in this part of the prostate are over-represented in TURP specimens. However, peripheral zone tissue is sometimes also resected and large peripheral zone cancers may involve the transition zone. Thus, TURP specimens include the same spectrum of cancers as needle biopsies, albeit with a different distribution. For example, small low-grade transition zone cancers are more often detected by TURP than by needle biopsies.

It has been demonstrated that the Gleason score of cancer detected at TURP predicts cancer-specific survival[22,23] and local progression.[24] Grading of cancer in TURP specimens was not specifically addressed in the International Society of Urological Pathology (ISUP) 2005 revision. In one study however, conventional Gleason score was compared to modified Gleason score including the highest Gleason grade regardless of amount.[22] Both were independent predictors of cancer-specific survival in multivariate analysis but conventional Gleason score showed slightly stronger correlation with outcome. No studies have been done on the validity of the ISUP 2014 grading system on TURP detected cancer but there is no reason to assume that this grading would not be valid when applied on TURP specimens. Moreover, the issue of how to deal with tertiary patterns is unresolved as there is not enough evidence at present to prove its validity. It is therefore required that the ISUP grade (Grade group) should be reported together with the Gleason score. Percent Gleason patterns 4 and 5 has been reported to predict cancer-specific survival independently of Gleason score.[22]

TURP is sometimes done for palliative reasons in patients with locally advanced prostate cancer. These cancers have usually been treated with androgen deprivation and a common reason for the TURP is that the tumour has become hormone refractory. It is important that information about the hormonal treatment is given on the request form. Prostate cancer showing morphological signs of hormonal treatment should not be graded as the treatment effect can mimic a higher grade. However, these tumours are almost invariably high-grade cancers.

The grade groups and associated definitions are outlined in Table 1.

Both the Gleason score and the ISUP grade (Grade group) should always be reported for the sake of clarity.

Table 1: ISUP grading system, core/needle biopsies and TURP specimens

ISUP grade (Grade group)	Gleason score	Definition
Grade 1	2-6	Only individual discrete well-formed glands
Grade 2	3+4=7	Predominantly well-formed glands with lesser component (*) of poorly- formed/fused/cribriform glands
Grade 3	4+3=7	Predominantly poorly-formed/fused/cribriform glands with lesser component (**) of well-formed glands
Grade 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 and lesser component (**) of well-formed glands (or with necrosis)
Grade 5	9-10	Lack gland formation (or with necrosis) with or without poorly formed/fused/cribriform glands

* Any component of the high-grade pattern (i.e. even if less than 5%) is included in the grade.
** The low-grade pattern is included in the grade only if it is at least 5%.

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Note 10 - Prostatic tissue involved by tumour (Required)

Reason/Evidentiary Support

In the TNM classification, incidentally detected cancer is substaged into cT1a (≤5% cancer) and cT1b (>5% cancer) based on the involvement of resected tissue. This substaging predicts cancer progression[25] and disease-specific survival.[26,27] The TNM classification does not specify how tumour extent should be measured, but the reported percentage of extent is commonly assumed to be calculated as the fraction of total tissue area in the sections.

It has recently been proposed that the percentage of number of chips positive for cancer over total number of chips be reported. With this method 10% involvement was a more useful cut-off for prediction of outcome than 5%.[27] This is expected as the percentage gets higher when a chip is considered positive regardless of the extent of cancer involvement. The advantage of this method is that it is simpler than estimating percentage of tissue area, but there is also a risk of overestimation

when only a minute focus of cancer is present in several chips. Either of these measures can be used but the report should specify what method was used. Percentage of positive chips can obviously not be used for open prostatectomy specimens and percent cancer of the total surface area in the sections should then be reported.

Whichever of these methods is used, for practical purposes it is only necessary to estimate the extent of tumour involvement to the nearest 10%, or for small tumours to state if the tumour comprises <5% of the specimen.

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Note 11 - Perineural invasion (Recommended)

Reason/Evidentiary Support

The significance of perineural invasion in prostate TURP or enucleation specimens is uncertain and there is little published literature specific to these particular specimen types. In needle core biopsy a systematic review of the literature concluded that the weight of evidence suggested that in clinically localised disease perineural invasion was a significant prognostic factor for extraprostatic extension (EPE) and subsequent local recurrence.[28] Hence, it may be significant and perineural invasion should be recorded when present in TURP and enucleation specimens.

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Note 12 - Seminal vesicle invasion (Recommended)

Reason/Evidentiary Support

Seminal vesicle invasion (SVI) is rarely identified in TUR specimens, hence its absence does not need to be explicitly stated. However, if seminal vesicle/ejaculatory duct invasion is present it should be recorded and the following comments apply.

SVI is defined as involvement of the muscular wall of the extraprostatic portion of the seminal vesicle.[29] If seminal vesicle tissue is present and involved by tumour, this should be reported since it indicates that the tumour may be pT3b in the American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) Staging system.[30,31] However, in TURP and enucleation specimens it is often difficult to distinguish between extraprostatic seminal vesicle and intraprostatic seminal vesicle or ejaculatory duct tissue, and it is important not to over interpret invasion of the latter two structures as SVI since their involvement by tumour does not constitute pT3b disease. If there is doubt as to whether the involved tissue represents the extraprostatic seminal vesicle or the intraprostatic seminal vesicle/ejaculatory duct, this should be stated in the report and SVI should not be definitively diagnosed.

