Keeping Your Lungs Healthy

Community Wellness Seminar

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Goals

- Understand the Societal impact of Air Pollution and Smoking
- Specifically, *their* impact on Lung Cancer
- List Diagnostic Tests Available for Lung Cancer
- Define the history and current recommendations on Lung Cancer Screening
- Discuss the Treatment options available for Lung Cancer with emphasis on newer surgical techniques available such as VATS or Robotic Lobectomy

Disclaimer

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

Air Pollution

Air Pollution

Two types dominate the problem in the US: Ozone and Particle Pollution

Ozone

- Extremely reactive gas molecule
- Primary ingredient in smog air pollution
- Very harmful to breathe
- Attacks lung tissue by reacting chemically with it

- At risk from breathing Ozone
  - Children and Teens
  - Age 65 and older
  - People who work or exercise outdoors
  - People with existing lung disease (COPD, Asthma)
  - "*Responders*" who are healthy but react more strongly to ozone
  - Some segments of society (high unemployment, high public transit use, and African Americans) face higher risks from dying prematurely secondary to ozone pollution

Air Pollution

- Harm to your Health
  - Shortness of breath
  - Chest pain with inhalation
  - Wheezing or Coughing
  - Asthma
  - Increased susceptibility to respiratory infections and pulmonary inflammation
  - Increased need for people with lung disease to go to the hospital
  - Reduced lung function
    - Decreased lung function in college freshman who were lifelong residents of Los Angeles or San Francisco
  - Increased risk or heart attacks, arrhythmias, stroke, and premature death
  - Premature death
    - *3700 deaths / yr* with 10 parts per billion increase in ozone level

Air Pollution

Particle Pollution

- EPA regulates particle pollution as $PM^{2.5}$ (fine particles) and PM^{10} (all particles 10 micrometers or less in diameter).
  - **Prenatal Harm**
    - Increased risk of preterm births with chronic exposure to high levels of air pollution during the last 6 weeks of pregnancy
  - **Newborn Harm**
    - Air pollution may increase the risk of sudden death syndrome (SIDS)
    - May increase risk of babies born with low birth weight
    - Prolonged exposure to Fine Particle Pollution Increases Odds of Severe Infant Bronchiolitis

For each 10 ug/m^3 in $PM^{2.5}$, risk of bronchiolitis increased by 9%

Air Pollution

Particle Pollution

- Harm to Children
  - Long term exposure to air pollutants associated with increased risk of asthmatic bronchitis, hay fever, eczema, and allergic sensitization
  - Worsening of Asthma
  - Increased prevalence and incidence of cough and bronchitis
  - Increased risk of upper / lower respiratory infections
  - Exacerbates cystic fibrosis
  - Diesel school buses expose children to four times the diesel exhaust versus car

  - Short and Long-term decreased lung function
    - 1759 children age 10-18 in Southern California who grew up in more polluted areas had an average drop in lung function 20% below what was expected for the child's age

Air Pollution

Particle Pollution

- Harm to Adults
  - California Air Resources Board estimates premature deaths in California from particle pollution at 14,000 – 24,000 annually with the possibility of as high as 41,000 annually
  - Dutch and British studies confirm that Long-term exposure to Air Pollution is Deadly and Shortens lives
  - Long term exposure to air pollution, especially from highway traffic appears to increase women's risk of lower lung function, COPD, and premature death from cardiopulmonary causes
  - Pollution from heavy highway traffic contributes to higher risks for heart attacks, allergies, premature births, and death of newborns
  - Long-term exposure to Air Pollution Increases risk of Developing COPD

Air Pollution

Particle Pollution

- **Harm to Adults**

  - Truck drivers, dockworkers, and railroad workers face **higher risk of death from lung cancer, heart disease, and COPD from breathing diesel emissions** on the job.

    - 50,000 members of Teamsters Union
    - Smoking rates were similar to general population

    - **49% higher death rate** from heart disease for truck drivers
    - **32% higher death rate** from heart disease for dockworkers
    - **10% higher Lung cancer death rate** for both truck drivers and dockworkers

Air Pollution

- Data from Women's Health Initiative: 36 US cities / 66,000 women
- Risk of Fatal and Nonfatal Cardiovascular Events Increases with increasing air pollution levels
  - For every increase of 10 ug/m^3 in PM$^{2.5}$, 76% increased risk of death from cardiovascular disease

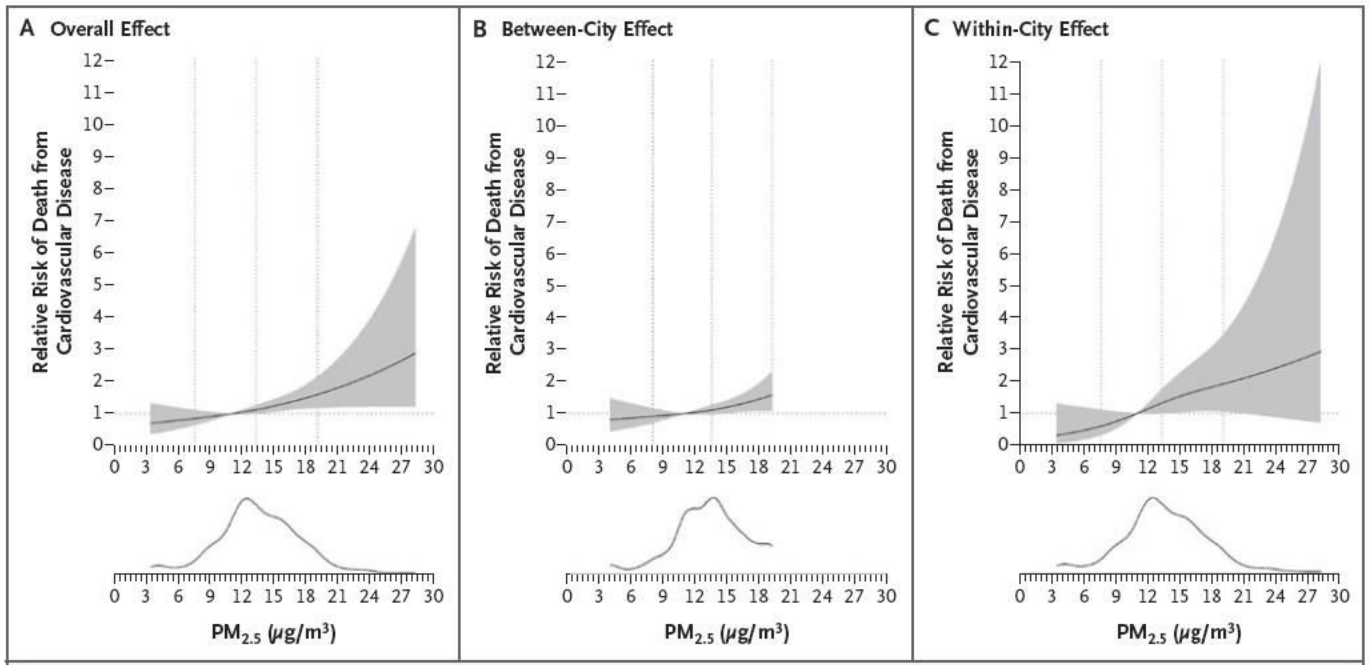

Figure 1. Level of Exposure to Fine Particulate Matter and the Risk of Death from Cardiovascular Causes in Women.

The graphs demonstrate the observed relationship between the risk of death from cardiovascular disease and the level of particulate matter of less than 2.5 μm in aerodynamic diameter ($PM_{2.5}$), including both definite and possible deaths from coronary heart disease or cerebrovascular disease. Panel A shows the overall relationship between the $PM_{2.5}$ level and death, Panel B the effects between metropolitan areas, and Panel C the effects within metropolitan areas, with an indicator variable used to adjust for each city. These results suggest a generally linear relationship between exposure and risk, though the 95% confidence intervals (shaded areas) are wide at the extremes of exposure. Risk is depicted in comparison with a reference value of 11 μg per cubic meter. The histogram in each panel illustrates the density of exposure distribution for air pollution. All estimates are adjusted for age, race or ethnic group, educational level, household income, smoking status, systolic blood pressure, body-mass index, and presence or absence of a history of diabetes, hypertension, or hypercholesterolemia.

What to Do about Air Pollution

Protect Yourself

- Pay attention to forecasts for high air pollution days to know when to take precautions
- Avoid exercising near high-traffic areas
- Avoid exercising outdoors when pollution levels are high, or substitute an activity that requires less exertion
- Do not let anyone smoke indoors and support measures to make all places smoke-free
- Reduce the use of fireplaces and wood-burning stoves.

Clean up Pollution

- Atlanta Georgia during 1996 Olympics
- Reduced traffic during the Olympics succeeded in not just reducing congestion, but in improving the health of children with asthma
- City brought in more buses, more subway cars, and encouraged ridesharing and telecommuting during the Summer Olympic Games
- These measures created a prolonged period of low ozone pollution that resulted in significantly lower rates of childhood asthma events for children aged 1–16
- The number of asthma acute care events (e.g., treatment and hospitalization) decreased 42 percent in the Georgia Medicaid claims files

Air Pollution

- Long-term improvement in Air Quality Benefits Lung function
- Reduction in $PM^{2.5}$ concentrations Would Increase Life Expectancy
  - Harvard Six Cities Study found that the deaths associated with exposure to fine particles occur primarily within two years of exposure, implying that reductions in air pollution levels can be expected to produce rapid improvements in public health
- Multiple studies and experts agree that reductions in air pollution levels with have an impact in the public health sector in years not decades of the reduction

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Smoking

Smoking

Smoking Facts

- Smoking is the most important preventable cause of morbidity and premature mortality Worldwide

- 438,000 Americans die each year from smoking related diseases
- Smoking is responsible for more than one in five US deaths
- About ½ of all regular smokers will die from the addiction
- Smoking costs the United States $193 billion in 2004

- Cigarette smoke contains over 4800 chemicals, of which 69 are known to cause cancer

- Smoking is directly responsible for 90% of the 161,000 Lung Cancer deaths
- Smoking is directly responsible for 80-90% of the 127,000 COPD deaths
- Smoking is major risk factor for Coronary artery disease, stroke, and lower respiratory infections

Smoking

Smoking Facts

- Smoking reduces the normal life expectancy by an average of 13-15 years
- 8.6 million Americans have a smoking related illness
- This means that for every 1 American who dies from smoking related disease, there are 20 more people who suffer from a smoking related disease

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List of diseases caused by smoking

COPD

Coronary Artery Disease

- 60 % Higher Risk of dying from heart attack in smokers over 65 than non smokers

Stroke

- Men over 65 who smoke are twice as likely to die from stroke than non smokers
- Women over 65 who smoke are 1 ½ times as likely to die from stroke than non smokers

AAA

Acute Myeloid Leukemia

Cataracts → 2-3 times the risk higher in smokers

Pneumonia

Periodontitis

Bladder cancer

Esophageal cancer

Laryngeal cancer

Lung cancer

Oral cancer

Throat cancer

Cervical cancer

Kidney cancer

Stomach cancer

Pancreatic cancer

Infertility

Peptic Ulcer Disease

Slow wound healing

Dementia / Alzheimer's

- Smokers have far greater chance of developing dementia than nonsmokers

Smoking

- Worldwide
  - Tobacco is leading cause of preventable death worldwide
  - Tobacco kills more than HIV/AIDS, Tuberculosis, and Malaria COMBINED
  - Tobacco responsible for 5 million deaths each year and will increase to 8 million / year in 2030
  - Tobacco was responsible for 100 million deaths in the 20th Century
  - With current usage, tobacco could kill 1 billion people in the 21st Century
  - 48% Men versus 10% Women smoke
  - China: 63% Men versus 3.8% Women → 300 million people smoke in China which is more than the entire US population

Smoking

Smoking Facts

- **45.3 million** Americans (**20.6 % of adults**) were current smokers in 2006
- **45.7 million** Americans were former smokers in 2006

- Prevalence of smoking decreased 40% between 1965 and 1990, but has been **UNCHANGED** since

Males	23.6%
Females	17.8%
American Indians/ Alaskan Natives	32.2%
Whites	21.8%
Blacks	22.6%
Hispanics	15.1%
Asians	10.3%

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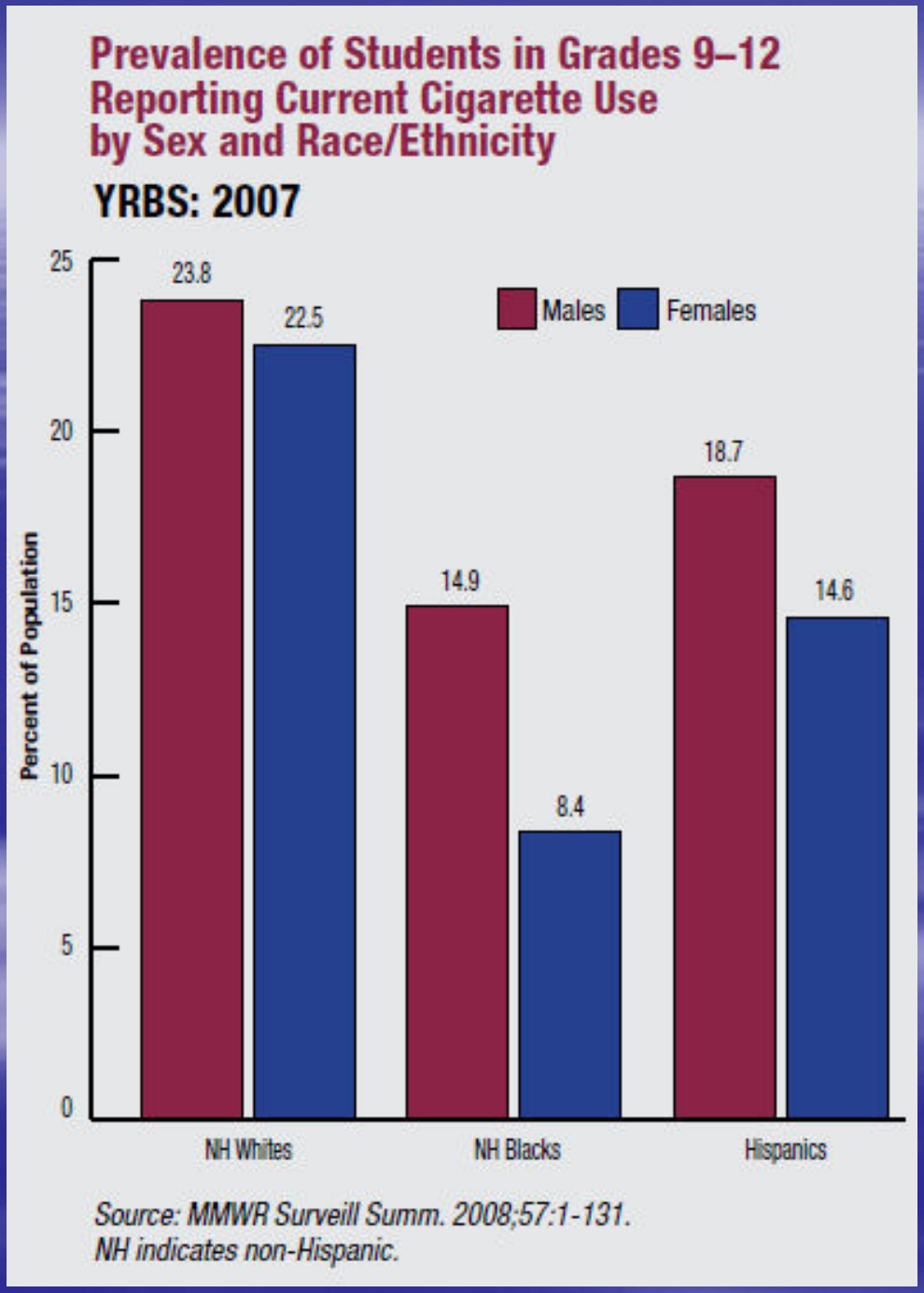

2007

20% high school students were smokers

6% middle school students were smokers

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Smoking

Smoking Facts

- 2005: Advertising by the 5 major tobacco companies totaled $13.1 billion → $35 million / day

- 90% of adults who smoke start by the age of 21
- 50% became regular smokers by the age of 18

- Average youth in the US is annually exposed to 559 tobacco ads
  - 617 tobacco ads for every adult female
  - 892 tobacco ads for every adult African American

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Second Hand Smoke

- Described by the EPA as a known human Group A carcinogen
- Contains more than 250 toxic or cancer causing chemicals, including formaldehyde, benzene, vinyl chloride, arsenic, ammonia, and hydrogen cyanide
- Current Surgeon General report concluded that there is NO risk free level of exposure to secondhand smoke
- Second hand smoke even in short exposures can cause platelets to become stickier, damage blood vessel lining, decrease coronary flow velocity, and reduce heart rate variability → all of these can increase the risk of a heart attack
- 3,400 lung cancer deaths / year
- 46,000 heart disease deaths / year

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Second Hand Smoke

- Smoking by Parents
  - Exacerbation of asthma
  - → 400,000 – 1,000,000 asthma episodes per year
  - Increased frequency of colds and ear infection
  - → 790,000 ear infections per year
  - Increased risk of respiratory infections
  - → 150,000 - 300,000 lower respiratory infections per year
  - Increased frequency of Sudden Infant Death Syndrome
  - → 430 cases per year
  - 21 million or 35% of children live with smokers on a regular basis

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What to do about Smoking

QUIT

DO NOT SMOKE

AVOID SECOND HAND SMOKE

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Lung Cancer

US Epidemiology

Estimated New Cases*	
Male	**Female**
Prostate 240,890 (29%)	Breast 230,480 (30%)
Lung & bronchus 115,060 (14%)	Lung & bronchus 106,070 (14%)
Colon & rectum 71,850 (9%)	Colon & rectum 69,360 (9%)
Urinary bladder 52,020 (6%)	Uterine corpus 46,470 (6%)
Melanoma of the skin 40,010 (5%)	Thyroid 36,550 (5%)
Kidney & renal pelvis 37,120 (5%)	Non-Hodgkin lymphoma 30,300 (4%)
Non-Hodgkin lymphoma 36,060 (4%)	Melanoma of the skin 30,220 (4%)
Oral cavity & pharynx 27,710 (3%)	Kidney & renal pelvis 23,800 (3%)
Leukemia 25,320 (3%)	Ovary 21,990 (3%)
Pancreas 22,050 (3%)	Pancreas 21,980 (3%)
All sites 822,300 (100%)	All sites 774,370 (100%)

