Lung Cancer Update

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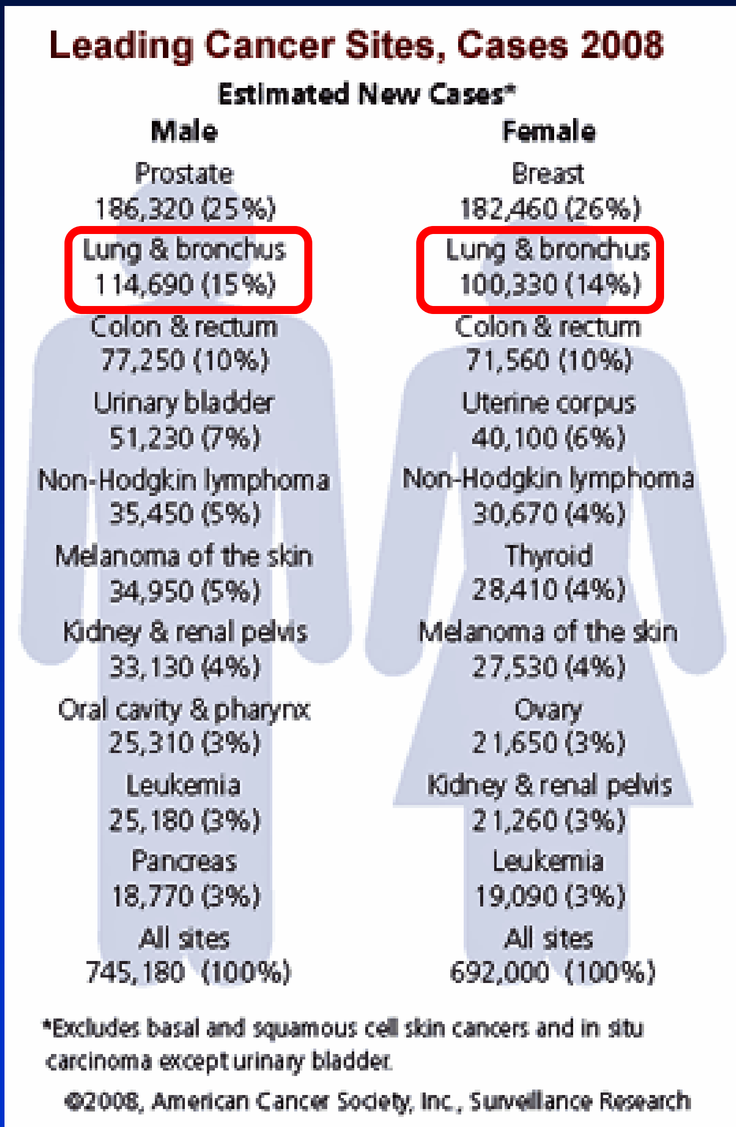
Goals

- Understand the Societal impact of Lung Cancer
- Identify Risk Factors for Lung Cancer
- List Diagnostic Tests Available for Lung Cancer
- Understand the history and current recommendations on Lung Cancer Screening
- Understand the Staging for Lung Cancer
- Understand the Treatment options available for Lung Cancer with emphasis on newer surgical techniques available such as VATS lobectomy

Disclaimer

I have NO personal financial relationship with any manufacturer of products or services that will be discussed in this lecture.

US Epidemiology



Leading Cancer Sites, Cases 2008

Estimated New Cases*

Male	Female
Prostate 186,320 (25%)	Breast 182,460 (26%)
Lung & bronchus 114,690 (15%)	Lung & bronchus 100,330 (14%)
Colon & rectum 77,250 (10%)	Colon & rectum 71,560 (10%)
Urinary bladder 51,230 (7%)	Uterine corpus 40,100 (6%)
Non-Hodgkin lymphoma 35,450 (5%)	Non-Hodgkin lymphoma 30,670 (4%)
Melanoma of the skin 34,950 (5%)	Thyroid 28,410 (4%)
Kidney & renal pelvis 33,130 (4%)	Melanoma of the skin 27,530 (4%)
Oral cavity & pharynx 25,310 (3%)	Ovary 21,650 (3%)
Leukemia 25,180 (3%)	Kidney & renal pelvis 21,260 (3%)
Pancreas 18,770 (3%)	Leukemia 19,090 (3%)
All sites 745,180 (100%)	All sites 692,000 (100%)

*Excludes basal and squamous cell skin cancers and in situ carcinoma except urinary bladder.

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- 215,020 new cases in the US in 2008
  - 114,690 in men
  - 100,330 in women
  - Accounts for 15% of all new cancer cases
  - Average age at diagnosis is 71
  - Lifetime risk is 1 in 13 for men and 1 in 16 for women
- 161,840 deaths in the US in 2008
  - 90,810 men
  - 71,030 women
  - Accounts for 29% of all cancer deaths

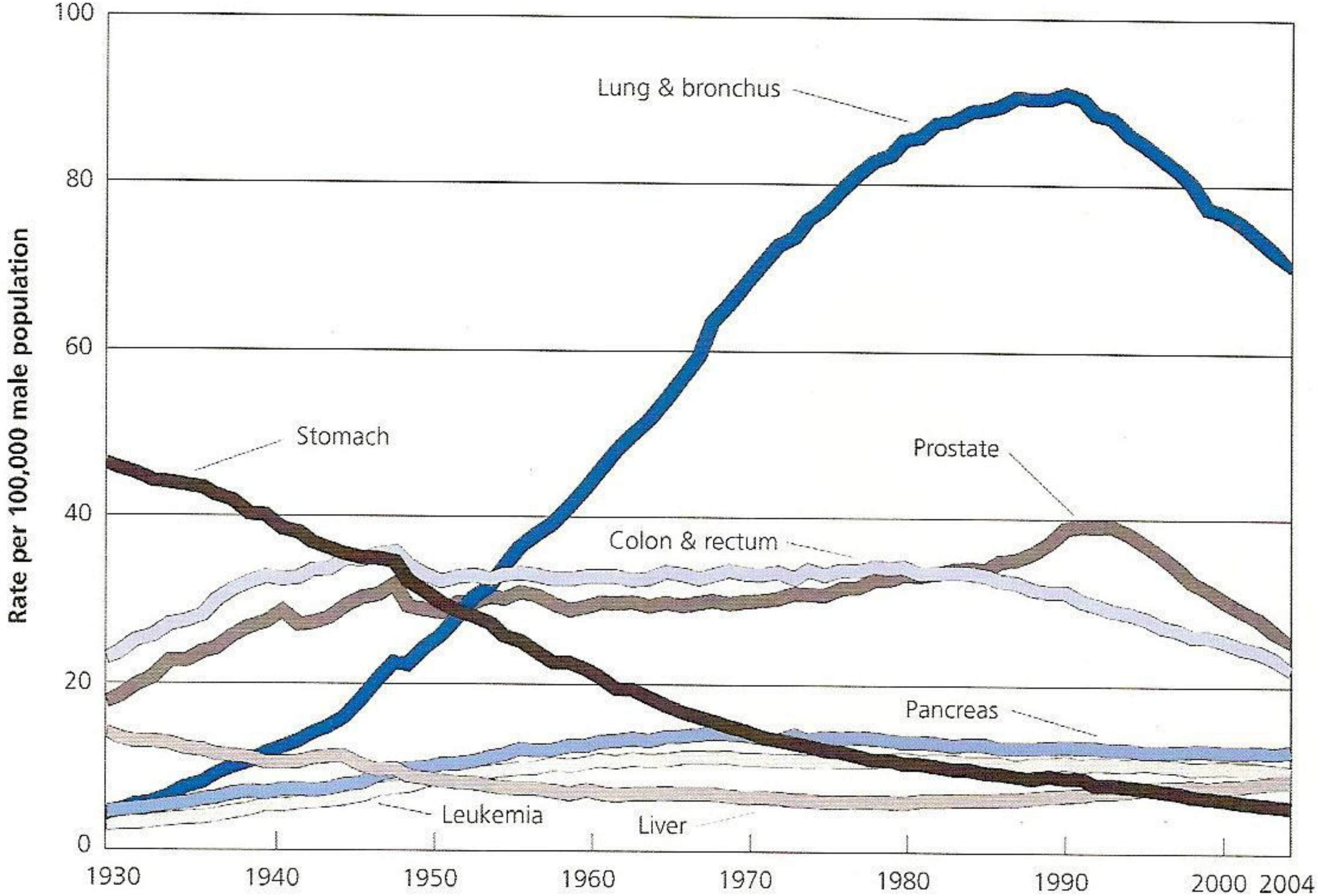
Lung cancer is the leading cause of cancer death for both men and women

More people die of Lung cancer than of Colon, Breast, and Prostate cancers COMBINED!

Lung Cancer Deaths in 2008
161,840

Colon Cancer Deaths =	49,960
Breast Cancer Deaths =	40,480
Prostate Cancer Deaths =	28,660
Combined Cancer Deaths =	119,100

Age-Adjusted Cancer Death Rates,* Males by Site, US, 1930-2004



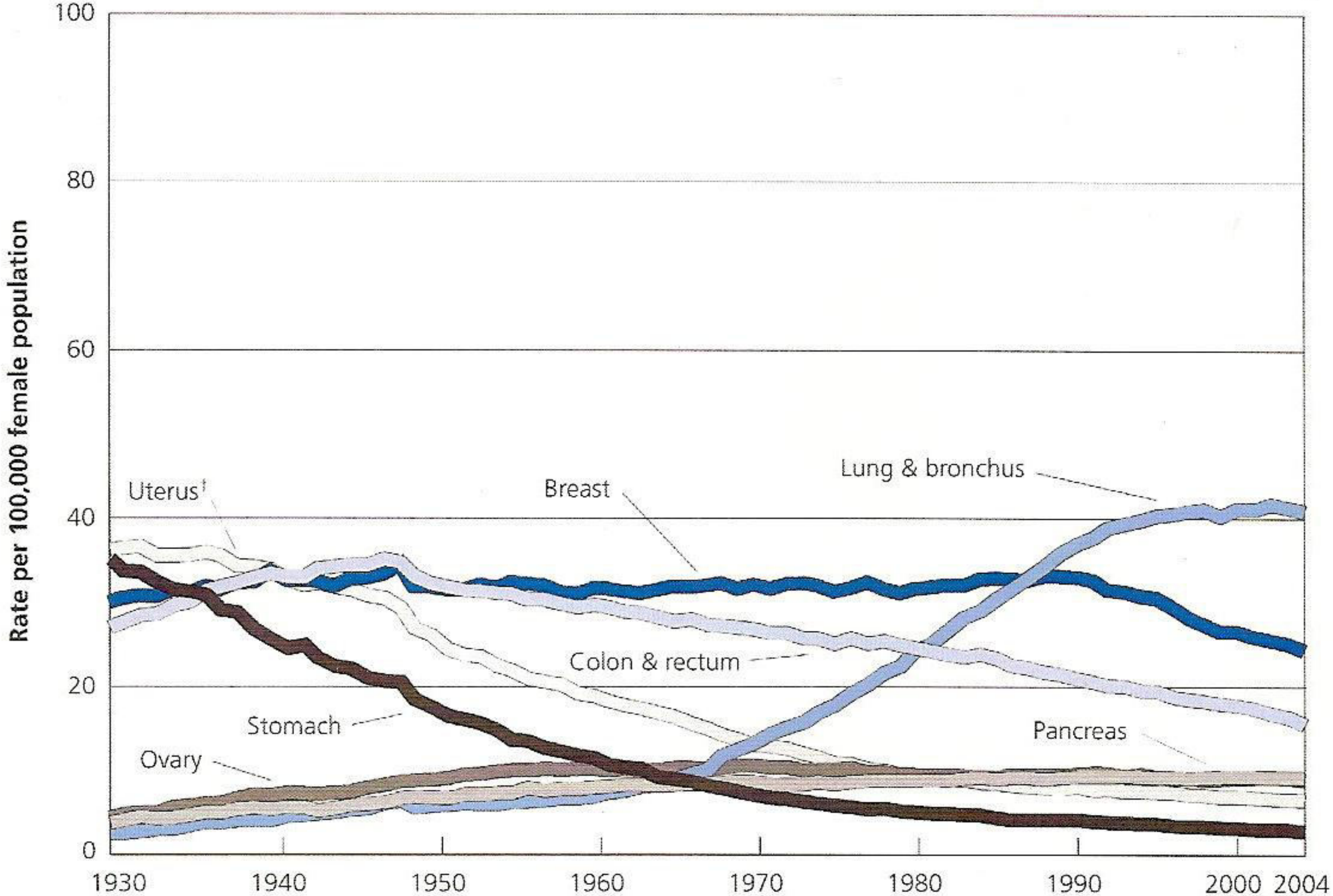
*Per 100,000, age-adjusted to the 2000 US standard population.

Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancer of the liver, lung and bronchus, and colon and rectum are affected by these coding changes.

Source: US Mortality Data 1960 to 2004, US Mortality Volumes 1930 to 1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2006.

American Cancer Society, Surveillance Research, 2008

Age-Adjusted Cancer Death Rates,* Females by Site, US, 1930-2004



*Per 100,000, age-adjusted to the 2000 US standard population. †Uterus cancer death rates are for uterine cervix and uterine corpus combined.

Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancer of the lung and bronchus, colon and rectum, and ovary are affected by these coding changes.

Source: US Mortality Data 1960 to 2004, US Mortality Volumes 1930 to 1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2006.

American Cancer Society, Surveillance Research, 2008

Worldwide Lung Cancer

- Estimated **1.5 million** new cases of Lung cancer expected each year
- Accounts for **12%** of total cancer diagnoses

- More than **1.3 million** people expected to die from Lung cancer each year

- Leading cause of cancer death in Men
- Second leading cause of cancer death in Women

Lung Cancer Survival Rates

Table 1. Changes in 5-Year Survival, Mortality, and Incidence for 20 Solid Tumors

Primary Site	5-Year Survival, % 1950-1954	5-Year Survival, % 1989-1995	Absolute Increase in 5-Year Survival, %	% Change (1950-1996) Mortality	% Change (1950-1996) Incidence
Prostate	43	93	50	10	190
Melanoma	49	88	39	161	453
Testis	57	96	39	–73	106
Bladder	53	82	29	–35	51
Kidney	34	61	27	37	126
Breast	60	86	26	–8	55
Colon	41	62	21	–21	12
Rectum	40	60	20	–67	–27
Ovary	30	50	20	–2	3
Thyroid	80	95	15	–48	142
Larynx	52	66	14	–14	38
Uterus	72	86	14	–67	0
Cervix	59	71	12	–76	–79
Oral cavity	46	56	10	–37	–38
Esophagus	4	13	9	22	–8
Brain	21	30	9	45	68
Lung	6	14	8	259	249
Stomach	12	19	7	–80	–78
Liver	1	6	5	34	140
Pancreas	1	4	3	16	9

Trends in 5-Year Relative Survival Rates* (%) by Race and Year of Diagnosis, US, 1975-2003

Site	White			African American			All Races		
	1975-77	1984-86	1996-2003	1975-77	1984-86	1996-2003	1975-77	1984-86	1996-2003
All sites	51	55	67†	40	41	57†	50	54	66†
Brain	23	28	34†	27	33	37†	24	29	35†
Breast (female)	76	80	90†	62	65	78†	75	79	89†
Colon	52	60	66†	46	50	55†	51	59	65†
Esophagus	6	11	18†	3	8	11†	5	10	16†
Hodgkin lymphoma	74	80	87†	71	75	81†	74	79	86†
Kidney	51	56	66†	50	54	66†	51	56	66†
Larynx	67	68	66	59	53	50	67	66	64
Leukemia	36	43	51†	34	34	40	35	42	50†
Liver#	4	6	10†	2	5	7†	4	6	11†
Lung & bronchus	13	14	16†	12	11	13†	13	13	16†
Melanoma of the skin	82	87	92†	60‡	70§	77	82	87	92†
Myeloma	25	27	34†	31	32	32	26	29	34†
Non-Hodgkin lymphoma	48	54	65†	49	48	56	48	53	64†
Oral cavity	55	57	62†	36	36	41	53	55	60†
Ovary	37	39	45†	43	41	38	37	40	45†
Pancreas	3	3	5†	2	5	5†	2	3	5†
Prostate	70	77	99†	61	66	95†	69	76	99†
Rectum	49	58	66†	45	46	58†	49	57	66†
Stomach	15	18	22†	16	20	24†	16	18	24†
Testis	83	93	96†	82‡	87‡	88	83	93	96†
Thyroid	93	94	97†	91	90	94	93	94	97†
Urinary bladder	75	79	81†	51	61	65†	74	78	81†
Uterine cervix	71	70	74†	65	58	66	70	68	73†
Uterine corpus	89	85	86†	61	58	61	88	84	84†

*Survival is adjusted for normal life expectancy and based on cases diagnosed in the SEER 9 areas from 1975-1977, 1984-1986, and 1996-2003, and followed through 2004. †The difference in rates between 1975-1977 and 1996-2003 is statistically significant ($p < 0.05$). ‡The standard error of the survival rate is between 5 and 10 percentage points. §The standard error of the survival rate is greater than 10 percentage points. #Includes intrahepatic bile duct.

