

THYROID CANCER STRUCTURED REPORTING PROTOCOL (1st Edition 2011)

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.*

ISBN: 978-1-74187-673-4

Publications number (SHPN): 110014

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First published: March 2011, 1st Edition (version 1.0)

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Scope

This protocol contains standards and guidelines for the preparation of structured reports for thyroid cancer.

Structured reporting aims to improve the completeness and usability of pathology reports for clinicians, and improve decision support for cancer treatment. The protocol provides the framework for the reporting of any thyroid cancer, 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
CD	Cluster of differentiation
CEA	Carcinoembryonic antigen
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
TTF	Thyroid transcription factor-1
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	<p>Commentary is text, diagrams or photographs that clarify the standards (see below) and guidelines (see below), provide examples and help with interpretation, where necessary (not every standard or guideline has commentary). Commentary is used to:</p> <ul style="list-style-type: none">• define the way an item should be reported, to foster reproducibility• explain why an item is included (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. <p>In this document, commentary is prefixed with 'CS' (for commentary on a standard) or 'CG' (for commentary on a guideline), numbered to be consistent with the relevant standard or guideline, and with sequential alphabetic lettering within each set of commentaries (eg CS1.01a, CG2.05b).</p>
General commentary	<p>General commentary is text that is not associated with a specific standard or guideline. It is used:</p> <ul style="list-style-type: none">• to provide a brief introduction to a chapter, if necessary• for items that are not standards or guidelines but are included in the protocol as items of potential importance, for which there is currently insufficient evidence to recommend their inclusion. (Note: in future reviews of protocols, such items may be reclassified as either standards or guidelines, in line with diagnostic and prognostic advances, following evidentiary review).

Guideline	<p>Guidelines are recommendations; they are not mandatory, as indicated by the use of the word 'should'. Guidelines cover items that are not essential for clinical management, staging or prognosis of a cancer, but are recommended.</p> <p>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.</p> <p>Guidelines are not used for research items.</p> <p>In this document, guidelines are prefixed with 'G' and numbered consecutively within each chapter (eg G1.10).</p>
Macroscopic findings	Measurements, or assessment of a biopsy specimen made by the unaided eye.
Microscopic findings	In this document, the term 'microscopic findings' refers to histological or morphological assessment.
Predictive factor	A <i>predictive factor</i> is a measurement that is associated with response or lack of response to a particular therapy.
Prognostic factor	A <i>prognostic factor</i> is a measurement that is associated with clinical outcome in the absence of therapy or with the application of a standard therapy. It can be thought of as a measure of the natural history of the disease.
Standard	<p>Standards are mandatory, as indicated by the use of the term 'must'. Their use is reserved for core items essential for the clinical management, staging or prognosis of the cancer.</p> <p>The summation of all standards represents the minimum dataset for the cancer.</p> <p>In this document, standards are prefixed with 'S' and numbered consecutively within each chapter (eg S1.02).</p>
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. In the context of structured pathology reporting, synthesis represents the integration and interpretation of information from two or more chapters to derive new information.

Introduction

Thyroid cancer

Thyroid cancer is the most common endocrine cancer in Australia and in other parts of the world. This malignancy is more common in women than in men and occurs primarily in young and middle aged adults, with approximately 122,000 new cases per year worldwide¹.

Thyroid cancers, like benign thyroid diseases, usually present as a thyroid nodule and/or enlargement of thyroid gland. In many instances, it is very difficult to differentiate them from benign thyroid lesions clinically. Thyroid nodules are common clinically (prevalence of approximately 5%) and even more common on ultrasound examination (prevalence of approximately 25%)². Approximately 5% of thyroid nodules are malignant.

Importance of histopathological reporting

Pathological reporting of resection specimens for thyroid cancer provides information both for the clinical management of the affected patient and for the evaluation of the health care systems as a whole. In thyroid cancer, there are many different histological types. Papillary carcinoma is the most common type, accounting for approximately three quarters of thyroid malignancies³. Many subtypes of papillary carcinoma have been described and some are known to have prognostic significance. Also, follicular lesions including follicular carcinoma, minimally invasive follicular carcinoma, follicular variant of papillary carcinoma, follicular adenoma and adenomatous nodule often be difficult to differentiate from each others. Some patients with thyroid cancer can progress to a more aggressive metastatic form of thyroid cancer with a high mortality⁴. Therefore, recognition of pathological parameters in thyroid cancer is very important for the management of these 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 have been recommended both in North America and the United Kingdom⁵⁻⁹.

The College of American Pathologists and the Royal College of Pathologists (UK) have recently published useful protocols for the reporting of cancer⁹⁻¹⁰. A protocol endorsed by the Royal College of Pathologists of Australasia and other Australasian organisations involved in the management of thyroid cancer 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 thyroid cancer.

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*¹¹
- *The Pathology Request-Test-Report Cycle — Guidelines for Requesters and Pathology Provider*¹²
- *AJCC Cancer Staging Manual, 7th edition*¹³
- *Pathology and Genetics of Tumours of Endocrine Organs. WHO Classification of Tumours, Volume 8, 2004*¹⁴

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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Acknowledgements

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

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

British Association of Head & Neck Oncologists (BAHNO)

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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)
Medical Software Industry Association (MSIA)
National Breast and Ovarian Cancer Centre (NBOCC)
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)
Representatives from laboratories specialising in anatomical pathology across Australia
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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Meagan Judge, Royal College of Pathologists of Australasia.

Development process

This protocol has been developed following the seven-step process set out in *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols*¹¹.

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

1 Clinical information and surgical handling

This chapter relates to information that should be collected before the pathology test, and procedures that are required before handover of specimens to the laboratory.

The standards and guidelines below specify the particular information and specimens required for thyroid cancer. Some of this information can be collected on generic pathology request forms; any additional information required specifically for the reporting of thyroid cancer may be recorded on a separate data sheet. Appendix 1 provides a standardised data sheet that may be useful in obtaining all relevant information.

S1.01 Adequate demographic and request information must be provided with the specimen by the requesting clinician.

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.¹² This document specifies the minimum information to be provided by the requesting clinician for any pathology test. Items relevant to cancer reporting protocols include:

- patient name
- date of birth
- sex
- identification and contact details of requesting doctor
- date of request

Additional information specified in the RCPA *The Pathology Request-Test-Report Cycle — Guidelines for Requesters and Pathology Providers* such as the specimen type and clinical information relevant to the investigation is catered for in the following standards and guidelines.

