

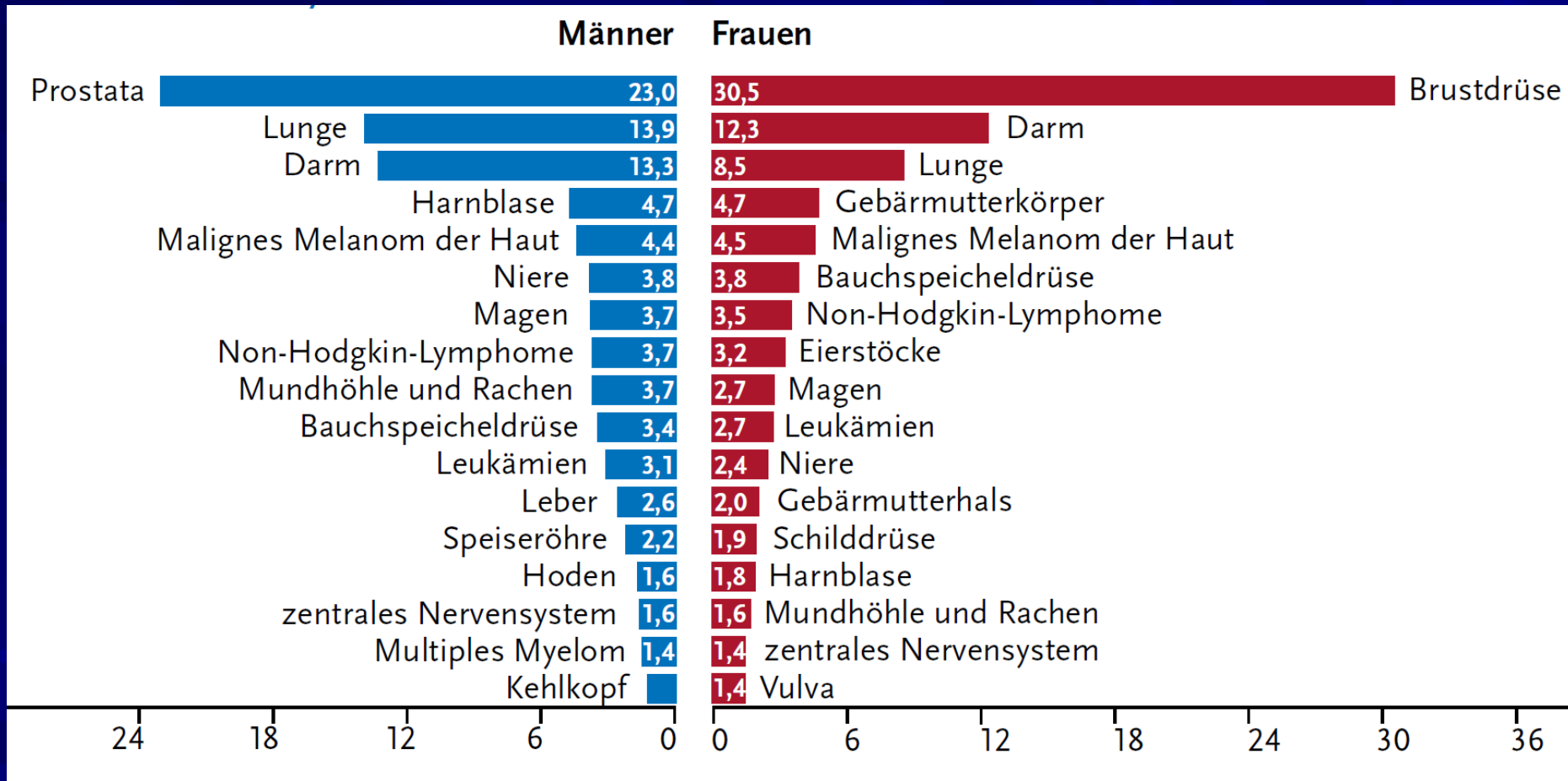
# Pulmonary oncology

József Lövey

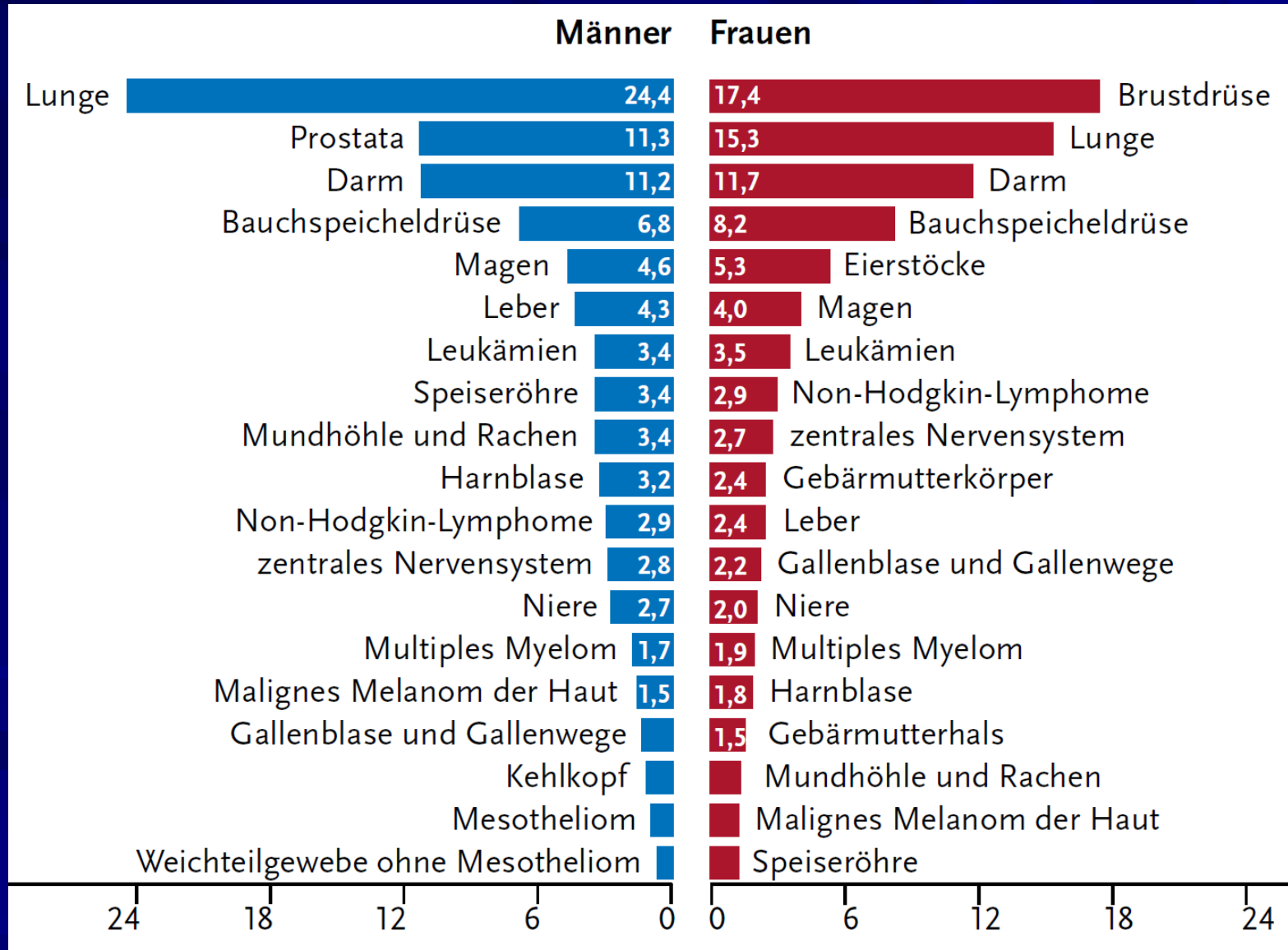
National Institute of Oncology

Budapest

# Epidemiology / incidence



# Epidemiology / mortality



# Epidemiology

Inzidenz	2013		2014		Prognose für 2018	
	Männer	Frauen	Männer	Frauen	Männer	Frauen
Neuerkrankungen	35.310	19.200	34.560	19.280	33.700	22.000
rohe Erkrankungsrate <sup>1</sup>	89,5	46,6	87,1	46,7	83,7	52,9
standardisierte Erkrankungsrate <sup>1,2</sup>	59,6	29,1	57,3	29,0	53,1	31,8
mittleres Erkrankungsalter <sup>3</sup>	70	69	70	69		

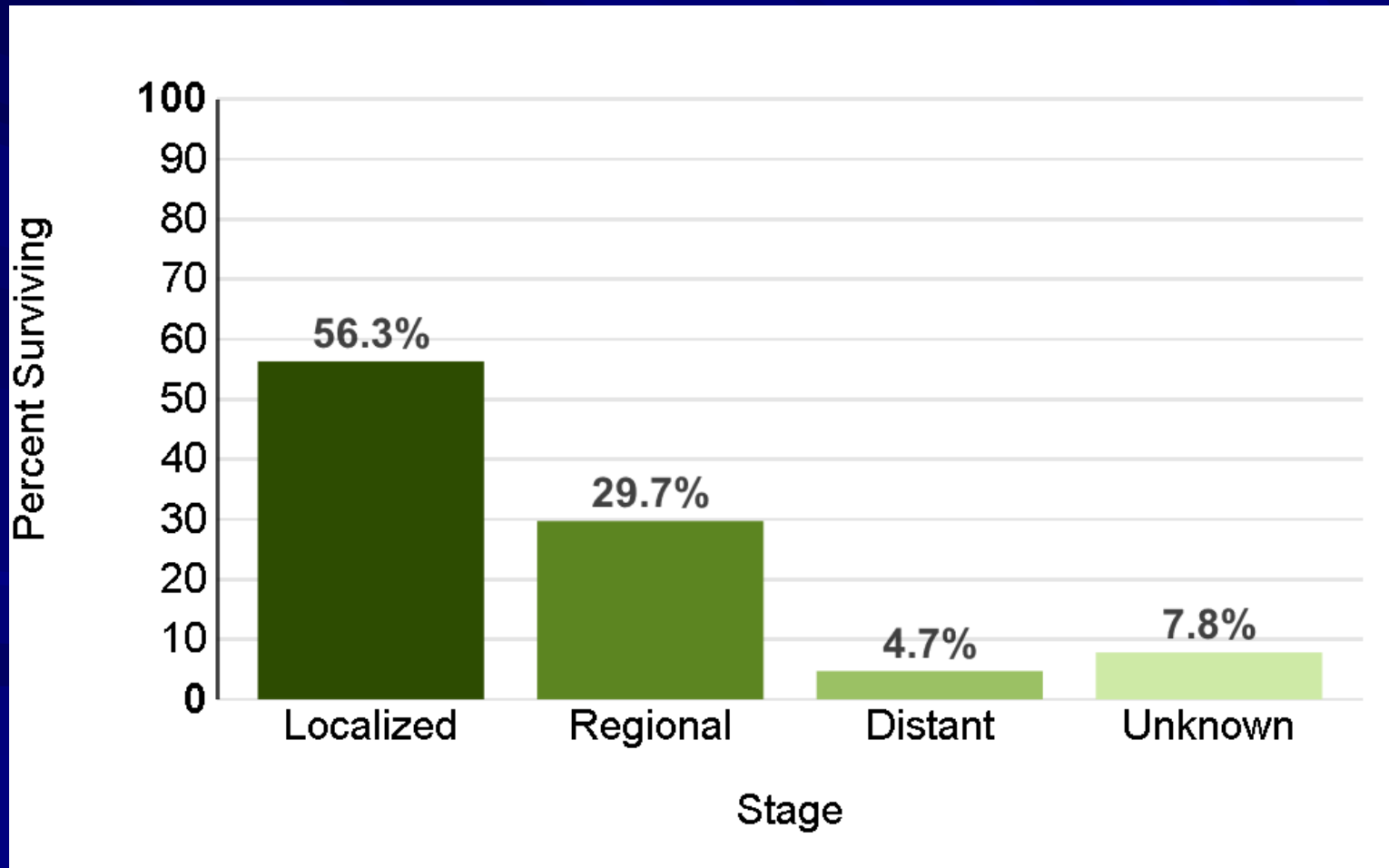
Mortalität	2013		2014		2015	
	Männer	Frauen	Männer	Frauen	Männer	Frauen
Sterbefälle	29.708	15.140	29.560	15.524	29.378	15.881
rohe Sterberate <sup>1</sup>	75,3	36,8	74,5	37,6	73,1	38,3
standardisierte Sterberate <sup>1,2</sup>	48,8	21,7	47,6	21,7	46,6	22,1
mittleres Sterbealter <sup>3</sup>	72	71	72	71	72	71

<sup>1</sup> je 100.000 Personen <sup>2</sup> altersstandardisiert nach alter Europabevölkerung <sup>3</sup> Median

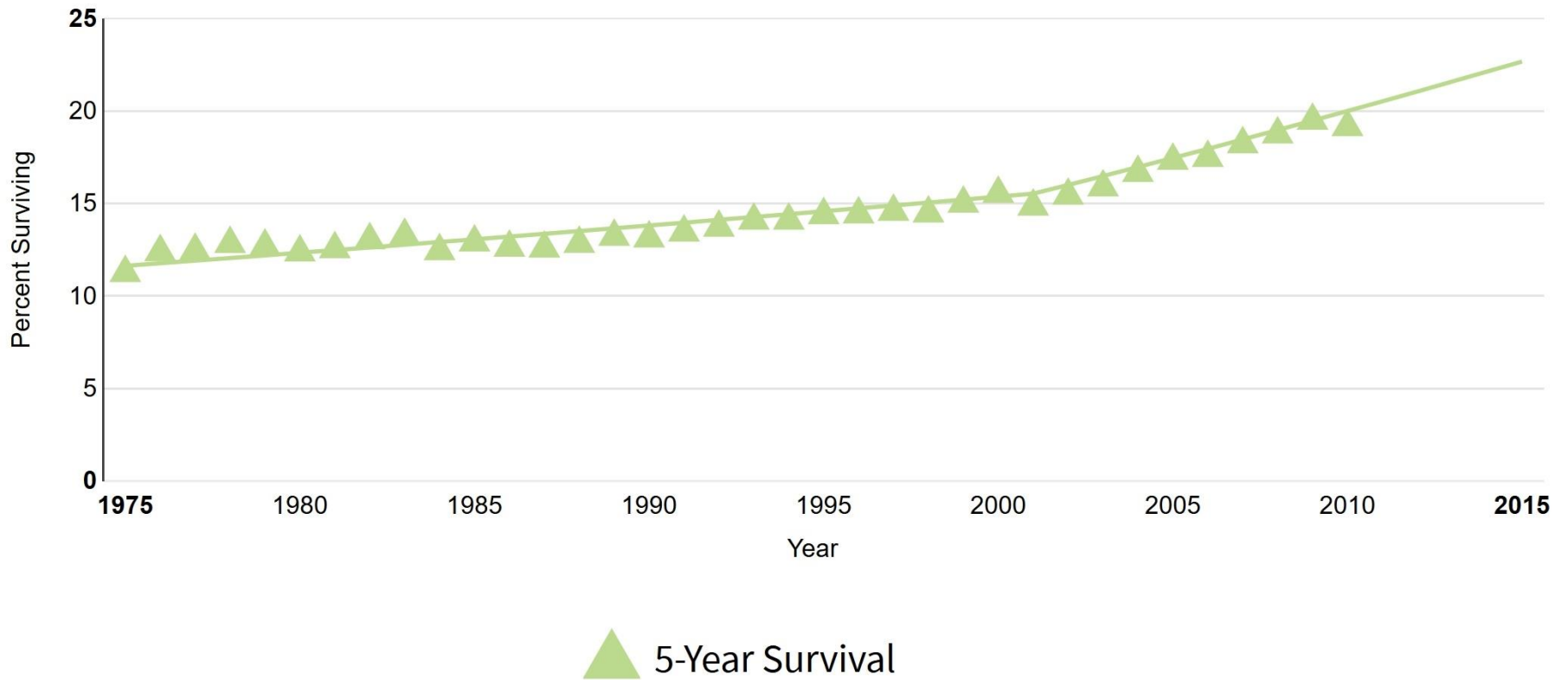
Prävalenz und Überlebensraten	5 Jahre		10 Jahre	
	Männer	Frauen	Männer	Frauen
Prävalenz	49.400	32.100	67.800	43.600
absolute Überlebensrate (2013–2014) <sup>4</sup>	13 (12–15)	18 (17–21)	8 (7–10)	12 (11–14)
relative Überlebensrate (2013–2014) <sup>4</sup>	15 (14–18)	20 (18–23)	11 (9–14)	16 (14–19)

# Survival by stage

- Estimated survival of lung cancer patients by SEER databases, USA



# Improvement of survival in 40 years



SEER database, USA

# Etiology

- Smoking
- Smoking
- Smoking
- Smoking
- Smoking
- Smoking
- Smoking
- Radon, asbestos, carcinogenes, air pollution, genetic background

A photograph of two cowboys on horseback, silhouetted against a bright orange and yellow sunset sky. They are walking away from the camera on a dirt path. The scene is framed by wooden fences on either side. The overall mood is somber and reflective.

**Bob, I've got cancer.**

Tobacco kills – don't be  
glamorous, be advertised, glam  
**WORLD NO TOBACCO**

©1999 World Health Organization, California Department of Public Health



iparks.com



 SINGAPORE CANCER SOCIETY





the  
art  
of  
quitting.com



SMOKING REDUCES YOUR ABILITY TO GET AN ERECTION



SMOKING REDUCES YOUR ABILITY TO GET AN ERECTION



Active in Smoking  
and Health

ADPH001



If you won't  
give up smoking  
for your lungs,  
heart or throat,

maybe you'll  
do it for  
your penis.

Did you know that there's  
a valve in your penis that  
traps the blood inside so  
you can get an erection?  
That every time you smoke,  
this valve is damaged?  
That if you don't quit now,  
it might stop working  
altogether? You do now.

Text HARD to 84118  
for a free information pack.  
Texts will be charged  
at your standard rate.  
Call 0800 159 0 159  
[www.stayinghard.info](http://www.stayinghard.info)

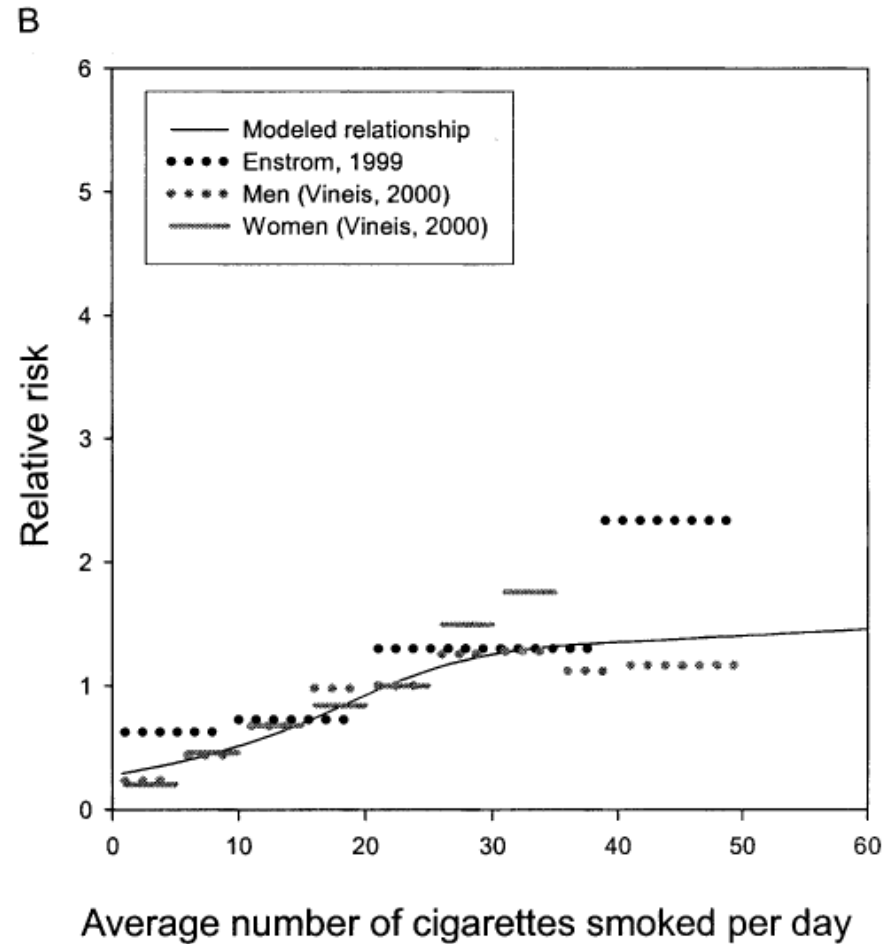
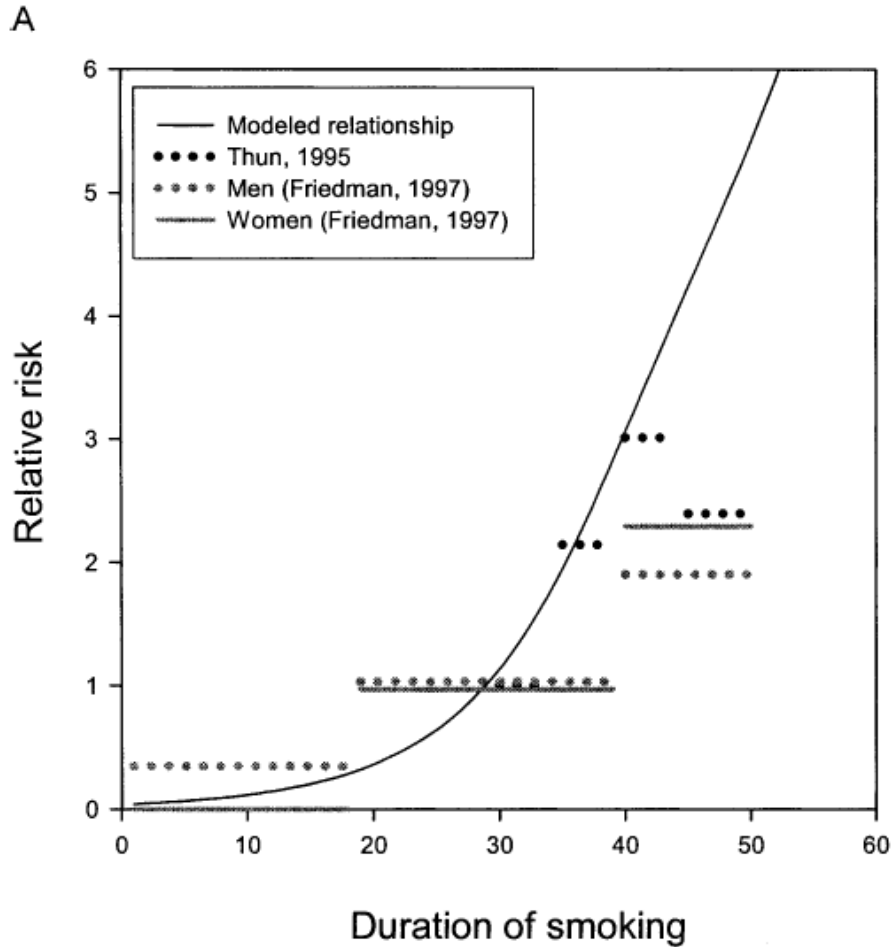


If you have any concerns about  
your health please contact your GP.





