

**Approach to Cut-Up; Macroscopic  
Examination as the Precursor to Accurate  
Microscopic Interpretation  
LUNG (AND THYMUS)**

***Professor Andrew G Nicholson***

***Royal Brompton and Harefield NHS Trust  
and NHLI Division of Imperial College  
School of Medicine, London***

# 10<sup>th</sup> BDIAP Educational Day on Cut-up



### Box A.1 Varieties of lung specimen

Needle aspiration  
Fibreoptic bronchoscopic  
    Bronchial biopsy  
    Transbronchial biopsy  
Rigid bronchoscopic bronchial biopsy  
Mediastinoscopy or mediastinotomy lymph node biopsy  
Transcutaneous drill biopsy  
Pleural punch biopsy  
'Medical' thoracoscopy  
Pleural biopsy  
Thoracotomy or 'surgical' (video-assisted) thoracoscopy  
    Pleural biopsy  
    Wedge lung biopsy  
    Segmentectomy  
    Lobectomy  
    Pneumonectomy  
Post mortem

Corrin, Nicholson: Pathology of the Lungs 2e © 2006 Elsevier Ltd

Primary lung cancer requires an anatomic resection (\*\*AIS)

Goal of metastatectomy is complete resection with minimum loss of lung

**Table A.1 A protocol for reporting lung tissue resected in the treatment of lung cancer**

**Specimen Type**

- |  |  |
|--|--|
| <input type="checkbox"/> Right                             | <input type="checkbox"/> Left                              |
| <input type="checkbox"/> VATS segmentectomy                | <input type="checkbox"/> VATS lobectomy                    |
| <input type="checkbox"/> Open segmentectomy                | <input type="checkbox"/> Open lobectomy/bi-lobectomy       |
| <input type="checkbox"/> Pneumonectomy (extra-pericardial) | <input type="checkbox"/> Pneumonectomy (intra-pericardial) |
| <input type="checkbox"/> Sleeve                            | <input type="checkbox"/> Wedge resection                   |
| <input type="checkbox"/> Other, e.g. chest wall            |  |

**Gross description**

**Location of Tumour**

- ☐ Main bronchus within 20 mm of carina (T3) – this will require clinical information  
☐ Main bronchus more than 20 mm from carina (T2)  
☐ Non-assessable

- |   |  |   |
|---|--|---|
| <input type="checkbox"/> Right upper lobe | <input type="checkbox"/> Right middle lobe | <input type="checkbox"/> Right lower lobe |
| <input type="checkbox"/> Left upper lobe  | <input type="checkbox"/> Left lower lobe   |   |

Tumour size ... mm (T1 ≤30 mm or superficial tumours confined to bronchial wall, T2 > 30 mm)

Distance from bronchial or medial resection margin ... mm

- Extent of atelectasis/obstructive pneumonitis: ☐ None  
☐ Involving hilar region but not whole lung (T2)  
☐ Involving whole lung (T3)

**Histology**

**Histological type**

- |   |   |   |
|---|---|---|
| <input type="checkbox"/> Squamous cell carcinoma                                    | <input type="checkbox"/> Adenocarcinoma       | <input type="checkbox"/> Bronchoalveolar cell carcinoma |
| <input type="checkbox"/> Large cell undifferentiated                                | <input type="checkbox"/> Small cell carcinoma |   |
| <input type="checkbox"/> Mixed tumours (please specify: .....)                      |   |   |
| <input type="checkbox"/> Other tumour (please specify, e.g. carcinoid, etc.: .....) |   |   |

**Local invasion**

- |  |  |  |
|--|--|--|
| <input type="checkbox"/> Visceral pleura (T2)  | <input type="checkbox"/> Parietal pleura/chest wall (T3) | <input type="checkbox"/> Mediastinal pleura (T3)                   |
| <input type="checkbox"/> Pericardium (T3)  | <input type="checkbox"/> Diaphragm (T3)                  |  |
| <input type="checkbox"/> Great vessel (aorta, central pulmonary artery or vein) (T4) |  | <input type="checkbox"/> Atrium, heart (T4)                        |
| <input type="checkbox"/> Malignant pleural effusion (T4)                             |  | <input type="checkbox"/> Separate tumour nodules in same lobe (T4) |

**Lymph node spread**

- |   |                                    |  |
|---|------------------------------------|--|
| Ipsilateral hilar/intrapulmonary (node stations 10–14)                                  | <input type="checkbox"/> Submitted | <input type="checkbox"/> Involved (N1) |
| Ipsilateral mediastinal (node stations 1–9)   | <input type="checkbox"/> Submitted | <input type="checkbox"/> Involved (N2) |
| Contralateral mediastinal, hilar, ipsilateral or contralateral scalene, supraclavicular | <input type="checkbox"/> Submitted | <input type="checkbox"/> Involved (N3) |

**Margins**

- |             |                                |                                   |
|-------------|--------------------------------|-----------------------------------|
| Bronchial   | <input type="checkbox"/> Clear | <input type="checkbox"/> Involved |
| Mediastinal | <input type="checkbox"/> Clear | <input type="checkbox"/> Involved |
| Vascular    | <input type="checkbox"/> Clear | <input type="checkbox"/> Involved |
| Chest wall  | <input type="checkbox"/> Clear | <input type="checkbox"/> Involved |

**Other Pathology**

- |   |   |
|---|---|
| <input type="checkbox"/> Emphysema (moderate/severe degree) | <input type="checkbox"/> Interstitial fibrosis; State cause (if known): ..... |
| <input type="checkbox"/> Other (please state: .....)        |   |

**Metastases**

- |  |                                      |
|--|--------------------------------------|
| <input type="checkbox"/> Unknown (MX)  | <input type="checkbox"/> Absent (M0) |
| <input type="checkbox"/> Present (M1) including tumour nodules in different lobes. (please state: .....) |                                      |

**Pathological staging**

- |                                   |                            |   |
|-----------------------------------|----------------------------|---|
| <input type="checkbox"/> T        | <input type="checkbox"/> N | <input type="checkbox"/> M (select highest stage from above data) |
| Complete resection at all margins |                            | <input type="checkbox"/> Yes <input type="checkbox"/> No          |

Copies can be downloaded from the Royal College of Pathologists website: [www.rcpath.org/resources/worddocs/dataset\\_lung\\_cancer\\_form\\_v2002.doc](http://www.rcpath.org/resources/worddocs/dataset_lung_cancer_form_v2002.doc)

T

N

M

2017/8

~~2015/6~~

~~2014~~

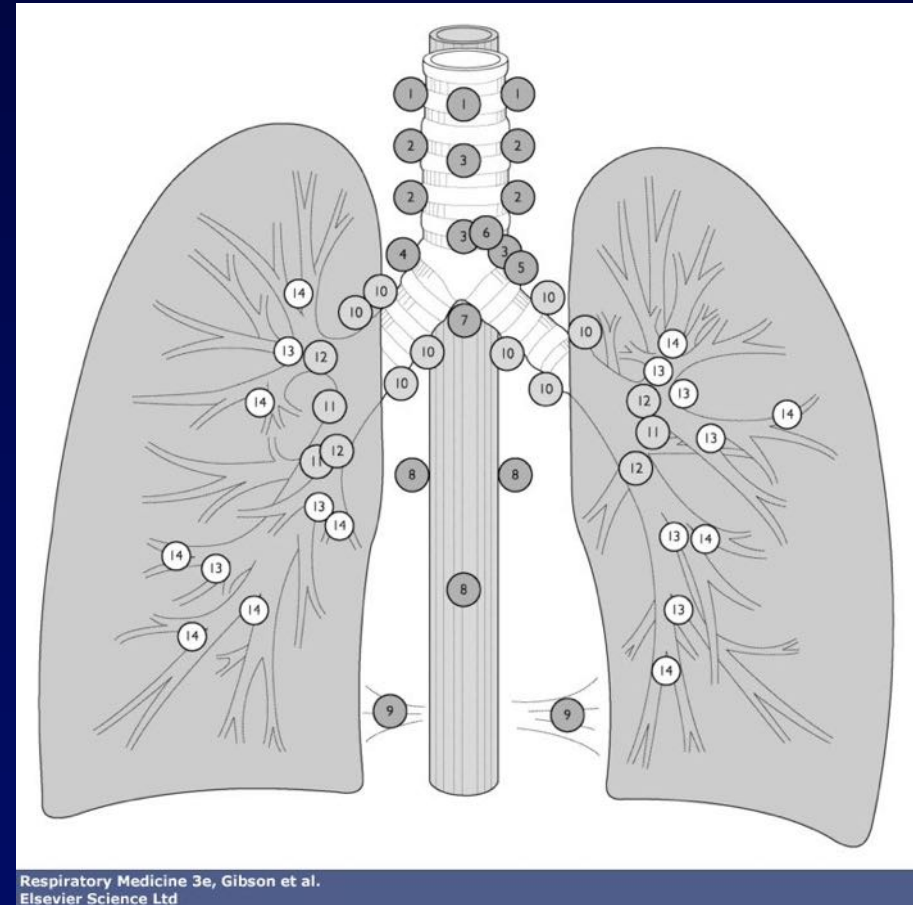
~~2011~~

# Lung ca – staging

**TNM remains the most important prognostic indicator**

(7<sup>th</sup> TNM major modifications 2009 - see [www.jto.org](http://www.jto.org) Rusch VW et al, JTO, 2009;4:568-577)

- **T descriptors**
  - T1 divided into T1a <2cm and T1b 2-3cm
  - T2 divided into T2a <5cm and T2b >5cm
  - T3 >7cm
  - Separate nodule same lobe T3
  - Ipsilateral lung nodules T4 not M1
- **M descriptors**
  - Distinction between types metastasis
    - Pleural/contralateral lung/malignant effusion M1a
    - Distant M1b
- **N descriptors (stayed the same)**
  - (Naruke map) – now internationally agreed between Japan and USA re anatomic landmarks



