



Standard Definitions and Polices

Institutional Kit of Specialty-Specific Summary Sheets



Introduction to Institutional Summary Kits of ITMIG Standard Definitions and Policies

Thymic malignancies are relatively uncommon, making it imperative to be able to pool data from different institutions. This requires a consistent definition of terms, standardization of basic practices and a consistent baseline for reporting outcomes. The International Thymic Malignancy Interest Group (ITMIG) has developed a set of consensus definitions which have been widely endorsed by thymic experts throughout the world. The full series of articles are available as a series of papers in the Journal of Thoracic Oncology, 2011, Volume 7, Supplement 3 (http://www.itmig.org/?page_id=315).

In order to have the salient points available at the time they are needed, ITMIG has assembled a series of summary sheets, specifically geared towards different specialties. This document is set up for double-sided printing. Ideally the relevant portions would be distributed to the respective specialists at an institution to facilitate clear communication within an institution as well as internationally. Alternatively individual portions can be downloaded as needed.

ITMIG has also developed laminated plastic sheets designed so that the surgeon can place a resected specimen on it, with an accompanying drawing on paper, in order to facilitate communication with the pathologist. The instructions in the surgeon's packet and the pathologist's packet provide guidance for consistent handling and reporting for those unfamiliar with the routine.

An entire Institutional Kit including 10 laminated sheets is available from ITMIG (www.itmig.org by contacting Pam Bruce pbruce@thymic.org). We have attempted to anticipate the needs of a moderate sized institution over the course of a year. Packets of laminated sheets are also available separately from ITMIG on request. We hope you will find this useful, and we believe this will foster better care and scientific advancement for patients with thymic malignancies.

With warm regards,

Jess Schwartz and Frank Detterbeck

Overview of Institutional Kits: ITMIG Standard Definitions and Policies

Cover Page

ITMIG Staging Kit

ITMIG Surgeon Kit

Mediastinal Diagram (paper)

Mediastinal Diagram (laminated plastic)

ITMIG Pathologist Kit

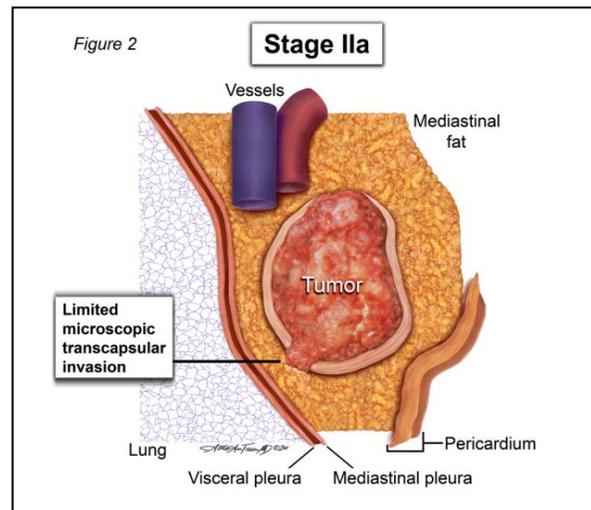
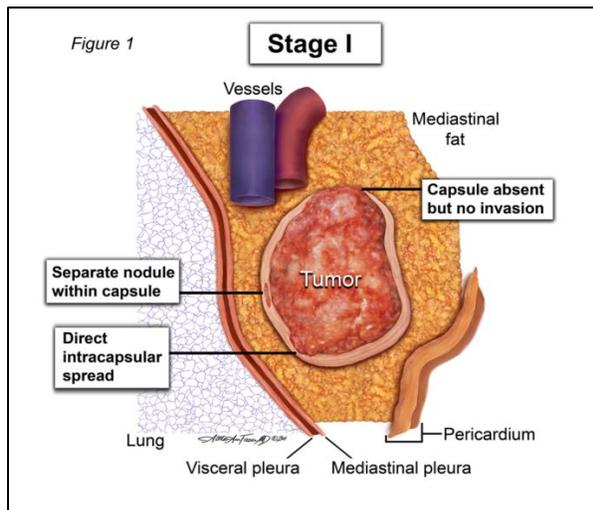
ITMIG CT Imaging Kit

