Sponsored by ISUP

Prostate Core Needle Biopsy Histopathology Reporting Guide Part 2 - Case Level Reporting

ICCR

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

☐ indicates multi-select values ◯ indicates single select values

SCOPE OF THIS DATASET

COMPLETE THE FOLLOWING AS A SUMMARY OF THE CASE

LOCATION OF POSITIVE SPECIMEN(S) (Note 1)

HISTOLOGICAL TUMOUR TYPE (select all that apply) (Note 2)

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

HISTOLOGICAL TUMOUR GRADE (Note 3)

HIGHEST GRADE[a] (select all that apply)

☐ Systematic biopsy ☐ Targeted biopsy

Gleason score

Primary pattern/grade

◯ 3 ◯ 4 ◯ 5

Highest remaining pattern/grade

◯ 3 ◯ 4 ◯ 5

◯ Indeterminate, *specify reason*

WHO/ISUP Grade (Grade Group)

- ◯ 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 (Grade Group) 5 (Gleason score 9-10)
- ◯ Indeterminate, *specify reason*

Percentage Glasson pattern 4

(Applicable for Gleason score 3+4=7 or WHO/ISUP Grade 2)

- ◯ 1-5%
- ◯ 6-10%
- ◯ 11-20%
- ◯ 21-30%
- ◯ 31-40%
- ◯ 41-50%

Percentage Gleason pattern 4

(Applicable for WHO/ISUP Grade ≥3)

%

Percentage Gleason pattern 5

(Applicable for WHO/ISUP Grade ≥4)

%

OVERALL (GLOBAL) GRADE[a] (select all that apply)

☐ Systematic biopsy ☐ Targeted biopsy

Gleason score

Primary pattern/grade

◯ 3 ◯ 4 ◯ 5

Highest remaining pattern/grade

◯ 3 ◯ 4 ◯ 5

◯ Indeterminate, *specify reason*

WHO/ISUP Grade (Grade Group)

- ◯ 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 (Grade Group) 5 (Gleason score 9-10)
- ◯ Indeterminate, *specify reason*

Percentage Glasson pattern 4

(Applicable for Gleason score 3+4=7 or WHO/ISUP Grade 2)

- ◯ 1-5%
- ◯ 6-10%
- ◯ 11-20%
- ◯ 21-30%
- ◯ 31-40%
- ◯ 41-50%

Percentage Gleason pattern 4

(Applicable for WHO/ISUP Grade ≥3)

%

Percentage Gleason pattern 5

(Applicable for WHO/ISUP Grade ≥4)

%

[a] *The highest grade and overall (global) grade should be documented. The highest grade and overall (global) grade can be derived from the systematic or targeted biopsies, or both.*

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TUMOUR GROWTH PATTERNS (Note 4)

Intraductal carcinoma of the prostate (IDC-P) AND/OR Invasive cribriform carcinoma (ICC)

- ◯ Indeterminate
- ◯ Not identified
- ◯ Present

If present, specify the tumour growth pattern (if apparent on H&E staining[b])

IDC-P

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

Invasive cribriform carcinoma

(Applicable for Gleason score 7 or 8)

- ◯ Not identified
- ◯ Present

[b] *Use of immunohistochemistry is optional.*

TUMOUR EXTENT (select all that apply) (Note 5)

☐ Systematic biopsy

Number of positive cores/total number of cores

/

AND

Greatest linear extent of prostatic tissue involved by carcinoma

- ◯ 1-5%
- ◯ 6-10%
- ◯ 11-20%
- ◯ 21-30%
- ◯ 31-40%
- ◯ 41-50%
- ◯ 51-60%
- ◯ 61-70%
- ◯ 71-80%
- ◯ 81-90%
- ◯ >90%

AND/OR

Greatest length of tissue involved by carcinoma ____ mm

☐ Targeted biopsy

Number of positive cores/total number of cores

/

AND

Greatest linear extent of prostatic tissue involved by carcinoma

- ◯ 1-5%
- ◯ 6-10%
- ◯ 11-20%
- ◯ 21-30%
- ◯ 31-40%
- ◯ 41-50%
- ◯ 51-60%
- ◯ 61-70%
- ◯ 71-80%
- ◯ 81-90%
- ◯ >90%