CS1.01b The patient's ethnicity must be recorded, if known.

G1.01 The patient's health identifiers should be recorded where provided.

CG1.01a The patient's health identifiers may include the patient's Medical Record Number as well as a national health number such as a NHI or the Individual Healthcare Identifier (IHI).

S1.02 The pathology accession number of the specimen must be recorded.

S1.03 The principal clinician and/or management unit involved in the patient's care and responsible for investigating the patient must be identified.

CS1.03a The requesting clinician (identified under S1.01) may be the doctor who performs the surgery or biopsy, and may not be the person with overall responsibility for investigating and managing the patient. The clinician is

likely to be either an endocrinologist or in some settings a nuclear medicine physician. Identification of the principal clinician and/or managing unit is essential, to ensure that clinical information is communicated effectively.

S1.04 The operating surgeon's identity and contact details must be recorded.

S1.05 The type of operation performed must be recorded.

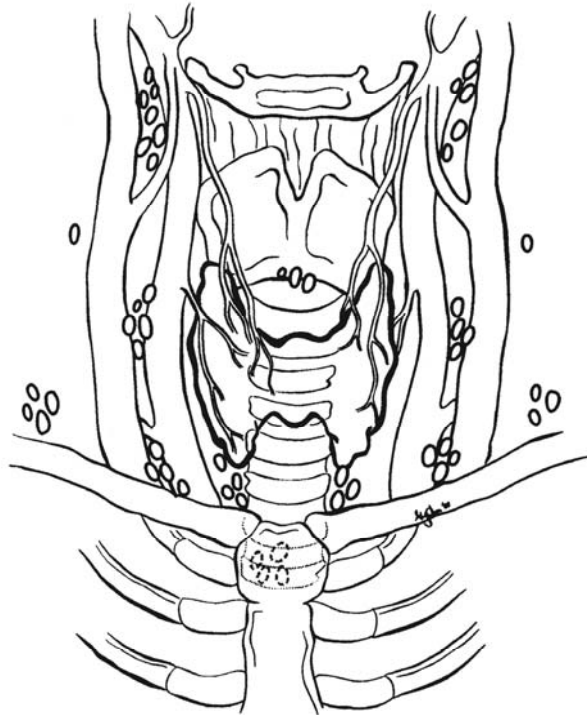
CS1.05a The requesting clinician should indicate the thyroid specimen type as:

- total thyroidectomy +/- neck dissection (including side and levels),
- near-total thyroidectomy+/-, neck dissection (including side and levels),
- subtotal thyroidectomy+/-, neck dissection (including side and levels),
- lobectomy with isthmusectomy (hemi-thyroidectomy) +/-, neck dissection (including side and levels),
- lobectomy+/-, neck dissection (including side and levels),
- partial lobectomy,
- completion thyroidectomy.

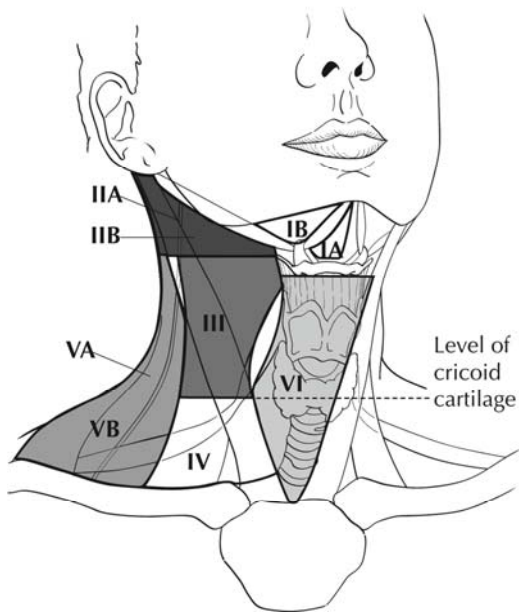
CS1.05b Additional surgical procedures should be mentioned: eg neck dissection. For neck dissections, clinicians should indicate whether it is central or lateral compartments in addition to side and levels. Clinicians often use only the term "central compartment" for levels 6 and 7 lymph nodes. (See figure CS1.05b)

Figure CS1.05b

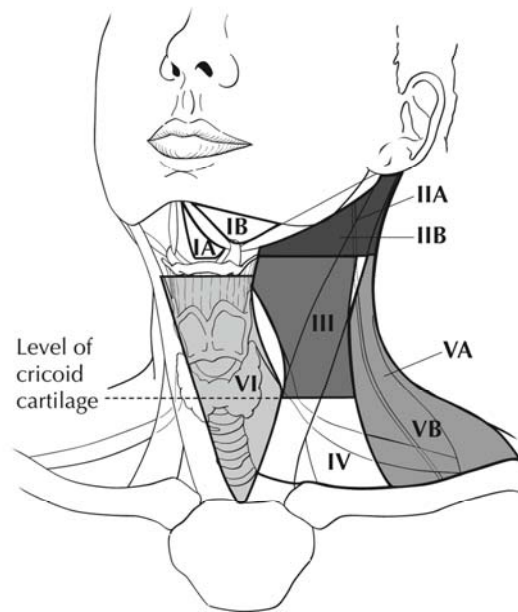
1.



2.



3.



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S1.06 Any previous operation on the thyroid must be recorded.

CS1.06a Previous surgery of the thyroid alters the shape and hence orientation of the thyroid.

S1.07 The anatomical site of the lesion(s) must be recorded.

CS1.07a Site is an important identifier especially when multiple lesions are present.

CS1.07b Sufficient information is required to localise the lesion(s) for subsequent therapy. A diagram or photograph can facilitate this.

CS1.07c Specimens other than thyroid should be identified (eg parathyroid gland, thymus, lymph nodes, neck dissection).

S1.08 The laterality of the lesion(s) must be recorded.

CS1.08a Laterality information is needed for identification purposes.

CS1.08b Left, right, isthmus should be recorded.

G1.02 Any clinical information relevant to the thyroid disease should be recorded.

CG1.02a Clinical or biochemical evidence of hyperthyroidism or hypothyroidism should be noted.

CG1.02b Previous medical treatments like anti-thyroid drug or radioactive iodine should be noted.

CG1.02c Previous exposure to the neck to radiotherapy (eg for treatment of Hodgkin lymphoma) should be noted.

CG1.02d The indication for performing the surgery should be recorded as many thyroid cancers are found incidentally in thyroid specimens removed for purpose other than cancer.

