The Royal College of Pathologists
Pathology: the science behind the cure

Standards and datasets for reporting cancers

Dataset for the histopathological reporting of thymic epithelial tumours

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Comments	This is an update to accommodate the 2015 WHO classification and ensure consistency with the International Collaboration on Cancer Reportingôs (ICCR) thymic epithelial tumour dataset. In accordance with the Collegeôs pre-publications policy, this document was placed on the College website for consultation from 15 August to 12 September 2017. It will replace the second edition of *Dataset for the histological reporting of thymic epithelial tumours,* published in 2016. **Dr Lorna Williamson** **Director of Publishing and Engagement**

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Foreword

The cancer datasets published by The Royal College of Pathologists (RCPath) are a combination of textual guidance, educational information and reporting proformas. The datasets enable pathologists to grade and stage cancers in an accurate, consistent manner in compliance with international standards and provide prognostic information, thereby allowing clinicians to provide a high standard of care for patients and appropriate management for specific clinical circumstances. It may rarely be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. The clinical risk of departing from the guidelines should be assessed by the relevant multidisciplinary team (MDT); just as adherence to the guidelines may not constitute defence against a claim of negligence, so a decision to deviate from them should not necessarily be deemed negligent.

Each dataset contains core data items that are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD ï previously the National Cancer Dataset) in England. Core data items are items that are supported by robust published evidence and are required for cancer staging, optimal patient management and prognosis. Core data items meet the requirements of professional standards (as defined by the Information Standards Board for Health and Social Care [ISB]) and it is recommended that at least 90% of reports on cancer resections should record a full set of core data items. Other, non-core data items are described. These may be included to provide a comprehensive report or to meet local clinical or research requirements. All data items should be clearly defined to allow the unambiguous recording of data.

The following stakeholder groups have been consulted:

- British Thoracic Oncology Group
- British Thoracic Society
- Society for Cardiothoracic Surgery in Great Britain and Ireland.

Evidence for the data items in the dataset is derived from consensus of recognised experts, in particular recent guidelines from the International Thymic Malignancy Interest Group (ITMIG), together with review of current literature. Evidence has been graded using modified SIGN guidance as recommended ï see Appendix H.

No major organisational changes or cost implications have been identified that would hinder the implementation of the dataset.

A formal revision cycle for all cancer datasets takes place on a 3-yearly basis. However, each year, the College will ask the author of the dataset, in conjunction with the relevant subspecialty adviser to the College, to consider whether or not the dataset needs to be updated or revised. A full consultation process will be undertaken if major revisions are required, i.e. revisions to core data items (the only exception being changes to international tumour grading and staging schemes that have been approved by the Specialty Advisory Committee on Cellular Pathology and affiliated professional bodies; these changes will be implemented without further consultation). If minor revisions or changes to non-core data items are required, an abridged consultation process will be undertaken, whereby a short note of the proposed changes will be placed on the College website for two weeks for membersô attention. If members do not object to the changes, the short notice of change will be incorporated into the dataset and the full revised version (incorporating the changes) will replace the existing version on the College website. All changes will be documented in the ódata controlôsection of the relevant dataset.

The dataset has been reviewed by the Clinical Effectiveness department, Working Group on Cancer Service (WGCS) and Lay Governance Group and placed on the College website for consultation with the membership from 15 August to 12 September 2017.

This dataset was developed without external funding to the writing group. The College requires the authors of datasets to provide a list of potential conflicts of interest; these are monitored by the Clinical Effectiveness department and are available on request. The authors have declared that they have previously received payment for advisory and educational work for commercial organisations involved in molecular testing and treatment of lung cancer. They give their assurances that these conflicts of interest have not influenced the content of this dataset.

1 Introduction

Due to the relative rarity of primary thymic epithelial tumours (TETs), and the fact that thymomas are sometimes reported by both pathologists with an interest in lymphoreticular pathology and/or thoracic pathology, thymic tumours were only covered for the first time by a cancer dataset in 2013. This was in part due to a lack of consensus agreement on pathological staging and histological subtyping. With regard to staging, several systems have been proposed,[1] with the Masaoka-Koga staging systems being most frequently used until recently.[2–5] However, this has been replaced in the *TNM Classification of Malignant Tumours (8th edition)* from the Union for International Cancer Control based on a retrospective dataset of over 8000 cases.[6–9] For histological subtyping, a WHO classification proposed in 2004 has been updated in the 2015 WHO classification,[10] and was included in the previous version. There has also been an initiative through the International Collaboration on Cancer Reporting (ICCR) for an international dataset and the RCPath dataset has been reviewed to ensure that all required ICCR parameters are within its dataset.[11] The ICCR dataset uses órecommendedô(non-core) and órequiredô(core), and some recommended elements remain as core items within the RCPath dataset, such as tumour size, although all ICCR elements are now within the RCPath dataset as either core or non-core elements.

During 2017 whilst there is transition to the 8th TNM, in relation to national data collection, it is recommended that the 8th TNM is a core item, but that Masaoka-Koga staging can additionally be provided as a non-core item, to facilitate any ongoing data collection using this system.

Consequently, features in both biopsy and resection specimens should be reported according to the following guidelines as the data is important for:

a) deciding on the most appropriate treatment for particular patients, including the need and choice of adjuvant therapy
b) providing prognostic information to clinicians and patients
c) providing more reliable staging than using clinical data alone
d) monitoring clinical effectiveness of therapeutic trials
e) providing accurate data for cancer registration.

Decisions about feasibility of surgical resection are made following clinical and radiological staging procedures. Correlation of these results with information obtained from resection specimens also allows for monitoring of the accuracy of staging procedures and the appropriateness of surgical intervention.