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Note 13 - Lymphovascular invasion (Recommended)

Reason/Evidentiary Support

Lymphovascular invasion (LVI) is rarely identified in TUR specimens, hence its absence does not need to be explicitly stated. However, if LVI is present it should be recorded and the following comments apply.

Invasion of lymphatic or blood vessels (i.e. thin-walled endothelial-lined spaces) is uncommonly identified in transurethral resection or enucleation specimens and there is little published data on the significance of LVI specifically relating to tissue obtained during these procedures. However, there is good evidence that LVI is a significant independent prognostic indicator of increased risk of recurrence post radical prostatectomy;[32-35] therefore, if LVI is identified in a TUR/enucleation specimen it may well be significant and its presence should be recorded. The presence of LVI does not affect assignment of the AJCC/UICC T category.

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Note 14 - Extraprostatic extension (Recommended)

Reason/Evidentiary Support

Extraprostatic extension (EPE) became accepted terminology at a 1996 consensus conference, and replaces earlier ambiguous terms such capsular penetration, perforation, or invasion.[36] In radical prostatectomy specimens EPE is an independent prognostic indicator of increased risk of recurrence post radical prostatectomy and is important in assignment of the AJCC/UICC T category.[37,38] There is little data specifically on the significance of EPE in TURP or enucleation specimens given that it is rarely identified; however, it may occasionally be seen and should be reported when present since it indicates that the tumour is at least pT3a in the TNM system.[30] In TURP specimens it is defined as tumour admixed with adipocytes.

The presence of bladder neck smooth muscle involvement by carcinoma in a TURP specimen may indicate that the tumour is at least category pT3a. Typically it is a high grade cancer infiltrating among well-formed and thick smooth muscle bundles with absence of normal prostate glands or stroma. These bladder neck chips are often admixed with chips showing either cancer in the prostate or just normal prostate tissue.

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Note 15 - Intraductal carcinoma of prostate (Recommended)

Reason/Evidentiary Support

Intraductal carcinoma of the prostate (IDC-P) is an uncommon finding in TUR specimens, hence its absence does not need to be explicitly stated. However, if IDC-P is present it should be recorded and the following comments apply.

IDC-P is usually associated with invasive prostate cancer, however, occasionally isolated IDC-P is found without invasive carcinoma; this latter situation is rare and beyond the scope of this dataset.

IDC-P has been well characterised at the histological and molecular levels over the past decade and its clinical significance is now also better understood.[39] The diagnosis of IDC-P is based on morphology and the key criteria include: 1) large calibre glands that are more than twice the diameter of normal non-neoplastic peripheral glands; 2) preserved (at least focally) basal cells identified on H&E staining or with basal cell markers, such as p63, keratin 34βE12 and keratin 5/6, however, the use of immunohistochemistry to identify basal cells is optional, rather than mandatory, for the diagnosis of IDC-P); 3) significant nuclear atypia including enlargement and anisonucleosis; and 4) comedonecrosis, which is often but not always present.[40,41] It is important to distinguish IDC-P from high grade prostatic intraepithelial neoplasia (HGPIN): compared to IDC-P, HGPIN has less architectural and cytological atypia, and cribriform HGPIN is rare.

IDC-P is strongly associated with high volume, high grade invasive prostate carcinoma and metastatic disease, hence the presence of IDC-P in a TURP specimen, even if invasive carcinoma cannot be identified, mandates either further investigation or definitive therapy (depending on the clinical situation).[42-44]

There was a strong consensus (82%) at the ISUP consensus meeting (Chicago 2014) that IDC-P should not be assigned an ISUP or Gleason grade.[45]

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Note 16 - Coexistent pathology (Recommended)

Reason/Evidentiary Support

In some cases clinical management decisions may be aided by knowledge of coexisting pathology, such as high grade prostatic intraepithelial neoplasia (HGPIN), glandular atypia suspicious for malignancy (atypical small acinar proliferation), prostatic urethral lesions, granulomatous prostatitis etc.

If there is carcinoma present, the presence of HGPIN is generally not significant, except perhaps occasionally in the situation where the carcinoma is of very limited extent. Low grade PIN should not be reported.

Likewise, if there is carcinoma present in a specimen, the presence of glandular atypia suspicious for malignancy (atypical small acinar proliferation) is generally not significant, except perhaps

occasionally in the situation where the carcinoma is of very limited extent. In TURP specimens where there is no cancer identified but atypical small aciner proliferation (ASAP) is present, the risk of carcinoma being present in subsequent specimens is not known, but in core biopsies is approximately 50%.[46-49]

Lesions of the prostatic urethra, e.g. urothelial carcinoma in situ (CIS), urethral polyps, nephrogenic adenoma, villous adenoma etc, should also be recorded if present.

Active prostatitis and granulomatous prostatitis may cause a rise in serum PSA, although inflammatory lesions may coexist with carcinoma and it is important not to assume that their presence always accounts for an unexplained increase in a patient's PSA.

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