**Further changes in  
8<sup>th</sup> edition in 2017/8**

# PROPOSED T CATEGORIES CHANGES

- **Subdivide T1:**
  - T1a:  $\leq 1$  cm; T1b:  $>1$  and  $\leq 2$  cm; T1c:  $< 2$ cm and  $\leq 3$  cm
- **Redefine T2a as  $>3$ -  $\leq 4$  cm**
- **Redefine T2b as  $>4$ -  $\leq 5$  cm**
- **Reclassify T2b that are  $>5$ -  $\leq 7$  cm as T3**
- **Reclassify T3 that are  $>7$  cm as T4**
- **Reclassify T3 by any endobronchial location as T2**
- **Reclassify T3 by invasion of diaphragm as T4**

The IASLC Lung Cancer Staging Project: Proposals for the Revisions of the T Descriptors in the Forthcoming Eighth Edition of the TNM Classification for Lung Cancer. Rami-Porta R et al. J Thorac Oncol. 2015 Jul;10(7):990-1003

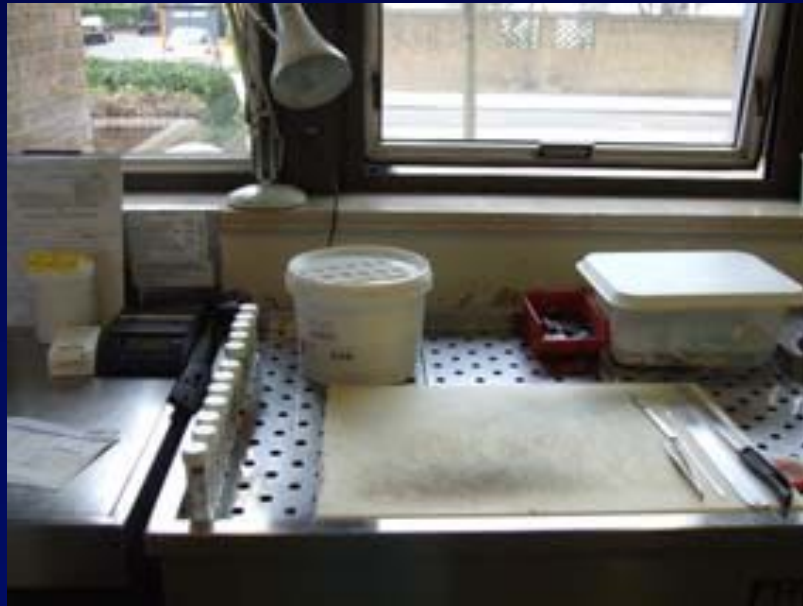


- The International Association for the Study of Lung Cancer Lung Cancer Staging Project: Proposals for the Revision of the N Descriptors in the Forthcoming 8th Edition of the TNM Classification for Lung Cancer. Asamura H et al J Thorac Oncol. 2015 Dec;10(12):1675-84
- The IASLC Lung Cancer Staging Project: Proposals for the Revision of the M Descriptors in the Forthcoming Eighth Edition of the TNM Classification of Lung Cancer. Eberhardt WE et al. J Thorac Oncol. 2015 Nov;10(11):1515-22
  - Cases with pleural/pericardial effusions, contralateral/bilateral lung nodules, contralateral/bilateral pleural nodules, or a combination of multiple of these parameters should continue to be grouped as M1a category.
  - Single metastatic lesions in a single distant organ should be newly designated to the M1b category.
  - Multiple lesions in a single organ or multiple lesions in multiple organs should be reclassified as M1c category.
  - This new division can serve as a first step into providing rational definitions for an oligometastatic disease stage in non-small-cell lung cancer in the future.





# Good bench, good assistant...



# 5P's

– Proper Preparation Prevents Poor Performance



- **Inflation of the specimen**
  - In theatre
  - In the laboratory
- **Fix for 24 hours (overnight)**
- **Cut-up next day (Can leave to fix further if chest wall/bone present)**

# FOR PERIPHERAL TUMOURS

## STEP 1: Assess:

- The clinical details
- Frozen section result
- External surface

in order to decide how to proceed with specimen



## **STEP 2: ASSESS AND PROCESS THE HILUM OF THE SPECIMEN**









Blocks:

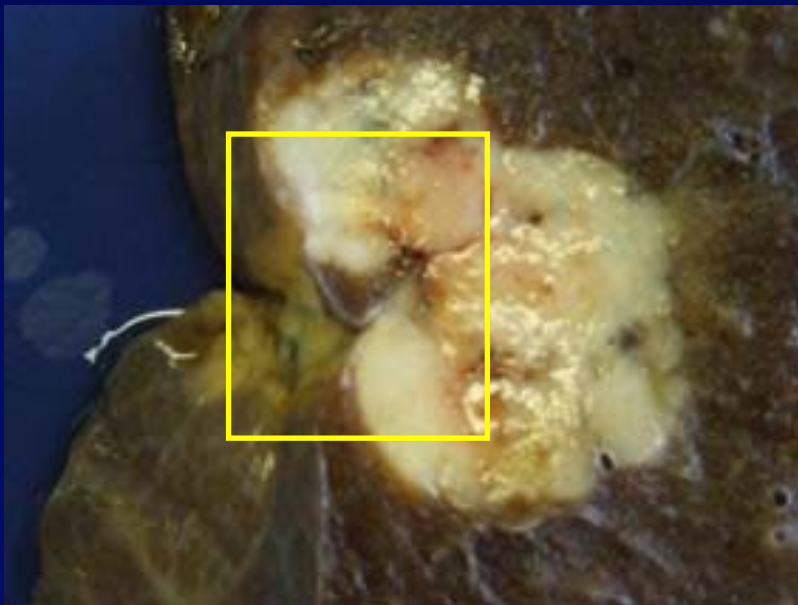
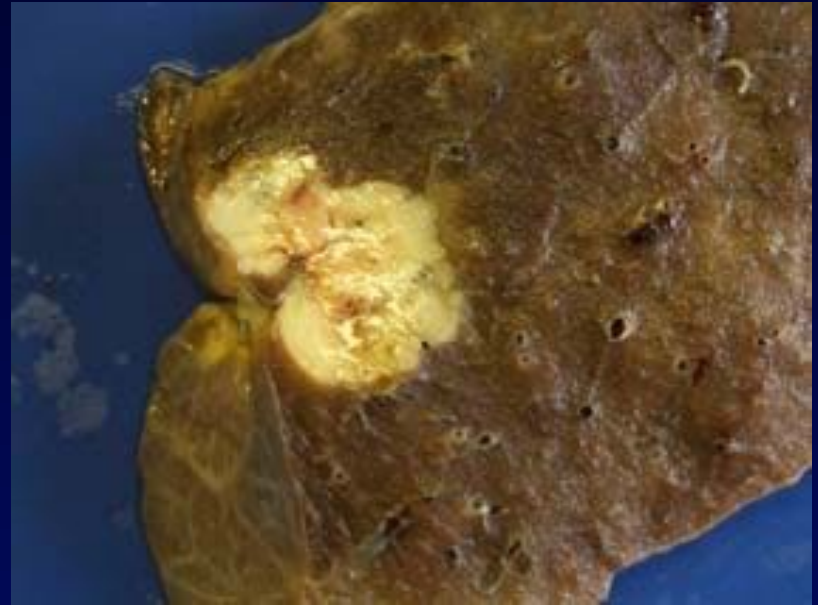
Bronchial and vascular (2) margins  
(\*may be more than one airway)

Specimen resection LNs





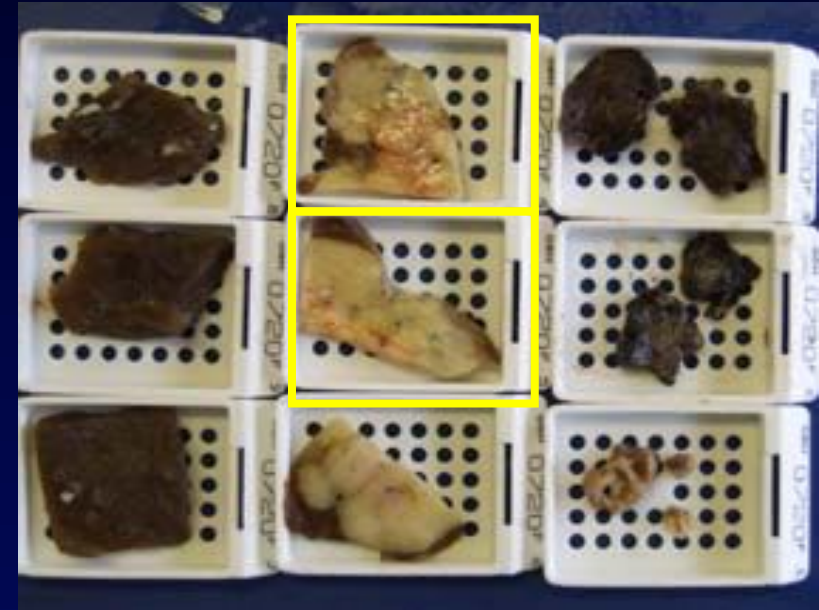
### STEP 3: ASSESS THE TUMOUR



## STEP 4: ASSESS THE BACKGROUND LUNG







EVGs on blocks abutting pleura

**F Right lower lobe of lung**  
**MACROSCOPIC DESCRIPTION**

Right lower lobe measuring 160x160x75mm in the inflated state. At the base of the lobe, there is a circumscribed tumour measuring 42x28mm x approximately 35mm, which abuts the visceral pleura. The tumour lies 75mm from the bronchial resection margin. The remaining lung is unremarkable.