AND/OR

Greatest length of tissue involved by carcinoma ____ mm

EXTRAPROSTATIC EXTENSION (Note 6)

- ◯ Indeterminate
- ◯ Not identified
- ◯ Present

Location (select all that apply)

- ☐ Left base
- ☐ Left mid
- ☐ Left apex
- ☐ Right base
- ☐ Right mid
- ☐ Right apex
- ☐ Other, *specify*

SEMINAL VESICLE/EJACULATORY DUCT INVASION (Note 7)

- ◯ Not identified
- ◯ Present

LYMPHOVASCULAR INVASION (Note 8)

- ◯ Not identified
- ◯ Present

PERINEURAL INVASION (Note 9)

- ◯ Not identified
- ◯ Present

COEXISTENT PATHOLOGY (Note 10)

- ◯ None identified
- ◯ Present, *specify*

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 evidence[1]). In rare circumstances, where level III-2 evidence is not available an element may be made a CORE element where there is unanimous agreement by the Dataset Authoring Committee (DAC).

Molecular and 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 the examination of prostate core needle biopsies. The dataset applies to invasive carcinomas of the prostate gland. Transurethral resection and enucleation specimens and radical prostatectomy specimens are dealt with in separate ICCR datasets.[2,3] Urothelial carcinomas arising in the bladder or urethra are dealt with in separate datasets.[4,5] Rare urothelial carcinomas arising within the prostate are included in a separate ICCR dataset.[5]

The second 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.[6] The ICCR dataset includes 5th edition Corrigenda, July 2024.[7] In development of this dataset, the DAC considered evidence up until July 2024.

The prostate biopsy reports can be done using *Specimen level reporting* or *Case level reporting*. The following commentary applies to both specimen level and case level reporting of prostate core needle biopsies. Reporting by either specimen level or case level will be sufficient or users may also use both.

Choosing which reporting to use will depend on your local practice or institutional preference, as well as regional or national recommendations.

A list of changes in this dataset edition can be accessed here.

The authors of this dataset can be accessed here.

Back

Note 1 – Location of positive specimen(s) (Core)

Biopsy cores are generally taken in a systematic way from multiple sites mapped in the prostate.[8-11] Systematic biopsies are now widely performed either by transperineal or transrectal approach, the former having the advantage of lesser infectious complications. If a lesion in prostate is identified on imaging, a magnetic resonance imaging (MRI)-targeted biopsy is additionally performed.[12-14] The targeted biopsy has a greater chance of detecting clinically significant cancer and has a lower risk of sampling clinically insignificant cancer. A usual prostate biopsy has 12 to 14 specimens from the systematic biopsy plus the additional specimens from the targeted biopsy.

The prostate biopsy reports can be done using *Specimen level reporting* or *Case level reporting*. Specimen level reporting can be used for every positive specimen site generating multiple reports. Case level reporting summarises all positive specimen sites generating a single report. For example, a 12-site systematic biopsy with 5 sites positive for cancer will have 5 specimen level reports or 1 case level report. Reporting by either specimen level or case level will be sufficient or users may also use both. Choosing which reporting to use will depend on your local practice or institutional preference, as well as regional or national recommendations.

In specimen level reporting, individual reports are specific for each positive specimen site and the specimen identification and location must be documented. When using a case level reporting, the location of all positive specimen sites should be documented. Targeted biopsies must be distinguished from the systematic biopsies.

Back

Note 2 – Histological tumour type (Core)

The vast majority (>95%) of prostate cancers are acinar adenocarcinomas.[6,15] 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 carcinoma, have a significantly poorer prognosis. The tumour type should be assigned in line with the 2022 WHO Classification and mixtures of different types should be indicated (Table 1).[16] Some prostate carcinoma subtypes, such as ductal and signet-ring cell-like, require full examination of the resected tumour with percent cut-offs to make the diagnosis. Thus, using descriptive diagnosis, for example ‘adenocarcinoma with ductal features’, is recommended in biopsy. Subtypes of prostate carcinoma (under acinar adenocarcinoma in Table 1) are often identified in combination with acinar type adenocarcinoma, and in such cases the tumour type should be classified according to the subtype(s) present.

