PHAEOCHROMOCYTOMA & PARAGANGLIOMA

STRUCTURED REPORTING PROTOCOL

(1st Edition 2020)

Incorporating the:

International Collaboration on Cancer Reporting (ICCR)

Phaeochromocytoma and Paraganglioma Dataset
www.ICCR-Cancer.org

Core Document versions:

- ICCR dataset: Phaeochromocytoma and Paraganglioma 1st edition v1.0[1]
- AJCC Cancer Staging Manual 8th edition[2]
- World Health Organization (2017) Classification of Tumours of Endocrine Organs (4th edition). Volume 10.[3]

Disclaimer

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. While each protocol includes "standards" and "guidelines" which are indicators of 'minimum requirements' and 'recommendations', the protocols are a first edition and have not been through a full cycle of use, review and refinement. Therefore, in this edition, the inclusion of "standards" and "guidelines" in each document are provided as an indication of the opinion of the relevant expert authoring group, but should not be regarded as definitive or as widely accepted peer professional opinion. The use of these standards and guidelines is subject to the clinician's judgement in each individual case.

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Contents

Scope

This protocol contains standards and guidelines for the structured reporting of adrenalectomy/partial adrenalectomy specimens for phaeochromocytoma, other excisions for paragangliomas, and biopsies of related specimens. Not covered in this protocol are: sarcoma, lymphoma, metastasis to the adrenal medulla, neuroblastoma and ganglioneuroblastoma specimens. Adrenal cortical tumours 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. This protocol can be used to define and report the minimum dataset, but the structure is scalable and can equally accommodate a maximum data set or fully comprehensive report.

Abbreviations

AJCC   American Joint Committee on Cancer
GAPP   Grading system for Adrenal Phaeochromocytoma and Paraganglioma
HPF   High power fields
ICCR   International Collaboration on Cancer Reporting
IHI   Individual Healthcare Identifier
LIS   The laboratory information system
MEN2   Multiple endocrine neoplasia type 2
mm   Millimetres
NHMRC   National Health and Medical Research Council
PASS   Phaeochromocytoma of the Adrenal gland Scaled Score
RCPA   Royal College of Pathologists of Australasia
TNM   Tumour-node-metastasis
UICC   International Union Against Cancer
UK   United Kingdom
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 (e.g. 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 National Health and Medical Research Council (NHMRC) level III-2 evidence.[4] 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 e.g. 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 (e.g. G1.10). |
Macroscopic findings	Measurements, or assessment of a biopsy specimen, made by the unaided eye.
Microscopic findings	In this document, the term 'microscopic findings' refers to histo-morphological assessment.
Predictive factor	A predictive factor is a measurement that is associated with response or lack of response to a particular therapy.
Prognostic factor	A prognostic factor is a measurement that is associated with clinical outcome in the absence of therapy or with the application of a standard therapy. It can be thought of as a measure of the natural history of the disease.

Standard	Standards are mandatory, as indicated by the use of the term 'must'. 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[4] 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 e.g. 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 (e.g. 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

Adrenal medullary tumours

ICCR – Anatomic sites of paraganglia

Paraganglia are neural crest-derived neuroendocrine organs derived from the second neuron of the autonomic chain and produce catecholamines. Tumours that arise within in the adrenal medulla are referred to as phaeochromocytomas, yet present only a special case of paraganglioma, as morphologically identical tumours arising from the chromaffin cells of the autonomic nervous system outside the adrenal medulla are also termed paraganglioma. Paragangliomas can be subdivided further into sympathetic and parasympathetic subtypes based on function and location. Sympathetic paragangliomas typically arise along the sympathetic chains in the thorax and abdomen. Parasympathetic paragangliomas originate from the parasympathetic autonomic nervous system, most commonly in the head and neck, where they are associated with the cranial nerves.

Benefits of structured reporting

The pathology report lays the foundation for a patient's cancer journey 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 challenging. 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[5,6] around the world. Both the United Kingdom,[7] and United States[8] 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 i.e. cancer registries.

Importance of histopathological reporting

The information contained within a pathology report includes prognostic information for the patient and treating clinical team. The content will assist in subsequent management, whether this may be surveillance, further surgery, radiotherapy or chemotherapy, or a combination of these modalities.

International Collaboration on Cancer Reporting

The International Collaboration on Cancer Reporting (ICCR), founded in 2011 by the Royal College of Pathologists of Australasia (RCPA), United States College of American Pathologists (US CAP) and Royal College of Pathologists United Kingdom (RCPath UK) Colleges of Pathology and the Canadian Association of Pathology - Association Canadienne des Pathologistes (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[9-12] 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 Phaeochromocytoma and Paraganglioma dataset as the foundation.

This protocol includes all 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 phaeochromocytoma and paraganglioma specimens.

ICCR dataset elements for phaeochromocytoma and paraganglioma specimens 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:

IC CR 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 nor indicated with an ICCR logo e.g.

IC CR 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

- ICCR dataset: Phaeochromocytoma and Paraganglioma 1st edition v1.0[1]
- Guidelines for Authors of Structured Cancer Pathology Reporting Protocols, Royal College of Pathologists of Australasia, 2009[13]
- World Health Organization (2017) Classification of Tumours of Endocrine Organs (4th edition). Volume 10.[14]

Changes since the last edition

Content has been incorporated from relevant sections of the Adrenal Gland Structured Reporting Protocol (1st edition).

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:

- This protocol is based on the ICCR dataset – Phaeochromocytoma and Paraganglioma 1st edition v1.0. All ICCR elements from this dataset, both core (mandatory) and non-core (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.

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

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Stakeholders

ACT Cancer Registry

ACT Health

Anatomical Pathology Advisory Committee (APAC)

Australian and New Zealand Endocrine Surgeons (ANZES)

Australian Commission on Safety and Quality in Health Care

Australian Digital Health Agency (ADHA)

Australian Institute of Health and Welfare (AIHW)

Australian Pathology

Cancer Australia

Cancer Council ACT

Cancer Council Australia and Australian Cancer Network (ACN)

Cancer Council NSW

Cancer Council Queensland

Cancer Council SA

Cancer Council Tasmania

Cancer Council Victoria

Cancer Council Western Australia

Cancer Institute NSW

Cancer Services Advisory Committee (CanSAC)

Cancer specific expert groups – engaged in the development of the protocols

Cancer Voices Australia

Cancer Voices NSW

Clinical Oncology Society of Australia (COSA)

Department of Health, Australian Government

Endocrine Society of Australia (ESA)

Health Informatics Society of Australia (HISA)

Independent Review Group of Pathologists

Medical Oncology Group of Australia (MOGA)

Medical Software Industry Association (MSIA)

National Pathology Accreditation Advisory Council (NPAAC)

New Zealand Cancer Control Agency

New Zealand Cancer Registry

Northern Territory Cancer Registry

Public Pathology Australia

Queensland Cooperative Oncology Group (QCOG)

Representatives from laboratories specialising in anatomical pathology across Australasia

Royal Australasian College of Physicians (RACP)

Royal Australasian College of Surgeons (RACS)

Royal Australian and New Zealand College of Radiologists (RANZCR)

Royal Australian College of General Practitioners (RACGP)

Royal College of Pathologists of Australasia (RCPA)

South Australia Cancer Registry

Southern Cancer Network, Christchurch, New Zealand

Standards Australia

Tasmanian Cancer Registry

Victorian Cancer Registry

Western Australia Clinical Oncology Group (WACOG)

Western Australian Cancer Registry

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 Adrenal gland tumours 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   Ideally the laboratory information system (LIS) should include documentation as to whether or not the patient identifies as Aboriginal and/ or Torres Strait Islander in Australia, or Māori in New Zealand. This is in support of government initiatives to monitor the health of those who identify as indigenous, particularly in relation to cancer.

