CARCINOMA OF THE URINARY BLADDER

STRUCTURED REPORTING PROTOCOL

(RADICAL CYSTECTOMY, PARTIAL CYSTECTOMY, DIVERTICULECTOMY, CYSTOPROSTATECTOMY)

(2nd Edition 2018)

Incorporating the:
International Collaboration on Cancer Reporting (ICCR)

Dataset for the reporting of Carcinoma of the Bladder – Cystectomy, Cystoprostatectomy and Diverticulectomy.
www.ICCR-Cancer.org
Core Document versions:

1. ICCR Dataset for the Reporting of Carcinoma of the Bladder – Cystectomy, Cystoprostatectomy and Diverticulectomy.
2. AJCC Cancer Staging Manual 8th edition
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   o Numbering of Standards and Guidelines must be retained in the checklist, but can be reduced in size, moved to the end of the checklist item or greyed out or other means to minimise the visual impact.
   
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   o Commentary from the Protocol may be added or hyperlinked to the relevant checklist item.

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The Royal College of Pathologists of Australasia ("College") has developed these protocols as an educational tool to assist pathologists in reporting of relevant information for specific cancers. Each protocol includes “standards” and “guidelines” which are indicators of ‘minimum requirements’ and ‘recommendations’, which reflect the opinion of the relevant expert authoring groups. The use of these standards and guidelines is subject to the clinician’s judgement in each individual case.

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Scope

This protocol contains standards and guidelines for the preparation of structured reports for carcinoma of the urinary bladder in adults. The guidelines can be used in the reporting of radical cystectomy, partial cystectomy, cystoprostatectomy and diverticulectomy specimens but does not include information on the handling and reporting of primary lymphadenectomy specimens. The protocol applies to primary carcinomas (non-invasive and invasive), with or without associated epithelial lesions. Urothelial tumours diagnosed as papilloma or papillary urothelial neoplasm of low malignant potential are not carcinomas and this data set does not apply to those diagnoses. Transurethral resection and biopsy specimens are dealt with in a separate protocol.

Structured reporting aims to improve the completeness and usability of pathology reports for clinicians, and improve decision support for cancer treatment. The protocol provides the framework for the reporting of any bladder tumour, whether as a minimum data set or fully comprehensive report.
Abbreviations

AJCC  American Joint Committee on Cancer
BCG  Bacillus Calmette-Guerin
CIS  Carcinoma in situ
CG  Commentary for a guideline
CS  Commentary for a standard
HG  High grade
ICCR  International Collaboration on Cancer Reporting
ISUP  International Society of Urological Pathology
LIS  laboratory information system
LG  Low grade
LMP  low malignant potential
LVI  lymphovascular invasion
PBS  Pharmaceutical Benefits Scheme
RCPA  Royal College of Pathologists of Australasia
TCC  Transitional cell carcinoma
TNM  tumour-node-metastasis
TUR  transurethral resection
TURBT  transurethral resection of bladder
UC  Urothelial carcinoma
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 unanimously agreed should be included in the dataset but are not supported by NHMRC 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.

Guidelines include 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 eg macroscopic tumour details, block identification key, may be included as either required or recommended elements by consensus of the expert committee. 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 specimen, made by the unaided eye.

Microscopic findings

In this document, the term ‘microscopic findings’ refers to histomorphological 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’. Standards 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 NHMRC levels of evidence document). In rare circumstances, where level III-2 evidence is not available an element may be made a Standard where there is unanimous agreement in the expert committee. An appropriate staging system eg Pathological TNM staging would normally be included as a required element. 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).

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structured report</td>
<td>A report format which utilises standard headings, definitions and nomenclature with required information.</td>
</tr>
<tr>
<td>Synoptic report</td>
<td>A structured report in condensed form (as a synopsis or precis).</td>
</tr>
<tr>
<td>Synthesis</td>
<td>Synthesis is the process in which two or more pre-existing elements are combined, resulting in the formation of something new.</td>
</tr>
<tr>
<td></td>
<td>The Oxford dictionary defines synthesis as “the combination of components or elements to form a connected whole”.</td>
</tr>
<tr>
<td></td>
<td>In the context of structured pathology reporting, synthesis represents the integration and interpretation of information from two or more modalities to derive new information.</td>
</tr>
</tbody>
</table>
Introduction

Cancer of the urinary bladder is the ninth most common cancer worldwide and the 13th most common cause of death from cancer.² At any point in time, 2.7 million people worldwide have a history of bladder cancer.³ Males are affected 3-4 times more commonly than females. The incidence of bladder cancer is high in many Southern and eastern European countries, parts of Africa, the Middle East, and in the USA. The highest mortality is in Egypt where the rates are more than 3 times that in Europe and 8 times that seen in the USA. In Western countries, the incidence of invasive cancer has decreased whereas the combined incidence of in situ and non-invasive cancer has increased over the years. There has been an overall decrease in mortality.

In Australia, bladder cancer is the 8th most common cancer in males with 2267 new cases predicted to occur in 2017.⁴ Between 1983 and 2003, reduction in mortality rates of 18%, with more pronounced decreases in men than women, have been found. Bladder cancer occurs in older individuals with the median age at diagnosis of 73 years.⁵ Approximately 0.1% are diagnosed under age 20; 0.4% between 20 and 34; 1.7% between 35 and 44; 7.4% between 45 and 54; 18.0% between 55 and 64; 27.2% between 65 and 74; 32.0% between 75 and 84; and 13.2% 85+ years of age.⁵

The most common type of bladder cancer in developed countries including Australia is urothelial carcinoma accounting for greater than 90% of bladder cancers. Urothelial carcinoma includes papillary and invasive UC and urothelial carcinoma in situ (CIS). Papillary urothelial neoplasms include papillomas, papillary urothelial neoplasms of low malignant potential (LMP) and low-grade (LG) and high-grade (HG) urothelial carcinoma. Invasive carcinoma is typically high grade. Low grade invasive urothelial carcinoma is extremely rare. Urothelial carcinoma has the propensity for divergent differentiation resulting in a variety of subtypes. Divergent differentiation is usually seen in association with high-grade and high stage disease. A variety of other carcinomas including adenocarcinoma, squamous cell carcinoma and small cell carcinoma are also seen.⁶ Standard therapies for bladder cancer include surgery, radiation therapy, chemotherapy, and immunotherapy or biological therapy. Accurate diagnosis and staging are essential to select appropriate therapy for each case. Therefore, it is important that these specimens are handled and reported in a systematic manner.

Importance of histopathological reporting

Information in the pathology report of the macroscopic and microscopic findings in cystectomy specimens (partial, total including radical cystoprostatectomy and diverticulectomy) is of both clinical and prognostic utility. The information gained from these specimens is used to guide clinical management of patients, particularly in relation to the role of definitive and adjuvant therapy and surveillance.
While the report must contain all information necessary for tumour staging, the treating clinician will often look for additional information in the report to further refine the patient’s likely prognosis and optimal treatment.

**Benefits of structured reporting**

The pathology report lays the foundation for a patient’s cancer management and conveys information which:

- Provides the definitive diagnosis
- Includes critical information for Tumour-Node-Metastasis (TNM) staging
- Evaluates the adequacy of the surgical excision
- Provides morphological and biological prognostic markers which determine personalised cancer therapy

However, there has been a rapid growth in ancillary testing such as immunohistochemistry, flow cytometry, cytogenetics, and molecular studies. The use of structured reporting checklists by pathologists ensures that all key elements are included in the report specifically those which have clinical management, staging or prognostic implications. Consequently minimum or comprehensive datasets for the reporting of cancer have been developed around the world. Both the United Kingdom, and United States have produced standardised cancer reporting protocols or “datasets” for national use for many years.

The use of cancer reporting checklists improves completeness and quality of cancer reporting and thereby ensures an improved outcome for cancer patients. This has long term cost implications for public health by ensuring the most effective and timely treatment based on accurate and complete information.

The use of a structured reporting format also facilitates easy extraction of the necessary information by secondary users of the information ie cancer registries.

**International Collaboration on Cancer Reporting**

The International Collaboration on Cancer Reporting (ICCR), founded in 2011 by the Australasian (RCPA), US (CAP) and UK (RCPath) Colleges of Pathology and the Canadian Association of Pathology (CAP-ACP) in association with the Canadian Partnership Against Cancer (CPAC), was established to explore the possibilities of a collaborative approach to the development of common, internationally standardised and evidence-based cancer reporting protocols for surgical pathology specimens.

The ICCR, recognising that standardised cancer datasets have been shown to provide significant benefits for patients and efficiencies for organisations through the ease and completeness of data capture undertook to use the best international approaches and the knowledge and experience of expert
pathologists, and produce cancer datasets which would ensure that cancer reports across the world will be of the same high quality – ensuring completeness, consistency, clarity, conciseness and above all, clinical utility.

Representatives from the four countries participating in the initial collaboration undertook a pilot project in 2011 to develop four cancer datasets - Lung, Melanoma, Prostate (Radical Prostatectomy), and Endometrium. Following on from the success of this pilot project, the ICCR was joined by the European Society of Pathology (ESP) in 2013 and in 2014 incorporated a not-for-profit organisation focussed on the development of internationally agreed evidence-based datasets developed by world leading experts. The ICCR Datasets are made freely available from its website www.ICCR-Cancer.org

**Design of this protocol**

This structured reporting protocol has been developed using the ICCR dataset on the reporting of Carcinoma of the Bladder – Cystectomy, Cystoprostatectomy and Diverticulectomy as the foundation.

