

Prostate Cancer Histopathology Reporting Guide Radical Prostatectomy Specimen



Family/Last name

Date of birth

Given name(s)

Patient identifiers

Date of request

Accession/Laboratory number

Elements in **black text** are **CORE**. Elements in **grey text** are **NON-CORE**.

SCOPE OF THIS DATASET

indicates multi-select values indicates single select values

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

- Information not provided
- Information provided
 - Previous history of prostate cancer (including the Gleason score or WHO/ISUP Grade/Grade Group of previous specimens if known), *specify*
 - Previous biopsy, *specify date and where performed*
 - Previous therapy, *specify*
 - Other clinical information, *specify*

PRE-BIOPSY SERUM PSA (Note 2)

ng/mL

SPECIMEN WEIGHT (Note 3)

(Weight of the prostate gland without the seminal vesicles)

g

SPECIMEN DIMENSIONS (Note 4)

(Of the prostate gland)

mm x mm x mm

SEMINAL VESICLES (Note 5)

- Absent
- Present (partially or completely resected)

LYMPH NODE DISSECTION SPECIMEN(S) (Note 6)

- Not submitted
- Present (partially or completely resected)
Site(s), specify

Laterality

- Left
- Right
- Bilateral
- Other

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 TUMOUR GRADE (Note 9)

Gleason score

Indicate how Gleason score is being reported

- Largest tumour nodule
- Highest score tumour nodule
- Highest pT category tumour nodule
- Global score (summation of Gleason patterns in all nodules)

Primary pattern

- 1
- 2
- 3
- 4
- 5

Secondary pattern

- 1
- 2
- 3
- 4
- 5

- Indeterminate, *specify reason*

Minor tertiary pattern (if present and higher than primary and secondary grade)

- 4
- <5
- Not applicable

HISTOLOGICAL TUMOUR GRADE (Note 9) continued**WHO/ISUP Grade (Grade Group)**

Indicate how WHO/ISUP Grade is being reported

- Largest tumour nodule
 Highest grade tumour nodule
 Highest pT category tumour nodule
 Global score (summation of Gleason patterns in all nodules)

Indicate WHO/ISUP Grade

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

TUMOUR GROWTH PATTERNS (Note 10)**Intraductal carcinoma of the prostate (IDC-P) AND/OR Invasive cribriform carcinoma**

- Indeterminate
 Not identified
 Present

If present, specify the tumour growth pattern (if apparent on H&E staining^a)**IDC-P**

- Not identified
 Present
 IDC-P incorporated into Gleason score
 IDC-P not incorporated into Gleason score

Invasive cribriform carcinoma

- Not identified
 Present

^a Use of immunohistochemistry is optional.**TUMOUR QUANTIFICATION (Note 11)**

(Amount of tumour identified)

Percentage of prostate involved by tumour

- $\leq 5\%$
 6-10%
 11-20%
 21-50%
 51-80%
 $\geq 80\%$

OR

Diameter of largest nodule

 mm
EXTRAPROSTATIC EXTENSION (Note 12)

- Indeterminate
 Not identified
 Present

Specify location(s)

Extent

- Focal
 Non-focal (established)

URINARY BLADDER NECK INVASION (Note 13)

- Not applicable^b
 Not identified
 Present

^b Refers to cases where bladder neck is not included in the specimen.**MARGIN STATUS (Note 14)**

- Cannot be assessed
 Not involved
 Involved, *specify margin(s) and their location, if possible*

Type of margin positivity (select all that apply)

- Indeterminate
 Extraprostatic (EPE)
 Intraprostatic (capsular incision)

Length of margin involved by carcinoma^c
 mm
Gleason pattern of tumour present at positive margin^d

- Gleason pattern 3
 Gleason pattern 4 or/and 5

^c If more than 1 positive margin the extent should reflect the cumulative length.^d If more than 1 pattern at margin select the highest.**SEMINAL VESICLE INVASION (Note 15)**

- Not applicable^e
 Not identified
 Present

^e Refers to rare cases where seminal vesicles are not included in the specimen.**LYMPHOVASCULAR INVASION (Note 16)**

- Indeterminate
 Not identified
 Present

LYMPH NODE STATUS (Note 17) No nodes submitted or foundNumber of lymph nodes examined Not involved InvolvedNumber of involved lymph nodes Number cannot be determinedMaximum dimension of largest deposit

mm

PATHOLOGICAL STAGING (UICC TNM 8th edition)^f (Note 18)**TNM Descriptors** (only if applicable) (select all that apply) m - multiple primary tumours r - recurrent y - post neoadjuvant therapy**Primary tumour (pT)** TX^g Primary tumour cannot be assessed T0 No evidence of primary tumour T2 Tumour confined within prostate T3 Tumour extends through the prostate capsule^{h,i} T3a Extracapsular extension^h (unilateral or bilateral) including microscopic bladder neck involvement T3b Tumour invades seminal vesicle(s) T4 Tumour is fixed or invades adjacent structures other than seminal vesicles external sphincter, rectum, levator muscles or pelvic wall**Regional lymph nodes (pN)** NX^g Regional nodes cannot be assessed N0 No regional lymph node metastasis N1 Regional lymph node metastasis**Distant metastasis (pM)^j** Not applicable^k M1 Distant metastasis M1a Non-regional lymph node(s) M1b Bone(s) M1c Other site(s)

^f Reproduced with permission. Source: UICC TNM Classification of Malignant Tumours, 8th Edition, eds by James D. Brierley, Mary K. Gospodarowicz, Christian Wittekind. 2016, Publisher Wiley. (incorporating any errata published up until 31st January 2024).

^g TX and NX should be used only if absolutely necessary.

^h The consensus of the dataset authors is that the term extraprostatic extension is preferred.

ⁱ Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is not classified as T3, but as T2.

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

^k No clinical and radiological correlation available.

Definitions

CORE elements

CORE elements are those which are essential for the clinical management, staging or prognosis of the cancer. These elements will either have evidentiary support at Level III-2 or above (based on prognostic factors in the National Health and Medical Research Council (NHMRC) levels of evidence¹). In rare circumstances, where level III-2 evidence is not available an element may be made a CORE element where there is unanimous agreement in the Dataset Authoring Committee (DAC). An appropriate staging system e.g., Pathological TNM staging would normally be included as a CORE element.

Non-morphological testing e.g., molecular or immunohistochemical testing is a growing feature of cancer reporting. However, in many parts of the world this type of testing is limited by the available resources. In order to encourage the global adoption of ancillary tests for patient benefit, International Collaboration on Cancer Reporting (ICCR) includes the most relevant ancillary testing in ICCR Datasets as CORE elements, especially when they are necessary for the diagnosis. Where the technical capability does not yet exist, laboratories may consider temporarily using these data elements as NON-CORE items.

The summation of all CORE elements is considered to be the minimum reporting standard for a specific cancer.

NON-CORE elements

NON-CORE elements are those which are unanimously agreed should be included in the dataset but are not supported by level III-2 evidence. These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.

Key information other than that which is essential for clinical management, staging or prognosis of the cancer such as macroscopic observations and interpretation, which are fundamental to the histological diagnosis and conclusion e.g., macroscopic tumour details, may be included as either CORE or NON-CORE elements by consensus of the DAC.

 [Back](#)

Scope

The dataset has been developed for radical prostatectomy specimens for prostate carcinoma. Core biopsies and transurethral resection (TUR) and enucleation specimens are dealt with in separate ICCR datasets.^{2,3} Rare urothelial carcinomas arising within the prostate are included in a separate ICCR dataset.⁴

The third edition of this dataset includes changes to align the dataset with the World Health Organization (WHO) Classification of Tumours, Urinary and Male Genital Tumours, 5th edition, 2022.⁵ The ICCR dataset includes 5th edition Corrigenda, November 2022.⁶

 [Back](#)

Note 1 – Clinical information (Core and Non-core)

It is the responsibility of the clinician requesting the pathological examination of a specimen 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 strongly encouraged to help ensure that important clinical data is provided by the clinicians with the specimen. Information about prior biopsies or 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 the cancer and the benign prostatic tissue. For this reason, information about any previous therapy is important for the accurate assessment of radical prostatectomy specimens.

Following irradiation, benign acinar epithelium shows nuclear enlargement and nucleolar prominence,⁷ while basal cells may show cytological atypia, nuclear enlargement and nuclear smudging.⁸ 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.^{8,9} Radiation may be associated with apparent upgrading of prostate cancer in prostatectomy specimens.¹⁰

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.¹¹ 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.¹²⁻¹⁴ 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.^{10,11} Hence, it has been suggested that in prostate glands resected following either radiotherapy or ADT, tumours that show significant treatment effect should not be graded.¹⁵

The Gleason score (GS) or International Society of Urological Pathology (ISUP)/WHO Grade (Grade Group) of prostate cancer in any previously submitted specimen should also be provided by the clinician.

↑ Back

Note 2 – Pre-biopsy serum PSA (Non-core)

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

Pre-biopsy serum PSA is a key parameter in some nomograms widely used to estimate the risk of recurrence post-operatively and guide clinical decision making on adjuvant therapy.¹⁶⁻¹⁸

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.¹⁹⁻²²

↑ Back

Note 3 – Specimen weight (Non-core)

The prostate gland should be weighed (ideally in the unfixed condition) without the seminal vesicles since the seminal vesicles can vary markedly in size. If only a combined weight is recorded, this will introduce error into the measurement of the prostate gland weight and distort comparisons, hence a working group at the 2009 ISUP Consensus Conference in Boston recommended that the prostate should be weighed following removal of the seminal vesicles.²³

↑ Back

Note 4 – Specimen dimensions (Non-core)

Although the shape of the prostate changes somewhat once removed from the pelvis, measurements of specimen size are generally considered part of a standard pathology report. In addition, measurements for apex to base, right to left and anterior to posterior enable comparison with clinical and imaging estimates of volume. Recording the volume of the prostate also allows comparisons with the pre-operative assessments of PSA density.

↑ Back

Note 5 – Seminal vesicles (Core)

A record of all organs/tissues received is typically a standard (core) item in gross/macroscopic pathology reports and assessment of invasion of the seminal vesicles is required for staging.

↑ Back

Note 6 – Lymph node dissection specimen(s) (Core and Non-core)

A record of all organs/tissues received is typically a standard (core) item in gross/macroscopic pathology reports and assessment of nodal metastasis is required for staging.

If present, the laterality of the pelvic lymph nodes submitted may be recorded as left, right, bilateral or other (as non-core).

