

Pulmonary oncology

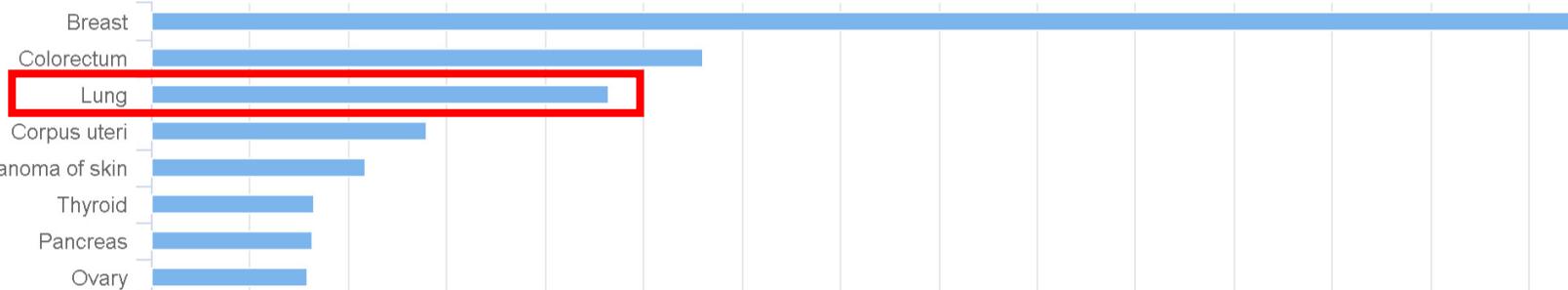
József Lövey

National Institute of Oncology
Budapest

Epidemiology / incidence in EU

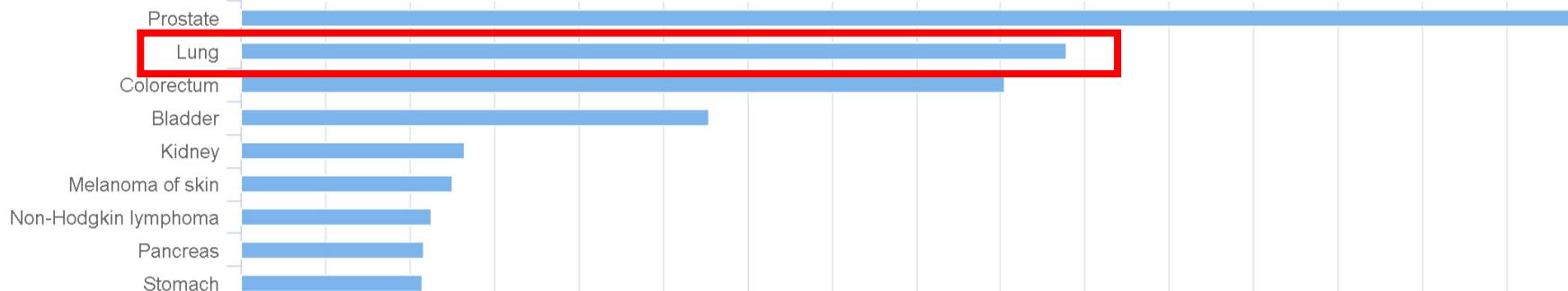
Estimated incidence by cancer

EU28, Female, All ages, 2018



Estimated incidence by cancer

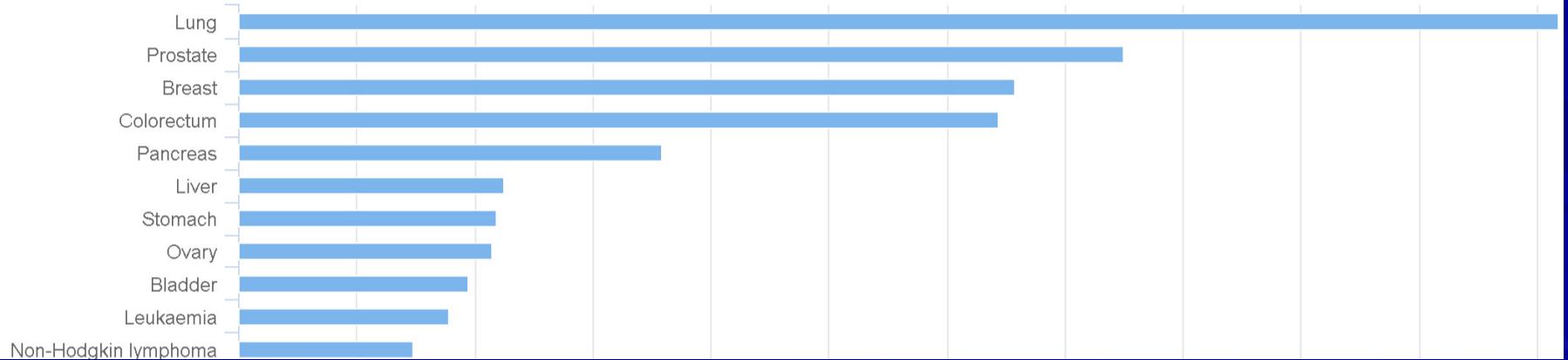
EU28, Male, All ages, 2018



Epidemiology / mortality in EU

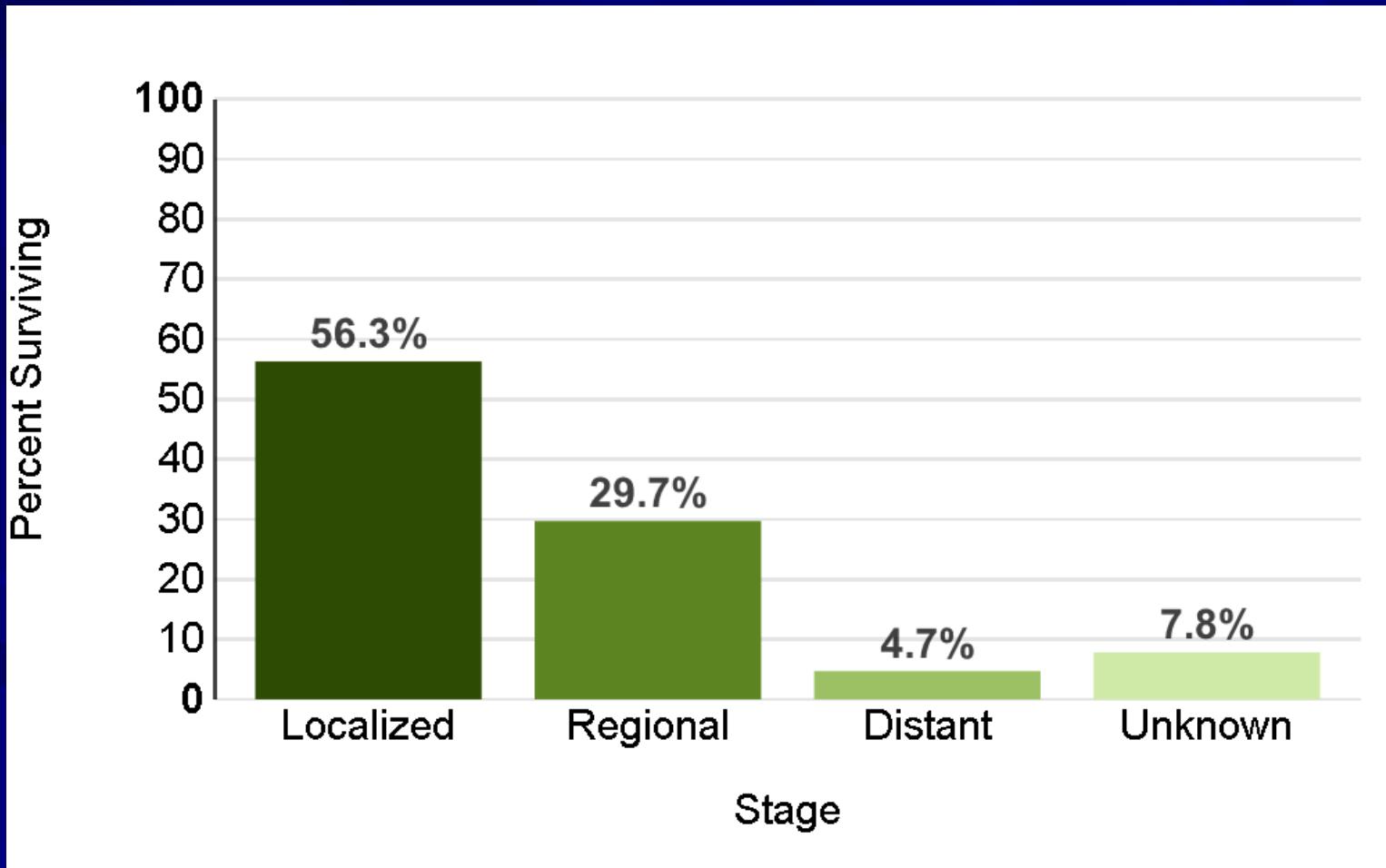
Estimated mortality by cancer

EU28, Both sexes, All ages, 2018

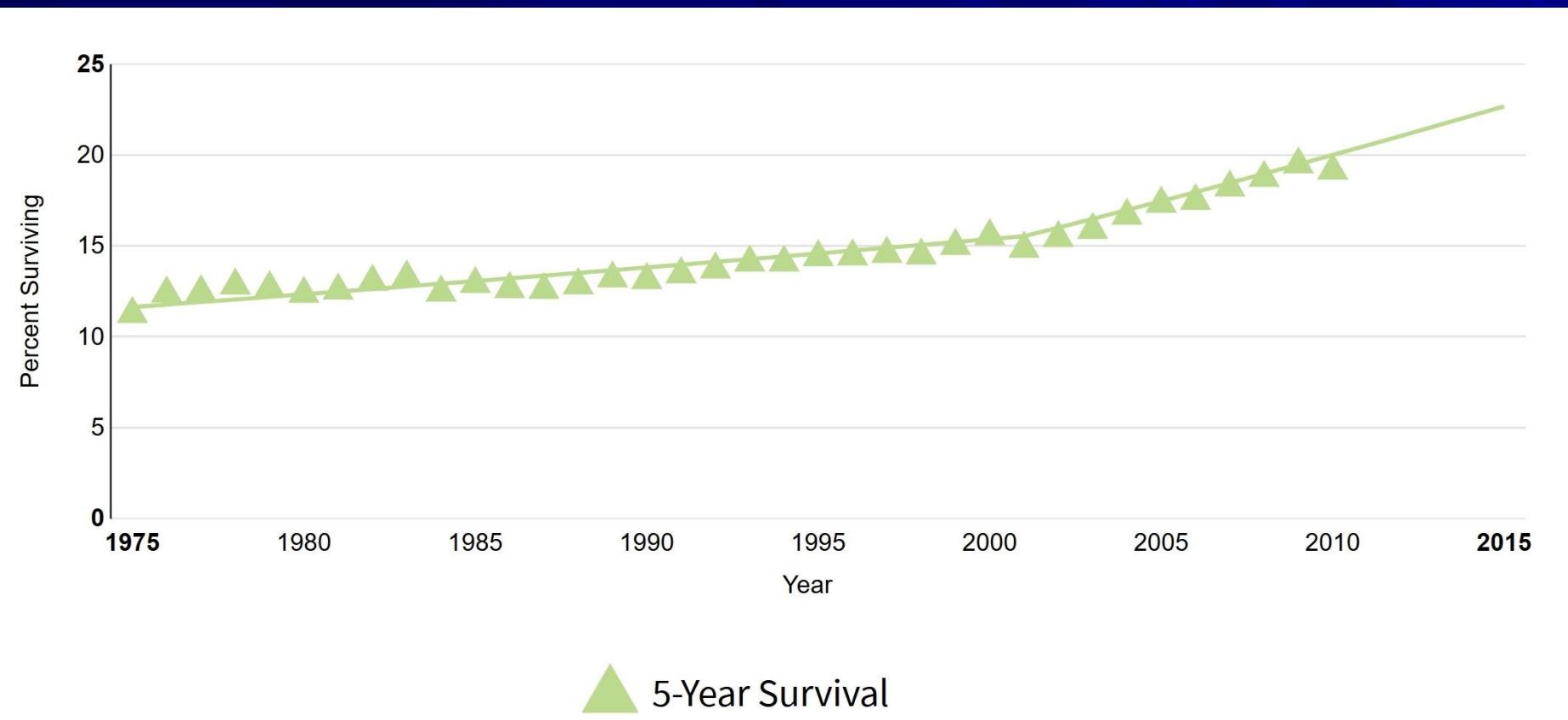


Survival by stage

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



Improvement of survival in 40 years



SEER database, USA

Etiology

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



Bob, I've got cancer.