CG1.02e Family history of thyroid cancers or features of other endocrine tumours or syndromes should be recorded. It is worth noting that gastrointestinal manifestations of an endocrine syndrome may present before identification of an endocrine tumour.

G1.03 If a pre-operative fine needle aspiration has been performed, this should be recorded.

CG1.03a Fine needle aspiration of the thyroid may alter the microscopic appearance of the tumour in the thyroid, including tumour infarction. The results of the procedure may sometimes make the judgement of the invasiveness of the thyroid tumour difficult as it can cause distortion of

the tissue, including the thyroid capsule.

- CG1.03b Correlations of histological and cytological findings are important for quality assurance purposes.
- G1.04 The results of clinical staging with ultrasound and fine needle aspiration should be recorded.
 - CG1.04a This is important for pathologic staging of cancer.
- G1.05 The involvement of adjacent organs or any distant metastases should be recorded.
 - CG1.05a This is important for staging of cancer.
- G1.06 The clinical diagnosis or differential diagnosis should be recorded.
 - CG1.06a Providing the provisional clinical diagnosis or differential diagnosis improves clinicopathological correlation and improves diagnostic accuracy.

Surgical handling

S1.09 The specimen must be orientated.

- CS1.09a 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.
- CS1.09b 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).

S1.10 The specimen must be handled properly.

- CS1.10a Specimens are best received fresh and without delay. This can help the process of tissue banking.
 - CS1.10b If the specimen cannot be handled without delay it should be fixed in an adequate volume of formalin. The usual recommended ratio is 8-10:1 formalin: specimen.
- G1.07 Research blocks should be taken by the pathologist in order to avoid compromising the diagnosis.

2 Specimen handling and macroscopic findings

This chapter relates to the procedures when the specimen is received in the laboratory.

Tissue banking

- G2.01 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

- G2.02 Requests for intra-operative frozen section of the thyroid should be discouraged as it will not help in providing additional information in most cases and may compromise the chance of making a proper diagnosis in paraffin section.
- CG2.02a 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.
- CG2.02b Care should be taken to prevent the spread of marking ink and distortions which may compromise subsequent paraffin section.
- CG2.02c Intra-operative frozen section will not help in the differential diagnosis of follicular neoplasm or in other instances in which the diagnosis is difficult to make by fine needle aspiration.
- CG2.02d Intra-operative frozen section may be beneficial in some instances eg identifying lymph node involvement by thyroid cancer.

Specimen handling

S2.01 The specimen must be orientated.

- CS2.01a Orientate the thyroid gland by identifying the inferiorly-placed isthmus, and the concavity of the posterior aspect of the lateral lobes.
- CS2.01b Some thyroid glands have an upwardly pointed pyramidal lobe, arising from the isthmus.
- CS2.01c Inspect the capsule of the thyroid to see whether it is intact or not.

S2.02 The external surface of the thyroid must be inked as the resection margin.

- CS2.02a It is preferable to use dyes of different colours for the different resection surfaces.

S2.03 The specimen must be serially sectioned.

- CS2.03a Serially section each thyroid lobe transversely, along the short axis, and maintain the proper orientation of the slices.
- CS2.03b The slices preferably should still be attached to one another, such that orientation is still preserved if re-sampling of the specimen is required.

G2.03 A diagram or photograph can facilitate the specimen orientation and block labelling.

S2.04 If the resection of thyroid is partial, the surgical resection margin should be blocked.

S2.05 In the presence of macroscopically noted thyroid cancer, blocks should be taken from the uninvolved thyroid, from the ipsilateral and contralateral lobe (when present) and perithyroid soft tissue.

S2.06 Submit sections to demonstrate any identifiable lymph nodes and parathyroid glands, if present.

S2.07 All lymph nodes and other tissue (parathyroid, thymus, etc) submitted by the surgeon(s) should be embedded.

- CS2.07a The neck dissection specimen should be processed as recommended by the head and neck reporting protocol.

S2.08 Block selection will differ for the different types of thyroid lesions.

- CS2.08a The blocks to be taken will vary with the clinical information, macroscopic appearance and cancer type.

CS2.08b When no focal lesion is identified (eg Graves' disease, Hashimoto's thyroiditis, completion thyroidectomy), all the white/cream or firm foci must be sampled because they may represent cancer.

If there is no suspicious lesion, it is recommended that random blocks from each lobe and the isthmus be taken.

CS2.08c For a multi-nodular goitre, all the white/cream or firm foci must be sampled because they may represent cancer.

If there is no suspicious lesion, it is recommended that random blocks, including nodules and adjacent thyroid tissue, be taken. Random blocks should be taken from each lobe and the isthmus.

CS2.08d In the setting of follicular neoplasm (dominant encapsulated nodule) there is no universal accepted sampling method. In practice, there are certain principles to be followed:

- The specimen should be widely sampled at the interface between the nodule, the capsule and the adjacent thyroid tissue to detect invasion.
- The specimen should be sampled more adequately where the lesion has worrisome features such as a thick capsule, fleshy cut surface, pale or very solid appearance.
- If the lesion is small i.e. $\leq 30\text{mm}$ in diameter), embed the whole nodule and the adjacent thyroid tissue.
- If the lesion is large, sample widely (at least 1 block per cm of maximum tumour dimension is recommended) and take additional blocks in the suspicious region.

CS2.08e In the setting of invasive thyroid cancer (papillary thyroid carcinoma, medullary thyroid carcinoma, undifferentiated carcinoma, etc):

(a) If the cancer is small (i.e. $\leq 20\text{mm}$), block the whole tumour and the adjacent thyroid tissue.

(b) If the cancer is large, it should be sampled widely enough (at least 1 block per cm of maximum tumour dimension is recommended) to permit a diagnosis and assess whether the tumour is of uniform type.

Blocks should be taken where the cancer comes closest to the soft tissue resection margin.

In the case of medullary carcinoma, some may recommend the whole specimen be blocked.

Macroscopic findings

S2.09 All measurements are in SI units, unless explicitly stated.

G2.04 The specimen should be weighed and findings recorded.

S2.10 The specimen dimensions must be recorded.

CS2.10a A measurement must be done for each lobe of the thyroid and isthmus (if present).

G2.05 Whether the capsule of the thyroid is intact or not should be recorded.

S2.11 The macroscopic description of any lesion(s) in the specimen must be recorded.

