ADRENAL GLAND TUMOURS

STRUCTURED REPORTING PROTOCOL

(1st Edition 2013)

Core Document versions:

- AJCC Cancer Staging Manual 7th edition (including errata corrected with 5th reprint 10th Aug 2010).
- World Health Organization Classification of Tumours Pathology and Genetics Tumours of Endocrine Organs. 2004. Volume 8.

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Contents

Scope

This protocol contains standards and guidelines for the preparation of structured reports for adult patient with tumour of the adrenal gland. It does not cover paediatric adrenal tumours eg neuroblastoma.

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 adrenal gland carcinoma, whether as a minimum data set or fully comprehensive report.

This protocol is based on information contained within multiple international publications and has been developed in consultations with practising pathologists and colleagues from different clinical disciplines. It is intended for use by pathologists, surgeons, physicians (endocrinologists), radiologists and oncologists.

Abbreviations

AJCC	American Joint Committee on Cancer
IHI	Individual Healthcare Identifier
LIS	The laboratory information system
MEN	Multiple Endocrine Neoplasia
mm	Millimetres
MRN	Medical Record Number
NHI	New Zealand National Health Identifier
PBS	Pharmaceutical Benefits Scheme
RCPA	Royal College of Pathologists of Australasia
SI	International System of Units
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 'pretest 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 (eg how does the item assist with clinical management or prognosis of the specific cancer). • cite published evidence in support of the standard or guideline • clearly state any exceptions to a standard or guideline. In this document, commentary is prefixed with 'CS' (for commentary on a standard) or 'CG' (for commentary on a guideline), numbered to be consistent with the relevant standard or guideline, and with sequential alphabetic lettering within each set of commentaries (eg CS1.01a, CG2.05b).
General commentary	General commentary is text that is not associated with a specific standard or guideline. It is used: • to provide a brief introduction to a chapter, if necessary • for items that are not standards or guidelines but are included in the protocol as items of potential importance, for which there is currently insufficient evidence to recommend their inclusion. (Note: in future reviews of protocols, such items may be reclassified as either standards or guidelines, in line with diagnostic and prognostic advances, following evidentiary review).

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

Adrenal tumours can occur in the cortex or medulla and with a wide range of morphologies. Many of these tumours have uncertain malignant potential on histopathological examination. Thus, in this protocol, we address the reporting of adrenal tumours rather than only on malignant tumours as many of the adrenal lesions may have a malignant potential. In fact, "borderline malignant potential" is a terminology often used in adrenocortical tumour.

The protocol discusses only primary adrenal tumours in adults as primary adrenal tumours in paediatric patients have a distinctive spectrum of diseases and should be presented in a separate protocol.

Importance of histopathological reporting

Pathological reporting of resection specimens for adrenal tumours provides information both for the clinical management of the affected patient and for the evaluation of the health care systems as a whole.

In the WHO classification and in the literature, there are many different types of adrenal tumour of borderline or malignant potential.[1] However, many of them are uncommon and are not described in detail in this protocol. The main adrenal tumours that will be covered in the protocol are adrenocortical neoplasms and pheochromocytoma. They are the tumours in which histological features and ancillary investigations may help in the management of the patients.

Benefits of structured reporting

Structured pathology reports with standardised definitions for each component have been shown to significantly enhance the completeness and quality of data provided to clinicians, and has been recommended both in North America and the United Kingdom.[2-6]

The College of American Pathologists and the Royal College of Pathologists (UK) have recently published useful protocols for the reporting of cancer.[6-7] A protocol endorsed by the Royal College of Pathologists of Australasia and other Australasian organisations involved in the management of adrenal carcinoma is timely.

Design of this protocol

This structured reporting protocol provides a complete framework for the assessment and documentation of all the pathological features of adrenal carcinoma.

Mandatory elements (standards) are differentiated from those that are not

mandatory but represent best practice (guidelines). Consistency and speed of reporting is improved by the use of discrete data elements recorded from the checklist. However, the pathologist is encouraged to include free text or narrative to document any other relevant issues, to give reasons for coming to a particular opinion and to explain any points of uncertainty.

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 checklist (Chapter 6) or report (Chapter 7). 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

This protocol draws on the following key documents:

- *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols*[8]
- *The Pathology Request-Test-Report Cycle — Guidelines for Requesters and Pathology Provider*[9]
- *AJCC Cancer Staging Manual*, 7th edition[10]
- *Pathology and Genetics of Tumours of Endocrine Organs. WHO Classification of Tumours, Volume 8, 2004*[1]

Changes since the last edition

Not applicable

Authority and development

This section provides details of the committee involved in developing this protocol and the process by which it was developed.

Protocol developers

This protocol was developed by an expert committee, with assistance from relevant stakeholders.

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Stakeholders

ACT Health

Anatomical Pathology Advisory Committee (APAC)

Australian Association of Pathology Practices Inc (AAPP)

Australian Cancer Network

Australian Commission on Safety and Quality in Health Care

Cancer Australia

Cancer Council ACT

Cancer Council NSW

Cancer Council Queensland

Cancer Council SA

Cancer Council Tasmania

Cancer Council Victoria

Cancer Council Western Australia

Cancer Institute NSW

Cancer Services Advisory Committee (CanSAC)

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

Cancer Voices

Clinical Oncology Society of Australia (COSA)

Colorectal Cancer Research Consortium

Department of Health and Ageing

Endocrine Society of Australia (ESA)

Grampians Integrated Cancer Services (GICS)

Health Informatics Society of Australia (HISA)

Independent review group of pathologists

Medical Software Industry Association (MSIA)

National Coalition of Public Pathology (NCOPP)

National E-Health Transition Authority (NEHTA)

National Pathology Accreditation Advisory Council (NPAAC)

National Round Table Working Party for Structured Pathology Reporting of Cancer.

New Zealand Guidelines Group (NZGG)

NSW Department of Health

Peter MacCallum Cancer Institute

Queensland Cooperative Oncology Group (QCOG)

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Royal Australasian College of Physicians (RACP)

Southern Cancer Network, Christchurch, New Zealand

Southern Melbourne Integrated Cancer Service (SMICS)

Standards Australia

The Medical Oncology Group of Australia

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)

Victorian Cooperative Oncology Group (VCOG)

Western Australia Clinical Oncology Group (WACOG)

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Development process

This protocol has been developed following the seven-step process set out in *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols.*[8]

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

1 Pre-analytical

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

The pathologist is reliant on the quality of information received from the clinicians or requestor. Some of this information may be received in generic pathology request forms; however, the additional information required by the pathologist specifically for the reporting of 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.[11] This document specifies the minimum information to be provided by the requesting clinician for any pathology test.

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

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

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

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

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

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

CS1.04a Knowledge of the clinical presentation is an essential part of the WHO classification yet it may not be available 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 procedure 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.