- **215,020 new cases**
  - **115,060 in men**
  - **106,070 in women**
  - **Accounts for 14% 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**

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Estimated New Cases*

Males				Females		
Prostate	240,890	29%		Breast	230,480	30%
Lung & bronchus	115,060	14%		Lung & bronchus	106,070	14%
Colon & rectum	71,850	9%		Colon & rectum	69,360	9%
Uninary bladder	52,020	6%		Uterine corpus	46,470	6%
Melanoma of the skin	40,010	5%		Thyroid	36,550	5%
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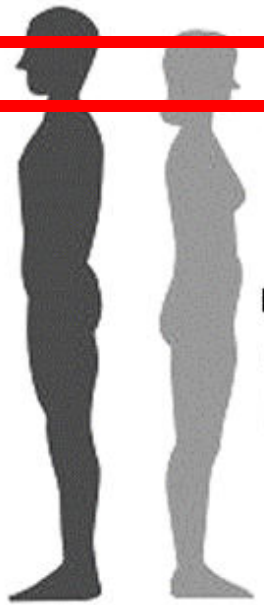
Leukemia	25,320	3%		Ovary	21,990	3%
Pancreas	22,050	3%		Pancreas	21,980	3%
All Sites	**822,300**	**100%**		**All Sites**	**774,370**	**100%**



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US Epidemiology

Estimated Deaths	
Male	**Female**
Lung & bronchus 85,600 (28%)	Lung & bronchus 71,340 (26%)
Prostate 33,720 (11%)	Breast 39,520 (15%)
Colon & rectum 25,250 (8%)	Colon & rectum 24,130 (9%)
Pancreas 19,360 (6%)	Pancreas 18,300 (7%)
Liver & intrahepatic bile duct 13,260 (4%)	Ovary 15,460 (6%)
Leukemia 12,740 (4%)	Non-Hodgkin lymphoma 9,570 (4%)
Esophagus 11,910 (4%)	Leukemia 9,040 (3%)
Urinary bladder 10,670 (4%)	Uterine corpus 8,120 (3%)
Non-Hodgkin lymphoma 9,750 (3%)	Liver & intrahepatic bile duct 6,330 (2%)
Kidney & renal pelvis 8,270 (3%)	Brain & other nervous system 5,670 (2%)
All sites 300,430 (100%)	All sites 271,520 (100%)

- **156,940 deaths**
  - **85,600 men**
  - **71,340 women**
  - **Accounts for 27% of all cancer deaths**

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

Estimated Deaths

Males				Females		
Lung & bronchus	85,600	28%		Lung & bronchus	71,340	26%
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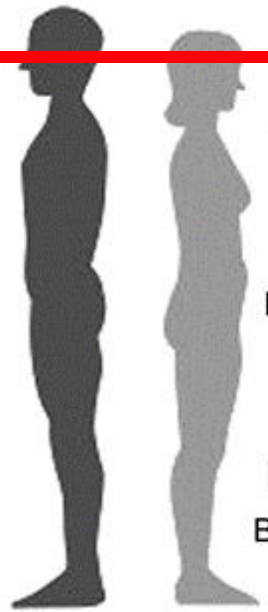
All Sites	**300,430**	**100%**		All Sites	**271,520**	**100%**



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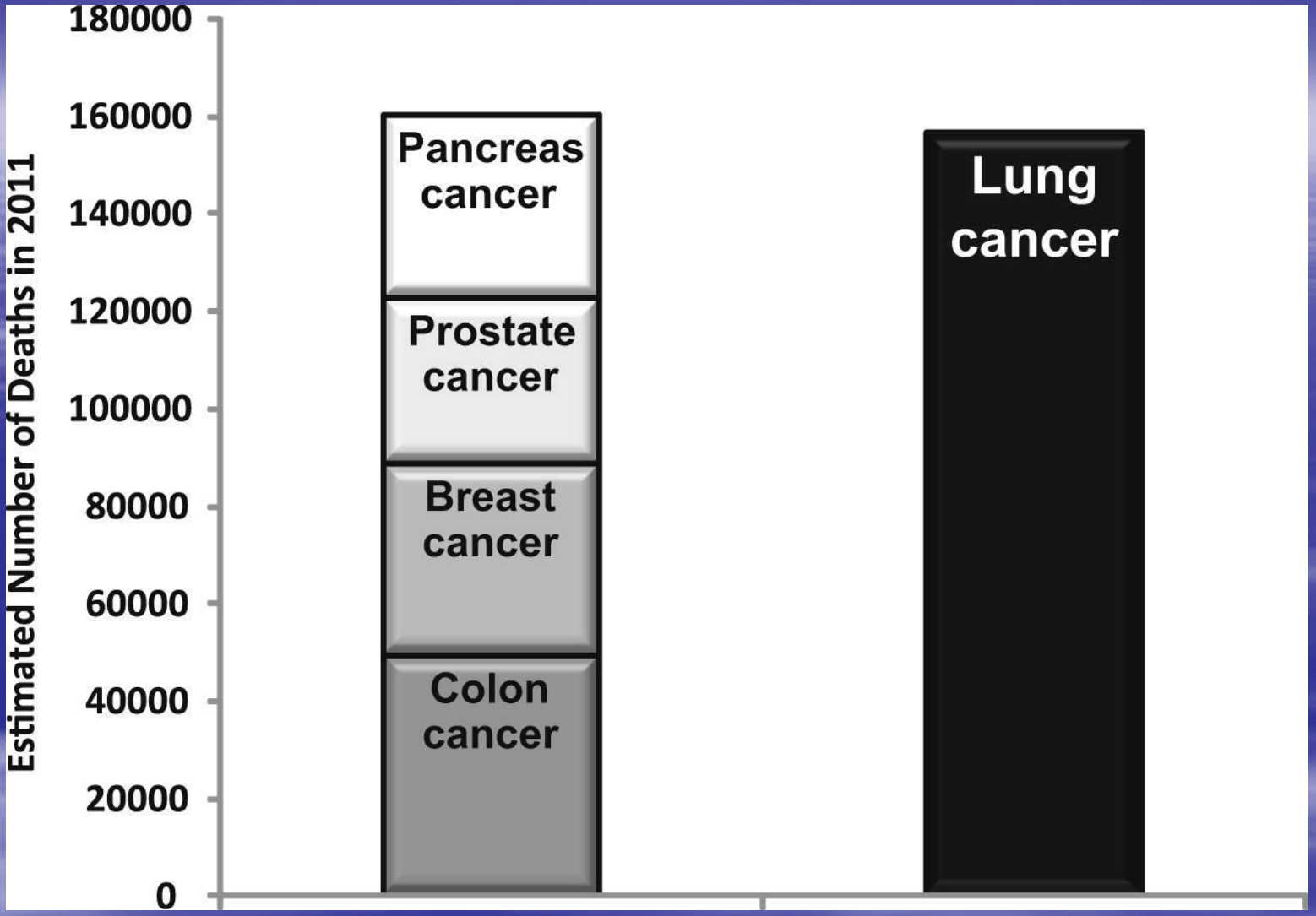
More people die of Lung cancer than of Colon, Breast, and Prostate cancers COMBINED!

Lung Cancer Deaths
156,940 deaths

Colon Cancer Deaths =	49,380
Breast Cancer Deaths =	39,520
Prostate Cancer Deaths =	33,720
Combined Cancer Deaths =	**122,620**



Clinics in Chest Medicine 2011 32, 605-644DOI: (10.1016/j.ccm.2011.09.001)

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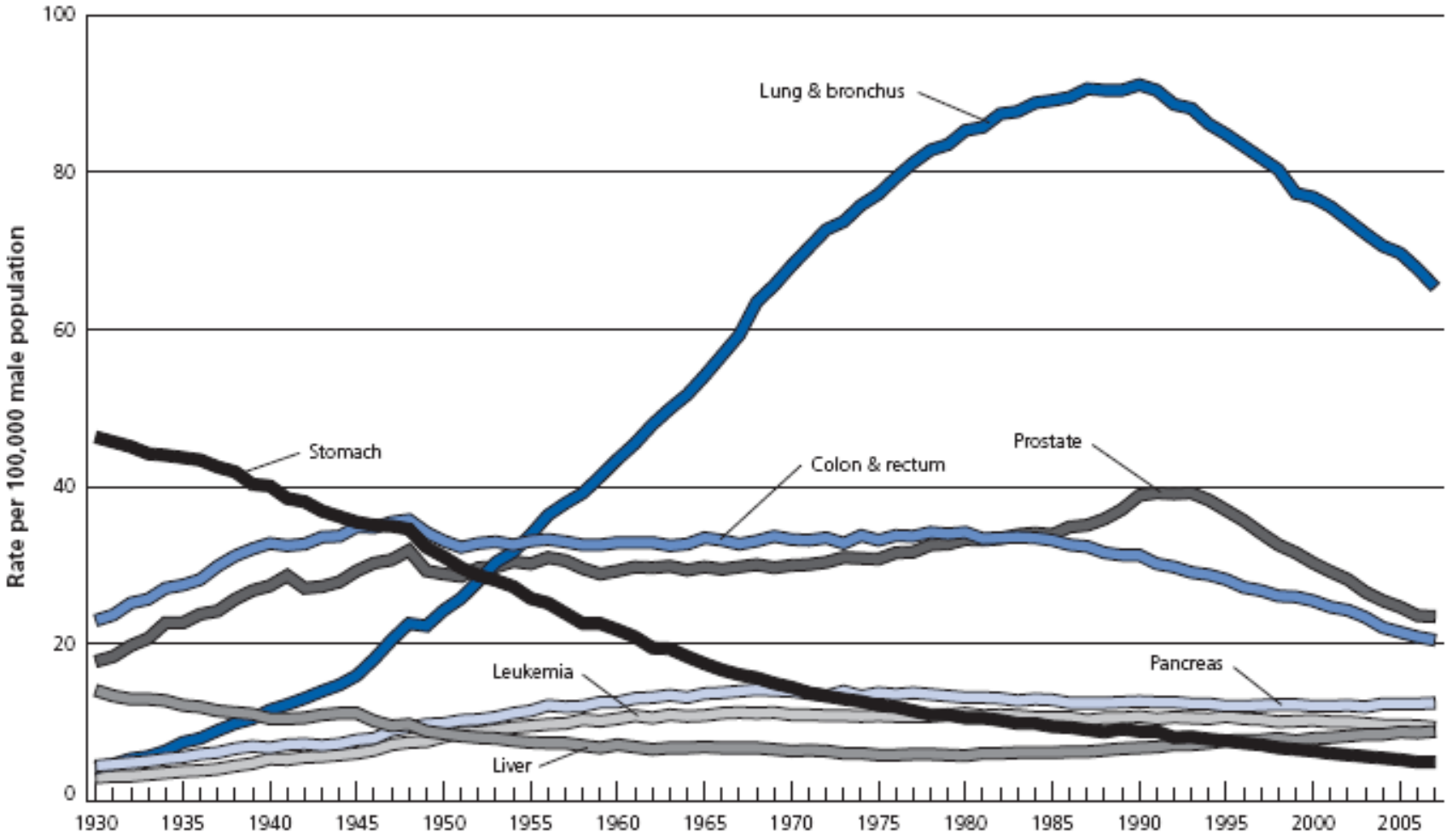
Age-adjusted Cancer Death Rates,* Males by Site, US, 1930-2007

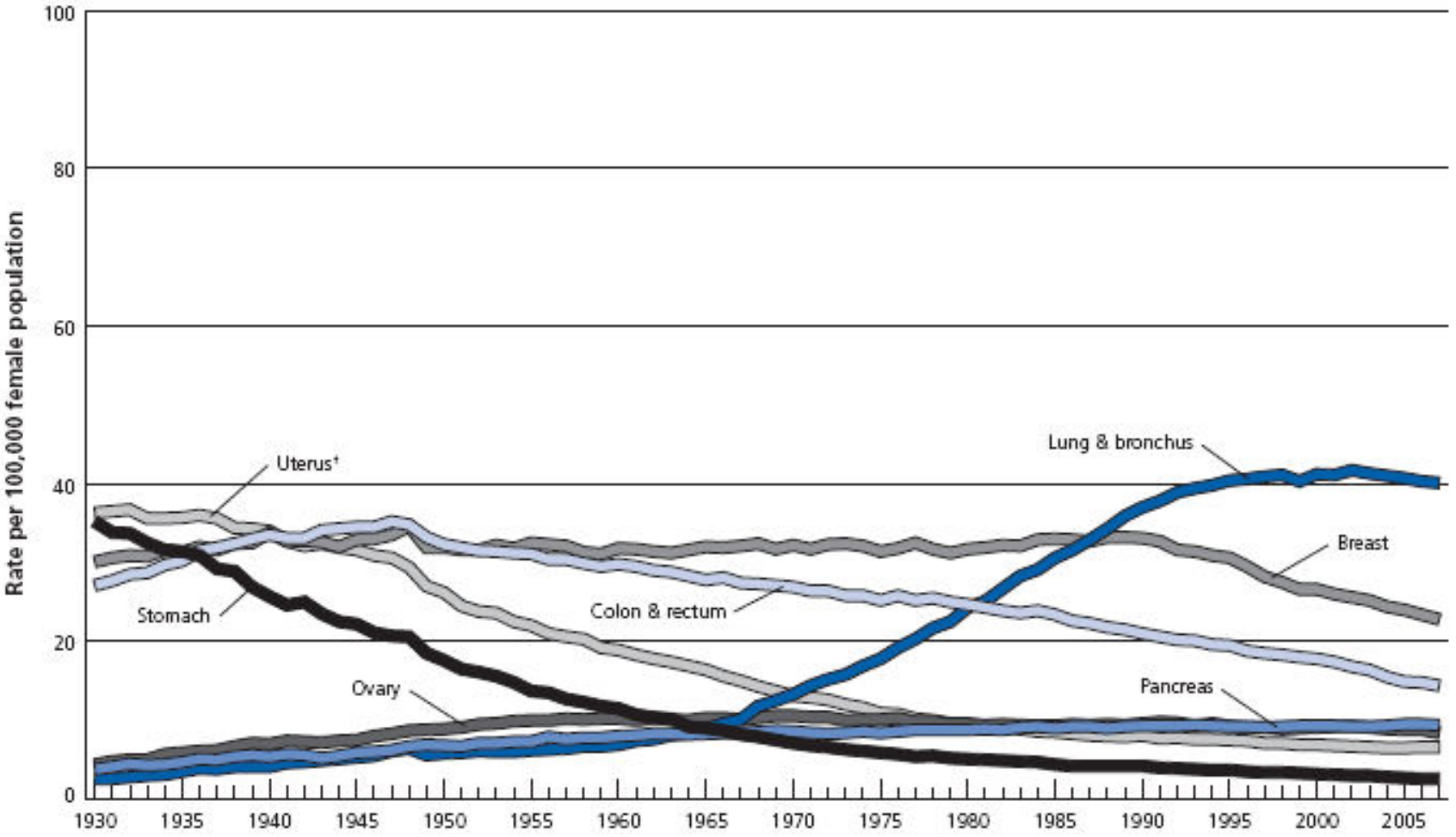


*Per 100,000, age adjusted to the 2000 US standard population.

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 changes.

Source: US Mortality Data, 1960 to 2007, US Mortality Volumes, 1930 to 1959, National Center for Health Statistics, Centers for Disease Control and Prevention.

Age-adjusted Cancer Death Rates,* Females by Site, US, 1930-2007



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Lung Cancer Survival Rates

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

Primary Site	5-Year Survival, %		Absolute Increase in 5-Year Survival, %	% Change (1950-1996)	
	1950-1954	1989-1995		Mortality	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, 1975-2006

	All races			White			African American		
	1975-77	1984-86	1999-2006	1975-77	1984-86	1999-2006	1975-77	1984-86	1999-2006
All sites	50	54	68†	51	55	69†	40	41	59†
Brain	24	29	36†	23	28	35†	27	32	41†
Breast (female)	75	79	90†	76	81	91†	62	65	78†
Colon	52	59	66†	52	60	67†	47	50	55†
Esophagus	5	10	19†	6	11	20†	3	9	13†
Hodgkin lymphoma	74	80	87†	74	80	88†	71	75	82†
Kidney	51	56	70†	51	56	70†	50	54	67†
Larynx	67	66	63†	68	68	65	59	53	49†
Leukemia	36	42	55†	36	43	56†	34	34	47†
Liver & bile duct	4	6	14†	4	6	14†	2	5	10†
Lung & bronchus	13	13	16†	13	14	17†	12	11	13†
Melanoma of the skin	83	87	93†	83	87	93†	60‡	70§	74‡
Myeloma	26	29	39†	26	27	39†	31	32	38†
Non-Hodgkin lymphoma	48	53	69†	49	54	71†	49	48	60†
Oral cavity & pharynx	53	55	63†	55	57	65†	36	36	45†
Ovary	37	40	45†	37	39	45†	43	41	37
Pancreas	3	3	6†	3	3	6†	2	5	5†
Prostate	69	76	100†	70	78	100†	61	66	97†
Rectum	49	57	69†	50	58	70†	45	46	60†
Stomach	16	18	27†	15	18	26†	16	20	26†
Testis	83	93	96†	83	93	97†	73‡#	87‡	87
Thyroid	93	94	97†	93	94	98†	91	90	95
Urinary bladder	74	78	81†	75	79	82†	51	61	66†
Uterine cervix	70	68	71	71	70	73	65	59	64
Uterine corpus	88	84	84†	89	85	86†	61	58	61

* Survival rates are adjusted for normal life expectancy and are based on cases diagnosed in the SEER 9 areas from 1975-77, 1984-86, 1999 to 2006, and followed through 2007. † The difference in rates between 1975-1977 and 1999-2006 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. # Survival rate is for 1978-1980.

Source: Altekruse SF, Kosary CL, Krapcho M, et al (eds.). *SEER Cancer Statistics Review, 1975-2007*, National Cancer Institute, Bethesda, MD, seer.cancer.gov/csr/1975_2007/, 2010.