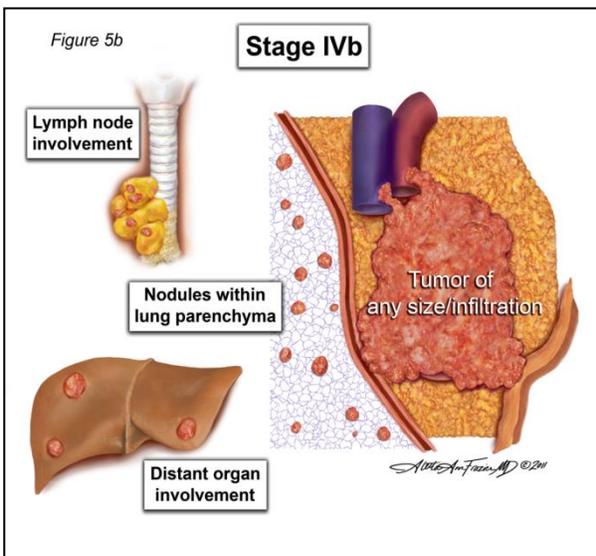
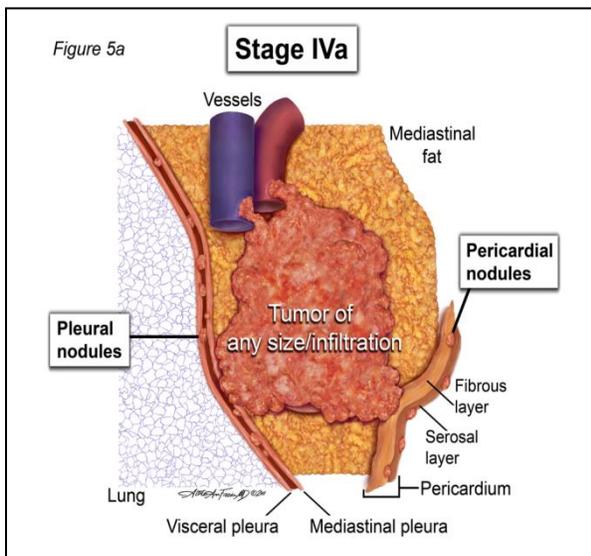
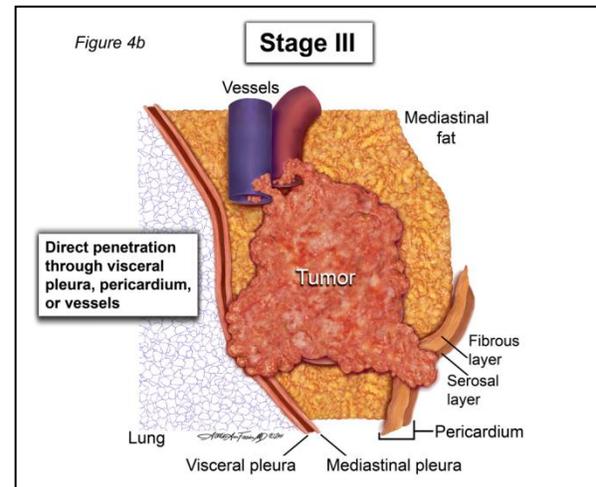
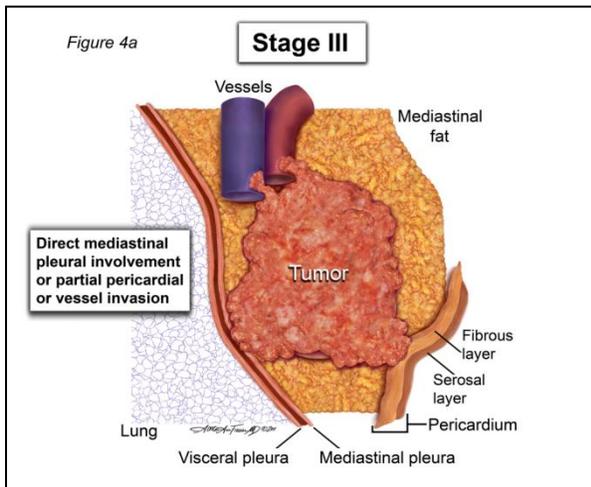
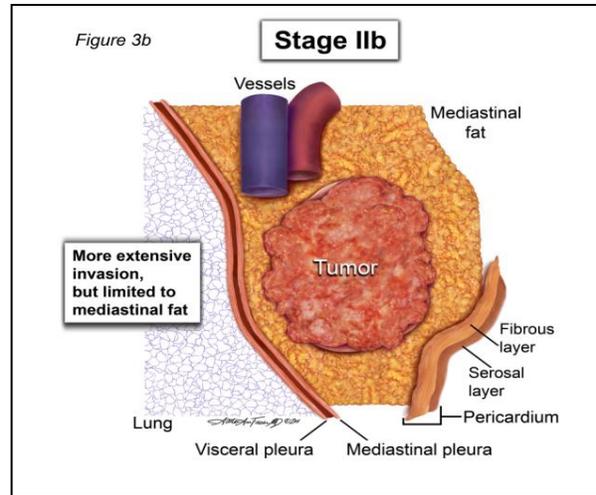
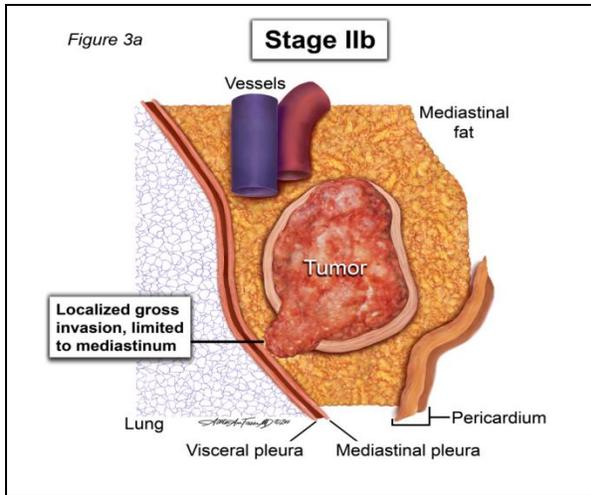
ITMIG Radiation Oncologist Kit

ITMIG Medical Oncologist Kit

ITMIG Staging Kit: Masaoka-Koga Staging System (with ITMIG Definition of Details)