CS2.11a Where there are multiple lesions, the total number of lesions must be recorded and each lesion should be identified and described.

CS2.11b For each lesion, the location, appearance, the borders (encapsulated or infiltrative), size (greatest dimension), and distance from the nearest excision margin must be recorded.

CS2.11c Thyroid cancer can be an incidental finding in thyroid glands surgically removed for reasons other than thyroid cancer.

G2.06 The appearance of the thyroid other than the lesion(s) detected should be documented.

G2.07 The presence or absence of parathyroid(s) and lymph nodes(s) should be recorded.

G2.08 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.

CG2.08a 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.

CG2.08b 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 tumour type must be based on the WHO histological classification of tumours of endocrine organs¹⁴.

The commoner types are papillary carcinoma, follicular carcinoma, medullary carcinoma, undifferentiated carcinoma and poorly-differentiated carcinoma. It is important to note that other types of benign and malignant tumours can occur in the thyroid gland.

- CS3.01b For follicular carcinoma, it is important to define the carcinoma on the basis of the extent of capsular and/or vascular invasion.

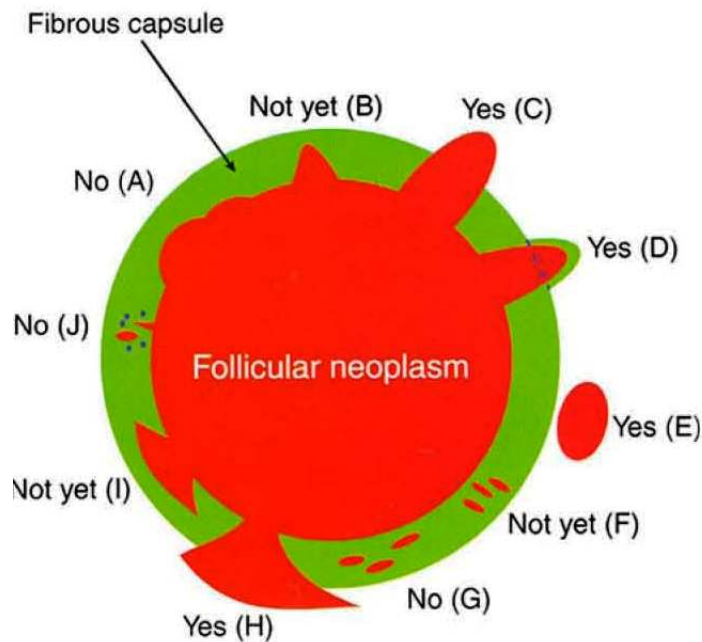
Follicular carcinoma is divided into widely invasive and minimally invasive type.

Widely invasive follicular carcinoma shows infiltration of thyroid parenchyma outside the capsule of the follicular lesion.

Minimally invasive follicular carcinoma shows significant focal invasion of the tumour capsule. It is important to indicate whether there is only capsular invasion or whether the tumour is angioinvasive. The number of foci of capsular or vascular invasion should be noted. (See figures CS3.01b(i), (ii) and (iii)).

Invasion must be differentiated from entrapments of follicles in the capsule and the pseudo-invasive changes following fine needle aspiration.

Figure CS3.01b (i) Capsular invasion (CI)



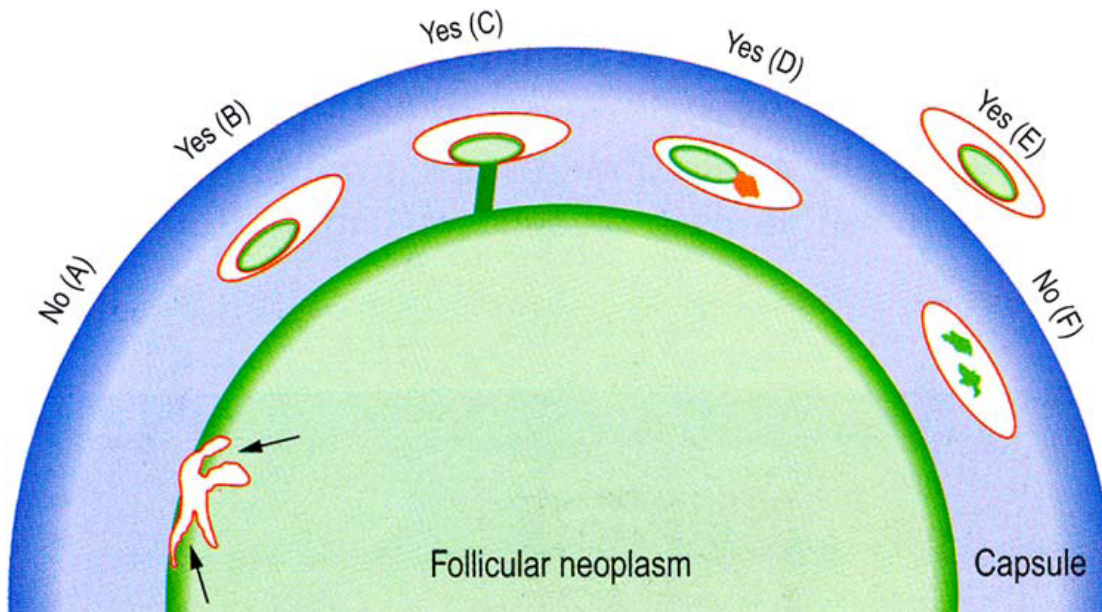
Schematic drawing for the interpretation of the presence or absence of CI. The diagram depicts a follicular neoplasm (orange) surrounded by a fibrous capsule (green).

- a) bosselation on the inner aspect of the capsule does not represent CI;
- b) sharp tumour bud invades into but not through the capsule suggesting invasion requiring deeper sections to exclude;
- c) tumour totally transgresses the capsule invading beyond the outer contour of the capsule qualifying as CI;
- d) tumour clothed by thin (probably new) fibrous capsule but already extending beyond an imaginary (dotted) line drawn through the outer contour of the capsule qualifying as CI;
- e) satellite tumour nodule with similar features (architecture, cytomorphology) to the main tumour lying outside the capsule qualifying as CI;
- f) Follicles aligned perpendicular to the capsule suggesting invasion requiring deeper sections to exclude
- g) follicles aligned parallel to the capsule do not represent CI;
- h) mushroom-shaped tumour with total transgression of the capsule qualifies as CI;
- i) mushroom-shaped tumour within but not through the capsule suggests invasion requiring deeper sections to exclude;
- j) neoplastic follicles in the fibrous capsule with a degenerated appearance accompanied by lymphocytes and siderophages does not represent CI but rather capsular rupture related to prior fine needle aspiration.