This protocol includes all of the ICCR cancer dataset elements as well as additional information, elements and commentary as agreed by the RCPA expert committee. It provides a comprehensive framework for the assessment and documentation of pathological features of cancers of the bladder.

ICCR dataset elements for bladder cancer are included verbatim. ICCR Required elements are mandatory and therefore represented as standards in this document. ICCR Recommended elements, that is, those which are not mandatory but are recommended, may be included as guidelines or upgraded to a standard based on the consensus opinion of the local expert committee.

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 is boarded by a grey box as shown below:

<table>
<thead>
<tr>
<th>G3.02</th>
<th>The intraglandular extent should be recorded as a percentage.</th>
</tr>
</thead>
</table>

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

<table>
<thead>
<tr>
<th>G2.03</th>
<th>If present, the laterality of the lymph nodes submitted may be recorded as left, right or bilateral.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS2.03a</td>
<td>If present, record site and number. All lymph node tissue should be submitted for histological examination.</td>
</tr>
</tbody>
</table>

Further information on the ICCR is available at www.iccr-cancer.org
Checklist

Consistency and speed of reporting is improved by the use of discrete data elements recorded from the checklist. Items suited to tick boxes are distinguished from more complex elements requiring free text or narrative. A structured or discrete approach to responses is favoured, however the pathologist is encouraged to include free text or narrative where necessary to document any other relevant issues, to give reasons for coming to a particular opinion and to explain any points of uncertainty.

Report format

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 that represent information from this protocol, organised and formatted differently to suit different purposes.

Key documentation

- Guidelines for Authors of Structured Cancer Pathology Reporting Protocols, Royal College of Pathologists of Australasia, 2009

Updates since last edition

Inclusion of ICCR agreed REQUIRED and RECOMMENDED elements.
Authority and development

This section provides information about the process undertaken to develop this protocol.

This 2nd edition of the protocol is an amalgam of two separate processes:

1. This protocol is based on the ICCR Dataset for the Reporting of Carcinoma of the Bladder – Cystectomy, Cystoprostatectomy and Diverticulectomy 1st edition. All ICCR elements from this dataset, both required (mandatory) and recommended (optional), are included in this protocol, verbatim. (It should be noted that RCPA feedback from all Anatomical Pathology fellows and specifically the local expert committee was sought during the development process of the ICCR dataset.) Details of the ICCR development process and the international expert authoring committee responsible for the ICCR dataset are available on the ICCR website: iccr-cancer.org.

2. Additional elements, values and commentary have been included as deemed necessary by the local expert committee. In addition, the standard inclusions of RCPA protocols eg example reports, request information etc, have also been added.

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Professor Brett Delahunt, Pathologist
Adjunct Professor Warick Delprado, Pathologist
Dr David Grimes, Oncologist
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Acknowledgements
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Stakeholders

ACT Health
ACT Cancer Registry
Australian Pathology
Australian Cancer Network
Australian Commission on Safety and Quality in Health Care
Australian Digital Health Agency
Australian Institute of Health and Welfare
Cancer Australia
Cancer Council ACT
Cancer Council Queensland
Cancer Council Victoria
Cancer Council Western Australia
Cancer Institute NSW
Cancer Services Advisory Committee (CanSAC)
Cancer Voices NSW
Clinical Oncology Society of Australia (COSA)
Department of Health, Australia
Department of Health, New Zealand
Faculty of Radiation Oncology Genito-Urinary Group (FROGG)
Health Informatics Society of Australia (HISA)
Independent Review Group of Pathologists
Medical Software Industry Association (MSIA)
National Pathology Accreditation Advisory Council (NPAAC)
New Zealand Cancer Registry
Northern Territory Cancer Registry
Public Pathology Australia
Queensland Cooperative Oncology Group (QCOG)
RCPA Anatomical Pathology Advisory Committee (APAC)
Representatives from laboratories specialising in anatomical pathology across Australia
Royal Australasian College of Physicians (RACP)
South Australia Cancer Registry
Standards Australia
Tasmanian Cancer Registry
The Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP)
The Medical Oncology Group of Australia
The Prostate Cancer Foundation of Australia (PCFA)
The Prostate Cancer Foundation of New Zealand (PCFNZ)
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)
Western Australia Clinical Oncology Group (WACOG)

Development process

This protocol has been developed following the ten-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 local expert group for local inclusions and the ICCR Dataset Authoring Committee for ICCR components denoted with the ICCR logo.
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 Bladder 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.\(^{15}\) This document specifies the minimum information to be provided by the requesting clinician for any pathology test.

CS1.01b Whether or not the patient identifies as Aboriginal and/or Torres Strait Islander. 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 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 in a structured format.

CS1.02b The copy doctors requested on the request form must be recorded.

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 should 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 procedure.
- The pathology request is often authored by the clinician performing the surgical excision/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 section 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
➢ Detailed fixation and specimen handling instructions are available from the RCPA online Cut-up Manual:

www.rcpa.edu.au/Library/Practising-Pathology/Macroscopic-Cut-Up

Macroscopic findings

S2.01 The labelling of the specimen(s) must be clearly recorded.

S2.02 The operative procedure must be recorded.

CS2.02a Recording of the operative procedure (if this information is provided) is essential in any pathology report. It helps to identify tissues that are not readily apparent for a variety of reasons including treatment effect.

S2.03 Additional specimens submitted must be recorded.

CS2.03a It is important to provide a comprehensive report that includes all specimens submitted. There may be involvement with bladder cancer or specific pathology pertaining to other organs eg prostate cancer.

S2.04 The bladder must be measured in three dimensions. The length of the urethra and ureters should be given. Three dimensional measurements of any other organs should also be reported if submitted.
<table>
<thead>
<tr>
<th>G2.01</th>
<th>Tumour focality should be recorded.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CG2.01a</td>
<td>Multifocality is relatively common in urothelial carcinoma of the urinary bladder. This can include an invasive carcinoma associated with non-invasive papillary carcinomas or multifocal invasive tumours. The presence of multifocal invasive carcinoma is a component of the SPARC score for predicting outcome after radical cystectomy for bladder cancer. In a meta-analysis of 13,185 patients the presence of multifocal disease was a significant risk factor for subsequent upper tract recurrence. Multifocality has also been found to be a risk factor for urethral recurrence following cystectomy in some but not all reports. When more than one tumour is present, it is important to sample all tumours as significant differences in histology can be present.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>G2.02</th>
<th>For multifocal tumours the number of foci of tumour should be recorded.</th>
</tr>
</thead>
<tbody>
<tr>
<td>G2.03</td>
<td>Macroscopic tumour site(s) should be recorded.</td>
</tr>
<tr>
<td>CG2.03a</td>
<td>Tumour location is important for several reasons including diagnosis and staging. Tumours arising in the dome and anterior wall region raise the possibility of an urachal origin. Most cases of secondary involvement of the urinary bladder are direct extension from adjacent organs. In males this is more often the prostate gland and in females the cervix and lower uterine segment. In both, colorectal adenocarcinoma is also a consideration. Depending on the histologic findings these possibilities may be raised and knowledge of location may be helpful. For staging purposes location in the posterior wall and bladder neck region is particularly relevant. It is in this area that adjacent organs are most often involved (stage pT4a). In the case of the prostate gland involvement can be by direct invasion or by <em>in situ</em> disease involving the urethra and subsequently the prostate gland (see PATHOLOGICAL STAGING). Knowledge of the tumour location may be helpful in making this distinction and correctly assigning pathologic stage.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>S2.05</th>
<th>The maximum dimension of the largest tumour must be recorded (in mm).</th>
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<tbody>
<tr>
<td>CS2.05a</td>
<td>Some studies have demonstrated the maximum diameter of the residual tumour at the time of cystectomy as an independent predictor of recurrence and cancer specific survival. In one report residual</td>
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<tr>
<td><strong>tumour diameter ≥ 3 cm was an independent predictor of cancer specific survival.</strong>&lt;sup&gt;22&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td><strong>G2.04</strong></td>
<td>Additional dimensions of the largest tumour may be recorded.</td>
</tr>
<tr>
<td><strong>G2.05</strong></td>
<td>The gross appearance of the tumour(s) should be recorded as polypoid, fungating, papillary, ulcerated or solid and indurated.</td>
</tr>
<tr>
<td><strong>CG2.05a</strong></td>
<td>This is useful for correlation with clinical findings as well as demonstrating that it has been adequately sampled.</td>
</tr>
<tr>
<td><strong>S2.06</strong></td>
<td>The macroscopic extent of invasion must be recorded.</td>
</tr>
<tr>
<td><strong>CS2.06a</strong></td>
<td>The staging of bladder cancer requires documentation of the gross extent of tumour (specifically for separation of pT3a from pT3b). It is also important for determination of the appropriateness of sampling of the tumour. Sites of prior transurethral resections of bladder tumours (TURBT) typically appear as scarred areas with fibrosis and a depressed mucosal surface. Calcifications are often present. Grossly the appearance mimics tumour and the fibrosis can extend into the perivesical fat mimicking a pT3b tumour. Correlating the gross and microscopic findings is necessary to accurately assign the pathologic stage.</td>
</tr>
<tr>
<td></td>
<td>Prostatic involvement by tumour can occur by direct invasion or by in situ involvement of the urethra with subsequent invasion of the prostate gland. These two mechanisms are staged differently and so the gross evaluation is critical in making the distinction. For invasive carcinomas located towards the bladder neck region of the urinary bladder submission of sections to include the invasive tumour and the adjacent prostate gland are important. Further, invasive tumours that are located posteriorly can directly invade the seminal vesicles and sections should be submitted to demonstrate the relationship between the invasive carcinoma and the seminal vesicles.</td>
</tr>
<tr>
<td></td>
<td>For tumours located in the dome the gross evaluation can be important in distinguishing tumours originating in the urachus from the urinary bladder proper. The current World Health Organization (WHO) classification system&lt;sup&gt;23&lt;/sup&gt; includes urachal tumours as a separate category irrespective of the histologic type of tumour. Although most urachal tumours are adenocarcinoma, all other histologic types are represented and an urothelial carcinoma in the dome area may also be of urachal origin.</td>
</tr>
<tr>
<td><strong>CS2.06b</strong></td>
<td>There is a high risk of prostatic adenocarcinoma in the age group undergoing cystectomy for bladder cancer,</td>
</tr>
</tbody>
</table>
high risk of finding incidental prostatic adenocarcinoma in cystoprostatectomy specimens\textsuperscript{24} and a significant risk of involvement of the prostate by urothelial carcinoma.\textsuperscript{25}

\textbf{S2.07} The presence or absence of macroscopic evidence of resection margin and peritoneal surface involvement.

