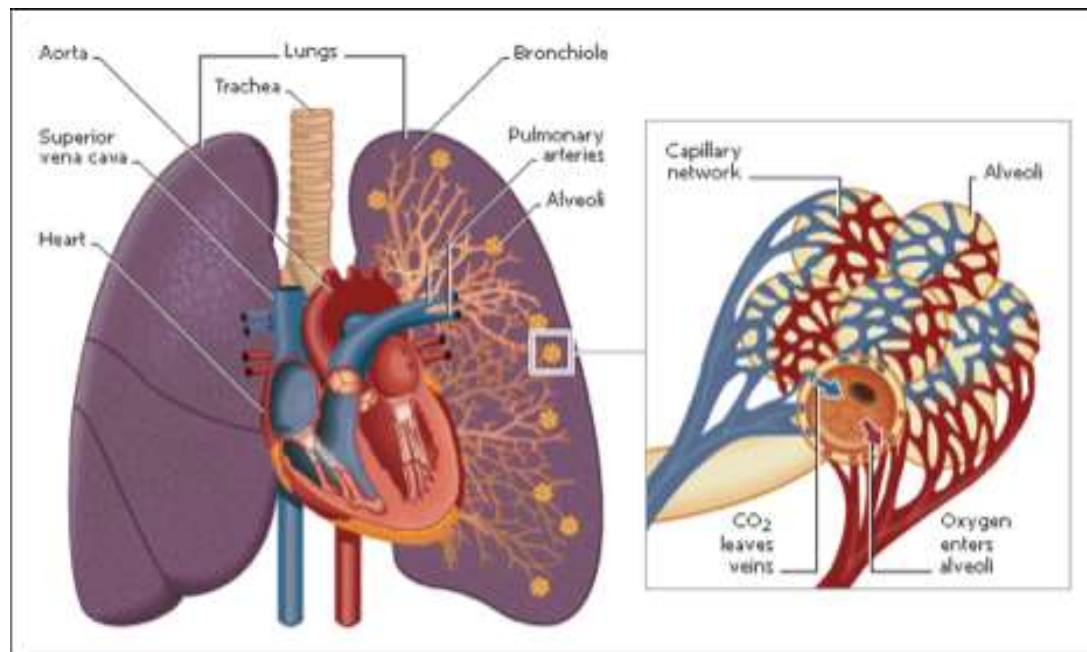


LUNGS

Nuclear Medicine Scans: Analysis of uptake mechanism and imaging protocols

Pulmonary imaging

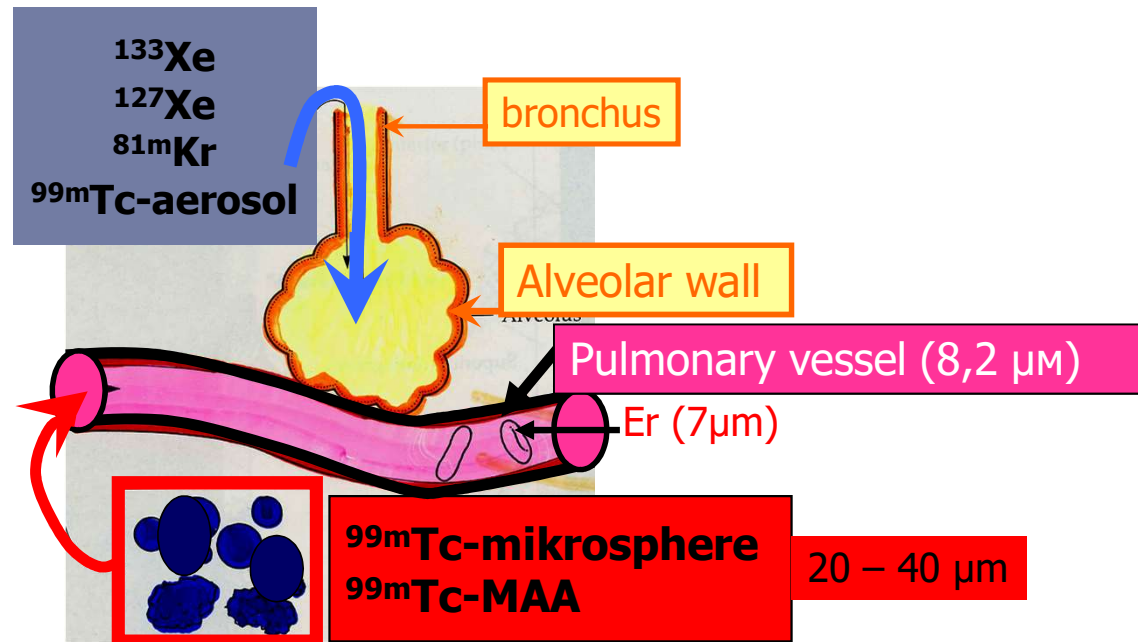
V/Q ventilation/perfusion scintigraphy



Pulmonary imaging

VENTILATION SCAN

PERFUSION SCAN



PERFUSION SCINTIGRAPHY

Microembolization of precapillarie vessels (1/1000) with particles whose diameter is larger (20-50 μ) than the diameter of pulmonary capillaries (8.2 μ).

Radiopharmaceuticals:

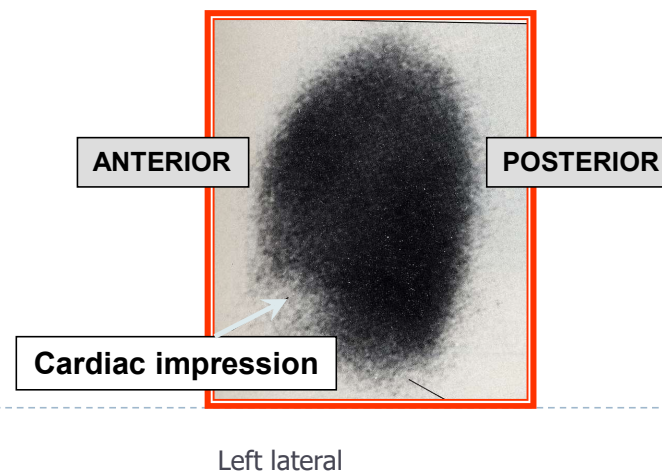
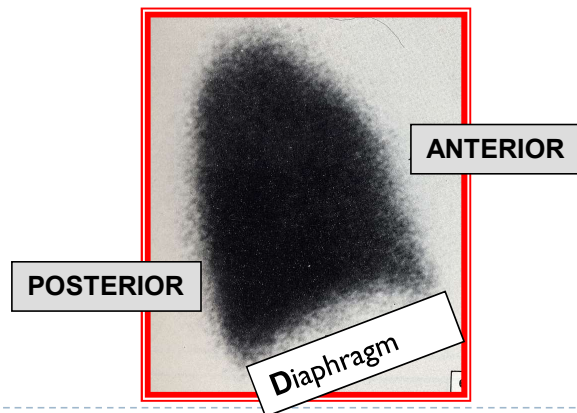
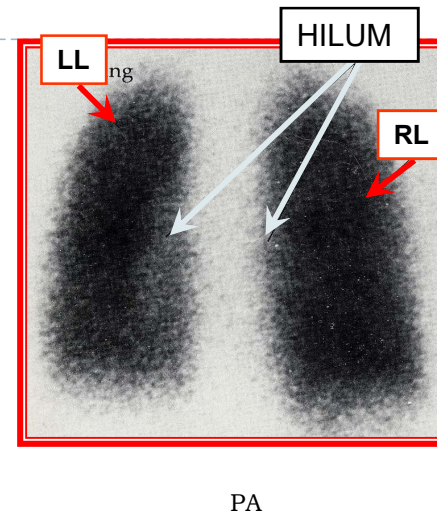
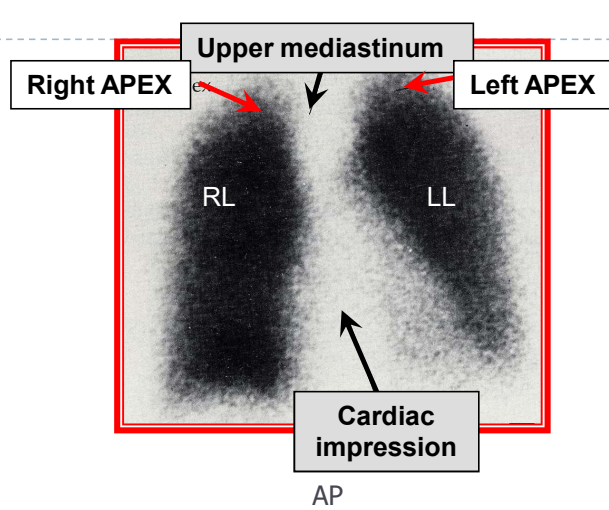
^{99m}Tc -macroaggregated human serum albumin (MAA) (minimum 100000 particles, optimal 200000-600000, caution with D-L shunt!!! $T_{1/2} \text{ biol} = 2\text{-}4\text{h}$)

^{99m}Tc -albumin microspheres

^{133}Xe dissolved in saline for i.v. application



PERFUSION SCINTIGRAPHY



VENTILATION SCINTIGRAPHY

^{133}Xe , ^{127}Xe и $^{81\text{m}}\text{Kr}$ radioactive gases

distal of the obstruction - reduced hypoperfusion "cold fields"

3 phases: "Wash-in, equilibrium and wash-out" scintigrams

1. Ventilation rate of different lung segments
2. Volume of gas distribution
3. Information on prolonged gas retention (COPD)



VENTILATION SCINTIGRAPHY

Technegas

- 0,02-0,2 μ m
- 100% Ar

Pertehnegas

- 0,02-0,2 μ m
- 95% Ar + 5% O₂



Radioactive aerosols produced in a commercial generator and used for lung scintigraphy. The aerosols are produced by first evaporating to dryness standard technetium-99m generator eluate ($^{99m}\text{TcO}_4$) in a graphite crucible (the simmer stage) and then heating this to 2500 degrees C (the "burn" stage).

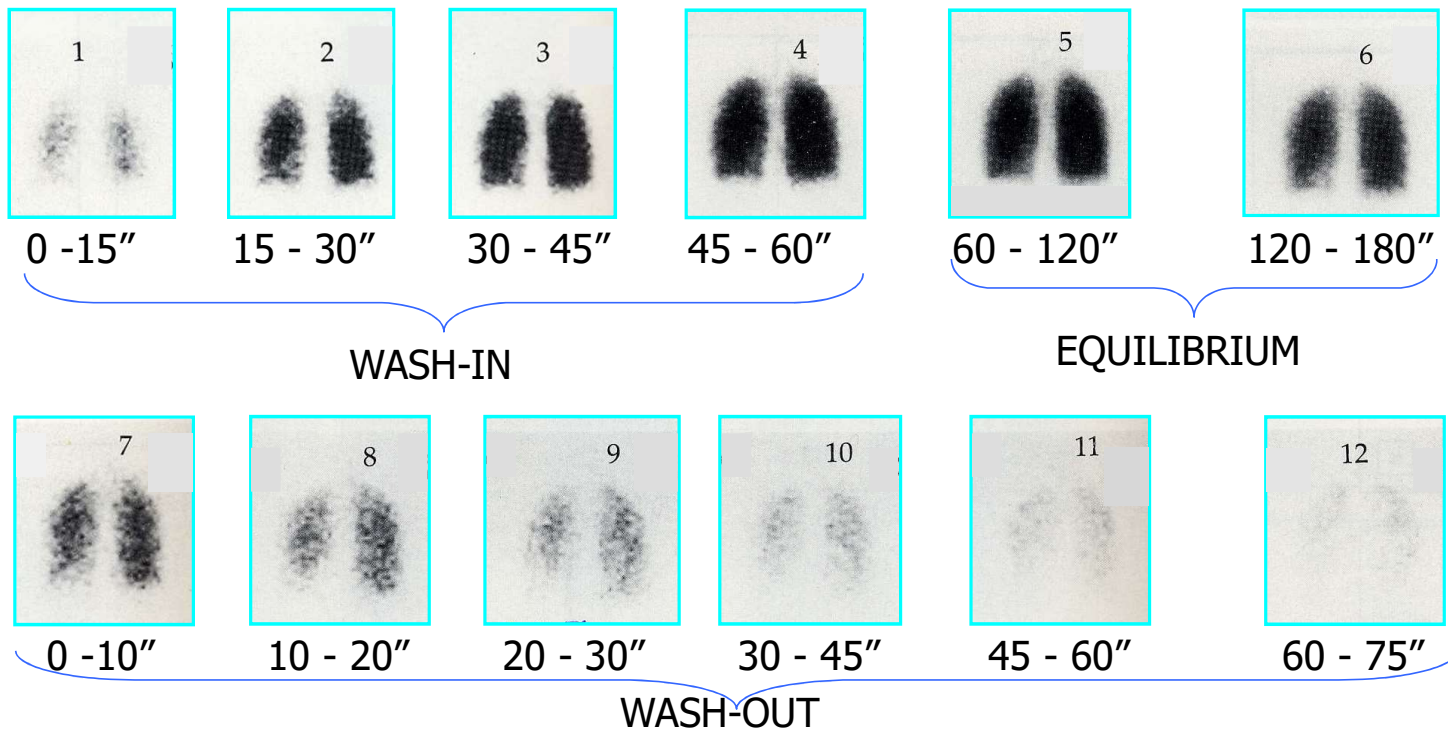
Patients inhale the Technegas via tubing and a mouthpiece, with particles lodging within the peripheral lungs.

Technegas has been reported to have better penetration of the peripheral lungs and less clumping of tracer in the central airways when compared to aerosolized Tc-99m DTPA. Technegas will remain lodged in the lungs as the isotope decays, with no absorption via the capillary beds or renal excretion.