*F1: bronchial & vascular resection margin (3 pieces); F2-F3: hilar lymph nodes (2 pieces in each); F4-F6: tumour (1 piece in each); F6-F8: random lung (1 piece in each). Tissue remains.*

## CLINICAL DETAILS

Adenocarcinoma in right lower lobe.

Specimen:

A Right upper lobe

### MACROSCOPIC DESCRIPTION

A piece of lung measuring 15x10x8mm. Cut surface shows an ill-defined firm area measuring 7x5x5mm.

*Bisected & all embedded in A1 (2 pieces).*

### MICROSCOPIC EXAMINATION

Sections show a localised area of fibrosis and inflammation within which are several epithelioid granulomas with very focal central necrosis. Acid fast bacilli (AFB) are noted on ZN stain. Special stain for fungi (Grocott) is negative. The features are of granulomatous inflammation due to mycobacterial infection. There is no evidence of malignancy.

B 10i C 11i; D 7; E 9

### MACROSCOPIC DESCRIPTION

Lymph nodes

*All embedded in B1 (3 pieces); B2 (3 pieces); C1 (1 piece);*

*D1 (2 pieces); E1 (2 pieces) and E2 (3 pieces.)*

### MICROSCOPIC EXAMINATION

All lymph nodes showing no granuloma formation or evidence of malignancy.

F Right lower lobe of lung

### MACROSCOPIC DESCRIPTION

Right lower lobe measuring 160x160x75mm in the inflated state. At the base of the lobe, there is a circumscribed tumour measuring 42x28mm x approximately 35mm, which abuts the visceral pleura. The tumour lies 75mm from the bronchial resection margin. The remaining lung is unremarkable.

*F1: bronchial & vascular resection margin (3 pieces); F2-F3: hilar lymph nodes (2 pieces in each); F4-F6: tumour (1 piece in each); F6-F8: random lung (1 piece in each). Tissue remains.*

### MICROSCOPIC EXAMINATION

Sections show a non-mucinous adenocarcinoma with mainly acinar (90%) pattern other than an occasional microscopic focus of micropapillary change (10%). The tumour breaches the visceral pleura, confirmed on EVG stain., but does not reach the surface. The resection margins are free of atypia and malignancy. The adjacent lung is unremarkable. The hilar lymph node shows no granuloma formation or evidence of malignancy. The adjacent lung is unremarkable.

G 11s; H right 2; J 12m; K Highest

L 12L; M 10s N Right 4

### MACROSCOPIC DESCRIPTION

Lymph nodes.

*G1 (2 pieces); H1 (4 pieces); J1 (4 pieces); K1 (4 pieces); L1: (2 pieces); M1 (1 piece); N1 (2 pieces); N2 (1 piece) & N3 (1 piece). All tissue embedded.*

### MICROSCOPIC EXAMINATION

All lymph nodes showing no granuloma formation or evidence of malignancy.

Right lower lobe of lung – Non-mucinous adenocarcinoma, acinar pattern, predominant. (pT2a N0 PL1, R0)

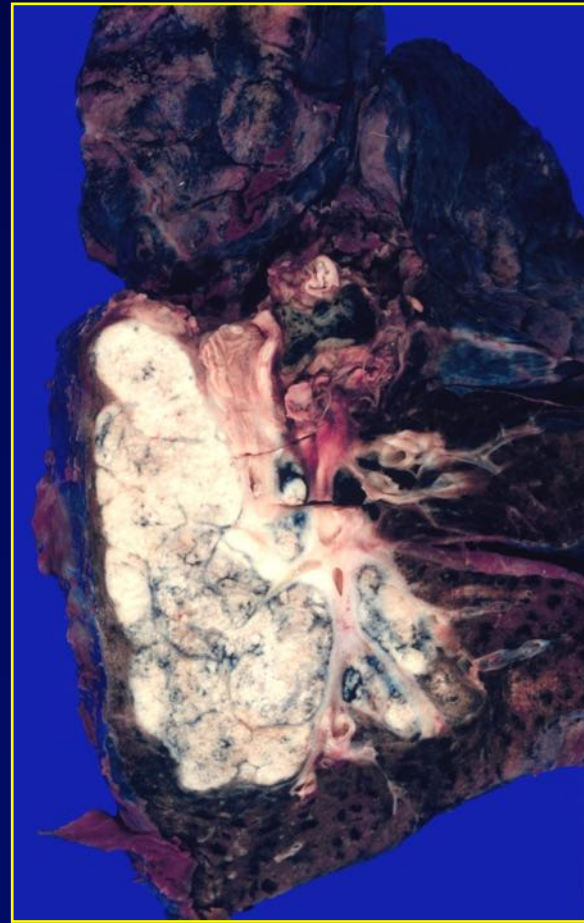
Right upper lobe of lung - Granulomatous inflammation due to mycobacterial infection.

## FOR CENTRAL TUMOURS (Liebow method)

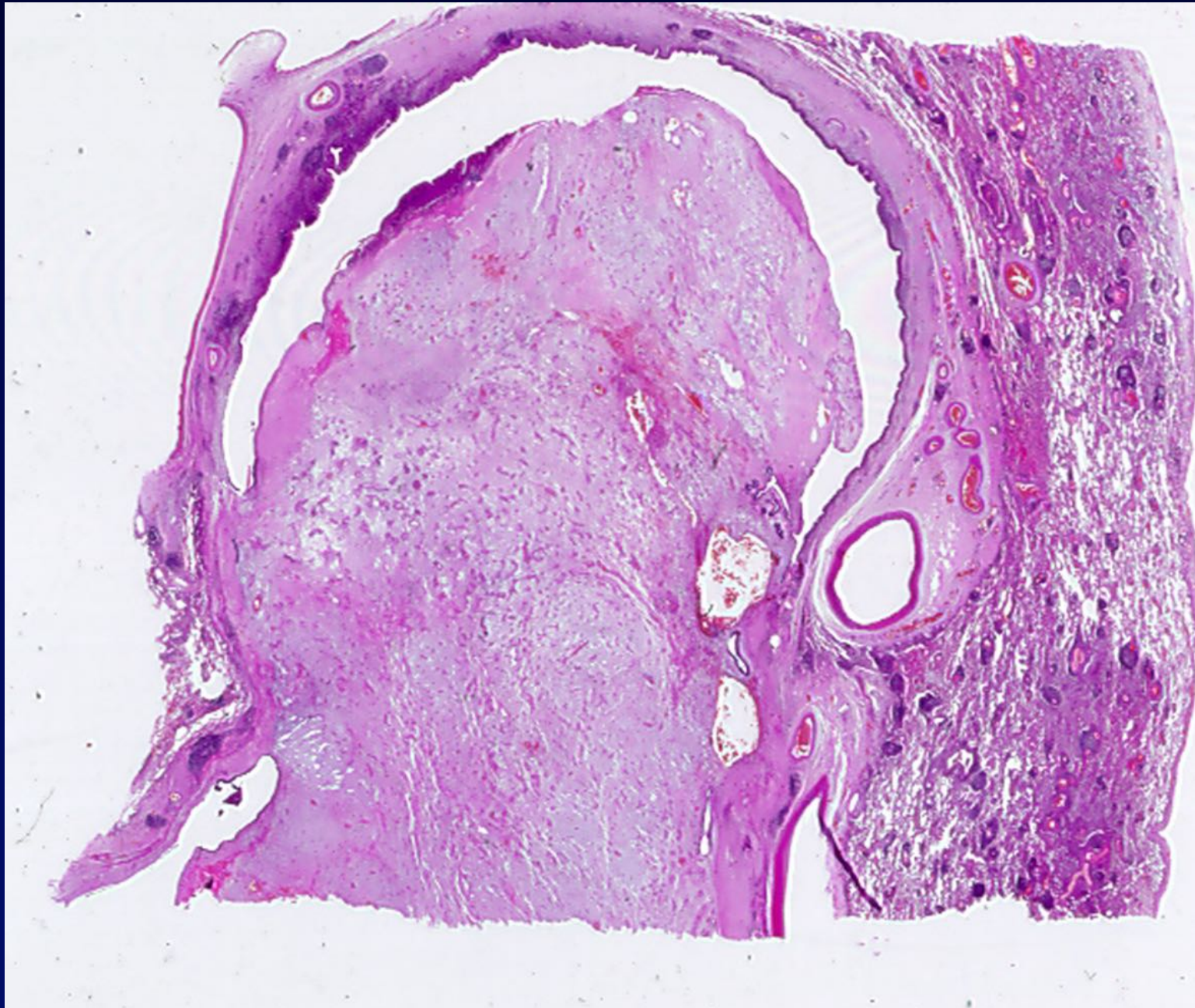
### STEP 1:



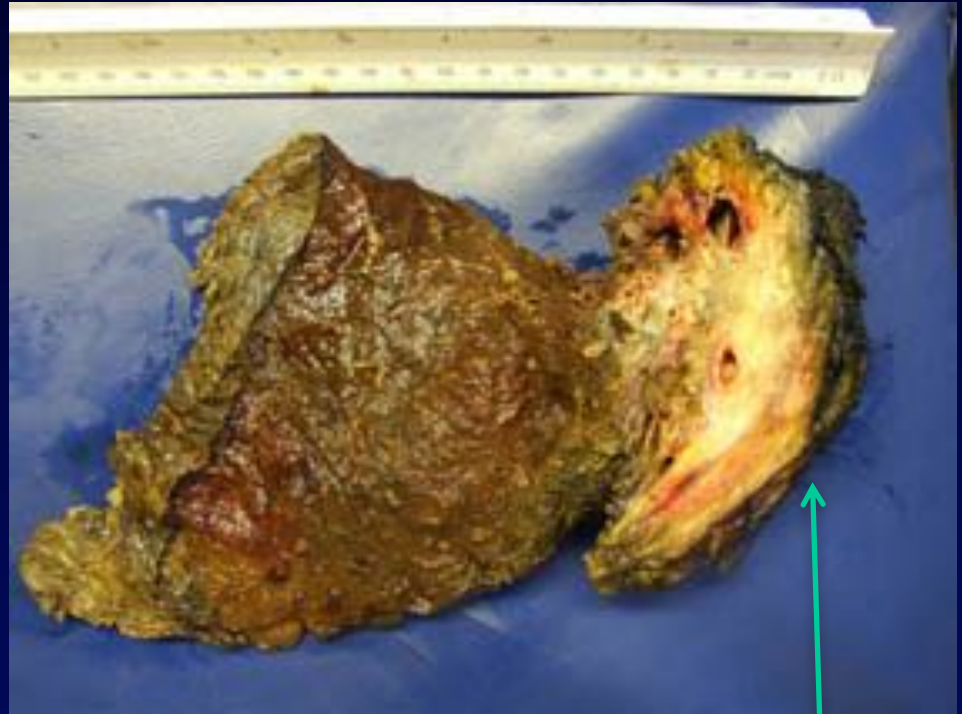
# Macroscopic features of lung carcinomas







## Lobectomy + Chest wall



## Wedge followed by lobectomy



**Ink only  
where you  
need to...**

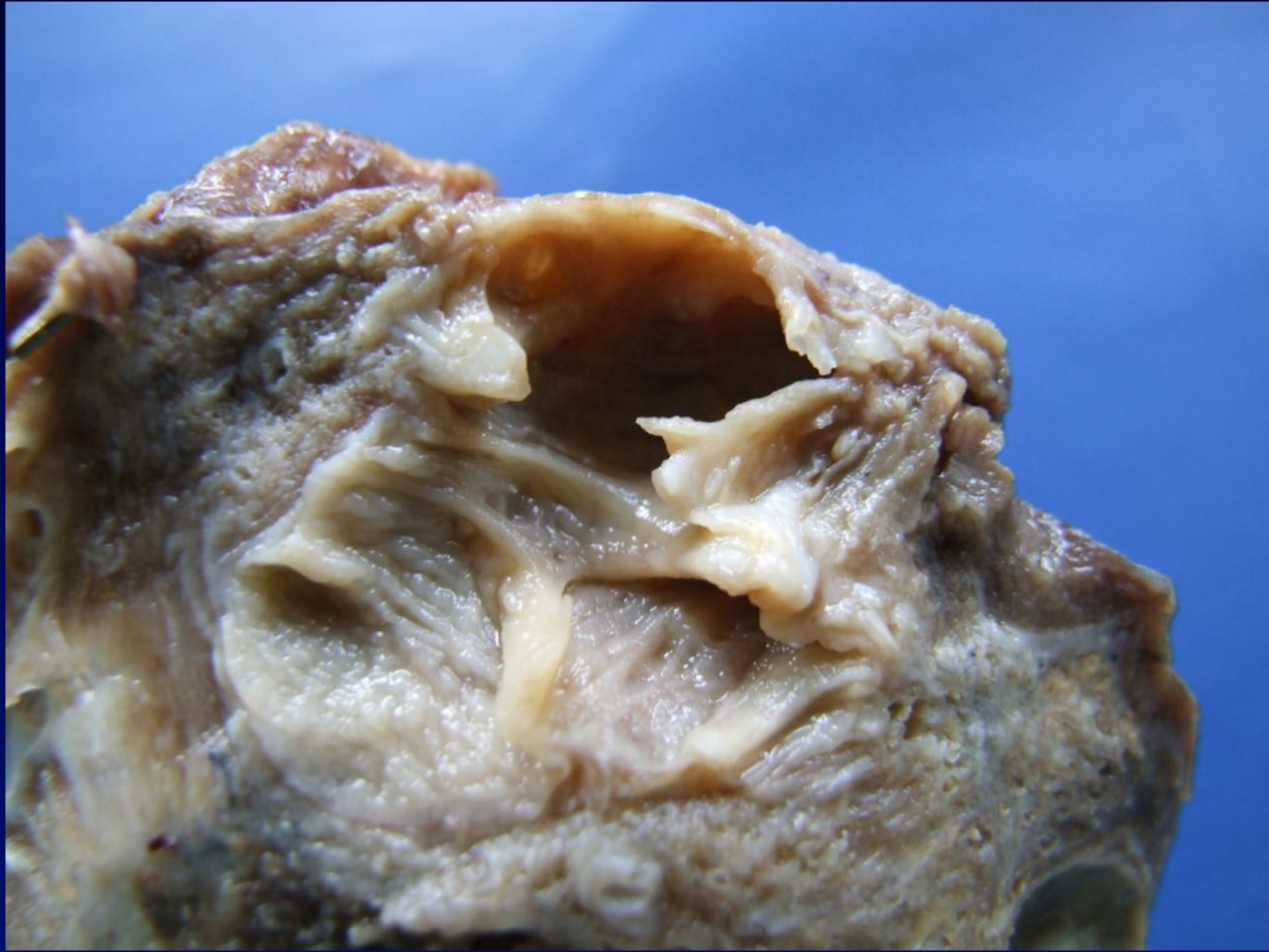






## Approach to cysts in the lung...



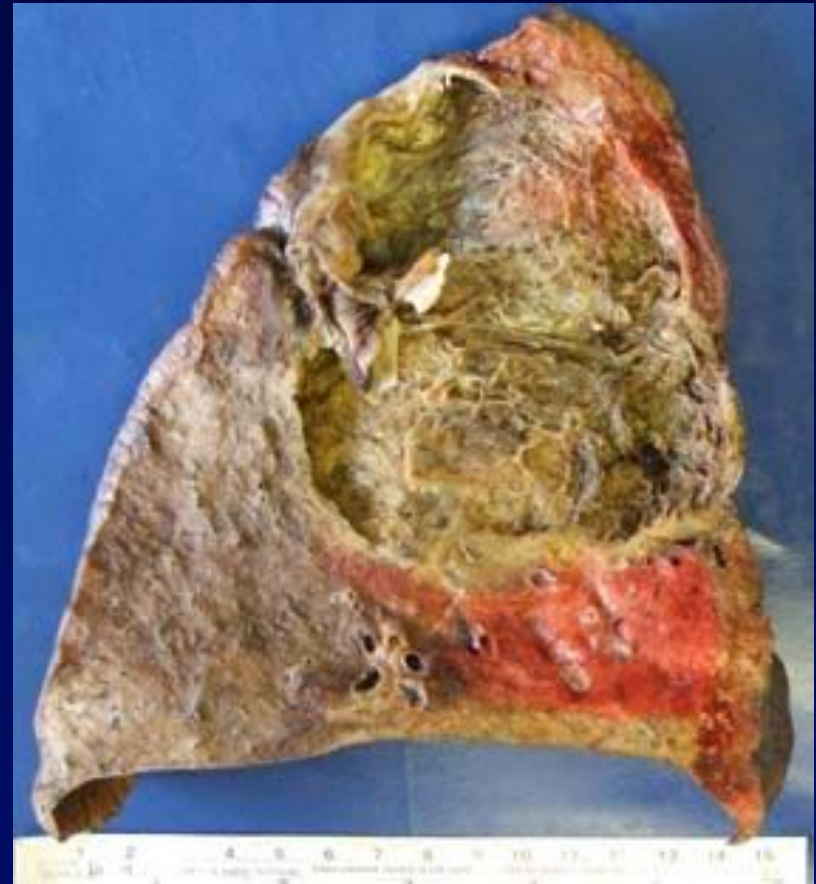




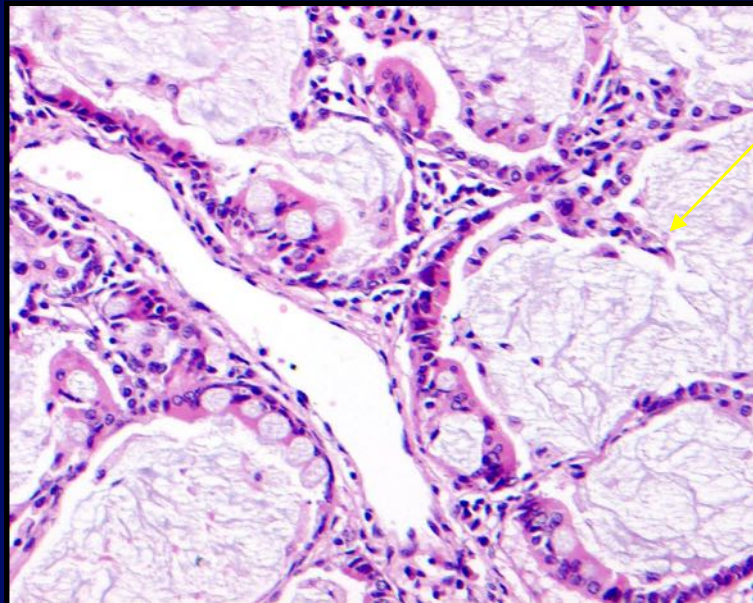




58 year old male with a single bulla in the left lower lobe



Review macroscopic specimen with 5mm sectioning...

