Mediastinal Staging

Samer Kanaan, M.D.

Overview

➢ **Importance of accurate nodal staging**

➢ **Accuracy of radiographic staging**

➢ **Mediastinoscopy**

➢ **EUS**

➢ **EBUS**

Staging

TNM Definitions

- **T Stage**
  - **Size of the Primary Tumor**
  - **Adjacent structures invaded into by Tumor**
- **N Stage**
  - **Nodal disease involvement**
- **M Stage**
  - **Metastatic disease involvement**

Stage	TNM Classifcation
IA	T1N0M0
IB	T2N0M0
IIA	T1N1M0
IIB	T2N1M0 or T3N0M0
IIIA	T1-3N2M0 or T3N1M0
IIIB	$T4N_{any}M0$ or $T_{any}N3M0$
IV	$T_{any}N_{any}M1$
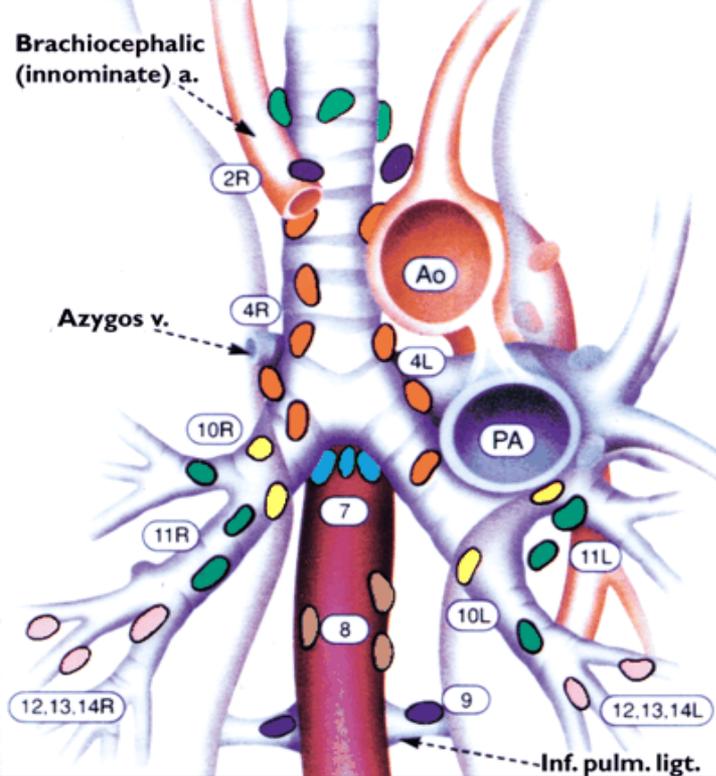
Brachiocephalic (innominate) a.

Azygos v.

2R

4R

4L

Ao

PA

10R

7

11R

11L

10L

8

12,13,14R

9

12,13,14L

Inf. pulm. ligt.

Superior Mediastinal Nodes
- 1 Highest Mediastinal
- 2 Upper Paratracheal
- 3 Prevascular and Retrotracheal
- 4 Lower Paratracheal (including azygos nodes)

N_2 = single digit, ipsilateral
N_3 = single digit, contratateral or supraclavicular

Aortic Nodes
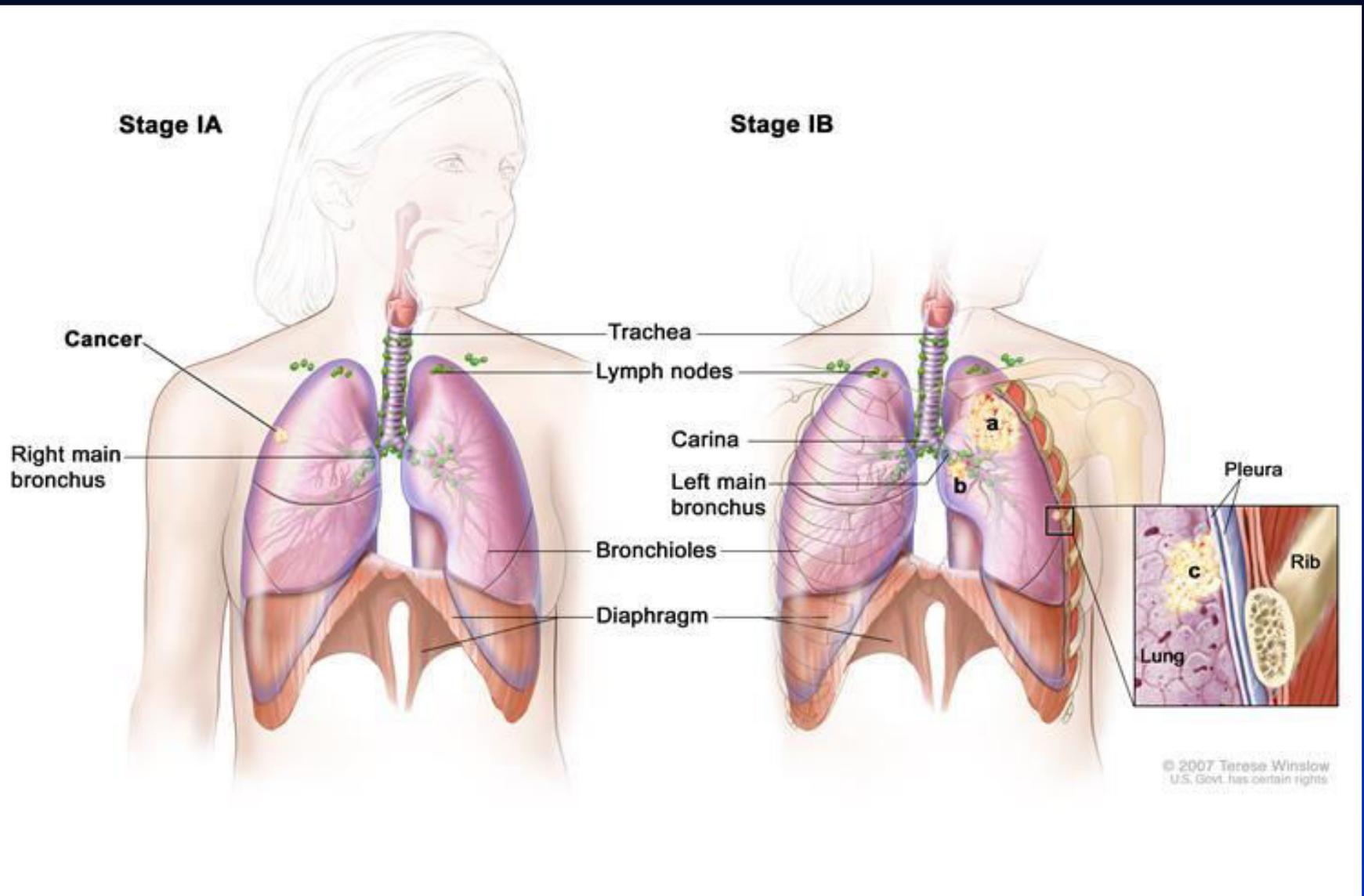- 5 Subaortic (AP window)
- 6 Para-aortic (Ascending aorta or phrenic)