Tobacco kills – don't be
advertized, glamorized

WORLD NO TOBACCO DAY

©1999 World Health Organization, California Department of Health Services







the
art
of
quitting.com



SMOKING REDUCES YOUR ABILITY TO GET AN ERECTION

ASHES



Action on
Smoking
and Health



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

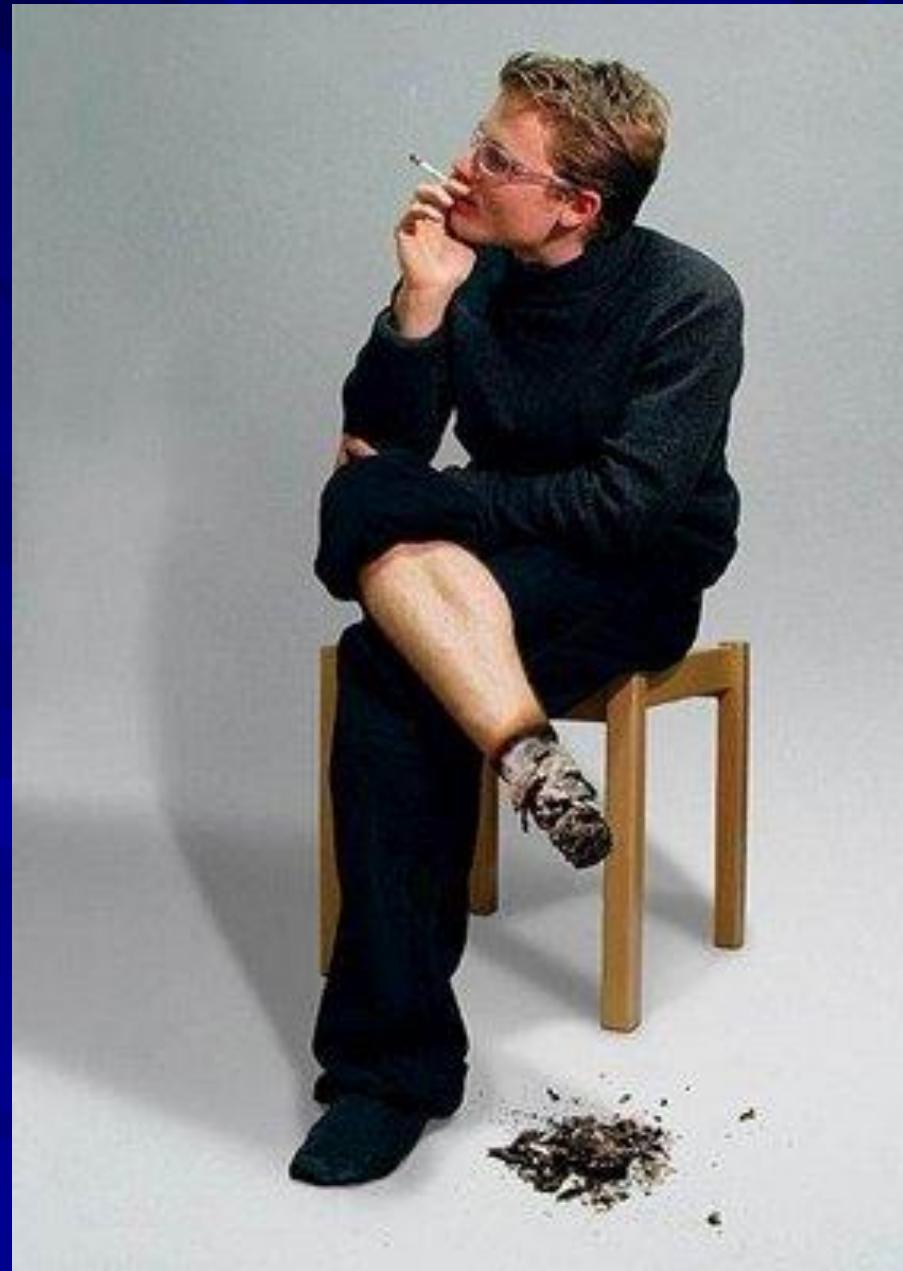
maybe you'll do it for your penis.

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 84198 for a free information pack. Texts will be charged at your standard rate. Call 0800 169 0169 www.stayinghard.info

NHS

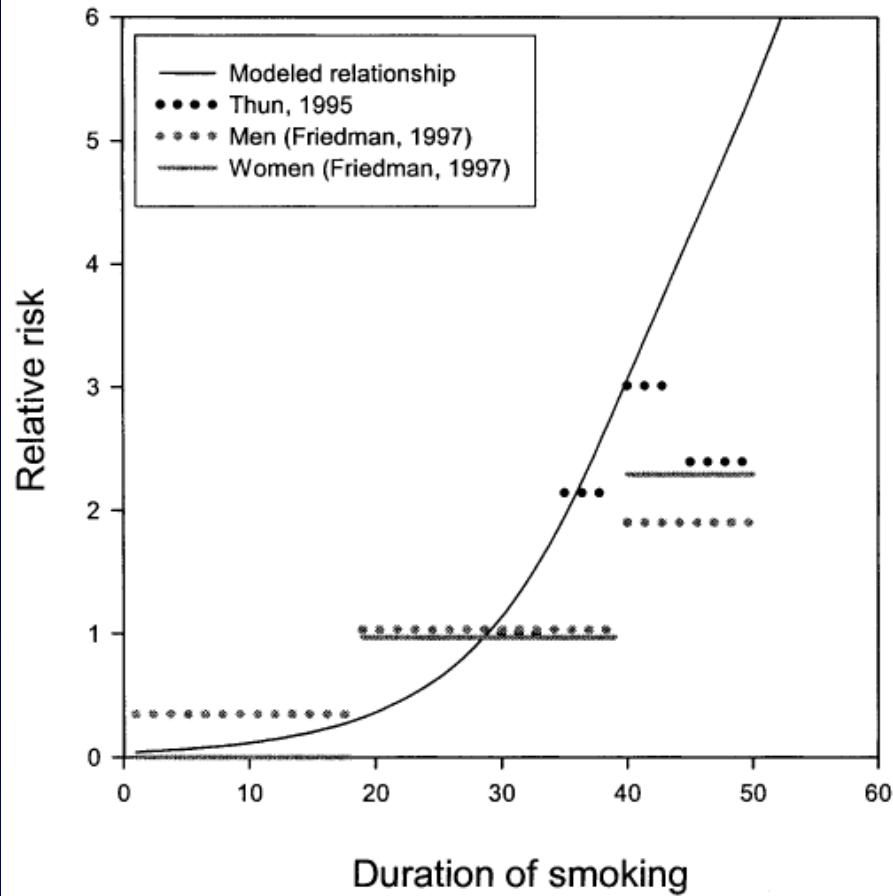
If you have any concerns about smoking please contact your GP.



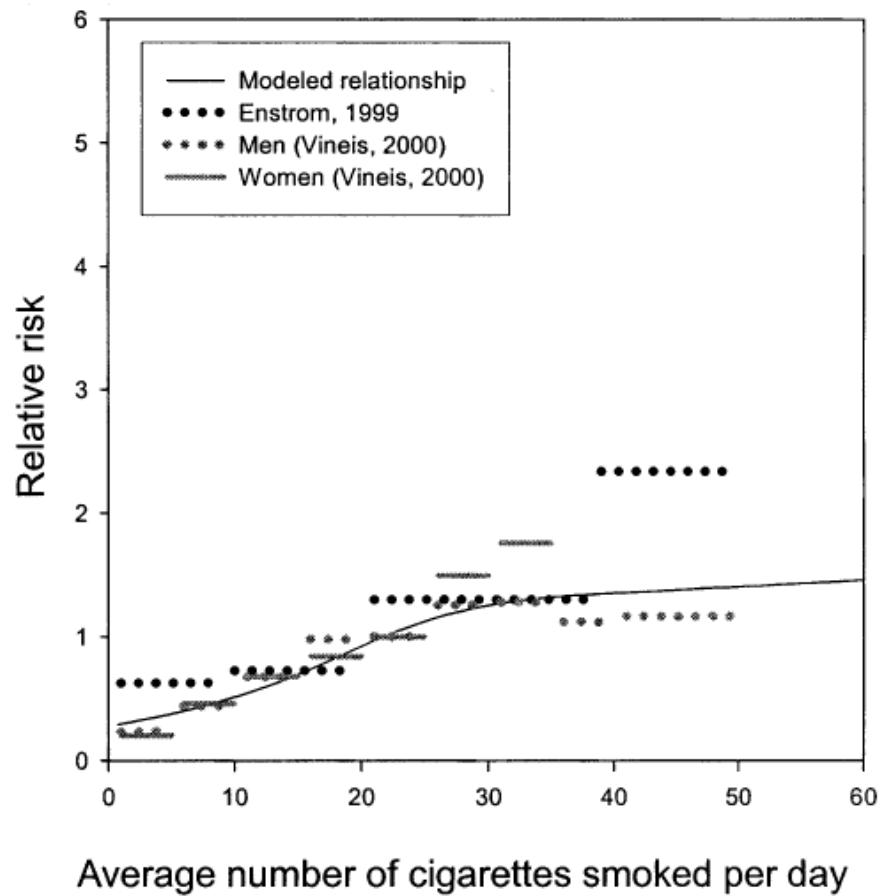


Etiology

A



B



Benz[<i>a</i>]anthracene	2A	<i>N</i> -Nitrosopyrrolidine	2B	Acetaldehyde	2B
Benzo[<i>b</i>]fluoranthene	2B	<i>N</i> -Nitrosopiperidine	2B	Catechol	2B
Benzo[<i>j</i>]fluoranthene	2B	<i>N</i> -Nitrosodiethanolamine	2B	Caffeic acid	2B
Benzo[<i>k</i>]fluoranthene	2B	<i>N,N</i> -Nitrosonornicotine	1	1,3-Butadiene	2A
Benzo[<i>a</i>]pyrene	1	4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone	1	Isoprene	2B
Dibenz[<i>a,h</i>]anthracene	2A	2-Toluidine	2A	Benzene	1
Dibenzo[<i>a,i</i>]pyrene	2B	2,6-Dimethylaniline	2B	Nitromethane	2B
Dibenzo[<i>a,e</i>]pyrene	2B	2-Naphthylamine	1	2-Nitropropane	2B
Indeno[1,2,3- <i>cd</i>]pyrene	2B	4-Aminobiphenyl	1	Nitrobenzene	2B
5-Methylchrysene	2B	A- \hat{I}^{\pm} -C	2B	Acetamide	2B
Furan	2B	MeA- \hat{I}^{\pm} -C	2B	Acrylamide	2A
Dibenz[<i>a,h</i>]acridine	2B	IQ	2A	Acrylonitrile	2B
Dibenzo[<i>a,j</i>]acridine	2B	Trp-P-1	2B	Vinyl chloride	1
Dibenzo[<i>c,g</i>]carbazole	2B	Trp-P-2	2B	1,1â€“Dimethylhydrazine	2B
Benzo[<i>b</i>]furan	2B	Glu-P-1	2B	Ethylene oxide	1
<i>N</i> -Nitrosodimethylamine	2A	Glu-P-2	2B	Propylene oxide	2B
<i>N</i> -Nitrosoethylmethylamine	2B	PhIP	2B	Urethane	2B
<i>N</i> -Nitrosodiethylamine	2A	Hydrazine	2B	Arsenic	1
		Radio-isotope Polonium-210	1	Beryllium	1
		Formaldehyde	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

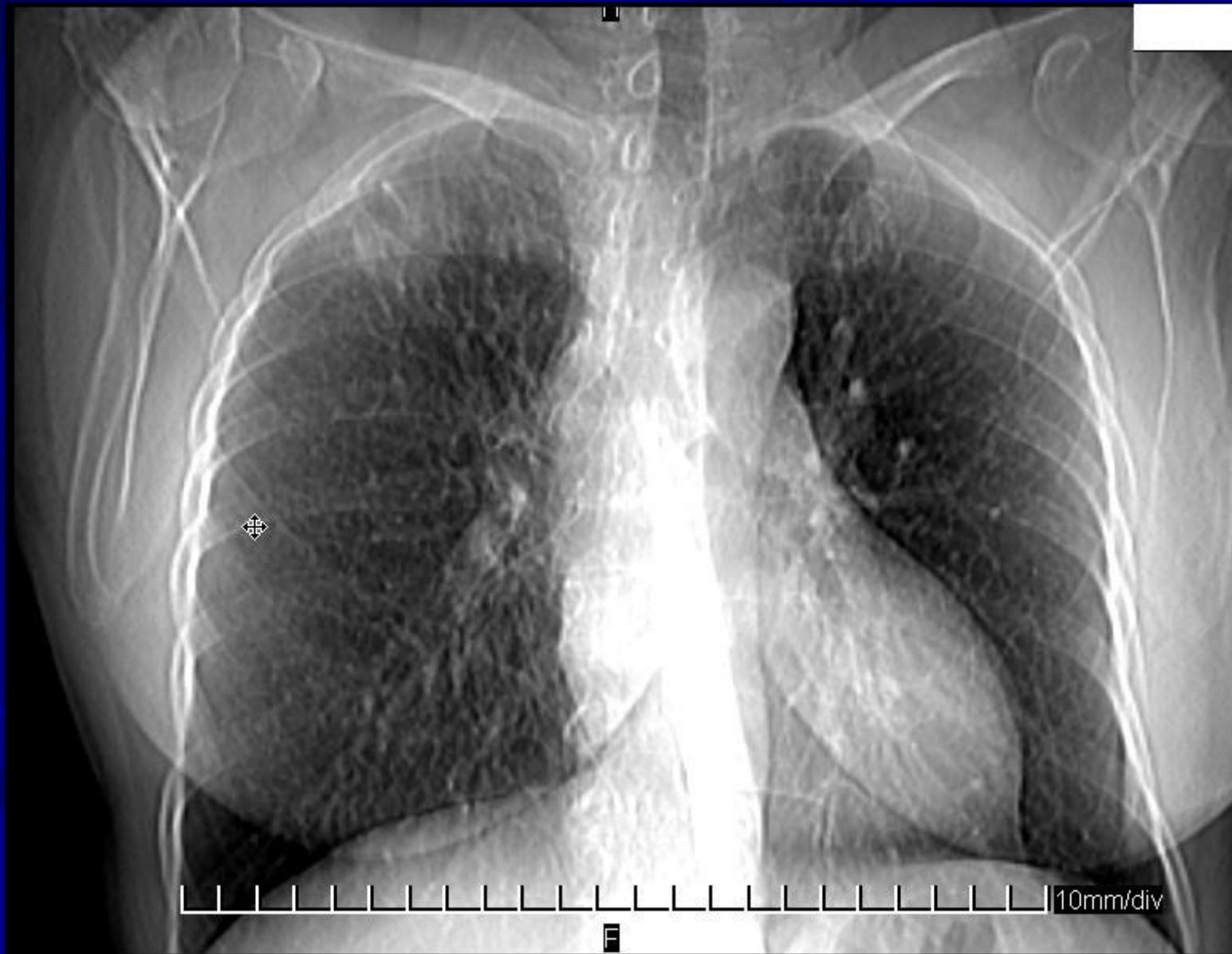
■ Statement of the EU:

- **Low-dose CT** is the method of screening
- Screening must be **risk adapted**
- **Informed involvement** of screenies 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 lifes**