Modified from Chan JKC; Chapter 18 Tumors of the thyroid and parathyroid glands. Diagnostic Histopathology of Tumors. 3rd ed. Fletcher CDM, editor. London, England: Churchill Livingstone; 2007. p. 997–1078. Reproduced with permission.

Figure CS3.01b (ii)

Vascular invasion (VI): Schematic drawing for the interpretation of the presence or absence of VI.



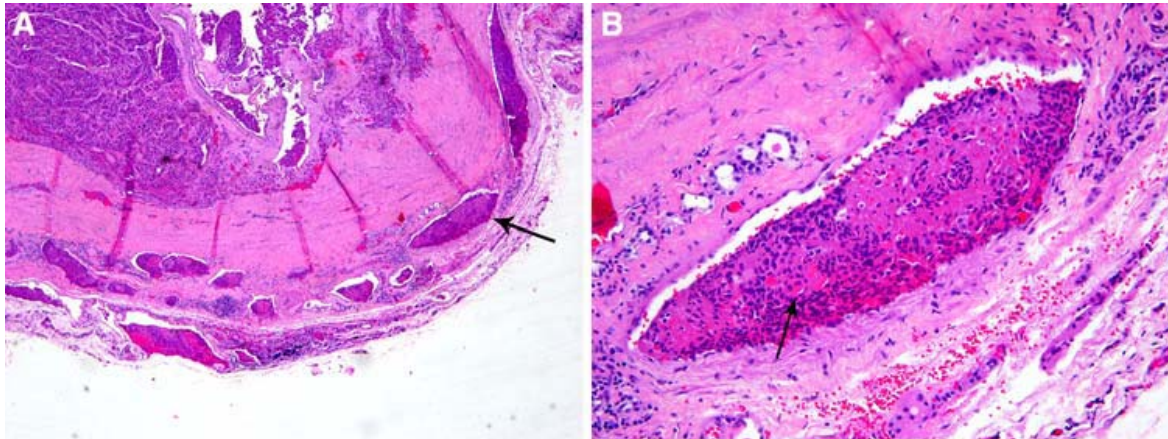
The diagram depicts a follicular neoplasm (green) surrounded by a fibrous capsule (blue).

- Bulging of tumour into vessels within the tumour proper does not constitute VI.
- Tumour thrombus covered by endothelial cells in intracapsular vessel qualifies as VI.
- Tumour thrombus in intracapsular vessel considered as VI since it is attached to the vessel wall.
- Although not endothelialized, this tumour thrombus qualifies for VI because it is accompanied by a fibrin thrombus.
- Endothelialized tumour thrombus in vessel outside the tumour capsule represents VI.
- Artefactual dislodgement of tumour manifesting as irregular tumour fragments into vascular lumen unaccompanied by endothelial covering or fibrin thrombus.

Modified from Chan JKC; Chapter 18 Tumors of the thyroid and parathyroid glands. Diagnostic Histopathology of Tumors. 3rd ed. Fletcher CDM, editor. London, England: Churchill Livingstone; 2007. p. 997–1078. Reproduced with permission.

Figure CS3.01b (iii)

Encapsulated follicular carcinoma



Encapsulated follicular carcinoma (FC), oncocytic variant with multiple foci of microscopic vascular invasion (VI) and no gross invasion.

In some classification schemes, these tumours are labelled as minimally invasive while others will use terms such as encapsulated angioinvasive FC or encapsulated FC with extensive angioinvasion to stress their potential for aggressive behaviour. This 50 year old patient developed bone metastases 10 years after thyroidectomy.

- A. Low power view showing multiple microscopic foci of VI in tumour capsule (arrow) and immediately outside the capsule.
- B. High power view of a tumour thrombus (arrow) attached to vessel wall and covered by endothelial cells.

Reproduced with kind permission from Springer Science+Business Media: Ghossein R. Update to the College of American Pathologists Reporting on Thyroid Carcinomas Head and Neck Pathol (2009) 3:86–93. Figure 3, pg 89

CS3.01c There is no doubt that minimally invasive follicular carcinoma with capsular invasion alone behaves like a benign tumour. The presence of vascular invasion should be noted but no definite prognostic implications have been demonstrated.¹⁵

CS3.01d For poorly-differentiated carcinoma, the pattern should be dominant for the carcinoma to be placed in this category.

CS3.01e For papillary, follicular or poorly-differentiated thyroid carcinomas, the presence of even a minor undifferentiated component should be noted as having a component of undifferentiated carcinoma confer a poorer prognosis.⁴

G3.01 Variants of tumour types should be recorded.

CG3.01a For papillary carcinoma, there are 15 histological variants documented by WHO¹⁴. Some variants have prognostic significance, while others do not.

Papillary microcarcinoma ($\leq 10\text{mm}$ in diameter) discovered incidentally is not thought to have a significant risk of recurrence or metastasis¹⁶. On the other hand, tall cell and columnar cell variants may show more aggressive clinical behaviour than conventional papillary thyroid carcinoma.

Some variants, in particular encapsulated follicular variant, oncocytic variant, etc may be difficult to differentiate from other tumours. It is recommended that expert opinion be sought if there are uncertainties.

CG3.01b For follicular carcinoma, the carcinoma is considered oncocytic if at least 75% of the carcinoma is composed of oncocytic cells¹⁴.

CG3.01c For poorly-differentiated and undifferentiated carcinomas, minor components of papillary or follicular carcinoma should be mentioned.

CG3.01d In familial medullary carcinoma, the tumour is preceded by expansion of the C cell population, termed *familial C cell hyperplasia* that is thought to be neoplastic¹⁷. The C cells are normally found in the upper and middle thirds of the lobes, so immunostaining of sections from these areas may be helpful in suggesting familial disease, although the thresholds for diagnosis are a matter of debate¹⁸⁻¹⁹. From a practical point of view, the presence of multiple groups or nodules of C cells in sections that do not contain the main tumour is suggestive of C cell hyperplasia. It should be noted, however, that *secondary C cell hyperplasia* may occur in a number of other circumstances such as hyperparathyroidism²⁰, Hashimoto's thyroiditis¹⁹ and around tumours of follicular origin²¹. It is now less important for the pathologist to identify C cell hyperplasia, as patients with medullary carcinoma in appropriate clinical settings should have genetic testing for the common mutations in the RET protooncogene²².

