PROSTATE CANCER

(RADICAL PROSTATECTOMY)

STRUCTURED REPORTING PROTOCOL

(2nd Edition 2014)

Core Document versions:

- AJCC Cancer Staging Manual 7th edition (including errata corrected with 5th reprint 10th Aug 2010).
- *World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Urinary System and Male Genital Organ*. (2004). Eble JN, Sauter G, Epstein JI and Sesterhenn IA. IARC Press, Lyon, France.

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Scope

This protocol contains standards and guidelines for the structured reporting of radical prostatectomy specimens for prostate carcinoma. There are separate protocols for core (needle) biopsies and transurethral resection (TUR) specimens.

Structured reporting aims to improve the completeness and usability of pathology reports for clinicians, and improve decision support for cancer treatment. This protocol can be used to define and report the minimum data set but the structure is scalable and can equally accommodate a maximum data set or fully comprehensive report.

Abbreviations

AJCC	American Joint Committee on Cancer
CI	capsular incision
EPE	extraprostatic extension
ICCR	International Collaboration on Cancer Reporting
ISUP	International Society of Urological Pathology
LIS	laboratory information system
LVI	lymphovascular invasion
PBS	Pharmaceutical Benefits Scheme
PIN	prostatic intraepithelial neoplasia
PSA	prostate specific antigen
PSM	positive surgical margin
RCPA	Royal College of Pathologists of Australasia
SVI	seminal vesicle involvement
TNM	tumour-node-metastasis
TUR	transurethral resection
TURP	transurethral resection of prostate
UICC	International Union Against Cancer
WHO	World Health Organization

Definitions

The table below provides definitions for general or technical terms used in this protocol. Readers should take particular note of the definitions for ‘standard’, ‘guideline’ and ‘commentary’, because these form the basis of the protocol.

Ancillary study	An ancillary study is any pathology investigation that may form part of a cancer pathology report but is not part of routine histological assessment.
Clinical information	Patient information required to inform pathological assessment, usually provided with the specimen request form, also referred to as “pre-test information”.
Commentary	Commentary is text, diagrams or photographs that clarify the standards (see below) and guidelines (see below), provide examples and help with interpretation, where necessary (not every standard or guideline has commentary). Commentary is used to: • define the way an item should be reported, to foster reproducibility • explain why an item is included (e.g. how does the item assist with clinical management or prognosis of the specific cancer). • cite published evidence in support of the standard or guideline • state any exceptions to a standard or guideline. In this document, commentary is prefixed with ‘CS’ (for commentary on a standard) or ‘CG’ (for commentary on a guideline), numbered to be consistent with the relevant standard or guideline, and with sequential alphabetic lettering within each set of commentaries (eg CS1.01a, CG2.05b).
General commentary	General commentary is text that is not associated with a specific standard or guideline. It is used: • to provide a brief introduction to a chapter, if necessary • for items that are not standards or guidelines but are included in the protocol as items of potential importance, for which there is currently insufficient evidence to recommend their inclusion. (Note: in future reviews of protocols, such items may be reclassified as either standards or guidelines, in line with diagnostic and prognostic advances, following evidentiary review).

Guideline	Guidelines are recommendations; they are not mandatory, as indicated by the use of the word 'should'. Guidelines cover items that are not essential for clinical management, staging or prognosis of a cancer, but are recommended. Guidelines include key observational and interpretative findings that are fundamental to the diagnosis and conclusion. Such findings are essential from a clinical governance perspective, because they provide a clear, evidentiary decision-making trail. Guidelines are not used for research items. In this document, guidelines are prefixed with 'G' and numbered consecutively within each chapter (eg G1.10).
Macroscopic findings	Measurements, or assessment of a biopsy specimen made by the unaided eye.
Microscopic findings	In this document, the term 'microscopic findings' refers to histo-morphological assessment.
Predictive factor	A predictive factor is a measurement that is associated with response or lack of response to a particular therapy.
Prognostic factor	A prognostic factor is a measurement that is associated with clinical outcome in the absence of therapy or with the application of a standard therapy. It can be thought of as a measure of the natural history of the disease.
Standard	Standards are mandatory, as indicated by the use of the term 'must'. Their use is reserved for core items essential for the clinical management, staging or prognosis of the cancer and key information (including observations and interpretation) which is fundamental to the diagnosis and conclusion. These elements must be recorded and at the discretion of the pathologist included in the pathology report according to the needs of the recipient of the report. The summation of all standards represents the minimum dataset for the cancer. In this document, standards are prefixed with 'S' and numbered consecutively within each chapter (eg S1.02).
Structured report	A report format which utilises standard headings, definitions and nomenclature with required information.
Synoptic report	A structured report in condensed form (as a synopsis or precis).

Synthesis

Synthesis is the process in which two or more pre-existing elements are combined, resulting in the formation of something new.

The Oxford dictionary defines synthesis as “the combination of components or elements to form a connected whole”.

In the context of structured pathology reporting, synthesis represents the integration and interpretation of information from two or more modalities to derive new information.

Introduction

Prostate cancer

Prostate cancer is the most common cancer with 21,808 new cases reported in Australia in 2009. It is also the third most common cause of cancer death, accounting for almost 3,235 in 2010.[1] Both the number of new cases and the number of deaths from prostate cancer are increasing, partly driven by the ageing of the population.[2] There is a wide variation in the biological behaviour of prostate cancer. Most tumours are relatively slow-growing; however, a significant minority have the propensity for aggressive behaviour, including metastasis, and such tumours can be fatal.[3]

Benefits of structured reporting

Structured pathology reports with standardised definitions for each component have been shown to significantly enhance the completeness and quality of data provided to clinicians, and have been recommended both in North America and the United Kingdom.[4-7]

Importance of histopathological reporting

Information from pathology reports on core biopsy and transurethral resection (TUR) specimens, particularly Gleason grade and pathological stage, has a key role in the rational planning of patient management and is a major component of the most common nomograms used to guide clinical decision making.[10] Likewise, accurate data from the pathological examination of radical prostatectomy specimens is essential in predicting the risk of cancer recurrence after prostatectomy and aids clinical decisions on surveillance, adjuvant therapy etc.[11-12]

Design of this protocol

This protocol defines the relevant information to be assessed and recorded in a pathology report for prostate cancer. Mandatory elements (standards) are differentiated from those that are not mandatory but are recommended (guidelines). Also, items suited to tick boxes are distinguished from more complex elements requiring free text or narrative. The structure provided by the following chapters, headings and subheadings describes the elements of information and their groupings, but does not necessarily represent the format of either a pathology report (Chapter 7) or checklist (Chapter 6). These, and the structured pathology request form (Appendix 1), are templates representing information from this protocol, organised and formatted differently to suit their respectively different purposes.

Key documentation

- *ISUP Boston 2009 Consensus Conference*
  - Egevad L, Srigley JR and Delahunt B. International Society of Urological Pathology (ISUP) Consensus Conference on Handling and Staging of Radical Prostatectomy Specimens: rationale and organization. Mod Pathol 24: 1-5

  - 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. 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
  - van der Kwast T, Amin MB, Billis A, Epstein JI, Griffiths DF, Humphrey PA, Montironi R, Wheeler TM, Srigley JR, Egevad L, Delahunt B and the ISUP Prostate Cancer Group. International Society of Urological Pathology (ISUP) Consensus Conference on Handling and Staging of Radical Prostatectomy Specimens. Working group 2: T2 substaging and prostate cancer volume. Mod Pathol 24: 16-25
  - Magi-Galluzzi C, Evans AJ, Delahunt B, Epstein JI, Griffiths DF, van der Kwast TH, Montironi R, Wheeler TM, Srigley JR, Egevad LL and Humphrey PA, and the ISUP Prostate Cancer Group. 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
  - 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 the ISUP Prostate Cancer Group. 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
  - Tan PH, Cheng L, Srigley JR, Griffiths DM, Humphrey PA, van der Kwast TH, Montironi R, Wheeler TM, Delahunt B, Egevad L, Epstein JI and the ISUP Prostate Cancer Group. 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

- *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols, Royal College of Pathologists of Austr*alasia, 2009[13]

- *Pathology and Genetics: Tumours of the Urinary System and Male Genital Organs.* World Health Organization Classification of Tumours, Volume 7, 2004[14]

- *AJCC Cancer Staging Manual*, 7th edition, American Joint Committee on Cancer, 2010[15]

- *Dataset for reporting of prostate carcinoma in radical prostatectomy specimens: recommendations from the International Collaboration on Cancer Reporting*. Kench J, Delahunt B, Griffiths DF, Humphrey PA, McGowan T, Trpkov K, Varma M, Wheeler TM and Srigley JR (2013).Histopathology 62:203-218[16]

Changes since last edition

- Rework of chapter 1 and appendix 1 in line with new framework

- Removal of numbering for specimen handling in Ch 2, with subsequent renumbering

- Inclusion of a new S5.02 and subsequent renumbering of this chapter

- Edits to G6.01

- Addition of G6.03

- Rework of the checklist in Ch 6.

- Inclusion of ICCR agreed REQUIRED and RECOMMENDED elements as follows:
    - Serum PSA
    - Specimen weight
    - Specimen dimensions (prostate)
    - Seminal vesicles
    - Lymph nodes
    - Histological tumour type
    - Histological grade
    - Intraglandular extent
    - Extraprostatic extension
        - EPE locations
        - EPE extent
    - Seminal vesicle involvement
    - Bladder neck involvement
    - Margin Status
        - Involvement
        - Location
        - Extent
        - Gleason score at the margin
        - Type of margin positivity
    - Lymphovascular invasion
    - Lymph nodes status
        - Number of lymph nodes examined
        - Number of positive lymph nodes
            - Laterality
            - Maximum dimension of deposit
    - Pathological staging (AJCC 7th edition)
        - Primary tumour (AJCC 7th edition)
        - Regional lymph nodes (AJCC 7th edition)
        - Distant Metastases (AJCC 7th edition)

Authority and development

This section provides details about the process undertaken in developing this protocol.