↑ Back

Note 7 – Block identification key (Non-core)

The origin/designation of all tissue blocks should be recorded. This information should ideally be documented in the final pathology report and is particularly important should the need for internal or external review arise. The reviewer needs to be clear about the origin of each block in order to provide an informed specialist opinion. If this information is not included in the final pathology report, it should be available on the laboratory computer system and relayed to the reviewing pathologist. It may be useful to have a digital image of the specimen and record of the origin of the tumour blocks in some cases.

Recording the origin/designation of tissue blocks also facilitates retrieval of blocks for further immunohistochemical or molecular analysis, research studies or clinical trials.

 **Back**

Note 8 – Histological tumour type (Core)

The vast majority (>95%) of prostate cancers are acinar adenocarcinomas.⁵ Other types and subtypes of carcinoma are rarer but must be recorded if present, since some, such as ductal adenocarcinoma, sarcomatoid carcinoma and pleomorphic giant cell adenocarcinoma, have a significantly poorer prognosis.²⁴⁻²⁸ The tumour type should be assigned in line with the 2022 WHO classification of epithelial tumours of the prostate, and mixtures of different types should be indicated (Table 1).²⁴

Table 1: World Health Organization classification of tumours of the prostate.²⁴

Descriptor	ICD-O codes ^a
Epithelial tumours of the prostate	
<i>Glandular neoplasms of the prostate</i>	
Cystadenoma	8440/0
Prostatic intraepithelial neoplasia, high grade	8148/2
Intraductal carcinoma	8500/2
Acinar adenocarcinoma	8140/3
Signet-ring cell-like acinar adenocarcinoma	8490/3
Pleomorphic giant cell acinar adenocarcinoma	8140/3
Sarcomatoid acinar adenocarcinoma	8572/3
Prostatic intraepithelial neoplasia-like carcinoma	8140/3
Ductal adenocarcinoma	8500/3
Adenocarcinoma with neuroendocrine differentiation	8574/3
<i>Squamous neoplasms of the prostate</i>	
Adenosquamous carcinoma	8560/3
Squamous cell carcinoma	8070/3
Adenoid cystic (basal cell) carcinoma [†]	8147/3
Mesenchymal tumours unique to the prostate	
<i>Stromal tumours of the prostate</i>	
Stromal tumour of uncertain malignant potential	8935/1
Stromal sarcoma	8935/3

^a These morphology codes are from the International Classification of Diseases for Oncology, third edition, second revision (ICD-O-3.2).²⁹ Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; /3 for malignant tumours, primary site; and /6 for malignant tumours, metastatic site. Behaviour code /6 is not generally used by cancer registries. Subtype labels are indented. Incorporates all relevant changes from the 5th edition Corrigenda, November, 2022.⁶

[†] Labels marked with a dagger have undergone a change in terminology of a previous code.

© World Health Organization/International Agency for Research on Cancer (IARC). Reproduced with permission.

 **Back**

Note 9 – Histological tumour grade (Core)

The Gleason system has been the worldwide standard for prostate cancer grading over several decades with its contemporary application outlined in detail in the 5th edition of the WHO Classification of Urinary and Male Genital Tumours, ISUP Consensus Conference and 2019 Genitourinary Pathology Society (GUPS) ‘White paper’.^{24,30,31} It is regarded as a core element since validation studies over the years have demonstrated that Gleason scoring is a robust independent predictor of biochemical recurrence, metastasis, and prostate cancer specific mortality.³²⁻³⁵

In summary, the GS of radical prostatectomy specimens is usually obtained by adding the two predominant Gleason patterns or doubling the pattern in cases of uniform pattern. In the 2005 ISUP revision it was recommended that a separate GS should be assigned for each dominant tumour nodule(s).³⁶ The rationale was that additional separate tumours of lower grade (e.g., transition zone cancers) would not be expected to mitigate the prognostic impact of the main tumour and, thus, their patterns should not be included in the global GS. Reporting of separate tumours may, however, be difficult in practice if the prostatectomy specimen is not totally embedded and multifocal tumour nodules may merge into a single large tumour mass. The 2019 ISUP Consensus Conference on the Grading of Prostate Carcinoma recommended that the GS of the (a) largest, (b) highest stage, and (c) highest grade tumour nodules should be recorded, if these are not one in the same. In the large majority of cases (approximately 90%) the highest GS, tumour volume, and stage are all seen in the one nodule.^{30,37}

Not uncommonly in radical prostatectomy specimens there are more than two Gleason patterns present and if there is a minor component of pattern 5 comprising the smallest volume it is referred to as a tertiary high grade pattern or minor tertiary pattern 5. If the tertiary pattern 5 carcinoma constitutes >5% of the estimated volume of the dominant tumour nodule(s) it used as the secondary pattern in Gleason scoring (and associated WHO/ISUP grade or Grade group). If there is <5% tertiary pattern 5 carcinoma present the GS remains unchanged but the presence of a minor or tertiary high grade pattern should be noted in the pathology report.^{24,30,31} This 5% cut-off point is somewhat arbitrary, but acknowledges that higher tertiary pattern 5 volumes are associated with a worse prognosis. Gleason scoring in radical prostatectomy and core needle biopsy specimens is summarised in the WHO Classification of Urinary and Male Genital Tumours, 5th edition (see Table 2).²⁴

At the 2014 ISUP expert consultation meeting on Gleason grading, a grouping of the GS into 5 grade categories was proposed (variously termed Grade groups, ISUP Grade or WHO grade).³⁸ The grade groupings and associated definitions are outlined in Table 2. Over the past decades GS below 6 have become less commonly used. There is also evidence that GS 7 (Grade groups 2 and 3) tumours have a worse outcome if there is a predominant pattern 4 (4+3) than if pattern 3 dominates (3+4). However, more precise quantification of the proportion of Gleason patterns 4 and 5 in radical prostatectomy specimens is currently considered a non-core element since the evidence for its significance is mixed.^{30,31}

Both the GS and the WHO grade/ISUP grade/Grade group must always be reported for the sake of clarity. It should also be stated whether or not any intraductal carcinoma of prostate (IDC-P) component, if present, has been included in the assignment of the tumour grade. If an IDC-P component has not been included in the assessment of prostate carcinoma grade, immunohistochemistry (IHC) may be necessary to differentiate IDC-P from invasive cribriform carcinoma (ICC) and comedocarcinoma.^{24,39,40}

Table 2: Gleason scoring in radical prostatectomy and core needle biopsy specimens.²²

Gleason score	Grade Group	Needle biopsy scoring ^a	Prostatectomy scoring ^b
≤ 3 + 3 = 6	1	Only pattern 3 present	Usually only pattern 3 present Very rarely lower grade patterns seen Minor higher grade pattern (International Society of Urological Pathology (ISUP) only) ^c
3 + 4 = 7	2	2 grade patterns present Most prevalent (primary) 3 Highest grade pattern (secondary) 4	2 or 3 grade patterns present Most prevalent (primary) 3 Second most prevalent (secondary) 4 Can have minor tertiary pattern 5 (≤5% tumour volume) ^d
4 + 3 = 7	3	2 grade patterns present Most prevalent (primary) 4 Highest grade pattern (secondary) 3	2 or 3 grade patterns present Most prevalent (primary) 4 Second most prevalent (secondary) 3 Can have minor tertiary pattern 5 (≤5% tumour volume) ^d
4 + 4 = 8	4	1, 2 or 3 grade patterns present	1, 2 or 3 grade patterns present
3 + 5 = 8		Only pattern 4 present OR Most prevalent (primary) 3 Highest grade pattern (secondary) 5	Pattern 4 ≥95% tumour volume ^e Pattern 3 ignored if third most prevalent or ≤5% tumour OR Most prevalent (primary) 3 Second most prevalent (secondary) 5 OR Most prevalent (primary) 3 Third most prevalent (>5% tumour) 5 OR Most prevalent (primary) 5 Second most prevalent (secondary) 3
5 + 3 = 8		Most prevalent (primary) 5 Highest grade pattern (secondary) 3	
4 + 5 = 9	5	1, 2 or 3 grade patterns present Most prevalent (primary) 4 Highest grade pattern (secondary) 5	1, 2 or 3 grade patterns present Most prevalent (primary) 4 Second most prevalent (secondary) 5 ^c OR Most prevalent (primary) 4 Third most prevalent pattern 5 (>5% tumour) OR Most prevalent (primary) 5 Second most prevalent (secondary) 4
5 + 4 = 9		Most prevalent (primary) 5 Highest grade pattern (secondary) 4	

5 + 5 = 10	OR	Only pattern 5 present	OR	Only pattern 5 present
------------	----	------------------------	----	------------------------

^a For needle core biopsies with multiples specimens there is uncertainty on whether the highest specimen score or the global (overall) Gleason score is superior in predicting the radical prostatectomy score and clinical outcome. ISUP recommends reporting a separate Gleason score for each biopsy site. Global scores should be assigned for each magnetic resonance imaging (MRI)-targeted lesion.^{30,31}

^b Most radical prostatectomy specimens show multifocal carcinoma⁴¹ and ISUP recommends that the Gleason score of the largest, highest grade and highest stage nodules are recorded.

^c ISUP 2019 recommendations would allow assignment of a minor Gleason pattern 4 or 5 in a 3 + 3 = 6 (GG1) carcinoma provided that the pattern 4 or 5 represents ≤5% of the tumour volume. Genitourinary Pathology Society (GUPS) 2020 defines minor tertiary pattern as requiring the presence of 3 different patterns, and confines its use to GG 2 or 3 cancers. Hence, in the GUPS system, a carcinoma with 96% pattern 3 and 4% pattern 4 would be scored as 3 + 4 = 7.

^d Minor tertiary grade patterns should be mentioned in report. However, if tertiary pattern 5 comprises >5% tumour volume it becomes the secondary pattern in the Gleason score (i.e. either 3 + 5 = 8 or 4 + 5 = 9).

^e Can have a minor component of Gleason pattern 5 (≤5% pattern 5 and >95% pattern 4) in a cancer scored as 4 + 4 = 8 (GG4) under ISUP 2019 recommendations. In contrast, according to the GUPS guidelines such a tumour would be scored 4 + 5 = 9 (GG5).

↑ Back

Note 10 – Tumour growth patterns (Core and Non-core)

Presence of either Intraductal carcinoma of the prostate (IDC-P) or Invasive cribriform carcinoma (ICC) (Core)

The presence or absence of either IDC-P or ICC is a core item in pathology reporting since several studies have demonstrated that the presence of cribriform growth patterns has a significant prognostic impact.^{30,31,42-51} However, it is not critically important to distinguish between these entities as there is currently little impact on post-surgical management.