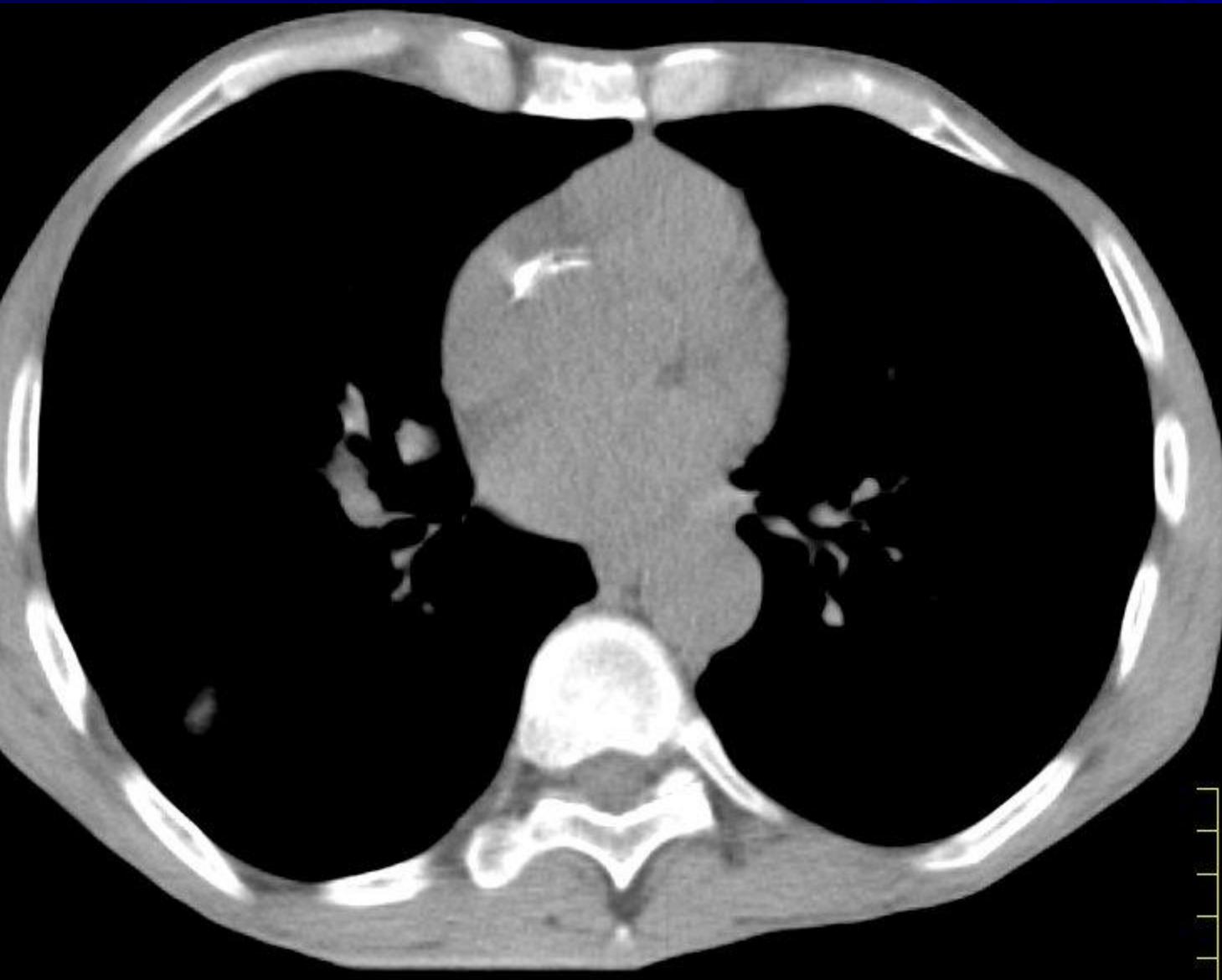
Diagnostics

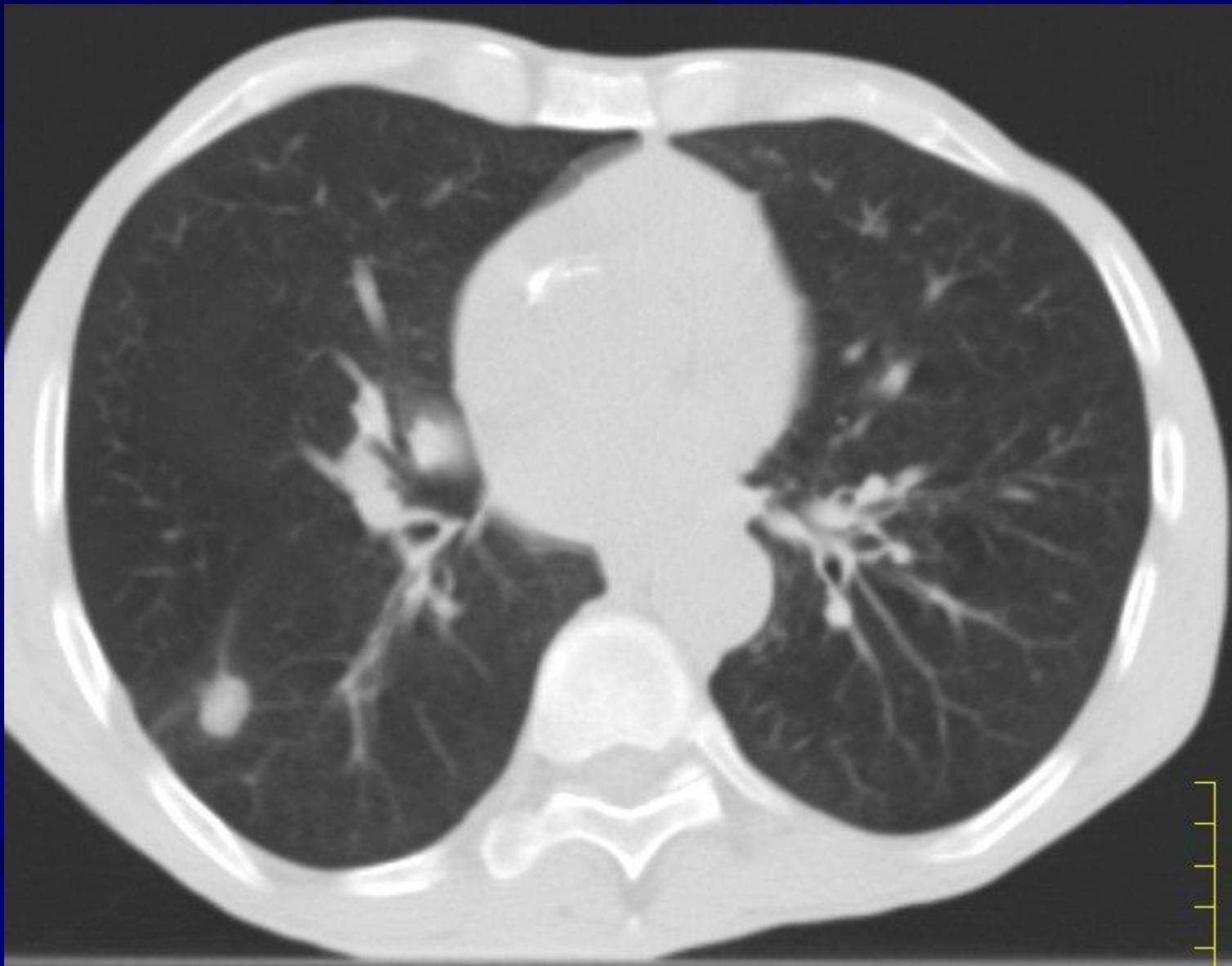
- Chest xR
- CAT scan
- Positron Emission Tomography (PET)
- Others (bone scan, MRI)
- Bronchoscopy
- Transthoracal biopsy (with xR or CAT assisted)
- Mediastinoscopy
- Video Assisted ThoracoScopy (VATS)

