Percutaneous Treatment of Thoracic Malignancy

Disclaimer

A good portion of this lecture was adopted/modified from lectures given by William Moore, MD to this Physics 210 class from previous years.

Credentials
Positions
NYU Langone Medical Center
Professor, Department of Radiology
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Board Certifications
American Board of Radiology - Diagnostic Radiology, 2004
Education and Training
Fellowship, NYU School of Medicine, Thoracic Radiology, 2004
Residency, Stony Brook University Medical Center, Diagnostic Radiology, 2004
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Objectives

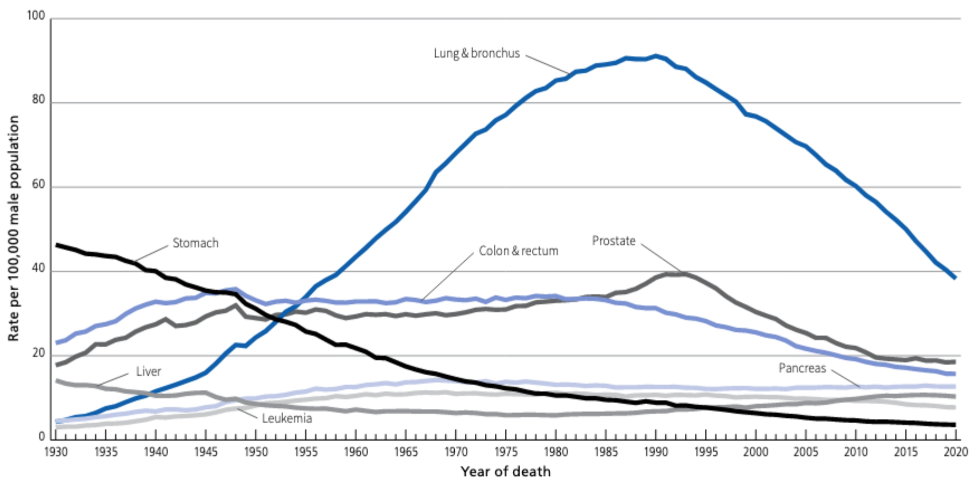
- Epidemiology of Lung Cancer.
- Technique of Percutaneous Ablation.
- Radiofrequency Biology of Cell Death.
- Cryobiology of Cell Death.
- Imaging Follow–up.
- Preliminary Data.

Epidemiology of lung cancer.

- Lung cancer is the leading cause of cancer related death for both men and women in the United States.
- In 2023:
  - estimated 238,000 cases of lung cancer will or have been diagnosed in the US and 1.95 million total US cancer cases.
  - 127,000 deaths from lung cancer and 610,000 overall are estimated in the United States in 2023.
  - This is down from a few years ago.

Cancer Deaths 1930 - 2020

Figure 1. Trends in Age-adjusted Cancer Death Rates* by Site, Males, US, 1930-2020



*Age adjusted to the 2000 US standard population. Rates exclude deaths in Puerto Rico and other US territories. Note: Due to changes in ICD coding, numerator information has changed over time for cancers of the liver, lung and bronchus, and colon and rectum.

Source: US Mortality Volumes 1930 to 1959, US Mortality Data 1960 to 2020, National Center for Health Statistics, Centers for Disease Control and Prevention.

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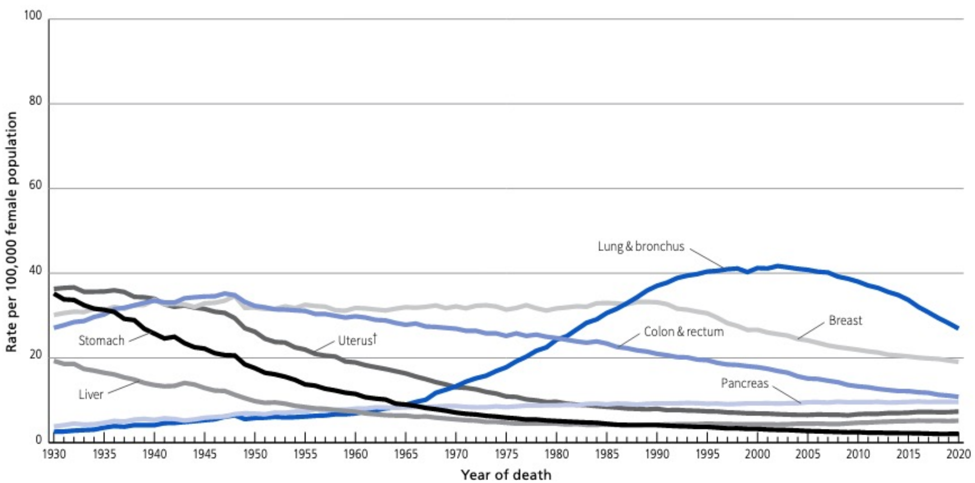
Figure 2. Trends in Age-adjusted Cancer Death Rates* by Site, Females, US, 1930-2020



*Age adjusted to the 2000 US standard population. Rates exclude deaths in Puerto Rico and other US territories. †Uterus refers to uterine cervix and uterine corpus combined. Note: Due to changes in ICD coding, numerator information has changed over time for cancers of the liver, lung and bronchus, colon and rectum, and uterus.

Source: US Mortality Volumes 1930 to 1959, US Mortality Data 1960 to 2020, National Center for Health Statistics, Centers for Disease Control and Prevention.

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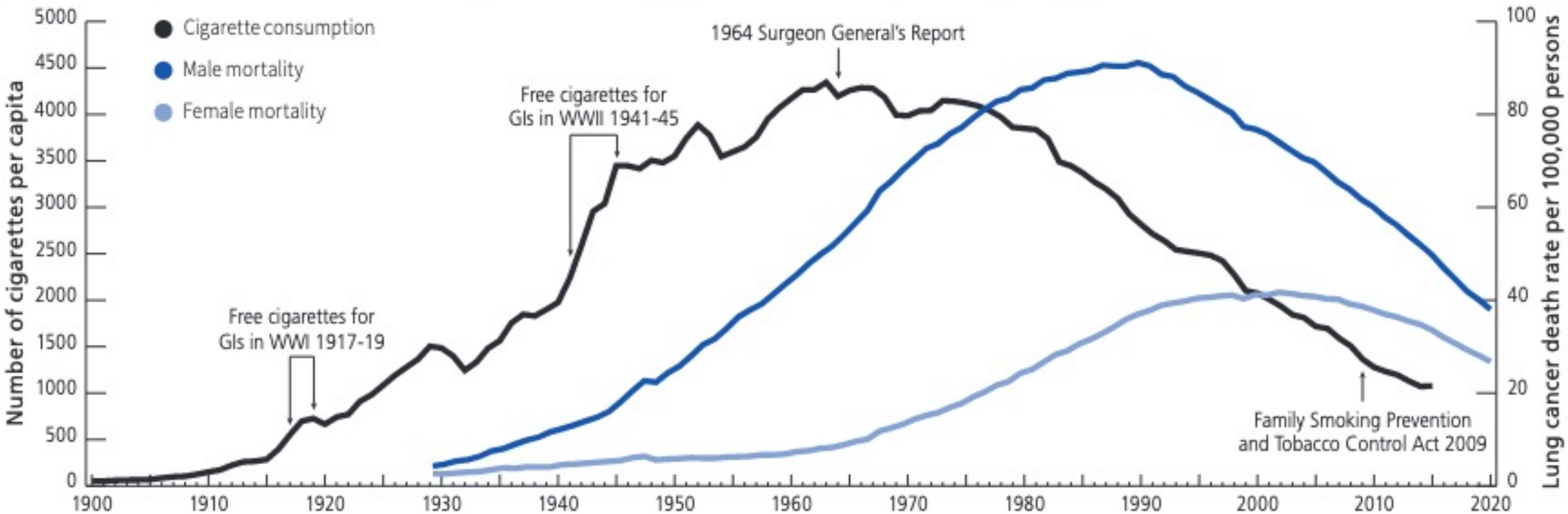
- Cancer deaths are generally on the decline since the early 1990s.
- Why the spike in lung/bronchus related deaths?
- What happened in the late 1930s for men? Late 1960s for women?
- Why the sharp decline in lung/bronchus related deaths after the early 1990's for men and leveling off for women?

Cancer Deaths 1930 - 2020

Figure S6. Trends in Tobacco Consumption and Lung Cancer Mortality Rates* by Sex, 1900-2020



*Age adjusted to the 2000 US standard population. Rates exclude deaths in Puerto Rico and other US territories. Note: Due to changes in ICD coding, numerator information for mortality rates has changed over time.

Source: Death rates: US Mortality Data, 1960-2020, US Mortality Volumes, 1930-1959, National Center for Health Statistics. Cigarette consumption: 1900-1999: US Department of Agriculture. 2000-2015: Consumption of Cigarettes and Combustible Tobacco – United States, 2000-2015. *MMWR Weekly Rep* 2016; 65(48);1357-1363.

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Cancer Deaths 1930 - 2020

Table 1. Estimated Number* of New Cancer Cases and Deaths by Sex, US, 2023

	Estimated New Cases			Estimated Deaths		
	Both sexes	Male	Female	Both sexes	Male	Female
All sites	1,958,310	1,010,310	948,000	609,820	322,080	287,740
Oral cavity & pharynx	54,540	39,290	15,250	11,580	8,140	3,440
Tongue	18,040	13,180	4,860	2,940	1,950	990
Mouth	14,820	8,680	6,140	3,090	1,870	1,220
Pharynx	20,070	16,340	3,730	4,140	3,260	880
Other oral cavity	1,610	1,090	520	1,410	1,060	350
Digestive system	348,840	194,980	153,860	172,010	99,350	72,660
Esophagus	21,560	17,030	4,530	16,120	12,920	3,200
Stomach	26,500	15,930	10,570	11,130	6,690	4,440
Small intestine	12,070	6,580	5,490	2,070	1,170	900
Colon & rectum†	153,020	81,860	71,160	52,550	28,470	24,080
Colon	106,970	54,420	52,550			
Rectum	46,050	27,440	18,610			
Anus, anal canal, & anorectum	9,760	3,180	6,580	1,870	860	1,010
Liver & intrahepatic bile duct	41,210	27,980	13,230	29,380	19,000	10,380
Gallbladder & other biliary	12,220	5,750	6,470	4,510	1,900	2,610
Pancreas	64,050	33,130	30,920	50,550	26,620	23,930
Other digestive organs	8,450	3,540	4,910	3,830	1,720	2,110
Respiratory system	256,290	131,150	125,140	132,330	71,170	61,160
Larynx	12,380	9,900	2,480	3,820	3,070	750
Lung & bronchus	238,340	117,550	120,790	127,070	67,160	59,910
Other respiratory organs	5,570	3,700	1,870	1,440	940	500
Bones & joints	3,970	2,160	1,810	2,140	1,200	940
Soft tissue (including heart)	13,400	7,400	6,000	5,140	2,720	2,420
Skin (excluding basal & squamous)	104,930	62,810	42,120	12,470	8,480	3,990
Melanoma of the skin	97,610	58,120	39,490	7,990	5,420	2,570
Other nonepithelial skin	7,320	4,690	2,630	4,480	3,060	1,420
Breast	300,590	2,800	297,790	43,700	530	43,170
Genital system	414,350	299,540	114,810	69,660	35,640	34,020
Uterine cervix	13,960		13,960	4,310		4,310
Uterine corpus	66,200		66,200	13,030		13,030
Ovary	19,710		19,710	13,270		13,270
Vulva	6,470		6,470	1,670		1,670
Vagina & other genital, female	8,470		8,470	1,740		1,740
Prostate	288,300	288,300		34,700	34,700	
Testis	9,190	9,190		470	470	
Penis & other genital, male	2,050	2,050		470	470	
Urinary system	168,560	117,590	50,970	32,590	22,680	9,910
Urinary bladder	82,290	62,420	19,870	16,710	12,160	4,550
Kidney & renal pelvis	81,800	52,360	29,440	14,890	9,920	4,970
Ureter & other urinary organs	4,470	2,810	1,660	990	600	390
Eye & orbit	3,490	1,900	1,590	430	240	190
Brain & other nervous system	24,810	14,280	10,530	18,990	11,020	7,970
Endocrine system	47,230	14,340	32,890	3,240	1,560	1,680
Thyroid	43,720	12,540	31,180	2,120	970	1,150
Other endocrine	3,510	1,800	1,710	1,120	590	530
Lymphoma	89,380	49,730	39,650	21,080	12,320	8,760
Hodgkin lymphoma	8,830	4,850	3,980	900	540	360
Non-Hodgkin lymphoma	80,550	44,880	35,670	20,180	11,780	8,400
Myeloma	35,730	19,860	15,870	12,590	7,000	5,590
Leukemia	59,610	35,670	23,940	23,710	13,900	9,810
Acute lymphocytic leukemia	6,540	3,660	2,880	1,390	700	690
Chronic lymphocytic leukemia	18,740	12,130	6,610	4,490	2,830	1,660
Acute myeloid leukemia	20,380	11,410	8,970	11,310	6,440	4,870
Chronic myeloid leukemia	8,930	5,190	3,740	1,310	780	530
Other leukemia‡	5,020	3,280	1,740	5,210	3,150	2,060
Other & unspecified primary sites‡	32,590	16,810	15,780	48,160	26,130	22,030

*Rounded to the nearest 10; cases exclude basal cell and squamous cell skin cancer and in situ carcinoma except urinary bladder. About 55,720 cases of female breast ductal carcinoma in situ and 89,070 cases of melanoma in situ will be diagnosed in 2023. †Cases and deaths for colon cancer include appendix. Deaths for colon and rectal cancers are combined because a large number of deaths from rectal cancer are misclassified as colon. ‡More deaths than cases may reflect lack of specificity in recording underlying cause of death on death certificates and/or an undercount in the case estimate.

Source: Estimated new cases are based on 2005-2019 incidence data reported by the North American Association of Central Cancer Registries (NAACCR). Estimated deaths are based on 2006-2020 US mortality data, National Center for Health Statistics, Centers for Disease Control and Prevention.

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Risk factors for Lung Cancer

- Cigarette smoking is by far the most important risk factor for lung cancer; risk increases with both quantity and duration of smoking. E-cigarettes & Vaping?

- Cigar and pipe smoking also increased risk.

- Exposure to radon gas released from soil and building materials is estimated to be the second leading cause of lung cancer in Europe and North America.

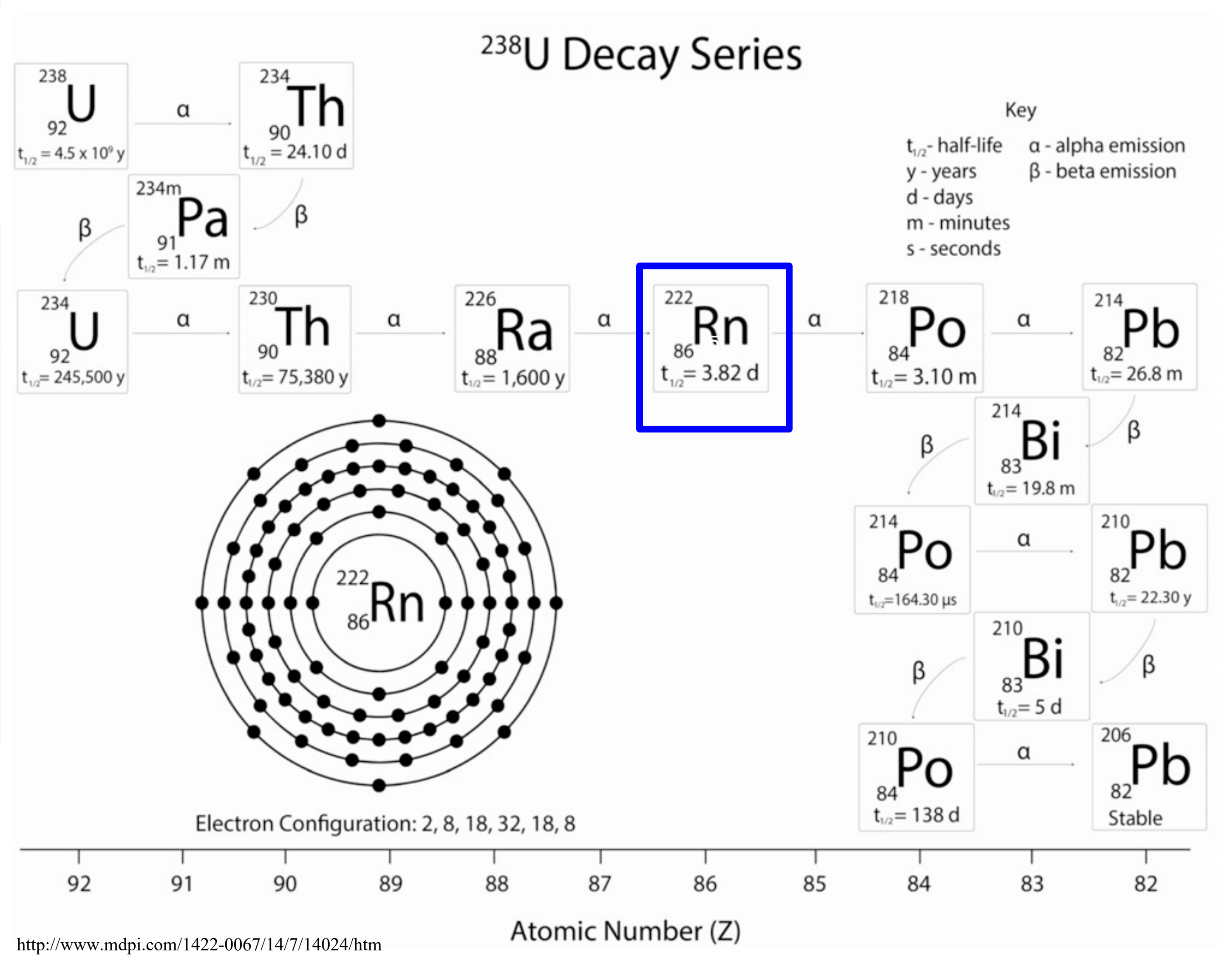
- Other risk factors include occupational or environmental exposure to secondhand smoke, asbestos (particularly among smokers), certain metals (chromium, cadmium, arsenic), some organic chemicals, radiation, air pollution, diesel exhaust, and paint.

- Risk is also probably increased among people with a medical history of tuberculosis.

- Genetic susceptibility plays a contributing role in the development of lung cancer, especially in those who develop the disease at a young age.

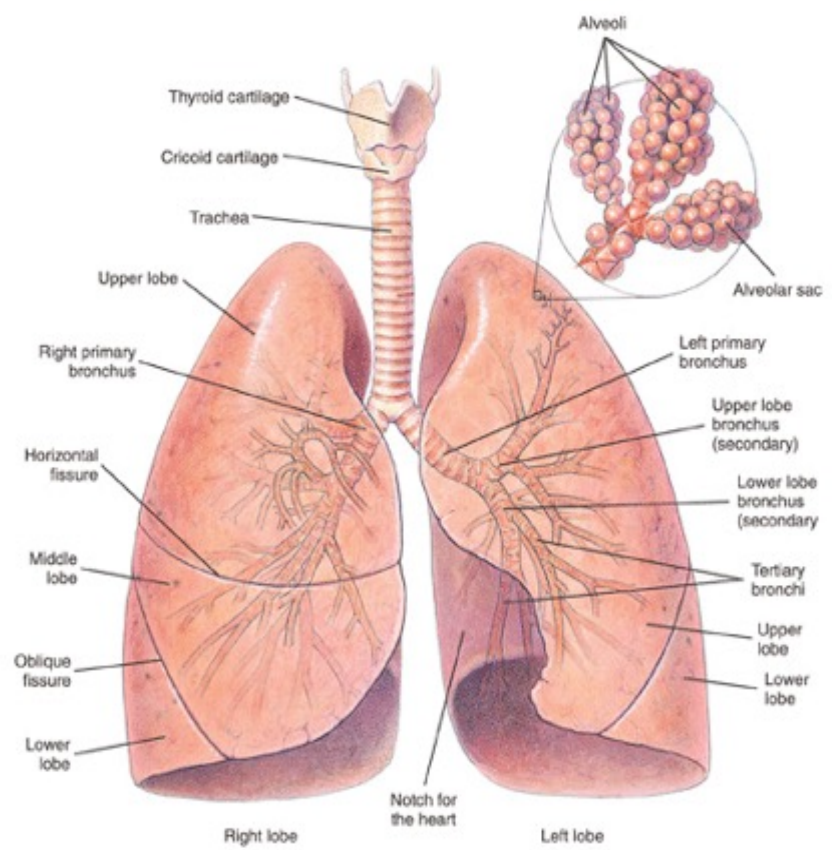
- Let’s look quickly at the secondary cause of lung cancer – radon gas.

Uranium Decay Chain

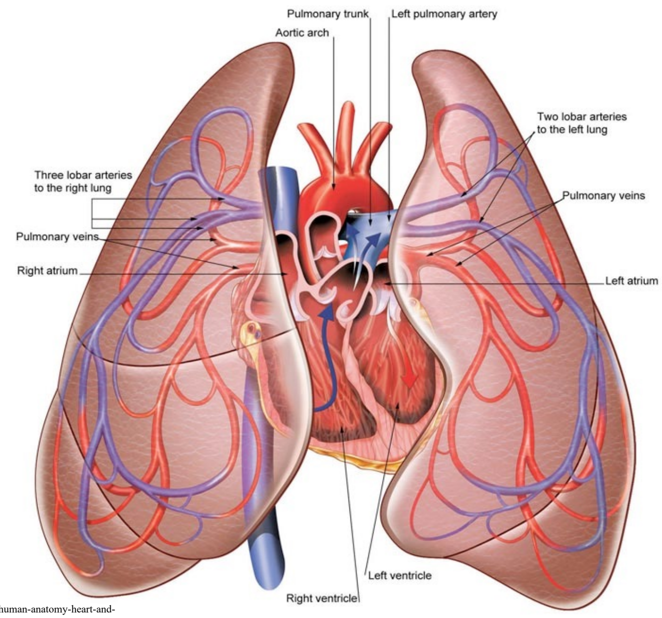


Radon is a radioactive gas that when airborne can be inhaled into the lungs where it decays by alpha emission.