# Etiology



Benz[ <i>a</i> ]anthracene	2A
Benzo[ <i>b</i> ]fluoranthene	2B
Benzo[ <i>j</i> ]fluoranthene	2B
Benzo[ <i>k</i> ]fluoranthene	2B
Benzo[ <i>a</i> ]pyrene	1
Dibenz[ <i>a,h</i> ]anthracene	2A
Dibenzo[ <i>a,i</i> ]pyrene	2B
Dibenzo[ <i>a,e</i> ]pyrene	2B
Indeno[ <i>1,2,3-cd</i> ]pyrene	2B
5-Methylchrysene	2B
Furan	2B
Dibenz[ <i>a,h</i> ]acridine	2B
Dibenz[ <i>a,j</i> ]acridine	2B
Dibenzo[ <i>c,g</i> ]carbazole	2B
Benzo[ <i>b</i> ]furan	2B
<i>N</i> -Nitrosodimethylamine	2A
<i>N</i> -Nitrosoethylmethylamine	2B
<i>N</i> -Nitrosodiethylamine	2A

<i>N</i> -Nitrosopyrrolidine	2B
<i>N</i> -Nitrosopiperidine	2B
<i>N</i> -Nitrosodiethanolamine	2B
<i>N</i> â€-Nitrosoornicotine	1
4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone	1
2-Toluidine	2A
2,6-Dimethylaniline	2B
2-Naphthylamine	1
4-Aminobiphenyl	1
A-Î±-C	2B
MeA-Î±-C	2B
IQ	2A
Trp-P-1	2B
Trp-P-2	2B
Glu-P-1	2B
Glu-P-2	2B
PhIP	2B
Hydrazine	2B
Radio-isotope Polonium-210	1
Formaldehyde	1

Acetaldehyde	2B
Catechol	2B
Caffeic acid	2B
1,3-Butadiene	2A
Isoprene	2B
Benzene	1
Nitromethane	2B
2-Nitropropane	2B
Nitrobenzene	2B
Acetamide	2B
Acrylamide	2A
Acrylonitrile	2B
Vinyl chloride	1
1,1-â€Dimethylhydrazine	2B
Ethylene oxide	1
Propylene oxide	2B
Urethane	2B
Arsenic	1
Beryllium	1
Nickel	1
Chromium (hexavalent)	1
Cadmium	1
Cobalt	2B
Lead (inorganic)	2A



# Lung cancer screening

## ■ Randomized trials

- NLST, MILD, ITALUNG, DANTE, DLCST, LUSI, UKLS

## ■ Statement of the EU:

- **Low-dose CT** is the method of screening
- Screening must be **risk adapted**
- **Informed involvement** of screenees has primary importance
- Screening should be semi-**automatized**, QA should be in place
- Procedures of screening has to be defined on national level
- Positively screened must be treated **multidisciplinary**
- Organization must start as screening **saves lives**

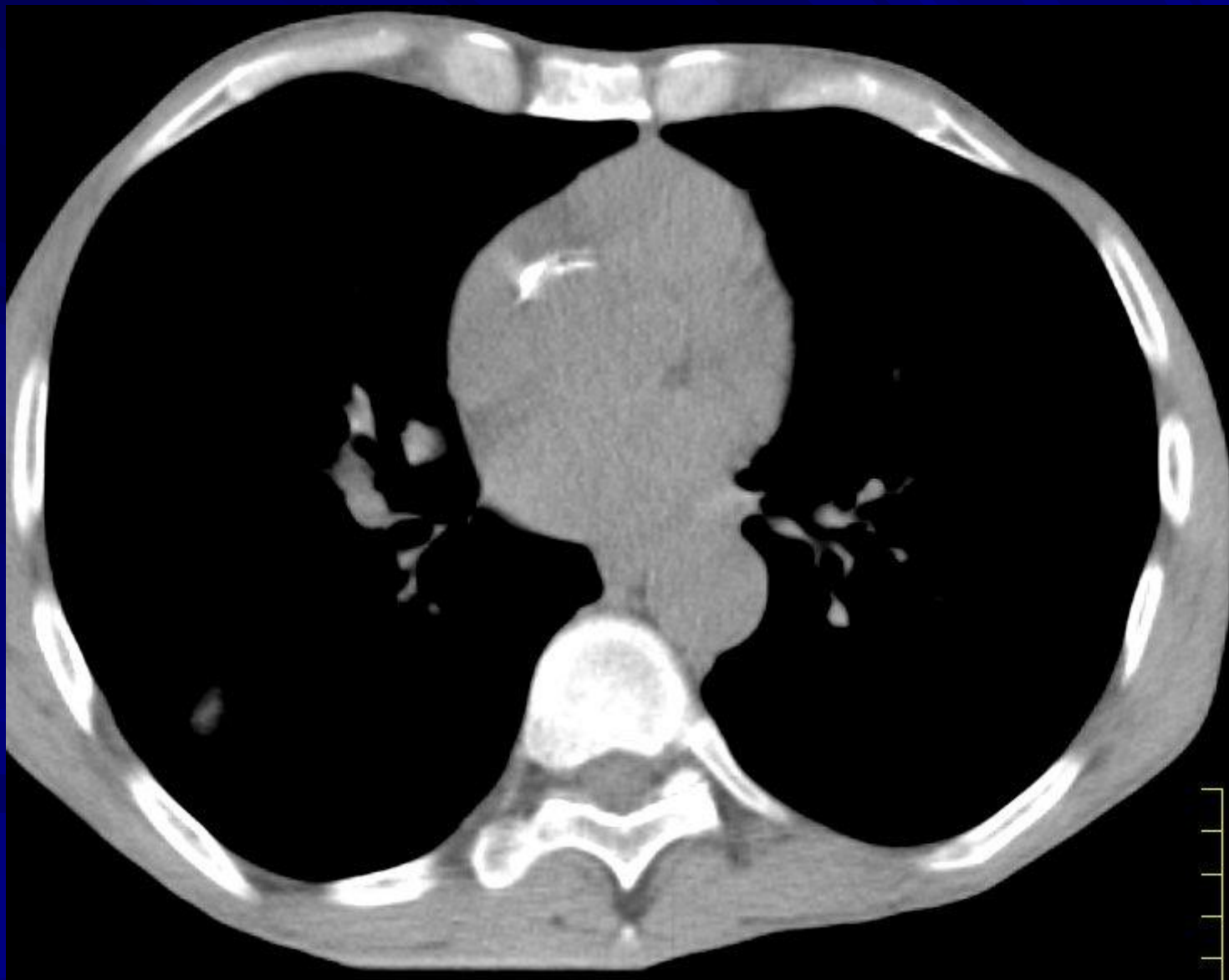
# Diagnostics

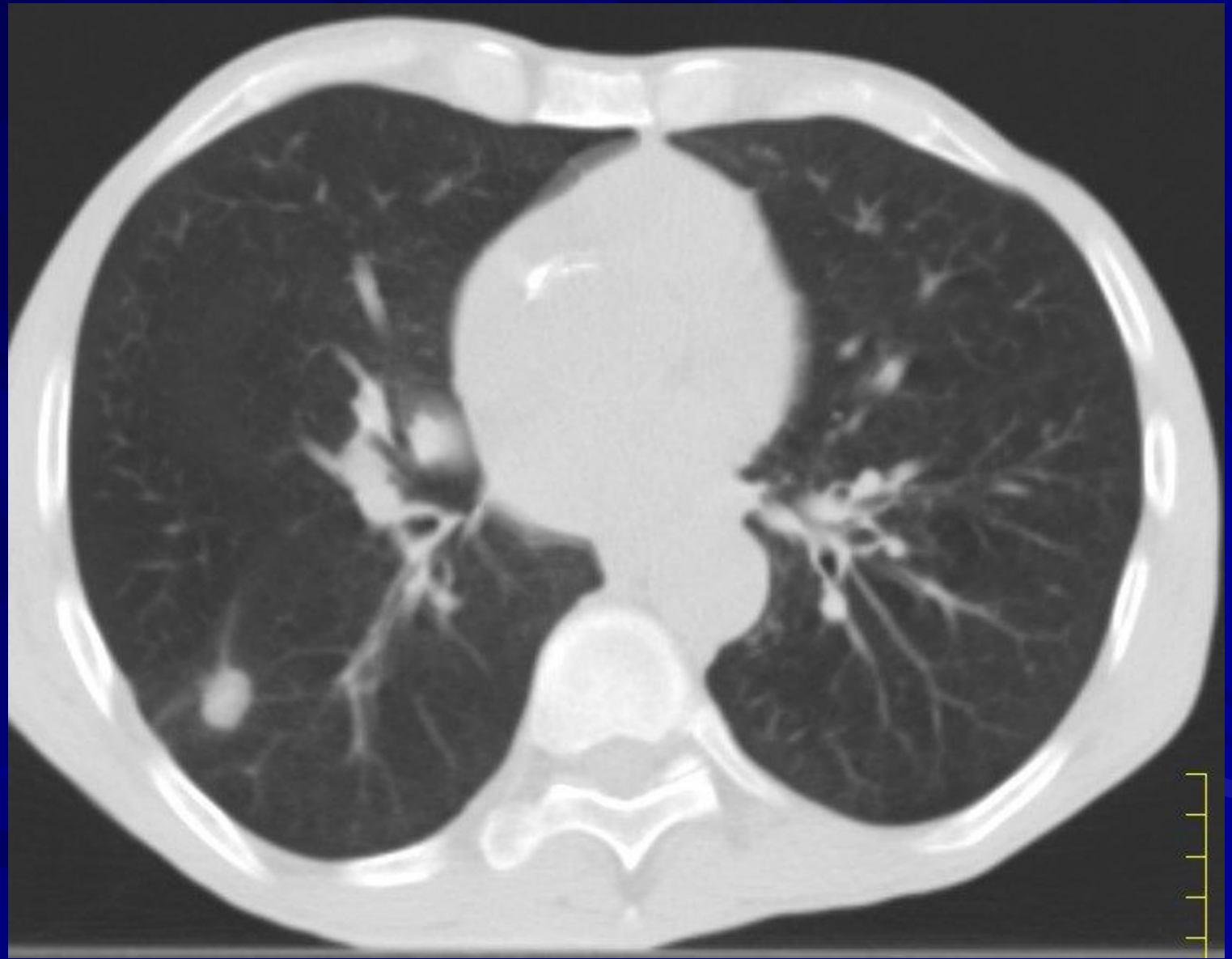
- Chest xR
- **CAT scan**
- **Positron Emission Tomography (PET)**
- Others (bone scan, **MRI**)
- Bronchoscopy
- Transthoracal biopsy (with xR or CAT assisted)
- Mediastinoscopy
- **Video Assisted ThoracoScopy (VATS)**