The reporting proformas and guidance in the following pages are based on the 8th TNM recommendations for staging, i.e. changing from the Masaoka-Koga system, in addition to using ITMIG recommendations for the reporting of small biopsies and handling of resections,[3,5] and the 2015 WHO classification for thymic epithelial neoplasms.[10,12]

Of note, the thymus is the primary site for several tumours other than TETs, such as germ cell tumours, mesenchymal tumours and lymphomas. These tumours are covered in other datasets.

The purpose of this document is to define the core data that should be determined for all resected cases with TETs, including neuroendocrine tumours of the thymus (NETT). These are guidelines and not rigid rules, and are intended to help pathologists provide the information necessary to local clinicians for effective management of their patients. Consistency in reporting and staging is improved by the use of standard terminology ï for example, precise definition of the extent of tumour invasion through the capsule, mediastinal pleura and visceral pleura. The reporting proforma is intended to supplement and not replace the usual ón-houseôtext report. The use of diagrams to show the extent of local invasion and involvement of lymph node stations can be advantageous. It is also important to realise that staging at the time of resection is only partly informed by pathological assessment of the specimen and that clinical details will be required with respect to some parameters, e.g. the presence of a nodule(s) seeding the pleural cavities/mediastinum.

1.1 Target users and health benefits of this guideline

The target primary users of the dataset are trainee and consultant cellular pathologists and, on their behalf, the suppliers of IT products to laboratories. The secondary users are surgeons and oncologists, cancer registries and the National Cancer Intelligence Network. Standardised cancer reporting and MDT working reduce the risk of histological misdiagnosis and help to ensure that clinicians have all of the relevant pathological information required for tumour staging, management and prognosis. Collection of standardised cancer-specific data also provides information for healthcare providers, epidemiologists, and facilitates international benchmarking and research.

2 Clinical information required on the specimen request form

Name, date of birth, hospital, hospital number, NHS/CHI number, procedure, specimen type, date of procedure and surgeon/physician should be provided.

In addition, the extent of thymic resection should be stated, along with any additional anatomic elements such as pericardium, lung wedge or wall of great vessel that are submitted. The latter are often adherent to the tumour and their presence should not only be recorded but should ideally be identified with sutures as areas of particular relevance to anatomical staging boundaries and completeness of resection.

Details of any previous biopsy or cytology, any previous malignancy and previous treatment such as neoadjuvant chemotherapy and/or radiotherapy should also be recorded.

3 Preparation of specimens before dissection

Anterior, posterior, and right and left aspects should be specifically identified after the anatomic landmarks of the tissue have been established. This can be facilitated either by submission of the specimen on a board pinned to a diagram of the mediastinum (see Appendix B) or by the appropriate use of marker sutures. It is critical that ambiguities be resolved by direct communication between the surgeon (or designee who was present during resection) and the pathologist prior to processing, as key areas may be lost once dissection begins. Inking of areas key to assess completeness of resection is recommended, although the whole specimen does not need to be inked. The specimen should be fixed appropriately and, if sliced to accelerate fixation, the anatomic relationship of the slices should be documented.[3]

[Level of evidence D – Expert opinion is that good communication between surgeon and pathologist improves the accuracy of determining completeness of resection.]

4 Specimen handling and block selection

It is ideal to bread-slice thymic resections from superior to inferior in thin sections, although this may not always be possible. Thymomas are well known for their potential microscopic heterogeneity,[13] such that different areas of the lesion may well have very dissimilar histological appearances, for example combined cases of thymic carcinoma and thymoma.[6] We recommend submission of at least one block of tissue for each centimetre of maximum tumour dimension (i.e. a 100 mm lesion would require ten blocks, a 50 mm lesion five blocks, etc.) Past publications suggest that systematic tissue sampling with at least five sections improves the reliability of the pathologic characterisation of thymic epithelial tumours.[13] If a thymic neoplasm is small, it should be submitted in its entirety for microscopy, usually in only two or three blocks. Sections of tumour with margins should be clearly documented in the block key, so that completeness of resection can be documented in relation to the anatomy, as adjuvant therapy may be targeted (e.g. radiotherapy). Any areas identified by either the surgeon or the pathologist as possibly being an involved margin must be sampled.

If tumours are extensively cystic, and especially if there is no pre-resection biopsy, the wall of the cyst should be thoroughly sampled to exclude other possible cystic neoplasms of the thymic region, such as germ cell tumours, and non-neoplastic cysts arising from thymoma.[14]

At least one random section of the uninvolved thymus should routinely be taken.

Finally, if at all feasible and there is appropriate consent, banking of fresh frozen tumour for future research is recommended.

[Level of evidence C – The basis for block selection is extrapolated from the need to provide microscopic confirmation or evaluation of prognostic and predictive factors.]

5 Core data items for resection specimens (see Appendix D)

5.1 Clinical

If previous treatment has been administered, this should be recorded, as should the specimen type and procedure.

[Level of evidence – good practice point (GPP).]

5.2 Pathological

5.2.1 Specimens submitted

All specimens submitted with the procedure should be listed.

[Level of evidence – GPP.]

5.2.2 Relationship of tumour to thymus and other intra-thoracic structures

The location of the tumour in the thymus as well as its relationship to adherent structures should be recorded. In particular, areas of likely invasion that pertain to staging should be assessed (capsule, mediastinal pleura, visceral pleura, lung, great vessels, pericardium). Separate tumour nodules in the main resection specimen or separately submitted samples (e.g. separate lung or pleural nodules) should also be documented. If the thymoma arises outside the thymus, it should be documented as ectopic.

[Level of evidence B – ITMIG staging analysis data.]

5.2.3 Size of tumour

The maximum diameter of the tumour should be measured to the nearest millimetre. Three dimensions can be recorded, but this is not essential. The ICCR dataset recommends that this parameter be only órecommendedô rather than órequiredô,[11] based on the paper on T staging that showed no prognostic significance in relation to tumour size, only correlation with recurrence at a 10 cm cut-off in a subset of patients.[8] However, as this is a mainstay of specimen description, not least as it dictates the number of recommended blocks, this remains a core item in the RCPath dataset.