This edition of the protocol is an amalgam of two separate but interwoven processes.

a) The first edition of the Prostate (Radical Prostatectomy) protocol was published in Feb 2010. It was developed by an expert committee as follows:

Expert committee

Professor James Kench (Chair and lead author), Pathologist
Dr David Clouston, Pathologist
Professor Brett Delahunt, Pathologist
Professor Warick Delprado, Pathologist
Dr Thomas Eade, Radiation Oncologist
Associate Professor David Ellis, Pathologist
Dr Lisa Horvath, Medical Oncologist
Dr Andrew Kneebone, Radiation Oncologist
Associate Professor Hema Samaratunga, Pathologist
Associate Professor Jurgen Stahl, Pathologist
Dr Alan Stapleton, Urologist

That edition of the protocol was developed following the nine-step process set out in *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols* [13]

b) In 2011 the International Collaboration of Cancer Reporting (ICCR) was established and developed an international cancer dataset for Prostate (Radical Prostatectomy) published to:

www.rcpa.edu.au/Publications/StructuredReporting/ICCR.htm

The ICCR dataset was developed by an international group of expert pathologists and clinicians. Representation of the international committee is as follows:

Dr John Srigley from the CAP-ACP serving as chair.

Dr James Kench	Pathologist	RCPA
Dr Brett Delahunt	Pathologist	RCPA
Dr David Griffiths	Pathologist	Royal College of Pathologists, UK
Dr Murali Varma	Pathologist	Royal College of Pathologists, UK
Dr Thomas Wheeler	Pathologist	College of American Pathologists
Dr Peter Humphrey	Pathologist	College of American Pathologists
Dr Kiril Trpkov	Pathologist	CAP-ACP
Dr Tom McGowan	Radiation Oncologist	CAP-ACP

The protocols developed by the ICCR member countries, including Australia's 1st edition Prostate (Radical Prostatectomy) protocol, were used as the basis for discussion of the ICCR dataset.

This 2nd edition of the Prostate (Radical Prostatectomy) protocol includes all of the ICCR cancer dataset elements as well as those elements and commentary from the first edition of the Prostate (Radical Prostatectomy) protocol which complement but do not overlap with the ICCR elements. The ICCR elements are identified in each chapter with the ICCR logo placed before the Standard or Guideline number or bullet and the ICCR element description and commentary boarded by a grey box as shown below:

G3.02	The intraglandular extent should be recorded as a percentage.

Additional commentary by the RCPA may be added to an ICCR element but is not included in the grey bordered area eg

G2.03	If present, the laterality of the lymph nodes submitted may be recorded as left, right or bilateral.

CS2.03a If present, record site and number. All lymph node tissue should be submitted for histological examination.

This 2nd edition of the Prostate Cancer (Radical Prostatectomy) protocol was reviewed, edited and endorsed by our Australasian expert committee as follows:

Professor James Kench (Chair and lead author), Pathologist
Dr David Clouston, Pathologist
Professor Brett Delahunt, Pathologist
Professor Warick Delprado, Pathologist
Dr Thomas Eade, Radiation Oncologist
Dr Lisa Horvath, Medical Oncologist
Associate Professor Hema Samaratunga, Pathologist
Associate Professor Jurgen Stahl, Pathologist

Stakeholders

ACT Health
Anatomical Pathology Advisory Committee (APAC)
Andrology Australia
Australian Cancer Network
Australian Commission on Safety and Quality in Health Care
Cancer Australia
Cancer Control New Zealand
Cancer Council ACT
Cancer Council NSW
Cancer Council Queensland
Cancer Council SA
Cancer Council Tasmania
Cancer Council Victoria
Cancer Council Western Australia
Cancer Institute NSW
Cancer Services Advisory Committee (CanSAC)
Cancer specific expert groups – engaged in the development of the protocols
Cancer Voices
Clinical Oncology Society of Australia (COSA)
Department of Health and Ageing
Faculty of Radiation Oncology Genito-Urinary Group (FROGG)
Grampians Integrated Cancer Services (GICS)
Independent Review Group of Pathologists
Health Informatics Society of Australia (HISA)
Medical Software Industry Association (MSIA)
National Coalition of Public Pathology (NCOPP)
National E-Health Transition Authority (NEHTA)
National Health Committee, Ministry of Health, New Zealand
National Pathology Accreditation Advisory Council (NPAAC)
National Round Table Working Party for Structured Pathology Reporting of Cancer.
New Zealand Cancer Registry Board
New Zealand Prostate Cancer Working Group
New Zealand Ministry of Health
NSW Ministry of Health
Pathology Australia
Peter MacCallum Cancer Institute
Prostate Cancer Foundation, New Zealand
Queensland Cooperative Oncology Group (QCOG)
Representatives from laboratories specialising in anatomical pathology across Australia
Royal Australasian College of Physicians (RACP)
Southern Melbourne Integrated Cancer Service (SMICS)
Standards Australia
The Medical Oncology Group of Australia
The Prostate Cancer Foundation of Australia (PCFA)
The Royal Australasian College of Surgeons (RACS)
The Royal Australian and New Zealand College of Radiologists (RANZCR)
The Royal Australian College of General Practitioners (RACGP)
The Royal College of Pathologists of Australasia (RCPA)
The Urological Society Of Australia And New Zealand (USANZ)
Victorian Cooperative Oncology Group (VCOG)
Western Australia Clinical Oncology Group (WACOG)

Secretariat

Meagan Judge, Royal College of Pathologists of Australasia

Development process

This protocol has been developed following the seven-step process set out in *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols.*[13]

Where no reference is provided, the authority is the consensus of the expert group.

1 Pre-analytical

This chapter relates to information that should be recorded on receipt of the specimen in the laboratory.

The pathologist is reliant on the quality of information received from the clinicians or requestor. Some of this information may be received in generic pathology request forms, however, the additional information required by the pathologist specifically for the reporting of prostate cancer is outlined in Appendix 1. Appendix 1 also includes a standardised request information sheet that may be useful in obtaining all relevant information from the requestor**.**

Surgical handling procedures affect the quality of the specimen and recommendations for appropriate surgical handling are included in Appendix 1.

S1.01 All demographic information provided on the request form and with the specimen must be recorded.

CS1.01a The Royal College of Pathologists of Australasia (RCPA) *The Pathology Request-Test-Report Cycle — Guidelines for Requesters and Pathology Providers* must be adhered to.[17] This document specifies the minimum information to be provided by the requesting clinician for any pathology test.

CS1.01b The patient's ethnicity must be recorded, if known. In particular whether the patient is of aboriginal or Torres Strait islander origin. This is in support of a government initiative to monitor the health of indigenous Australians particularly in relation to cancer.

CS1.01c The patient's health identifiers may include the patient's Medical Record Number as well as a national health number such as a patient's Medicare number (Australia), Individual Healthcare Identifier (IHI) (Australia) or the National Healthcare Identifier (New Zealand).

S1.02 All clinical information as documented on the request form must be recorded verbatim.

CS1.02a The request information may be recorded as a single text (narrative) field or it may be recorded atomically.

S1.03 The pathology accession number of the specimen must be recorded.

S1.04 The principal clinician involved in the patient's care and responsible for investigating the patient must be recorded.

CS1.04a The principle clinician can provide key information regarding the clinical presentation of the patient. Follow up may be required with the principle clinician for a number of reasons:

- The clinical assessment and staging may be incomplete at the time of biopsy.

- The pathology request is often authored by the clinician performing the biopsy rather than the clinician who is investigating and managing the patient.

- The identity of this clinician is often not indicated on the pathology request form

In practice therefore, it is important in such cases that the reporting pathologist should be able to communicate with the managing clinician for clarification.

G1.01 Any clinical information received in other communications from the requestor or other clinician should be recorded together with the source of that information.

2 Specimen handling and macroscopic findings

This chapter relates to the procedures required after the information has been handed over from the requesting clinician, and the specimen has been received in the laboratory.

Tissue banking

- Pathologists may be asked to provide tissue samples from fresh specimens for tissue banking or research purposes. The decision to provide tissue should only be made if the pathologist is sure that the diagnostic process will not be compromised. As a safeguard, research use of the tissue samples may be put on hold until the diagnostic process is complete.

Specimen handling

- **The specimen must be handled in a systematic and thorough fashion to ensure completeness and accuracy of pathological data.**

    - The pathological findings from examination of radical prostatectomy specimens are important in guiding the patient's subsequent clinical management; for example, in predicting a patient's prognosis, or in deciding whether adjuvant therapy such as radiotherapy or chemotherapy is needed. Hence, these specimens must be handled in a systematic and thorough fashion to ensure the completeness and accuracy of the pathological data, such as Gleason score,[18] resection margin status, pathological stage etc. The radical prostatectomy specimen may be submitted in its entirety for histological assessment or partially sampled in a standardised manner.

    - Total and partial sampling methods for examination of radical prostatectomy specimens have been outlined in several articles.[19-20] In summary, the outer surface of the specimen is carefully inked (more than one colour may be used to aid in section orientation) to enable determination of the margin status. The apical segment (distal 10mm) is transversely amputated and sectioned in a perpendicular fashion, generating a series of sagittal slices that are all submitted for histological examination. Likewise, the base of the prostate (bladder neck portion) is transversely amputated and used to generate a series of perpendicular slices that are all submitted. The seminal vesicles can be handled in a variety of ways (eg transverse or longitudinal sections, provided that the junction between each seminal vesicle and the prostate is submitted for histological examination).