Stage	Definition
I	Grossly and microscopically completely encapsulated tumor <i>This includes tumors with invasion into but not through the capsule, or ... Tumors in which the capsule is missing but without invasion into surrounding tissues</i>
II a	Microscopic transcapsular invasion <i>Microscopic transcapsular invasion (not grossly appreciated)</i>
b	Macroscopic invasion into thymic or surrounding fatty tissue, or grossly adherent to but not breaking through mediastinal pleura or pericardium <i>Gross visual tumor extension into normal thymus or perithymic fat surrounding the thymoma (microscopically confirmed), or ... Adherence to pleura or pericardium 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)</i>
III	Macroscopic invasion into neighboring organ (i.e. pericardium, great vessel or lung) <i>This includes extension of the primary tumor to any of the following tissues: Microscopic involvement of mediastinal pleura (either partial or penetrating the elastin layer); or ... Microscopic involvement of the pericardium (either partial in the fibrous layer or penetrating through to the serosal layer); or ... Microscopically confirmed direct penetration into the outer elastin layer of the visceral pleura or into the lung parenchyma; or ... Invasion into the phrenic or vagus nerves (microscopically confirmed, adherence alone is not sufficient); or ... Invasion into or penetration through major vascular structures (microscopically confirmed); Adherence (i.e. fibrous attachment) of lung or adjacent organs only if there is mediastinal pleural or pericardial invasion (microscopically confirmed)</i>
IV a	Pleural or pericardial metastases <i>Microscopically confirmed nodules, separate from the primary tumor, involving the visceral or parietal pleural surfaces, or the pericardial or epicardial surfaces,</i>
b	Lymphogenous or hematogenous metastasis <i>Any nodal involvement (e.g. anterior mediastinal, intrathoracic, low/anterior cervical nodes, any other extrathoracic nodes) Distant metastases (i.e. extrathoracic and outside the cervical perithymic region) or pulmonary parenchymal nodules (not a pleural implant)</i>





Reference: Detterbeck F, Nicholson A, Kondo K et al. The Masaoka-Koga Stage Classification for Thymic Malignancies: Clarification and Definition of Terms. J Thorac Oncol 2011;6(7,Suppl 3):S1710-6
 Available for download at: http://www.itmig.org/?page_id=315

ITMIG Surgeon Kit

Intraoperative Policies for the Surgeon during Resection:

Marking

- Mark areas of concern immediately upon dissection, both on the specimen and in the patient
- Routinely mark a representative area adjacent to the pericardium and innominate vein (or mark these structures if resected)
- Routinely mark right/left mediastinal pleural surfaces (if resected)
- Mark a representative area adjacent to the SVC, if the tumor is nearby
- Place marking stitches through loose tissue as well as into more substantial deeper tissue in order to prevent tissue disruption

Orientation

- The surgeon should be involved with orientation of the specimen
- The surgeon should either orient the specimen together with the pathologist or use a system of communicating the orientation of the specimen to the pathologist
- Orienting the unfurled specimen on a mediastinal board or diagram is encouraged
- A digital photo of the mounted specimen is encouraged
- A sketch of the specimen with adjacent structures and marking stitches is encouraged

Lymph Nodes

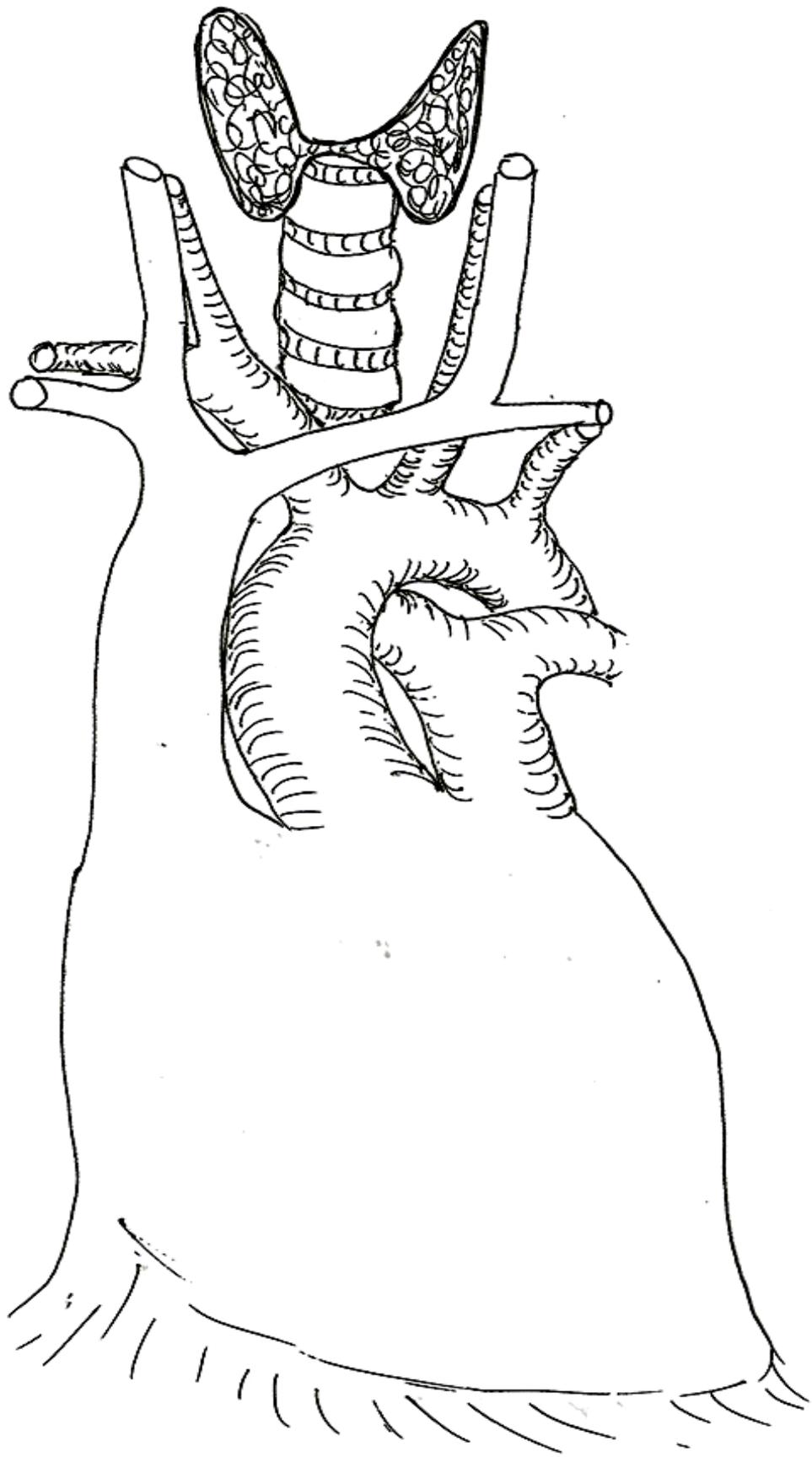
- Any suspicious nodes should be routinely removed in patients with a thymoma
- For stage I,II thymoma removal of adjacent nodes and anterior mediastinal nodes is encouraged
- For stage III thymoma a systematic anterior mediastinal node dissection is recommended, and a systematic sampling of appropriate intrathoracic sites is encouraged (i.e. paratracheal, aortopulmonary window, subcarinal etc).
- For thymic carcinoma at least a systematic sampling of anterior mediastinal, intrathoracic, supraclavicular and lower cervical nodes should be done (if the diagnosis is suspected or known).