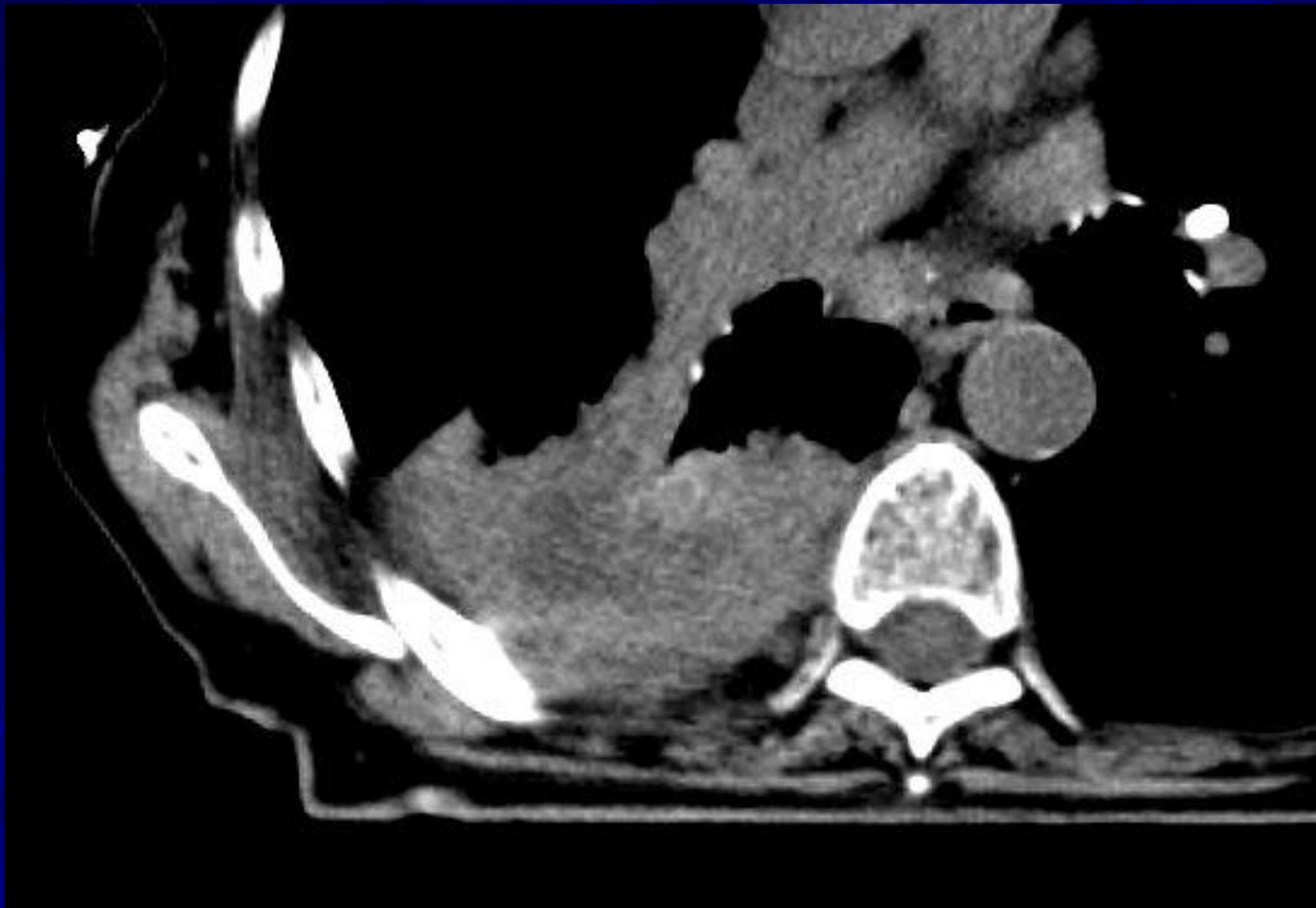
Chest xR

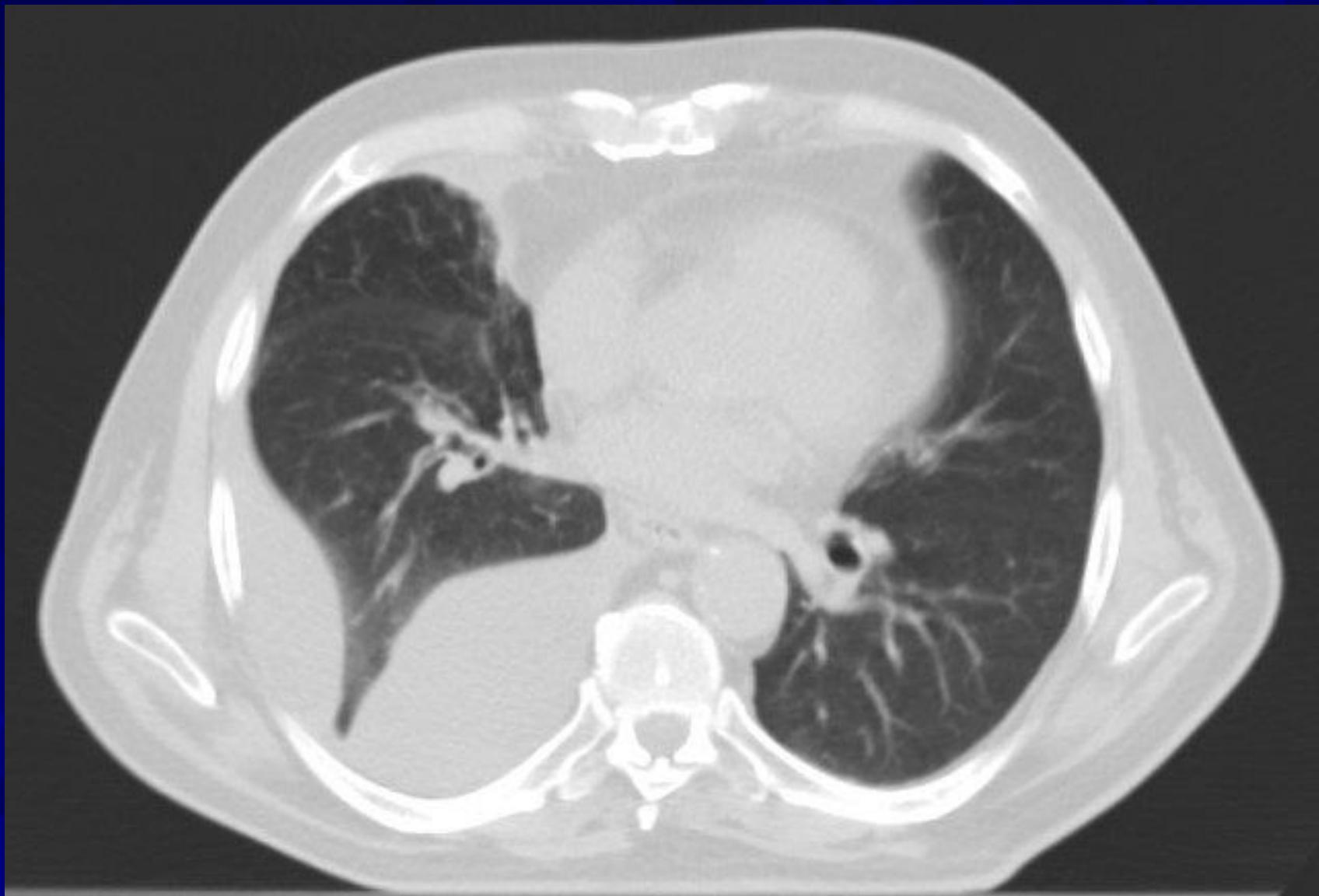


CAT









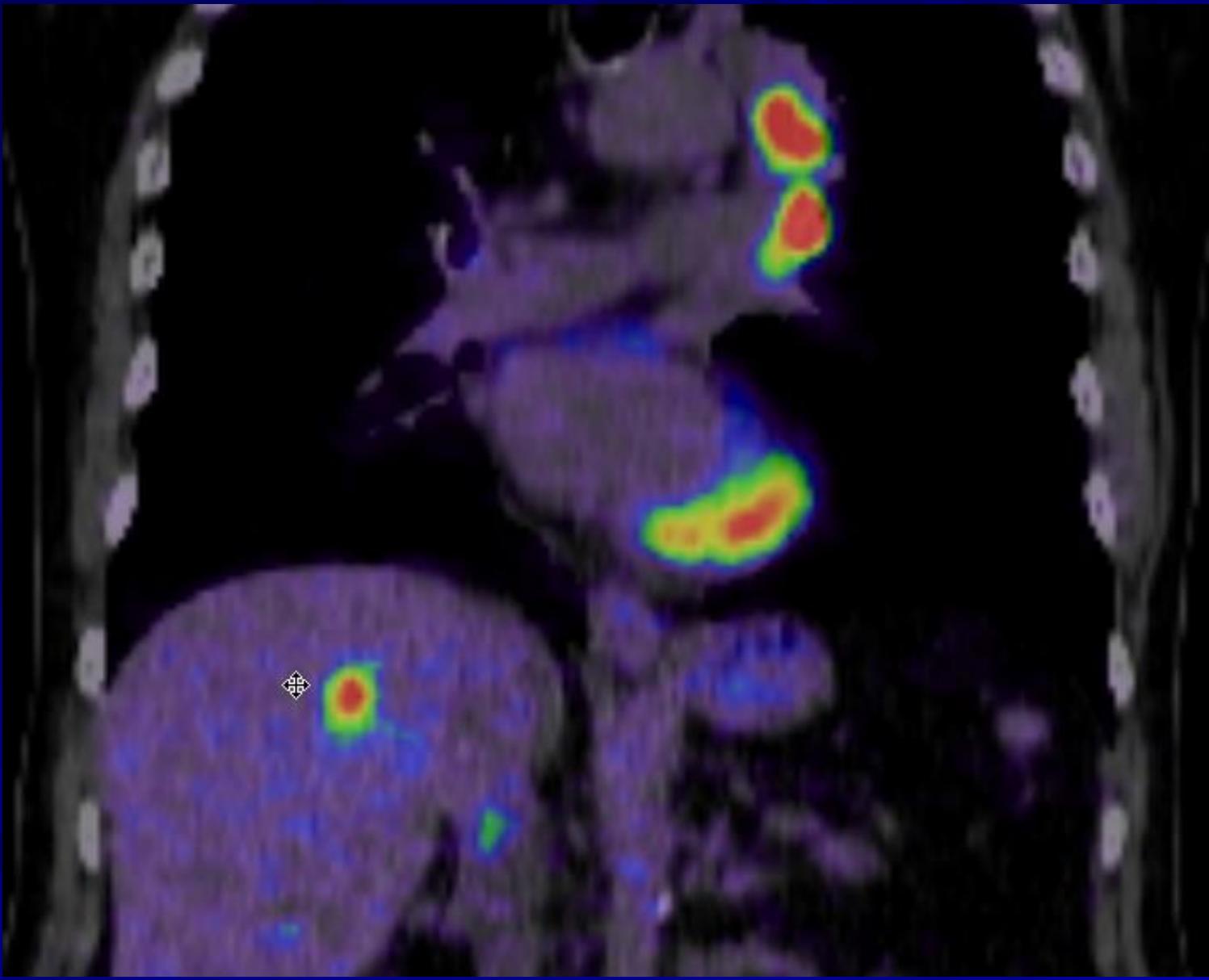




25
S

X : 0.0 mm
Y : 0.0 mm
Z : 46.9 mm
Zoom: 2.19 X

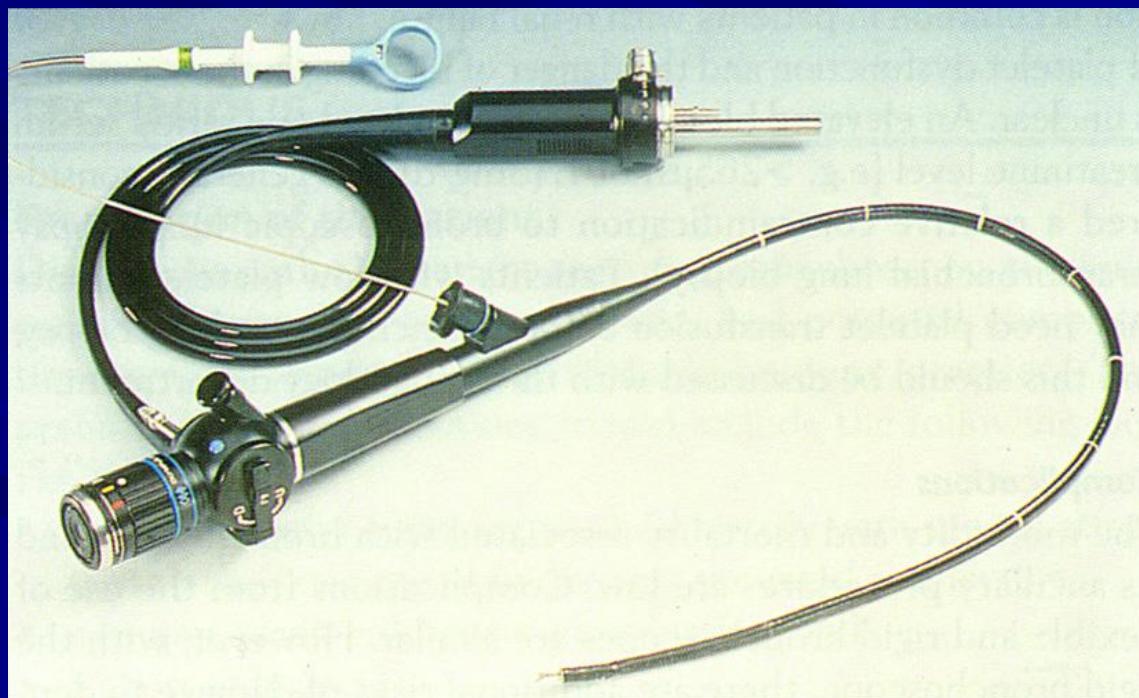


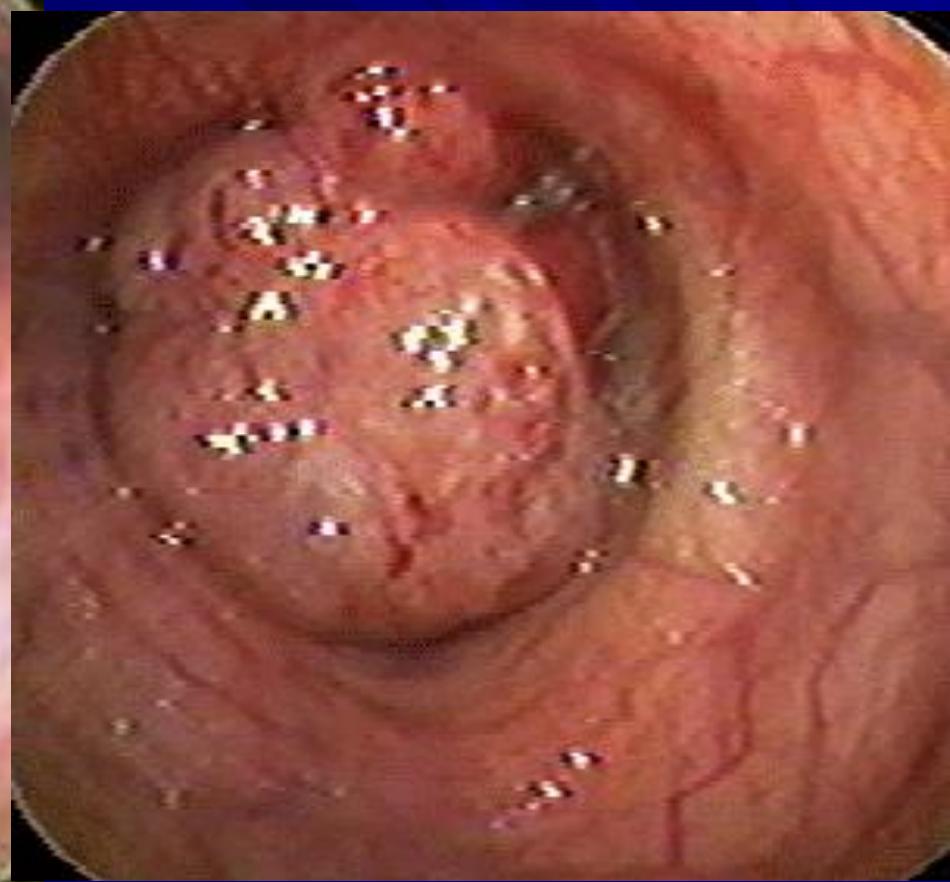
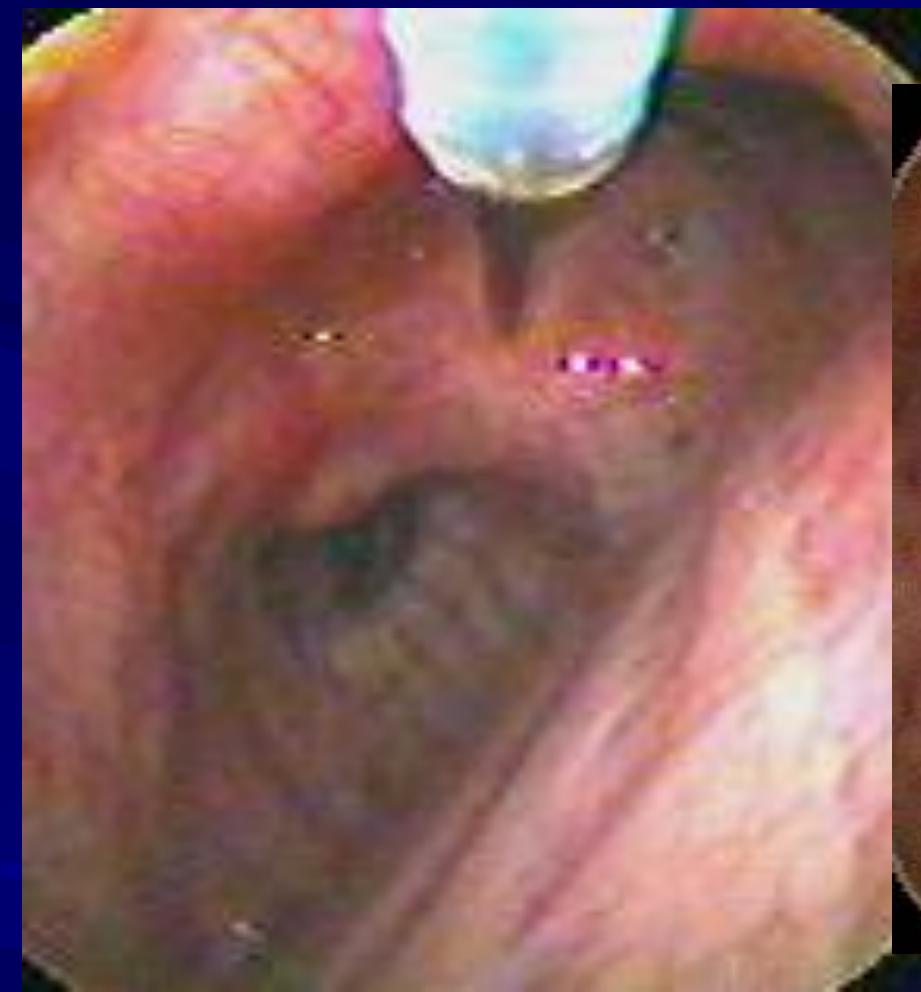


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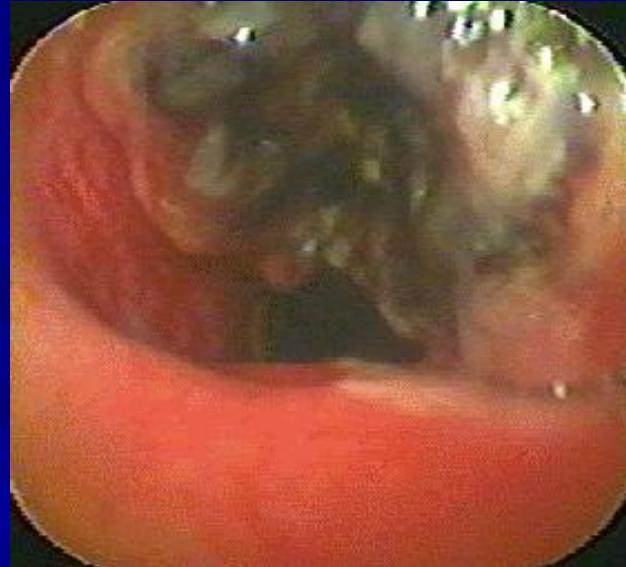
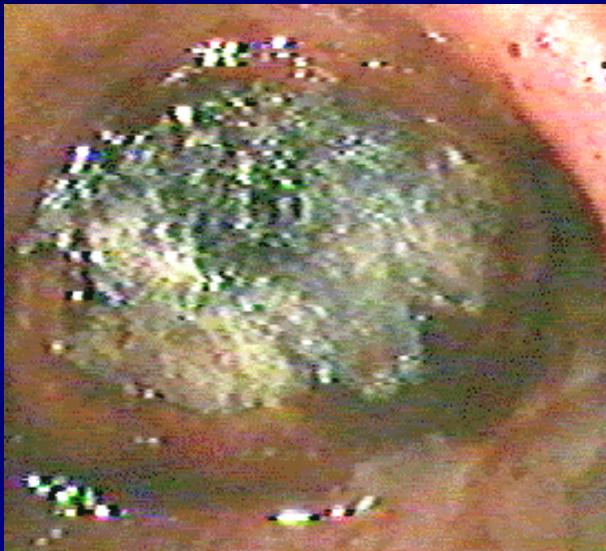
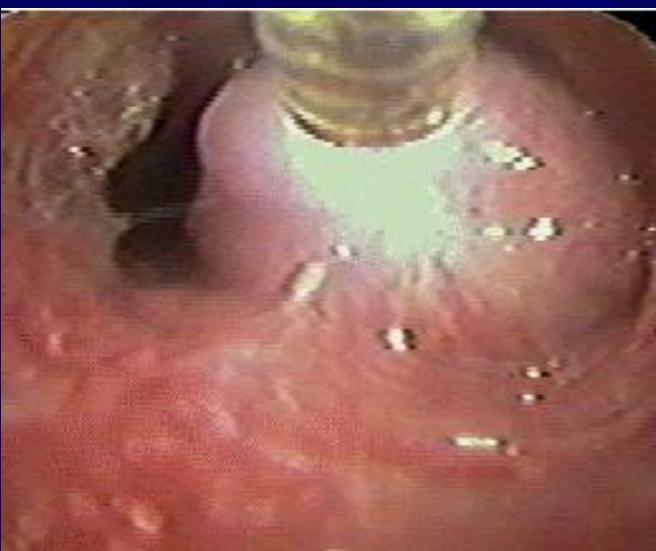
Bronchoscopy