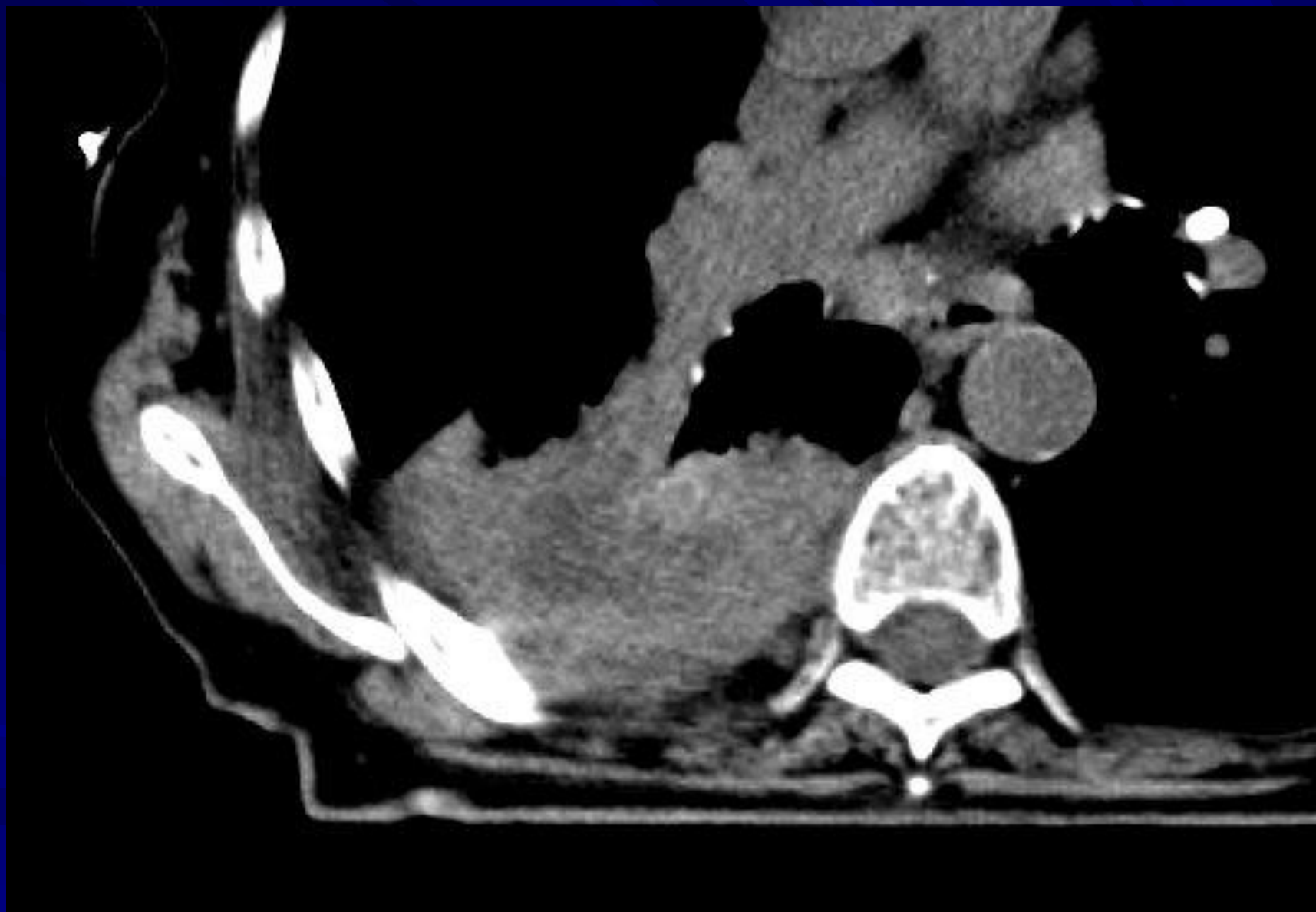
# Chest xR

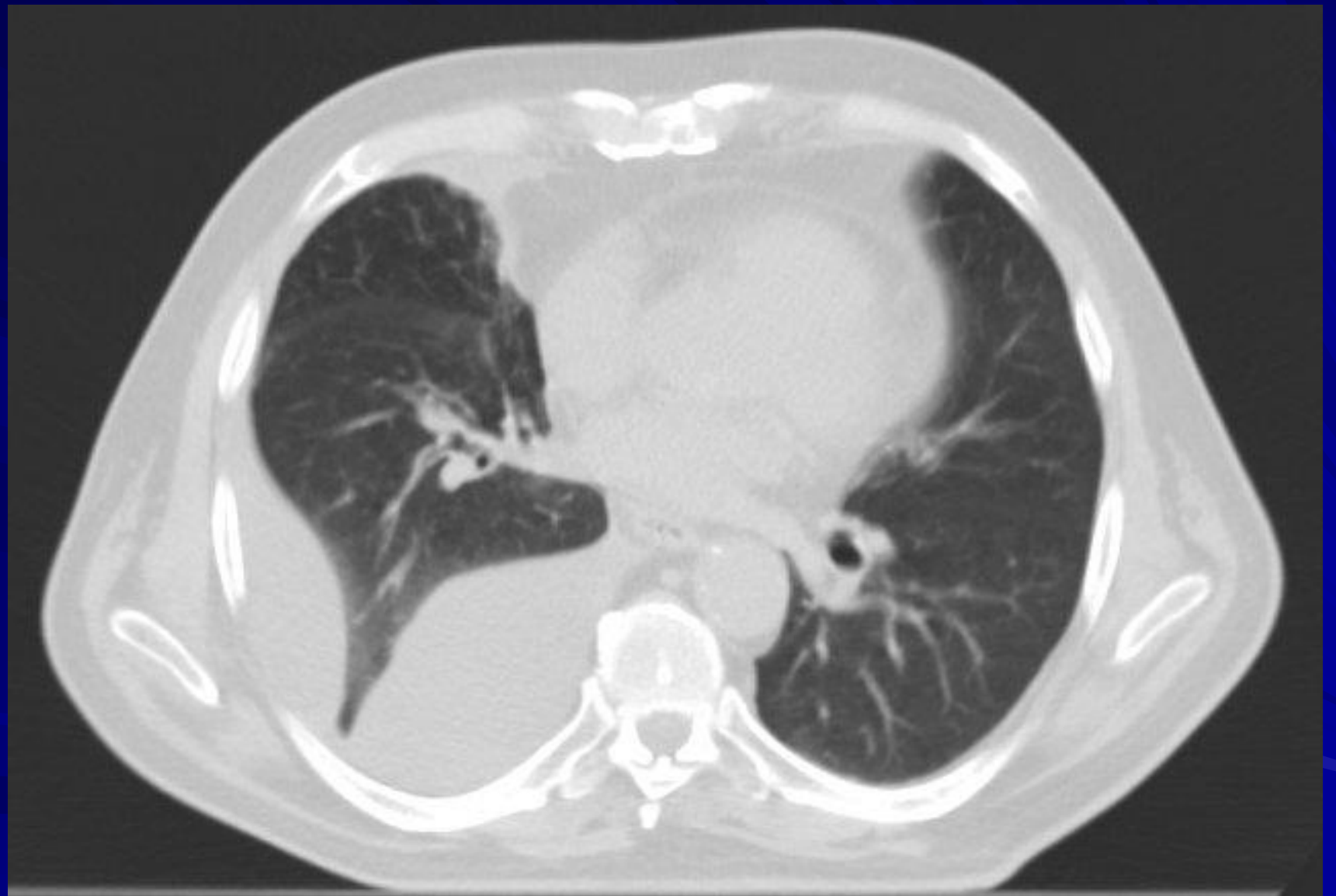


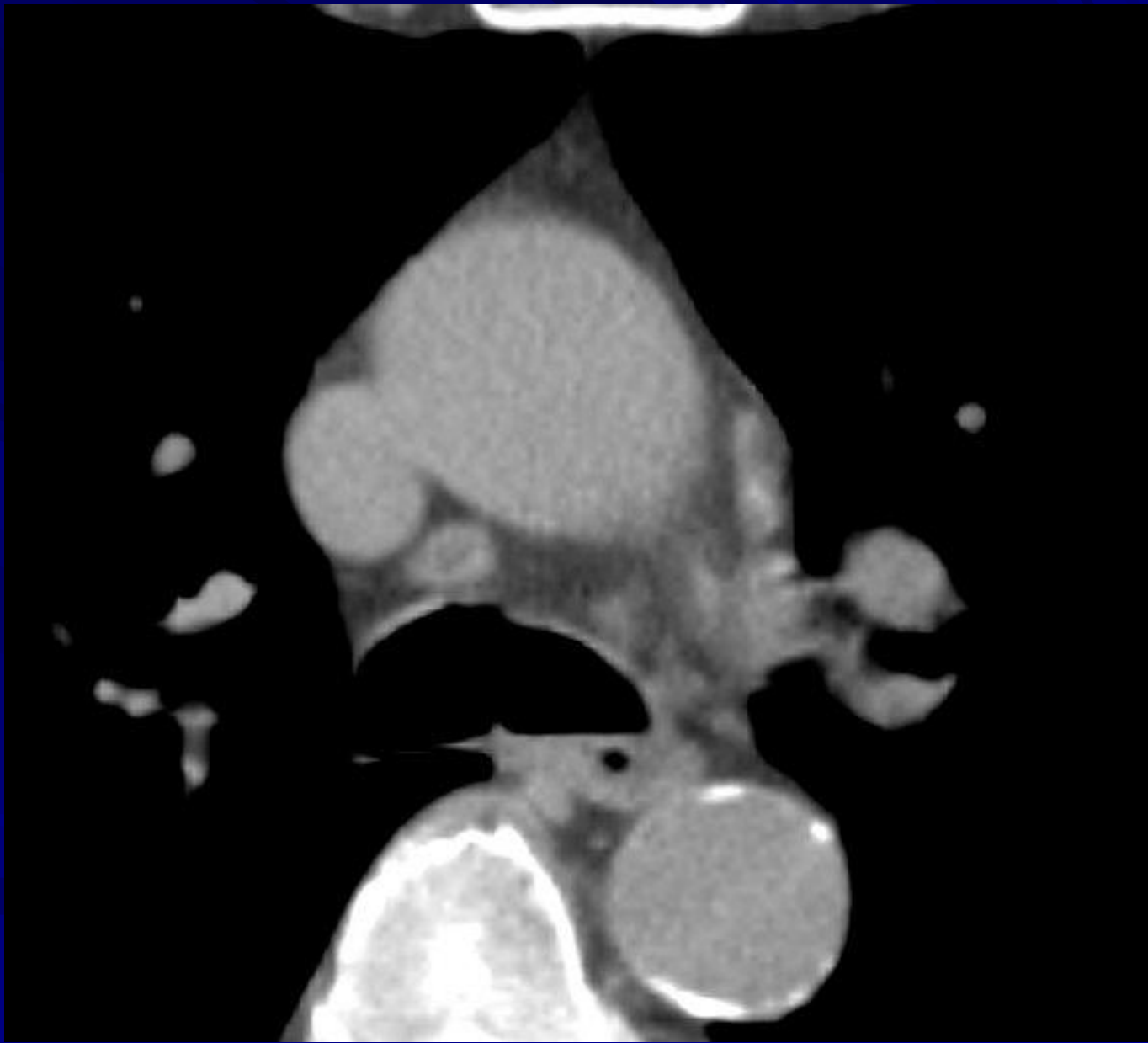
# CAT



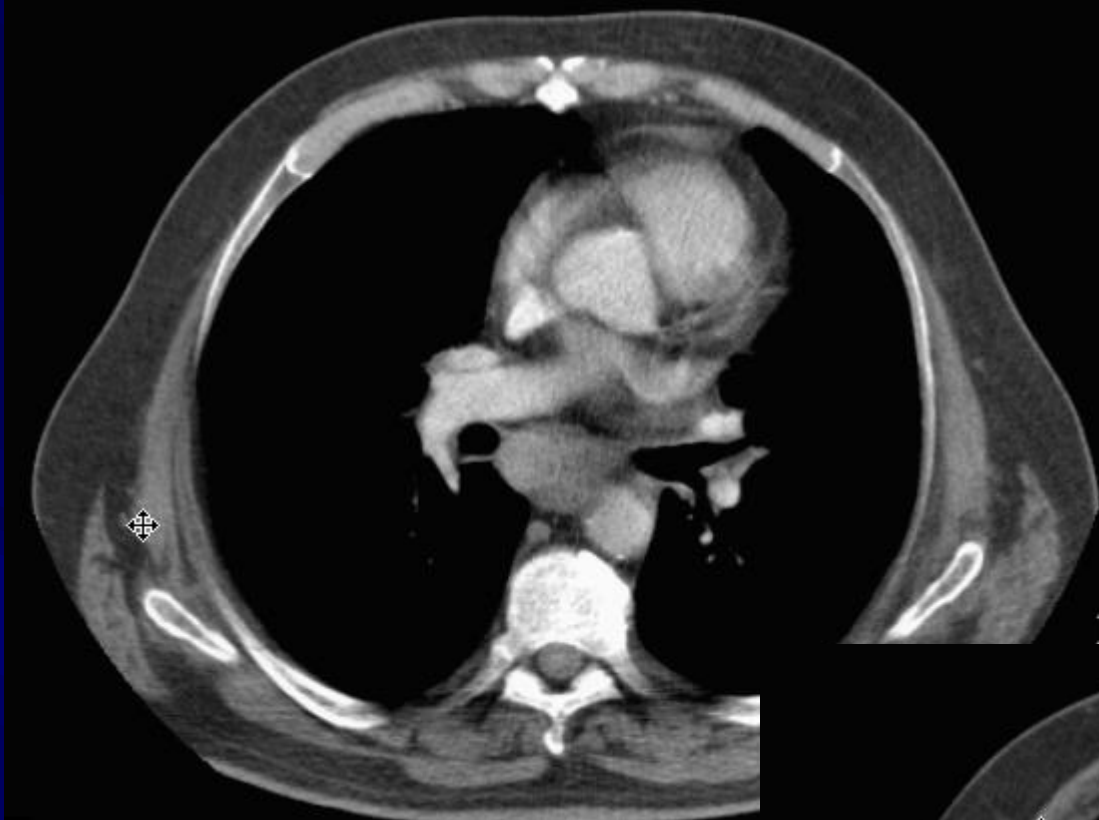


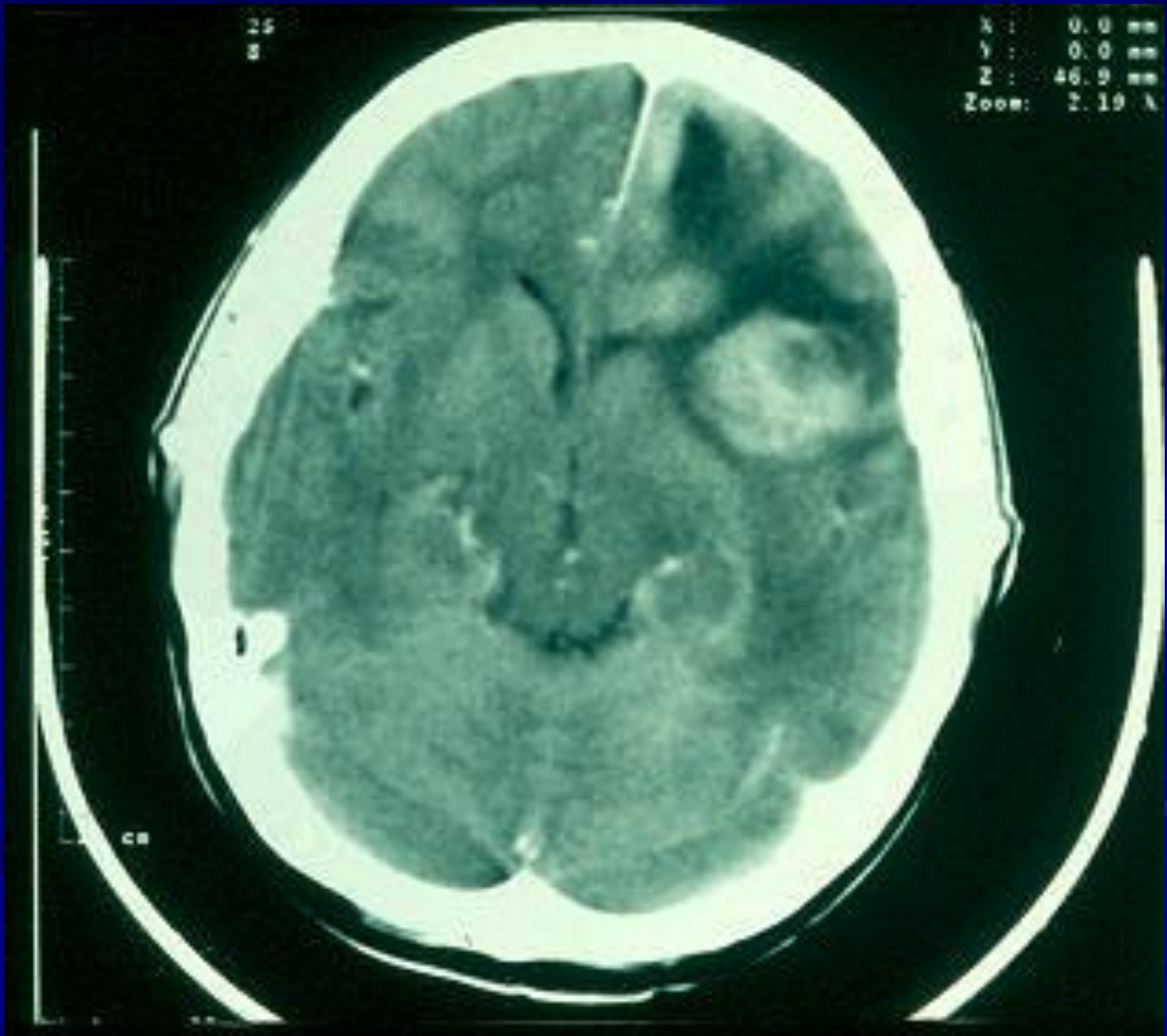


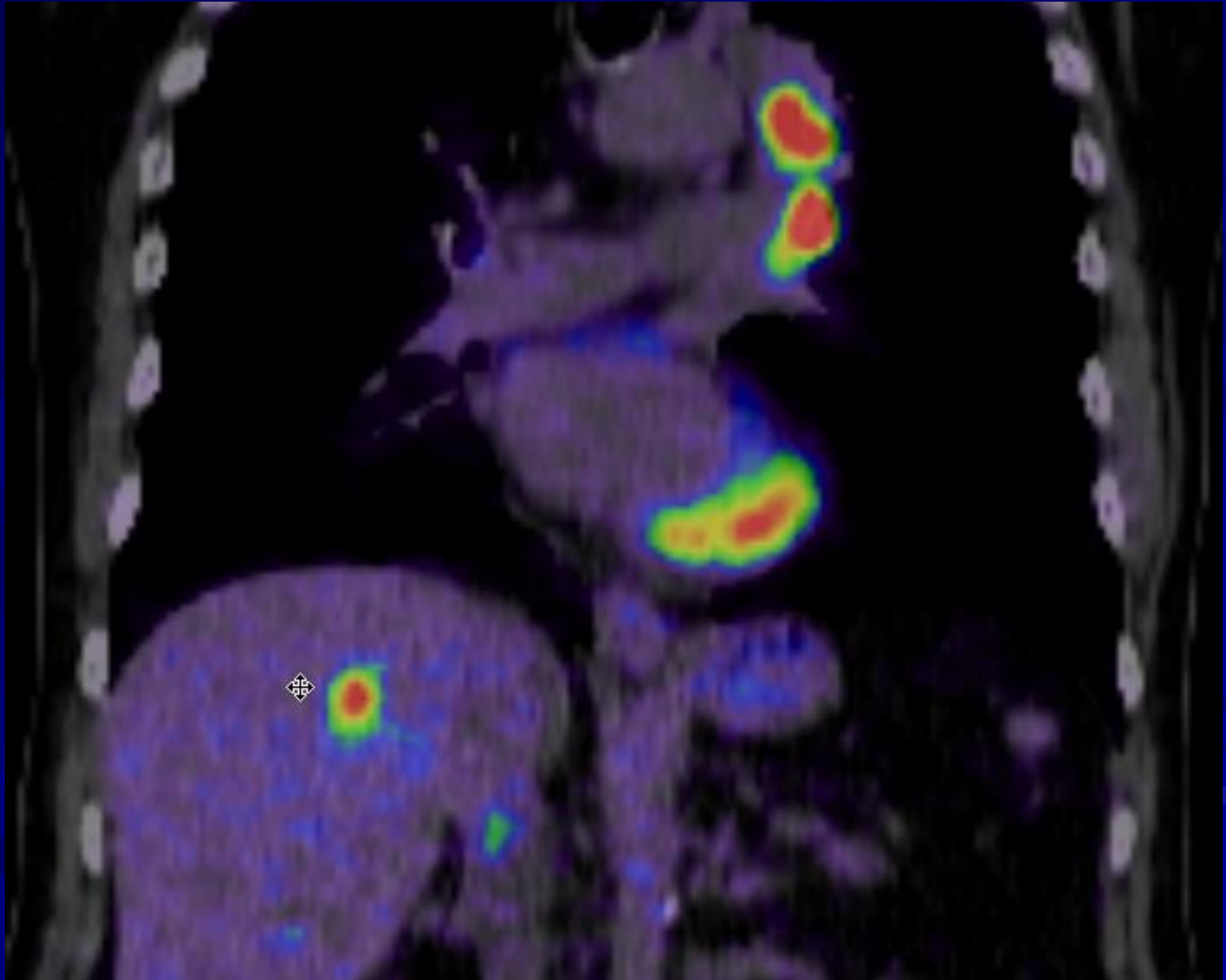


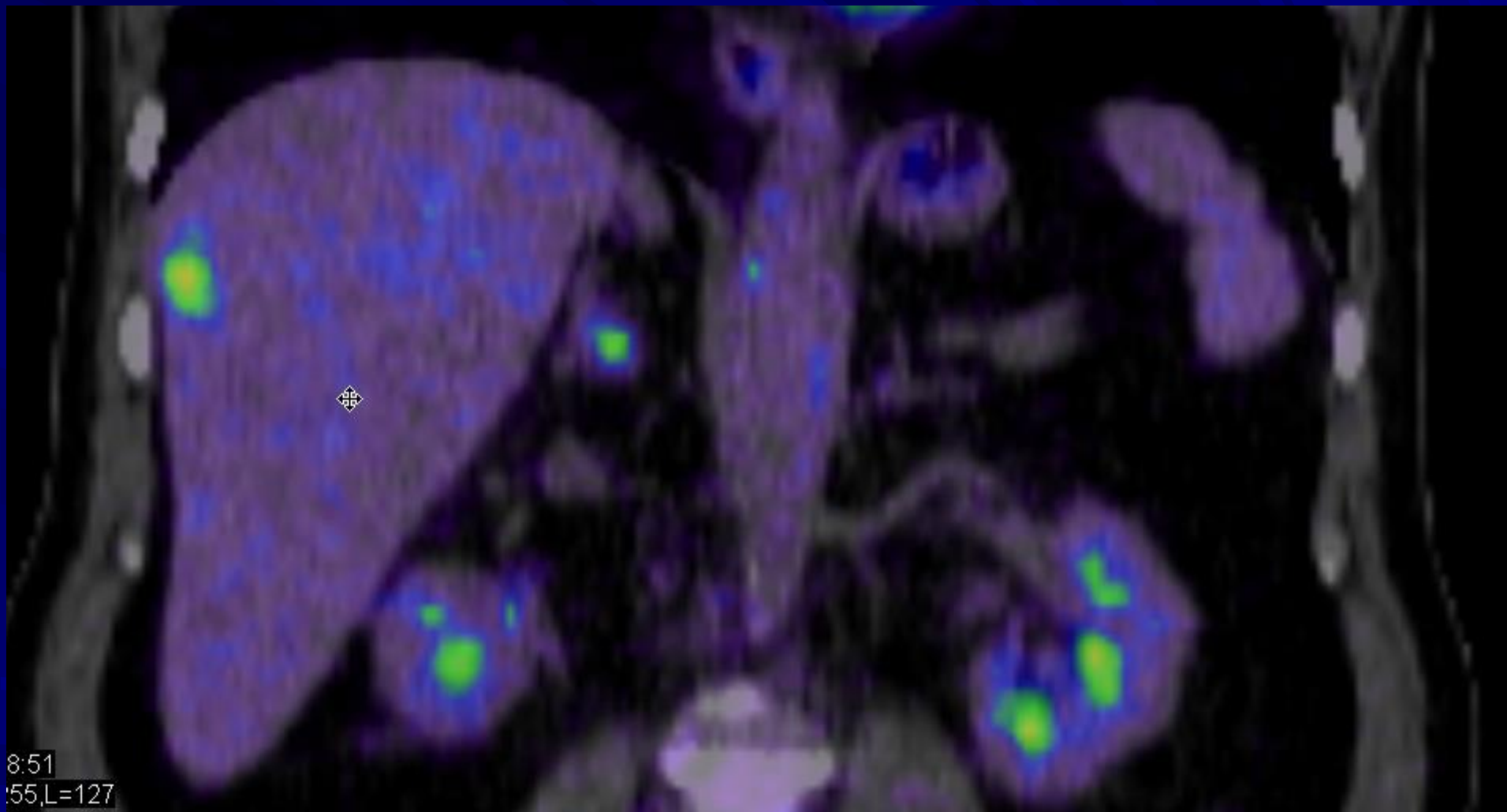






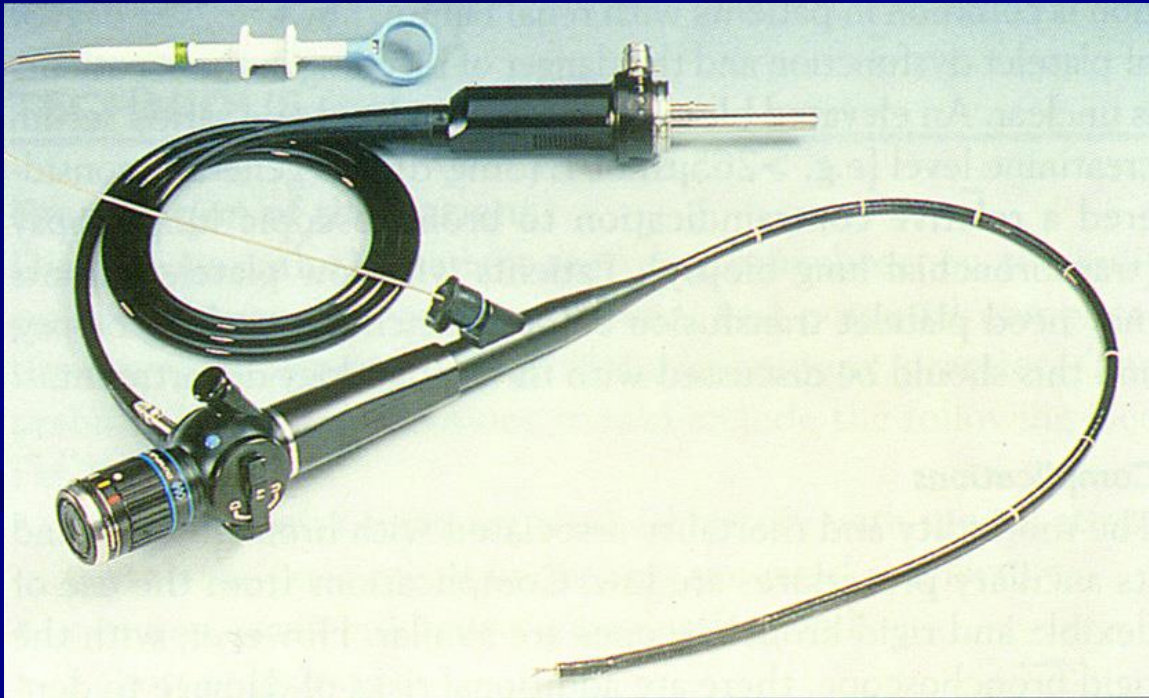


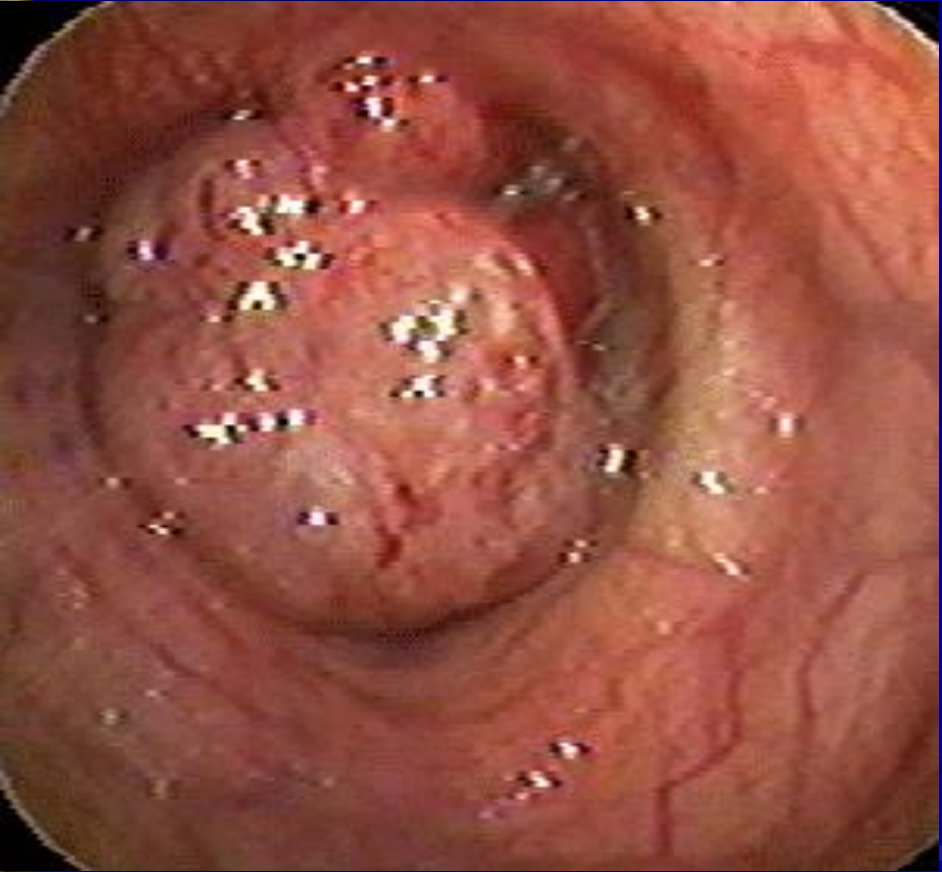
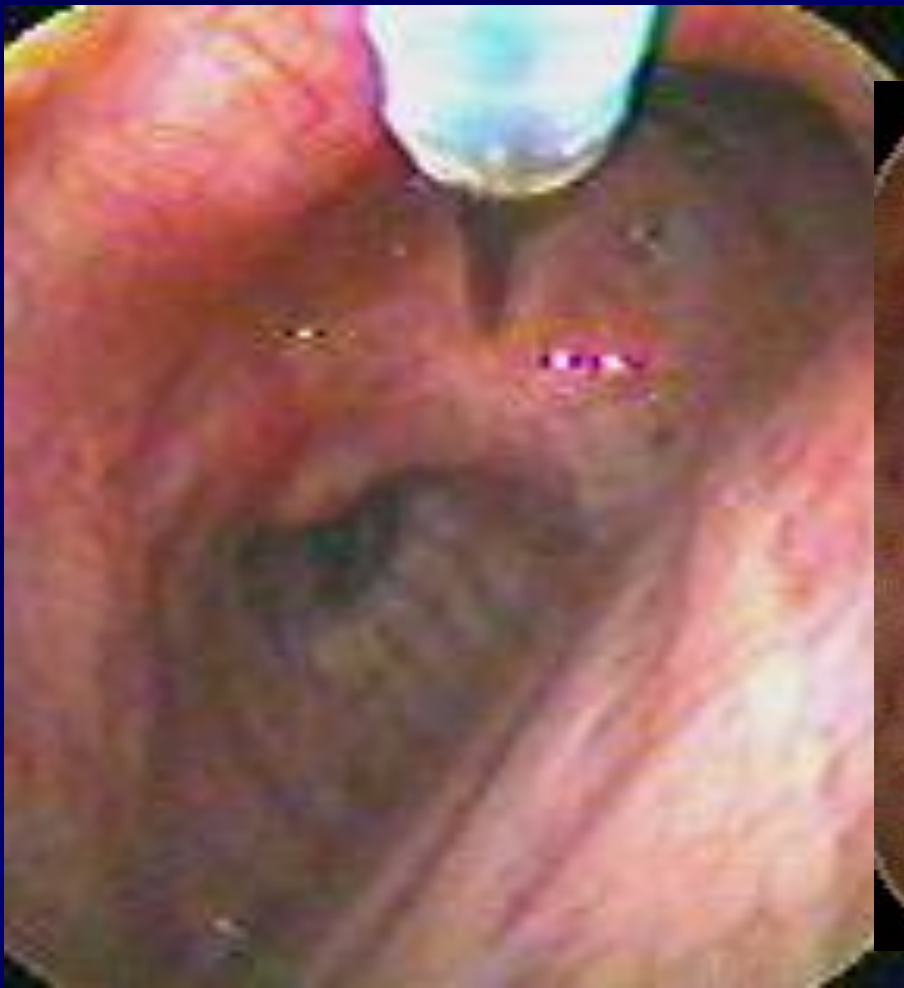




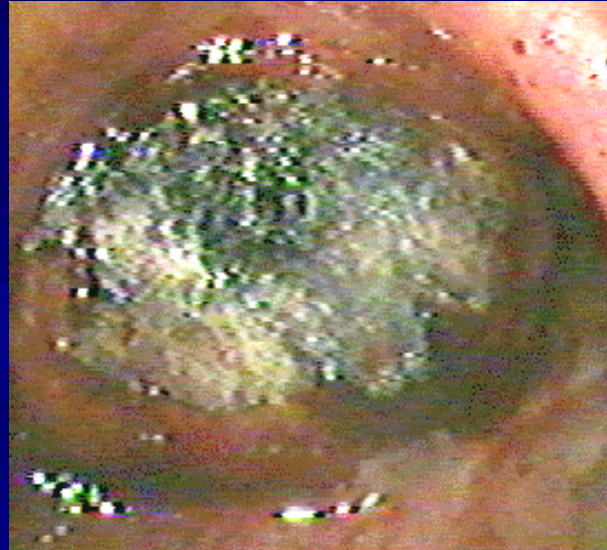
# Bronchoscopy





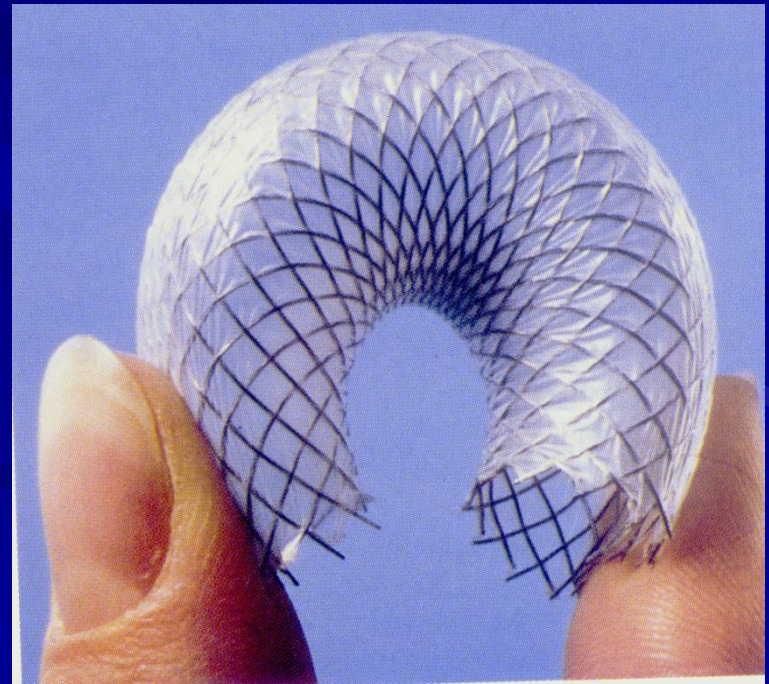
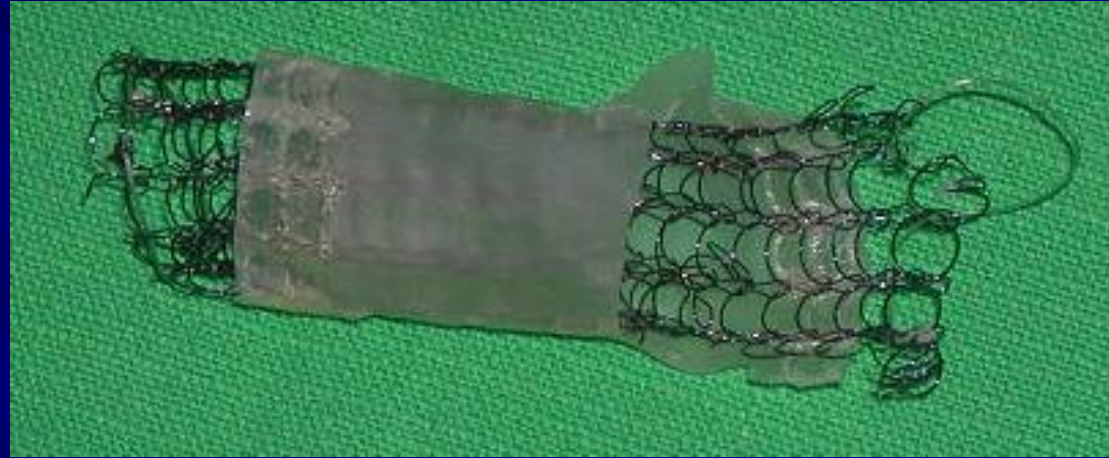
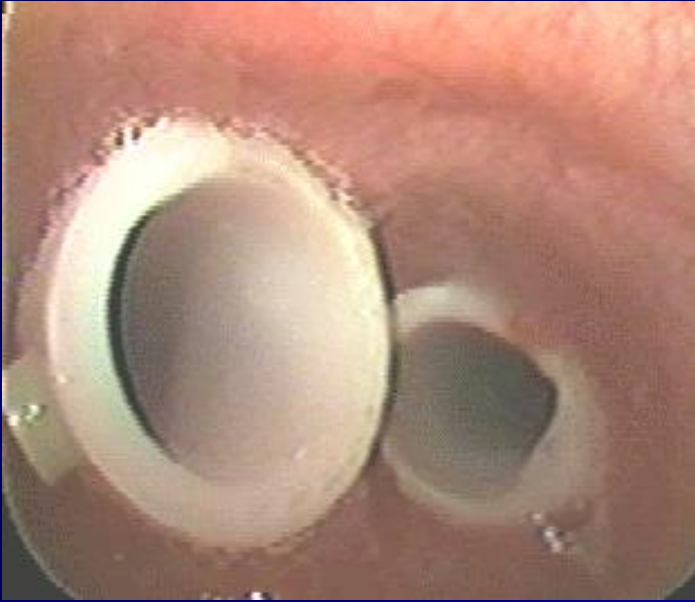