[Level of evidence B – ITMIG staging analysis data.]

5.2.4 Histological type

Histological typing of thymomas is recorded according to the classification based on the 2015 WHO typing of thymic tumours (A, B1, B2, B3).[10] If there is a combination of patterns (e.g. AB, B2 and B3), these should all be documented and the percentage of each component recorded. Rare variants of thymoma (e.g. micronodular) should be documented under ó Other Thymomasô Thymic carcinomas are rare but are classified separately, with squamous subtype being the most common.[10] NETTs should be classified as typical carcinoid, atypical carcinoid, large cell neuroendocrine cell carcinoma or small cell carcinoma.[10]

[Level of evidence B.[10]]

5.2.5 Direct local invasion

Invasion of the capsule is no longer a core item. pT1 thymoma can be either encapsulated or unencapsulated, with (pT1b) or without extension (pT1a) into mediastinal fat. The borders of the mediastinum may be difficult to identify, but this is facilitated by EVG staining and through discussion with the surgeon.

A tumour with direct invasion into the pericardium only is designated as pT2a. Invasion of the pericardium is defined as tumour cells present at least into the fibrous layer and may be partial or complete.

A tumour with direct invasion into the lung, brachiocephalic vein, superior vena cava, chest wall, and/or phrenic nerve is designated as pT3. Invasion into lung is defined as tumour present inside the outer elastin layer of the visceral pleura.

A tumour with direct invasion into the aorta, main pulmonary artery, myocardium, trachea or oesophagus is designated as pT4.

[Level of evidence B – ITMIG staging analysis data.]

5.2.6 Lymph nodes

Lymph nodes are often not sampled in thymic resections. If sampled, the presence or absence of a tumour should be recorded. Lymph nodes are currently divided into two areas within the mediastinum, namely anterior (perithymic) and deep intrathoracic or cervical regions,[6] with involved nodes in the anterior (perithymic) region being pN1 and deep intrathoracic or cervical regions being pN2. Lymph nodes outside these regions are classified as pM1b.[7]

[Level of evidence B – ITMIG staging analysis data.]

5.2.7 Separate nodules/metastases

Pleural or pericardial tumour nodules (seeding) that are separate from the primary tumour indicate classification as pM1a. These separate tumour nodules may be located on the visceral or parietal pleural or pericardial surfaces.

Pulmonary nodules that are in the lung, with a rim of normal lung between the nodule and the pleural surface, are regarded as distant metastases and classified as pM1b. Involvement of extrathoracic tissues (including lymph nodes outside of anterior and deep mediastinal regions) should be classified as distant metastases (pM1b).

[Level of evidence B – ITMIG staging analysis data.]

5.2.8 Resections following therapy

Gross preparation of a resected specimen after preoperative (neoadjuvant) therapy should follow the same principles outlined for primary resected specimens. However, it is likely that some of the tumour will have become necrotic and more sections will need to be examined in order to have a valid representation of the histological appearance. Also, preoperative steroid therapy can decrease the number of lymphocytes within the tumour, which may affect interpretation. Ideally, a complete cross section of the tumour should be examined and the percentage of remaining viable tumour can be reported. As a core item, scoring should be limited to ónoo or minimal responseô, ópartial responseô or ócomplete or near complete responseô, as recommended for other malignancies.[11]

[Level of evidence – GPP.]

5.2.9 Margins

Any area where there is concern over completeness of the resection should be marked by the surgeon and sampled by the pathologist, with subsequent reporting on whether or not the margins are clear. R0 indicates complete resection, R1 indicates microscopic evidence of tumour at the resection margin (incomplete resection) and R2 indicates macroscopic evidence of tumour at the resection margin (incomplete resection). Distance from nearest margin should be recorded. In cases submitted in multiple pieces, the relationship of the specimens will often need to be discussed with the surgeon to ensure accurate assignment of R status.

[Level of evidence B – ITMIG staging analysis data.]

6 Non-core data items

Various additional parameters have been recommended, but as yet there is insufficient evidence that these influence patient management for them to be included as core items. They may be prospectively recorded at a local level, according to needs and interest.

6.1 Clinical, surgical and specimen information

It is helpful to know whether the patient has myasthenia gravis or other conditions including neoplasms that can be associated with thymomas. This is recorded as órecommendedôin the ICCR dataset, along with the surgical procedure (extended, radical/partial/total/other), block identification key and the specimen integrity (intact/surface disrupted/fragmented).

6.2 Ancillary data

Ancillary data should be recorded if any testing is undertaken. Immunohistochemistry may aid in the distinction between various TET subtypes (e.g. TdT, CD5, CD117). Testing for gene mutations is not commonly undertaken at present. Fluorescent *in situ* hybridisation detection of the 15:19 translocation confirms the diagnosis as a particularly aggressive type of thymic carcinoma. Compared to lung cancer, molecular abnormalities, particularly in relation to targeted therapies, are not in routine clinical usage, but should be recorded if any are identified.

6.3 Background thymus

Evidence of coexistent pathology in the background thymus should be recorded, such as true (enlarged size) or follicular hyperplasia.

6.4 Variations in capsular integrity

In some patients, the capsule is partially absent; this should not be interpreted as invasion, rather this situation can be documented in the report (i.e. thymoma, partially unencapsulated). It should be recognised that the capsule is not a native anatomical structure, rather a reflection of desmoplasia induced by the tumour; hence, thymomas are not always encapsulated. The ICCR recommends division into 'intact', 'disrupted' and 'fragmented'[11]

7 Diagnostic coding and pathological staging

The site and histological diagnosis and procedure should be coded using SNOMED or SNOMED-CT (see Appendix C).