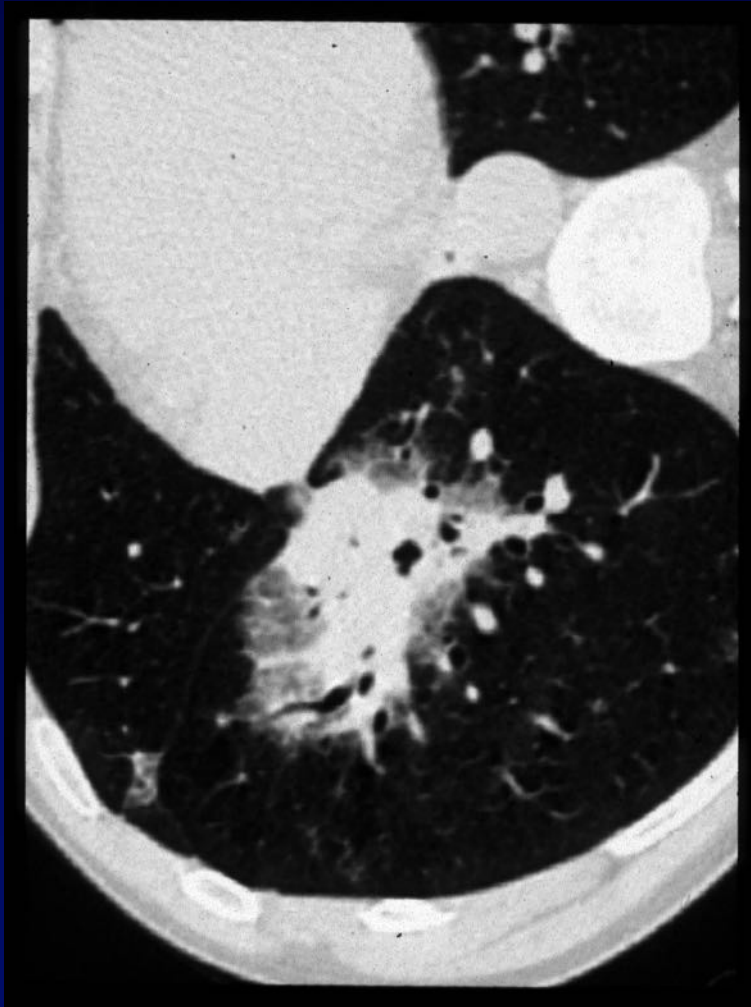


## DIAGNOSIS

Invasive mucinous  
adenocarcinoma arising in a type  
1 congenital cystic adenomatoid  
malformation (CCAM) (pT2N0)



**Review of imaging/clinical data often is useful with regard to macroscopic appearances**



### Box A.1 Varieties of lung specimen

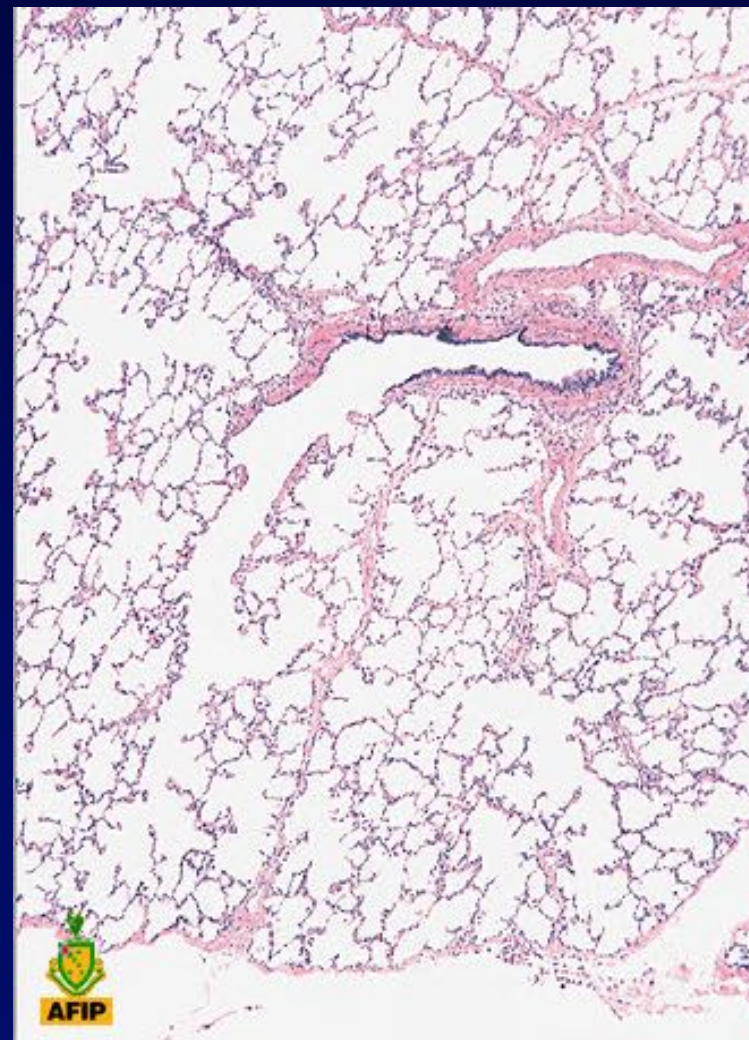
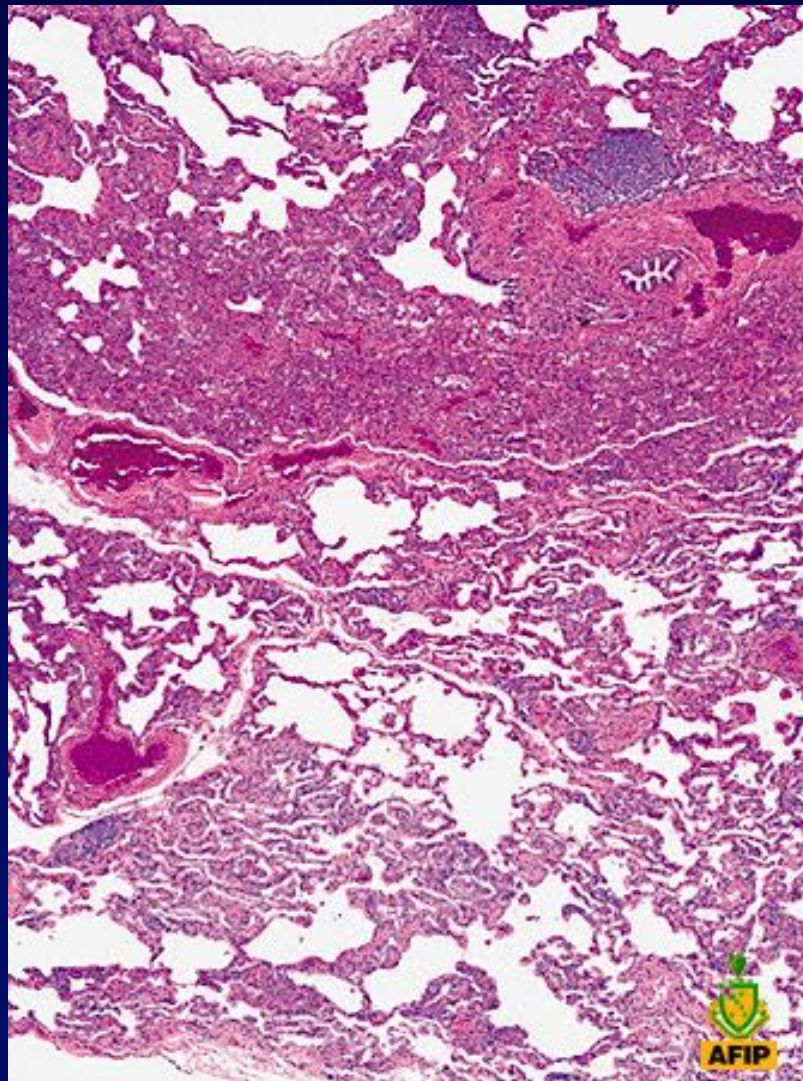
- Needle aspiration
- Fibreoptic bronchoscopic
  - Bronchial biopsy
  - Transbronchial biopsy
- Rigid bronchoscopic bronchial biopsy
- Mediastinoscopy or mediastinotomy lymph node biopsy
- Transcutaneous drill biopsy
- Pleural punch biopsy
- 'Medical' thoracoscopy
- Pleural biopsy
- Thoracotomy or 'surgical' (video-assisted) thoracoscopy
  - Pleural biopsy
  - Wedge lung biopsy
- Segmentectomy
- Lobectomy
- Pneumonectomy
- Post mortem

## Gentle inflation fixation with a small bore needle





# Better microscopic morphology





# Should surgical lung biopsies be inflated?

- **Yes**

- Reduces artefact due to collapse
- Allows better analysis of morphology, especially interstitium

- **No**

- May alter the architecture by overinflation (misdiagnosis of lymphangectasia)
- May 'wash out' macrophages in cases of respiratory bronchiolitis and DIP

### Box A.1 Varieties of lung specimen

- Needle aspiration
- Fibreoptic bronchoscopic
  - Bronchial biopsy
  - Transbronchial biopsy
- Rigid bronchoscopic bronchial biopsy
- Mediastinoscopy or mediastinotomy lymph node biopsy
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- Thoracotomy or 'surgical' (video-assisted) thoracoscopy
  - Pleural biopsy
  - Wedge lung biopsy
  - Segmentectomy
  - Lobectomy
  - Pneumonectomy
- Post mortem

With increasing molecular requirements, use tissue judiciously...