Information on histological tumour type may be recorded at a specimen level or at a case level depending on local practice. The response type 'No evidence of primary tumour' should only be used if specimen level reporting is utilised.

Table 1: World Health Organization classification of epithelial tumours of the prostate.[16]

Descriptor	ICD-O codes[a]
Epithelial tumours of the prostate	
Glandular neoplasms of the prostate	
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 carcinorna	8140/3
Ductal adenocarcinoma	8500/3
Adenocarcinoma with neuroendocrine differentiation	8574/3
Squamous neoplasms of the prostate	
Adenosquamous carcinoma	8560/3
Squamous cell carcinoma	8070/3
Adenoid cystic (basal cell) carcinoma†	8147/3
Mesenchymal tumours unique to the prostate	
Stromal tumours of the prostate	
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-0-3.2).[17] Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour: /2 for carcinoma in situ and grade Ill 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, July 2024.[7]

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

Back

Note 3 – Histological tumour grade (Core and Non-core)

The Gleason grading system is the foundation of grading for prostatic adenocarcinoma.[15,18-21] The Gleason score is traditionally obtained by adding the two predominant Gleason patterns or doubling the pattern in cases with uniform grade. This was modified in the International Society of Urological Pathology (ISUP) 2005 revision by always including the highest grade in the Gleason score of needle biopsies, regardless of its

amount.[22] At the 2014 ISUP Consensus Conference, the Gleason system was further modified that mainly focused on the Gleason patterns.[23] It was decided that Gleason pattern 4 should include fused or poorly formed glands, glomerulations and all cribriform patterns of acinar adenocarcinoma. Additional refinements were made in the 2019 ISUP Consensus Conference and the 2019 Genitourinary Pathology Society (GUPS) 'White paper' mainly on reporting of Gleason scores and its components.[24,25] Many of these changes have been incorporated into the 4th and 5th editions of the WHO Classification.[6,26]

Over the past decades, Gleason scores below 6 have become less commonly used, especially on needle biopsies.[27] There is also an understanding that Gleason score 7 tumours have a worse prognosis if there is a predominant pattern 4 (4+3) than if pattern 3 dominates (3+4).[28] Grouping of the Gleason scores (6 or less, 3+4, 4+3, 8 and 9-10) into 5 grade categories (1 to 5) that was endorsed by ISUP is now recommended in the WHO Classification (WHO/ISUP Grade or Grade Group).[29-33]

The WHO/ISUP grades and associated definitions are outlined in Table 2.

Both the Gleason score and the WHO/ISUP Grade should always be reported for the sake of clarity. For specimen level reporting, separate grade is rendered on every positive specimen site. In targeted biopsies, grade should be rendered on every positive lesion. Occasionally, multiple cores are taken from one target lesion and is rendered an overall (global) grade.

For case level reporting, the highest (or worst) grade and overall (global) grade should be documented. Studies have shown that the highest and overall grades are good predictors of prostate cancer and adding a case level overall score showed comparable or slightly improved concordance with radical prostatectomy grade.[34,35] There are also worldwide geographic variations in the use of highest grade and/or overall (global) grade, and thus, both are required for case level reporting.

The highest grade and overall (global) grade can be derived from the systematic or targeted biopsies, or both. The overall (global) grade is the aggregate grade of multiple positive sites and can be *global* or *composite* grade. Global grade considers all positive sites whereas composite grade takes into consideration the location of the positive sites that may represent the dominant nodule.[36] Because of the challenges in deriving the composite grade, recording the global grade will be sufficient as the overall grade.

In the presence of significant treatment effects, prostate cancer may not be gradable. In rare instances, grading may not be feasible in very small tumour (tumour microfocus) or in tissues showing processing artifacts. In such challenging cases, grade can be documented as indeterminate.