S1.05 The operating surgeon's identity and contact details must be recorded.

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 be encouraged. However, the pathologist should make sure that the diagnostic process including the measurement of maximum extent and other important parameters that influence patient prognosis and management will not be compromised. Also, the pathologist should ensure that appropriate ethical approval has been obtained for tissue banking. As a safeguard, research use of the specimen may be put on hold until the diagnostic process is complete so that the specimen can be retrieved.

Intra-operative consultations

- Requests for an intra-operative frozen section of the adrenal gland is uncommon.
    - If being done, try to limit the number of blocks taken from the lesion to a minimum, to ensure that there are tumour tissues that have not been frozen.
    - Care should be taken to prevent the spread of marking ink and distortions which may compromise subsequent paraffin section.
    - Intra-operative frozen section may happen in some instances eg identifying metastases and infection that may mimic cancer.

Specimen handling

- **The specimen must be orientated.**

  - The right adrenal gland is roughly pyramidal in shape whereas the left is more elongated. The medial one-third is designated as head and the lateral outer third as tail. The concave surface represents the infero-lateral aspect.

- **The specimen must be weighed.**

  - The combined weighed of both adrenal glands are often less than 12g.[12] The left adrenal gland is often heavier than the right adrenal gland. The amount of adipose tissue adjacent to the gland, co-existing diseases and other factors may affect the actual weight of the adrenal gland and must be taken in account.[10]

  - The weight is an important criterion to predict malignancy in both adrenocortical neoplasms and pheochromocytoma (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.

- **The external surface of the specimen must be inked as the resection margin.**

- A diagram or photograph can facilitate the specimen orientation and block labelling.

- **The specimen should be serially sectioned perpendicular to its long axis.**

- **Blocks should be sampled from the macroscopically noted adrenal tumour.**

- Submit blocks to show the relationship of the tumour to the capsule and the adjacent adrenal tissue.

  There is no definite protocol for tumour sampling. At least one block for each 10mm of the largest dimension of the tumour is recommended. Blocks should also be taken from areas of different appearance e.g. necrotic tissue. If the tumour is small, it is recommended to sample the whole tumour.

- **Blocks should be taken from uninvolved adrenal gland.**

- **Blocks should be taken from other tissues if submitted.**

    - Soft tissues, lymph nodes and adjacent structures may be sampled and submitted.

Macroscopic findings

S2.01 All measurements are in SI units, unless explicitly stated.

S2.02 The labelling of the specimen must be recorded.

S2.03 Specimen weight must be recorded in grams.

G2.01 The specimen dimensions should be recorded.

S2.04 Whether the tumour capsule is intact or not should be recorded.

S2.05 Where there are multiple lesions, the total number of lesions must be recorded.

S2.06 The macroscopic description of any lesion(s) in the specimen must be recorded.

CS2.06a Where possible, for each lesion, the location (cortex versus medulla), appearance, the borders (encapsulated or infiltrative), size (greatest dimension), and distance from the nearest excision margin must be recorded.

S2.07 The appearance of the adrenal gland other than the lesion(s) detected must be documented.

CS2.07a This should include whether the cortex, medulla of the adrenal gland appears unremarkable, atrophic (thin) or hypertrophic (thickened).

CS2.07a The presence of cortical nodules should be noted. In most cases, the nodule should be less than 10mm in size.

CS2.07a The presence of medullary hyperplasia/nodule should be noted.

It is worth noting that in a normal gland, there is little or no medullary tissue in the tail. Thus, medulla tissue in the tail indicates medullary hyperplasia. Medullary nodule is defined as a lesion of 10mm or less, any larger than that it is labelled pheochromocytoma.[13]

G2.02 The presence or absence of lymph nodes(s) or adjacent structure should be recorded.

G2.03 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.

CG2.03a 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.

CG2.03b 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

Microscopic findings 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 The tumour type must be recorded.

CS3.01a The classification of tumours of the adrenal gland is from the WHO 2004 classification[1] (refer to Appendix 4).

G3.01 Variants of tumour types should be recorded.

CG3.01a Variants of adrenocortical carcinoma include oncocytic, myxoid and sarcomatous variants.

Pure oncocytic tumour should be greater than 90% oncocytes.

Pheochromocytoma can be composite which means areas of ganglioneuroma, ganglioneuroblastoma can be found in additional to pheochromocytoma.[14]

S3.02 The diameter of the largest tumour must be recorded.

CS3.02a Size of the cortical neoplasm is important in the staging system for adrenal cortical tumour. In particular, the size is a criterion for prediction of malignant behaviour for oncocytic adrenocortical neoplasms.[15-16]

In cases of multifocal tumours, the diameter of the largest tumour must be recorded.

S3.03 The presence or absence of invasion of the adrenal vein or vena cava must be recorded.

CS3.03a This is associated with a poor prognosis refer to CG3.02a and b.

S3.04 The presence or absence of capsular invasion must be recorded.

CS3.04a This is associated with a poor prognosis refer to CG3.02a and b.

S3.05 If conventional or oncocytic adrenocortical neoplasm, the presence or absence of sinusoidal invasion must be recorded.

CS3.05a This is associated with a poor prognosis refer to CG3.02a and b.

S3.06 If pheochromocytoma, the presence or absence of extension into adipose tissue must be recorded.

CS3.06a This is associated with a poor prognosis and increased recurrence, refer to CG3.02c.

S3.07 The extension of the tumour into adjacent organs must be recorded.

CS3.07a In adrenocortical neoplasm, the pathological staging (T stage) depends on the size of the cancer, presence of extra-adrenal invasion (invasion through the capsule) and involvement of adjacent organs such as the kidney, etc.

S3.08 Mitotic rate must be recorded.

CS3.08a For conventional and oncocytic adrenocortical neoplasms the mitotic rate should be calculated per 50 high power fields (HPF at 40x objective).

High mitotic rate is associated with poorer prognosis, refer to CG3.02a and b.

CS3.08b For pheochromocytoma the mitotic rate should be calculated per 10 high power fields.

High mitotic rate is associated with poorer prognosis, refer to CG3.02a and b.

S3.09 The presence or absence of atypical mitotic figures must be recorded.

S3.10 The presence or absence of central or confluent necrosis must be recorded.

CS3.10a For pheochromocytoma. record if the central (middle of large nests) or confluent tumour necrosis is present. Necrosis should be distinguished from degenerative changes.

Necrosis is associated with poorer prognosis, refer to CG3.02b.

S3.11 If conventional adrenocortical neoplasm, nuclear grade must be recorded.

CS3.11a This is based on criteria of Fuhrman, refer to CG3.02a and b.

S3.12 If conventional adrenocortical neoplasm, the percentage of tumour comprising clear or vacuolated cells must be recorded.