8 Reporting of small biopsy specimens

There are no evidence-based or expert consensus guidelines available for the interpretation of needle core biopsies of the mediastinum. Biopsy findings should be closely correlated with the imaging findings and other clinical information, especially to help exclude metastatic disease. However, as TETs can be heterogeneous, it may only be possible to classify a biopsy as 'thymoma, not otherwise specified', rather than attempt subdivision. However, differentiation between NETTs and thymic carcinoma may be possible using antibodies, such as CD5 and TdT, and neuroendocrine markers. Lymphoid and epithelial markers (cytokeratins) are also useful to help distinguish TETs from mediastinal lymphomas.[5,12]

It is recommended that a pathway for second opinion be available as many institutions will lack pathologists that have extensive experience in the interpretation of such lesions, particularly in small biopsies. A reporting proforma is provided in Appendix E.

[Level of evidence D – recommendation based on collective opinion of ITMIG.]

9 Reporting of cytology specimens

There are no available evidence-based or expert consensus guidelines for the interpretation of mediastinal fine needle aspiration (FNA) specimens. As with biopsies, cytological findings should be correlated with the clinical and imaging findings to establish whether the available cytological material is sufficient to render a specific diagnosis or a clinically applicable differential diagnosis. In patients where malignant lymphoma is being considered in the differential diagnosis, information about immunostains should be incorporated in the cytological report. A reporting proforma is provided in Appendix E.

[Level of evidence D – recommendation based on collective opinion of ITMIG.]

10 Reporting of frozen sections

Biopsies of mediastinal lesions are frequently sent for frozen section, which may be as much to confirm adequacy for diagnosis as for immediate diagnosis. In the former situation, as the frozen section procedure introduces technical artefacts that can preclude adequate

diagnoses, additional tissue fixed in formalin should be submitted to ensure greatest diagnostic accuracy. This is particularly important as lymphoma is often one of the differential diagnoses.

[Level of evidence D – recommendation based on collective opinion of ITMIG.]

11 Prognostic and predictive markers

At present, neither predictive nor prognostic immunohistochemical nor molecular markers are recommended for diagnostic use.

12 Criteria for audit of the dataset

In keeping with the recommended key performance indicators published by The RCPath (www.rcpath.org/profession/clinical-effectiveness/key-performance-indicators-kpi.html), reports on thymic epithelial tumours should be audited for the following:

- The inclusion of SNOMED or SNOMED-CT codes:
  - standard: 95% of reports should have T, M and P codes.
- The availability of pathology reports and data at MDT meetings:
  - standard: 90% of cases discussed at MDT meetings where biopsies or resections have been taken should have pathology reports/core data available for discussion
  - standard: 90% of cases where pathology has been reviewed for the MDT meeting should have the process of review recorded.
- The use of electronic structured reports or locally agreed proformas (it is assumed that these processes will ensure that 90% of core data items are recorded):
  - standard: 80% of resection specimens will include 100% data items presented in a structured format.
- Turnaround times for biopsies and resection specimens:
  - standard: 80% of diagnostic biopsies will be reported within seven calendar days of the biopsy being taken
  - standard: 80% of all histopathology specimens (excluding those requiring decalcification) will be reported within 10 calendar days of the specimen being taken.

In addition, the following are suggested as some of the criteria that might be used in periodic reviews of thymic epithelial tumour reporting:

- assessment of anatomic parameters used for staging of TETs using the updated Masaoka-Koga staging system
- inter- and intra-observer studies in classification of tumours
- accuracy of cytology diagnosis by correlating the histological and cytological diagnoses.

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Appendix A Staging of thymic epithelial neoplasms – 8th TNM staging[6–9]

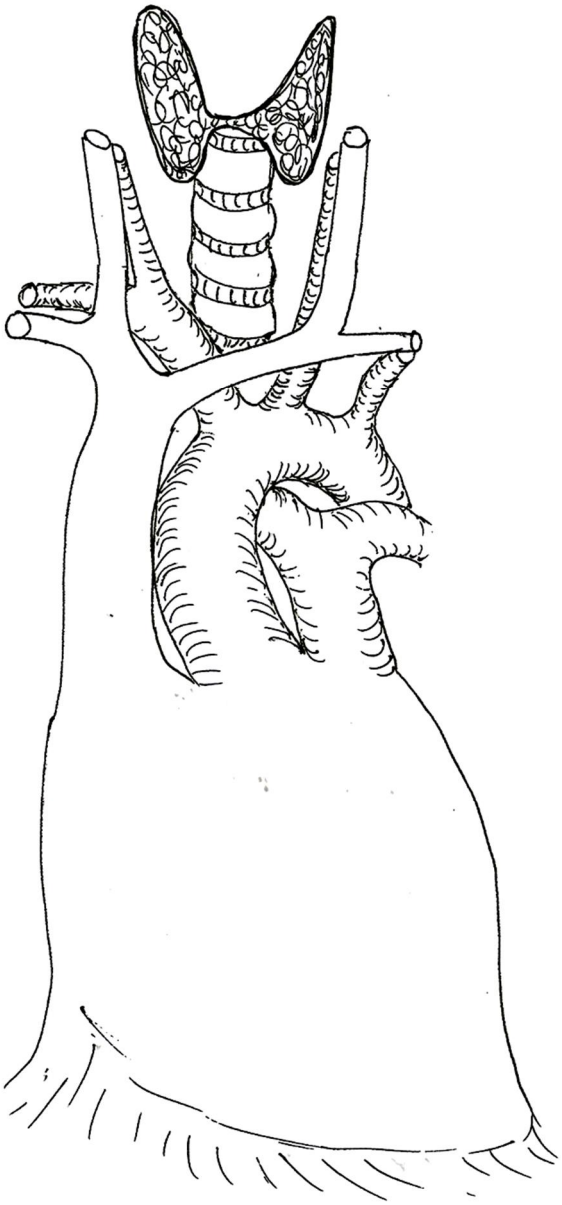
T	Descriptors
T1	**A tumor that either is limited to the thymus with or without encapsulation, directly invades into the mediastinum only, or directly invades the mediastinal pleura but does not involve any other mediastinal structure.** For further testing T1 is subdivided into T1a (no mediastinal pleural involvement) and T1b (direct invasion of the mediastinal pleura)
T2	**A tumor with direct invasion of the pericardium (either partial or full thickness)**
T3	**A tumor with direct invasion into any of the following: lung, brachiocephalic vein, superior vena cava, phrenic nerve, chest wall or extrapericardial pulmonary artery or veins**
T4	**A tumor with invasion into any of the following: aorta (ascending, arch or descending), arch vessels, intrapericardial pulmonary artery, myocardium, trachea, oesophagus**