\textbf{CS2.07a} Perivesical, ureteric and urethral margins and peritoneal surface involvement must be recorded.

\textbf{CS2.07b} Resection margins are examined to assess the adequacy of resection. Peritoneal surface involvement may be associated with peritoneal carcinomatosis.\textsuperscript{26}

\textbf{CS2.07c} For partial cystectomy specimens, the ureteric and urethral margin resection may be recorded as “Not applicable”.

\textbf{G2.06} Features of the uninvolved bladder must be recorded.

\textbf{CG2.06a} Careful examination of apparently uninvolved bladder is needed to identify multifocal urothelial CIS and foci of unexpected tumour without a surface papillary component but directly invasive. Rarely these foci can be more deeply invasive than a grossly apparent tumour.

\textbf{S2.08} The number and sites of any lymph nodes submitted must be recorded.

\begin{tabular}{|c|p{0.8\textwidth}|}
\hline
\textbf{S2.09} & A block identification key listing the nature and origin of all tissue blocks must be recorded. \\
\hline
\textbf{CS2.09a} & The origin/designation of all tissue blocks should be recorded and it is preferable to document this information in the final pathology report. This is particularly important should the need for internal or external review arise. The reviewer needs to be clear about the origin of each block in order to provide an informed specialist opinion. If this information is not included in the final pathology report, it should be available on the laboratory computer system and relayed to the reviewing pathologist. \\
& Recording the origin/designation of tissue blocks also facilitates retrieval of blocks, for example for further immunohistochemical or molecular analysis, research studies or clinical trials. \\
\hline
\textbf{G2.07} & 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 \\
\hline
\end{tabular}
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.

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.
### Microscopic findings

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

<table>
<thead>
<tr>
<th>S3.01</th>
<th>Histological tumour type and sub-type/variant must be recorded.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS3.01a</td>
<td>The 2016 WHO classification is utilised for assigning histological tumour type. As in the 2004 WHO Classification, a tumour is classified as a urothelial carcinoma if there is any identifiable urothelial component no matter how small and including urothelial carcinoma in situ (CIS). The one exception to this rule is for cases with a neuroendocrine component (small cell neuroendocrine carcinoma or large cell neuroendocrine carcinoma) where classification is in the neuroendocrine tumour category. For those cases that are mixed, the other elements should be reported with an estimated percentage. In the above scheme, this would be managed by placing the other component in the histological tumour type element. For example, a mixed tumour with 70% small cell neuroendocrine carcinoma and 30% urothelial carcinoma would be reported under the histological tumour type as Neuroendocrine tumour (small cell neuroendocrine carcinoma) and then under histological tumour type – Other, specify - urothelial carcinoma (30%).</td>
</tr>
</tbody>
</table>

For biopsies and TURs that contain pure adenocarcinoma or pure squamous cell carcinoma, they should be diagnosed as such. Subsequent evaluation of the entire lesion in the cystectomy specimen should allow for definitive classification. It is not unusual for a tumour with pure squamous or glandular differentiation on biopsy/TURBT to prove to represent a urothelial carcinoma with squamous or glandular differentiation. It is for this reason that a definitive diagnosis of either should be made with caution in biopsy or TURBT material.

The 2016 WHO classification now includes carcinomas arising in the urachus as a separate category. These are defined as carcinomas arising from urachal remnants. It is generally not possible to diagnose these in biopsy and TURBT material based on the morphologic findings alone. Criteria for the diagnosis of urachal carcinoma include location in the bladder dome or anterior wall, an epicentre in the bladder wall or perivesical tissue, the absence of diffuse cystitis glandularis/intestinal metaplasia outside of the
dome/anterior wall region and the absence of a known primary elsewhere.28 The majority (over 80%) of urachal carcinomas are adenocarcinoma followed by urothelial carcinoma, squamous cell carcinoma and small cell neuroendocrine carcinoma. If a diagnosis of urachal carcinoma is rendered the histologic type should be specified. Adenocarcinomas of the urachus are most often mucinous and can be either solid or cystic. Other variants of adenocarcinoma including enteric and signet ring-cell also occur. The WHO does include a category of “mucinous cystic tumour of low malignant potential.”23,29 There are no reliable immunohistochemical markers to distinguish adenocarcinomas of urachal origin from primary adenocarcinomas of the bladder proper or from secondary adenocarcinomas of gastrointestinal origin.28-30 The gross examination is an important parameter in making this distinction in the resection specimen.

Also new in the 2016 WHO classification is the category of Müllerian tumours. For the purposes of this dataset this consists primarily of clear cell carcinoma and rare examples of endometrioid carcinoma. These tumours are morphologically the same as their counterparts in the female genital tract. They are rare tumours and most often when clear cell carcinoma presents as a primary bladder tumour it represents secondary involvement most often originating in a urethral diverticulum.31 Diagnosis therefore requires clinical correlation to support diagnosis as a primary bladder tumour. Clear cell carcinoma and endometrioid carcinoma may arise from endometriosis or rarely Müllerianosis.32-35 Clear cell carcinoma must also be distinguished from urothelial carcinoma with divergent differentiation along Müllerian lines in which case it would be classified under urothelial carcinoma.36 Markers such as p63, GATA3 and high molecular weight cytokeratin are not expressed by clear cell carcinoma and expression of these markers even in the absence of a recognisable urothelial component would suggest this possibility.37 Müllerian type clear cell carcinoma has similar immunohistochemical profile to primary tumours of the female genital tract and cannot be used to distinguish a primary from a secondary origin.34,38-40

The neuroendocrine tumour category includes small cell neuroendocrine carcinoma, large cell neuroendocrine carcinoma, well-differentiated neuroendocrine tumour and paraganglioma. Small cell neuroendocrine carcinoma is by far the most common of these. By definition this is a malignant neoplasm with neuroendocrine differentiation. About one-half of cases are pure and one-half are mixed with another component with urothelial carcinoma being most frequent. In some cases the biopsy/TURBT specimen does not include a small cell neuroendocrine component.
and it is only discovered in the resection specimen. Cases with mixed differentiation are included in this category. There does remain some controversy regarding the percentage of the neuroendocrine component required to classify a tumour as a neuroendocrine carcinoma. From a practical standpoint cases with a small cell neuroendocrine carcinoma component irrespective of the amount are managed as small cell neuroendocrine carcinoma with the larger series in the literature including cases with only a focal component of small cell carcinoma.\textsuperscript{41-44} For example the National Comprehensive Cancer Network (NCCN) includes tumours with “any small-cell component’ in the category of non-urothelial cell carcinoma.\textsuperscript{45,46} The diagnosis is defined by morphologic criteria but most cases do demonstrate evidence of neuroendocrine differentiation by immunohistochemistry. The most sensitive immunohistochemical markers are CD56 and synaptophysin.\textsuperscript{47} TTF-1 is expressed in about 50% of cases and hence would not be indicative of metastasis from the lung.\textsuperscript{48,49} In cases with pure small cell morphology the possibility of direct spread from an adjacent organ or metastasis must be excluded clinically.

Lastly, there are carcinomas arising in the urinary bladder that have no specific differentiation and based on exclusion of metastasis from another site are considered to be primary in the urinary tract. In the 2004 WHO classification these were included as a variant of urothelial carcinoma but given that by definition they have no urothelial differentiation these should be reported using the “carcinoma, type cannot be determined” category.\textsuperscript{27}

**Histologic subtype/variant**

The 2016 WHO classification includes a number of recognised morphologic variants as outlined in the table below.\textsuperscript{23} Because urothelial carcinoma has a remarkable capacity for morphologic variation the number of histologic variants that have been described in the literature is extensive.\textsuperscript{50,51} In the 2016 WHO classification not all of these are included. In general the variants that have been specifically recognised fall into three broad categories. Variants that have a deceptively bland morphology, such as the nested variant, could be misdiagnosed as benign or considered low grade although their behaviour is the same as for high grade tumours. In the second category are tumours that have a morphology that mimics other tumours. Lastly are those tumour variants that have important prognostic or therapeutic implications.