Worldwide Lung Cancer

- Over **1.6 million** new cases of Lung cancer

- Accounts for **13%** of total cancer diagnoses
- Accounts for **18%** of total cancer Deaths

- Over **1.4 million** died from Lung cancer

- Leading cause of cancer death in Men
- 2nd leading cause of cancer death in Women

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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
- **Air pollution**
  - ***Worldwide, 5% of deaths from Lung cancer may be due to air pollution***
- **Asbestos Exposure**
  - Synergy with Tobacco (***50-90 times the risk*** of cancer)

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Second Hand Smoke

- Described by the EPA as a known human **Group A carcinogen**
- Contains more than **250 toxic or cancer causing chemicals**, including formaldehyde, benzene, vinyl chloride, arsenic, ammonia, and hydrogen cyanide
- Current Surgeon General report concluded that there is **NO risk free level of exposure** to secondhand smoke

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Risk Factors

- Race / Ethnicity
  - African Americans have similar rate of smoking as Whites (20% vs 22%); 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%) 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:
    - Hispanics 26.2%
    - African Americans 17.1%
    - Whites 31.5%

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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

Sign and Symptoms

- Cough (that does not resolve) 29-87%
- Hemoptysis 9-57%
- Pleuritic chest pain 6-60%
- Shortness of Breath / Dyspnea 3-58%

- **ASYMPTOMATIC**
  - All patients with Lung cancer 5-20%
  - Patients detected screening programs 60%

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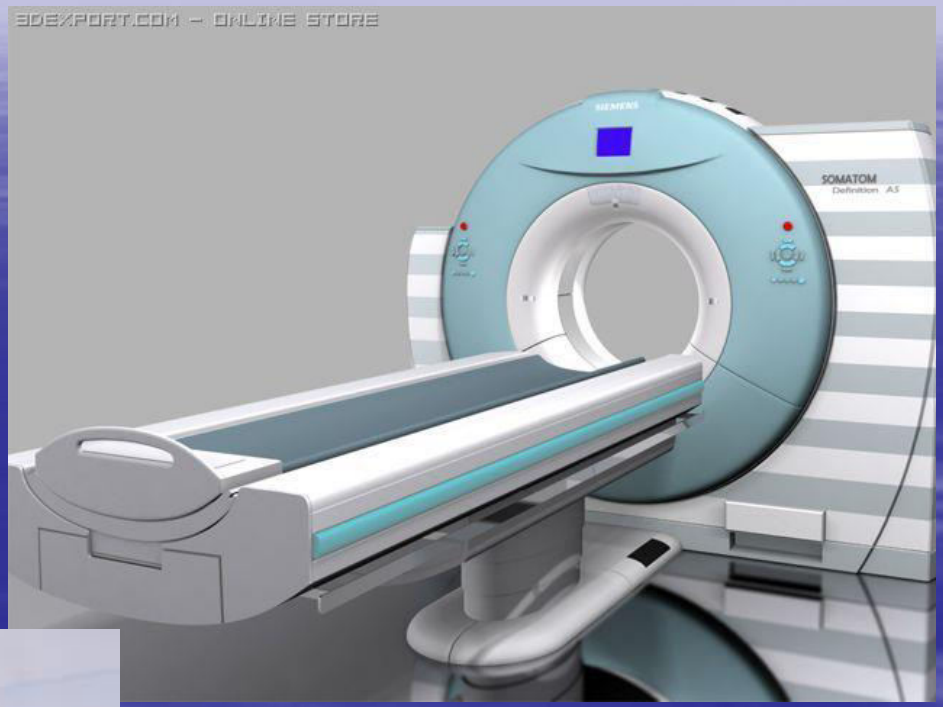
Diagnosis - Imaging

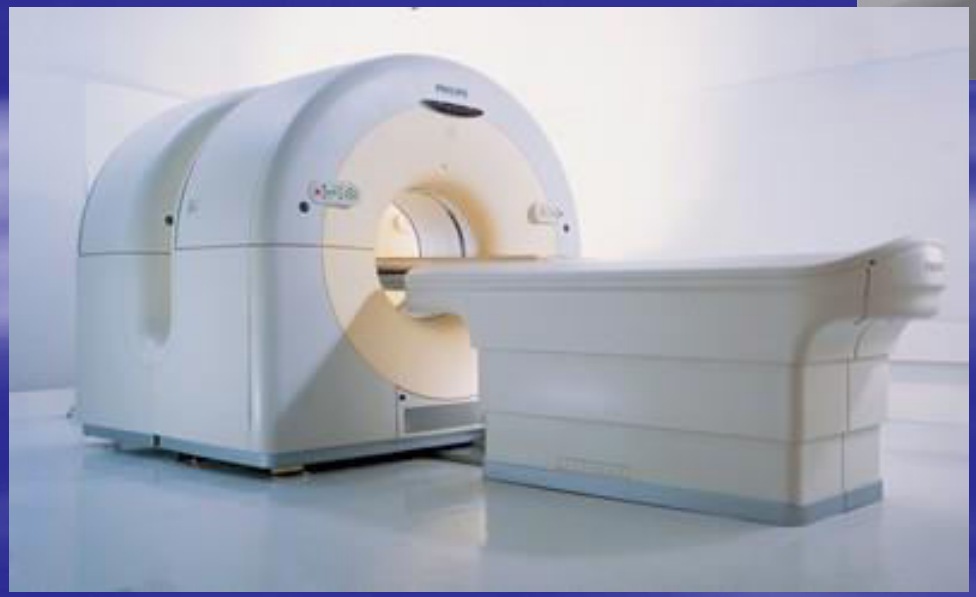
Chest X ray

CT scan

PET Scan

PET and CT scan combined





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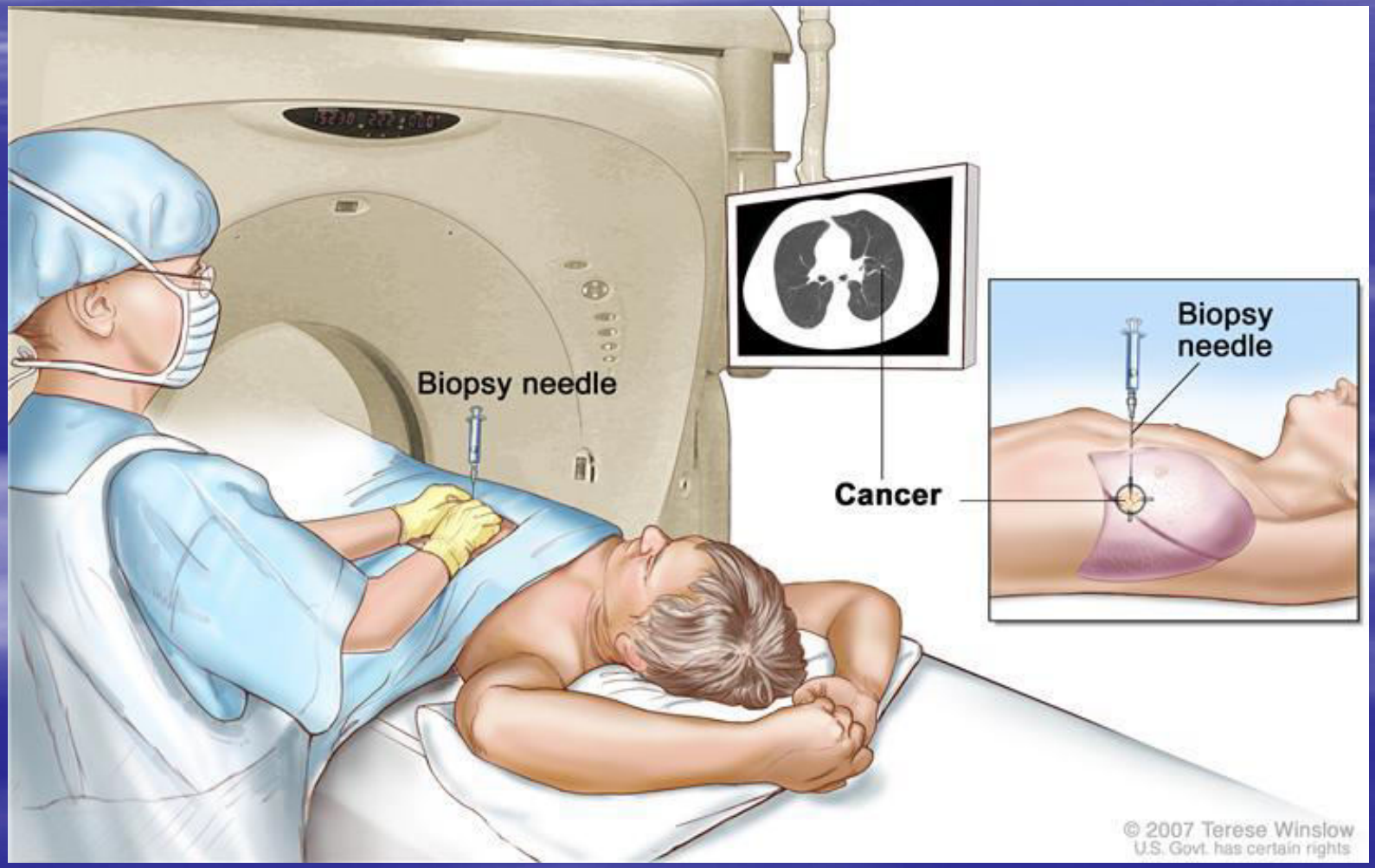
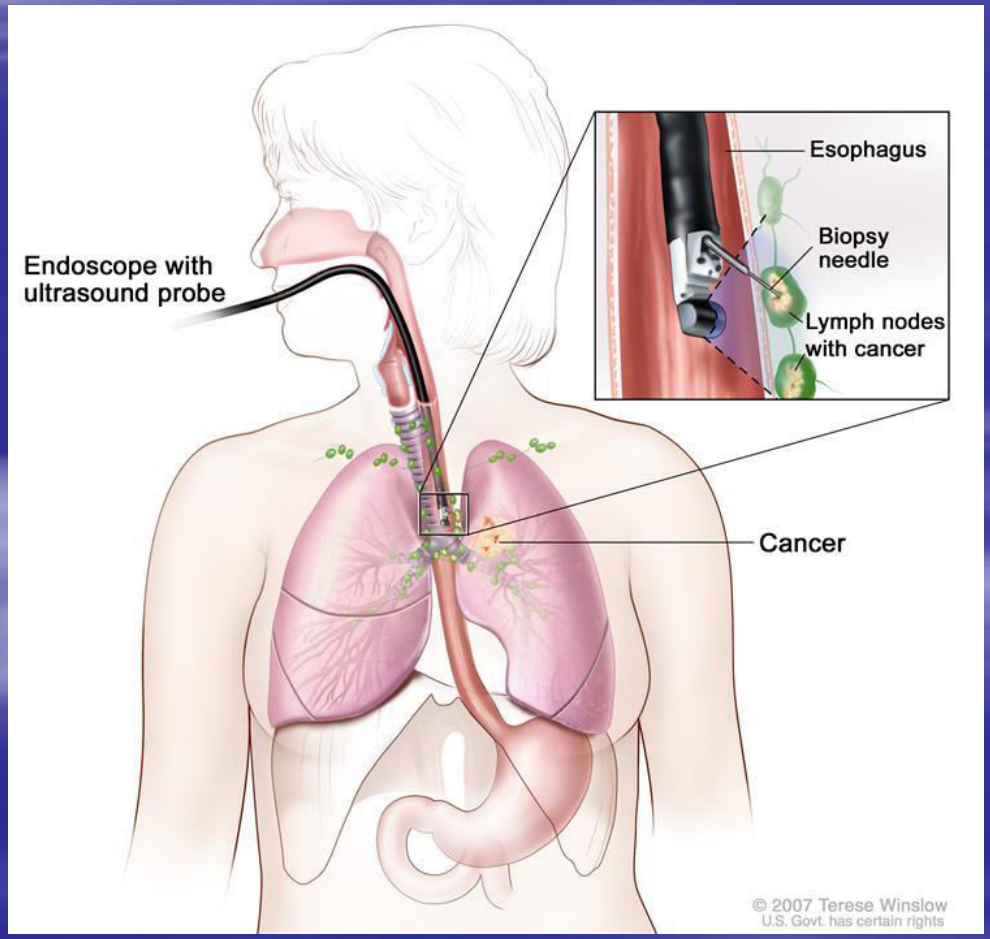
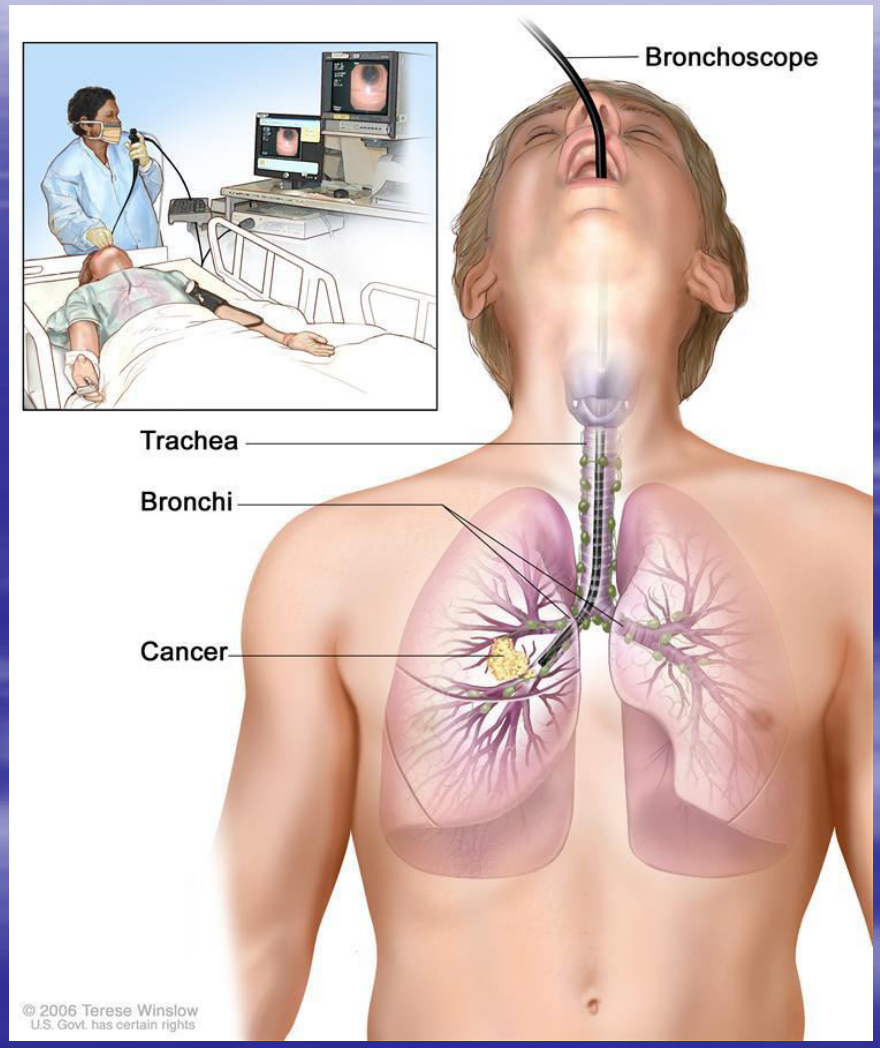
Fine Needle Aspiration

