

**CARCINOMA OF THE RENAL
PELVIS AND URETER
STRUCTURED REPORTING
PROTOCOL
(NEPHROURETERECTOMY AND
URETERECTOMY)
(1st Edition 2018)**

Incorporating the:

**International Collaboration on Cancer Reporting
(ICCR)**

Dataset for the reporting of carcinoma of the renal pelvis
and ureter – nephroureterectomy and ureterectomy.

www.ICCR-Cancer.org

Core Document versions:

1. ICCR Dataset for the reporting of carcinoma of the renal pelvis and ureter – nephroureterectomy and ureterectomy.
2. AJCC Cancer Staging Manual 8th edition
3. World Health Organization (WHO). Classification of tumours. Pathology and genetics of the urinary system and male genital organs. 4th edition.

ISBN: 978-1-76000-929-8

Publications number (SHPN): (CI) 180565

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First published: August 2018, 1st Edition (version 1.0)

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Scope

This protocol contains standards and guidelines for the reporting of resection specimens from patients with primary carcinoma of the ureter and renal pelvis. The protocol applies to 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 protocol does not apply to those diagnoses. Transurethral resection and biopsy specimens are dealt with in a separate protocol. For bilateral tumours, complete a separate dataset for each.

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 upper urinary tract urothelial cancer, whether as a minimum data set or fully comprehensive report.

Abbreviations

AJCC	American Joint Committee on Cancer
BCG	Bacillus Calmette-Guerin
CIS	Carcinoma <i>in situ</i>
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
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
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	<p>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).</p> <p>Commentary is used to:</p> <ul style="list-style-type: none">• 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. <p>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).</p>
General commentary	<p>General commentary is text that is not associated with a specific standard or guideline. It is used:</p> <ul style="list-style-type: none">• 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	<p>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.¹ These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.</p> <p>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.</p> <p>Guidelines are not used for research items.</p> <p>In this document, guidelines are prefixed with 'G' and numbered consecutively within each chapter (eg G1.10).</p>
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	<p>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 evidence¹ 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.</p> <p>The summation of all standards represents the minimum dataset</p>

for the cancer.

In this document, standards are prefixed with 'S' and numbered consecutively within each chapter (eg S1.02).

Structured report	A report format which utilises standard headings, definitions and nomenclature with required information.
Synoptic report	A structured report in condensed form (as a synopsis or precis).
Synthesis	Synthesis is the process in which two or more pre-existing elements are combined, resulting in the formation of something new.

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

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

Introduction

Upper urinary tract carcinoma accounts for approximately 5% of all genitourinary malignancies² and 5-10 % of all urothelial cancers.³ It occurs more commonly in older individuals, most commonly at >70 years of age and it is more common in males.⁴ The incidence of these tumours appears to be increasing.³ Several aetiological factors are incriminated. The most common of these are cigarette smoking, occupational exposure to carcinogens and Hereditary non-polyposis colorectal cancer (HNPCC) or Lynch syndrome.^{5,6} Ingestion of Aristolochic acid which is a bioactive component found in Chinese herbs, dietary supplements, slimming pills and contaminated flour is a risk factor in exposed populations worldwide.⁷ Lynch syndrome increases the risk of developing an upper tract urothelial carcinoma, 14-22 times that in the general population.⁸ While urothelial carcinoma is the commonest type, a variety of other carcinomas including squamous cell carcinoma, adenocarcinoma and neuroendocrine carcinoma have been reported in this location.⁶ Urothelial carcinoma has a great propensity for divergent differentiation resulting in a number of subtypes similar to that occurring in the bladder and elsewhere in the urinary tract.⁶ Given that diagnosis is difficult in most cases with biopsies often insufficient for diagnosis and for grading and staging accurately, most cases are at a high stage at nephroureterectomy.⁴

Importance of histopathological reporting

Information in the pathology report of the macroscopic and microscopic findings in nephroureterectomy and ureterectomy 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, the rapid growth in ancillary testing such as immunohistochemistry, flow cytometry, cytogenetics, and molecular studies, have made the task of

keeping abreast of advances on specific cancer investigations extremely difficult for pathologists. 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,⁹ and United States¹⁰ 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 capture¹¹⁻¹⁴ 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 renal pelvis and ureter – nephroureterectomy and ureterectomy 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 renal pelvis and ureter.

ICCR dataset elements for carcinoma of the renal pelvis and ureter 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:

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

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

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

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

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*¹⁵
- *World Health Organization (WHO). Classification of tumours. Pathology and genetics of the urinary system and male genital organs. Humphrey PA, Moch H, Reuter VE, Ulbright TM editors. 4th edition. Lyon, France: IARC Press;2016.*¹⁶
- *AJCC Cancer Staging Manual, 8th edition, American Joint Committee on Cancer, 2016*¹⁷

Updates since last edition

Not applicable.

Authority and development

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

This 1st 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 renal pelvis and ureter 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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Acknowledgements

The expert committee wish to thank all the pathologists and clinicians who contributed to the discussion around this document.

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)

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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

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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*.¹⁵

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 carcinoma of the renal pelvis and ureter 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.¹⁸ 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	<p>The term partial refers to cases where the entire ureter is not removed.</p> <p>A complete (radical) nephroureterectomy assumes that the bladder cuff is present. This is the standard operation for high risk urothelial carcinoma of the upper urinary tract irrespective of location.^{19,20}</p> <p>In the past the role for segmental ureterectomy in urothelial carcinoma has been largely limited to patients with specific indication, in particular patients with an absent or non-functioning kidney on the opposite side. More recently, this approach has also been used in patients with a normal functioning contralateral kidney, particularly those patients with low risk disease.^{19,21,22} Low-risk upper tract urothelial carcinoma is defined by</p>

		the European Association of Urology (EAU) as those that are unifocal, <1 cm in size, with low-grade cytology, low-grade histology on ureteroscopic biopsy and are non-invasive on multidetector computed tomography urography. ¹⁹ When segmental ureterectomy specimens are submitted for pathological examination it is crucial that the tissue be oriented as to lower and upper ends should a margin prove to be positive.
 S2.03	Additional specimens submitted must be recorded.	