S3.02 The presence or absence of multifocal lesions must be recorded.

CS3.02a Multifocal lesions are not uncommon in patients with papillary carcinoma and medullary carcinoma.

S3.03 The diameter of the tumour must be recorded.

CS3.03a For multifocal tumours, the diameter of the largest tumour must be recorded.

S3.04 The extension of the tumour into adjacent tissues or organs must be recorded.

- CS3.04a The pathological staging (T stage) depends on the size of the cancer and the extent of involvement of thyroid gland and adjacent tissues.
- The extension into peri-thyroid soft tissue and the sternohyoid muscles is recorded as T3 regardless of size of the cancer.
- Cancer extending beyond the thyroid capsule into subcutaneous soft tissue, larynx, trachea, oesophagus or recurrent laryngeal nerve, etc should be recorded as T4.
- S3.05 The presence or absence of cancer at the resection margins must be recorded.**
- CS3.05a The location of the involved margin(s) must be specified.
- S3.06 The presence, location and status of lymph nodes must be recorded.**
- CS3.06a If regional lymph nodes were identified the location must be specified.
- CS3.06b The total number of lymph nodes sampled must be stated.
- CS3.06c The number of lymph nodes containing metastatic tumour must be stated.
- CS3.06d The presence and sites of lymph node metastases of thyroid carcinoma affect the pathological staging (N stage) of thyroid cancer.
- S3.07 The presence or absence of parathyroid tissue must be recorded.**
- CS3.07a The presence of parathyroid tissue may provide correlation with the clinical data on calcium status.
- G3.02 The presence or absence of coexistent pathological abnormalities in the thyroid gland should be recorded.
- CG3.02a Hashimoto's thyroiditis, lymphocytic thyroiditis, diffuse parenchymatous goitre and nodular hyperplasia, etc are often additional findings and may help elucidate the aetiological relationship or the differential diagnosis.
- G3.03 Any additional relevant microscopic comments should be recorded.

4 Ancillary studies findings

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

S4.01 Immunohistochemistry must be done for some cancers in the thyroid gland. Where performed, the findings must be recorded.

- CS4.01a In cases in which the diagnosis is suspected to be medullary carcinoma, immunostaining for calcitonin should be done to confirm the diagnosis. The immunostain is also helpful to identify nodular or C-cell hyperplasia in the settings of multiple endocrine neoplasia (MEN) and familial medullary thyroid carcinoma. Neuroendocrine markers and /or carcinoembryonic antigen (CEA) should be done in less well-differentiated medullary carcinomas in which calcitonin immunoreactivity is lost.
- CS4.01b In cases in which the diagnosis is suspected to be lymphoma, the tumours must be investigated in the pathway as adopted for lymphoma.
- CS4.01c Follicular neoplasm with vascular invasion has a higher risk of metastasis and increases with the extent of vascular involvement. CD31 or other vascular markers may be helpful in delineating the vascular invasion. However, the findings by such endothelial markers in this setting should be interpreted with care.
- CS4.01d Epithelial markers, thyroglobulin and thyroid transcription factor-1 (TTF-1) may define that a tumour is of thyroid origin in the right clinical settings, for instance, for metastatic thyroid carcinoma. TTF-1 is more sensitive than thyroglobulin but TTF-1 can be positive in other cancers such as lung adenocarcinoma and small cell carcinoma of any primary site. Undifferentiated thyroid carcinoma is often negative for both thyroglobulin and TTF-1, but PAX-8 is often positive.
- CS4.01e Uncommon tumours (eg angiosarcoma, carcinoma showing thymus-like differentiation, paraganglioma, etc) can occur in the thyroid gland. Immunohistochemistry can help in the diagnosis or in confirming the diagnosis.
- CS4.01f It is not possible to differentiate benign and malignant thyroid tumours by using immunohistochemistry. Although cytokeratin 19, other high molecular weight cytokeratins and some other markers have been demonstrated to have stronger positivity in thyroid carcinomas than benign thyroid lesions, there are many exceptions and the interpretation has to be taken in the context of morphology of the lesion.

G4.01 Any molecular investigation performed should have the results incorporated into the pathology report.

CG4.01a Molecular investigation can be useful in the management of patients with medullary thyroid carcinoma in the context of appropriate advice from a genetic counsellor or from a clinician with experience in following through on the implications of positive or negative tests.

Identification of germline *RET* mutation carriers allows prophylactic surgery as well as biochemical follow-up for metastatic and recurrent medullary thyroid carcinoma, and for development of MEN 2-associated pheochromocytoma and parathyroid disease.

Somatic *RET* mutations can be performed for the prognosis of patients with medullary thyroid carcinoma. Somatic *RET* mutations can be detected in tumour tissue of 23–69% of sporadic medullary thyroid carcinoma patients. It has been demonstrated that the somatic *RET* mutation (M918T) correlates with stage of the disease, a higher probability of persistence of the disease after total thyroidectomy, increased chance of recurrence and metastatic potential, and a reduced survival.

CG4.01b 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.

CG4.01c 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 Manual¹³. (See Appendices 5 and 6)

- CS5.01a In thyroid cancer, the staging depends also on the age of the patients and the type of cancer. At the moment, staging information is only available for papillary carcinoma, follicular carcinoma, medullary carcinoma and undifferentiated carcinoma.
- CS5.01b For papillary and follicular carcinomas of thyroid, young patients (age under 45 years) have a different cancer staging.
- CS5.01c For medullary carcinoma, the age of the patient does not affect the cancer staging.
- CS5.01d Undifferentiated carcinoma is considered to be stage IV but being subdivided to stage IVA, IVB and IVC based on the criteria of TNM.

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. Operation type (S1.05)
- b. Tumour site and laterality (S1.07 and S1.08)
- c. Tumour type (S3.01)
- d. Tumour stage (S5.01)
- e. Completeness of excision (S3.05).

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

overarching case comment.

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

- 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.
- 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.