CS3.12a <25% clear or vacuolated cells is one of 9 criteria for determining malignant potential, refer to CG3.02a and b.

S3.13 If conventional adrenocortical neoplasm or pheochromocytoma, tumour architecture must be assessed and recorded.

CS3.13a Tumour architecture may be:

- Non-diffuse
- Diffuse architecture
    - For conventional adrenocortical neoplasms this is defined as more than 1/3 of the tumour forms patternless sheets of cells; trabecular, cord, columnar, alveolar or nesting is not considered to be diffuse.
    - For pheochromocytoma, this is defined as large nests or diffuse growth >10%. The pattern should be recognized as either zellabellen, irregular nests of diffuse growth or having pseudorosette.

S3.14 If pheochromocytoma, cellular and other nuclear features should be recorded. (Refer to CG3.02c below).

CS3.14a Cellularity should be described and the presence of:

- Cellular monotony
- Tumour cell spindling
- Profound nuclear pleomorphism
- Nuclear hyperchromasia

should be recorded.

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

CG3.02a **Conventional adrenocortical neoplasm.**

Each of the below parameters is scored 0 when absent and 1 when present. 3 or more of these factors are required for a diagnosis of adrenocortical carcinoma:

- Nuclear grade - high nuclear grade (grade 3 or 4) is scored 1 and the others are scored 0.
- >5 mitotic figures/50 high power field (HPF at 40x

objective)

- Presence of atypical mitotic figures
- Clear or vacuolated cells comprising 25% or less of tumor
- Diffuse architecture (more than 1/3 of tumor forms patternless sheets of cells; trabecular, cord, columnar, alveolar or nesting is not considered to be diffuse)
- Microscopic necrosis
- Venous invasion
- Sinusoidal invasion
- Capsular invasion

The scoring for adrenocortical neoplasm is based on the recognition at light microscopy of at least three among nine morphological parameters, according to the Weiss scoring system, which has been introduced in 1984 and nowadays is the most widely employed.[17-18] Nevertheless, the diagnostic performance of this system is very high but does not reach a sensitivity and specificity of 100%, its diagnostic applicability is potentially low among non-expert pathologists, and a group of borderline cases with only one or two criteria exist of uncertain behaviour.

Several multi-parameter systems have been published in an attempt to delineate malignancy (see Appendix 5). The earliest one is in 1979 by Hough who have used 7 histological criteria and 5 non-histological criteria.[19] The disadvantage of this system is the reliance on clinical parameters and some of these clinical parameters, may not be available when examining the specimen.

In 1985 Van Slooten *et al*. developed a system based on seven histopathological parameters, each combined with a numerical value, and currently known as the Van Slooten index (VSI).[20] In 2002 Aubert *et al*. simplified the Weiss system, eliminating four parameters with limited discrimination, retaining only the most reliable criteria. For this new index they coined the term Weiss revisited index (WRI) consisting of five histological parameters (2.mitotic rate + 2.cytoplasm + abnormal mitoses + necrosis + capsular invasion).[21]

None of these systems have been universally adopted.

From a practical perspective, the most useful criteria to separate adenomas from carcinomas include tumour size,

presence of necrosis, mitotic activity including atypical mitoses, invasive growth and high nuclear grade. Capsular invasion may be difficult to recognize because the expanding capsule may be a pre-existing adrenal capsule. Invasion of adjacent soft tissue, kidney or liver is definitive sign of malignancy.[22]

CG3.02b **Oncocytic adrenocortical neoplasm**

If all the 3 major histological criteria listed below are present, the tumour is malignant. The presence of any of the minor criteria indicates that the tumour is of borderline malignant potential. In the absence of all these criteria, the tumour is benign.

Major histological criteria:

- Mitotic rate >5 per 50 HPF
- Atypical mitotic figures
- Venous invasion

Minor histological criteria:

- Necrosis
- Capsular invasion
- Sinusoidal invasion
- Size > 10cm and/or 200g

Specifically for the pure oncocytic neoplasms that seem to have a better prognosis in comparison to the conventional ACCs, a modified system (the Lin-Weiss-Bisceglia) has been proposed.[16]

CG3.02c **Pheochromocytoma**

There is no reliable histological criterion to differentiate benign or malignant pheochromocytoma. In the literature, there are two scoring system. These include the PASS score based only on histological criteria and a Japanese scoring system based on histological criteria plus Ki-67 immunoreactivity and types of catecholamine produced. 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[23] (Appendix 5):

- High cellularity (2),
- Central or confluent tumor 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 pheochromocytoma has a score of less than 4 and malignant pheochromocytoma has a PASS score higher than 6. Patients with a PASS score >4 should be followed closely for recurrence.

The Japanese scoring system (Kimura et al)[24] 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 pheochromocytoma appears to be correlated with potential for metastases and survival rates. Patients with poorly-differentiated pheochromocytoma are malignant and

reported to have 0% survival rate.

S3.15 The status of the non-tumour adrenal gland must be recorded.

CS3.15a The presence of adrenal cortical atrophy, hyperplasia, cortical nodules should be noted.

CS3.15b The presence of medullary hyperplasia/nodule 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. Medullary nodule is defined as a lesion of 10mm or less, any larger than that it is labelled pheochromocytoma.

S3.16 The presence or absence of tumour at the resection margins must be recorded.

S3.17 The presence of positive lymph nodes must be recorded.

CS3.17a The presence of lymph node metastases affects the pathological staging (N stage) of adrenal gland carcinoma. It is worth noting that TNM staging only applies to adrenal cortical carcinoma. In pheochromocytoma, is by definition, the first evidence of malignancy.

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.

4 Ancillary studies findings

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

S4.01 The findings of any ancillary studies, where performed, must be recorded.

CS4.01a Diagnostic purpose

Neuroendocrine markers like chromogrannin, synaptophysin, CD 56 can be used to document the neuroendocrine nature of the pheochromocytoma. S-100 would be useful for documenting substantacular cells if present. The lack of S-100 substantacular cells have been reported in some but not all of malignant pheochromocytomas.[1]

In metastatic pheochromocytoma, carcinoid (neuroendocrine tumour/carcinoma)can be a differential diagnosis. In this situation, cytokeratin could be done. Pheochromocytoma is usually negative for cytokeratin but carcinoid (neuroendocrine tumour/carcinoma) is positive.

Adrenocortical neoplasm can be positive for inhibin and melan-A. It may be positive for synaptophysin but not chromogranin. Also, negativity to EMA may help to differentiate cortical neoplasm from renal cell carcinoma. Cytokeratin is not useful as the staining is variable in adrenocortical carcinoma.[1]

Anti-mitochondrial antibody mES-13 has been proposed to confirm the oncocytic nature (numerous mitochondria) in the oncocytic variant of adrenocortical neoplasm.[15]

CS4.01b Prognostic purpose

Ki-67 labeling index has been used in differentiating benign from malignant pheochromocytoma.[24]

CS4.01c Genetic counseling

As a group at least 30% of pheochromocytomas and paragangliomas are hereditary.