Frozen Section

- A frozen section for diagnosis should be interpreted cautiously, and should be limited to cases with unexpected features or suspected to not be a thymic malignancy (e.g. lymphoma, germ cell tumor). The clinical diagnosis of thymoma is generally at least as reliable as a frozen section diagnosis.
- Frozen section determination of adequacy of margins is difficult (high false negative and false positive rates); the clinical impression should be carefully considered as well as the microscopic impression.

Operative Note

- The operative note should specifically mention the following:
 - Whether gross tumor was left behind, and if so, where
 - The extent of resection performed (i.e. complete thymectomy)
 - The presence and location of any adhesions that were simply divided (not suspicious for involvement)
 - Any additional structures (i.e. mediastinal pleura, pericardium, phrenic nerve, innominate vein) or organs removed (i.e. lung)
 - Any sites of intraoperative concern, including how these were marked on the specimen and in the patient
 - Which nodal areas were explored and the extent of assessment (i.e. sampling vs. complete dissection)
 - Whether the pleural and pericardial spaces were (able to be) inspected for metastases



General Principles for Minimally Invasive Resection

Overall the planned and or completed resection should not be diminished or compromised in any way in order to accomplish the resection in a minimally invasive manner. Opening should be considered standard expectation, and not a complication, if variation from the planned resection is encountered.

- 1- A minimally invasive resection of a thymic malignancy should involve **no** rib spreading or sternal cutting. The intent should be to perform a complete resection and a significant portion should be done with visualization on a video monitor.
- 2- Resection should involve the thymoma, thymus and mediastinal fat.
- 3- Dissection and visualization of innominate vein and both phrenic nerves should be done.
- 4- Conversion to open is required if oncologic principles are being compromised or violated: e.g. perforation of the capsule, incomplete resection, risk of a discontinuous (not en bloc) resection or disruption of the tissues exposing the tumor.
- 5- The access incision for retrieval should be large enough to prevent specimen disruption.
- 6- Exploration of pleura should be done if the thymoma invades the mediastinal pleura.
- 7- Retrieval in the bag.
- 8- Examination of the removed specimen to assess for completeness of the resection is required.
- 9- Communication with pathologist about suspicious areas is essential. The issues are orientation of the specimen, marking of several routine areas both on the specimen and in the patient, and identification of areas of tissue disruption that were not “close” during the dissection.

Details of Operative Report for Minimally Invasive Resection

1. The number, placement and size of incisions (e.g. cervical incision)
2. Was any sternal lifting used?
3. Was the xiphoid or a rib cartilage removed?
4. Was any rib spreading, sternal splitting or rib cutting done?
5. Is there invasion of adjacent structures of organs? These should be listed.
6. Which mediastinal structures were visualized (i.e. right/left phrenic nerves, innominate vein, right/left mediastinal pleura, pericardium, SVC, major vessels, A-P window)?
7. Extent of exploration: were the right/left and pericardial cavities visually inspected?
8. Details of the resected tissue (i.e. thymus, with attached adjacent structures, adjacent fat, nodes)
9. Was the thymic tumor resected en bloc? Was the surface of the tumor exposed?
10. Which nodal areas were explored; was systematic sampling or lymphadenectomy performed?
11. Resection of fatty tissue (i.e. pericardiophrenic, mediastinal, cervical; en bloc or separately resected?)
12. Suspected areas in close proximity to tumor and whether or not they were marked (on the specimen and in the patient at the time of identification during resection)
13. Hemostatic material used (type, amount and where it was placed)
14. Reason of conversion to open approach

Reference: Toker S, Sonett J, Zielinski M et al. Standard Terms, Definitions, and Policies for Minimally Invasive Resection of Thymoma. J Thorac Oncol 2011;6(7,Suppl 3):S1730-8

Available for download at: http://www.itmig.org/?page_id=315

Policies Regarding Surgical Incisional Biopsies of Mediastinal Lesions

Technical Aspects when Obtaining Incisional Biopsies

Frozen Section is useful to assess whether the tissue is representative

Frozen section diagnoses should be interpreted cautiously

Additional tissue not processed for frozen section should be obtained

Multiple biopsies are recommended due to frequent heterogeneity of mediastinal tumors