The importance of variant histology in clinical management decisions has been receiving increasing clinical attention.\textsuperscript{52,53} Some variants have been
highlighted because of the high frequency of under staging when present in biopsy or TURBT specimens, as discussed in the ICCR Urinary tract carcinoma – Biopsy and Transurethral resection specimen dataset.\textsuperscript{54,55}

There are an increasing number of therapeutic algorithms that incorporate variant histology as a significant factor.\textsuperscript{56}

The level of evidence for specific variants having independent prognostic information varies from the variant having no clinical significance but being important diagnostically (e.g. nested, microcystic, etc), to no data, to data indicating the variant has prognostic significance (e.g. micropapillary, plasmacytoid, sarcomatoid). Rather than making reporting of specific subtypes that have some supporting data mandatory and others lacking data recommended it is considered best to make the entire category a required element.

Reporting the percentage of variant histology when present is recommended as in the WHO 2016 monograph. The data supporting this is very limited and only available for selected variants (micropapillary, sarcomatoid, lymphoepithelioma-like), with divergent differentiation (glandular, squamous). There is also insufficient data available for setting specific amounts of each specific variant in order for it to be clinically significant. Given the lack of data, if variant histology is identified, it should be reported and the estimated approximate percentage of the tumour it makes up reported. For cases with more than one variant present, the percentage of each is recommended to be documented.

\textbf{S3.02} The presence of non-invasive carcinoma must be reported.

\textbf{CS3.02a} The majority of surgical resections of bladder tumours are performed for invasive carcinoma, however patients with carcinoma \textit{in situ} that fail intra-vesical therapy are also usually managed by cystectomy.\textsuperscript{57} Cystectomy is also recommended for patients with recurrent high grade papillary carcinomas refractory to BCG or recurring after completion of BCG maintenance.\textsuperscript{57} For patients that are BCG intolerant this may also be an indication for cystectomy. Occasionally patients have such large and extensive non-invasive papillary tumours that cystectomy also becomes necessary. In those cases this category will represent the tumour that was the indication for the procedure.

For patients undergoing cystectomy for invasive carcinoma, it may sometimes be important to document non-invasive carcinoma if present. In large cystectomy series concomitant carcinoma \textit{in situ} is found in 19\% to 54\% of cases with most series at the higher end of this range.\textsuperscript{58-61} The presence of urothelial
carcinoma *in situ* in these cases has been associated with an increased risk of recurrence in a limited number of studies.\(^{62}\) However, in the majority of reports the presence of carcinoma *in situ* has not been found to be associated with either recurrence or cancer specific survival.\(^{59,60,63,64}\) In a meta-analysis of 13,185 patients undergoing radical cystectomy, the presence of carcinoma *in situ* was not a significant risk factor for subsequent upper tract recurrence.\(^{17}\) Similarly most reports have not found carcinoma *in situ* in the bladder to be associated with a higher likelihood of urethral recurrence in contrast to prostatic involvement by *in situ* carcinoma which is a major risk factor of urethral recurrence in men.\(^{18-20}\)

<table>
<thead>
<tr>
<th>G3.01</th>
<th>The presence of associated epithelial lesions should be reported.</th>
</tr>
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<tbody>
<tr>
<td>CG3.01a</td>
<td>A variety of neoplastic lesions that fall short of carcinoma are recognised in the urinary tract. These include papillary lesions such as urothelial papilloma, papillary urothelial neoplasm of low malignant potential and inverted urothelial papilloma. Similarly flat lesions such as urothelial dysplasia, keratinizing squamous metaplasia with dysplasia and intestinal metaplasia with dysplasia can be seen. Identification of these may have diagnostic implications (e.g. the presence of keratinizing squamous metaplasia with dysplasia supporting the diagnosis of primary squamous cell carcinoma) but do not have known proven prognostic or clinical significance otherwise. While for completeness it may be useful to report such findings, it is not considered to be a required element in the context of a carcinoma diagnosis.</td>
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<tr>
<th>S3.03</th>
<th>The histological grade must be reported.</th>
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<tbody>
<tr>
<td>CS3.03a</td>
<td>Histologic grading of urothelial tumours is best considered in two categories, non-invasive papillary tumours and invasive carcinoma. For non-invasive papillary tumours the 2016 WHO remains the same as in the 2004 WHO and continues to recommend the grading system first put forward by the International Society of Urological Pathology (ISUP) in 1997.(^{65}) The system is now recommended by almost all major pathology and urology organisations as the preferred grading system.(^{66,67}) Papillary urothelial neoplasm of low malignant potential is not reported using this dataset. It is nonetheless a significant diagnosis and does indicate an increased risk for the development of other neoplasms in the urinary tract. Grade heterogeneity is not uncommon in papillary urothelial carcinoma being reported in up to 32% of</td>
</tr>
</tbody>
</table>
It is currently recommended that tumour grade be assigned based on the highest grade present.

The 2016 WHO recommends grading based on the highest grade component and acknowledges the uncertainty of how to approach cases with a small proportion of high grade tumour. It does indicate that “it may be prudent to state the proportion of high-grade disease.”

The 1973 WHO grading system for papillary tumours remains in use in many regions and some published guidelines specifically recommend the reporting of both the current WHO grade with the 1973 grade while others provide for the 1973 grade to be included by institutional choice. The grading of invasive urothelial carcinoma is another area of controversy. In North America the vast majority of invasive urothelial carcinomas have been diagnosed as high grade in contrast to European studies where a substantial percentage of invasive tumours have been graded as 2 or even 1. Currently there is general agreement that grade 1 tumours (WHO 1973), largely corresponding to papillary urothelial neoplasm of low malignant potential, lack the capacity to invade. In studies using the 1998 ISUP/WHO 2004 grading system the vast majority of invasive tumours are high grade. We recommend the 2016 WHO approach of continuing to grade invasive carcinoma using the WHO 2004 system while recognising that the vast majority of tumours will be high grade. If invasive tumours are graded using an alternative grading system this should be indicated.

For further information refer to the ICCR dataset.

Although the current categories are thought to overlap with the 1973 categories, a study comparing the 2 systems showed that there was no good correlation with a larger proportion of LMP tumours and high grade cancers in the current system than grade 1 and 3 cancers.

There is no generally accepted grading system for adenocarcinoma of the bladder.

Squamous cell carcinoma is graded using criteria used for these tumours in other viscera. Invasive SCC may be well differentiated with well defined nests of squamous cells with prominent keratinisation, intercellular bridges and minimal nuclear pleomorphism, moderately differentiated with more cellular atypia, minimal keratinisation but with obvious squamous features or poorly differentiated with marked nuclear pleomorphism and only focal evidence of
The microscopic extent of invasion must be given.

<table>
<thead>
<tr>
<th>CS3.04a</th>
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</table>
| Determining the extent of invasion is the key feature for the assignment of pathologic stage.\(^7\) In most cases this determination is relatively straightforward but a few situations are worth specific discussion. There are several publications providing guidelines for the optimal gross examination and sampling of radical cystectomy specimens.\(^80\)-\(^82\) In contemporary cystectomy series there is no residual tumour identified in the radical cystectomy specimen in between 5% and 20% of specimens.\(^83\)-\(^86\) It is likely that this frequency will continue to increase with the more frequent treatment of T1 tumours by radical cystectomy and the increased use of neoadjuvant chemotherapy. In most cases the site of the prior TURBT is evident grossly and this area can be completely submitted for microscopic examination (or if large extensively sampled). In cases with no grossly apparent lesion the clinical information including radiologic findings may be helpful in guiding sampling. Sampling of areas with mucosal lesions such as erythema may identify foci of carcinoma in situ as may random samples of apparently normal mucosa. As long as the site of the prior TURBT is identified microscopically the case can be reported as “no residual tumour” without resorting to extensive sampling of grossly normal bladder tissue.

Determination of peri-vesical fat invasion seems on the face of it to be relatively straightforward. However, unlike in the colon, the junction between the muscle of the muscularis propria and the perivesical fat is not well defined. Adipose tissue is present throughout the bladder wall and at the deep aspect of the muscularis propria typically results in haphazardly separated muscle bundles forming a poorly formed demarcation.\(^87\) Ananthanarayanan and colleagues demonstrated the inconsistency among expert urologic pathologists in defining peri-vesical fat extension.\(^88\) We are unaware of a definition that has been validated with outcome data to provide guidance. It may be that this variability in part explains the variation in prognostic differences between pT2b and pT3a tumours in different reports. Some reports have found no significant difference between pT2b and pT3a carcinomas,\(^89\),\(^90\) while others have found there to be a significant difference.\(^91\) Distinction of pT3a from pT3b tumours is however consistently found to be significant.\(^89\),\(^90\),\(^92\) In many of the larger cystectomy series the data compares pT2 and pT3 tumours without subdividing them.\(^59\),\(^60\),\(^86\)
Documentation of invasion into adjacent structures represents pT4 disease and is important to document. Involvement of the prostate gland represents a unique group in that the invasion can occur by two routes: direct invasion by the invasive tumour from the bladder or invasion by in situ disease involving the prostatic urethra and/or prostatic ducts. The significance of this is discussed in detail in PATHOLOGICAL STAGING.

Carcinoma arising in diverticula represent less than 2% of urothelial carcinomas of the bladder. The urothelium in diverticula is however known to be at significantly higher risk for the development of carcinoma than that of the urinary bladder. The majority of carcinomas arising in diverticula are urothelial carcinoma but all histologic types can occur. In most series squamous cell carcinoma is more frequent than in the bladder proper. Most diverticula in adults are acquired and by definition do not have a muscularis propria therefore there are no pT2 tumours. Invasive carcinomas are staged as either pT1, pT3a or pT3b only. It should be noted that acquired diverticula usually have fibres of the muscularis mucosae and these can be hypertrophic and should not be confused with muscularis propria. In one report hypertrophic muscularis mucosae was found in 59% of diverticula resected for carcinoma. Carcinomas arising in diverticula can be treated by diverticulectomy, partial cystectomy or radical cystectomy.