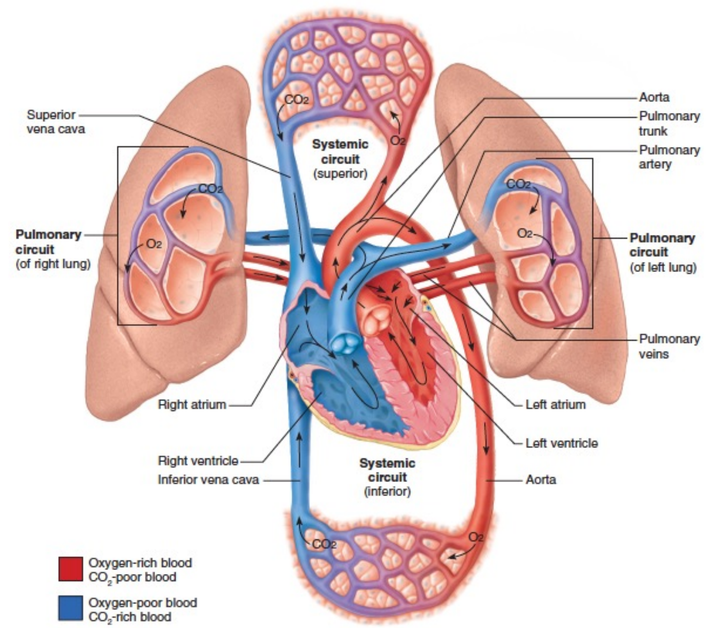
Anatomy of the Lungs



http://anatomy-medicine.com/respiratory-system/57-the-lungs.html

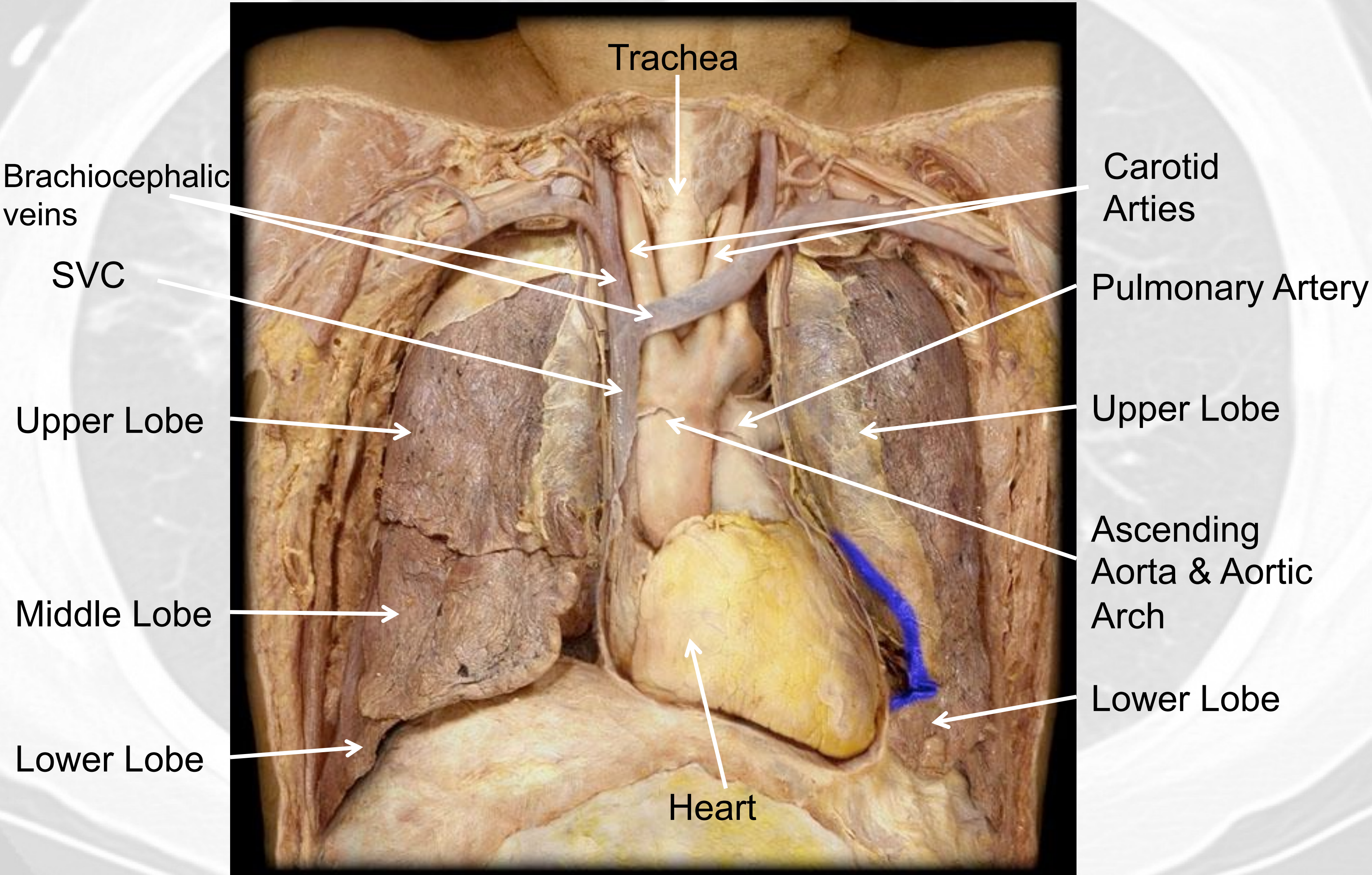


http://www.stylepinner.com/human-anatomy-heart-and-lungs/aHVtYW4tYW5hdG9teS1oZWFydC1hbmQtbHVuZ3M/

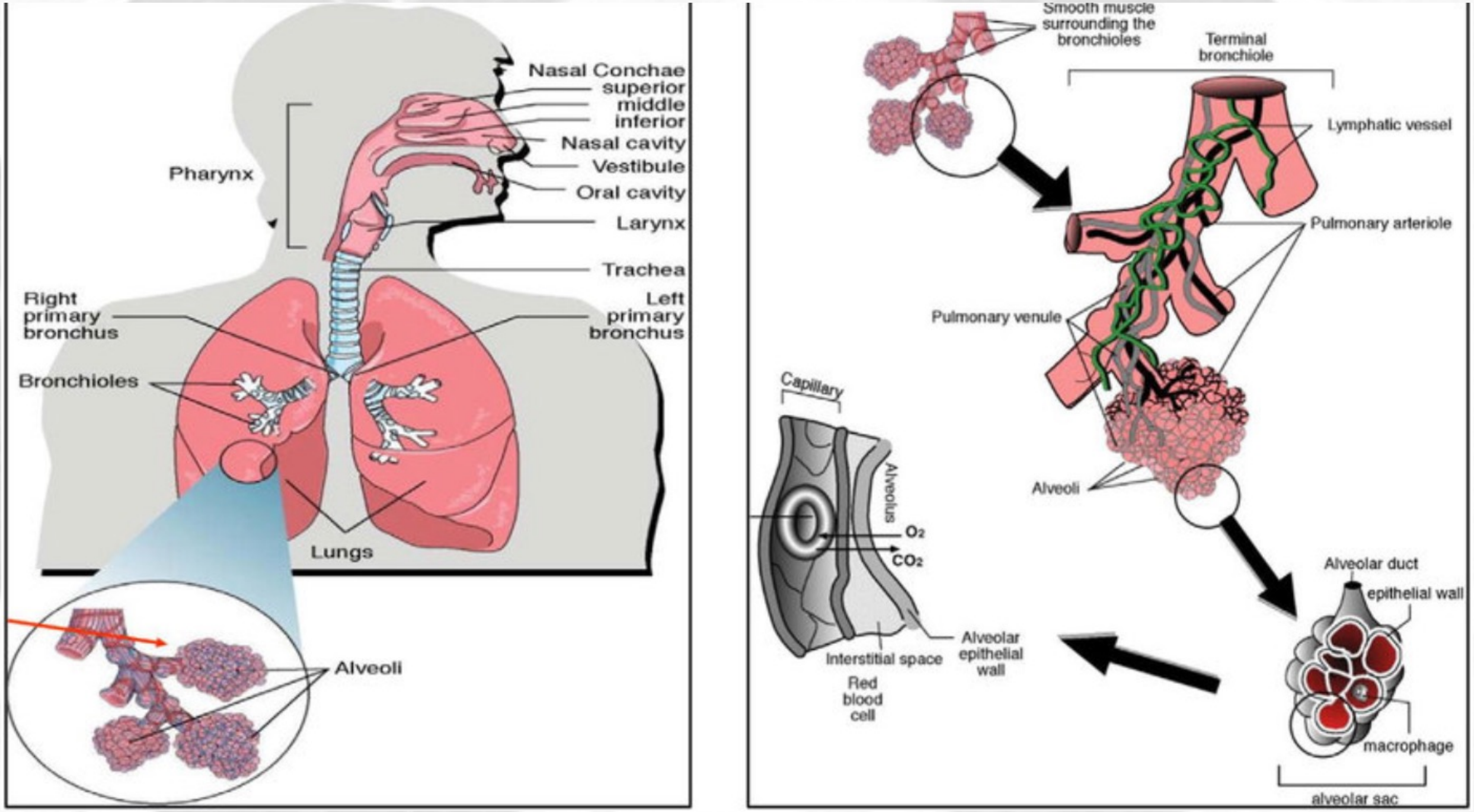


https%3A%2F%2Fgrayson.instructure.com%2Fcourses%2F63%2Ffiles%2F745964%2Fdownload%3Fwrap%3D1&bvm

Anatomical View of the Thoracic Cavity

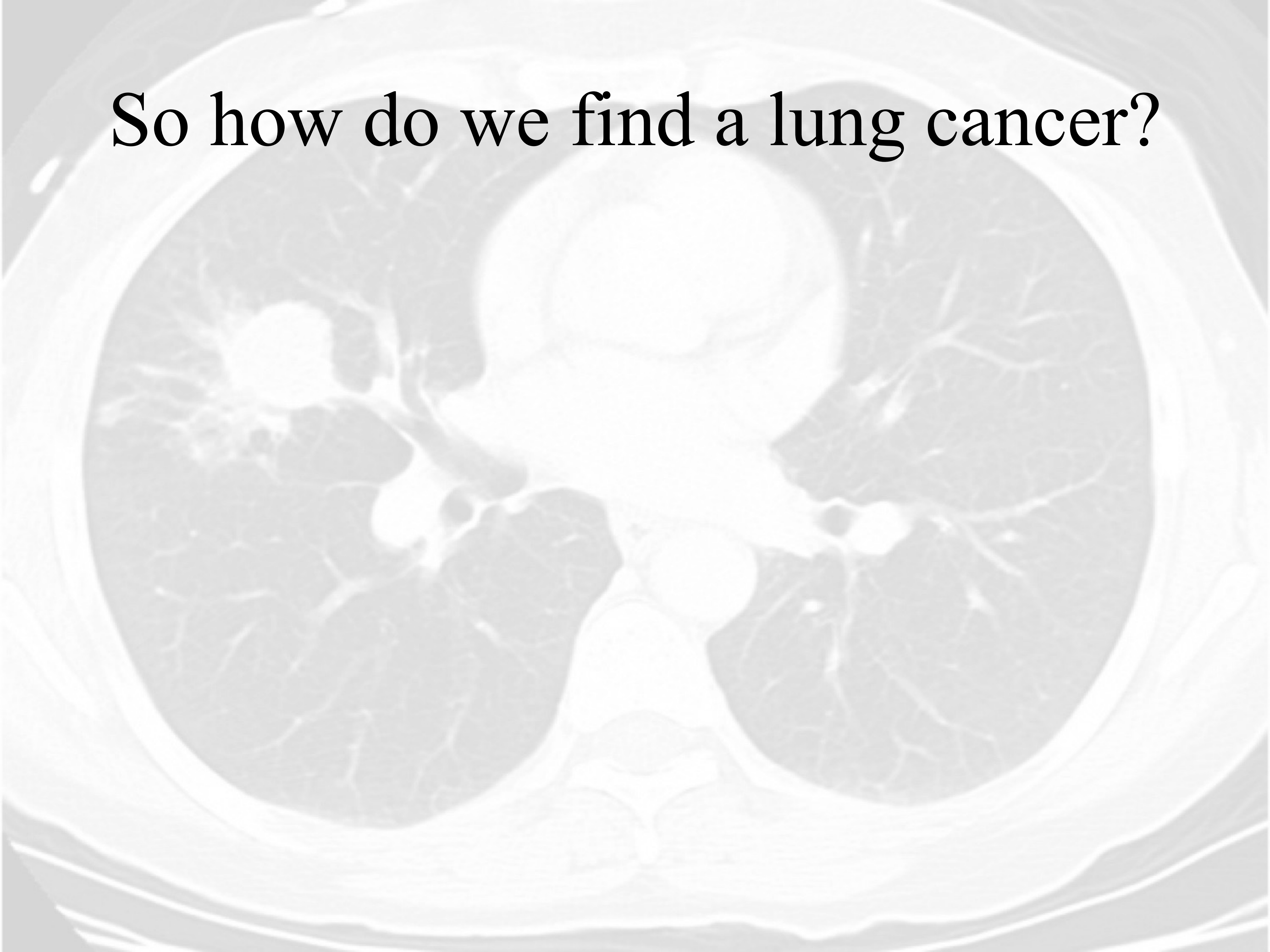


Anatomy of the Lungs



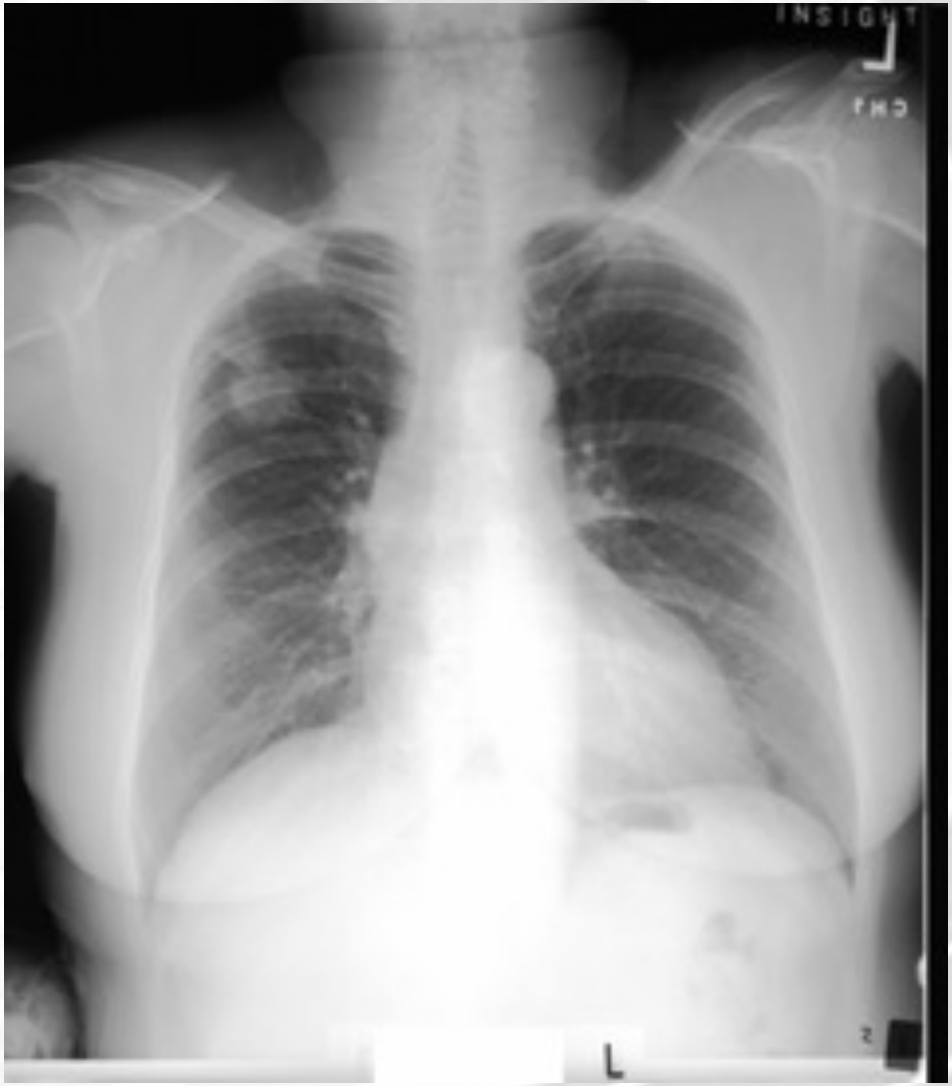
Chen, J., et al., A review of biomass burning: Emissions and impacts on air quality, health and climate in China, Sci Total Environ (2016), http://dx.doi.org/10.1016/j.scitotenv.2016.11.025

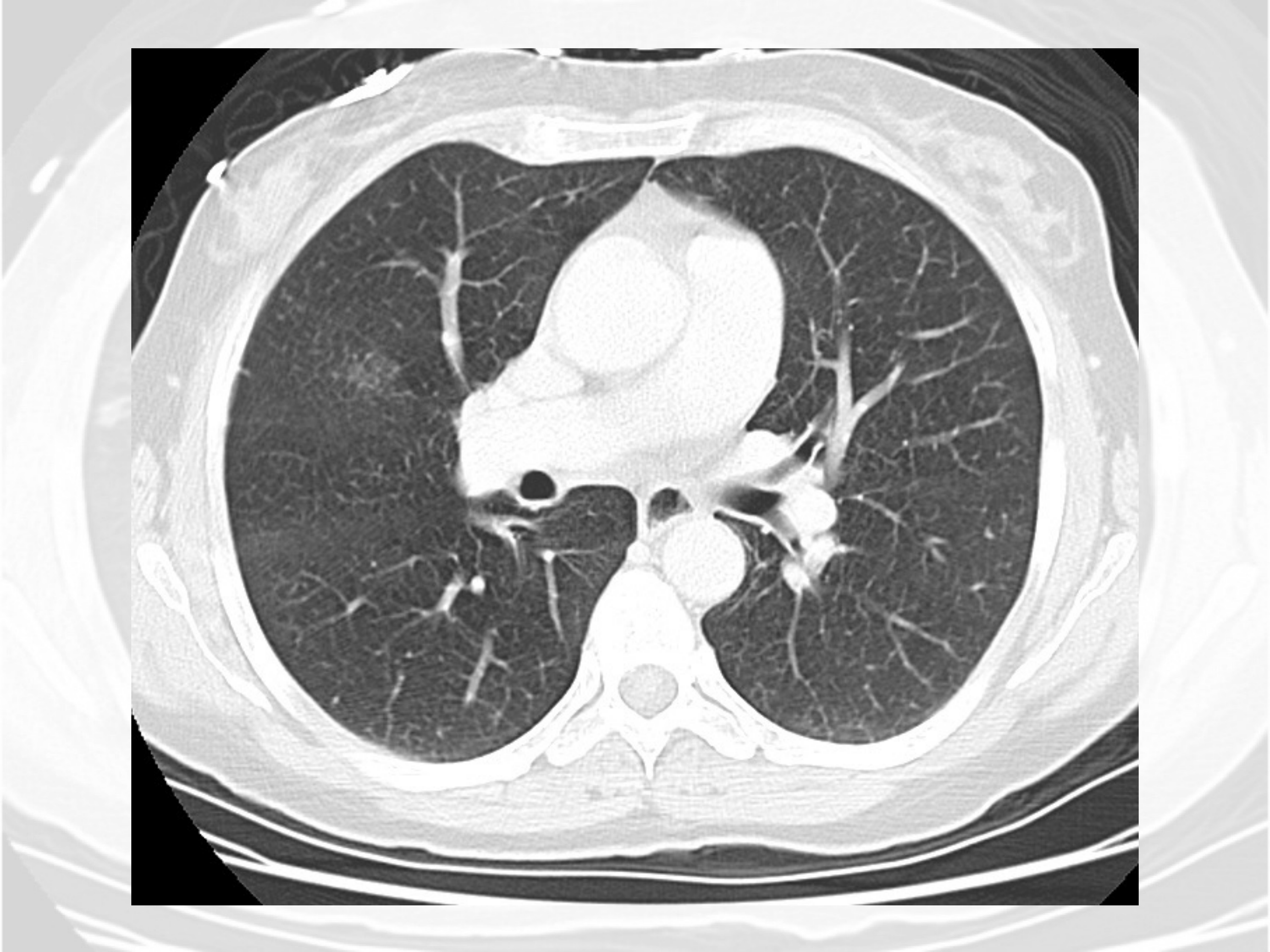
So how do we find a lung cancer?