Inferior Mediastinal Nodes
- 7 Inferior Mediastinal Nodes
- 8 Paraesophageal (below carina)
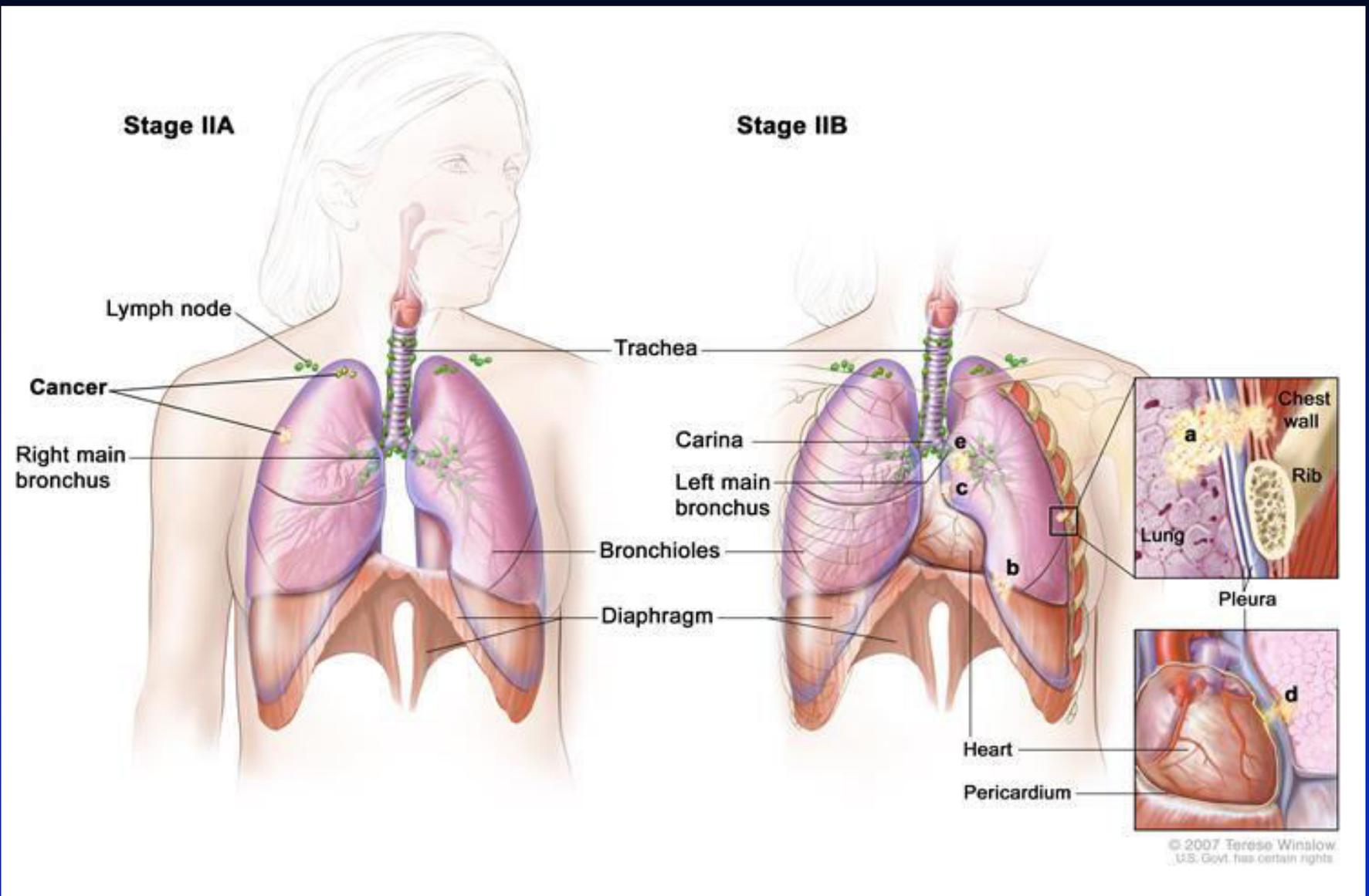- 9 Pulmonary Ligament

N_1 Nodes
- 10 Hilar
- 11 Interlobar
- 12 Lobar
- 13 Segmental
- 14 Subsegmental

Phrenic n.

3

Ligamentum arteriosum

L. pulmonary a.

Ao

6

5

PA
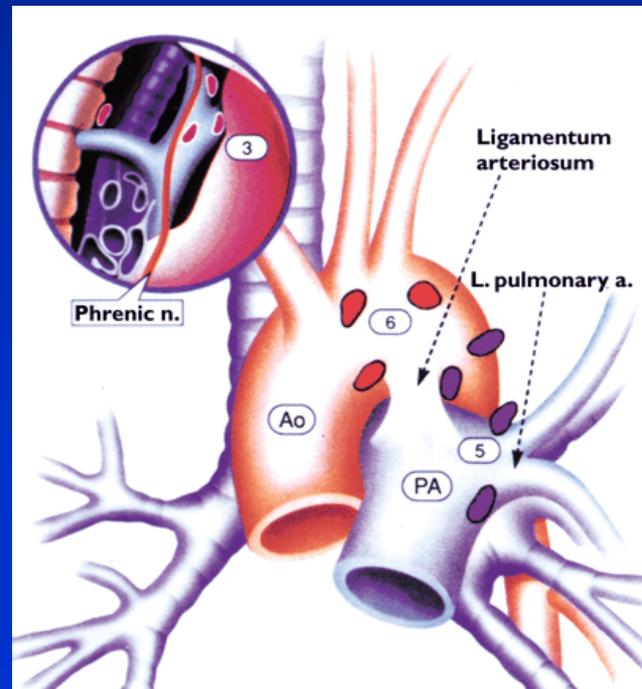
**Stage IA**, cancer is in the lung only, less than 3cm in size.
Stage IB, the cancer is: **(a)** greater than 3cm in size **(b)** involve the main bronchus **(c)** invade visceral pleura **(d)** associated with obstructive pneumonitis.

Stage IIA, cancer is less than 3cm in size and involves ipsilateral hilar lymph nodes.
Stage IIB, cancer is either the same as in stage IB and has also spread to ipsilateral hilar lymph nodes or Cancer has not spread to lymph nodes but has spread to one or more of the following: **(a)** the chest wall, **(b)** the diaphragm, **(c)** mediastinal pleura, **(d)** pericardium, **(e)** the main bronchus less than 2cm from the carina, and/or **(f)** associated obstructive pneumonitis of the entire lung.
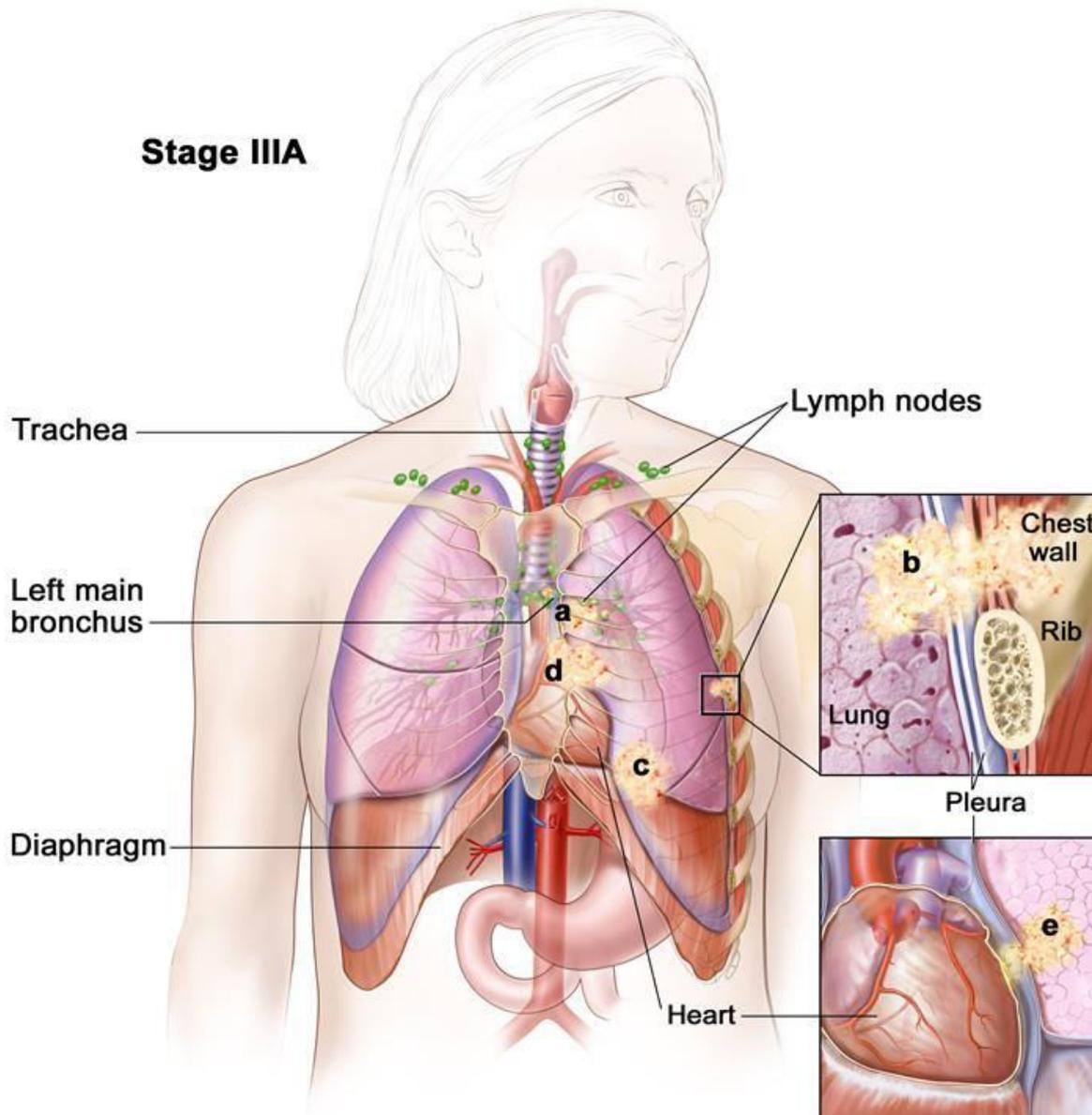
Stage IIIA