Immunohistochemistry (IHC) may be required to differentiate intraductal cribriform patterns seen in IDC-P from ICC when standard morphological criteria are equivocal.^{42,52,53} Hence, the differentiation between IDC-P and ICC is recommended as a non-core element (see below) to mitigate the risk of overuse of IHC in distinguishing intraductal from ICC.

Intraductal carcinoma of the prostate (IDC-P) (Non-core)

Intraductal carcinoma of the prostate (IDC-P) is found in 15-30% of radical prostatectomy specimens and is usually associated with invasive prostate cancer.⁵⁴ Occasionally isolated IDC-P ('precursor-type' IDC-P) is found without invasive carcinoma; this latter situation is very rare and beyond the scope of this dataset and IDC-P without an associated invasive carcinoma should not be assigned an GS or Grade group.⁵⁵

Intraductal carcinoma of the prostate (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.⁵⁶ In the 5th edition of the WHO Classification of Tumours the essential diagnostic criteria for IDC-P are: 1) expansile epithelial proliferation in the pre-existing duct-acinar system; 2) lumen spanning solid, cribriform and/or comedo

patterns; 3) loose cribriform or micropapillary patterns with enlarged pleomorphic nuclei; and 4) residual basal cells.²⁴ Desirable diagnostic criteria include IHC demonstrating at least partial basal cell retention.

It is important to distinguish IDC-P from high grade prostatic intraepithelial neoplasia (HGPIN). Compared to IDC-P, HGPIN does not have necrosis, marked nuclear pleomorphism or brisk mitotic activity. Cribriform HGPIN is a controversial entity and it has been proposed that such lesions which do not meet the threshold for diagnosis of IDC-P should instead be referred to as 'atypical intraductal proliferation' (AIP) or 'atypical proliferation suspicious for intraductal carcinoma' (ASID).^{24,31,39}

When present in combination with invasive carcinoma in radical prostatectomy specimens, IDC-P is strongly associated with high volume, high grade and stage (extraprostatic extension (EPE) or seminal vesicle invasion (SVI) positive) carcinoma.⁵⁷ Moreover the presence of IDC-P is independently associated with biochemical recurrence, regional lymph node metastasis and cancer specific survival.^{48,49,58} Hence, in radical prostatectomy specimens, the presence of IDC-P in association with invasive carcinoma should be recorded. It is unnecessary to measure the extent of the IDC-P.

Invasive cribriform carcinoma (ICC) (Non-core)

The presence of ICC should be recorded in the pathology report. In 2021, ISUP proposed a consensus definition of cribriform pattern in prostate carcinoma, namely 'A confluent sheet of contiguous malignant epithelial cells with multiple glandular lumina that are easily visible at low power (objective magnification x10).⁵⁹ There should be no intervening stroma or mucin separating individual or fused glandular structures.' Additional criteria have also been proposed based on an interobserver reproducibility study among urological pathologists which found that transluminal bridging and a clear luminal space along the periphery of gland occupying <50% of gland circumference were reliable diagnostic features of cribriform adenocarcinoma.⁶⁰

Several studies in radical prostatectomy specimens have shown that the presence of cribriform pattern 4 carcinoma in GS 7, 8 and 9 (WHO/ISUP grades or Grade groups 2-5) tumours confers a worse prognosis, including biochemical-free, metastasis-free and disease specific survival.^{30,31,39,44-47,61-63} Differentiating between large and small cribriform glands is not currently recommended due to the varying definitions used and findings in the published studies.

 [Back](#)

Note 11 – Tumour quantification (Non-core)

Some measurement of the size or extent of the tumour forms part of the generic ICCR dataset for all tumour types. However in prostate, while cancer volume is a prognostic factor on univariate analysis, it is significantly correlated with other clinicopathological features, including GS, EPE, surgical margin status and pathological TNM stage, and the majority of studies have not demonstrated independent prognostic significance on multivariate analysis.⁶⁴⁻⁶⁹ Hence, the DAC regarded this element as non-core.

The irregular distribution and often multifocal nature of prostate cancer makes accurate calculation of tumour volume challenging for the pathologist in routine diagnostic practice; a situation where precise methods, such as computerised planimetry or image analysis, are too time and labour intensive to be practical. However, there was consensus at the 2009 ISUP Consensus Conference that some quantitative measure of the extent of the tumour in a prostatectomy specimen should be recorded. This can be done either as a visual estimate of intraglandular percentage of cancer,^{70,71} or by measuring the maximum size of dominant tumour nodule.^{72,73} The latter has been shown to correlate with tumour volume and has also been recommended as a readily assessed surrogate for tumour volume in some studies and protocols.^{69,72,73} In the

future more widespread utilisation of artificial intelligence based methods may make precise tumour quantification more feasible in routine practice.

↑ Back

Note 12 – Extraprostatic extension (Core)

Extraprostatic extension (EPE), defined as the extension of tumour beyond the confines of the gland into the periprostatic soft tissue, is a core element as it is a significant predictor of recurrence in node negative patients.^{64,74} EPE replaced earlier, less clearly defined terms such as capsular penetration, perforation or invasion, following a 1996 Consensus Conference.⁷⁵

The assessment of EPE can be difficult, as the prostate is not surrounded by a discrete, well defined fibrous capsule,⁷⁶ but rather by a band of concentrically placed fibromuscular tissue that is an inseparable component of the prostatic stroma.⁷⁷ EPE can be recognised in several different settings: 1) the presence of neoplastic glands abutting on or within periprostatic fat or beyond the adjacent fat plane in situations where no fat is present in the immediate area of interest (most useful at the lateral, posterolateral and posterior aspects of the prostate); 2) neoplastic glands surrounding nerves in the neurovascular bundle (posterolaterally) beyond the boundary of the normal prostatic glandular tissue; and 3) the presence of a nodular extension of tumour bulging beyond the periphery of the prostate or beyond the compressed fibromuscular prostatic stroma at the outer edge of the gland—since there is often a desmoplastic reaction in the vicinity of EPE and the neoplastic extraprostatic glands may then be seen in fibrous tissue, rather than in fat.^{77,78} Extraprostatic tumour in fibrous tissue is best identified initially at low power magnification, but should be then confirmed by high power magnification examination verifying that the neoplastic glands are in stroma that is fibrous and beyond the condensed smooth muscle of the prostate.^{64,78} The presence of cancer within fibrous stroma that is in the same tissue plane as adipose tissue on either side is a helpful indicator of EPE.

The boundary of the prostate gland cannot be readily identified anteriorly and at the base or apex of the prostate. Moreover, at the apex benign glands are frequently admixed with skeletal muscle and the presence of neoplastic glands within skeletal muscle does not necessarily constitute EPE. Hence, in this region it is more important to accurately assess the completeness of surgical resection. Similarly, the assessment of EPE at the anterior aspect of the prostate may be difficult as the prostatic stroma blends in with extraprostatic fibromuscular tissue, but in this location EPE can be diagnosed (in the manner described in the previous paragraph) when the carcinoma appears to bulge beyond the boundary of the normal prostate gland.^{78,79}

Extent of EPE

Categorisation of the extent of EPE as focal or non-focal (also referred to as ‘extensive’ or ‘established’) is a core item. Focal EPE was originally defined as no more than ‘a few’ neoplastic glands just outside the prostate which is now interpreted in a more semi-quantified manner as extraprostatic glands which occupy no more than one high power field (HPF) in no more than two sections, with extensive EPE representing anything more than this.⁶⁴ More rigorous quantification of the extent of EPE by measuring the maximum distance that the tumour bulges beyond the outer edge of the fibromuscular prostatic stroma radially has been proposed by some investigators.⁸⁰ However, the practical value of such parameters is limited by the difficulty in precisely defining the outer limit of the prostate gland, especially when the tumour is associated with a desmoplastic reaction.

The identification of EPE is important, as both focal and non-focal EPE are associated with a significantly higher risk of recurrence, with non-focal EPE demonstrating higher rates of biochemical recurrence (BCR) and also an association with lymph node metastasis.^{64,74,81-83}

Location of EPE

Since it was considered a generic element forming part of a comprehensive pathology report, the location of any EPE has been included as a non-core item based on the consensus of the DAC, despite the lack of published evidence for its influence on staging, prognosis or treatment.⁷⁸ It provides potentially useful information to the urologist, enabling correlation with clinical findings and any pre-operative imaging studies performed.

 [Back](#)

Note 13 – Urinary bladder neck invasion (Core)

Microscopic invasion of the urinary bladder neck can be identified when there are neoplastic glands within the thick smooth muscle bundles of the bladder neck in sections from the base of the prostate in the absence of associated benign prostatic glandular tissue.⁸⁴ Microscopic bladder neck involvement is a significant predictor of PSA-recurrence in univariate analysis, although not in multivariate modelling in most studies.⁸⁵⁻⁸⁷ Neoplastic glands intermixed with benign prostatic glands at the bladder neck margin is equivalent to capsular incision (CI) rather than true bladder neck invasion.^{85,88,89} In the 8th editions of the Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC) Cancer Staging Manual microscopic bladder neck invasion is classified as stage pT3a disease since it has a similar biochemical recurrence-free survival and cancer specific survival to patients with SVI or EPE.^{90,91} Macroscopic invasion of the bladder wall is categorised as pT4.