CS1.01c   The patient's health identifiers may include the patient's Medical Record Number as well as a national health number such as a patient's Medicare number (Australia), Individual Healthcare Identifier (IHI) (Australia) or the National Healthcare Index (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   In most cases all clinical information should be transcribed: however, in a small number of cases the pathologist may exercise discretion regarding the inclusion of provided clinical information, for instance, possibly erroneous information or information that may impact on patient privacy. In such case reference should be made as to the location of the complete clinical information e.g. 'Further

clinical information is available from the scanned request form.'

G1.01   The copy doctors requested on the request form should 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 principal clinician can provide key information regarding the clinical presentation of the patient. Follow up may be required with the principal clinician for a number of reasons:

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

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

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

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

CS1.04b   The Australian Healthcare identifiers i.e. Healthcare Provider Identifier - Individual (HPI-I) and Healthcare Provider Identifier - Organisation (HPI-O) should be included, where possible, to identify the principal clinician involved in the patient's care.

| IC❋CR G1.02 | 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.

➢ If tissue is sampled for banking or research, this should be done in consultation with a pathologist and recorded in the report.

Specimen handling

➢ Detailed fixation and specimen handling instructions are available from the RCPA online Cut-up Manual:

https://www.rcpa.edu.au/Manuals/Macroscopic-Cut-Up-Manual

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

Macroscopic findings

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

IC CR S2.02	Clinical information must be recorded.	
IC CR	CS2.02a	Clinical data provide important guidance to pathologists for establishing a diagnosis and for assisting clinicians in planning patient management. Optimally, information should be provided on biochemical function, individual and family history, presence of multiple tumours and additional endocrine or non-endocrine tumours that may be components of a syndrome.[16] Almost 50% of phaeochromocytomas/paragangliomas are hereditary,

| | | making them the most hereditarily determined of all human tumours, and more than 20 hereditary susceptibility genes are now associated with their development.[17,18] Distinct correlations exist between genotype, biochemical phenotype,[19] tumour distribution, prognosis, and syndromic associations.[20,21]

Most phaeochromocytomas and sympathetic paragangliomas are capable of synthesising catecholamines and are also associated with clinical signs and symptoms related to catecholamine excess. In contrast, parasympathetic paragangliomas are rarely symptomatic and often lack tyrosine hydroxylase, the enzyme required for catecholamine synthesis, making them biochemically as well as clinically silent.[22] There is overwhelming evidence that biochemical testing for phaeochromocytoma/paraganglioma should assess (nor)metanephrines, measured either in plasma or urine, as these are superior to measurements of catecholamines.[23] Many clinically silent paragangliomas, particularly of the sympathicoadrenal type, will result in excess production of (nor)metanephrines and/or methoxytyramine and therefore are amenable to biochemical testing.[17,19]

Similarly to other neuroendocrine neoplasms, phaeochromocytomas and extra-adrenal paragangliomas are also capable of producing and secreting peptides that can cause clinical syndromes.[24] Production of adrenocorticotropic hormone, ß-endorphin, corticotropin-releasing hormone, calcitonin gene-related peptide, vasoactive intestinal peptide, growth hormone-releasing hormone, neuropeptide Y, peptide YY, insulin-like growth factor-1, galanin, adrenomedullin, serotonin, somatostatin, and gastrin like neuropeptide have been reported.[21]

As with other tumours, previous procedures can alter the microscopic appearance of a tumour and should be recorded. Fine needle aspiration or core needle biopsy may cause tumour infarction or interfere with assessment of invasion. Preoperative embolization is an established cause of necrosis in head and neck paragangliomas.[22] Partial adrenalectomy, which is increasingly utilised in treating patients with phaeochromocytomas,[25] might also be expected to cause long term changes in histology of the residual adrenal. |
|---|---|---|
| **IC CR S2.03** | | **The operative procedure must be recorded.** |
| IC CR | CS2.03a | Laparoscopic surgery is frequently used, and this may lead to some disruption or fragmentation of the gland/tumour. This may cause problems in assessing |

		tumour size, integrity of the tumour capsule and completeness of excision and may also cause distortion of vascular channels, making assessment of lymphovascular invasion difficult. In the rare cases where the specimen has been morcellated, tumour size should be obtained from either the surgeon or from pre-operative cross-sectional imaging studies.
IC CR S2.04	**The specimen(s) submitted and laterality must be recorded.**	
IC CR	CS2.04a	All anatomical structures removed or biopsied as part of the procedure should be identified. Examples of 'other' specimens may include additional tissues or organs (e.g. kidney, larynx), or deposits of recurrent or metastatic tumour.

Laterality information is needed for correct identification of specimens. The designation of laterality may include right, left or midline. |

S2.05 **Specimen weight must be recorded in grams.**

CS2.05a   The weight is an important criterion to predict malignancy in phaeochromocytoma (see microscopic section) thus removal of adipose tissue for an accurate weight is important. However, consideration should be given to ensuring any invasion of the tumour in the adrenal capsule or adjacent tissue is not missed. The removal of adipose tissue should not jeopardise the identification of extra-adrenal invasion.

G2.01   Specimen size should be recorded to the first decimal in mm in three dimensions.

IC CR S2.06	**Tumour focality must be recorded.**	
IC CR	CS2.06a	The presence of multiple or multifocal tumours is an important clue to the presence of hereditary disease.[26] Multifocality is defined as separate foci of tumour in the same organ, in contrast to multiple tumours in separate organs (e.g. two or three removed paragangliomas or a paraganglioma and a phaeochromocytoma). These designations apply to primary tumours, not metastases, and require histologic confirmation that tumour is present. In some cases it may not be possible to determine whether a tumour specimen represents a metastasis or a separate primary (e.g. a suspected lymph node with no residual lymph node architecture or a solitary pulmonary nodule).[27] Similarly, it may not be possible to determine whether a fragmented specimen is multifocal. These examples would be classified as indeterminate. Specimens should be carefully examined both macroscopically and microscopically to determine whether multiple or

		multifocal tumours are present. In most cases, multifocality specifically applies to the adrenal gland. However, occasional adrenal specimens may contain both a phaeochromocytoma and a nearby extraadrenal paraganglioma.
IC CCR **S2.07**		**The tumour sites must be recorded, where possible.**
IC CCR	CS2.07a	This element is defined as the site from which the surgeon has removed tumour tissue, and requires histologic confirmation that tumour is present. The anatomic location of a paraganglioma has important clinical correlations with predictive value concerning genotype, hormonal function, likelihood of additional and syndromically associated tumours, and risk of metastasis.[28] Metastatic sites such as bone, liver, lung, lymph node, etc. should specifically indicate which bone(s)/ which lung(s)/which lymph node(s), and the number of tumours, independently for each site.

	S2.08	**The macroscopic description of any lesion(s) in the specimen must be recorded.**
	CS2.08a	Where possible, for each lesion, the location (cortex versus medulla), appearance, the border (encapsulated or infiltrative), size (greatest dimension), and distance from the nearest excision margin must be recorded.