Source: Ries LAG, Melbert D, Krapcho M, et al (eds.). *SEER Cancer Statistics Review, 1975-2004*, National Cancer Institute, Bethesda, MD, www.seer.cancer.gov/csr/1975_2004/, 2007.

American Cancer Society, Surveillance Research, 2008

Risk Factors

- Smoking
  - Responsible for 87% of Lung Cancer Deaths Annually
  - Latent period of 20-25 years
  - Dose related
    - (9-10 fold risk average smoker, 20 fold risk for heavy smoker)
  - Smoking *reduces the lifespan of average American by* ***14 years***
- Secondhand smoke
  - Non-smoking spouses who live with a smoker have a 20-30% greater risk
- Radon Exposure
- Asbestos Exposure
  - Synergy with Tobacco (*50-90 times the risk* of cancer)
- Other Environmental exposures
  - Arsenic, Chromium, Nickel, Silica, Soot or Tar
  - Benzopyrene, Vinyl Chloride, Diesel exhaust
- Beta carotene supplements – only in smokers

Risk Factors

- Genetic Factors
  - p53 tumor suppressor gene mutation
  - k-ras oncogene activation
- Personal or Family History Lung Cancer

- Air pollution
  - *Worldwide, 5% of deaths from Lung cancer may be due to air pollution*

- Recurring inflammation
  - Scarring from Tuberculosis or recurrent pneumonias can increase risk
- Prior Radiation Treatment
  - Mantle cell lymphoma
  - Breast cancer - Non smoking women with radiation to breast after lumpectomy do NOT have increased risk of lung cancer

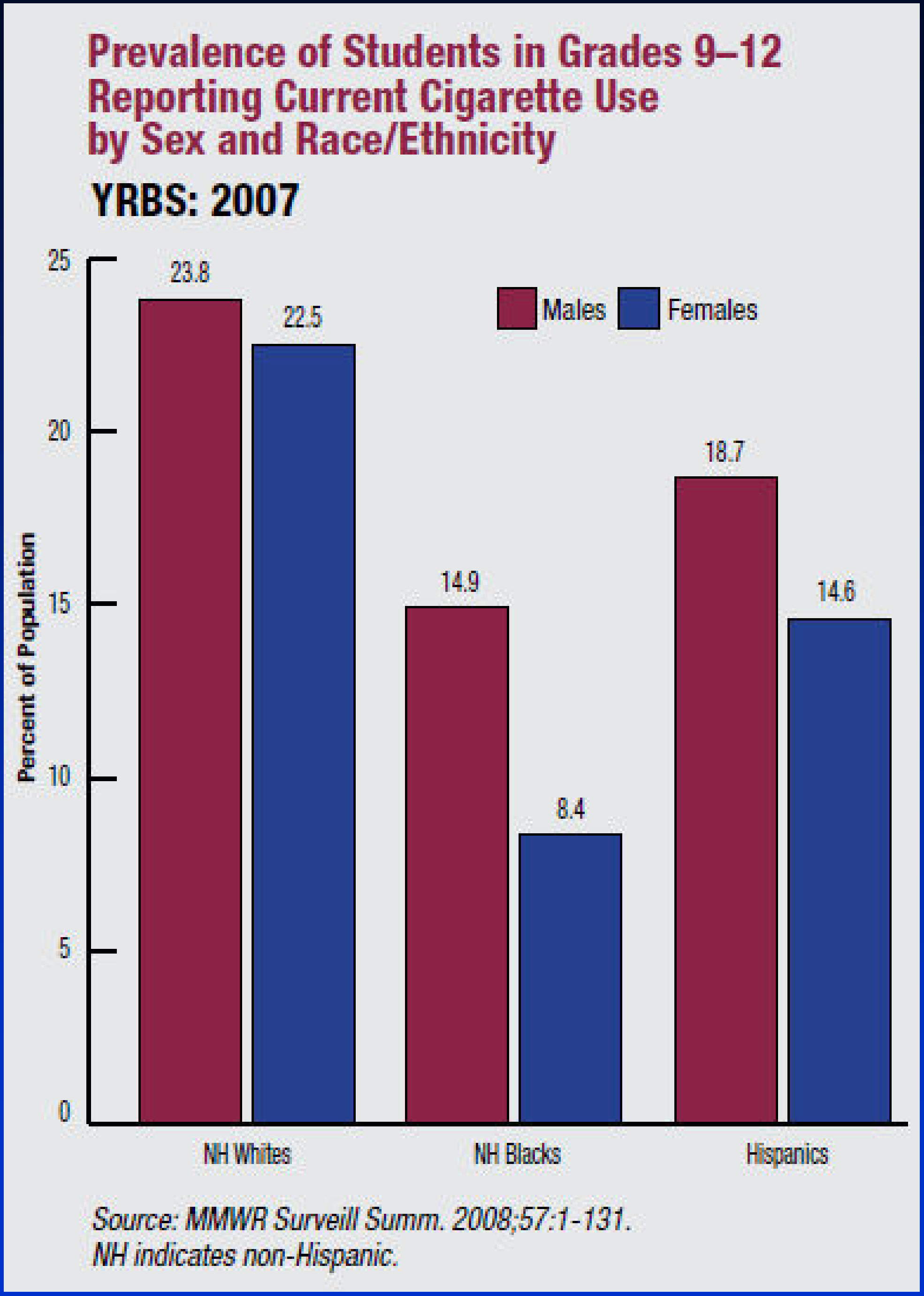
Risk Factors

- Race / Ethnicity

  - African Americans have similar rate of smoking as Whites (20% vs 22% in 2004); yet
    - Black men are 50% more likely to develop lung cancer
    - 30% more likely to die from lung cancer than White men

  - Hispanics smoke less (15% in 2004) than Whites or African Americans
    - 50% lower lung cancer rate than Whites
    - 60% lower lung cancer rate than African Americans

  - High school students smoking trend is alarming: data from 2004 →
    - Hispanics 26.2%
    - African Americans 17.1%
    - Whites 31.5%



2007

20% high school students were smokers

6% middle school students were smokers

Risk Factors

- Race and Gender Trends (SEER database)

SubGroup	Incidence/100,000	Death/100,000
White Men	79.4	78.1
White Women	51.9	41.5
African American Men	120.4	107
African American Women	54.8	40
Asian American Men	62.1	40.9
Asian American Women	28.4	19.1
Hispanic Men	46.1	40.7
Hispanic Women	24.4	15.1
American Indian Men	45.6	52.9
American Indian Women	23.4	26.2

C-STATS Report

Age-adjusted lung cancer mortality rates

MORTALITY *(age-adjusted)*

	Number of cases	Rate
• NAPA	78	50.4
• SOLANO	198	54.0
• SONOMA	229	45.6
• STATEWIDE	13,168	40.4

Sign and Symptoms

Cough (that does not resolve)	29-87%
Hemoptysis	9-57%
Pleuritic chest pain	6-60%
Shortness of Breath / Dyspnea	3-58%
Wheezing (new onset) / Stridor	2-14%
Hoarseness	1-18%
Pleural Effusion	7%
Dysphagia	2-6%
Superior vena cava syndrome	4-11%
Pancoast's Syndrome / Horner's Syndrome	3-5%
Phrenic Nerve paralysis	1%
Neurologic Metastasis	10%
Bone Metastasis	22%
Liver Metastasis	5%
Adrenal Metastasis	2-4%
Paraneoplastic Syndromes	10-20%
➢ SIADH 1-27% Hypercalcemia 1-12% Cushing's 2-6%	
ASYMPTOMATIC	
➢ All patients with Lung cancer	5-20%
➢ Patients detected in screening programs	60%

Diagnosis - Imaging

Chest X ray

- Tumor
  - Sensitivity = 26%
  - Specificity = 93%

CT scan

- Tumor
  - Sensitivity = 63%
  - Specificity = 84%
- Mediastinum
  - Sensitivity = 51-75%
  - Specificity = 66-86%

PET Scan

- Tumor
  - Sensitivity = 83-96%
  - Specificity = 73-78%
- Mediastinum
  - Sensitivity = 64-91%
  - Specificity = 77-93%
- Distant Metastasis
  - Sensitivity = 95%
  - Specificity = 83%

PET and CT scan combined

- Mediastinum
  - Sensitivity = 93%
  - Specificity = 95%

Diagnosis - Imaging

MRI scan

- Tumor
  - Sensitivity = 56%
  - Specificity = 80%
- Mediastinum
  - Sensitivity = 48%
  - Specificity = 64%
- Brain
  - 7% detection rate for occult metastasis
  - 4% Stage I and Stage II
  - 11% for Stage III

Bone scan

(with clinical indicators such as pain or increased alkaline phoshatase)

- Sensitivity = 73-100%
- Specificity = 54%

Sputum Cytology

(at least 3 specimens)

- Sensitivity = 50-71%
  (Lower in peripheral versus central tumors)
- Specificity = 99%

- DNA Methylation Analysis increases Sensitivity

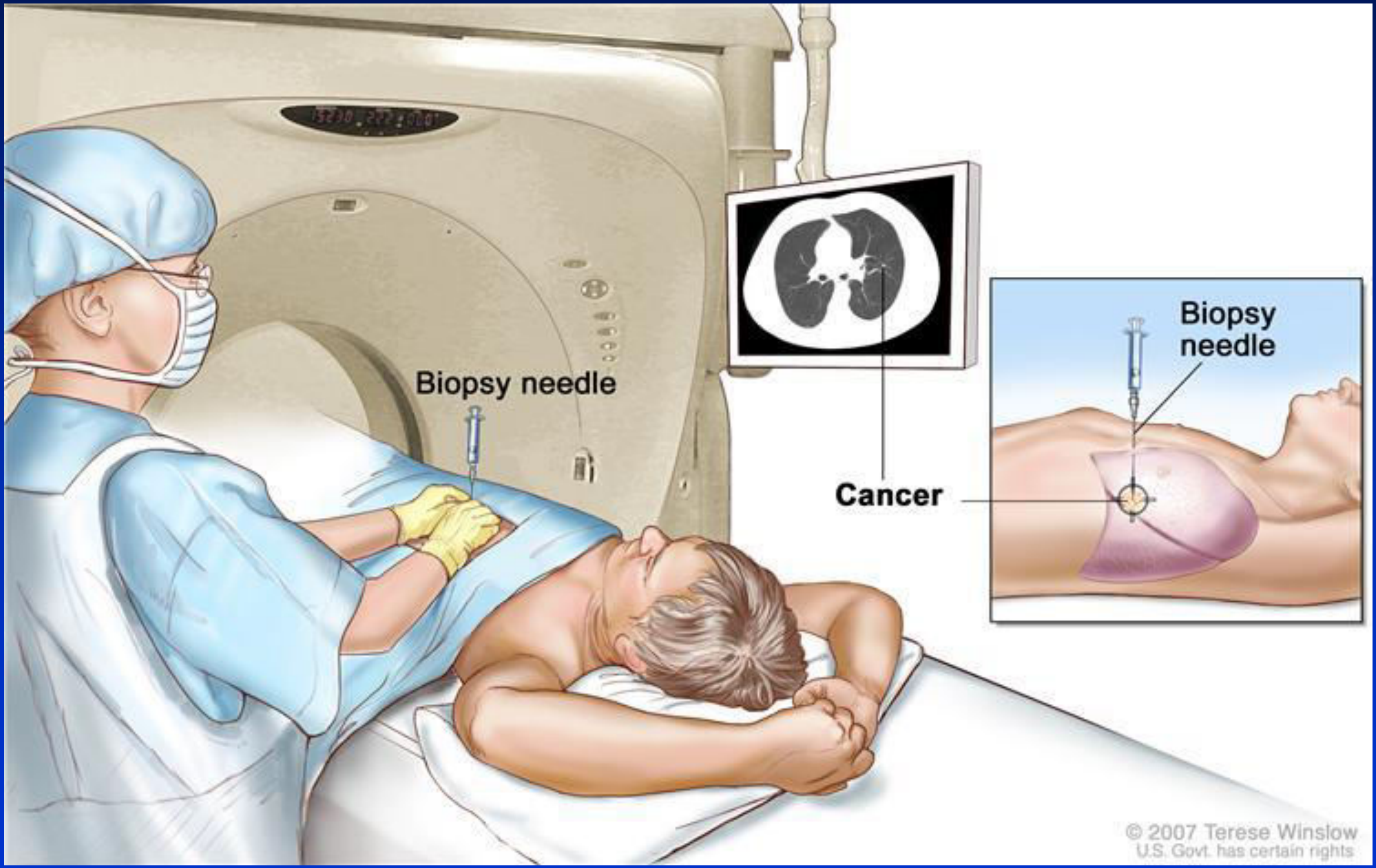
- Methylation disturbs normal gene expression

- p16 & MGMT (O^6-methylguanine DNA methyltransferase)
  - Methylated in 100% of squamous cell cancer sputum samples
  - Methylated in 25% of long-term smokers
  - Marker of risk

- Up to 25% of sputum samples are inadequate for analysis

Fine Needle Aspiration

- Sensitivity = 50-98%
- Specificity = 97%
- Pneumothorax risk 15-37% with 10-15% requiring CT placement