 [Back](#)

Note 14 – Margin status (Core and Non-core)

A positive surgical margin (PSM) is regarded as a core element since it significantly reduces the likelihood of progression-free survival, including PSA recurrence-free survival, local recurrence-free survival and development of metastases after radical prostatectomy in some multivariate analyses.^{79,92-96} In some studies positive margins are associated with an increased risk of prostate cancer specific mortality.⁹⁷⁻⁹⁹ Careful inking of the outer surface of the radical prostatectomy specimen before macroscopic dissection (grossing) greatly facilitates the determination of margin status. A PSM can then be defined as cancer extending to the inked surface of the specimen, representing a site where the urologist has cut through cancer.^{79,100}

The presence of prostate carcinoma close to, but not touching the inked margin should not be labelled as a PSM as this finding has been shown to have little, if any, prognostic significance.¹⁰¹⁻¹⁰⁴ Close surgical margins are most commonly seen posterolaterally in cases where neurovascular bundle preservation leaves virtually no extraprostatic tissue. Studies on such nerve sparing cases have shown that additional tissue removed from these sites did not contain any carcinoma and a close margin was not associated with a worse prognosis.^{101,103}

Stating the location of the PSM is useful information for the urologist. The site of the PSM and the number of positive margins have been shown to influence biochemical recurrence and risk of progression. For instance,

a margin involving the bladder neck or the posterolateral surface of the prostate has a more significant adverse impact on prognosis than an involved apical or anterior margin.^{105,106}

Type of margin positivity

The type of margin positivity is regarded as a non-core item. Intraprostatic margin involvement or CI occurs when the urologist inadvertently develops the resection margin within the plane of the prostate rather than outside the capsule. CI with a PSM is diagnosed when malignant glands are cut across adjacent to benign prostatic glands.⁷⁷ In these cases, the edge of the prostate in this region is left in the patient. Data on the prognostic significance of CI vary among studies.¹⁰⁷⁻¹⁰⁹ In one large series, a significantly higher recurrence rate is found in patients with CI/intraprostatic margin involvement than in patients with organ confined disease with negative margins, or focal EPE with negative margins, although CI has a significantly better outcome than that associated with non-focal EPE and positive margins.¹¹⁰

Margin involvement associated with EPE is diagnosed when malignant glands in extraprostatic tissue are transected by the resection margin. This can be difficult to distinguish from CI in some cases, particularly posteriorly and posterolaterally if there is a desmoplastic reaction. Cancer extending to a margin which is beyond the normal contour of the prostate gland, or beyond the compressed fibromuscular prostatic stroma at the outer edge of the prostate, can be diagnosed as a PSM with EPE, similarly to margin involvement when there is cancer in adipose tissue.¹⁰⁸ At the apex, the histological boundaries of the prostate gland can be difficult to define and again EPE with a positive margin can be difficult to differentiate from CI/intraprostatic margin involvement. Hence, if carcinoma extends to an inked margin at the apex where benign glands are not transected, this is considered a positive margin in an area of EPE by some authors.^{79,108} In contrast, other authors, and the majority of survey participants at the 2009 ISUP Consensus Conference, believe there is no reliable method to diagnose EPE in sections from the prostatic apex.⁷⁸

Extent (total) of margin involvement

Although a PSM has a significant adverse impact on the overall likelihood of progression-free survival, in most published series only about a third of individual patients with a PSM will experience biochemical recurrence.^{92,93,111,112} The DAC considered that there is sufficient evidence to include measurement of the length of margin involved by carcinoma as an element in the dataset (as non-core).^{101,103,110,112-118} However, in one series, Cao et al (2011)¹¹⁵ found that the linear length of a positive margin was an independent prognostic factor for organ confined tumours only, i.e., pT2 not pT3, while, another investigation found that the impact of a PSM after radical prostatectomy was greater in intermediate and high risk groups (based on GS and pre-biopsy PSA) than in low risk patients.⁹⁵ Further studies of such factors potentially affecting the impact of PSMs are required before there is sufficient evidence justifying their inclusion as core data elements. The optimal method of assessing the extent of margin involvement when multiple positive margins are present is currently uncertain, but, until more evidence is available, it is suggested that extent is measured as the linear cumulative length of all positive margins.¹¹⁹

Gleason pattern at the margin

Gleason pattern at the surgical margin is classified as a non-core item since some studies have found that Gleason pattern or score of the tumour at the PSM is an independent predictor of biochemical recurrence and may aid optimal selection of patients for adjuvant therapy.^{112,120-126} In one of these studies patients with Gleason pattern 4 or 5 carcinoma (GS 3+4, 4+3, 4+4 or 4+5) at a PSM had double the risk of PSA relapse compared to those with only Gleason pattern 3 (score 3+3) at the margin. Moreover, men with Gleason pattern 3 at the PSM had a similar 5 year biochemical relapse-free survival rate to those with negative margins.¹¹² Another study, restricted to men with dominant nodule GS 7 and non-focal EPE, also found that the grade of cancer at the site of a PSM was associated with biochemical recurrence.¹²⁰ A meta-analysis of 10 eligible studies also demonstrated that GS, primary Gleason pattern and Grade Group at the PSM were significantly associated with increased risk of BCR.¹²³

In these studies, the potential problem of cautery/thermal artefact was considered - in slides where the cancer at the margin was distorted by cautery/thermal or crush artifact and could not be reliably assessed, the margin pattern, or score, was designated as that of the closest, well preserved carcinoma in direct continuity with the distorted neoplastic glands.^{112,120-122} Limiting assessment to only the highest pattern present at the PSM may simplify measurement of this parameter,¹²⁴ however, it should be noted that in most of the published studies GS could be reported.¹²⁰⁻¹²² In the event there are multiple positive margins with differently scored cancers present, the highest pattern or score should be recorded.

 **Back**

Note 15 – Seminal vesicle invasion (Core)

The DAC included SVI as a core element as SVI is a well-established, independent, adverse prognostic factor,^{79,127,128} is required for staging, and constitutes an integral component of the commonly used nomograms and tables that predict risk of post prostatectomy cancer recurrence.¹⁶⁻¹⁸ The finding of SVI at the time of radical prostatectomy is associated with a significantly increased risk of PSA recurrence,¹²⁷⁻¹²⁹ and the presence of SVI and a PSM may also influence the response to adjuvant radiotherapy.^{130,131} Bilaterality and extent of extraprostatic SVI are not independently predictive of prognosis and were not included in the ICCR dataset.¹¹³

Different definitions of SVI complicate comparison of the published survival analyses.^{130,132} Older definitions including involvement of the adipose tissue or adventitia around the seminal vesicle are problematic with regard to distinction from EPE. In other studies a distinction between intraprostatic and extraprostatic SVI has not always been made, impeding comparisons between series.^{133,134} At the 2009 ISUP meeting, the proposal that SVI should be defined as carcinomatous invasion of the muscular wall of the seminal vesicle exterior to the prostate was endorsed.¹³² Only extraprostatic seminal vesicle is included in this definition of SVI, since it is difficult to differentiate between intraprostatic seminal vesicle and ejaculatory duct invasion as these structures merge without a clear histological cut off.¹³⁵ It was concluded that older definitions that include invasion of the adipose tissue around the seminal vesicle are imprecise and should be discarded.^{130,132}

 **Back**

Note 16 – Lymphovascular invasion (Core)

Lymphovascular invasion (LVI) is defined as the unequivocal presence of tumour cells within endothelial-lined spaces with no or only thin underlying muscular walls.^{136,137} Lymphatic and venous invasion should be assessed together due to the difficulties in distinguishing between the two by routine light microscopy and it is important that artefacts, such as retraction or mechanical displacement of tumour cells into vessels, are excluded. IHC for endothelial markers, e.g., CD31, CD34 or D2-40, may aid in the assessment of equivocal cases but is not recommended for routine use at present.

Lymphovascular invasion (LVI) has been reported to be associated with decreased time to biochemical progression, distant metastases and overall survival after radical prostatectomy.¹³⁶⁻¹⁴⁴ Multivariate analysis, controlling for other pathological variables known to affect clinical outcome, showed that LVI is an independent predictor of disease recurrence in some studies.^{136,137,139,141-145}

 **Back**

Note 17 – Lymph node status (Core and Non-core)

Lymph node involvement is a well-established independent adverse prognostic factor,^{79,132} and is an integral component of the commonly used nomograms that predict the risk of post prostatectomy disease recurrence.¹⁶ Stating the number of examined lymph nodes and the number of involved nodes is a useful quality indicator for urologists and pathologists.

There is little published data on the prognostic significance of isolated tumour cells (clusters less than <200 micrometre (µm) in greatest dimension) in prostate cancer and insufficient evidence at present to support the routine use of IHC as an ancillary technique in the identification of lymph node involvement.

Maximum dimension of largest deposit

As the diameter of the largest metastatic deposit correlated with distant metastasis and cancer-specific survival in two studies but not in another,¹⁴⁶⁻¹⁴⁸ maximum dimension of largest deposit has been included as a non-core item rather than as a core item. There was consensus (81% of respondents) at the 2009 ISUP Consensus Conference that that the diameter of the largest lymph node metastasis should be included in the pathology reports on radical prostatectomy specimens.¹³²

↑ Back

Note 18 – Pathological staging (Core and Non-core)

Staging data must be assessed according to either the 8th editions of the UICC or AJCC Staging Manuals.^{90,91}

It should also be noted that that the UICC 8th edition Stage Grouping differs from the AJCC 8th edition Prognostic Stage Groups.^{90,91}

Reporting of pathological staging categories (pT,pN,pM) is based on the evidence available to the pathologist at the time of reporting. As indicated in UICC/AJCC TNM8,^{90,91} the final stage grouping of a patient's tumour is based on a combination of pathological staging and other clinical and imaging information.

The reference document TNM Supplement: A commentary on uniform use, 5th edition (C Wittekind et al. editors) may be of assistance when staging.¹⁴⁹

↑ Back

References

- 1 Merlin T, Weston A and Tooher R (2009). Extending an evidence hierarchy to include topics other than treatment: revising the Australian 'levels of evidence'. *BMC Med Res Methodol* 9:34.
- 2 International Collaboration on Cancer Reporting (2024). *Prostate Core Needle Biopsy Histopathology Reporting Guide. 2nd edition*. Available from: <https://www.iccr-cancer.org/datasets/published-datasets/urinary-male-genital/prostate-biopsy-page-2/> (Accessed TBC 2024).
- 3 International Collaboration on Cancer Reporting (2024). *Prostate Cancer, Transurethral Resection and Enucleation Histopathology Reporting Guide. 2nd edition*. Available from: <https://www.iccr-cancer.org/datasets/published-datasets/urinary-male-genital/prostate-tr/> (Accessed TBC 2024).