IC CCR **S2.09**		**The tumour dimensions must be recorded.**
IC CCR	CS2.09a	Tumour measurements should not include adjacent fat or other non-neoplastic tissue. The dimensions recorded should be the most complete as determined by accurately assessing gross and microscopic measurements. Large tumour size (>50 mm) correlates to metastatic potential in some, but not all studies, although possibly not as an independently useful criterion.[29,30] It is worth noting that tumour size ≥50 mm is included as a staging criterion in the American Joint Committee on Cancer (AJCC) TNM 8 Staging Manual.[2,31] Tumour sampling for microscopy should represent all variations in the gross appearance and consistency of the tumour, as well as margins and other specific features of interest. The general guideline of at least 1 section per cm of tumour should be considered. In the rare cases where the specimen has been morcellated, tumour size should be obtained from either the surgeon or from the pre-operative cross-sectional

			imaging studies.
IC CR **S2.10**		**The appearance of the adrenal gland other than the lesion(s) detected must be documented.**	
IC CR		CS2.10a	Adrenal medullary nodules either coexisting with phaeochromocytoma/paraganglioma, or in a background of diffuse adrenal medullary expansion are an important clue to the presence of hereditary disease.[26] They most often are associated with multiple endocrine neoplasia type 2 (MEN2), but have recently been described in other disorders.[32] Historically, nodules <10 mm have been arbitrarily called hyperplastic nodules or nodular adrenal medullary hyperplasia. Current molecular evidence suggests they are more appropriately considered microphaeochromocytomas.[33]

Sequential sections of roughly equal thickness are made in the transverse plane to display the distribution and amount of medullary tissue in the general regions - head, body and tail.[34] Medulla is normally present only in the head and body of the gland, with only minimal extension into the alae but not into the tail. The presence of substantial adrenal medullary tissue in the tail or alae strongly suggests adrenal medullary hyperplasia. Normal medulla usually does not represent more than one-third of the gland thickness, with cortex on each side comprising the other two thirds. However, anatomic variants exist, and definitive diagnosis of medullary hyperplasia in the absence of nodules may require quantitative morphometric analysis.[35]

Although it is sometimes difficult to define the tail of an adrenal gland distorted by a phaeochromocytoma, it should be remembered that adrenal medullary nodules[35] and phaeochromocytomas can occur in adrenals in MEN2 syndrome without an obvious background of diffuse hyperplasia. The adrenal gland adjacent to an apparently sporadic phaeochromocytoma should therefore be sectioned as above and carefully examined for small nodules.[21] |
| IC CR **S2.11** | | **Whether the tumour capsule is intact or not must be recorded.** | |
| IC CR | | CS2.11a | Tumour fragmentation often results from laparoscopic surgery and may cause problems in assessing tumour size, integrity of the tumour capsule, lymphovascular invasion and completeness of excision. |

S2.12 A block identification key[7] listing the nature and origin of all tissue blocks must be recorded.

CS2.12a 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. Photography of macroscopic specimen(s) is considered best practice. Annotation of captured images can be very helpful and aids with review of the case later. It can also provide useful information in the context of multidisciplinary meetings.

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.

Because of the importance of resection margin status, it is recommended that all surgical surfaces are painted prior to specimen dissection. Occasionally different colours can be used to identify specific surgical margins. This information should also be recorded in the block key.

G2.02 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.

CG2.02a The traditional macroscopic narrative recorded at the time of specimen dissection is often reported separately from the cancer protocol. Although this remains an option, it is recommended that macroscopic information be recorded within the overall structure of this protocol.

CG2.02b 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.

CG2.02c A traditional macroscopic description may be required when the LIS does not allow a structured approach.

CG2.02d Where the LIS offers an electronic interface for structured data entry the need for narrative can be significantly reduced to describe only information not otherwise captured.

3   Microscopic findings

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

IC CR **S3.01**	**The histological tumour type must be recorded.**	
IC CR	CS3.01a	All tumours of the adrenal medulla and extra-adrenal paraganglia should be given a type based on the most recent edition of the World Health Organization (WHO) Classification of Tumours of Endocrine Organs.[16] A composite tumour is defined as a tumour that combines morphological features of paraganglioma or phaeochromocytoma with those of a developmentally related neurogenic tumour including, ganglioneuroma, ganglioneuroblastoma, neuroblastoma or malignant peripheral nerve sheath tumour.[16] There is no specified percentage of the second tumour type.[16] However, complete histoarchitecture of the second tumour type is required. Scattered neuron-like cells often seen in phaeochromocytomas are not enough to make diagnosis of composite tumour. This designation is separate from mixed corticomedullary neoplasms, which would be included in 'other'. The most common second component of composite tumours is ganglioneuroma (70-80% of cases) followed by ganglioneuroblastoma (15-20%). Although the latter is morphologically comparable to paediatric ganglioneuroblastoma, it differs in molecular and clinical perspectives and confers only a low risk of metastases.[16,34]
IC CR G3.01	Any adverse tumour features should be assessed and recorded.	
IC CR	CG3.01a	While the cumulative summary of adverse features may be clinically helpful it is not a required component of the pathology report and is therefore listed as non-core. Individual features (tumour size and location) that are core are so listed in other sections. Several categories of histological features are putative risk factors for development of metastases in multiple publications and overlap in the two major proposed scoring systems for risk stratification, PASS[36] and GAPP.[37] However, the individual parameters within the categories are assessed and weighted differently in the two systems. No scoring system is currently required or endorsed, but histologic features may be considered in

		conjunction with other data for cumulative risk stratification in order to optimally guide patient management. Comedonecrosis and growth pattern are the most readily recognised and possibly the most predictive parameters, while cellularity is potentially highly subjective. To reduce subjectivity, it was recommended that cellularity be quantitated by counting the number of cells within an area (U) encompassed by a square grid in a 10x ocular viewed with a 40x HPF, corresponding to 0.0625 mm.[3,37] Necrosis does not include ischemic necrosis secondary to therapeutic embolization or spontaneous infarction. PASS was designed for phaeochromocytomas, while GAPP was intended for both phaeochromomocytomas and sympathetic paragangliomas. No scoring system currently applies to head and neck paragangliomas, although individual parameters may provide useful information for those tumours.[38] Use of either scoring system is optional. A 2019 meta-analysis of multiple papers employing PASS or GAPP, concludes that a low score with either histological system is a stong predictor of low metastatic risk but that high scores have little predictive value in the absence of additional features including genotype and biochemical testing.[39] Poor concordance between expert pathologists has been noted in a PASS study.[40] Coarse nodularity is a gross finding reported to be associated with metastatic risk.[41]
IC CR **S3.02**	**The extent of invasion must be recorded.**	
IC CR	CS3.02a	Invasion is a reported risk factor for development of metastases when considered in conjunction with other adverse features. However, invasion is currently categorised and weighted inconsistently.[26] Precise descriptions of the nature and extent of invasion are required in conjunction with other adverse factors in order to optimally guide patient management. As phaeochromocytomas usually do not have a capsule,[34] the adrenal capsule becomes the capsule of the tumour in most cases. Within other organs an encapsulated tumour may be more likely. If a tumour capsule is present, invasion of the organ capsule and tumour capsule should be documented separately. Capsular invasion is not assessed in a biopsy.
	CS3.02b	The presence or absence of capsular invasion or invasion of the adrenal vein or vena cava is associated with poor prognosis. Refer to CG3.02b and c.

S3.03 If phaeochromocytoma, the presence or absence of extension into adipose tissue must be recorded.

CS3.03a   This is associated with a poor prognosis and increased recurrence, refer to CG3.01a.

ICCR S3.04	**The presence of lymphovascular invasion must be recorded.**
ICCR	CS3.04a Vessel invasion is a reported risk factor for development of metastases when considered in conjunction with other adverse features.[26] Precise descriptions of the nature and extent of vascular invasion are required in conjunction with other adverse factors in order to optimally guide patient management.[26] There are currently no firm data for phaeochromocytoma or paraganglioma to assess whether metastatic risk increases progressively with involvement of small to larger vessels, although extrapolation from other tumours would suggest that is the case. In the adrenal, invasion of one or more tributaries of the central vein may be an important event leading to involvement of the adrenal vein and the vena cava. This may be facilitated by the normal anatomy within the adrenal where arcades of mural smooth muscle provide gaps through which normal cortex and/or medulla or tumours derived from them can protrude into the vascular space(s).[34]
ICCR S3.05	**Mitotic count and/or Ki-67 proliferation index must be recorded.**
ICCR	CS3.05a Mitotic count and/or Ki-67 proliferation index is now widely utilised in risk stratification for other neuroendocrine tumours. A high proliferative fraction based on either mitoses[42] or Ki-67[37] is a reported risk factor for development of metastases for phaeochromocytoma and paraganglioma. Mitotic count should be performed in a minimum area of 2 mm^2, which is equivalent to approximately 10 high power fields (HPFs) in many microscopes. There is currently no standard approach to scoring a Ki-67 labelling index in phaeochromocytoma and paraganglioma and this has been emphasised. On the basis of established methodology for other neuroendocrine tumours,[16] it is recommended that the Ki-67 index should be reported as percentage of positive tumour cells per 40x field HPF (0.2 mm^2) in area of highest nuclear labelling.[21,37] Counts should ideally be based on manual counts of printed images or appropriately validated automated image analysis; visual estimates have proven less accurate for multiple tumour types.[16]

S3.06   The status of the non-tumour adrenal gland must be recorded.