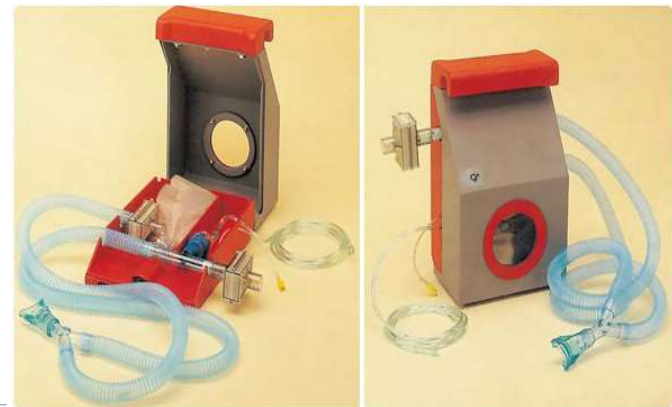
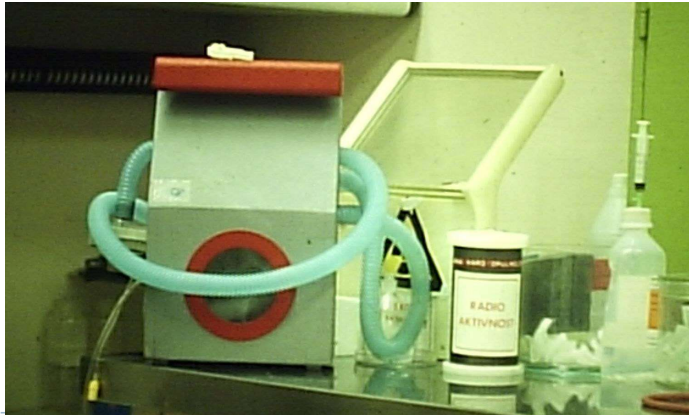
VENTILATION SCINTIGRAPHY

^{133}Xe , 80 keV, 5,3 days T1/2,

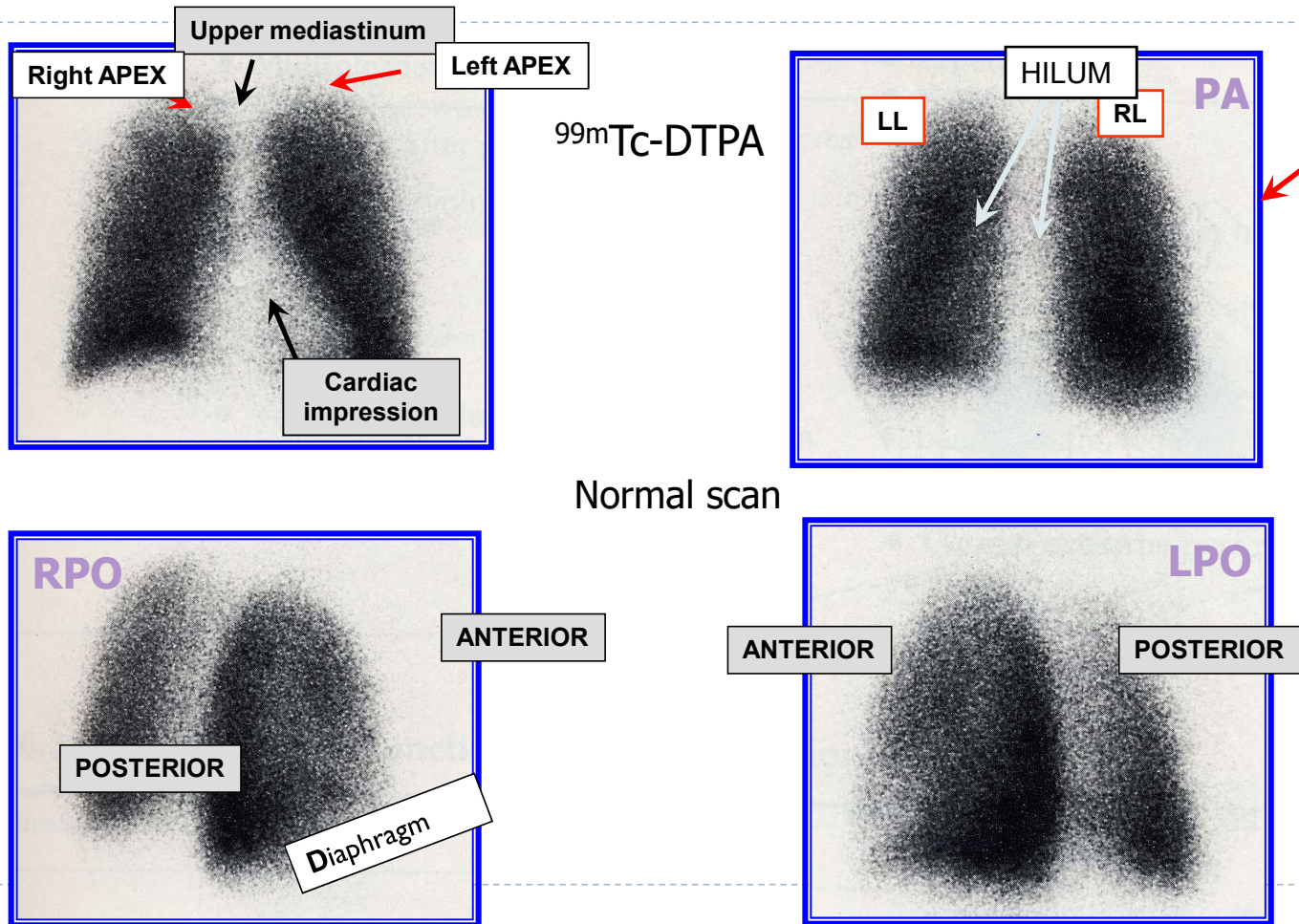


VENTILATION SCINTIGRAPHY

- ▶ Aerosols ^{99m}Tc -diethylenetriaminepentaacetate (DTPA)
- ▶ An aerosol of ^{99m}Tc -DTPA was produced using pressurised air. The jet nebuliser produces an aerosol with a median aerodynamic diameter of less than $1\text{ }\mu\text{m}$.
- ▶ Patients are sitting in front of a gamma camera and inhaled the aerosol during normal tidal breathing through a mouthpiece with a one way valve and noseclip in place.
- ▶ Airway obstruction „hot spot“, distal of the obstruction “cold spot”



VENTILATION SCINTIGRAPHY



V/Q ventilation/perfusion scintigraphy

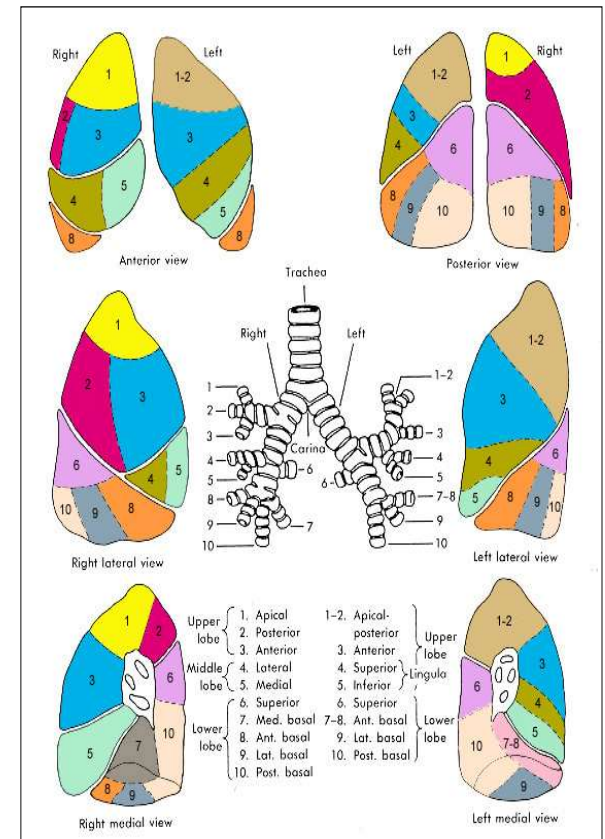
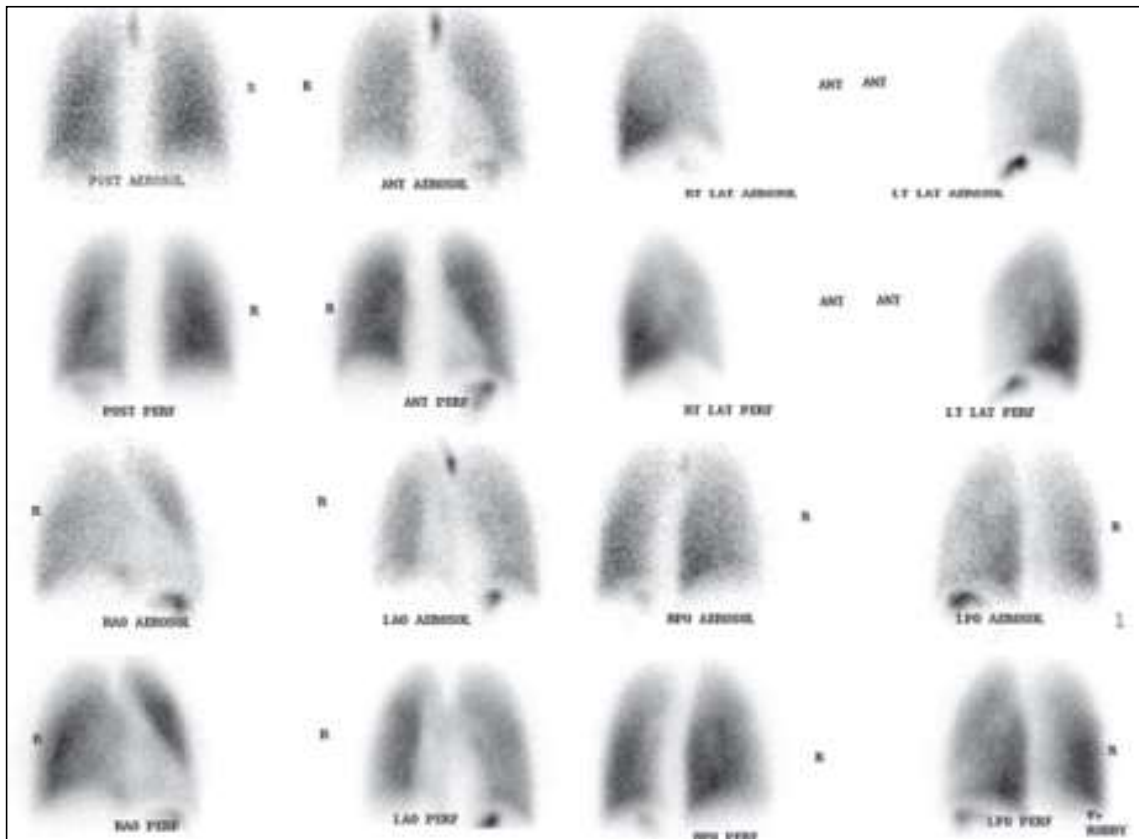
Normal scan

V

P

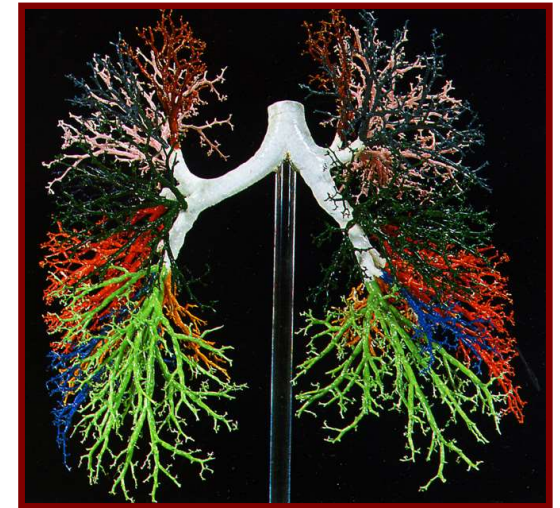
V

P



ANATOMY AND PHYSIOLOGY OF THE LUNGS

For the interpretation of the scan its an important knowledge of pulmonary vascular segmental anatomy which almost completely follows bronchopulmonary segmental anatomy except in the apical parts of the lungs



V/Q ventilation/perfusion scintigraphy

Indications:

- ▶ **pulmonary embolism,**
- ▶ **F/U pulmonary embolism after anti-coagulant therapy,**
- ▶ **CTEPH** (Chronic thromboembolic pulmonary hypertension)
- ▶ perfusion change secondary to lung tumor,
- ▶ pre-operative evaluation for pneumonectomy, post-operative F/U...