- 4 International Collaboration on Cancer Reporting (2024). *Carcinoma of the urethra - urethrectomy specimen Histopathology Reporting Guide. 2nd edition*. Available from: <https://www.iccr-cancer.org/datasets/published-datasets/urinary-male-genital/urethra-urethrectomy/> (Accessed TBC 2024).
- 5 WHO Classification of Tumours Editorial Board (2022). *Urinary and Male Genital Tumours, WHO Classification of Tumours, 5th edition, Volume 8*, IARC Publications, Lyon.
- 6 WHO Classification of Tumours Editorial Board (2022). *Urinary and Male Genital Tumours, WHO Classification of Tumours, 5th edition, Volume 8 - Corrigenda November 2022*. Available from: <https://publications.iarc.fr/Book-And-Report-Series/Who-Classification-Of-Tumours/Urinary-And-Male-Genital-Tumours-2022> (Accessed 2nd April 2024).
- 7 Cheng L, Cheville JC and Bostwick DG (1999). Diagnosis of prostate cancer in needle biopsies after radiation therapy. *Am J Surg Pathol* 23(10):1173-1183.
- 8 Magi-Galluzzi C, Sanderson HBS and Epstein JI (2003). Atypia in non-neoplastic prostate glands after radiotherapy for prostate cancer: duration of atypia and relation to type of radiotherapy. *Am J Surg Pathol* 27:206-212.
- 9 Herr HW and Whitmore WF, Jr (1982). Significance of prostatic biopsies after radiation therapy for carcinoma of the prostate. *Prostate* 3(4):339-350.
- 10 Grignon DJ and Sakr WA (1995). Histologic effects of radiation therapy and total androgen blockage on prostate cancer. *Cancer* 75:183-1841.
- 11 Vailancourt L, Ttu B, Fradet Y, Dupont A, Gomez J, Cusan L, Suburu ER, Diamond P, Candas B and Labrie F (1996). Effect of neoadjuvant endocrine therapy (combined androgen blockade) on normal prostate and prostatic carcinoma. A randomized study. *Am J Surg Pathol* 20(1):86-93.
- 12 Montironi R, Magi-Galluzzi C, Muzzonigro G, Prete E, Polito M and Fabris G (1994). Effects of combination endocrine treatment on normal prostate, prostatic intraepithelial neoplasia, and prostatic adenocarcinoma. *J Clin Pathol* 47(10):906-913.
- 13 Civantos F, Marcial MA, Banks ER, Ho CK, Speights VO, Drew PA, Murphy WM and Soloway MS (1995). Pathology of androgen deprivation therapy in prostate carcinoma. A comparative study of 173 patients. *Cancer* 75(7):1634-1641.
- 14 Bostwick DG and Meiers I (2007). Diagnosis of prostatic carcinoma after therapy. *Arch Pathol Lab Med* 131(3):360-371.
- 15 Epstein JI and Yang XJ (2002). Benign and malignant prostate following treatment. In: *Prostate Biopsy Interpretation*, Lippincott Williams and Wilkins, Philadelphia, Pennsylvania, 209-225.
- 16 Kattan MW, Wheeler TM and Scardino PT (1999). Postoperative nomogram for disease recurrence after radical prostatectomy for prostate cancer. *J Clin Oncol* 17(5):1499-1507.
- 17 Partin AW, Piantadosi S, Sanda MG, Epstein JI, Marshall FF, Mohler JL, Brendler CB, Walsh PC and Simons JW (1995). Selection of men at high risk for disease recurrence for experimental adjuvant therapy following radical prostatectomy. *Urology* 45(5):831-838.

- 18 Han M, Partin AW, Zahurak M, Piantadosi S, Epstein JI and Walsh PC (2003). Biochemical (prostate specific antigen) recurrence probability following radical prostatectomy for clinically localised prostate cancer. *J Urol* 169:517-523.
- 19 Guess HA, Gormley GJ, Stoner E and Oesterling JE (1996). The effect of finasteride on prostate specific antigen: review of available data. *J Urol* 155(1):3-9.
- 20 Oesterling JE, Roy J, Agha A, Shown T, Krarup T, Johansen T, Lagerkvist M, Gormley G, Bach M and Waldstreicher J (1997). Biologic variability of prostate-specific antigen and its usefulness as a marker for prostate cancer: effects of finasteride. The Finasteride PSA Study Group. *Urology* 50(1):13-18.
- 21 Marberger M, Freedland SJ, Andriole GL, Emberton M, Pettaway C, Montorsi F, Teloken C, Rittmaster RS, Somerville MC and Castro R (2012). Usefulness of prostate-specific antigen (PSA) rise as a marker of prostate cancer in men treated with dutasteride: lessons from the REDUCE study. *BJU Int* 109(8):1162-1169.
- 22 Andriole GL, Humphrey P, Ray P, Gleave ME, Trachtenberg J, Thomas LN, Lazier CB and Rittmaster RS (2004). Effect of the dual 5alpha-reductase inhibitor dutasteride on markers of tumor regression in prostate cancer. *J Urol* 172(3):915-919.
- 23 Samaratunga H, Montironi R, True L, Epstein JI, Griffiths DF, Humphrey PA, van der Kwast T, Wheeler TM, Srigley JR, Delahunt B, Egevad L and The ISUP Prostate Cancer Group (2011). International Society of Urological Pathology (ISUP) consensus conference on handling and staging of radical prostatectomy specimens. Working group 1: specimen handling. *Mod Pathol* 24:6-15.
- 24 Kench JG, Berney DM, De Marzo A, et al. Prostatic acinar adenocarcinoma. In: *Urinary and Male Genital Tumours, WHO Classification of Tumours, 5th edition, Volume 8*, IARC Publications, Lyon; 2022; 203-219.
- 25 Christensen WN, Steinberg G, Walsh PC and Epstein JI (1991). Prostatic duct adenocarcinoma. Findings at radical prostatectomy. *Cancer* 67:2118-2124.
- 26 Dundore PA, Cheville JC, Nascimento AG, Farrow GM and Bostwick DG (1995). Carcinosarcoma of the prostate. Report of 21 cases. *Cancer* 76:1035-1042.
- 27 Hansel DE and Epstein JI (2006). Sarcomatoid carcinoma of the prostate. A study of 42 cases. *Am J Surg Pathol* 30:1316-1321.
- 28 Alharbi AM, De Marzo AM, Hicks JL, Lotan TL and Epstein JI (2018). Prostatic Adenocarcinoma With Focal Pleomorphic Giant Cell Features: A Series of 30 Cases. *Am J Surg Pathol* 42(10):1286-1296.
- 29 Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM and Whelan S (eds) (2020). *International Classification of Diseases for Oncology, Third edition, Second revision ICD-O-3.2*. Available from: http://www.iacr.com/fr/index.php?option=com_content&view=category&layout=blog&id=100&Itemid=577 (Accessed 16th December 2023).

- 30 van Leenders G, van der Kwast TH, Grignon DJ, Evans AJ, Kristiansen G, Kweldam CF, Litjens G, McKenney JK, Melamed J, Mottet N, Paner GP, Samaratunga H, Schoots IG, Simko JP, Tsuzuki T, Varma M, Warren AY, Wheeler TM, Williamson SR and Iczkowski KA (2020). The 2019 International Society of Urological Pathology (ISUP) Consensus Conference on Grading of Prostatic Carcinoma. *Am J Surg Pathol* 44(8):e87-e99.
- 31 Epstein JI, Amin MB, Fine SW, Algaba F, Aron M, Baydar DE, Beltran AL, Brimo F, Cheville JC, Coicchia M, Comperat E, da Cunha IW, Delprado W, DeMarzo AM, Giannico GA, Gordetsky JB, Guo CC, Hansel DE, Hirsch MS, Huang J, Humphrey PA, Jimenez RE, Khani F, Kong Q, Kryvenko ON, Kunju LP, Lal P, Latour M, Lotan T, Maclean F, Magi-Galluzzi C, Mehra R, Menon S, Miyamoto H, Montironi R, Netto GJ, Nguyen JK, Osunkoya AO, Parwani A, Robinson BD, Rubin MA, Shah RB, So JS, Takahashi H, Tavora F, Tretiakova MS, True L, Wobker SE, Yang XJ, Zhou M, Zynger DL and Trpkov K (2021). The 2019 Genitourinary Pathology Society (GUPS) White Paper on Contemporary Grading of Prostate Cancer. *Arch Pathol Lab Med* 145(4):461-493.
- 32 Berney DM, Beltran L, Fisher G, North BV, Greenberg D, Møller H, Soosay G, Scardino P and Cuzick J (2016). Validation of a contemporary prostate cancer grading system using prostate cancer death as outcome. *Br J Cancer* 114(10):1078-1083.
- 33 Grogan J, Gupta R, Mahon KL, Stricker PD, Haynes AM, Delprado W, Turner J, Horvath LG and Kench JG (2017). Predictive value of the 2014 International Society of Urological Pathology grading system for prostate cancer in patients undergoing radical prostatectomy with long-term follow-up. *BJU Int* 120(5):651-658.
- 34 Epstein JI, Zelefsky MJ, Sjoberg DD, Nelson JB, Egevad L, Magi-Galluzzi C, Vickers AJ, Parwani AV, Reuter VE, Fine SW, Eastham JA, Wiklund P, Han M, Reddy CA, Ciezki JP, Nyberg T and Klein EA (2016). A Contemporary Prostate Cancer Grading System: A Validated Alternative to the Gleason Score. *Eur Urol* 69(3):428-435.
- 35 Delahunt B, Egevad L, Srigley JR, Steigler A, Murray JD, Atkinson C, Matthews J, Duchesne G, Spry NA, Christie D, Joseph D, Attia J and Denham JW (2015). Validation of International Society of Urological Pathology (ISUP) grading for prostatic adenocarcinoma in thin core biopsies using TROG 03.04 'RADAR' trial clinical data. *Pathology* 47(6):520-525.
- 36 Epstein JI, Allsbrook WCJ, Amin MB and Egevad LL (2005). The 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma. *Am J Surg Pathol* 29(9):1228-1242.
- 37 Huang CC, Deng FM, Kong MX, Ren Q, Melamed J and Zhou M (2014). Re-evaluating the concept of "dominant/index tumor nodule" in multifocal prostate cancer. *Virchows Arch* 464(5):589-594.
- 38 Epstein JI, Egevad L, Amin MB, Delahunt B, Srigley JR and Humphrey PA (2016). The 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma: Definition of Grading Patterns and Proposal for a New Grading System. *Am J Surg Pathol* 40(2):244-252.
- 39 Kench JG, Amin MB, Berney DM, Compérat EM, Cree IA, Gill AJ, Hartmann A, Menon S, Moch H, Netto GJ, Raspollini MR, Rubin MA, Tan PH, Tsuzuki T, Turjalic S, van der Kwast TH, Zhou M and Srigley JR (2022). WHO Classification of Tumours fifth edition: evolving issues in the classification, diagnosis, and prognostication of prostate cancer. *Histopathology* 81(4):447-458.