The cancer has spread to ipsilateral mediastinal or subcarinal lymph nodes (N2).

Similar to Stage IIB, It may also spread to one or more of the following: (a) the chest wall, (b) the diaphragm, (c) mediastinal pleura, (d) pericardium, (e) the main bronchus less than 2cm from the carina, and/or (f) associated obstructive pneumonitis of the entire lung.
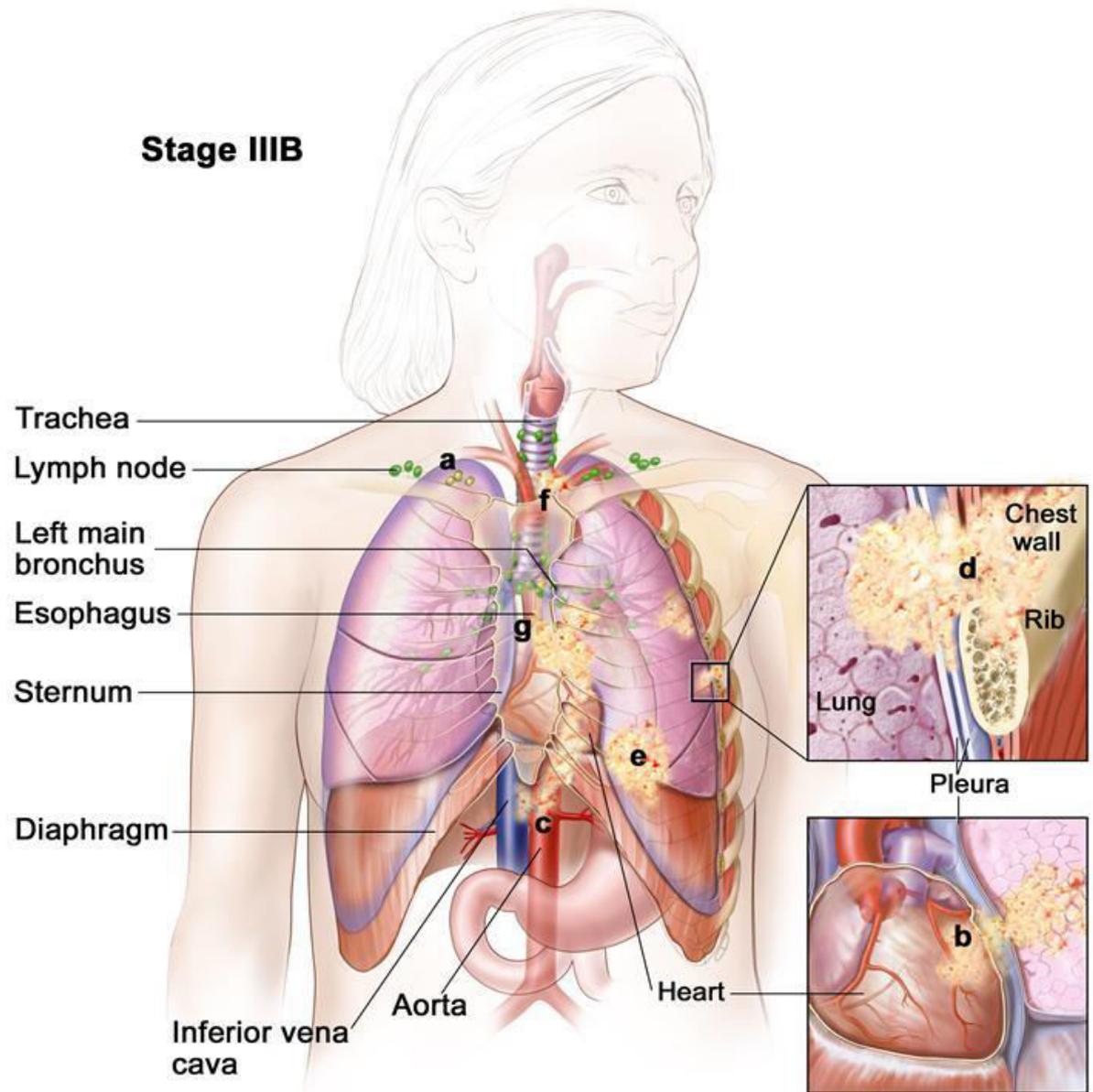
Stage IIIB
The cancer has spread to (a) contralateral mediastinal or hilar nodes or ipsilateral supraclavicular nodes.

The cancer may also spread to one or more of the following: (b) the heart, (c) the inferior vena cava and the aorta, (f) the trachea, and (g) the esophagus.

Cancer may also spread to the pleural fluid (T4).

Separate nodules in the same lobe is also (T4)*

Stage IIIB

Trachea
Lymph node
Left main bronchus
Esophagus
Sternum
Diaphragm
Inferior vena cava
Aorta
Heart

Chest wall
Rib
Lung
Pleura

© 2007 Terese Winslow
U.S. Govt. has certain rights

Stage IV

Lung cancer has spread to other parts of the body:
- Brain
- Lymph node
- Another lobe of the lung
- Adrenal gland
- Liver
- Kidney
- Bone