PULMONARY EMBOLISM

- ❑ A pulmonary embolism is a sudden blockage in your pulmonary arteries, the blood vessels that send blood to your lungs. It usually happens when a blood clot in the deep veins in leg breaks off and travels to your lungs
- ❑ Clinical symptoms: chest pain, dyspnea, hemoptysis

Lab tests:

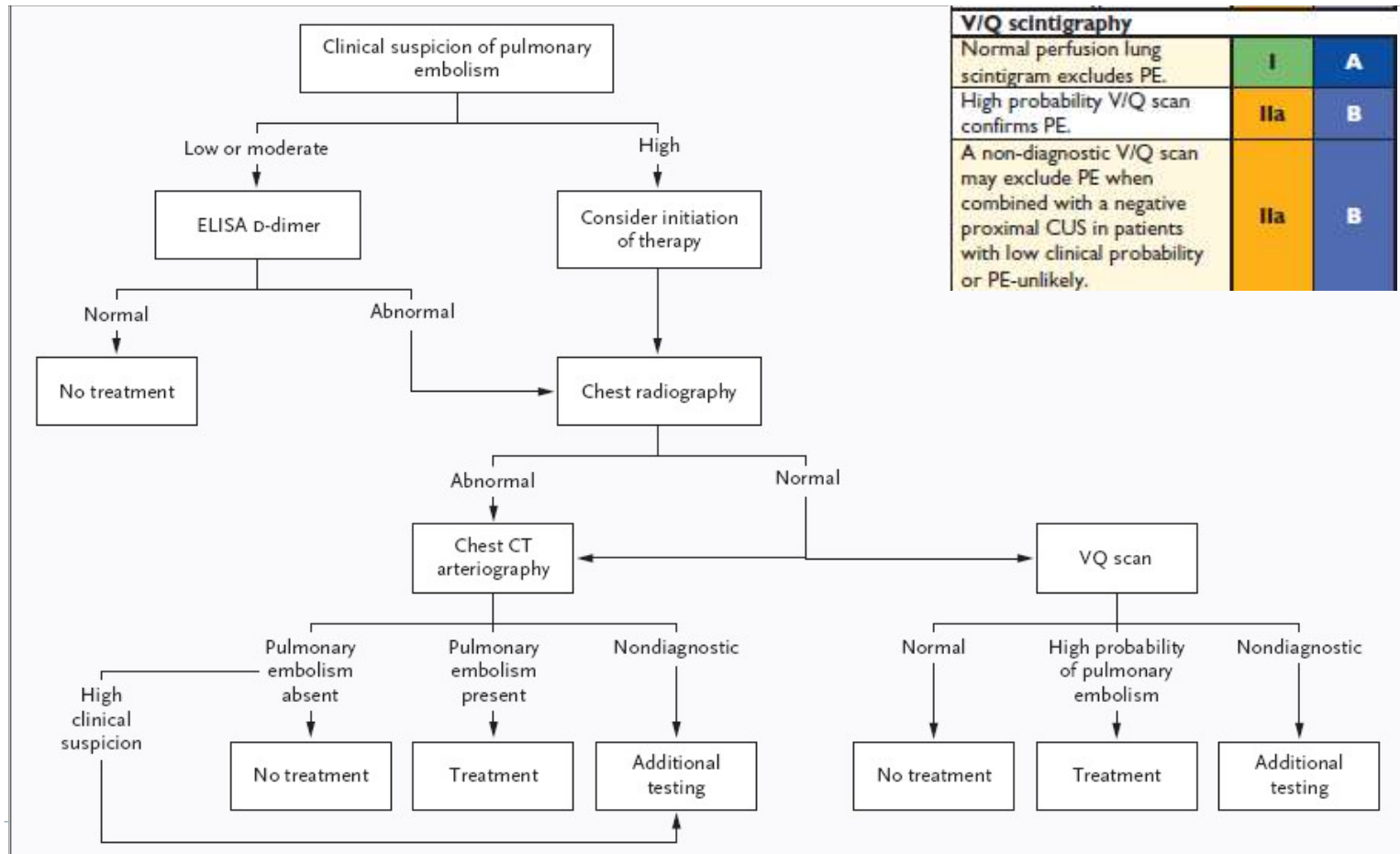
- D-dimer, gass analysis
- ECG – sinus tachycardia, C1Q3T3, PБББ, P pulmonale

Imaging :

- RTG
- MDCT
- V/Q scan
- Angiography

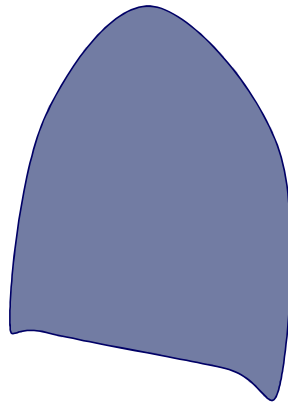


PULMONARY EMBOLISM



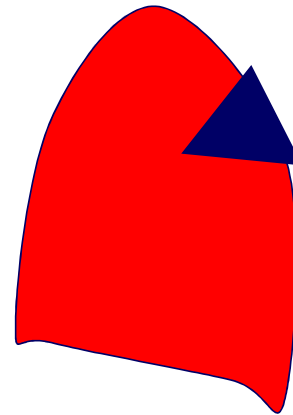
PULMONARY EMBOLISM

“V/P Mismatch”



Ventilation

\geq

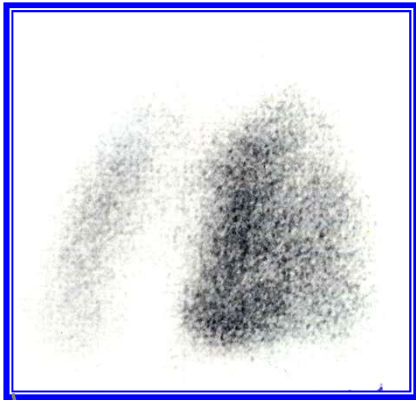


Perfusion

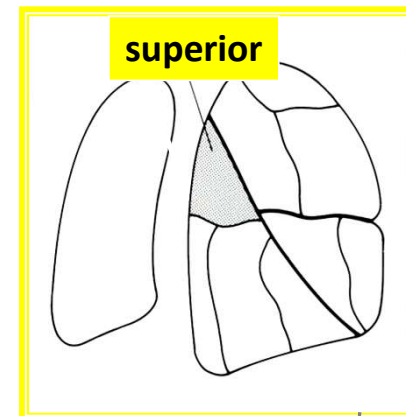
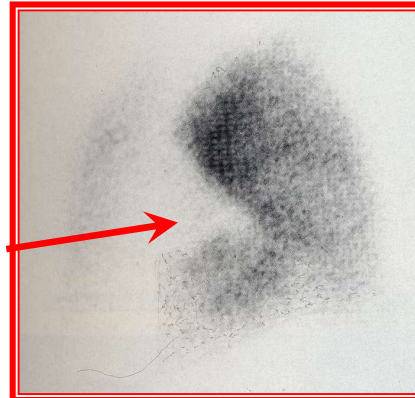


PULMONARY EMBOLISM

Ventilation



Perfusion

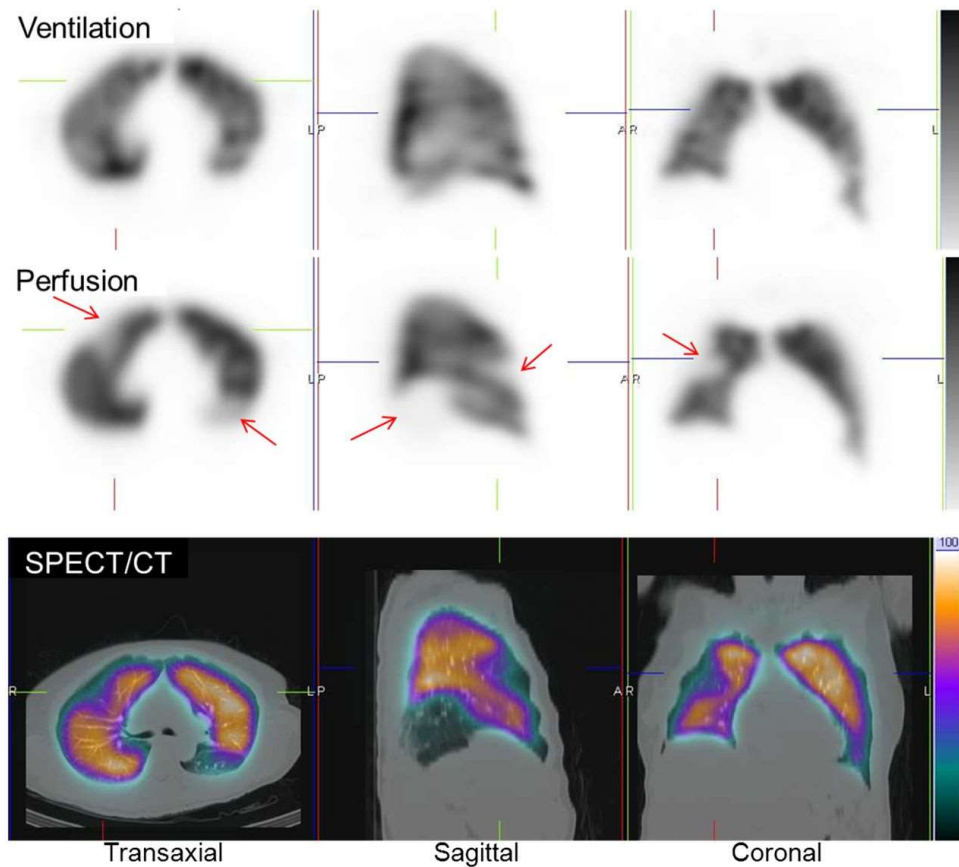


RPO

1 segment

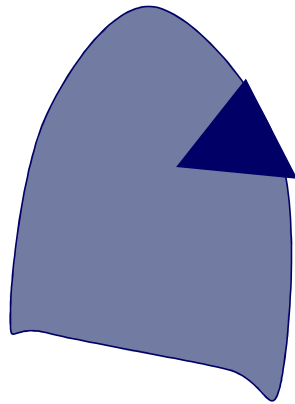


PULMONARY EMBOLISM



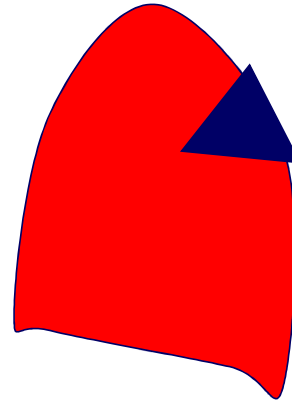
Parenchymal lung disease

“V/P Match”



Ventilation

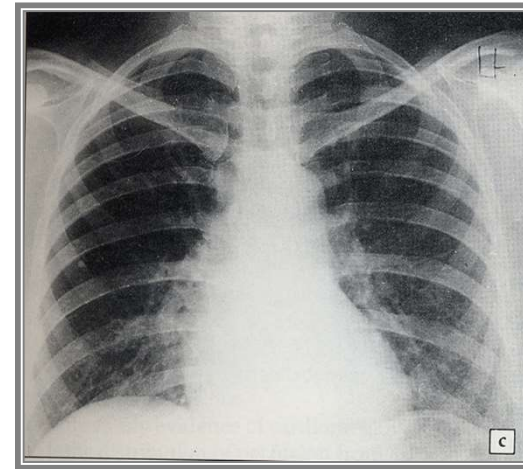
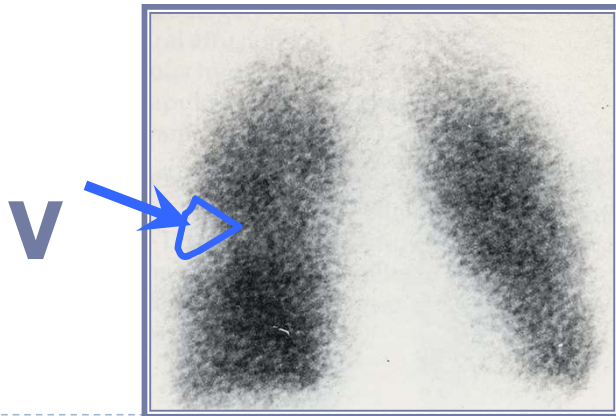
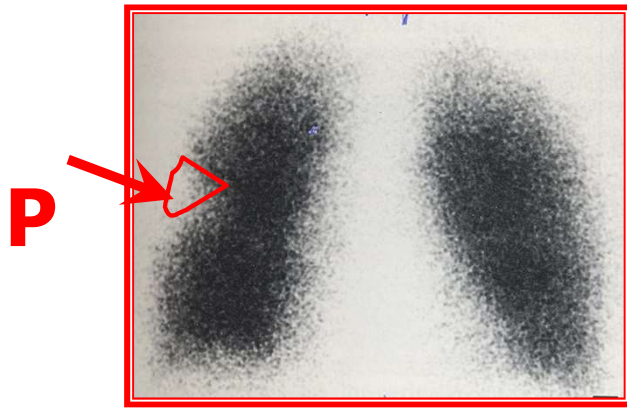
=



Perfusion



Parenchymal lung disease



Rtg

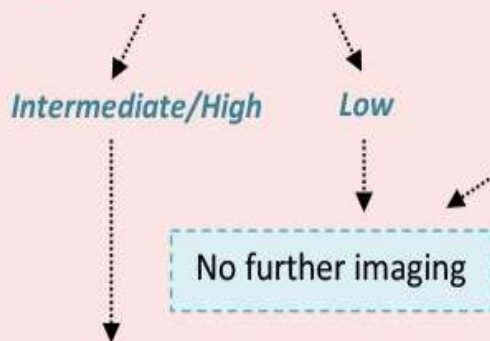
Previous tuberculosis can lead to of significantly larger P defects in relation to the X-ray findings.

PIOPED	Modified PIOPED II	Perfusion-only modified PIOPED II	Perfusion-only PISAPED
High LR >2 large mismatched (V:Q) segmental defects*	High LR ≥2 large mismatched (V:Q) segmental defects*	PE present ≥2 large mismatched (Q:CXR) segmental defects*	PE present ≥1 wedge-shaped Q defects
Borderline high LR 2 large mismatched (V:Q) segmental defects*			
Intermediate LR 2 moderate or 1 large mismatched (V:Q) defect* Difficult to categorize as high or low	Nondiagnostic All other findings	Nondiagnostic All other findings	Nondiagnostic Cannot classify as PE-present or PE-absent
Borderline low LR 1 matched (V:Q) defect, CXR-negative			
Low LR Nonsegmental perfusion defects [†] Q defect substantially < CXR defect Matched (V:Q) defects, CXR-negative Any number of small Q defects*			
Normal No Q defects	Very low LR Nonsegmental [†] Q defect < CXR lesion 1–3 small segmental* defects Solitary matched (V:Q:CXR) defect (≤1 segment) in mid or upper lung Stripe sign [‡] Solitary large pleural effusion [§] ≥2 matched (V:Q) defects, regionally normal CXR	PE absent Very low probability Nonsegmental [†] Q defect < CXR lesion 1–3 small segmental* defects Solitary matched (Q:CXR) defect (≤1 segment) in mid or upper lung Stripe sign [‡] Solitary large pleural effusion [§]	PE absent Non-wedge-shaped Q defect Contour defect caused by enlarged heart, mediastinum, or diaphragm Near-normal Q Normal Q
	Normal No Q defects		

PISAPED criteria

Stepwise approach of ventilation-perfusion (V/Q) scan for pulmonary embolism (PE) detection