- 40 Varma M and Epstein JI (2021). Head to head: should the intraductal component of invasive prostate cancer be graded? *Histopathology* 78(2):231-239.
- 41 Wise AM, Stamey TA, McNeal JE and Clayton JL (2002). Morphologic and clinical significance of multifocal prostate cancers in radical prostatectomy specimens. *Urology* 60(2):264-269.
- 42 Hollemans E, Verhoef EI, Bangma CH, Rietbergen J, Roobol MJ, Helleman J and van Leenders G (2020). Clinical outcome comparison of Grade Group 1 and Grade Group 2 prostate cancer with and without cribriform architecture at the time of radical prostatectomy. *Histopathology* 76(5):755-762.
- 43 Hollemans E, Verhoef EI, Bangma CH, Rietbergen J, Osanto S, Pelger RCM, van Wezel T, van der Poel H, Bekers E, Helleman J, Roobol MJ and van Leenders G (2021). Cribriform architecture in radical prostatectomies predicts oncological outcome in Gleason score 8 prostate cancer patients. *Mod Pathol* 34(1):184-193.
- 44 Iczkowski KA, Torkko KC, Kotnis GR, Wilson RS, Huang W, Wheeler TM, Abeyta AM, La Rosa FG, Cook S, Werahera PN and Lucia MS (2011). Digital quantification of five high-grade prostate cancer patterns, including the cribriform pattern, and their association with adverse outcome. *Am J Clin Pathol* 136(1):98-107.
- 45 Trudel D, Downes MR, Sykes J, Kron KJ, Trachtenberg J and van der Kwast TH (2014). Prognostic impact of intraductal carcinoma and large cribriform carcinoma architecture after prostatectomy in a contemporary cohort. *Eur J Cancer* 50(9):1610-1616.
- 46 Hollemans E, Verhoef EI, Bangma CH, Rietbergen J, Helleman J, Roobol MJ and van Leenders G (2019). Large cribriform growth pattern identifies ISUP grade 2 prostate cancer at high risk for recurrence and metastasis. *Mod Pathol* 32(1):139-146.
- 47 Kweldam CF, Wildhagen MF, Steyerberg EW, Bangma CH, van der Kwast TH and van Leenders GJ (2015). Cribriform growth is highly predictive for postoperative metastasis and disease-specific death in Gleason score 7 prostate cancer. *Mod Pathol* 28(3):457-464.
- 48 Kimura K, Tsuzuki T, Kato M, Saito AM, Sassa N, Ishida R, Hirabayashi H, Yoshino Y, Hattori R and Gotoh M (2014). Prognostic value of intraductal carcinoma of the prostate in radical prostatectomy specimens. *Prostate* 74(6):680-687.
- 49 Kryvenko ON, Gupta NS, Virani N, Schultz D, Gomez J, Amin A, Lane Z and Epstein JI (2013). Gleason score 7 adenocarcinoma of the prostate with lymph node metastases: analysis of 184 radical prostatectomy specimens. *Arch Pathol Lab Med* 137(5):610-617.
- 50 Downes MR, Liu KN, Yu Y, Lajkosz K, Kroon LJ, Hollemans E, Fleshner N, Finelli A, van Leenders G, Iczkowski KA and van der Kwast TH (2024). Addition of Cribriform and Intraductal Carcinoma Presence to Prostate Biopsy Reporting Strengthens Pretreatment Risk Stratification Using CAPRA and NCCN Tools. *Clin Genitourin Cancer* 22(1):47-55.

- 51 Marra G, van Leenders G, Zattoni F, Kesch C, Rajwa P, Cornford P, van der Kwast T, van den Bergh RCN, Briers E, Van den Broeck T, De Meerleer G, De Santis M, Eberli D, Farolfi A, Gillessen S, Grivas N, Grummet JP, Henry AM, Lardas M, Lieuw M, Linares Espinós E, Mason MD, O'Hanlon S, van Oort IM, Oprea-Lager DE, Ploussard G, Rouvière O, Schoots IG, Stranne J, Tilki D, Wiegel T, Willemse PM, Mottet N and Gandaglia G (2023). Impact of Epithelial Histological Types, Subtypes, and Growth Patterns on Oncological Outcomes for Patients with Nonmetastatic Prostate Cancer Treated with Curative Intent: A Systematic Review. *Eur Urol* 84(1):65-85.
- 52 Wobker SE and Epstein JI (2016). Differential Diagnosis of Intraductal Lesions of the Prostate. *Am J Surg Pathol* 40(6):e67-82.
- 53 Iczkowski KA, Egevad L, Ma J, Harding-Jackson N, Algaba F, Billis A, Camparo P, Cheng L, Clouston D, Comperat EM, Datta MW, Evans AG, Griffiths DF, Guo CC, Hailemariam S, Huang W, Humphrey PA, Jiang Z, Kahane H, Kristiansen G, La Rosa FG, Lopez-Beltran A, MacLennan GT, Magi-Galluzzi C, Merrimen J, Montironi R, Osunkoya AO, Picken MM, Rao N, Shah RB, Shanks JH, Shen SS, Tawfik OW, True LD, Van der Kwast T, Varma M, Wheeler TM, Zynger DL, Sahr N and Bostwick DG (2014). Intraductal carcinoma of the prostate: interobserver reproducibility survey of 39 urologic pathologists. *Ann Diagn Pathol* 18(6):333-342.
- 54 Zhou M EL, Fine SW, et al. (2022). Intraductal carcinoma of the prostate. In: *Urinary and Male Genital Tumours, WHO Classification of Tumours, 5th edition, Volume 8*, IARC Publications, Lyon; 2022; 200-202.
- 55 Epstein JI, Egevad L, Amin MB, Delahunt B, Srigley JR and Humphrey PA (2015). The 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma: Definition of Grading Patterns and Proposal for a New Grading System. *Am J Surg Pathol* 40(2):244-52.
- 56 Zhou M (2013). Intraductal carcinoma of the prostate: the whole story. *Pathology* 45(6):533-539.
- 57 McNeal JE and Yemoto CE (1996). Spread of adenocarcinoma within prostatic ducts and acini. Morphologic and clinical correlations. *Am J Surg Pathol* 20(7):802-814.
- 58 Miyai K, Divatia MK, Shen SS, Miles BJ, Ayala AG and Ro JY (2014). Heterogeneous clinicopathological features of intraductal carcinoma of the prostate: a comparison between "precursor-like" and "regular type" lesions. *Int J Clin Exp Pathol* 7(5):2518-2526.
- 59 van der Kwast TH, van Leenders GJ, Berney DM, Delahunt B, Evans AJ, Iczkowski KA, McKenney JK, Ro JY, Samaratunga H, Srigley JR, Tsuzuki T, Varma M, Wheeler TM and Egevad L (2021). ISUP Consensus Definition of Cribriform Pattern Prostate Cancer. *Am J Surg Pathol* 45(8):1118-1126.
- 60 Shah RB, Cai Q, Aron M, Berney DM, Cheville JC, Deng FM, Epstein J, Fine SW, Genega EM, Hirsch MS, Humphrey PA, Gordetsky J, Kristiansen G, Kunju LP, Magi-Galluzzi C, Gupta N, Netto GJ, Osunkoya AO, Robinson BD, Trpkov K, True LD, Troncoso P, Varma M, Wheeler T, Williamson SR, Wu A and Zhou M (2021). Diagnosis of "cribriform" prostatic adenocarcinoma: an interobserver reproducibility study among urologic pathologists with recommendations. *Am J Cancer Res* 11(8):3990-4001.
- 61 Oufattole J, Dey T, D'Amico AV, van Leenders G and Acosta AM (2023). Cribriform morphology is associated with higher risk of biochemical recurrence after radical prostatectomy in patients with Grade Group 5 prostate cancer. *Histopathology* 82(7):1089-1097.

- 62 Kweldam CF, Kümmerlin IP, Nieboer D, Verhoef EI, Steyerberg EW, van der Kwast TH, Roobol MJ and van Leenders GJ (2016). Disease-specific survival of patients with invasive cribriform and intraductal prostate cancer at diagnostic biopsy. *Mod Pathol* 29(6):630-636.
- 63 Kweldam CF, Kümmerlin IP, Nieboer D, Verhoef EI, Steyerberg EW, Incrocci L, Bangma CH, van der Kwast TH, Roobol MJ and van Leenders GJ (2016). Prostate cancer outcomes of men with biopsy Gleason score 6 and 7 without cribriform or intraductal carcinoma. *Eur J Cancer* 66:26-33.
- 64 Wheeler TM, Dilliogluligil O, Kattan MW, Arakawa A, Soh S, Suyama K, Ohori M and Scardino PT (1998). Clinical and pathological significance of the level and extent of capsular invasion in clinical stage T1-2 prostate cancer. *Hum Pathol* 29(8):856-862.
- 65 Epstein JI, Carmichael M, Partin AW and Walsh PC (1993). Is tumor volume an independent predictor of progression following radical prostatectomy? A multivariate analysis of 185 clinical stage B adenocarcinomas of the prostate with 5 years of followup. *J Urol* 149(6):1478-1481.
- 66 Kikuchi E, Scardino PT, Wheeler TM, Slawin KM and Ohori M (2004). Is tumor volume an independent prognostic factor in clinically localized prostate cancer? *J Urol* 172:508-511.
- 67 Van Oort IM, Witjes JA, Kok DE, Kiemeny LALM and Hulsbergen-vandeKaa CA (2008). Maximum tumor diameter is not an independent prognostic factor in high-risk localised prostate cancer. *World J Urol* 26:237-241.
- 68 Wolters T, Roobol MJ, van Leeuwen PJ, van den Bergh RC, Hoedemaeker RF, van Leenders GJ, Schröder FH and van der Kwast TH (2010). Should pathologist routinely report prostate tumor volume? The prognostic value of tumor volume in prostate cancer. *Eur Urol* 57(5):735-920.
- 69 Dvorak T, Chen MH, Renshaw AA, Loffredo M, Richie JP and D'Amico AV (2005). Maximal tumor diameter and the risk of PSA failure in men with specimen-confined prostate cancer. *Urology* 66:1024-1028.
- 70 Epstein JI, Oesterling JE and Walsh PC (1988). Tumor volume versus percentage of specimen involved by tumor correlated with progression in stage A prostatic cancer. *J Urol* 139:980-984.
- 71 Partin AW, Epstein JI, Cho KR, Gittelsohn AM and Walsh PC (1989). Morphometric measurement of tumor volume and per cent of gland involvement as predictors of pathological stage in clinical stage B prostate cancer. *J Urol* 141:341-345.
- 72 Wise AM, Stamey TA, McNeal JE and Clayton JL (2002). Morphologic and clinical significance of multifocal prostate cancers in radical prostatectomy specimens. *Urology* 60(2):264-269.
- 73 Renshaw AA, Richie JP, Loughlin KR, Jirutek M, Chung A and D'Amico AV (1999). Maximum diameter of prostatic carcinoma is a simple, inexpensive, and independent predictor of prostate-specific antigen failure in radical prostatectomy specimens. Validation in a cohort of 434 patients. *Am J Clin Pathol* 111(5):641-644.
- 74 Epstein JI, Partin AW, Sauvageot J and Walsh PC (1996). Prediction of progression following radical prostatectomy. A multivariate analysis of 721 men with long-term follow-up. *Am J Surg Pathol* 20(3):286-292.