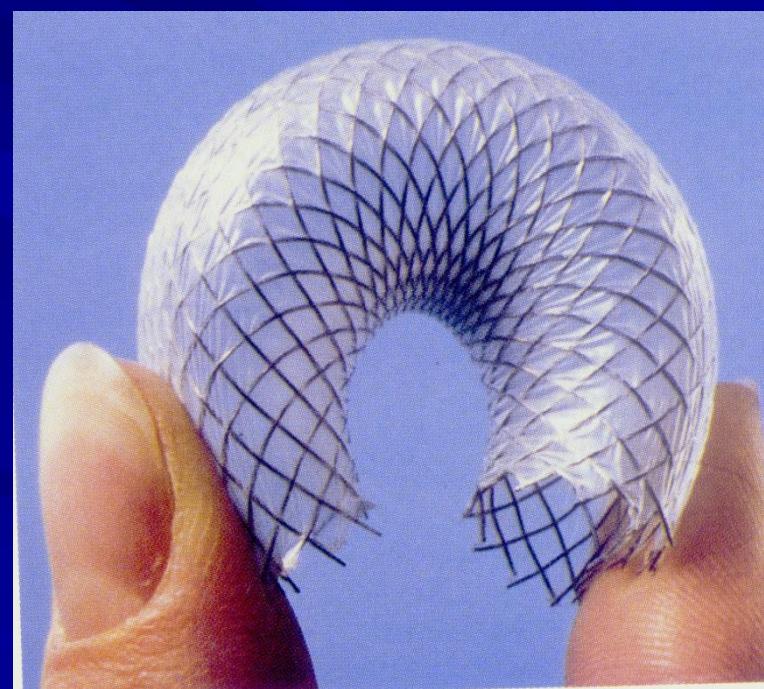
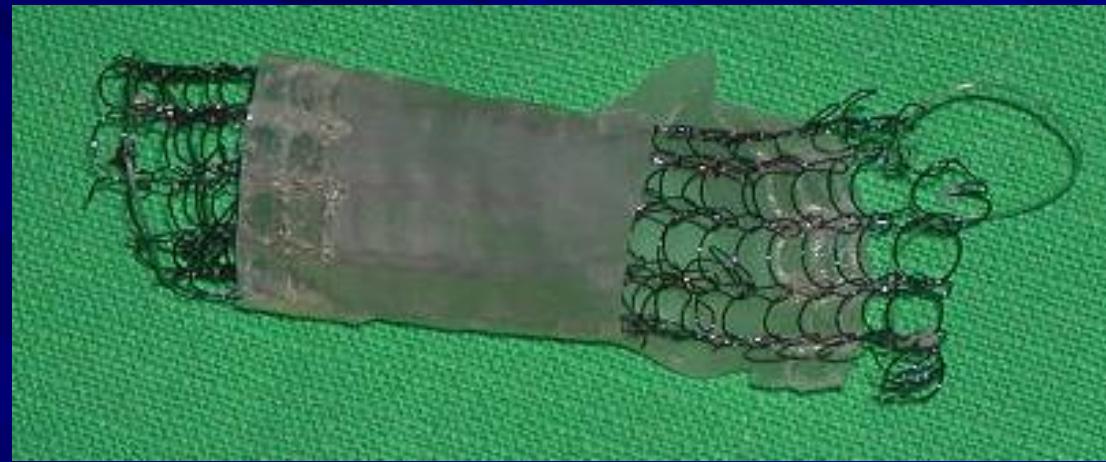
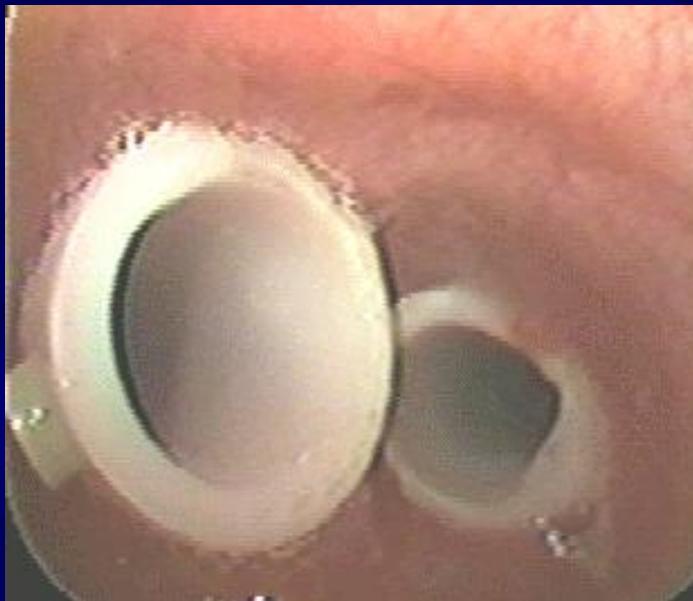




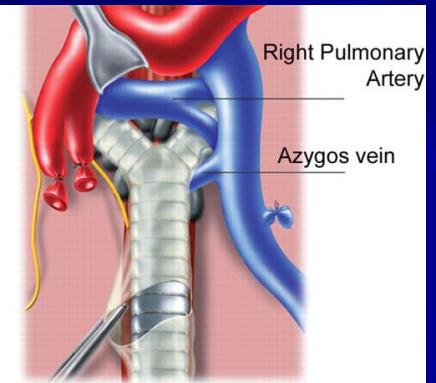
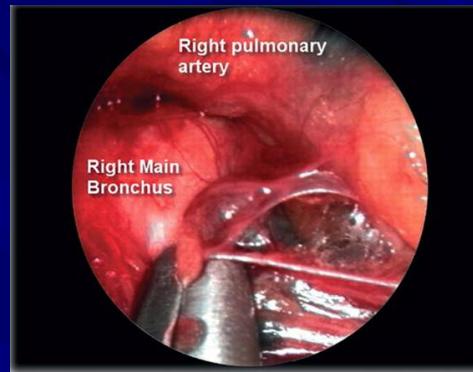
Special endobronchial techniques



Stenting

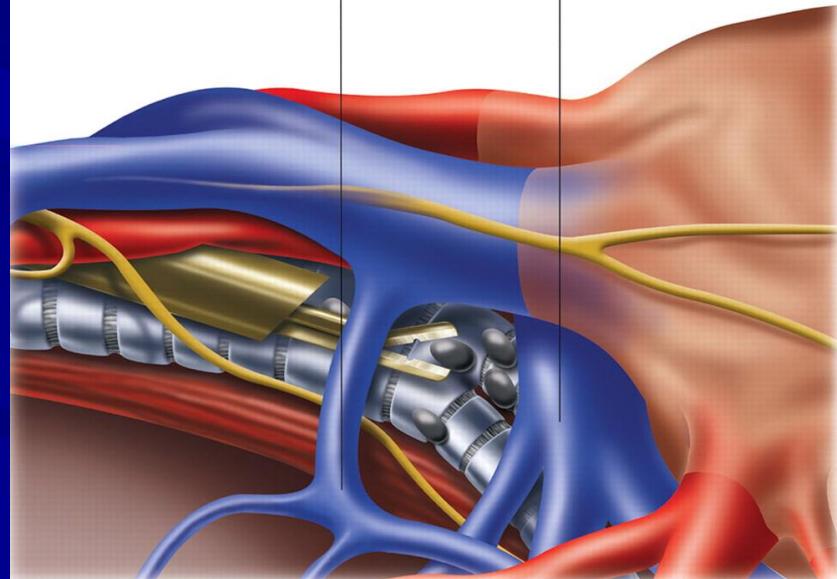
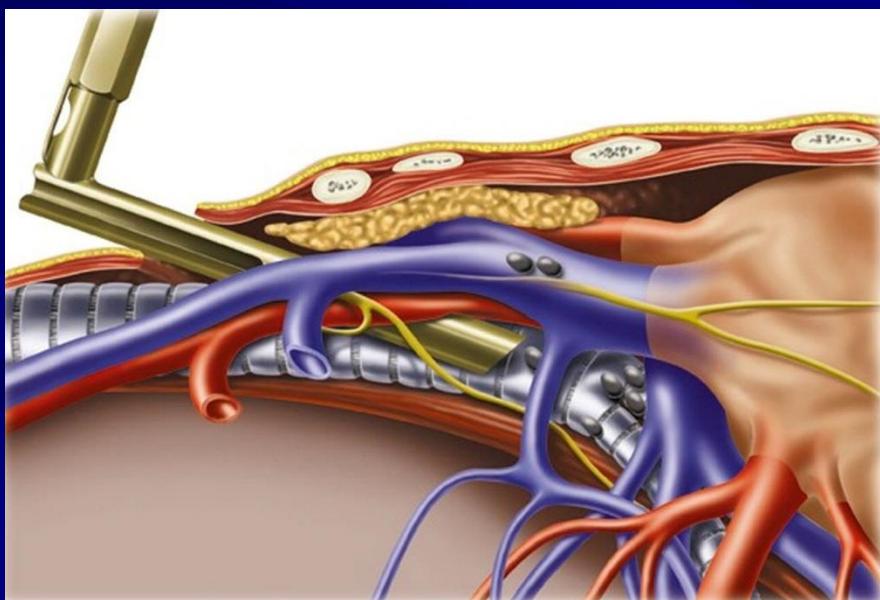


Mediastinoscopy

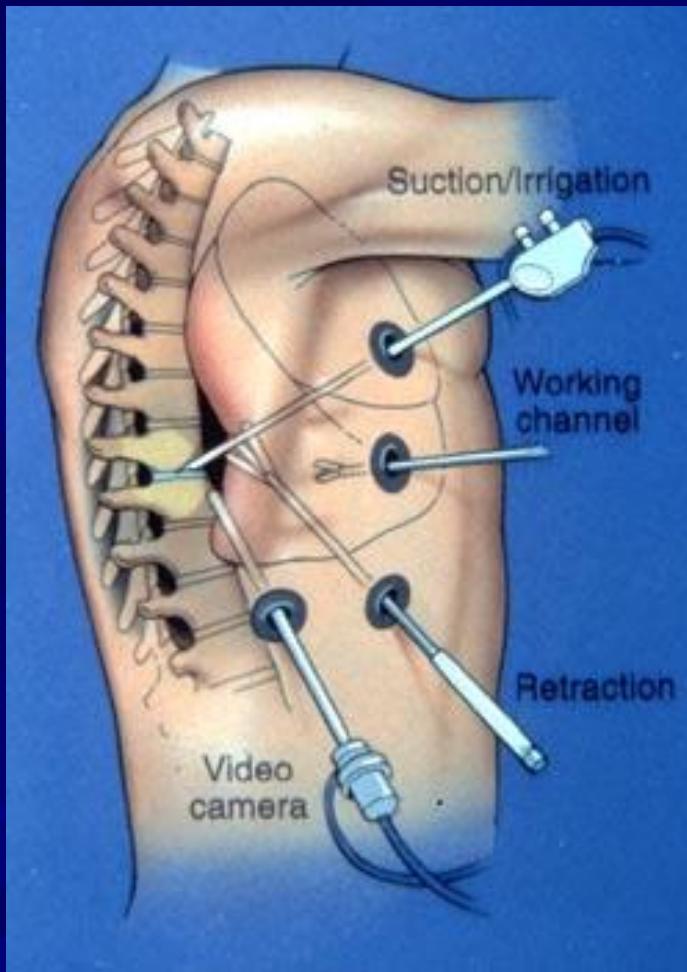


Azygos vein

Right Pulmonary Artery



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
- Immunootherapy
 - 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) ¹
T1mi		Minimally invasive adenocarcinoma ²
T1a		Tumour 1 cm or less in greatest dimension ¹
T1b		Tumour more than 1 cm but not more than 2 cm in greatest dimension ¹
T1c		Tumour more than 2 cm but not more than 3 cm in greatest dimension ¹
T2		Tumour more than 3 cm but not more than 5 cm; or tumour with any of the following features ³ <ul style="list-style-type: none">• Involves main bronchus regardless of distance to the carina, but without involving the carina• Invades visceral pleura• Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, either involving part of the lung or the entire lung
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

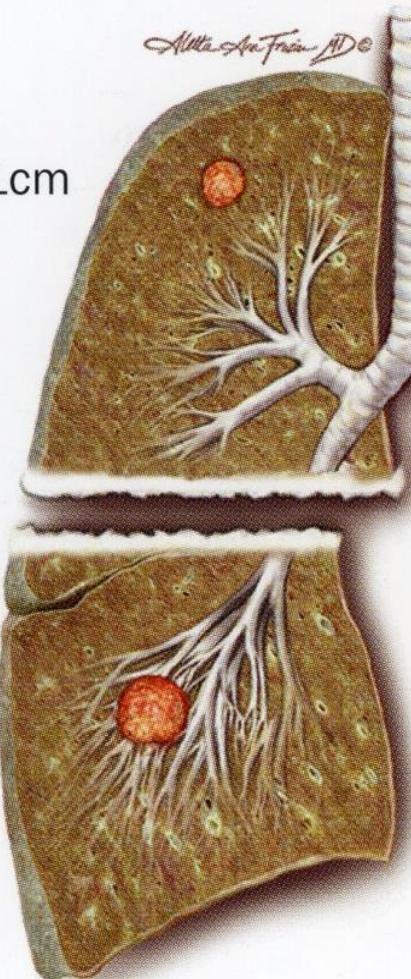
N – Regional Lymph Nodes

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 ⁴
	M1b	Single extrathoracic metastasis in a single organ ⁵
	M1c	Multiple extrathoracic metastases in one or several organs