# Special endobronchial techniques

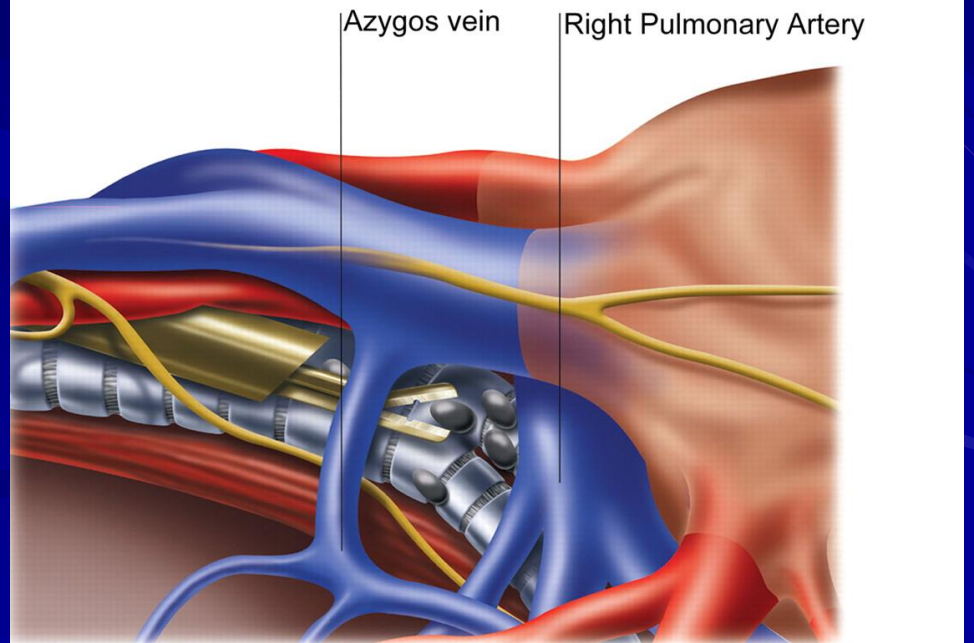
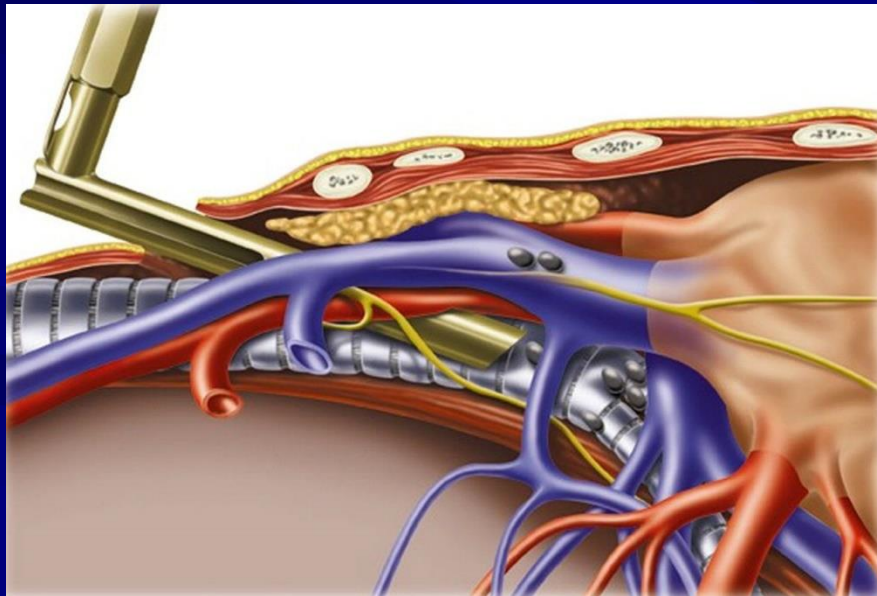
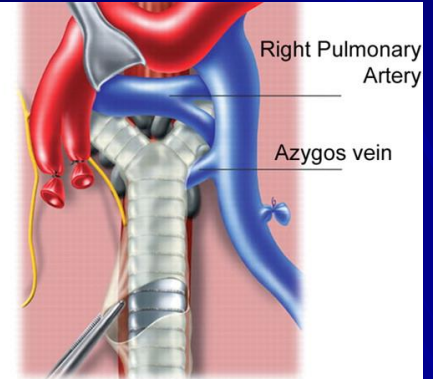
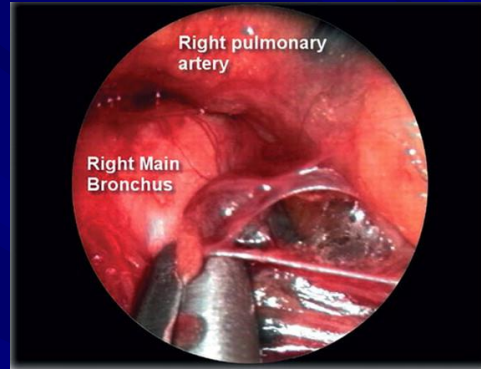




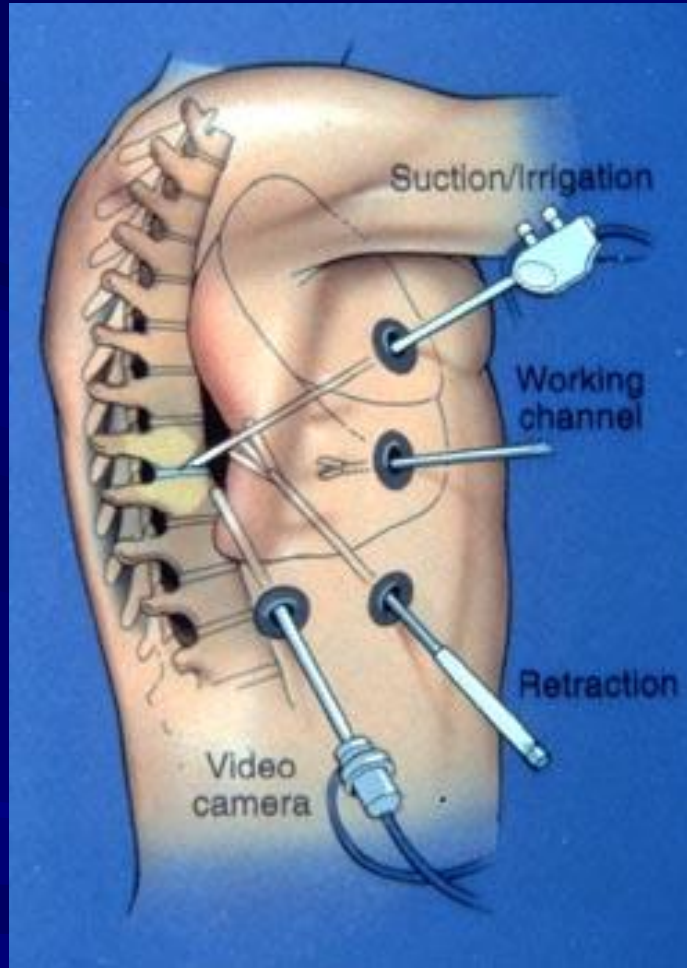
# Stenting



# Mediastinoscopy



# Video Assisted ThoracoScopy (VATS)



# Histology – WHO classification

## ■ Epithelial tumors

### – Benign

- Papilloma
- Adenoma
- Dysplasia / in situ cc.

### – Malignant

- Squamous cell cc.
- Adenocc.
- Small cell cc.
- Large cell cc.
- Adenosquamous cc.
- Carcinoid
- Bronchio-alveolar cc.

## ■ Soft tissue tumors

## ■ Mesothelial tumors

### – Benign

### – Malignant

## ■ Mixed tumors

## ■ Secondary tumors

## ■ Non-classified tumors

## ■ Tumor like lesions

# Molecular pathology

- From histology
- From good quality / quantity cytology
- Liquid biopsy from blood
- Targeted therapy
  - EGFR, KRAS, ALK, ROS-1, BRAF
- Immunotherapy
  - PD-L1

# Staging (TNM 8. 2017)

## T – Primary Tumour

TX	Primary tumour cannot be assessed, or tumour proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
T0	No evidence of primary tumour
Tis	Carcinoma in situ
T1	Tumour 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus) <sup>1</sup>
T1mi	Minimally invasive adenocarcinoma <sup>2</sup>
T1a	Tumour 1 cm or less in greatest dimension <sup>1</sup>
T1b	Tumour more than 1 cm but not more than 2 cm in greatest dimension <sup>1</sup>
T1c	Tumour more than 2 cm but not more than 3 cm in greatest dimension <sup>1</sup>
T2	Tumour more than 3 cm but not more than 5 cm; or tumour with any of the following features <sup>3</sup> <ul style="list-style-type: none"> <li>• Involves main bronchus regardless of distance to the carina, but without involving the carina</li> <li>• Invades visceral pleura</li> <li>• Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, either involving part of the lung or the entire lung</li> </ul>
T2a	Tumour more than 3 cm but not more than 4 cm in greatest dimension
T2b	Tumour more than 4 cm but not more than 5 cm in greatest dimension
T3	Tumour more than 5 cm but not more than 7 cm in greatest dimension or one that directly invades any of the following: chest wall (including superior sulcus tumours), phrenic nerve, parietal pericardium; or associated separate tumour nodule(s) in the same lobe as the primary
T4	Tumours more than 7 cm or one that invades any of the following: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, oesophagus, vertebral body, carina; separate tumour nodule(s) in a different ipsilateral lobe to that of the primary

## N – Regional Lymph Nodes

NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2		Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3		Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene or supraclavicular lymph node(s)

## M- Distant Metastasis

M0		No distant metastasis
M1		Distant metastasis
	M1a	Separate tumour nodule(s) in a contralateral lobe; tumour with pleural or pericardial nodules or malignant pleural or pericardial effusion <sup>4</sup>
	M1b	Single extrathoracic metastasis in a single organ <sup>5</sup>
	M1c	Multiple extrathoracic metastases in one or several organs

# T1a, T1b

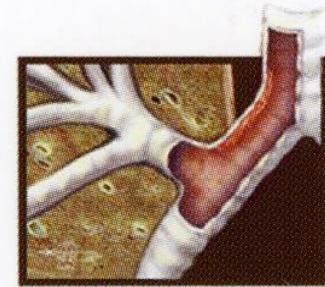
Tumour:  $\leq 1\text{cm}$



*Allan Fran MD*

# T1c

Tumour:  
 $>2\text{cm}, \leq 3\text{cm}$



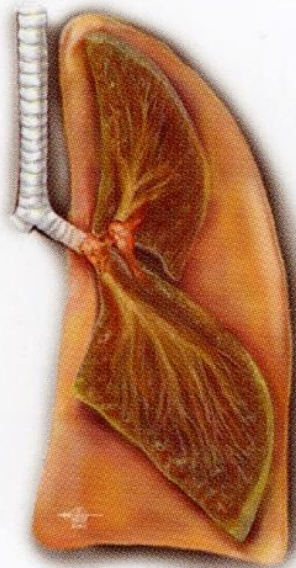
Superficial spreading tumour of any size with its invasive component limited to the bronchial wall, which may extend proximal to the main bronchus is T1

Tumour:  
 $>1\text{cm}, \leq 2\text{cm}$

Tumour  $\leq 3\text{cm}$ ; any associated bronchoscopic invasion should not extend proximal to the lobar bronchus



Tumour in the main bronchus < 2cm from the carina (without involvement of the carina) and/or associated atelectasis or obstructive pneumonitis of the entire lung



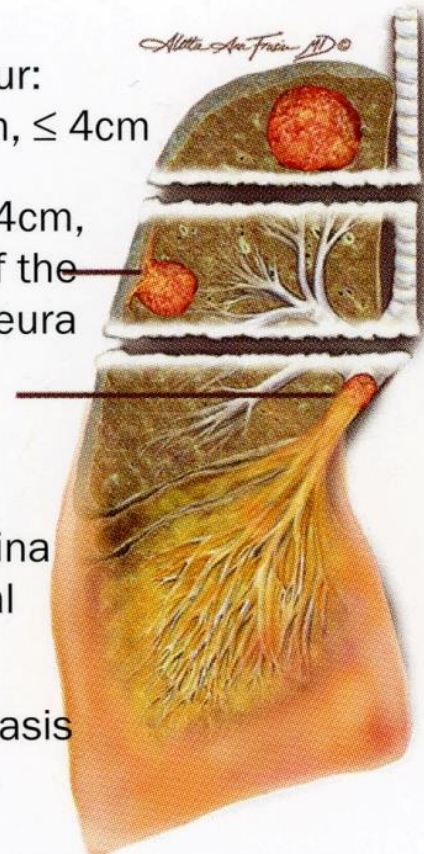
Tumour: > 3cm, ≤ 4cm  
Tumour ≤ 4cm, invasion of the visceral pleura

Tumour involves main bronchus, regardless of distance from carina but without carinal involvement

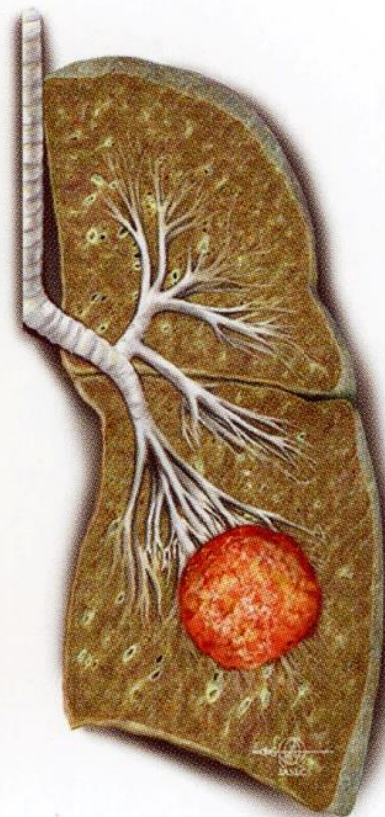
Associated atelectasis or obstructive pneumonitis that extends to the hilar region, either involving part of the lung or the entire lung

Note: if the tumour is associated with atelectasis or pneumonitis, it is T2a if lesion ≤ 4cm or if tumour size cannot be measured; it is T2b if lesion > 4cm, ≤ 5cm.

# T2a



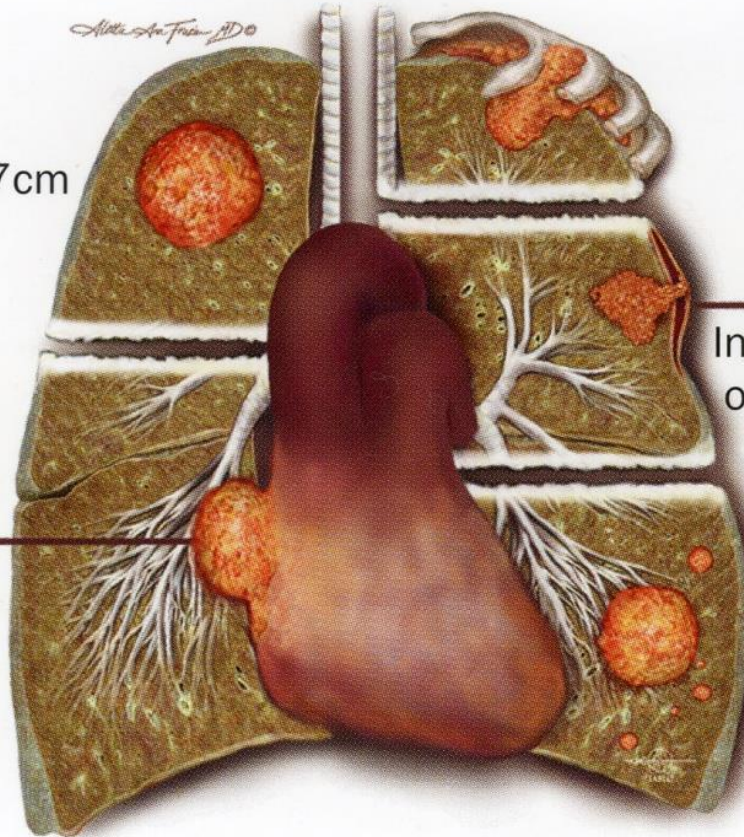
# T2b



Tumour: > 4cm, ≤ 5cm (with or without other T2 descriptors)

# T3

Tumour:  
> 5cm, ≤ 7cm



Phrenic nerve  
or parietal  
pericardium  
invasion

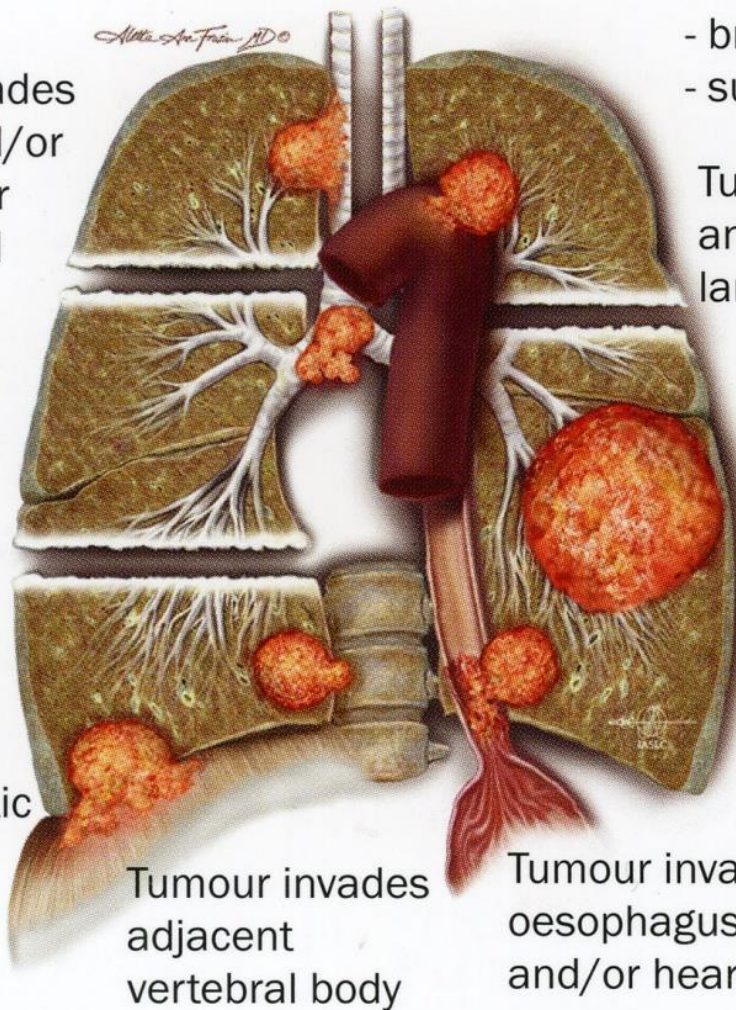
Chest wall invasion, including Pancoast tumours without invasion of vertebral body or spinal canal, encasement of the subclavian vessels, or unequivocal involvement of the superior branches of the brachial plexus (C8 or above)

Invasion  
of parietal  
pleura



Separate tumour  
nodule(s) in the  
lobe of the primary

# T4



Tumour invades trachea and/or SVC or other great vessel

Tumour involves carina

Diaphragmatic invasion

Tumour invades adjacent vertebral body

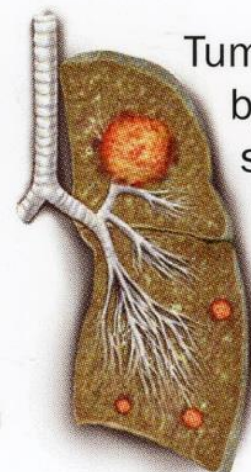
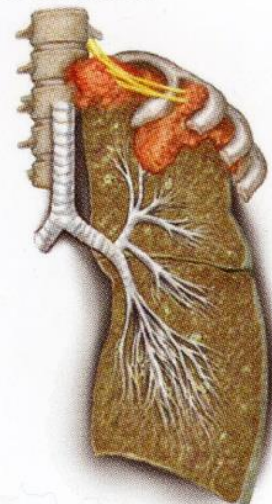
Tumour invades oesophagus, mediastinum and/or heart

Pancoast tumours with invasion of one or more of the following structures:

- vertebral body or spinal canal
- brachial plexus (C8 or above)
- subclavian vessels

Tumour invades aorta and/or recurrent laryngeal nerve

Tumour > 7cm



Tumour accompanied by ipsilateral, separate tumour nodules, different lobe

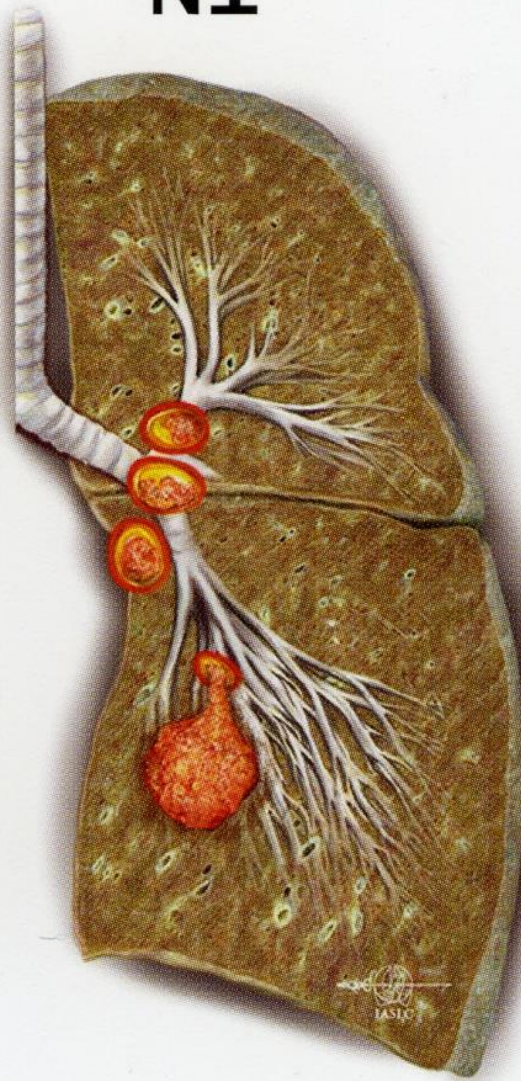
**NO**

*Alta Ana Frazin MD ©*



No regional lymph node metastases

**N1**

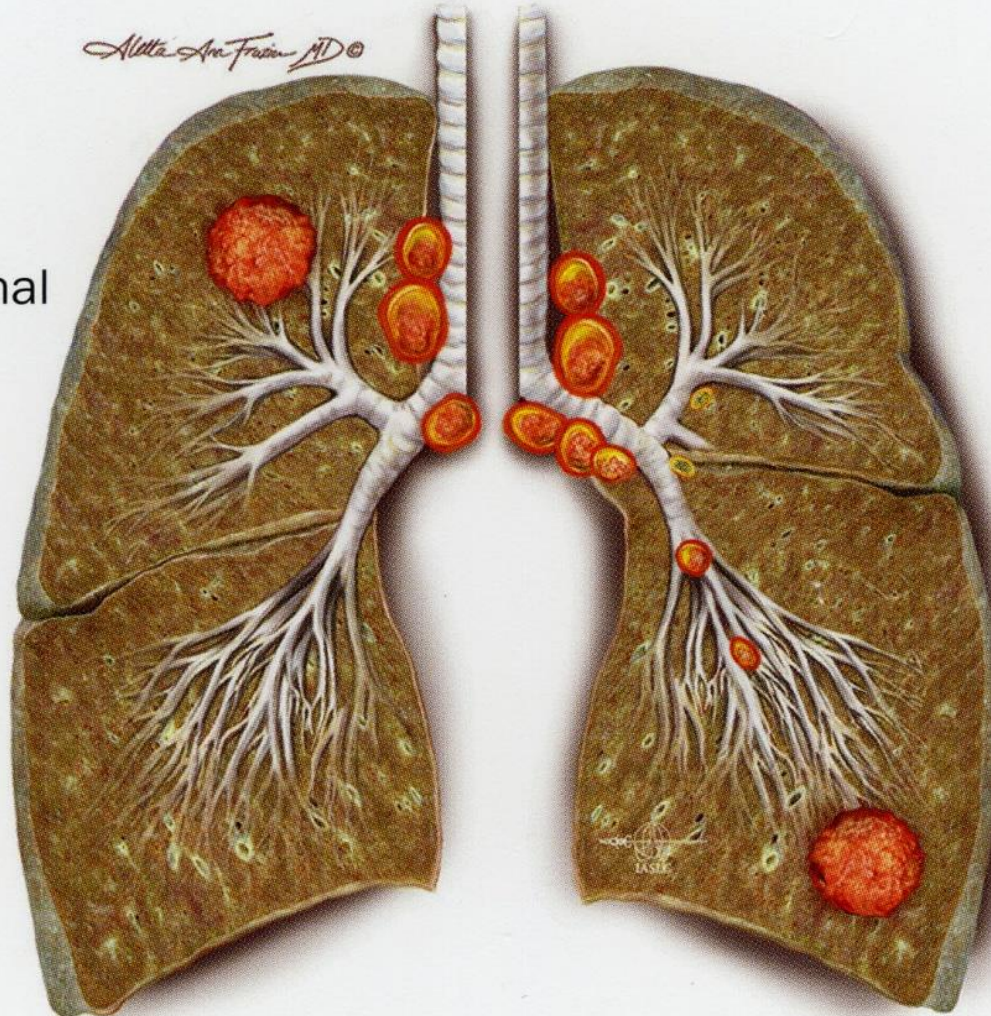


Metastasis in ipsilateral intrapulmonary/peribronchial/hilar lymph node(s), including nodal involvement by direct extension