Biopsies that are deep rather than wide are suggested

Reference: Marchevsky A, Marx A, Ströbel P et al. Policies and Reporting Guidelines for Small Biopsy Specimens of Mediastinal Masses. J Thorac Oncol 2011;6(7,Suppl 3):S1724-9

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Masaoka-Koga Staging System (with ITMIG Definition of Details)

Stage	Definition
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b	Lymphogenous or hematogenous metastasis <i>Any nodal involvement (e.g. anterior mediastinal, intrathoracic, low/anterior cervical nodes, any other extrathoracic nodes)</i> <i>Distant metastases (i.e. extrathoracic and outside the cervical perithymic region) or pulmonary parenchymal nodules (not a pleural implant)</i>

ITMIG Pathologist Kit

Recommended Surgeon's Preparation of the Gross Specimen:

Marking

- Mark areas of concern immediately upon dissection, both on the specimen and in the patient
- Routinely mark a representative area adjacent to the pericardium and innominate vein (or mark these structures if resected)
- Routinely mark right/left mediastinal pleural surfaces (if resected)
- Mark a representative area adjacent to the SVC, if the tumor is nearby
- Place marking stitches through loose tissue as well as into more substantial deeper tissue in order to prevent tissue disruption

Orientation

- The surgeon should be involved with orientation of the specimen
- The surgeon should either orient the specimen together with the pathologist or use a system of communicating the orientation of the specimen to the pathologist
- Orienting the unfurled specimen on a mediastinal board or diagram is encouraged
- A digital photo of the mounted specimen is encouraged
- A sketch of the specimen with adjacent structures and marking stitches is encouraged

Recommended Pathologist's Preparation of the Gross Specimen:

Gross Preparation of the Excised Specimen

- Resolution of ambiguities by communication between the surgical and pathological team immediately at the time of resection
- Identify areas of concern prior to sectioning
- Identify areas of tissue disruption that occurred during handling
- Anterior, posterior, right and left surfaces should be clearly distinguished (e.g. inked with different colors or with a detailed block key)
- Tumor bread-loafed (e.g. from superior to inferior) with sections serially ordered and submitted
- One block per cm of tumor should be submitted
- At least 5 representative sections should be taken regardless of the tumor diameter
- Random sections from the remaining uninvolved thymus should be submitted
- As much tissue as possible should be banked without compromising the diagnostic assessment; adjacent sections in paraffin should be taken for comparison

Reference: Detterbeck F, 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):S1730-8

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Recommended Routine Policies for Microscopic Findings:

Reporting Policies for Margins

Capsular Integrity and Invasion

Thymoma, localized (encapsulated, although capsule may be partially absent)

Thymoma, minimally invasive (penetration through capsule but only minimally into adjacent fat, i.e. ≤ 3 mm)

Thymoma, invasive (with infiltration of surrounding structures including mediastinal fat)

Margin Status

Negative

intact normal tissue overlying the tumor, or

invasion of structures bounded by a space (i.e. pleura or pericardium) or

inked outer surface of specimen consisting of intact capsule, or

tumor extending up to inked margin in an area of tissue disruption that was identified as not grossly concerning intraoperatively (with additional text identifying this situation)

Positive (tumor extending to an inked cut margin)

Distance to closest margin

Distance in mm reported whenever ≤ 3 mm

If ≤ 1 mm (or ≤ 1 hpf) at least 3 additional levels should be examined

Processing and Reporting Policies after Neoadjuvant Therapy

Gross preparation should follow the same principles as a primarily resected specimen

At least 5 representative sections should be taken regardless of the tumor diameter

At least one block per cm of tumor should be submitted;

Careful sampling is required according to the policies defined for a primary specimen before a complete pathologic response can be defined

The percent of viable tumor (in 10% increments) should be reported based on an aggregate assessment of multiple representative sections of the resected tumor.

Reference: Detterbeck F, 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):S1730-8

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Policies Regarding FNA Biopsies of Mediastinal Lesions

Technical Aspects when Obtaining FNA (Fine Needle Aspiration) Biopsies

22-gauge needle (or larger)

Either ROSE or at least 3 passes

Either ROSE or at least 6 smears (2 smears per pass). and collection of materials in CYTORICH® red collection fluid or similar solution

Preparation of a cell block is suggested

A sample for flow cytometry is recommended if lymphoma is suspected

Interpretation and Reporting of FNA Biopsies

Interpretation should be correlated with clinical and radiologic findings

Specimen adequacy should be reported*

Immunostains should be used as suggested by the differential diagnosis

Consultation with an experienced second pathologist is recommended whenever there is any diagnostic difficulty

*No general criteria are possible, but should be assessed relative to the clinically applicable differential diagnosis
FNA, Fine Needle Aspiration; ROSE, Real-time On-Site Examination

Policies Regarding Needle Core Biopsies of Mediastinal Lesions

Technical Aspects when Obtaining Needle Core Needle Biopsies

19-gauge needle (or larger)

3 passes (or more)

Interpretation and Reporting of Needle Core Biopsies

Interpretation should be correlated with clinical and radiologic findings

Immunostains should be used as suggested by the differential diagnosis

Consultation with an experienced second pathologist is recommended whenever there is any diagnostic difficulty

Policies Regarding Surgical Incisional Biopsies of Mediastinal Lesions

Technical Aspects when Obtaining Incisional Biopsies

Frozen Section is useful to assess whether the tissue is representative

Frozen section diagnoses should be interpreted cautiously

Additional tissue not processed for frozen section should be obtained

Multiple biopsies are recommended due to frequent heterogeneity of mediastinal tumors