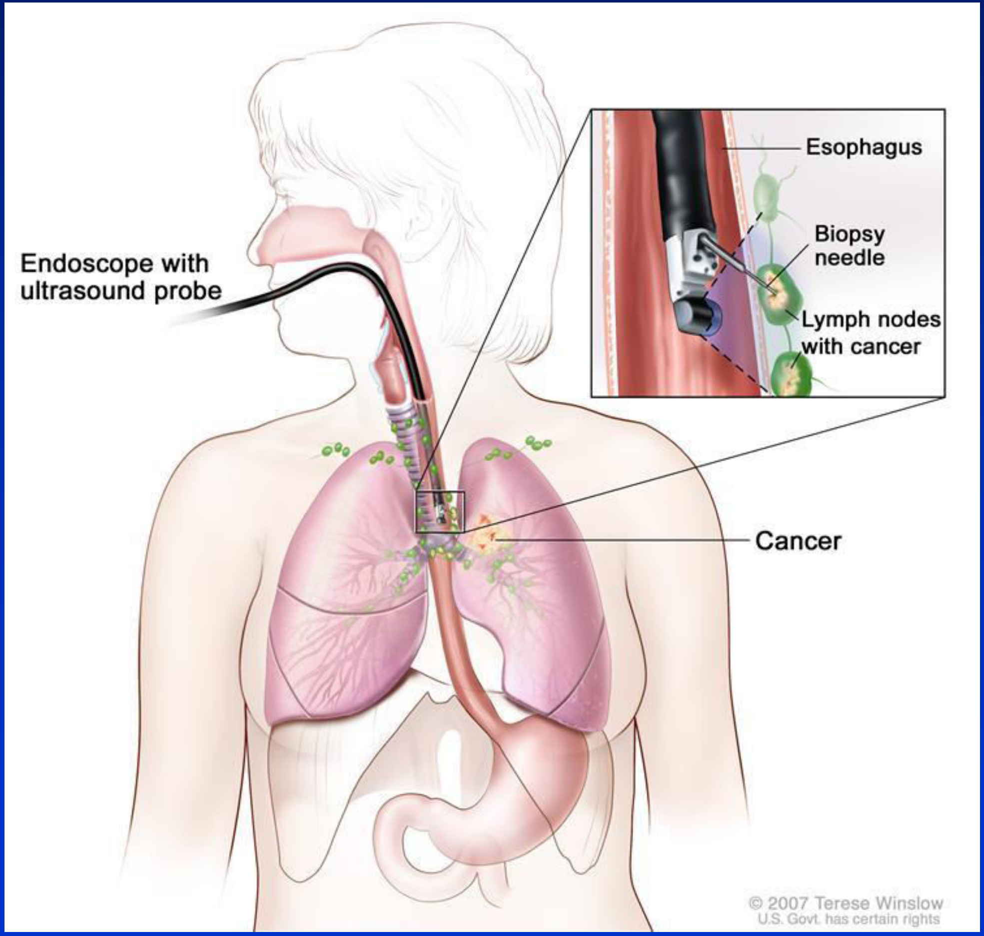


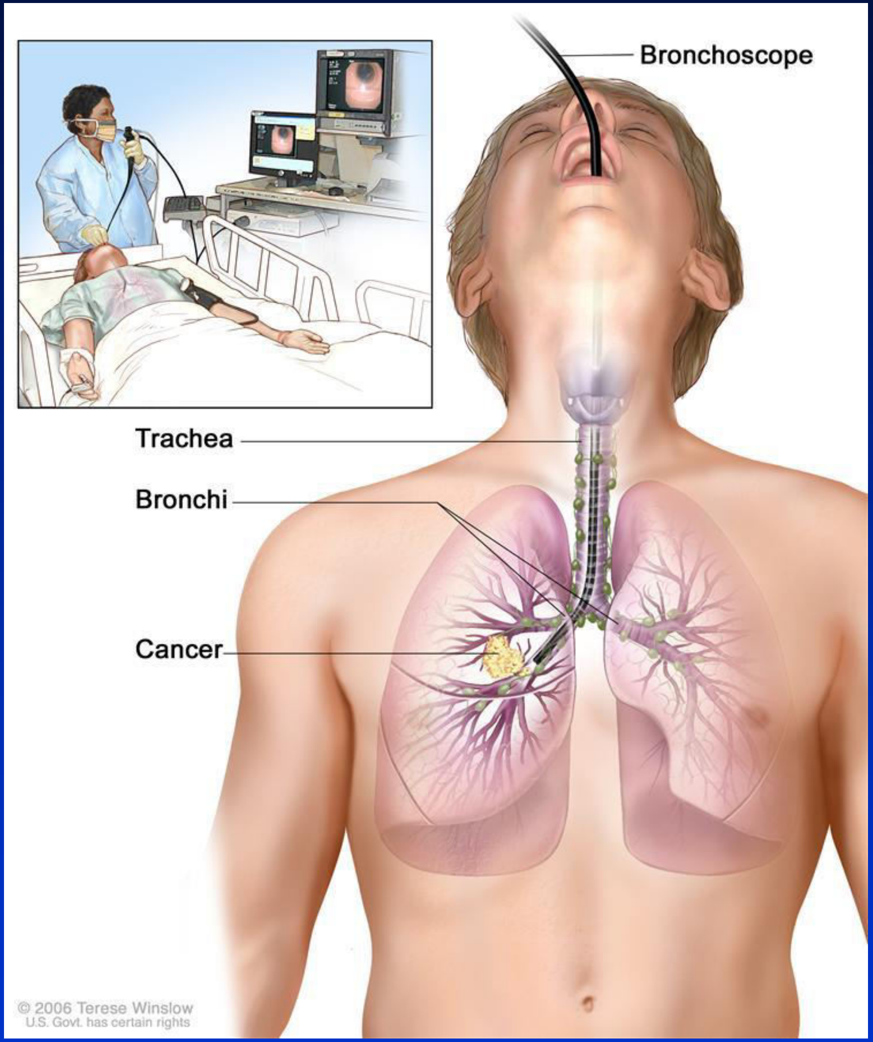
Bronchoscopy with Endoscopic / Endobronchial Ultrasound

- Sensitivity = 58-97%

(Lower with peripheral tumors)

- Specificity = 90-97%
- Complication rate = 1%





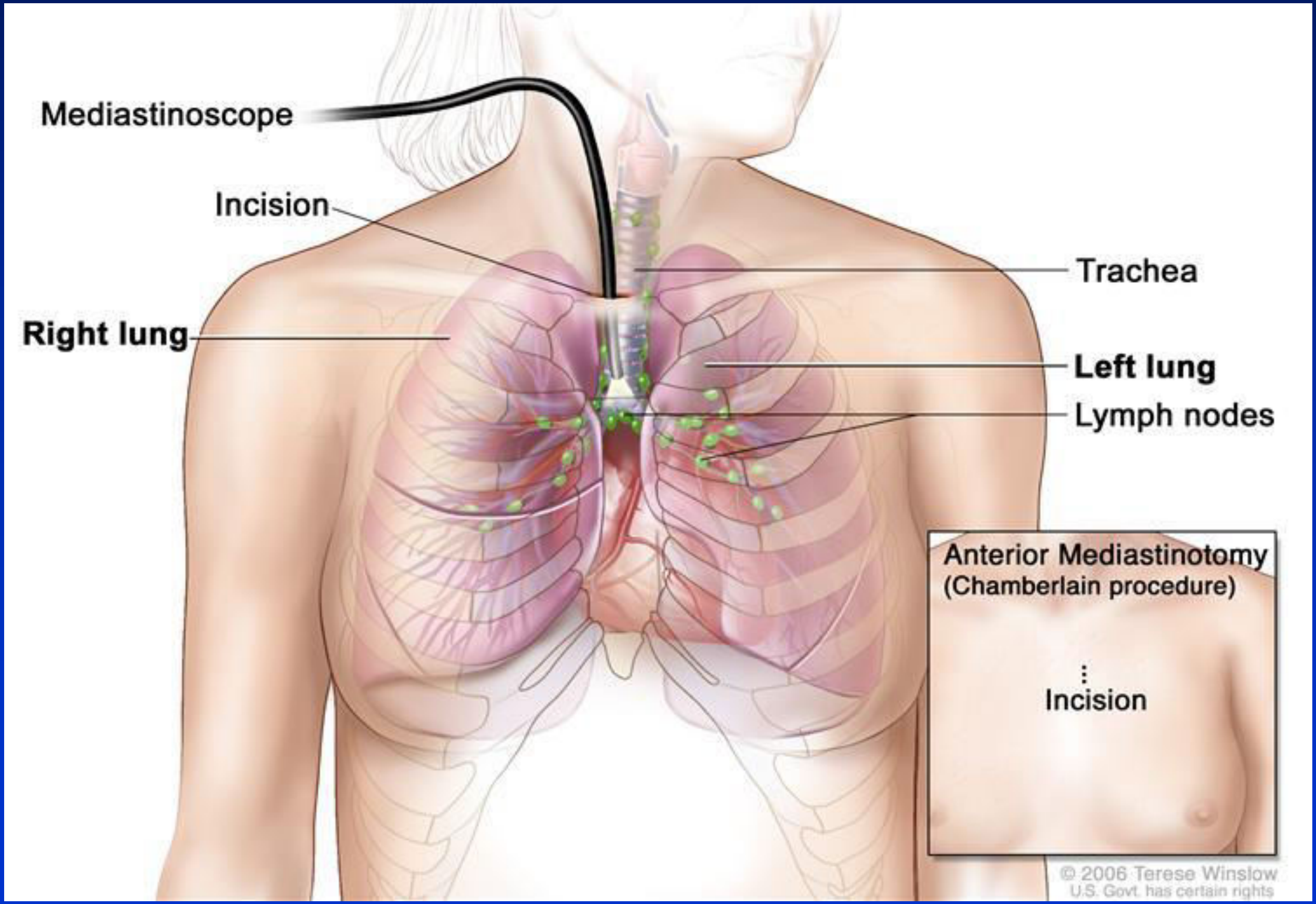
Thoracentesis

- Sensitivity = 80%
- Specificity = 90%

Thoracoscopy

Mediastinoscopy

- Sensitivity = 70-95%
- Specificity = 100%
- Complication rate = 0.6%
- Mortality rate = 0.2%



Screening

Chest Xray and/or Sputum Cytology

- **Benefits**
  - **Based on Fair evidence → Screening does *NOT* reduce mortality from lung cancer**

- **Harms**
  - **Based on Solid evidence → Screening would lead to false-positives and unnecessary invasive procedures and treatments**

- **Studies:**
  - **Philadelphia Pulmonary Neoplasm Research Project**
  - **Veterans Administration study**
  - **South London Lung Cancer Study**
  - **North London Lung Cancer Study**
  - **Kaiser Foundation Health Plan multiphasic screening trial**
  - **Czechoslovak Study**
  - **German Democratic Republic Study**
  - **Japan Study**
  - **Mayo Lung Project**
  - **Johns Hopkins Study**
  - **Memorial Sloan-Kettering Study**

CXR /Sputum cytology <u>NOT </u>helpful

	MSKCC	Hopkins	Mayo	Czech
Accrual	1974-1982	1973-1982	1971-1983	1976-1980
Screened Protocol Cancers at baseline Cancers at screen Lung cancer mortality (per 1000 person-years)	N=4968 Annual CXR, sputum Q4m 30 114 **2.7**	5226 Annual CXR, sputum Q4m 39 194 **3.4**	4618 CXR & sputum Q4m NA 206 **3.2**	3172 CXR & sputum Q6m NA 39 **3.6**
Control Protocol Cancers at baseline Cancers at screen Lung cancer mortality (per 1000 person-years)	N= 5072 Annual CXR 23 121 **2.7**	5161 Annual CXR 40 202 **3.8**	4593 Annual CXR & sputum NA 160 **3.0**	3174 CXR & sputum Q3y NA 27 **2.6**

Mayo Lung Project: Incidence Screening

	Experimental group	Control group
Population	4,618	4,593
Incidence	206	160 (p=0.016)
Resectability	46 percent	32 percent
Five year survival (actuarial)	33 percent	15 percent
Fatality (actual)	59 percent	72 percent (p=0.016)
Mortality	122	115

Data from Fontana, R, Sanderson, DR, Woolner, LB, et al, J Occupat Med 1986; 28:746 and Fontana, R, Sanderson, DR, Woolner, LB, et al, Cancer 1991; 67:1155.

Czechoslovak Study: Incidence Screening

	Experimental group	Control group
Population	3,172	3,174
Incidence	36	19
Resectability	25 percent	15 percent
Five year survival (actuarial)	23 percent	0 percent (p=0.0001)
Mortality	28	18

Data from Kubik, A, Polak, J, Cancer 1986; 57:2428 and Kubik, A, Parkin, DM, Khlat, M, et al, Int J Cancer 1990; 45:26.

Low-Dose Helical CT Scan (LDCT)

- **Benefits**
  - **Evidence is inadequate to determine whether screening reduces mortality from lung cancer**

- **Harms**
  - **Based on Solid evidence → Screening would lead to false-positives and unnecessary invasive procedures and treatments**

- **Studies:**
  - **Early Lung Cancer Action Project (ELCAP)**
  - **Mayo Clinic Study**
  - **University of Munster study**
  - **Shinshu University study**
  - **Anti-Lung Cancer Association (ALCA)**

Low-dose CT Screening Trials

	Mayo Clinic Study	Shinshu University	Early Lung Cancer Action Project (ELCAP)	Anti-Lung Cancer Association (ALCA)	University of Munster
Prevalence					
N	1520	5483	1000	1611	817
Abnormal CT	51%	35%	23%	11.5%	43%
# cancers on CXR	NA	1	7	5	NA
# cancers on CT	26	19	27	14	11
Stage I NSCLC	79%	84%	85%	71%	64%
Incidence					
N	1438	4781	1184	1180	
# cancers on CT	10	37	7	19	
Stage 1 NSCLC	67%	86%	82%	79%	
Interval cancers not detected on screening CT	2	NA	2	3	

Guidelines for Lung Cancer Screening

Organization	Recommendation	Year
US Preventive Services Task Force	Evidence is insufficient to recommend for or against screening asymptomatic persons for lung cancer with either low dose computerized tomography, chest x-ray, sputum cytology, or a combination of these tests.	2004
American College of Chest Physicians	Recommends that individuals should only be screened with low-dose CT in the context of well-designed clinical trials	2003
American Cancer Society	Recommends against routine screening of asymptomatic persons	2002
American Academy of Family Physicians	Recommends against the use of chest x-ray and/or sputum cytology in asymptomatic persons	1997
Canadian Task Force on the Periodic Health Examination	Recommends against the use of chest x-ray or sputum cytology in asymptomatic persons	1994
American College of Radiology	Recommends against the use of chest x-ray in asymptomatic persons	1993
American College of Physicians	Recommends against the use of chest x-ray in asymptomatic persons	1991
American Thoracic Society	Recommends against mass lung cancer screening programs except as part of well-designed, controlled clinical trials	1983

NLST National Lung Screening Trial

The **National Lung Screening Trial** (NLST) is a **lung cancer screening** trial sponsored by the National Cancer Institute (NCI).

Launched in 2002, NLST is comparing: spiral computed tomography (CT) and standard chest X-ray. This study will aim to show if either test is better at reducing deaths from this disease.

By February 2004, nearly 50,000 current or former smokers had joined NLST at more than 30 study sites across the country. The trial, now closed to further enrollment, is slated to collect and analyze data for eight years, and will examine the risks and benefits of spiral CT scans compared to chest X-rays.

This trial is a **randomized, controlled study** and is large enough to determine if there is a 20 percent or greater drop in lung cancer mortality from using spiral CT compared to chest X-ray.

CT-screening vs. Mammography

	Breast cancer detection in women ≥ 40	Lung cancer detection in people ≥ 40
Baseline screening	**0.6 - 1.0%**	**1.3%**
Annual screening	**0.2 - 0.4%**	**0.3%**

Henschke et al. NEJM 2006; 355

Who are the at-risk patients?

- History of smoking
- Work related exposure history
- Significant second-hand smoke exposure
- Chronic cough
- Hemoptysis
- Pleuritic chest pain

What do you do for these patients?

- **For symptomatic at-risk patients:**
  - **CT scan of the Chest**
  - **Further Workup as Indicated**
- **For asymptomatic patients who are at-risk:**
  - **No indication to date for CT scan**
  - **Await NLST results**

Pathology

WHO Classification (1999) for NSCLC (80% of Lung CA)

- Squamous Cell Carcinoma (30%)
  - Most commonly in Men
  - Tends to spread Locally and usually central lesions
  - Related to Smoking
  - More readily detected in Sputum
- Adenocarcinoma (30-50%)
  - Most commonly in Women and Non-smokers, but Smoking is risk factor
  - Usually peripheral lesions
  - Metastasize early
  - Bronchoalveolar Carcinoma (BAC) is a subtype
- Large Cell Carcinoma (10-25%)
  - Undifferentiated, primitive cells
  - Metastasize early
  - Usually peripheral lesions
- Adenosquamous Carcinoma
- Carcinomas with Pleomorphic or Sarcomatous elements (0.5%)
- Carcinoid tumor (3-5%)
- Carcinomas of Salivary-gland type
- Unclassified Carcinoma

Staging

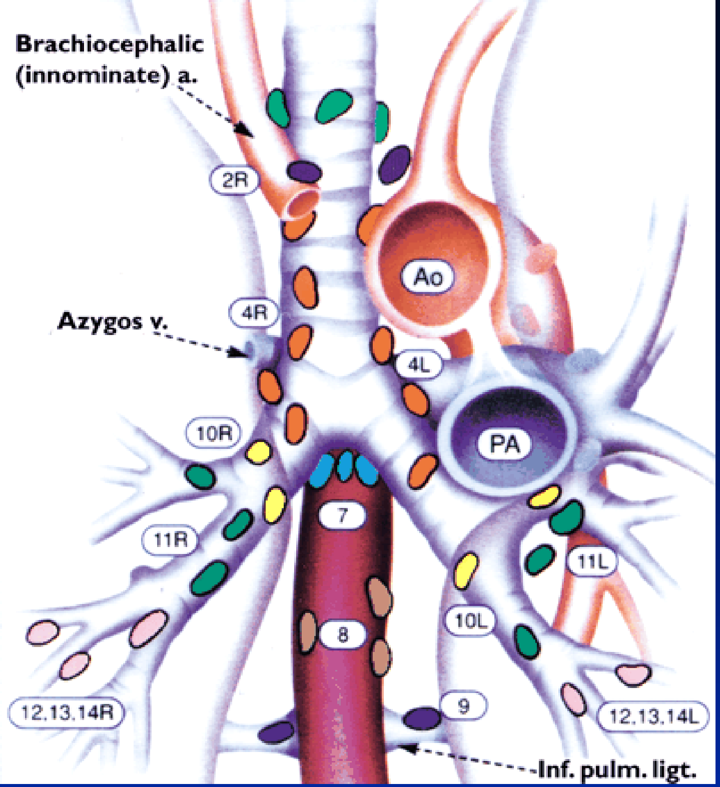
TNM Definitions

- 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	$T_{any}N_{any}M1$

T and M		N0	N1	N2	N3
6th Ed TNM	7th Ed TNM	Stage	Stage	Stage	Stage
T1 (<2cm)	T1a	IA	IIA	IIIA	IIIB
T1 (2-3cm)	T1b	IA	IIA	IIIA	IIIB
T2 (<5cm)	T2a	IB	IIA (IB)	IIIA	IIIB
T2 (5-7cm)	T2b	IIA (IB)	IIB	IIIA	IIIB
T2 (>7cm)	T3	IIB (IB)	IIIA (IB)	IIIA	IIIB
T3 invasion	T3	IIB	IIIA	IIIA	IIIB
T4 (same lobe nodules)	T3	IIB (IIIB)	IIIA (IIIB)	IIIA (IIIB)	IIIB
T4 (extension)	T4	IIIA (IIIB)	IIIA (IIIB)	IIIB	IIIB
M1 (ipsilat lung)	T4	IIIA (IV)	IIIA (IV)	IIIB (IV)	IIIB (IV)
T4 (pleural effusion)	M1a	IV (IIIB)	IV (IIIB)	IV (IIIB)	IV (IIIB)
M1 (contralat lung)	M1a	IV	IV	IV	IV
M1 (distant)	M1b	IV	IV	IV	IV