Cancer

Blood

Lymph nodes

To other parts of the body

© 2007 Terese Winslow
U.S. Govt. has certain rights
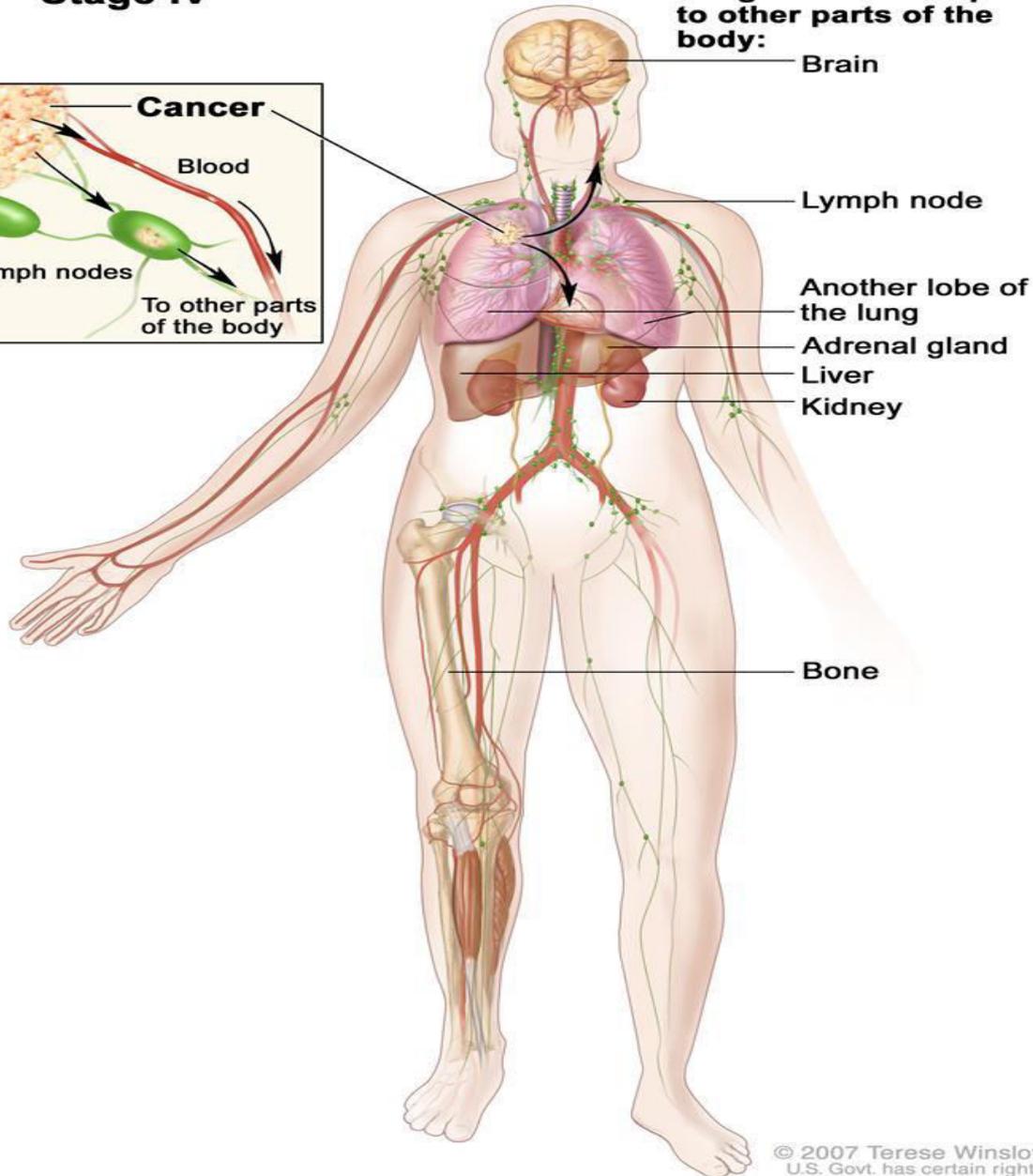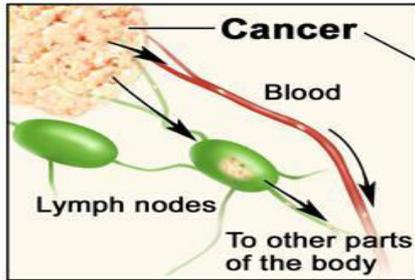
Staging

NSCLC Incidence by Stage
US Population, 2006
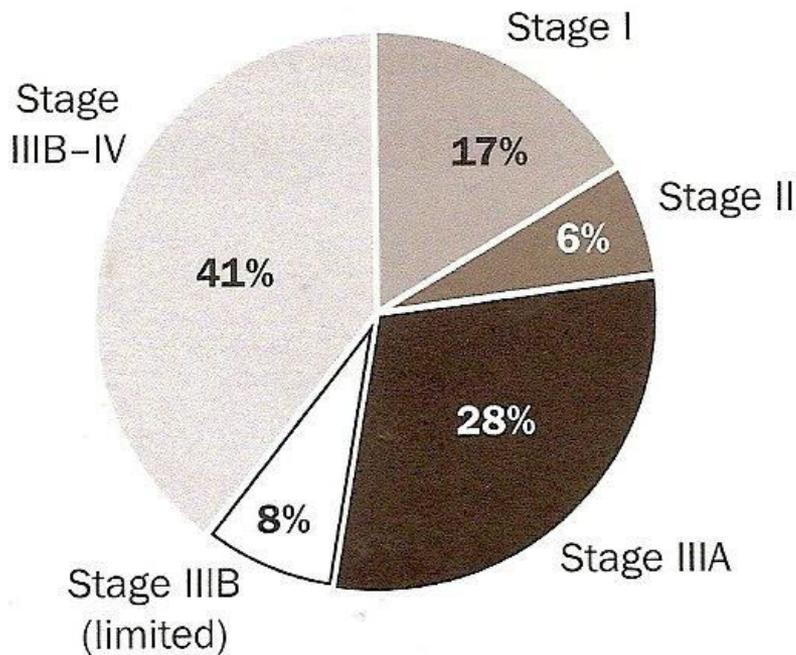
Disease and Stage	Annual Incidence	1-Year Survival	5-Year Survival
NSCLC	140,000	—	17%
I	24,000	90%	70%
II	9,000	80%	40%
IIIA	42,000	70%	20%
IIIB (limited)	11,000	50%	4%
IIIB–IV	57,000	35%	3%

Stage	TNM Classifcation	5 Year Survival
IA	T1N0M0	67
IB	T2N0M0	57
IIA	T1N1M0	55
IIB	T2N1M0 or T3N0M0	39
IIIA	T1-3N2M0 or T3N1M0	23
IIIB	T4N_{any}M0 or T_{any}N3M0	5
IV	$T_{any}N_{any}$M1	1

Why is accurate nodal staging essential?

- ➢ **N1 disease**
- ➢ **N2 disease**
- ➢ **N3 disease**

Treatment of Lung Cancer According to Stage

Stage	Primary treatment	Adjuvant therapy	Five-year survival rate (%)
Non-small cell carcinoma			
I	Resection	Chemotherapy	60 to 70
II	Resection	Chemotherapy with or without radiotherapy	40 to 50
IIIA (resectable)	Resection with or without preoperative chemotherapy	Chemotherapy with or without radiotherapy	15 to 30
IIIA (unresectable) or IIIB (involvement of contralateral or supraclavicular lymph nodes)	Chemotherapy with concurrent or subsequent radiotherapy	None	10 to 20
IIIB (pleural effusion) or IV	Chemotherapy or resection of primary brain metastasis and primary T1 tumor	None	10 to 15 (two-year survival)
Small cell carcinoma			
Limited disease	Chemotherapy with concurrent radiotherapy	None	15 to 25
Extensive disease	Chemotherapy	None	< 5

Treatment – Stage IIIA

- Stage IIIA N2 disease 5 year survival is 10-15% overall
- Stage IIIA bulky mediastinal involvement (visible on CXR) have **5 year survival of 2-5%**

Radiation:
- Treatment with 60 Gy can achieve long term survival benefit in 5-10% of patients

Chemotherapy and Radiation:
- Meta analysis from 11 randomized studies showed **cisplatin based chemotherapy with radiation resulted in 10% reduction in the risk of death compared to radiation therapy alone.**

Combined SurgicalTherapy:
- **Neoadjuvant** chemotherapy plus surgery had median survival **> 3X** versus surgery alone
- **Neoadjuvant** chemotherapy and radiation allowed 65-75% patients to undergo surgical resection → these patients had **27% 3 year survival.**

N2 Disease

➢ **Patients benefit from neoadjuvant therapy and surgery *versus* resection followed by adjuvant therapy.**

➢ **Patients are more likely to complete chemotherapy regimen pre operatively than post operatively.**

➢ **Awaiting definitive results of the NATCH (Neoadjuvant Taxol Carboplatin Hope) trial available 2009**

Alam N, et al. Lung Cancer 2005;47:385-394

Depierre A, et al. J Clin Oncol 2002;20:247-253

What is the accuracy of radiographic staging?