The 2019 ISUP Consensus Conference and 2019 GUPS 'White paper' also recommended that the percentage of Gleason pattern 4 be reported in cases with WHO/ISUP Grades 2 or 3.[37-39] The rationale for this is to indicate if the tumour is bordering on the lower or higher ends of Gleason score 7. In some protocols, Gleason score 7 tumours with low or ≤10% pattern 4 are considered for active surveillance.[40,41] Since clinical use of this information has been mainly for active surveillance, reporting of percentage Gleason pattern 4 is currently required only for Gleason 3+4 tumours. The percentage of Gleason pattern 4 and 5 is reported by some pathologists for Gleason score 4+3 and higher tumours,[42,43] but this information is not widely used in clinical decision making. This element is therefore optional (non-core).

Table 2: World Health Organization (WHO)/International Society of Urological Pathology (ISUP) grading system, core needle biopsies and transurethral resection of the prostate (TURP) specimens.[16,23]

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 (or with necrosis) and lesser component (**) of well-formed glands
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%.

⬆ **Back**

Note 4 – Tumour growth patterns (Core and Non-core)

Several studies have shown the importance of invasive cribriform carcinoma (ICC) and intraductal carcinoma of prostate (IDC-P) as independent adverse prognosticators.[44-47] Both the 2019 ISUP Consensus Conference and 2019 GUPS 'White paper' recommended reporting of these two elements in biopsies with prostate cancer. Presence of either of these growth patterns would make the patients suboptimal for active surveillance.[48,49]

Invasive cribriform carcinoma (ICC) is one of the basic architectures for Gleason pattern 4. Presence of luminal necrosis upgrades the cribriform gland to Gleason pattern 5. Among the Gleason pattern 4 architectures, cribriform morphology has been shown to be associated with higher biochemical recurrence rate or poorer survival after radical prostatectomy or radiotherapy. Many of these findings were shown in Gleason score 7 prostate cancers.[50-54] Several studies have shown that cribriform pattern can also be prognostic in Gleason score 9-10 cancers.[49,55] However, because of the lack of clinical actionability on the presence of cribriform in Gleason score 9-10 cancers, reporting is only required for Gleason score 7 or 8 prostate cancers.

Both small and large cribriform glands are associated with poorer outcome, although the definition of small or large cribriform is still under debate.[56-58] To improve interobserver agreement, ISUP has proposed a definition for cribriform pattern as a confluent sheet of contiguous malignant epithelial cells with multiple glandular lumina that are easily visible at low power (objective magnification X10) and that there should be no intervening stroma or mucin separating individual or fused glandular structures.[59]

Intraductal carcinoma of prostate (IDC-P) is seen usually associated with invasive prostate cancer. However rarely, isolated IDC-P is found without invasive carcinoma.[60,61]

Intraductal carcinoma of prostate (IDC-P) has been well characterised at the histological and molecular levels over the past decade and its clinical significance is now better understood.[62] 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.[16] Desirable diagnostic criteria include immunohistochemistry demonstrating at least partial basal cell retention.[63,64]

Intraductal carcinoma of prostate (IDC-P) is strongly associated with high volume, high grade invasive prostate carcinoma and metastatic disease.[49,51,65,66] Hence, the presence of IDC-P in a biopsy, even if invasive carcinoma cannot be identified, mandates immediate repeat biopsy or definitive therapy (depending on the clinical situation). In patients treated with radiation with or without androgen deprivation therapy, the presence of IDC-P in the needle biopsy was an independent predictor of early biochemical recurrence, survival and metastasis.[53,67]

Presence of IDC-P in biopsy should be documented regardless of the grade. In terms of grading, it is recommended that pure IDC-P without invasive should not be graded. However, there is controversy in terms of grading IDC-P with invasive cancer.[68,69] ISUP recommended incorporating IDC-P into grade, whereas GUPS recommended excluding IDC-P from grading of invasive cancer. The prostate biopsy dataset allows either manner of grading invasive cancer with IDC-P, however, the approach should be documented in the report.

Distinction between ICC and IDC-P should be made based on morphology. Use of immunohistochemistry for basal cell markers to distinguish these two growth patterns is not recommended. If the grading approach is to exclude IDC-P in invasive carcinoma grade, it was recommended by GUPS to perform immunohistochemistry when biopsy shows Gleason score 6 cancer and cribriform glands that include a differential diagnosis of IDC-P versus Gleason pattern 4 cancer, or if the results would change the highest Gleason score of the case. Such approach can be opted in regions of the world with adequate resources available to support performing immunohistochemistry.