Biopsies that are deep rather than wide are suggested

Policies in Interpretation and Reporting of Surgical Incisional Biopsies

Interpretation should be correlated with clinical and radiologic findings

Consultation with an experienced second pathologist is recommended whenever there is any diagnostic difficulty

Immunostains may be helpful in addressing issues related to subtyping of thymic malignancies and differentiation from other mediastinal malignancies

Reference: Marchevsky A, Marx A, Ströbel P et al. Policies and Reporting Guidelines for Small Biopsy Specimens of Mediastinal Masses. J Thorac Oncol 2011;6(7,Suppl 3):S1724-9

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Selected Immunohistochemical Markers Used in the Differential Diagnosis of Mediastinal Lesions

	Epithelial markers	Miscellaneous markers of Thymic carcinoma	Neuroendocrine markers	Germ cell tumor markers	Markers of pulmonary origin	Lymphoid markers of mature T phenotype	Lymphoid markers of immature T phenotype	Lymphoid markers: CD20	
	Cyto-keratin	CD117, CD5*, CD70, EMA*	Synaptophysin, chromogranin, CD56	Oct 3 / 4, α fetoprotein, CD30, PLAP	TTF-1, Napsin, Surfactant apoprotein	CD3, CD45	CD99, Tdt, CD1a	LY	EC
Thymoma	+	-	-	-	-	+	+	-	-/+
Thymic hyperplasia	+	-	-	-	-	+	+	+	-
Thymic carcinoma	+	+	+/-	-	-	+	-	-	-
Thymic neuroendocrine tumors	+	-	+	-	-	-	-	-	-
Lymphoma	-	-	-	+ (CD30°)	-	+	+	+	-
Germ cell tumors	+/-	-	-	+	-	-	-	-	-
Metastases	+/-	-*	+/-	-	+	-	-	-	-

Legend: among several antibodies (Ab) useful in the evaluation of anterior mediastinal masses, it should be remembered that some markers have to be evaluated for the epithelial cell (EC) component or for putative Germ cells, whereas other are useful in the evaluation of the Lymphoid cell (LY) component. Moreover, some few Ab originally established to characterize hematolymphoid cells (CD5, CD20, CD117) proved to be of value in the diagnosis of thymic epithelial tumors, because aberrantly expressed in selected thymoma subtypes or in thymic carcinomas. Morphological criteria and antibody panels should be applied in selected cases in order to establish the diagnosis.²⁷⁻³²

CD30°: in mediastinal lymphomas, CD30 is expressed (in different settings) in Hodgkin lymphoma and sometimes in Primary mediastinal B cell lymphoma.

*Adenocarcinomas of extrathymic origin frequently express CD5 and EMA immunoreactivity.

ITMIG CT Imaging Kit

Documentation of Primary Tumor Characteristics

VARIABLE	MENU OPTION
Size (cm)	X-axis (longest dimension on axial slice) Y-axis (perpendicular to longest dimension) Z-axis (cranio-caudal dimension)
Contour	Smooth Lobulated
Internal density	Homogenous Heterogeneous Cystic
Calcification	Yes No
Infiltration of surrounding fat	Yes No
Abutment of $\geq 50\%$ of mediastinal structure with loss of fat plane	Yes (list which structure/s) No
Additional mediastinal structures tumor abuts	Yes (list) No
Direct vascular endoluminal invasion	Yes (list vessel name) No

Documentation of Involvement of Surrounding Structures

VARIABLE	MENU OPTION
Abnormalities in adjacent lung parenchyma	Yes No
Presence of a pleural effusion	Unilateral Bilateral No
Presence of a pleural nodule	No Unilateral/bilateral 1 2-5 >5/diffuse
Mediastinal lymph node enlargement (> 1 cm in short axis on an axial image)	Yes (location according to node map ²⁶) No
Abutment of expected location of phrenic nerve	Yes No
Elevated hemidiaphragm	Yes No
Presence of a pulmonary nodule	Yes No
Extrathoracic suspected metastases	Yes (location) No

Reference: Marom E, Rosado-de-Christenson M, Bruzzi J et al. Standard Report Terms for Chest Computed Tomography Reports of Anterior Mediastinal Masses Suspicious for Thymoma. J Thorac Oncol 2011;6(7,Suppl 3):S1717-23

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ITMIG Radiation Oncology Kit

Reporting Guideline for Thymic Malignancies Treated with Radiotherapy

Intent:

Curative – with the intent to definitively treat the disease, i.e. for long-term disease control

Palliative – for symptom improvement and/or reduction in tumor size but not eradication of tumor

Clinical Context (Setting):

Preoperative, RT alone or with concurrent or sequential chemotherapy.

Postoperative, indicate whether this is following a complete resection (R0), microscopic residual disease (R1) or gross residual disease (R2), and whether postoperative chemotherapy (concurrent or sequential) is given as well.

Definitive RT (i.e. no plans for surgery) RT alone or chemoradiation given with curative intent

RT for recurrent disease – area of recurrence needs to be specified, as well as the type of RT (external beam, endobronchial brachytherapy, intraoperative)

Area Treated:

Gross Tumor with Margin: primary tumor or lymph nodes

Tumor Bed with Margin: as delineated by preoperative and postoperative imaging and surgical findings, including surgical clips

Elective Sites Beyond Initially Involved Area: (e.g. mediastinum, lymph nodes)

Sites of Pleural metastases: either postoperative, definitive (curative intent) or palliative

Entire hemithorax (right or left)

Radiation Dose:

Date Initiated and Date Completed

Radiation Dose, Initial Volume (Gy)

Radiation Fraction Size, Initial Volume (Gy)

Boost Given: yes/no

Boost Timing: Sequential/Concurrent

Boost Dose (Gy)