Noninvasive Staging of Non-small Cell Lung Cancer: ACCP Evidenced-Based Clinical Practice Guidelines (2nd Edition)

Gerard A. Silvestri, Michael K. Gould, Mitchell L. Margolis, Lynn T. Tanoue, Douglas McCrory, Eric Toloza and Frank Detterbeck

CT Scan

Information gained by CT

- ➢ **Tumor size**
- ➢ **Tumor number**
- ➢ **Central tumor or Peripheral**
- ➢ **Lymph node enlargement (>1 cm)**
- ➢ **Extent**
  - ➢ **Discrete lymph nodes versus mediastinal infiltration**
- ➢ **Metastatic disease**

Accuracy of CT in Staging

CT scan

- **Tumor**
  - **Sensitivity = 63%**
  - **Specificity = 84%**
- **Mediastinum**
  - **Sensitivity = 51-75%**
  - **Specificity = 66-86%**
  - **Positive predictive value = 60%**
  - **Negative predictive value = 80%**

Toloza E, et al. Chest 2003(suppl):137s–146s
Gould MK, et al. Ann Intern Med 2003; 139:879–892
Dwamena et al. Radiology 1999; 213:530–536

Accuracy of CT in Staging the Mediastinum

➤ **CT scanning alone is not sufficient to determine nodal staging**

➤ **However, certain characteristics can guide further staging**

CT Staging of the Mediastinum

- **Group A: mediastinal infiltration**

- **Group B: discrete mediastinal lymph node enlargement**

- **Group C: central tumor or suspected N1 disease**

- **Group D: peripheral tumor, no mediastinal involvement**

- **Invasive biopsy**

- **Invasive biopsy**

- **N2, N3 involvement 20-25% → Invasive biopsy**

- **???**

Prevalence of N2 disease in clinical stage I

➢ **Location?**
  ➢ **Central** ➔ **9-11%**
  ➢ **Peripheral** ➔ **6-19%**

➢ **Cell Type?**
  ➢ **Adenocarcinoma** ➔ **14%**
  ➢ **Squamous** ➔ **8.9%**

➢ **Tumor Stage?**
  ➢ **T1** ➔ **8.4%**
  ➢ **T2** ➔ **10.4%**

Suzuki K et al, JTCVS; 1999;117:593-8

Daly BD, et al. JTCVS; 1993;105:904-10

Uy KFL et al, Difficult Decisions in Thoracic Surgery; 2007:68-74.

CT Staging of the Mediastinum

- **Group A:** mediastinal infiltration

- **Group B:** discrete mediastinal lymph node enlargement

- **Group C:** central tumor or suspected N1 disease

- **Group D:** peripheral tumor, no mediastinal involvement

- **Invasive biopsy**

- **Invasive biopsy**

- **N2, N3 involvement 20-25% → Invasive biopsy**

- **??? → But must assume at least 10% chance of N2 disease → Invasive biopsy**

PET Scan

PET in Staging

- Detecting both size and activity of tumor
- Detecting size and activity of lymph nodes
- Provides whole-body information
  - M1 disease found in **1-8%** of patients thought to be stage I by CT
  - M1 disease found in **7-18%** of patients thought to be stage II by CT

Reed CE, et al. JTCVS 2003; 126:1943–1951
MacManus MP, et al. Int J Radiat Oncol Biol Phys 2001; 50:287–293

Accuracy of PET in Staging the Mediastinum

PET Scan

> **Tumor**

>> **Sensitivity = 83-96%**

>> **Specificity = 73-78%**

> **Mediastinum**

>> **Sensitivity = 64-91%**

>> **Specificity = 77-93%**

> **Distant Metastasis**

>> **Sensitivity = 95%**

>> **Specificity = 83%**

Recommendations of PET in Staging the Mediastinum

➢ **Stage IA** ➔ **consider**

➢ **Stage IB-IIIB** ➔ **should undergo PET**

➢ **Any abnormal result in the mediastinum should prompt lymph node sampling**

PET/CT combined

Accuracy of Helical Computed Tomography and [18F] Fluorodeoxyglucose Positron Emission Tomography for Identifying Lymph Node Mediastinal Metastases in Potentially Resectable Non–Small-Cell Lung Cancer

Francisco Pozo-Rodríguez, José L. Martín de Nicolás, María A. Sánchez-Nistal, Antonio Maldonado, Santiago García de Barajas, Rosa Calero-García, Miguel A. Pozo, Pedro Martín-Escribano, Isabel Martín-García, Ricardo García-Lujan, Angel Lopez-Encuentra, and Angel Arenas de Pablo

	Sensitivity	Specificity
CT	86%	67%
PET	94%	59%
PET/CT	97%	44%

Is the combination of PET/CT good enough to obviate mediastinoscopy?

- **Radiographic N2, N3 = need for tissue biopsy prior to neoadjuvant therapy**
  - **NO**

- **Radiographic N1 = 20-25% occult N2 disease**
  - **NO**

- **Radiographic N0**
  - **CONTROVERSIAL**

What is the prevalence of undetected N2 disease after PET/CT

➢ **PET/CT staging was node negative**

➢ **At mediastinoscopy found to have N2 disease 11.7% of the time (n=137)**

Gonzalez-Stawinski et al. JTCVS 2003;126:1900-1905

What is the prevalence of undetected N2 disease after PET/CT

➢ **After CT → 19.2% (n=2224)**

➢ **After CT + PET → 6.7% (n=906)**

➢ **After CT + mediastinoscopy → 8.3% (n=869)**

➢ **After CT + PET + mediastinoscopy → 4.5% (n=178)**

Uy KFL et al, Difficult Decisions in Thoracic Surgery; 2007:68-74.

What is the prevalence of undetected N2 disease after PET/CT

➢ **PET/CT staging was node negative but at thoracotomy found to have N2 disease 5.6%**

➢ **PET/CT/mediastinoscopy staging was node negative but at thoracotomy found to have N2 disease 4.5%**

Choice of lymph node sampling

Table 1—*Techniques of Invasive Mediastinal Staging*

Mediastinoscopy
EUS-NA
TBNA
EBUS-NA
TTNA
VATS staging
Chamberlain procedure
Extended cervical mediastinoscopy

Mediastinoscopy

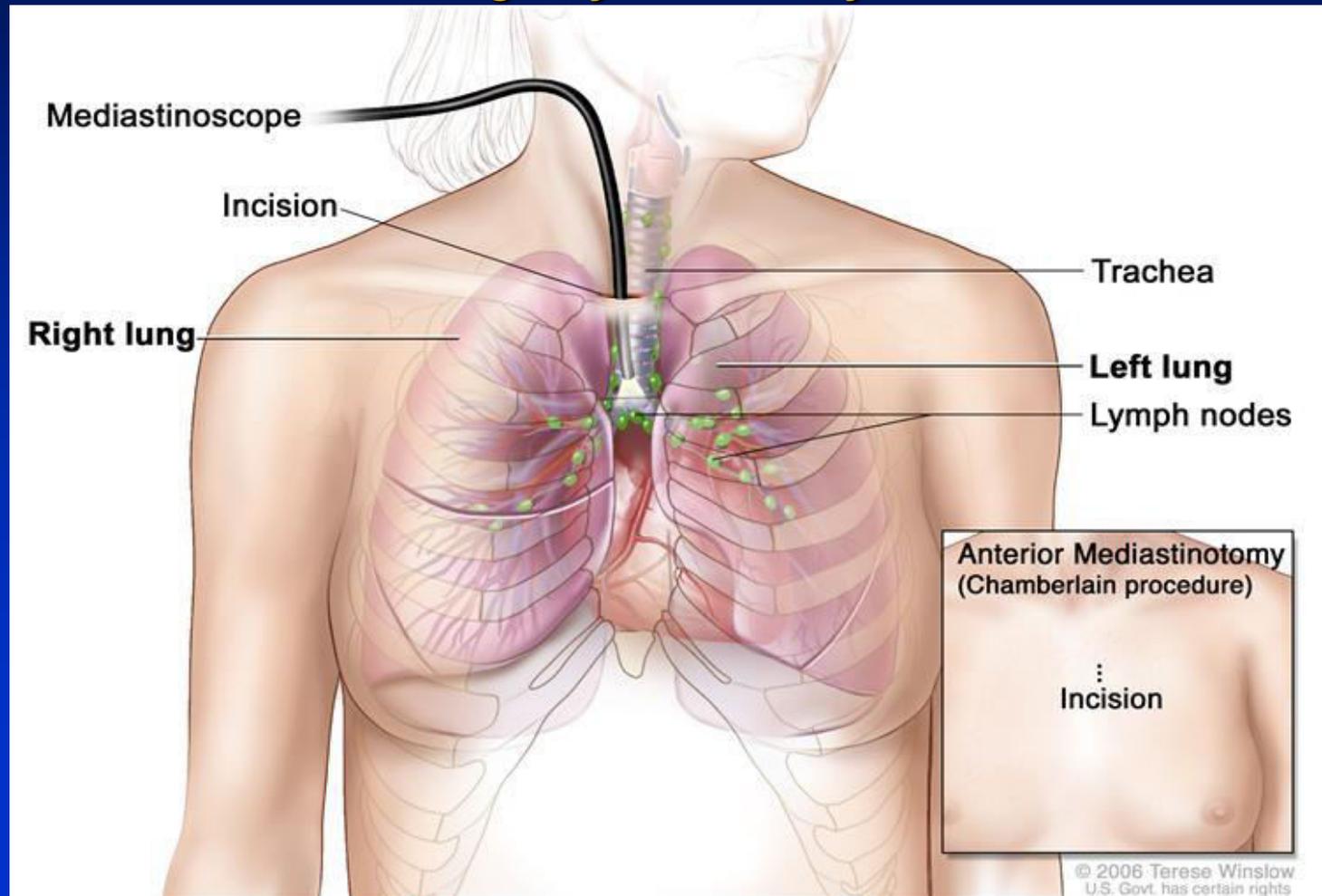**Sensitivity** = 70-95%   **Specificity** = 100%