S2.04 The kidney must be measured in three dimensions and weighed. The length and diameter of the ureters must be recorded. Three dimensional measurements of any other organs should also be reported if submitted.

 S2.05	Tumour focality must be recorded.	
	CS2.05a	<p>A large meta-analysis found tumour multifocality to be a significant predictor of subsequent development of an intravesical tumour.²³ In this study other significant pathologic predictors of an increased risk for intravesical recurrence were tumour location (ureter), pT stage, and tumour necrosis; features that were not significant were tumour size, tumour grade, concomitant carcinoma <i>in situ</i> (CIS) and lymphovascular invasion. In a different meta-analysis predictors of intravesical recurrence were location (ureter higher), pT stage (lower=higher risk), and tumour size (higher with tumour >3 cm); features that were not significant were concomitant CIS, multifocality and tumour grade.²⁴</p> <p>In the most recent EAU guidelines,¹⁹ multifocality is not listed as a significant prognostic indicator postoperatively. It is listed as significant preoperatively. In contrast, in a comprehensive literature review, Lughezzani <i>et al</i>²⁵ concluded that multifocality was an independent predictor of cancer specific survival. This reflected several large series in the literature.^{26,27}</p>

G2.01 For multifocal tumours the number of foci of tumour should be recorded.

 S2.06	Macroscopic tumour site(s) must be recorded.	
	CS2.06a	<p>Studies evaluating the significance of tumour location of upper tract urothelial carcinoma have had inconsistent results.^{20,28-31} In the most recent analysis of the subject by the EAU, it was concluded that ureteral location was associated with a worse prognosis than renal pelvic location.¹⁹</p>

		<p>Several reports have also demonstrated that tumour location is a significant predictor of subsequent development of intravesical disease. These reports have consistently noted an increased risk to be associated with ureteral rather than renal pelvic origin.^{23,24} It has also been found that location in the lower ureter is associated with a higher risk than the upper ureter.³²</p> <p>Further knowledge of the gross location of the tumour is important in the evaluation of histologic sections. In cases where examination of the sections does not show the relationship of the tumour to renal stroma, a gross description describing location as renal pelvis should prompt re-examination of the specimen and submission of additional sections as appropriate.</p>
 S2.07	The maximum dimension of the largest tumour must be recorded (in mm).	
	CS2.07a	<p>Tumour size is prognostic for upper tract tumours pre-surgical resection. In the current EAU guidelines they conclude that it is not prognostic post resection.¹⁹ Small (<1 cm) is considered in these guidelines to be part of the definition of low-risk disease. A recent comprehensive review did however conclude that size was a significant predictor of progression-free and recurrence free survival.^{20,33,34} Given the limited size of the referenced studies this parameter requires additional larger studies to confirm its independent significance. Nonetheless tumour size remains an integral part of the gross description of a tumour and documentation of at least the largest dimension of a tumour is considered to be a required element of this dataset.</p>
 G2.02	Additional dimensions of the largest tumour may be recorded.	

G2.03 The gross appearance of the tumour(s) should be recorded as polypoid, fungating, papillary, ulcerated or solid and indurated.

 S2.08	The macroscopic extent of invasion must be recorded.	
	CS2.08a	<p>In contrast to the urinary bladder the gross evaluation of tumour extent is not an element of the pathologic staging system. Nonetheless, estimating the gross extent of disease can help in block selection and reporting cases if there is a discrepancy between the gross evaluation and the microscopic findings. When a discrepancy is found between the two, this should be resolved by re-evaluating the gross appearance and submitting additional blocks if appropriate. It is recognised that the gross estimation may both over and under estimate the microscopic extent of disease</p>

		and assignment of pathologic stage is based on the latter. For further information refer to the ICCR dataset. ³⁵
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S2.09 The presence or absence of macroscopic evidence of resection margin involvement.

CS2.09a Renal hilar, perinephric ureteric and periureteric margin involvement must be recorded.

G2.04 Features of uninvolved tissue must be recorded.

S2.10 The number and sites of any lymph nodes submitted must be recorded.

 S2.11	A block identification key listing the nature and origin of all tissue blocks must be recorded.	
	CS2.11a	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.

G2.05 A descriptive or narrative field should be provided to record any macroscopic information that is not recorded in the above standards and guidelines, and that would normally form part of the macroscopic description.

CG2.05a The traditional macroscopic narrative recorded at the time of specimen dissection is often reported separately from the cancer dataset. Although this remains an option, it is recommended that macroscopic information be recorded within the overall structure of this protocol.

CG2.05b Much of the information recorded in a traditional macroscopic narrative is covered in the standards and guidelines above and in many cases, no further description is required.

3 Microscopic findings

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

 S3.01	Histological tumour type and sub-type/variant must be recorded.	
	CS3.01a	<p>The majority of primary carcinomas of the upper tracts are urothelial carcinoma with non-urothelial carcinomas accounting for approximately 2% of tumours.³⁶ Primary squamous cell carcinoma, adenocarcinoma and small cell neuroendocrine carcinoma account for almost all other types and generally exist in the literature as small institutional case series.³⁶⁻³⁸</p> <p>The 2016 World Health Organization (WHO) classification is utilised for assigning histological tumour type.³⁹ As in the 2004 WHO Classification,⁴⁰ a tumour is classified as a urothelial carcinoma if there is any identifiable urothelial component no matter how small and including urothelial CIS. The one exception to this rule is for cases with a (small cell neuroendocrine carcinoma or large cell neuroendocrine carcinoma) where classification is now 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%).</p> <p>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. As in the urinary bladder, in the upper tract about one-half of cases are pure and one-half are mixed with another component with urothelial carcinoma being most frequent. 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</p>