   CS3.06a   The presence of medullary hyperplasia or microphaeochromocytoma should be noted. In a normal gland, there is little or no medullary tissue in the tail. Thus, medullary tissue in the tail indicates medullary hyperplasia. A lesion of 10 mm or less in the adrenal medulla is regarded as a microphaeochromocytoma.

G3.02   The malignant potential of the neoplasm should be recorded.

   CG3.02a   There is no reliable histological criterion to differentiate metastatic from non-metastatic phaeochromocytoma. In the literature, there are two scoring system. These include the PASS score based only on histological criteria and a more recent Japanese scoring system based on histological criteria plus Ki-67 immunoreactivity and types of catecholamine produced.[43] However, both systems need to be further validated. The information below is for reference.

   The following items and their values (in parentheses) determine the PASS score[36]:

   •   High cellularity (2),

   •   Central or confluent tumour necrosis (2),

   •   Vascular invasion (1),

   •   Capsular invasion (1),

   •   Extension into adipose tissue (2)

   •   Large nests or diffuse >10% growth (2),

   •   Tumour cell spindling (2),

   •   Cellular monotony (2),

   •   Greater than 3 of 10 HPF mitotic figures (2),

   •   Atypical mitotic figures (2),

   •   Profound nuclear pleomorphism (1),

   •   Nuclear hyperchromasia (1)

   Benign phaeochromocytoma has a score of less than 4 and malignant phaeochromocytoma has a PASS score higher than 6. Patients with a PASS score >4 should be followed closely for recurrence.

   The Japanese scoring system, GAPP (Grading System for Adrenal Pheochromocytoma and Paraganglioma)[43]

depends on:

- Histological pattern (zellballen =0; large irregular nests=1; pseduorosette =1, if both =2)
- Cellularity (low -0; moderate =1; high=2)
- Coagulation necrosis (negative =0; positive=2)
- Vascular/ capsular invasion (negative =0; positive =1)
- Ki-67 immunoreactivity (very few cells =0; 1-3% = 1; >3% =2)
- Types of catecholamine produced (non-functional/epinephrine=0; norepinephrine=1)

The tumours were classified as well (score= 0-2), moderately (score =3-6), and poorly differentiated (score = 7-10) types according to their scores. The differentiation of the phaeochromocytoma appears to be correlated with potential for metastases and survival rates. Patients with poorly differentiated phaeochromocytoma are malignant and reported to have 0% survival rate.

ICCR S3.07	**The margin status must be recorded.**

ICCR	CS3.07a	Incomplete excision has been associated with local recurrence.[44] Positive margins are defined both grossly, as tumour obviously transected and microscopically as 'tumour on ink', if the surface is inked. Adrenalectomy specimens especially are frequently damaged and very irregular, often precluding both the application of ink, and reliable gross assessment. In these cases, the margins cannot be assessed.

ICCR S3.08	**The presence of positive lymph nodes must be recorded.**

ICCR	CS3.08a	Regional lymph nodes are found within the anatomic area in which a tumour is located and receive lymphatic drainage from that area. They are, therefore, anatomically related to the tumour and may be the earliest sites of lymph node metastases. In keeping with practices applied to other tumours to stratify risk of early nodal involvement, the pathology report should state the total number of lymph nodes examined and the number of nodes with metastases. Size of tumour deposit within the lymph node may be correlated with outcome, and thus it is recommended to report the greatest tumour dimension identified within the lymph node dissection/biopsy sample. Lymph node biopsies are sometimes received as intact resections and sometimes as multiple fragments. In the latter, the number of nodes will be known only if

		specified by the surgeon and otherwise is undetermined.
	CS3.08b	The presence of lymph node metastases affects the pathological staging (N stage) of phaeochromocytoma.
ICCR **S3.09**	**The presence or absence of histologically confirmed distant metastases must be recorded.**	
ICCR	CS3.09a	A diagnosis of metastasis is appropriate when phaeochromocytoma or paraganglioma is present in a site where normal paraganglia do not exist. The sites are bone and lymph node. It is crucial to remember the normal anatomic distribution of paraganglia in order to consider the possibility of multiple primary tumours.[45] The assessment of distant metastasis can be particularly challenging in some cases because primary paragangliomas do also occur in rare anatomic sites such as thyroid, pituitary, gallbladder, liver and lung. Therefore, tumour in these rare locations should not automatically be considered metastatic. In addition, due to the ease of performing needle core biopsies of various organs, metastatic disease is now increasingly seen histologically and in many cases biopsies may be the only tissue sample available due to the advanced nature of the primary tumour or the comorbidities associated with surgical resection.

G3.03   The presence or absence of coexistent pathological abnormalities in the adrenal gland should be recorded.

G3.04   Any additional relevant microscopic comments should be recorded. For example, the presence of calcification could be mentioned for correlations with radiological findings.

CG3.04a   Free text entry to allow any additional, unusual or unexpected findings to be reported.

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.

IC CR G4.01	The findings of any ancillary studies, where performed, should be recorded.	
IC CR	CG4.01a	The differential diagnosis of phaeochromocytoma or paraganglioma often requires use of generic immunohistochemical markers to establish the neuroendocrine nature of a tumour together with additional more specific markers to confirm the diagnosis or exclude other entities, including other neuroendocrine neoplasms.[22,45,46] The most frequently utilized positive generic markers in most contexts are chromogranin A (CgA) and synaptophysin. However, synaptophysin is expressed in adrenal cortex and must not be used to distinguish phaeochromocytomas from cortical neoplasms. Additional useful positive markers include tyrosine hydroxylase to demonstrate capacity for catecholamine synthesis, and S100 to demonstrate sustentacular cells. Useful negative markers include keratins and inhibin. A caveat is that head and neck paragangliomas are often completely negative for tyrosine hydroxylase and also negative or only focally positive for CgA and synaptophysin.[22] In those cases the presence of sustentacular cells can be particularly helpful; however, sustentacular-like cells can also be found in other neuroendocrine tumours and are therefore not diagnostic. Additional potentially useful positive markers that have been proposed include dopamine beta-hydroxylase,[47] INSM1,[48] NKX2.2[49] and GATA-3.[45,50] In addition to aiding diagnosis, immunohistochemistry is increasingly used as a genetic screen. This particularly applies to staining for loss of SDHB, which also serves as a prognostic marker.[51,52]
	CG4.01b	Neuroendocrine markers like chromogrannin, synaptophysin, CD 56 can be used to document the neuroendocrine nature of the phaeochromocytoma. S-100 would be useful for documenting sustentacular cells if present. The lack of S-100 sustentacular cells have been reported in some but not all of malignant phaeochromocytomas.[53] In metastatic phaeochromocytoma, neuroendocrine tumour/neuroendocrine carcinoma can be differential

diagnoses. In this situation, cytokeratin could be done. Pheochromocytoma is usually negative for cytokeratin but neuroendocrine tumour and carcinoma are positive.