As of 2012, there are 12 known genes responsible for the pathogenesis of pheochromocytoma/paraganglioma [RET, VHL, NF1, TMEM127, MAX, KIF1Bb, PHD2, SDHA, SDHB, SDHC, SDHD and SDHAF2.]. Depending on the clinical circumstance, mutation testing for some, most or all of

these genes should be considered in individuals presenting with apparently sporadic pheochromocytoma /paraganglioma.[25]

Positive staining for SDHB (when performed in experienced centres) excludes germlilne 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.[26]

Approximately 4% of pheochromocytomas 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 pheochromocytomas 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 paragagnliomas. SDHD and SDHC mutation are more commonly found in head and neck paragangliomas.[26]

CS4.01d 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 (eg 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.

CS4.01e 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 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 tumour stage and stage grouping must be recorded according to the most recent TNM staging system of the AJCC Cancer Staging Manual.[10] (See Appendix 6)

CS5.01a The AJCC lists the staging system for adrenal cortical cancer. At the moment, there is no staging system for medullary tumours such as pheochromocytoma.

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 type (S2.02)

b. Tumour type (S3.01)

c. Diameter of largest tumour (S3.02)

d. Tumour stage (S5.01)

e. Completeness of excision (S3.16)

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:

- list any relevant ancillary tests,
- document any noteworthy adverse gross and/or

histological features,

- express any diagnostic subtlety or nuance that is beyond synoptic capture, and
- document further consultation or results still pending.

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

6 Structured checklist

The following checklist contains all the standards and guidelines for this protocol in the simplest possible form. The summation of all "Standards" is equivalent to the "Minimum Data Set" for thyroid cancer. 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.[27]

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.

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:**	
	Functionality of the adrenal gland	**Single selection value list:** • Functional • Non-functional	**If functional, specific type of presentation**
	Type of presentation	***Text***	
	Operative procedure	**Text**	
	Any previous adrenal surgery	**Text**	
	Site of lesion(s)	**Text**	
	Laterality of lesion	**Single selection value list:** • Left • Right • Both	
	Any accompanying specimens	**Single selection value list:**	**If Other, provide details**

S/G	Item description	Response type	Conditional
		• Lymph nodes • Kidney • Other	
	Details	***Text***	
	Relevant clinical information	**Text**	
	Pre-operative biopsy	**Single selection value list:** • Not performed • Performed	**If performed, provide details**
	Details	***Text***	
	Clinical stage	**Text**	
	Involvement of adjacent organs	**Single selection value list:** • Not involved • Involved	**If involved, describe involved organs**
	Involved organs	***Text***	
	Clinical or differential diagnosis	**Text**	
	New primary or recurrence	**Single selection value list:** • New primary cancer • Regional (local) recurrence • Distant metastasis	**If distant metastasis, provide details**
	Details	***Text***	

S/G	Item description	Response type	Conditional
S1.03	**Pathology accession number**	**Alpha-numeric**	
S1.04	**Principal clinician caring for the patient**	**Text**	
S1.05	**Surgeon's identity and contact details**	**Text**	
G1.01	Other clinical information received	**Text**	
Macroscopic findings			
S2.02	**Specimen labelled as**	**Text**	
G2.01	Specimen dimensions	**Numeric: __x__x__mm** **OR** **Cannot be recorded**	
S2.03	**Specimen weight**	**Numeric: ___g**	
S2.04	**Tumour capsule**	**Single selection value list:** • Not intact • Intact	
S2.05	**Number of macroscopically visible tumour(s)**	**Numeric: _____**	
S2.06	**MACROSCOPIC APPEARANCE OF LESION(S)**	Note: that the macroscopic appearance will need to be repeated for each primary tumour identified.	

S/G	Item description	Response type	Conditional
	Location	**Single selection value list:** • Cortex • Medulla • Indeterminate • Other	**If other provide details**
	Details	***Text***	
	Borders	**Single selection value list:** • Encapsulated • Infiltrative	
	Description	**Text**	
	Size in greatest dimension	**Numeric: __mm**	
	Distance to nearest excision margin	**Numeric: __mm**	
S2.07	**APPEARANCE OF UNINVOLVED ADRENAL GLAND**		
	Cortex	**Single selection value list:** • Unremarkable • Atrophic (thin) • Hypertrophic (thickened) • Not identified	

S/G	Item description	Response type	Conditional
	Medulla	**Single selection value list:** • Unremarkable • Atrophic (thin) • Hypertrophic (thickened) • Not identified	
	Cortical nodules	**Single selection value list:** • Absent • Present • Not assessable	**If present, record the size of the largest nodule**
	Size of largest nodule	***Numeric: ___mm OR <10mm***	
	Medullary hyperplasia/nodule	**Single selection value list:** • Absent • Present • Not assessable	
G2.02	ANY ACCOMPANYING SPECIMENS		
	Lymph nodes	**Single selection value list:** • Absent • Present	
	Other adjacent structures	**Text**	
G2.03	Other macroscopic comment	**Text**	

S/G	Item description	Response type	Conditional
Microscopic findings			
S3.01	**Tumour type**	**Single selection value list from WHO Classification of Adrenal gland tumours.**	
G3.01	Tumour type variants	**Multi select value list from WHO Classification of Adrenal gland tumours.**	
S3.02	**Diameter of largest tumour**	**Numeric: ___mm**	

FOR PHEOCHROMOCYTOMA

S3.13	**Cellular pattern**	**Single selection value list:** • Non-diffuse • Zellballen • Large and irregular cell nests • Pseudorosette Note: For pheochromocytoma, diffuse architecture is defined as large nests or diffuse growth >10%. The pattern should be recognized as either zellabellen, irregular nests of diffuse growth or having pseduorosette.	
S3.14	**Cellularity**	**Single selection value list:** • Low • Moderate • High	

S3.10	**Central or confluent necrosis**	**Single selection value list:** • Absent • Present	
S3.03	**Adrenal vein or vena cava invasion**	**Single selection value list:** • Absent • Present	
S3.04	**Capsular invasion**	**Single selection value list:** • Absent • Present	
S3.06	**Extension into adipose tissue**	**Single selection value list:** • Absent • Present	
S3.07	**Adjacent organs**	**Single selection value list:** • Not involved • Involved	**If involved, list involved organs**
	Involved organs	***Text***	
S3.14	**Cellular monotony**	**Single selection value list:** • Absent • Present	
	Tumour cell spindling	**Single selection value list:** • Absent • Present	
	Profound nuclear	**Single selection value list:**	

	pleomorphism	• Absent • Present	
	Nuclear hyperchromasia	**Single selection value list:** • Absent • Present	
S3.08	**Mitotic rate**	**Numeric: _____ per 10HPF**	
S3.09	**Atypical mitotic figures**	**Single selection value list:** • Absent • Present	