IASIC

# N2

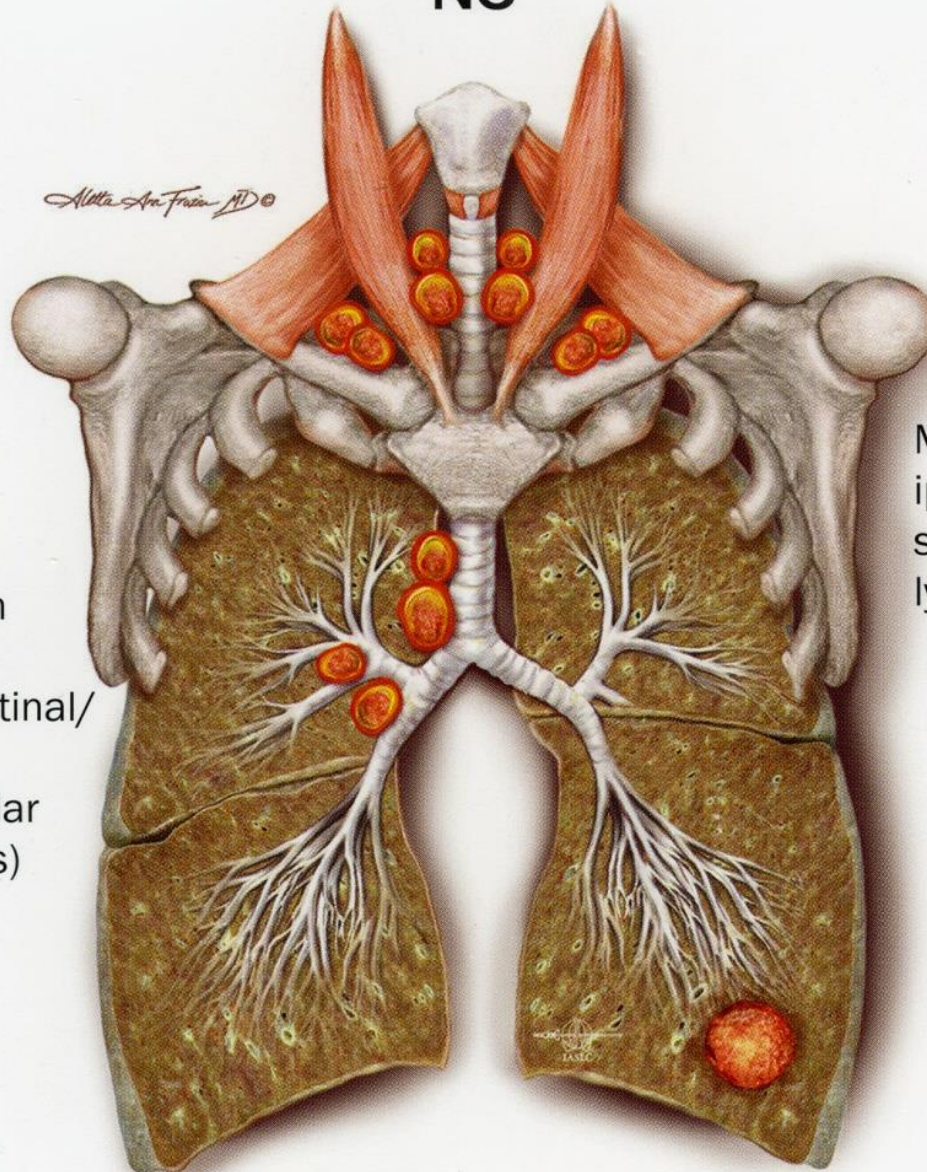
*Allan Am Frasin MD ©*



Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s), including “skip” metastasis without N1 involvement

Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s) associated with N1 disease

N3



Metastasis in  
contralateral  
hilar/mediastinal/  
scalene/  
supraclavicular  
lymph node(s)

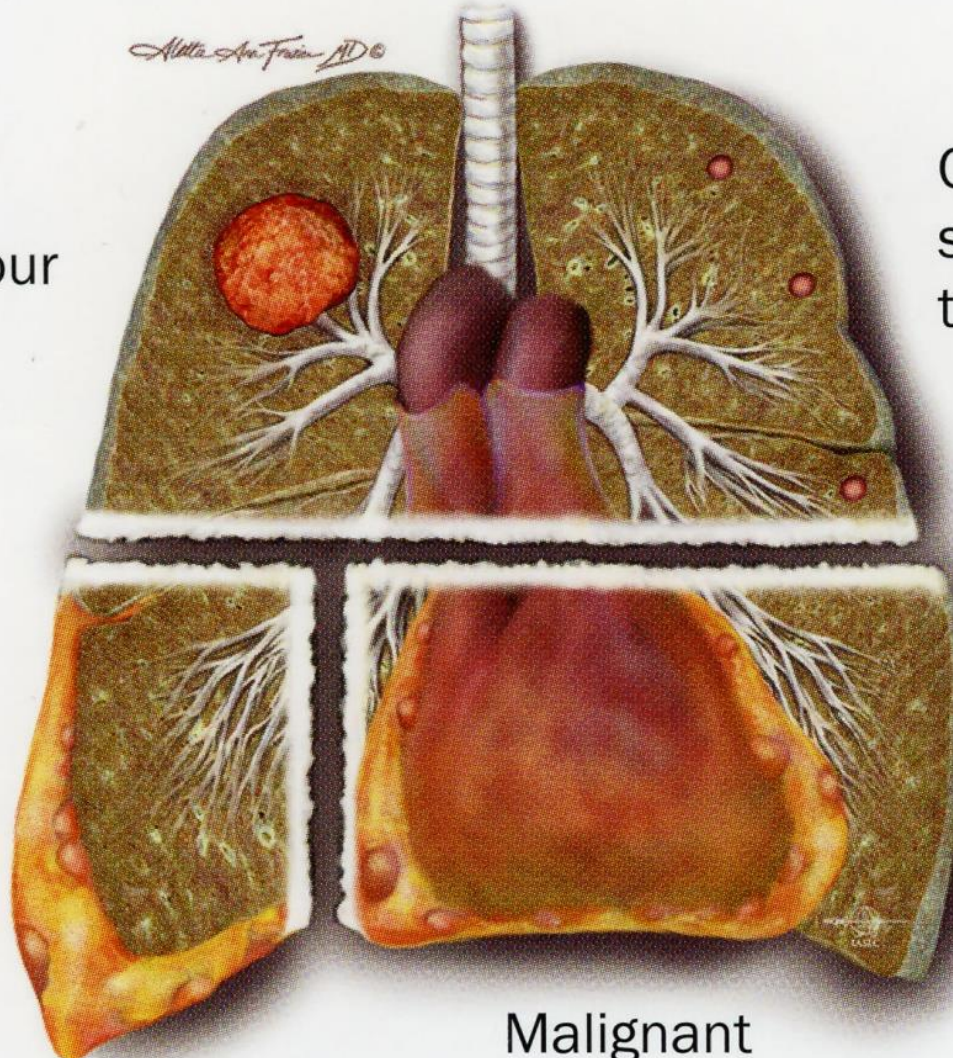
Metastasis in  
ipsilateral scalene/  
supraclavicular  
lymph node(s)

# M1a

*Attila An. Frasin MD ©*

Primary tumour

Contralateral,  
separate  
tumour nodule(s)



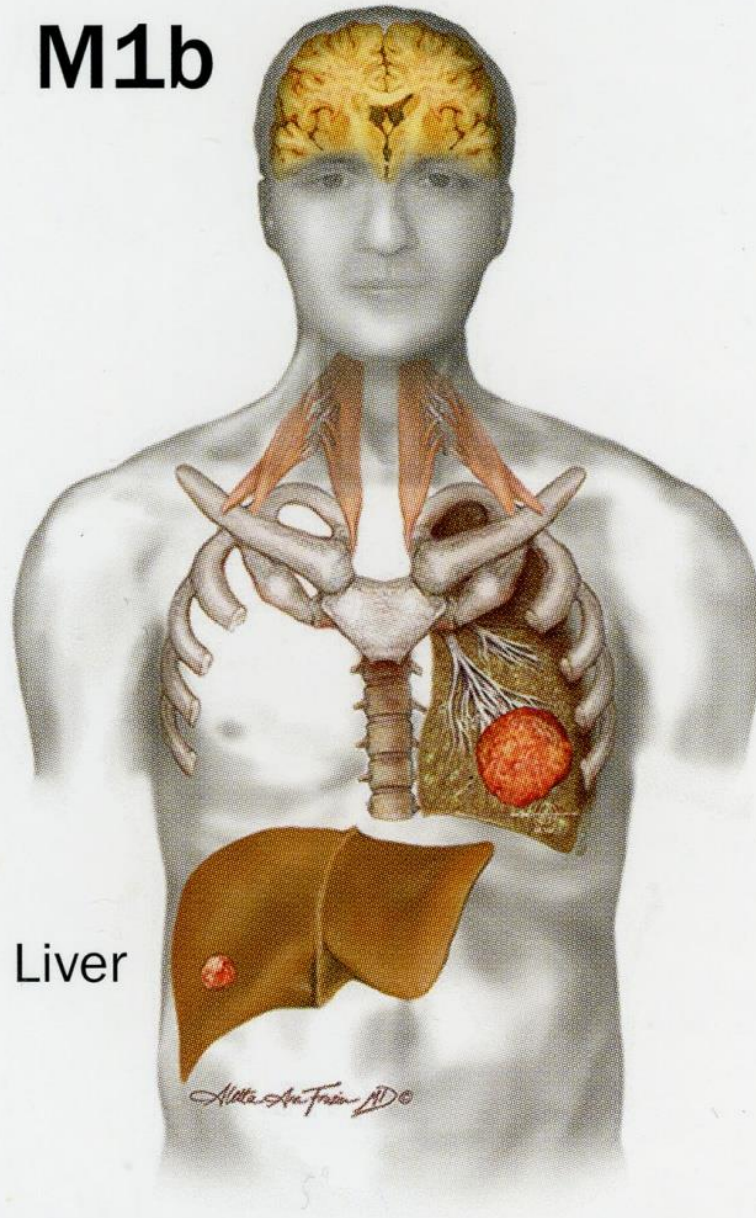
Malignant  
pleural effusion/nodule(s)

Malignant  
pericardial effusion/nodule(s)

**M1b**

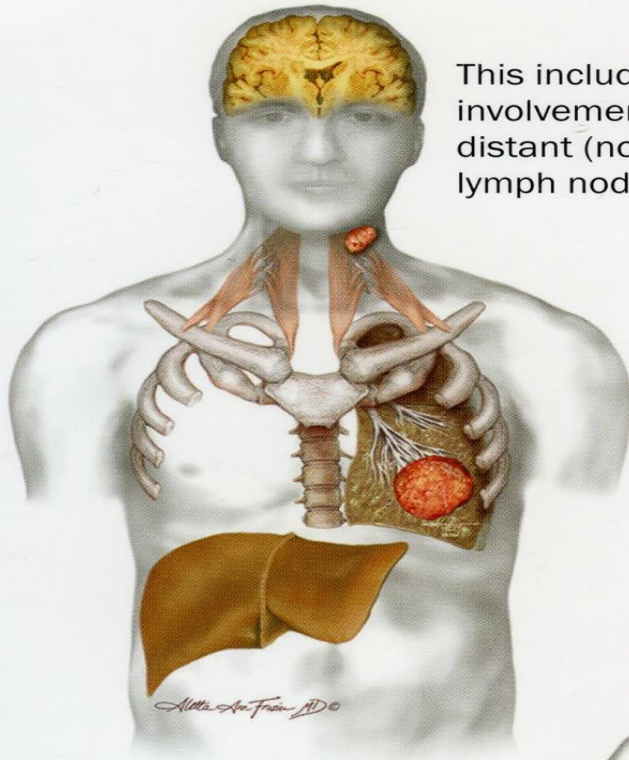
Single  
extrathoracic  
metastasis

Liver



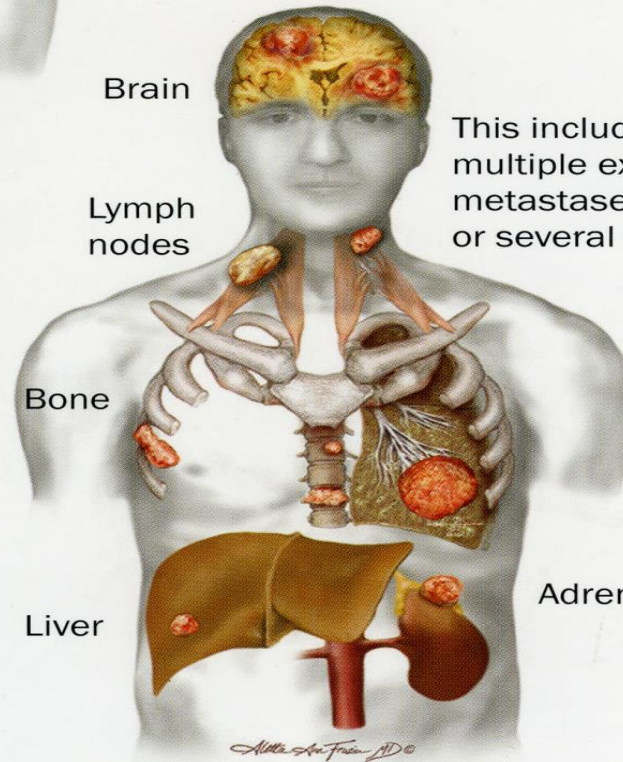


## M1b



This includes involvement of a single distant (non-regional) lymph node

## M1c



Brain

Lymph nodes

Bone

Liver

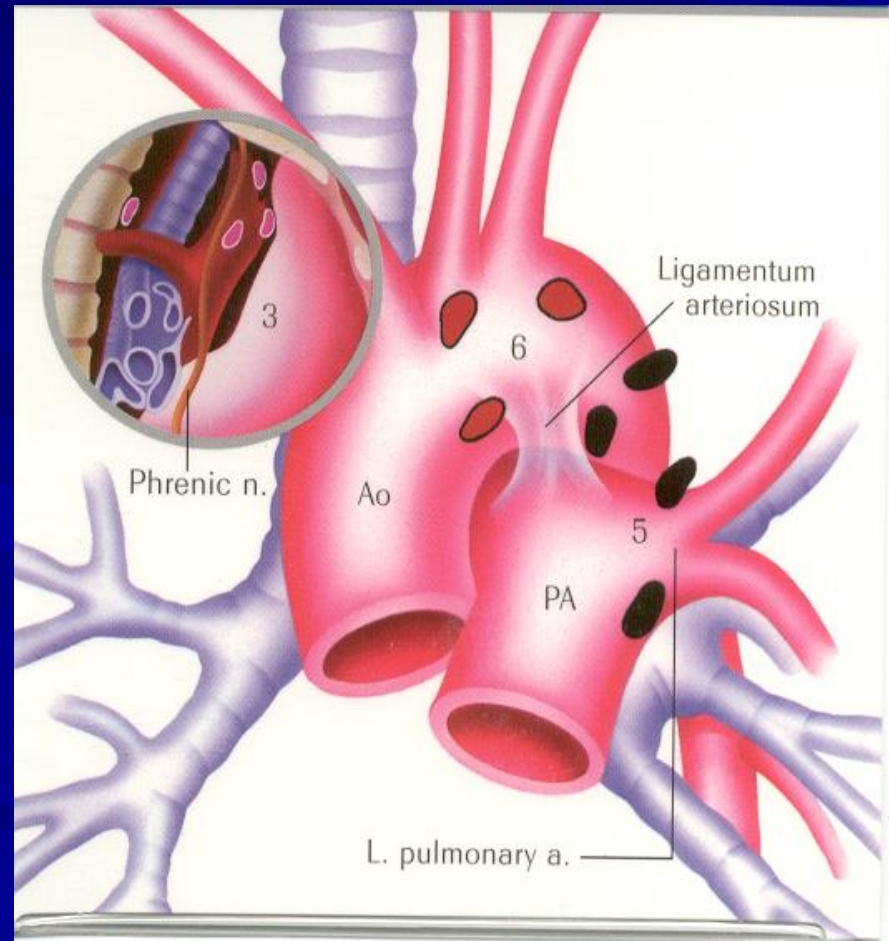
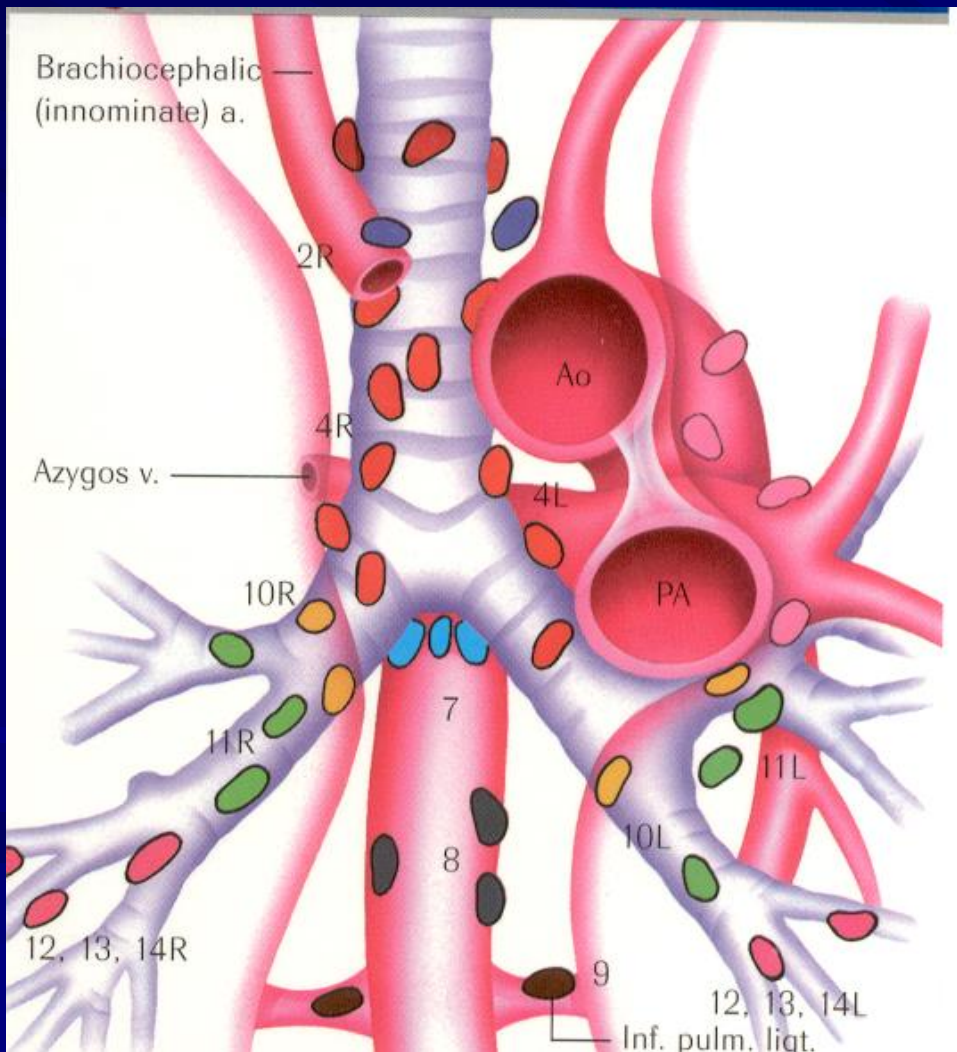
This includes multiple extrathoracic metastases in one or several organs

Adrenal

# Stage grouping

	N0	N1	N2	N3	M1a	M1b	M1c
T1a	IA1	IIB	IIIA	IIIB	IVA	IVA	IVB
T1b	IA2	IIB	IIIA	IIIB	IVA	IVA	IVB
T1c	IA3	IIB	IIIA	IIIB	IVA	IVA	IVB
T2a	IB	IIB	IIIA	IIIB	IVA	IVA	IVB
T2b	IIA	IIB	IIIA	IIIB	IVA	IVA	IVB
T3	IIB	IIIA	IIIB	IIIC	IVA	IVA	IVB
T4	IIIA	IIIA	IIIB	IIIC	IVA	IVA	IVB

# Lymph node regions



# Staging of SCLC

## (Veteran administration system)

- Limited-stage (LD)
  - Tumour confined to one hemithorax and can be safely irradiated
- Extended-stage (ED)
  - Extend beyond one hemithorax / malignant pleural or pericardial effusion / distant metastasis

# Principles of treatment - NSCLC

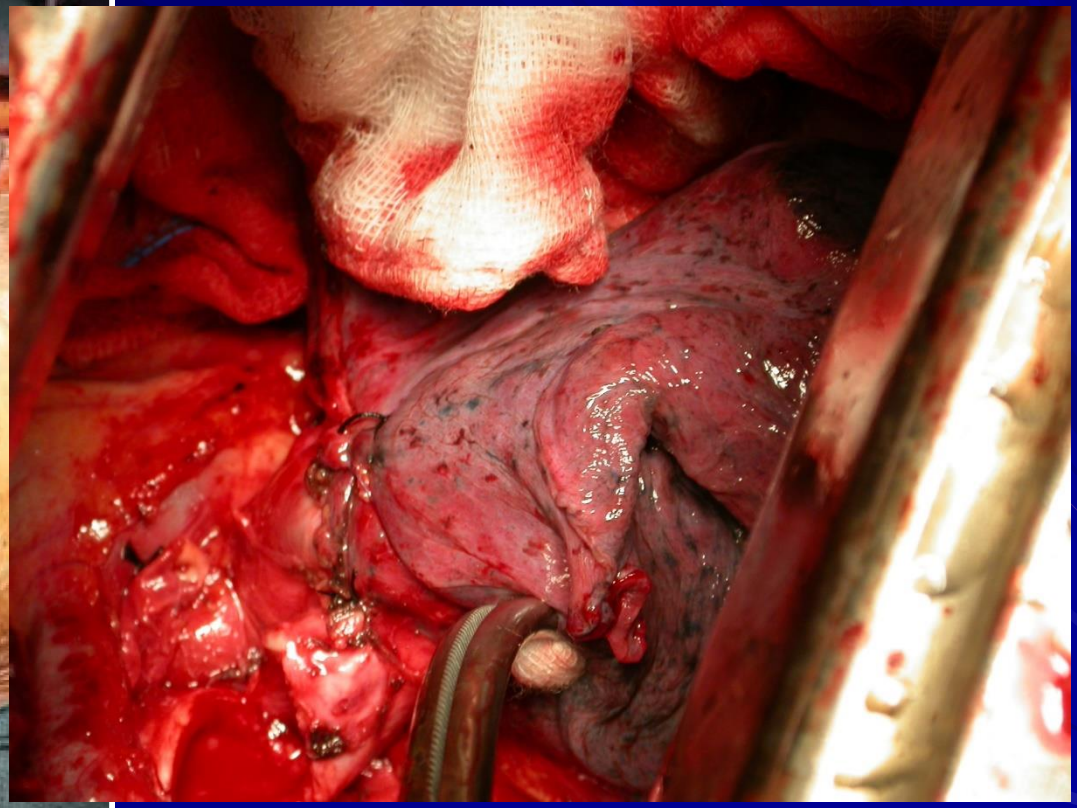
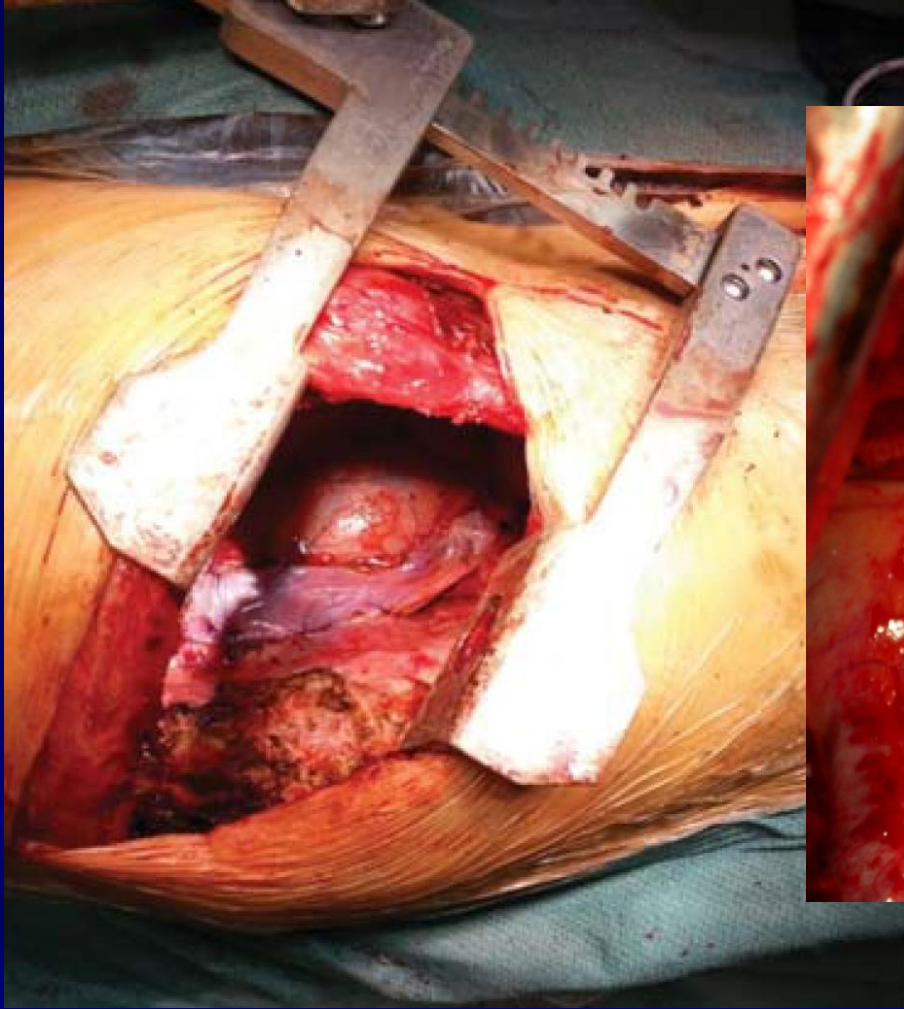
- **Resectable disease** (generally up to T3 N2)
  - Surgery
  - Adjuvant chemotherapy (>T2b, N+)
  - Adjuvant radiotherapy (adenocarcinoma N2, sublobar resection)
- **Locally advanced**, not resectable, non-metastatic (st. III/A-III/B)
  - Chemo+radiotherapy (concurrent / sequential) (maintenance immunotherapy?)
- **Metastatic**
  - Chemo-, targeted-, immunotherapy