- 75 Sakr WA, Wheeler TM, Blute M, Bodo M, Calle-Rodrigue R, Henson DE, Mostofi FK, Seiffert J, Wojno K and Zincke H (1996). Staging and reporting of prostate cancer-sampling of the radical prostatectomy specimen. *Cancer* 78(2):366-368.
- 76 Ayala AG, Ro JY, Babaian R, Troncoso P and Grignon DJ (1989). The prostatic capsule: does it exist? Its importance in the staging and treatment of prostatic carcinoma. *Am J Surg Pathol* 13:21-27.
- 77 Chuang AY and Epstein JI (2008). Positive surgical margins in areas of capsular incision in otherwise organ-confined disease at radical prostatectomy: histologic features and pitfalls. *Am J Surg Pathol* 32(8):1201-1206.
- 78 Magi-Galluzzi C, Evans AJ, Delahunt B, Epstein JI, Griffiths DF, van der Kwast TH, Montironi R, Wheeler TM, Srigley JR, Egevad LL, Humphrey PA and ISUP Prostate Cancer Group (2011). International Society of Urological Pathology (ISUP) consensus conference on handling and staging of radical prostatectomy specimens. Working group 3: extraprostatic extension, lymphovascular invasion and locally advanced disease. *Mod Pathol* 24:26-38.
- 79 Epstein JI, Amin M, Boccon-Gibod L, Egevad L, Humphrey PA, Mikuz G, Newling D, Nilsson S, Sakr W, Srigley JR, Wheeler TM and Montironi R (2005). Prognostic factors and reporting of prostate carcinoma in radical prostatectomy and pelvic lymphadenectomy specimens. *Scand J Urol Nephrol Suppl* 216:34-63.
- 80 Sung MT, Lin H, Koch MO, Davidson DD and Cheng L (2007). Radial distance of extraprostatic extension measured by ocular micrometer is an independent predictor of prostate specific antigen recurrence: a new protocol for the substaging of pT3a prostate cancer. *Am J Surg Pathol* 31:311-318.
- 81 Jeong BC, Chalfin HJ, Lee SB, Feng Z, Epstein JI, Trock BJ, Partin AW, Humphreys E, Walsh PC and Han M (2015). The relationship between the extent of extraprostatic extension and survival following radical prostatectomy. *Eur Urol* 67(2):342-346.
- 82 Teramoto Y, Numbere N, Wang Y and Miyamoto H (2022). The Clinical Significance of Either Extraprostatic Extension or Microscopic Bladder Neck Invasion Alone Versus Both in Men With pT3a Prostate Cancer Undergoing Radical Prostatectomy: A Proposal for a New pT3a Subclassification. *Am J Surg Pathol* 46(12):1682-1687.
- 83 Ball MW, Partin AW and Epstein JI (2015). Extent of extraprostatic extension independently influences biochemical recurrence-free survival: evidence for further pT3 subclassification. *Urology* 85(1):161-164.
- 84 Pierorazio PM, Epstein JI, Humphreys E, Han M, Walsh PC and Partin AW (2010). The significance of a positive bladder neck margin after radical prostatectomy: the American Joint Committee on Cancer Pathological Stage T4 designation is not warranted. *J Urol* 183:151-157.
- 85 Zhou M, Reuther AM, Levin HS, Falzarano SM, Kodjoe E, Myles J, Klein E and Magi-Galluzzi C (2009). Microscopic bladder neck involvement by prostate carcinoma in radical prostatectomy specimens is not a significant independent prognostic factor. *Mod Pathol* 22(3):385-392.
- 86 Dash A, Sanda MG, Yu M, Taylor JM, Fecko A and Rubin MA (2002). Prostate cancer involving the bladder neck: recurrence-free survival and implications for AJCC staging modification. American Joint Committee on Cancer. *Urology* 60(2):276-280.

- 87 Yossepowitch O, Engelstein D, Konichezky M, Sella A, Livne PM and Baniel J (2000). Bladder neck involvement at radical prostatectomy: positive margins or advanced T4 disease? *Urology* 56(3):448-452.
- 88 Poulos CK, Koch MO, Eble JN, Daggy JK and Cheng L (2004). Bladder neck invasion is an independent predictor of prostate-specific antigen recurrence. *Cancer* 101(7):1563-1568.
- 89 Rodriguez-Covarrubias F, Larre S, Dahan M, De La Taille A, Allory Y, Yiou R, Vordos D, Hoznek A, Abbou CC and Salomon L (2009). Prognostic significance of microscopic bladder neck invasion in prostate cancer. *BJU Int* 103(6):758-761.
- 90 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). *Union for International Cancer Control. TNM Classification of Malignant Tumours, 8th Edition*, Wiley, USA.
- 91 Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM and Meyer LR (eds) (2017). *AJCC Cancer Staging Manual. 8th ed.*, Springer, New York.
- 92 Blute ML, Bostwick DG, Bergstralh EJ, Slezak JM, Martin SK, Amling CL and Zincke H (1997). Anatomic site-specific positive margins in organ-confined prostate cancer and its impact on outcome after radical prostatectomy. *Urology* 50:733-739.
- 93 Swindle P, Eastham JA, Ohori M, Kattan MW, Wheeler T, Maru N, Slawin K and Scardino PT (2005). Do margins matter? The prognostic significance of positive surgical margins in radical prostatectomy specimens. *J Urol* 174(3):903-907.
- 94 Pfitzenmaier J, Pahernik S, Tremmel T, Haferkamp A, Buse S and Hohenfellner M (2008). Positive surgical margins after radical prostatectomy: do they have an impact on biochemical or clinical progression? *BJU Int* 102(10):1413-1418.
- 95 Alkhateeb S, Alibhai S, Fleshner N, Finelli A, Jewett M, Zlotta A, Nesbitt M, Lockwood G and Trachtenberg J (2010). Impact of a positive surgical margin after radical prostatectomy differs by disease risk group. *J Urol* 183:145-150.
- 96 Ploussard G, Agamy MA, Alenda O, Allory Y, Mouracade P, Vordos D, Hoznek A, Abbou CC, de la Taille A and Salomon L (2011). Impact of positive surgical margins on prostate-specific antigen failure after radical prostatectomy in adjuvant treatment-naïve patients. *BJU Int* 107:1748-1754.
- 97 Wright JL, Dalkin BL, True LD, Ellis WJ, Stanford JL, Lange PH and Lin DW (2010). Positive surgical margins at radical prostatectomy predict prostate cancer specific mortality. *J Urol* 183:2213-2218.
- 98 Zhang B, Zhou J, Wu S, Guo M, Zhang Y and Liu R (2020). The impact of surgical margin status on prostate cancer-specific mortality after radical prostatectomy: a systematic review and meta-analysis. *Clin Transl Oncol* 22(11):2087-2096.
- 99 Yossepowitch O, Briganti A, Eastham JA, Epstein J, Graefen M, Montironi R and Touijer K (2014). Positive surgical margins after radical prostatectomy: a systematic review and contemporary update. *Eur Urol* 65(2):303-313.

- 100 Tan PH, Cheng L, Srigley JRS, Griffiths D, Humphrey PA, van der Kwast, Montironi R, Wheeler TM, Delahunt B, Egevad L, Epstein JI and ISUP Prostate Cancer Group (2011). International Society of Urological Pathology (ISUP) consensus conference on handling and staging of radical prostatectomy specimens. Working group 5: surgical margins. *Mod Pathol* 24:48-57.
- 101 Epstein JI and Sauvageot J (1997). Do close but negative margins in radical prostatectomy specimens increase the risk of postoperative progression? *J Urol* 157(1):241-243.
- 102 Emerson RE, Koch MO, Daggy JK and Cheng L (2005). Closest distance between tumor and resection margin in radical prostatectomy specimens: lack of prognostic significance. *Am J Surg Pathol* 29(2):225-229.
- 103 Epstein JI (1990). Evaluation of radical prostatectomy capsular margins of resection. The significance of margins designated as negative, closely approaching, and positive. *Am J Surg Pathol* 14(7):626-632.
- 104 Gupta R, O'Connell R, Haynes AM, Stricker PD, Barrett W, Turner JJ, Delprado W, Horvath LG and Kench JG (2015). Extraprostatic extension (EPE) of prostatic carcinoma: is its proximity to the surgical margin or Gleason score important? *BJU Int* 116(3):343-350.
- 105 Eastham JA, Kuroiwa K, Ohori M, Serio AM, Gorbonos A, Maru N, Vickers AJ, Slawin KM, Wheeler TM, Reuter VE and Scardino PT (2007). Prognostic significance of location of positive margins in radical prostatectomy specimens. *Urology* 70(5):965-969.
- 106 Obek C, Sadek S, Lai S, Civantos F, Rubinowicz D and Soloway MS (1999). Positive surgical margins with radical retropubic prostatectomy: anatomic site-specific pathologic analysis and impact on prognosis. *Urology* 4(54):682-688.
- 107 Barocas DA, Han M, Epstein JI, Chan DY, Trock BJ, Walsh PC and Partin AW (2001). Does capsular incision at radical retropubic prostatectomy affect disease-free survival in otherwise organ-confined prostate cancer? *Urology* 58(5):746-751.
- 108 Kumano M, Miyake H, Muramaki M, Kurahashi T, Takenaka A and Fujisawa M (2009). Adverse prognostic impact of capsular incision at radical prostatectomy for Japanese men with clinically localized prostate cancer. *Int Urol Nephrol* 41(3):581-586.
- 109 Shuford MD, Cookson MS, Chang SS, Shintani AK, Tsiatis A, Smith JA, Jr. and Shappell SB (2004). Adverse prognostic significance of capsular incision with radical retropubic prostatectomy. *J Urol* 172(1):119-123.
- 110 Chuang AY, Nielsen ME, Hernandez DJ, Walsh PC and Epstein JI (2007). The significance of positive surgical margin in areas of capsular incision in otherwise organ confined disease at radical prostatectomy. *J Urol* 178(4 pt. 1):130-1310.
- 111 Simon MA, Kim S and Soloway MS (2006). Prostate specific antigen recurrence rates are low after radical retropubic prostatectomy and positive margins. *J Urol* 175:140-145.
- 112 Savdie R, Horvath LG, Benito RP, Rasiyah KK, Haynes AM, Chatfield M, Stricker PD, Turner JJ, Delprado W, Henshall SM, Sutherland RL and Kench JG (2012). High Gleason grade carcinoma at a positive surgical margin predicts biochemical failure after radical prostatectomy and may guide adjuvant radiotherapy. *BJU Int* 109:1794-1800.