FOR ADRENOCORTICAL TUMOURS

S3.11	**Nuclear grade (Fuhrman)**	**Single selection value list:** • grade 1 • grade 2 • grade 3 • grade 4	
S3.12	**Tumour comprising clear or vacuolated cells**	**Numeric: _____%**	
S3.08	**Mitotic rate**	**Numeric: _____ per 50HPF**	
S3.09	**Atypical mitotic figures**	**Single selection value list:** • Absent • Present	

S3.13	**Cellular pattern**	**Single selection value list:** • Non-diffuse • Diffuse architecture Note: For conventional adrenocortical neoplasms diffuse growth is defined as more than 1/3 of the tumour forms patternless sheets of cells; trabecular, cord, columnar, alveolar or nesting is not considered to be diffuse.	
S3.10	**Central or confluent necrosis**	**Single selection value list:** • Absent • Present	
S3.03	**Adrenal vein or vena cava invasion**	**Single selection value list:** • Absent • Present	
S3.04	**Capsular invasion**	**Single selection value list:** • Absent • Present	
S3.07	**Adjacent organs**	**Single selection value list:** • Not involved • Involved	**If involved, list involved organs**
	Involved organs	***Text***	
S3.05	**Sinusoidal invasion**	**Single selection value list:** • Absent • Present	**Require only if conventional or oncocytic adrenocortical neoplasm in S3.01**

For ALL TUMOURS

G3.02	MALIGNANT POTENTIAL		
	Scoring system (eg PASS, Weiss etc)	**Text**	
	Score for malignant potential	**Numeric**	
S3.15	**Non-tumour adrenal gland**	**Unremarkable** **OR** **Not identified/not assessable** **OR** **Multi select value list (select all that apply)** • Adrenal cortical atrophy • Hyperplasia • Cortical nodules • Medullary hyperplasia/nodule	
S3.16	**Margin status**	**Single selection value list:** • Clear • Involved	**If clear, record distance to closest margin** **If involved, record involved margin(s)**
	Distance to closest margin	***Numeric: ___mm***	
	Involved margin(s)	***Text***	

S3.17	***Lymph node status***	***Single selection value list:*** • *Clear* • *Involved*	***Only if received in G2.02.*** ***If involved, record the number of positive nodes***
	Number of positive nodes	***Numeric: ____/_____*** *Note: Number of positive nodes out of total number of nodes.*	
G3.03	Coexistent pathological abnormalities	**Single selection value list:** • Absent • Present	**If present, describe**
	Description	***Text***	
G3.04	Other relevant microscopic comments	**Text**	
Ancillary test findings			
S4.01	**Ancillary Tests**	**Single selection value list:** • Not performed • Performed	**If performed, record the test result type(s) and result.** **If performed externally also include laboratory performing the test, substrate, method and person responsible for reporting.**
	Test result type eg FISH, IHC, cytogenetics etc	***Text*** *Note: Repeat for each other ancillary test*	

		performed.	
	Result	***Text*** *<u>Note:</u> Repeat for each other ancillary test performed.*	
	Conclusion	***Text*** *<u>Note:</u> Repeat for each other ancillary test performed.*	
	Laboratory performing the test	***Text*** *<u>Note:</u> Repeat for each other ancillary test performed.*	
	Method	***Text*** *<u>Note:</u> Repeat for each other ancillary test performed.*	
	Substrate (eg cytology smears, fluid in special media, paraffin block, fresh tissue, etc)	***Text*** *<u>Note:</u> Repeat for each other ancillary test performed.*	
	Person responsible for reporting	***Text*** *<u>Note:</u> Repeat for each other ancillary test performed.*	
Synthesis and overview			
S5.01	***PATHOLOGICAL TUMOUR STAGE***		**Required only for adrenal cortical cancer**
	T stage	***Single selection value list:***	

		TX *Primary tumour cannot be assessed* *T0* *No evidence of primary tumour* *T1* *Tumour 5 cm or less in greatest dimension, no extra-adrenal invasion* *T2* *Tumour greater than 5 cm, no extra-adrenal invasion* *T3* *Tumour of any size with local invasion, but not invading adjacent organs** *T4* *Tumour of any size with invasion of adjacent organs** **Adjacent organs include kidney, diaphragm, great vessels, pancreas, spleen, and liver.*	
	N stage	***Single selection value list:*** *NX* *Regional lymph nodes cannot be assessed* *N0* *No regional lymph node metastasis* *N1* *Metastasis in regional lymph node(s)*	
	M stage	***Single selection value list:*** *M0* *No distant metastasis* *M1* *Distant metastasis*	
	Stage Group	***Single selection value list:*** ***Stage*** ***T*** ***N*** ***M*** *Stage I* *T1* *N0* *M0* *Stage II* *T2* *N0* *M0*	

		Stage III	*T1*	*N1*	*M0*	
			T2	*N1*	*M0*	
			T3	*N0*	*M0*	
		Stage IV	*T3*	*N1*	*M0*	
			T4	*N0*	*M0*	
			T4	*N1*	*M0*	
			Any T	*Any N*	*M1*	
S5.02	***Year of publication and edition of the cancer staging system***	***Text***				**Required only if S5.01 completed.**
G5.01	Diagnostic summary Include: a. Specimen type (S2.02) b. Tumour type (S3.01) c. Diameter of largest tumour (S3.02) d. Tumour stage, if applicable (S5.01) e. Completeness of excision (S3.16)	**Text**				
S5.03	**Overarching comment**	**Text**				

7 Formatting of pathology reports

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

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

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 adrenal gland tumours 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
    - The patient's ethnicity should be recorded, if known. In particular whether the patient is of aboriginal or Torres Strait islander origin. This is in support of a government initiative to monitor the health of indigenous Australians particularly in relation to cancer.
- The patient's health identifiers should be provided.
    - The patient's health identifiers may include the patient's Medical Record Number as well as a national health number such as a patient's Medicare number (Australia), Individual Healthcare Identifier (IHI) (Australia) or the National Healthcare Identifier (New Zealand).

Clinical Information

- **Whether or not the adrenal gland is functional should be**

recorded.

- If the adrenal gland is functional the specific type of presentation should be recorded.

➢ **The type of operation performed should be recorded.**

- 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.

➢ **Any previous operation on the adrenal gland should 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.

➢ **The anatomical site of the lesion(s) should be recorded.**

- Site is an important identifier especially when multiple lesions are present.

- Sufficient information is required to localise the lesion(s) for subsequent therapy. A diagram or photograph can facilitate this.

- Specimens other than adrenal gland should be identified eg lymph nodes, kidney.