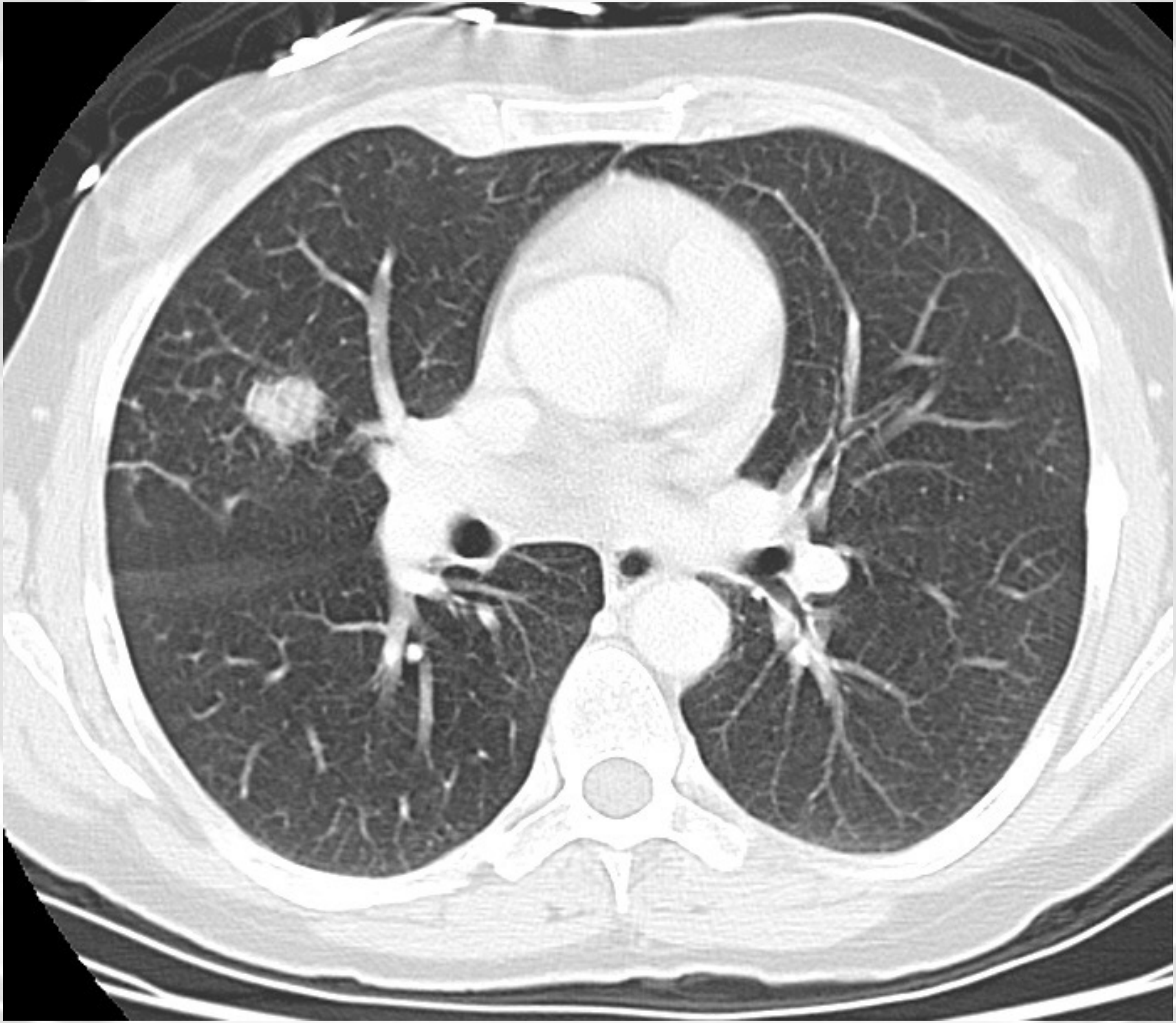


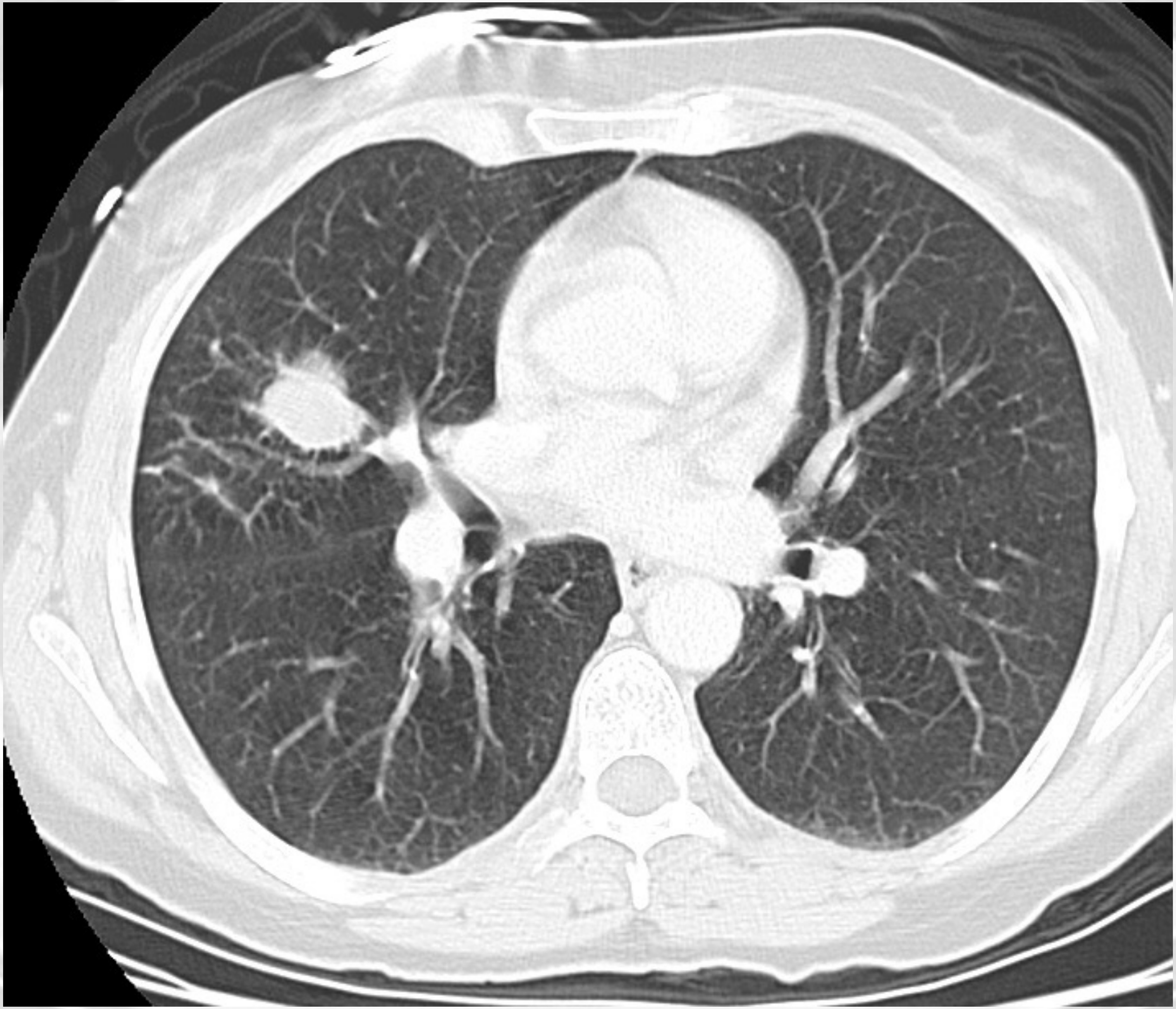
So how do we find a lung cancer?

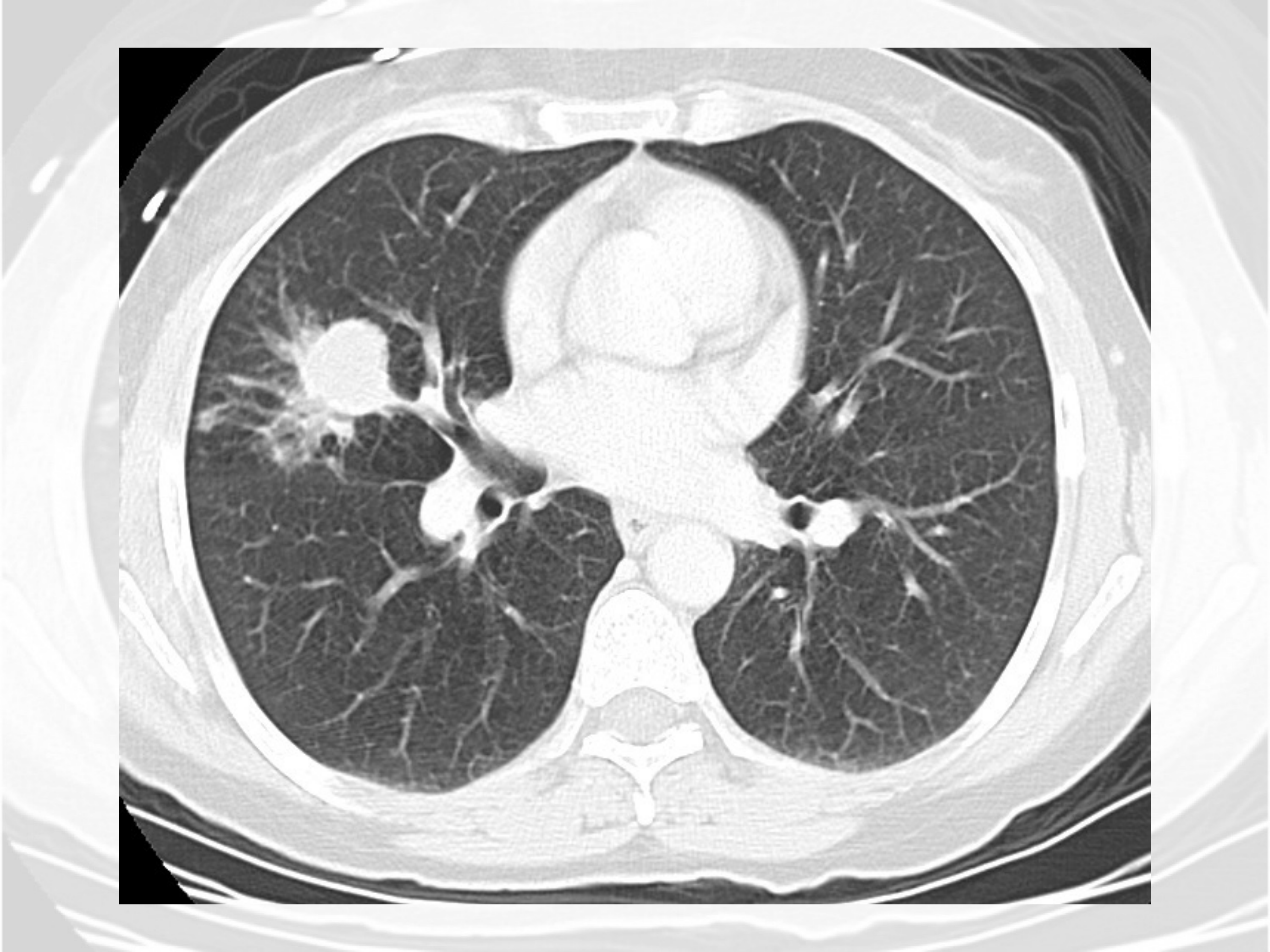
- Chest x-ray
- CT

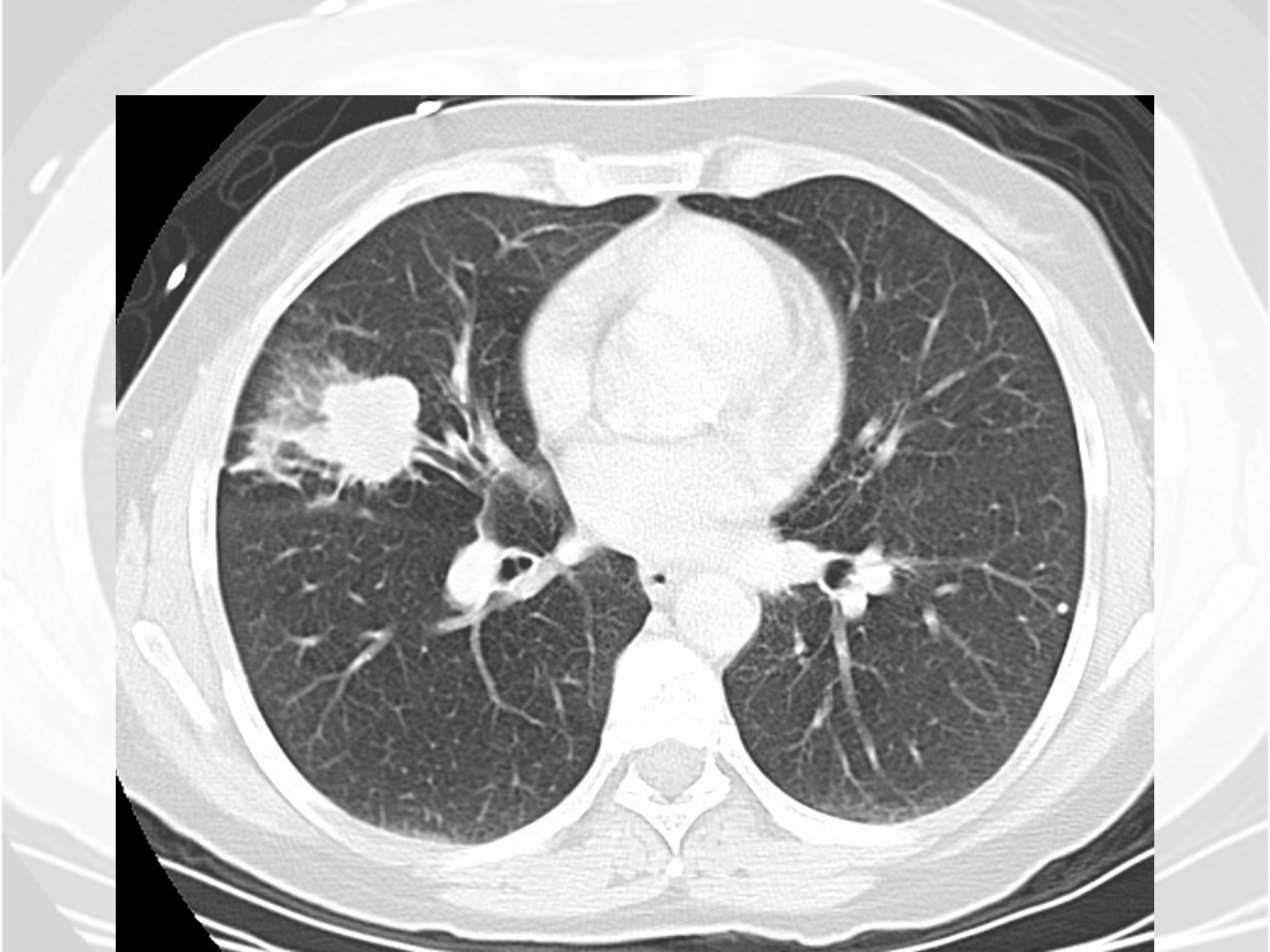


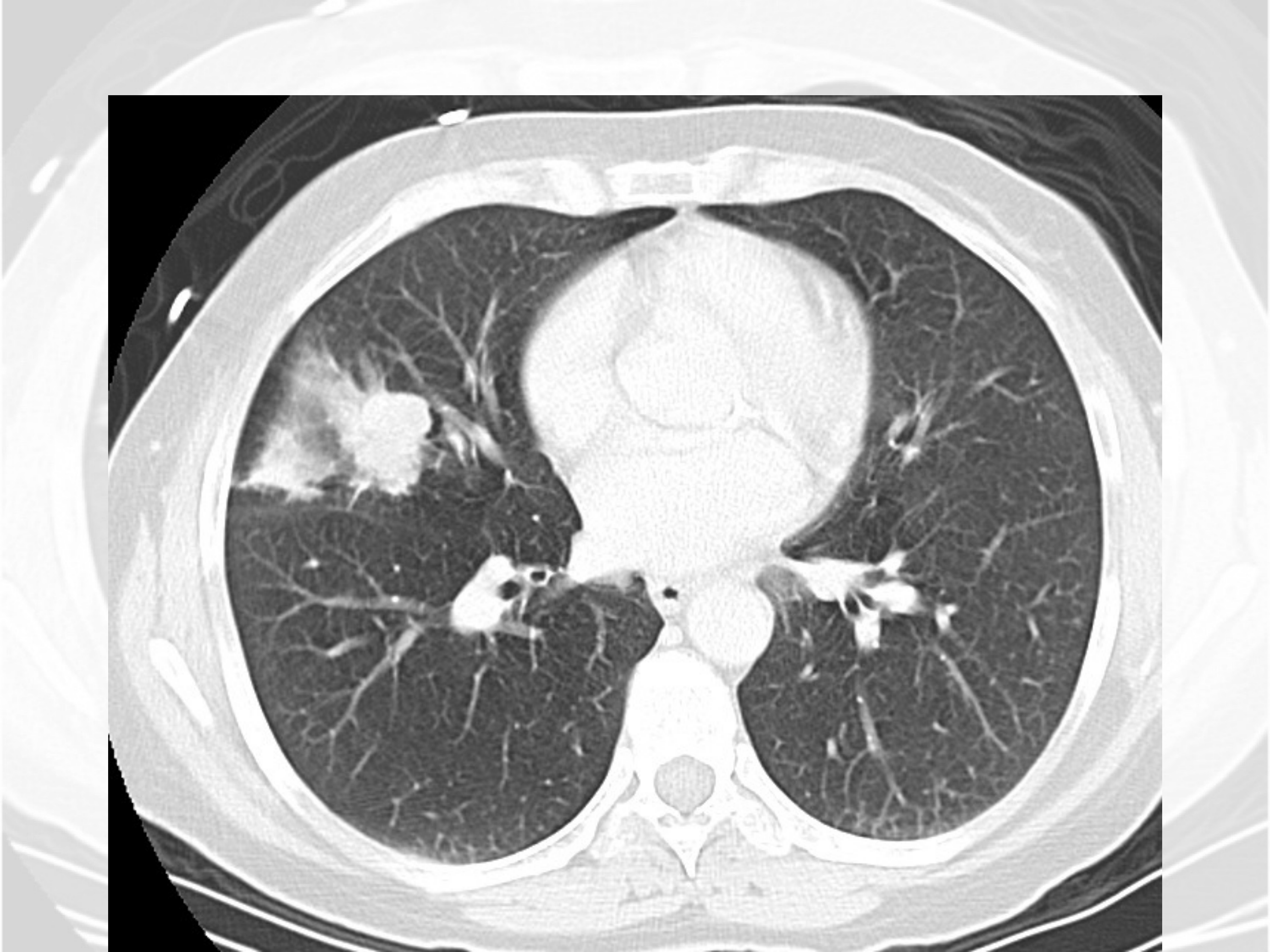


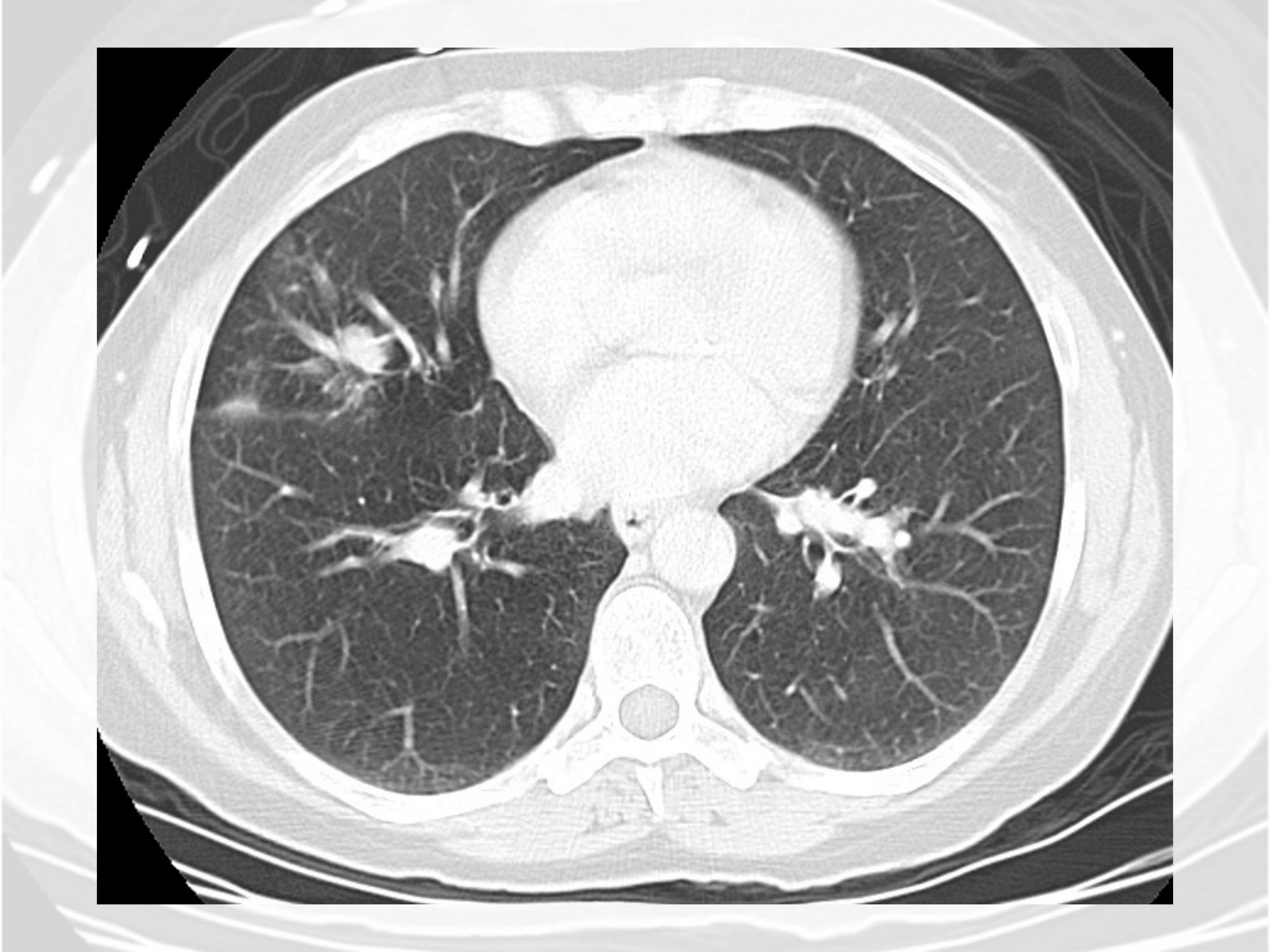








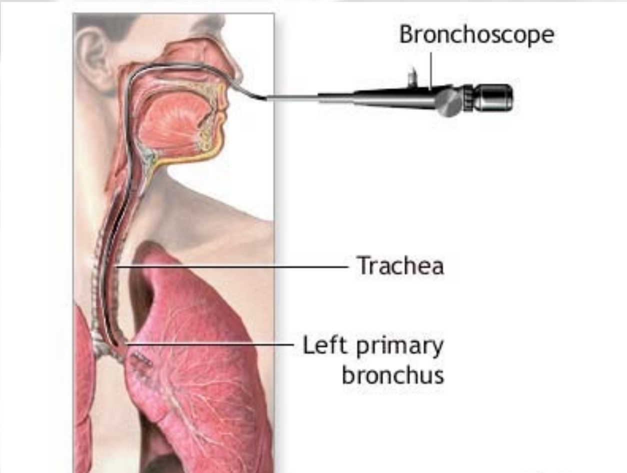




So how do we find a lung cancer?