Category	Definition (involvement of):[a]
N0	No nodal involvement
N1	Anterior (perithymic) nodes
N2	Deep intrathoracic or cervical nodes
M0	No metastatic pleural, pericardial or distant sites
M1 a	Separate pleural or pericardial nodule(s)
b	Pulmonary intraparenchymal nodule or distant organ metastasis

Stage	T	N	M
I	T1	N0	M0
II	T2	N0	M0
IIIa	T3	N0	M0
IIIb	T4	N0	M0
IVa	T any	N1	M0
	T any	N0,1	M1a
IVb	T any	N2	M0, M1a
	T any	N any	M1b

Appendix B Mediastinal diagram

This diagram may be printed off and used to pin specimens to facilitate macroscopy.



Appendix C SNOMED codes

SNOMED T codes

Descriptor	SNOMED 2 code	SNOMED 3 code	SNOMED-CT terminology	SNOMED-CT code
Thymus	T-98000	T-C8000	Thymus gland structure (body structure)	9875009

SNOMED M codes

Descriptor	ICD-O codes	SNOMED-CT terminology	SNOMED-CT code
Epithelial tumours			
Thymoma			
Type A thymoma, including atypical variant	8581/3*	Thymoma, type A, malignant (morphologic abnormality)	128708008
Type AB thymoma	8582/3*	Thymoma, type AB, malignant (morphologic abnormality)	128710005
Type B1 thymoma	8583/3*	Thymoma, type B1, malignant (morphologic abnormality)	128712002
Type B2 thymoma	8584/3*	Thymoma, type B2, malignant (morphologic abnormality)	128714001
Type B3 thymoma	8585/3*	Thymoma, type B3, malignant (morphologic abnormality)	128716004
Micronodular thymoma with lymphoid stroma	8580/1*	Thymoma, no International Classification of Diseases for Oncology (ICD-O) subtype (morphologic abnormality)	128856005
Metaplastic thymoma	8580/3	Thymoma, malignant (morphologic abnormality)	15949004
Other rare thymomas			
Microscopic thymoma	8580/0	Thymoma, benign (morphologic abnormality)	21181001
Sclerosing thymoma	8580/3	Thymoma, malignant (morphologic abnormality)	15949004
Lipofibroadenoma	9010/0*	Fibroadenoma, no ICD-O subtype (morphologic abnormality)	65877006

Descriptor	ICD-O codes	SNOMED-CT terminology	SNOMED-CT code
Thymic carcinoma			
Squamous cell carcinoma	8070/3	Squamous cell carcinoma, no ICD-O subtype (morphologic abnormality)	28899001
Basaloid carcinoma	8123/3	Basaloid carcinoma (morphologic abnormality)	5843004
Mucoepidermoid carcinoma	8430/3	Mucoepidermoid carcinoma (morphologic abnormality)	4079000
Lymphoepithelioma-like carcinoma	8082/3	Lymphoepithelial carcinoma (morphologic abnormality)	7300000
Clear cell carcinoma	8310/3	Clear cell adenocarcinoma (morphologic abnormality)	30546008
Sarcomatoid carcinoma	8033/3	Pseudosarcomatous carcinoma (morphologic abnormality)	23109009
Adenocarcinomas			
Papillary adenocarcinoma	8260/3	Papillary adenocarcinoma (morphologic abnormality)	4797003
Thymic carcinoma with adenoid cystic carcinoma-like features	8200/3	Adenoid cystic carcinoma (morphologic abnormality)	11671000
Mucinous adenocarcinoma	8480/3	Mucinous adenocarcinoma (morphologic abnormality)	72495009
Adenocarcinoma, NOS	8140/3	Adenocarcinoma, no subtype (morphologic abnormality)	35917007
NUT carcinoma	8023/3*	No code exists yet	No code exists yet
Undifferentiated carcinoma	8020/3	Carcinoma, undifferentiated (morphologic abnormality)	38549000
Other rare thymic carcinomas			
Adenosquamous carcinoma	8560/3	Adenosquamous carcinoma (morphologic abnormality)	59367005
Hepatoid carcinoma	8576/3	Hepatoid adenocarcinoma (morphologic abnormality)	128706007
Thymic carcinoma, NOS	8586/3	Thymoma, type C (morphologic abnormality)	128717008

Descriptor	ICD-O codes	SNOMED-CT terminology	SNOMED-CT code
Thymic neuroendocrine tumours			
Carcinoid tumours			
Typical carcinoid	8240/3	Carcinoid tumor, no ICD-O subtype (morphologic abnormality)	81622000
Atypical carcinoid	8249/3	Atypical carcinoid tumor (morphologic abnormality)	128658008
Large cell neuroendocrine carcinoma	8013/3	Large cell neuroendocrine carcinoma (morphologic abnormality)	128628002
Combined large cell neuroendocrine carcinoma	8013/3	Combined large cell neuroendocrine carcinoma (morphologic abnormality)	448546006
Small cell carcinoma	8041/3	Small cell carcinoma (morphologic abnormality)	74364000
Combined small cell carcinoma	8045/3	Combined small cell carcinoma (morphologic abnormality)	21326004

Notes

a. The morphology codes are from the International Classification of Diseases for Oncology (ICD-O). Behaviour is coded:
/0 for benign tumours
/1 for unspecified, borderline or uncertain behaviour
/2 for carcinoma *in situ* and grade III intraepithelial neoplasia
/3 for malignant tumours.

b. The classification is modified from the previous WHO classification, taking into account changes in our understanding of these lesions.