CS3.04b For partial cystectomy specimens, the relationship of the tumour to structures which are not included in the resection can be recorded as “Not applicable”.

CS3.04c Level of invasion or pathological category is the most important prognostic indicator in bladder cancer.

CS3.04d Where adenocarcinoma of the prostate is identified, the protocol for carcinoma of the prostate should be used.
Figure 1  Assessment of bladder tumour extent

This figure shows the clinical landmarks used to assess the extent of bladder cancer invasion. Picture courtesy of Kiara Klopfer, BSc, AQUESTA Uropathology.

S3.05  Microscopic tumour site(s) must be recorded.

CS3.05a  A single tumour can involve several of these locations or there can be separate tumours involving different locations.

G3.02  Tumour size should be recorded as greatest dimension of the largest tumour.

G3.03  A response to pre-operative therapy should be given.

CG3.03a  Neoadjuvant chemotherapy is commonly part of the management of patient with high risk bladder cancer prior to cystectomy. \(^\text{45,100}\) In the 2013 European Association of Urology (EAU) guidelines neoadjuvant chemotherapy was “recommended for T2-T4 cN0 M0 bladder cancer and should always be cisplatinum-based combination therapy.” \(^\text{100}\) The recommendation was a “grade A” recommendation. \(^\text{100}\)

At cystectomy patients treated with neoadjuvant chemotherapy are often down staged and may be pT0. This has been demonstrated to be associated with improved survival. \(^\text{101-104}\) pT0 at cystectomy after TURBT is also associated with significantly improved survival but pT0 is more frequent in patients having neoadjuvant chemotherapy. \(^\text{103}\)

Improved survival following neoadjuvant chemotherapy
has also been studied for specific histologic types and generally had similar results.\textsuperscript{105}

There is minimal data however on morphologic alterations in the tumour itself following neoadjuvant chemotherapy and what the significance of such alterations might be. Fleischmann \textit{et al} developed a “tumour regression grade” by comparing the tumour in the TURBT with residual tumour in the cystectomy following neoadjuvant chemotherapy.\textsuperscript{106} The grade was based on the amount of residual tumour with respect to the size of the TURBT site scar. Three grades were assigned: TRG1 – no identifiable residual tumour (complete response), TRG2 – residual tumour occupying <50\% of the area of fibrosis and TRG3 – residual tumour overgrowing or occupying \geq 50\% of the fibrotic area. The TRG correlated significantly with overall survival. The study is limited by small numbers and many other issues but this is one of the first efforts to come up with some measurement of response. Of note is that the TRG2 group did better than the TRG3 group.

**S3.06** The presence or absence of lymphovascular invasion (LVI) must be recorded.

**CS3.06a** The data on lymphovascular invasion (LVI) in urothelial carcinoma in the urinary bladder has continued to grow with very large series now reported,\textsuperscript{16,59,61,64,107,108} These have included very large multi-institutional series (e.g. Kluth \textit{et al}\textsuperscript{59}), cases from phase 3 clinical trials (von Rundstedt \textit{et al}\textsuperscript{108} – SWOG4B951/NCT00005047) and in the generation of prognostic scores (Eisenberg \textit{et al}\textsuperscript{16} – SPARC Score) all of which have found LVI to be a highly significant independent predictor of outcome. This is therefore a required element.

**CS3.06b** Criteria used in other locations also apply here.

**S3.07** The margin status must be reported.

**CS3.07a** Evaluation of surgical margin status is a core component of evaluation of resection specimens in most areas of surgical oncology. The prognostic significance of this finding in resection specimens for urinary bladder carcinoma has had variable significance in studies in the literature. Gross evaluation of the surgical margins is important primarily to ensure that tissue sections are taken at the locations that are most likely to have involvement confirmed histologically. For cases where the gross examination suggests a positive surgical margin and the histological sections do not reflect this submission of additional sections may be appropriate. Confirmation by microscopic examination is necessary as the stromal response to invasive
tumour or a prior TURBT may mimic a positive margin.

Studies have reported positive surgical margins to be present in 4% to 15% of radical cystectomy specimens. Positive margins are generally placed in three categories: urethral, ureteral and soft tissue. Urethral and ureteral margins can be involved by in situ carcinoma and/or invasive carcinoma. Ureteric margins are frequently evaluated by frozen section as is the urethral margin to a lesser extent. For this reason in most studies of radical cystectomy specimens positive margins most frequently involve the soft tissues followed by the urethra and then the ureters. Positive soft tissue surgical margins have been an independent predictor of an increased risk of recurrence and decreased cancer specific survival. In a multi-institutional case control study, Neuzillet et al (2013) showed a significantly higher recurrence rate and decreased cancer specific survival for patients with positive urethral and soft tissue surgical margins but not for ureteral margins. In the multivariable analysis both urethral and soft tissue margins remained significant for recurrence with only soft tissue margins being significant for cancer specific survival. It has also been reported that patients with positive soft tissue margins (as well as positive lymph nodes) have greater benefit from adjuvant chemotherapy than those without.

Ureter margins are typically controlled for by frozen section evaluation at the time of cystectomy. Frozen section interpretation is reliable with low false positive and false negative rates. Several studies have evaluated the utility of routine frozen sections with varying conclusions. In larger series ureteral involvement by carcinoma in situ is present in up to 9% of cases. In most cases with ureteric involvement there is carcinoma in situ in the urinary bladder leading some to recommend performing frozen sections only in those cases, while others have recommended against routine use of frozen section in general. Overall subsequent recurrence in the ureter occurs in up to 13% of patients, with most studies reporting upper tract recurrence in the 4% to 6% range and with recurrence of invasive carcinoma at the ureterointestinal anastomosis in less than 1%. Recurrence is significantly higher in patients with documented ureteric involvement. This increased risk remains but is reduced if a negative margin is subsequently obtained with frozen section control. The latter may in part be related to “skip lesions” that can be present in up to 4.8% of patients.

Although urethral margins are positive in up to 10% of cases, frozen sections are less often performed for...
margin control.\textsuperscript{121,126,127} It is most often used in the setting of orthotopic diversions and/or when there has been documented prostatic urethral involvement. Patients with positive urethral margins are at increased risk of the development of recurrence in the urethra. Limited data suggests that documentation of a negative urethral margin at frozen section is associated with a low likelihood of urethral recurrence.\textsuperscript{126}

<table>
<thead>
<tr>
<th><strong>S3.08</strong> Regional lymph node status must be recorded.</th>
</tr>
</thead>
</table>
| **CS3.08a** | Lymph node dissection is a standard procedure performed at the time of radical cystectomy for bladder cancer. The past decade has seen considerable expansion of the literature on this topic addressing such issues as the optimal extent of the lymph node dissection, the significance of the number of lymph nodes examined and the proportion of positive lymph nodes (lymph node density) in cases with metastases.

For cases with lymph node metastases, a number of studies have evaluated the significance of extranodal extension. Most of these have found the presence of extranodal extension to be associated with worse cancer specific survival\textsuperscript{128-131} but this has not been uniform.\textsuperscript{132} In a multi-institutional study of 748 cases with positive lymph nodes, extranodal extension was present in 50\%.\textsuperscript{131} In a multivariable analysis, the presence of extranodal extension was the most significant independent predictor of disease recurrence and cancer-specific mortality.\textsuperscript{131} |
| **CS3.08b** | It is recommended that separate lymph node packets should be extensively sampled as this improves the lymph node detection.\textsuperscript{133} |

<table>
<thead>
<tr>
<th><strong>G3.04</strong></th>
<th>The presence of extranodal spread should be recorded.</th>
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<tbody>
<tr>
<td><strong>S3.09</strong> The presence of histologically confirmed distant metastases must be recorded.</td>
<td></td>
</tr>
</tbody>
</table>
| **CS3.09a** | In some patients there will be known metastases that have been confirmed histologically. When these are known they should be included in the report. It is helpful to include in the report the relevant pathology identifier as a reference to the metastases.

In the 8\textsuperscript{th} edition of the American Joint Committee on Cancer (AJCC)/TNM manual\textsuperscript{14} the M category has been revised. M1 is now subdivided into M1a for distant metastases limited to lymph nodes beyond the common iliac nodes and M1b for non-lymph node metastases. |
| **G3.05** | Any coexistent pathology should be recorded. |
| CG3.05a | A wide range of non-neoplastic changes can be found in radical cystectomy specimens. These include those found in the urinary bladder as well as in other organs that are often removed as part of the radical cystectomy (prostate gland and seminal vesicles; uterus and cervix with and without fallopian tubes and ovaries). For the urinary bladder findings such as keratinizing squamous metaplasia and intestinal metaplasia may be relevant in cases of squamous cell carcinoma and adenocarcinoma but for the most part these findings are not critical and so this element is not required standard. |
| CG3.05b | Significant pathology in other organs submitted would however be considered required for reporting. The topic of urothelial carcinoma involving the urethra and prostate gland is discussed in detail in the staging section. Prostate adenocarcinoma is a frequent incidental finding in cystoprostatectomy specimens. When this occurs the prostatectomy dataset should be inserted in the pathology report and completed as appropriate. |

G3.06 Any additional relevant microscopic comments should be recorded.
4 Ancillary studies findings

Ancillary studies may be used to determine lineage, clonality or disease classification or subclassification; as prognostic biomarkers; or to indicate the likelihood of patient response to specific biologic therapies.