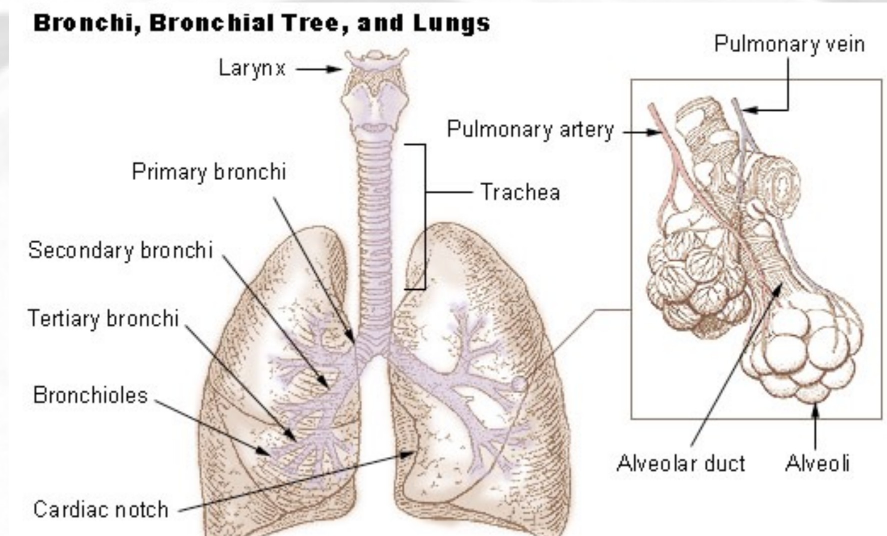
- Chest x-ray
- CT
- Bronchoscopy
- Findings metastatic disease elsewhere

Bronchoscopy



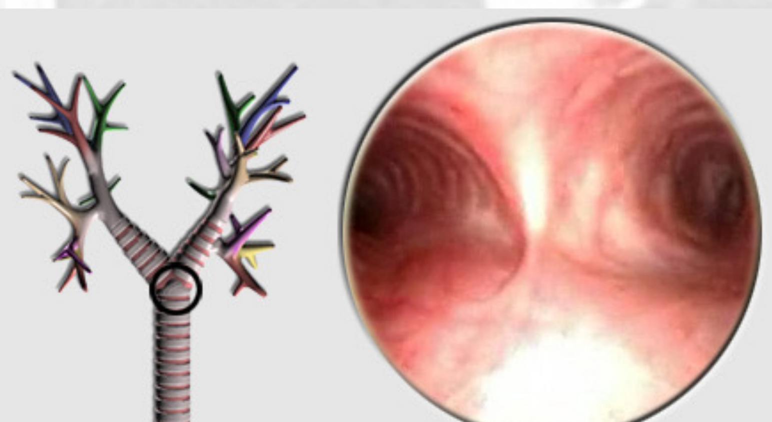
http://www.healthcentral.com/encyclopedia/adam/bronchoscopy-4020401/

Bronchoscopy Procedure



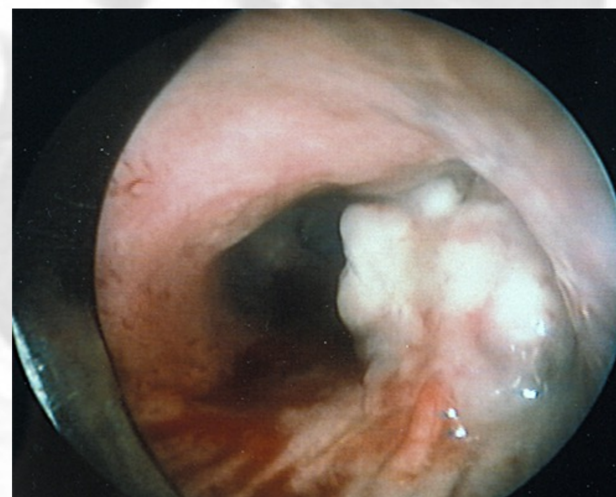
http://training.seer.cancer.gov/anatomy/respiratory/passages/bronchi.html

Anatomy of the Bronchi/Lungs



http://www.bronchotraining.org/spip.php?article95

Normal Main Right and Left Bronchi



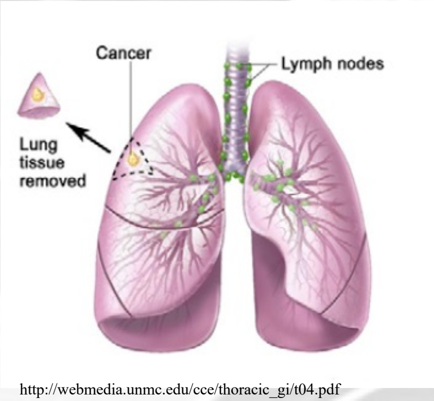
http://www.cancernetwork.com/oncology-journal/management-centrally-located-non-small-cell-carcinoma

Abnormal Bronchi

Standard Therapy for Lung Cancer:

- Lobectomy is the standard therapy for stage I non-small cell lung cancer (NSCLC).
- 5-year survivals as great as 80-90% and local recurrence rates of 5%.
- Unfortunately, only 30% of cases are resectable at the time of diagnosis.

- For the moderately compromised patient, sublobar resection is an option.
  - The main concern with sublobar resection is the increased local recurrence relative to lobectomy.
- For patients who are unable to tolerate pulmonary resection, external beam radiation (XRT) has traditionally been used.



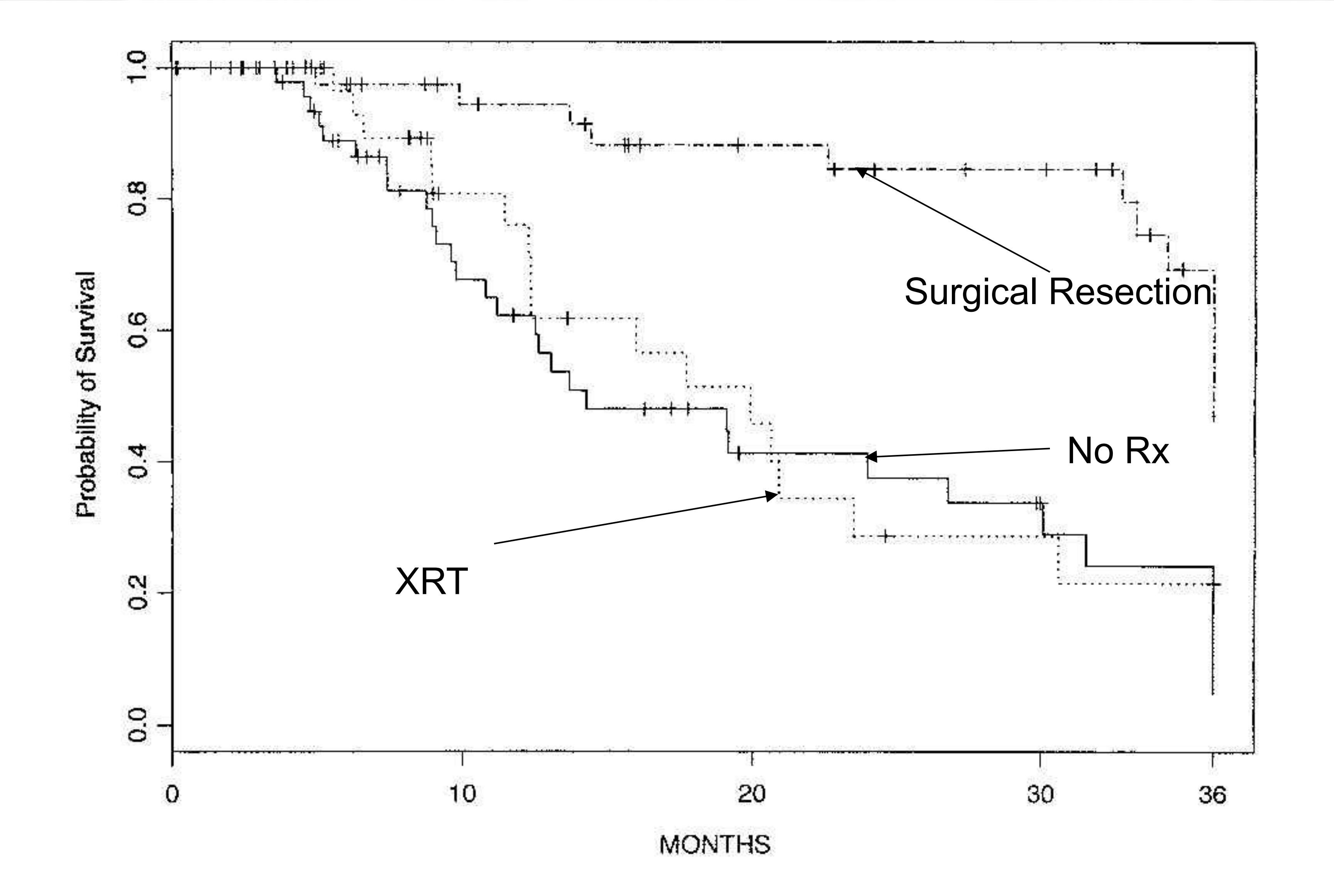
http://webmedia.unmc.edu/cce/thoracic_gi/t04.pdf

External Beam Radiation (XRT):

- Treatment results are inferior to those of resection.
  - In a study of Stage 1 Lung cancers who received XRT of at least 60 Gy.
    - 3-year survival 19%.*
    - 5-year survivals 12%.*
  - Median survival is estimated at 19.9 months.**

*Kupelian PA, Komaki R, Allen P. Int J Radiat Oncol Biol Phys. 1996;36:607-613.
** Chest: 2002;121;1155-1158

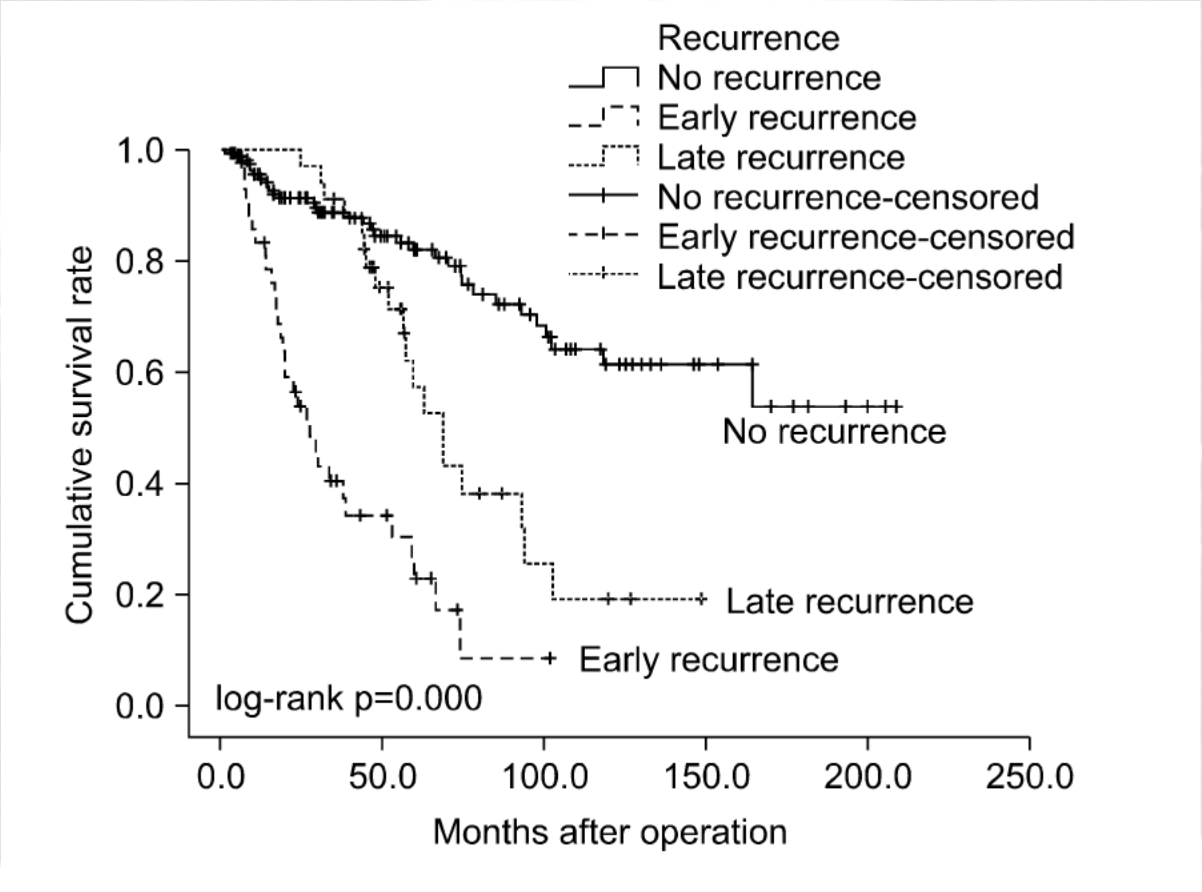
External Beam Radiation (XRT) versus Surgical Resection versus Nothing



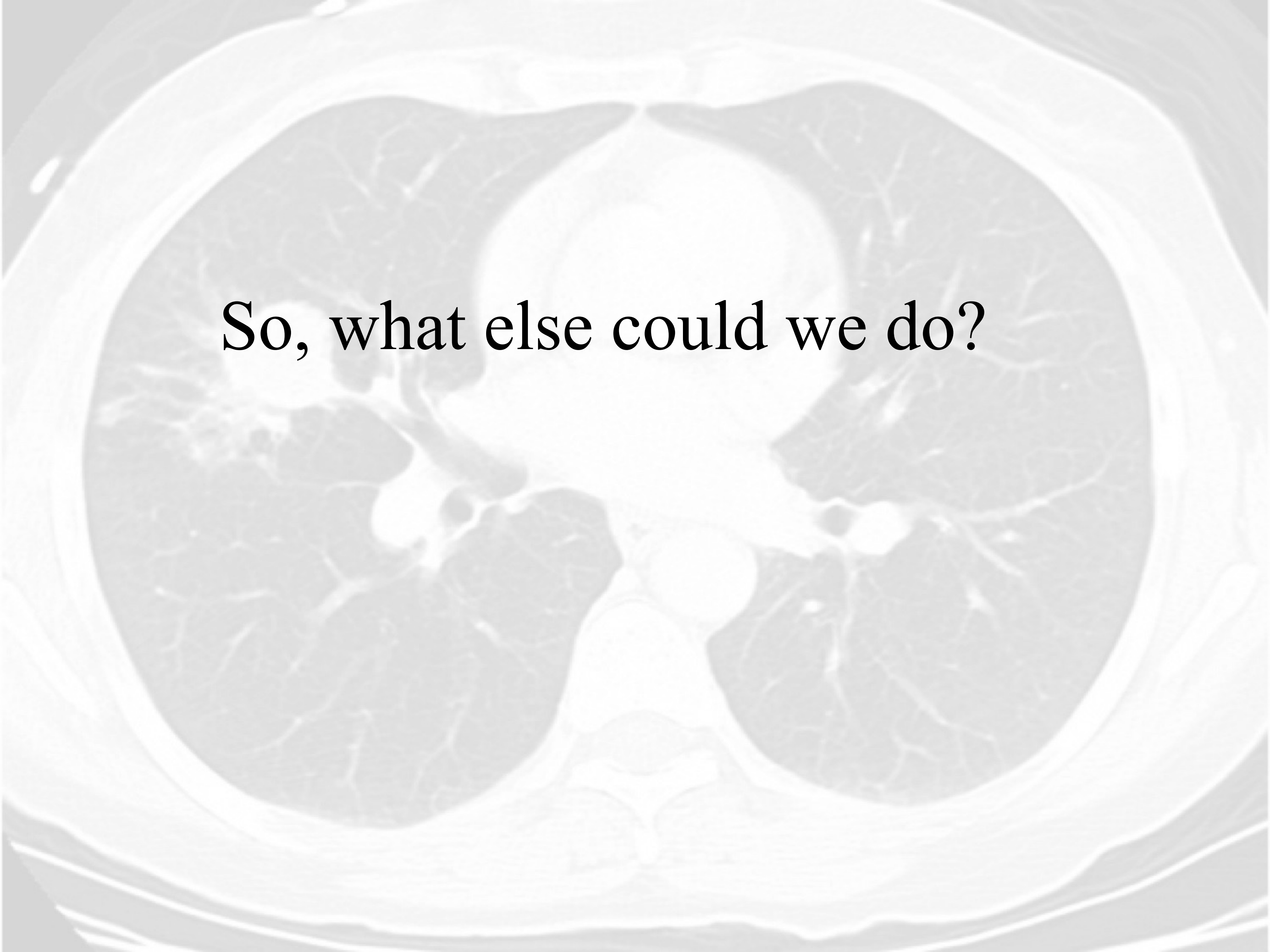
Chest: 2002;121;1155-1158
Chest: 2007; 123; 193-200

Observation-only management of early stage, medically inoperable lung cancer: Poor outcome
McGarry, Ronald C; Song, Guobin; Paul des Rosiers; Timmerman, Robert. **Chest**;
Chicago Vol. 121, Iss. 4, (Apr 2002): 1155-8.

Surgical Resection Survival Probability



Choi, Pil & Jeong, Sang & Yoon, Sung. (2013). Prognosis of Recurrence after Complete Resection in Early-Stage Non-Small Cell Lung Cancer. The Korean journal of thoracic and cardiovascular surgery. 46. 449-56. 10.5090/kjtcs.2013.46.6.449.



So, what else could we do?