T1a, T1b

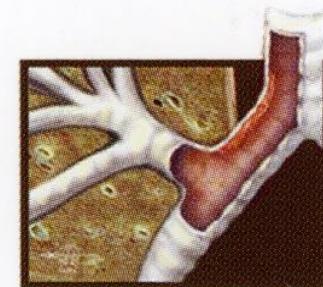


Tumour: $\leq 1\text{cm}$

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

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 $\leq 3\text{cm}$; 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



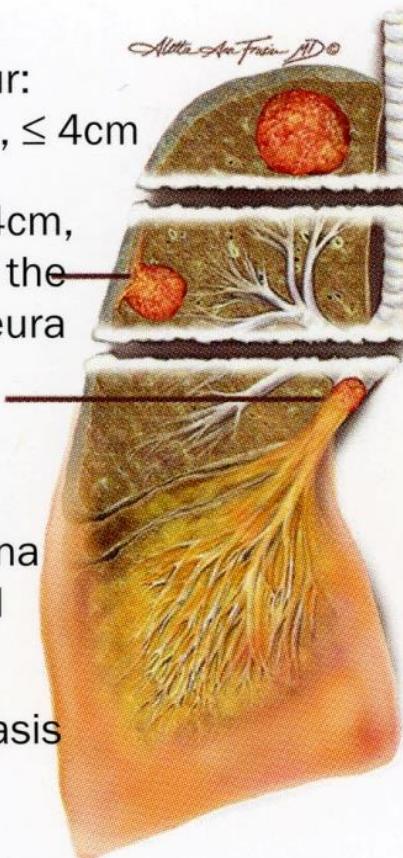
Tumour involves main bronchus, regardless of distance from carina but without carinal involvement

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

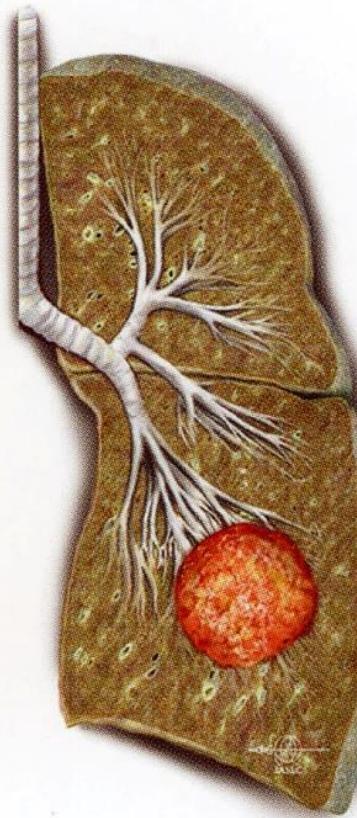
Tumour:
 $> 3\text{cm}, \leq 4\text{cm}$

Tumour $\leq 4\text{cm}$,
invasion of the
visceral pleura

T2a



T2b



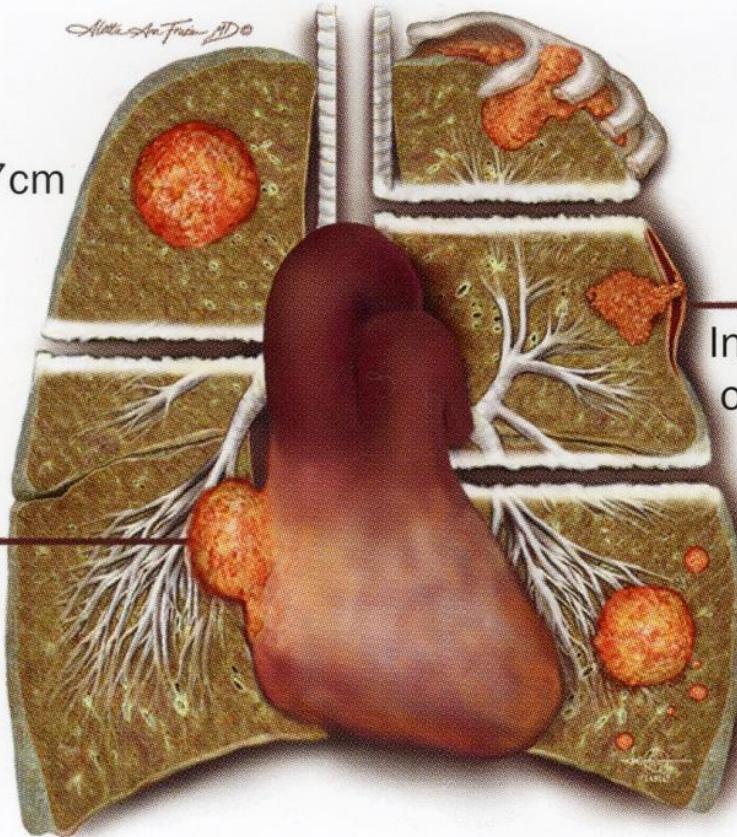
Tumour:
 $> 4\text{cm}, \leq 5\text{cm}$
(with or without other T2 descriptors)

Note: if the tumour is associated with atelectasis or pneumonitis, it is T2a if lesion $\leq 4\text{cm}$ or if tumour size cannot be measured; it is T2b if lesion $> 4\text{cm}, \leq 5\text{cm}$.

T3

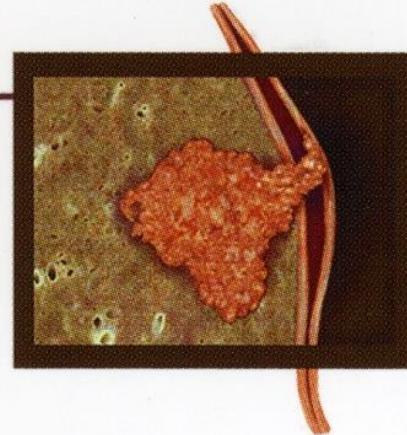
Tumour:
> 5cm, ≤ 7cm

Phrenic nerve
or parietal
pericardium
invasion



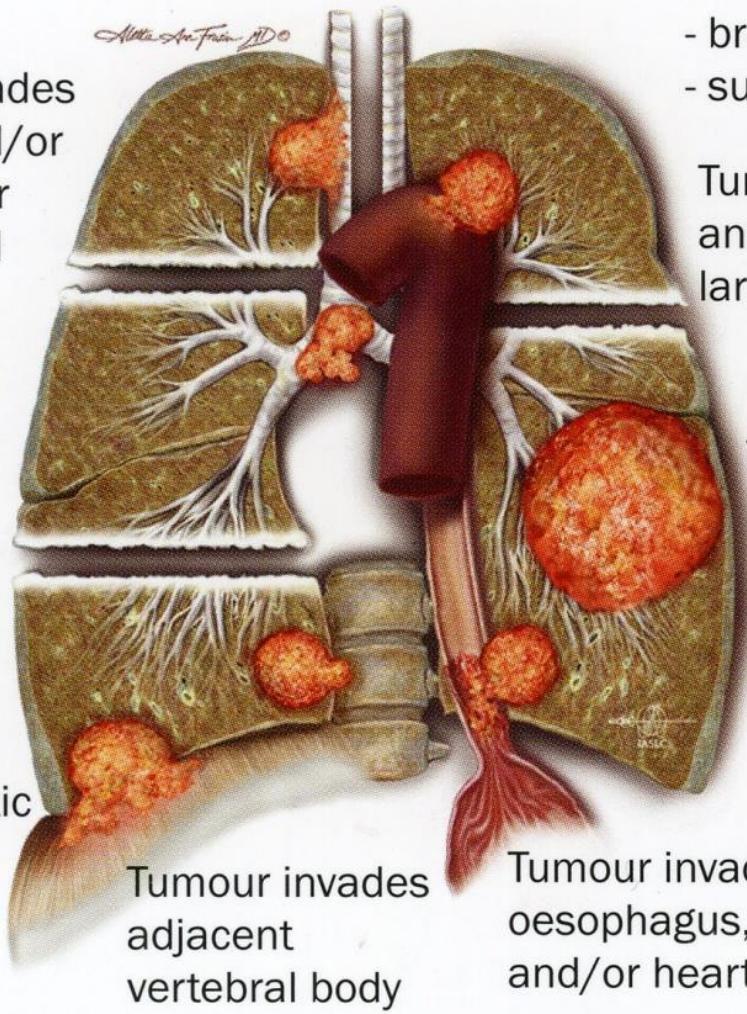
Chest wall invasion, including Pancoast tumours without invasion of vertebral body or spinal canal, encasement of the subclavian vessels, or unequivocal involvement of the superior branches of the brachial plexus (C8 or above)

Invasion
of parietal
pleura



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

T4

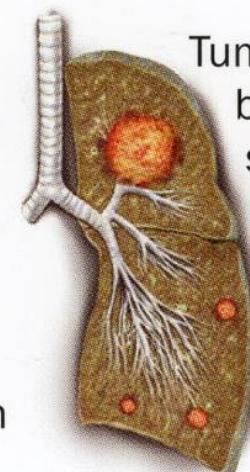
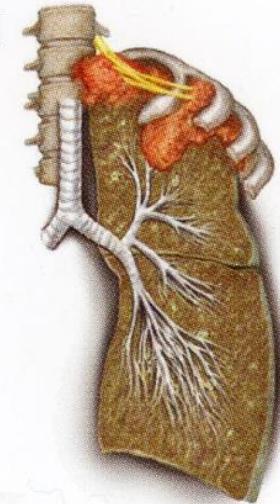


Pancoast tumours with invasion of one or more of the following structures:

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

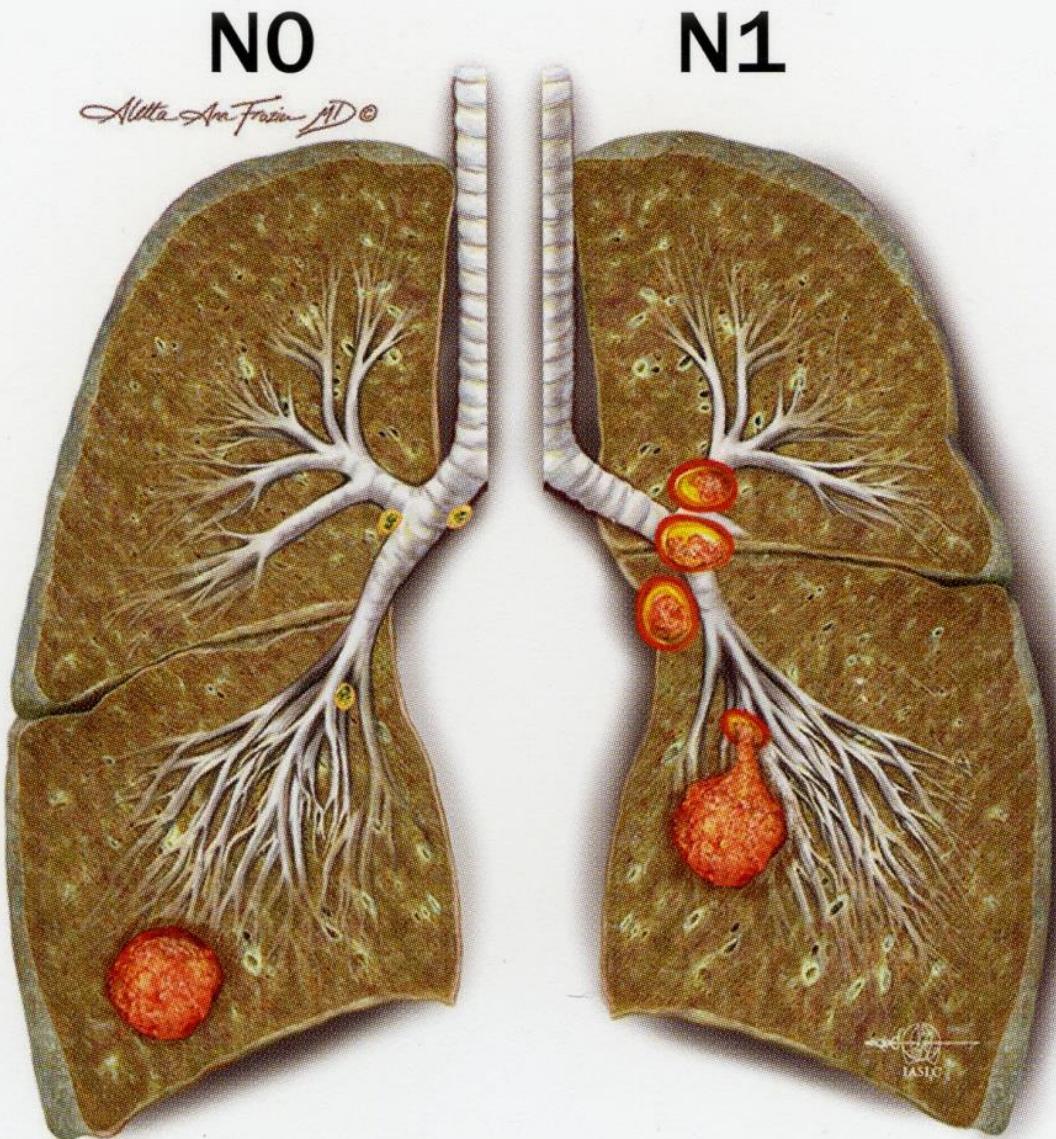
Tumour invades aorta and/or recurrent laryngeal nerve