International Association for the Study of Lung Cancer, *2009*



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

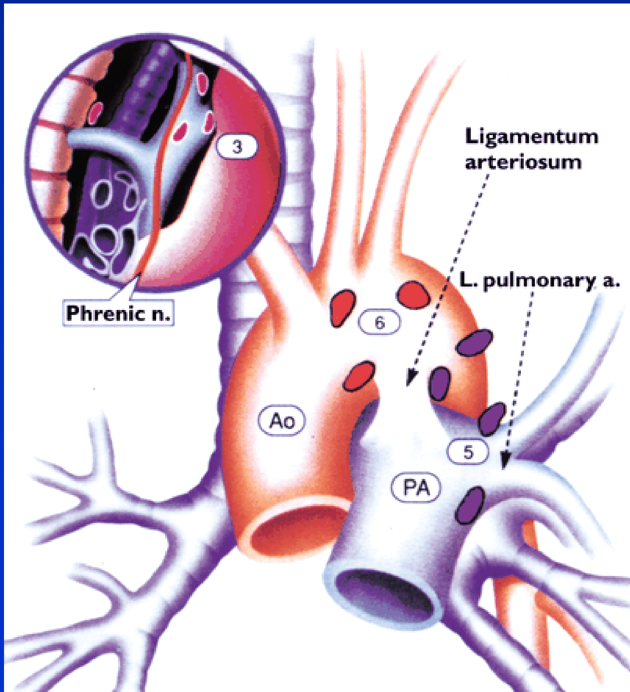
- 5 Subaortic (AP window)
- 6 Para-aortic (Ascending aorta or phrenic)

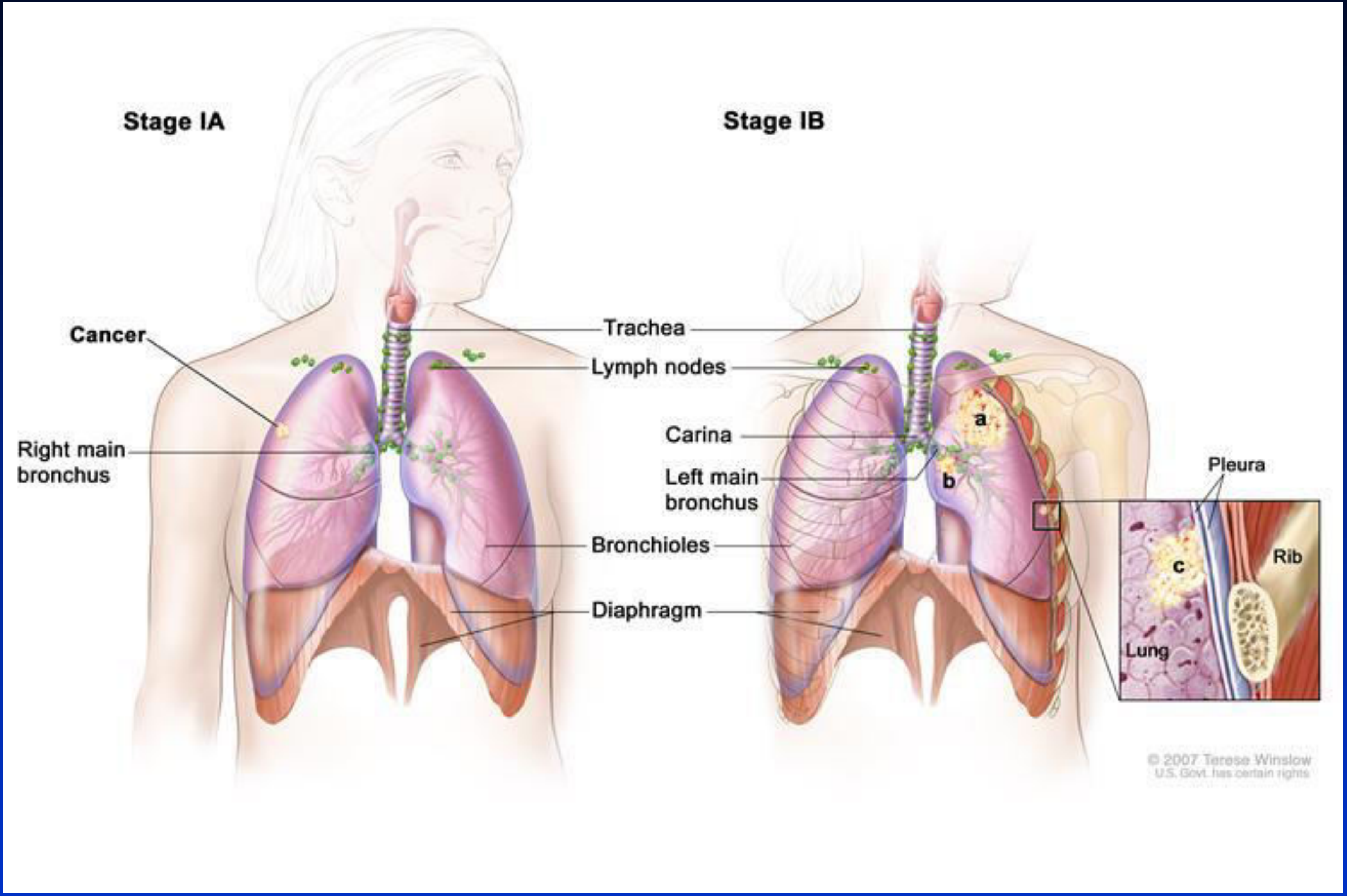
Inferior Mediastinal Nodes

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

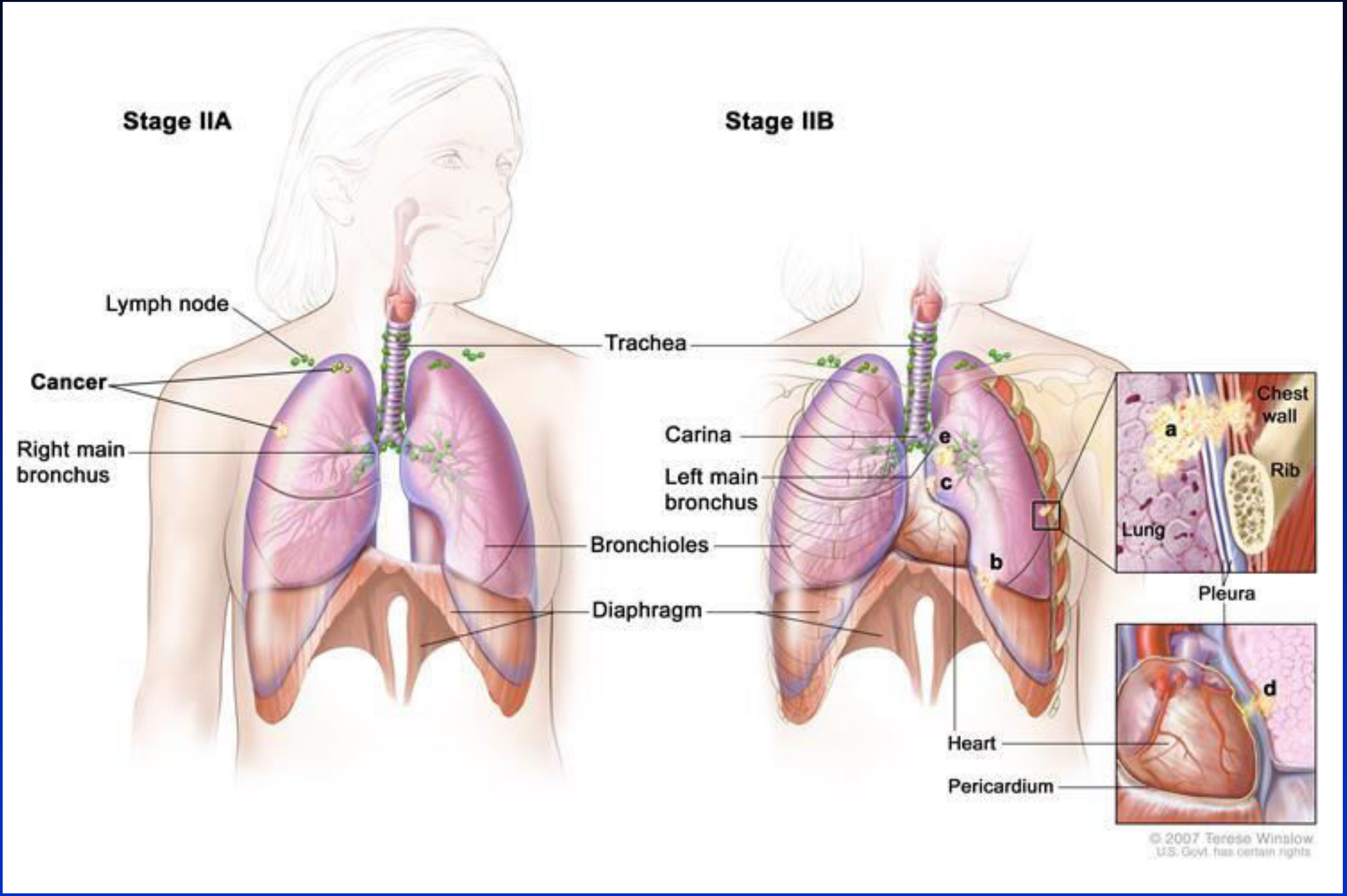
N_1 Nodes

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



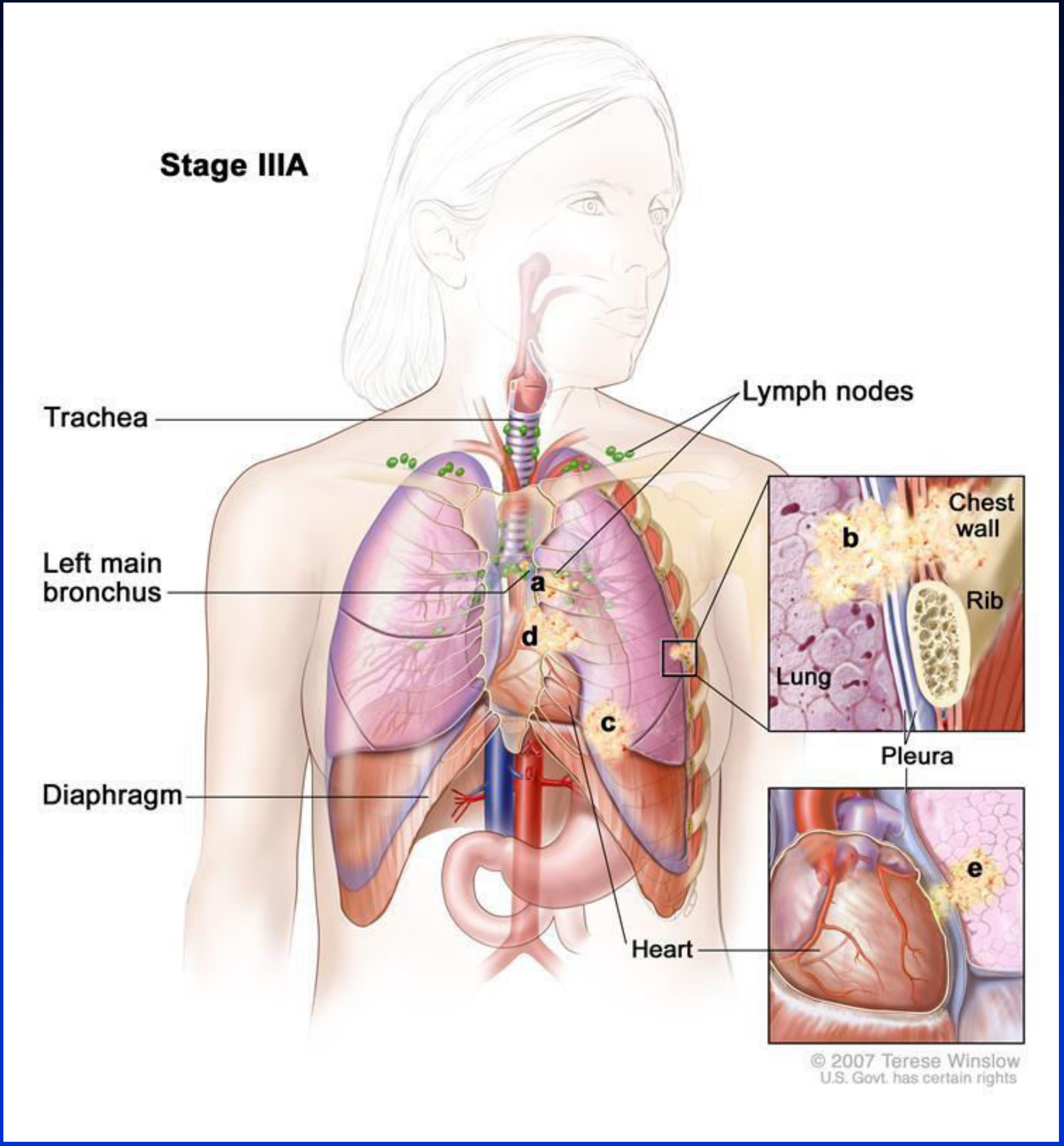


Stage IA, cancer is in the lung only, less than 3cm in size.
Stage IB, the cancer is: **(a)** greater than 3cm in size **(b)** involve the main bronchus **(c)** invade visceral pleura **(d)** associated with obstructive pneumonitis.



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.