Local therapy has been tried

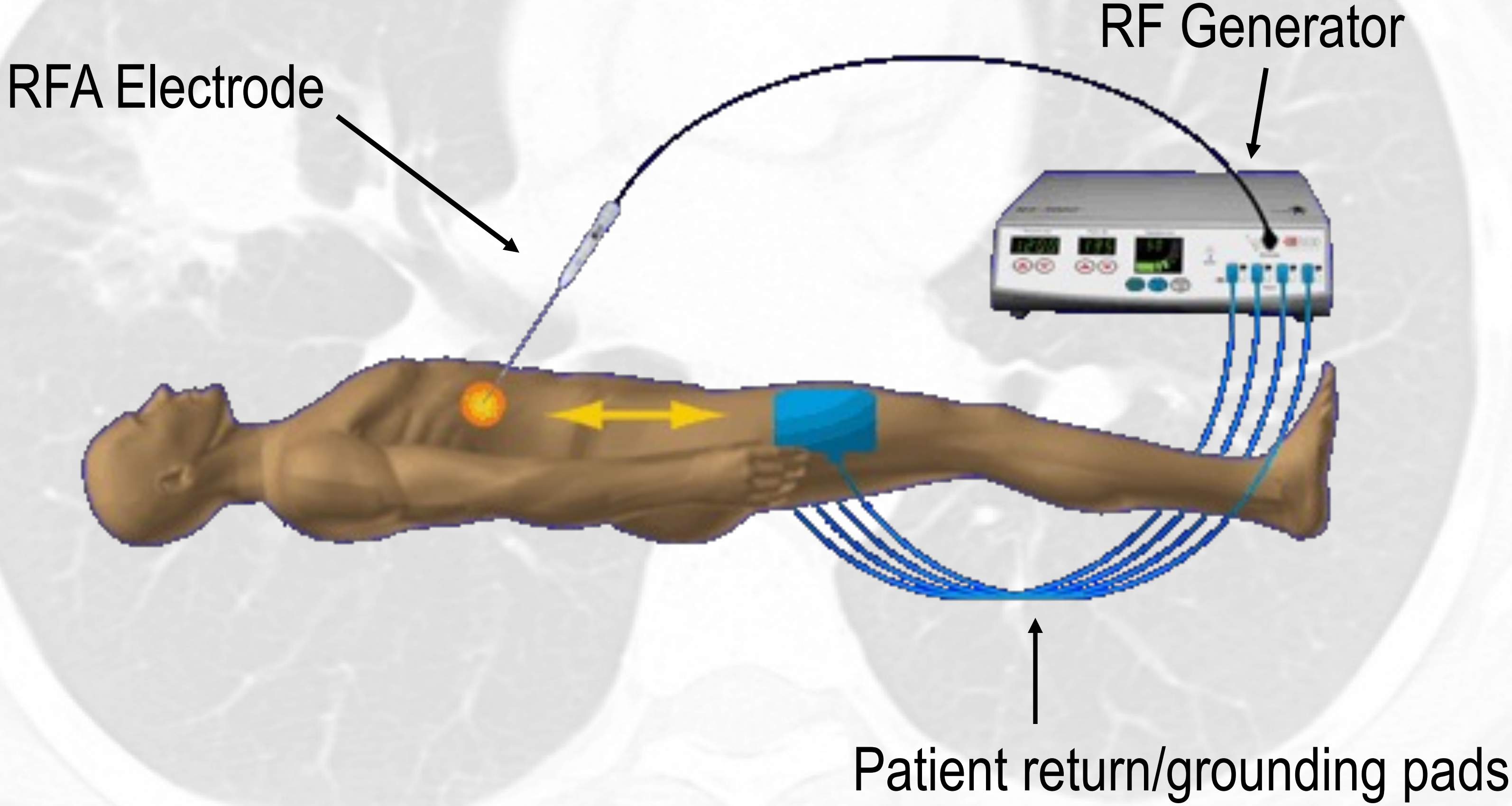
- What is the goal?
  - Cure
- What could we use?
  - Laser
  - Radionuclides
  - Radiofrequency
  - Freezing
  - Heating

General Ablation Technique:

- CT guidance is used for ALL lung applications

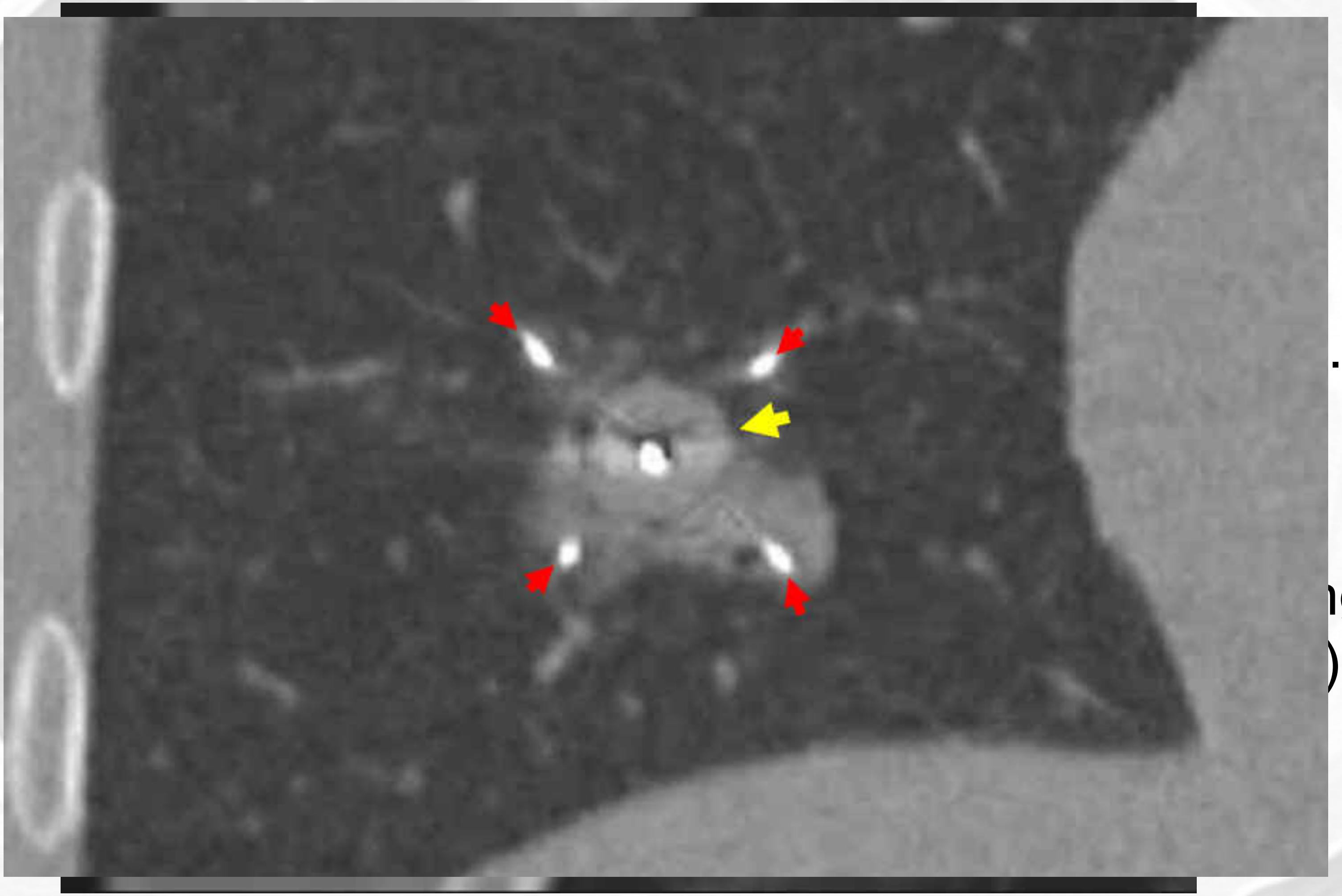
- We use general Anesthesia for all procedures.
  - Total anesthesia time is about 1-1.5 hours.

RFA technique:

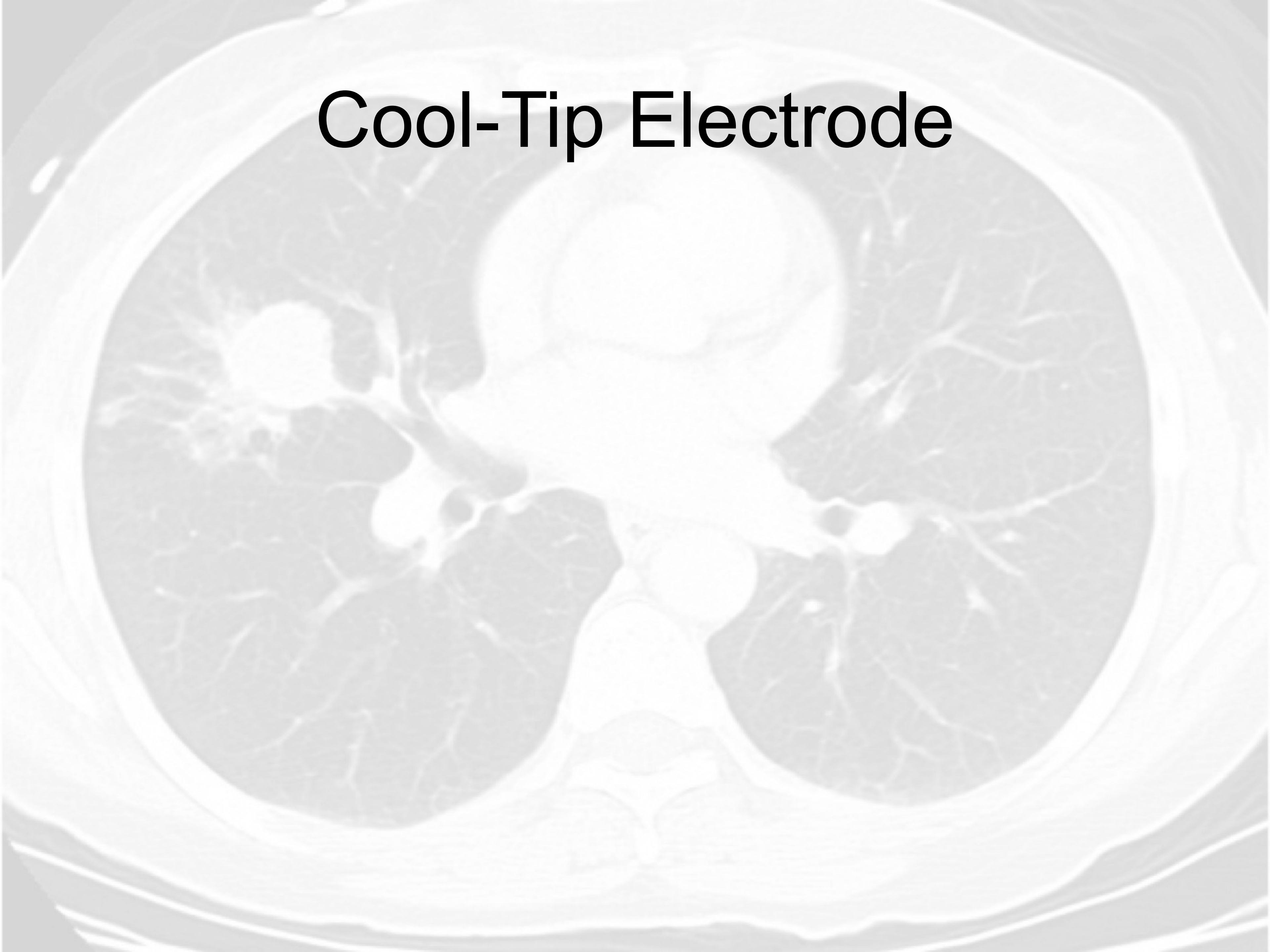


RFA technique:

RITA/Angiodynamics



Cool-Tip Electrode



RFA technique:

Valley-labs

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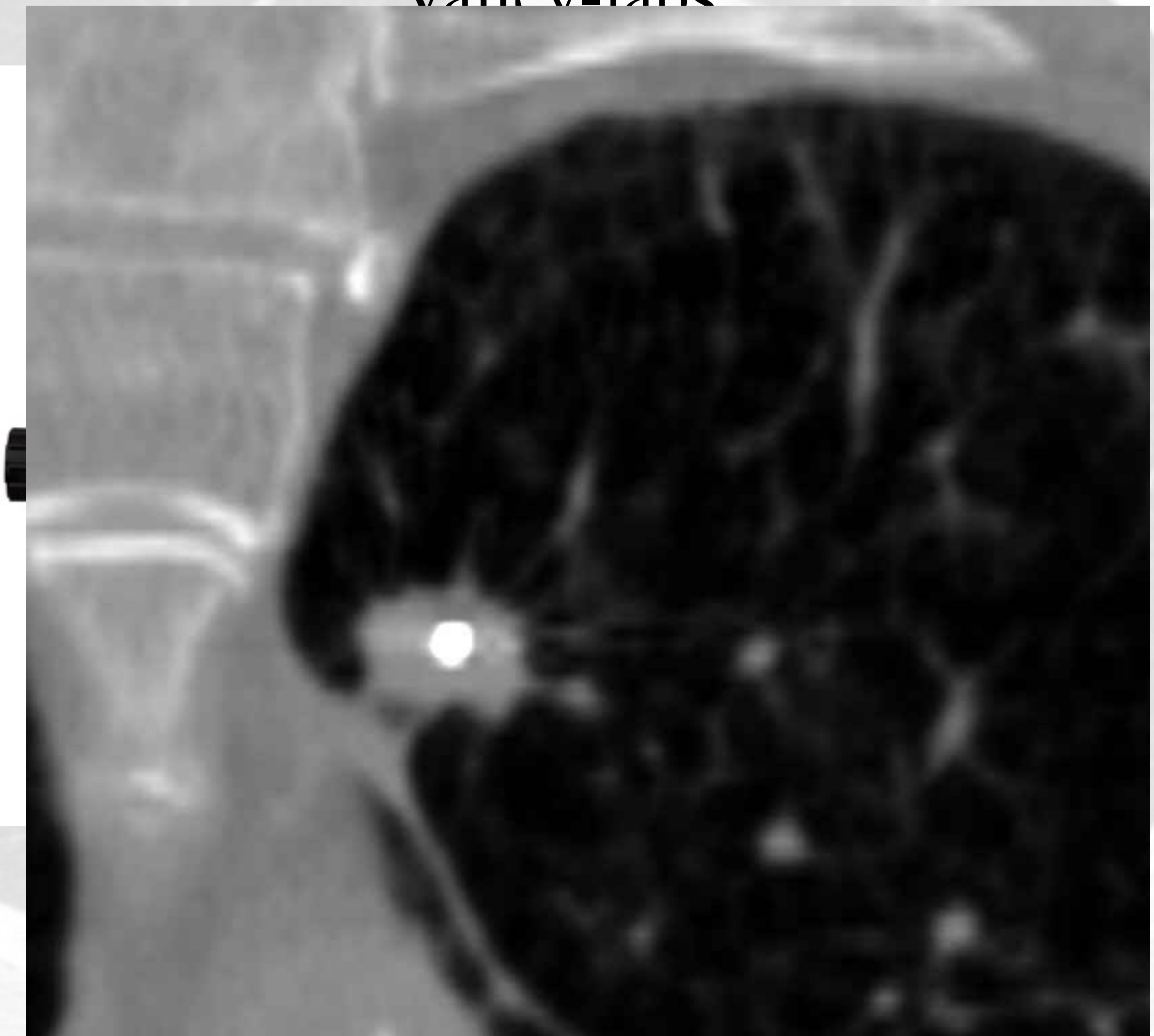
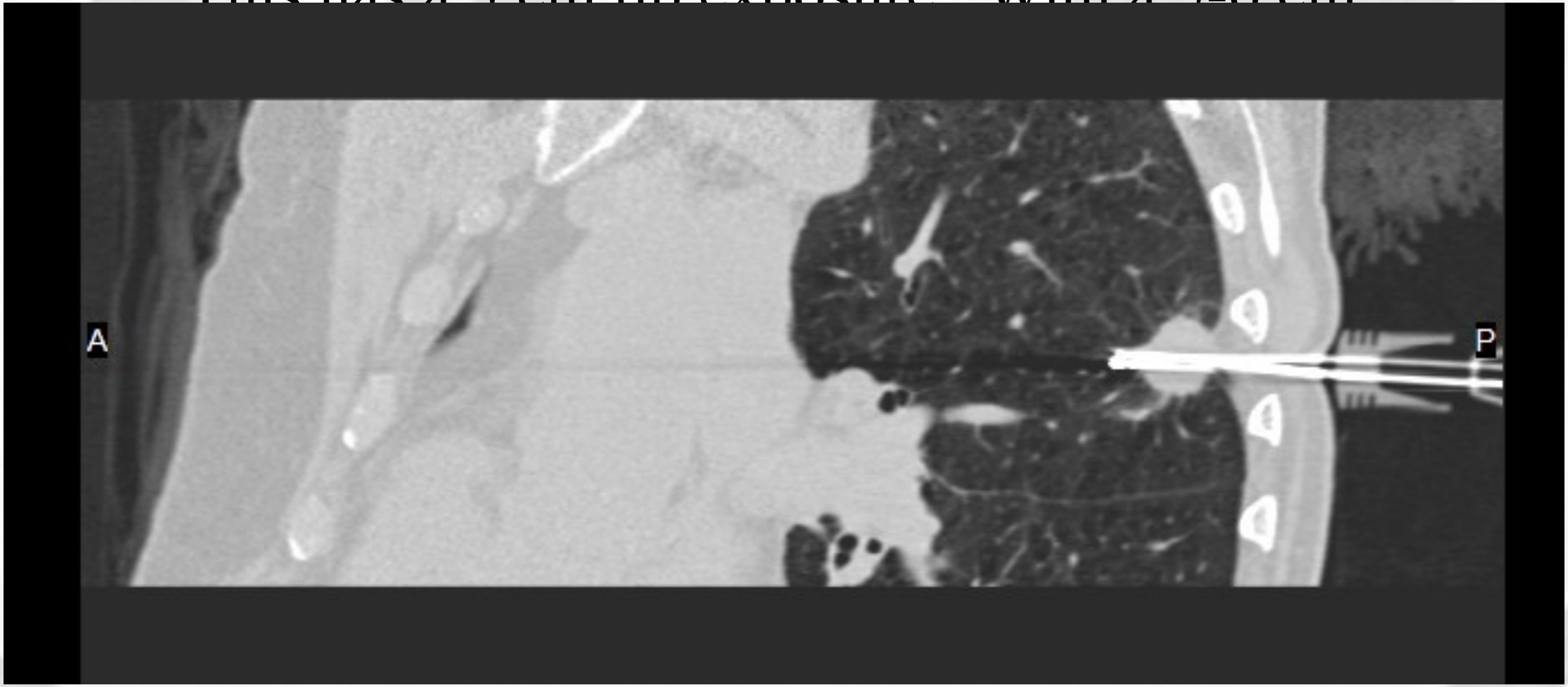
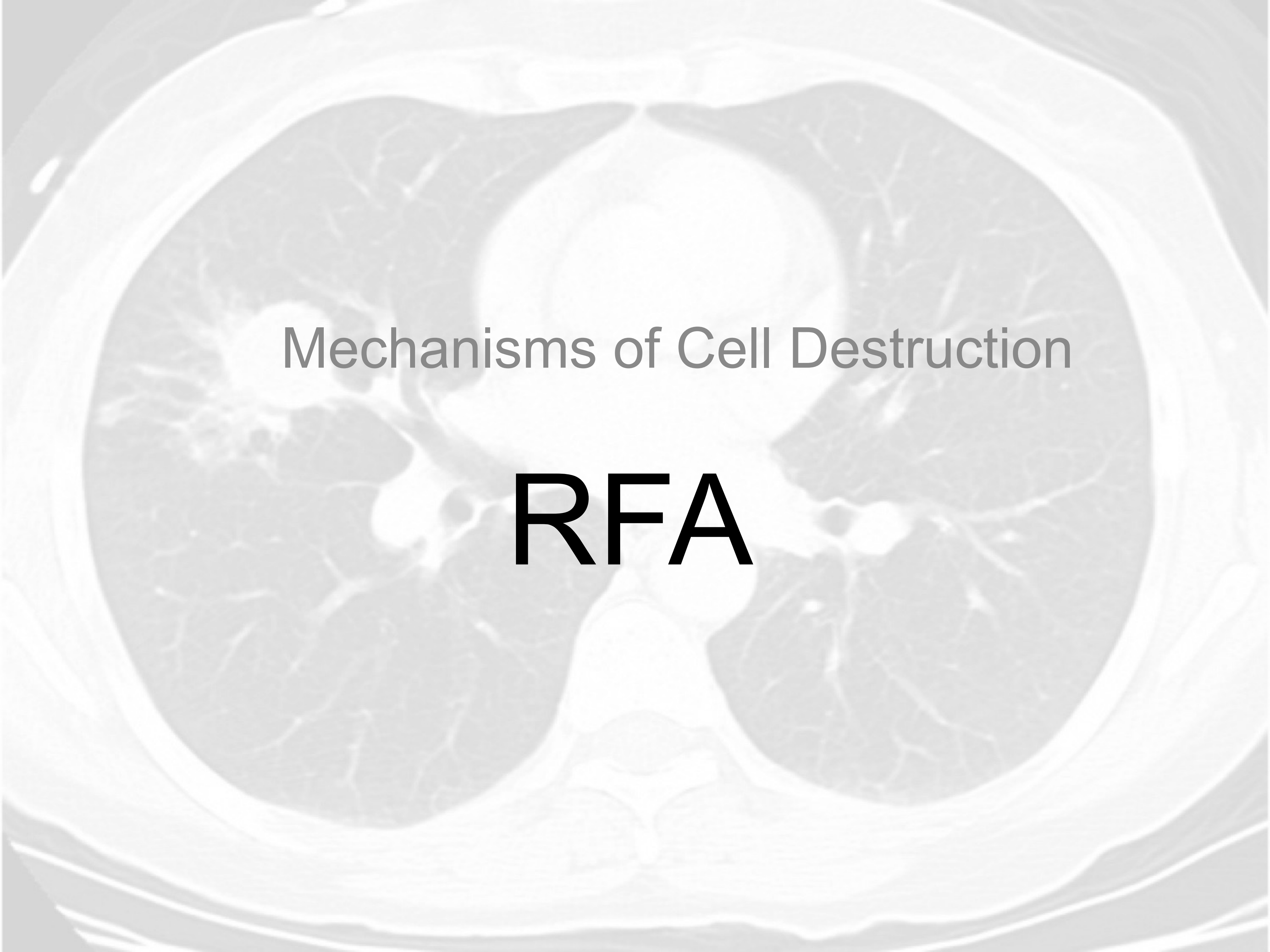


Cluster tip probe.

– Three separate tips are on this single shaft probe. This has a 3 cm tip exposure. With a 5-6 cm





Mechanisms of Cell Destruction

RFA

Tumor Biology with RFA:

- At $45^{0}C$ cellular swelling begins.
- The minimal acceptable tissue temperature for cell death is $60^{0}C$.
  - Cellular proteins are denatured
  - enzymes are deactivated
  - cellular death results.

- At $100 \; - 105^{0}C$ charring of tissue can occur.
  - Cavitation or gas formation also occur at this temperature.

- The impedance (tissue resistance to energy flow) increases dramatically.

- This is a problem in the lung because of possible air emboli to the brain.
  - Stroke is a known risk with RFA.

