Protocol for the Examination of Specimens From Patients With Thymic Tumors

Version: 4.1.0.0
Protocol Posting Date: June 2021
CAP Laboratory Accreditation Program Protocol Required Use Date: March 2022
The changes included in this current protocol version affect accreditation requirements. The new deadline for implementing this protocol version is reflected in the above accreditation date.

For accreditation purposes, this protocol should be used for the following procedures AND tumor types:

Procedure	Description
Resection	Includes specimens designated thymectomy and partial thymectomy
Tumor Type	**Description**
Thymoma	
Carcinoma	Includes neuroendocrine carcinoma
Carcinoid tumor	

This protocol is NOT required for accreditation purposes for the following:

Procedure
Biopsy
Primary resection specimen with no residual cancer (eg, following neoadjuvant therapy)
Cytologic specimens

The following tumor types should NOT be reported using this protocol:

Tumor Type
Carcinoma not involving the thymus
Mediastinal germ cell tumors
Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)
Sarcoma (consider the Soft Tissue protocol)

Authors
Frank Schneider, MD*; Anja Roden, MD; Sanja Dacic, MD.

With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.
* Denotes primary author.

Replaced by version 5.0.0.0 on December 11, 2024, Obsolete as of September 2025 (8 months after newest release date)

Accreditation Requirements
This protocol can be utilized for a variety of procedures and tumor types for clinical care purposes. For accreditation purposes, only the definitive primary cancer resection specimen is required to have the core and conditional data elements reported in a synoptic format.

- Core data elements are required in reports to adequately describe appropriate malignancies. For accreditation purposes, essential data elements must be reported in all instances, even if the response is "not applicable" or "cannot be determined."
- Conditional data elements are only required to be reported if applicable as delineated in the protocol. For instance, the total number of lymph nodes examined must be reported, but only if nodes are present in the specimen.
- Optional data elements are identified with "+" and although not required for CAP accreditation purposes, may be considered for reporting as determined by local practice standards.

The use of this protocol is not required for recurrent tumors or for metastatic tumors that are resected at a different time than the primary tumor. Use of this protocol is also not required for pathology reviews performed at a second institution (ie, secondary consultation, second opinion, or review of outside case at second institution).

Synoptic Reporting
All core and conditionally required data elements outlined on the surgical case summary from this cancer protocol must be displayed in synoptic report format. Synoptic format is defined as:

- Data element: followed by its answer (response), outline format without the paired Data element: Response format is NOT considered synoptic.
- The data element should be represented in the report as it is listed in the case summary. The response for any data element may be modified from those listed in the case summary, including "Cannot be determined" if appropriate.
- Each diagnostic parameter pair (Data element: Response) is listed on a separate line or in a tabular format to achieve visual separation. The following exceptions are allowed to be listed on one line:
    - Anatomic site or specimen, laterality, and procedure
    - Pathologic Stage Classification (pTNM) elements
    - Negative margins, as long as all negative margins are specifically enumerated where applicable
- The synoptic portion of the report can appear in the diagnosis section of the pathology report, at the end of the report or in a separate section, but all Data element: Responses must be listed together in one location

Organizations and pathologists may choose to list the required elements in any order, use additional methods in order to enhance or achieve visual separation, or add optional items within the synoptic report. The report may have required elements in a summary format elsewhere in the report IN ADDITION TO but not as replacement for the synoptic report ie, all required elements must be in the synoptic portion of the report in the format defined above.

Summary of Changes

v 4.1.0.0

- General Reformatting
- New WHO 5th Edition Histological Updates
- Revised Margins Section
- Revised Lymph Nodes Section
- Added Distant Metastasis Section
- Removed pNX Staging Classification
- Added Modified Masaoka Stage

Reporting Template

Protocol Posting Date: June 2021
Select a single response unless otherwise indicated.