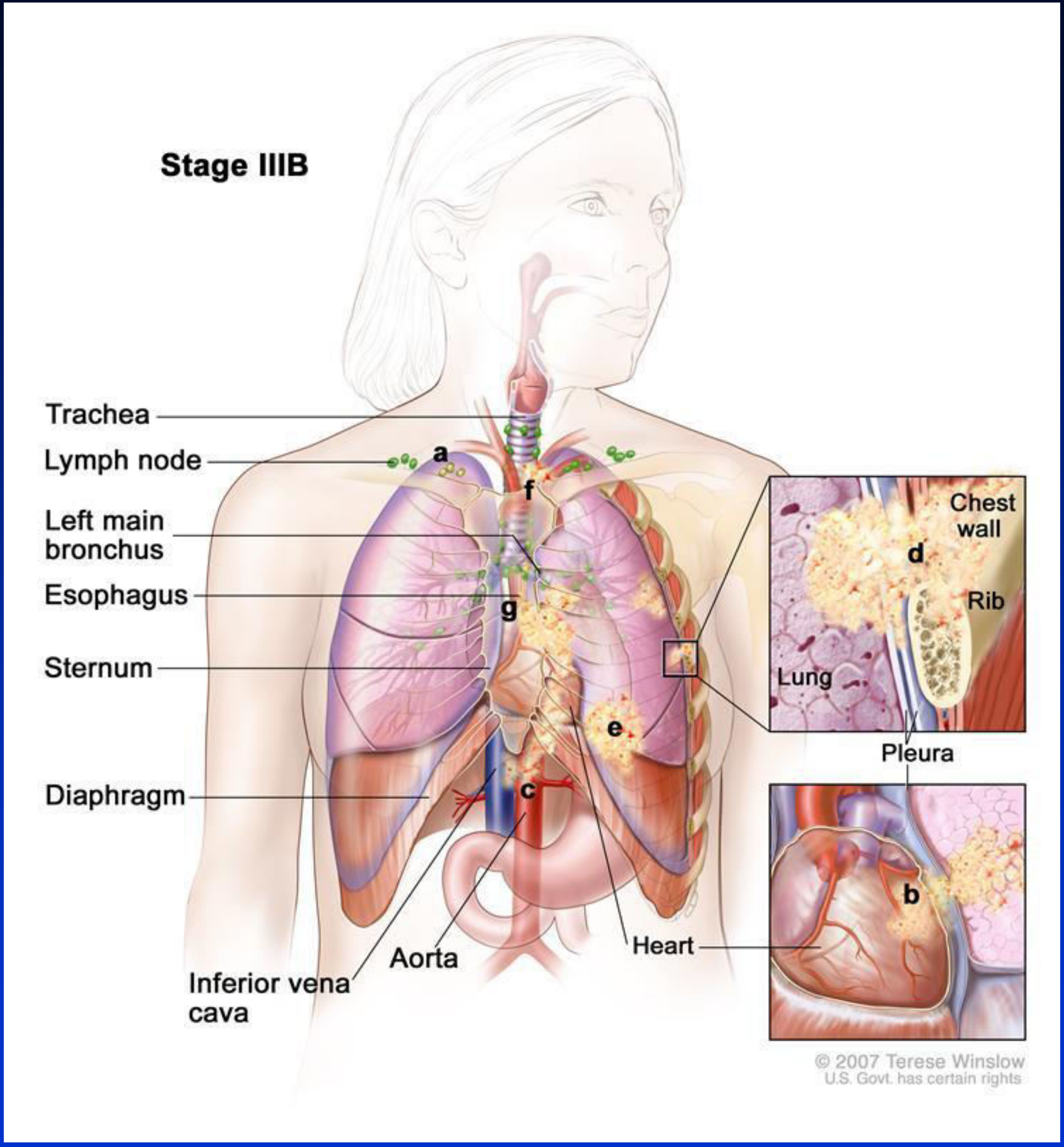
Stage IIIB

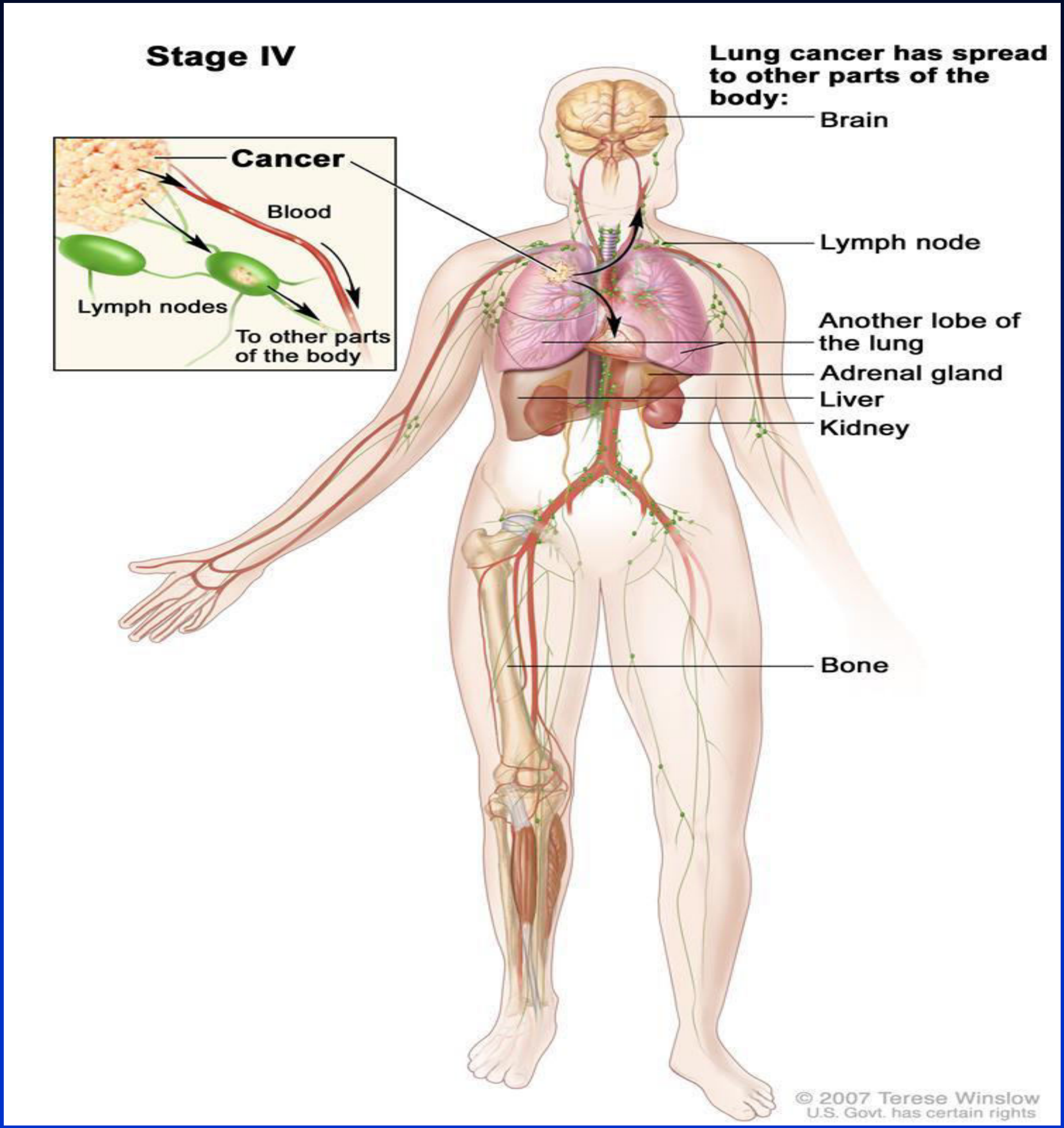
The cancer has spread to (a) contralateral mediastinal or hilar nodes or ipsilateral supraclavicular nodes.

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 IV
Lung cancer has spread to other parts of the body:
Brain
Cancer
Blood
Lymph nodes
To other parts of the body
Lymph node
Another lobe of the lung
Adrenal gland
Liver
Kidney
Bone
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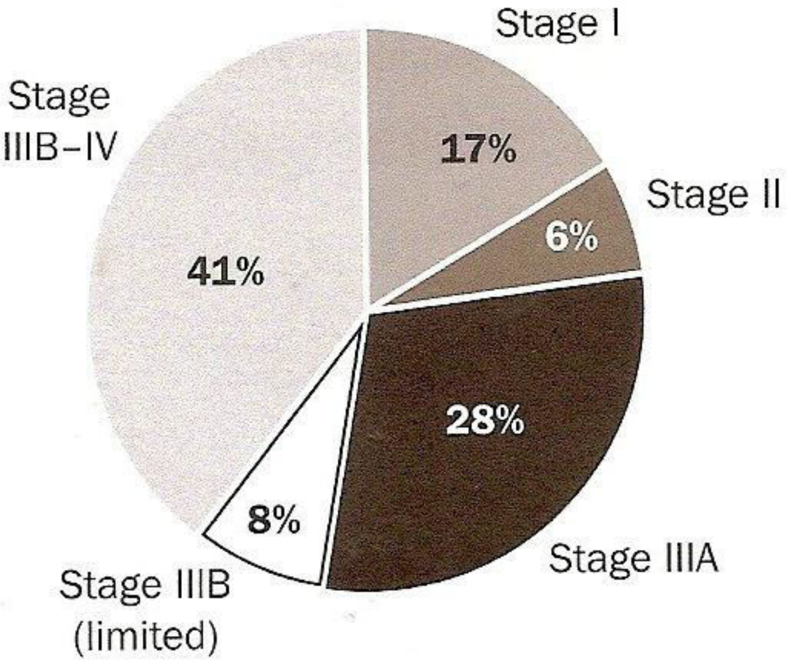
Staging

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

Mountain, *Chest* 1997

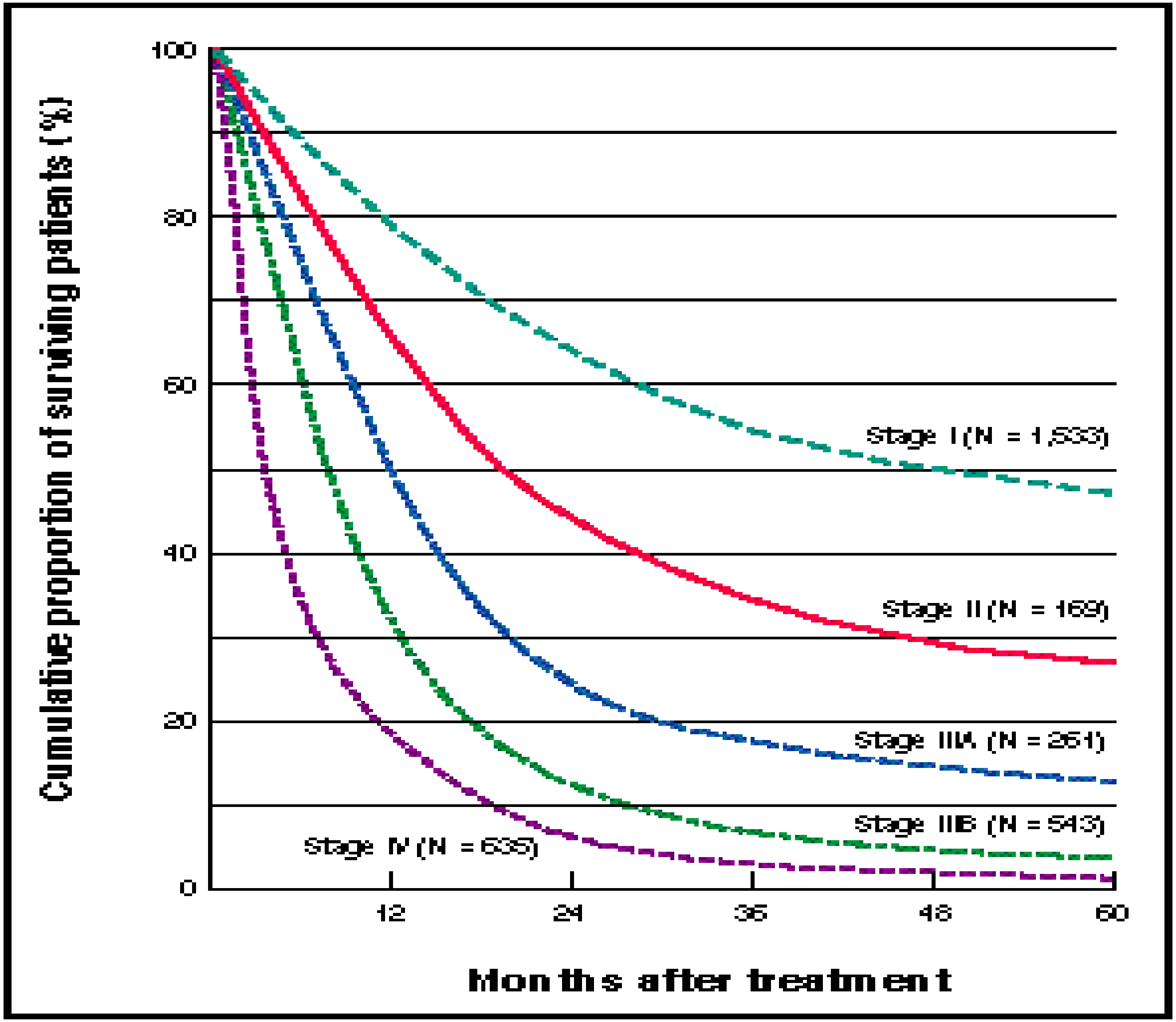


Figure 3. Survival rates after surgical resection by stage of disease (P < .001).

Adapted from Mountain (10).

Non-small cell lung cancer survival by stage*

Stage	5-year relative survival rate
I	56%
II	34%
III	10%
IV	2%

NCI Surveillance, Epidemiology, and End Results (SEER) Database 1988-2001

Treatment

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

Adapted with permission from Spira A, Ettinger DS. Multidisciplinary management of lung cancer. N Engl J Med 2004;350:388.

Treatment – Stage I

- **Surgery is the treatment of choice.**
- **Lobectomy is recommended if patient's medical condition and pulmonary function tests are acceptable.**
- **Postoperative Mortality 3-5% with Lobectomy**
- **Segmental or wedge resection recommended for patients with impaired pulmonary function**

- **Lung Cancer Study Group study (Ginsberg and Rubinstein)**
- **Lobectomy versus limited resection Stage I lung cancer**
- **Reduction in local recurrence with lobectomy (6.4% vs 17.2%)**
- **No significant difference in overall survival (68% vs 50%)**

- **Warren et al showed: Survival Advantage with Lobectomy for patients with tumors more than 3cm**

Treatment – Stage I

- **Inoperable Stage I: Radiation**
- ***Dosoretz et al* & *Gauden et al*:**
  - **5 year survival 10-27%**
  - **For Stage IA (T1N0) 5 year survival was 32-60%**
- **Radiation dose is 60 Gy**

- **Adjuvant Radiation:**
  - **Meta analysis of 9 randomized trials for postoperative radiation in Stage I showed a 7% reduction in overall survival**

- **Adjuvant Chemotherapy:**
- **The Lung Adjuvant Cisplatin Evaluation (LACE), which was based on a pooled analysis of five randomized trials, has demonstrated that cisplatin-based adjuvant chemotherapy improved survival in patients with completely resected NSCLC**
- **This analysis has suggested that platinum-based adjuvant chemotherapy may have NO benefit for patients with stage IA and only a marginal benefit for patients with stage IB.**
    - **Tumor > 5cm in size**
    - **Poorly differentiated**

Treatment – Stage II

- Surgery is the treatment of choice.
- Lobectomy is recommended if patient's medical condition and pulmonary function tests are acceptable.
- Postoperative Mortality 3-5% with Lobectomy
- Postoperative Mortality 5-8% with Pneumonectomy
- Segmental or wedge resection recommended for patients with impaired pulmonary function

Inoperable Stage II: Radiation

- Dosoretz et al:
  - 5 year survival 10%
  - For T1N1 5 year survival was 60%
- Radiation dose is 60 Gy

Treatment – Stage II

Adjuvant Radiation:

- Postoperative radiotherapy reduces rates of local recurrence by 11% to 18% among patients with completely resected, pathologically confirmed stage II NSCLC. Therefore, if the outcome of interest is a reduction in the frequency of local tumour recurrence, radiotherapy is recommended. However, there is no evidence of a survival benefit from postoperative radiotherapy alone.

Adjuvant Chemotherapy:

- The Lung Adjuvant Cisplatin Evaluation (LACE), which was based on a pooled analysis of five randomized trials, has demonstrated that cisplatin-based adjuvant chemotherapy improved survival in patients with completely resected NSCLC
- This benefit depended on stage, being greatest in patients with stage II or IIIA disease.
- With a median followup of 5.1 years, the overall hazard ratio of death was 0.89 (95% C.I.; 0.82–0.96; *$p<0.005$) which corresponds to a 5-year absolute benefit of 4.2% with chemotherapy*. Hazard Ratio for stage II was 0.83 (95% C.I.; 0.73–0.95).

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%
- All patients are candidates for treatment on clinical trials since long term survival is poor

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.

Treatment – Stage IIIA

Adjuvant Chemotherapy alone:

- **The Lung Adjuvant Cisplatin Evaluation (LACE) has demonstrated that cisplatin-based adjuvant chemotherapy improved survival in patients with completely resected NSCLC**
- **With a median followup of 5.1 years, the overall hazard ratio of death was 0.89 (95% C.I.; 0.82–0.96; *p<0.005) which corresponds to a 5-year absolute benefit of 4.2% with chemotherapy*. Hazard Ratio for stage III was 0.83 (95% C.I.; 0.73–0.95)**

Adjuvant Radiation Therapy alone:

- **Meta analysis of nine randomized trials of postoperative radiation versus surgery alone → NO difference in overall survival for all patients or the subset of N2 positive patients.**
- **Postoperative radiotherapy reduces rates of <u>local recurrence</u> by 11% to 18% among patients with completely resected, pathologically confirmed IIIA NSCLC**

Treatment – Stage IIIB / IV

- Chemotherapy
- Radiation alone
- Chemotherapy plus radiation
  - Meta analysis of 54 randomized trials showed an **absolute survival benefit of 4% at 2 years** with combination of chemotherapy and radiation

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

Adapted with permission from Spira A, Ettinger DS. Multidisciplinary management of lung cancer. N Engl J Med 2004;350:388.