- Pneumothorax risk requiring CT placement

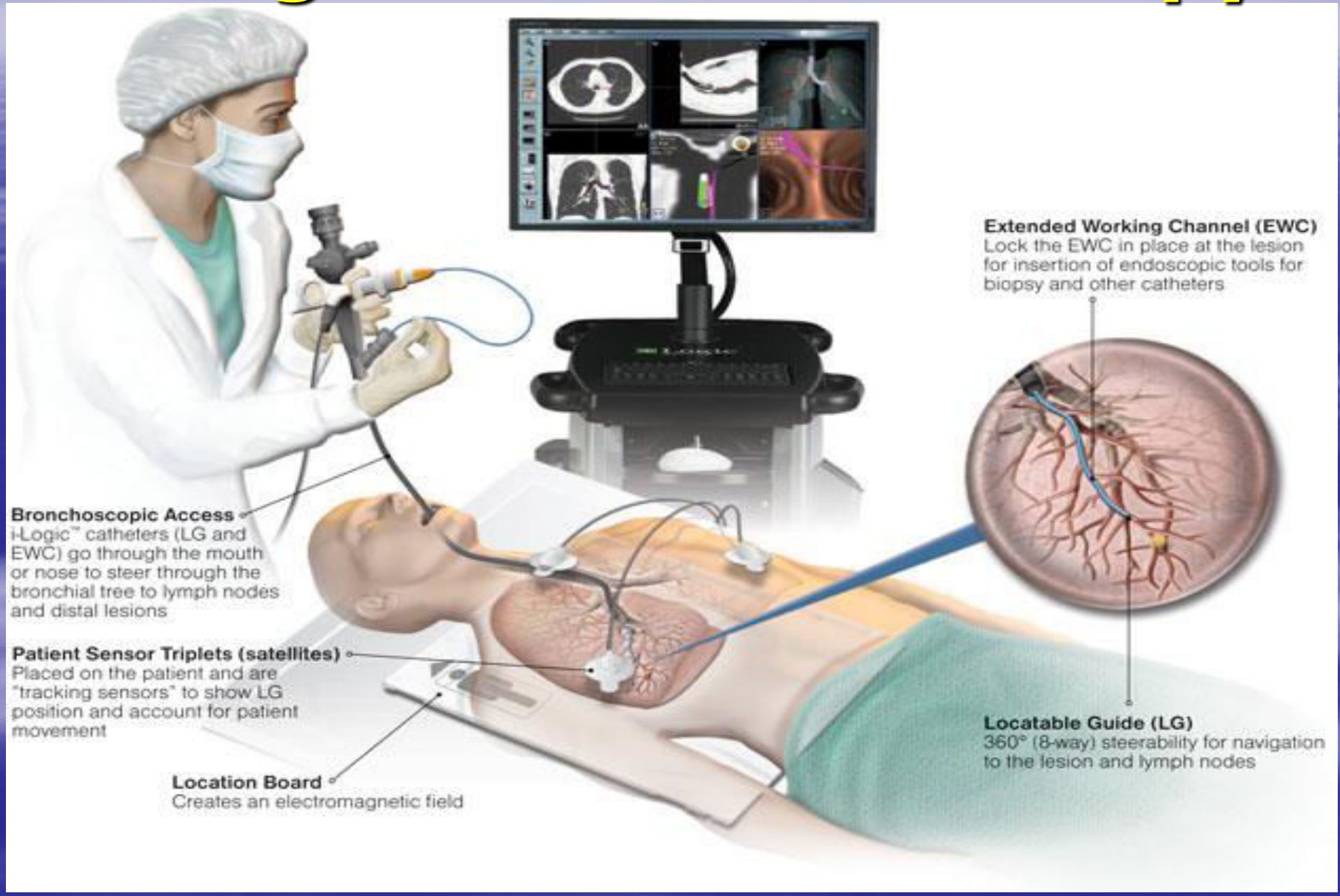


Bronchoscopy with Endoscopic / Endobronchial Ultrasound



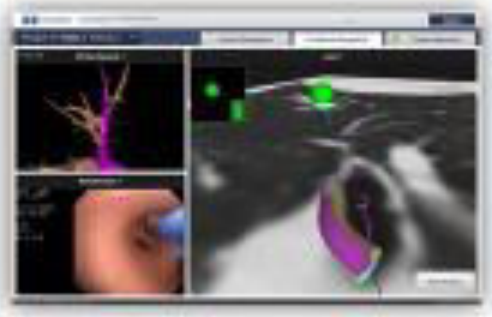


Navigational Bronchoscopy

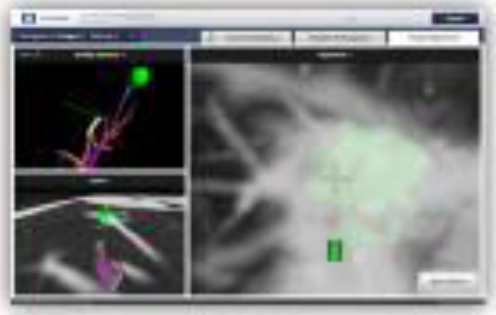


superDimension™ Navigation System

Central Navigation



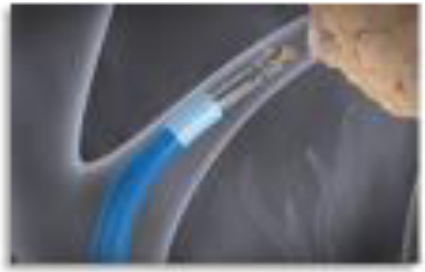
Peripheral Navigation



Target Alignment

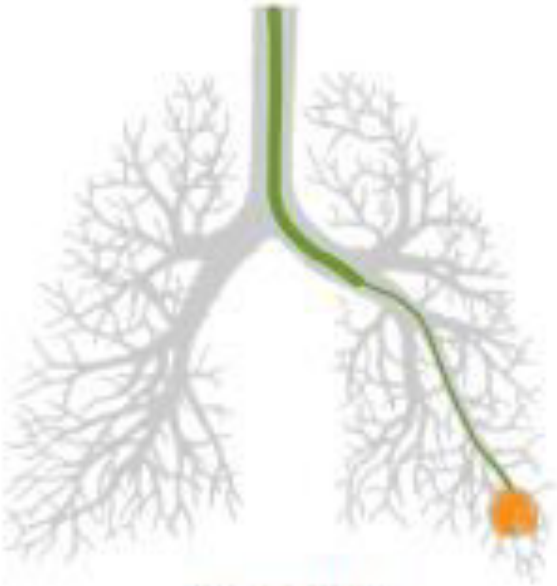
COVIDIEN

Complete Procedure



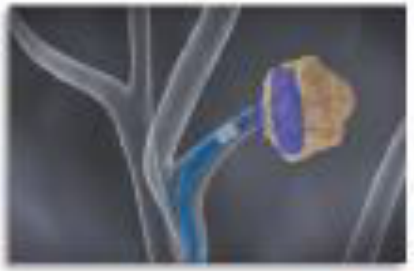
Acquire Tissue

Place Fiducial Markers



Navigate

Stage



Dye Localization

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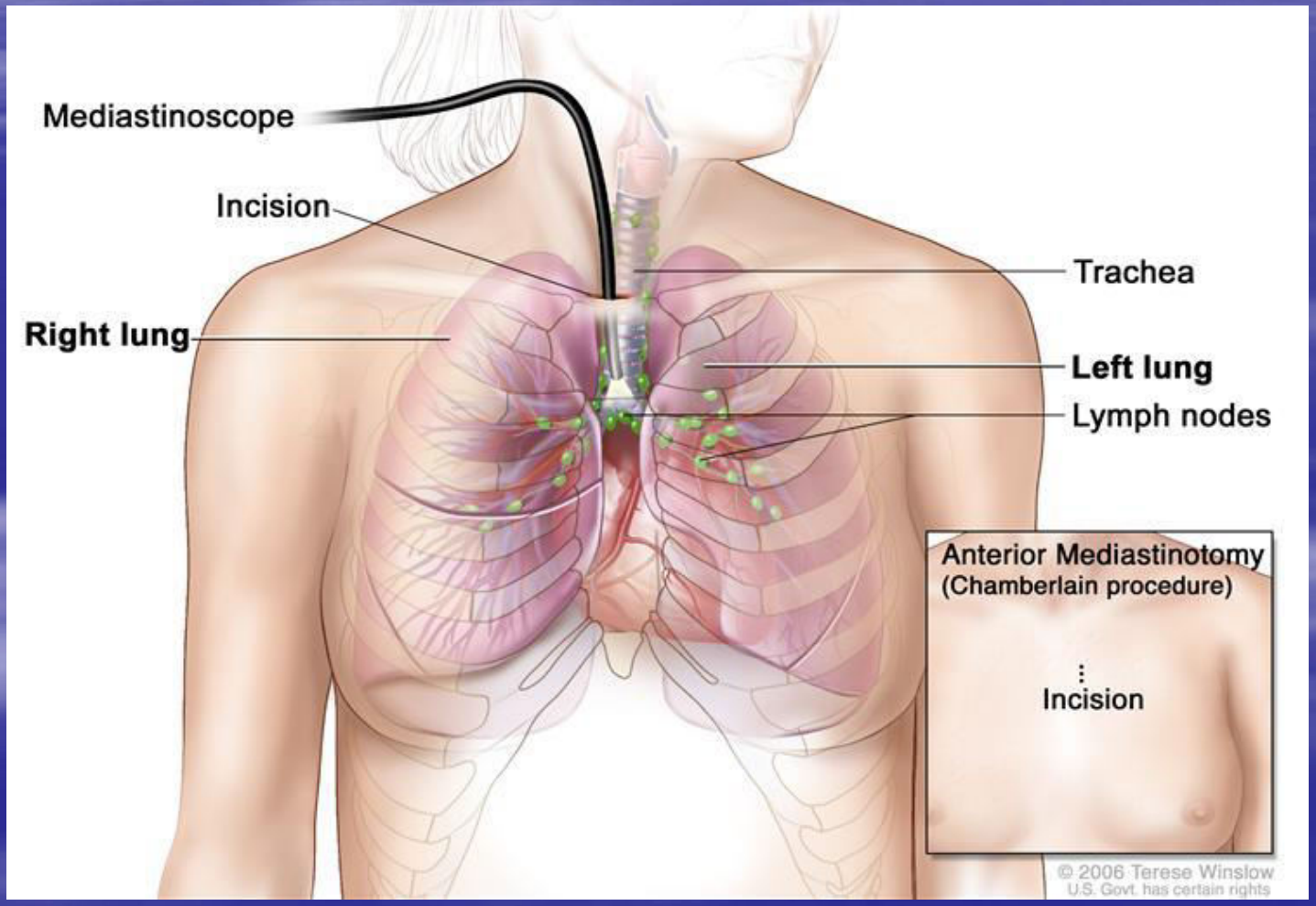
Thoracentesis
Mediastinoscopy
Thoracoscopy



Pathology

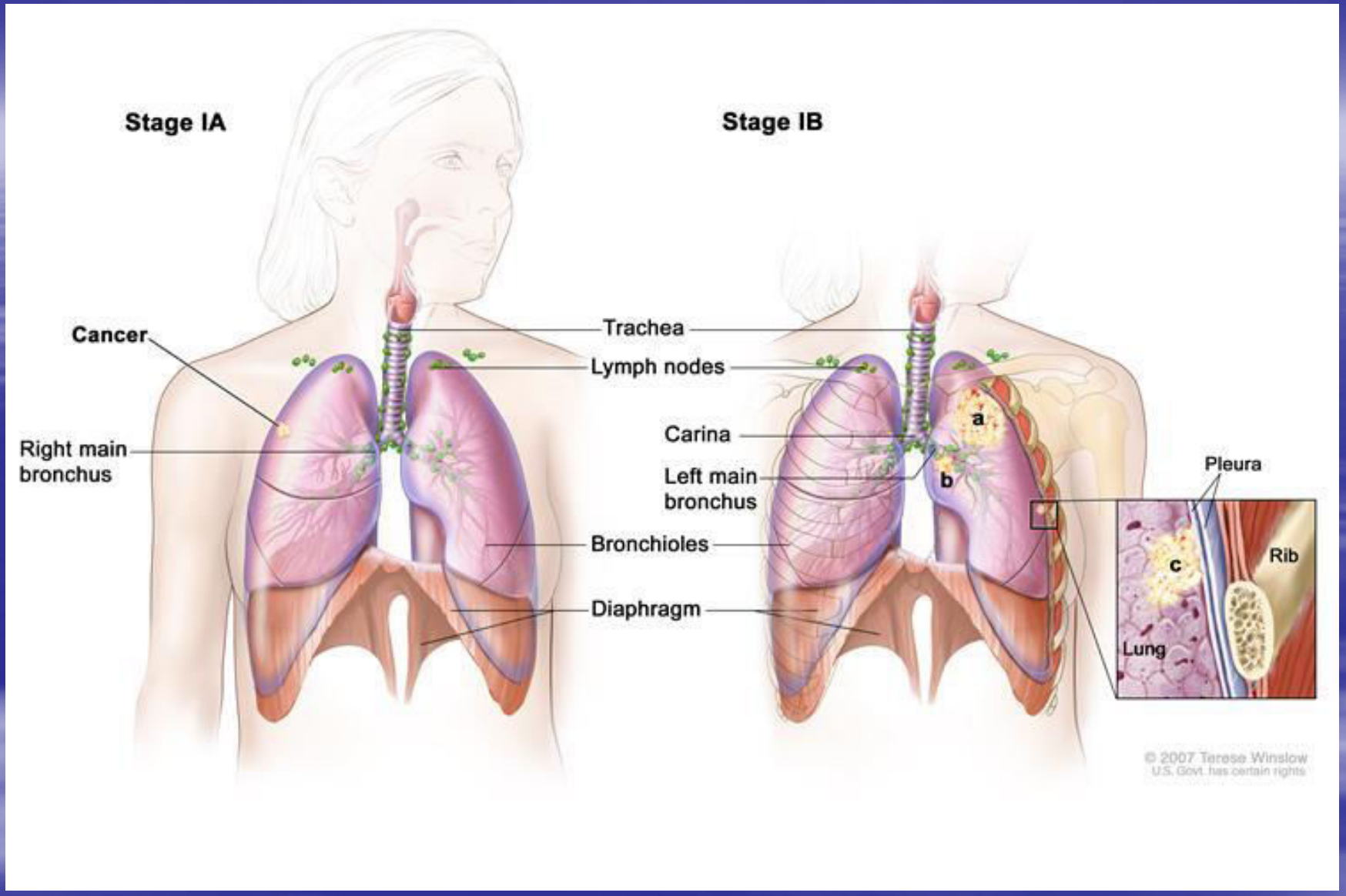
WHO Classification (1999) for NSCLC (80% of Lung CA)

- Squamous Cell Carcinoma (30%)
  - Most commonly in Men
  - Tends to spread Locally and usually central lesions
  - Related to Smoking
- 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
- Carcinoid tumor (3-5%)

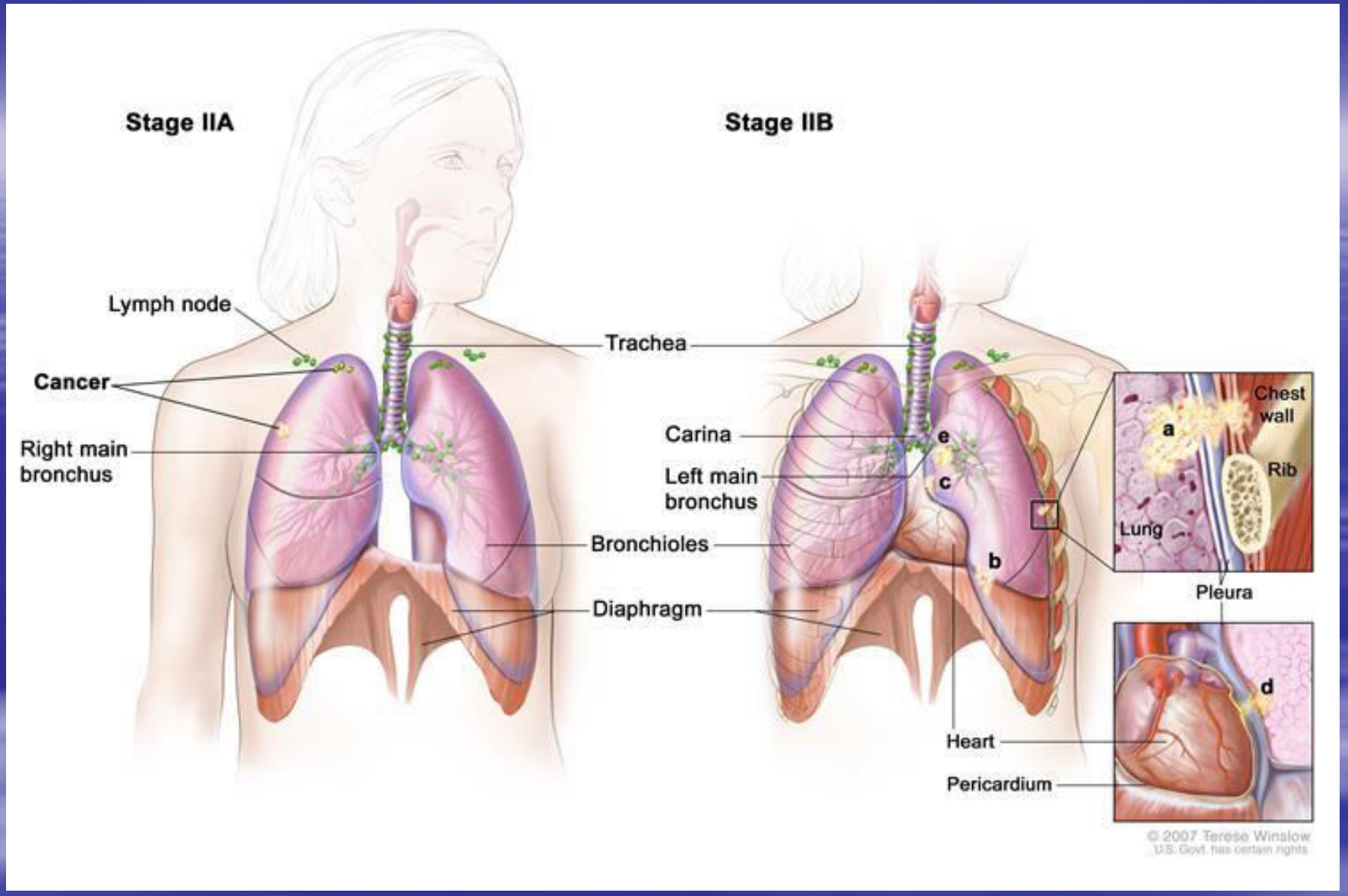
Staging

TNM Definitions

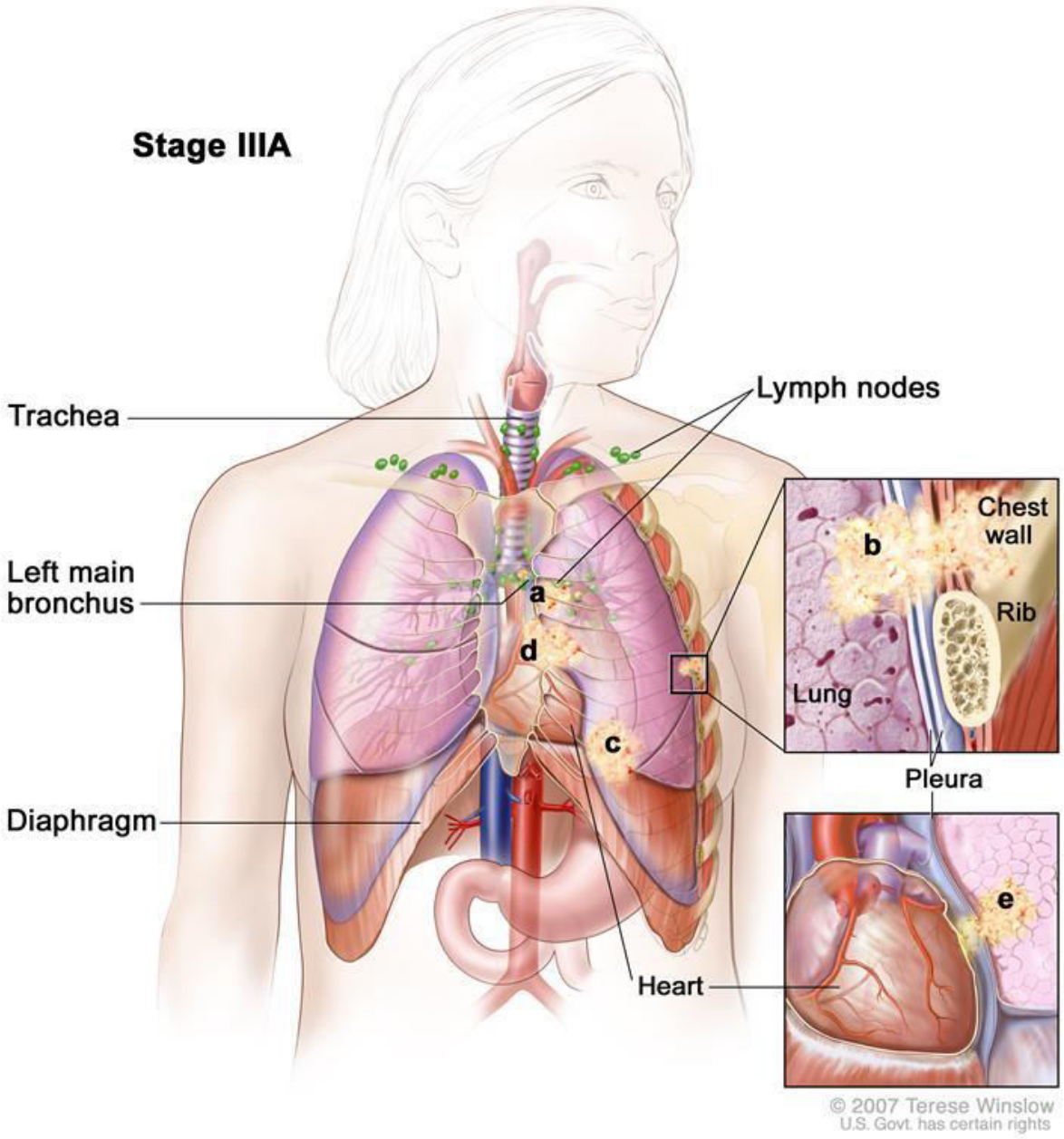
- T Stage
  - Size of the Primary Tumor
  - Adjacent structures invaded into by Tumor
- N Stage
  - Nodal disease involvement
- M Stage
  - Metastatic disease involvement



Stage 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.