Clinical information and surgical handling

S1.01 Patient name _____

Date of birth _____

Sex _____

Identification and contact details of requesting doctor _____

Date of request _____

Ethnicity:

Aboriginal or Torres Strait Islander _____

Other ethnicity _____

Unknown _____

G1.01 Patient identifiers (eg MRN, IHI, NHI) _____

S1.02 Pathology accession number _____

S1.03 Principal clinician involved in the patient's care _____

S1.04 Operating surgeon _____

Contact details _____

S1.05 Type of operation:

total thyroidectomy _____

near-total thyroidectomy _____

subtotal thyroidectomy _____

lobectomy with isthmusectomy (hemi-thyroidectomy) _____

Isthmus _____

Not stated _____

G1.02 Any relevant clinical information:

Thyroid function status _____

Relevant medical treatments (eg anti-thyroid drug, radioactive iodine) _____

Previous exposure of neck to radiotherapy _____

Indication for performing surgery _____

Family history (eg thyroid cancer, endocrine tumours or syndromes) _____

Other (specify) _____

G1.03 Pre-operative fine needle aspiration:

No _____

Yes _____

If yes, specify details _____

G1.04 Clinical staging

G1.05 Involvement of adjacent organs or distant metastases:

No _____

Yes _____

If yes, specify details _____

G1.06 Clinical or differential diagnosis _____

Macroscopic findings

G2.04 Weight of specimen _____ g

S2.10 Specimen dimensions:

Right lobe _____ x _____ x _____ mm

Left lobe _____ x _____ x _____ mm

Isthmus _____ x _____ x _____ mm

G2.05 Thyroid capsule:

Intact _____

Not intact _____

S2.11 Macroscopic description of lesion(s):

Multiple lesions?

No _____

Yes _____

If yes, indicate number and complete the following items for each tumour as appropriate

Lesion 1

Location _____

Appearance _____

Borders: encapsulated _____

infiltrative _____

Size in greatest dimension _____ mm

Distance from nearest excision margin _____ mm

Lesion 2

Location _____

Appearance _____

Borders: **encapsulated** _____

infiltrative _____

Size in greatest dimension _____ mm

Distance from nearest excision margin _____ mm

Lesion 3

Location _____

Appearance _____

Borders: **encapsulated** _____

infiltrative _____

Size in greatest dimension _____ mm

Distance from nearest excision margin _____ mm

Lesion 4

Location _____

Appearance _____

Borders: **encapsulated** _____

infiltrative _____

Size in greatest dimension _____ mm

Distance from nearest excision margin _____ mm

G2.06 Appearance of other portion of thyroid _____

G2.07 Parathyroid

absent _____

present _____

Lymph nodes

absent _____

present _____

If yes, indicate type _____

G2.08 Other macroscopic comment

Microscopic findings

S3.01 Tumour type:

Papillary carcinoma _____

Follicular carcinoma _____

Medullary carcinoma _____

Others (please state) _____

Level of invasion (for follicular carcinoma)

Minimally invasive _____

Widely invasive _____

If minimally invasive, record:

Vascular invasion

present _____

absent _____

Number of foci of capsular and/or vascular invasion (if known) _____

G3.01 Tumour variant

S3.02 Multifocal lesions

absent _____

present _____

S3.03 Diameter of tumour (for _____ mm
multifocal tumours measure
largest)

**S3.04 Extension into adjacent
tissues/organs**

absent _____
present _____

**If present,
into which
tissue**

Sternohyoid _____
muscle
Perithyroid soft _____
tissue
Subcutaneous _____
soft tissues
Larynx _____
Trachea _____
Oesophagus _____
Recurrent _____
laryngeal nerve
Other (specify) _____

S3.05 Cancer at resection margin

absent _____
present _____

If absent, clearance from _____ mm
resection margin
If present, which _____
margin(s)

S3.06 Lymph node status

Location 1 _____

Total number of _____
nodes resected

Number of positive nodes _____

Location 2 _____

Total number of nodes resected _____

Number of positive nodes _____

S3.07 Parathyroid tissue

absent _____

present _____

If present, state where _____

G3.02 Co-existing pathology:

Hashimoto's thyroiditis _____

Lymphocytic thyroiditis _____

Diffuse parenchymatous goitre _____

Nodular hyperplasia _____

Other (specify) _____

G3.03 Other microscopic comment

Ancillary test findings

S4.01 Immunohistochemical stains:

Antibodies:

Positive antibodies _____

Negative antibodies _____

Equivocal antibodies _____

Interpretation _____

**Clinical
significance** _____

G4.01 Molecular investigation

performing laboratory _____

result _____

conclusion _____

Person responsible for
reporting _____

Synthesis and overview

S5.01 Tumour stage (AJCC)

T _____

N _____

M _____

Stage Grouping _____

S5.02 Year of publication and
edition of cancer staging
system _____

G5.01 Diagnostic summary _____

S5.03 Other relevant information
and comments _____

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 form for thyroid cancer

S1.01 Patient name _____

Date of birth _____

Sex _____

Identification and contact details of requesting doctor _____

Date of request _____

Ethnicity:

Aboriginal or Torres Strait Islander _____

Other ethnicity _____

Unknown _____

G1.01 Patient identifiers (eg MRN, IHI, NHI) _____

S1.03 Principal clinician involved in the patient's care _____

S1.04 Operating surgeon: _____

Contact details _____

S1.05 Type of operation:

total thyroidectomy _____

near-total thyroidectomy _____

subtotal thyroidectomy _____

lobectomy with isthmusectomy (hemi-thyroidectomy) _____

lobectomy _____

partial lobectomy _____
completion thyroidectomy _____

Neck dissection:

No _____
Yes _____

If yes, complete the following details:

Side Right _____
 Left _____
Compartment Central _____
 Lateral _____
Levels _____

Additional procedures

S1.06 Details of any previous thyroid operation

S1.07 Anatomical site(s) (insert diagram or photograph if possible)

a. _____
b. _____
c. _____

Other specimens :

No _____
Yes _____

If yes, specify details

S1.08 Laterality of the lesion

Left _____
Right _____
Isthmus _____

G1.02 Any relevant clinical information:

Thyroid function status _____

Relevant medical treatments (eg anti-thyroid drug, radioactive iodine) _____

Previous exposure of neck to radiotherapy _____

Indication for performing surgery _____

Family history (eg thyroid cancer, endocrine tumours or syndromes) _____

Other (specify) _____

G1.03 Pre-operative fine needle aspiration:
No _____
Yes _____
If yes, specify details _____

G1.04 Clinical staging _____

G1.05 Involvement of adjacent organs or distant metastases:
No _____
Yes _____
If yes, specify details _____