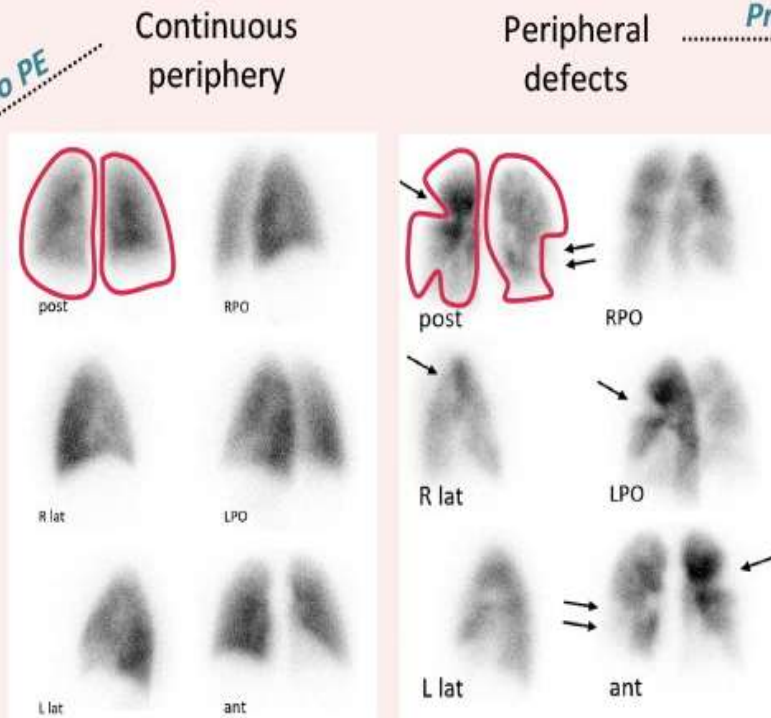
1 PRETEST PROBABILITY



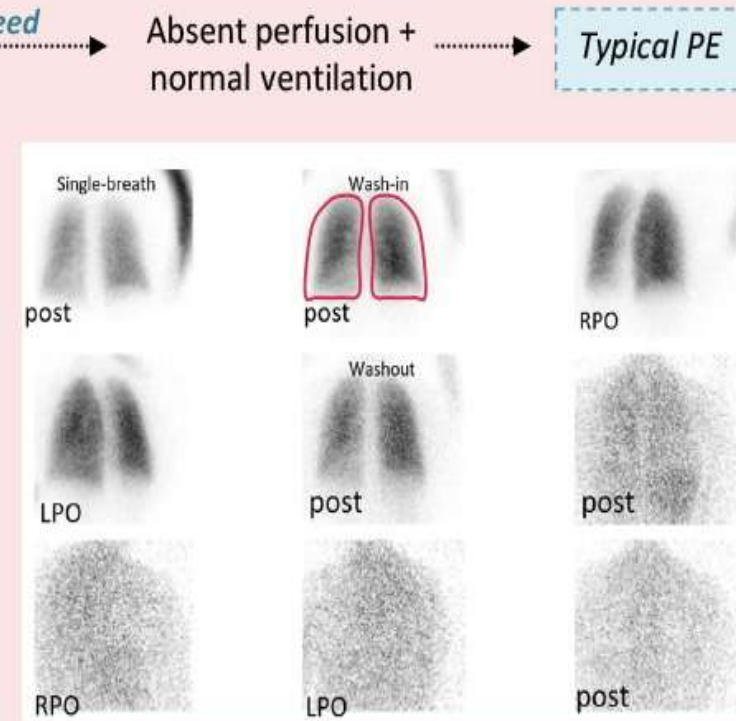
2 BASELINE IMAGING

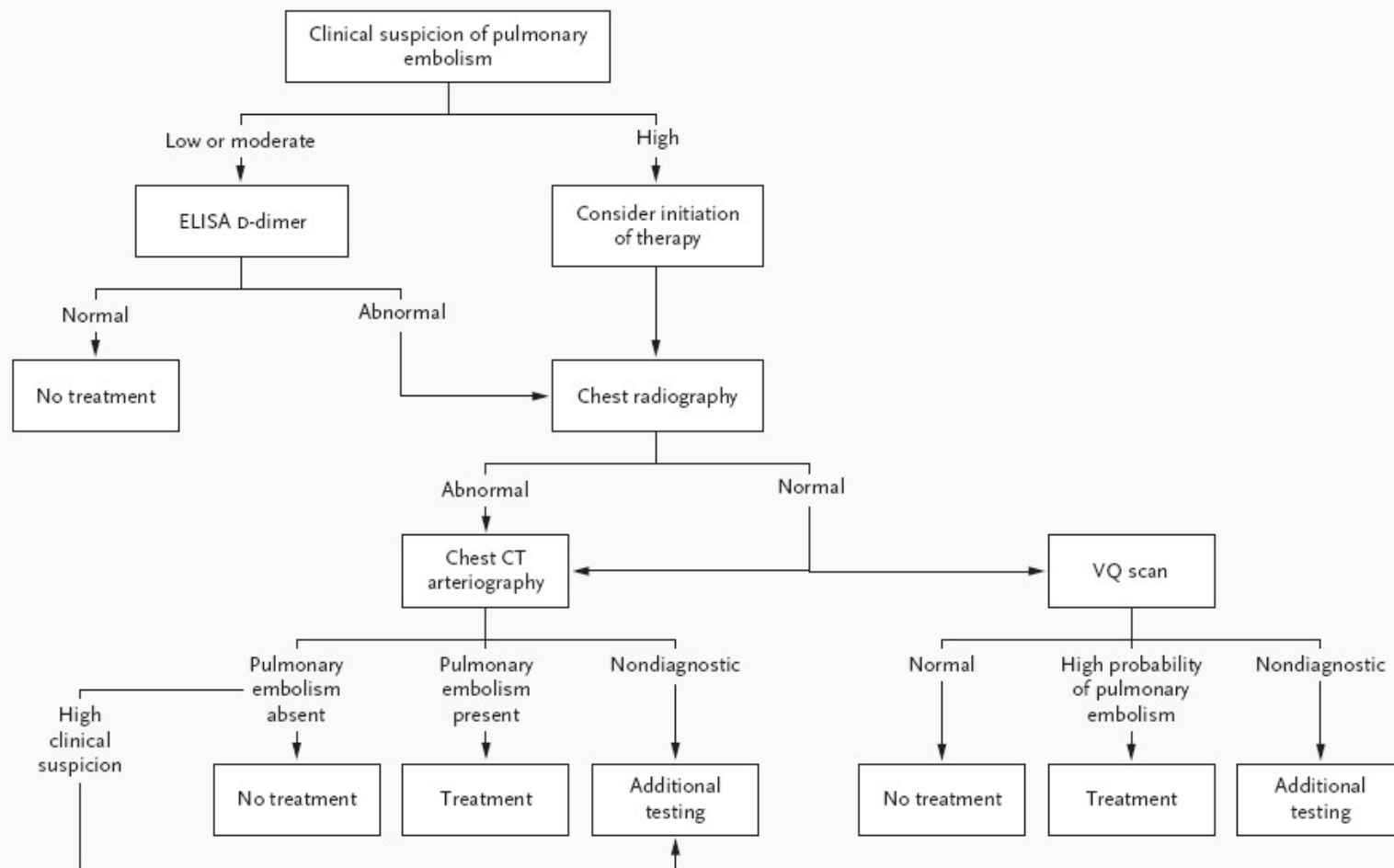


3 PERFUSION SCAN



4 VENTILATION SCAN





V/Q scintigraphy

Normal perfusion lung scintigram excludes PE.

I

A

High probability V/Q scan confirms PE.

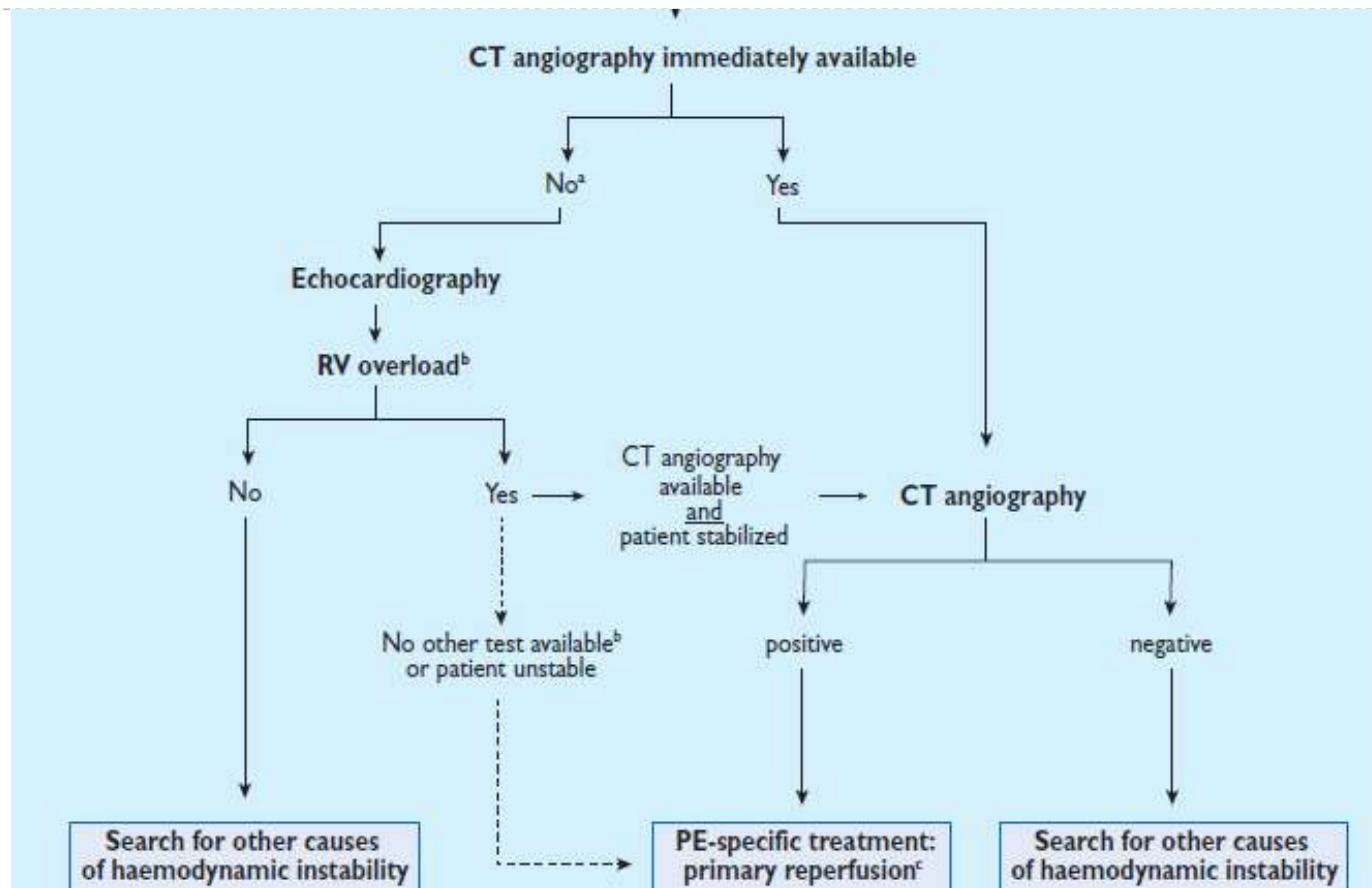
IIa

B

A non-diagnostic V/Q scan may exclude PE when combined with a negative proximal CUS in patients with low clinical probability or PE-unlikely.

IIa

B



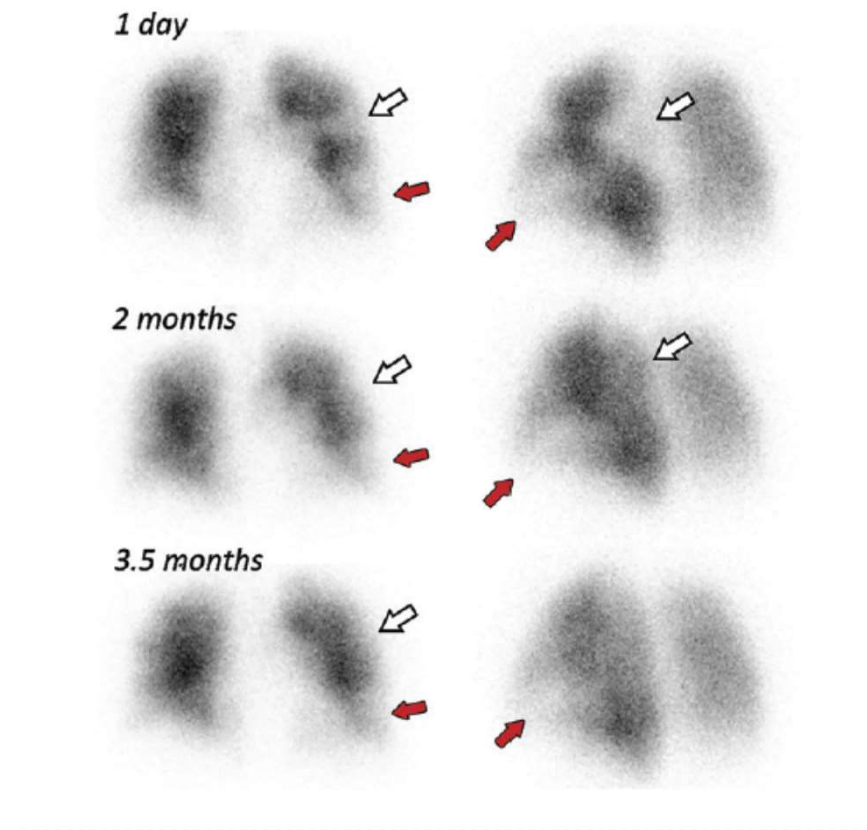
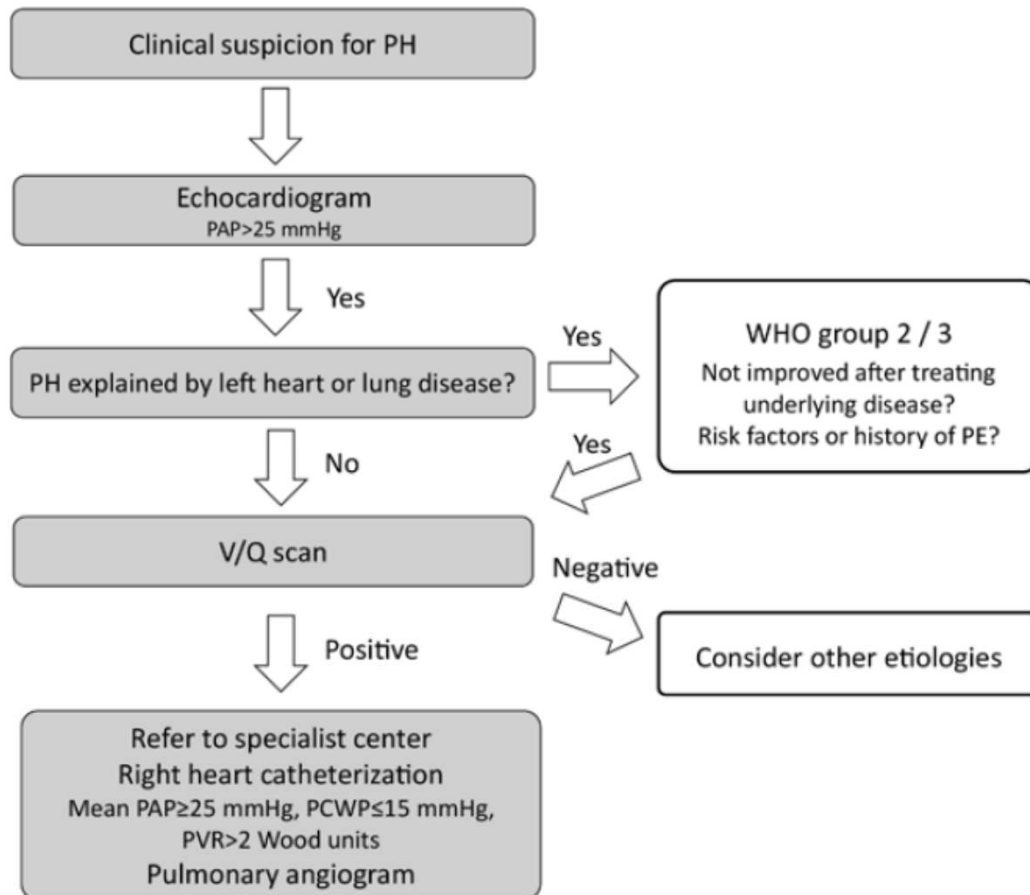
V/Q scan in pregnancy