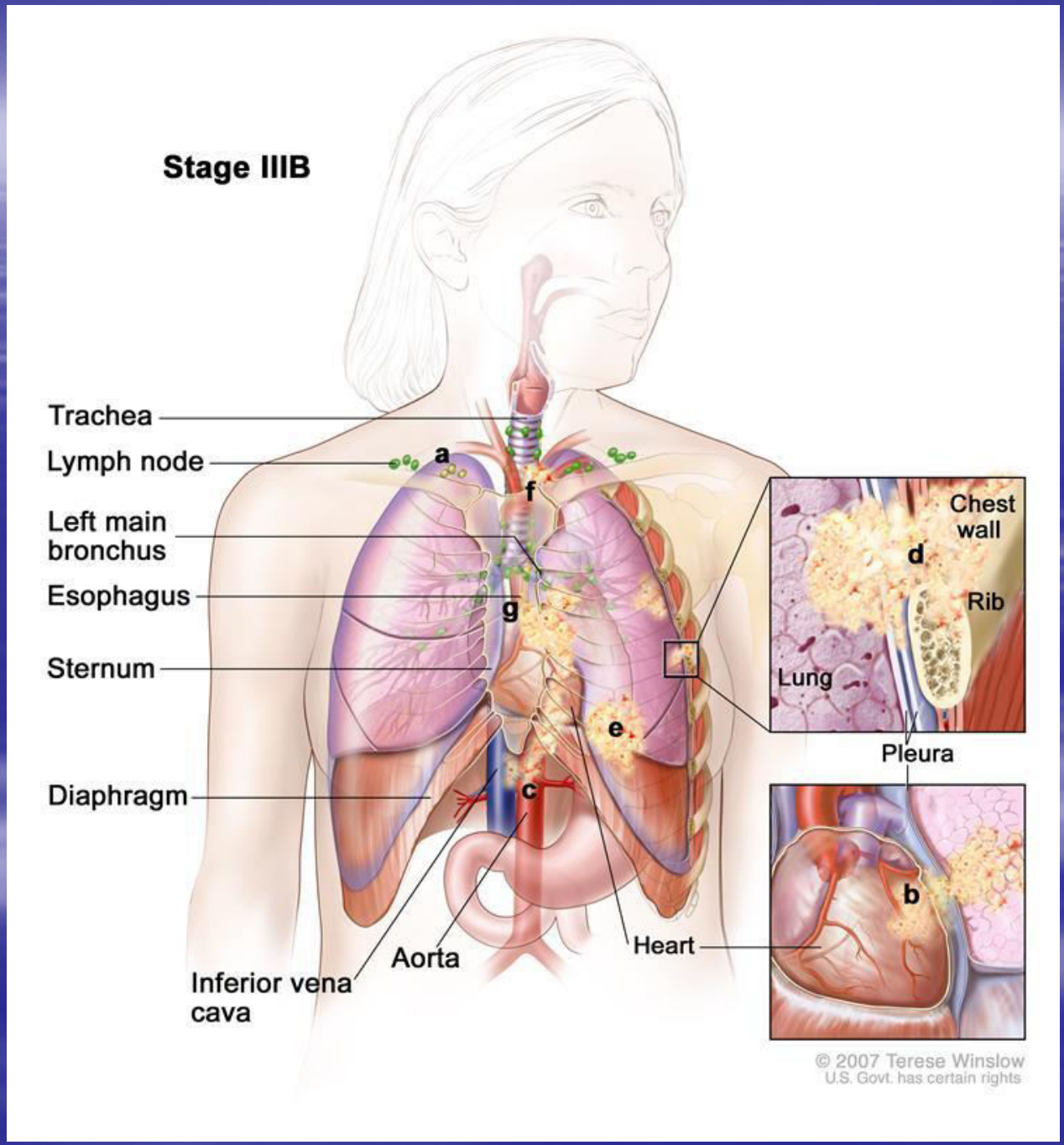
Stage IIIB

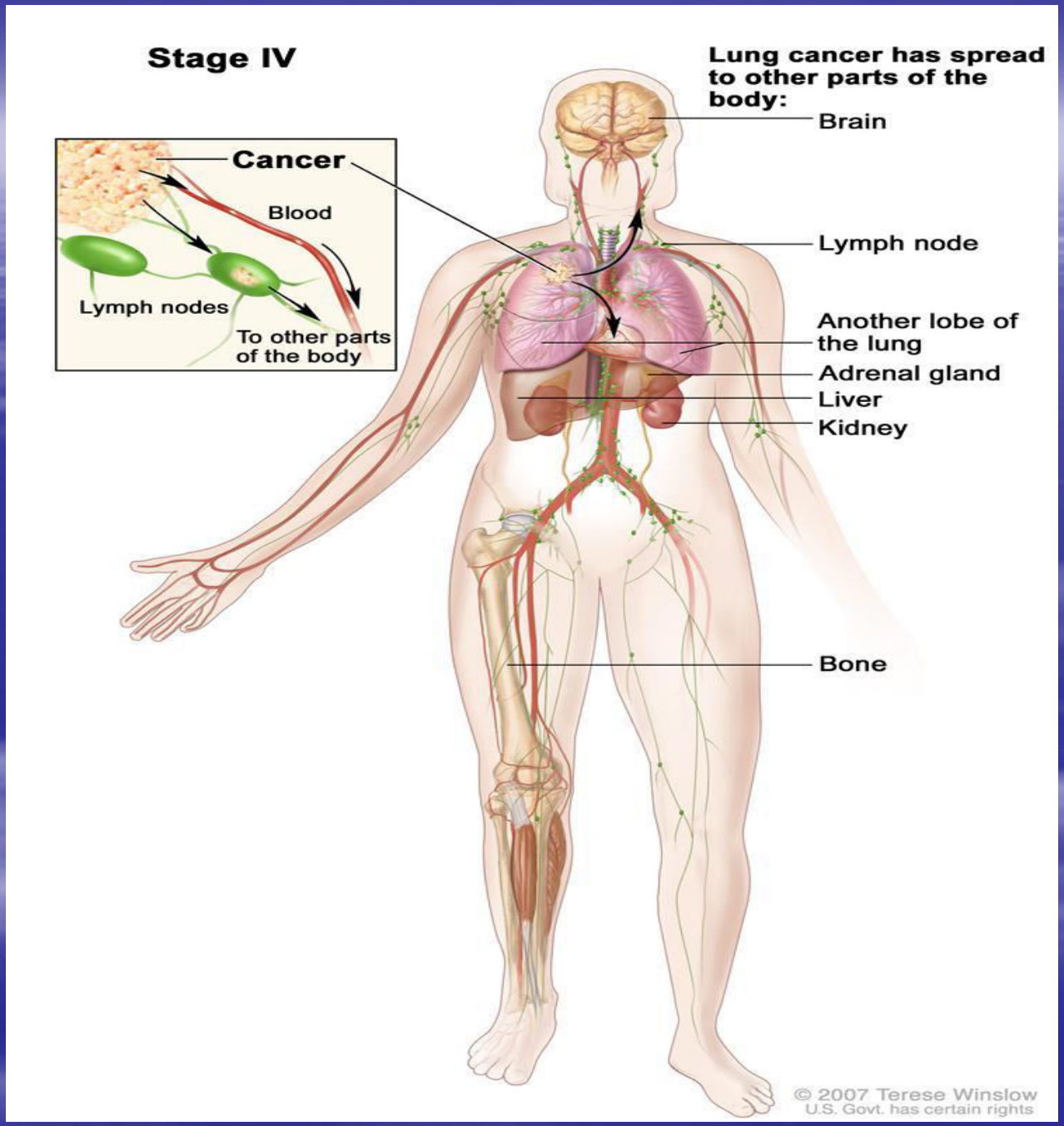
The cancer has spread to (a) contralateral mediastinal or hilar nodes or ipsilateral supraclavicular nodes.

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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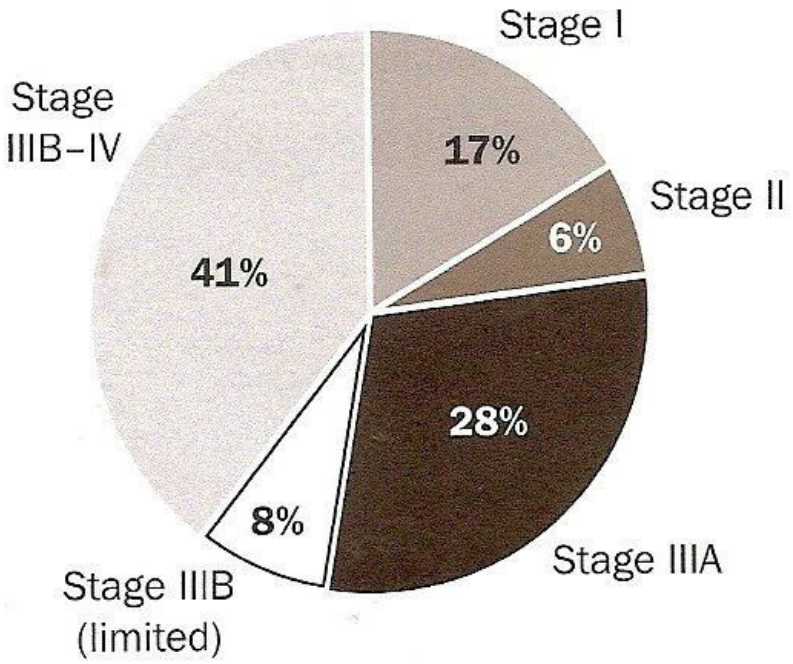
Staging



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%

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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

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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	

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 compared: low-dose helical computed tomography (CT) and standard chest X-ray. **53,456 current and former heavy smokers ages 55 to 74 with at least a 30 pack year history** were enrolled and **randomized** to compare the effects on mortality.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 4, 2011 VOL. 365 NO. 5

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*

Results

- **LUNG CANCER** Mortality Results
  - CT scan: 356 deaths 247/100,000
  - Radiography: 443 deaths 309/100,000

RELATIVE REDUCTION IN THE RATE OF DEATH FROM LUNG CANCER WITH LOW DOSE CT SCREENING OF 20% (P= 0.004)

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- **OVERALL** Mortality Results
  - CT scan: 1877 deaths
  - Radiography: 2000 deaths

RELATIVE REDUCTION IN THE RATE OF DEATH FROM ANY CAUSE WITH LOW DOSE CT SCREENING OF 6.7% (P= 0.02)

National Lung Screening Trial

Results:

20% reduction in lung cancer mortality with low-dose helical CT scan versus standard CXR

An additional 7% reduction in all cause mortality with low-dose helical CT scan

Translation:

156,940 Lung cancer deaths x 20.0% reduced

= 31,388 Lives Saved per year

(additional 10, 515 Lives Saved per year)

Annals of Internal Medicine

U.S. Preventive Services TASK FORCE
www.USPreventiveServicesTaskForce.org

SCREENING FOR LUNG CANCER
CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Asymptomatic adults aged 55 to 80 y who have a 30 pack-year smoking history and currently smoke or have quit smoking within the past 15 y
Recommendation	Screen annually for lung cancer with low-dose computed tomography. Discontinue screening when the patient has not smoked for 15 y. Grade: B

Risk Assessment	Age, total cumulative exposure to tobacco smoke, and years since quitting smoking are the most important risk factors for lung cancer. Other risk factors include specific occupational exposures, radon exposure, family history, and history of pulmonary fibrosis or chronic obstructive lung disease.
Screening Tests	Low-dose computed tomography has high sensitivity and acceptable specificity for detecting lung cancer in high-risk persons and is the only currently recommended screening test for lung cancer.
Treatment	Non–small cell lung cancer is treated with surgical resection when possible and also with radiation and chemotherapy.
Balance of Benefits and Harms	Annual screening for lung cancer with low-dose computed tomography is of moderate net benefit in asymptomatic persons who are at high risk for lung cancer based on age, total cumulative exposure to tobacco smoke, and years since quitting smoking.
Other Relevant USPSTF Recommendations	The USPSTF has made recommendations on counseling and interventions to prevent tobacco use and tobacco-caused disease. These recommendations are available at www.uspreventiveservicestaskforce.org.

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Organization	Groups eligible for screening	Year
American Academy of Family Practice1	Evidence is insufficient to recommend for or against screening.	2013
American Association for Thoracic Surgery2	1. Age 55 to 79 years with ≥ 30 pack year smoking history. 2. Long-term lung cancer survivors who have completed 4 years of surveillance without recurrence and who can tolerate lung cancer treatment following screening to detect second primary lung cancer until the age of 79. 3. Age 50 to 79 years with a 20 pack year smoking history and additional comorbidity that produces a cumulative risk of developing lung cancer ≥ 5% in 5 years.	2012
American Cancer Society3	Age 55 to 74 years with ≥ 30 pack year smoking history, who either currently smoke or have quit within the past 15 years, and who are in relatively good health.	2015
American College of Chest Physicians4	Age 55 to 74 years with ≥ 30 pack year smoking history, who either currently smoke or have quit within the past 15 years.	2013
American College of Chest Physicians and American Society of Clinical Oncology5	Age 55 to 74 years with ≥ 30 pack year smoking history, who either currently smoke or have quit within the past 15 years.	2012

American Lung Association6	Age 55 to 74 years with ≥ 30 pack year smoking history and no history of lung cancer.	2012
Centers for Medicare and Medicaid Services7	Age 55 to 77 years with ≥ 30 pack year smoking history and smoking cessation < 15 years.	2015
National Comprehensive Cancer Network8	1. Age 55 to74 years with ≥ 30 pack year smoking history and smoking cessation < 15 years. 2. Age ≥ 50 years and ≥ 20 pack year smoking history and 1 additional risk factor (other than secondhand smoke exposure).b	2015
U.S. Preventive Services Task Force9	Age 55 to 80 years with ≥ 30 pack year smoking history and smoking cessation < 15 years.	2013

Additional risk factors include cancer history, lung disease history, family history of lung cancer, radon exposure, occupational exposure, and history of chronic obstructive pulmonary disease or pulmonary fibrosis. Cancers with increased risk of developing new primary lung cancer include survivors of lung cancer, lymphomas, cancer of the head and neck, and smoking-related cancers. Occupational exposures identified as carcinogens targeting the lungs include silica, cadmium, asbestos, arsenic, beryllium, chromium (VI), diesel fumes, and nickel.