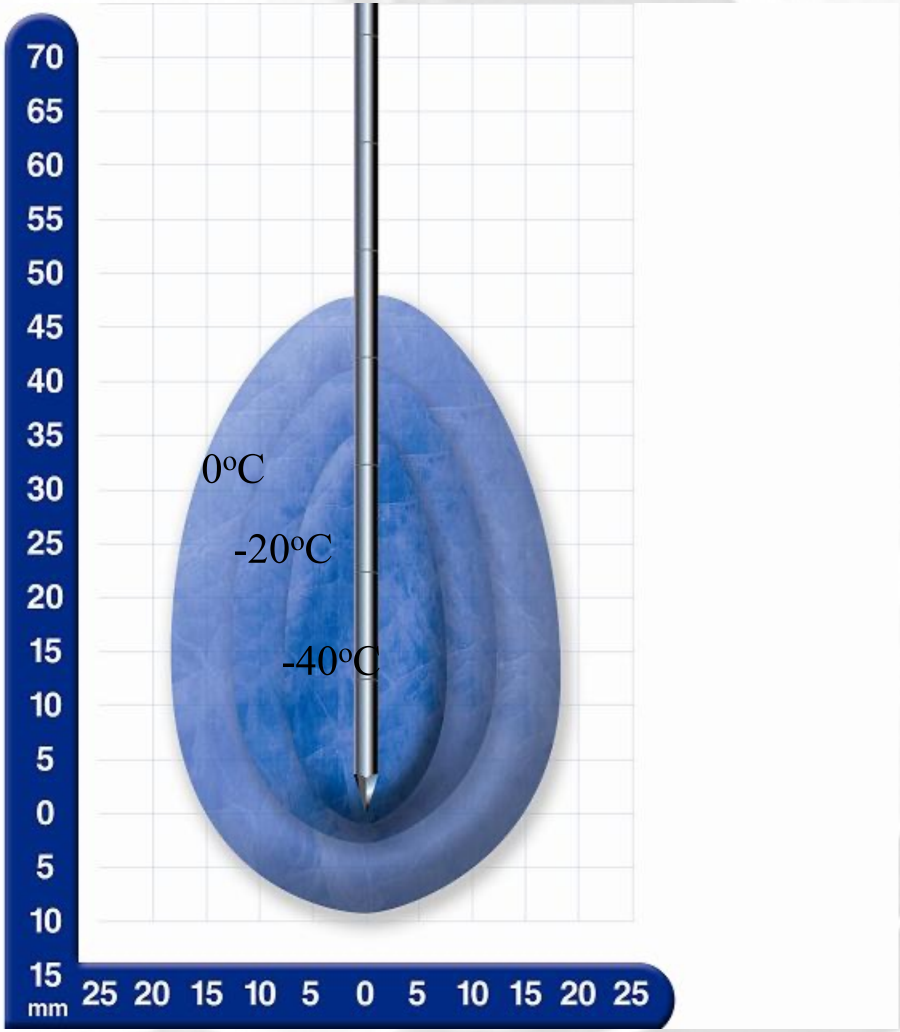
Cryoablation

- This is a freezing procedure.
- Just like the RFA we place a needle into the lesion and rather than heat it up we freeze it.

Isotherms form

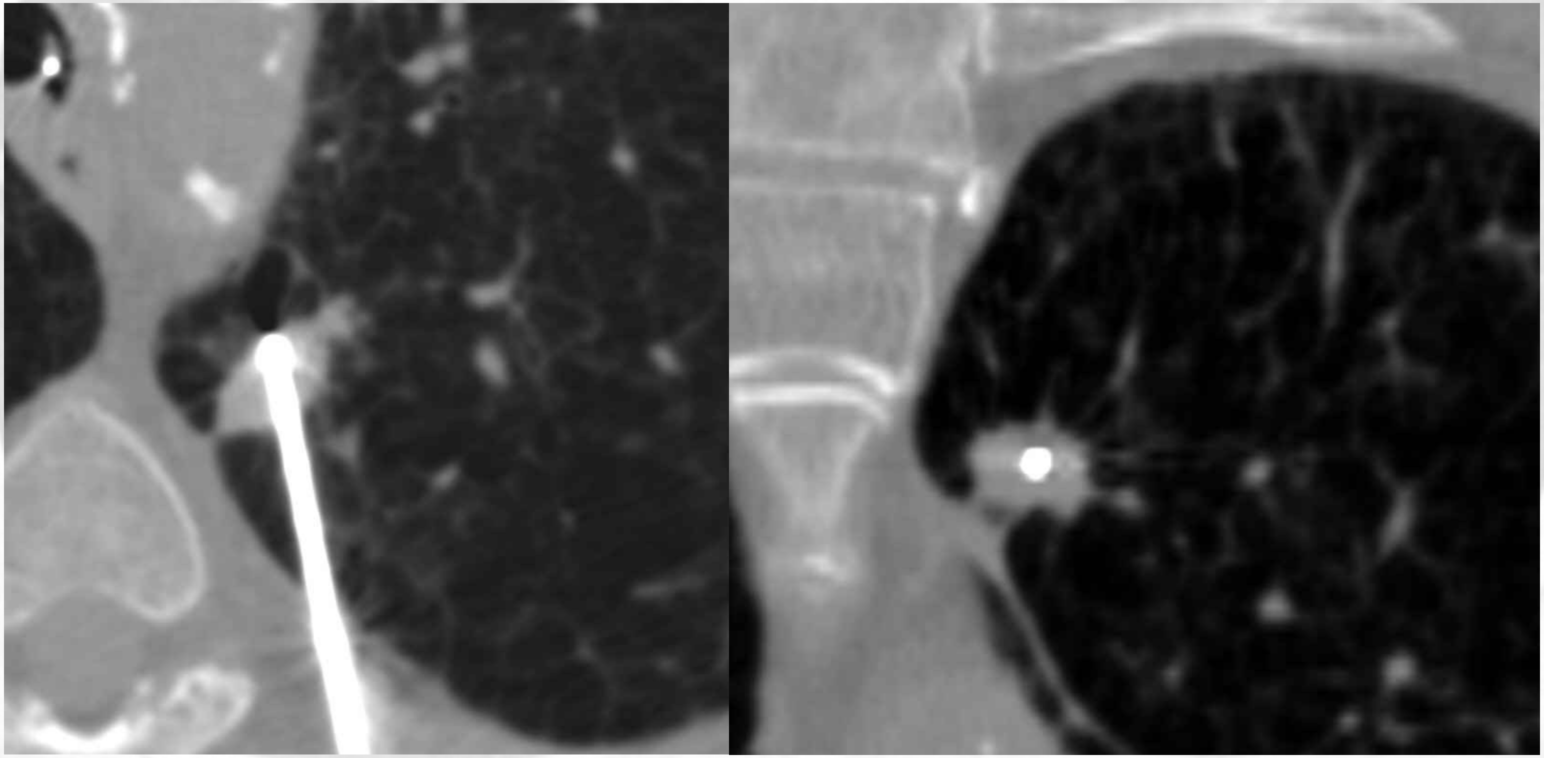
Right Angle CryoProbe

	DIAMETER (MM)	LENGTH (MM)
0ºC	37	56
-20ºC	24	44
-40ºC	16	36

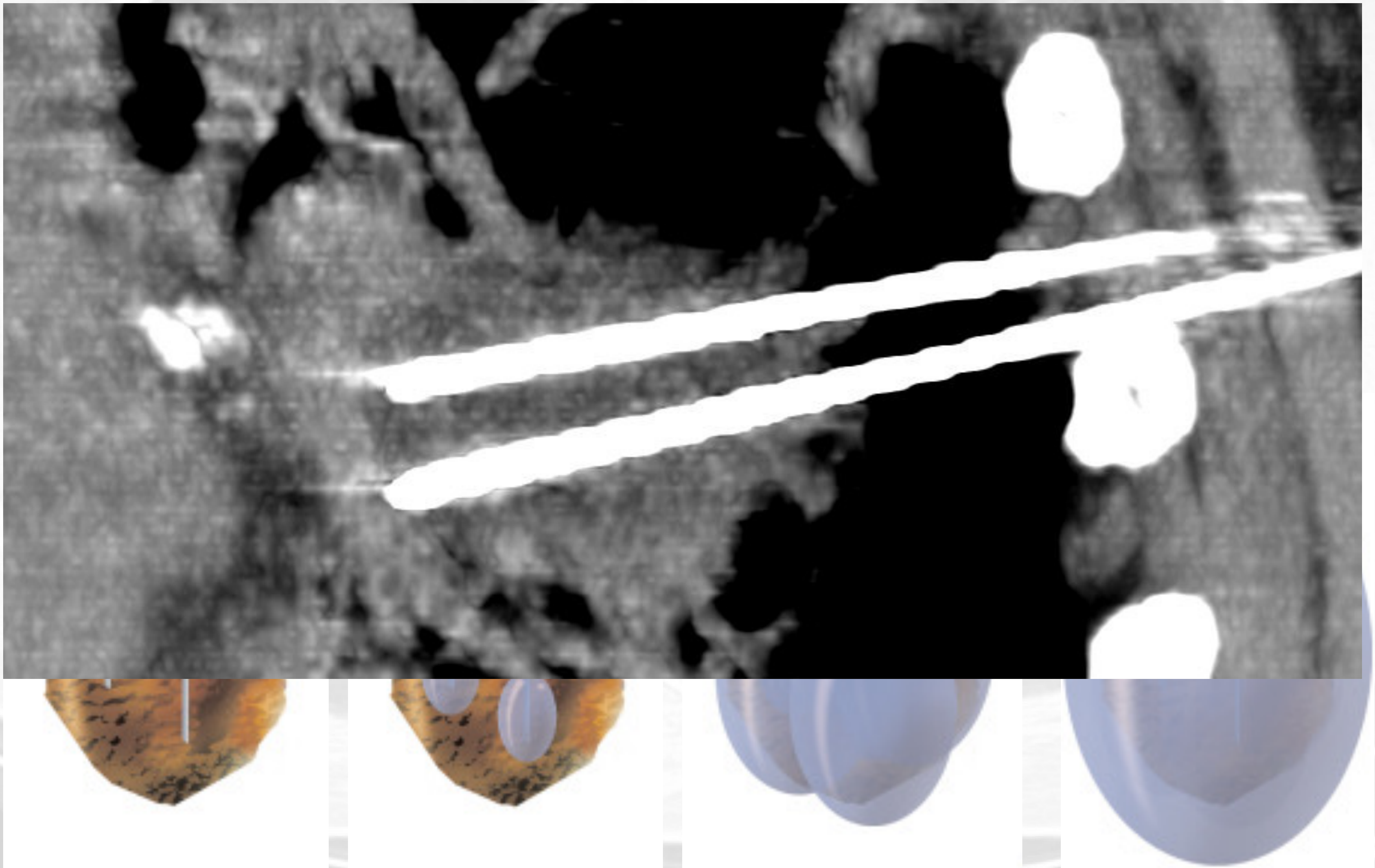


PCT Technique:

- Depends on the size of the lesion.

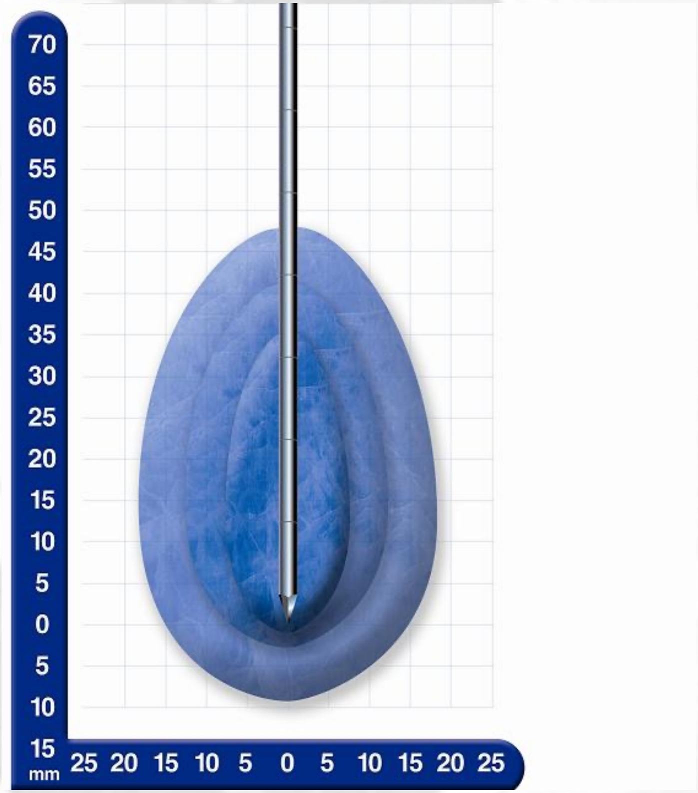


PCT Technique:



Cryoablation Protocol

- We perform a freeze-thaw-freeze cycle on all tumors.
- 10-minute freeze
  - (-40^0C)
- 8-minute thaw
  - (Never go above 0^0C)
- 10-minute freeze
- 3-minute thaw to remove the needle from the ice block.

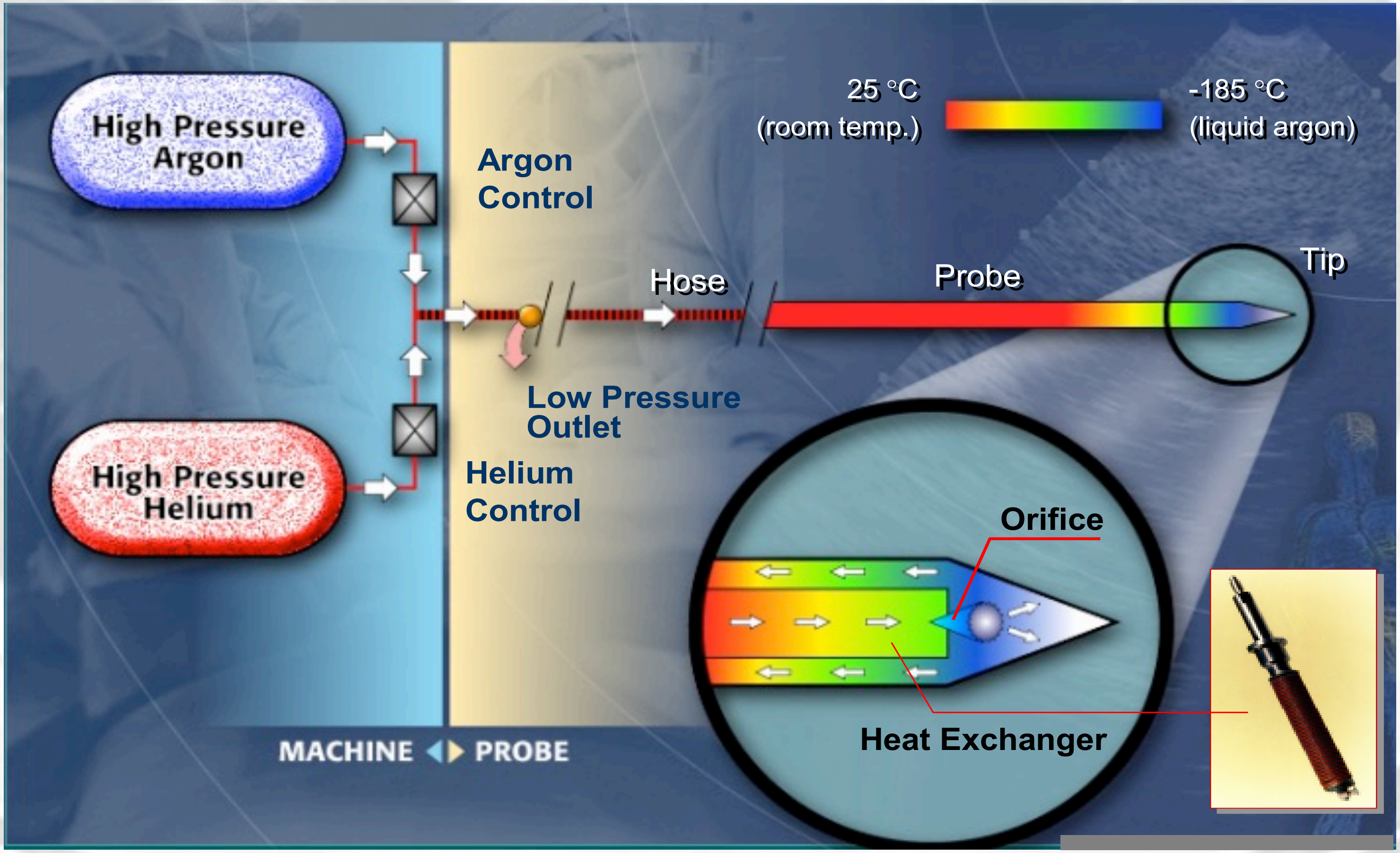


Total Ablation time 28 minutes

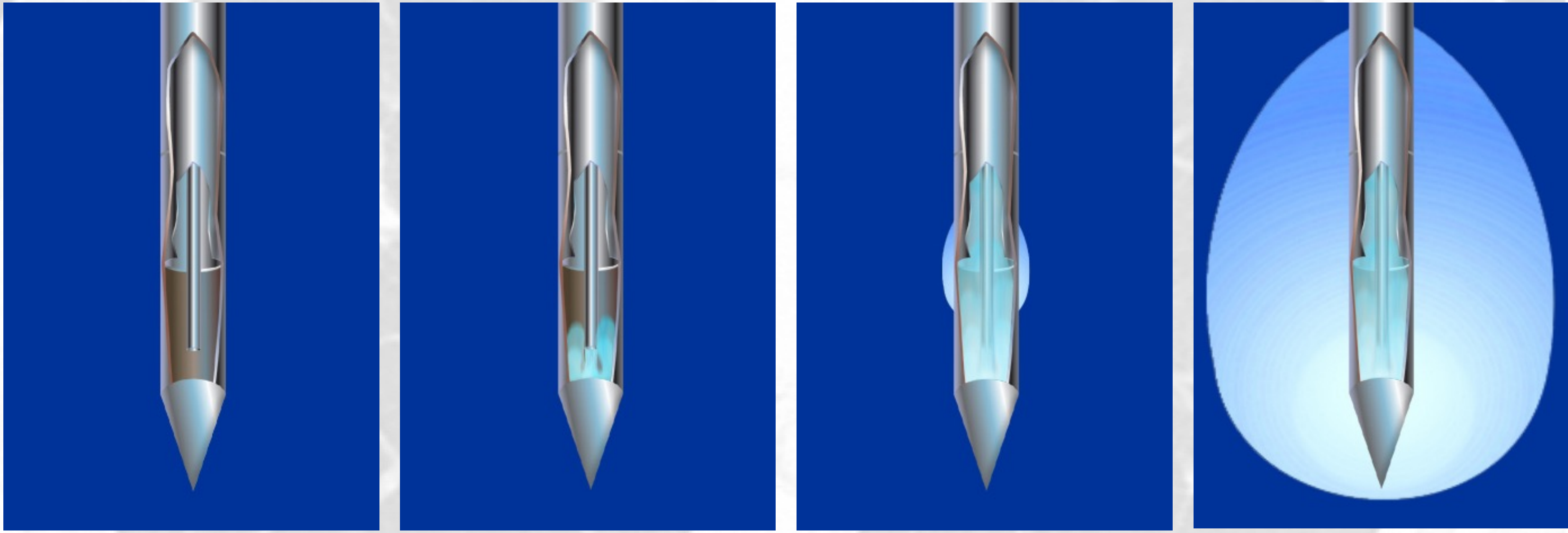
1996
Argon Based
Joule-Thompson Cryoprobes

To freeze

To warm



Ice Ball Formation

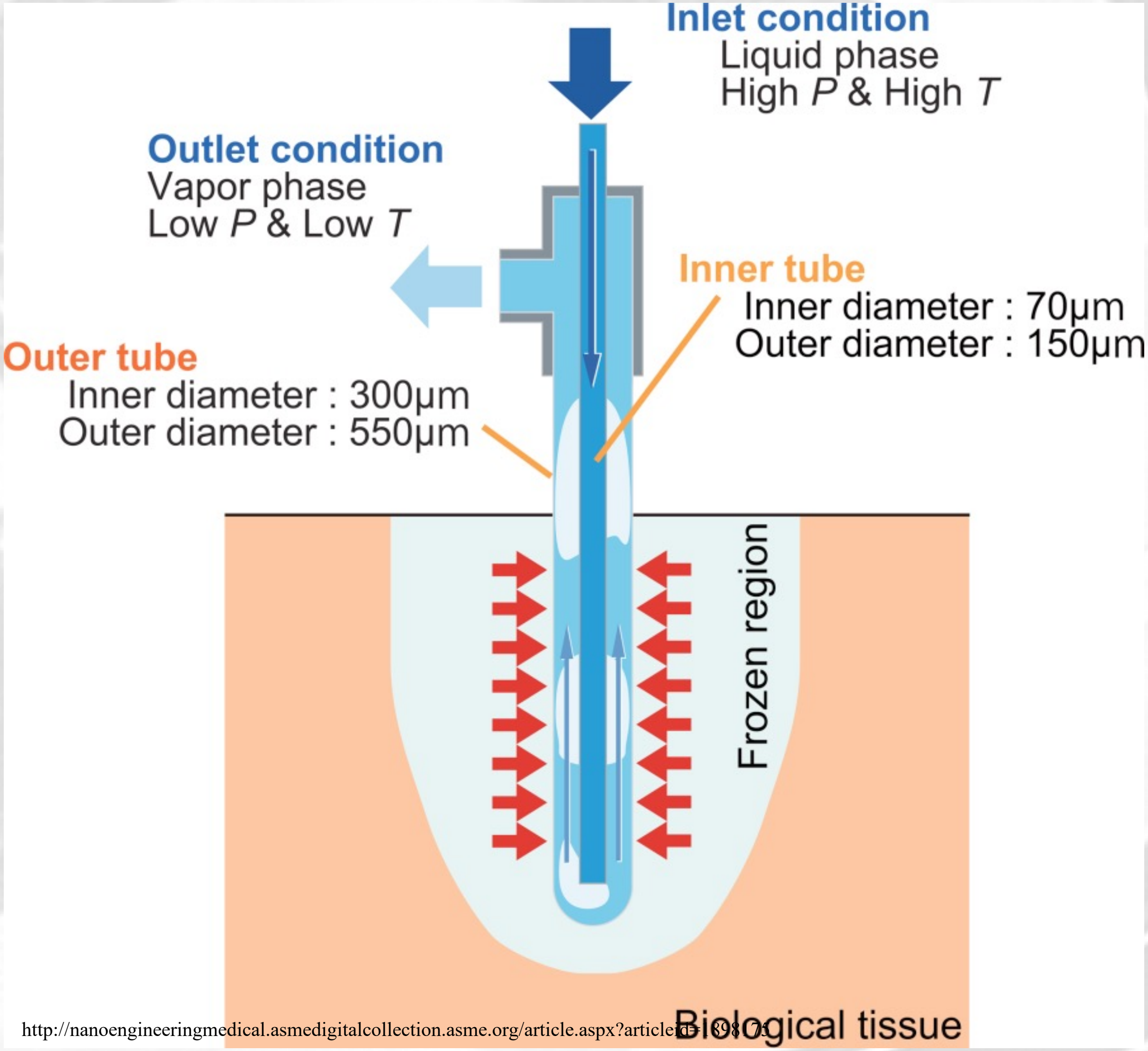


- Different gases have different Joule–Thomson (Kelvin) coefficients
- Helium is warmer at 1 atmosphere while most other gases like Argon get colder.
- We use the argon flowing through the orifice to freeze and then helium to warm.