<table>
<thead>
<tr>
<th>G4.01</th>
<th>Whether or not ancillary tests are performed should be recorded and the results incorporated into the pathology report.</th>
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</thead>
<tbody>
<tr>
<td>CG4.01a</td>
<td>Currently there are no ancillary studies that are recommended for routine use in urothelial carcinoma. In cases where immunohistochemistry is used diagnostically these should be reported in this section.</td>
</tr>
</tbody>
</table>
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 report ‘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.

<table>
<thead>
<tr>
<th>S5.01</th>
<th>The pathologic tumour staging categories - Primary Tumour (pT) and Regional Lymph Node (pN) must be recorded according to the AJCC TNM Classification 2016 (Eighth Edition).</th>
</tr>
</thead>
</table>
| CS5.01a | Pathologic stage remains the single most important prognostic parameter in patients treated by radical cystectomy. In prior sections several issues related to pathologic staging including cases with no residual tumour in the cystectomy specimen (Extent of invasion), separation of pT2b from pT3a disease (Extent of invasion) and the importance of various lymph node parameters (Regional lymph node status) have been reviewed.

An important issue that has not been covered in detail is the assignment of pathologic stage in cases with involvement of the prostatic urethra and prostate gland in cystoprostatectomy specimens. It has long been recognised that in patients with bladder cancer, involvement of the prostatic urethra can also be present. In contemporary cystoprostatectomy series involvement of the prostatic urethra with or without prostate gland involvement is reported in 16% to 48% of patients. Pagano et al reported that prostatic gland involvement in such cases could be classified as contiguous or non-contiguous with the latter having a significantly better prognosis. Similar results have been reported by others.

The prostatic stroma can be invaded by two different mechanisms. The first is direct (transmural) extension of the invasive bladder cancer into the prostatic stroma. A second mechanism would be extension of urothelial carcinoma in situ into the prostatic urethra and/or prostatic ducts with subsequent prostatic stromal invasion. There are data that indicate that there are
significant prognostic differences between these two groups with the former having a substantially worse prognosis.\textsuperscript{140,142,144,145} It is therefore critical that when assigning pathologic stage in cases where the prostate gland is involved the mechanism of involvement be determined. The current TNM has clarified the handling of prostatic involvement.\textsuperscript{14} For cases with direct extension of the invasive tumour into the prostate gland, a stage of pT4a is assigned. For cases where the involvement is related to carcinoma \textit{in situ} involving the prostatic urethra and or prostatic ducts, stage is assigned using the urethra staging system.\textsuperscript{144,145} Using this approach, prostatic stromal invasion would be pT2.\textsuperscript{14}

\textbf{S5.02} The year of publication or the edition of the cancer staging system used in S5.01 must be included in the report.

\textbf{G5.01} The "Diagnostic summary" section of the final formatted report should include:

\begin{itemize}
  \item a. Operative procedure and any additional specimens
  \item b. Tumour type with different subtypes specified
  \item c. Tumour grade
  \item d. Tumour extent (Level of invasion)
  \item e. Microscopic tumour site
  \item f. Lymphovascular invasion
  \item g. Surgical margin status (completeness of excision)
  \item h. Lymph node involvement
  \item i. Tumour stage
  \item j. Presence of non-invasive carcinoma
\end{itemize}

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

\textbf{CS5.03a} This field may be used, for example, to:

\begin{itemize}
  \item document any noteworthy adverse gross and/or histological features
  \item explain any elements of clinicopathological ambiguity
  \item express any diagnostic subtlety or nuance that is beyond synoptic capture
  \item document further consultation or results still pending
\end{itemize}
CS5.03b  Use of this field is at the discretion of the reporting pathologist.

G5.02  The edition/version number of the RCPA protocol on which the report is based should be included on the final report.

CG5.02a  For example, the pathology report may include the following wording at the end of the report: “the data fields within this formatted report are aligned with the criteria as set out in the RCPA document “XXXXXXXXXX” XXXX Edition dated XXXXXXXX”.
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 bladder cancers. For emphasis, standards (mandatory elements) are formatted in bold font.

S6.01 The structured checklist provided below 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 CancerProtocols.146

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.
Values in italics are conditional on previous responses.
Values in all caps are headings with sub values.

<table>
<thead>
<tr>
<th>S/G</th>
<th>Item description</th>
<th>Response type</th>
<th>Conditional</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Pre-analytical</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S1.01</td>
<td><strong>Demographic information provided</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S1.02</td>
<td><strong>Clinical information provided on request form</strong></td>
<td><strong>Text</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>OR</strong></td>
<td><strong>Structured entry as below:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>CLINICAL INFORMATION</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Previous history of urinary tract disease or distant metastasis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Information not provided</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• No previous history</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>OR</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Multi select value list (select all that apply):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Non-invasive papillary</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Carcinoma <em>in situ</em>, flat</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Invasion into lamina propria</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Muscle invasive disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Distant metastasis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Other, <em>specify</em></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Previous therapy | • Information not provided  
|                 | • No previous therapy  
| **OR** |  
| **Multi select value list (select all that apply):** |  
|              | • Transurethral resection (TURBT)  
|              | • Bacillus Calmette-Guerin (BCG)  
|              | • Chemotherapy, intravesical, *specify*  
|              | • Chemotherapy, systemic  
|              | • Radiation therapy  
|              | • Other, *specify*  
| Other clinical information | **Text**  
| Clinical extent of disease | **Text**  
| **Operative procedure** | **Single selection value list:**  
|              | • Not specified  
|              | • Cystectomy, partial  
|              | • Cystectomy, simple  
|              | • Cystectomy, radical (female)  
|              | • Cystoprostatectomy (male)  
|              | • Diverticulectomy  
|              | • Anterior exenteration (female)  


| Procedure(s) submitted | Additional specimen(s) submitted | OR | Multi select value list (select all that apply):
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Urethrectomy</td>
<td></td>
<td></td>
<td>Prostate gland</td>
</tr>
<tr>
<td>Lymphadenectomy</td>
<td></td>
<td></td>
<td>Seminal vesicles</td>
</tr>
<tr>
<td>Other, specify</td>
<td></td>
<td></td>
<td>Penile urethra</td>
</tr>
<tr>
<td></td>
<td>Not submitted</td>
<td></td>
<td>Uterus</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Fallopian tubes</td>
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<td>- Left</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- Right</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Laterality not specified</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ovaries</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Left</td>
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<td></td>
<td>- Right</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- Laterality not specified</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Vaginal cuff</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ureter</td>
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<tr>
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<td></td>
<td></td>
<td>- Left</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Right</td>
</tr>
<tr>
<td>S1.03</td>
<td>Pathology accession number</td>
<td>Alpha-numeric</td>
<td></td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------</td>
<td>---------------</td>
<td></td>
</tr>
<tr>
<td>S1.04</td>
<td>Principal clinician caring for the patient</td>
<td>Text</td>
<td></td>
</tr>
<tr>
<td>G1.01</td>
<td>Other clinical information received</td>
<td>Text</td>
<td></td>
</tr>
</tbody>
</table>

### Macroscopic findings

<table>
<thead>
<tr>
<th>S2.01</th>
<th>Specimen labelled as</th>
<th>Text</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>S2.02</strong></td>
<td>Operative procedure</td>
<td><strong>Single selection value list:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Not specified</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cystectomy, partial</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cystectomy, simple</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cystectomy, radical (female)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cystoprostatectomy (male)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Diverticulectomy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Anterior exenteration (female)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Urethrectomy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Lymphadenectomy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Other, specify</td>
</tr>
<tr>
<td></td>
<td>Additional specimen(s) submitted</td>
<td>Not submitted</td>
</tr>
<tr>
<td>---</td>
<td>---------------------------------</td>
<td>---------------</td>
</tr>
<tr>
<td></td>
<td><strong>OR</strong> Multi select value list (select all that apply):</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Prostate gland</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Seminal vesicles</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Penile urethra</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Uterus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Fallopian tubes</td>
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<td></td>
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<td></td>
<td>o Right</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o Not specified</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Ovaries</td>
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<td>o Right</td>
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<td>o Not specified</td>
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</tr>
<tr>
<td></td>
<td>• Vaginal cuff</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Ureter</td>
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<tr>
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<td></td>
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<tr>
<td></td>
<td>o Right</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o Not specified</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Other, specify</td>
<td></td>
</tr>
</tbody>
</table>

|   | Bladder measurements | Numeric: \_\_x\_\_x\_\_mm |   |
| **G2.01** | Tumour focality | **Single selection value list:**  
• Unifocal  
• Multifocal  
• Cannot be assessed, specify | If multifocal, consider recording the number of tumours at G2.02 |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>G2.02</strong></td>
<td>Number of tumours</td>
<td><strong>Numeric:</strong></td>
<td></td>
</tr>
</tbody>
</table>
| **G2.03** | Macroscopic tumour site | **Single selection value list:**  
• Indeterminate  
• No macroscopically visible tumour | |
### TUMOUR DIMENSIONS

**S2.05**

**Multi select value list (select all that apply):**
- Trigone
- Right lateral wall
- Left lateral wall
- Anterior wall
- Posterior wall
- Dome
- Other, specify

**TUMOUR DIMENSIONS**

**Single selection value list:**
- No macroscopically visible tumour
- Cannot be assessed

*OR complete the following element(s)*

| **Maximum tumour dimension (largest tumour)** | Numeric: ____mm |
| **Additional dimensions (largest tumour)** | Numeric: ____x____mm |