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)

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

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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

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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

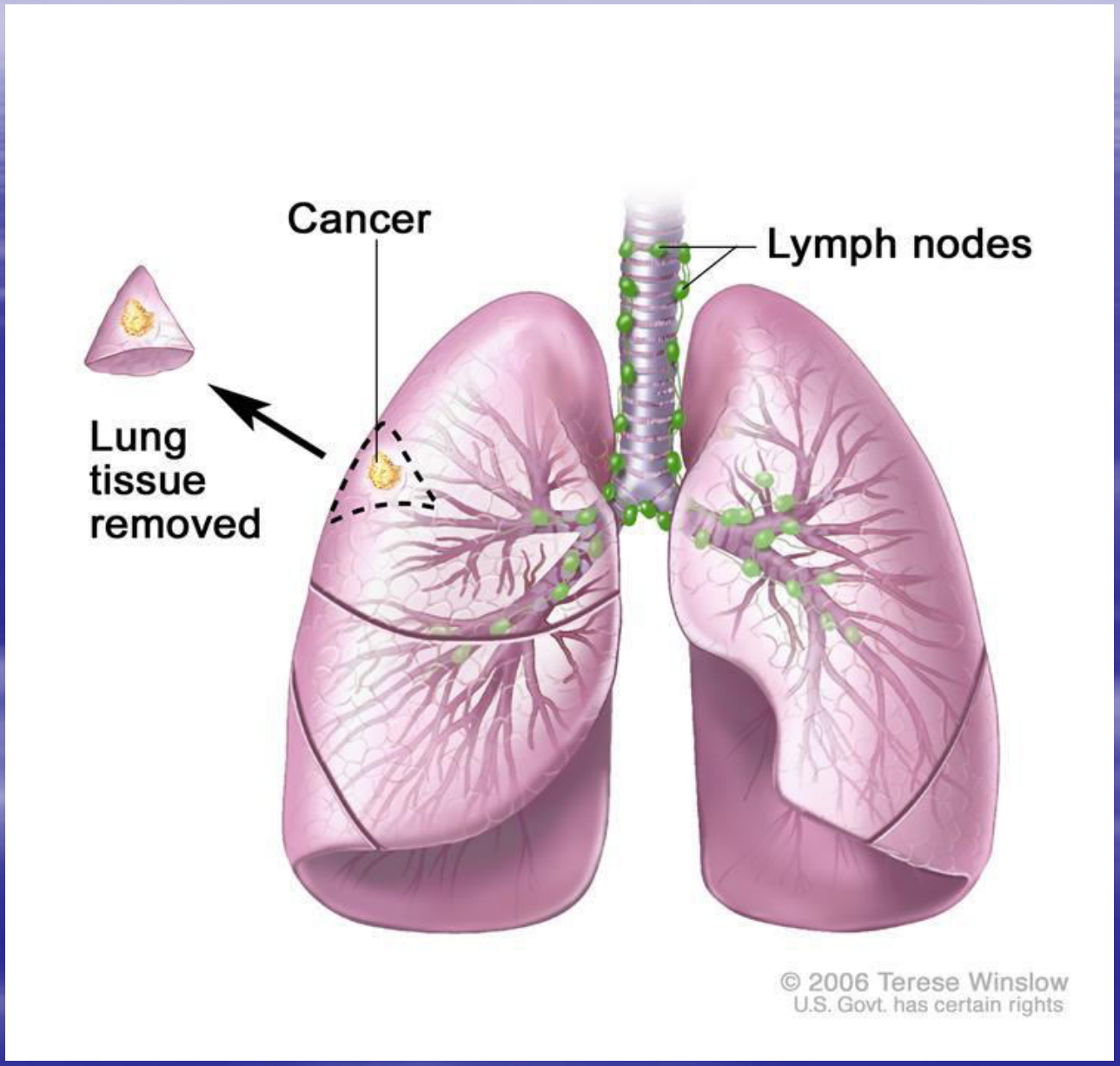
- **Radiation:**
  - Treatment with 60 Gy can achieve long term survival benefit in 5-10% of patients
- **Chemotherapy and Radiation:**
  - Meta analysis from 11 randomized studies showed cisplatin based chemotherapy with radiation resulted in 10% reduction in the risk of death compared to radiation 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.

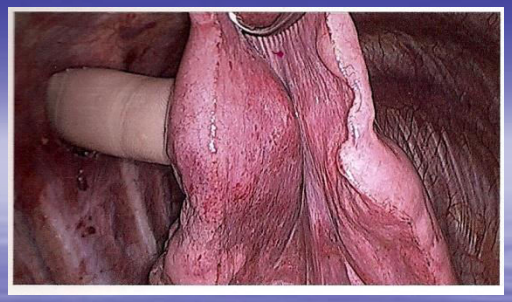
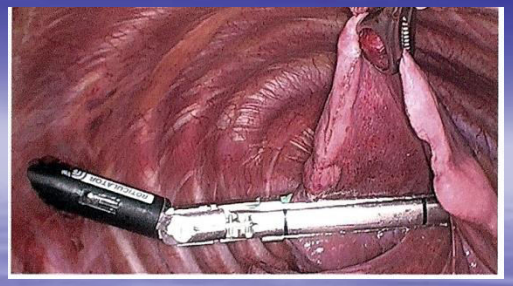
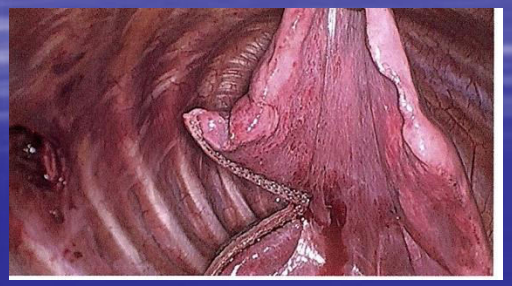
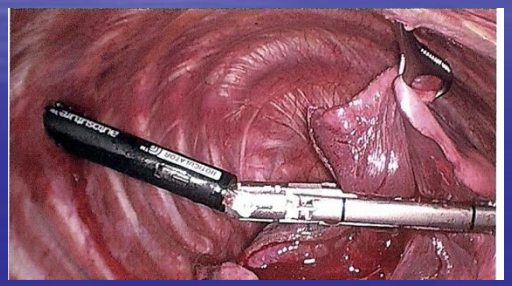
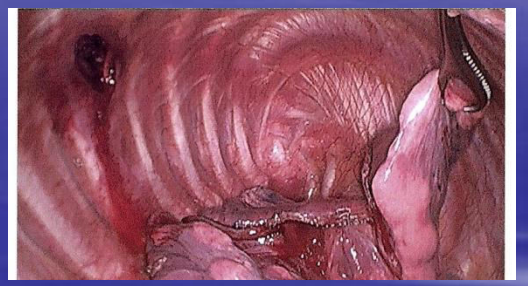
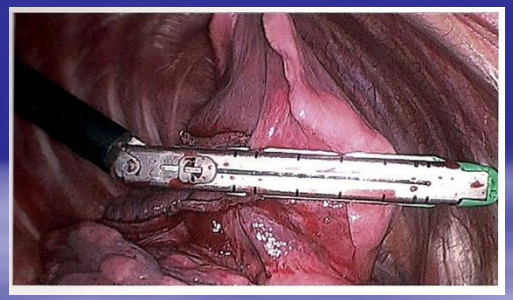
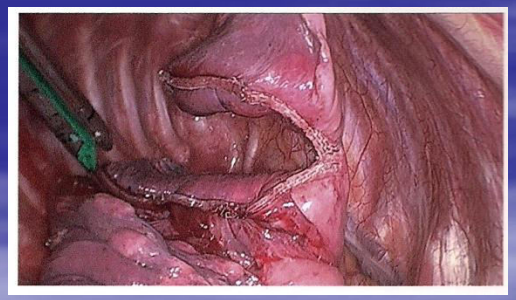
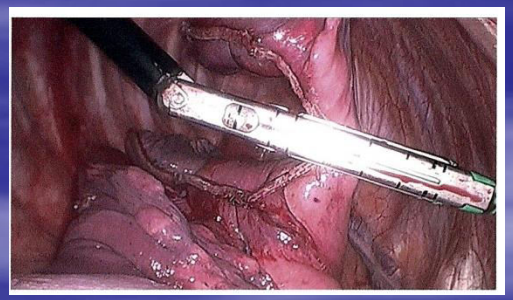
Treatment – Stage IIIB / IV

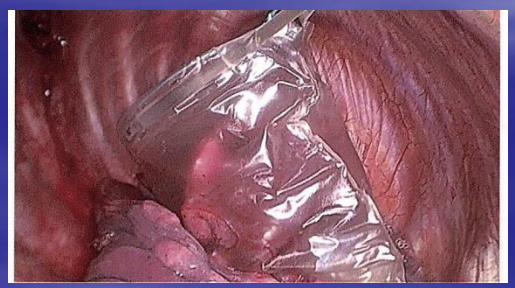
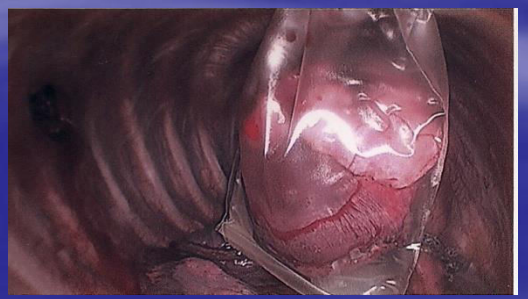
- Chemotherapy
- Radiation alone
- Chemotherapy plus radiation
  - Meta analysis of 54 randomized trials showed an **absolute survival benefit of 4% at 2 years** with combination of chemotherapy and radiation

Surgery

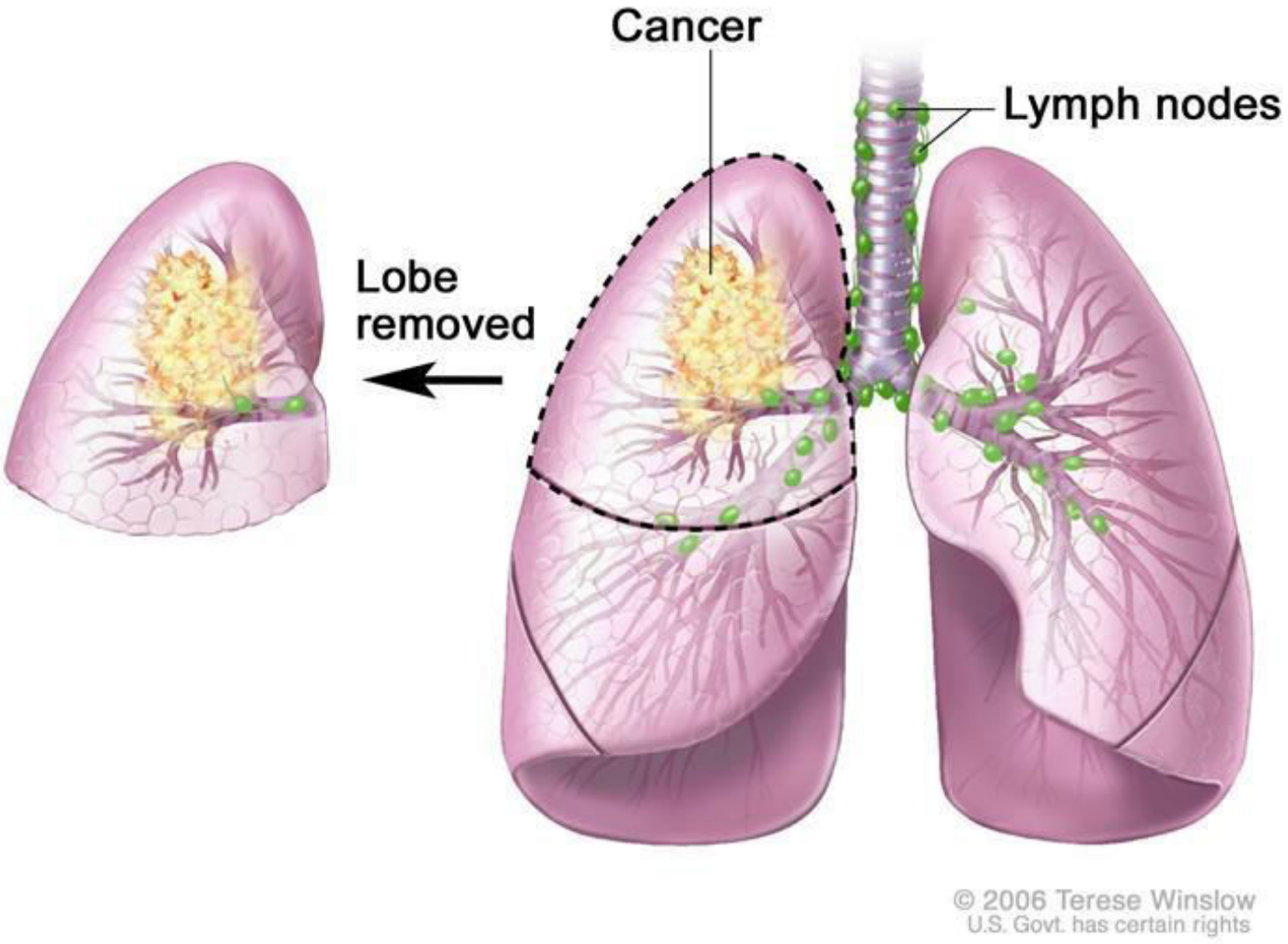
Wedge Resection



Lobectomy


Cancer
Lymph nodes
Lobe
removed
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Lobectomy

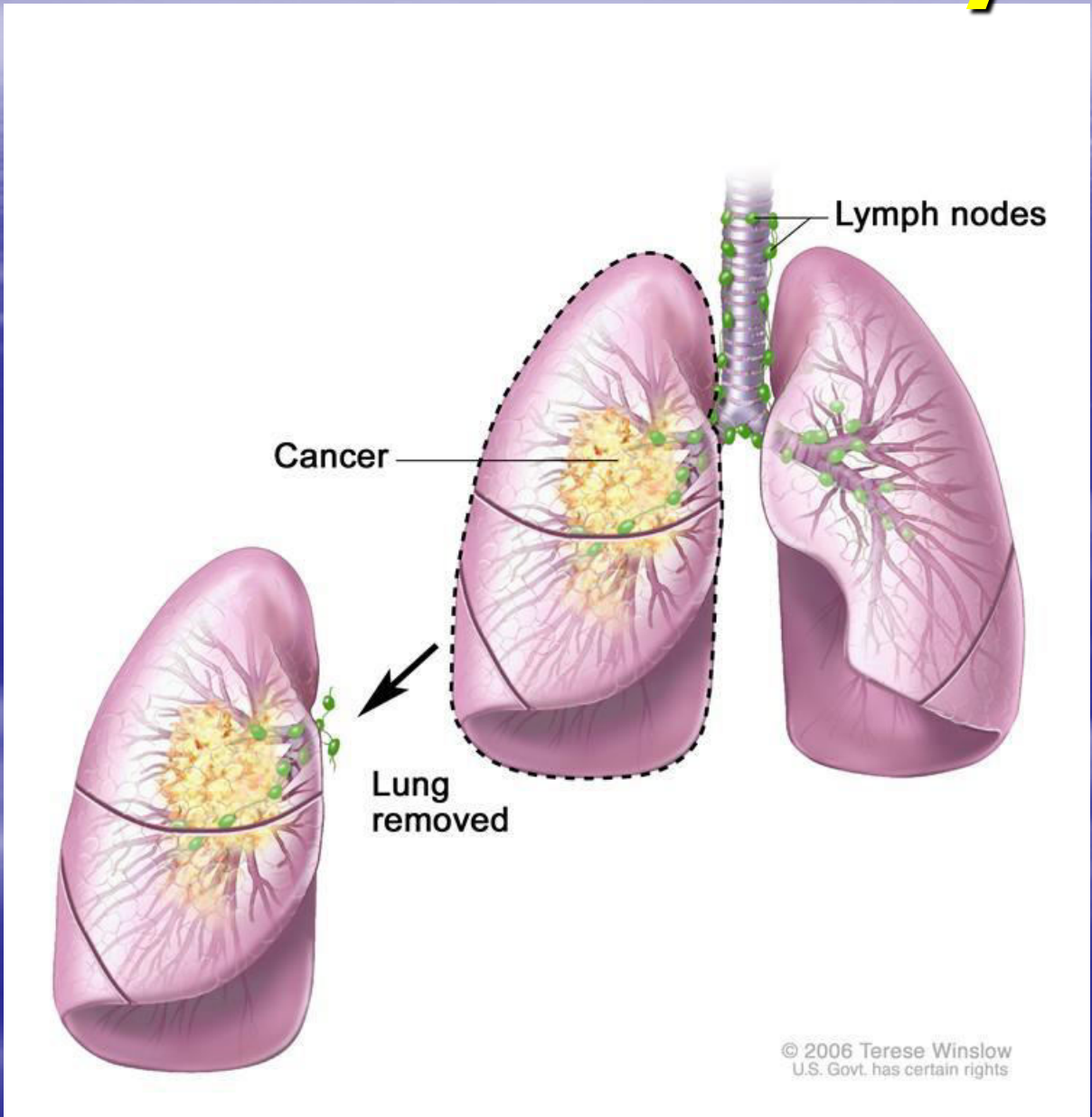
Lobectomy is the removal of a lobe of the lung, usually to treat lung cancer. Traditionally, a thoracotomy was used to accomplish this, but the incision was large, painful, led to many postsurgical complications.

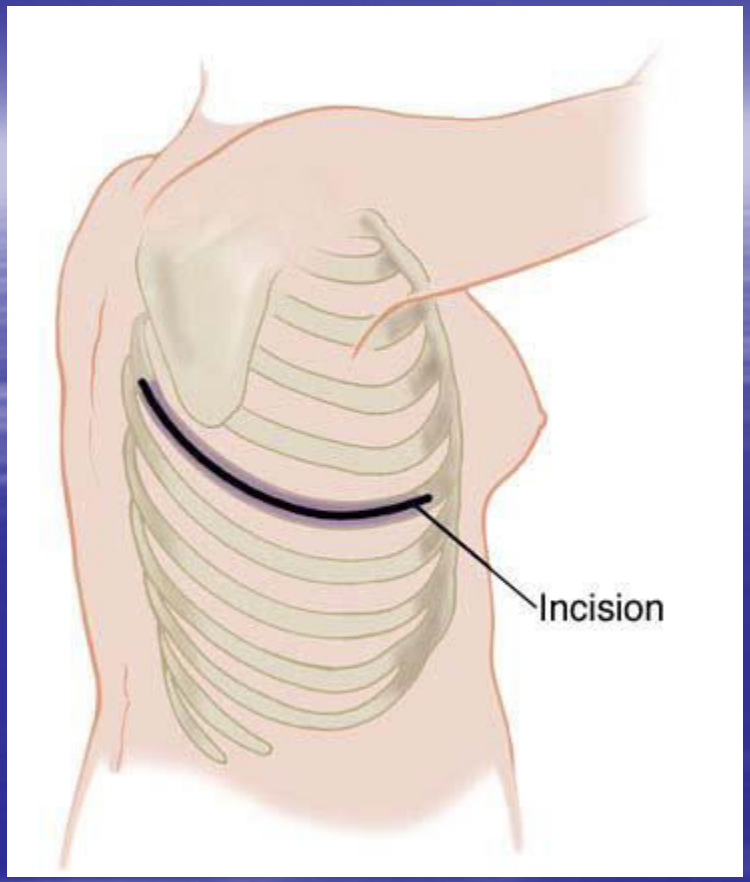
Today, we can perform a lobectomy **minimally invasively** thru a VATS or Robotic approach.