Ice Ball Formation – JT Effect

The cryotube is cooled by rapid expansion of a cooled gas through a narrow opening.

Since



http://nanoengineeringmedical.asmedigitalcollection.asme.org/article.aspx?articleid=1898175

Cryobiology

Mechanisms of Cell Destruction

Freezing Damage Mechanisms

Freezing tissue damages cells in two ways:

1. Direct damage (to the cells) at the time of cryoablation
   - Slow cooling injury

     When cells are frozen slowly:

     - Ice forms in the extracellular matrix
     - The cell dehydrates but now has more concentrated cytoplasm
     - Upon thawing cell rehydrates and expands beyond the membrane resulting in lysis or the breakdown of the cell membrane

   - Fast cooling injury

     When cells are frozen quickly:

     - Water is trapped inside the cell because of how fast the temperature decreases
     - This results in Intracellular Ice Formation (IIF)
     - The cytoplasm becomes supercooled
     - This damages the cell membrane.
     - Holding the freeze causes recrystallization increasing cell damage.

Freezing Damage Mechanisms

2. Indirect damage (to the tissue) following cryoablation

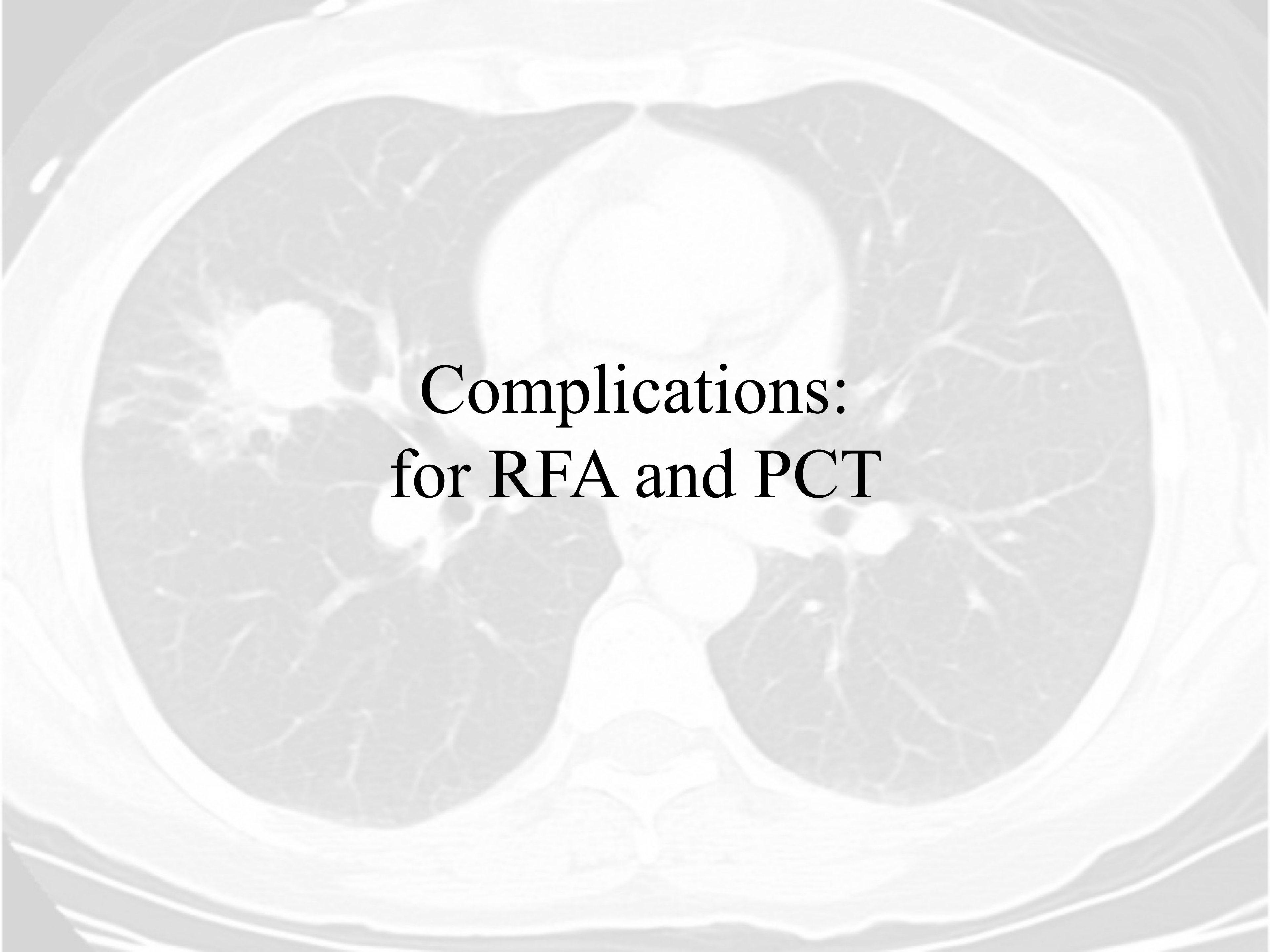
– Ischemia
  - an inadequate blood supply to an organ or part of the body.

– Apoptosis
  - process of programmed cell death that occurs in multicellular organisms

Indirect Damage

- Two theories
  - Blood vessel engorgement
    - Ice formation causes vessel wall engorgement and distention resulting in stasis or blood reduced flow.
  - Damage to the endothelial cells
    - Almost all tissues depend on a blood supply, and the blood supply depends on endothelial cells, which form the linings of the blood vessels.
    - Endothelial cells have a remarkable capacity to adjust their number and arrangement to suit local requirements.
    - They create an adaptable life-support system, extending by cell migration into almost every region of the body.
    - If it were not for endothelial cells extending and remodeling the network of blood vessels, tissue growth and repair would be impossible.
    - Cancerous tissue is as dependent on a blood supply as is normal tissue
    - It is hoped that by blocking/stopping the formation of new blood vessels, it may be possible to block the growth of tumors
    - Much like direct causes but this results in decreased blood flow to the tumor.

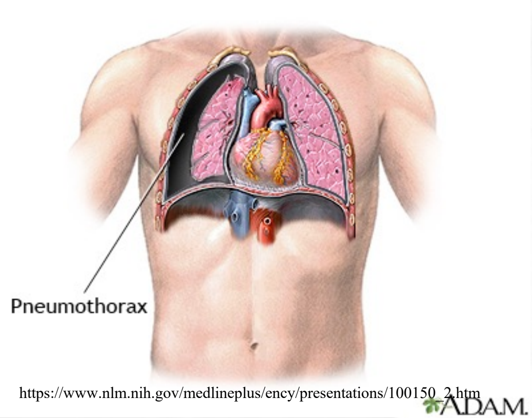
Final result necrosis



Complications: for RFA and PCT

Immediate complications:

- ***Pneumothorax*** - a collapsed lung. A pneumothorax occurs when air leaks into the space between your lung and chest wall. This air pushes on the outside of your lung and makes it collapse. In most cases, only a portion of the lung collapses.
  - Small: 30% of cases performed
    - Up to 50% in literature
  - Large: 20%; all required chest tubes
    - Three required prolonged hospitalization.



https://www.nlm.nih.gov/medlineplus/ency/presentations/100150_2.htm

Pulmonary Hemorrhage: acute bleeding from the lung, especially in the upper respiratory tract and the trachea

- Minor degrees in almost all cases.

Hemoptysis: the coughing up of blood.

- Moderate (200 cc ~ 1/5 L) in 1 case.

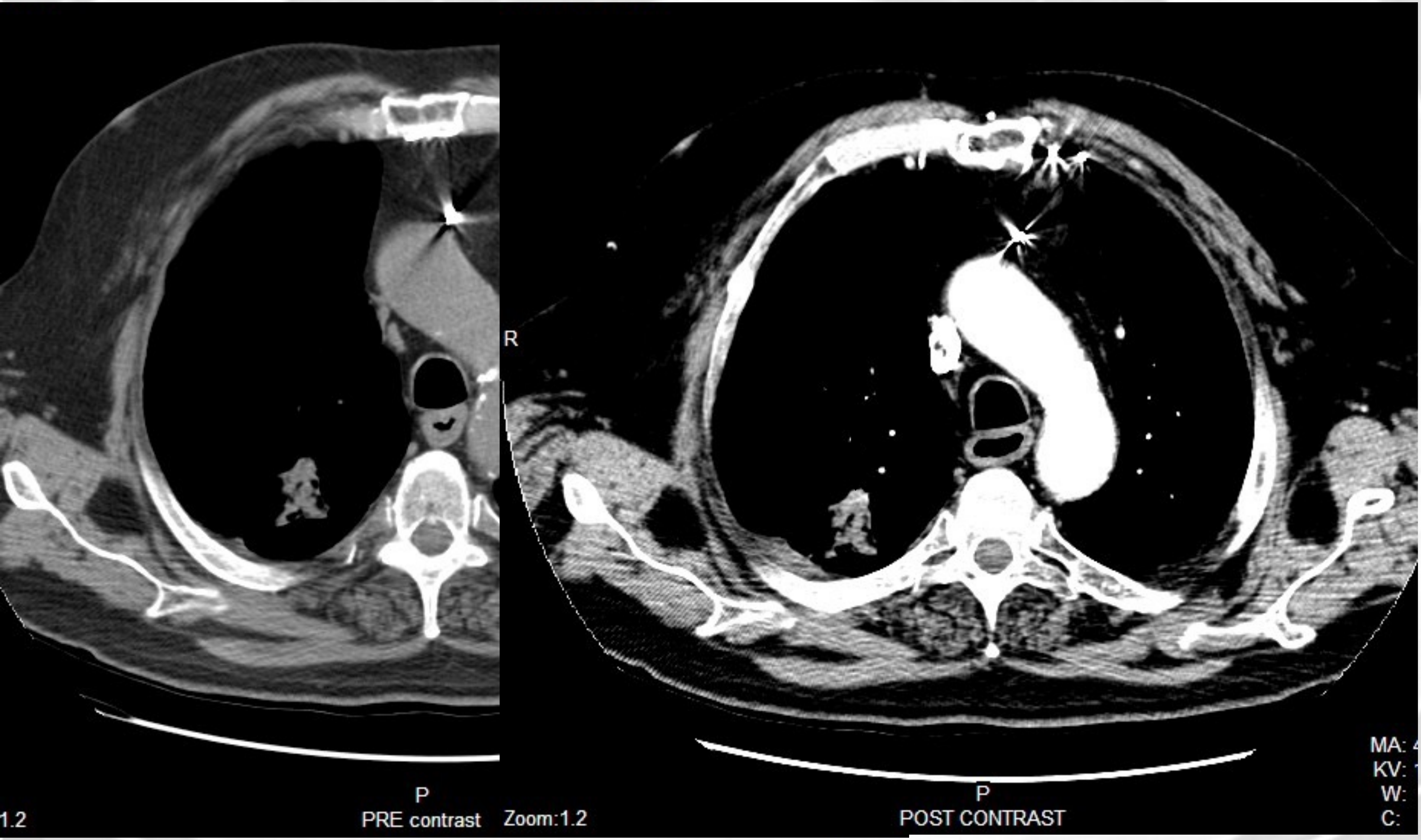
Follow-up?

We follow patient with CT with contrast and Positron Emission Tomography (PET) imaging.

Contrast CT

- CT works by stopping the beam of radiation (x-rays) as it passes through a structure.
  - The radiation is collected by the detector and then depending on the density of the structure it will give a specific level of gray – Hounsfield Unit.

- When we add contrast (aka Iodine) structures that are vascular have more iodine in them
  - More iodine means more attenuation of x-ray beams.
  - Why would you want this?



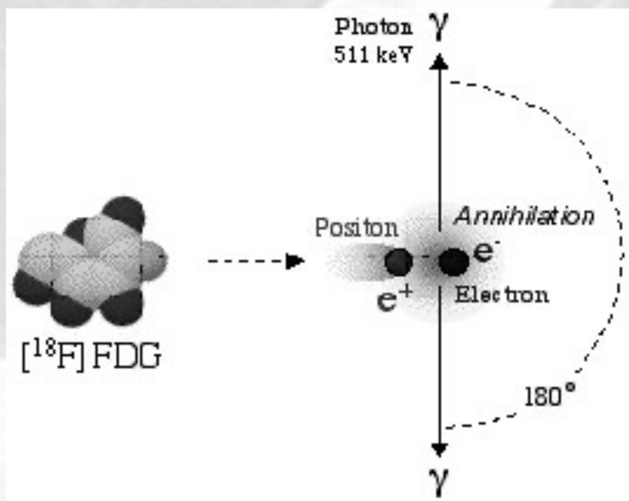
R
P
1.2
PRE contrast
Zoom:1.2
P
POST CONTRAST
MA:
KV:
W:
C:

Positron-Emission Tomography (PET)

- Works by giving a radioactive substance to the patient which emits a high energy particle.
- This high energy particle (a positron) which quickly annihilates with an electron to form two gamma rays.
  - The radioactive substance (fluorine) is given to the patient coupled to a glucose analog.
  - This particle is radioactive and breaks down with half-time of about 2 hours.
  - We inject a standard amount $10 - 13mCi$ and image 1 hour later.

Positron-Emission Tomography (PET)

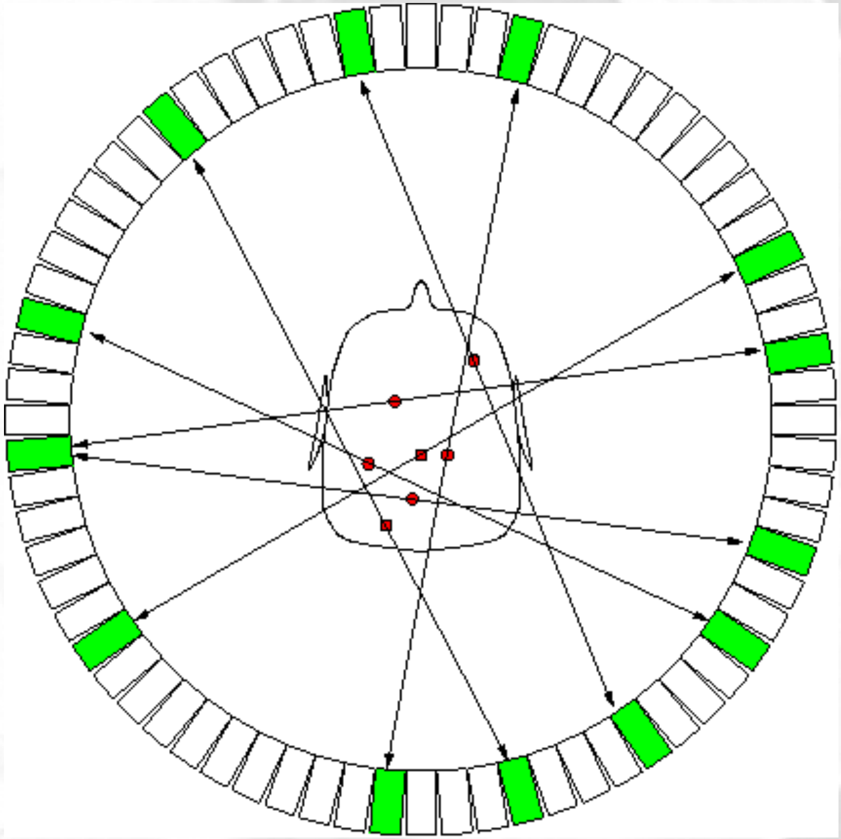
- The radioactive Fluorine decays and gamma rays are produced by annihilation.
  - This means that the particle (positron) meets its antimatter counterpart (electron), and the two masses disappear and to conserve mass/energy two photons are produced and each photon goes in opposite directions to conserve momentum.
  - $511 keV$ at 180 degrees to each other.

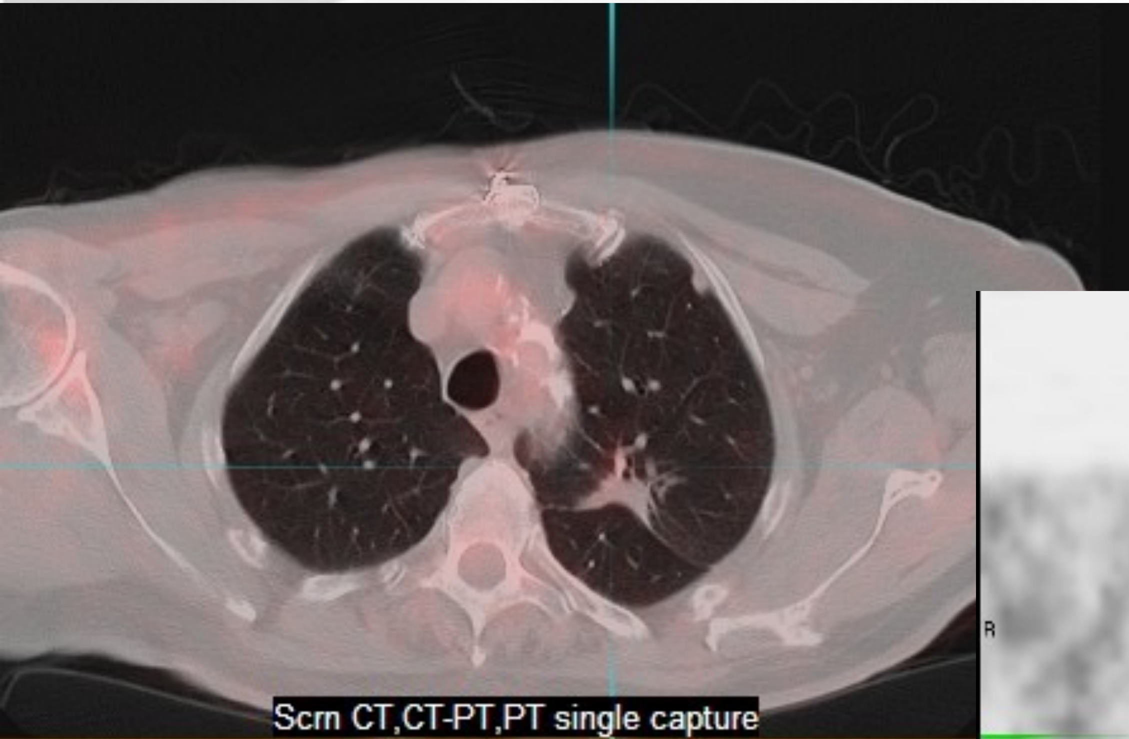


Positron-Emission Tomography (PET)

- The detector will only image the particles that hit the detectors at the same time at 180 degrees.

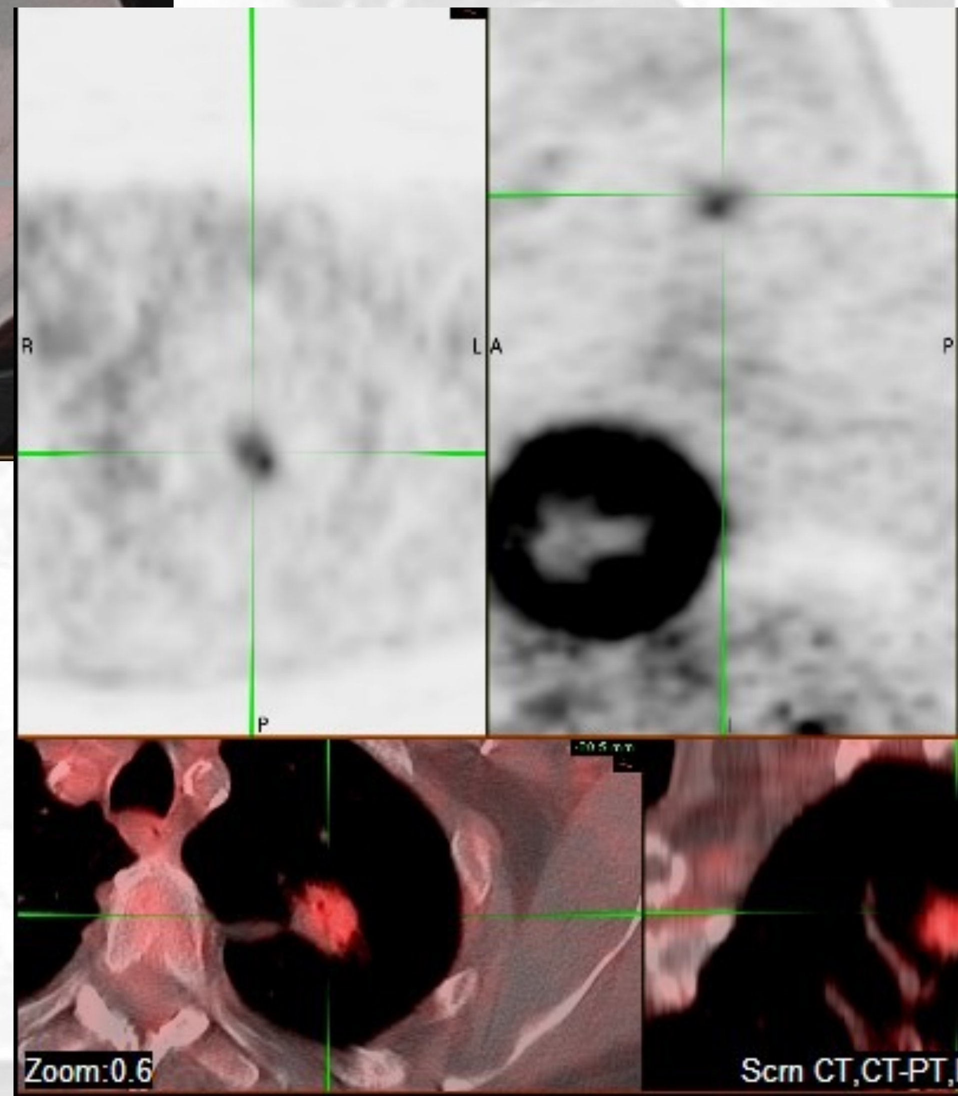
- The glucose is held in the metabolically active cells because of the fluoride which is added to the glucose.