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

SNOMED P codes

Local P codes should be recorded. At present, P codes vary according to the SNOMED system in use in different institutions.

Appendix D Reporting proforma for resections of thymic epithelial tumours

Surnameé é é é é é é é é é . Forenamesé é é é é é é é é ... Date of birthé é é é .. Sexé ....

Hospitalé é é é .é é é .é é ..... Hospital noé é é é é é .é é é é é é . NHS/CHI noé é é é .é é é ..

Date of surgeryé é é é .é ..... Date of report authorisationé é é é é . Report noé é é é é .é .....

Date of receipté é é é .é é é é .. Pathologisté é é .é é é é é é é é é . Surgeoné é é é é é .é é é .

Previous treatment (neoadjuvant chemotherapy/radiotherapy)ÿ Yes □ No □ Not known □

Specimens submitted ÿ

Partial thymus □ Complete thymus □ Thymus plus surrounding tissue (radical thymectomy) □

Lung Right □ Wedge □ Lobe □ Entire lung □

Left □ Wedge □ Lobe □ Entire lung □

Pericardium □

Mediastinal pleura □

Phrenic nerve □

Great vessels □ *(specify: innominate vein, aorta (descending/ascending, SVC, Arch vessels, intrapericardial pulmonary artery)* é é é .....

Myocardium □ Diaphragm □ Chest wall □ Oesophagus □

Lymph nodes: Anterior □ Deep intrathoracic/cervical □ Extrathoracic □

Separate extrathymic nodules □ (specify number and sites) é é é é é é é é é é é é é é é é é

Other □ (specify) é é é ..é é .....é é

Macroscopic features Àÿ

Location of tumour (intrathymic, ectopic, multiple sites): é é é é ..é .....

Tumour size é é é .mm (maximum dimension) Not assessable □

Microscopic features

Histological type Àÿ

Thymoma A □ Thymoma AB □ Thymoma B1 □ Thymoma B2 □ Thymoma B3 □

Other thymoma (e.g. micronodular) é é é é é é é é é é é é é é é é é ..é é é é é é é é é .

Combined tumour □ (specify percentages of types) é é é é é ..é é é é é é é é é é ....é é é é .

Thymic carcinoma □ (specify subtype, see Appendix C) é é é é é é é é é é .é é é é é é é é ..

Neuroendocrine thymic tumours (specify subtype/grade, see Appendix C) é é é é é é é é é é

Direct invasion

Mediastinal pleura À	Not involved □	Involved □	Not assessable □	Not applicable □
Pericardium À	Not involved □	Involved □	Not assessable □	Not applicable □
Lung/Visceral À pleura	Not involved □	Involved □	Not assessable □	Not applicable □
Great vessels				
Innominate vein À	Not involved □	Involved □	Not assessable □	Not applicable □
Aorta À	Not involved □	Involved □	Not assessable □	Not applicable □
SVC À	Not involved □	Involved □	Not assessable □	Not applicable □
Arch vessels À	Not involved □	Involved □	Not assessable □	Not applicable □
Extrapericardial PA À	Not involved □	Involved □	Not assessable □	Not applicable □
Intrapericardial PA À	Not involved □	Involved □	Not assessable □	Not applicable □
Phrenic nerve À	Not involved □	Involved □	Not assessable □	Not applicable □
Chest wall	Not involved □	Involved □	Not assessable □	Not applicable □
Other involved organ sites (by direct spread)	Àé é é é	Involved □	Not assessable □	Not applicable □

Lymph node involvement À

Anterior (perithymic):	Not involved □	Involved □	Not assessable □	Not applicable □
Deep intrathoracic/cervical:	Not involved □	Involved □	Not assessable □	Not applicable □
Other é é é é é é é :	Not involved □	Involved □	Not assessable □	Not applicable □

Separate extrathymic tumour nodules/metastases

Pleural or pericardial (stage pM1a) Àÿ

Present □ Not identified □

Number: .....

Location(s) é é é é é é é . é é é é é é é é é é é é ..

Other nodules (stage pM1b) Àÿ

Lung, intraparenchymal	Present □	Not identified □
Distant organ	Present □	Not identified □

If present, specify……

Response to neoadjuvant therapy

N/A □ Complete/Near complete □ Partial □ None/Minimal □

Margins ÿ

Excision complete (R0) Yes □ No □ Cannot be assessed □

If excision not complete:

Microscopic involvement (R1) Yes □ No □

Macroscopic involvement (R2) Yes □ No □

Sites of involvement if R1 or R2: é é é é é é é é é é

Closest margin if excision complete: ..... distance .....mm

Summary of pathological staging ÿ

(Select highest stage from above data; Use prefix ýyôfor resection during or following treatment and ýrôfor recurrence after treatment) é é pT é é é ..pN é é é é pM (if known) é é é Version:é ..

SNOMED and SNOMED-CT codes ÿ

Comments

Signature .....…… Date ……../……../……..

Notes

À Data items included in the 1st edition of the ICCR lung cancer resection dataset.

ÿ Data items that are currently part of the Cancer Outcomes and Services Dataset (COSD) version 7.