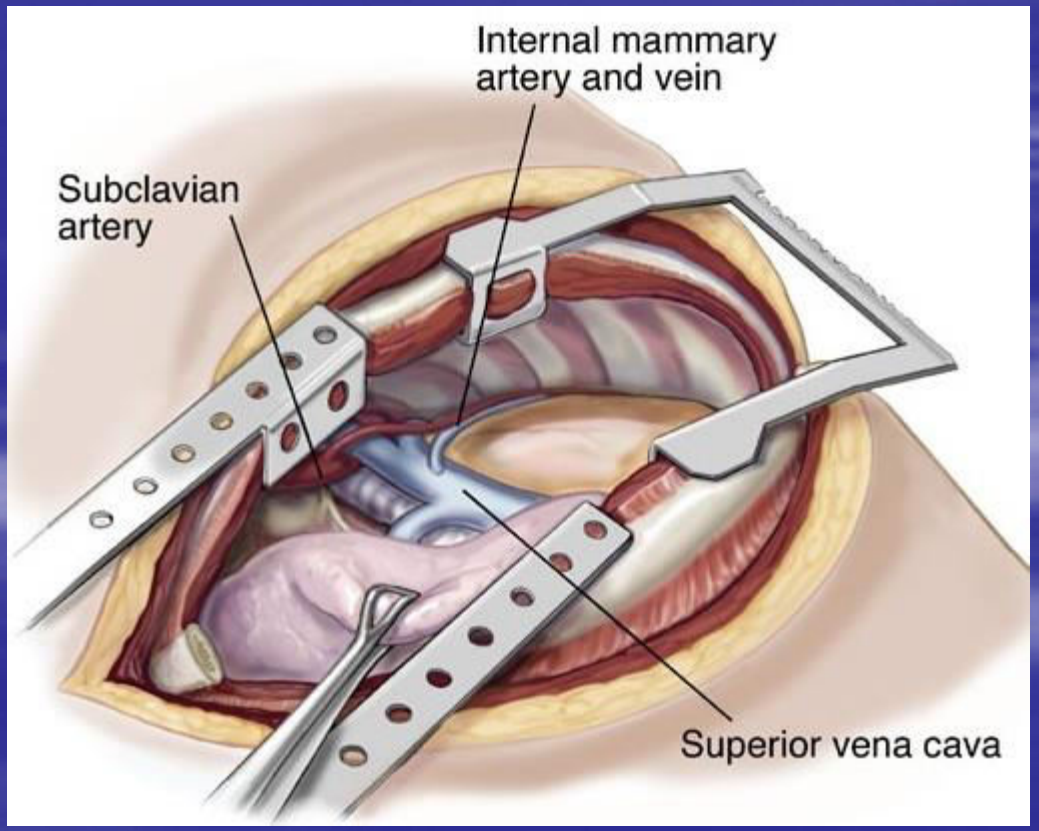
The advantages include smaller incision, no rib spreading or cutting, **less pain, less pneumonia (3% vs 19% in open lobectomy), less atrial fibrillation (3% vs 20% in open lobectomy), shorter hospital stay (4 days vs 9 days in open lobectomy), and earlier return to normal activity and work.**

Also, the minimally invasive technique allows us to offer surgery to higher risk patients who would otherwise not be candidates for traditional surgery.

Pneumonectomy




Incision


Internal mammary
artery and vein
Subclavian
artery
Superior vena cava

Minimally Invasive Surgery

Video Assisted Thorascopic Surgery

Robotic Assisted Thoracic Surgery

VATS Lobectomy

Video Assisted Thorascopic Surgery

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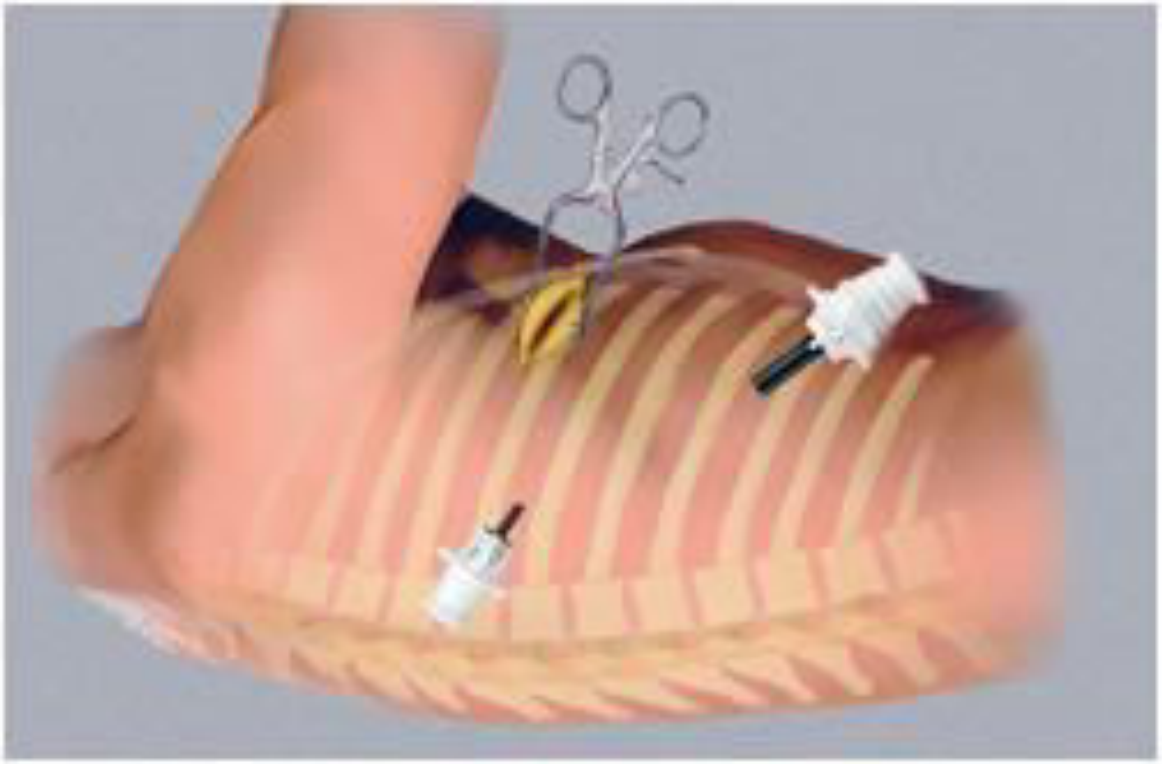


Example of VATS Incisions

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

Stephen M. Cattaneo, MD, Bernard J. Park, MD, Andrew S. Wilton, MS, Venkatraman E. Seshan, PhD, Manjit S. Bains, MD, Robert J. Downey, MD, Raja M. Flores, MD, Nabil Rizk, MD, and Valerie W. Rusch, MD

Departments of Surgery and Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, New York

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 = 76 years

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)	

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

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

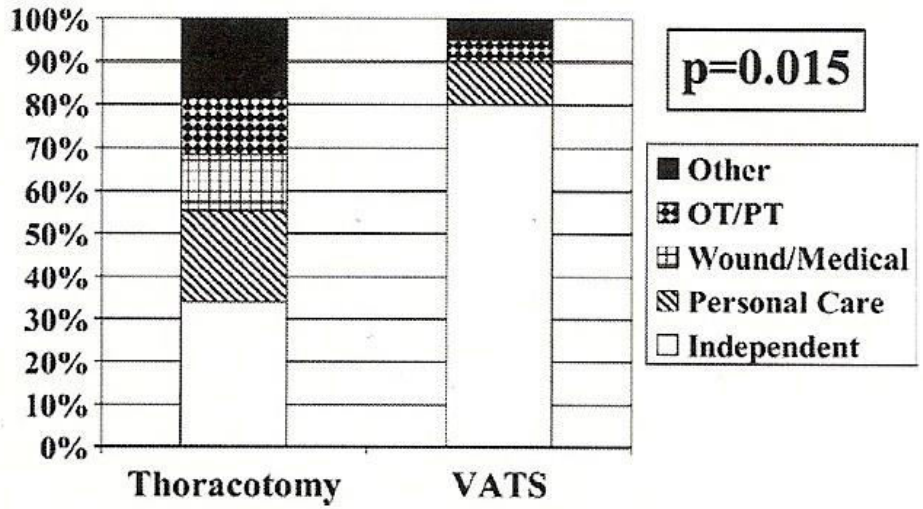


Fig 1. Discharge independence after thoracoscopic lobectomy. The bar graphs demonstrate a much lower need for home health services in the video-assisted thoracic surgery (VATS) group. The types of services needed for each procedure type are displayed as well. (OT = occupational therapy; other = other 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.

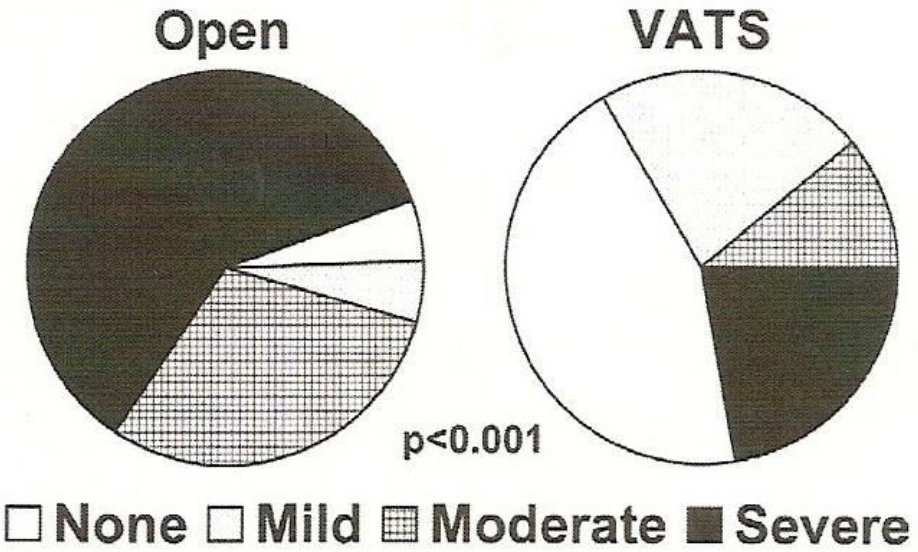
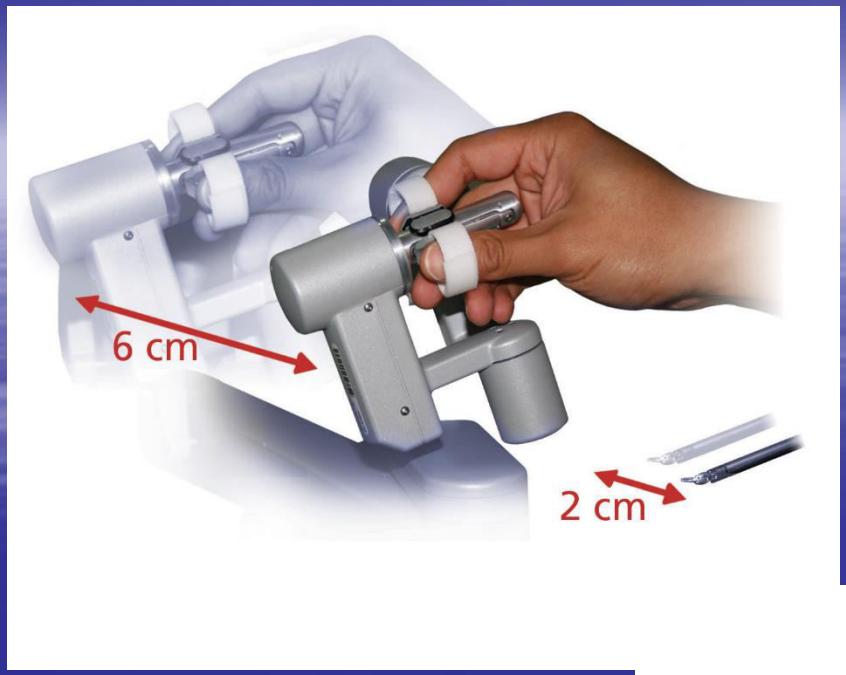


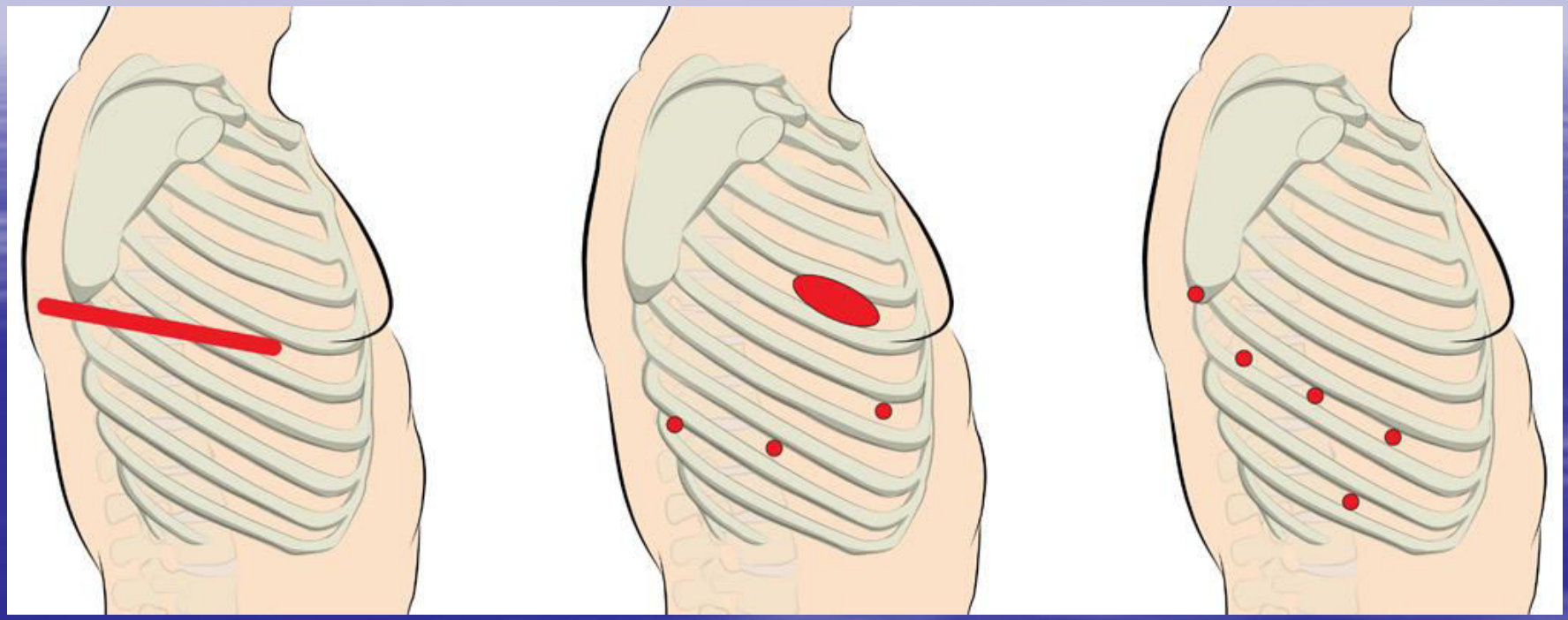
Fig 2. Pain control at 3 weeks after video assisted thoracic surgery (VATS) lobectomy. The pie charts show that VATS patients have significantly ($p < 0.01$) less pain as measured by the most potent analgesic still required: severe—schedule 2 narcotic; moderate—schedule 3 or lower; mild–nonsteroidal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