# Principles of treatment - SCLC

- Very early stage (T1-2 N0)
  - Surgery, chemotherapy és profilactic cranial irradiation (PCI)
- Limited disease (LD)
  - Chemo+radiotherapy (concurrent + PCI)
- Extended disease (ED)
  - Chemotherapy +- PCI
  - Best supportive care

# Surgery

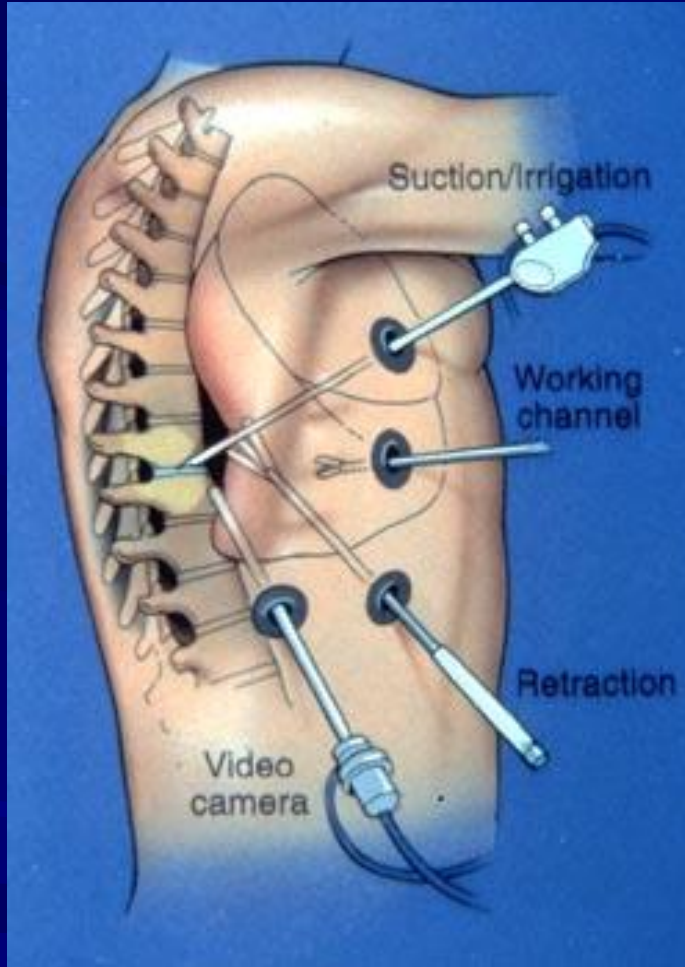
- (Wedge resection)
- (Atypical resection)
- (Segmentectomy)
- Lobectomy
- Bi-lobectomy
- Pneumonectomy (PNO)
- Pleuro-pneumonectomy (mesothelioma)
- Ultra-radical resections (e.g. carina resection)
- Mediastinal lymph node dissection

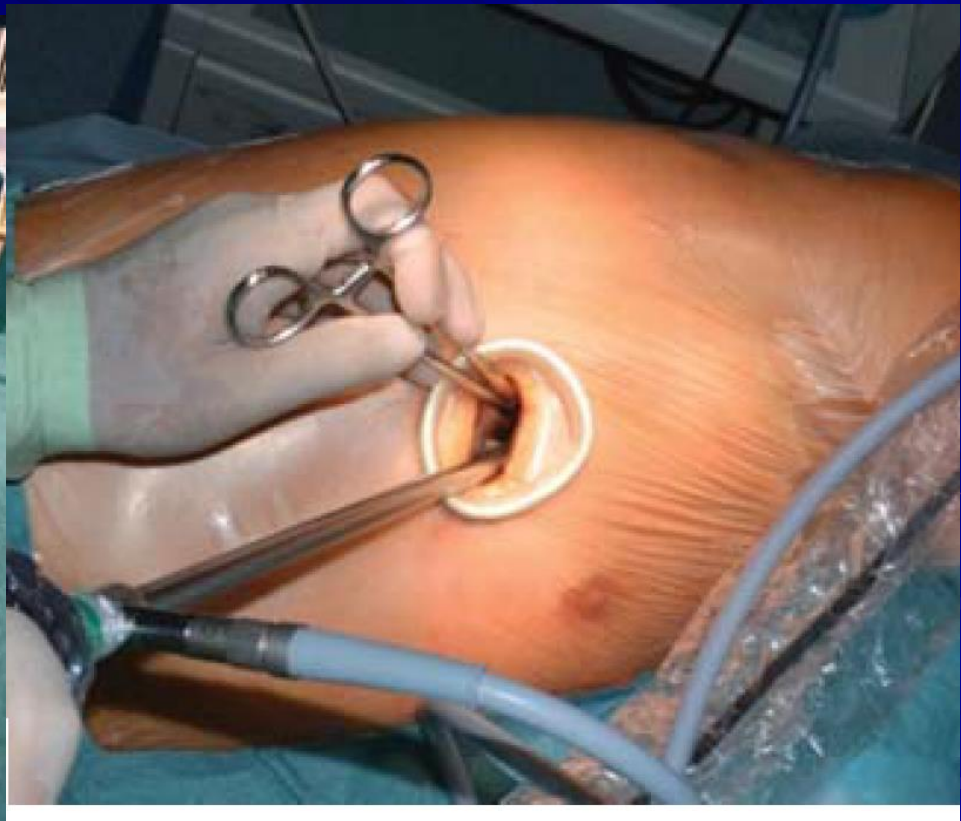
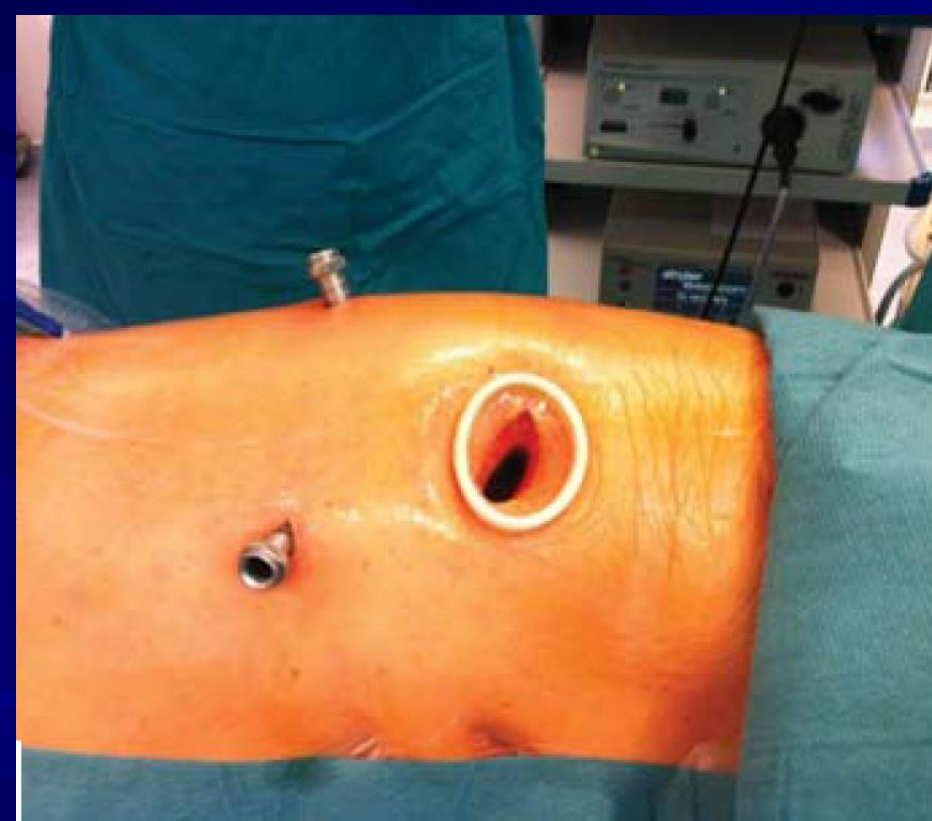


Courtesy of dr. Rényi-Vámos and dr. Agócs

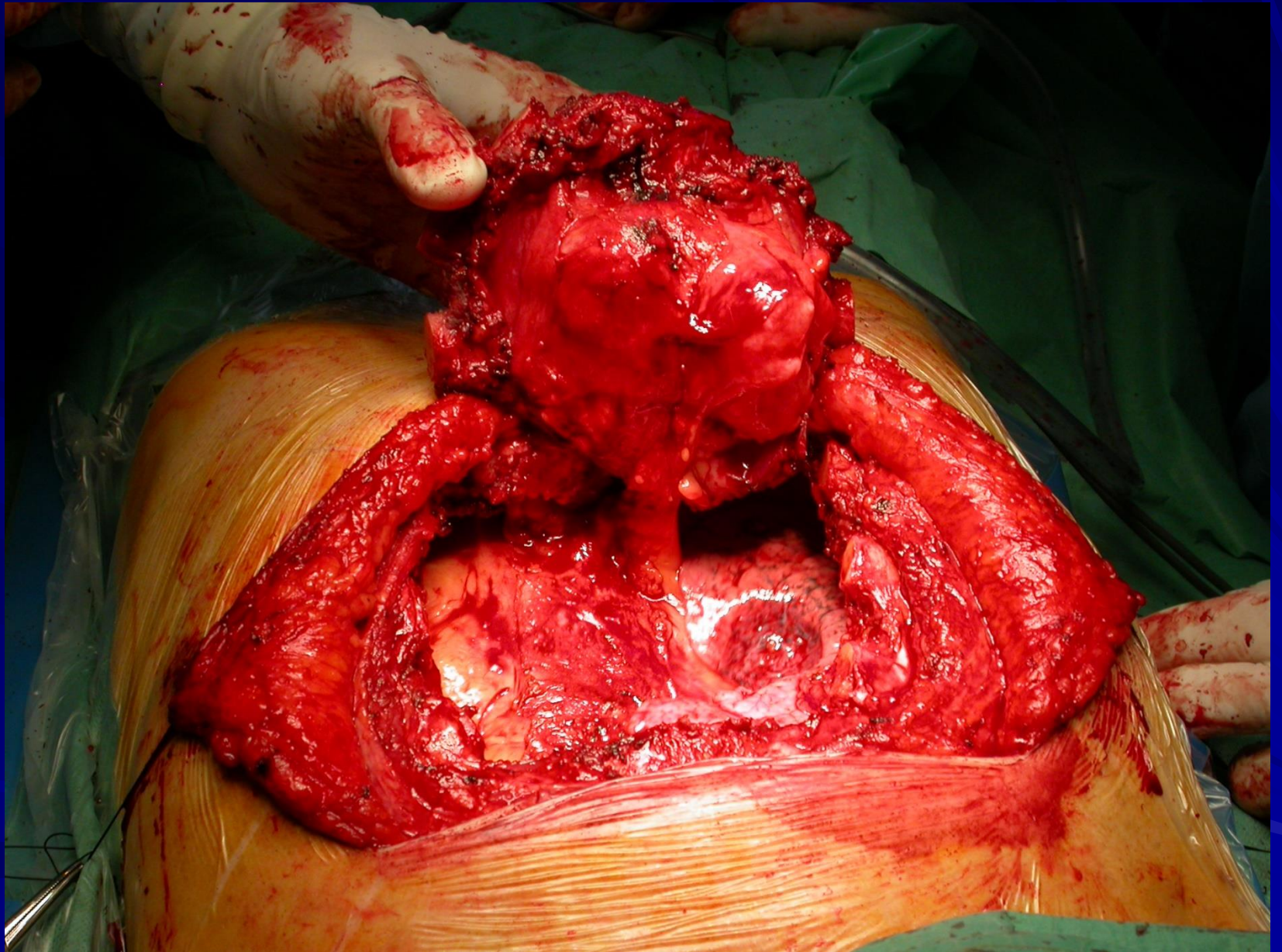


# Video Assisted ThoracoScopy (VATS)

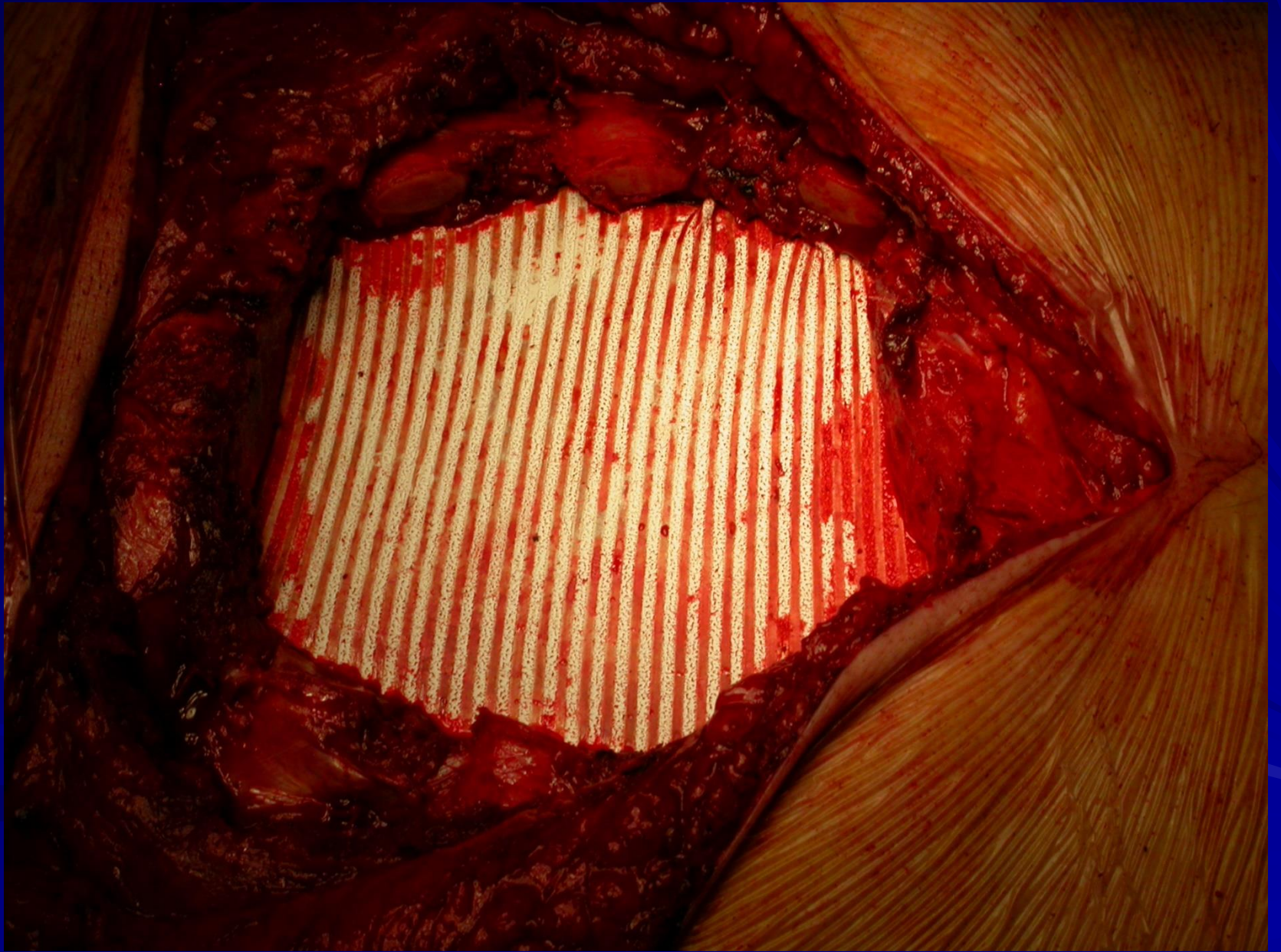




Courtesy of dr. Rényi-Vámos



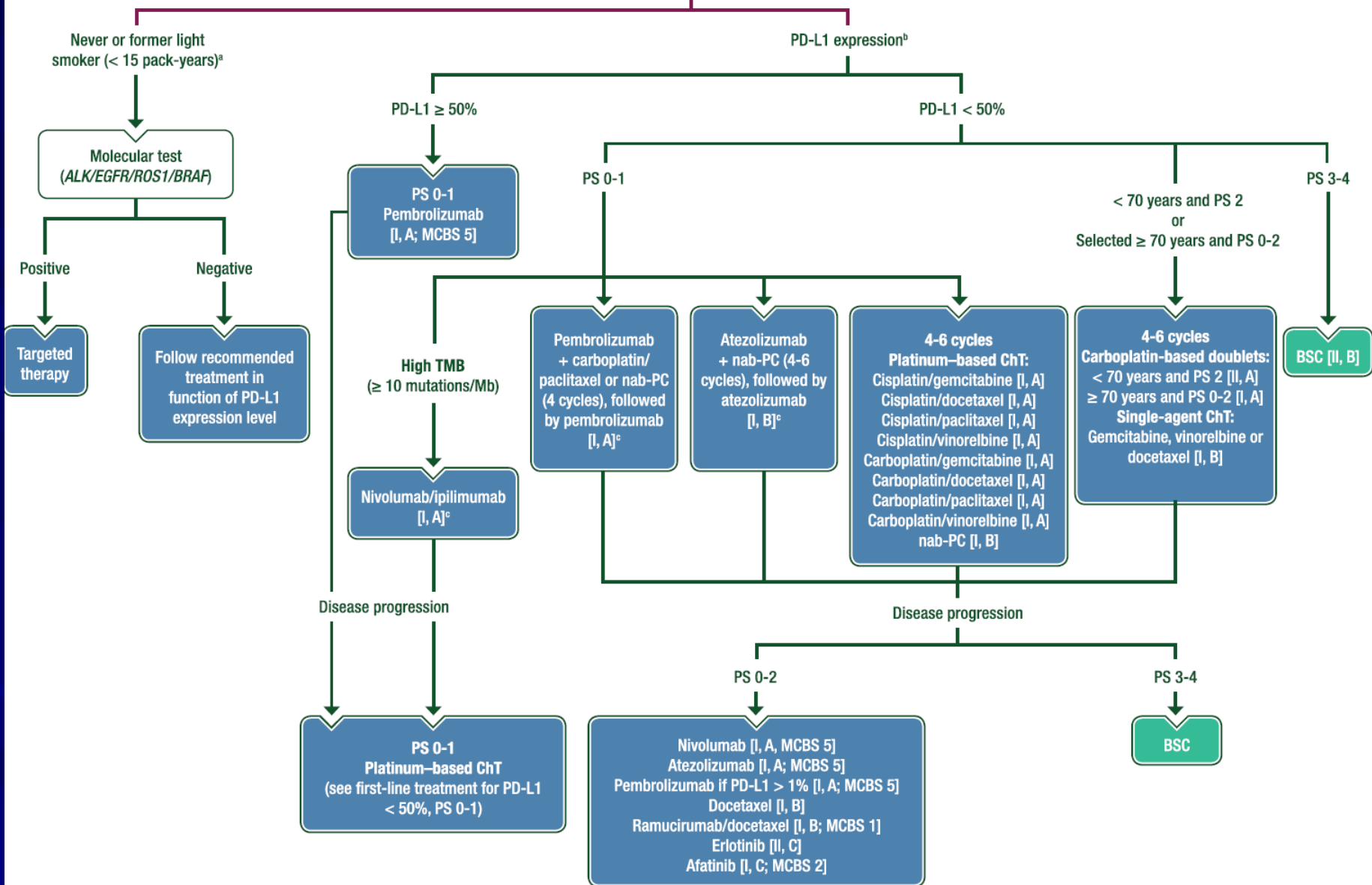
Courtesy of dr. Agócs



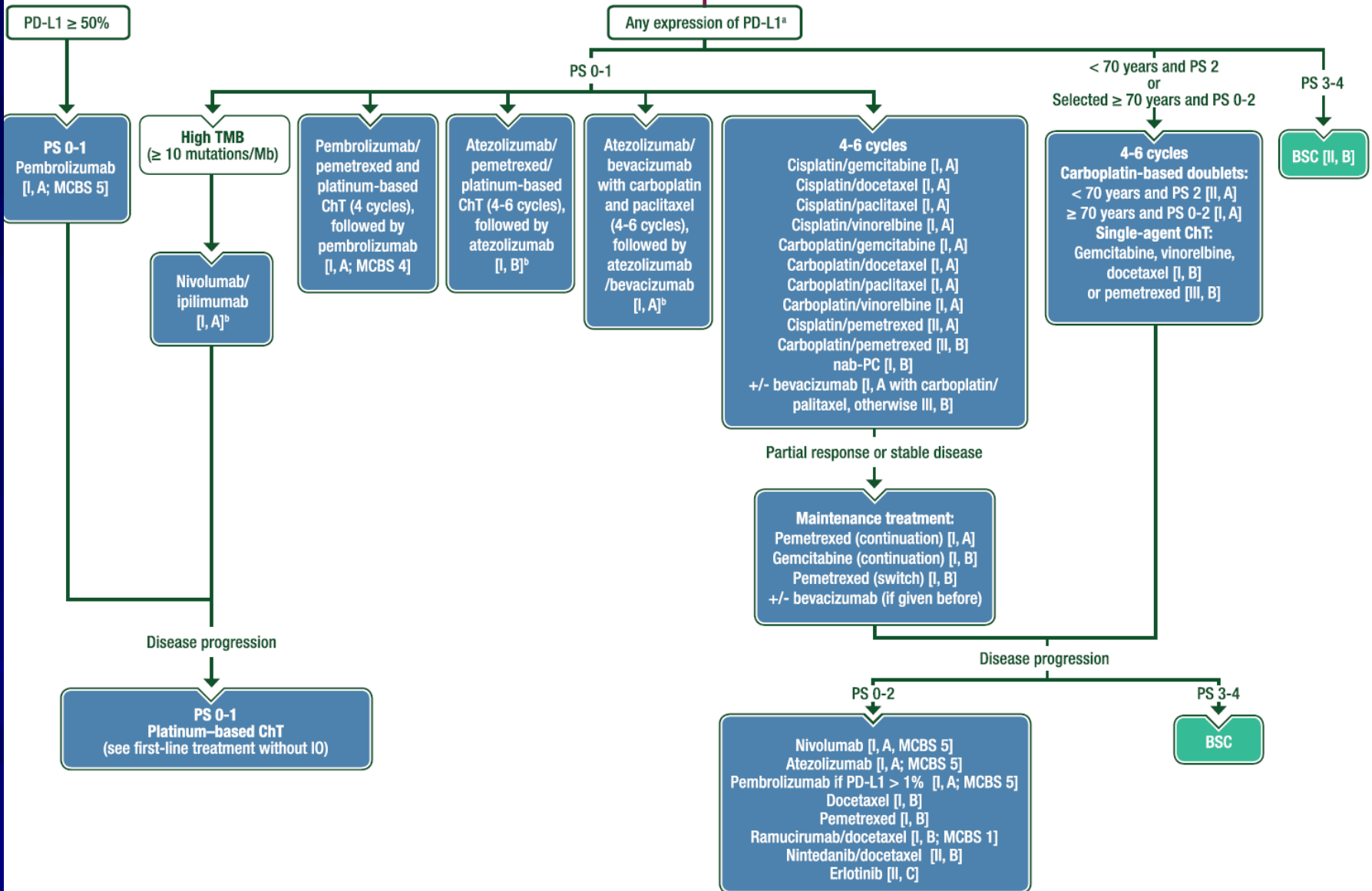
# Pharmaceutical therapy

- First generation chemotherapy
  - Platinum based: cisplatin, carboplatin
  - Etoposide
- Second generation chemotherapy
  - Taxanes: paclitaxel, docetaxel
  - Gemcitabine, Vinorelbine, Pemetrexed
- Targeted therapy
  - EGFR-TKI, VEGF, ALK, combined inhibitors
- Immunotherapy
  - PD-L1, CTLA-4 inhibitors
- SCLC: platinum-etoposid, ECO, hycamtin