    - Following this, the remaining middle portion of the prostate is serially sectioned transversely at 3–4-mm intervals perpendicular to the rectal surface. These sections are carefully laid out in an orderly manner, and both sides of each slice are macroscopically examined

for the presence of grossly visible tumour. These slices can then be entirely submitted for histological assessment (with the origin of each block recorded on an appropriate diagram, template or macroscopic photograph of the slices). Submitting the entire gland in this fashion facilitates accurate estimation of tumour volume and extent.

- Less comprehensive, partial sampling methods have also been described (eg submission of alternate transverse slices or submission of the posterior half of each transverse slice along with a midanterior section from each of the right and left sides).[19-20] However, some studies have found that partial sampling can miss a proportion of cases (15%) with extraprostatic extension and also some with involved resection margins.[19,21-22]

Macroscopic findings

S2.01	**The weight of the prostate gland without the seminal vesicles must be recorded.**

CS2.01a Weigh the prostate gland without the seminal vesicles. The seminal vesicles can vary markedly in size; thus, if only a combined weight is recorded, this will introduce error into the measurement of the prostate gland weight and distort comparisons with the radiologically estimated weight. Given this, a working group at the 2009 International Society of Urological Pathology (ISUP) Consensus Conference in Boston recommended that the prostate should be weighed following removal of the seminal vesicles.[23]

G2.01	Specimen dimensions of the prostate gland should be recorded in three dimensions (in millimetres).

CG2.01a Measurements for apex to base, right to left and anterior to posterior enable comparison with clinical and imaging estimates of volume.

S2.02	**The presence or absence of seminal vesicles must be recorded.**
S2.03	**The presence or absence of lymph nodes must be recorded.**
G2.02	If present, the laterality of the lymph nodes submitted may be recorded as left, right or bilateral.

CG2.02a If present, record site and number. All lymph node tissue should be submitted for histological examination.

G2.03	A block identification key listing the nature and origin of all tissue blocks should be recorded.

G2.04 A descriptive or narrative field should be provided to record any macroscopic information that is not recorded in the above standards and guidelines, and that would normally form part of the macroscopic description.

CG2.04a The traditional macroscopic narrative recorded at the time of specimen dissection is often reported separately from the cancer dataset. Although this remains an option, it is recommended that macroscopic information be recorded within the overall structure of this protocol.

CG2.04b Much of the information recorded in a traditional macroscopic narrative is covered in the standards and guidelines above and in many cases, no further description is required.

3 Microscopic findings

This section relates to purely histological or morphological assessment. Information derived from multiple investigational modalities, or from two or more chapters, is described in Chapter 5.

S3.01	**The histological tumour type must be recorded.**	
	CS3.01a	Choose from the following values taken from the World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs (2004)[14]: • Adenocarcinoma (Acinar, usual type) • Adenocarcinoma (Acinar variant eg foamy, pseudohyperplastic) (specify type) • Prostatic ductal adenocarcinoma • Adenosquamous carcinoma • Small cell carcinoma • Sarcomatoid carcinoma • Undifferentiated carcinoma, not otherwise specified • Other (specify)
	CS3.01b	The large majority (>95%) of prostate cancers are acinar adenocarcinomas.[14] Other types of carcinoma are rarer but must be recorded if present, since some variants, such as ductal adenocarcinoma, small cell carcinoma, sarcomatoid carcinoma and urothelial-type adenocarcinoma, have a significantly poorer prognosis.[14,24-29] The tumour type should be assigned in line with the 2004 WHO classification[14] and mixtures of different types should be indicated.

G3.01 The tumour location should be recorded.

CG3.01a Record in which quadrants tumour is present. (Specify for the dominant or largest tumour nodule, and also for other nodules >10 mm diameter, if present).

Specify whether right anterior, right posterior, left anterior or left posterior.

CG3.01b Specify the location in another plane (eg apex, mid, base of prostate). This information is important for correlation with needle biopsy findings, imaging results, etc.

G3.02	The intraglandular extent should be recorded as a percentage.	
	CG3.02a	Some measurement of the size or extent of the tumour is typically given in histopathology reports for most sites and this parameter 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 Gleason score, EPE, surgical margin status and pathological TNM stage, and the majority of studies have not demonstrated independent prognostic significance on multivariate analysis.[30-35] Hence, the ICCR expert panel regarded this factor as a recommended (non-core) rather than required item. 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 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[36-37] or by measuring the maximum size of dominant tumour nodule.[38-39] 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.[35,38-39]
G3.03	The maximum size of the dominant nodule should be recorded in millimetres.	
S3.02	**The Histological grade using the Gleason grading system (ISUP 2005) must be recorded.[18]**	
	CS3.02a	The 2005 ISUP modified Gleason score is a required (core) element for all radical prostatectomy specimens containing adenocarcinoma, except for those showing morphological changes consistent with androgen withdrawal or significant radiation therapy changes. The Gleason grading system has been in use for over 40 years and is the current, internationally accepted grading system for prostate cancer.[40] It has undergone several significant modifications over time, with an updated version developed at the 2005 ISUP Consensus Conference on Gleason Grading of Prostatic Carcinoma.[18] The Gleason score is an important, independent predictor of tumour behaviour and is a key parameter in the tables and nomograms commonly used to guide decisions on clinical treatment.[11-12,41]

		The method for Gleason scoring is described in the 2005 ISUP Consensus Conference recommendations.[18] Gleason grading is based solely on the architectural patterns of the tumour, best assessed at low power magnification, using a 4x or 10x objectives, and is not influenced by nuclear or cytoplasmic features. Following the ISUP recommendations, the Gleason score for radical prostatectomy specimens is based on assessment of the dominant tumour nodule (the largest nodule) and derived by adding the primary grade (defined as that occupying the greatest area) to the secondary grade (that occupying the second largest area). In general, the dominant nodule has the highest Gleason score; however, in the unusual situation where there is a smaller nodule (non-dominant nodule) that is composed of higher Gleason grade patterns, the Gleason score of that nodule must also be reported. In radical prostatectomy specimens the dominant or highest grade tumour nodule may show more than two Gleason grades. The grade that is the third most prevalent (i.e., occupies the third largest area in the tumour nodule) is referred to as the tertiary grade.[42] In a radical prostatectomy specimen, where the tertiary grade (usually grade 5) is higher than the primary or secondary grades the tertiary grade is also recorded.[18] There is strong evidence, including a 2007 meta-analysis, that small volumes of tertiary grade 5 patterns (See Fig. S3.02 below) are associated with aggressive pathological features and a higher risk of biochemical recurrence.[43-48] Moreover, a recently published study in a retrospective cohort showed an association between the presence of a tertiary Gleason grade of 4 or 5 in the radical prostatectomy specimen and clinical progression, defined as either local failure or metastasis.[49] The question of how extensive clusters of individual cells, strands or nests without lumina need to be to qualify as tertiary grade 5 is unresolved (for example, whether tertiary grade 5 should exceed 5% of the tumour overall or not).[50] One survey of the current grading practises among genitourinary pathologists found the large majority required identification of such clusters at less than x40 magnification.[51] Another investigation, while reporting under diagnosis of Gleason grade/pattern 5 in prostatic needle biopsies specimens, stressed that pathologists should have a high threshold before diagnosing Gleason pattern 5, and not assign this grade on the basis of a few individual cells or solid nests that could represent tangential sectioning of poorly formed Gleason pattern 4 glands.[52]

Figure S3.02 Gleason grade 5 carcinoma

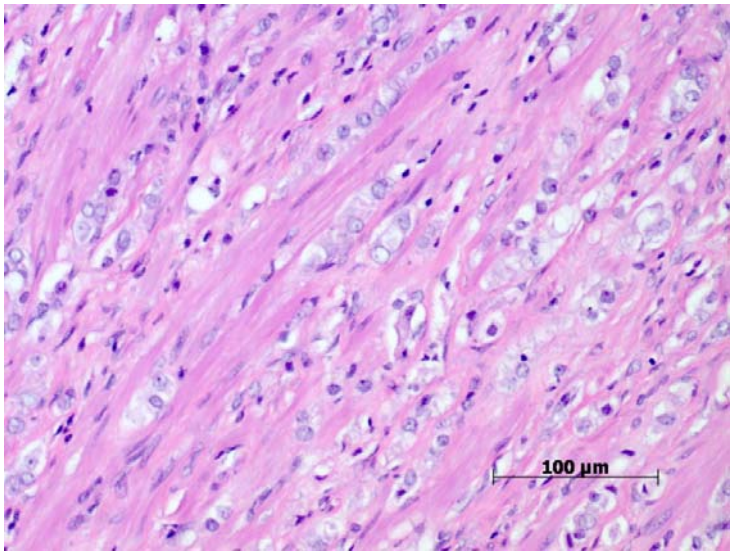


Table S3.02a Gleason grading

Gleason grade	Criteria	Comments
1	Closely packed small regular glands forming a circumscribed rounded nodule	Very rarely used in radical prostatectomy specimen reports. Do not use for needle biopsy specimens
2	Glands more loosely arranged; not quite as uniform; fairly circumscribed but may have minimal infiltration at margins	May be used in radical prostatectomy and TURP specimen reports. Do not use for needle biopsies
3	Discrete glandular units/acini with marked variation in size and shape; infiltrates in and amongst benign prostatic tissue Very rarely cribriform (see below)	
4	Fused micro acinar glands; ill-defined glands with poorly formed lumina; large cribriform irregular glands; hypernephroid	
5	Minimal if any glandular differentiation – solid sheets, cords or single cells. Comedocarcinoma	

Table S3.02b Gleason scoring

Number of different grades present	Proportion of grades present	Comments
1	One of 2, 3, 4 or 5 only	Double grade to get score (eg 4+4=8) Record for dominant nodule +/- nondominant (smaller) nodule if of higher grade (if present)
2 – Primary and secondary	Grades mixed	Report both grades, dominant pattern* first (2+3, 3+4, 4+3 ..) Record for dominant nodule +/- nondominant (smaller) nodule if of higher grade (if present)
	Secondary grade is lower and of limited amount (<5%)	Ignore lower grade – 4+3 becomes 4+4 Record for dominant nodule +/- non dominant (smaller) nodule if of higher grade (if present)
	Secondary grade is higher and of limited amount (<5%)	Include higher grade – 3+3 becomes 3+4 Record for dominant nodule +/- non dominant (smaller) nodule if of higher grade (if present)
3 – Primary, secondary and tertiary	Grades 2, 3, 4 or 5	Report dominant grade (largest area) first, then secondary grade (second largest area), then tertiary grade (only if 4 or 5) eg 3+4=7 with tertiary grade 5 eg 2+3=5 with tertiary grade 4 Record for dominant nodule +/- non dominant (smaller) nodule if of higher grade (if present)

Notes:
Dominant (primary) grade is that which occupies the greatest area.
For radical prostatectomy specimens secondary grade is defined as that which occupies the second greatest area.
For radical prostatectomy specimens tertiary grade is defined as that which occupies the third greatest area (provided that it is higher than the primary and secondary grades).