**G2.05**

**Gross appearance of tumour(s)**

**Multi select value list (select all that apply):**
- Polypoid
- Fungating
<table>
<thead>
<tr>
<th>S2.06</th>
<th>Macropscopic extent of invasion</th>
<th>Single selection value list:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>• No macroscopically visible tumour</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Non-invasive tumour visible</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cannot be assessed</td>
</tr>
<tr>
<td>OR</td>
<td>Multi select value list (select all that apply):</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Invasion into bladder wall</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Invasion into perivesical tissue</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Involvement of peritoneal surface</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Involvement of adjacent structures, specify</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>S2.07</th>
<th>Macropscopic evidence of margin involvement</th>
<th>Single selection value list:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>• Absent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Present</td>
</tr>
</tbody>
</table>

**Margins involved**

<table>
<thead>
<tr>
<th></th>
<th>Multi select value list (select all that apply):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• <em>Perivesical fat margin</em></td>
</tr>
</tbody>
</table>
| G2.06 | Appearance of uninvolved bladder | • Normal  
  OR  
  **Multi select value list (select all that apply):**  
  • Ulcerated  
  • Erythematous  
  • Other, *specify* |
|-------|---------------------------------|---------------------------------------------------------------|
| S2.08 | Lymph nodes                     | **Single selection value list**  
  • Submitted  
  • Not submitted |
|       | **Site(s) and number of nodes** | **Text:** Site  
  **AND**  
  **Numeric:** Number of LN’s  
  **Notes:**  
  Note that the site and number of LN’s for that site will need to be repeated for each site received. |
<p>| S2.09 | Block identification key        | <strong>Text</strong> |
| G2.07 | Other macroscopic comment       | <strong>Text</strong> |
| <strong>Microscopic findings</strong> |
|--------------------------|-------------------------------------------------|-------------------------------------------------|
| <strong>S3.01</strong>                | <strong>Histological tumour type</strong>                     | <strong>Single selection value list:</strong>                |
|                          | • Urothelial carcinoma                          | If urothelial carcinoma, record the           |
|                          | • Squamous cell carcinoma                       | Histological sub-type/variant                 |
|                          | • Adenocarcinoma                                |                                                 |
|                          | • Tumours of Müllerian type                     |                                                 |
|                          |   • Clear cell carcinoma                        |                                                 |
|                          |   • Endometrioid carcinoma                      |                                                 |
|                          | • Neuroendocrine tumour                         |                                                 |
|                          |   • Small cell neuroendocrine carcinoma         |                                                 |
|                          |   • Large cell neuroendocrine carcinoma         |                                                 |
|                          | • Other, <em>specify</em>                              |                                                 |
|                          |                                                 |                                                 |
|                          | <strong>Histological sub-type(s)/variant(s)</strong> (urothelial carcinoma) | <strong>Single selection value list:</strong>                |
|                          | • Not identified                                |                                                 |
|                          | • Present                                      |                                                 |
|                          | <strong>Sub-type/variant</strong>                            | <strong>Multi select value list (select all that apply):</strong> |
|                          | • Squamous                                     |                                                 |
|                          | • Glandular                                    |                                                 |
|                          | • Nested                                       |                                                 |
|                          | • Micropapillary                                |                                                 |
|                          | • Plasmacytoid                                  |                                                 |</p>
<table>
<thead>
<tr>
<th></th>
<th>Percentage</th>
<th>Numeric: ____ %</th>
</tr>
</thead>
</table>
| **S3.02** | **Non-invasive carcinoma** | Single selection value list:  
- Not identified  
- Indeterminate  
OR  
Multi select value list (select all that apply):  
- Carcinoma *in situ*, flat  
  - Multifocal  
  - Focal  
- Papillary carcinoma, non-invasive  
- Other, specify |
| **G3.01** | **Associated epithelial lesions** | Single selection value list:  
- Not identified  
- Present, specify |
| **S3.03** | **Histological grade** | Single selection value list:  
- Not applicable  
- Cannot be determined  
**Urothelial carcinoma**  
  - Low-grade  
  - High-grade |
| S3.04 | Microscopic extent of invasion | Single selection value list:  
- Cannot be assessed  
- No evidence of primary tumour  
**OR**  
**Multi select value list (select all that apply):**  
- Non-invasive tumour present  
- Tumour invades lamina propria  
- Tumour invades muscularis propria  
  - Tumour invades superficial muscularis propria (inner half)  
  - Tumour invades deep muscularis propria (outer half)  
- Tumour invades perivesical tissue  
  - Microscopically  
  - Macroscopically (extravesical mass)  
- Tumour involves adjacent structures | If prostatic stroma is selected record mechanism of prostatic stromal invasion |
<table>
<thead>
<tr>
<th>Mechanism of prostatic stromal invasion</th>
<th>Single selection value list:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct</td>
<td>Extension from prostatic ducts</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>S3.05</th>
<th>Microscopic tumour site(s)</th>
<th>Multi select value list (select all that apply):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trigone</td>
<td>Right lateral wall</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Left lateral wall</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anterior wall</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Posterior wall</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dome</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other, specify</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>G3.02</th>
<th>Microscopic tumour size</th>
<th>Numeric: _____mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>G3.03</td>
<td>Response to pre-operative therapy</td>
<td>Single selection value list:</td>
</tr>
<tr>
<td>-------</td>
<td>----------------------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Complete response (ypT0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Incomplete response</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• No response</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• No prior treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Response cannot be assessed, explain reasons</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>S3.06</th>
<th>Lymphovascular invasion</th>
<th>Single selection value list:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>• Not identified</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Present</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Indeterminate</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>S3.07</th>
<th>Margin status</th>
<th>Single selection value list:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>• Cannot be assessed</td>
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<td></td>
<td></td>
<td>• Not involved</td>
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<td></td>
<td>• Involved</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Multi select value list (select all that apply):</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o Macroscopic, specify</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o Microscopic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Invasive carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Urethral</td>
</tr>
<tr>
<td><strong>Regional lymph node status</strong></td>
<td><strong>Single selection value list:</strong></td>
<td></td>
</tr>
<tr>
<td>--------------------------------</td>
<td>---------------------------------</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• No regional nodes submitted</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Not involved</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Involved</td>
<td></td>
</tr>
</tbody>
</table>

If involved, record the following elements and consider recording G3.04. If not involved, record the number of lymph nodes examined.

| **Number of lymph nodes examined** | **Numeric:** ___ |

| **Number of positive lymph nodes** | **Number cannot be determined** OR **Numeric:** ___ |

| **Size of largest metastasis** | **Numeric:** ___mm |

- Ureteral, specify side
- Soft tissue
- Other, specify

- Carcinoma *in situ*/non-invasive high-grade urothelial carcinoma
- Urethral
- Ureteral, specify side
- Other, specify
<table>
<thead>
<tr>
<th>Location(s) of involved lymph nodes</th>
<th>Text</th>
</tr>
</thead>
</table>
| G3.04 | **Extranodal spread** | **Single selection value list:**  
- Not identified  
- Present |
| S3.09 | **Histologically confirmed distant metastases** | **Single selection value list:**  
- Not identified  
- Indeterminate  
- Present, specify site(s) |
| G3.05 | **Coexistent pathology** | None identified  
OR  
**Multi select value list (select all that apply):**  
- Adenocarcinoma of prostate  
- Urothelial carcinoma involving urethra, prostatic ducts and acini with or without stromal invasion  
- Inflammation/regenerative changes  
- Therapy-related changes  
- Cystitis cystica et glandularis  
- Keratinizing squamous metaplasia  
- Intestinal metaplasia  
- Other, specify |
### Ancillary test findings

<table>
<thead>
<tr>
<th>G4.01</th>
<th>Ancillary studies</th>
<th>Single selection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Not performed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Performed, specify</td>
</tr>
</tbody>
</table>

### Synthesis and overview

<table>
<thead>
<tr>
<th>S5.01</th>
<th>PATHOLOGICAL STAGING (AJCC TNM 8th edition)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TNM descriptors</td>
</tr>
<tr>
<td></td>
<td>Multi select value list (select all that apply):</td>
</tr>
<tr>
<td></td>
<td>m (multiple primary tumours)</td>
</tr>
<tr>
<td></td>
<td>r (recurrent)</td>
</tr>
<tr>
<td></td>
<td>y (post therapy)</td>
</tr>
</tbody>
</table>

<p>|       | Primary tumour (pT)                         |
|       | Single selection value list:               |
|       | TX Primary tumour cannot be assessed       |
|       | T0 No evidence of primary tumour           |
|       | Ta Non-invasive papillary carcinoma        |
|       | Tis Urothelial carcinoma in situ: “flat tumour” |
|       | T1 Tumour invades lamina propria (subepithelial connective tissue) |</p>
<table>
<thead>
<tr>
<th><strong>Regional lymph nodes (pN)</strong></th>
<th><strong>Single selection value list:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• NX Lymph nodes cannot be assessed</td>
<td></td>
</tr>
<tr>
<td>• N0 No lymph node metastasis</td>
<td></td>
</tr>
<tr>
<td>• N1 Single regional lymph node metastasis in the true pelvis (perivesical, obturator, internal and external iliac, or sacral lymph node)</td>
<td></td>
</tr>
<tr>
<td>• N2 Multiple regional lymph node metastasis in the true pelvis (perivesical, obturator, internal and external iliac, or sacral lymph node metastasis)</td>
<td></td>
</tr>
</tbody>
</table>