➢ **The laterality of the lesion(s) should be recorded.**

- Laterality information is needed for identification purposes.

➢ Any relevant clinical information should be recorded.

- Clinical or biochemical evidence of hyper-functional or hypo-functional status as a result of changes in the adrenal hormones level should be reported.

- Previous medical treatments should be noted.

- The presence, clinical suspicion and results of genetic tests of familial predisposition of adrenal tumours like multiple endocrine neoplasia (MEN) type 2, neuroectodermal syndromes etc should be reported.

➢ If a pre-operative biopsy has been performed, this should be recorded.

- 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.

➢ The results of clinical staging with radiological imaging and fine needle aspiration should be recorded.

- This is important for pathologic staging of cancer.

➢ The involvement of adjacent organs should be recorded.

- This is important for staging of cancer.

➢ 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.

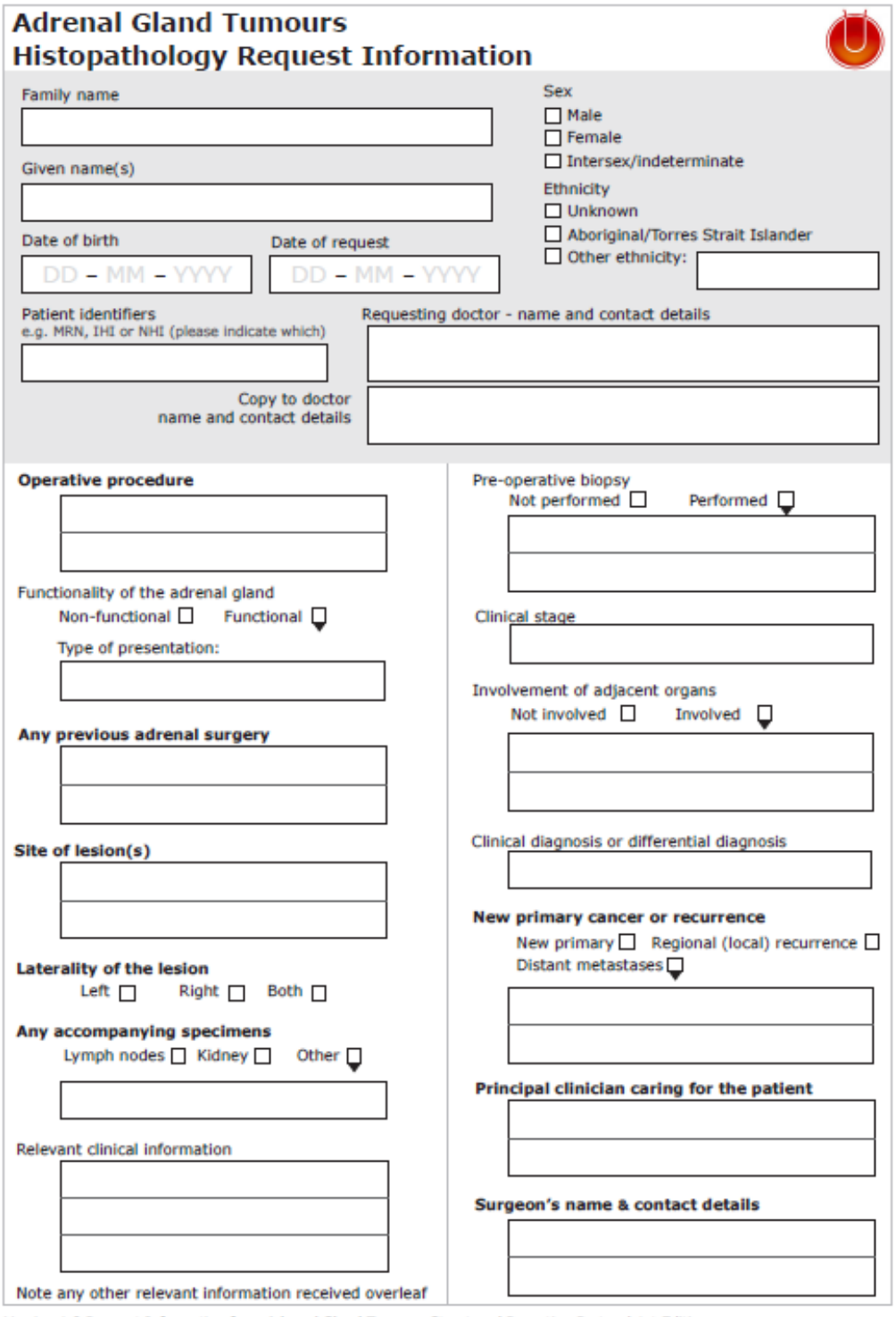
  Distant metastasis refers to the spread of cancer of the same histologic type as the original (primary) tumour to distant organs or distant lymph nodes.

- 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.

Surgical handling

- **The specimen must be orientated.**
  - The specimen must be capable of orientation if the status of specific surgical margins is critical in determining the need for, or extent of, further surgery.
  - Where there are no anatomical landmarks, specimen orientation may be indicated with marking sutures or other techniques. If a specimen is orientated, the orientation should be indicated on the specimen request form (this may be facilitated by the use of a diagram).
- **The specimen must be handled properly.**
  - Specimens are best received fresh and without delay. This can help the process of tissue banking.
  - If the specimen cannot be handled without delay it should be fixed in an adequate volume of formalin. The usual recommended ratio is 8-10:1formalin: specimen.
- Research blocks should be taken by or supervised by the pathologist in order to avoid compromising the diagnosis.

Example Request Information Sheet



Adrenal Gland Tumours
Histopathology Request Information

Family name

Given name(s)

Date of birth DD – MM – YYYY

Date of request DD – MM – YYYY

Sex
☐ Male
☐ Female
☐ Intersex/indeterminate

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

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

Requesting doctor - name and contact details

Copy to doctor
name and contact details

Operative procedure

Functionality of the adrenal gland
Non-functional ☐ Functional ☐

Type of presentation:

Any previous adrenal surgery

Site of lesion(s)

Laterality of the lesion
Left ☐ Right ☐ Both ☐

Any accompanying specimens
Lymph nodes ☐ Kidney ☐ Other ☐

Relevant clinical information

Note any other relevant information received overleaf

Pre-operative biopsy
Not performed ☐ Performed ☐

Clinical stage

Involvement of adjacent organs
Not involved ☐ Involved ☐

Clinical diagnosis or differential diagnosis

New primary cancer or recurrence
New primary ☐ Regional (local) recurrence ☐
Distant metastases ☐

Principal clinician caring for the patient

Surgeon's name & contact details

Version 1.0 Request Information from Adrenal Gland Tumours Structured Reporting Protocol 1st Edition

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

Appendix 2 Guidelines for formatting of a pathology report

Layout

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

- Grouping like data elements under headings and using 'white space' assists in rapid transfer of information.[28]