6 month
SUV 1

12 month
SUV 3.8



Standardized Uptake Values

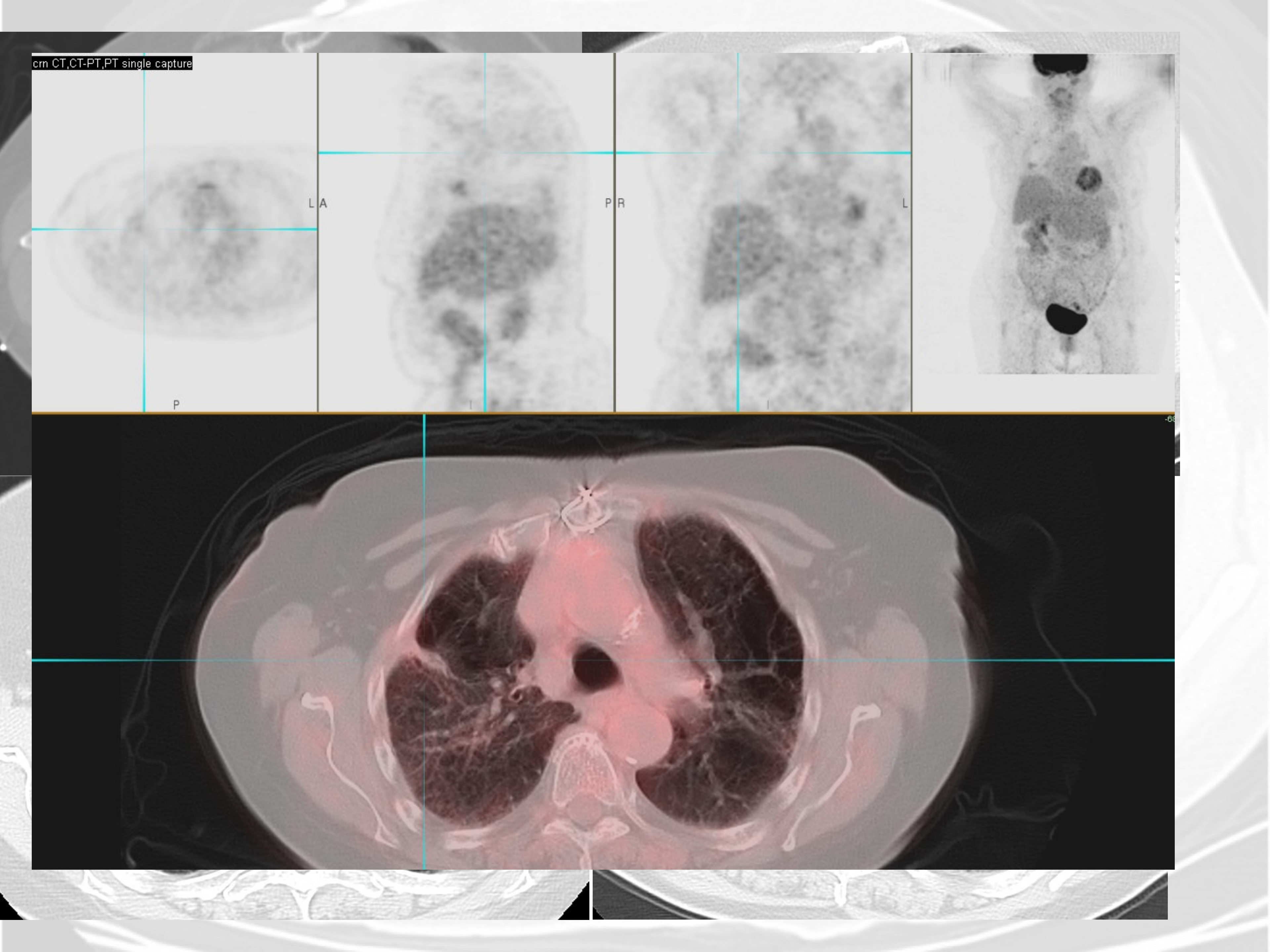
SUV = Standardized Uptake Values

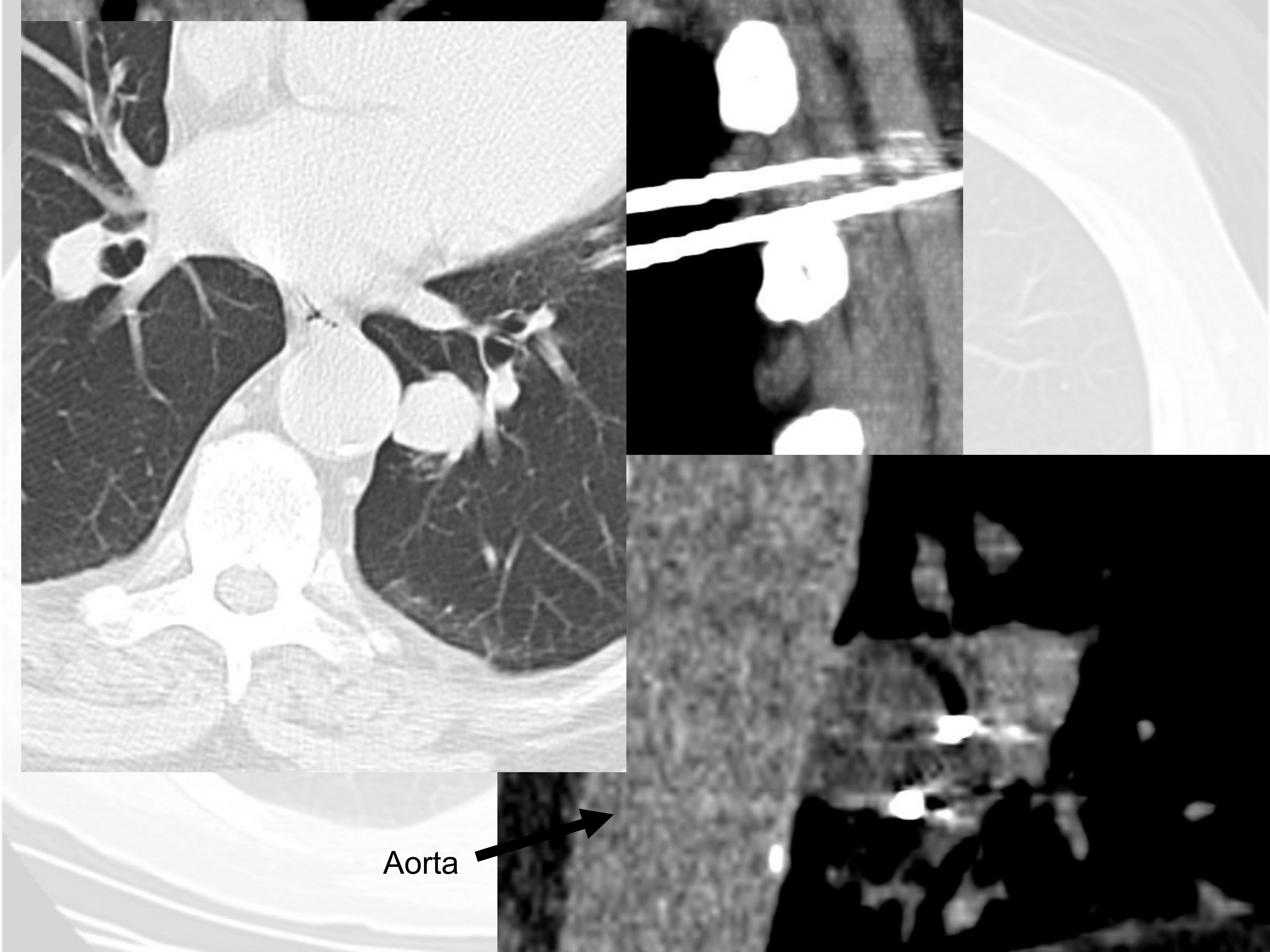
$$SUB = \frac{r}{\left({a'}/{w}\right)}$$

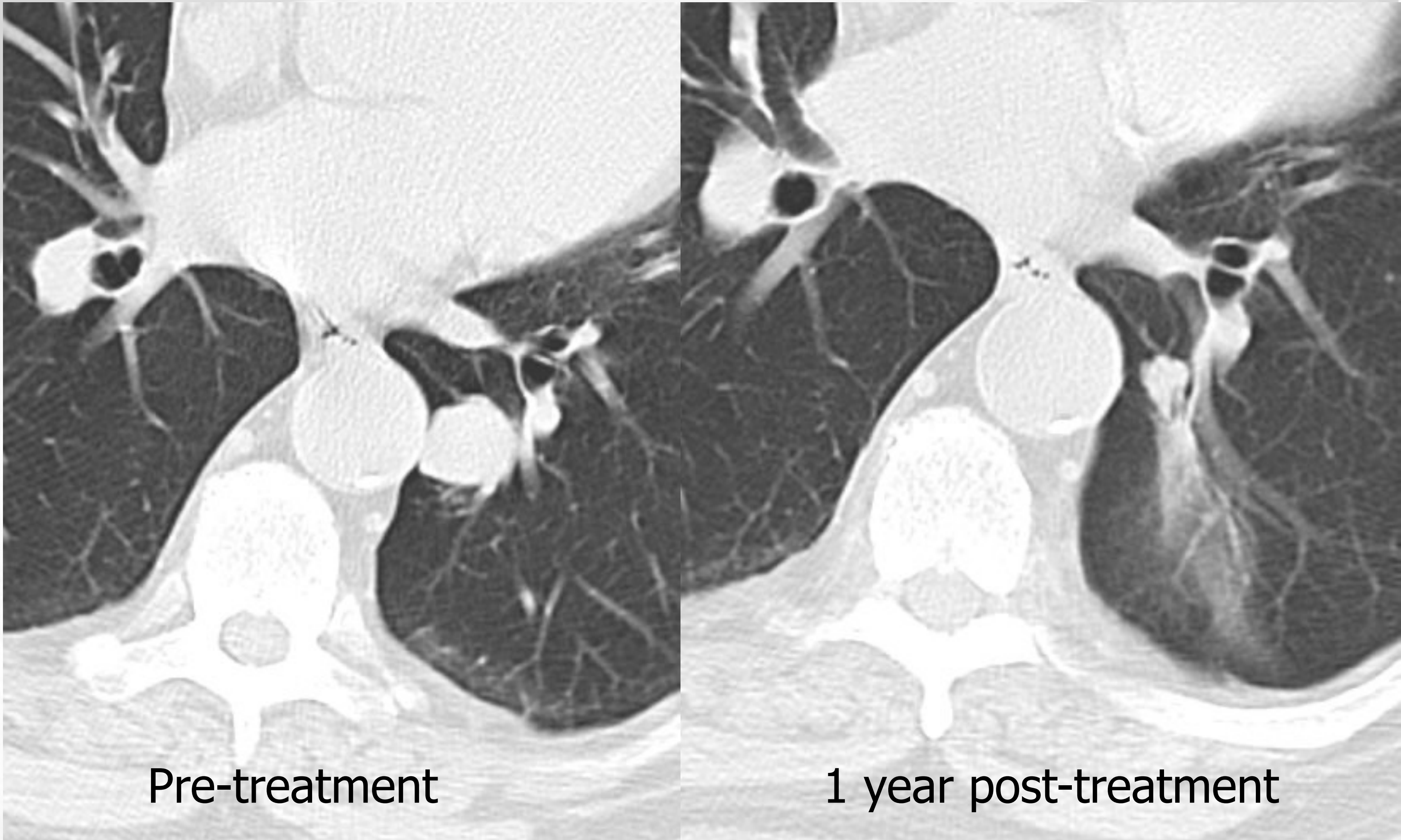
Where r is the radioactive activity concentration $\left(\frac{kBq}{ml}\right)$ measured by the PET scanner within some region of interest (ROI), a' is the decay-corrected amount of injected radiolabeled FDG $[kBq]$, and w is the weight of the patient in grams.

The use of SUVs as a measurement of relative tissue/organ uptake facilitates comparisons between patients and has been suggested as a basis for diagnosis.

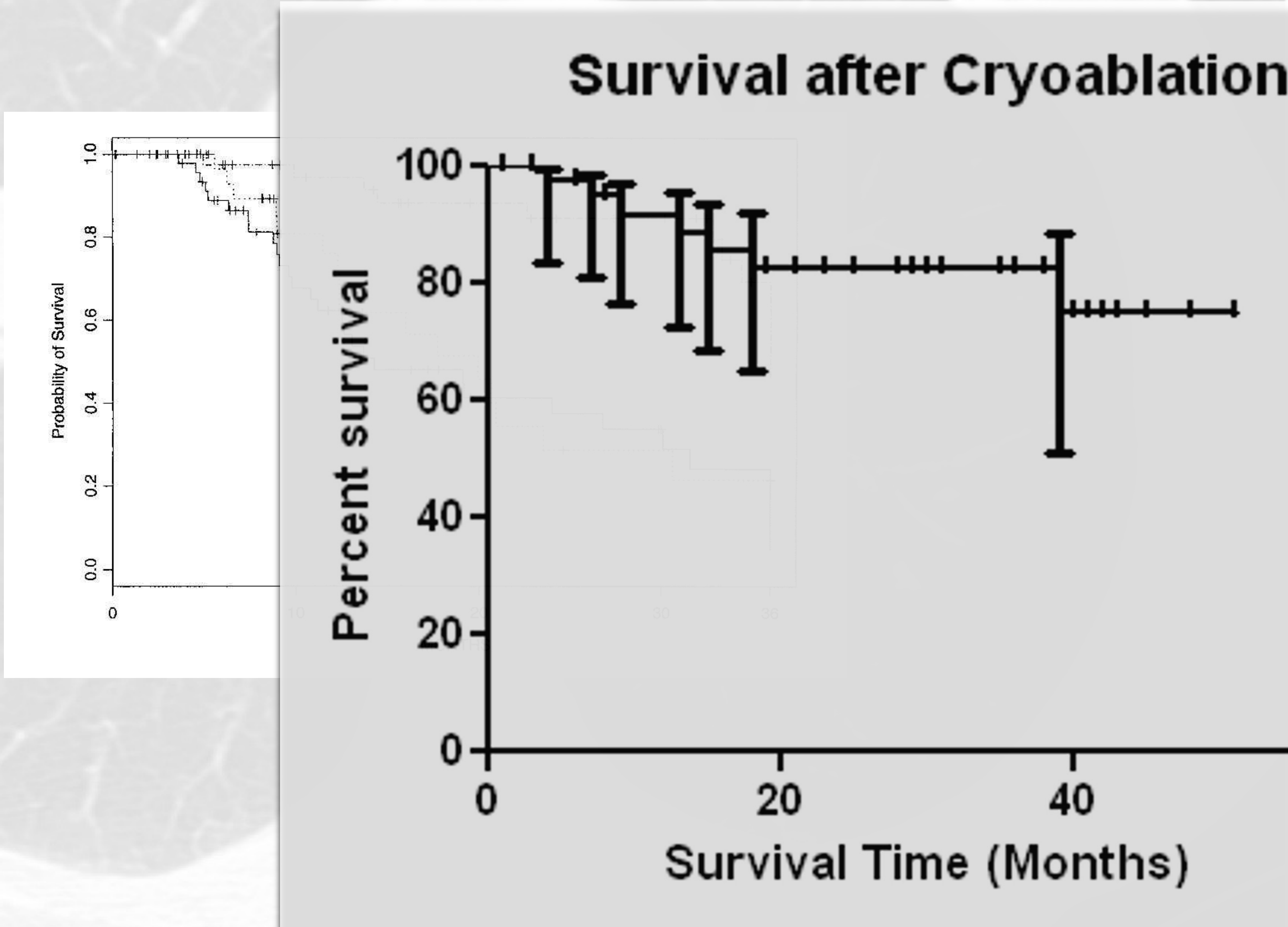
The greater the uptake value in a large lesion the greater the chance it’s a cancer.


crn CT,CT-PT,PT single capture
L
A
P
R
L
P

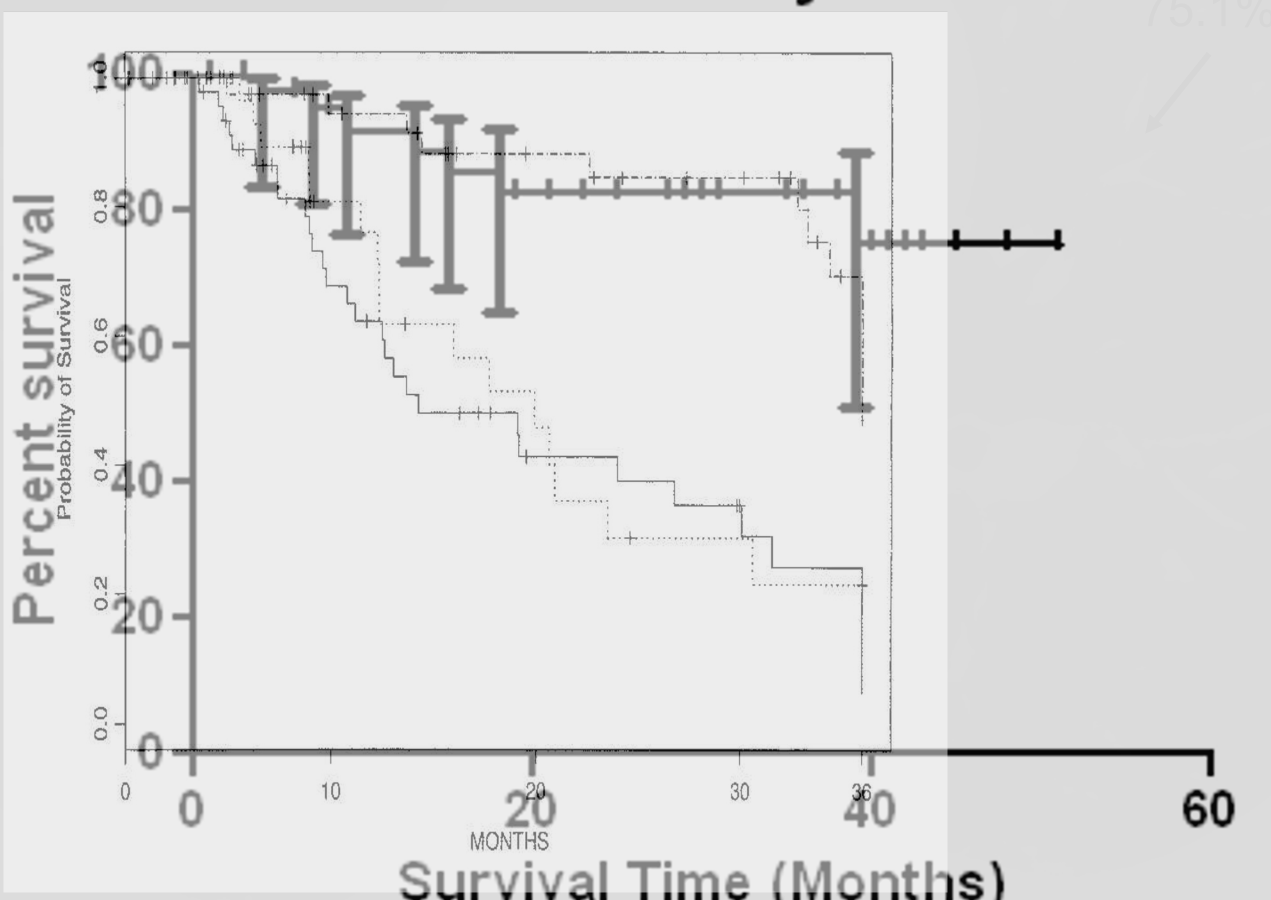

Aorta


Pre-treatment
1 year post-treatment

Did we do any better?



Survival after Cryoablation



Conclusions:

- RFA and Cryoablation are safe alternatives to standard non-surgical therapy for lung cancer and pulmonary metastatic disease.
-
- Long term data in the lung is starting to surface for RFA but not PCT.
- Carefully, performed clinical trials are necessary to determine the exact role of these interventions in patients with lung cancer.

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