Boost Fraction Size (Gy)

Radiation Technique:

i.e. 2D Planning, 3D Conformal Therapy, IMRT, Proton Therapy, Other

Suggested Guidelines for Treatment Parameters

Margins

GTV to CTV margin: 0.5-1.0 cm

CTV to PTV margin, without 4D CT simulation (or equivalent) and without daily kV imaging: 1.0-1.5 cm

ITV to PTV margin, with 4D CT simulation (or equivalent) but without daily kV imaging: 0.5-1.0 cm

ITV to PTV margin, with 4D CT simulation and daily kV imaging: 0.5 cm

Outer Boundary Definitions for Timing and Dose for Postoperative RT

Treatment should start within 3 months (if sequential RT is given after chemotherapy, the chemotherapy should have been initiated within 3 months of surgery)

Differentiate planned postoperative RT vs. RT for progressive disease

At least 40 Gy (1.8-2 Gy fractions) for R0,1 and ≥ 54 Gy for R2 resections

Reference: Gomez D, Komaki R, Yu J et al. Radiation Therapy Definitions and Reporting Guidelines for Thymic Malignancies. J Thorac Oncol 2011;6(7,Suppl 3):S1743-8

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Definition of Recurrences

- Tumor regrowth after palliative RT should be classified as progression of disease
- Distant recurrence – Outside the thorax or Intraparenchymal pulmonary nodules
- Regional recurrence – intrathoracic, but not contiguous with original tumor or thymus (this includes pleural or pericardial nodules)
- Local Recurrence – at site of original tumor (including curatively treated pleural implants), or in thymic bed including adjacent nodes. This should be further classified according to the RT treatment field:
- Out of field recurrence – Outside the RT field; i.e. center lies outside of the 50% isodose field
- Marginal Miss – geographic center of the recurrence lies in a region receiving 50-100% of the prescription dose

Toxicity Definition

Define according to CTCAE v 4.02 (Common Toxicity Criteria for Adverse Events, available at www.acrin.org/Portals/0/Administration/Regulatory/CTCAE_4.02_2009-09-15_QuickReference... · PDF file)

Should include at least grade 3-5, and categories of Esophagus, Respiratory, Cardiac and Other
Include maximal toxicity, toxicity duration, and whether it represents a dose-limiting toxicity

Proposed Dosimetric Constraints for Treatment of Thymic Malignancies⁵

	RT Alone	Chemo and RT	Chemo and RT Before Surgery
Spinal cord ¹	$D_{max} < 45$ Gy	$D_{max} < 45$ Gy	$D_{max} < 45$ Gy
Lung ²	MLD ≤ 20 Gy $V_{20} \leq 40\%$	MLD ≤ 20 Gy $V_{20} \leq 35\%$ $V_{10} \leq 45\%$ $V_5 \leq 65\%$	MLD ≤ 20 Gy $V_{20} \leq 30\%$ $V_{10} \leq 40\%$ $V_5 \leq 55\%$
Heart	$V_{30} \leq 45\%$ Mean dose < 26 Gy	$V_{30} \leq 45\%$ Mean dose < 26 Gy	$V_{30} \leq 45\%$ Mean dose < 26 Gy
Esophagus	$D_{max} \leq 80$ Gy $V_{70} < 20\%$ $V_{50} < 50\%$ Mean dose < 34 Gy	$D_{max} \leq 80$ Gy $V_{70} < 20\%$ $V_{50} < 40\%$ Mean dose < 34 Gy	$D_{max} \leq 80$ Gy $V_{70} < 20\%$ $V_{50} < 40\%$ Mean dose < 34 Gy
Kidney ³	20 Gy $< 32\%$ of bilateral kidney	20 Gy $< 32\%$ of bilateral kidney	20 Gy $< 32\%$ of bilateral kidney
Liver	$V_{30} \leq 40\%$ Mean dose < 30 Gy	$V_{30} \leq 40\%$ Mean dose < 30 Gy	$V_{30} \leq 40\%$ Mean dose < 30 Gy

RT, radiotherapy; chemo, chemotherapy; MLD, mean lung dose; D_{max} = maximal dose

¹The size of the treated volume of the spinal cord should be considered; when PTV is close (< 1 cm) to spinal cord, the cord may receive a dose higher than the recommended threshold in order to maintain adequate dose to the GTV target volume, but should be < 60 Gy, even in a very limited volume, and ~ 40 Gy if large fractions (i.e. 3-Gy) are used.

² V_{20} = the effective lung volume (total lung volume – gross tumor volume) receiving 20 Gy or more. For patients who undergo pneumonectomy before RT, we recommend an MLD of < 8 Gy, a V_{20} of $< 10\%$ and $V_5 < 60\%$. Note that in the setting of postoperative treatment in which a gross total resection has been achieved, there is no GTV, so the lung constraint will be representative of solely the total lung, not the total lung minus the CTV.