Table S3.02c Gleason scoring of cribriform patterns

Cribriform pattern	Morphology	Comments
Grade 3	Small, well circumscribed, round with smooth regular edges	Rare. Should be used only rarely in scoring
Grade 4	Irregular cribriform and fused gland masses visible at low power	Should include nearly all cribriform patterns
Grade 5	Any cribriform area with necrosis	Comedonecrosis
PIN		Do not include in score
Intraductal carcinoma	Branched architecture of high grade intraductal proliferation filling lumen	Include as Grade 4 (or 5 if comedonecrosis)

PIN = prostatic intraepithelial neoplasia

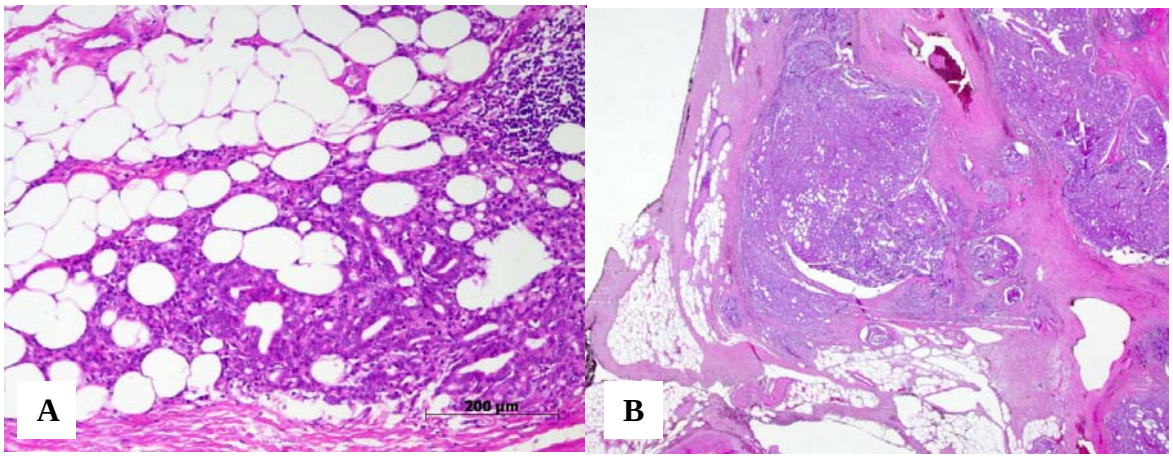
Table S3.02d Gleason scoring of unusual patterns

Pattern	Morphology	Comment
Vacuoles	Cytoplasmic change seen in all grades	Grade as if vacuoles were absent, on the underlying architecture
Mucin extravasation		Grade as if were absent
Mucinous fibroplasia	Collagenous micronodules	Grade as if were absent
Glomeruloid structures		Grade as 4
Foamy gland change		Grade as if were absent
Small cell neuroendocrine		Do not assign a grade

S3.03	**Extraprostatic extension (EPE) must be recorded.**	
	CS3.03a	Extraprostatic extension (EPE), defined as the extension of tumour beyond the confines of the gland into the periprostatic soft tissue, is a required (core) element of the ICCR dataset as it is a significant predictor of recurrence in node negative patients.[30,53] EPE replaced earlier, less clearly defined terms, such capsular penetration, perforation or invasion, following a 1996 Consensus Conference.[54] The assessment of EPE can be difficult, as the prostate is not surrounded by a discrete, well defined fibrous capsule,[55] but rather of a band of concentrically placed fibromuscular tissue that is an inseparable component of the prostatic stroma.[56] 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) (See Fig. S3.03 (i)A below); (2) neoplastic glands surrounding nerves in the neurovascular bundle (posterolaterally); (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—as 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.[56-57] 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 (See Fig. S3.03 (i)B below).[30,57] The presence of cancer within fibrous stroma that is in the same tissue plane as adipose tissue on either side is a helpful indictor 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 prostatic glandular tissue.[57-58]

Figure S3.03 (i) Extraprostatic extension (EPE)



A. Carcinoma infiltrating extraprostatic adipose and fibrous tissue.
B. A nodular extension of tumour bulging beyond the normal contour of the prostate gland.

Figure S3.03 (ii) Extraprostatic extension.

A. Carcinoma confined to prostate gland

LEGEND:

Inked surgical margin

Benign prostatic glands

Fatty tissue

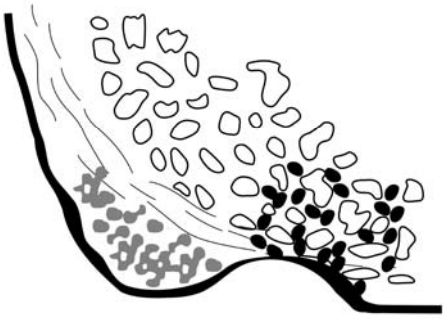
Fibromuscular stroma

Cancer cells

B. Extraprostatic extension with stromal reaction; margin not involved

C. Extraprostatic extension with tumour cells within fat; margin not involved.

D. Positive surgical margin in an area of capsular incision



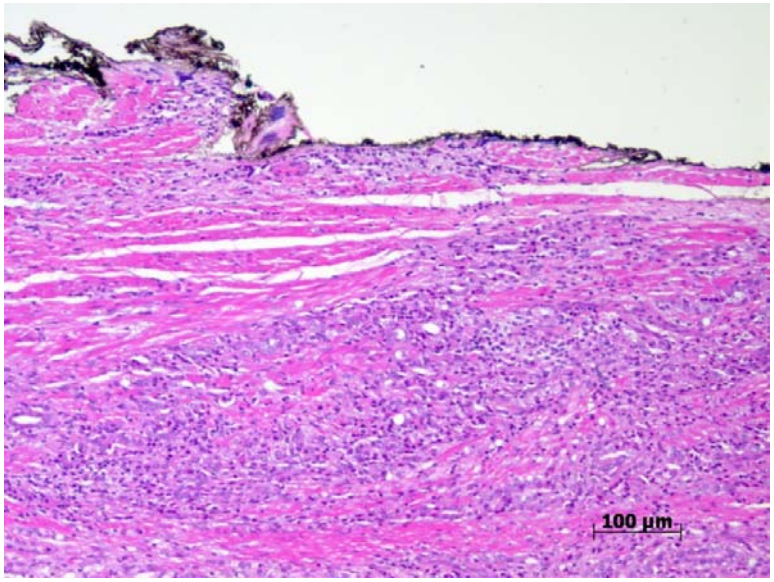
S3.04	**The EPE extent must be reported as focal or non-focal.**	
	CS3.04a	Categorisation of the extent of EPE as focal or non-focal (also referred to as 'established' or 'extensive') is a required (core) item in the ICCR dataset. Focal EPE was originally defined no more than "a few " neoplastic glands just outside the prostate, then subsequently, in a more semi-quantified manner, as extraprostatic glands which occupy no more than one high power field in no more than two sections, with extensive EPE representing anything more than this.[30] 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.[59] 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 any EPE is important, as both focal and extensive EPE are associated with a significantly higher risk of recurrence at both 5 and 10 years.[30,53] Following radical prostatectomy, the progression-free probability for node negative patients with uninvolved seminal vesicles at 10 years for organ confined disease is 85–89%, falling to 67–69% for focal EPE and to 36–58% for extensive EPE.[30,53]
G3.04	The location of extraprostatic extension (EPE) may be recorded.	
	CG3.04a	Select all that apply: • Lateral • Postero-lateral • Posterior • Anterior • Bladder neck • Apical • Other (specify)
	CG3.04b	Since it was considered a generic element forming part of a comprehensive pathology report, the location of any extraprostatic extension present has been included in the recommended (non-core) dataset, despite the lack of published evidence for its influence on staging, prognosis or treatment.[57] It provides potentially useful information to the urologist, enabling correlation with clinical findings and any pre-

		operative imaging studies performed.
S3.05	**Margin status must be recorded.**	
	CS3.05a	Record the following: • whether margins are involved, not involved or indeterminate • the location(s) (select all that apply): – Lateral – Postero-lateral – Posterior – Anterior – Bladder neck – Apical – Other (specify)
	CS3.05b	A positive surgical margin (PSM) 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 multivariate analysis.[58,60-64] Moreover, positive margins are associated with a 2.6-fold increased unadjusted risk of prostate cancer specific mortality.[65] 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[58,66] (See Fig. S3.05 below). PSMs are reported in between 10 – 48% of patients treated by radical prostatectomy for both organ confined and non-organ confined prostate cancer with the rates in the lower range typically found in more modern cohorts.[64,67-69] 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.[70-72] 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.[70,72]