- 113 Babaian RJ, Troncoso P, Bhadkamkar VA and Johnston DA (2001). Analysis of clinicopathologic factors predicting outcome after radical prostatectomy. *Cancer* 91:1414-1422.
- 114 Watson RB, Civantos F and Soloway MS (1996). Positive surgical margins with radical prostatectomy: detailed pathological analysis and prognosis. *Urology* 48(1):80-90.
- 115 Cao D, Humphrey PA, Gao F, Tao Y and Kibel AS (2011). Ability of length of positive margin in radical prostatectomy specimens to predict biochemical recurrence. *Urology* 77:1409-1414.
- 116 Marks RA, Koch MO, Lopez-Beltran A, Montironi R, Juliar BE and Cheng L (2007). The relationship between the extent of the surgical margin positivity and prostate specific antigen recurrence in radical prostatectomy specimens. *Hum Pathol* 38:1207-1211.
- 117 Matti B, Reeves F, Prouse M and Zargar-Shoshtari K (2021). The impact of the extent and location of positive surgical margins on the risk of biochemical recurrence following radical prostatectomy in men with Gleason 7 prostate cancers. *Prostate* 81(16):1428-1434.
- 118 Porcaro AB, Tafuri A, Sebben M, Amigoni N, Shakir A, Corsi P, Processali T, Pirozzi M, Rizzetto R, Bernasconi R, Cerrato C, Tiso L, Migliorini F, Novella G, Brunelli M, De Marco V, Siracusano S and Artibani W (2020). Linear extent of positive surgical margin impacts biochemical recurrence after robot-assisted radical prostatectomy in a high-volume center. *J Robot Surg* 14(4):663-675.
- 119 van Oort IM, Bruins HM, Kiemeneij LA, Knipscheer BC, Witjes JA and Hulsbergen-van de Kaa CA (2010). The length of positive surgical margins correlates with biochemical recurrence after radical prostatectomy. *Histopathology* 56:464-471.
- 120 Brimo F, Partin AW and Epstein JI (2010). Tumor grade at margins of resection in radical prostatectomy specimens is an independent predictor of prognosis. *Urology* 76:1206-1209.
- 121 Cao D, Kibel AS, Gao F, Tao Y and Humphrey PA (2010). The Gleason score of tumor at the margin in radical prostatectomy specimens is predictive of biochemical recurrence. *Am J Surg Pathol* 34:994-1001.
- 122 Kates M, Sopko NA, Han M, Partin AW and Epstein JI (2015). Importance of Reporting The Gleason Score at the Positive Surgical Margin Site: An Analysis of 4,082 Consecutive Radical Prostatectomy Cases. *J Urol* 195(2):337-4.
- 123 John A, John H, Catterwell R, Selth LA and Callaghan MO (2021). Primary Gleason grade and Gleason grade group at positive surgical margins: a systematic review and meta-analysis. *BJU Int* 127 Suppl 1:13-22.
- 124 Iremashvili V, Pelaez L, Jorda M, Parekh DJ and Punnen S (2019). A Comprehensive Analysis of the Association Between Gleason Score at a Positive Surgical Margin and the Risk of Biochemical Recurrence After Radical Prostatectomy. *Am J Surg Pathol* 43(3):369-373.
- 125 Hollemans E, Verhoef EI, Bangma CH, Rietbergen J, Helleman J, Roobol MJ and van Leenders G (2020). Prostate Carcinoma Grade and Length But Not Cribriform Architecture at Positive Surgical Margins Are Predictive for Biochemical Recurrence After Radical Prostatectomy. *Am J Surg Pathol* 44(2):191-197.

- 126 Chapin BF, Nguyen JN, Achim MF, Navai N, Williams SB, Prokhorova IN, Wang X, Tapia E, Davis JW and Troncoso P (2018). Positive margin length and highest Gleason grade of tumor at the margin predict for biochemical recurrence after radical prostatectomy in patients with organ-confined prostate cancer. *Prostate Cancer Prostatic Dis* 21(2):221-227.
- 127 Debras B, Guillonneau B, Bougaran J, Chambon E and Vallancien G (1998). Prognostic significance of seminal vesicle invasion on the radical prostatectomy specimen. Rationale for seminal vesicle biopsies. *Eur Urol* 33(3):271-277.
- 128 Tefilli MV, Gheiler EL, Tiguert R, Banerjee M, Sakr W, Grignon DJ, Pontes JE and Wood Jr DP (1998). Prognostic indicators in patients with seminal vesicle involvement following radical prostatectomy for clinically localized prostate cancer. *J Urol* 160(3):802-806.
- 129 Epstein JI, Partin AW, Potter SR and Walsh PC (2000). Adenocarcinoma of the prostate invading the seminal vesicle: prognostic stratification based on pathologic parameters. *Urology* 56(2):283-288.
- 130 Potter SR, Epstein JI and Partin AW (2000). Seminal vesicle invasion by prostate cancer: prognostic significance and therapeutic implications. *Rev Urol* 2(3):190-195.
- 131 Swanson GP, Goldman B, Tangen CM, Chin J, Messing E, Canby-Hagino E, Forman JD, Thompson IM and Crawford ED (2008). The prognostic impact of seminal vesicle involvement found at prostatectomy and the effects of adjuvant radiation: data from Southwest Oncology Group 8794. *J Urol* 180(6):2453-2457.
- 132 Berney DM, Wheeler TM, Grignon DJ, Epstein JI, Griffiths DF, Humphrey PA, van der Kwast T, Montironi R, Delahunt B, Egevad L, Srigley JR and ISUP Prostate Cancer Group (2011). International Society of Urological Pathology (ISUP) consensus conference on handling and staging of radical prostatectomy specimens. Working group 4: seminal vesicles and lymph nodes. *Mod Pathol* 24:39-47.
- 133 Jewett HJ, Eggleston JC and Yawn DH (1972). Radical prostatectomy in the management of carcinoma of the prostate: probable causes of some therapeutic failures. *J Urol* 107:1034-1040.
- 134 Soh S, Arakawa A and Suyama K et al (1998). The prognosis of patients with seminal vesicle involvement depends upon the level of extraprostatic extension. *J Urol* 159:296A.
- 135 Otori M, Scardino PT, Lapin SL, Seale-Hawkins C, Link J and Wheeler TM (1993). The mechanisms and prognostic significance of seminal vesicle involvement by prostate cancer. *Am J Surg Pathol* 17:1252-1261.
- 136 Herman CM, Wilcox GE, Kattan MW, Scardino PT and Wheeler TM (2000). Lymphovascular invasion as a predictor of disease progression in prostate cancer. *Am J Surg Pathol* 24(6):859-863.
- 137 Cheng L, Jones TD, Lin H, Eble JN, Zeng G, Carr MD and Koch MO (2005). Lymphovascular invasion is an independent prognostic factor in prostatic adenocarcinoma. *J Urol* 174(6):2181-2185.
- 138 van den Ouden D, Hop WCJ, Kranse R and Schroder FH (1997). Tumour control according to pathological variables in patients treated by radical prostatectomy for clinically localized carcinoma of the prostate. *Brit J Urol* 79:203-211.

- 139 Van den Ouden D, Kranse R, Hop WC, van der Kwast TH and Schroder FH (1998). Microvascular invasion in prostate cancer: prognostic significance in patients treated by radical prostatectomy for clinically localized carcinoma. *Urol Int* 60:17-24.
- 140 Loeb S, Roehl KA, Yu X, Antenor JA, Han M, Gashti SN, Yang XJ and Catalona WJ (2006). Lymphovascular invasion in radical prostatectomy specimens: prediction of adverse prognostic features and biochemical progression. *Urology* 68:99-103.
- 141 Yee DS, Shariat SF, Lowrance WT, Maschino AC, Savage CJ, Cronin AM, Scardino PT and Eastham JA (2011). Prognostic significance of lymphovascular invasion in radical prostatectomy specimens. *BJU Int* 108:502-507.
- 142 Rakic N, Jamil M, Keeley J, Sood A, Vetterlein M, Dalela D, Arora S, Modonutti D, Bronkema C, Novara G, Peabody J, Rogers C, Menon M and Abdollah F (2021). Evaluation of lymphovascular invasion as a prognostic predictor of overall survival after radical prostatectomy. *Urol Oncol* 39(8):495.e491-495.e496.
- 143 Jamil M, Rakic N, Sood A, Keeley J, Modonutti D, Novara G, Jeong W, Menon M, Rogers CG and Abdollah F (2021). Impact of Lymphovascular Invasion on Overall Survival in Patients With Prostate Cancer Following Radical Prostatectomy: Stage-per-Stage Analysis. *Clin Genitourin Cancer* 19(5):e319-e325.
- 144 Fajkovic H, Mathieu R, Lucca I, Hiess M, Hübner N, Al Hussein Al Awamlh B, Lee R, Briganti A, Karakiewicz P, Lotan Y, Roupret M, Rink M, Kluth L, Loidl W, Seitz C, Klatte T, Kramer G, Susani M and Shariat SF (2016). Validation of lymphovascular invasion is an independent prognostic factor for biochemical recurrence after radical prostatectomy. *Urol Oncol* 34(5):233.e231-236.
- 145 May M, Kaufmann O, Hammermann F and Siegsmond M (2007). Prognostic impact of lymphovascular invasion in radical prostatectomy specimens. *BJU Int* 99:539-544.
- 146 Cheng L, Bergstralh EJ, Chevillie JC, Slezak J, Corica FA, Zincke H, Blute ML and Bostwick DG (1998). Cancer volume of lymph node metastasis predicts progression in prostate cancer. *Am J Surg Pathol* 22(12):1491-1500.
- 147 Boormans JL, Wildhagen MF, Bangma CH, Verhagen PC and van Leenders GJ (2008). Histopathological characteristics of lymph node metastases predict cancer-specific survival in node-positive prostate cancer. *BJU Int* 102:1589-1593.
- 148 Sgrignoli AR, Walsh PC, Steinberg GD, Steiner MS and Epstein JI (1994). Prognostic factors in men with stage D1 prostate cancer: identification of patients less likely to have prolonged survival after radical prostatectomy. *J Urol* 152:1077-1081.
- 149 Wittekind C, Brierley JD, van Eycken AL and van Eycken E (eds) (2019). *TNM Supplement: A Commentary on Uniform Use, 5th Edition* Wiley, USA.