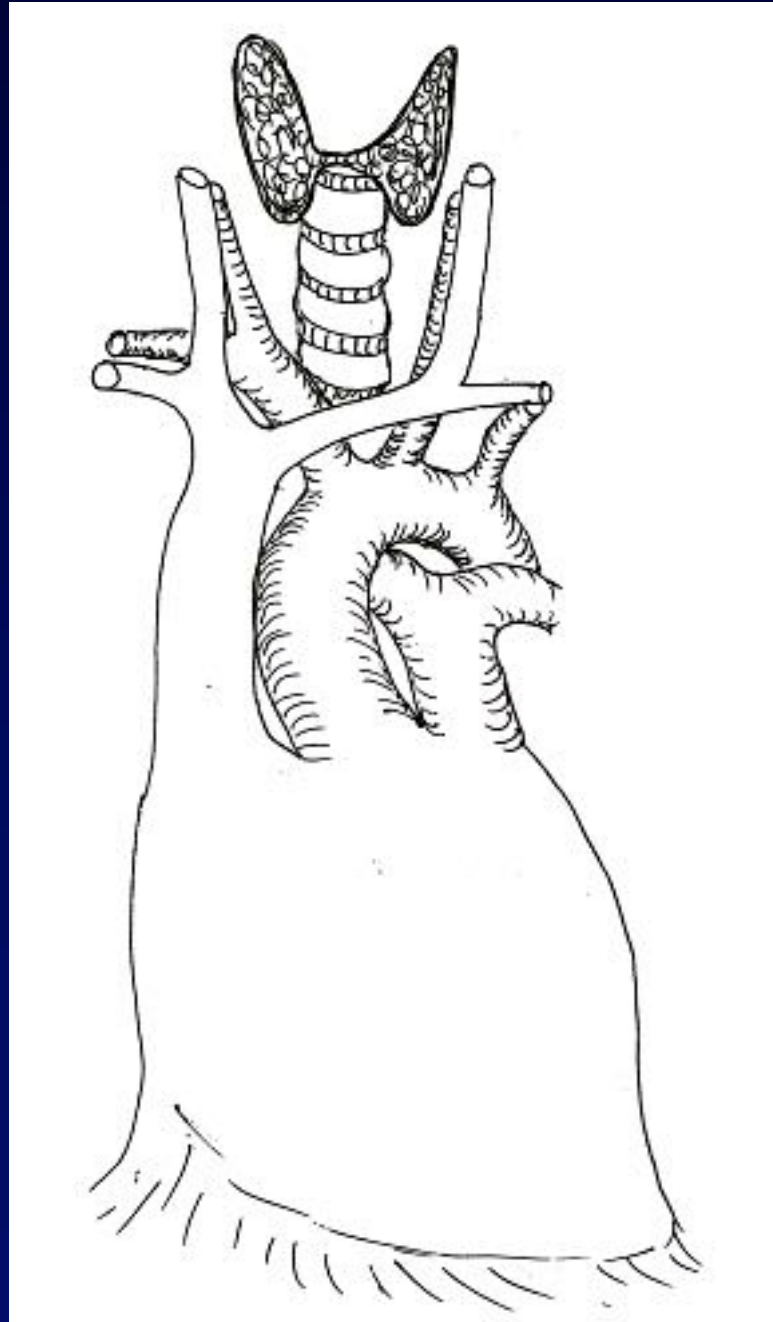
? Multiple blocks  
? Less IHC

# THYMUS

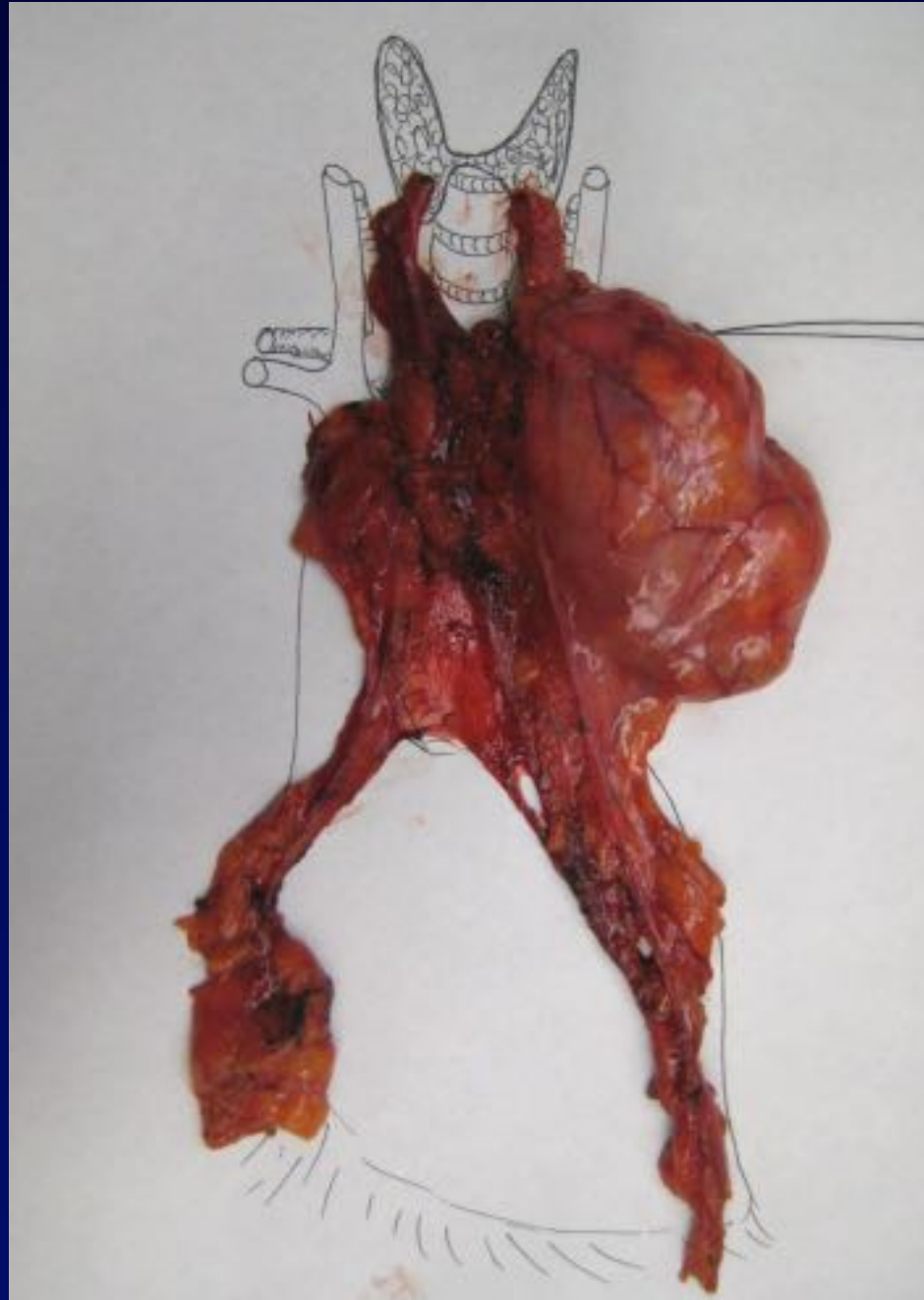
- **Which Way is Up? Policies and Procedures for Surgeons and Pathologists Regarding Resection Specimens of Thymic Malignancy**
- **Detterbeck FC, Moran C, Huang J, Suster S, Walsh G, Kaiser L, Wick M.**
- ***Journal of Thoracic Oncology*, 2011;6(7 Suppl 3):S1730-8**