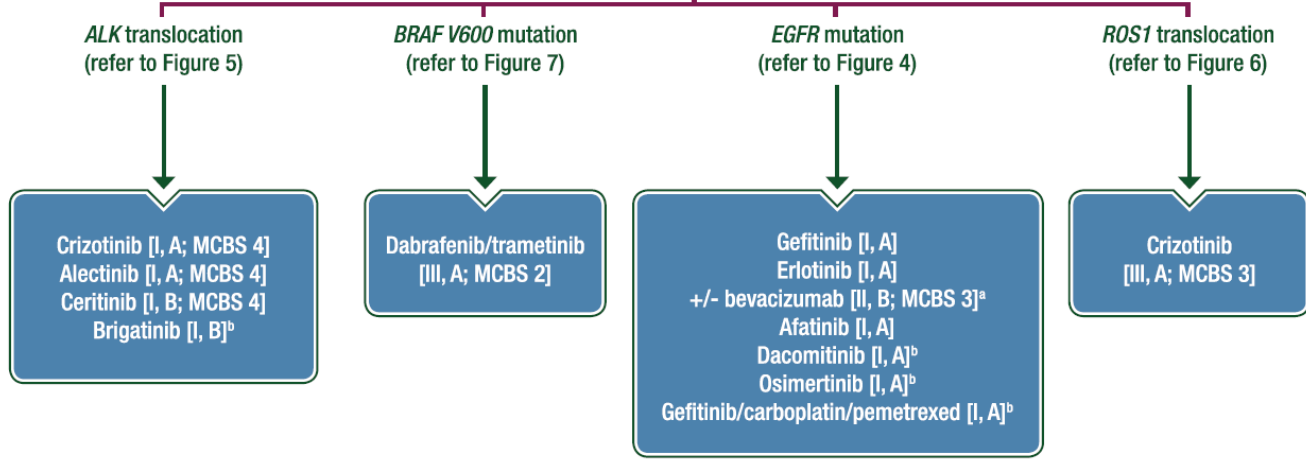
# Stage IV SCC



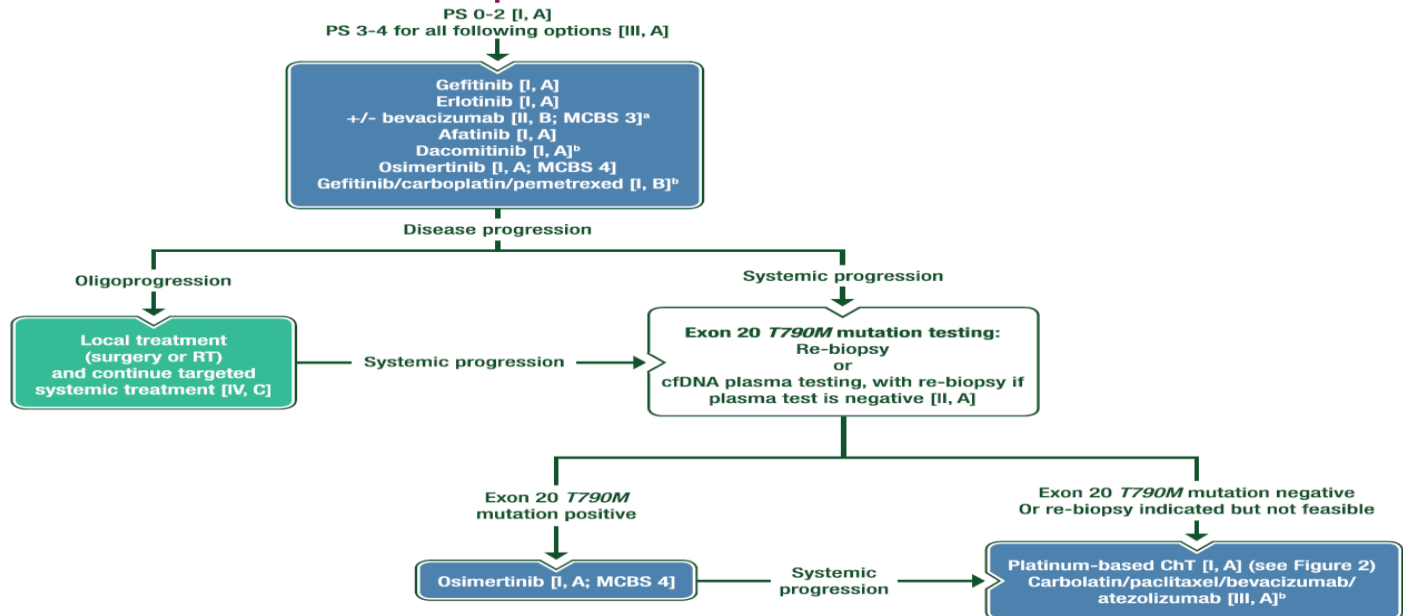
**Stage IV NSCC: Molecular tests negative (ALK/BRAF/EGFR/ROS1)**



**Stage IV NSCC: Molecular tests positive (ALK/BRAF/EGFR/ROS1)**



**Stage IV lung carcinoma with EGFR-activating mutation**



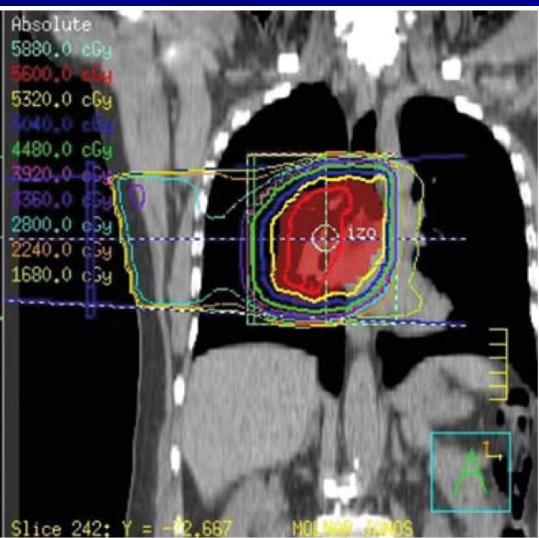
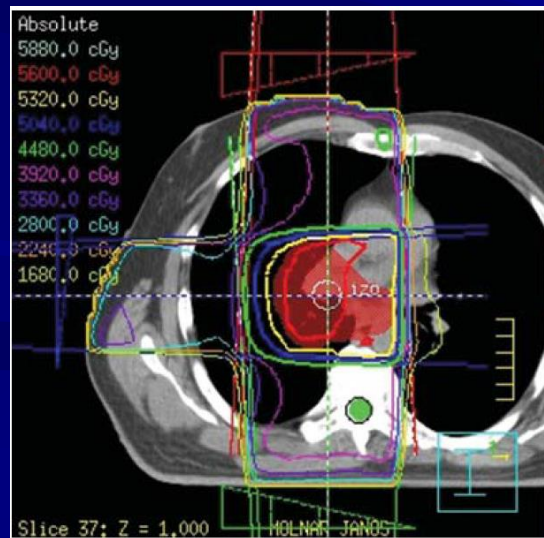
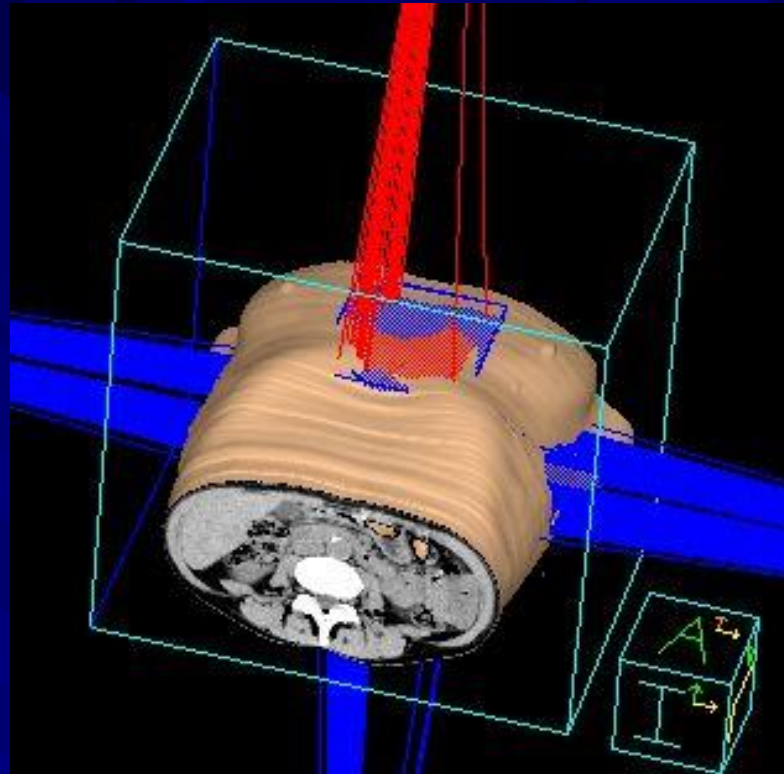
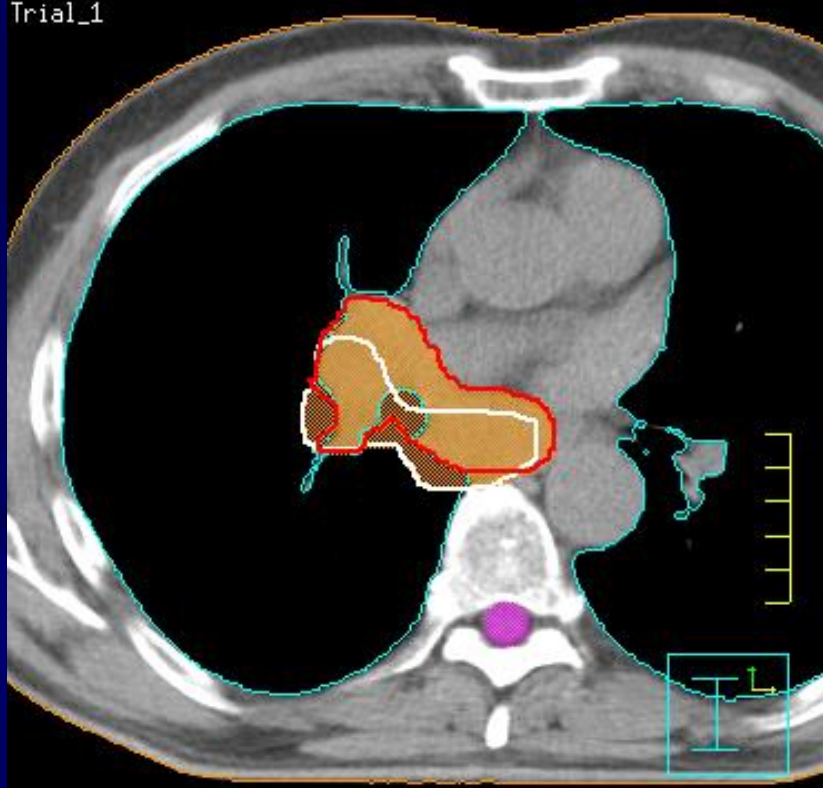


# Radiotherapy

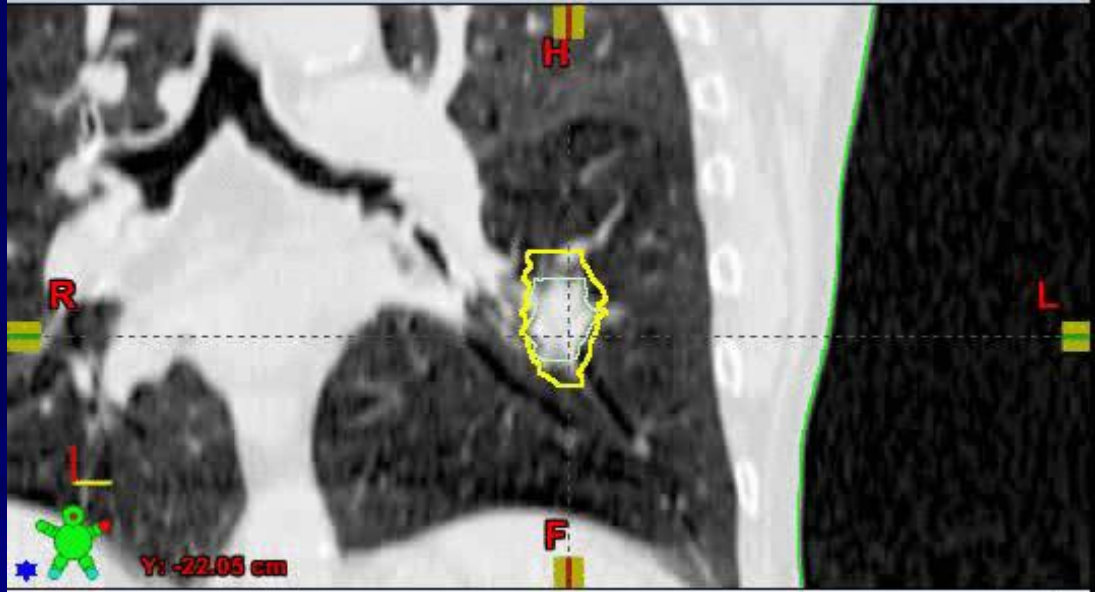
- External beam and brachytherapy
- High dose treatment
  - Always CT / PET-CT based treatment planning  
high level QA, respiratory motion compensation
  - 3D conformal / IMRT, 60-70 Gy
  - SABRT: curative if surgery no feasible,  
3x20/5x12Gy
- Palliative treatment: simple technique, short treatment course
- Brachytherapy
  - Palliative, airway maintaining (1x10Gy, 3x8Gy)



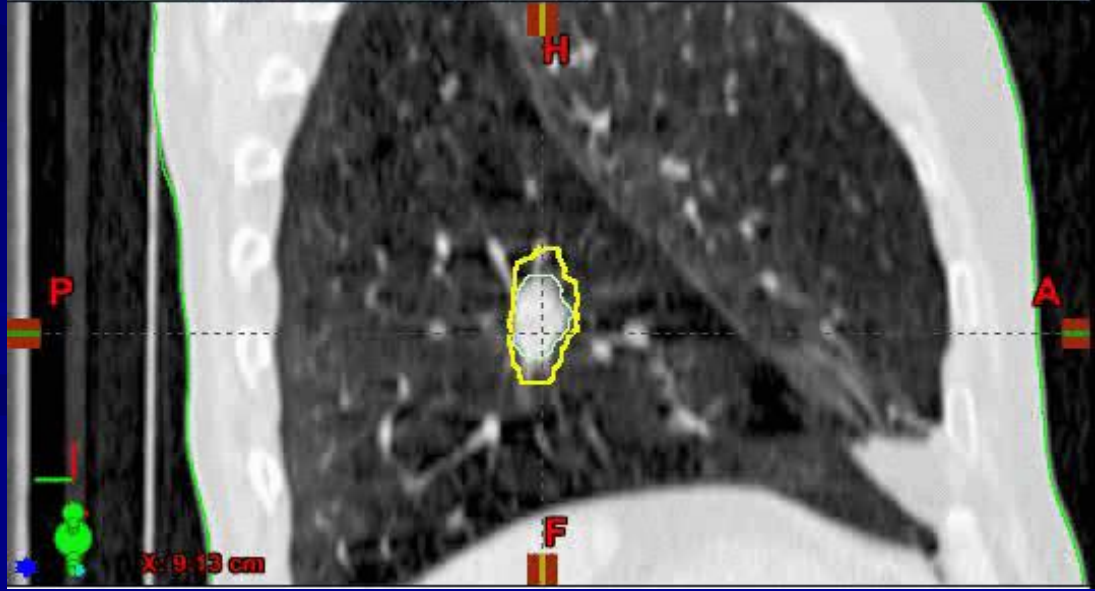
Trial\_1



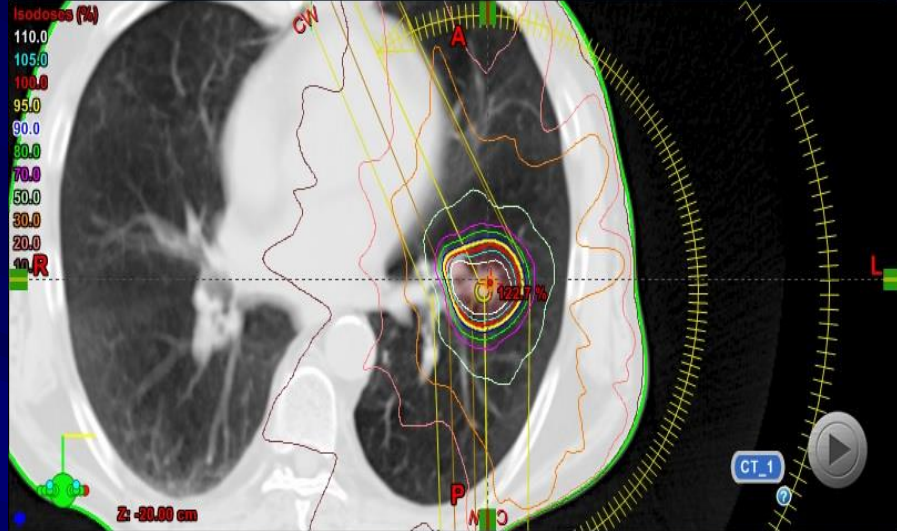
CT\_1 (Avg) - Showing registered image: CT85 (85)



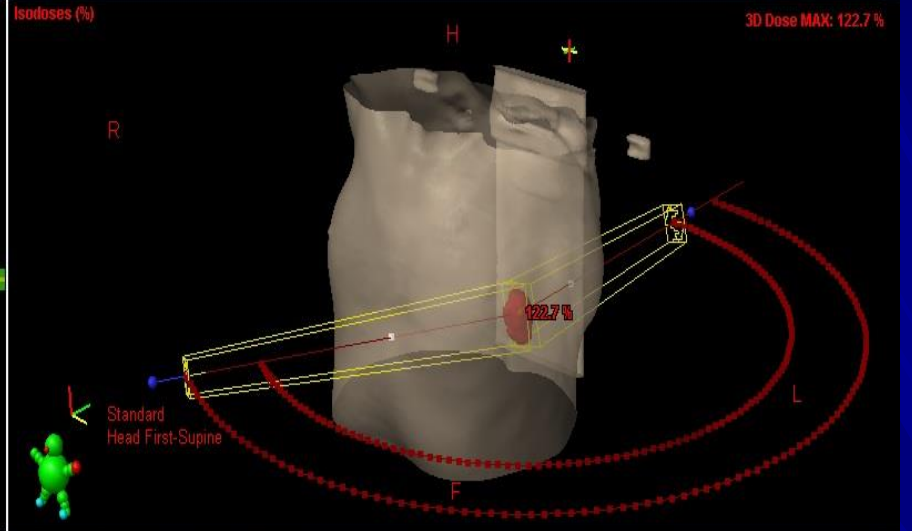
CT\_1 (Avg) - Showing registered image: CT85 (85)



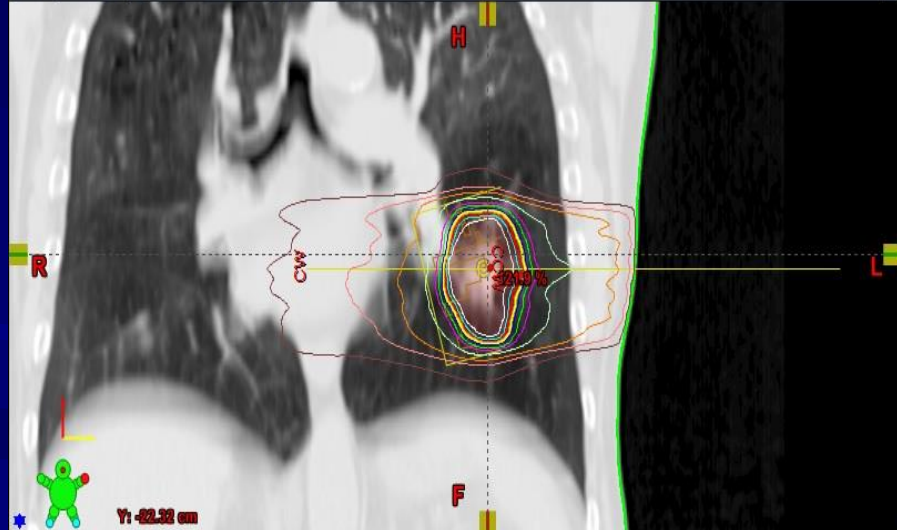
8x7.5Gy - 3rd Party Approval - Transversal - CT\_1 (Avg)



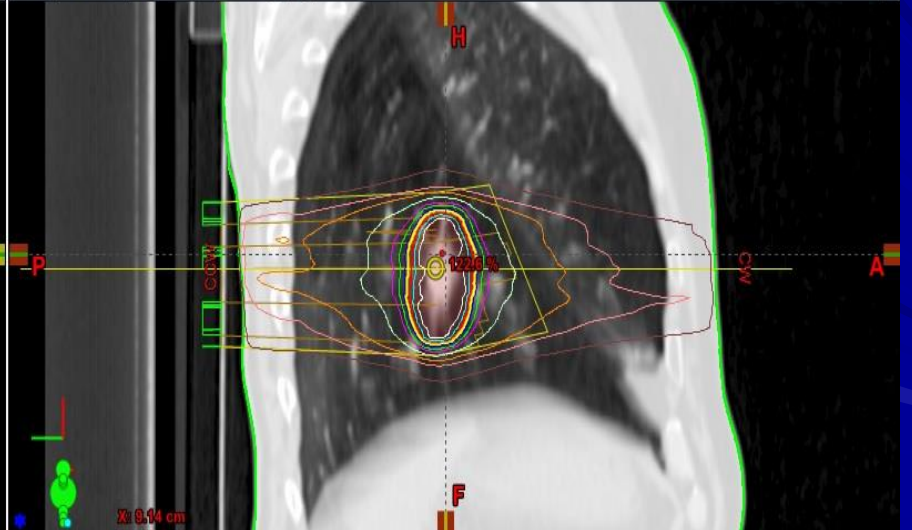
8x7.5Gy - 3rd Party Approval - Model View - CT\_1 (Avg)