G1.06 Clinical or differential diagnosis _____

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.²³

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.²³
- 'Clutter' should be reduced to a minimum.²³ 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 Wreck Bay Resort Nar Nar Goon East, 3181 Female DOB 1/7/1951 MRN FMC1096785	Lab Ref: 10/P28460 Referred: 30/8/2010
Copy to: Dr N.G.Chapman Rainforest Cancer Centre. 46 Smith Road, Woop Woop, 3478	Referred by: Dr V. Smith Suite 3, AJC Medical Centre, Bunyip Crescent Nar Nar Goon West, 3182

THYROID CANCER STRUCTURED REPORT

Page 1 of 2

Diagnostic Summary

Total thyroidectomy:

Right upper lobe, Papillary carcinoma, Stage pT1a, pNX (AJCC 7th edition, 2010), Resection margins negative

Comment: Nil

Supporting Information

CLINICAL

Type of operation:	Total thyroidectomy
Previous thyroid operation:	Details not provided
Anatomical site/Laterality:	Right upper lobe
Other specimens received:	No
Clinical information:	Suspicious of papillary carcinoma Confined to thyroid No enlarged lymph node
Pre-operative fine needle aspiration:	Yes - St Bart's Hospital, 21 st July 2010

MACROSCOPIC

Weight of specimen:	40g
Specimen dimensions	
Right lobe:	40 x 20 x 15mm
Left lobe:	45 x 30 x 15mm
Isthmus:	10 x 3 x 3mm
Thyroid capsule:	intact
Tumour Morphology	
Multiple lesions:	No - single lesion
Location:	right upper portion
Appearance:	white, partly cystic
Border:	infiltrative
Size (greatest dimension):	15 mm
Distance from nearest excision margin:	5mm
Appearance of other portion of thyroid:	Nodular with colloid nodules

MICROSCOPIC

Tumour type:	Papillary carcinoma
Tumour variant:	Conventional
Multifocal:	Absent
Largest tumour dimension	15 mm

Extension into adjacent tissue/organ: Limited to thyroid (T1)

Cancer at resection margin: Absent
Clearance from margin: 5mm

Lymph nodes

Location: Detected near isthmus
Total number resected: 2
Number positive 0

Parathyroid: Present - Parathyroid tissue noted near right lobe

Co-existing pathology: Nodular hyperplasia

ANCILLARY TESTS

None performed.

Reported by Dr Bernard Mg

Authorised 4/9/2010

Appendix 4 WHO histological classification of thyroid tumours

Papillary carcinoma	8260/3
Follicular carcinoma	8330/3
Poorly differentiated carcinoma	
Undifferentiated (anaplastic) carcinoma	8020/3
Squamous cell carcinoma	8070/3
Mucoepidermoid carcinoma	8430/3
Sclerosing mucoepidermoid carcinoma with eosinophilia	8480/3
Mucinous carcinoma	8480/3
Medullary carcinoma	8345/3
Mixed medullary and follicular cell carcinoma	8346/3
Spindle cell tumour with thymus-like differentiation	8588/3
Carcinoma showing thymus-like differentiation	8589/3

Thyroid adenoma and related tumours:

Follicular adenoma	8330/0
Hyalinizing trabecular tumour	8336/0

Other thyroid tumours:

Teratoma	9080/1
Primary lymphoma and plasmacytoma	
Ectopic thymoma	8580/1
Angiosarcoma	9120/3
Smooth muscle tumours:	
Peripheral nerve sheath tumours	
Paraganglioma	8693/1
Solitary fibrous tumour	8815/0
Follicular dendritic cell tumour	9758/3
Langerhans cell histiocytosis	9751/1
Secondary tumours	

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Appendix 5 AJCC TNM classification of thyroid carcinomas

Primary Tumour (T)	
<i>Note: All categories may be subdivided: (s) solitary tumour and (m) multifocal tumour (the largest determines the classification).</i>	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Tumour 2cm or less in greatest dimension limited to the thyroid.
T1a	Tumour 1cm or less, limited to the thyroid.
T1b	Tumour more than 1cm but not more than 2cm in greatest dimension limited to the thyroid.
T2	Tumour more than 2cm but not more than 4cm in greatest dimension limited to the thyroid.
T3	Tumour more than 4cm in greatest dimension limited to the thyroid or any tumour with minimal extrathyroid extension (eg extension to sternothyroid muscle or perithyroid soft tissues).
T4a	Moderately advanced disease. Tumour of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, oesophagus or recurrent laryngeal nerve.
T4b	Very advanced disease. Tumour invades prevertebral fascia or encases carotid artery or mediastinal vessels.
All anaplastic carcinomas are considered T4 tumours	
T4a	Intrathyroidal anaplastic carcinoma
T4b	Anaplastic carcinoma with gross extrathyroid extension

Regional Lymph Nodes (N)	
Regional lymph nodes are the central compartment, lateral cervical, and upper mediastinal lymph nodes.	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph nodes metastasis
N1a	Metastasis to Level VI (Pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes)
N1b	Metastasis to unilateral, bilateral, or contralateral cervical (Levels I, II, III, IV, or V) or retropharyngeal or superior mediastinal lymph nodes (Level VII)

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

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Appendix 6 AJCC Staging Grouping

Separate stage groupings are recommended for papillary or follicular (differentiated), medullary, and anaplastic (undifferentiated) carcinoma.

<i>Papillary or follicular (differentiated)</i>			
UNDER 45 YEARS			
Stage	T	N	M
Stage I	Any T	Any N	M0
Stage II	Any T	Any N	M1
45 YEARS AND OLDER			
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1a	M0
	T2	N1a	M0
	T3	N1a	M0
Stage IVA	T4a	N0	M0
	T4a	N1a	M0
	T1	N1b	M0
	T2	N1b	M0
	T3	N1b	M0
	T4a	N1b	M0
Stage IVB	T4b	Any N	M0
Stage IVC	Any T	Any N	M1
<i>Medullary carcinoma (all age groups)</i>			
Stage I	T1	N0	M0
Stage II	T2	N0	M0
	T3	N0	M0
Stage III	T1	N1a	M0
	T2	N1a	M0
	T3	N1a	M0
Stage IVA	T4a	N0	M0
	T4a	N1a	M0
	T1	N1b	M0
	T2	N1b	M0
	T3	N1b	M0
	T4a	N1b	M0
Stage IVB	T4b	Any N	M0
Stage IVC	Any T	Any N	M1
<i>Anaplastic carcinoma</i>			
All anaplastic carcinomas are considered Stage IV			
Stage IVA	T4a	Any N	M0
Stage IVB	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

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