CASE SUMMARY: (THYMUS)
Standard(s): AJCC-UICC 8

SPECIMEN

Procedure
___ Thymectomy
___ Partial thymectomy
___ Other (specify): _____
___ Not specified

TUMOR

Tumor Site
___ Thymus
___ Other (specify): _____

Histologic Type (Note A)
Thymoma
___ Type A thymoma (including atypical subtype)
___ Type AB thymoma
___ Type B1 thymoma
___ Type B2 thymoma
___ Type B3 thymoma
___ Micronodular thymoma with lymphoid stroma
___ Metaplastic thymoma
___ Thymoma with more than one histological pattern
+Histological Patterns Present (may include percentages totaling 100%) (select all that apply)
___ A: _____ %
___ B1: _____ %
___ B2: _____ %
___ B3: _____ %
___ Other (specify): _____
Thymic Carcinoma
___ Squamous cell carcinoma
___ Basaloid carcinoma
___ Lymphoepithelial carcinoma
___ NUT carcinoma
___ Clear cell carcinoma
___ Low-grade papillary adenocarcinoma
___ Mucoepidermoid carcinoma
___ Thymic carcinoma with adenoid cystic carcinoma-like features
___ Enteric-type adenocarcinoma
___ Adenocarcinoma NOS

Replaced by version 5.0.0.0 on December 11, 2024, Obsolete as of September 2025 (8 months after newest release date)

___ Adenosquamous carcinoma
___ Sarcomatoid carcinoma
___ Undifferentiated carcinoma
___ Thymic carcinoma NOS
Thymic Neuroendocrine Tumors
___ Typical carcinoid / Neuroendocrine tumor, grade 1
___ Atypical carcinoid / Neuroendocrine tumor, grade 2
___ Large cell neuroendocrine carcinoma
___ Small cell carcinoma
___ Other histologic type not listed (specify): _____
___ Cannot be determined (explain): _____
+Histologic Type Comment: _____

Tumor Size
___ Greatest dimension in Centimeters (cm): _____ cm
+Additional Dimension in Centimeters (cm): ____ x ____ cm
___ Cannot be determined (explain): _____

Lymphovascular Invasion
___ Not identified
___ Present
___ Cannot be determined: _____

Treatment Effect
___ No known presurgical therapy
___ Not identified
___ Present
Percentage of Residual Viable Tumor
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined: _____
___ Cannot be determined: _____

Site(s) Involved by Direct Tumor Invasion (select all that apply)
___ Encapsulated tumor or capsule missing but without invasion into surrounding tissue
___ Microscopic transcapsular invasion into thymic or perithymic fat
___ Macroscopic invasion into thymic or perithymic fat
___ Confined to thymus
___ Invades mediastinal pleura
___ Invades pericardium
___ Invades diaphragm
___ Lung (specify lobe(s) involved): _____
___ Brachiocephalic vein
___ Superior vena cava
___ Phrenic nerve
___ Chest wall
___ Extrapericardial pulmonary artery
___ Extrapericardial pulmonary veins
___ Ascending aorta

Replaced by version 5.0.0.0 on December 11, 2024, Obsolete as of September 2025 (8 months after newest release date)

___ Aortic arch
___ Descending aorta
___ Arch vessels
___ Intrapericardial pulmonary artery
___ Myocardium
___ Trachea
___ Esophagus
___ Other (specify): _____
___ Cannot be determined: _____
___ Not applicable: _____
___ No evidence of primary tumor

+Tumor Comment: _____

MARGINS (Note B)

Margin Status
___ All margins negative for tumor
Distance from Tumor to Closest Margin
Specify in Millimeters (mm)
___ Exact distance: _____ mm
___ Greater than: _____ mm
___ At least: _____ mm
___ Less than: _____ mm
___ Less than 1 mm
___ Other (specify): _____
___ Cannot be determined (explain): _____
___ Tumor present at margin
Margin(s) Involved by Tumor
___ Specify involved margin(s): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____
___ Not applicable

+Margin Comment: _____

REGIONAL LYMPH NODES

Regional Lymph Node Status
___ Not applicable (no regional lymph nodes submitted or found)
___ Regional lymph nodes present
___ All regional lymph nodes negative for tumor
___ Tumor present in regional lymph node(s)
Number of Lymph Nodes with Tumor
___ Exact number (specify): _____
___ At least (specify): _____
___ Other (specify): _____

___ Cannot be determined (explain): _____

Nodal Site(s) with Tumor (select all that apply)

___ Anterior (perithymic): _____
___ Deep intrathoracic: _____
___ Cervical: _____
___ Other (specify): _____
___ Cannot be determined: _____