	<p>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.⁴¹⁻⁴⁵ For example the National Comprehensive Cancer Network (NCCN) includes tumours with “any small-cell component” in the category of non-urothelial cell carcinoma.^{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.⁴⁷ TTF-1 is expressed in about 50% of cases.^{48,49}</p> <p>Lastly there are carcinomas arising in the urinary tract 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.³⁹</p> <p>Histologic subtype/variant</p> <p>The 2016 WHO classification includes a number of recognised morphologic variants as outlined in the table below.³⁹ Because urothelial carcinoma has a remarkable capacity for morphologic variation the number of histologic variants that have been described in the literature is extensive.^{50,51} In the development of the 2016 WHO classification not all of these are included.³⁹ 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 tumours that have important prognostic or therapeutic implications.</p> <p>There are therefore data on histologic variants in upper tract tumours though not as robust as for primary bladder urothelial carcinoma. One large series of 1648 patients reported variant histology in 24% of cases with squamous (9.9%) and glandular (4%) differentiation being most common.⁵² Patients with variant histology had worse recurrence-free and cancer-specific survival although it was not independent for either. An additional study of 417 cases found variant histology in 22% (also with squamous and glandular being most common) and found variant histology to be an independent predictor of cancer specific survival.⁵³</p>
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		<p>Practically all of the described variants of urothelial carcinoma have been reported in the upper tracts.^{54,55} These are mostly isolated case reports or small case series. One report of 39 upper tract micropapillary urinary carcinoma (out of 519 cases) found the micropapillary variant to be associated with advanced stage and reduced cancer specific survival.⁵⁶</p> <p>Reporting the percentage of variant histology when present is recommended (this is recommended in the WHO 2016 monograph).³⁹ The data supporting this is very limited and only available for selected variants (micropapillary, sarcomatoid, lymphoepithelioma-like), and those with divergent differentiation (glandular, squamous) in series from the urinary bladder. 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 as well as the estimated percentage of this component. For cases with more than one variant present, the percentage of each is recommended to be documented.</p>
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CS3.01b The classification of tumours is from the WHO 2016 classification¹⁶ (refer to Appendix 4).

 S3.02	The presence of non-invasive carcinoma must be reported.	
	CS3.02a	<p>There is substantial data that the presence of concomitant urothelial CIS is associated with a worse recurrence-free and cancer-specific survival.^{25,57-59} It is therefore important in these specimens to sample grossly normal portions of the resected ureter and renal pelvis for evaluation. These studies have not specifically recorded the extent of the associated CIS. For the purposes of this dataset we have divided CIS into focal and multifocal and arbitrarily defined these as involvement of a single versus multiple blocks.</p>

CS3.02b The extent of CIS may have an impact on the risk of involvement of other urinary tract sites.⁶⁰

 G3.01	The presence of associated epithelial lesions should be reported.	
	CG3.01a	<p>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</p>

		<p>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.</p>
 S3.03	The histological grade must be reported.	
	CS3.03a	<p>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 WHO³⁹ remains the same as in the 2004 WHO⁴⁰ and continues to recommend the grading system first put forward by the International Society of Urological Pathology (ISUP) in 1997.⁶¹ The system is now recommended by almost all major pathology and urology organizations as the preferred grading system.^{62,63}</p> <p>Histologic grade is a significant predictor of cancer specific survival in urothelial carcinoma of the upper urinary tract.^{25,64} In contrast to the urinary bladder where relatively few patients with low grade non-invasive papillary tumours are managed by cystectomy, many such patients do undergo nephroureterectomy or segmental ureterectomy. Histologic grade is one suggested determining factor in selecting patients for segmental ureterectomy versus nephroureterectomy.¹⁹ Low grade tumours may also be managed endoscopically and not come to resection.^{19,65,66} For those patients undergoing surgical resection for papillary tumours, grade is a significant prognostic indicator. It is included as a variable in the nomograms based on the largest series in the literature.⁶⁷⁻⁶⁹ The nomograms both from Seisen <i>et al</i>⁶⁸ and from Cha <i>et al</i>⁶⁷ utilised the 1998 WHO/ISUP grading system (equivalent to the 2004 and 2016 WHO grading systems).</p> <p>The use of 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,⁷⁰⁻⁷² while others suggest that the 1973 grade be provided by institutional choice.^{39,62,63}</p> <p>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.⁷³⁻⁷⁵ In</p>

		<p>studies using the 1998 ISUP/WHO 2004 grading system the vast majority of invasive tumours are high grade.^{76,77} The 2016 WHO recommends continuing to grade invasive carcinoma using the WHO 2004 system recognising that the vast majority of tumours will be high grade.³⁹ If invasive tumours are graded using an alternative grading system this should be indicated.</p> <p>For further information refer to the ICCR dataset.³⁵</p>
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CS3.03b Squamous cell carcinoma is graded using criteria used for these tumours in other viscera.⁷⁸ 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 squamous differentiation.

CS3.03c There is no generally accepted grading system for adenocarcinoma of the upper urinary tract.¹⁶

 S3.04	The microscopic extent of invasion must be given.	
	CS3.04a	<p>Pathologic stage is a major prognostic indicator postoperatively. It is included in all three of the published nomograms based on the largest datasets available in the literature.⁶⁷⁻⁶⁹ The diagnosis of invasion in upper tract tumours can be complicated by the distortion induced by the expansile mass growing in a confined space. This can result in thinning of the wall in the ureter or renal pelvis. Tumours with inverted architecture can compress the muscularis propria with near complete absence of this layer in tissue sections and diagnosis of invasion requires identification of a clearly infiltrative component. Given the very thin layer of subepithelial connective tissue in the ureter and renal pelvis, there is essentially no identifiable muscularis mucosae and invasion of any smooth muscle should be considered to represent T2 disease.</p> <p>For tumours arising in the renal pelvis involvement of the renal parenchyma is an important element in the staging system. Invasion of the renal stroma is included in the definition of pT3 disease. This must be distinguished from <i>in situ</i> spread of the tumour into the collecting ducts of the kidney which does not impact stage assignment. There have been proposals to substage pT3a tumours with renal stromal involvement. None of these approaches have been adopted in the 8th edition of the AJCC Staging Manual.⁷⁹</p> <p>Invasive carcinomas can also extend through the renal</p>

		stroma and extend into the perinephric fat. Those tumours are staged as pT4. This needs to be distinguished from involvement of sinus fat in cases with renal stromal invasion that would still be considered pT3. Direct invasion of an adjacent organ, including the adrenal gland, is also staged as pT4.
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CS3.04b Level of invasion or pathological category is the most important prognostic indicator in upper urinary tract cancer.⁸⁰

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.