Newer Treatments

- Cyber knife
- Radiofrequency Ablation (RFA)
- Photodynamic Therapy (PDT)
- Targeted Therapies

Newer Treatments

CyberKnife

- CyberKnife is a frameless robotic radiosurgery method of delivering radiotherapy, with the intention of targeting treatment more accurately than standard radiotherapy.
- Two main elements are the small linear particle accelerator which produces radiation and a robotic arm that allows energy to be directed to the body from any direction.
- Used for Inoperable early stage lung cancer, or
- Metastatic disease

CyberKnife Results

Stereotactic radiotherapy for primary lung cancer and pulmonary metastases: a noninvasive treatment approach in medically inoperable patients,
***Int J Radiat Oncol Biol Phys* 2004**

Twenty patients with Stage I-II NSCLC and
41 patients with 51 pulmonary metastases

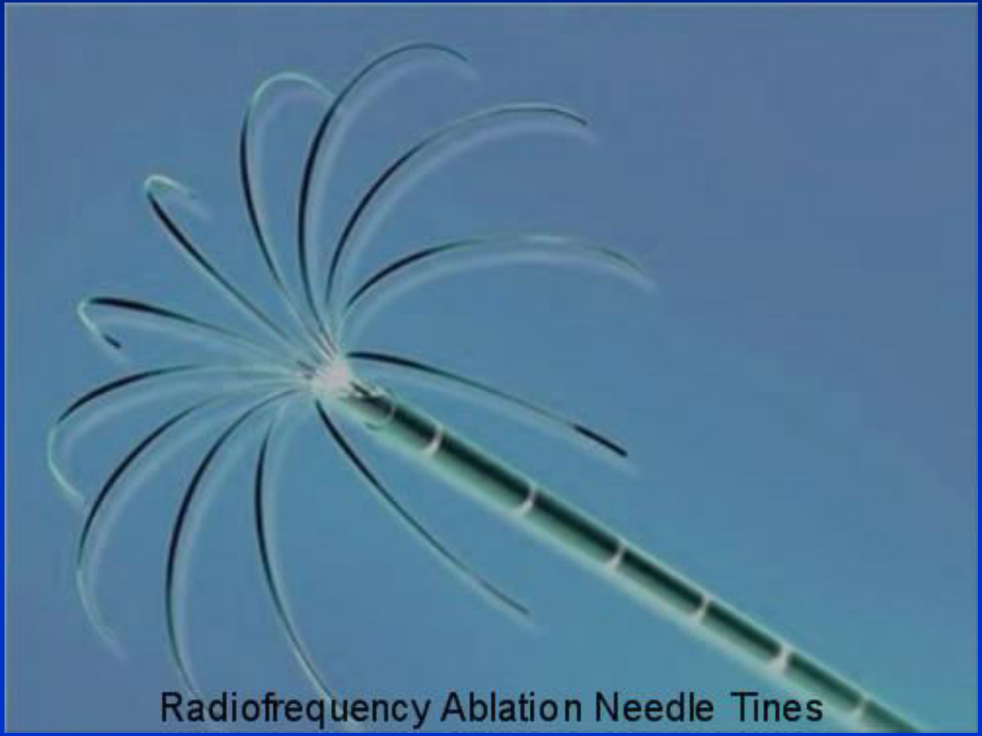
Overall survival rate:
Lung Cancer Patients
1 year = 52%   2 year = 32%

Metastasis Patients
1 year = 85%   2 year = 33%

Newer Treatments

Radiofrequency Ablation (RFA)

- Ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI) are used to help guide a needle electrode into a cancerous tumor.
- High-frequency electrical current is then used to heat a specific volume of tissue to temperatures high enough to cause destruction of undesired malignant cells.
- Used for Inoperable early stage lung cancer, or
- Metastatic disease



RFA Results

Pulmonary Radiofrequency Ablation: Long-term Safety and Efficacy in 153 Patients, *Radiology* 1997

Overall long-term survival rates for stage I non–small cell lung cancer (NSCLC):

1 year = 78%   2 year = 57%
3 year = 36%   4 year = 27%
5 year = 27%

Pneumothorax rate 28.4%
Other Complication rate 14.3%
30 day Mortality rate 3.9%
→ 2.6% procedure specific

Newer Treatments

Photodynamic Therapy (PDT)

- Involves the use of photosensitizing agents that are selectively retained within tumor cells.
- The agents remain inactive until exposed to light of the proper wavelength.
- When activated by light, these compounds generate toxic oxygen radicals that result in tumor necrosis.
- In lung cancer, PDT can be used for both carcinoma in situ and for the treatment of unresectable disease with endobronchial obstruction.

Table 1

Photodynamic Therapy in Early-Stage Lung Cancer

Study	Number of Tumors	Clinical Stage	Drug	Complete Response Rate	Partial Response Rate	Rate of Nonresponses	Recurrence Rate
Edell and Cortese[46]	14	IA	HPD	93%	7%	0%	21%
Kato et al[47]	95	CIS and IA	Porfimer sodium	83%	17%	0%	6%
Furuse et al[48]	59	CIS and IA	Porfimer sodium II	85%	10%	5%	10%
Sutedja et al[49]	39	CIS (N = 17)	Porfimer sodium	100%	0%	0%	29%
		IA (N = 22)		50%	45%	5%	
Cortese et al[50]	23	Early stage	HPD	70%	30%	0%	48%

CIS = Carcinoma in situ; HPD = hematoporphyrin derivative.

Long-term survival of patients treated with photodynamic therapy for carcinoma in situ and early non-small-cell lung carcinoma, *Laser Surg Med* 2007

Two Year Overall Survival = 73%

Five year Overall Survival = 59%

Ost, *Oncology*, 2000

Selected targeted agents in clinical development for lung cancer treatment

Target	Drug	Trade name	Stage of development in lung cancer
EGFR pathway inhibitors			
EGFR	Gefitinib	Iressa	Approved for advanced NSCLC[A]
EGFR	Erlotinib	Tarceva	Approved for advanced NSCLC
EGFR	Cetuximab	Erbitux	Phase II/III
EGFR	Matuzumab		Phase I
EGFR	Panitumumab	Vectibix	Phase II
EGFR, HER2	Lapatinib	Tykerb	Phase II
EGFR, HER2	HKI-272		Phase II
EGFR, HER2, ERB4	CI-1033		Phase II
VEGF/VEGFR pathway inhibitors			
VEGF-A	Bevacizumab	Avastin	Approved for advanced NSCLC
VEGFR-2, EGFR	ZD6474; Vandetanib	Zactima	Phase II/III
VEGFR-1-3	AZD2171	Recentin	Phase II/III
VEGFR-1-3, PDGFR, c-KIT, FLT-3	SU11248; Sunitinib	Sutent	Phase II
VEGFR-1-3, PDGFR-β, c-KIT, c-fms	PTK787; Vatalanib		Phase II
VEGFR-1-3, PDGFR, c-KIT	AG-013736; Axitinib	Champix	Phase II
VEGFR-1-3, PDGFR, c-KIT	AMG 706		Phase I
Ras/Raf/MEK pathway inhibitors			
Ras	Tipifarnib (FTI)	Zarnestra	Phase III
Ras	Lonafarnib (FTI)	Sarasar	Phase III
Raf-1, VEGFR-2 and -3, PDGFR, c-KIT	BAY 43-9006; Sorafenib	Nexavar	Phase II
MEK	CI-1040		Phase II
MEK	PD-0325901		Phase I/II
MEK	AZD6244		Phase I
PI3K/Akt/PTEN pathway inhibitors			
PI3K	LY294002		Phase I
mTOR	Rapamycin; Sirolimus	Rapamune	Phase I
mTOR	CCI-779; Temsirolimus		Phase I/II
mTOR	RAD001; Everolimus		Phase I/II
mTOR	AP23573		Phase I
Tumor suppressor gene therapies			
p53	p53 retrovirus		Phase I
p53	p53 adenovirus (Ad5CMV-p53)	Advexin	Phase I
FUS1	FUS1 nanoparticle		Phase I
Proteasome inhibitors			
Proteasomes	Bortezomib	Velcade	Phase II
HDAC inhibitors			
HDAC	SAHA; Vorinostat	Zolinza	Phase II
HDAC	Depsipeptide		Phase I
Telomerase inhibitors			
Telomerase	GRN163L		Phase I

Iressa
Tarceva
Erbitux
Avastin

New molecularly targeted therapies for lung cancer

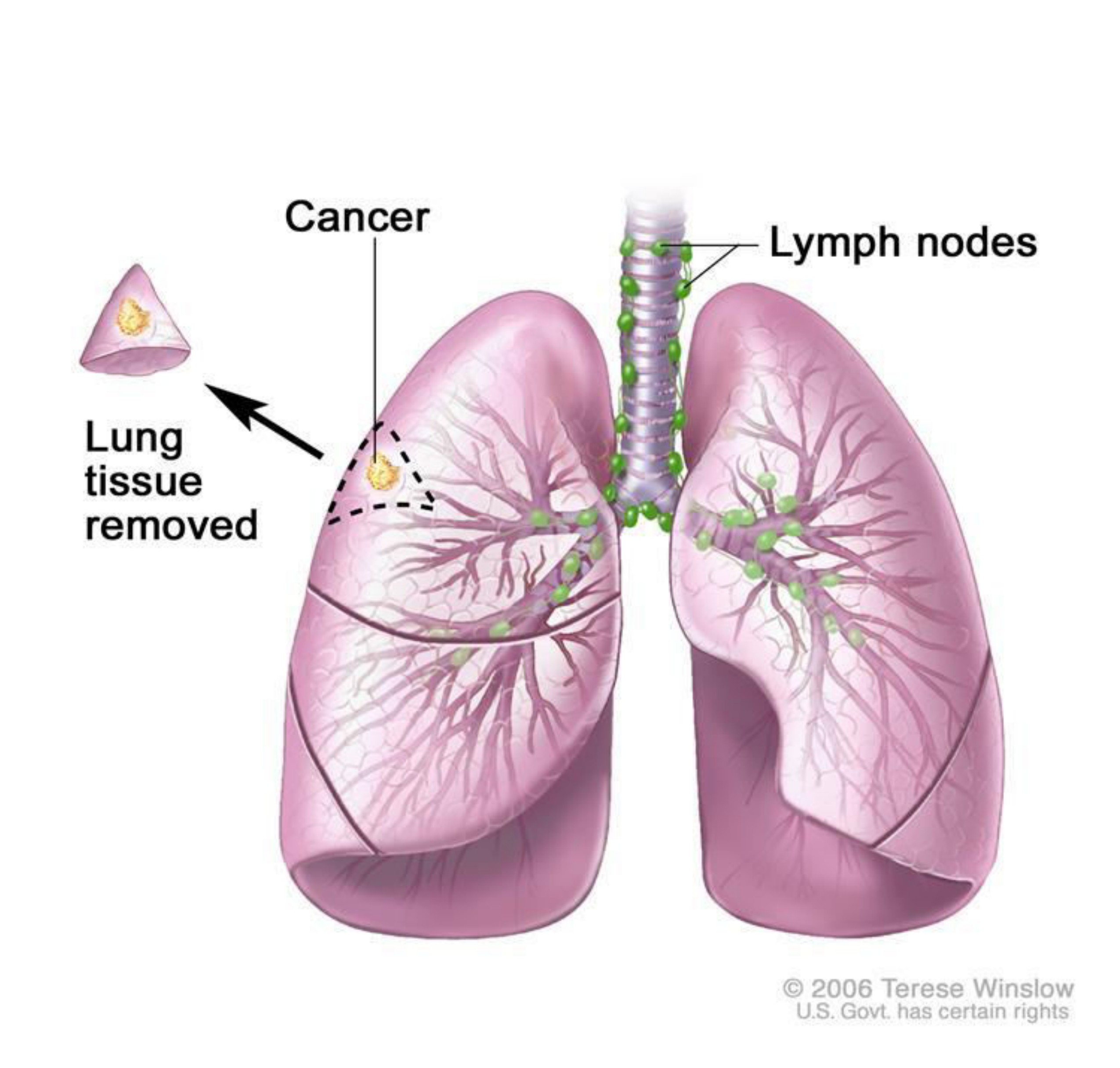
Sophie Sun,[1,2] Joan H. Schiller,[1,2] Monica Spinola,[2,3] and John D. Minna[1,2,3]

[1]Division of Hematology and Oncology, [2]Simmons Comprehensive Cancer Center, and [3]Hamon Center for Therapeutic Oncology Research, University of Texas Southwestern Medical Center, Dallas, Texas, USA.

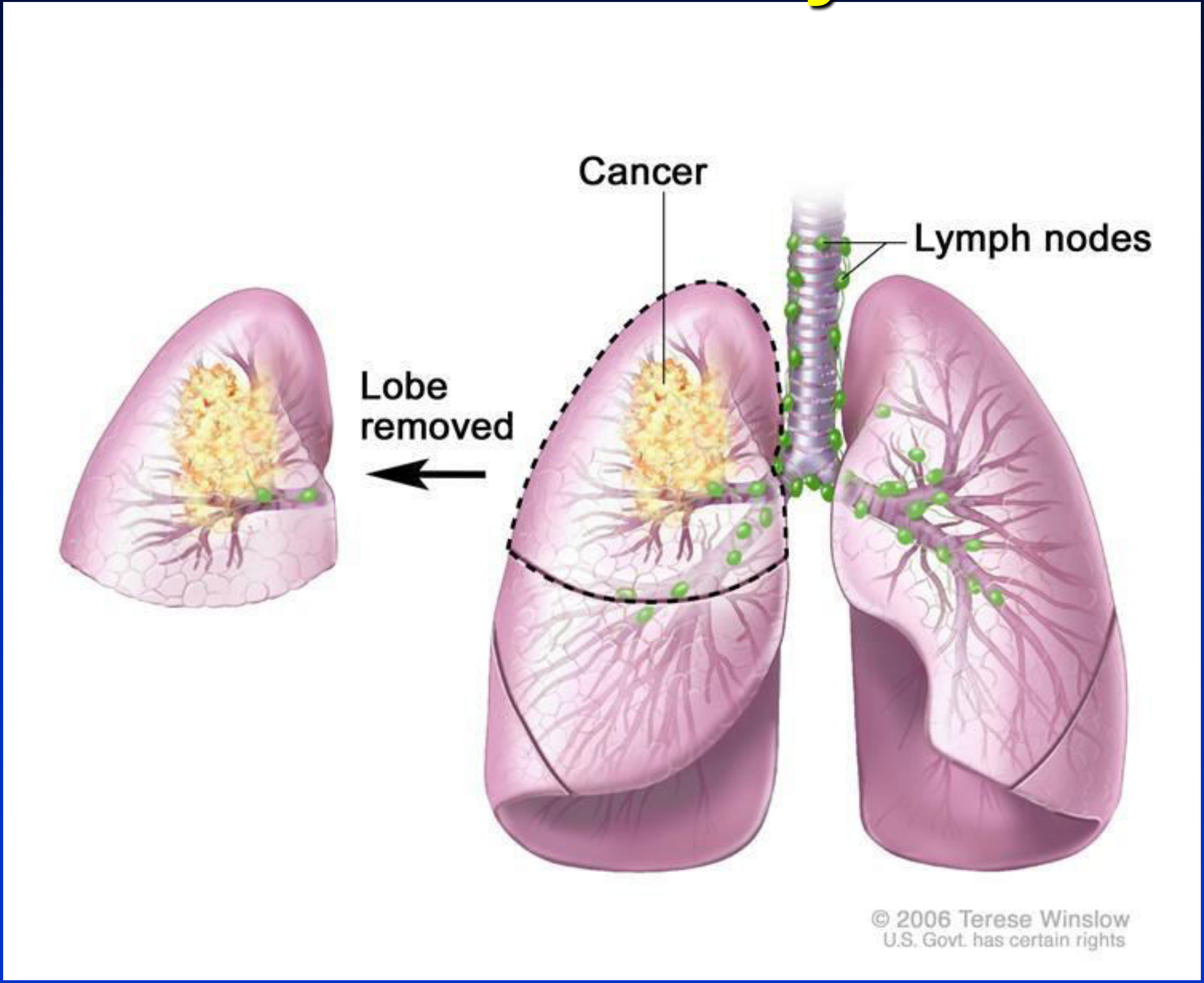
The Journal of Clinical Investigation http://www.jci.org Volume 117 Number 10 October 2007