___ Other (specify): _____
___ Cannot be determined (explain): _____

Number of Lymph Nodes Examined

___ Exact number (specify): _____
___ At least (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Regional Lymph Node Comment: _____

DISTANT METASTASIS

Distant Site(s) Involved, if applicable (select all that apply)

___ Not applicable
___ Pleural metastasis: _____
___ Pericardial metastasis: _____
___ Pleural nodule(s): _____
___ Pericardial nodule(s): _____
___ Intraparenchymal pulmonary nodule(s): _____
___ Other distant organs (specify): _____
___ Cannot be determined: _____

PATHOLOGIC STAGE CLASSIFICATION (pTNM, AJCC 8th Edition) (Note C)

Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. As per the AJCC (Chapter 1, 8th Ed.) it is the managing physician's responsibility to establish the final pathologic stage based upon all pertinent information, including but potentially not limited to this pathology report.
Involvement must be microscopically confirmed in pathological staging, if possible.

TNM Descriptors (select all that apply)

___ Not applicable: _____
___ m (multiple primary tumors)
___ r (recurrent)
___ y (post-treatment)

pT Category

T categories are defined by "levels" of invasion; they reflect the highest degree of invasion regardless of how many other (lower-level) structures are invaded. T1, level 1 structures: thymus, anterior mediastinal fat, mediastinal pleura; T2, level 2 structures: pericardium; T3, level 3 structures: lung, brachiocephalic vein, superior vena cava, phrenic nerve, chest wall, hilar pulmonary vessels; T4, level 4 structures: aorta (ascending, arch, or descending), arch vessels, intrapericardial pulmonary artery, myocardium, trachea, esophagus.

___ pT not assigned (cannot be determined based on available pathological information)
___ pT0: No evidence of primary tumor

pT1: Tumor encapsulated or extending into the mediastinal fat; may involve the mediastinal pleura

___ pT1a: Tumor with no mediastinal pleura involvement

___ pT1b: Tumor with direct invasion of mediastinal pleura
___ pT1 (subcategory cannot be determined)
___ pT2: Tumor with direct invasion of the pericardium (either partial or full thickness)
___ pT3: 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
___ pT4: Tumor with invasion into any of the following: aorta (ascending, arch, or descending), arch vessels, intrapericardial pulmonary artery, myocardium, trachea, esophagus

pN Category
___ pN not assigned (no nodes submitted or found)
___ pN not assigned (cannot be determined based on available pathological information)
___ pN0: No regional lymph node metastasis
___ pN1: Metastasis in anterior (perithymic) lymph nodes
___ pN2: Metastasis in deep intrathoracic or cervical lymph nodes

pM Category (required only if confirmed pathologically)
___ Not applicable - pM cannot be determined from the submitted specimen(s)
pM1: Pleural, pericardial, or distant metastasis
___ pM1a: Separate pleural or pericardial nodule(s)
___ pM1b: Pulmonary intraparenchymal nodule or distant organ metastasis
___ pM1 (subcategory cannot be determined)

+Modified Masaoka Stage (applies only to thymomas in addition to TNM categories)
___ Stage I: Grossly and microscopically encapsulated (includes microscopic invasion into, but not through, the capsule)
___ Stage IIa: Microscopic transcapsular invasion
___ Stage IIb: Macroscopic capsular invasion into thymic or perithymic fat, or grossly adherent to, but not breaking through, mediastinal pleura or pericardium
___ Stage III: Macroscopic invasion of neighboring organs
+Great Vessel Involvement
___ Not identified
___ Present
___ Cannot be determined: _____
___ Stage IVa: Pleural or pericardial dissemination
___ Stage IVb: Hematogenous or lymphatic dissemination
___ Cannot be determined: _____

ADDITIONAL FINDINGS

+Additional Findings (select all that apply)
___ Age-appropriate involutional changes
___ Fibrosis
___ Follicular thymic hyperplasia
___ Epithelial thymic hyperplasia
___ True thymic hyperplasia
___ Cystic changes in tumor
___ Cystic changes in adjacent thymus
___ Other (specify): _____

SPECIAL STUDIES (Note D)