Tumour > 7cm



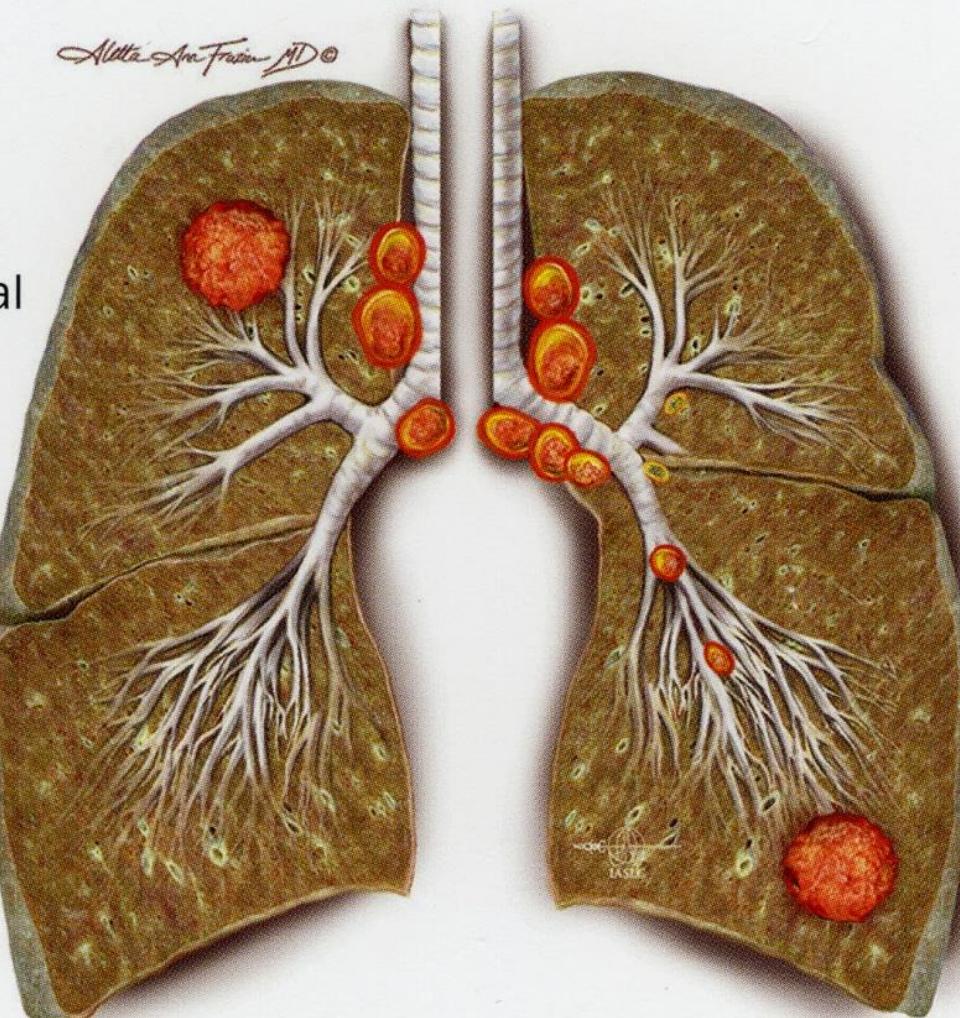
Tumour accompanied by ipsilateral, separate tumour nodules, different lobe

No regional lymph node metastases



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

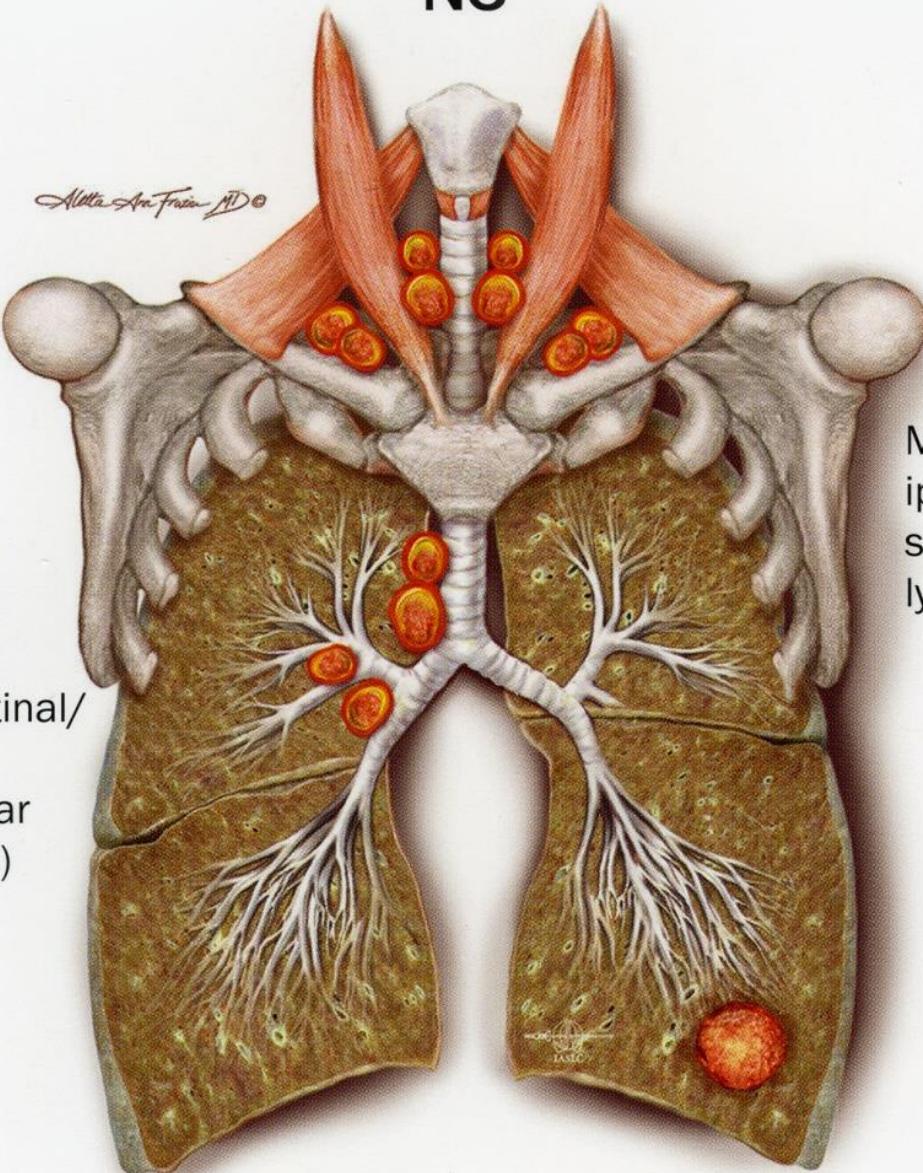
N2



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

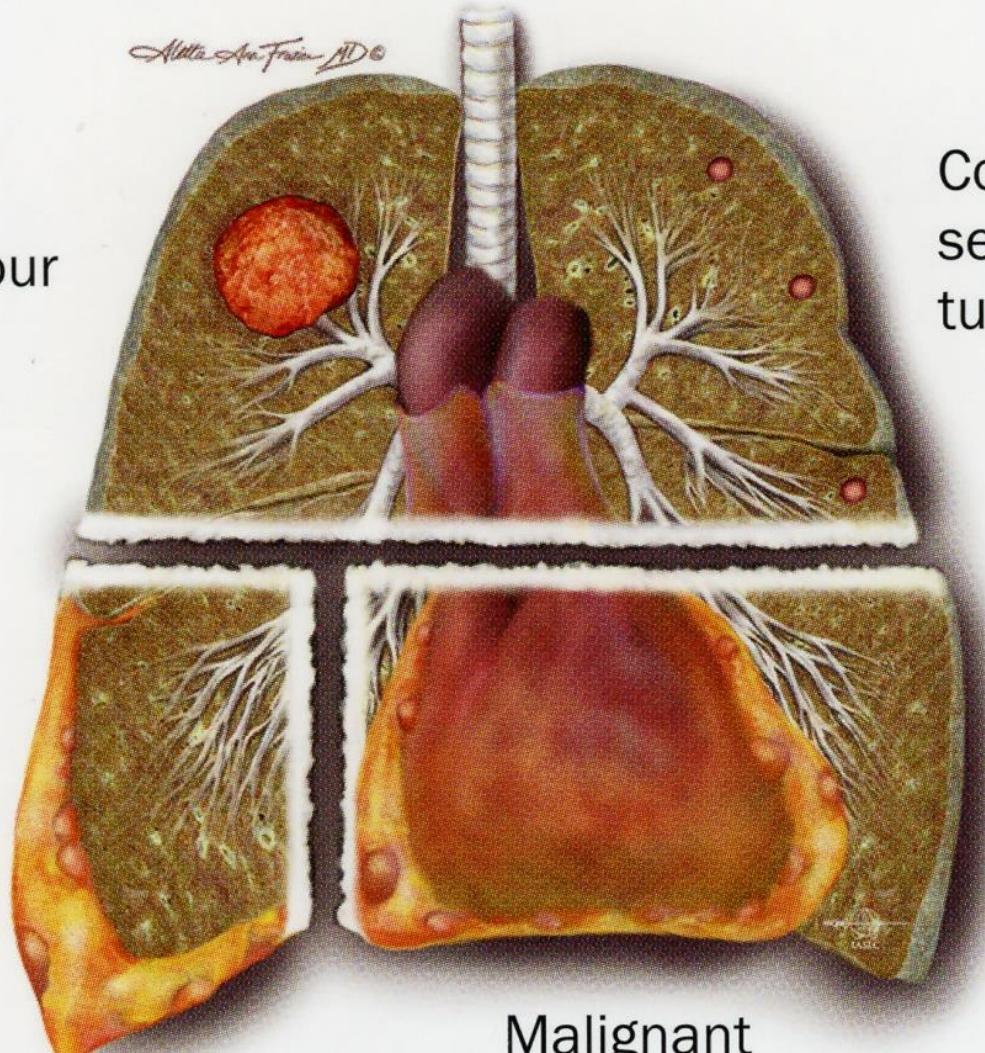
N3



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

Metastasis in
ipsilateral scalene/
supraclavicular
lymph node(s)

M1a



Primary tumour

Malignant
pleural effusion/nodule(s)

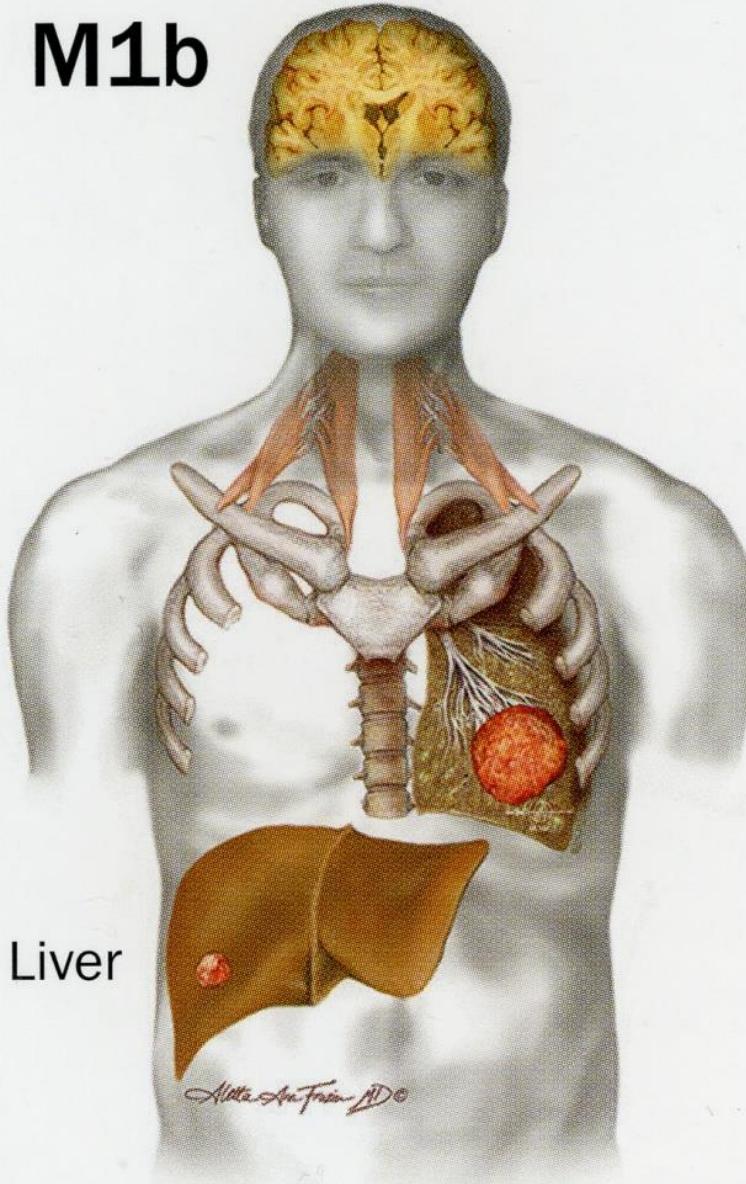
Contralateral,
separate
tumour nodule(s)

Malignant
pericardial effusion/nodule(s)