- **T2** Tumour invades muscularis propria
- **T2a** Tumour invades superficial muscularis propria (inner half)
- **T2b** Tumour invades deep muscularis propria (outer half)
- **T3** Tumour invades perivesical soft tissue
- **T3a** Tumour invades perivesical soft tissue microscopically
- **T3b** Tumour invades perivesical soft tissue macroscopically (extravesical mass)
- **T4** Extravesical tumour directly invades any of the following: prostatic stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall
- **T4a** Extravesical tumour invades directly into prostatic stroma, uterus, vagina
- **T4b** Extravesical tumour invades pelvic wall, abdominal wall
<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>S5.02</strong></td>
<td><strong>Year and edition of staging system</strong></td>
<td><strong>Numeric:</strong> year AND <strong>Text:</strong> Edition eg 1\textsuperscript{st}, 2\textsuperscript{nd} etc</td>
</tr>
<tr>
<td><strong>G5.01</strong></td>
<td><strong>Diagnostic summary</strong>&lt;br&gt;Include:&lt;br&gt;a. Operative procedure and any additional specimens&lt;br&gt;b. Tumour type with different subtypes specified&lt;br&gt;c. Tumour grade&lt;br&gt;d. Tumour extent (Level of invasion)&lt;br&gt;e. Microscopic tumour site&lt;br&gt;f. Lymphovascular invasion&lt;br&gt;g. Surgical margin status (completeness of excision)&lt;br&gt;h. Lymph node involvement&lt;br&gt;i. Tumour stage&lt;br&gt;j. Presence of non-invasive</td>
<td><strong>Text</strong></td>
</tr>
<tr>
<td></td>
<td>carcinoma</td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>-----------</td>
<td></td>
</tr>
<tr>
<td><strong>S5.03</strong></td>
<td><strong>Overarching comment</strong></td>
<td>Text</td>
</tr>
<tr>
<td><strong>G5.02</strong></td>
<td>Edition/version number of the RCPA protocol on which the report is based</td>
<td>Text</td>
</tr>
</tbody>
</table>
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.
Appendix 1  Pathology request information and surgical handling procedures

This appendix describes the information that should be collected before the pathology test. Some of this information can be provided on generic pathology request forms; any additional information required specifically for the reporting of bladder 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:
  i patient name
  ii date of birth
  iii sex
  iv identification and contact details of requesting doctor
  v date of request

- Whether or not the patient identifies as Aboriginal and/ or Torres Strait Islander. 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 Individual Healthcare Identifier (IHI) (Australia) or the National Healthcare Identifier (New Zealand).

➢ The Australian Healthcare identifiers i.e. Healthcare Provider Identifier - Individual (HPI-I) and Healthcare Provider Identifier - Organisation (HPI-O) should be use, where possible, to identify the requesting doctor.
Clinical Information

- Clinical information should be recorded.

- Knowledge of any relevant history is critical in the accurate diagnosis of tumours throughout the urinary tract.\textsuperscript{55,66,67,81} This may be relevant to the specific diagnosis being entertained. This is a recommended rather than a required item as it is the responsibility of the clinician requesting the pathological examination of a specimen to provide information that will have an impact on the diagnostic process or affect its interpretation. Patients with a history of urothelial neoplasia are at risk for urothelial tumours throughout the urinary tract and this may inform the interpretation in subsequent specimens. Urothelial tumours in the urinary bladder and upper tract may have been treated with therapies such as Bacillus Calmette-Guerin (BCG), mitomycin C and others. These can be associated with morphologic changes that have the potential for misdiagnosis if the pathologist is unaware of the prior treatment.\textsuperscript{147,148} Radiation therapy (to the bladder or to adjacent organs) can be associated with pseudocarcinomatous hyperplasia that can be misdiagnosed as invasive carcinoma.\textsuperscript{149,150} Neoadjuvant chemotherapy may result in significant tumour response and necessitate very careful macroscopic and microscopic assessment for residual tumour.

- Relevant past medical history, family history and known risk factors associated with bladder cancers should be provided. The past history of urothelial neoplasms elsewhere in the urinary tract should be recorded.

- Previous history of bladder disease may include:
  - Superficial bladder disease
  - Muscle invasive disease.

- Distant metastasis refers to the spread of cancer of the same histologic type as the original (primary) tumour to distant organs or distant lymph nodes.

- This information will provide an opportunity for previous reports to be reviewed during the reporting process, which may provide valuable information to the pathologist. This information also has implications for recording cancer incidence and evidence based research.

- Previous chemotherapy may cause extensive or complete tumour necrosis. This must be taken into account by the reporting pathologist.

- Information regarding the extent of disease as determined from clinical assessment, cystoscopy, prior histology and imaging should be provided.
• Relevant information regarding the extent of disease, particularly biopsy positivity gives extra information that is useful for adequately sampling for accurate staging. For example, the principal tumour may not be the most invasive. There may be non-papillary tumours that are deeply invasive.

➢ The operative procedure and nature of additional specimen(s) submitted should be stated.
Example Request Information Sheet

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.\(^{151}\)

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.

- Configuring reports in such a way that they ‘chunk’ data elements into a single unit will help to improve recall for the clinician.\(^{151}\)
- ‘Clutter’ should be reduced to a minimum.\(^{151}\) Thus, information that is not part of the protocol (e.g. billing information, SNOMED codes, etc) should not appear on the reports or should be minimized.
- Injudicious use of formatting elements (e.g. too much bold, underlining or use of footnotes) constitutes 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.
### URINARY BLADDER STRUCTURED REPORT

**CLINICAL INFORMATION RECEIVED**

- **Prev. hx of urinary tract disease:** No previous history
- **Previous therapy:** No previous therapy
- **Other clinical information:** Haematuria
- **Clinical extent of disease:** Muscle invasive high grade TCC found on left lateral bladder biopsy
- **Operative procedure:** Radical cystectomy
- **Additional specimens submitted:** Not submitted

**MACROSCOPIC**

- **Specimen labelled as:** Bladder and prostate
- **Operative procedure:** Radical cysto-prostatectomy
- **Additional specimens submitted:** Not submitted

**SPECIMEN MEASUREMENTS**

- **Bladder measurements:** 80 x 65 x 45mm
  - Superior to inferior x transverse x anterior to posterior
- **Length of ureters:** 45 mm Right, 55 mm Left
- **Length of urethra:** 7mm
- **Prostate measurements:** 45x35x30 mm
- **Right seminal vesicle:** 25x15x10 mm
- **Left seminal vesicle:** 35x25x10 mm
- **Tumour focality:** Unifocal
- **Macro. tumour site:** Left lateral wall, posterior wall, dome

**TUMOUR DIMENSIONS**

- **Max tumour dimension (largest tumour):** 42mm
- **Additional Tumour dimensions:** 19mm x 6mm
- **Gross appearance of tumour:** Ulcerated, Solid and indurated.
- **Macro extent of invasion:** Invasion into bladder wall
- **Macro evidence of margin involvement:** Absent
- **Appearance of uninvolved bladder:** Normal
- **Lymph nodes:** Not submitted
- **Other macroscopic comment:** Nil of significance
Block identification key: A: Right ureter resection margin; B: Left ureter resection margin; C: Urethra resection margin; D: T: Tumour; K: Trigone; L: Anterior wall bladder; M: Right lateral wall bladder; N: Posterior wall bladder; O: Left wall bladder; P: Q: Bladder dome; R-U: Basal slice of prostate; V-AG: Body of prostate (Superior to inferior RA, RP, LP, LA); AH-AR: Apical prostate R-L.

MICROSCOPIC

Tumour

Histological tumour type: Urothelial carcinoma
Histological grade: High-grade
Micro tumour site: Left lateral wall, posterior wall, dome
Tumour size (max dimension): 42mm
Response to pre-operative therapy: No prior treatment

Extent of invasion

Tumour invades Lamina propria
Muscularis propria
- superficial (inner half)
- deep (outer half)

Lymphovascular invasion: Present

Margin status: Not involved
Lymph node status: No regional nodes submitted
Histologically confirmed distant metastases: Not identified
Non-invasive carcinoma: Not identified
Co-existing pathology: None identified
Other microscopic comment: No evidence of prostatic adenocarcinoma

Diagnostic Summary

Radical cystectomy:

High grade urothelial carcinoma
In left lateral wall, posterior wall, dome
Invading into lamina propria and inner and outer muscularis propria.
Clear surgical margins
Lymphovascular invasion present
Pathological Stage pT2b (AJCC 8th edition, 2016)

Reported by Dr Bernard Beckstein Authorised 4/9/2017
Appendix 4  WHO Classification of Tumours

WHO 2016: Variants of Urothelial Carcinoma

Urothelial carcinomas with divergent differentiation
  Squamous differentiation
  Glandular differentiation
  Trophoblastic differentiation
  Müllerian differentiation

Nested, including large nested

Microcystic

Micropapillary

Lymphoepithelioma-like

Plasmacytoid/diffuse

Sarcomatoid

Giant cell

Lipid-rich

Clear cell

Poorly differentiated tumours (including those with osteoclast-like giant cells)
References

1 Merlin T, Weston A and Tooher R (2009). Extending an evidence hierarchy to include topics other than treatment: revising the Australian 'levels of evidence'. BMC Med Res Methodol 9:34.


13 RCPA (Royal College of Pathologists of Australasia (2009 ). *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols*. RCPA, Surry Hills NSW.