Recommendations	Class ^a	Level ^b	Ref ^c
Suspicion of PE in pregnancy warrants formal diagnostic assessment with validated methods.	I	C	
D-dimer measurement may be performed in order to avoid unnecessary irradiation, as a negative result has a similar clinical significance as in non-pregnant patients.	IIb	C	418, 419
Venous compression ultrasonography may be considered in order to avoid unnecessary irradiation, as a diagnosis of proximal DVT confirms PE.	IIb	C	
Perfusion scintigraphy may be considered to rule out suspected PE in pregnant women with normal chest X-ray.	IIb	C	
CT angiography should be considered if the chest X-ray is abnormal or if lung scintigraphy is not readily available.	IIa	C	
A weight-adjusted dose of LMWH is the recommended therapy during pregnancy in patients without shock or hypotension.	I	B	432, 433

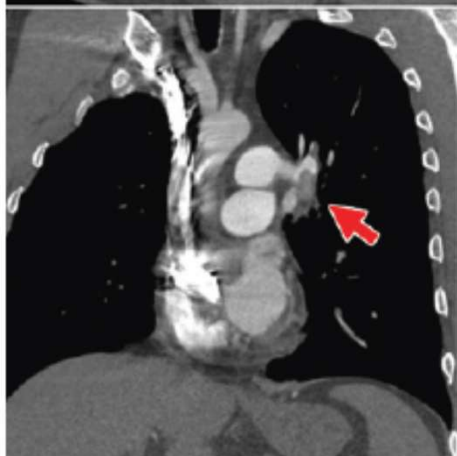
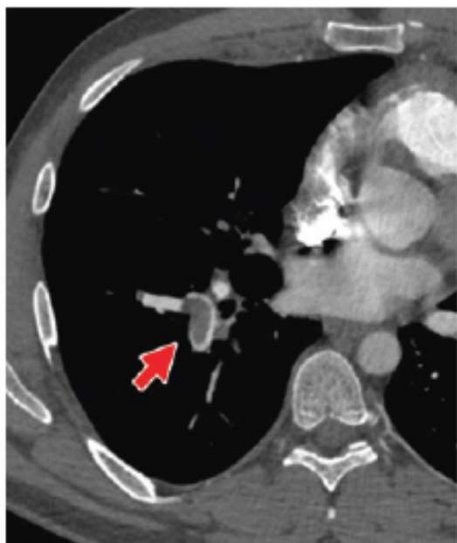
V/Q scan in pregnancy

Test	Estimated radiation	
	uGy	mSv
Chest radiography	<10	0.01
Perfusion lung scan with technetium 99m-labelled albumin	60–120	0.06–0.12
V/Q scan	200	0.2
CT angiography		
First trimester	3–20	0.003–0.02
Second trimester	8–77	0.008–0.08
Third trimester	51–130	0.051–0.13
Pulmonary angiography by femoral access	2210–3740	2.2–3.7

Chronic thromboembolic pulmonary hypertension (CTEPH)



Chronic thromboembolic pulmonary hypertension (CTEPH)



3 days

3.5 months

1 year

ANT Q

POST Q

LPO Q

RPO Q

PULMONARY CARCINOMA

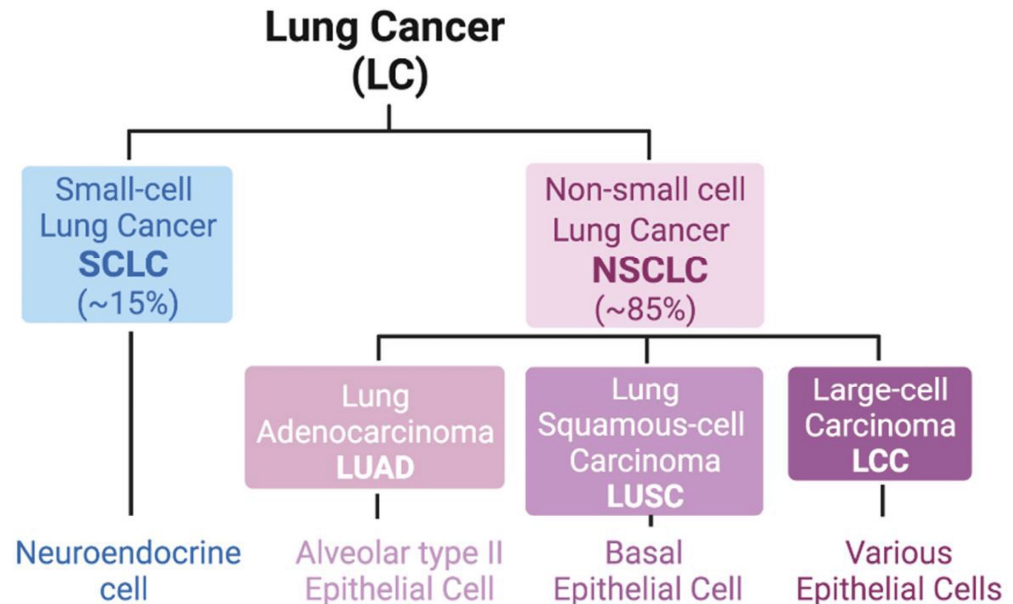
Lung cancer is a disease of great sociomedical importance, due to its high incidence and mortality. Etiologically, it is associated with the inhalation of tobacco smoke. Previously, it occurred much more often in men, but the percentage of affected women is increasing.



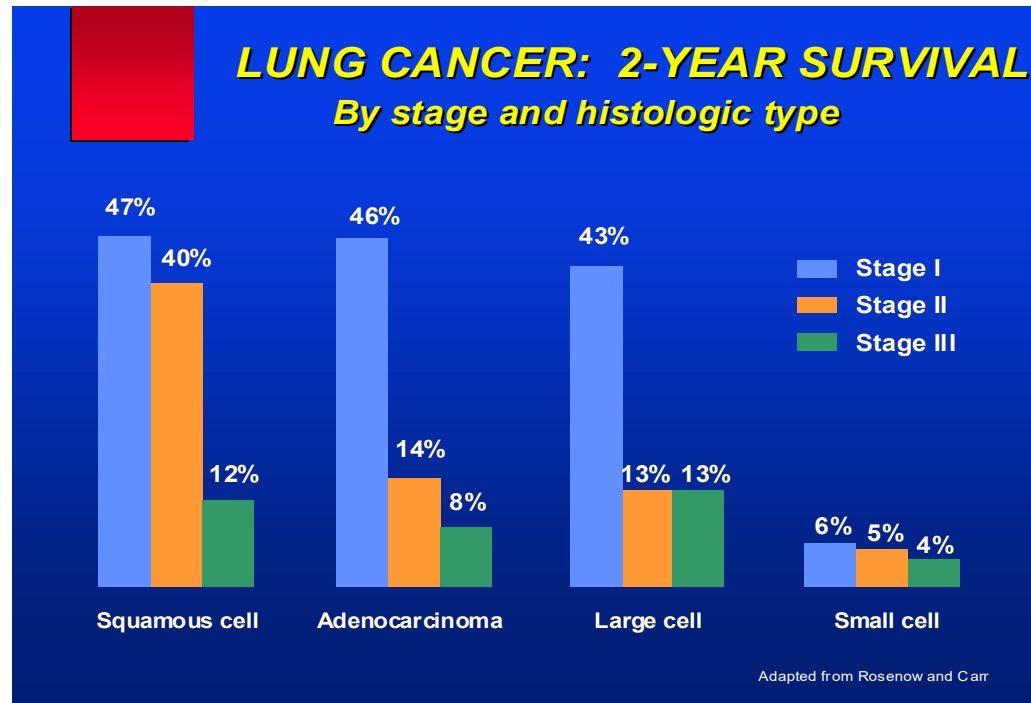
SUB-TYPE



ORIGIN



- Small cell carcinoma produces regional and distant metastases very early, and the chance of a radical cure is very small. Most often, no surgery is performed.
- Other histological types are less malignant and in less advanced cases, radical surgery and adjuvant chemotherapy and radiotherapy can be successful.
- Reliable diagnostics are needed to clearly distinguish patients with good chances of recovery from those with poor ones.



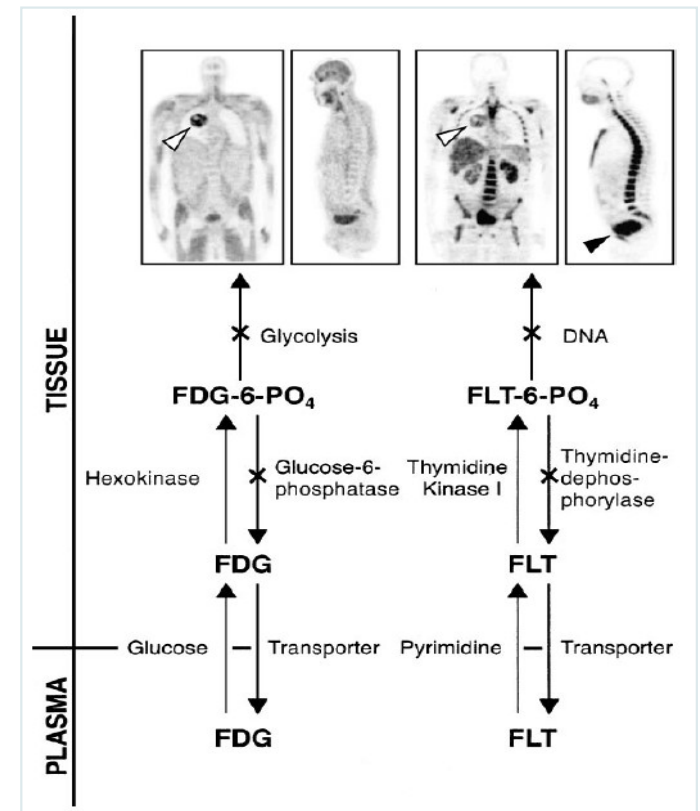
IMAGING LUNG CANCER

■ Glucose uptake	[¹⁸F]FDG	NSCLC
■ NETs SSTR	[¹¹¹In]Octreotate [⁶⁸Ga] DOTATOC	SCLC
■ Protein synthesis	[¹¹ C]methionine	
■ Phospholipids synthesis	[¹¹ C]Choline	
■ Cell proliferation	[¹⁸ F]FLT	
■ Cell hypoxia	[¹⁸ F]FMISO [¹⁸ F]FAZA [⁶⁴ Cu]ATSM	
■ Apoptosis	[¹⁸ F]Annexin V	
■ Angiogenesis	[¹⁸ F]NGR-peptide	



^{18}F (^{18}F FDG)

Fluorodeoxyglucose (FDG) is phosphorylated to FDG-6-PO₄ by hexokinase. Since the activity of glucose-6-phosphatase is negligible, FDG-6-phosphate is essentially trapped in tumor cells. Unfortunately it is also trapped in activated macrophages.

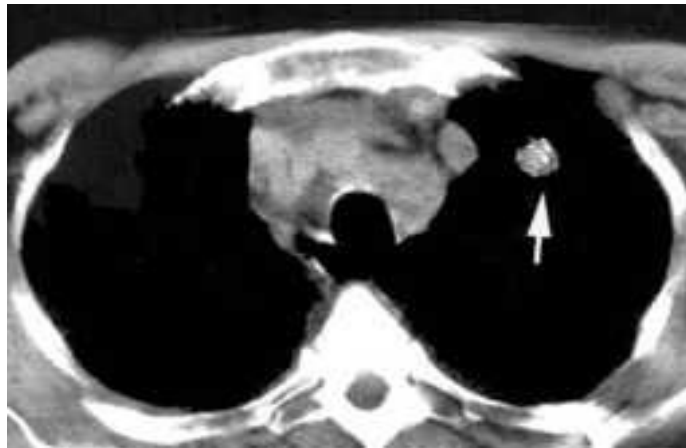


PET with FDG in ONCOLOGY LUNG CANCER

1. Diagnosis and “grading” of malignant disease
2. Definition of disease extent: staging and restaging
3. Identification and localisation of disease foci unknown primary (paraneoplastic syndromes)
4. Evaluation and monitoring of response to therapy
5. Identification of recurrent disease in comparison with “raising” tumour markers and anatomic/structural changes (CT and MR)
6. Guide for biopsy
7. Therapy guidance and “management”

Evaluation of Solitary Pulmonary Nodule

- ▶ Large numbers of SPNs detected, ~10 for every case of cancer.
 - ▶ Lung biopsies: significant morbidities & costs.
 - ▶ CT: Limited ability to characterize tissue*.