CS3.05c	In very rare cases, it can be impossible to ascertain whether the surgical margin is truly positive.[73] This can be due to marked crush or thermal artefact causing glandular distortion along the margin so that it cannot be histologically determined whether the crushed glands are malignant or whether the margin is actually positive rather than artificially retracted due to heat coagulation or tissue compression. This can be associated with haemostatic staples, surgical dissection or retraction. On these rare occasions, the margins should be reported as equivocal.
CS3.05d	Another cause of difficulty is irregular tracking of ink in areas of tears or lacerations.[73-74] This can occur during handling of the specimen in the operating theatre, transportation or processing in the laboratory. It is important not to misdiagnose PSM, as some of these patients receive postoperative radiotherapy with the associated risk of significant complications.[75]
CS3.05e	Stating the location of the PSM is useful information for the urologist who can then modify future operations to avoid iatrogenic margin positivity and increase the likelihood of curative surgery. 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.[69,76]

Figure S3.05 **Positive surgical margin (PSM). Prostatic adenocarcinoma extending to black inked margin (top)**



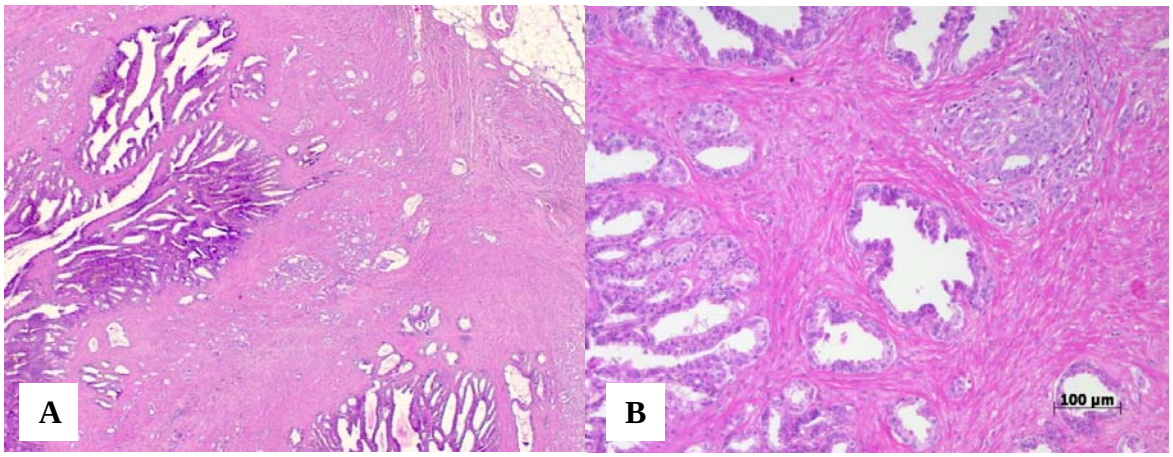
G3.05	The extent (total) of margin involvement may be recorded.	
	CG3.05a	Extent is measured as the linear cumulative length of all positive margins.[77] Although a positive surgical marginal (PSM) has a significant adverse impact on the overall likelihood of progression-free survival, in most published series only about a third of individual patients with a PSM will experience biochemical recurrence.[60-61,67,78] Studies aiming to better quantify the risk associated with a PSM have focussed on a number of factors such as number, location and extent of positive margins. However, the published data relating to these parameters are somewhat contradictory, and the expert panel considered that there is only sufficient evidence to include measurement of the length of margin involved by carcinoma as an element in the ICCR dataset at present.[70,72,74,78-82] In particular, the 5 year PSA recurrence risk appears to be significantly greater when the length of the involved margin is 3mm or more, (53% versus 14%).[79-80] However, in one series, Cao *et al* [81]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 positive surgical margin after radical prostatectomy was greater in intermediate and high risk groups (based on Gleason score and pre-biopsy PSA) than in low risk patients.[63] Further studies of such factors potentially affecting the impact of PSMs are required before there is sufficient evidence justifying their inclusion as required (core) data elements.

G3.06	Gleason score at involved margins may be recorded.	
	CG3.06a	Following review of feedback on the draft prostate cancer (radical prostatectomy) dataset and commentary, the expert panel has included the Gleason score of the tumour at the positive surgical margin as a recommended (non-core) element of the ICCR dataset. Three recently published papers have found that Gleason score or grade of the tumour at the positive surgical margin is an independent predictor of biochemical recurrence and may aid optimal selection of patients for adjuvant therapy.[78,83-84] In one of these studies patients with Gleason grade 4 or 5 carcinoma (score 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 grade 3 (score 3+3) at the margin. Moreover, men with Gleason score 3 at the PSM had a similar 5-year biochemical relapse-free survival rate to those with negative margins.[78] Another study, restricted to men with dominant nodule Gleason score 7 and non-focal EPE, also found that the grade of cancer at the site of a PSM was associated with biochemical recurrence.[83] In the event there are multiple positive margins with differently scored cancers present, the highest score should be recorded.
G3.07	The type of margin positivity may be recorded.	
	CG3.07a	This should be recorded as: • EPE • Intraprostatic (capsular incision)
	CG3.07b	Intraprostatic margin involvement or capsular incision (CI) occurs when the urologist inadvertently develops the resection margin within the plane of the prostate rather than outside the capsule. CI with a positive surgical margin is diagnosed when malignant glands are cut across adjacent to benign prostatic glands.[56] 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.[85-87] According to the largest series published, 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 nonfocal EPE and positive margins.[80] 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 capsular incision 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 positive surgical margin with EPE, similarly to margin involvement when there is cancer in adipose tissue.[86] 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.[58,86] 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.[57]
S3.06	**Presence or absence of seminal vesicle involvement must be recorded.**	
	CS3.06a	State if seminal vesicles are involved or not involved.
	CS3.06b	The expert panel included seminal vesicle invasion (SVI) as a required (core) element of the ICCR dataset as SVI is a well-established, independent, adverse prognostic factor[58,88-89] and an integral component of the commonly used nomograms and tables that predict risk of post prostatectomy cancer recurrence.[11-12,41] The finding of SVI at the time of radical prostatectomy is associated with a significantly increased risk of PSA recurrence[88-90] and the presence of SVI and a positive surgical margin may also influence the response to adjuvant radiotherapy.[91-92] Bilaterality and extent of extraprostatic SVI are not independently predictive of prognosis and were not included as required or recommended items in the ICCR dataset.[79] Different definitions of seminal vesicle invasion have been used over the years complicating comparison of the published survival analyses.[91,93] Older definitions including involvement of the adipose tissue or adventitia around the seminal vesicle are problematic with regard to distinction from EPE; while in other studies a distinction between intraprostatic and extraprostatic seminal vesicle invasion has not always been made, impeding comparisons between series.[94-95] 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 (See Fig.S3.06 below).[93] Only extraprostatic seminal vesicle is included in this definition of SVI, since it is difficult differentiating between intraprostatic seminal vesicle and ejaculatory duct invasion as these structures merge without a clear histological cut off.[96] It was concluded that older definitions that include invasion of the adipose tissue around the seminal vesicle are

		imprecise and should be discarded.[91,93]
	CS3.06c	If one or more of the seminal vesicles are involved by cancer, specify whether left side, right side or both.

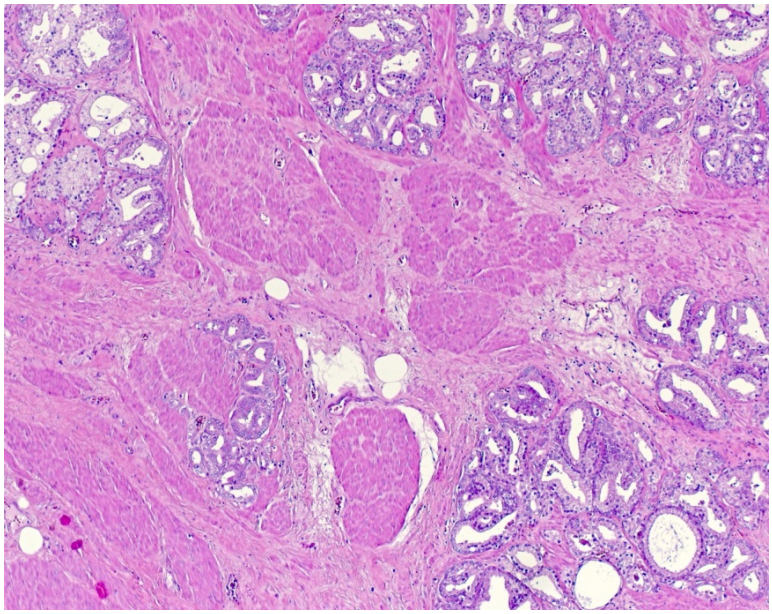
Figure S3.06 Seminal vesicle invasion (SVI)



A. Low power view showing carcinoma centre and seminal vesicle lumen on left.
B. Medium power view of seminal vesicle invasion by prostatic adenocarcinoma (top right)

G3.08	Presence or absence of bladder neck involvement should be recorded.	
	CG3.08a	Microscopically, 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 (Fig. G3.08).[97] Microscopic bladder neck involvement is a significant predictor of PSA-recurrence in univariate analysis, although not in multivariate modelling in most studies.[98-100] Neoplastic glands intermixed with benign prostatic glands at the bladder neck margin is equivalent to capsular incision rather than true bladder neck invasion.[98,101-102] In the 7th Edition of the 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.[15,97]

Figure G3.08 **Neoplastic glands within the thick smooth muscle bundles of the bladder neck.**



S3.07	**Lymph node status must be recorded.**	
	CS3.07a	State the number of lymph nodes examined and the number of positive lymph nodes.
	CS3.07b	Lymph node involvement is a well established independent adverse prognostic factor[58,93] and is an integral component of the commonly used nomograms that predict the risk of post prostatectomy disease recurrence.[12] There is little published data on the prognostic significance of isolated tumour cells (clusters less than <200 µm in greatest dimension) in prostate cancer and insufficient evidence at present to support the routine use of immunohistochemistry as an ancillary technique in the identification of lymph node involvement.
G3.09	The laterality of any lymph node involvement should be recorded.	
	CG3.09a	The site of involved lymph nodes may also be recorded.