Appendix E Reporting proforma for biopsy/cytology specimens of thymic epithelial tumours

Surnameé é é é é é é é é é . Forenamesé é é é é é é é é ... Date of birthé é é é .. Sexé ....

Hospitalé é é é .é é é .é é ..... Hospital noé é é é é é .é é é é é é . NHS/CHI noé é é é .é é é ..

Date of surgeryé é é é .é ..... Date of report authorisationé é é é é . Report noé é é é é .é .....

Date of receipté é é é .é é é é .. Pathologisté é é .é é é é é é é é é . Surgeoné é é é é é .é é é .

Previous treatment (neoadjuvant chemotherapy/radiotherapy)ÿ

Yes □ No □ Not known □

Origin of specimen ÿ

Thymus □ Mediastinum, other than thymus NOS □

Pleura □ Lung □ Other é é é é . □

Sample type (more than one box may be ticked) ÿ

Biopsy:

Transthoracic needle biopsy □ Incisional biopsy □

Lymph node biopsy □ Specify site(s) é é ..é é é .....

Pleural biopsy □ Other metastatic site(s) □ Details.....

Cytology:

Transthoracic FNA mediastinum □ Pleural effusion □ Other □ é é é é é é é é é ..

Microscopic features ÿ

Histological/cytological type

Thymic epithelial tumour, not otherwise specified □

Specify WHO subtype present if assessable .....é .....

Other tumour type (specify) é .

SNOMED and SNOMED-CT codes : ÿ

Comments

Signature .....…… Date ……...../……../……...

ÿ Data items that are currently part of the Cancer Outcomes and Services Dataset (COSD) version 7.

Appendix F Reporting proforma for resections of thymic epithelial tumours in list format

Element name	Values	Implementation comments
Previous treatment (neoadjuvant chemotherapy/radiotherapy)	Single selection value list: • Yes • No	
Specimens submitted	Multiple selection value list: • Partial thymus • Complete thymus • Thymus plus surrounding tissue (radical thymectomy) • Right lung wedge • Right lung lobe • Entire right lung • Left lung wedge • Left lung lobe • Entire left lung • Pericardium • Mediastinal pleura • Phrenic nerve • Great vessels • Myocardium • Chest wall • Oeosphagus • Lymph nodes, anterior • Lymph nodes, deep intrathoracic/cervical • Lymph nodes, extrathoracic • Separate extrathymic nodules • Other	
Great vessels, specify	Free text	Only applicable if ôSpecimens submitted, Great vesselsôis selected.
Separate extrathymic nodules, specify number and sites	Free text	Only applicable if ôSpecimens submitted, Separate extrathymic nodulesôis selected.
Specimens submitted, other (specify)	Free text	Only applicable if ôSpecimens submitted, Otherôis selected.

Element name	Values	Implementation comments
Location of tumour	Free text	
Tumour size	Size in mm	
Tumour size, assessable	Single selection value list: • Assessable • Not assessable	Assessable if ôTumour sizeôis completed.
Histological type	Single selection value list: • Thymoma A • Thymoma AB • Thymoma B1 • Thymoma B2 • Thymoma B3 • Other thymoma • Combined tumour • Thymic carcinoma • Neuroendocrine thymic tumours	
Other thymoma, specify	Free text	Only applicable if ôHistological type, Other thymomaôis selected.
Combined tumour, specify percentages of types	Free text	Only applicable if ôHistological type, Combined tumourôis selected.
Thymic carcinoma, specify subtype	Free text	Only applicable if ôHistological type, Thymic carcinomaôis selected.
Neuroendocrine thymic tumour, specify subtype/grade	Free text	Only applicable if ôHistological type, Neuroendocrine thymic tumourôis selected.
Mediastinal pleura	Single selection value list: • Not involved (pT1a) • Involved (pT1b) • Not assessable • Not applicable	
Pericardium	Single selection value list: • Not involved • Involved (pT2) • Not assessable • Not applicable	

Element name	Values	Implementation comments
Lung/visceral pleura	Single selection value list: • Not involved • Involved (pT3) • Not assessable • Not applicable	
Innominate vein	Single selection value list: • Not involved • Involved (pT3) • Not assessable • Not applicable	
Chest wall	Single selection value list: • Not involved • Involved (pT3) • Not assessable • Not applicable	
Phrenic nerve	Single selection value list: • Not involved • Involved (pT3) • Not assessable • Not applicable	
Superior vena cava	Single selection value list: • Not involved • Involved (pT3) • Not assessable • Not applicable	
Extrapericardial pulmonary artery	Single selection value list: • Not involved • Involved (pT3) • Not assessable • Not applicable	
Aorta	Single selection value list: • Not involved • Involved (pT4) • Not assessable • Not applicable	

Element name	Values	Implementation comments
Arch vessels	Single selection value list: • Not involved • Involved (pT4) • Not assessable • Not applicable	
Intrapericardial pulmonary artery	Single selection value list: • Not involved • Involved (pT4) • Not assessable • Not applicable	
Other involved organ sites by direct spread	Free text	
Lymph nodes, anterior (perithymic)	Single selection value list: • Not involved • Involved (pN1) • Not assessable • Not applicable	
Lymph nodes, deep intrathoracic/cervical	Single selection value list: • Not involved • Involved (pN2) • Not assessable • Not applicable	
Lymph nodes, other	Single selection value list: • Not involved • Involved (pM1b) • Not assessable • Not applicable	
Lymph nodes, other specify	Free text	
Separate extrathymic tumour nodules, pleural or pericardial	Single selection value list: • Present (pM1a) • Not identified	