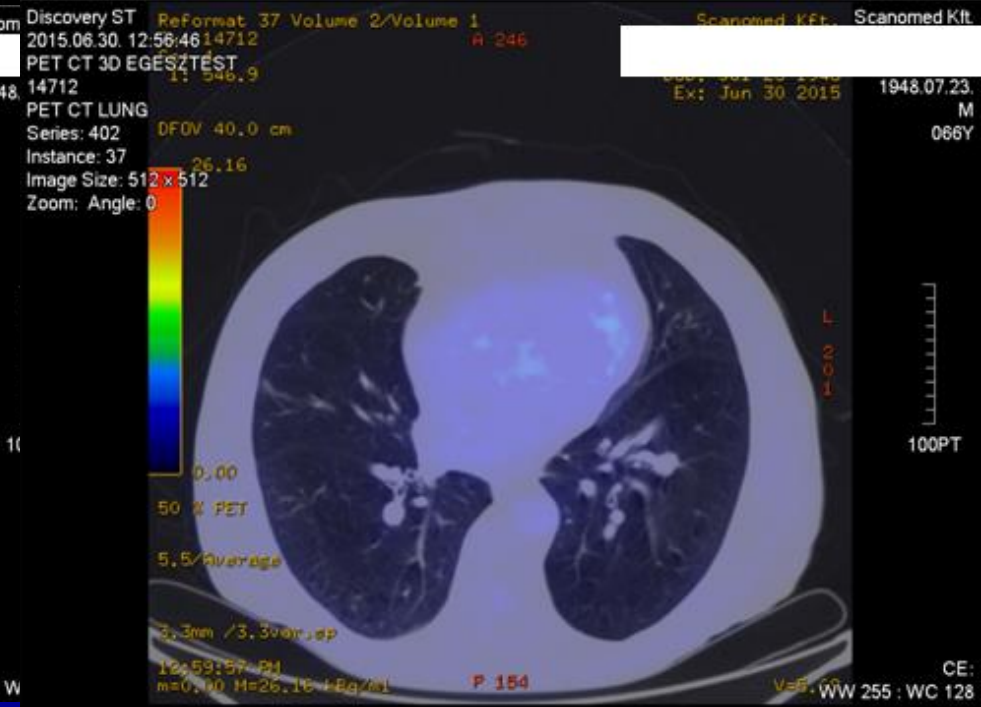
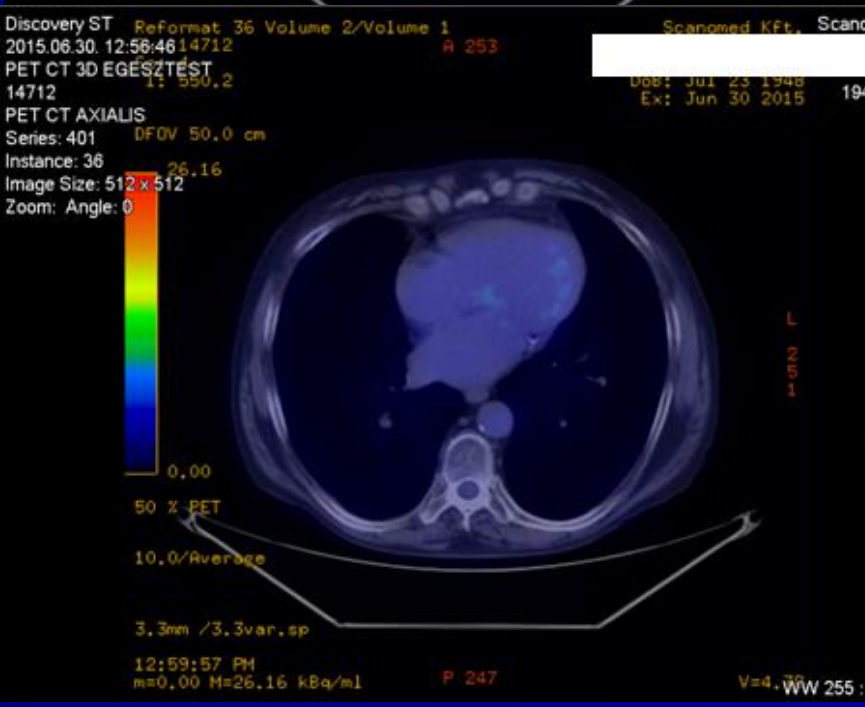
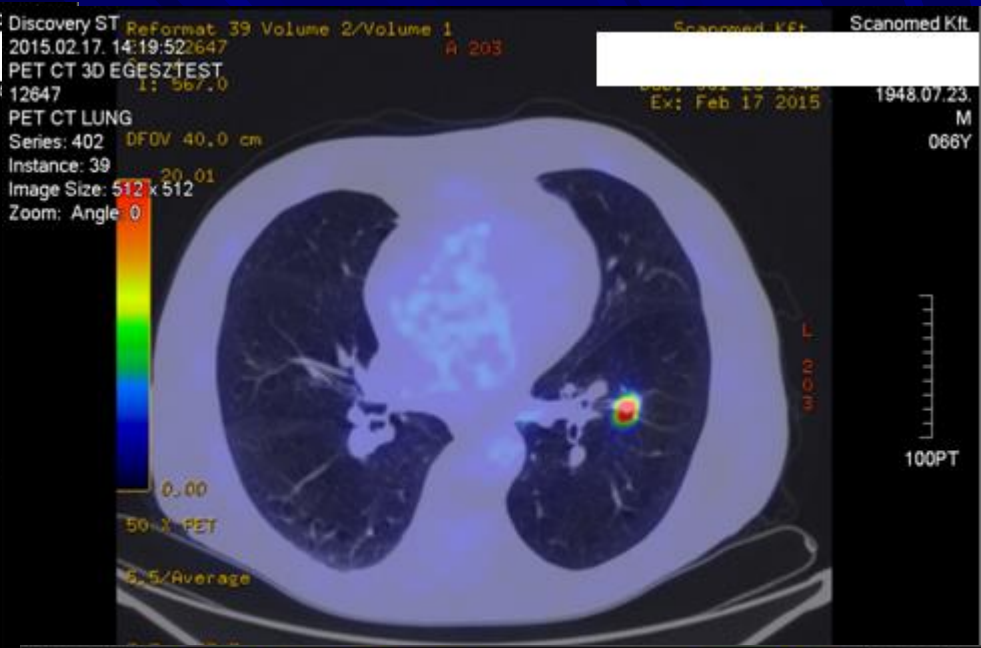
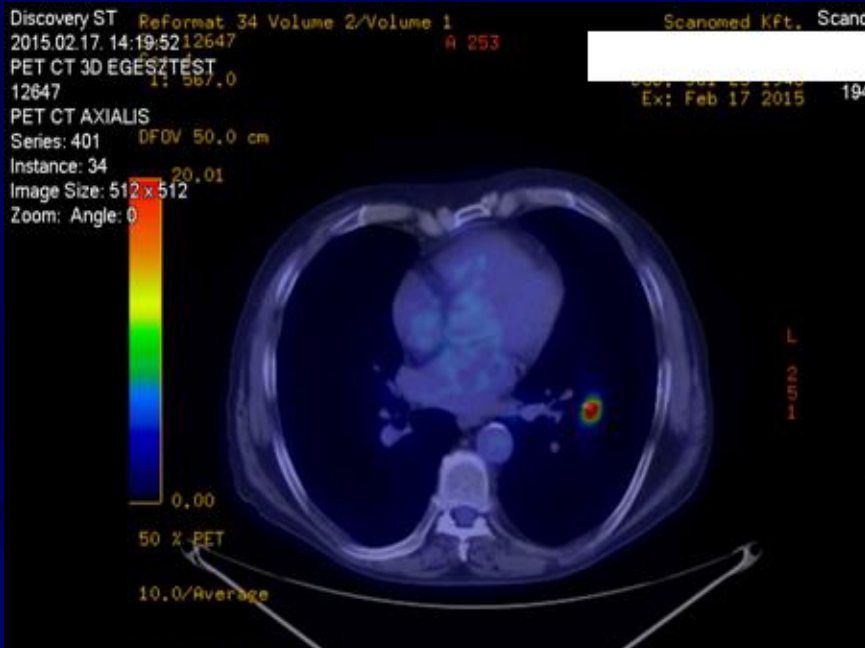


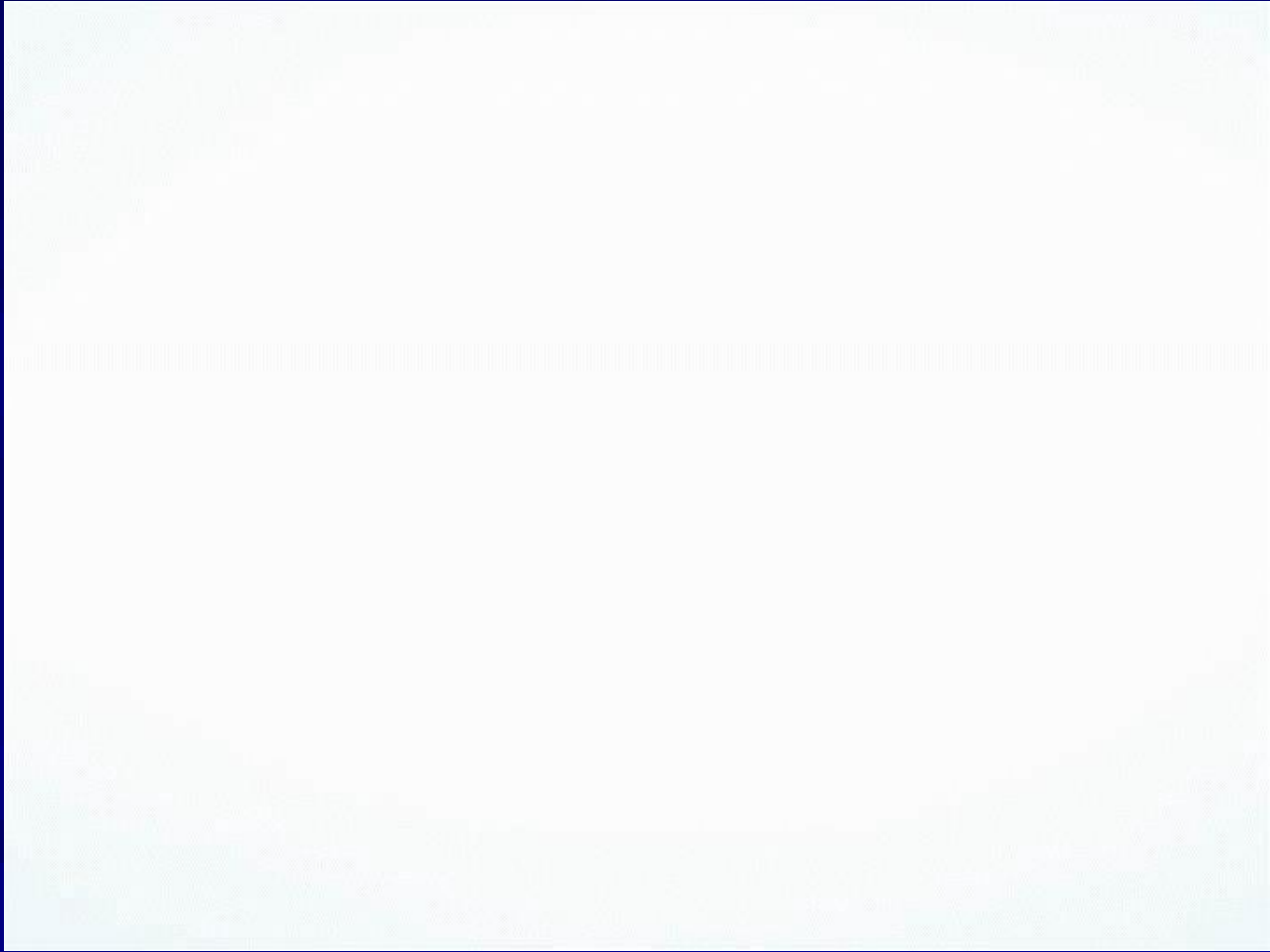
8x7.5Gy - 3rd Party Approval - Frontal - CT\_1 (Avg)



8x7.5Gy - 3rd Party Approval - Sagittal - CT\_1 (Avg)



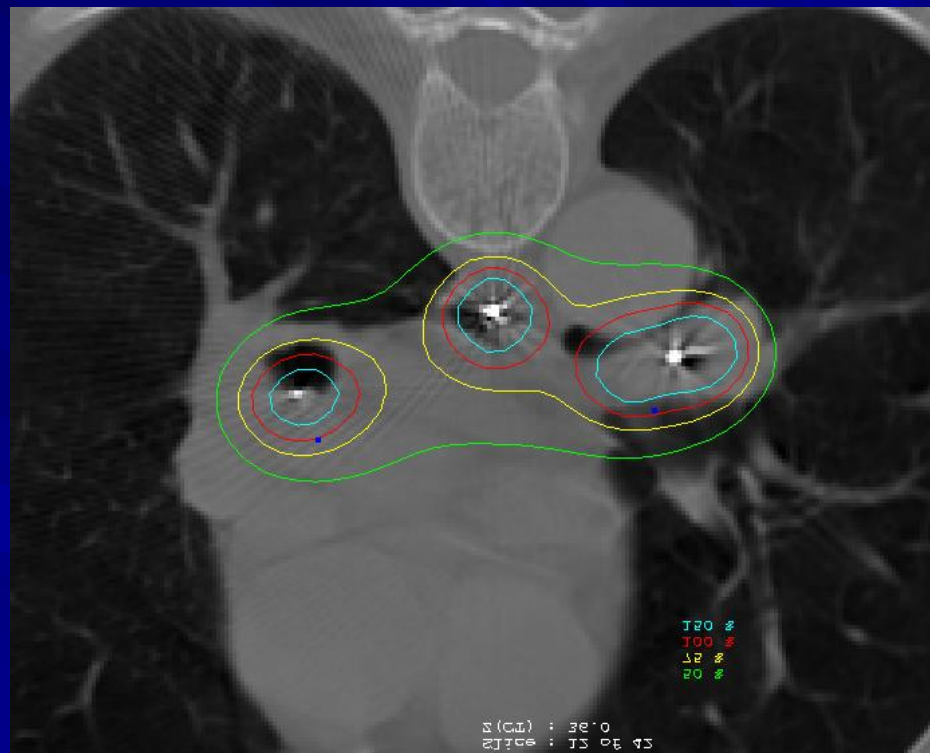
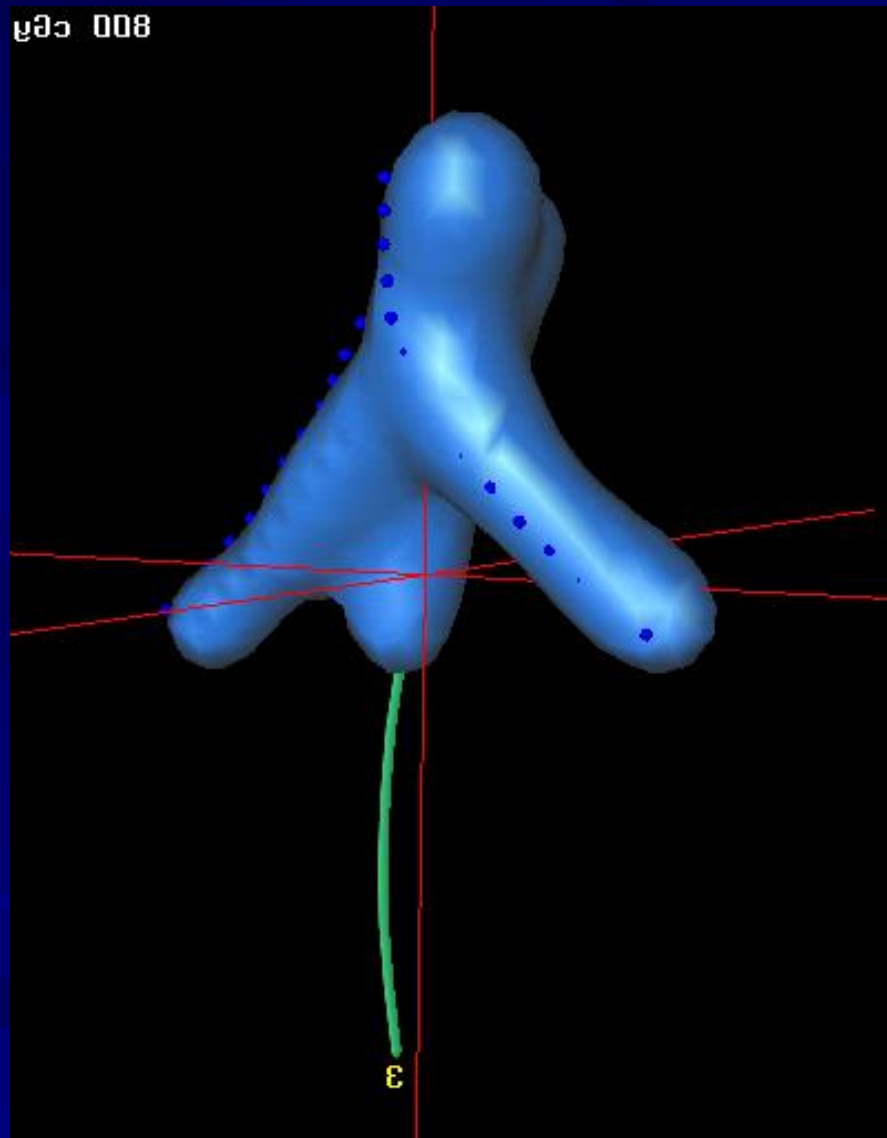


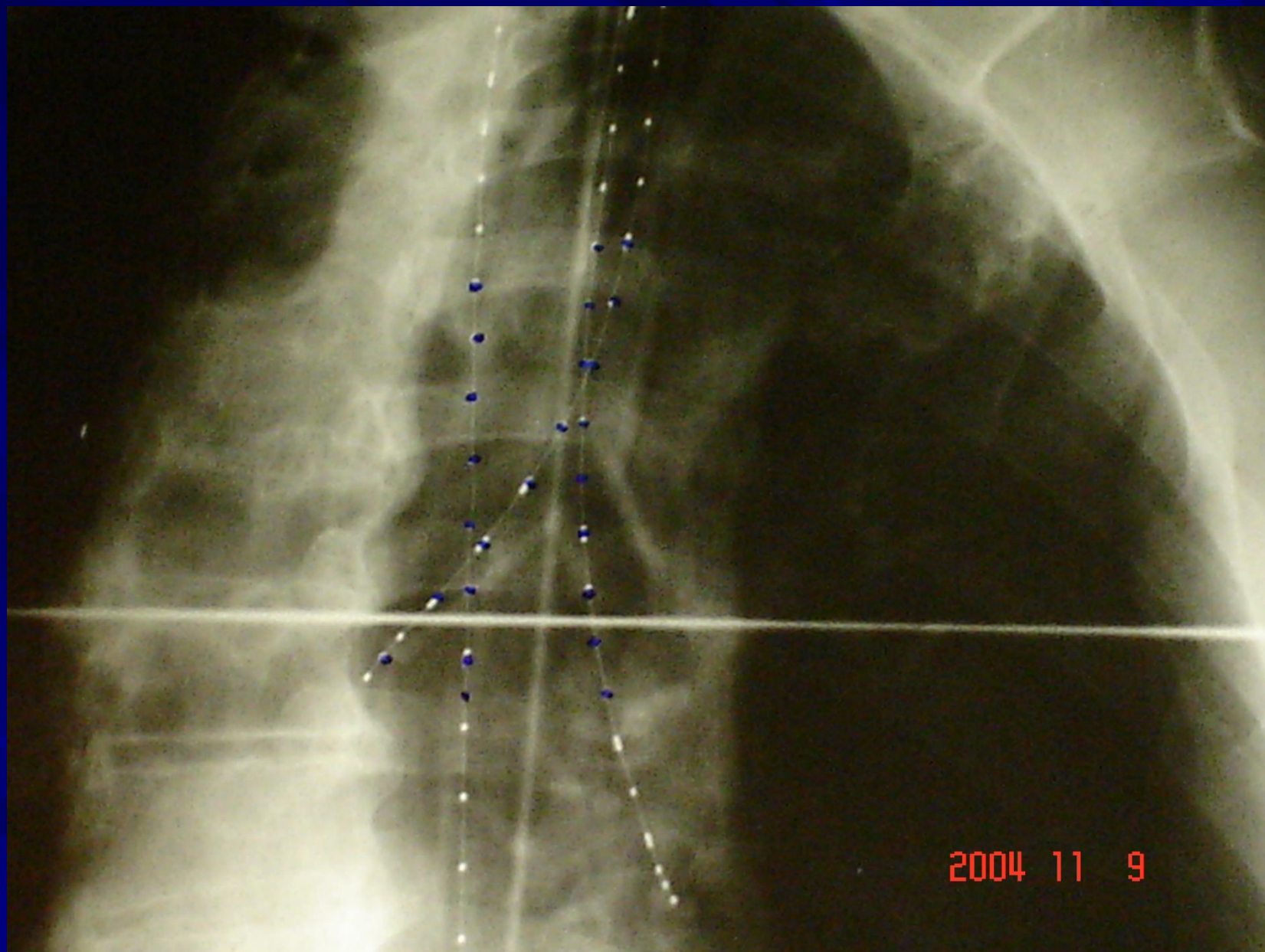






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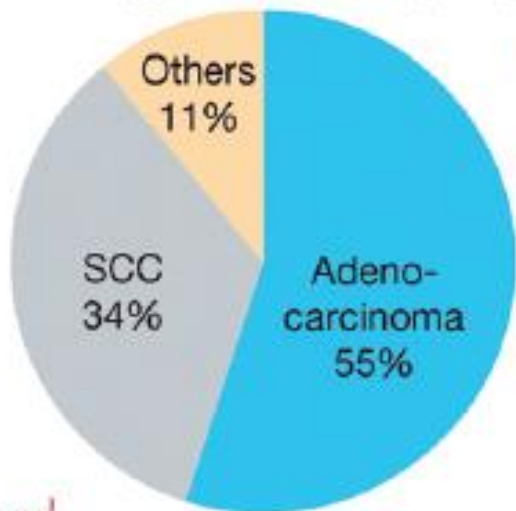


# 5-year survival by histology and extension

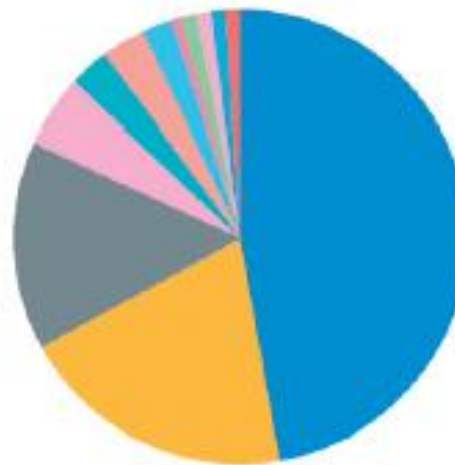
Histology	All stage	Local	Regional	Mets
<b>All histology</b>	<b>13.9</b>	<b>39.6</b>	<b>14.4</b>	<b>1.5</b>
Squamous cell cc.	15.4	34.3	14.9	1.5
Adenocarcinoma	16.6	49.9	16.1	1.5
Bronchioalveolar cc.	42.1	65.1	31.8	4.2
Papillaris adenocc.	23.7	57.4	25.8	5.4
Adenosquamous cc.	21.6	49.6	19.1	2.2
<b>SCLC</b>	<b>4.6</b>	<b>12.3</b>	<b>7.5</b>	<b>1.4</b>
Large cell cc.	11.4	34.8	13.2	1.6



Histology-based subtyping

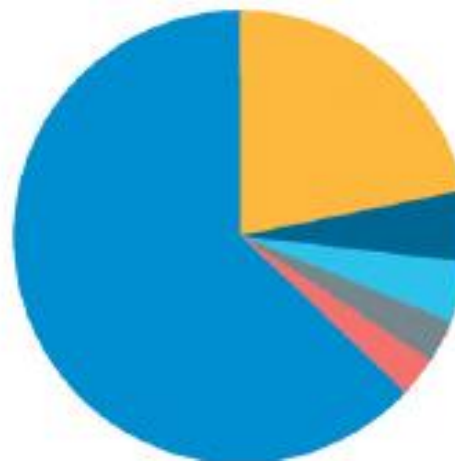


Adenocarcinoma



- ALK
- HER2
- BRAF
- PIK3CA
- AKT1
- MAP2K1
- NRAS
- ROS1
- RET
- EGFR
- KRAS
- Unknown

SCC



- EGFRvIII
- PIK3CA
- EGFR
- DDR2
- FGFR1 Amp
- Unknown



Understanding Disease