G3.10	The maximum dimension of the largest lymph node deposit may be recorded.	
	CG3.10a	The diameter of the largest metastatic deposit correlated with distant metastasis and cancer-specific survival in two studies but not in another[103-105] and this factor has been included in the recommended (non-core) dataset rather than as a required (core) item. There was consensus

		(81% respondents) at the 2009 ISUP Conference that that the diameter of the largest lymph node metastasis should be included in the pathology reports on radical prostatectomy.[93]
G3.11	Lymphovascular invasion should be recorded.	

CG3.11a Lymphovascular invasion is defined as the unequivocal presence of tumour cells within endothelial-lined spaces with no underlying muscular walls.[106-107] 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. Immunohistochemistry 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 (LVI) invasion has been reported to be associated with decreased time to biochemical progression, distant metastases and overall survival after radical prostatectomy.[106-111] 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.[106-107,109,111-112] However, the independent prognostic value of LVI is uncertain as definitions of LVI have varied between studies and most included a substantial number of patients with lymph node metastases or SVI, failing to stratify patients into clinical meaningful categories. Further well designed studies with standardised definitions are necessary to confirm the independent prognostic significance of LVI.

G3.12 Comments should be included, if appropriate.

CG3.12a Free text entry to allow any additional, unusual or unexpected findings to be reported.

General commentary

The tumour zone may be reported.

Specification of zones (ie peripheral, central, transition) involved by tumour may be included, if desired. Zonal location of prostate cancer is not an independent prognostic indicator on multivariate analysis. The zonal location of the cancer can be difficult to determine with tumours commonly overlapping the peripheral and transition zones.

4 Ancillary studies findings

No ancillary tests are currently used on a routine diagnostic basis for prostate cancer.

5 Synthesis and overview

Information that is synthesised from multiple modalities and therefore cannot reside solely in any one of the preceding chapters is described here.

For example, *tumour stage* is synthesised from multiple classes of information – clinical, macroscopic and microscopic.

By definition, synthetic elements are inferential rather than observational, often representing high-level information that is likely to form part of the 'Summary' or 'Diagnosis' section in the final formatted report.

Overarching case comment is synthesis in narrative format. Although it may not necessarily be required in any given report, the provision of the facility for overarching commentary in a cancer report is essential.

S5.01	**The tumour stage must be recorded according to the AJCC/UICC TNM system (7th edition).[15]** Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science and Business Media LLC, www.springerlink.com.	
	CS5.01a	The pathological tumour (T) and lymph node (N) categories were considered as generic required (core) elements for all ICCR cancer datasets Staging data should be assessed according to the most recent edition of the AJCC/UICC Staging Manuals (7th Edition)[15] except pT2 subcategorization should be considered optional in line with ISUP recommendations as it lacks additional prognostic significance.[113] The reference document: TNM Supplement: A commentary on uniform use, 4th Edition (C Wittekind editor) may be of assistance when staging.[114]
	CS5.01b	*Pathologic* **primary tumour (T)** pTX Primary tumour cannot be assessed pT0 No evidence of primary tumour * pT2 Organ Confined pT2a Unilateral, one-half of one side or less pT2b Unilateral, involving more than one-half of side but not both sides pT2c Bilateral disease pT3 Extraprostatic extension

		pT3a Extraprostatic extension or microscopic invasion of bladder neck** pT3b Seminal vesicle invasion pT4 Invasion of rectum, levator muscles and/or pelvic wall. Notes: 1. Invasion into the prostate apex or into (but not beyond) the prostate capsule is not classified as T3, but as T2. **Note:* There is no pathologic T1 classification for radical prostatectomy specimens *** Note:* Positive surgical margin should be indicated by an R1 descriptor (residual microscopic disease)
		Pathologic **regional lymph nodes (N)** pNX Regional lymph nodes not sampled pN0 No positive regional nodes. pN1 Metastasis in regional node(s).
		Clinical and pathologic **distant metastasis (M)** Not applicable **OR** M0 No distant metastasis M1 Distant metastasis M1a Non-regional lymph node(s)* M1b Bone(s) M1c Other site(s) with or without bone disease **Note:* When more than one site of metastasis is present, the most advanced category is used. pM1c is most advanced.

S5.02 The year of publication and edition of the cancer staging system used in S5.01 must be included in the report.

G5.01 The 'Diagnostic summary' section of the final formatted report should include:

a. nature of specimen (S1.02)

b. tumour type (S3.01)

c. Gleason score (S3.02)

d. tumour stage (S5.01 & S5.02)

e. whether or not the specimen margins are involved (S3.05)

S5.03 The reporting system must provide a field for free text or narrative in which the reporting pathologist can give overarching case comment.

CS5.03a This field may be used, for example, to:

- explain the decision-making pathway, or any elements of clinicopathological ambiguity, or factors affecting diagnostic certainty, thereby allowing communication of diagnostic subtlety or nuance that is beyond synoptic capture
- give recommendations for further action or investigation
- document further consultation or results still pending.

CS5.03b Use of this field is at the discretion of the reporting pathologist.

6 Structured checklist

The following checklist includes the standards and guidelines for this protocol which must be considered when reporting, in the simplest possible form. The summation of all 'standards' is equivalent to the 'minimum data set' for prostate cancer. For emphasis, standards (mandatory elements) are formatted in bold font.

S6.01 The structured checklist provided may be modified as required but with the following restrictions:

a. All standards and their respective naming conventions, definitions and value lists must be adhered to.

b. Guidelines are not mandatory but are recommendations and where used, must follow the naming conventions, definitions and value lists given in the protocol.

G6.01 The order of information and design of the checklist may be varied according to the laboratory information system (LIS) capabilities and as described in *Functional Requirements for Structured Pathology Reporting of Cancer* Protocols.[115]

CG6.01a Where the LIS allows dissociation between data entry and report format, the structured checklist is usually best formatted to follow pathologist workflow. In this situation, the elements of synthesis or conclusions are necessarily at the end. The report format is then optimised independently by the LIS.

CG6.01b Where the LIS does not allow dissociation between data entry and report format, (for example where only a single text field is provided for the report), pathologists may elect to create a checklist in the format of the final report. In this situation, communication with the clinician takes precedence and the checklist design is according to principles given in Chapter 7.

G6.02 Where the checklist is used as a report template (see G6.01), the principles in Chapter 7 and Appendix 2 apply.

CG6.02a All extraneous information, tick boxes and unused values should be deleted.

G6.03 Additional comment may be added to an individual response where necessary to describe any uncertainty or nuance in the selection of a prescribed response in the checklist. Additional comment is not required where the prescribed response is adequate.

Item descriptions in italics are conditional on previous responses.

Values in all caps are headings with sub values.

S/G	Item description	Response type	Conditional
Clinical information and surgical handling			
S1.01	**Demographic information provided**		
S1.02	**Clinical information provided on request form**	**Text** OR **Structured entry as below:**	
	Surgical procedure	**Text**	
	Nature of specimen	**Text**	
	Clinical history (including Gleason grade and score of previous specimens)	**Text**	
	Previous therapy	**Text**	
	**Pre-biopsy serum PSA**	**Numeric: ___ ng/mL** **OR** **Not available**	
	Relevant clinical information for clinicopathological staging	**Text**	
S1.03	**Pathology accession number**	**Alpha-numeric**	

S1.04	**Principal clinician**	**Text**	
G1.01	Comments	**Text**	
Macroscopic findings			
S2.01	**Specimen weight (ie Prostate without seminal vesicles)**	**Numeric: ____g**	
G2.01	Specimen dimensions (prostate)	**Numeric: __x__x__mm**	
S2.02	**Seminal vesicles**	**Single selection value list:** • Absent • Present (partially or completely resected)	
S2.03	**Lymph nodes**	**Single selection value list:** • Absent • Present	**If present consider recording G2.02.**
G2.02	*Laterality*	***Single selection value list:*** • *Left* • *Right* • *Bilateral*	

	Site(s) and numbers of lymph nodes	***Text:*** *Site* ***AND*** ***Numeric:*** *Number of LNs* ***from this site*** *Notes:* *Note that the site and number of LNs for that site may need to be repeated for each site received.*	
G2.03	Block identification key	**Text**	
G2.04	Additional macroscopic comments	**Text**	
Microscopic findings			
S3.01	**Histological tumour type**	**Multi selection value list (select all that apply):** • Adenocarcinoma (Acinar, usual type) • Adenocarcinoma (Acinar variant eg, foamy, pseudohyperplastic) • Prostatic ductal adenocarcinoma • Adenosquamous carcinoma • Small cell carcinoma • Sarcomatoid carcinoma • Undifferentiated carcinoma, not otherwise specified • Other	**If other, record other type.** **If Adenocarcinoma (Acinar variant eg foamy, pseudohyperplastic) record variant.**

	Other type	***Text***	
	Acinar variant	***Text***	
G3.01	TUMOUR LOCATION		
	Largest nodule located by quadrant	**Single selection value list:** • Right anterior • Right posterior • Left anterior • Left posterior	
	Largest nodule located by plane	**Single selection value list:** • Apex • Mid • Base of prostate	
	Other nodules >10mm in diameter	**Single selection value list:** • None identified • Present	***If present, record the locations in quadrant and plane***
	Locations by quadrant	***Multi select value list (select all that apply):*** • *Right anterior* • *Right posterior* • *Left anterior* • *Left posterior*	
	Locations by plane	***Multi select value list (select all that apply):*** • *Apex*	