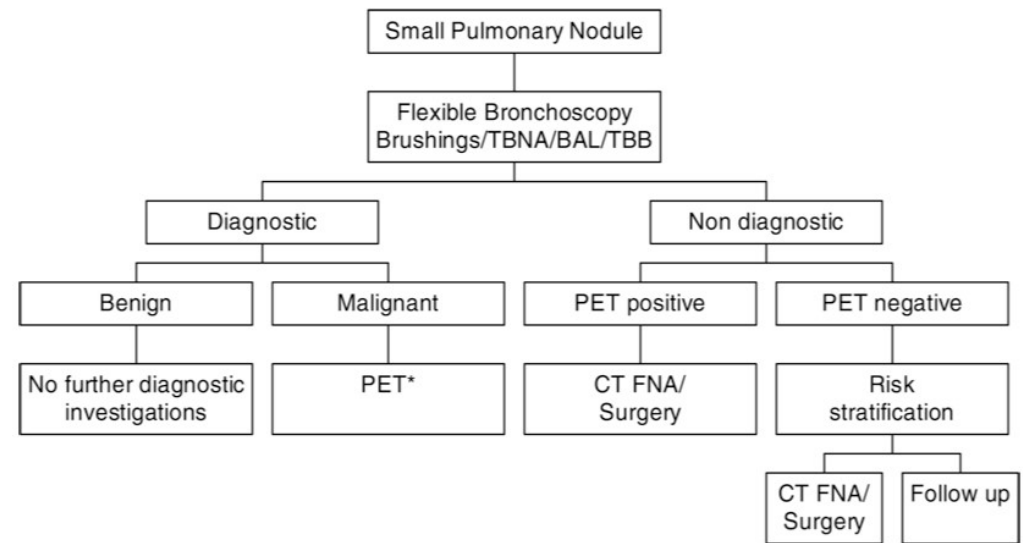
▶ * Fletcher JW, Kymes SM, Gould M, et al. A comparison of the diagnostic accuracy of 18F-FDG PET and CT in the characterization of solitary pulmonary nodules. J Nucl Med 2008; 49:179-185.

Evaluation of Solitary Pulmonary Nodule

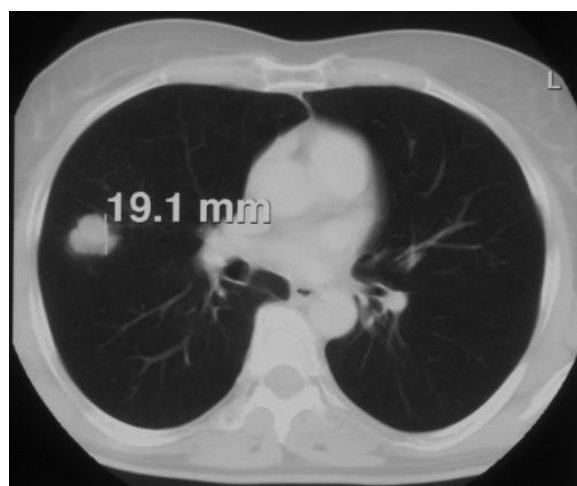
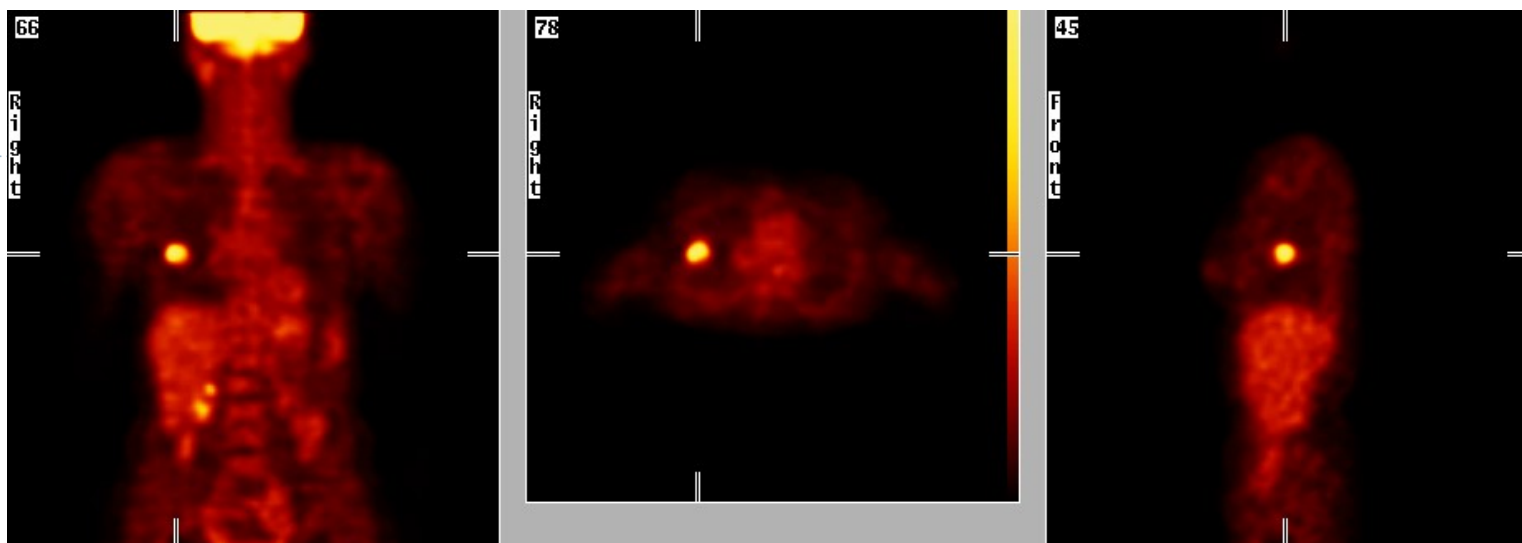
Sn 97% (83-100%) Sp 78% (52-100%)

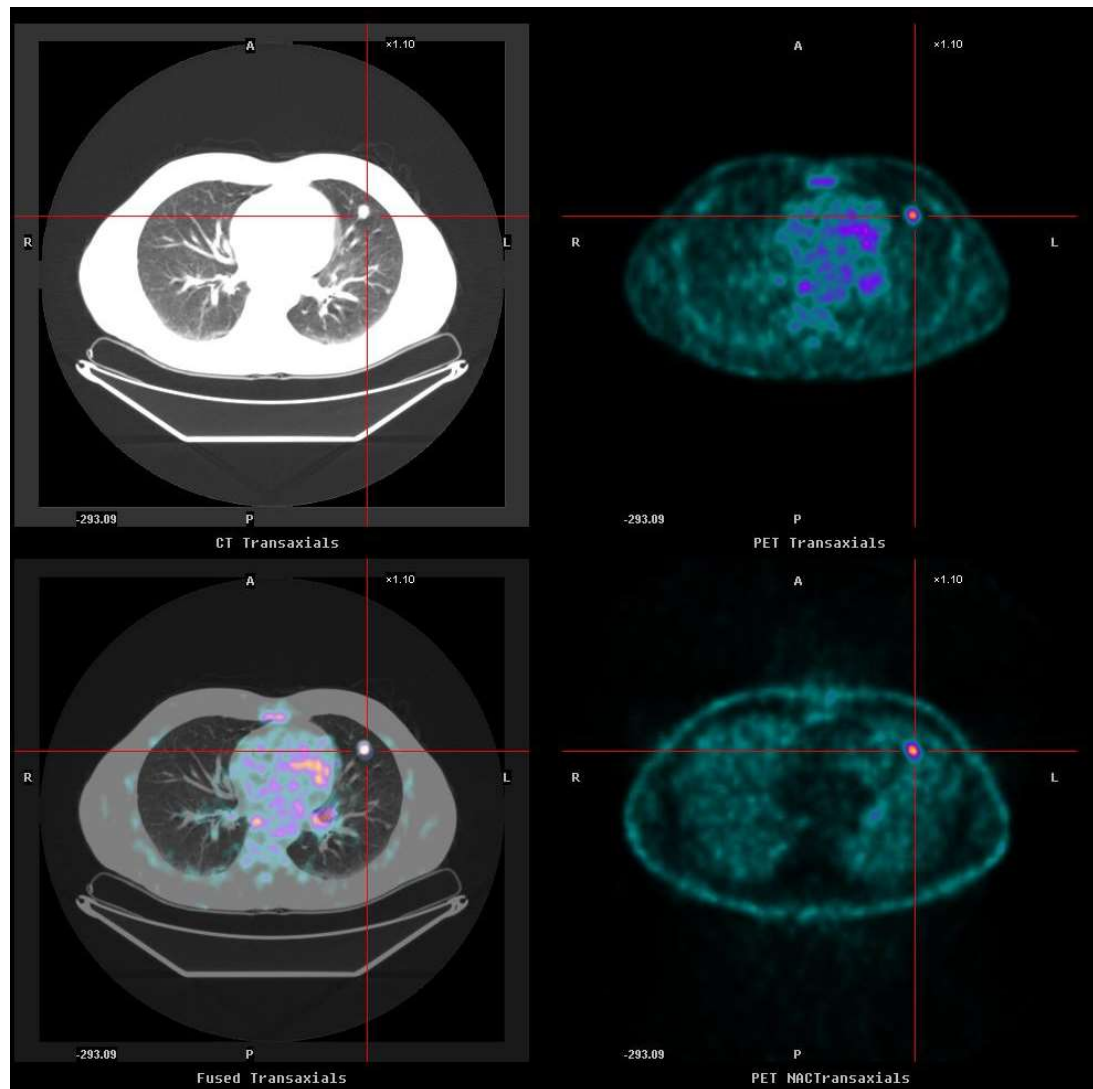
❖ False negative (SPN<5mm)

Application of FDG-PET in patients with SPN reduces unnecessary resections by 20%



Meta analiza, Dwamena et.al., Radiology, 2000: 513-536





Staging” NSCLC

The primary goal of pre-treatment staging is to determine the extent of disease so that management and prognostication can be done.

Staging is based on:

- ✓ Tumor Size
- ✓ Location
- ✓ Nodal Involvement
- ✓ Presence/Absence of Metastasis
- ✓ Precise Primary Tumor and Nodal Staging

CT

Sn 20-86% (65%)

Sp 43-90% (80%)

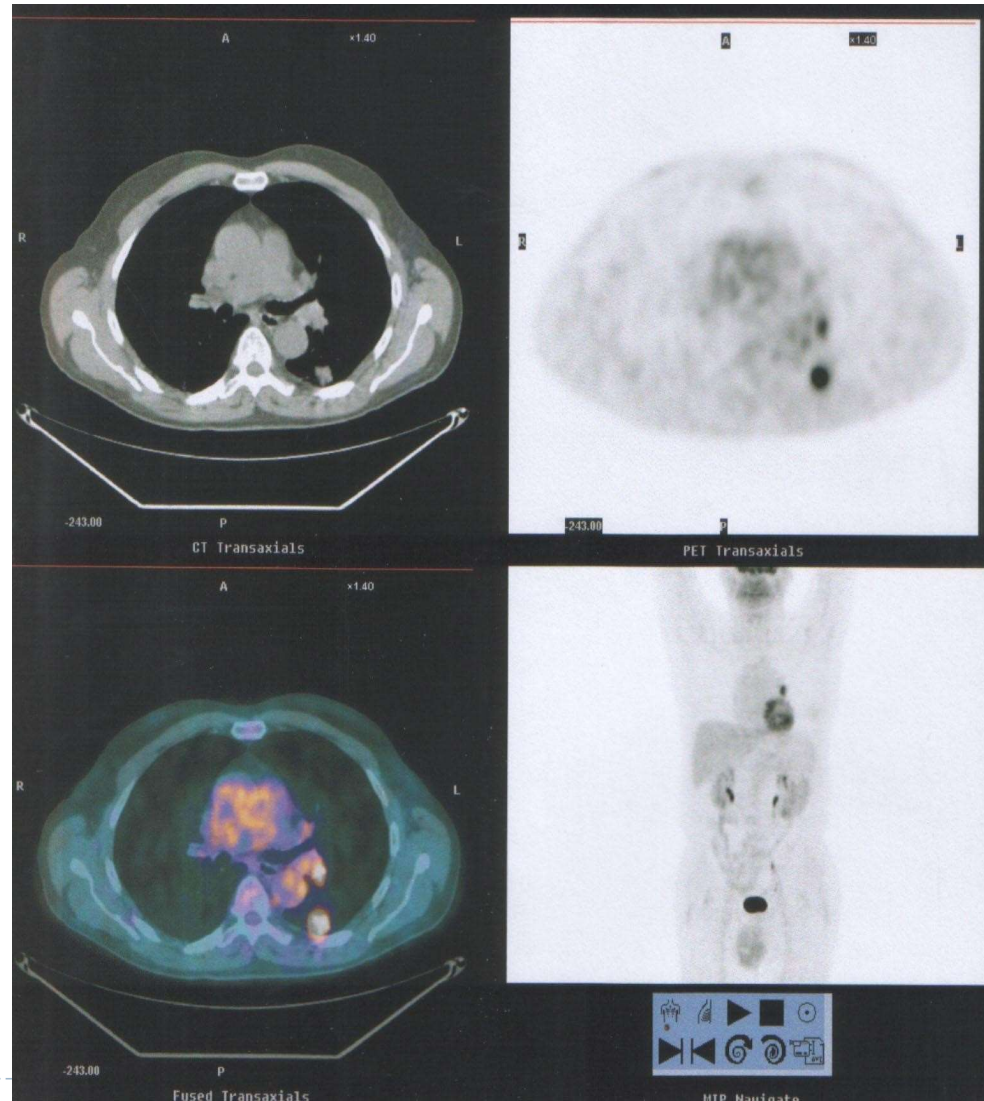
Acc 52-79% (75%)

FDG-PET

Sn 67-100% (89%)

Sp 79-100% (92%)