Negative Predictive value = 88-93%   **Positive Predictive value** = 100%

Complication rate = 0.6%   **Mortality rate** = 0.08%
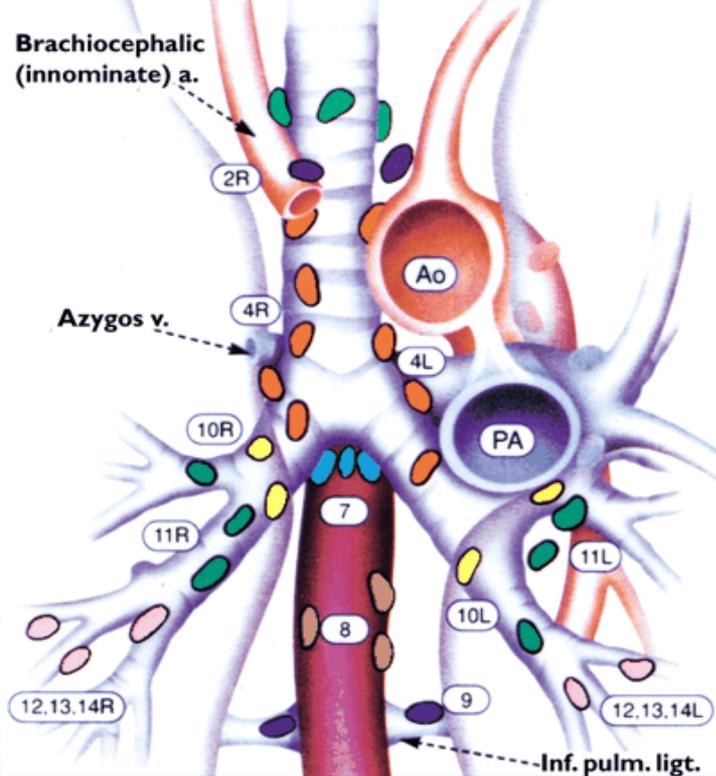
Emergency Sternotomy = 0.12%

Staging with Mediastinoscopy

➢ **Define N1, N2, N3 disease**

➢ **1, 3, 2L, 2R, 4L, 4R, 7 + enlarged nodes**

➢ **Not 5,6,8,9**

Luke WP, Pearson FG, et al. JTCVS; 1986: 91(1) 53-56.
Kiser AC, Detterbeck FC. Diagnosis and treatment of lung cancer: an evidencebased guide for the practicing
clinician. Philadelphia, PA: WB Saunders, 2001; 133–147

Brachiocephalic (innominate) a.

Azygos v.

Ao

PA

2R
4R
4L
10R
11R
11L
10L
7
8
9
12,13,14R
12,13,14L
Inf. pulm. ligt.

Superior Mediastinal Nodes
- 1 Highest Mediastinal
- 2 Upper Paratracheal
- 3 Prevascular and Retrotracheal
- 4 Lower Paratracheal (including azygos nodes)

N_2 = single digit, ipsilateral
N_3 = single digit, contratateral or supraclavicular

Aortic Nodes
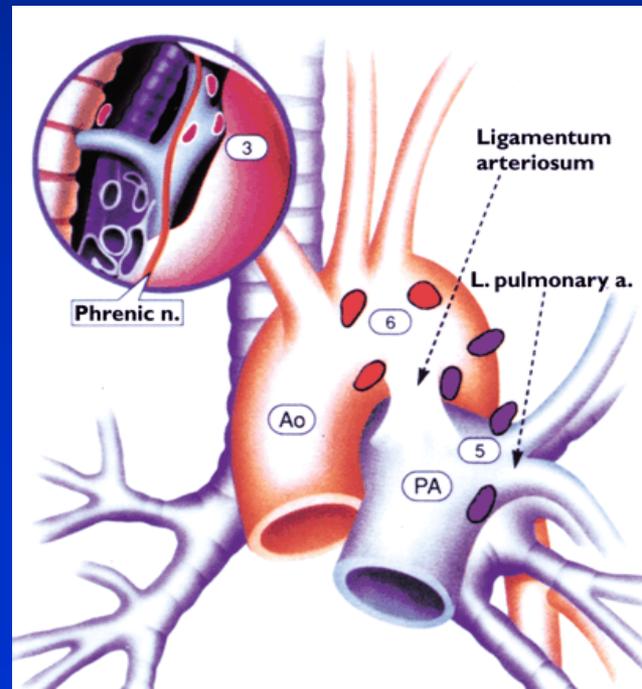- 5 Subaortic (AP window)
- 6 Para-aortic (Ascending aorta or phrenic)

Inferior Mediastinal Nodes
- 7 Inferior Mediastinal Nodes
- 8 Paraesophageal (below carina)
- 9 Pulmonary Ligament

N₁ Nodes
- 10 Hilar
- 11 Interlobar
- 12 Lobar
- 13 Segmental
- 14 Subsegmental

Phrenic n.

Ligamentum arteriosum

L. pulmonary a.

Ao

PA

3
6
5

What's the real problem with mediastinoscopy?

Patterns of Surgical Care of Lung Cancer Patients

Alex G. Little, MD, Valerie W. Rusch, MD, James A. Bonner, MD,
Laurie E. Gaspar, MD, Mark R. Green, MD, W. Richard Webb, MD, and
Andrew K. Stewart, MA

- ➤ **ACS survey in 2001 of 729 hospitals including 40,090 patients**

- ➤ **Mediastinoscopy performed in 27.1% of patients going to curative resection**

- ➤ **Of these mediastinoscopies, only 46.6% had documented node biopsy**

Patterns of Surgical Care of Lung Cancer Patients

Alex G. Little, MD, Valerie W. Rusch, MD, James A. Bonner, MD,
Laurie E. Gaspar, MD, Mark R. Green, MD, W. Richard Webb, MD, and
Andrew K. Stewart, MA

- **Perhaps they are utilizing PET/CT?**
  - **26.5% received PET**

- **Perhaps they are sampling at the time of thoracotomy?**
  - **Only 42.2% of surgical resections had mediastinal lymph nodes**