³Consider a kidney scan if a large volume of one kidney will be treated with a high dose

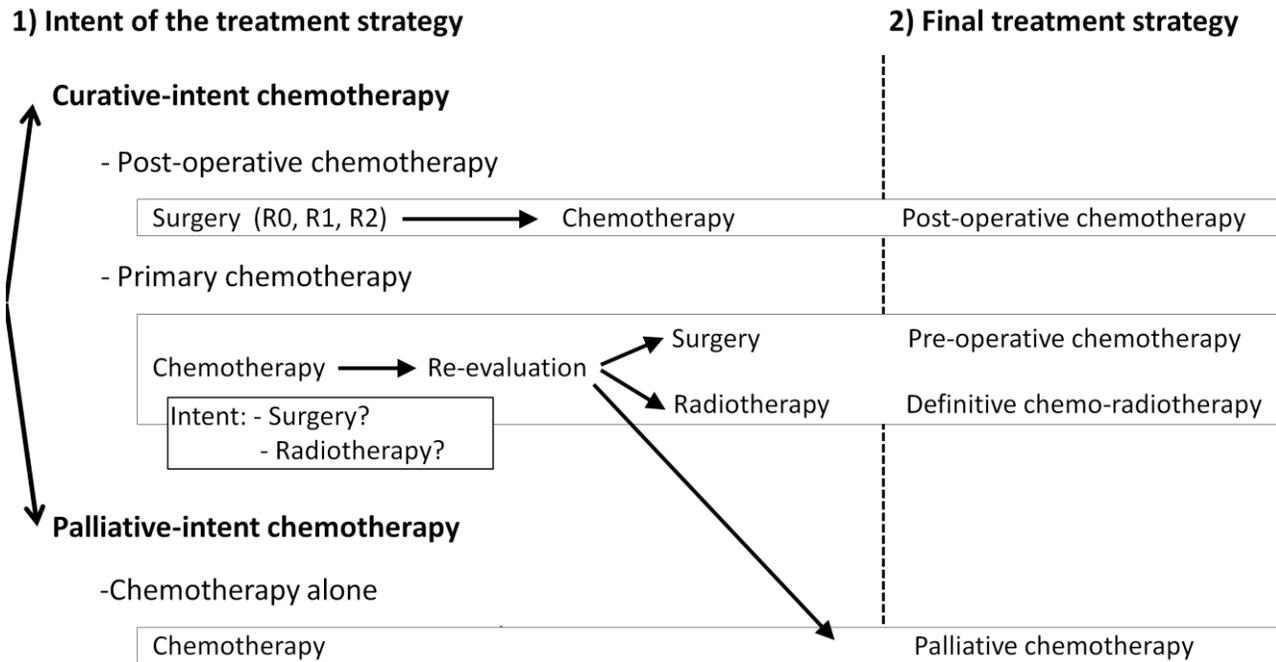
Reference: Marks LB, Yorke ED, Jackson A, et al: Use of normal tissue complication probability models in the clinic. *Int J Radiat Oncol Biol Phys* 2010;76:S10-9

ITMIG Medical Oncologist Kit

Reporting Guidelines for Thymic Malignancies Treated with Chemotherapy

CHEMOTHERAPY STRATEGIES		
Initial treatment		
<i>Curative-intent</i>	Primary chemotherapy	Chemotherapy prior to another focal treatment – surgery or RT Intent of the treatment should be documented, i.e. primary chemotherapy prior to surgery or prior to RT Final strategy has to be indicated: primary preoperative chemotherapy or primary chemo-radiotherapy.
	Post-operative chemotherapy	Chemotherapy delivered following surgery. Completeness of resection (R0, R1 or R2) should be noted.
<i>Palliative-intent</i>	Palliative chemotherapy	Chemotherapy alone in cases for which there is no plan for surgery or radiotherapy.
Chemotherapy for recurrence		Chemotherapy delivered for tumor recurrence appearing after previous curative-intent treatment. Chemotherapy for recurrence may be curative-intent (primary preoperative/chemoradiation, post-operative) or palliative-intent (chemotherapy alone). Intent of the treatment and final strategy have to be documented as for initial treatment.
CHEMOTHERAPY GENERAL REPORTING GUIDELINES		
Modalities	Chemotherapy regimen Number of cycles administered Dose intensity: > or < 70% of the planned dose-intensity	
Analysis	Treatment outcome evaluated separately for thymoma and thymic carcinoma.	
Toxicities	Grade 3-5 and dose limiting toxicities should be reported using the NCI-Common Toxicity Criteria Adverse Event (CTCAE) v4.02. Report both acute and late toxicities (especially late events such as cardiac toxicities).	
Response	Assessment of tumor response as described in “Standard Outcome Measures for Thymic Malignancies” paper. Whether the tumor contains a substantial lymphocyte component should be noted Octreoscan results should be reported for patients treated with octreotide. Report effect of antitumor treatment on associated paraneoplastic manifestations Report Corticosteroid treatment doses (equivalent to prednisone doses above 0.5mg/kg/day) and durations.	
Follow-Up	After R0 surgical resection – annual CT (with contrast) for 5 years, then annual CXR alternating with CT for 5 years is suggested as a minimum After curative intent treatment for stage III, IVa – CT every 6 months for 3 years, then schedule noted above	
Recurrence	Tumor regrowth should be classified as progression if treatment was palliative. Recurrence should denote regrowth after complete resection or radiographic complete response to curative intent therapy. Time of recurrence should be defined as when clinical suspicion of recurrence first occurred, regardless of whether a biopsy was done (unless the finding is subsequently demonstrated not to be a recurrence). Rebound hyperplasia must be considered when tumor re-growth occurs within 15 months following treatment cessation. Local Recurrence – at site of original tumor, or in thymic bed including adjacent nodes Regional recurrence – intrathoracic, but not contiguous with original tumor or thymus (this includes pleural or pericardial nodules) Distant recurrence – outside of the thorax, or Intraparenchymal nodules	

Schematic Diagram of Treatment Strategies Involving Chemotherapy in Thymic Malignancies



Reference: Girard N, Lal R, Wakelee H et al. Chemotherapy Definitions and Policies for Thymic Malignancies.. J Thorac Oncol 2011;6(7,Suppl 3):S1749-55
 Available for download at: http://www.itmig.org/?page_id=315