 S3.06	The presence or absence of lymphovascular invasion (LVI) must be recorded.	
	CS3.06a	<p>Lymphovascular invasion has been repeatedly found to be an important prognostic indicator for urothelial carcinoma of the upper tracts. The most recent EAU guidelines conclude that it is an independent predictor of outcome in these tumours.¹⁹ It is included in both the Cha <i>et al</i> and Seisen <i>et al</i> nomograms.^{67,68} There are many other studies where it has been reported to be an independent predictor as well.^{57,69,81-83}</p> <p>As in other datasets the use of immunohistochemistry (IHC) to determine the presence or absence of lymphovascular invasion is considered optional. It should be noted that none of the major studies referenced above used IHC as a routine part of the evaluation.</p>

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

 S3.07	The margin status must be reported.	
	CS3.07a	<p>Positive surgical margins (generally the bladder cuff in nephroureterectomy series) have been correlated with increased risk of subsequent development of an intravesical tumour.^{84,85} In the meta-analysis by Seisen <i>et al</i>²³ this was a statistically significant indicator of an increased risk of bladder recurrence.</p> <p>Positive surgical margins (generally the bladder cuff in nephroureterectomy series) have also been correlated with increased risk of distant metastases and cancer</p>

		specific survival. ⁸⁶ This has not however been a consistent finding ⁸⁷ and was not a significant predictor of cancer specific survival in the meta-analysis by <i>Seisen et al</i> (2015). ²³ Of interest margin status was not tested in the development of the nomograms by Cha et al (2012) ⁶⁷ or <i>Seisen et al</i> (2014). ⁶⁸
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CS3.07b Involvement of ureter margin by CIS or invasive carcinoma must be stated. Involvement of renal hilar, perinephric fat or periureteric margins by invasive carcinoma must be stated.

	S3.08	Regional lymph node status must be recorded.
	CS3.08a	<p>The staging system for tumours of the renal pelvis and ureter differs from the urinary bladder in that it includes both the number of lymph nodes involved and the size of the metastases in assigning the pN category.⁸⁸ It is therefore necessary to both determine the number of lymph nodes involved by tumour (one or greater than one) and the greatest dimension of the metastasis (cutpoint is at 2 cm). By definition for tumours of the renal pelvis, the renal hilar, paracaval, aortic and retroperitoneal lymph nodes not otherwise specified are considered regional. For carcinomas of the ureter the regional lymph nodes are the renal hilar, Iliac (common, internal/hypogastric, external), paracaval, periureteral, and pelvic not otherwise specified. Involvement of lymph nodes other than as defined is considered to represent pM1 disease.</p> <p>There are limited published data indicating that the number of lymph nodes removed, the number of positive nodes and the lymph node density (% positive nodes) are significant prognostic indicators in patients with upper tract carcinoma and lymph node positive disease.^{89,90} In contrast, another study did not find the number of nodes removed or the number of positive nodes to correlate with outcome; lymph node density was however significant.⁹¹ Similarly Fajkovic <i>et al</i>⁹² did not find either the number of nodes removed or the number of positive nodes to correlate with outcome.</p> <p>For patients with node-negative disease it has been reported that the number of nodes resected correlates with the likelihood that the patient is a true pN0.⁹³ This study used a statistical modelling method and was based on 814 lymph node dissections. To reach >95% confidence that a pN0 result was "true" a minimum of 15 nodes needed to be examined. With only 1 lymph node they estimated that 44% of true pN+ cases would be misclassified as pN0. Another study reported that removal of 8 lymph nodes had a >75% probability of finding a positive lymph node and with 13 lymph nodes a >90% probability was achieved.⁹⁴</p>

		In the most recent EAU guidelines for upper tract carcinoma it is stated that "extranodal extension is a powerful predictor of clinical outcome in upper tract urothelial carcinomas and positive lymph node metastases". ¹⁹ This conclusion was based on a study by Fajkovic <i>et al</i> ⁹² in which the presence of extranodal extension was an independent predictor of tumour recurrence and cancer specific mortality. In another study the presence of extranodal extension was "marginally" associated with a worse prognosis. ⁹⁵ Studies of metastatic carcinoma of the urinary bladder have also evaluated the significance of extranodal extension with similar findings in most ⁹⁶⁻⁹⁸ but not all. ⁹⁹
 G3.03	The presence of extranodal spread should be recorded.	
 S3.09	The presence of histologically confirmed distant metastases must be recorded.	
 CS3.09a	Documentation of known metastatic disease is an important part of the pathology report. Such information, if available, should be recorded with as much detail as is available including the site and reference to any relevant prior surgical pathology or cytopathology specimens.	
 S3.10	Any coexistent pathology must be recorded.	
 CS3.10a	It is important to recognise that medical kidney diseases may be present in non-neoplastic renal tissue in nephrectomy specimens. ¹⁰⁰⁻¹⁰² It is presumed that similar findings may be present in nephroureterectomy specimens and likely would have similar clinical significance although specific studies are not yet available. Assessment of the non-neoplastic kidney may be complicated by changes related to urinary tract obstruction with hydronephrosis and other sequelae. No formal definition exists for insufficient renal stromal tissue. In nephroureterectomy specimens this is generally not relevant as the entire kidney is removed.	

G3.04 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.