da Vinci® Surgery

Less invasive • More precise • Faster recovery


6 cm
2 cm


da Vinci



Open Surgery Incision

VATS Incisions

Da Vinci Surgery Incisions

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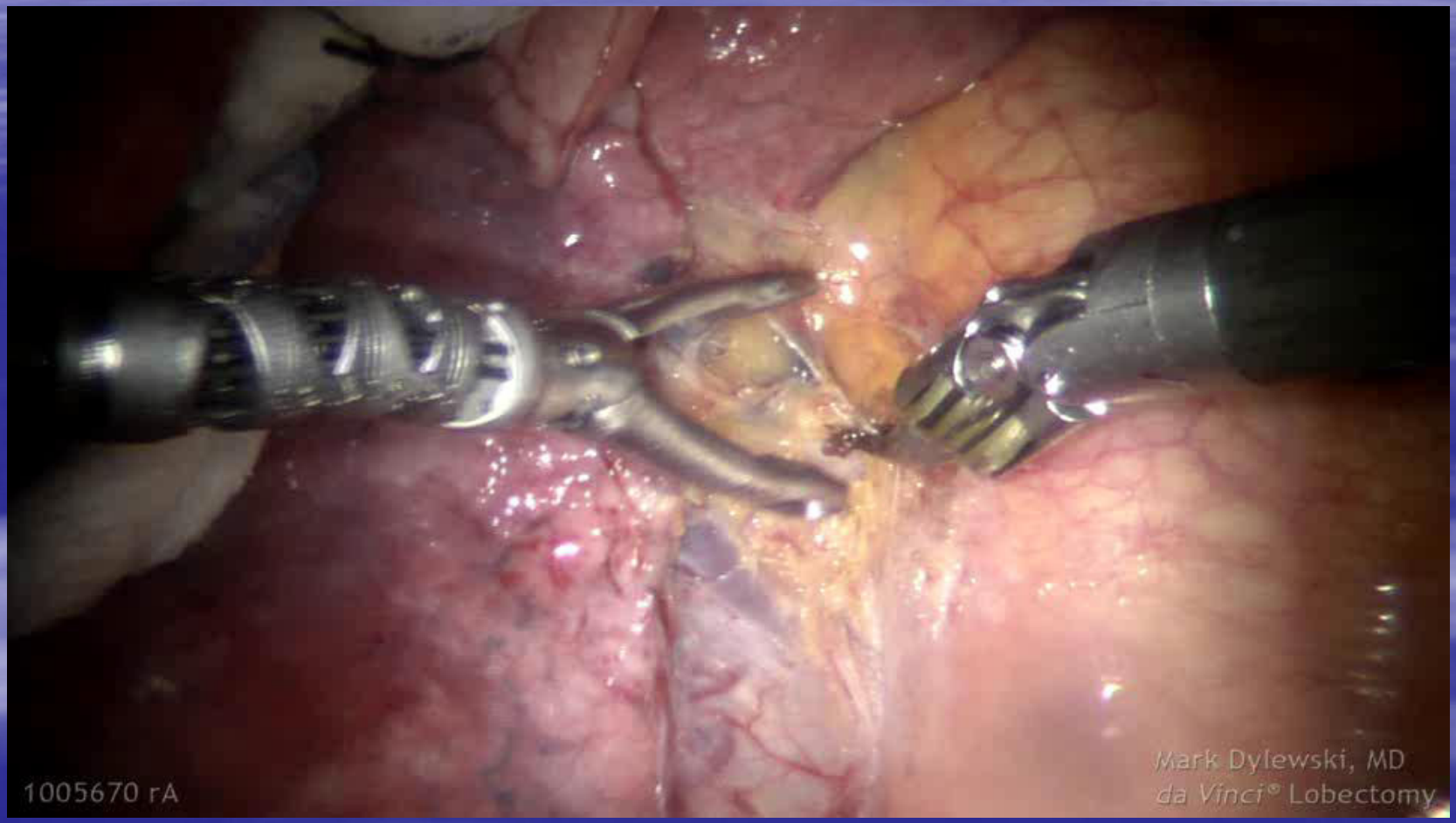
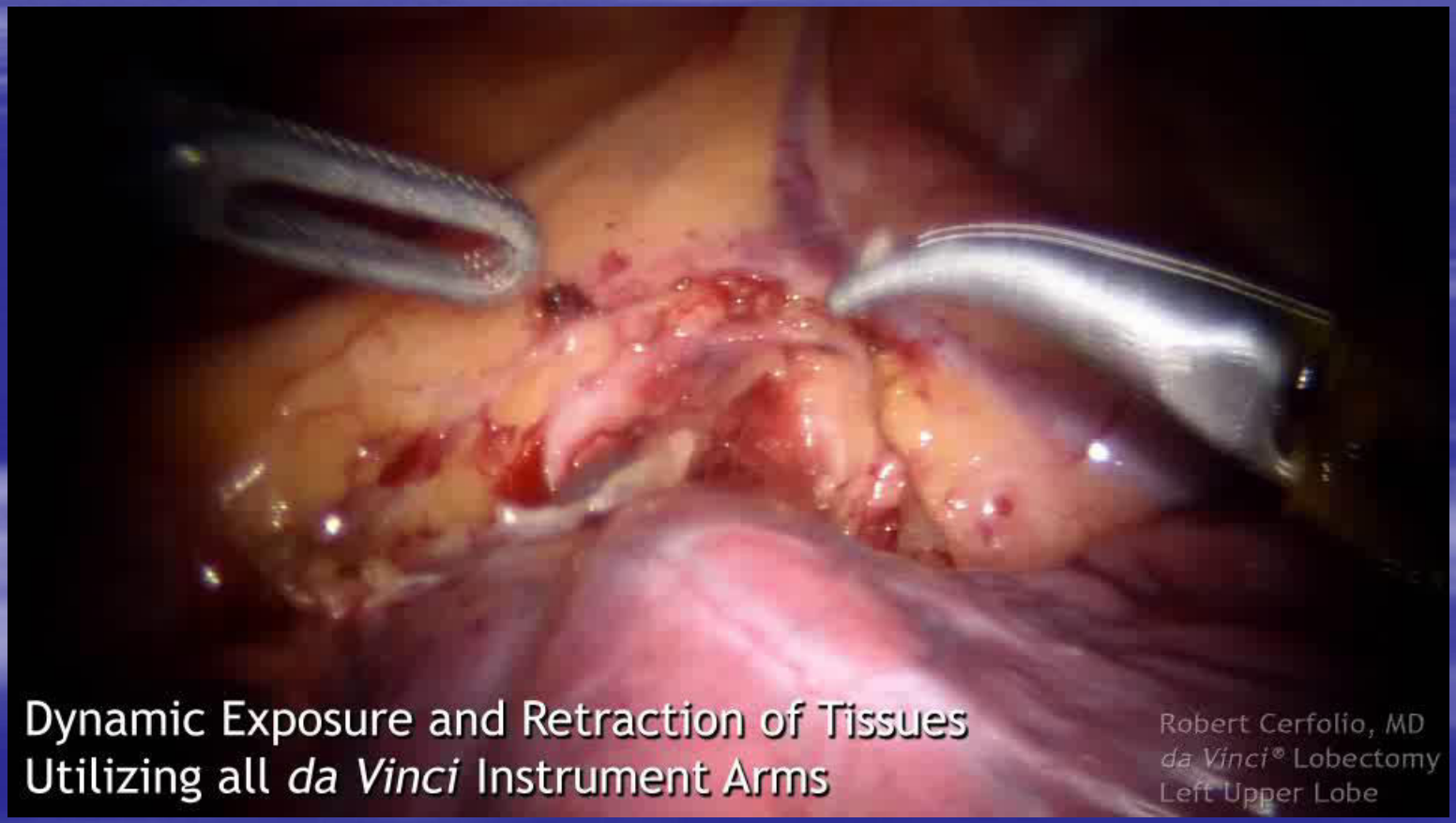
Robotic and VATS Advantage Summary

- 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

Mediastinal & Hilar Lymph Node Dissection



Dynamic Exposure & Retraction



Alternative Treatments

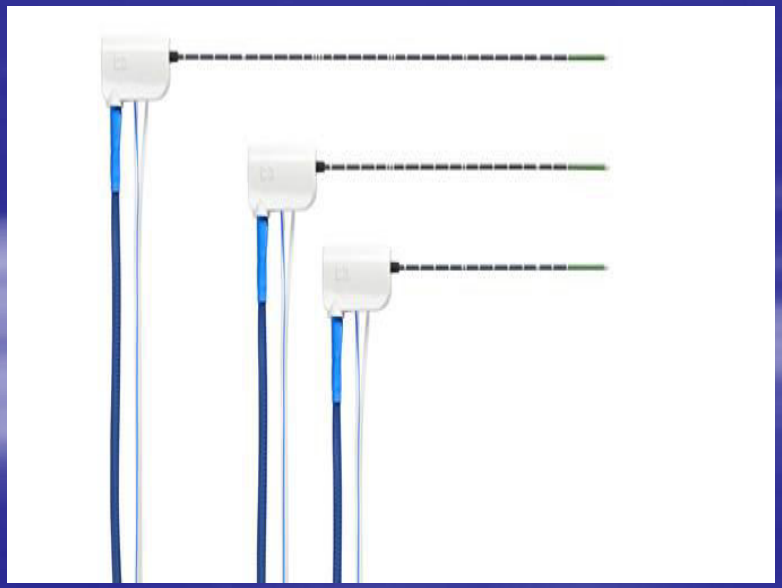
- Cyber knife
- Radiofrequency Ablation (RFA)
- Microwave Ablation
- PDT
- Targeted Therapies

CyberKnife

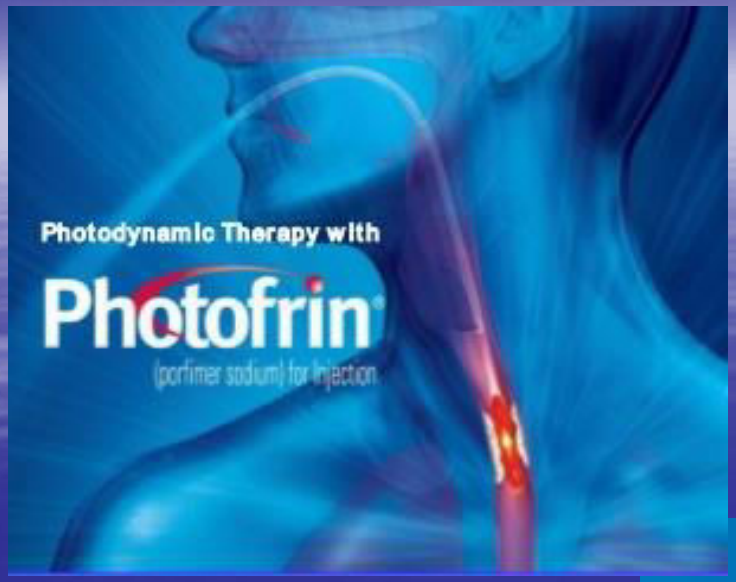
- CyberKnife is a frameless robotic radiosurgery method of delivering radiotherapy, with the intention of targeting treatment more accurately than standard radiotherapy.
- Used for Inoperable early stage lung cancer, or
- Metastatic disease

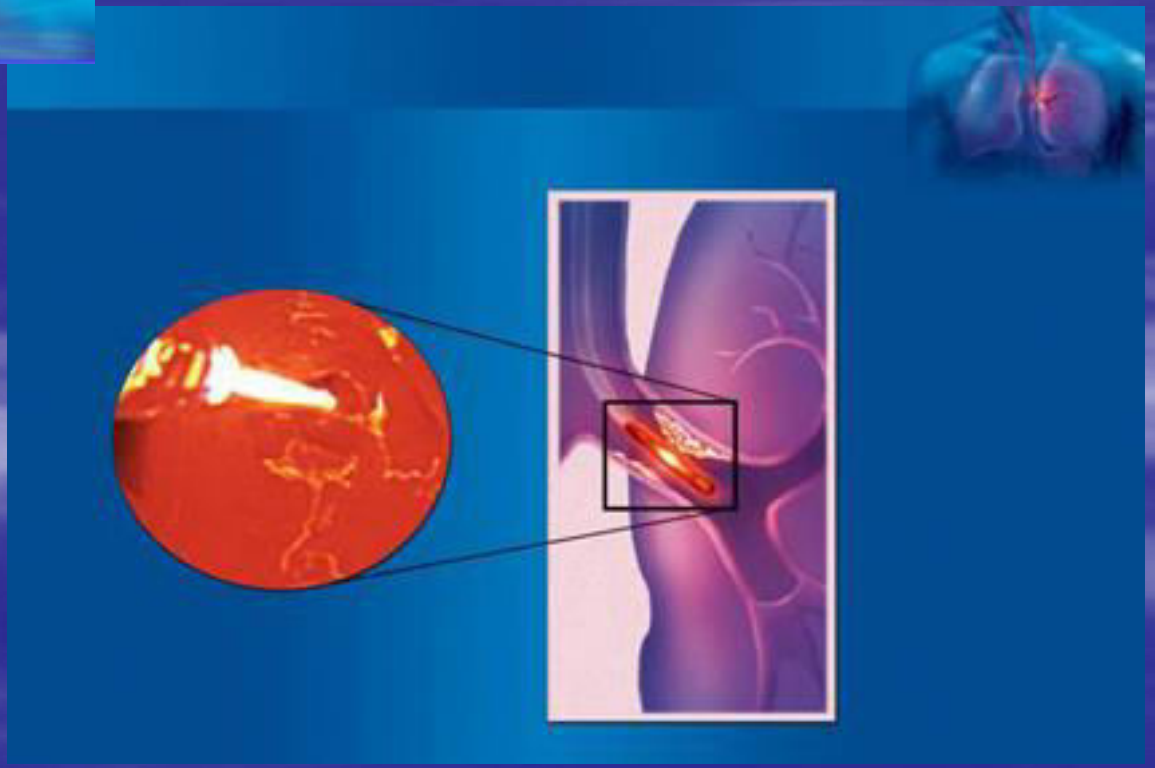
Radiofrequency Ablation (RFA)/ Microwave Ablation

- 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 or microwave 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



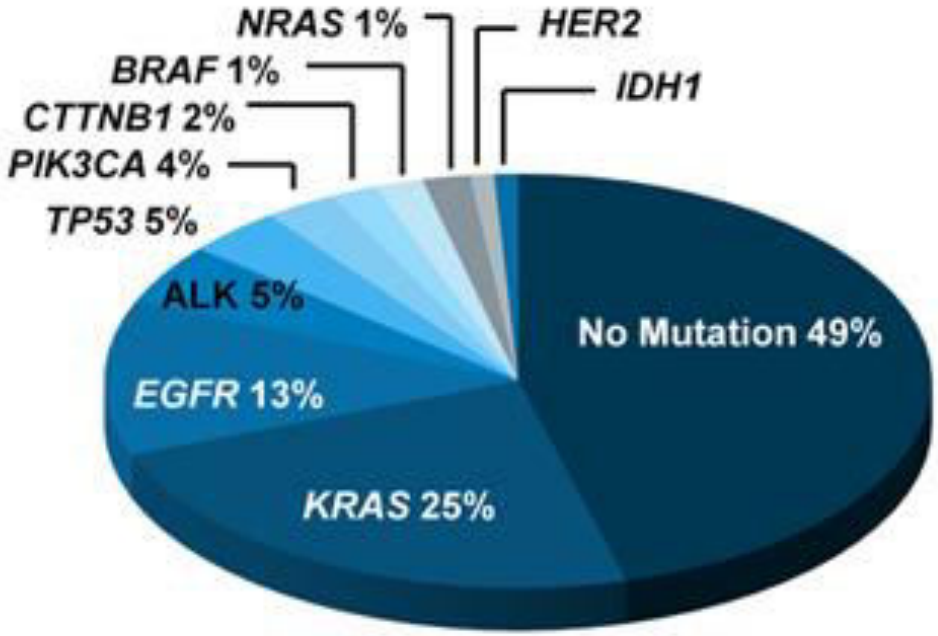
PhotoDynamic Therapy





Targeted Therapy

Incidence of Driver Mutations in NSCLC



HER2 = human epidermal growth factor receptor 2; IDH1 = isocitrate dehydrogenase; PIK3CA = phosphoinositide-3-kinase-catalytic alpha

Sequist LV, et al. *J Clin Oncol.* 2011;29: abstract 7518.

Table 1. Lung cancer genetic aberrations and associated targeted therapy.

Biomarker gene	Aberration	Targeted therapeutic	Frequency of aberration [%]
EGFR	Mutation or amplification	Gefitinib, erlotinib, cetuximab	[10-25] (35% in Asian patients)
HER2 (ERBB2)	Mutation or amplification	Trastuzumab	[5-10]
BRAF	Mutation	Sorafenib	[2-3]
p53	Mutation or deletion	Advexin a p53 adenoviral vector	[30-50]
VEGF	Overexpression	Bevacizumab, afibercept	
PI3K	Modified and activated	BEZ235, LY294002	[1-3]
mTOR	Activated	Rapamycin, RAD001, CCL-779	[70-75]
RAS	Mutation leading to activation	Tipifarnib, lonafarnib	[10-15] (20-30% in Adenocarcinoma)
MEK	Activated	Trametinib, salumetinib	[1-2]
c-KIT	Overexpressed	Imatinib	[1-2]
EML/ALK	Fusion	Crizotinib	[5-13]

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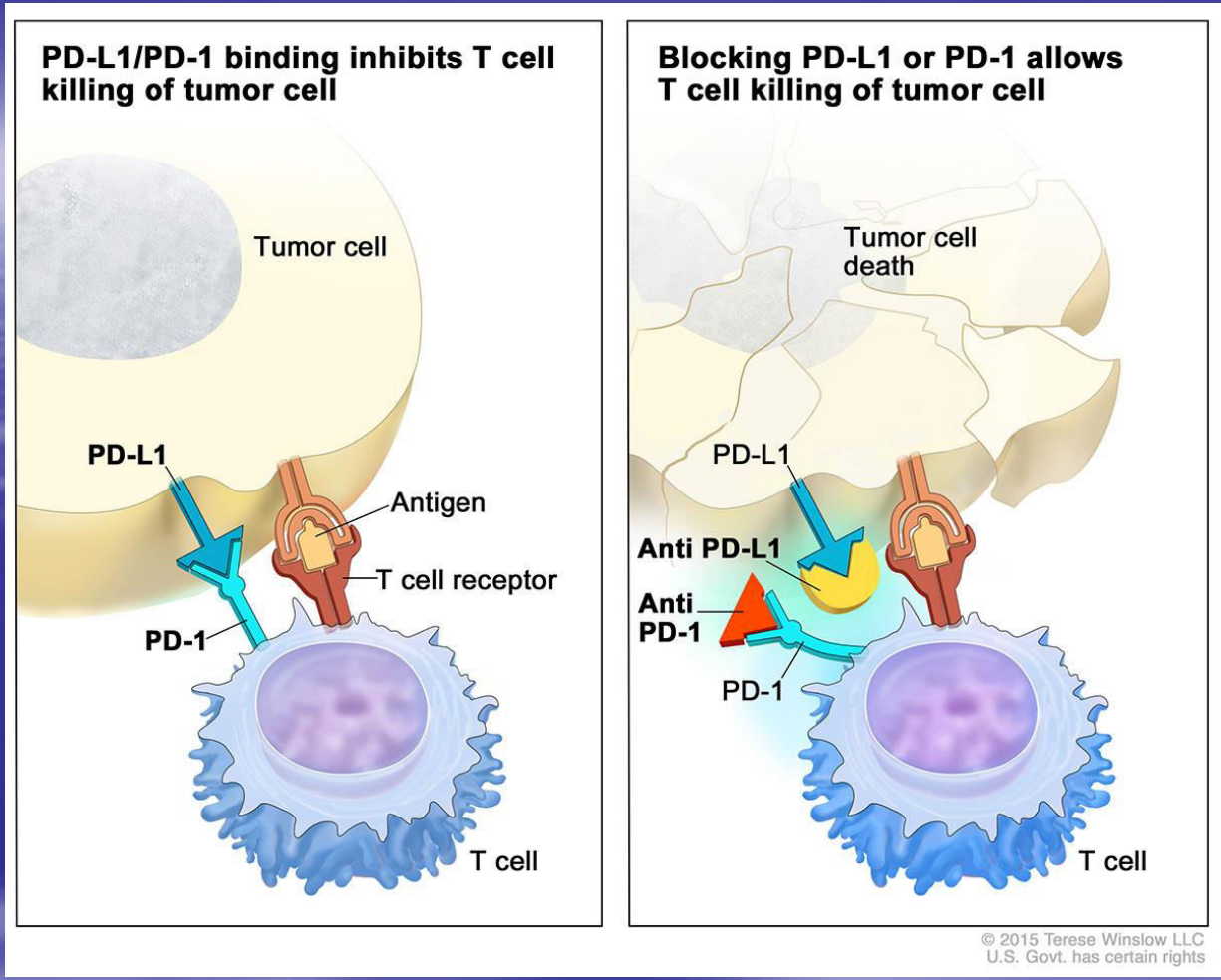

Pembrolizumab targets a protein on immune cells called PD-1, one of a family of so-called checkpoint proteins that can restrain the immune response.

Credit: National Cancer Institute / Terese Winslow

Questions?

Thank U