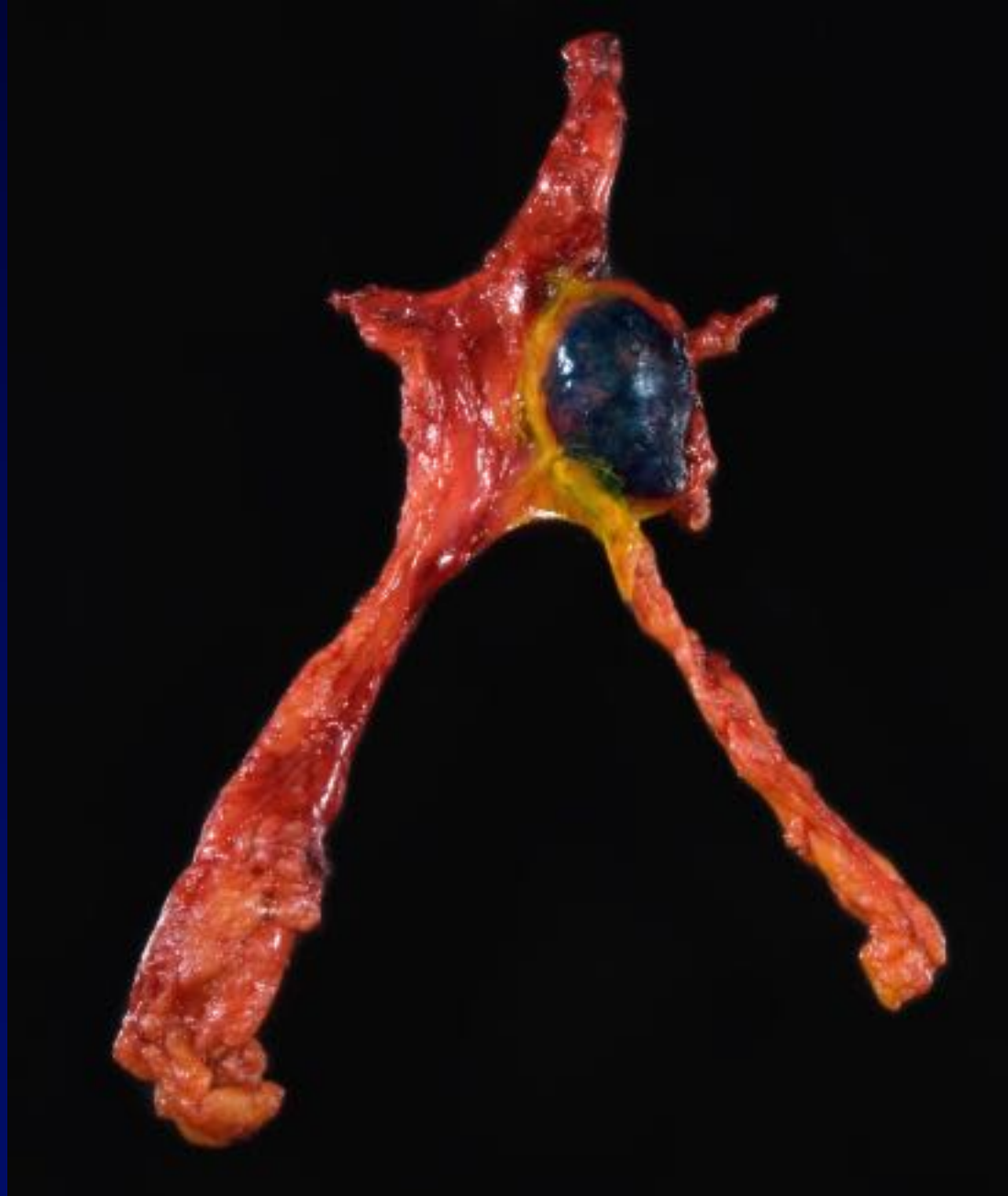
# Figure 1: Mediastinal Board



**Figure 2: Specimen oriented on Mediastinal Board**

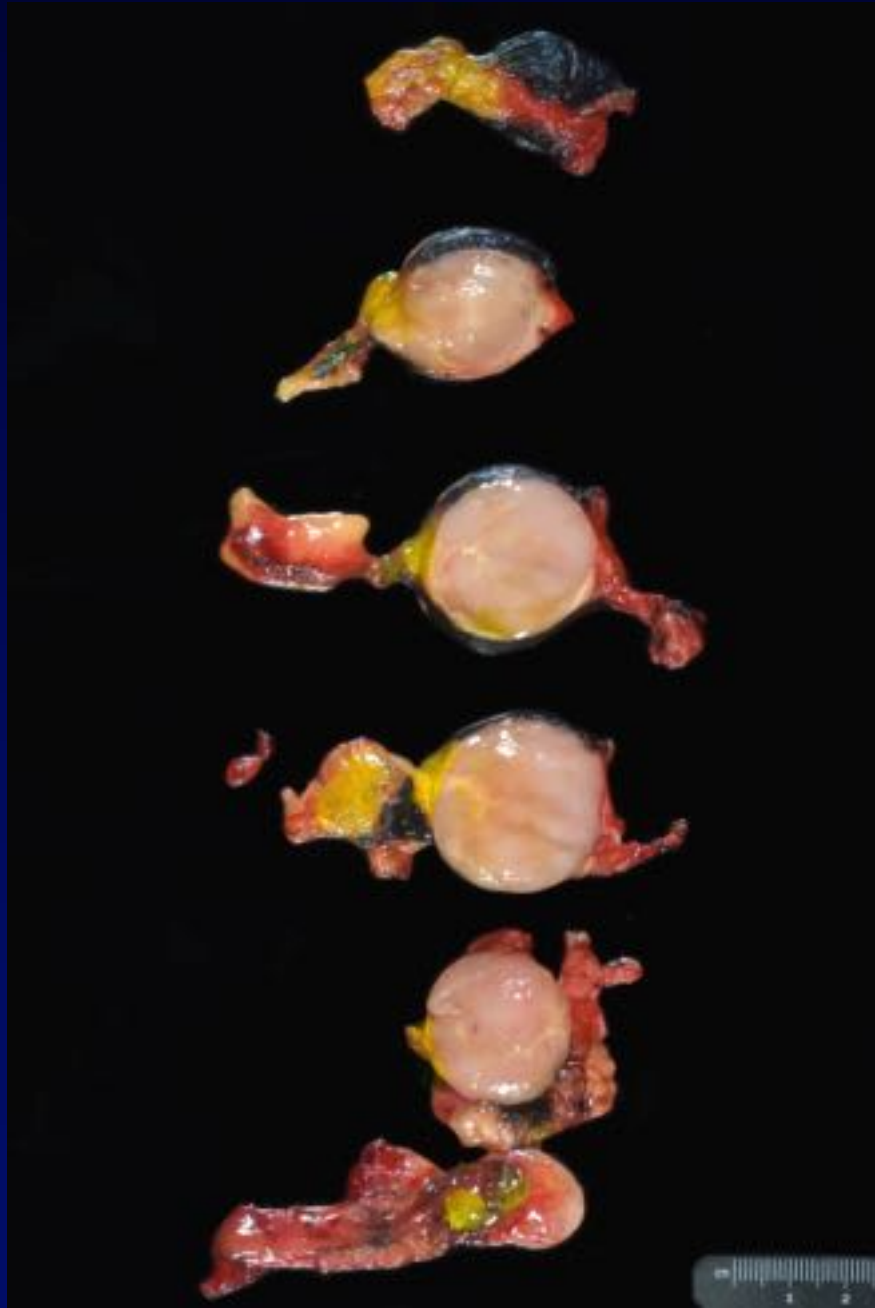


**Figure 3: Inked Specimen, Anterior Aspect**





# Figure 4: Bread-loafed Tumor Specimen



One block per cm max diameter...

Minimum data published in 2014....

# Masaoka-Koga Staging System

---

- I**                      **Grossly and microscopically completely encapsulated tumor**
  
- II**                    **a**                      **Microscopic transcapsular invasion**
  - b**                      **Macroscopic invasion into thymic or surrounding fatty tissue, or grossly adherent to but not breaking through the mediastinal pleura or pericardium**
  
- III**                    **Macroscopic invasion into neighboring organs (i.e. pericardium, great vessel or lung)**
  
- IV**                    **a**                      **Pleural or pericardial metastases**
  - b**                      **Lymphogenous or hematogenous metastasis**

# T stage descriptors

T	Descriptors
<b>T1</b>	<p><b>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.</b></p> <p>For further testing T1 is subdivided into T1a (no mediastinal pleural involvement) and T1b (direct invasion of the mediastinal pleura)</p> <p><i>(Level 1 structures – thymus, anterior mediastinal fat, mediastinal pleura)</i></p>
<b>T2</b>	<p><b>A tumor with direct invasion of the pericardium (either partial or full thickness)</b></p> <p><i>(Level 2 structures – pericardium)</i></p>
<b>T3</b>	<p><b>A tumor with direct invasion into any of the following: lung, brachiocephalic vein, superior vena cava (SVC), phrenic nerve, chest wall or extrapericardial pulmonary artery or veins</b></p> <p><i>(Level 3 structures – lung, brachiocephalic vein, SVC, phrenic nerve, chest wall, hilar pulmonary vessels)</i></p>
<b>T4</b>	<p><b>A tumor with invasion into any of the following: aorta (ascending, arch or descending), arch vessels, intrapericardial pulmonary artery, myocardium, trachea, esophagus</b></p> <p><i>(Level 4 structures – aorta (ascending, arch or descending), arch vessels, intrapericardial pulmonary artery, myocardium, trachea, esophagus)</i></p>

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.

Nicholson AG, Detterbeck FC, Marino M, Kim J, Stratton K, Giroux D, Asamura H, Crowley J, Falkson C, Filosso PL, Giaccone G, Huang J, Kondo K, Lucchi M, Marom EM, Okumura M, Ruffini E, Van Schil P J  
 Thorac Oncol. 2014 Sep;9(9 Suppl 2):S73-80



# TNM proposals (based on ITMIG retrospective database of >8000 cases)

Category	Definition (Involvement of): <sup>a,b</sup>
<b>T1</b>	a
	b
<b>T2</b>	
<b>T3</b>	
<b>T4</b>	

Category	Definition (Involvement of): <sup>a</sup>
<b>N0</b>	
<b>N1</b>	
<b>N2</b>	
<b>M0</b>	
<b>M1</b>	a
	b