+Immunohistochemistry (specify stains and results): _____

COMMENTS

Comment(s): _____

Explanatory Notes

A. Histologic Type

For consistency in reporting, the histologic classification published by the World Health Organization (WHO) for tumors of the thymus is recommended.[1]

Type A, AB, and B thymomas show thymic architectural features.[1] Sclerosing thymoma was removed from the fifth edition of the WHO classification because it is thought to represent sclerotic changes in various types of thymomas rather than a distinctive form of thymoma. The protocol now supports reporting of thymomas exhibiting more than one histological pattern. It is recommended that the diagnosis lists the predominant histological pattern observed, followed by minor components (e.g., "thymoma, with type B2 (80%) and type B3 (20%) components".[1] However, type AB thymoma should be reported as such and not divided into type A and type B components. Thymic carcinomas are a heterogeneous group of malignant epithelial tumors with diverse morphology showing morphologies that resemble carcinomas encountered outside the thymus.[1] The nomenclature and diagnostic criteria for thymic neuroendocrine tumors (typical and atypical carcinoids, large cell neuroendocrine carcinoma [LCNEC], and small cell carcinoma) are retained from previous editions of the WHO classification.[1,2] The descriptive terms "well-differentiated neuroendocrine carcinoma" (referring to carcinoids) and "poorly differentiated neuroendocrine carcinoma" (referring to LCNEC and small cell carcinoma) should not be used.[1,2]

References

1. WHO Classification of Tumours Editorial Board. *Thoracic tumours*. Lyon (France): International Agency for Research on Cancer; 2021. (WHO classification of tumours series, 5th ed.; vol. 5). https://publications.iarc.fr/595.
2. Marx A, Chan JK, Coindre JM, Detterbeck F, et al. The 2015 World Health Organization Classification of Tumors of the Thymus: Continuity and Changes. *J Thorac Oncol.* 2015;10(10):1383-1395.

B. Margins

Thymectomy involves dissection and mobilization of the thymus from the pericardium and mediastinal pleura. In most thymectomy specimens, the posterior surface constitutes a true margin. Unless it has been marked by the surgeon, the posterior surface of thymectomy specimens is difficult to locate. If the completeness of excision is in question, the orientation of the specimen should be confirmed by the surgeon before grossing, and all surgical margins inked. In addition to thymus, some specimens also include attached neighboring structures (eg, pleura, pericardium, lung). The margins of any attached structures should be properly identified by the surgeon and inked to facilitate accurate histologic assessment of margin status. In addition to tumor stage and histologic type, completeness of resection is an important prognostic parameter.[1,2]

References

1. Huang J, Detterbeck FC, Wang Z, Loehrer PJ Sr. Standard outcome measures for thymic malignancies. *J Thorac Oncol.* 2010;5(12):2017-2023.
2. Detterbeck FC, Moran C, Huang J, et al. Which way is up?: policies and procedures for surgeons and pathologists regarding resection specimens of thymic malignancy. *J Thorac Oncol.* 2011;6(7 Suppl 3):S1730.

C. Pathologic Staging of Thymic Epithelial Neoplasms

The 8th edition of the AJCC staging manual introduced a TNM classification and staging system for thymic tumors. It includes thymoma, thymic carcinoma, thymic neuroendocrine tumors, and combined thymic carcinoma. The AJCC staging is based on the proposal by the International Association for the Study of

Lung Cancer (IASLC) and the International Thymic Malignancy Interest Group (ITMIG) that is founded on the analyses of an international database with 10,808 patients from 105 sites.[1,2,3]

The Masaoka-Koga system is the most frequently used staging system for thymic neoplasms.[4,5,6] However, there are significant discrepancies in the interpretation of ambiguously defined criteria between different institutions. Classification of a thymoma according to the Masaoka-Koga system should always be accompanied by (and does not replace) TNM classification.

The modified Masaoka staging scheme requires assessment of capsular invasion and invasion of adjacent structures. Encapsulated thymomas are completely surrounded by a fibrous capsule of variable thickness. Tumors that invade into, but not through, the capsule should still be considered encapsulated. Assessment of capsular invasion is sometimes difficult, because a capsule may be either partially or entirely lacking in some thymomas and in a substantial proportion of thymic carcinomas.