Ki-67 labelling index has been used in differentiating metastatic from non-metastatic phaeochromocytoma.[54]

As a group, up to 40% of phaeochromocytomas and paragangliomas are hereditary.[18]

There are more than 20 known genes responsible for the pathogenesis of phaeochromocytoma/paraganglioma (*RET, VHL, NF1, TMEM127, MAX, KIF1Bb, PHD2, SDHA, SDHB, SDHC, SDHD and SDHAF2*).[18] Depending on the clinical circumstance, mutation testing for some, most or all of these genes should be considered in individuals presenting with apparently sporadic phaeochromocytoma/paraganglioma.[55]

Positive staining for SDHB (when performed in experienced centres) excludes germline mutation of *SDHA*, *SDHB*, *SDHC* or *SDHD* whereas negative staining for SDHB indicates dysfunction of the mitochondrial complex 2 which is usually due to germline mutations of *SDHA, SDHB, SDHC* or *SDHD* but can occur in sporadic syndromic disease (the Carney triad). In addition to negative staining for SDHB, tumours associated with *SDHA* mutation also show negative staining for SDHA.[56]

Approximately 4% of phaeochromocytomas will show negative staining for SDHB and therefore be associated with germline mutations in *SDHA, SDHB, SDHC, SDHD*. Negative staining for SDHB occurs in close to half of all extra-adrenal paragangliomas. Therefore, SDHB immunohistochemistry should be performed to guide genetic testing in all phaeochromocytomas and paragangliomas. SDHA immunohistochemistry should also be performed on SDHB negative tumours to help further guide the order in which genes are tested. Mutation of *SDHB* carries a high risk of metastasis after surgery (estimated as 30 to 70%) and is more commonly seen in intra-abdominal extra-adrenal paragangliomas. *SDHD* and *SDHC* mutations are more commonly found in head and neck paragangliomas.[56]

CG4.01c   Ancillary tests performed externally may contain information needed for compliance with NPAAC and RCPA requirements, but they are not relevant to cancer reporting protocols. The specific elements of an ancillary study report needed for cancer reporting include the following:

- laboratory performing the test,

- substrate (e.g. cytology smears, fluid in special media, paraffin block, fresh tissue, etc.),

- method (where relevant),

- results,

- conclusion (usually a text field,) and

- person responsible for reporting the ancillary test.

CG4.01d   Documentation of all relevant ancillary study findings is essential for overarching commentary (see Synthesis and Overview, Chapter 5), in which the significance of each finding is interpreted in the overall context of the case.

5   Synthesis and overview

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

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

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

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

ICCR S5.01	**The tumour stage and stage grouping must be recorded according to the most recent TNM staging system of the AJCC Cancer Staging Manual (8th edition).**	
ICCR	CS5.01a	The AJCC staging system for phaeochromocytomas and sympathetic paragangliomas was implemented in 2017 in order to guide clinicians in determining the therapies and follow-up that patients require.[2] It is expected that extensive staging and survival data to be collected will also lead to increased understanding of these tumours and to future improvements in patient care.[2,31]

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

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

a. Specimen submitted

b. Histological tumour type

c. Completeness of excision

d. Tumour dimensions

e. Tumour stage

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

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

- explain the decision-making pathway, or any elements of clinicopathological ambiguity, or factors affecting diagnostic certainty, thereby allowing communication of diagnostic subtlety or nuance that is beyond synoptic capture

- give recommendations for further action or investigation

- document further consultation or results still pending

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

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 ' XXXXXXXXX' XXXX Edition dated XXXXXXX'.

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 phaeochromocytoma and paraganlioma. For emphasis, standards (mandatory elements) are formatted in bold font.

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

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

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

G6.01 The order of information and design of the checklist may be varied according to the LIS capabilities and as described in *Functional Requirements for Structured Pathology Reporting of Cancer* Protocols.[57]

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

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

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

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

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

Item descriptions in italics are conditional on previous responses.

Values in all caps are headings with sub values.

S/G	Item description	Response type	Conditional
Pre-analytical			
S1.01	**Demographic information provided**		
S1.02	**Clinical information provided on request form**	**Text** OR **Information not provided** OR **Structured entry as below:**	

ICCR	**Hormonal status**	**Single selection value list:**
		
		• Biochemically functioning (select all that apply)
		
		    o Metanephrine and/or adrenaline
		
		    o Normetanephrine and/or noradrenaline
		
		    o Methoxytyramine and/or dopamine
		
		    o Other, *specify*
		
		• Biochemically silent
		
		• Biochemical analysis not performed
		
		• Cannot be determined (testing status	

		not known)		
ICCR	**Imaging findings**	**Text**	
ICCR	**Relevant biopsy/cytology results**	**Text**	
ICCR	**Previous therapy (including pre-operative embolization, chemotherapy, radiotherapy, targeted therapy, immunotherapy)**	**Text**	
ICCR	**Relevant familial history**	**Text**	
ICCR	**Presence of endocrine or other tumours**	**Text**	
ICCR	**Germline mutation or familial syndrome**	**Text**	*Specify mutation, if known*
G1.01	Copy To doctors recorded	**Text**	
S1.03	**Pathology accession number**	**Alpha-numeric**	
S1.04	**Principal clinician**	**Text**	
ICCR G1.02	Other clinical information received	**Text**	
Macroscopic findings			
S2.01	**Specimen labelled as**	**Text**	
ICCR S2.02	**Clinical information**	**Text**	
ICCR S2.03	**Operative procedure**	Not specified OR	

39 Structured Reporting Protocol for Phaeochromocytoma and Paraganglioma 1st edition

		Multi selection value list (select all that apply): • Biopsy (core needle, incisional, excisional), *specify* • Open resection, *specify procedure, including other organs if present (e.g. adrenal resection and liver biopsy)* • Laparoscopic • Organ-sparing • Other (e.g. conversion, laparoscopic to open), *specify*	

IC CR S2.04	**Specimen(s) submitted**	**Single selection value list:**
		
		• Not specified
		
		OR
		
		Multi selection value list (select all that apply):
		
		• Adrenal tumour
		    o Left
		    o Right
		
		• Biopsy tissue*, specify site(s) and laterality*
		
		• Lymph nodes, *specify biopsy/dissection, site(s) and laterality*
		
		• Other (e.g. right neck mass, midline abdominal mass), *specify site(s) and laterality*	

S2.05	**Specimen weight**	**Numeric: ____g**	

G2.01	Specimen dimensions	**Numeric: __x__x__mm**	
ICCR **S2.06**	**Tumour focality**	**Single selection value list:** • Indeterminate • Cannot be assessed, *specify* • Unifocal • Multiple	
ICCR	***Number of tumours in same organ***	**Numeric: _____**	
ICCR	***Number of tumours in separate organs***	**Numeric: _____**	**If multiple tumours from different organs are present, separate protocols should be used to record all following elements for each tumour.**
ICCR **S2.07**	**Tumour site**	**Single selection value list:** • Not specified OR **Multi selection value list (select all that apply):** • Adrenal tumour 　○ Left 　○ Right • Other abdominal or pelvic 　○ Paraaortic 　○ Urinary bladder 　○ Other, *specify*	

		• Head and neck	
		o Carotid body	
		▪ Left	
		▪ Right	
		o Middle ear (jugulotympanic)	
		▪ Left	
		▪ Right	
		o Vagal	
		▪ Left	
		▪ Right	
		o Laryngeal	
		▪ Left	
		▪ Right	
		o Other, *specify site(s) and laterality*	
S2.08	**MACROSCOPIC APPEARANCE OF LESION(S)**	<u>Note:</u> that the macroscopic appearance will need to be repeated for <u>each</u> primary tumour identified.	
	Location	**Single selection value list:** • Medulla • Indeterminate • Other	**If other provide details**
	Details	*Text*	
	Borders	**Single selection value list:** • Encapsulated	

		• Infiltrative	
	Description	**Text**	
	Distance to nearest excision margin	**Numeric: __mm**	
ICCR S2.09	**Tumour dimensions**	**Single selection value list:** • Cannot be assessed, *specify* OR **Text**: Tumour identification AND **Numeric**: ___mm maximum dimension (largest tumour) Note: Repeat tumour identification and maximum dimension for each tumour identified.	
ICCR	Additional dimensions (largest tumour)	Numeric**: ____mm x ____mm**	
ICCR S2.10	**APPEARANCE OF UNINVOLVED ADRENAL GLAND**	**Not applicable** OR	**Applicable to adrenal specimens only**
ICCR	**Medullary nodules (microphaeochromocytoma) (<10 mm)**	**Single selection value list:** • Present • Absent • Indeterminate • Cannot be assessed, *specify*	

IC CR		**Diffuse hyperplasia**	**Single selection value list:** • Present • Absent • Indeterminate • Cannot be assessed, *specify*	
IC CR	S2.11	**Specimen integrity**	**Single selection value list:** • Not applicable • Specimen intact • Fragmented specimen • Cannot be assessed, *specify*	
	S2.12	**Block identification key**	**Text**	
	G2.02	Other macroscopic comments	**Text**	
Microscopic findings				

IC CR	S3.01	**Histological tumour type**	**Single selection value list from WHO Classification of Adrenal Carcinomas.**
			
			Single selection value list:
			
			• Phaeochromocytoma
			
			• Extra-adrenal paraganglioma
			
			• Composite phaeochromocytoma
			
			    o Neuroblastoma, *specify*
			
			    o Ganglioneuroma, *specify*
			
			    o Malignant peripheral nerve sheath tumour, *specify*
			
			• Composite paraganglioma
				For each tumour type, specify the percentage.