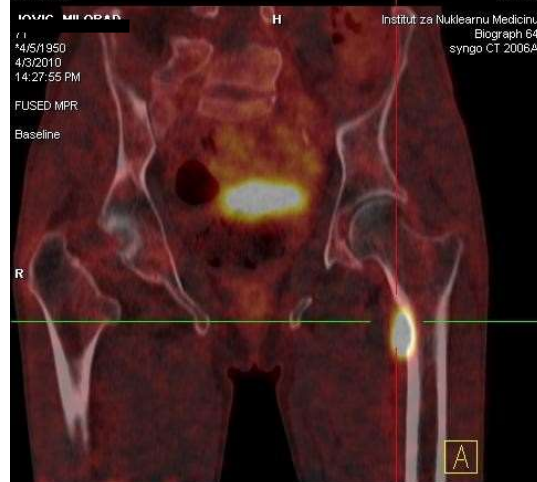
Acc 78-100% (90%)





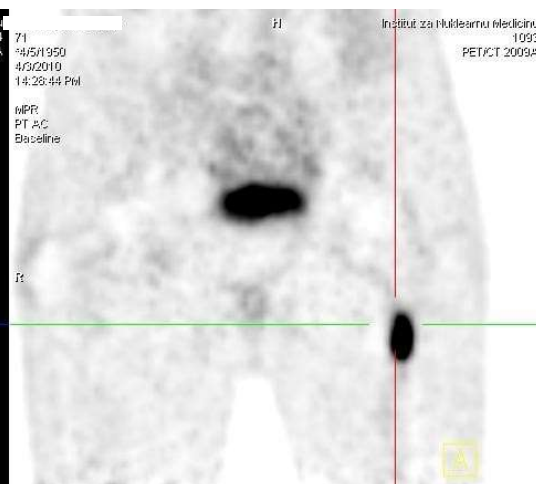
SP A100.7
SL: 3.000

W 1500
C 450



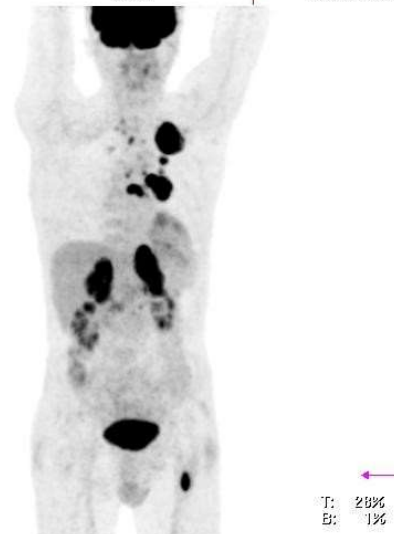
SP A100.7
SL: 5.000

CT,PT: 50/ 50
W 1500 T 4.89 SUV bw
C 450 B 0.23 SUV bw



SP A100.7
SL: 5.000

T 4.89 SUV bw
B 0.23 SUV bw



TNM

TNM STAGING OF LUNG CANCER (2009)

2009

M1a
- Satellite (separate) tumor nodule(s) in contralateral lung
- Pleural nodules or malignant pleural or pericardial effusion
M1b
Distant metastasis

Stage IV (Any T, Any N, M1)

(Distant metastasis present)

M1

M0

DISTANT METASTASIS (M)

(No distant metastasis)

Scapular (ipsi./ contralateral)	Supraclavicular	Hilar	Mediastinal	Subcarinal	Mediastinal	Hilar	Peribronchial	LYMPH NODE (N)
● ● ● ●								N3
- - - -				● ●				N2
- - - -				- -		● ●		N1
- - - -				- -		- -		N0

Explanation of lymph node staging:

-For any N category, one or more of the groups marked by ● must be involved and the involvement of all groups marked by □ should be absent.

-The presence or absence of involvement in groups marked by ▨ does not alter N staging in the corresponding category.

Stage III B

Stage III A

Stage II A

II B

Stage I A

I B

II A

Stage II B

PRIMARY TUMOR (T)

T1a

T1b

T2a

T2b

T3

T4

Stage 0
(Tis N0 M0)

1- Size

≤ 2 cm

> 2 cm

≤ 3 cm

> 3 cm

≤ 5 cm

Any size ≤ 7 cm if 1 or more of the criteria of extent are present*

> 5 cm

≤ 7 cm

> 7 cm or Any size if 1 or more of the criteria of extent are present

Any size if 1 or more of the criteria of extent are present

Tis: Carcinoma in situ

Occult Carcinoma
(Tx N0 M0)

Tx: Tumor is proven histopathologically (+ Cytology) but not detected by imaging or bronchoscopy)

No extension proximal to the lobar bronchus**

Vs. Atelectasis or obstructive pneumonitis extending to the hilum but not involving the entire lung

Main bronchus < 2 cm distal to the carina***
Vs. Atelectasis or obstructive pneumonitis involving the entire lung

Involvement of the carina

2- Criteria of Extent

Endo-bronchial Location

Local Invasion

Satellite Nodule(s)

None; the tumor is surrounded by lung or visceral pleura

Visceral pleura

None

None

Chest wall***, diaphragm, phrenic nerve, mediastinal pleura and/or parietal pericardium

Separate tumor nodule(s) in the same lobe

Mediastinum, trachea, heart, great vessels, recurrent laryngeal nerve, esophagus, vertebral body

Separate tumor nodule(s) in a different ipsilateral lobe

The 2009 TNM staging system applies to non-small cell lung carcinoma as well as to small cell lung carcinoma and carcinoid tumor of the lung

*: A tumor with these features is classified as T2a if ≤ 5 cm in size and T2b if > 5 cm and ≤ 7 cm

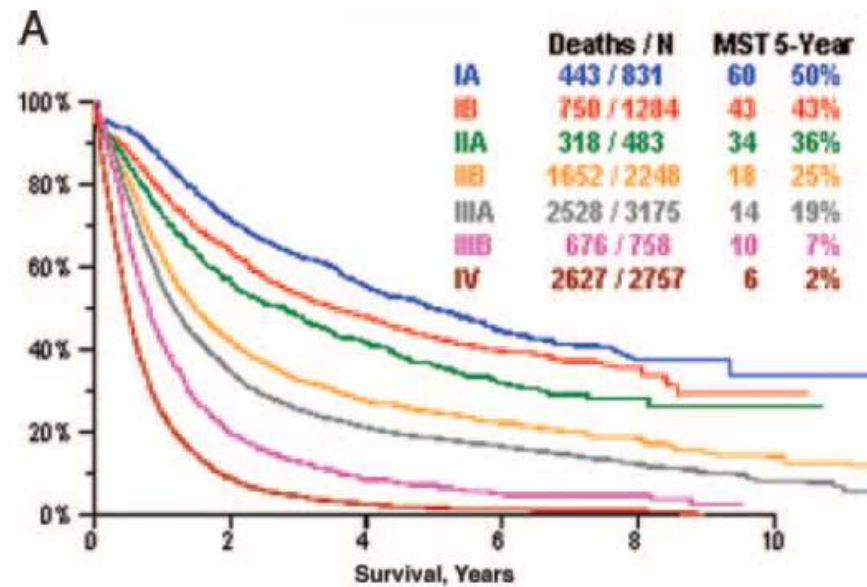
** : The uncommon superficial spreading tumor with invasion limited to the bronchial wall is considered T1a regardless of size and extension to the main bronchus

***: Including superior sulcus tumors

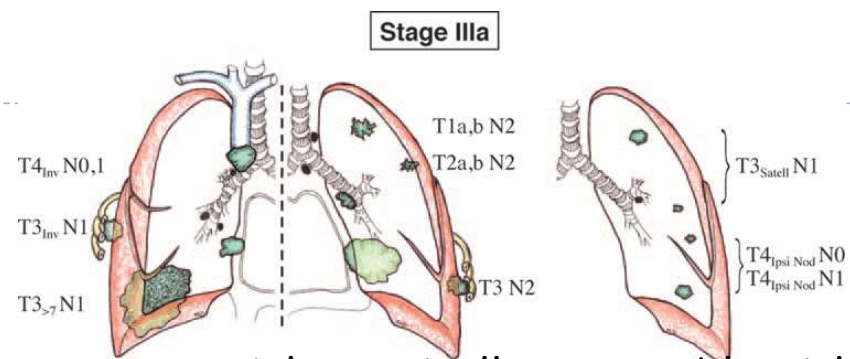
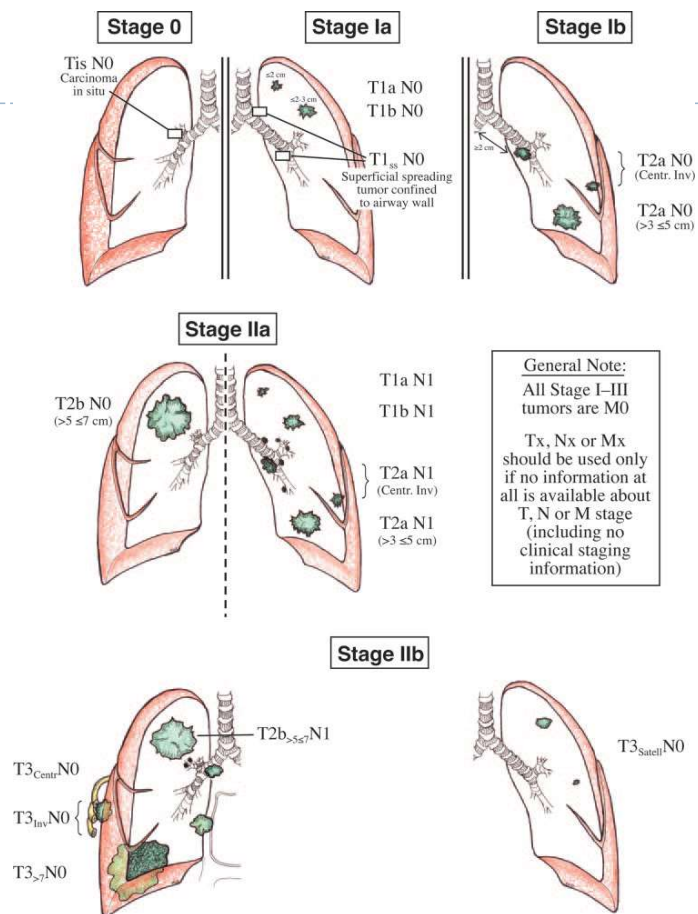
Lababede O, Chest
2011; 139: 183-189

TNM

Stage Groups	Descriptors, % of all		
	T	N	M
Ia	T1a,b	N0	M0
Ib	T2a	N0	M0
IIa	T1a,b	N1	M0
	T2a	N1	M0
	T2b	N0	M0
IIb	T2b	N1	M0
	T3	N0	M0
IIIa	T1-3	N2	M0
	T3	N1	M0
	T4	N0,1	M0
IIIb	T4	N2	M0
	T1-4	N3	M0
IV	T _{Any}	N _{Any}	M1a,b



Detterbeck F, Chest
2009; 136: 260-271



potentially surgically resectable with CHT

not surgically resectable

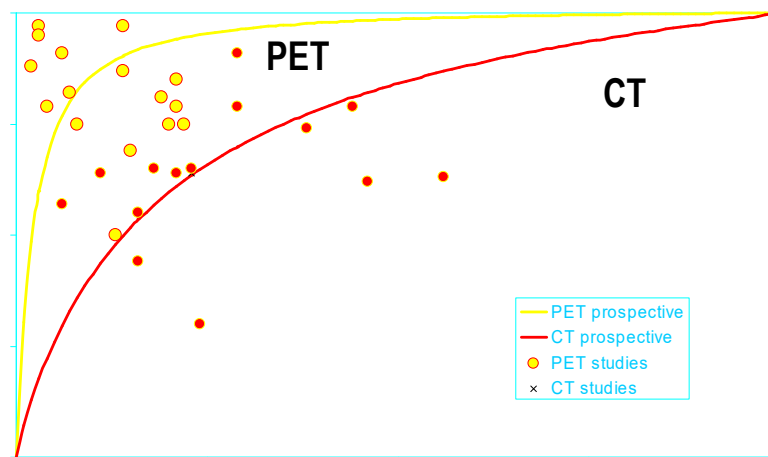
surgically resectable.

