

Protocol for the Examination of Specimens from Patients with Thymoma and Thymic Carcinoma

Protocol applies to thymic epithelial tumors located in any area of the mediastinum.

No AJCC/UICC TNM Staging System

Protocol web posting date: October 2009

Procedure

- Resection

Authors

Kelly J. Butnor, MD, FCAP*

Department of Pathology and Laboratory Medicine, Fletcher Allen Health Care/University of Vermont, Burlington, Vermont

Mary Beth Beasley, MD, FCAP

Department of Pathology, Mt. Sinai Medical Center, New York, New York

Feng-Ming Kong, MD, PhD, MPH

Veterans Administration Health Center/University of Michigan, Ann Arbor, Michigan

Alberto Marchevsky, MD, FCAP

Department of Pathology, Cedars-Sinai Medical Center, Los Angeles, California

Robert J. McKenna, MD

Department of Thoracic Surgery, Cedars-Sinai Medical Center, Los Angeles, California

Nader T. Okby, MD, FCAP

Orange Pathology Associates, Orange Regional Medical Center, Middletown, New York

Victor L. Roggli, MD, FCAP

Department of Pathology, Duke University Medical Center, Durham, North Carolina

Henry D. Tazelaar, MD, FCAP

Department of Laboratory Medicine and Pathology, Mayo Clinic Scottsdale, Scottsdale, Arizona

William D. Travis, MD, FCAP

Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, New York

Saul Suster, MD, FCAP

Department of Pathology, The Medical College of Wisconsin, Milwaukee, Wisconsin

For the Members of the Cancer Committee, College of American Pathologists

*denotes primary author

Previous lead contributors: Alberto Marchevsky, MD; M. Elizabeth H. Hammond, MD; Cesar Moran, MD; Saul Suster, MD

© 2009 College of American Pathologists (CAP). All rights reserved.

The College does not permit reproduction of any substantial portion of these protocols without its written authorization. The College hereby authorizes use of these protocols by physicians and other health care providers in reporting on surgical specimens, in teaching, and in carrying out medical research for nonprofit purposes. This authorization does not extend to reproduction or other use of any substantial portion of these protocols for commercial purposes without the written consent of the College.

The CAP also authorizes physicians and other health care practitioners to make modified versions of the Protocols solely for their individual use in reporting on surgical specimens for individual patients, teaching, and carrying out medical research for non-profit purposes.

The CAP further authorizes the following uses by physicians and other health care practitioners, in reporting on surgical specimens for individual patients, in teaching, and in carrying out medical research for non-profit purposes: (1) **Dictation** from the original or modified protocols for the purposes of creating a text-based patient record on paper, or in a word processing document; (2) **Copying** from the original or modified protocols into a text-based patient record on paper, or in a word processing document; (3) The use of a **computerized system** for items (1) and (2), provided that the Protocol data is stored intact as a single text-based document, and is not stored as multiple discrete data fields.

Other than uses (1), (2), and (3) above, the CAP does not authorize any use of the Protocols in electronic medical records systems, pathology informatics systems, cancer registry computer systems, computerized databases, mappings between coding works, or any computerized system without a written license from CAP. Applications for such a license should be addressed to the SNOMED Terminology Solutions division of the CAP.

Any public dissemination of the original or modified Protocols is prohibited without a written license from the CAP.

The College of American Pathologists offers these protocols to assist pathologists in providing clinically useful and relevant information when reporting results of surgical specimen examinations of surgical specimens. The College regards the reporting elements in the “Surgical Pathology Cancer Case Summary (Checklist)” portion of the protocols as essential elements of the pathology report. However, the manner in which these elements are reported is at the discretion of each specific pathologist, taking into account clinician preferences, institutional policies, and individual practice.

The College developed these protocols as an educational tool to assist pathologists in the useful reporting of relevant information. It did not issue the protocols for use in litigation, reimbursement, or other contexts. Nevertheless, the College recognizes that the protocols might be used by hospitals, attorneys, payers, and others. Indeed, effective January 1, 2004, the Commission on Cancer of the American College of Surgeons mandated the use of the checklist elements of the protocols as part of its Cancer Program Standards for Approved Cancer Programs. Therefore, it becomes even more important for pathologists to familiarize themselves with these documents. At the same time, the College cautions that use of the protocols other than for their intended educational purpose may involve additional considerations that are beyond the scope of this document.

The inclusion of a product name or service in a CAP publication should not be construed as an endorsement of such product or service, nor is failure to include the name of a product or service to be construed as disapproval.

Surgical Pathology Cancer Case Summary (Checklist)

Protocol web posting date: October 2009

THYMUS: Resection

Select a single response unless otherwise indicated.