		○ Neuroblastoma, *specify* ○ Ganglioneuroblastoma, *specify* ○ Ganglioneuroma, *specify* ○ Malignant peripheral nerve sheath tumour, *specify* • Other, *specify*	
IC CR G3.01	ADVERSE FEATURES		

IC CR	Histological features	**Multi selection value list (select all that apply):**
		
		• Growth pattern
		  ○ Large and irregular nests
		  ○ Diffuse
		  ○ Pseudorosette (even focal)
		• Cellularity
		  ○ Moderate (150-250 cells/U)
		  ○ High (>250 cells/U)
		  ○ Indeterminate
		• Cytological features
		  ○ Spindle cells
		• Necrosis
		  ○ Comedonecrosis
		  ○ Other, *specify*
		• Other, *specify*	

IC•CR	Other features	**Multi selection value list (select all that apply):** • Extra-adrenal abdominal or mediastinal location • Size >50 mm • Negative staining for SDHB • Biochemical testing showing high levels of methoxytyramine	
	Other histopathological features	**Multi selection value list (select all that apply):** • Adenoma • Hyperplasia • Other, *specify*	
IC•CR	**Other**	**Text**	
IC•CR S3.02	**Extent of invasion**	**Single selection value list:** • Cannot be assessed • Capsular invasion not present OR **Multi selection value list (select all that apply):** • Microscopic transcapsular penetration of tumour capsule within an organ • Microscopic transcapsular penetration of organ capsule • Invasion into peritumoural soft tissue	

			• Invasion into adjacent structure(s)/organ(s), *specify*	
S3.03	**Extension into adipose tissue (for phaeochromocytoma)**	**Single selection value list:** • Absent • Present		**If present, specify distance**
		Distance	***Numeric: __mm***	

IC&CR S3.04	**Lymphovascular invasion**	Not identified
		
		OR
		
		Multi selection value list (select all that apply):
		
		• Present
		
		    o Periadrenal or peritumoural for extra-adrenal tumours, *specify*
		
		        ▪ Intracapsular
		
		        ▪ Extracapsular
		
		    o Adrenal vein
		
		    o Vena cava
		
		    o Other (e.g. adrenal central vein and tributaries), *specify*		

IC&CR S3.05	**Mitotic count**	**Numeric**: ____ mitotic figures/2 mm^2* **Single selection value list:** • Cannot be assessed, *specify* **AND/OR**		
	Atypical mitoses	**Single selection value list:**		

		• Cannot be assessed • Absent • Present	
IC(L)CR	**Ki-67 proliferation index**	**Numeric**: ____ % **OR** **Single selection value list:** • Cannot be assessed, *specify*	
S3.06	**Non-tumour appearance**	**Unremarkable** **OR** **Not identified/not assessable** **OR** **Multi select value list (select all that apply)** • Adrenal cortical atrophy • Hyperplasia • Cortical nodules • Medullary hyperplasia/nodule	
G3.02	MALIGNANT POTENTIAL		
	Scoring system (e.g. PASS, Weiss etc.)	**Text**	
	Score for malignant potential	**Numeric**	
IC(L)CR S3.07	**Margin status**	**Single selection value list:** • Not involved (R0), *specify distance to closest margin*	**If not involved by invasive carcinoma record the distance of tumour to closest margin**

			• Involved, *specify R1 (microscopic) or R2 (macroscopic) extent and location of involvement if possible* • Cannot be assessed, *specify*	**If involved by invasive carcinoma specify the extent of margin involvement, if possible**
IC CR		*Distance to closest margin*	***Numeric: __mm***	
IC CR		*Closest margin*	***Text***	
IC CR		***Extent of margin involvement***	**Single selection value list:** • ***Numeric: __mm*** R1 (microscopic), *specify if possible* • ***Numeric: __mm*** R2 (macroscopic), *specify if possible*	
IC CR		***Location of involved margin***	***Text***	
IC CR	S3.08	**LYMPH NODE STATUS**	No nodes submitted or found OR	
IC CR		**Lymph node biopsy site(s)**	**Text**	**Specify site(s), if possible**
IC CR			**Single selection value list:** • Not involved • Involved	**Record the number of LN examined.** **If involved, specify the number of positive LN**
IC CR		**Number of lymph nodes examined**	**Numeric: ____**	
IC CR		**Number of positive lymph nodes**	**Numeric: ____**	**Not required if number cannot be determined is entered above.**
IC CR		**Extranodal extension (ENE)**	**Single selection value list:** • Not identified	**If ENE present, specify number of nodes**

		• Present	
		• Cannot be determined	
IC·CR	**Number of nodes with ENE**	**Numeric: ____**	
IC·CR	**Maximum dimension of largest lymph node metastasis**	**Numeric: ____mm**	
IC·CR S3.09	**Distant metastases**	**Single selection value list:** • Not identified • Not assessed • Present, *specify site(s)*	
G3.03	Coexistent pathological abnormalities	**Single selection value list:** • Absent • Present, *specify*	**If present, specify**
G3.04	Additional microscopic comment	**Text**	
Ancillary findings			

IC·CR G4.01	Ancillary studies	Not performed
		
		OR
		
		Multi select value list :
		• Immunohistochemistry performed
		    ○ Synaptophysin, *specify result*
		    ○ S-100, *specify result*
		    ○ SDHB, *specify result*
		    ○ Tyrosine hydroxylase, *specify result*	

		○ Other, *specify*	
		• Molecular testing performed, *specify result(s) if available*	
		• Other, s*pecify*	
Synthesis and overview			
IC CR S5.01	**PATHOLOGICAL STAGING (AJCC 8TH EDITION)**		
IC CR	**TNM descriptors**	**Multi select value list :** • m - multiple primary tumours • r – recurrent • y – post therapy	
IC CR	**Primary tumour (T)**	**Single select value list :** TX Primary tumour cannot be assessed T1 Phaeochromocytoma <5 cm in greatest dimension, no extra-adrenal invasion T2 Phaeochromocytoma $\geq$5 cm or paraganglioma-sympathetic of any size, no extra-adrenal invasion T3 Tumour of any size with invasion into surrounding tissues (e.g. liver, pancreas, spleen, kidneys) Phaeochromocytoma: within adrenal gland Paraganglioma sympathetic: functional Paraganglioma parasympathetic: nonfunctional, usually in the head and neck region	**Parasympathetic paraganglioma are not staged because they are largely benign.**

	Regional lymph node (N)	**Single selection value list:**	
		NX Regional lymph nodes cannot be assessed	
		N0 No lymph node metastasis	
		N1 Regional lymph node metastasis	
S5.02	**Year and edition of staging system**	**Numeric:** year **AND** **Text:** Edition e.g. 1st, 2nd etc.	
G5.01	Diagnostic summary Include: a. Specimen submitted b. Histological tumour type c. Tumour dimensions d. Completeness of excision e. Tumour stage	**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. An example of a pathology report is shown in Appendix 3.