LIMITATIONS OF CT

- ▶ Limited ability to differentiate benign from malignant lesions
- ▶ Limited usefulness in the detection of chest wall and mediastinal invasion
 - ▶ Sensitivity & Specificity = 50-70%¹
- ▶ Several meta-analysis reported low sensitivity and specificity of CT for mediastinal LN involvement:
 - ▶ Sensitivity = 50-65%²
 - ▶ Specificity = 65-85%

-
- ▶
1. Vesselle H et al. J Thorac Cardiovasc Surg 2002; 124: 511-519
 2. Birim O et al. Ann Thorac Surg 2005; 79: 375-381

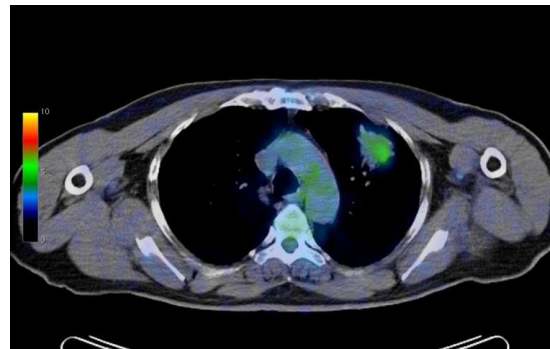
PET/CT NSCLC N-Staging



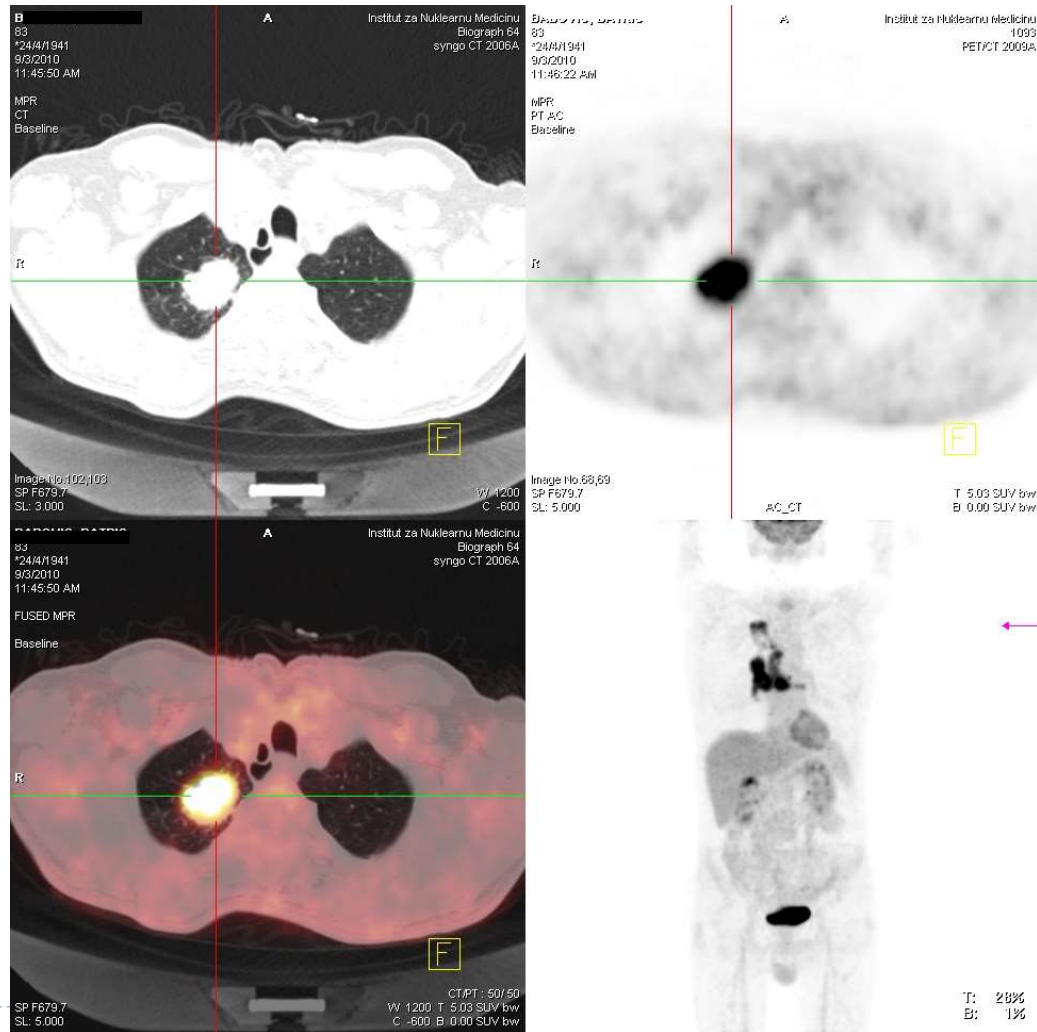
PET is more accurate than CT for N-Staging NSCLC.
(Baum et al. Q J Nucl Med Mol Imaging 2004)

PET changes N Staging u 21% of patients planning for surgery (Beadsmoore et al. Eur J Radiol 2003)

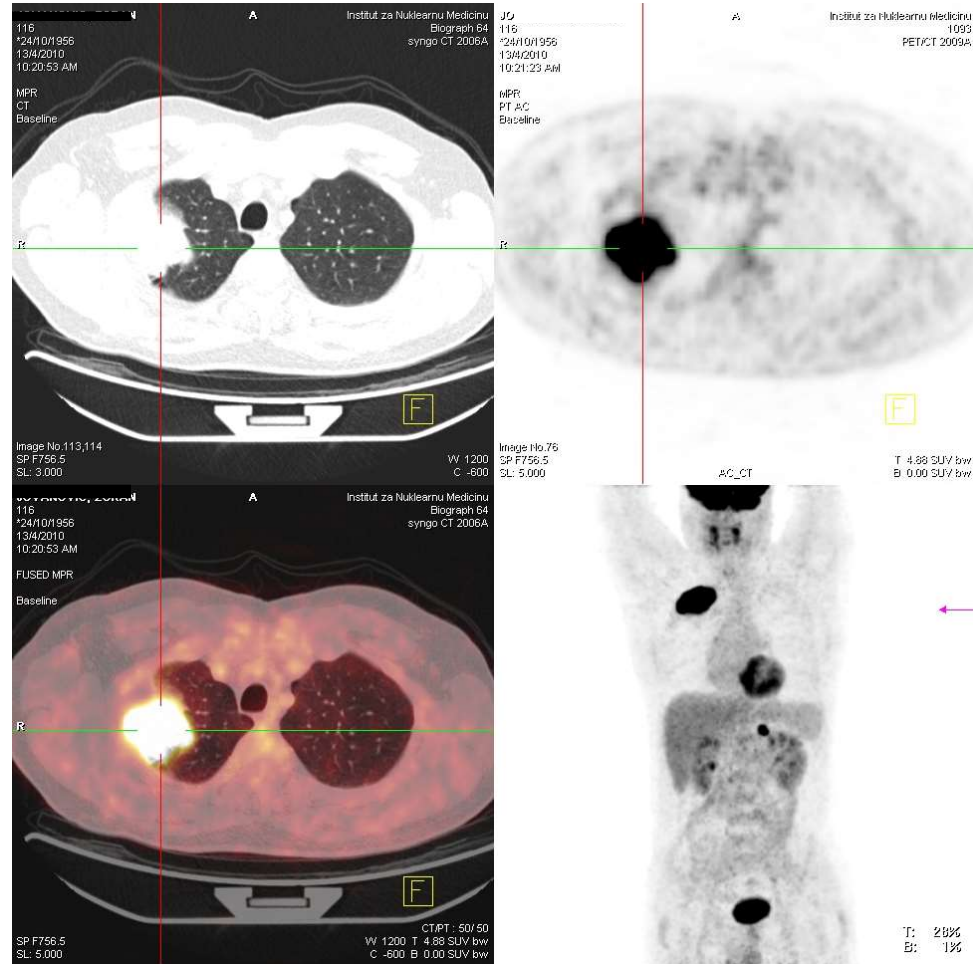
T2-N0-M0: Stage IB



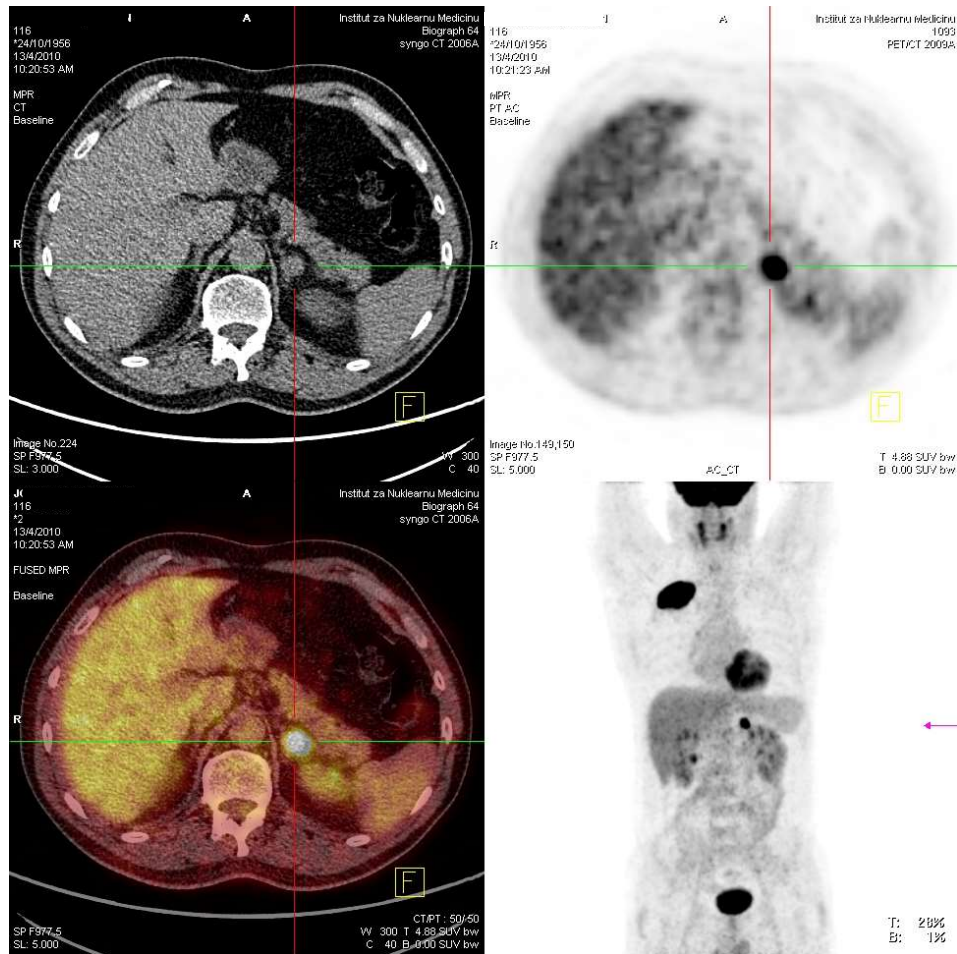
Stage IIIA: T3, N2, M0



Stage IV: T3, N0, M1b



Stage IV: T3, N0, M1b



Small Cell Lung Cancer

Neuroendocrine aggressive tumor

Two stage classification:

- ▶ Limited: tumor confined to unilateral chest
- ▶ Treatment: Chemotherapy and radiation
- ▶ Extensive: Contralateral or distant disease
- ▶ Treatment: Chemotherapy + PPRT
- ▶ Change of management due to FDG PET: 8-29%

Blum R et al. Am J Clin Oncol 2004;27:164-171.

Bradley JD et al. J Clin Oncol 2004;22:3248-3254.

▶ For neuroendocrine lung tumors

- ^{18}F -DOPA
- ^{68}Ga -DOTA TOC/TATE/NOC

▶ For dedifferentiation of neuroendocrine lung tumors


- ^{18}F -FDG



small cell lung cancer- SCLC

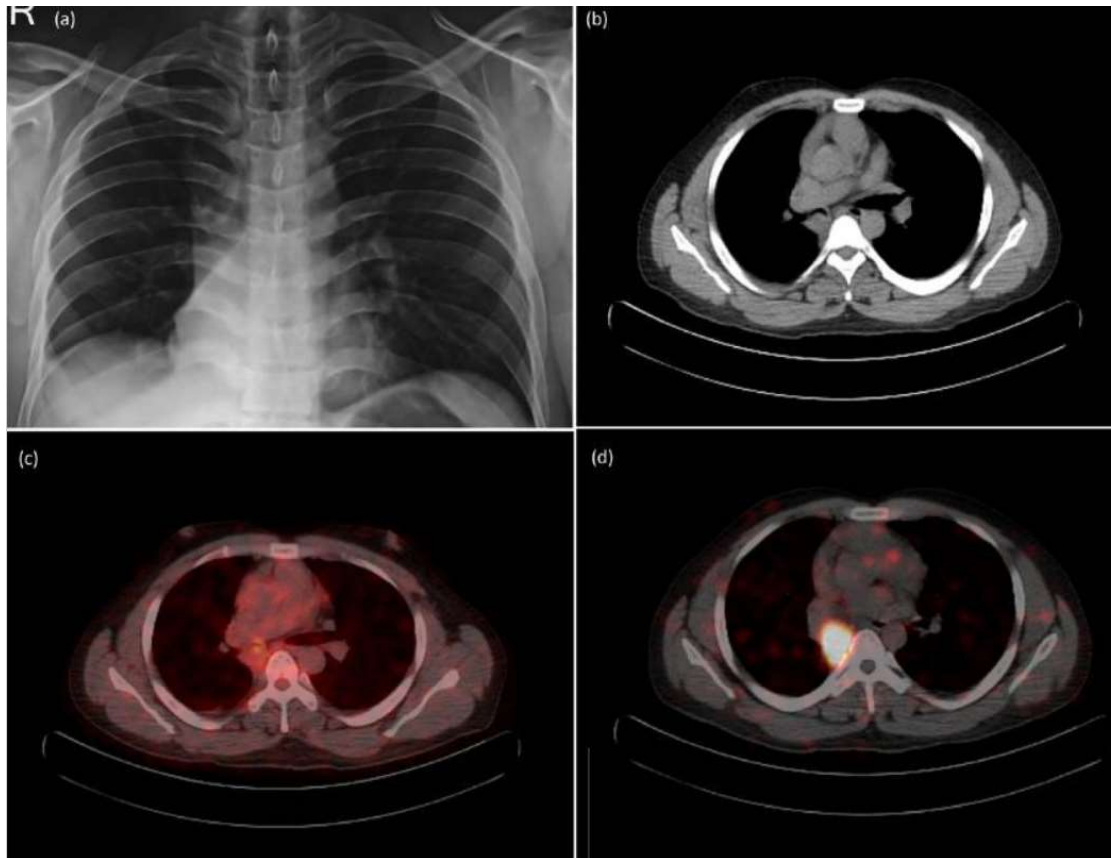
SSTR imaging (Octreoscan®)

well-differentiated NETs express somatostatin receptors, so this method can not only detect NETs and their metastases, but also opens up the possibility of therapeutic application of somatostatin analogs

	Well-differentiated		Poorly differentiated
Grade (ENETS)	Low (G1)	Intermediate (G2)	High (G3)
Ki-67 index (%)	≤2	3-20	>20
Anatomic imaging	more rapid growth on serial imaging		
Functional imaging			
Prognosis	Indolent (slowly growing)		Aggressive
Treatment options	Surgery for localised +/- resectable metastatic disease		
	Observation Somatostatin analogues Radionuclide therapy		Chemotherapy
	Everolimus, sunitinib, α-interferon Liver metastases: radiofrequency ablation, hepatic embolisation, TACE, SIR-Spheres		



small cell lung cancer- SCLC



^{18}F FDG (-)

^{68}Ga -Dotatoc (+)



CONCLUSION

- ▶ Integrated PET/CT provides:
 - ▶ More precise staging than all the other imaging techniques
 - ▶ Allows better selection of patients for new modalities of treatment
 - ▶ Helps in re-staging after induction therapy
 - ▶ It is cost-effective
 - ▶ Precise delineation - EBRT Planning
 - ▶ Helps in follow up evaluation by differentiating Residual or recurrent tumor from Post-treatment scarring