Specimen

- ☐ Thymus
- ☐ Thymus and other (specify): _____
- ☐ Not specified

Procedure

- ☐ Thymectomy
- ☐ Partial thymectomy
- ☐ Other (specify): _____
- ☐ Not specified

Specimen Integrity

- ☐ Intact
- ☐ Disrupted
- ☐ Indeterminate

Specimen Weight

Specify: ____ grams

Tumor Size

Greatest dimension: ____ cm

*Additional dimensions: ____ x ____ cm

☐ Cannot be determined (see Comment)

Histologic Type (Note A)

Thymoma, specify:

- ☐ Type A thymoma
- ☐ Type AB thymoma
- ☐ Type B1 thymoma
- ☐ Type B2 thymoma
- ☐ Type B3 thymoma
- ☐ Other (specify): _____

Thymic carcinoma, specify:

- ☐ Squamous cell carcinoma
- ☐ Basaloid carcinoma
- ☐ Mucoepidermoid carcinoma
- ☐ Lymphoepithelioma-like carcinoma
- ☐ Sarcomatoid carcinoma

* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

- ☐ Clear cell carcinoma
- ☐ Adenocarcinoma
- ☐ Well-differentiated neuroendocrine carcinoma, typical carcinoid
- ☐ Well-differentiated neuroendocrine carcinoma, atypical carcinoid
- ☐ Poorly differentiated neuroendocrine carcinoma, large cell neuroendocrine carcinoma
- ☐ Poorly differentiated neuroendocrine carcinoma, small cell carcinoma, neuroendocrine type
- ☐ Other (specify): _____

Other (specify): _____

Tumor Extension (select all that apply)

- ☐ Not applicable
- ☐ Not identified
- ☐ Cannot be assessed
- ☐ Pulmonary parenchyma
 - *Specify lobe(s) of lung: _____
- ☐ Pleura
 - *Specify location: _____
- ☐ Pericardium
- ☐ Diaphragm
- ☐ Other (specify): _____

Margins (Note B)

- ☐ Cannot be assessed
- ☐ Margins uninvolved by tumor
 - Distance of tumor from closest margin: ____ mm
- ☐ Margin(s) involved by tumor
 - Specify margin(s): _____

Treatment Effect

- ☐ Not applicable
- ☐ Cannot be determined
- ☐ Not identified
- ☐ Present (specify: ____% residual viable tumor)

Lymph-Vascular Invasion

- ☐ Not identified
- ☐ Present
- ☐ Indeterminate

Regional Lymph Nodes

- ☐ Cannot be assessed
 - ☐ No regional lymph node metastasis
 - ☐ Regional lymph node metastasis
- Specify: Number examined: ____
Number involved: ____

* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

Pathologic Staging for Thymomas (Modified Masaoka Stage) (applies only to thymomas) (Note C)

- ☐ 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
- ☐ Stage III: Macroscopic invasion of neighboring organs
- ☐ Stage IVa: Pleural or pericardial dissemination
- ☐ Stage IVb: Hematogenous or lymphatic dissemination
- ☐ Cannot be determined

Implants/Distant Metastasis (select all that apply) (Note D)

- ☐ Cannot be assessed
- ☐ Not identified
- ☐ Present
- Specify site(s):
- ☐ Pleura
- ☐ Pericardium
- ☐ Other (specify) _____

Pathologic Staging for Thymic Carcinomas (pTNM) (does not apply to thymomas) (Note C)TNM Descriptors (required only if applicable) (select all that apply)

- ☐ m (multiple primary tumors)
- ☐ r (recurrent)
- ☐ y (post-treatment)

Primary Tumor (pT)

- ☐ pTX: Primary tumor cannot be assessed
- ☐ pT0: No evidence of primary tumor
- ☐ pT1: Tumor completely encapsulated
- ☐ pT2: Tumor invades pericapsular connective tissue
- ☐ pT3: Tumor invades neighboring structures, such as pericardium, mediastinal pleura, thoracic wall, great vessels, and lung
- ☐ pT4: Tumor with pleural or pericardial dissemination

Regional Lymph Nodes (pN)

- ☐ pNX: Regional lymph nodes cannot be assessed
- ☐ pN0: No regional lymph node metastases
- ☐ pN1: Metastasis in anterior mediastinal lymph nodes
- ☐ pN2: Metastasis in other intrathoracic lymph nodes, excluding anterior mediastinal lymph nodes
- ☐ pN3: Metastasis in scalene and/or supraclavicular lymph nodes

Distant Metastasis (pM)

- ☐ Not applicable
- ☐ pM1: Distant metastasis
- *Specify site(s), if known: _____

* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

***Additional Pathologic Findings (select all that apply)**

- * ☐ Age-appropriate involution changes
- * ☐ Fibrosis
- * ☐ Cortical hyperplasia
- * ☐ Cystic changes in tumor
- * ☐ Cystic changes in adjacent thymus
- * ☐ Other (specify): _____