Appendix 1 Pathology request form for adrenal medulla tumours

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 adrenal cortical specimens may be provided by the clinician on a separate request information sheet. An example request information sheet is included below. Elements which are in bold text are those which pathologists consider to be required information. Those in non-bold text are recommended.

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

Patient information

- **Adequate demographic and request information should be provided with the specimen.**

    - Items relevant to cancer reporting protocols include:

        - patient name

        - date of birth

        - gender

        - identification and contact details of requesting doctor

        - date of request

    - Document whether or not the patient identifies as Aboriginal and/ or Torres Strait Islander in Australia, or Māori in New Zealand. This is in support of government initiatives to monitor the health of those who identify as indigenous, 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 Index (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

> **Surgical handling procedures affect the quality of the specimen.**

- The specimen should be fixed in 10% neutral buffered formalin as soon as possible after resection or after tissue banking (if applicable).

- It is useful for the surgeon to identify the location of the adrenal gland (right or left) as well as the anatomical orientation of the gland.

IC CR	**The type of operation performed must be recorded.**
IC CR	• Laparoscopic surgery is frequently used and this may lead to some disruption or fragmentation of the gland/tumour. This may cause problems in assessing tumour size, integrity of the tumour capsule and completeness of excision and may also cause distortion of vascular channels, making assessment of lymphovascular invasion difficult. In the rare cases where the specimen has been morcellated, tumour size should be obtained from either the surgeon or from pre-operative cross-sectional imaging studies.

- The requesting clinician should indicate that whether it is an open or laparoscopic surgery.

  Surgery may cause fragmentation of the gland, distortion of capsule and problems in assessing tumour size. It may also distort the vascular channels, making assessment of vascular invasion difficult.

IC CR	**Any previous hormonal status must be recorded.**
>	• Most phaeochromocytomas and sympathetic paragangliomas are capable of synthesizing catecholamines and are also associated with clinical signs and symptoms related to catecholamine excess. In contrast, parasympathetic paragangliomas are rarely symptomatic and often lack tyrosine hydroxylase, the enzyme required for catecholamine synthesis, making them biochemically as well as clinically silent.[22] There is overwhelming evidence that biochemical testing for phaeochromocytoma/paraganglioma should include metanephrines, measured either in plasma or urine, as these are superior to measurements of catecholamines.[23] Many clinically silent paragangliomas, particularly of the sympathoadrenal type, will produce metanephrines and/or methoxytyramine and therefore are amenable to biochemical testing.[17,19] • Similarly to other neuroendocrine neoplasms, phaeochromocytomas and extra-adrenal paragangliomas are also capable of producing and secreting peptides that can cause clinical syndromes.[24] Production of adrenocorticotropic hormone, ß-endorphin, corticotropin-releasing hormone, calcitonin gene-related peptide, vasoactive intestinal peptide, growth hormone-releasing hormone, neuropeptide Y, peptide YY, insulin-like growth factor-1, galanin, adrenomedullin, serotonin,

	somatostatin, and gastrin like neuropeptide have been reported.[21]
IC CR	**Any imaging findings must be recorded.**
IC CR	**Any previous history of endocrine/adrenal tumour or related abnormality must be recorded.**

- Previous surgery of the adrenal gland alters the shape and hence orientation of the adrenal gland.

  Operation on the 'same adrenal gland' or 'contralateral adrenal gland' as a staged procedure for bilaterality, should be indicated.

IC CR	**If a pre-operative biopsy, or cytology has been performed, this must be recorded.**

- Any information about prior adrenal biopsy or resection should be included.

- Fine needle aspiration of the adrenal gland may alter the microscopic appearance of the tumour, including tumour infarction. The results of the procedure may sometimes make the judgement of the invasiveness of the adrenal gland tumour difficult as it can cause distortion of the tissue.

- Correlations of histological and cytological findings are important for quality assurance purposes.

IC CR	**Any previous surgery or therapy must be recorded.**
IC CR	• As with other tumours, previous procedures can alter the microscopic appearance of a tumour, and should be recorded. Fine needle aspiration or core needle biopsy may cause tumour infarction or interfere with assessment of invasion. Preoperative embolization is an established cause of necrosis in head and neck paragangliomas.[22] Partial adrenalectomy, which is increasingly utilised in treating patients with phaeochromocytomas,[25] might also be expected to cause long term changes in histology of the residual adrenal.

- Relevant information about prior therapy (e.g. chemotherapy) should be included.

IC CR	**Any relevant family history must be recorded.**
IC CR	• Almost 50% of phaeochromocytomas/paragangliomas are hereditary, making them the most hereditarily determined of all human tumours, and at least 15 hereditary susceptibility genes are now associated with their development.[17]

- Relevant information regarding familial predisposition to cancer (e.g. Li-Fraumeni, Beckwith-Wiedemann and Lynch syndromes), including family history and results of genetic testing, should also be recorded.

ICCCR	**The presence of endocrine or other tumours must be recorded.**

- History of other cancers, which may metastasize to the adrenal glands, should be included.

ICCCR	**The presence of any germline mutations or familial syndrome must be recorded.**
ICCCR	• Distinct correlations exist between genotype, biochemical phenotype,[19] tumour distribution, prognosis, and syndromic associations.[20,21]

➢ The clinical diagnosis or differential diagnosis should be recorded.

- Providing the provisional clinical diagnosis or differential diagnosis improves clinicopathological correlation and improves diagnostic accuracy.

➢ **Record if this is a new primary cancer or a recurrence of a previous cancer, if known.**

- The term recurrence defines the return, reappearance or metastasis of cancer (of the same histology) after a disease free period.

  Recurrence should be classified as distant metastases or regional (local) recurrence.

  Regional (local) recurrence refers to the recurrence of cancer cells at the same site as the original (primary) tumour or the regional lymph nodes.

  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.

ICCCR	Any other clinical information should be included, if appropriate.

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

Example Request Information Sheet

Phaeochromocytoma & Paraganglioma Request Information

Family name

Given name(s)

Date of birth
DD – MM – YYYY

Date of request
DD – MM – YYYY

Ethnicity
- ○ Unknown/inadequately described
- ○ Aboriginal/Torres Strait Islander (AU)
- ○ Māori (NZ)
- ○ Other ethnicity:

Accession/Laboratory number

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

Requesting doctor - name and contact details

Copy to doctor
name and contact details

CLINICAL INFORMATION

OR
- ○ Information not provided

OR
Hormonal status
- ○ Cannot be determined (testing status not known)
- ○ Biochemically silent
- ○ Biochemical analysis not performed
- ○ Biochemically functioning (select all that apply)
  - ☐ Metanephrine and/or adrenaline
  - ☐ Normetanephrine and/or noradrenaline
  - ☐ Methoxytyramine and/or dopamine
  - ☐ Other, *specify*

Imaging findings

Relevant biopsy/cytology results

Previous therapy (including pre-operative embolization, chemotherapy, radiotherapy, targeted therapy, immunotherapy)

Relevant familial history

Presence of endocrine or other tumours

Germline mutation or familial syndrome

PRINCIPAL CLINICIAN

OTHER CLINICAL INFORMATION

OPERATIVE PROCEDURE (select all that apply)

- ○ Not specified

OR
- ☐ Laparoscopic
- ☐ Organ-sparing
- ☐ Biopsy (Incisional, excisional), *specify*

- ☐ Open resection, *specify procedure, including other organis if present (e.g. adrenal resection and liver biopsy)*

- ☐ Other, *specify*

V1.0 Request Info from Phaeochromocytoma and Paraganglioma Structured Reporting Protocol 1st Edition

The above Request Information Sheet is also available on the RCPA Cancer Protocols webpage.

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.[58]

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

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

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

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

- Configure reports in such a way that data elements are 'chunked' into a single unit to help improve recall for the clinician.[58]

- Reduce 'clutter' to a minimum.[58] Thus, information that is not part of the protocol (e.g. billing information or SNOMED codes) should not appear on the reports or should be minimised.