Surgery

Wedge Resection



Lobectomy



Cancer
Lymph nodes
Lobe removed
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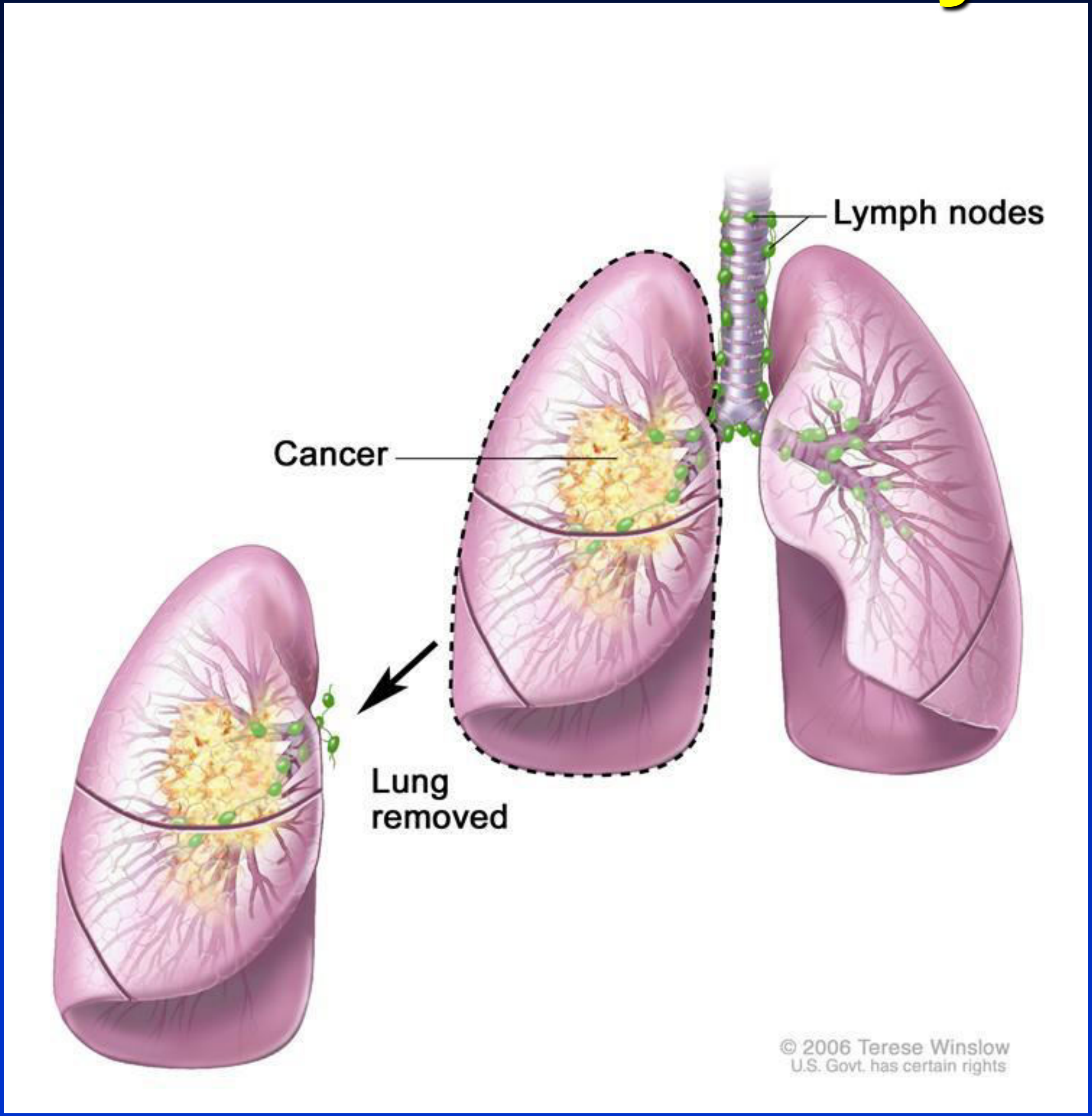
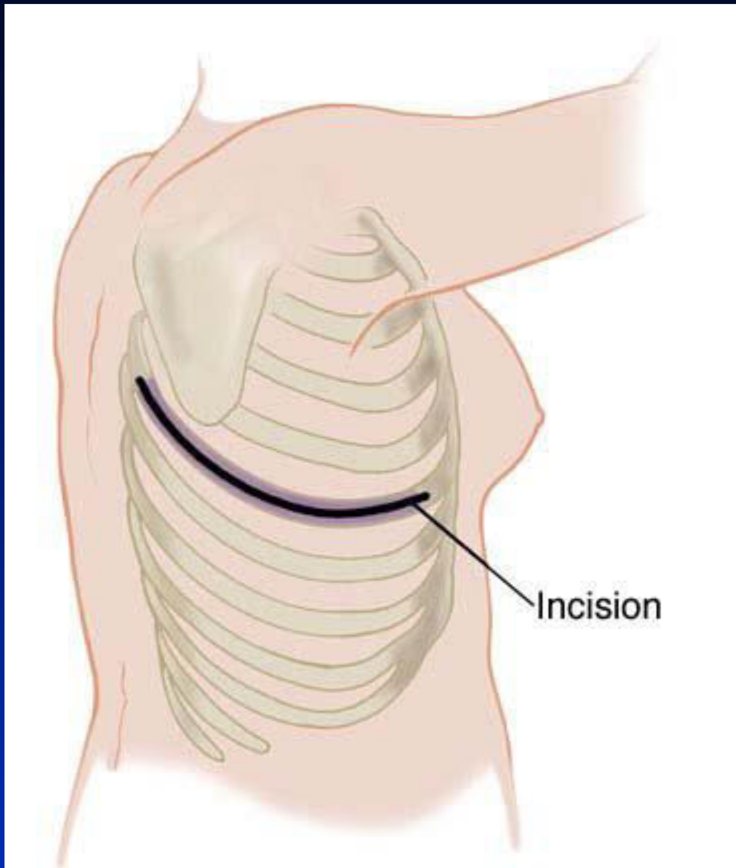
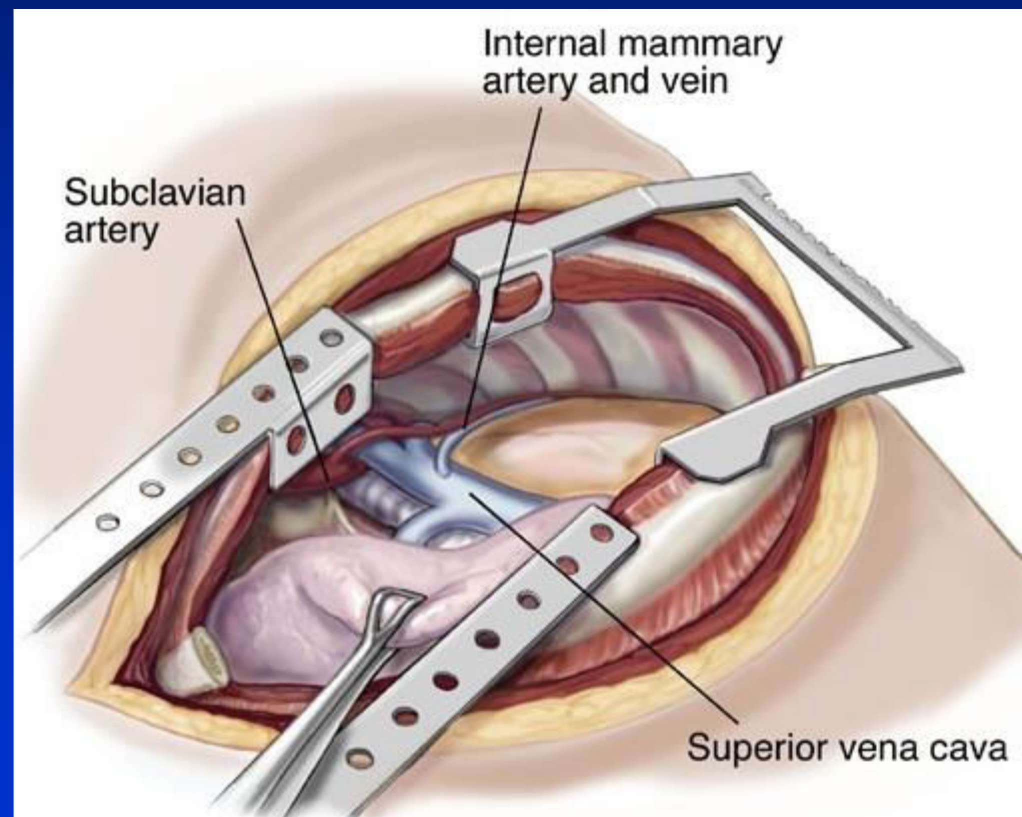
Pneumonectomy




Incision


Internal mammary
artery and vein
Subclavian
artery
Superior vena cava

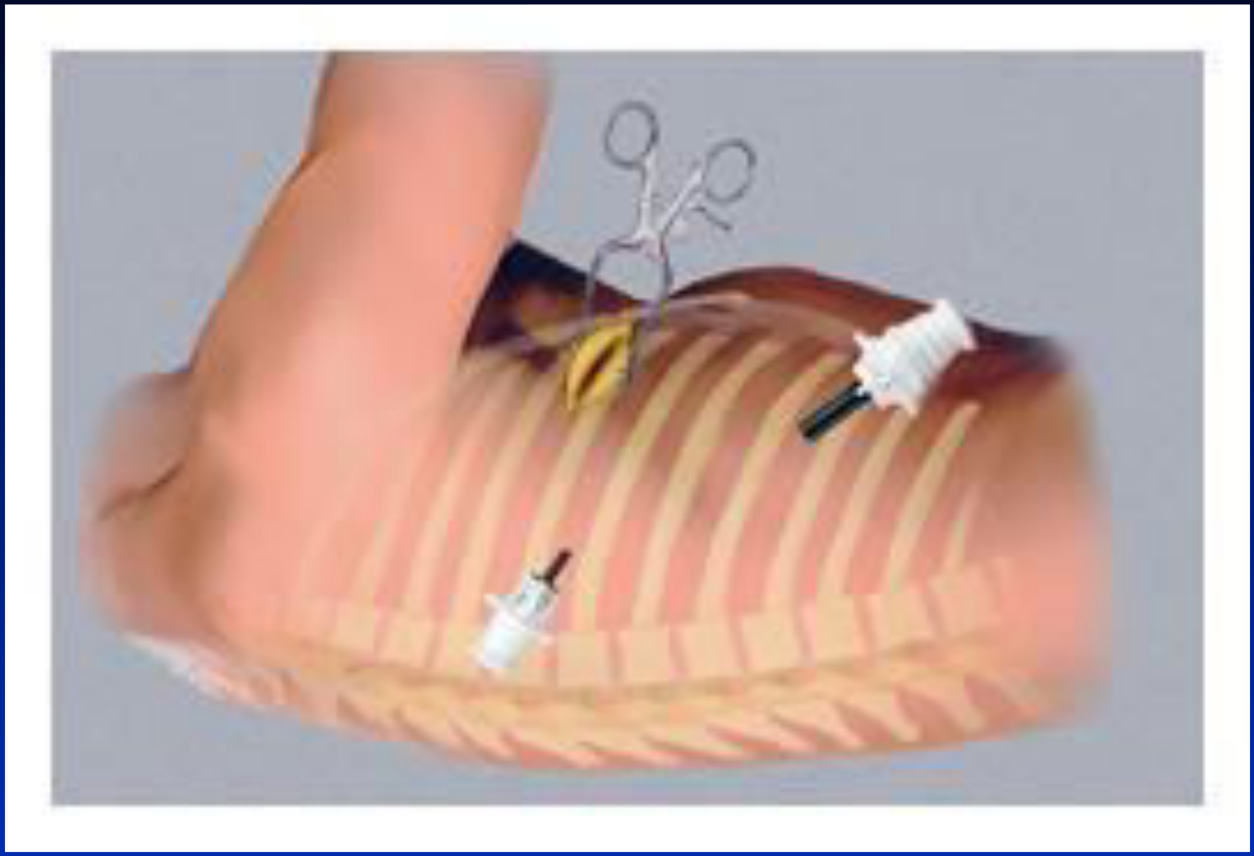
VATS Lobectomy

Video Assisted Thorascopic Surgery

VATS Lobectomy

- Standardize the definition of a VATS lobectomy to encompass a true anatomic lobectomy with individual ligation of lobar vessels and bronchus as well as hilar lymph node dissection or sampling using the video screen for guidance, two or three ports, and no retractor use or rib spreading.

CALBG 39802, 2007



Example of VATS Incisions

VOLUME 25 · NUMBER 31 · NOVEMBER 1 2007

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Video-Assisted Thoracic Surgery Lobectomy: Report of CALGB 39802—A Prospective, Multi-Institution Feasibility Study

Scott J. Swanson, James E. Herndon II, Thomas A. D'Amico, Todd L. Demmy, Robert J. McKenna Jr, Mark R. Green, and David J. Sugarbaker

Table 2. Operative Data (N = 127)

Operative Characteristic	Value
Stage I NSCLC	
No. of patients	111
%	87
Successful VATS lobectomy	
No. of patients/total	96/111
%	86.5
95% CI, %	80% to 93%
Lobe resected, No. of patients	
RUL	23
RML	2
RLL	17
LUL	35
LLL	12
Unknown/other	7
Operative time, minutes	
Median	130
Range	47-428
Chest tube duration, days	
Median	3
Range	1-14

Abbreviations: NSCLC, non–small-cell lung cancer; VATS, video-assisted thoracic surgery; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe.

Table 4. Complications Among Patients Who Underwent Successful Resection With Video-Assisted Thoracic Surgery

Complication	Grade of Complications						
	Grade 3: Severe		Grade 4: Life Threatening		Grade 5: Lethal		Total No. of Patients Evaluated
	No. of Patients	%	No. of Patients	%	No. of Patients	%	
Cardiovascular: arrhythmia							
Arrhythmia, other	3	3	1	1	0	0	95
Supraventricular arrhythmias	1	1	0	0	0	0	95
Cardiovascular: general							
Hypotension	1	1	0	0	0	0	95
Cardiac ischemia/infarction	0	0	0	0	0	0	95
Thrombosis/embolism	0	0	0	0	0	0	95
Operative injury of vein/artery	0	0	0	0	0	0	95
Dermatology/skin							
Wound infection	0	0	0	0	0	0	95
Hemorrhage							
Hemorrhage/bleeding associated	0	0	1	1	0	0	95
Infection/febrile neutropenia							
Infection without neutropenia	0	0	0	0	0	0	95
Catheter-related infection	0	0	0	0	0	0	95
Infection/other	0	0	0	0	0	0	95
Pulmonary							
Pleural effusion	1	1	0	0	0	0	95
Adult respiratory distress syndrome	0	0	0	0	0	0	95
Pneumothorax	0	0	0	0	0	0	95
Pulmonary, other	0	0	1	1	0	0	95
Summary							
Maximum toxicity	4	4	3	3	0	0	95

Results

- Mortality Rate = 2.7%
- Complication Rate = 7.4%
- Arrhythmias = 5.6%
- Prolonged Air Leak = <1%

- Conversion Rate = 11%
- More than 1/3 of patients were older than 70 years of age

<u>ACOSOG Z0030 Trial</u>:

- Open thoracotomy in patients older than 70 years, morbidity of 40-50%
- Atrial Arrhythmias = 15%
- Prolonged Air Leak = 8%

<u>Thomas et al</u>:

- Open thoracotomy in patients older than 70 years, mortality rate 12.8%

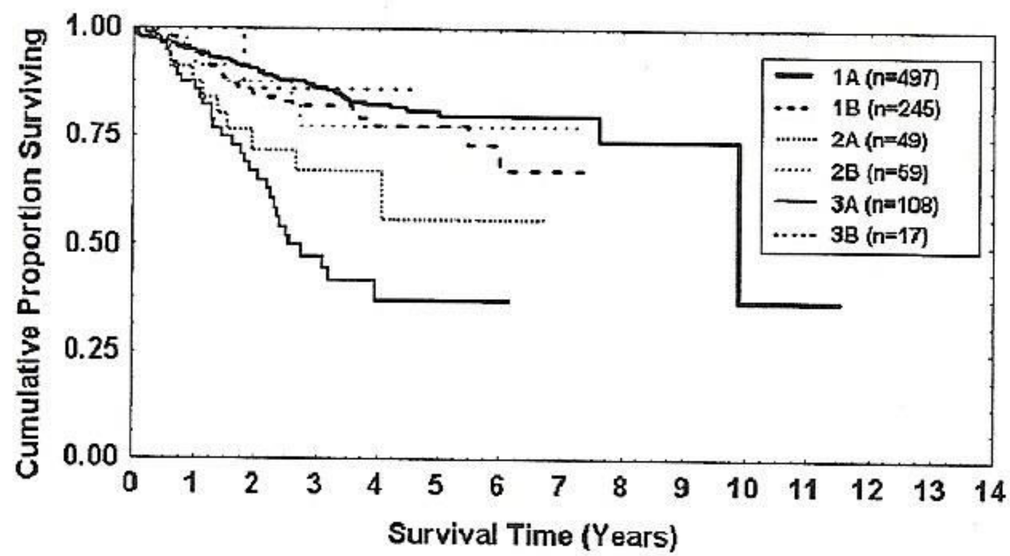
Video-Assisted Thoracic Surgery Lobectomy: Experience With 1,100 Cases

Robert J. McKenna, Jr, MD, Ward Houck, MD, and Clark Beeman Fuller, MD

Cedars Sinai Medical Center, Los Angeles, California

Table 1. Anatomic Pulmonary Resections Done With Video-Assisted Thoracic Surgery

Type of Resection	Number
Right upper lobectomy	403
Right middle lobectomy	92
Right lower lobectomy	158
Pneumonectomy	14
Segmentectomy	19
Sleeve lobectomy	3
Bilobectomy	18
Bilateral lobectomy	1
Left upper lobectomy	279
Left lower lobectomy	113



At Risk

1A	403	283	199.5	136	84.5	47	26.5	11	3	2	1	.5
1B	193.5	154	124	96.5	70.5	53	32.5	20	13.5	6.5	2	.5
2A	37	26.5	21.5	17	13.5	9.5	6.5	4	35	2	1	.5
2B	44	32.5	25	18.5	14	9	7	6	5	3	1	.5
3A	83.5	60	46	36	27.5	17.5	11.5	8.5	6	3	1	.5
3B	12	8.5	8	7.5	7	6	5	4	4	3	1.5	.5

Results

- Mortality Rate = 0.8%
- Complication Rate = 15.3%
- Arrhythmias = 2.9%
- Prolonged Air Leak = 5.1%

- Conversion Rate = 2.5%
- Mean Age of Patients = 71.2 years
- Mean LOS = 4.78 days
- 20% discharged POD 1 or 2

<u>ACOSOG Z0030 Trial</u>:

- Open thoracotomy in patients older than 70 years, morbidity of 40-50%
- Atrial Arrhythmias = 15%
- Prolonged Air Leak = 8%
- Mortality Rate = 2.3% (Older than 70 years)

<u>Thomas et al</u>:

- Open thoracotomy in patients older than 70 years, mortality rate 12.8%

Video-Assisted Thoracoscopic Lobectomy: State of the Art and Future Directions

Jason P. Shaw, MD, Francine R. Dembitzer, MD, Juan P. Wisnivesky, MD, MPH, Virginia R. Litle, MD, Todd S. Weiser, MD, Jaime Yun, MD, Cynthia Chin, MD, and Scott J. Swanson, MD

Division of Thoracic Surgery and Departments of Medicine and Pathology, The Mount Sinai Medical Center, New York, New York

Table 2. Summary of Studies of Video-Assisted Thoracoscopic Procedures and Overall Results

First Author	No.	Year	Patient Group	Procedure Performed	Conversion Rate, %	LOS, Mean/ Median Days	Peri-Op Morbidity, %	Peri-Op Mortality, %	Survival, %
McKenna [4]	1100	2006	Benign + stage I–III NSCLC	Lobectomy	2.5	4.8	15	0.8	5 y: 1A, 84.5; 1B, 70.5; 2A, 13.5; 2B, 14; 3A, 27.5
Onaitis [5]	500	2006	Benign + NSCLC	Lobectomy	1.6	3	NR	1.0	2 y: 80
Yim [6]	214	1998	Benign + NSCLC	Lobectomy + others	0.9	6.8/NR	22	0.5	23 mon: 93
Kaseda [7]	204	2000	Benign + NSCLC	Lobectomy + others	1.5	NR/NR	2.3	0.8	5 y: stage I, 97
Roviaro [8]	171	2004	Clinical stage IA NSCLC	Lobectomy + others	5.3	NR/NR	8.7	0.6	3 y, 77; 5 y, 63.6
Walker [9]	159	2003	Stage I, II NSCLC	Lobectomy, lingulectomy	11.2	NR/6	NR	1.8	Stage I, 77.9; stage II, 51
Iwasaki [10]	140	2004	Stage IA NSCLC	Lobectomy + segmentectomy	2.1	NR	NR	0	5 y, 7
Swanson [11]	128	2002	Benign + NSCLC	Lobectomy	13	3	8.2	2.1	NR
Daniels [12]	110	2002	Benign + NSCLC	Lobectomy	1.8	NR/3	19	3.6	NR
Ohtsuka [13]	106	2004	Stage I NSCLC	Lobectomy + others	10	7.6	NR	0.9	3 y, 79
Solaini [14]	105	2001	Benign + NSCLC	Lobectomy + others	5.7	6.2/NR	12	NR	3 y, 85
Sugi [15]	100	2000	Stage 1A NSCLC	Lobectomy	4.2	NR	NR	NR	5 y, 90
Shiraishi [16]	95	2006	T1 N0 M0 NSCLC	Lobectomy	14/95	NR	NR	0	5 y, 89
Kirby [3]	61	1995	Stage I NSCLC (6 excluded)	Lobectomy	10	7.1	6	0	NR
Whitson [17]	59	2007	Stage I NSCLC	Lobectomy	11/70	6.4/NR	NR	NR	4 y, 72

LOS = length of stay; NR = not reported; NSCLC = non-small cell lung cancer.

Oncologic Benefit of VATS?

Petersen et al:

- VATS lobectomy has greater likelihood of planned delivery of adjuvant therapy after surgery

- 61% VATS lobectomy received 75% or more planned adjuvant therapy without delay or dose reduction

versus

- 40% open lobectomy received 75% or more planned adjuvant therapy

VATS Lobectomy Reduces Cytokine Responses Compared With Conventional Surgery

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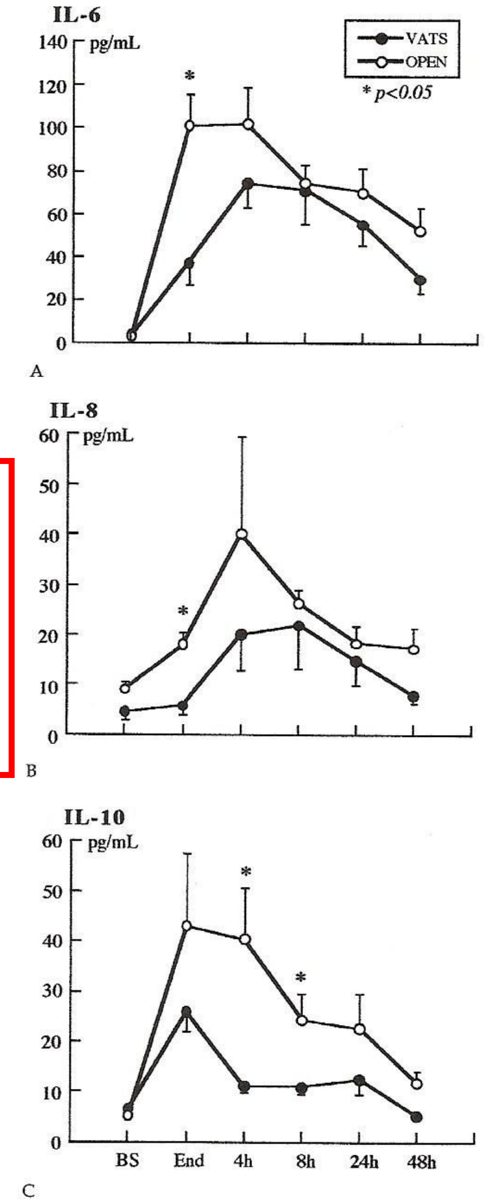

Fig 2. Plasma levels of IL-6 (A), IL-8 (B), and IL-10 (C) in patients undergoing video-assisted thoracic surgery (n = 18) or conventional (n = 18) lobectomy. Data are mean ± SEM. (BS = before surgery; End = at the end of surgery; 4, 8, 24, and 48 hours = time points after surgery.)

Quality of Life:
Demmy et al, *Ann Thor Surg* 2008

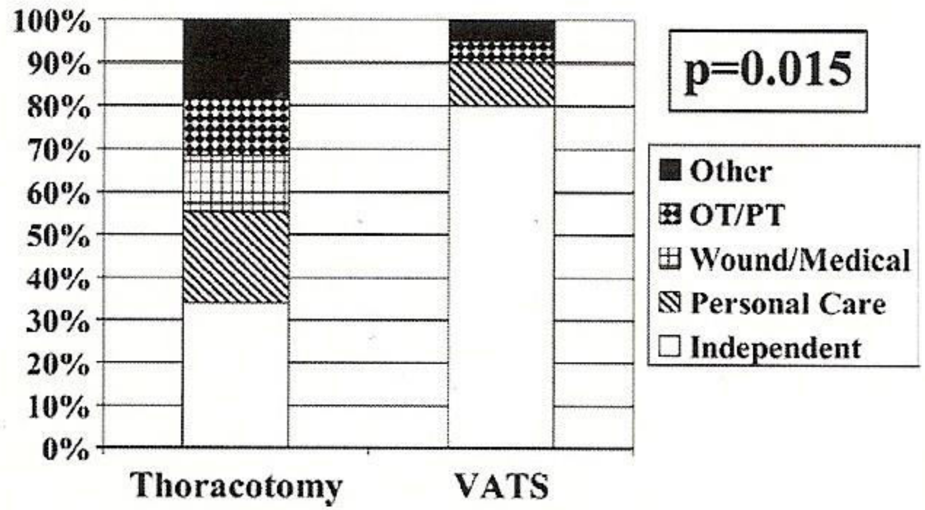

Fig 1. Discharge independence after thoracoscopic lobectomy. The bar graphs demonstrate a much lower need for home health services in the video-assisted thoracic surgery (VATS) group. The types of services needed for each procedure type are displayed as well. (OT = occupational therapy; other = other miscellaneous care needs; PT = physical therapy.) Adapted from Demmy TL, et al. Discharge independence with minimally invasive lobectomy. Am J Surg 2004;188:698–702.

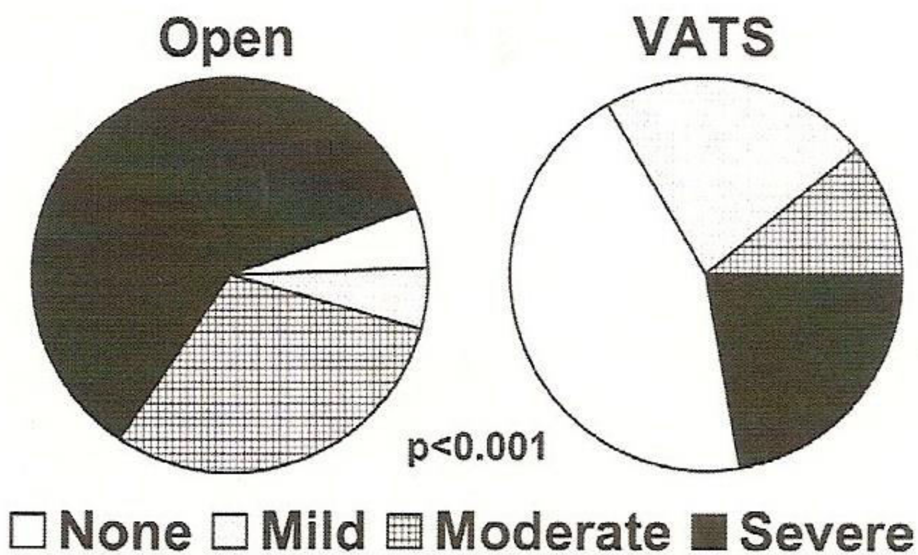

Fig 2. Pain control at 3 weeks after video assisted thoracic surgery (VATS) lobectomy. The pie charts show that VATS patients have significantly (p < 0.01) less pain as measured by the most potent analgesic still required: severe—schedule 2 narcotic; moderate—schedule 3 or lower; mild–nonsteroidal anti-inflammatory drugs or acetaminophen. These data represent an updated series of high-risk reported previously [49, 61].

Benefit of VATS Lobectomy in the Elderly

<u>Koizumi et al</u>:

- 32 octogenarian or nonagenarian patients
- 5 year survival rate of 56% with VATS lobectomy with early stage cancer

Versus

- 5 year survival rate of 0% with open lobectomy with early stage cancer

Use of Video-Assisted Thoracic Surgery for Lobectomy in the Elderly Results in Fewer Complications

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Table 2. Perioperative Data

Characteristics	THOR (n = 82)	VATS (n = 82)	*p* Value[a]
Histology			
Adenocarcinoma	24 (29)	24 (29)	0.14
Adeno w/BAC	27 (33)	32 (39)	
Squamous	24 (29)	13 (16)	
Other	7 (10)	13 (16)	
Tumor diameter (range), cm	2.0 (0.3–8.0)	1.8 (0.1–7.5)	0.11
Pathologic stage			
IA	49 (60)	56 (68)	0.13
IB	15 (18)	19 (23)	
II	8 (10)	3 (4)	
III–IV	10 (12)	4 (5)	
Length of stay (range), days	6 (2–27)	5 (2–20)	<0.001
Complications, n (%)	37 (45)	23 (28)	0.04
Death, n (%)	3 (3.6)	0 (0)	0.10

Average age = <u>76 years</u>

Table 4. Complication Profile

Type, n (%)	THOR (n = 82)	VATS (n = 82)	*p* Value[a]
None	45 (55)	59 (72)	0.04
Pulmonary	27 (33)	12 (15)	0.01
Cardiac (atrial fibrillation)	19 (23)	14 (17)	0.44
Genitourinary	5 (6)	2 (2)	
Gastrointestinal	4 (5)	0 (0)	
Infectious	4 (5)	1 (1)	
Neurologic	1 (1)	3 (4)	
Other	2 (2)	0 (0)	

VATS Cost

Costs of Videothoracoscopic Surgery versus Open Resection for Patients with of Lung Carcinoma

Nakajima et al, *Cancer* 2000

TABLE 1
Clinical Features and Itemized Costs for the Open Thoracotmy and Videothorascopic Surgery Patient Groups[a]

Feature	Open thoracotomy	Thoracoscopic surgery	*P* value
No. of patients	66	36	
Age in yrs (mean)	35–77 (61.2)	42–83 (64.9)	N.S.
Tumor pathology			
Primary lung carcinoma	65	14	—
Metastatic lung carcinoma	1	22	< 0.0001
Surgical procedure			
Lobectomy	64	8	—
Pargial resection or segmentectomy	2	28	< 0.0001
Length of hospitalization (days)	23.8 ± 7.8	17.3 ± 7.8	< 0.0001
Charges (U.S. dollars)			
Medication	904 ± 1568	874 ± 780	N.S.
Laboratory examination	1335 ± 632	990 ± 529	0.0064
Total surgical charges	6174 ± 1383	5097 ± 747	< 0.0001
Anesthesia	1853 ± 416	1534 ± 309	0.0004
Surgical fee	2746 ± 423	2746 ± 37	N.S.
Disposable equipment	573 ± 274	0	< 0.0001
Hospitalization	3064 ± 1233	2319 ± 775	0.0015
Total hospital charges	12,178 ± 3877	9825 ± 2296	0.0012

Video Clips

VATS Utility Incision Placement.avi

RUL Bronchus Division.avi

Right Superior Pulmonary Vein Division.avi

Right Major and Minor Fissure Division.avi

Right Pulmonary Artery Division.avi

RUL Specimen Removal.avi

VATS Summary

- Enhanced visualization
- Decreased trauma to the tissue
- Decreased postoperative pain
- Decreased postoperative respiratory and other complications
- Decreased Hospital Stay
- Shortened Recovery time, allowing return to work and daily activities sooner
- Ability to offer surgery to higher risk patients who would not be candidates otherwise