		• *Mid* • *Base of prostate*	
G3.02	Intraglandular extent	**Numeric: ___%**	
G3.03	Maximum size of dominant nodule	**Numeric: ___mm**	
S3.02	**HISTOLOGICAL GRADE**		
	Primary Gleason grade	**Numeric: ___ (1-5)**	
	Secondary Gleason grade	**Numeric: ___(1-5)**	
	Tertiary Gleason grade	**Numeric: ___(3-5) or Not applicable**	
	Gleason score	**Text**	
S3.03	**Extraprostatic extension**	**Single selection value list:** • Not identified • Present • Indeterminate	**If present, record S3.04 extent.** **If present, consider recording G3.04**
S3.04	***Extent***	***Single selection value list:*** • *Non-focal* • *Focal*	

G3.04	*Location(s) of EPE*	***Multi select value list (select all that apply):*** • *Lateral* • *Postero-lateral* • *Posterior* • *Anterior* • *Bladder neck* • *Apical* • *Other*	**If other, specify the other location.**
	Other location	***Text***	
S3.05	**Margin status**	**Single selection value list:** • Not involved • Involved • Indeterminate	**If involved record the location(s) and optionally G3.05**
	Location(s)	***Multi select value list (select all that apply):*** • *Lateral* • *Postero-lateral* • *Posterior* • *Anterior* • *Bladder neck* • *Apical* • *Other (specify)*	

G3.05	*Extent (total)*	***Numeric: ___mm*** <u>*Notes:*</u> *If more than 1 positive margin, record the cummulative length.*	***Conditional on margin involvement***
G3.06	*Gleason score at margin*	***Numeric:*** __ <u>*Notes*</u>*:* *If more than 1 positive margin, record the highest score*	***Conditional on margin involvement***
G3.07	*Type of margin positivity*	***Multi select value list (select all that apply):*** • *EPE* • *Intraprostatic (capsular incision)*	***Conditional on margin involvement***
S3.06	**Seminal vesicles**	**Single selection value list:** • Not applicable • Not involved • Involved	**If involved, record side**
	Side	***Single selection value list:*** • *Left side* • *Right side* • *Both*	
G3.08	Bladder neck	**Single selection value list:** • Not applicable	

		• Not involved • Involved	
S3.07	***LYMPH NODE STATUS***		***This is conditional on receipt of LNs in S2.03.***
	Number of lymph nodes examined	***Numeric:*** ___	
	Number of positive lymph nodes	***Numeric:*** ___	***If >0 consider recording G3.09 and G3.10.***
G3.09	*Laterality*	***Single selection value list:*** • *Left* • *Right* • *Bilateral*	***Consider recording the site(s) of involved nodes***
	Site(s) of involved nodes	***Text***	
G3.10	*Maximum dimension of largest deposit*	***Numeric:*** ___***mm***	
G3.11	Lymphovascular invasion	**Single selection value list:** • Not identified • Present • Indeterminate	
G3.12	Additional microscopic comment	**Text**	
Synthesis and overview			
S5.01	**PATHOLOGICAL STAGING (AJCC 7TH EDITION)**		

	Primary tumour (T)	**Single selection value list :** TX Primary tumour cannot be assessed T0 No evidence of primary tumour* T2 Organ Confined T2a Unilateral, one-half of one side or less T2b Unilateral, involving more than one-half of side but not both sides T2c Bilateral disease T3 Extraprostatic extension T3a Extraprostatic extension or microscopic invasion of bladder neck** T3b Seminal vesicle invasion T4 Invasion of rectum, levator muscles and/or pelvic wall. Notes: 1. Invasion into the prostate apex or into (but not beyond) the prostate capsule is not classified as T3, but as T2. * There is no pathologic T1 classification for radical prostatectomy specimens ** Positive surgical margin should be indicated by an R1 descriptor (residual microscopic disease)	

	Regional lymph nodes (N)	**Single selection value list :** NX Regional lymph nodes not sampled. N0 No positive regional nodes. N1 Metastasis in regional node(s).	
	Distant metastasis (M)	**Single selection value list :** Not applicable **OR** M0 No distant metastasis. M1 Distant metastasis M1a Non-regional lymph node(s)* M1b Bone(s) M1c Other site(s) with or without bone disease **Note:* When more than one site of metastasis is present, the most advanced category is used. M1c is most advanced.	
S5.02	**Year and edition of staging system**	**Numeric:** year **AND** **Text:** Edition eg 1st, 2nd etc	
G5.01	Diagnostic summary Include:	**Text**	

	a. specimen type b. tumour type c. Gleason score d. tumour stage e. whether or not the specimen margins are involved		
S5.03	**Overarching comment**	**Text**	

7 Formatting of pathology reports

Good formatting of the pathology report is essential for optimising communication with the clinician, and will be an important contributor to the success of cancer reporting protocols. The report should be formatted to provide information clearly and unambiguously to the treating doctors, and should be organised with their use of the report in mind. In this sense, the report differs from the structured checklist, which is organised with the pathologists' workflow as a priority.

Uniformity in the format as well as in the data items of cancer reports between laboratories makes it easier for treating doctors to understand the reports; it is therefore seen as an important element of the systematic reporting of cancer. For guidance on formatting pathology reports, please refer to Appendix 2. An example of a pathology report is shown in Appendix 3.

Appendix 1 Pathology request form for prostate cancer

This appendix describes the information that should be collected before the pathology test.

Clinical information relating to presenting symptoms and spread of disease — including pretreatment prostate specific antigen (PSA) — are necessary for staging of the tumour. Details of previous therapy are required because this often impacts upon the grading of the tumour and this needs to be taken into account by the examining pathologist. Similar information is required regardless of whether the specimen is a core biopsy, transurethral resection (TUR) or radical prostatectomy.

Some of this information can be provided on generic pathology request forms; any additional information required specifically for the reporting of Prostate cancer may be provided by the clinician on a separate request information sheet. An example request information sheet is included below. Elements which are in bold text are those which pathologists consider to be required information. Those in non-bold text are recommended.

Also included in this appendix are the procedures that are recommended before handover of specimens to the laboratory.

Patient information

- **Adequate demographic and request information should be provided with the specimen.**
  - Items relevant to cancer reporting protocols include:
    - patient name
    - date of birth
    - sex
    - identification and contact details of requesting doctor
    - date of request
  - The patient's ethnicity should be recorded, if known. In particular whether the patient is of aboriginal or Torres Strait islander origin. This is in support of a government initiative to monitor the health of indigenous Australians particularly in relation to cancer.
- The patient's health identifiers should be provided.
  - The patient's health identifiers may include the patient's Medical Record Number as well as a national health number such as a patient's Medicare number (Australia), Individual Healthcare Identifier (IHI) (Australia) or the National Healthcare Identifier (New Zealand).

Clinical Information

- **The nature of the specimen should be clearly stated.**

  - For prostatectomy specimens, it is important to state the nature of the surgical procedure — open prostatectomy (for benign disease), or radical prostatectomy (for cancer) and the completeness of excision of the tumour. On those occasions where the surgeon is aware that a surgical incision into the prostate has produced an artificial margin inside the true resection margin, this should be specified in order to ensure that a positive surgical excision margin is not incorrectly reported.

- Clinical history should be recorded.

  - In many cases the clinical history will influence the ultimate diagnosis and may provide information which will assist in providing prognostic information. Specifically, the Gleason grade and score of prostate cancer in any previously submitted specimen should be provided. This permits assessment of any progression of the tumour towards a more undifferentiated state, which itself is of prognostic significance.

  - Symptoms due to prostate cancer are often nonspecific and are often similar to those of benign prostatic hyperplasia. Impotence, priapism or haemospermia may be the presenting feature but such cases are rare. Metastatic tumour is usually associated with bone pain and, in advanced disease, symptoms secondary to organ involvement may be the first clinical evidence of prostate cancer. Most organ-confined prostate cancers are asymptomatic.[116] Approximately 25% of prostate cancers are diagnosed as a result of symptoms and in nearly all of these cases extraprostatic spread of tumour has occurred.[117]

- Previous therapy should be described.

  - Adjuvant radiation and endocrine therapy for prostate cancer has 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 specimens. This applies to prostate biopsies taken to evaluate local disease or to salvage radical prostatectomy specimens; to transurethral resection of the prostate (TURP) undertaken to relieve obstructive symptoms; and to biopsies of metastatic tumour.

  - Following irradiation, benign, acinar epithelium shows nuclear enlargement and nucleolar prominence[118] while basal cells may show cytologic atypia, nuclear enlargement and nuclear smudging.[119] There may also be increased stromal fibrosis, which may resemble tumour-induced desmoplasia. These changes may persist for a

considerable period, have 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.[119-120] It is important to document any previous radiotherapy to help the pathologist to interpret changes accurately. Failure to do so could lead to an incorrect diagnosis of malignancy.