- Reduce the use of formatting elements (e.g. bold, underlining or use of footnotes) because these increase clutter and may distract the reader from the key information.

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

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

As a report is transferred between systems:

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

Appendix 3   Example of a pathology report

Citizen, Geraldine W.
C/O Paradise Close
Wreck Bay Resort
Nar Nar Goon East, 3181

Female

DOB 17/8/1978
MRN M1196788

Lab Ref: **18/P28460**
Referred: 28/4/2020

Copy to: **Dr N.G.Chappie**
Rainforest Cancer Centre.
46 Smith Road,
Woop Woop, 3478

Referred by: **Dr E. Throat**
Suite 3, AJC Medical Centre,
Nose Drive
Nar Nar Goon West, 3182

PHAEOCHROMOCYTOMA STRUCTURED REPORT

Diagnostic Summary

Right adrenalectomy: Phaeochromocytoma; 11 mm; Completely excised

AJCC 8th Edition Staging Parameters: pT1b, pNX

Supporting Information

CLINICAL INFORMATION RECEIVED

(Provided on the request form and obtained at the Endocrine MDT 30 April 2020):

Hormone status:	Biochemically silent
Imaging findings:	Nil
Relevant biopsy/cytology results:	Nil
Relevant therapy:	Nil
Relevant familial history:	Nil
Presence of endocrine or other tumours:	Nil
Germline mutation or familial syndrome:	Nil
Other clinical information:	Nil

MACROSCOPIC

Specimen label / Specimen submitted:	Right adrenal tumour
Operative procedure:	Laproscopic adrenalectomy
Specimen weight:	2.5 g
Specimen dimensions:	12 mm x 10 mm x 5 mm
Tumour focality:	Unifocal
Number of tumours in same organ:	1
Number of tumours in separate organs:	0
Tumour site:	Right adrenal tumour

MACROSCOPIC APPEARANCE OF LESION

Location:	Medulla, head
Borders:	Encapsulated
Description:	Dusky red, well circumscribed, round border
Distance to nearest excision margin:	2 mm
Tumour dimensions:	11mm x 8 mm x 4mm

APPEARANCE OF UNINVOLVED ADRENAL GLAND

Medullary nodules (microphaeochromocytoma):	Absent
Diffuse hyperplasia:	Absent
Specimen integrity:	Specimen intact
Block identification key:	A to B adrenal tumour; C – non-tumour adrenal
	Photographs taken: M/PTH1234
Other macroscopic comments:	Nil

MICROSCOPIC

Histologic tumour type:	Phaeochromocytoma
Adverse features	
Growth pattern:	Zellballen
Cellularity:	Low
Necrosis:	Absent
Extent of invasion:	Confined to adrenal gland, capsular invasion not present
Extension into adipose tissue:	Absent
Lymphovascular invasion:	Not identified
Mitotic count:	<1 mitotic figures/2 mm^2
Atypical mitoses:	Absent
Ki-67 proliferation index:	2%
Non-tumour appearance:	Unremarkable

Margin status

Distance to closest margin:	2 mm
Closest margin:	Anterior
Margin status:	Not involved (R0)

Lymph node (LN) status   No nodes submitted or found

Distant metastases:	Not identified
Coexistent pathological abnormalities:	Absent
Additional microscopic comments:	Nil

ANCILLARY TESTS

Immunohistochemistry:	Chromogranin A: Positive
	Synaptophysin: Positive
	S100: Positive in sustentacular cells
	SDHB: Positive (normal pattern of staining)

Reported by Dr Bernadette Beckstein   Authorised 1/5/2020

Citizen, Gerald W.
C/O Paradise Close
Wreck Bay Resort
Nar Nar Goon East, 3181

Male

DOB 1/7/1971
MRN M1196788

Lab Ref: **18/P28460**
Referred: 28/4/2020

Copy to: **Dr N.G.Chappie**
Rainforest Cancer Centre.
46 Smith Road,
Woop Woop, 3478

Referred by: **Dr E. Throat**
Suite 3, AJC Medical Centre,
Nose Drive
Nar Nar Goon West, 3182

PARAGANGLIOMA STRUCTURED REPORT

Diagnostic Summary

Carotid body excision: **Paraganglioma; 42 mm; Completely excised**

AJCC 8th Edition Staging Parameters: pT3a, pN0

Supporting Information

CLINICAL INFORMATION RECEIVED

(Provided on the request form and obtained at the Endocrine MDT 30 April 2020):

Hormone status:	Biochemical analysis not performed
Imaging findings:	Nil
Relevant biopsy/cytology results:	Nil
Relevant therapy:	Nil
Relevant familial history:	Nil
Presence of endocrine or other tumours:	Nil
Germline mutation or familial syndrome:	Nil
Other clinical information:	Nil

MACROSCOPIC

Specimen label / Specimen submitted:	Right carotid body tumour
Operative procedure:	Carotid body excision
Specimen weight:	3.8 g
Specimen dimensions:	44 mm x 12 mm x 10 mm
Tumour focality:	Unifocal
Number of tumours in same organ:	1
Number of tumours in separate organs:	0
Tumour site:	Right carotid body

MACROSCOPIC APPEARANCE OF LESION

Location:	Right carotid body
Borders:	Infiltrative
Description:	Dusky red, irregular
Distance to nearest excision margin:	1 mm
Tumour dimensions:	42mm x 10mm x 8mm

APPEARANCE OF UNINVOLVED ADRENAL GLAND

Medullary nodules (microphaeochromocytoma):   Not applicable

Diffuse hyperplasia: Not applicable

Specimen integrity: Not applicable

Block identification key: A to D adrenal tumour; E – non-tumour adrenal

Photographs taken: M/PTH1234

Other macroscopic comments: Nil

MICROSCOPIC

Histologic tumour type: Extra-adrenal paraganglioma

Adverse features

Growth pattern: Pseudorosettes

Cellularity: High

Necrosis: Present

Extent of invasion: Widespread soft tissue invasion is seen up to 0.7mm in maximum extent

Extension into adipose tissue: Present, 0.5mm in maximum extent

Lymphovascular invasion: Present

Mitotic count: 4 mitotic figures/2 mm^2

Atypical mitoses: Present

Ki-67 proliferation index: 25%

Non-tumour appearance: No residual normal carotid body is seen

Margin status

Distance to closest margin: 1 mm

Closest margin: Posterior

Margin status: Not involved (R0)

Lymph node (LN) status   0 / 4 lymph nodes involved

Distant metastases: Not identified

Coexistent pathological abnormalities: Absent

Additional microscopic comments: Nil

ANCILLARY TESTS

SDHB immunohistochemistry: Negative/abnormal pattern of staining (with internal control endothelial cell staining present), highly suggestive of SDH deficiency. Molecular testing is recommended for further characterisation.

Reported by Dr Bernadette Beckstein   Authorised 1/5/2020

Appendix 4   WHO histological classification of adrenal gland tumours

Phaeochromocytoma	8700/3

Extra-adrenal paragangliomas

Head and neck paragangliomas

Carotid body paraganglioma	8692/3*
Jugulotympanic paraganglioma	8690/3*
Vagal paraganglioma	8693/3
Laryngeal paraganglioma	8693/3
Sympathetic paragangliomas	8693/3

Neuroblastic tumours of the adrenal gland

Neuroblastoma	9500/3
Ganglioneuroblastoma, nodular	9490/3
Ganglioneuroblastoma, intermixed	9490/3
Ganglioneuroma	9490/0

Composite phaeochromocytoma	8700/3
Composite paraganglioma	8693/3

The morphology codes are from the International Classification of Diseases for Oncology (ICD-O).[59] Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours.
The classification is modified from the previous WHO classification, taking into account changes in our understanding of these lesions.

*These new codes were approved by the IARC/WHO Committee for ICD-O.

From WHO Classification of Tumours Pathology and Genetics. Tumours of Endocrine Organs 2017, Volume 10, 4th Edition. IARC.[16]

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