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.[28]
- 'Clutter' should be reduced to a minimum.[28] Thus, information that is not part of the protocol (eg billing information, Snomed codes, etc) should not appear on the reports or should be minimized.
- Injudicious use of formatting elements (eg 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

Citizen, Georgina W.
C/O Paradise Close
Nar Nar Goon East, 3181
Tasmania

Female

DOB 1/7/1964
MRN FMC1096785

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

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

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

ADRENAL GLAND TUMOUR STRUCTURED REPORT

Diagnostic Summary

Right adrenalectomy: **Pheochromocytoma;**
30mm in greatest dimension;
Margins clear

Supporting Information

CLINICAL

Operative procedure:	Adrenalectomy
Laterality of the lesion:	Right
Functionality of the adrenal:	Non-functional
Involvement of adjacent organ:	Not involved

MACROSCOPIC

Specimen labelled as:	Adrenal, right
Specimen dimensions:	70mm x 40mm x 5mm
Specimen weight:	68g
Tumour capsule:	Intact
Number of macro. visible tumour(s):	1

Appearance of tumour

Location of tumour:	Medulla
Borders:	Encapsulated
Description:	Well demarcated
Size in greatest dimension:	30mm
Dist. to nearest excision margin:	5mm

Appearance of uninvolved adrenal

Cortex:	Unremarkable
Medulla:	Unremarkable
Cortical nodules:	Absent
Medullary hyperplasia/nodule:	Absent

MICROSCOPIC

Tumour type:	Pheochromocytoma
Cellular pattern:	Zellballen
Cellularity:	Moderate
Central or confluent necrosis:	Absent
Adrenal vein or vena cava invasion:	Absent
Capsular invasion:	Absent
Extension into adipose tissue	Absent
Adjacent organs:	Not involved
Tumour cell spindling:	Present
Cellular monotony:	Absent
Mitotic rate:	2 per 10HPF
Atypical mitotic figures:	Absent
Profound nuclear pleomorphism:	Absent
Nuclear hyperchromasia:	Present
Malignant potential:	PASS = 3 benign
	Japanese score = 1 well differentiated
Non-tumour adrenal gland:	Unremarkable
Margin status:	Clear
Distance to closest margin:	5mm
Lymph node status:	Not received

ANCILLARY STUDIES

Immunohistochemical stains:	Tumour cells positive for chromogrannin and CD56 and substanticular cells highlighted by S-100, Ki-67 index: less than 1%

Reported by Dr Robert Chong Authorised 4 /3/2013

Appendix 4 WHO histological classification of adrenal gland tumours

Adrenal cortical tumours	
Adrenal cortical carcinoma	8370/3
Adrenal cortical adenoma	8370/0
Adrenal medullary tumours	
Malignant phaeochromocytoma	8700/3
Benign phaeochromocytoma	8700/0
Composite phaeochromocytoma/paraganglioma	
Extra-adrenal paraganglioma	**8693/1**
Carotid body	8692/1
Jugulotympanic	8692/1
Vagal	8690/1
Laryngeal	8693/1
Aortico-pulmonary	8691/1
Gangliocytic	8683/0
Cauda equina	8693/1
Orbital Nasopharyngeal	8693/1
Extra-adrenal sympathetic paraganglioma	8693/1
Superior and inferior para-aortic paraganglioma	8693/1
Urinary bladder	8693/1
Intrathoracic and cervical paravertebral	8693/1
Other adrenal tumours	
Adenomatoid tumour	9054/0
Sex-cord stromal tumour	8590/1
Soft tissue and germ cell tumours	
Myelolipoma	8870/0
Teratoma	9080/1
Schwannoma	9560/0
Ganglioneuroma	9490/0

Angiosarcoma	9120/3

Secondary tumours

* Morphology code of the International Classification of Diseases for Oncology (ICD-O) and the Systematized Nomenclature of Medicine (http://snomed.org). Behaviour is coded /0 for benign tumours, /3 for malignant tumours, and /1 for borderline or uncertain behaviour.

From WHO Classification of Tumours Pathology and Genetics. Tumours of Endocrine Organs 2004, Volume 8, Third Edition. IARC.

APPENDIX 5 Histological features for adrenal neoplasms

Weiss Histological Criteria[1718]

1. Nuclear grade III or IV based on criteria of Fuhrman
2. >5 mitotic figures/50 HPF (40x objective), counting 10 random fields in area of greatest number of mitotic figures on 5 slides with greatest number of mitoses
3. Presence of atypical mitotic figures (abnormal distribution of chromosomes or excessive number of mitotic spindles)
4. Clear or vacuolated cells comprising 25% or less of tumor
5. Diffuse architecture (more than 1/3 of tumor forms patternless sheets of cells; trabecular, cord, columnar, alveolar or nesting is not considered to be diffuse
6. Microscopic necrosis
7. Venous invasion (veins must have smooth muscle in wall; tumor cell clusters or sheets forming polypoid projections into vessel lumen or polypoid tumor thrombi covered by endothelial layer)
8. Sinusoidal invasion (sinusoid is endothelial lined vessel in adrenal gland with little supportive tissue, no smooth muscles in wall; consider only sinusoids within tumor)
9. Capsular invasion (nests or cords of tumor extending into or through the capsule with a stromal reaction); either incomplete or complete

Criteria of malignancy

Each is scored 0 when absent and 1 when present. 3 or more of these factors are required for a diagnosis of adrenocortical carcinoma.

Scoring systems for the assessment of adrenal cortical neoplasms by Hough et al[19]

Histological criteria	Score
1. Diffuse growth pattern	0.92
2. Vascular invasion	0.92
3. Tumour cell necrosis (>2 HPF in diameter)	0.69
4. Broad fibrous trabeculae (>1 HPF in diameter)	1.00
5. Capsular invasion	0.37
6. Mitotic index	0.60
7. Pleomorphism (moderate/marked)	0.39

Non-histological criteria

1. Tumour mass (>100g)	0.60
2. Urinary 17-ketosteroids (>10 mg/g creatinine/24hours)	0.50
3. Lack of response to ACTH	0.42
4. Cushing's syndrome with virilism, or no clinical manifestations	0.42
5. Weight loss (>10 pounds/3 months)	2.00

Criteria of malignancy:
Not explicitly stated; but mean histological value for malignant, indeterminate and benign tumors are 2.91, 1.00 and 0.17 respectively.