Adherence to pleura or pericardium is interpreted by the ITMIG as, "making removal of these [structures] necessary during resection, with microscopic confirmation of perithymic invasion, but without microscopic extension into or through the mediastinal pleura or into the fibrous layer of the pericardium."[6] Areas of tumor adherence to mediastinal or other structures could be the result of tumor invasion or only chronic inflammation with fibrosis.

There are currently not enough data to support a particular T category for thymomas extending directly into the diaphragm because they are exceedingly rare. Until this situation is revisited in an upcoming edition of the AJCC Staging Manual, it is probably best subsumed under chest wall invasion and classified T3.

References

1. Detterbeck FC, Asamura H, Crowley J, et al. The IASLC/ITMIG thymic malignancies staging project: development of a stage classification for thymic malignancies. *J Thorac Oncol.* 2013;8(12):1467-1473.
2. Detterbeck FC, Stratton K, Giroux D, et al. The IASLC/ITMIG Thymic Epithelial Tumors Staging Project: proposal for an evidence-based stage classification system for the forthcoming (8th) edition of the TNM classification of malignant tumors. *J Thorac Oncol.* 2014;9(9 Suppl 2):S65-S72.
3. Nicholson AG, Detterbeck FC, Marino M, et al. The IASLC/ITMIG Thymic Epithelial Tumors Staging Project: proposals for the T component for the forthcoming (8th) edition of the TNM classification of malignant tumors. *J Thorac Oncol.* 2014;9(9 Suppl 2):S73-S80.
4. Masaoka A, Monden Y, Nakahara K, Tanioka T. Follow-up study of thymomas with special reference to their clinical stages. *Cancer*. 1981;48:2485-2492.
5. Koga K, Matsuno Y, Noguchi M, et al. A review of 79 thymomas: modification of staging system and reappraisal of conventional division into invasive and non-invasive thymoma. *Pathol Int.* 1994;44:359-367.
6. Detterbeck FC, Nicholson AG, Kondo K, Van Schil P, Moran C. The Masaoka-Koga stage classification for thymic malignancies and definition of terms. *J Thorac Oncol.* 2011;6(7 Suppl 3);S1710-S1716.

D. Ancillary Studies

Ancillary studies, such as immunohistochemistry, are often employed in the diagnosis of thymic epithelial neoplasms. The types of ancillary studies utilized vary with the histologic appearance of the tumor. Immunostaining for cytokeratins is helpful in distinguishing between thymomas and lymphoid lesions. In selected cases, the use of immunohistochemistry for CD1a and terminal deoxynucleotidyl transferase (TdT) may be helpful in defining the cortical thymocyte phenotype of thymoma, as distinguished from the typical

peripheral T-cell phenotype of tumor-infiltrating lymphocytes associated with other tumors. CD5, CD117, and MUC1 are expressed in about 70% of all thymic carcinomas and in about 80% of thymic squamous cell carcinomas, and may potentially be helpful in separating thymic carcinoma from thymoma. It should be noted that about 3% of thymomas, particularly B3 type, may express CD5 and CD117.[1,2] Pax8 immunohistochemical staining in thymic epithelial tumors is commonly seen with polyclonal, but not monoclonal, Pax8 antibodies.[3] Immunostains for human chorionic gonadotropin (HCG), placental alkaline phosphatase (PLAP), carcinoembryonic antigen (CEA), α-fetoprotein, SALL4, OCT4, and CD30 are helpful in differentiating between thymic carcinomas and mediastinal germ cell tumors. The diagnosis of NUT carcinoma is confirmed by immunohistochemical, FISH, or molecular studies.[1]

References

1. WHO Classification of Tumours Editorial Board. *Thoracic tumours*. Lyon (France): International Agency for Research on Cancer; 2021. (WHO classification of tumours series, 5th ed.; vol. 5). https://publications.iarc.fr/595.
2. Marx A, Chan JK, Coindre JM, Detterbeck F, et al. The 2015 World Health Organization Classification of Tumors of the Thymus: Continuity and Changes. *J Thorac Oncol.* 2015;10(10):1383-1395.
3. Weissferdt A, Moran CA. Pax8 expression in thymic epithelial neoplasms: an immunohistochemical analysis. *Am J Surg Pathol*. 2011 Sep;35(9):1305-1310.