 G4.01	Whether or not ancillary tests are performed should be recorded and the results incorporated into the pathology report.	
	CG4.01a	<p>In addition to specifying ancillary studies performed, results should be provided (if available).</p> <p>The current EAU guidelines recommend evaluation for Hereditary Nonpolyposis Colorectal Cancer (HNPCC or Lynch syndrome) at the time of medical history taking.¹⁰³ They also recommend DNA sequencing to identify hereditary cancers misclassified as sporadic. In a recent comprehensive review,¹⁰⁴ the authors recommend tissue testing of upper tract urothelial carcinomas (IHC and/or molecular) similar to gastrointestinal tract guidelines in any one of the following situations: (i) the patient is <60 years of age or (ii) there is a family history of an upper tract urothelial carcinoma, endometrial carcinoma, or a colon cancer diagnosis in a relative <60 years of age, or (iii) if there is a personal history of colon or endometrial cancer.</p> <p>It has been shown that upper tract tumours associated with microsatellite instability frequently have an inverted growth pattern.¹⁰⁵ There is at least one report indicating that these tumours are more responsive to adjuvant chemotherapy.¹⁰⁶</p>

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.

 S5.01	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).	
	CS5.01a	<p>Pathologic stage is the single most important prognostic parameter for patients that have undergone nephroureterectomy or ureterectomy for upper tract carcinoma.²⁵ Pathologic stage is also a significant predictor of subsequent intravesical recurrence.²³ Stage may also be an important parameter in the consideration of the use of adjuvant chemotherapy. Accurate assignment of pathologic stage is therefore of considerable clinical significance. A careful gross examination with appropriate submission of sections is integral to the determination of pathologic stage. Knowledge of the anatomical origin of the sections can also be important to interpretation of the microscopic findings given the complex anatomy, particularly in the renal hilar region.</p> <p>Understanding the anatomy and histology of the various parts of the upper tract are important to the subsequent interpretation of the specimen.¹⁰⁷ As discussed earlier, throughout the upper tract the subepithelial connective tissue tends to be very thin and is often distorted by the intraluminal tumour. The muscularis propria can be similarly attenuated. Further in the region of the renal sinus and calyces there may be no visible muscle fibres and the distinction of subepithelial connective tissue invasion (pT1) from the renal sinus connective tissue (pT3) may be quite arbitrary. In such cases identification of a convincing focus of invasion can change the stage assignment from pTa to pT2 or even pT3.¹⁰⁸ In the area of the renal papillae the urothelium sits on the renal stroma with an essentially invisible zone of subepithelial connective</p>

		<p>tissue such that virtually any invasion will result in designation as pT3 tumour.</p> <p>For tumours in the renal sinus and calyces the relationship of the tumour with the renal stroma can be complex. Non-invasive tumour extending into the renal collecting ducts does not constitute renal stroma invasion and over staging as pT3 must be avoided. Fortunately when urothelial carcinoma invades renal stroma it almost always elicits a response and this can be helpful in difficult cases.</p> <p>Invasive carcinomas can also extensively infiltrate the kidney and extend into the perinephric fat. Those tumours are staged as pT4. This needs to be distinguished from involvement of sinus fat in cases with renal stroma invasion that would still be considered pT3.</p> <p>Assessment of pathological stage can also be challenging in tumours with an inverted architecture. In the renal pelvis and calyces this is problematic given the histological anatomy of that location. Non-invasive tumours with inverted architecture can push on renal sinus fat. Problematic cases should be extensively sampled in an effort to document unequivocal invasion.</p> <p>For further information refer to the ICCR dataset.³⁵</p>
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S5.02 The year of publication or the edition of the cancer staging system used in S5.01 must be included in the report.

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

- a. Operative procedure (S2.03) and any additional specimens (S2.04)
- b. Tumour site (S2.06)
- c. Tumour type with different subtypes specified (S3.01)
- d. Tumour grade (S3.03)
- e. Tumour extent (Level of invasion) (S3.04)
- f. Lymphovascular invasion (S3.06)
- g. Surgical margin status (completeness of excision) (S3.07)
- h. Lymph node involvement (S3.08)
- i. Tumour stage (S5.01)
- j. Presence of non-invasive carcinoma (S3.02)

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

overarching case comment.

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

- document any noteworthy adverse gross and/or histological features
- explain any elements of clinicopathological ambiguity
- express any diagnostic subtlety or nuance that is beyond synoptic capture
- document further consultation or results still pending.

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 Cancer Protocols*.¹⁰⁹

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.

S/G	Item description	Response type	Conditional
Pre-analytical			
S1.01	Demographic information provided		
S1.02	Clinical information provided on request form	Text OR Structured entry as below:	
	CLINICAL INFORMATION		
	Previous history of urinary tract disease or distant metastasis	<ul style="list-style-type: none"> • Information not provided • No previous history OR Multi select value list (select all that apply): <ul style="list-style-type: none"> • Non-invasive papillary • Carcinoma <i>in situ</i>, flat • Invasion into lamina propria • Muscle invasive disease • Distant metastasis • Other, <i>specify</i> 	

	Previous therapy	<ul style="list-style-type: none"> • Information not provided • No previous therapy OR Multi select value list (select all that apply): <ul style="list-style-type: none"> • Bacillus Calmette-Guerin (BCG) • Chemotherapy, intravesical, <i>specify</i> • Chemotherapy, systemic • Radiation therapy • Other, <i>specify</i> 	
	Other clinical information	Text	
	Clinical extent of disease	Text	
	Operative procedure	Single selection value list: <ul style="list-style-type: none"> • Not specified • Nephroureterectomy • Ureterectomy, partial • Ureterectomy, complete • Ureterectomy with cystectomy • Ureterectomy with cystoprostatectomy • Other, <i>specify</i> 	
	Additional specimen(s) submitted	Single selection value list: <ul style="list-style-type: none"> • Not submitted 	

		Submitted, <i>specify</i>	
S1.03	Pathology accession number	Alpha-numeric	
S1.04	Principal clinician caring for the patient	Text	
G1.01	Other clinical information received	Text	
Macroscopic findings			
S2.01	Specimen labelled as	Text	
 S2.02	Operative procedure	Single selection value list: <ul style="list-style-type: none"> • Not specified • Nephroureterectomy • Ureterectomy, partial • Ureterectomy, complete • Ureterectomy with cystectomy • Ureterectomy with cystoprostatectomy • Other, <i>specify</i> 	
 S2.03	Additional specimen(s) submitted	Single selection value list: <ul style="list-style-type: none"> • Not submitted • Submitted, <i>specify</i> 	