- Radiotherapy has a variable effect on prostate carcinoma. There is debate as to whether or not Gleason grading is appropriate [118,121] because radiation may be associated with apparent upgrading in prostatectomy specimens.[122] It has been suggested that in biopsies undertaken following radiotherapy, tumours that do not show any radiation effect should be graded, while tumours that show a treatment effect should not.[123]

- Neoadjuvant androgen blockade induces basal cell hyperplasia and cytoplasmic vacuolation in benign prostatic tissue, and this is unlikely to be confused with malignancy.[124] 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.[122,124] The current consensus is that these tumours should not be graded.[125]

➢	Pre-biopsy serum PSA value should be recorded.	
	•	Pre-biopsy serum PSA is essential for stage grouping in the 7th Edition of the AJCC/UICC TNM staging system.[15] In addition, 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.[11-12,41]

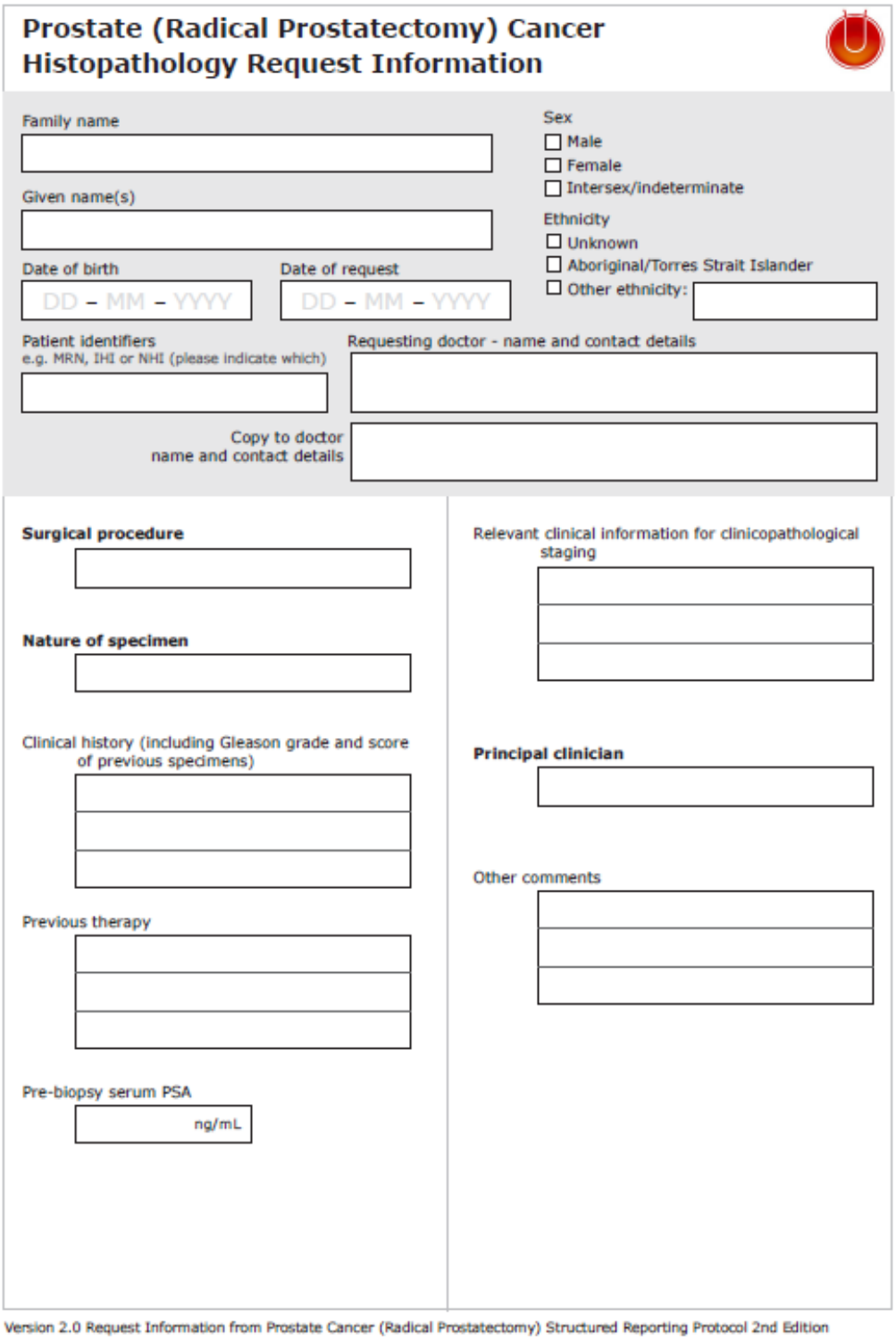
➢ Relevant clinical information should be recorded to enable accurate clinicopathological staging.

- Clinical details about the anatomical extent of the tumour should be provided. For radical prostatectomy specimens the details should include a comment about the apparent completeness of resection, the presence or absence of clinically known metastatic disease and the site of any known metastases. Information relating to the presence or absence of extraprostatic tumour, as well as metastases, is rarely evident from examination of the surgical specimen, and details of this should be included in the specimen request form to facilitate accurate staging.

➢ Comments should be included, if appropriate.

- Space for free text should be included to encourage reporting of ambiguity, or for the addition of other comments.

Example Request Information Sheet



Prostate (Radical Prostatectomy) Cancer Histopathology Request Information

Family name

Given name(s)

Date of birth DD – MM – YYYY

Date of request DD – MM – YYYY

Sex
- ☐ Male
- ☐ Female
- ☐ Intersex/indeterminate

Ethnicity
- ☐ Unknown
- ☐ Aboriginal/Torres Strait Islander
- ☐ Other ethnicity:

Patient identifiers
e.g. MRN, IHI or NHI (please indicate which)

Requesting doctor - name and contact details

Copy to doctor name and contact details

Surgical procedure

Nature of specimen

Clinical history (including Gleason grade and score of previous specimens)

Previous therapy

Pre-biopsy serum PSA ng/mL

Relevant clinical information for clinicopathological staging

Principal clinician

Other comments

Version 2.0 Request Information from Prostate Cancer (Radical Prostatectomy) Structured Reporting Protocol 2nd Edition

The above Request Information Sheet is published to the RCPA website.

Appendix 2 Guidelines for formatting of a pathology report

Layout

Headings and spaces should be used to indicate subsections of the report, and heading hierarchies should be used where the LIS allows it. Heading hierarchies may be defined by a combination of case, font size, style and, if necessary, indentation.

Grouping like data elements under headings and using 'white space' assists in rapid transfer of information.[126]

Descriptive titles and headings should be consistent across the protocol, checklist and report.

When reporting on different tumour types, similar layout of headings and blocks of data should be used, and this layout should be maintained over time.

Consistent positioning speeds data transfer and, over time, may reduce the need for field descriptions or headings, thus reducing unnecessary information or 'clutter'.

Within any given subsection, information density should be optimised to assist in data assimilation and recall. The following strategies should be used:

- Configure reports in such a way that data elements are 'chunked' into a single unit to help improve recall for the clinician.[126]
- Reduce 'clutter' to a minimum.[126]Thus, information that is not part of the protocol (eg billing information or SNOMED codes) should not appear on the reports or should be minimised.
- Reduce the use of formatting elements (eg bold, underlining or use of footnotes) because these increase clutter and may distract the reader from the key information.

Where a structured report checklist is used as a template for the actual report, any values provided in the checklist but not applying to the case in question must be deleted from the formatted report.

Reports should be formatted with an understanding of the potential for the information to 'mutate' or be degraded as the report is transferred from the LIS to other health information systems.

As a report is transferred between systems:

- text characteristics such as font type, size, bold, italics and colour are often lost
- tables are likely to be corrupted as vertical alignment of text is lost when fixed font widths of the LIS are rendered as proportional fonts on screen or in print
- spaces, tabs and blank lines may be stripped from the report, disrupting the formatting
- supplementary reports may merge into the initial report.

Appendix 3 Example of a pathology report

Citizen, George W.
C/O Paradise Close
Sunset Bay Resort
Nar Nar Goon East, 3181

Male

DOB 1/7/1951
MRN FMC1096785

Lab Ref: **13/P28460**
Referred: 30/2/2013

Copy to: Dr G. Gleason
Rainforest Cancer Centre.
46 Smith Road,
Woop Woop, 3478

Referred by: Dr V. Smith
Suite 3, AJC Medical Centre,
Bunyip Crescent
Nar Nar Goon West, 3182

RADICAL PROSTATECTOMY STRUCTURED REPORT

Diagnostic Summary

Radical prostatectomy:

Adenocarcinoma (Acinar);
Gleason score (ISUP 2005) 4+3 = 7, tertiary grade 5;
AJCC Stage T3a, N0, M0; PSM (R1).

Comment:
1. Focal urothelial carcinoma *in situ* (CIS) is noted in the prostatic urethra. The urethral resection margin appears clear.
2. Equivocal margin involvement (due to crush artefact) by prostatic adenocarcinoma is noted at the apex focally.

Supporting Information

CLINICAL

Surgical procedure:	Radical prostatectomy
Pre-biopsy serum PSA:	8.9 ng/mL
Clinical history:	No symptoms Previous biopsy: Gleason 3+3=6
Previous therapy:	Nil
Clinical stage:	No known metastases

MACROSCOPIC

Specimen weight:	23g without seminal vesicles
Specimen dimensions:	40 x 37 x 30mm
Seminal vesicles:	Present
Lymph nodes:	Present Right pelvic: 2 Left pelvic: 3

MICROSCOPIC

Histological tumour type:	Adenocarcinoma (Acinar, usual type)
Tumour location	
Largest nodule	
Located by quadrant:	Right anterior and right posterior.
Located by plane:	Apex and mid prostate. Focally crosses midline posteriorly.
Other nodules (>10mm)	
Located by quadrant:	Left posterior.
Located by plane:	Base of prostate. Smaller nodules are present.
Maximum size of dominant nodule:	22mm

Histological Grade (ISUP2005):	
Primary Gleason grade:	4
Secondary Gleason Grade:	3
Tertiary Gleason grade:	5
Gleason score:	4+3=7
Extraprostatic extension:	Present
Extent of EPE:	Focal
Location of EPE:	Right posterior quadrant
Margin status:	Involved
Locations:	Right posterior quadrant
Extent(total):	1.3mm linear length
Gleason score of cancer at PSM:	3+4 = 7
Type of margin positivity:	EPE
Seminal vesicles:	Not involved
Bladder neck:	Not involved
Lymph node status	
No. of lymph nodes examined:	5
No. of positive lymph nodes:	0
Lymphovascular invasion:	Not identified

Reported by Dr Bernard Beckstein Authorised 4/3/2013

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