It is important to distinguish IDC-P from atypical intraductal proliferation (AIP) and high grade prostatic intraepithelial neoplasia (HGPIN).[70] AIP when present suggests an undersampled or concomitant IDC-P.[6,71-73] Compared to IDC-P, AIP and HGPIN have less architectural and cytological atypia.

Back

Note 5 – Tumour extent (Core)

Number of biopsy cores positive for cancer and linear extent of cancer in the cores correlate with tumour volume, postoperative stage and outcome.[74-76] Number of positive cores should be reported but may be difficult to determine because of fragmentation when multiple cores have been submitted together. The number of positive cores should not be greater than the number of cores taken (as specified in **Part 1 Clinical Information/Specimen Receipt Reporting Guide**). Site specific labelling and single core submission facilitates the assessment of cancer extent.[77]

Linear extent is a core data element and may be recorded either as percentage of cancer or millimetres (mm) cancer length in each core or as a composite measure of linear extent (mm or percentage) in multiple or fragmented cores in a specimen.[78,79] One approach to calculate percentage of cancer is to measure the length of cancer and divide by the entire length of prostatic tissue. The methods for reporting of discontinuous cancer remain controversial. Most (78%) discontinuous tumour foci in biopsy corresponded to a single tumour focus on radical prostatectomy and can be measured including the intervening stroma as one continuous tumour. However, this approach will also result to overestimating the tumour extent in a minority of cases. Whether intervening benign tissue is included or subtracted from the extent measurement may determine eligibility for active surveillance. A patient with WHO/ISUP Grade 1 cancer in no more than three cores may be a candidate for active surveillance. In some protocols, if a positive core is greater than 50% involved by tumour, a patient would be ineligible for active surveillance. In such a case it is recommended that the tumour extent of a discontinuous cancer should be reported by both including and subtracting the intervening benign tissue, e.g., in a 20 mm core there are two 1 mm discontinuous foci of cancer WHO/ISUP Grade 1 cancer spanning a distance of 12 mm (60% linear extent) and measuring 1+1 mm (10% linear extent).[78]

Since most active surveillance protocols use a cut-off determined by the greatest extent of core involvement, documenting the greatest linear extent and/or length of tissue involved by carcinoma will be sufficient for case level reporting.

Back

Note 6 – Extraprostatic extension (Core and Non-core)

Extraprostatic extension (EPE) is now the accepted terminology and replaces earlier ambiguous terms such capsular penetration, perforation, or invasion.[6,80] 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 Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC) T category.[81-84] There is limited data specifically on the significance of EPE in core needle biopsies given that it is relatively uncommon; however, it may be occasionally be seen and should be reported when.[85-87] One study showed that EPE in biopsy is strongly correlated with aggressive disease features.[85] In core needle biopsies, EPE is defined as tumour admixed with adipocytes, usually at the end of a biopsy core. 'Indeterminate' should be used sparingly but may be applicable to cases where the tumour involves fibrous tissue without directly involving adipocytes.

It is recommended that the site of any EPE present is recorded since this information is useful for correlation with MRI results and may assist the urologist or radiation oncologist with the technical aspects of treatment planning.

'Indeterminate' should be used sparingly but may be applicable to cases where the tumour involves fibrous tissue without directly involving adipocytes.

Back

Note 7 – Seminal vesicle/ejaculatory duct invasion (Non-core)

Seminal vesicle invasion (SVI) is rarely identified in core needle biopsies, hence its absence does not need to be explicitly stated.[88] However, if seminal vesicle/ejaculatory duct invasion is present it should be recorded and the following comments apply.

Seminal vesicle invasion (SVI) is defined as involvement of the muscular wall of the extraprostatic portion of the seminal vesicle.[89] If possible seminal vesicle tissue is present (either unintentionally or intentionally, as in a targeted biopsy) and involved by carcinoma, this may be significant since it indicates that the tumour could be T3b in the UICC/AJCC staging system.[81,82] However, assessment of SVI is problematic in needle biopsy specimens since it is impossible to reliably distinguish between extraprostatic seminal vesicle and intraprostatic seminal vesicle or ejaculatory duct tissue, therefore it is important not to over interpret invasion of the latter two structures as SVI since their involvement by tumour does not constitute T3b disease. Unless one is dealing with a targeted seminal vesicle biopsy, it is recommended to report tumour involvement of such structures in a core needle biopsy as 'seminal vesicle/ejaculatory duct invasion' rather than as SVI.