S2.04	Specimen measurements	Numeric: __x__x__mm <u>Notes:</u> (Superior to inferior x transverse x anterior to posterior)	
	Length of ureters	Numeric: ___mm (Right) AND Numeric: ___mm (Left)	
	Measurements of other organs	Text: <i>Other organ</i> AND Numeric: __x__x__mm <u>Notes:</u> <i>Record for each other organ submitted.</i>	Conditional on other organs submitted being recorded in S2.03.
 S2.05	Tumour focality	Single selection value list: <ul style="list-style-type: none"> • Unifocal • Multifocal • Cannot be assessed, <i>specify</i> 	If multifocal, consider recording the number of tumours at G2.01
G2.01	<i>Number of tumours</i>	Numeric: _____	
 S2.06	Macroscopic tumour site	Single selection value list: <ul style="list-style-type: none"> • Indeterminate • No macroscopically visible tumour 	

		OR Multi select value list (select all that apply):	
		<ul style="list-style-type: none"> • Ureter • Renal pelvis • Other, <i>specify</i> 	
 S2.07	TUMOUR DIMENSIONS	Single selection value list: <ul style="list-style-type: none"> • No macroscopically visible tumour • Cannot be assessed <i>OR complete the following element(s)</i>	
	Maximum tumour dimension (largest tumour)	Numeric: ___mm	
 G2.02	Additional dimensions (largest tumour)	Numeric: ___x___mm	
G2.03	Gross appearance of tumour(s)	Multi select value list (select all that apply): <ul style="list-style-type: none"> • Polypoid • Fungating • Papillary • Ulcerated • Solid and indurated <u>Notes:</u>	

		Tumour appearance should be recorded for <i>each</i> tumour identified in G2.01 if recorded.	
 S2.08	Macroscopic extent of invasion	<p>Single selection value list:</p> <ul style="list-style-type: none"> • Non-invasive tumour visible • No macroscopically visible tumour • Cannot be assessed <p>OR</p> <p>Multi select value list (select all that apply):</p> <ul style="list-style-type: none"> • Invasion into wall • Invasion into periureteral/peripelvic tissue • Invasion into renal stroma • Invasion into perinephric fat • Involvement of other adjacent structures, <i>specify</i> 	
S2.09	Macroscopic evidence of margin involvement	<p>Single selection value list:</p> <ul style="list-style-type: none"> • Absent • Present 	If present, record the margins involved
	<i>Margins involved</i>	<p>Multi select value list (select all that apply):</p> <ul style="list-style-type: none"> • Renal hilar • Perinephric fat • Ureteric • Periureteric 	

G2.04	Appearance of uninvolved tissue	Normal OR Multi select value list (select all that apply): <ul style="list-style-type: none"> • Ulcerated • Erythematous • Other, <i>specify</i> 	
S2.10	Lymph nodes	Single selection value list <ul style="list-style-type: none"> • Submitted • Not submitted 	If submitted, record site(s) and number of nodes
	Site(s) and number of nodes	Text: Site AND Numeric: Number of LN's <i>Notes:</i> <i>Note that the site and number of LN's for that site will need to be repeated for each site received.</i>	
 S2.11	Block identification key	Text	
G2.05	Other macroscopic comment	Text	
Microscopic findings			
 S3.01	Histological tumour type	Single selection value list: <ul style="list-style-type: none"> • Urothelial carcinoma 	If urothelial carcinoma, record the Histological sub-type/variant

		<ul style="list-style-type: none"> • Squamous cell carcinoma • Adenocarcinoma • Tumours of Müllerian type <ul style="list-style-type: none"> ○ Clear cell carcinoma ○ Endometrioid carcinoma • Neuroendocrine tumour <ul style="list-style-type: none"> ○ Small cell neuroendocrine carcinoma ○ Large cell neuroendocrine carcinoma • Other, <i>specify</i> 	
	Histological sub-type(s)/variant(s) (urothelial carcinoma)	Single selection value list: <ul style="list-style-type: none"> • Not identified • Present 	<i>If present, record sub-type/variant and estimated % for each applicable variant</i>
	<i>Sub-type/variant</i>	Multi select value list (select all that apply): <ul style="list-style-type: none"> • Squamous • Glandular • Nested • Micropapillary • Plasmacytoid • Sarcomatoid • Other, <i>specify</i> 	
	Percentage	Numeric: ____ %	

 S3.02	Non-invasive carcinoma	Single selection value list: <ul style="list-style-type: none"> • Not identified • Indeterminate OR Multi select value list (select all that apply): <ul style="list-style-type: none"> ▪ Carcinoma <i>in situ</i>, flat <ul style="list-style-type: none"> ○ Multifocal ○ Focal ▪ Papillary carcinoma, non-invasive ▪ Other, <i>specify</i> 	
 G3.01	Associated epithelial lesions	Single selection value list: <ul style="list-style-type: none"> • Not identified • Present, <i>specify</i> 	
 S3.03	Histological grade	Single selection value list: <ul style="list-style-type: none"> • Not applicable • Cannot be determined Urothelial carcinoma <ul style="list-style-type: none"> ○ Low-grade ○ High-grade ○ Other, <i>specify</i> Squamous cell carcinoma or adenocarcinoma <ul style="list-style-type: none"> ○ GX: Cannot be assessed 	

		<ul style="list-style-type: none"> ○ G1: Well differentiated ○ G2: Moderately differentiated ○ G3: Poorly differentiated ○ Other, <i>specify</i> 	
IC ¹ CR	S3.04 Microscopic extent of invasion	<ul style="list-style-type: none"> • Cannot be assessed • No evidence of primary tumour <p>OR</p> <p>Multi select value list (select all that apply):</p> <ul style="list-style-type: none"> • Papillary carcinoma, non-invasive • Carcinoma <i>in situ</i>, flat • Tumour invades subepithelial connective tissue (lamina propria) • Tumour invades the muscularis propria • Tumour invades beyond muscularis propria into periureteric or peripelvic (renal sinus) fat • Tumour invades into the renal stroma • Tumour invades through the kidney into the perinephric fat • Tumour invades adjacent structures, <i>specify</i> 	
	S3.05 Microscopic tumour site(s)	<p>Multi select value list (select all that apply):</p> <ul style="list-style-type: none"> • Renal pelvis, <i>specify</i> • Ureter, <i>specify</i> • Kidney, <i>specify</i> 	