Scoring system for the assessment of adrenal cortical neoplasms by Van Slooten et al[20]

Histological criteria	Score
Extensive regressive changes (necrosis, haemorrhage, fibrosis, calcification)	5.7
Loss of normal structure	1.6
Nuclear atypia (moderate/marked)	2.1
Nuclear hyperchromasia (moderate/marked)	2.6
Abnormal nucleoli	4.1
Mitotic activity [>2/10 HPF (x400)]	9.0
Vascular or capsular invasion	3.3

Criteria of malignancy:
Score for malignant tumor $\geq$8
Score for benign tumor <8

Lin-Weiss-Bisceglia (LWB) criteria for assessing the malignant potential of oncocytic adrenocortical neoplasms[16]

Major Criteria
Mitotic rate >5 per 50 HPF
Atypical mitotic figures
Venous invasion

Minor criteria
Size >10cm and/or weight >200 g
Necrosis*
Capsular invasion
Sinusoidal invasion

NOTE. Presence of any major criteria = malignant; presence of any minor criteria = borderline malignant potential; absence of all criteria = benign

*****Microscopic necrosis

Thompson PASS scores assigned to the histological features of pheochromocytoma[23]

Microscopic features	**Score**
Capsular invasion	1
Vascular invasion*	1
Extension into the peri-adrenal adipose tissue	2
Presence of large nests of diffuse growth (in >10% of tumor volume)!	2
Central tumor necrosis (in middle of large nests) or confluent necrosis	2
High cellularity	2
Tumor cell spindling even when focal	2
Cellular monotony	2
Increased mitotic figures #	2
Atypical mitotic figures	2
Profound nuclear pleomorphism	1
Nuclear hyperchromasia	1

*Defined by direct extension into the vessel lumen, intravascular attached tumor thrombi, and/or tumor nests covered by endothelium identified in a capsular or extracapsular vessel.
!Defined as 3-4 times the size of a zellballen or the normal size of the medullary paraganglia nests or diffuse growth.
#3/10 high power fields (x400) using an Olympus microscope (U-DO model; Olympus America Inc, Melville,NY

Appendix 6 AJCC TNM classification of adrenal carcinomas

Primary Tumour (T)	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Tumour 5 cm or less in greatest dimension, no extra-adrenal invasion
T2	Tumour greater than 5 cm, no extra-adrenal invasion
T3	Tumour of any size with local invasion, but not invading adjacent organs*
T4	Tumour of any size with invasion of adjacent organs*

*Adjacent organs include kidney, diaphragm, great vessels, pancreas, spleen, and liver.

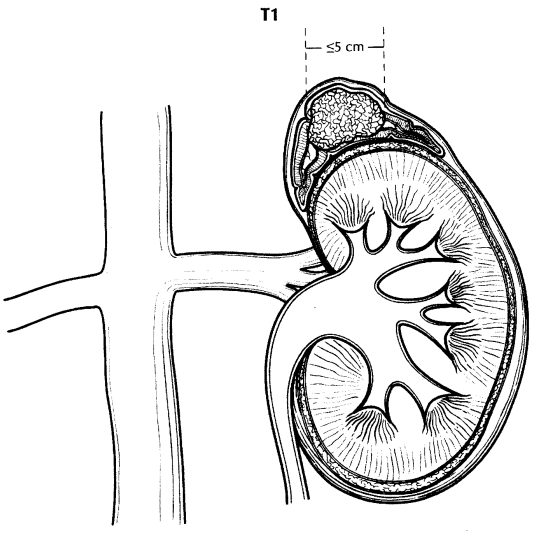
Regional Lymph Nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in regional lymph node(s)

Distant Metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis

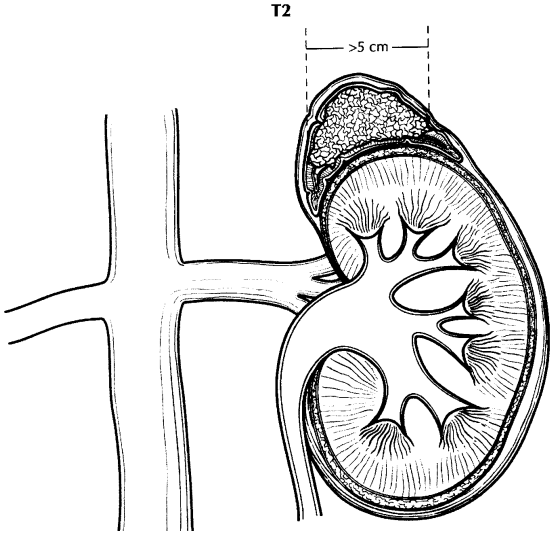
Anatomic Stage/Prognostic groups

Stage	**T**	**N**	**M**
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1	N1	M0
	T2	N1	M0
	T3	N0	M0
Stage IV	T3	N1	M0
	T4	N0	M0
	T4	N1	M0
	Any T	Any N	M1

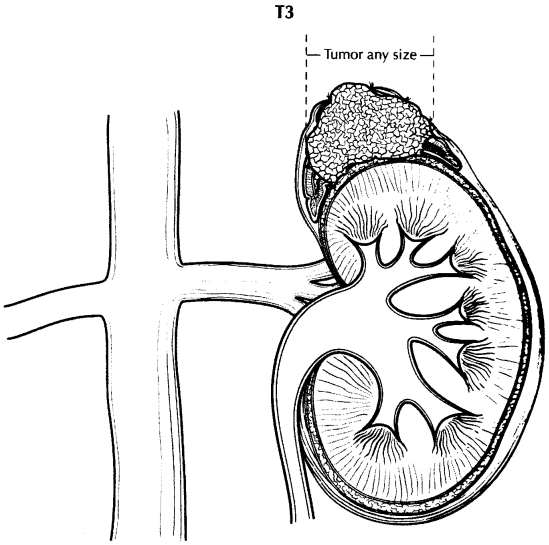
Figure A6: T stage categories



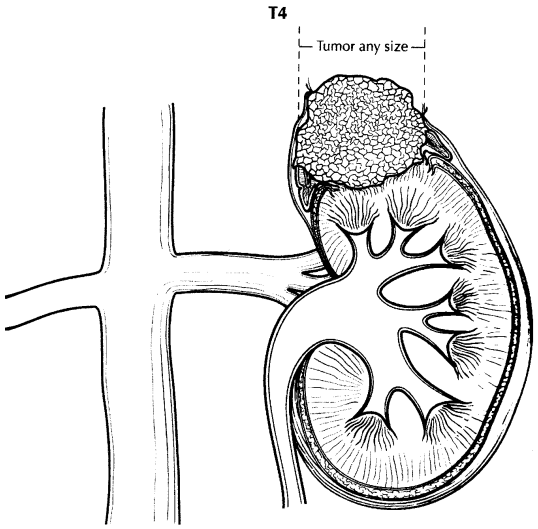
T1: Tumour 5cm or less in greatest dimension, no extra-adrenal invasion



T2: Tumour greater than 5cm, no extra-adrenal invasion



T3: Tumour of any size with local invasion, but not invading adjacent organs



T4: Tumour of any size with invasion of adjacent organs

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