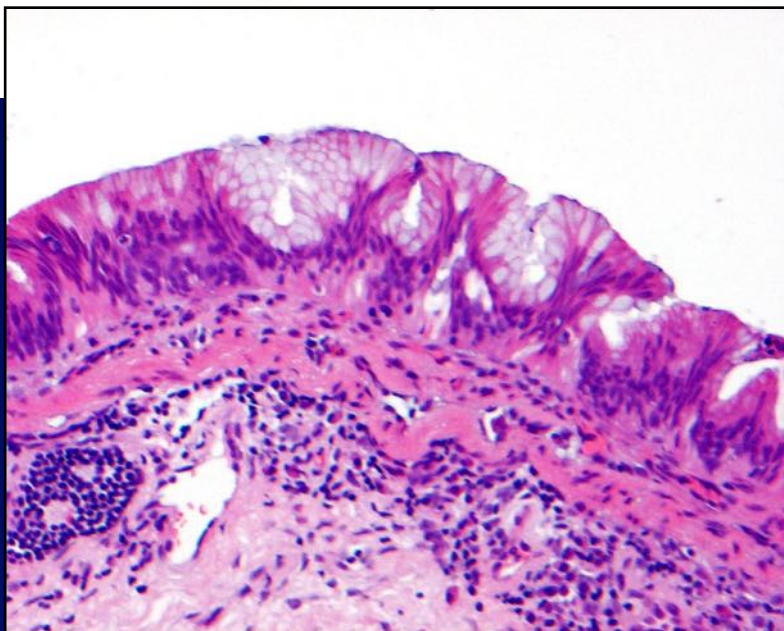
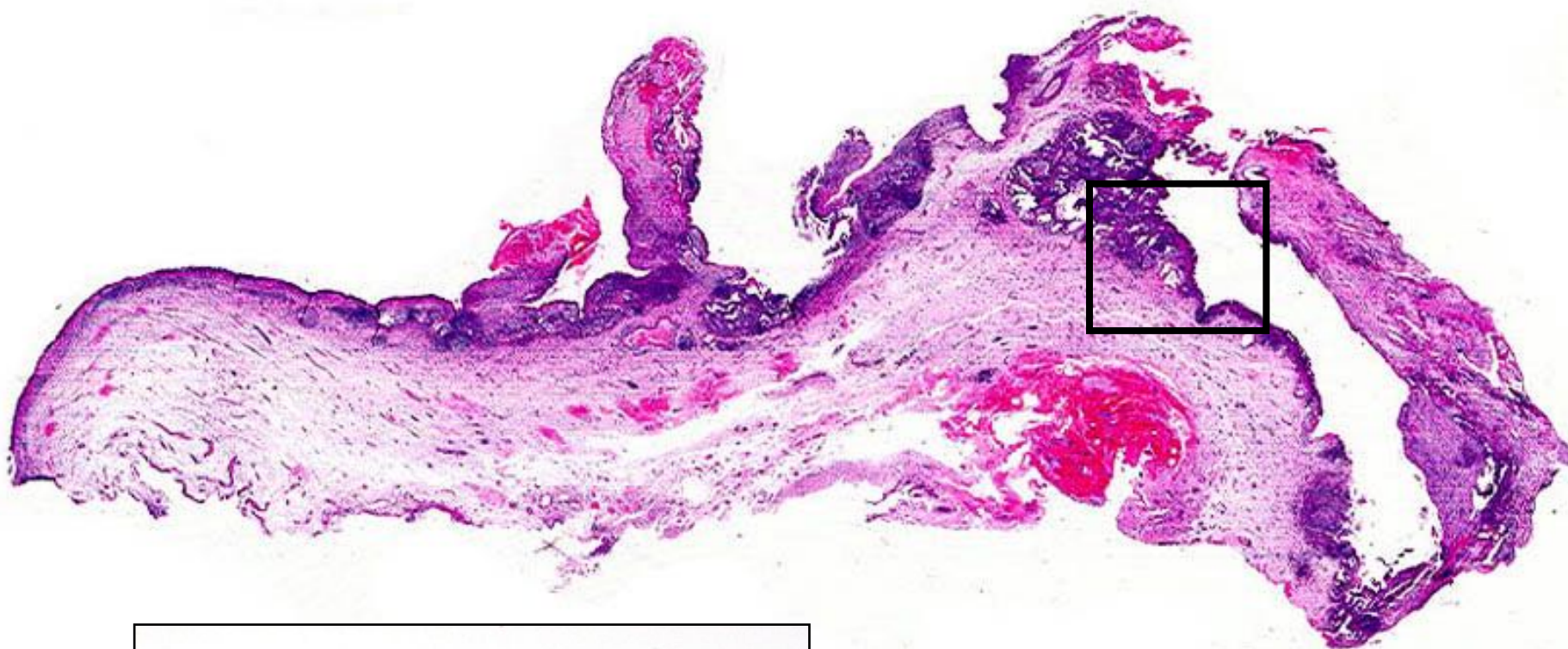
Stage	T	N	M
<b>I</b>	T1	N0	M0
<b>II</b>	T2	N0	M0
<b>IIIa</b>	T3	N0	M0
<b>IIIb</b>	T4	N0	M0
<b>IVa</b>	T any	N1	M0
	T any	N0,1	M1a
<b>IVb</b>	T any	N2	M0,1a
	T any	N any	M1b

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. Detterbeck FC, Stratton K, Giroux D, Asamura H, Crowley J, Falkson C, Filosso PL, Frazier AA, Giaccone G, Huang J, Kim J, Kondo K, Lucchi M, Marino M, Marom EM, Nicholson AG, Okumura M, Ruffini E, Van Schil P et al. J Thorac Oncol. 2014 Sep;9(9 Suppl 2):S65-72

# **Approach to Cut-Up; Macroscopic Examination as the Precursor to Accurate Microscopic Interpretation LUNG and THYMUS**

## **CONCLUSIONS**

- 24 hours inflation fixation is optimal
- Know (or have a diagram to hand) the anatomy (segments) and have nodal map to hand.
- Dissect hilum first (unless good reason)
- Assess tumour (\*approach may be dependent on site)
- Assess background lung and airways, if not already done so.
- Ensure that description and blocks taken will fulfil the minimum data set\*.
  - Localised mass or diffuse,
  - Tumour location - involvement of pleura/airways
  - Proximity to surgical margins
  - Tumour size
  - Satellite nodules
  - Description of surrounding lung
- Return to specimen/discuss with surgeon and radiologist as appropriate
- Thymus – follow recommended approach from ITMIG. New TNM staging system proposed.

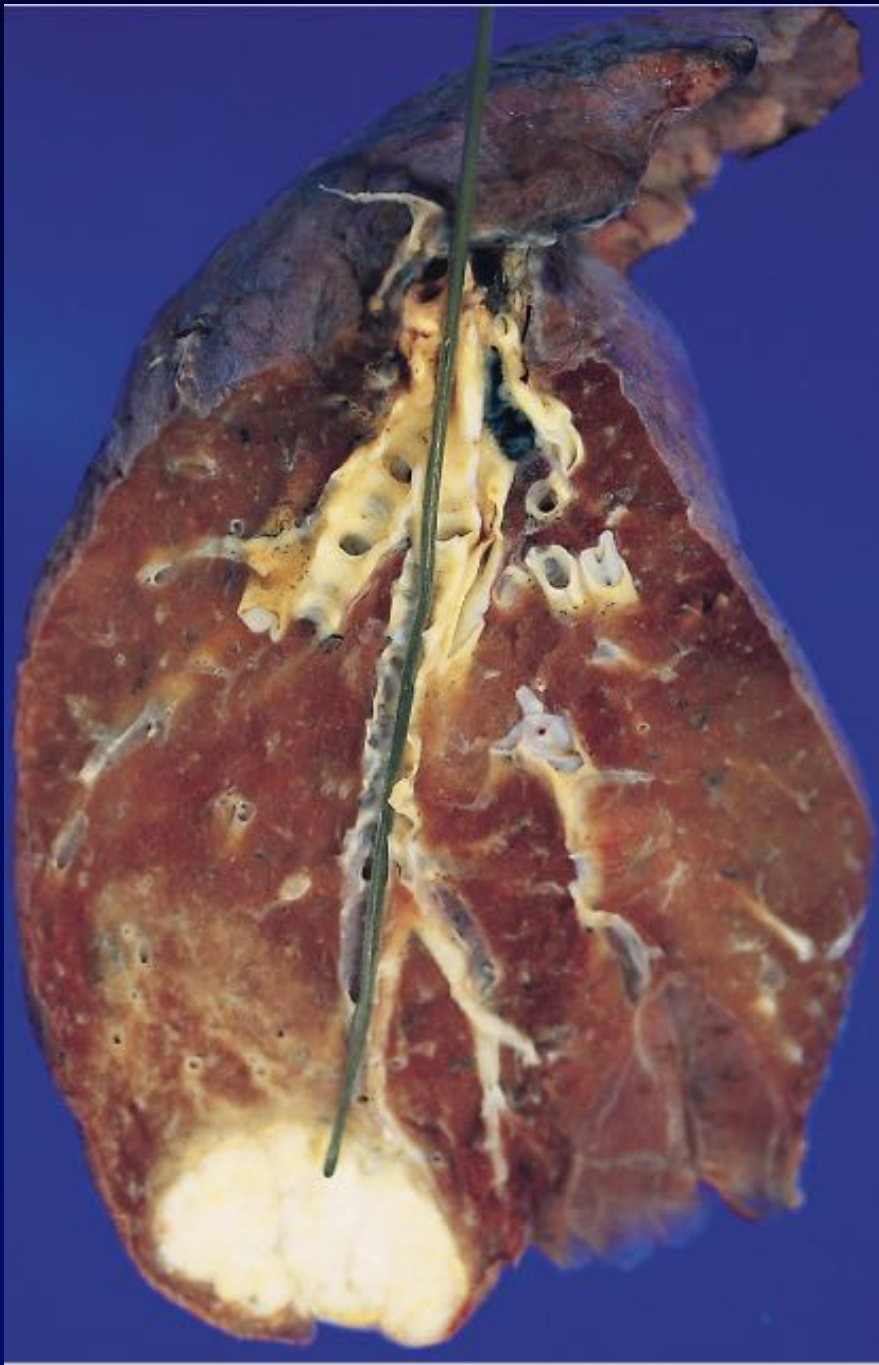




# **Specimen Handling**

- **Identify areas of concern prior to sectioning, and areas of tissue disruption occurring 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 from superior to inferior, and sections serially ordered and submitted**
- **One block per cm of tumor should be submitted;**
- **Take at least 5 representative sections should be taken regardless of the tumor diameter**
- **Random sections from the remaining uninvolved thymus should be submitted**

## FOR PERIPHERAL TUMOURS (Liebow method)



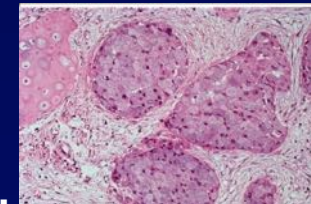
# Best Practice for Usage of Tissue – Everyone has a Role to Play!

## ■ Pre-examination phase

- Identify those who you would consider for targeted therapy
- Handle tissue appropriately (right media, timely fixation etc)
- Put core biopsies in separate pots

## ■ Examination phase (“judicious use of tissue”)

- Consider separate blocks for different cores
- Cut into the tissue carefully (if cutting levels, take spare sections)
- Selection for testing based on histology
  - ADC versus SQCC
  - Apply immunohistochemistry appropriately (ideally only once)
  - Specific antibodies (ALK)
    - ALK IHC correlates with gene rearrangement



Boland JM et al. *Hum Pathol.* 2009;40(8):1152-1158; Conklin CM et al. *J Thorac Oncol.* 2013;8(1):45-51.

## ■ Post-examination phase

- Enhance tumour load by microdissection