**59.5% Stage I, 17.5% Stage II,
17.0% Stage III, 6.0% Stage IV**

Bronchoscopy
Endoscopic Ultrasound
Endobronchial Ultrasound

Endoscope with ultrasound probe

Esophagus

Biopsy needle

Lymph nodes with cancer

Cancer

© 2007 Terese Winslow
U.S. Govt. has certain rights

Bronchoscope

Trachea

Bronchi

Cancer

© 2006 Terese Winslow
U.S. Govt. has certain rights
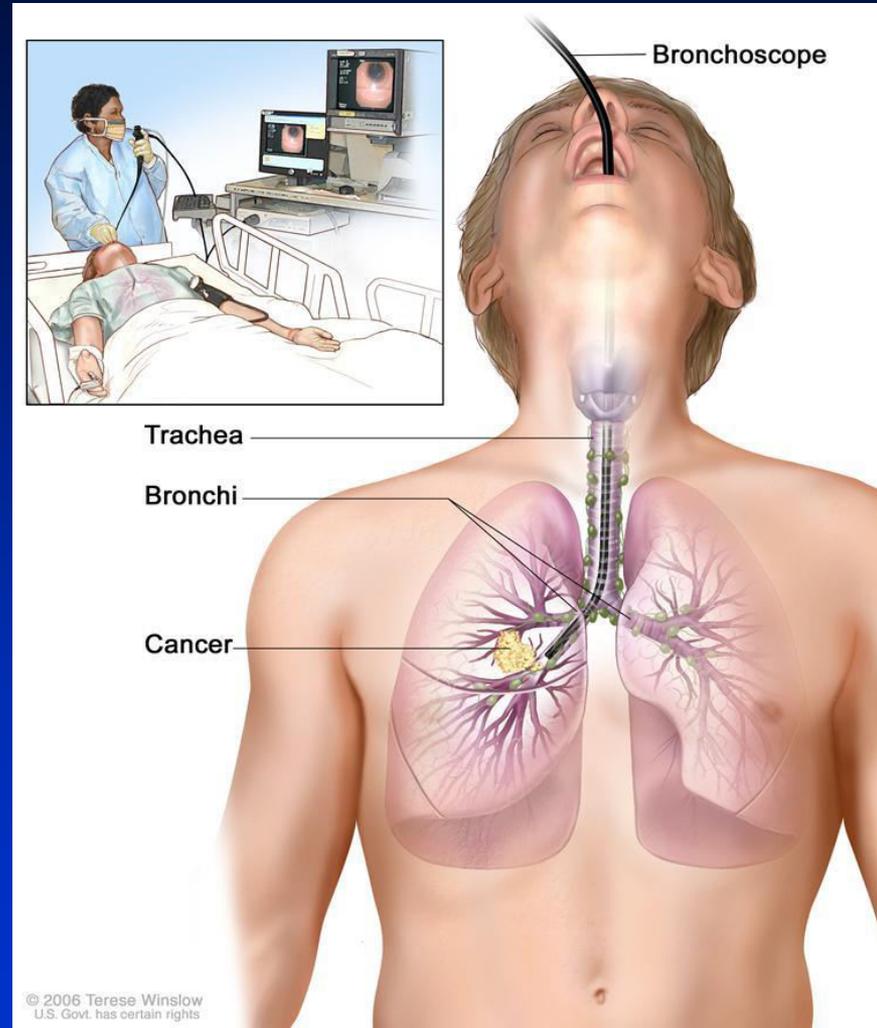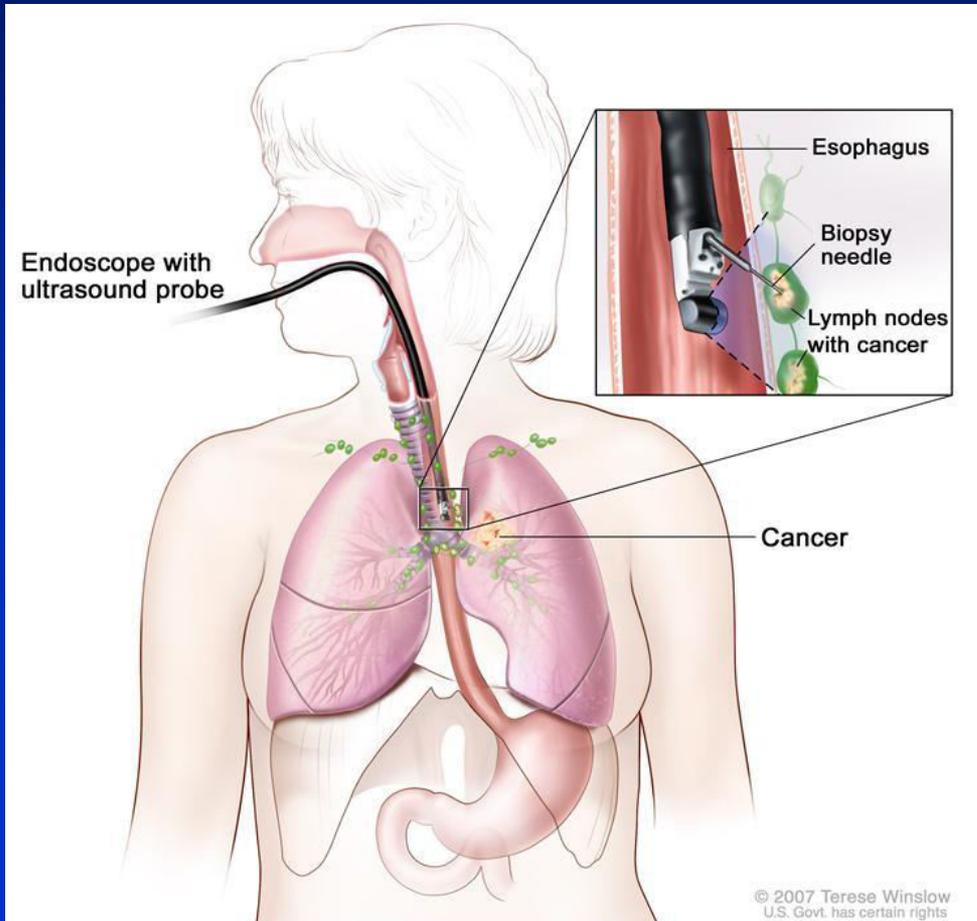
EUS

- ➢ **Can be done with conscious sedation**
- ➢ **Can detect and biopsy adrenal, celiac, liver metastasis**
- ➢ **Can detect T4 invasion into the mediastinum**
  - ➢ **EUS for T staging**
    - ➢ **Sensitivity 88%**
    - ➢ **Specificity 98%**
    - ➢ **False Negative 1%**
    - ➢ **False Positive 30%**
  - ➢ **EUS for N staging**
    - ➢ **Sensitivity 84%**
    - ➢ **Specificity 100%**
    - ➢ **False Negative 19%**
    - ➢ **False Positive 8%**

Varadarajulu S, et al. Gastrointest Endosc 2004; 59:345–348
Detterbeck et al. Chest;2007:132 (3 Supplement): 202S.
Annema JT, et al. JAMA 2005; 294:931–936, only study to investigate positive lymph with surgical incision

EUS

Table 4—EUS-NA of the Mediastinum in Lung Cancer Patients*

Study/Year	Patients, No.	Patient Type	Feasibility, %	Sensitivity, %	Specificity, %	FP, %	FN, %	Prevalence, %	Notes
Annema et al[34]/2005	193	cN0–3†	100	90	100	0	27	79	
Annema et al[29]/2004	36	?		93	100	0	20	78	All PET+
Caddy et al[89]/2005	33	?	100	91	100	0	15	67	
Fritscher-Ravens et al[90]/ 2003	33	cN0–3†	100	88	100	0	11	48	Excluding bulky
Larsen et al[27]/2005	55	cN0–3†		92					
Subtotal	350	cN0–3	100	91					
Wallace et al[22]/2001	107	cN2,3‡	100	87					
Annema et al[23]/2005	93	cN2,3	100	71					
Kramer et al[21]/2004	81	cN2,3‡	100	72					
Wiersema et al[20]/2001	33	cN2,3	100	100					
Larsen et al[28]/2002	29	cN2,3		90					
Silvestri et al[19]/1996	26	cN2,3‡		88					
Fritscher-Ravens et al[18]/ 2000	25	cN2,3		96					
Gress et al[17]/1997	24	cN2,3	100	93					
Subtotal	418	cN2,3	100	87	98	2	22	68	
Eloubeidi et al[26]/2005	104	cN0,1‖	100	93	100	0	4	38	Prior negative mediastinoscopy findings
Wallace et al[24]/2004	64	cN0,1	100	61	100	0	18	36	
LeBlanc et al[31]/2005	67	cN0,1	100	45	100	0	21	33	
Subtotal	235	cN0,1	100	66	100	0	14	36	
Total	1,003			84	99.5	0.7	19	61	

Pre-selected patient population

CT evidence of N2, N3 nodal disease

Detterbeck et al. Chest;2007:132 (3 Supplement): 202S.