		<ul style="list-style-type: none"> • Pelvicalyceal, <i>specify</i> 	
G3.02	Tumour size (maximum dimension of the largest tumour)	Numeric: _____mm	
 S3.06	Lymphovascular invasion	Single selection value list: <ul style="list-style-type: none"> • Not identified • Present • Indeterminate 	
 S3.07	Margin status	Single selection value list: <ul style="list-style-type: none"> • Cannot be assessed • Not involved • Involved <p>Multi select value list (select all that apply):</p> <ul style="list-style-type: none"> ▪ Invasive carcinoma <ul style="list-style-type: none"> • Renal hilar • Perinephric fat • Ureteric • Periureteric • Distal • Proximal • Soft tissue • Other, <i>specify</i> 	

		<ul style="list-style-type: none"> ▪ Carcinoma <i>in situ</i>/non-invasive high-grade urothelial carcinoma <ul style="list-style-type: none"> • Distal mucosal • Proximal mucosa • Other, <i>specify</i> 	
 S3.08	Regional lymph node status	Single selection value list: <ul style="list-style-type: none"> • No regional nodes submitted • Not involved • Involved 	<p>If involved, record the following elements and consider recording G3.03</p> <p>If not involved, record the number of lymph nodes examined.</p>
	Number of lymph nodes examined	Numeric: ____	
	Number of positive lymph nodes	<i>Number cannot be determined</i> OR Numeric: ____	
	Size of largest metastasis	Numeric: ____ mm	
	Location(s) of involved lymph nodes	Text	
 G3.03	<i>Extranodal spread</i>	Single selection value list: <ul style="list-style-type: none"> • <i>Not identified</i> 	

		<ul style="list-style-type: none"> • <i>Present</i> 	
 S3.09	Histologically confirmed distant metastases	Single selection value list: <ul style="list-style-type: none"> • Not identified • Indeterminate • Present, <i>specify site(s)</i> 	
 S3.10	Coexistent pathology	Non-neoplastic renal tissue <ul style="list-style-type: none"> • Not applicable • Insufficient tissue • No significant pathologic alterations • Significant pathologic alterations, <i>specify</i> Other histopathological features <ul style="list-style-type: none"> • None identified • Present, <i>specify</i> 	
G3.04	Other microscopic comment	Text	
Ancillary test findings			
 G4.01	Ancillary studies	Single selection <ul style="list-style-type: none"> • Not performed • Performed, <i>specify</i> 	

Synthesis and overview		
 S5.01	PATHOLOGICAL STAGING (AJCC TNM 8th edition)	
	TNM descriptors	Multi select value list (select all that apply): <ul style="list-style-type: none"> • m (multiple primary tumours) • r (recurrent) • y (posttreatment)
	Primary tumour (pT)	Single selection value list: <ul style="list-style-type: none"> • TX Primary tumour cannot be assessed • T0 No evidence of primary tumour • Ta Papillary non invasive carcinoma • Tis Carcinoma <i>in situ</i> • T1 Tumour invades subepithelial connective tissue • T2 Tumour invades the muscularis • T3 <i>For renal pelvis only:</i> Tumour invades beyond muscularis into peripelvic fat or into the renal parenchyma** <i>For ureter only:</i> Tumour invades beyond muscularis into perinephric fat • T4 Tumour invades adjacent organs, or through the kidney into the perinephric fat <p>**use of terminology is incorrect¹¹⁰ Stroma should be substituted for parenchyma.</p>

	Regional lymph nodes (pN)	Single selection value list: <ul style="list-style-type: none"> • NX Regional lymph nodes cannot be assessed • N0 No lymph node metastasis • N1 Metastasis in a single lymph node, ≤2 cm in greatest dimension • N2 Metastasis in a single lymph node, >2 cm; or multiple lymph nodes 	Conditional on Lymph nodes being submitted
S5.02	Year and edition of staging system	Numeric: year AND Text: Edition eg 1 st , 2 nd etc	

G5.01	<p>Diagnostic summary Include:</p> <ul style="list-style-type: none"> a. Operative procedure (S2.03) and any additional specimens (S2.04) b. Tumour site (S2.06) c. Tumour type with different subtypes specified (S3.01) d. Tumour grade (S3.03) e. Tumour extent (Level of invasion) (S3.04) f. Lymphovascular invasion (S3.06) g. Surgical margin status (completeness of excision) (S3.07) h. Lymph node involvement (S3.08) i. Tumour stage (S5.01) j. Presence of non-invasive carcinoma (S3.02) 	Text	
S5.03	Overarching comment	Text	
G5.02	Edition/version number of the RCPA protocol on which the report is based	Text	

7 Formatting of pathology reports

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

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

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 carcinoma of the renal pelvis and ureter 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 used, where possible, to identify the requesting doctor.

Clinical Information

	<p>Clinical information should be recorded.</p>
	<ul style="list-style-type: none"> • In addition to demographic information about the patient and details of destination of the report, several items of clinical information can help the pathologist in the handling and reporting of specimens of the upper urinary tract. Knowledge of any relevant history is critical in the accurate diagnosis of tumours throughout the urinary tract.^{62,63,111,112} 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. <p>Specific observations on the upper tract epithelium are not available and may or may not be similar to those described in the urinary bladder. The application of Bacillus Calmette-Guerin (BCG) and other "intravesical" agents is used in upper tract tumours however.¹¹³</p>

- Relevant past medical history, family history and known risk factors associated with urinary tract cancers should be provided.
 - 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, ureteroscopy, 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