Element name	Values	Implementation comments
Separate extrathymic tumour nodules, pleural or pericardial, number	Integer	Only applicable if 'Separate extrathymic tumour nodules, Pleural or pericardial' is 'Present'
Separate extrathymic tumour nodules, pleural or pericardial, locations	Free text	Only applicable if 'Separate extrathymic tumour nodules, Pleural or pericardial' is 'Present'
Other nodules, lung intraparenchymal	Single selection value list: • Present (pM1b) • Not identified	
Other nodules, distant organ	Single selection value list: • Present (pM1b) • Not identified	
Other nodules, distant organ, specify	Free text	Only applicable if 'Other nodules, Distant organ' is 'Present'
Response to neoadjuvant therapy	Single selection value list: • N/A • Complete/near complete • Partial • None/minimal	N/A if 'Previous treatment (neoadjuvant chemotherapy/radiotherapy)' is 'No'
Margins, excision complete	Single selection value list: • Yes • No • Cannot be assessed	Only applicable if 'Residual invasive tumour type, components: Other' selected.
Margins, microscopic involvement	Single selection value list: • Yes • No	Only applicable if 'Margin, Excision complete' is Yes.
Margins, macroscopic involvement	Single selection value list: • Yes • No	Only applicable if 'Margin, Excision complete' is Yes.
Margins, site of involvement	Free text	Only applicable if 'Margin, Excision complete' is Yes.
Closest margin	Free text	Only applicable if 'Margin, Excision complete' is No.
Closest margin, distance	Size in mm	Only applicable if 'Margin, Excision complete' is No.

Element name	Values	Implementation comments
pT stage	Single selection value list: • X • 0 • 1 • 2 • 3 • 4	
pN stage	Single selection value list: • X • 0 • 1 • 2	
pM stage	Single selection value list: • No applicable • 1a • 1b	
TNM version	Single selection value list: • 8 • 9 • 10	
SNOMED Topography code	May have multiple codes. Look up from SNOMED tables.	
SNOMED Morphology code	May have multiple codes. Look up from SNOMED tables.	

Appendix G Reporting proforma for biopsy/cytology specimens of thymic epithelial tumours in list format

Element name	Values	Implementation comments
Previous treatment	Single selection value list: • Yes • No • Not known	
Origin of specimen	Multiple selection value list: • Thymus • Mediastinum, other than thymus NOS • Pleura • Lung • Other	Only applicable if ôSpecimens submitted, Great vesselsôis selected.
Origin of specimen, other	Free text	Only applicable if ôOrigin of specimen, Otherôis selected.
Sample type	Multiple selection value list: • Transthoracic needle biopsy • Incisional biopsy • Lymph node biopsy • Pleural biopsy • Other metastatic site(s) • Transthoracic FNA mediastinum • Pleural effusion • Cytology, other	
Lymph node biopsy, sites	Free text	Only applicable if ôSample type, Lymph node biopsyôis selected.
Other metastatic sites, details	Free text	Only applicable if ôSample type, Other metastatic site(s)ô is selected.
Cytology, other, specify	Free text	Only applicable if ôSample type, Cytology: Otherôis selected.
Histological type	Single selection value list: • Thymic epithelial tumour, not otherwise specified • WHO subtype present • Other tumour	

Element name	Values	Implementation comments
WHO subtype, specify	Free text	Only applicable if 'Histological type, WHO subtype present' is selected.
Other tumour type, specify	Free text	Only applicable if 'Histological type, Other tumour' is selected.
SNOMED Topography code	May have multiple codes. Look up from SNOMED tables.	
SNOMED Morphology code	May have multiple codes. Look up from SNOMED tables.	

Appendix H Summary table – explanation of levels of evidence

(modified from Palmer K *et al. BMJ* 2008; 337:1832)

Level of evidence	Nature of evidence
Level A	At least one high-quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target cancer type or A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type.
Level B	A body of evidence demonstrating consistency of results and comprising mainly high-quality systematic reviews of case-control or cohort studies and high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in A.
Level C	A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high-quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in B.
Level D	Non-analytic studies such as case reports, case series or expert opinion or Extrapolation evidence from studies described in C.
GPP	Recommended best practice based on the clinical experience of the authors of the writing group.

Appendix I AGREE compliance monitoring sheet

The cancer datasets of The Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines (www.agreetrust.org). The sections of this dataset that indicate compliance with each of the AGREE II standards are indicated in the table below.

AGREE standard	Section of guideline
Scope and purpose	
1 The overall objective(s) of the guideline is (are) specifically described	Foreword, 1
2 The health question(s) covered by the guideline is (are) specifically described	Foreword, 1
3 The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described	1
Stakeholder involvement	
4 The guideline development group includes individuals from all the relevant professional groups	Foreword
5 The views and preferences of the target population (patients, public, etc.) have been sought	Foreword
6 The target users of the guideline are clearly defined	1
Rigour of development	
7 Systematic methods were used to search for evidence	Foreword
8 The criteria for selecting the evidence are clearly described	Foreword
9 The strengths and limitations of the body of evidence are clearly described	Foreword, 1
10 The methods for formulating the recommendations are clearly described	Foreword
11 The health benefits, side effects and risks have been considered in formulating the recommendations	Foreword, 1
12 There is an explicit link between the recommendations and the supporting evidence	3ï 10
13 The guideline has been externally reviewed by experts prior to its publication	Foreword
14 A procedure for updating the guideline is provided	Foreword
Clarity of presentation	
15 The recommendations are specific and unambiguous	2ï 11
16 The different options for management of the condition or health issue are clearly presented	2ï 11
17 Key recommendations are easily identifiable	2ï 11
Applicability	
18 The guideline describes facilitators and barriers to its application	Foreword
19 The guideline provides advice and/or tools on how the recommendations can be put into practice	Appendices Aï G
20 The potential resource implications of applying the recommendations have been considered	Foreword
21 The guideline presents monitoring and/or auditing criteria	12
Editorial independence	
22 The views of the funding body have not influenced the content of the guideline	Foreword
23 Competing interest of guideline development group members have been recorded and addressed	Foreword