***Ancillary Studies (Note E)**

- * ☐ Immunohistochemical staining
 - *Specify results: _____

***Comment(s)**

* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

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 The histologic types are listed in this protocol in the order they appear in the WHO classification. Difficulties in diagnostic reproducibility have been encountered with the WHO classification scheme and this protocol does not preclude the use of other systems of classification of histologic types.^{2,3}

Type A, AB, and B thymomas show thymic architectural features.¹ Thymic carcinomas are a heterogeneous group of malignant epithelial tumors with diverse morphology showing morphologies that resemble carcinomas encountered outside the thymus (designated type C thymomas in the previous WHO classification).¹ Because thymic carcinoids have the capacity to recur and metastasize, they are classified as neuroendocrine carcinomas.^{1,4}

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

C. Pathologic Staging of Thymic Epithelial Neoplasms

No TNM protocol has been officially authorized by the American Joint Committee on Cancer (AJCC) or the International Union Against Cancer (UICC) for the staging of thymic epithelial neoplasms. The scheme developed by Masaoka for thymoma and revised by others is frequently used for staging.⁵⁻⁸ A tentative classification for thymic carcinoma and other malignant thymic epithelial tumors appeared in the UICC TNM Supplement.⁹

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. Minimally invasive tumors are those that focally invade through the capsule (ie, transcapsular invasion) into the mediastinal fat, whereas widely invasive tumors directly extend into adjacent structures such as the lung or pericardium.¹

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.¹ Areas of adherence to other mediastinal structures may be the only indication of capsular penetration by tumor and hence the only indicator of aggressive

behavior. However, adherence to adjacent structures does not necessarily indicate invasion. Such areas should be carefully sampled. Uncertainties regarding the nature and degree of capsular adherence should be discussed with the surgeon. Any areas of macroscopic adherence or foci otherwise deemed suggestive of invasion should be sampled and evaluated histologically.

D. Implants and Distant Metastases

Thymomas sometimes exhibit tumor nodules separate from the main mass on the pericardial or pleural surface that have been referred to as implants by the WHO.¹ The WHO designates distant metastases as metastases to distant sites, most commonly the lung, liver, and skeletal system. From a practical standpoint, there are no reliable morphologic criteria for determining whether dissemination to the pericardium and/or pleura represents implants or metastatic disease. For this reason, these items are incorporated into a single heading in this protocol.

It is important to note that metastases to lymph nodes or local extension into adjacent organs are not included under the heading of distant metastases, but instead are reflected in the pN category and under the tumor extension section, respectively.¹

E. 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 reactivity can be somewhat helpful in separating thymic carcinoma from thymoma and other tumors that have a tendency to involve the mediastinum, but it should be noted that some B3 thymomas express CD5.¹⁰⁻¹² Immunostains for human chorionic gonadotropin (HCG), placental alkaline phosphatase (PLAP), carcinoembryonic antigen (CEA), and α -fetoprotein are helpful in differentiating among thymic carcinomas and mediastinal germ cell tumors.

References

1. Travis WD, Brambilla E, Muller-Hermelink HK, Harris CC, eds. *World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of the Lung, Pleura, Thymus and Heart*. Lyon, France: IARC Press; 2004.
2. Suster S, Moran CA. Problem areas and inconsistencies in the WHO classification of thymoma. *Semin Diagn Pathol*. 2005;22:188-197.
3. Suster S, Moran CA. Thymoma classification: current status and future trends. *Am J Clin Pathol*. 2006;125:542-554.
4. Moran CA, Suster S. Neuroendocrine carcinomas of the thymus (thymic carcinoid): clinicopathologic study of 80 cases with a proposal for histologic grading and clinical staging. *Am J Clin Pathol*. 2000;114:100-110.
5. 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.

6. 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.
7. Tsuchiya R, Koga K, Matsuno Y, et al. Thymic carcinoma: proposal for pathological TNM and staging. *Pathol Int.* 1994;44:505-512.
8. Yamakawa Y, Masaoka A, Hashimoto T, et al. A tentative tumor-node-metastasis classification of thymoma. *Cancer.* 1991;68:1984-1987.
9. International Union Against Cancer (UICC). *TNM Supplement: A Commentary on Uniform Use.* 3rd ed. New York: Wiley-Liss; 2003.
10. Tateyama H, Eimoto T, Tada T, et al. Immunoreactivity of a new CD5 antibody with normal epithelium and malignant tumors including thymic carcinoma. *Am J Clin Pathol.* 199;111:235-240.
11. Dorfman DM, Shahsafaei A, Chan JK. Thymic carcinomas, but not thymomas and carcinomas of other sites, show CD5 immunoreactivity. *Am J Surg Pathol.* 1997;21:936-940.
12. Alexiev BA, Drachenberg CB, Burke AP. Thymomas: a cytological and immunohistochemical study, with emphasis on lymphoid and neuroendocrine markers. *Diagn Pathol.* 2007;2:13.