EUS in the Setting of a Negative CT

TABLE 1. ENDOSCOPIC ULTRASOUND–GUIDED FINE-NEEDLE ASPIRATION FINDINGS THAT PRECLUDED SURGERY

EUS-FNA Finding	n
Positive celiac lymph node	2
Esophageal wall invasion (T4)	1
Synchronous esophageal cancer	1
Positive contralateral mediastinal lymph node	5
Total	9

Saved an inappropriate thoracotomy in 9/67 = 13%

EUS in the Setting of a Negative CT

TABLE 3. SURGICAL RESULTS OF MALIGNANT IPSILATERAL (N2) MEDIASTINAL LYMPH NODES

Location of NSCLC	Patient	ATS Lymph Node Station(s)	Accessible to EUS Imaging*
Right upper lobe	1	2	N
	2	4	N
	3	4	N
Left upper lobe	4	5	Y
	5	6, 11	N
	6	6, 11	N
Right hilum	7	7, 11	Y
	8	10	Y
Left hilum	9	7, 11	Y
Lingula	10	8	Y[†]
Right lower lobe	11	7	Y
	12	7, 10	Y
	13	7, 11, 12	Y[‡]
Left lower lobe	14	5, 6	Y[‡]
	15	5, 9, 10	Y
	16	7	Y[†]
	17	7, 10	Y[†]

Failed to detect N2 disease in 17/67 = 25%

Would never be able to detect N2 disease in 5/67 = 7%

LeBlanc et al. Am J Resp and Crit Care Med. 171 (2): 177. (2005)

Endobronchial Ultrasound-Guided Needle Aspiration (EBUS)

➤ **Stations 1, 2, 3, 4, 7, 10**

➤ **Not 5, 6, 8, 9**

➤ **Only EBUS-positive nodes sampled**
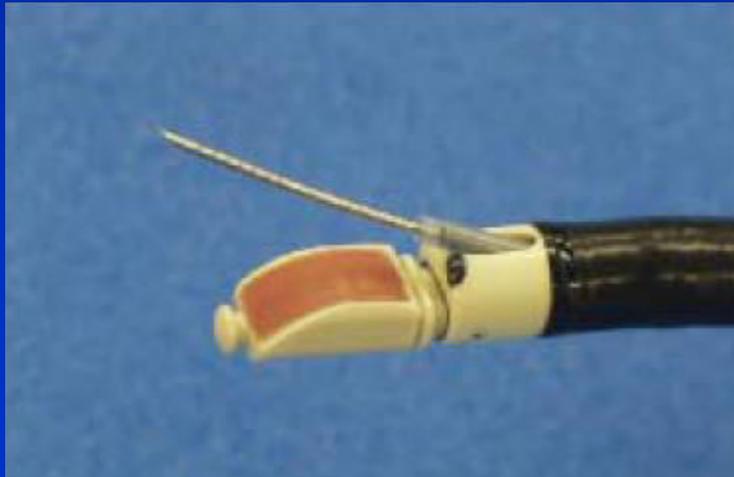
EBUS

- Sensitivity **90%**
- Specificity **100%**
- False Positive **0%**
- False Negative **20%**

- Few complications
- Up to 25% suspected malignancy can be benign
- Minimize mediastinal scarring for future biopsy or resection
- Can be done with conscious sedation, no need for intubation

Detterbeck et al. Chest;2007:132 (3 Supplement): 202S.
Doelken P, Reed C, Silvestri G, et al. Ann Thorac Surg 2008;85:224 –30

EBUS

Table 6—EBUS-NA of the Mediastinum in Lung Cancer Patients*

Study/Year	Patients, No.	Patient Type	Technique	Feasibility, %	Sensitivity, %	Specificity, %	FP, %	FN, %	Prevalence, %
Herth et al[46]/2006	502	cI–III	RT-US bronch (22 ga)		94	100	0	(89)†	98
Yasufuku et al[101]/2005	108	cII–III	RT-US bronch (22 ga)	100	95	100	0	11	69
Yasufuku et al[102]/2004	70	cII–III	RT-US bronch (22 ga)	100	95	100	0	10	67
Vilmann et al[103]/2005‡	31	cII–III	RT-US bronch (22 ga)	100	85	100	0	28	65
Rintoul et al[112]/2005	20	cII–III	RT-US bronch (22 ga)	100	79	100	0	30	70
Kanoh et al[104]/2005	54	cII–III	Catheter probe (19 ga)	100	86	100	0	37	81
Plat et al[105]/2006	33	cII–III	Catheter (histo needle)		93	100	0	25	82
Herth et al[47]/2006	100	cI	RT-US bronch 22 ga		94	100	0	1	17
Summary	918				90	100	0	20	68

EBUS in Patients with Normal CT

Eur Respir J 2006; 28: 910–914

Endobronchial ultrasound-guided transbronchial needle aspiration of lymph nodes in the radiologically normal mediastinum

F.J.F. Herth*, A. Ernst*,#, R. Eberhardt*, P. Vilmann¶, H. Dienemann+ and M. Krasnik§

- 100 patients
- Biopsies taken from any identifiable lymph node 2, 4, 7, 10, 11
- 199 lymph nodes
- Average size 8mm
- Measured against pathologic specimen

- Sensitivity **92.3%**
- Specificity **100%**
- Negative predictive value **96.3%**

EBUS in Patients with Normal CT

Endobronchial ultrasound-guided transbronchial needle aspiration of lymph nodes in the radiologically normal mediastinum

F.J.F. Herth*, A. Ernst*,#, R. Eberhardt*, P. Vilmann[¶], H. Dienemann[+] and M. Krasnik[§]

- Upstaged to N1 disease in **3%** patients
- Upstaged to N2 disease in **13%** patients
- Upstaged to N3 disease in **3%** patients

- Saved an inappropriate thoracotomy in **16%**
- Failed to identify N2 or N3 disease in **2%** of patients

EUS + EBUS

- **EBUS: stations 1-4, 7**
- **EUS: stations 8, 9**
- **Conscious sedation**
- **52 minutes**

Procedure	Sensitivity	Specificity
Bronch-FNA	45%	100%
EBUS-FNA	83%	100%
EUS-FNA	83%	100%
Bronch+EBUS	86%	100%
EUS+EBUS	97%	100%

Per patient accuracy

Procedure	Sensitivity	Specificity	p value
Bronchoscopy-FNA	36%	100%	
EBUS-FNA	70%	100%	<0.002 (vs bronch)
EUS- FNA	73%	100%	<0.001 (vs bronch), > 0.2 (vs ebus)
Bronch + EBUS	82%	100%	
EBUS + EUS	95%	100%	<0.03 (vs bronch + ebus), <0.025 (vs eus + bronch)
Bronch + EUS	77%	100%	=0.09 (vs eus + ebus), > 0.2 (vs bronch + ebus)

EUS + EBUS = Medical Mediastinoscopy

- **Vilmann P, Puri R.**
- **The complete "medical" mediastinoscopy (EUS-FNA + EBUS-TBNA).Minerva Med. 2007 Aug;98(4):331-8.**

- **Sensitivity 100%**
- **Specificity 100%**

	Sensitivity	Specificity	False Neg	False Pos	Station	Limitations
Med	78-95	100	11	0	1, 3, 2, 4, 7	Utilization
EUS	87	100	19	8	5, 6, 8, 9	Limited location
EBUS	90	100	20	0	1, 3, 2, 4, 7, 10	No standard protocol
EUS+ EBUS	95	100			1, 2, 3, 4, 8, 9, 10	No data

	*	Sensitivity	Specificity	False Neg	False Pos	Station	Limitations
Med	**42**	78-95	100	11	0	1, 3, 2, 4, 7	Utilization
EUS	**66**	87	100	19	8	5, 6, 8, 9	Limited location
EBUS	**94**	90	100	20	0	1, 3, 2, 4, 7, 10	No standard protocol
EUS+ EBUS	**97**	95	100			1, 2, 3, 4, 8, 9, 10	No data

* Sensitivity in the setting of radiographic stage 1 disease

Summary

➢ **Mediastinum should be staged invasively utilizing mediastinoscopy, EUS, EBUS or EUS+EBUS.**

➢ **PET/CT alone will miss N2 disease (5-12%)**

➢ **Perhaps future lies with medical mediastinoscopy of EUS+EBUS**