Carcinoma of the Renal Pelvis & Ureter Histopathology Request Information		
Family name <input style="width: 100%;" type="text"/>	Indigenous Status <input type="radio"/> Aboriginal but not Torres Strait Islander origin <input type="radio"/> Torres Strait Islander but not Aboriginal origin <input type="radio"/> Both Aboriginal and Torres Strait Islander origin <input type="radio"/> Neither Aboriginal nor Torres Strait Islander origin <input type="radio"/> Not stated/inadequately described	
Given name(s) <input style="width: 100%;" type="text"/>		
Date of birth <input style="width: 100%;" type="text"/>	Date of request <input style="width: 100%;" type="text"/>	
Patient identifiers e.g. MRN, IHI or NHI (please indicate which) <input style="width: 100%;" type="text"/>	Requesting doctor - name and contact details <input style="width: 100%;" type="text"/>	
Copy to doctor name and contact details <input style="width: 100%;" type="text"/>		
CLINICAL INFORMATION Previous history of urinary tract disease or distant metastasis <input type="checkbox"/> Non-invasive papillary <input type="radio"/> No previous history <input type="checkbox"/> Carcinoma in situ, flat <input type="checkbox"/> Invasion into lamina propria <input type="checkbox"/> Muscle invasive disease <input type="checkbox"/> Distant metastasis <input type="checkbox"/> Other, specify <input style="width: 100%;" type="text"/>	OPERATIVE PROCEDURE <input type="radio"/> Nephroureterectomy <input type="radio"/> Ureterectomy, partial <input type="radio"/> Ureterectomy, complete <input type="radio"/> Ureterectomy with cystectomy <input type="radio"/> Ureterectomy with cystoprostatectomy <input checked="" type="radio"/> Other, specify <input style="width: 100%;" type="text"/>	
Previous therapy <input type="checkbox"/> Radiation therapy <input type="radio"/> No previous therapy <input type="checkbox"/> Chemotherapy, systemic <input type="checkbox"/> Bacillus Calmette-Guerin (BCG) <input type="checkbox"/> Chemotherapy, intravesical, specify <input style="width: 100%;" type="text"/>	ADDITIONAL SPECIMEN(S) SUBMITTED <input style="width: 100%; height: 20px;" type="text"/> <input style="width: 100%; height: 20px;" type="text"/> <input style="width: 100%; height: 20px;" type="text"/> <input type="radio"/> Not submitted	
<input type="checkbox"/> Other, specify <input style="width: 100%;" type="text"/>	PRINCIPAL CLINICIAN <input style="width: 100%;" type="text"/>	
Other clinical information <input style="width: 100%; height: 20px;" type="text"/> <input style="width: 100%; height: 20px;" type="text"/> <input style="width: 100%; height: 20px;" type="text"/>	OTHER COMMENTS <input style="width: 100%; height: 20px;" type="text"/>	
CLINICAL EXTENT OF DISEASE <input style="width: 100%; height: 20px;" type="text"/>		
Version 1.0 Request Information from Carcinoma of the Renal Pelvis & Ureter Structured Reporting Protocol 2ndEdition		

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.¹¹⁴

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.¹¹⁴
- 'Clutter' should be reduced to a minimum.¹¹⁴ 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.

Appendix 3 Example of a pathology report

Page 1 of 2	
Citizen, Gerald W. C/O Paradise Close Wreck Bay Resort Nar Nar Goon East, 3181 Male DOB 1/7/1992 MRN M1196785	Lab Ref: 17/P28460 Referred: 30/8/2017 <div style="display: flex; justify-content: space-between; margin-top: 10px;"> <div style="width: 45%; padding: 5px;"> Copy to: Dr N.G.Chappie Rainforest Cancer Centre, 46 Smith Road, Woop Woop, 3478 </div> <div style="width: 45%; padding: 5px;"> Referred by: Dr V. Brown Suite 3, AJC Medical Centre, Bunyip Crescent Nar Nar Goon West, 3182 </div> </div>
RENAL PELVIS/URETER 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:	Renal pelvi-calyceal tumour
Operative procedure:	Right nephroureterectomy
Additional specimens submitted:	Not submitted
MACROSCOPIC	
Specimen labelled as:	Right kidney and ureter
Operative procedure:	Right nephroureterectomy
Additional specimens submitted:	Not submitted
Kidney measurements:	180 x 70 x 45 mm Superior to inferior x transverse x anterior to posterior
Length of ureter:	240 mm
Measurements of bladder cuff:	12 x 10 x 4mm
Tumour focality:	Unifocal
Macro. tumour site:	Upper renal pelvi-calyceal system
Tumour dimensions:	52 x 40 x 15 mm
Gross appearance of tumour:	Ulcerated, Solid and indurated, polypoid.
Macro extent of invasion:	Invasion into wall and periureteral/peripelvic tissue and involving kidney and renal sinus
Macro evidence of margin involvement:	Absent
Appearance of uninvolved tissue:	Normal
Lymph nodes:	Not submitted
Other macroscopic comment:	Nil of significance
Block identification key:	A: Bladder cuff resection margin; B: Hilar blood vessel margin; C: Further section of hilar blood vessels; D, E: Lower ureter; F, G: Mid ureter; H, I: Upper ureter; J-O: Pelvicalyceal tumour; P, Q: Kidney with tumour; R, S: Tumour with renal sinus; T: Perinephric fat; U, V: Kidney away from tumour

MICROSCOPIC

Tumour

Histological tumour type and grade:	High-grade Urothelial carcinoma
Tumour size (max dimension):	52mm
Micro tumour site:	Upper renal pelvi-calyceal system

Extent of invasion

Tumour invades:	Subepithelial connective tissue (lamina propria) and beyond muscularis propria into periureteric or peripelvic (renal sinus) fat Renal parenchyma
Lymphovascular invasion:	Present

Resection margins:	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

Diagnostic Summary

Right nephroureterectomy:

**High grade urothelial carcinoma
In upper renal pelvi-calyceal system
Invading through full thickness of renal pelvic wall with invasion into renal sinus and renal parenchyma;
Clear surgical resection margins;
Lymphovascular invasion present
Pathological Stage pT3a (AJCC 8th edition, 2016)**

Reported by Dr Bernard Beckstein

Authorised 4/9/2017

Appendix 4 WHO Classification of Tumours

WHO 2016: Variants of Urothelial Carcinoma¹⁶

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)

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