Back

Note 8 – Lymphovascular invasion (Non-core)

Lymphovascular invasion (LVI) is rarely identified in core needle biopsies, hence its absence does not need to be explicitly stated. However, if LVI is present it should be recorded.

Invasion of lymphatic or blood vessels (i.e., thin-walled endothelial-lined spaces) is uncommonly identified in core needle biopsy specimens and there is little published data on its significance specifically relating to prostate core biopsies. However, there is good evidence that LVI identified at radical prostatectomy is an independent prognosticator associated with adverse pathology, increased recurrence, metastasis and poorer outcome including those receiving radiotherapy.[90-94] Therefore, if LVI is identified in a core needle biopsy it may well be significant and its presence should be recorded. The presence of LVI does not affect assignment of the UICC/AJCC T category.[81,82]

Back

Note 9 – Perineural invasion (Non-core)

The significance of perineural invasion in prostate core biopsy specimens is uncertain.[95] Some studies show a correlation with EPE in the corresponding radical prostatectomy specimens or an association with adverse outcome in patients treated with radical prostatectomy or radiotherapy.[96-101] Other investigators have questioned prognostic value of biopsy perineural invasion in univariate or multivariate analyses.[102-105] The weight of evidence suggested that in clinically localised disease perineural invasion was a significant prognostic factor for EPE and subsequent local recurrence.[106,107] In advanced disease perineural invasion is common and probably not of prognostic significance. It should also be noted that nerves are not necessarily present in biopsy material, therefore it is not always possible to assess the possibility of perineural invasion.

Back

Note 10 – Coexistent pathology (Non-core)

In some cases clinical management decisions may be aided by knowledge of coexisting pathology, such as HGPIN, glandular atypia suspicious for malignancy (atypical small acinar proliferation (ASAP)), AIP, granulomatous prostatitis, etc.[15]

If there is carcinoma present, the presence of HGPIN is generally not clinically meaningful. Even if no cancer is identified in the specimen, the significance of finding HGPIN in core needle biopsies has been controversial with some studies finding an increased risk for detection of prostatic adenocarcinoma in subsequent biopsies, while others did not.[108] Studies, including one analysing data from a large Canadian cohort, found that this risk was related to the extent of HGPIN, i.e., the number of involved sites; only patients with multifocal HGPIN had a significantly increased risk of prostate cancer.[109,110] Low grade prostatic intraepithelial neoplasia (PIN) should not be reported.

Likewise, if there is carcinoma present in a specimen, the presence of ASAP is generally not significant, except occasionally in the situation where the carcinoma is bordering the criteria for active surveillance. In this situation, thorough evaluation, and reclassification of glandular atypia to carcinoma may influence the management decision. In specimens where there is no cancer identified but glandular atypia is present, the risk of carcinoma being present in subsequent biopsies is approximately 35%, a high proportion of these are clinically insignificant cancer.[111-115]

Atypical intraductal proliferation (AIP) is the preferred term to describe intraductal neoplasm that has complexity or atypia greater than HGPIN but falls short for the diagnosis of IDC-P.[6,71-73] AIP is characterised by loose cribriform proliferation and/or nuclear atypia falling short for IDC-P and encompasses what was previously known as cribriform HGPIN. Because of the association of AIP with IDC-P, documenting their presence in biopsy is recommended especially in lower grade prostate cancers. Presence of AIP alone in biopsy specimens is uncommon and is managed with repeat follow-up biopsy.

Active prostatitis and granulomatous prostatitis may cause a rise in serum prostate-specific antigen (PSA), although inflammatory lesions may coexist with carcinoma and it is important not to assume that their presence always accounts for an unexplained or disproportional increase in a patient's PSA.[116-118]

In negative targeted biopsy, it is recommended by ISUP to report the presence of non-cancerous lesions that may explain the radiologic abnormality.[24]

⬆ Back

References

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