M1b

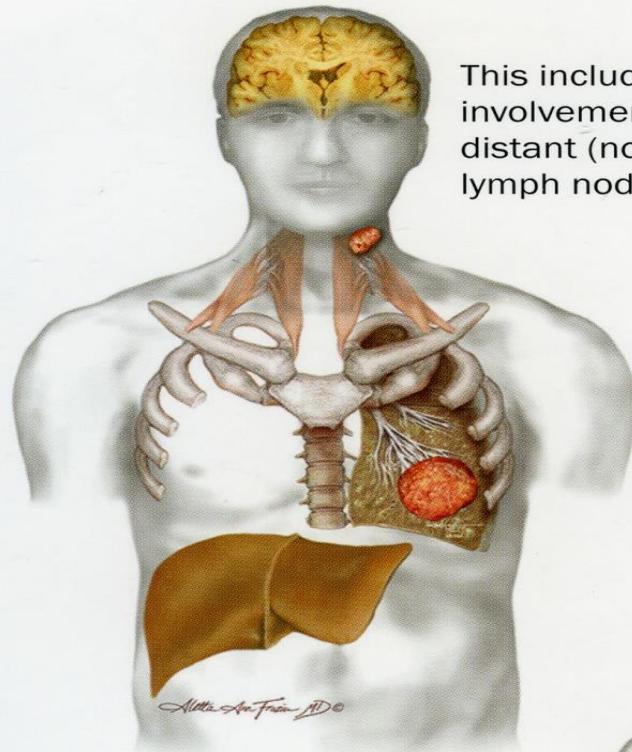
Single
extrathoracic
metastasis

Liver



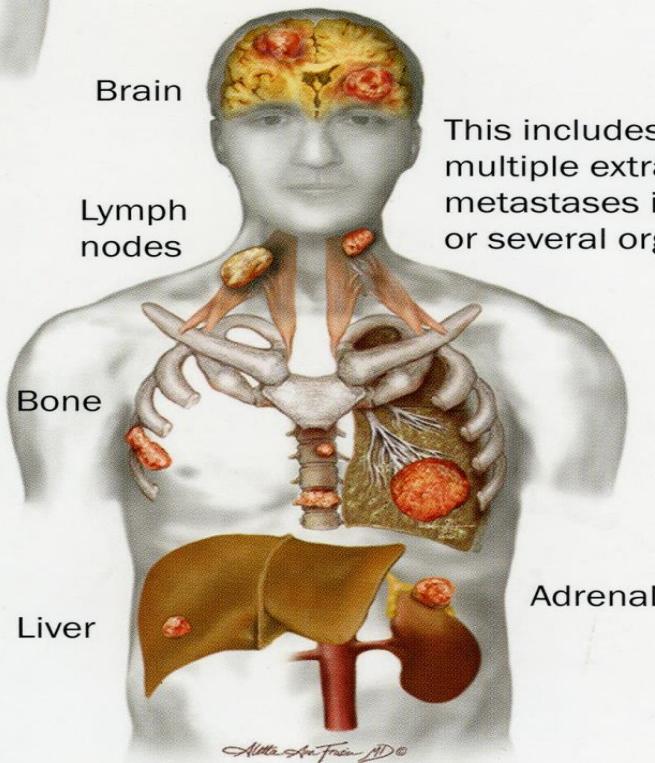
Alta An Fria MD ©

M1b



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

M1c

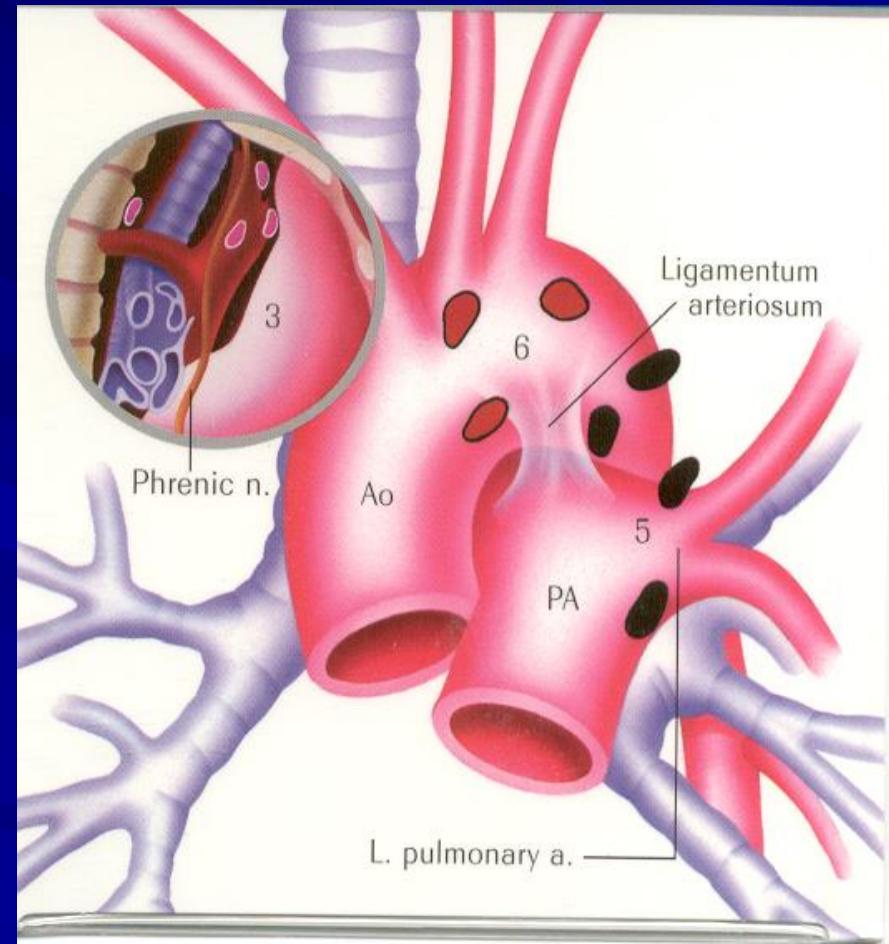
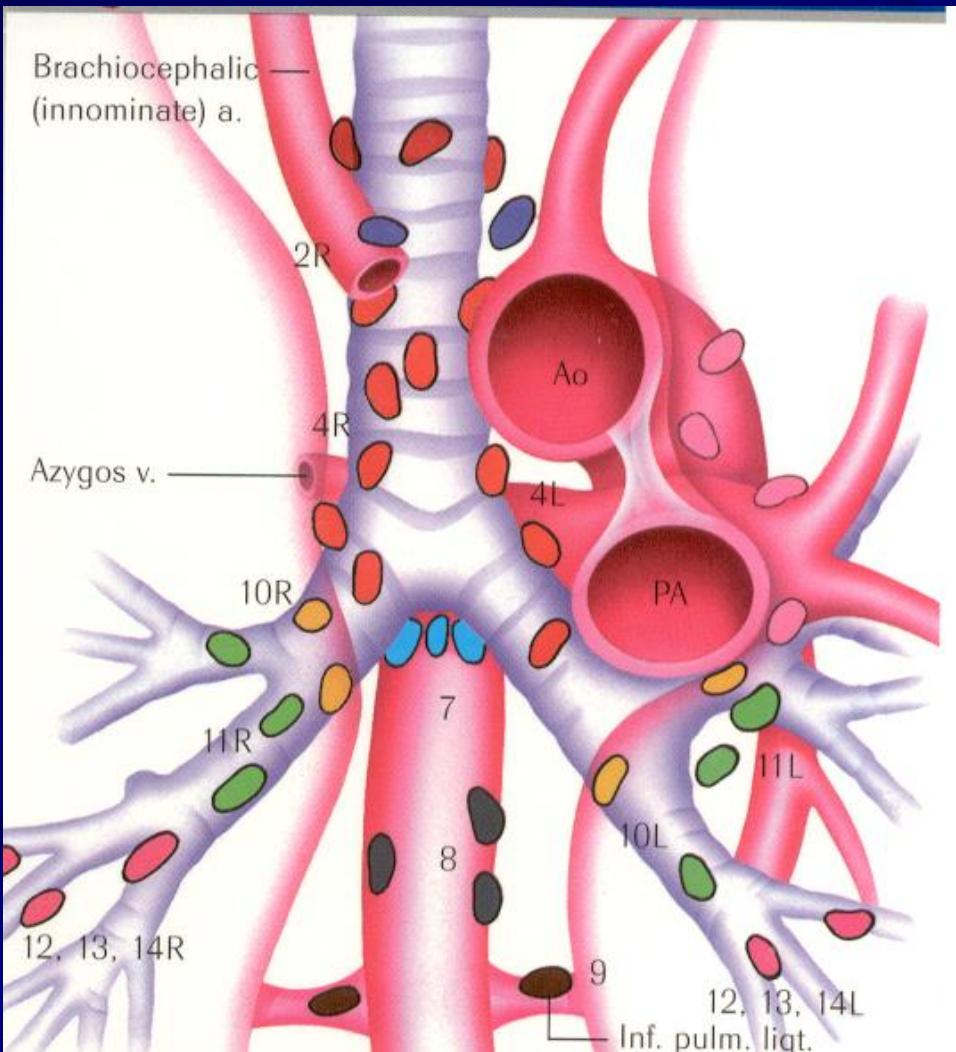


This includes
multiple extrathoracic
metastases in one
or several organs

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 (adenocc N2, sublobar resection)

■ **Locally advanced**, not resectable, non-metastatic (st. III/A-III/B)

- Chemo+radiotherapy (concurrent / sequential) + maintenance immunotherapy

■ **Metastatic**

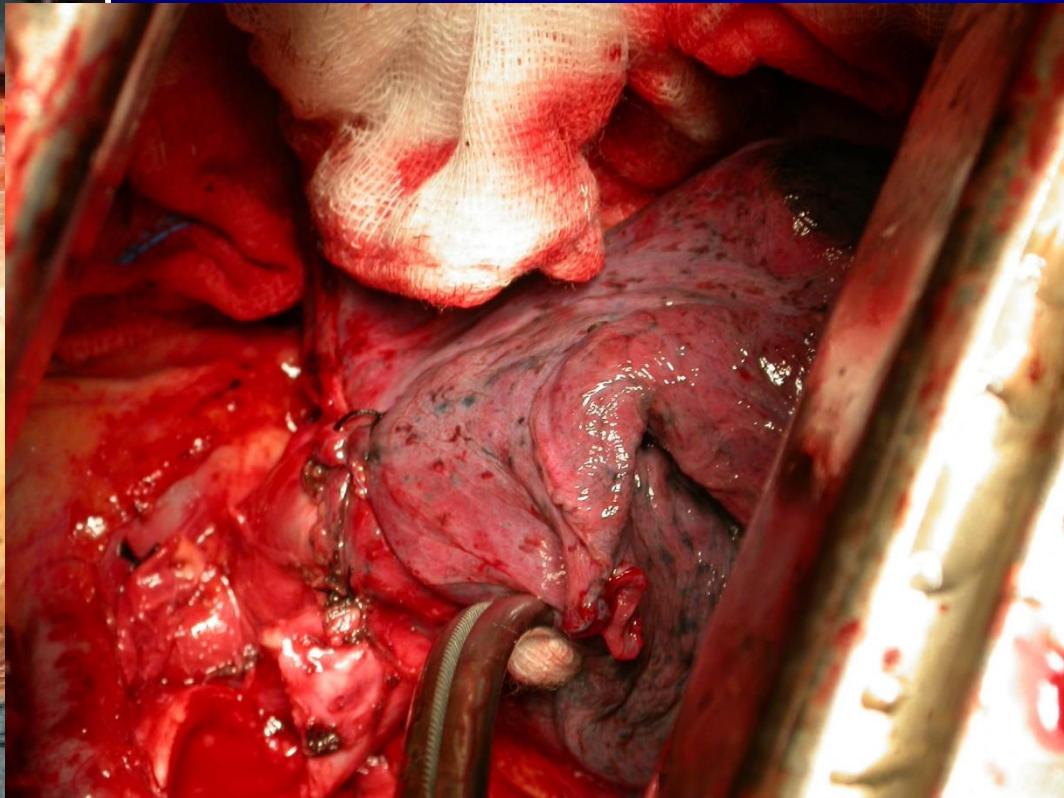
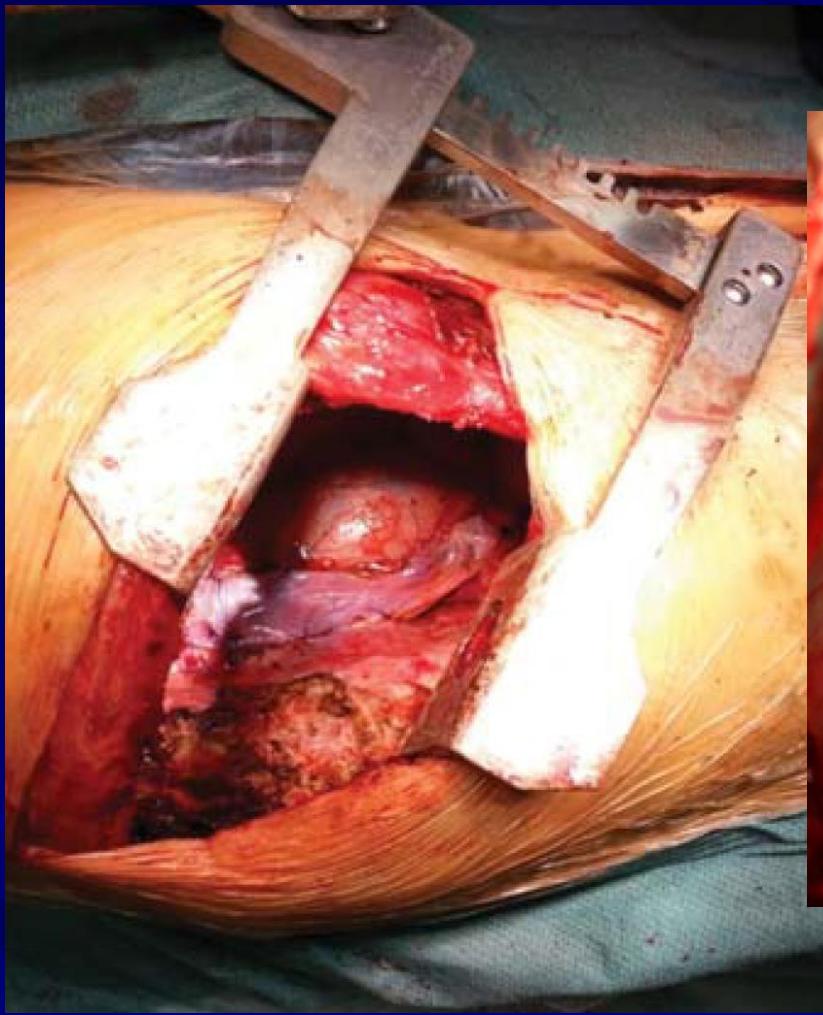
- Chemo-, targeted-, immunotherapy

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

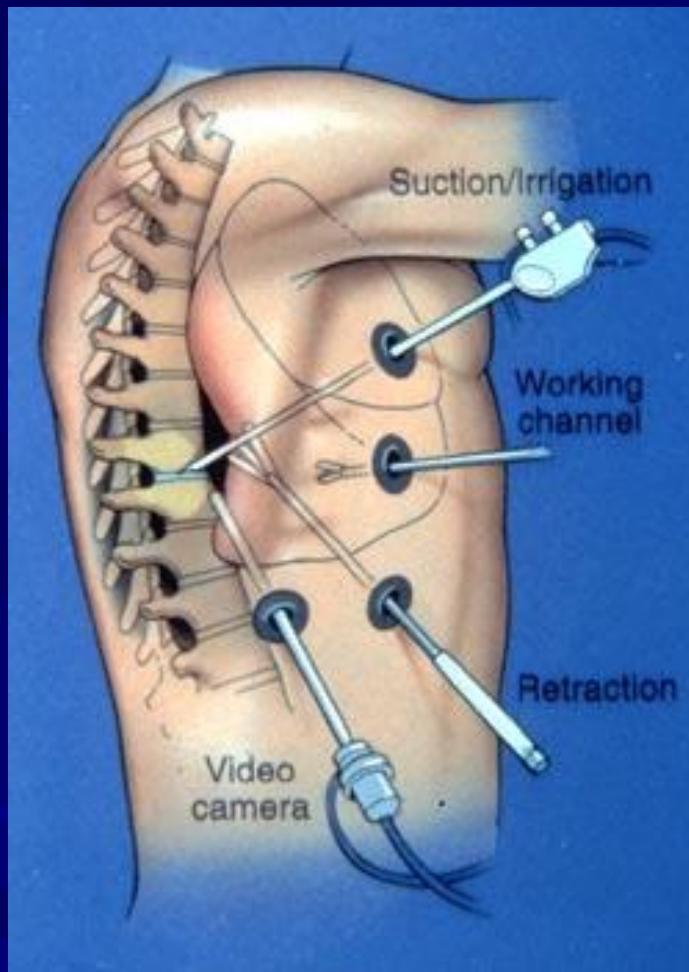
Surgery

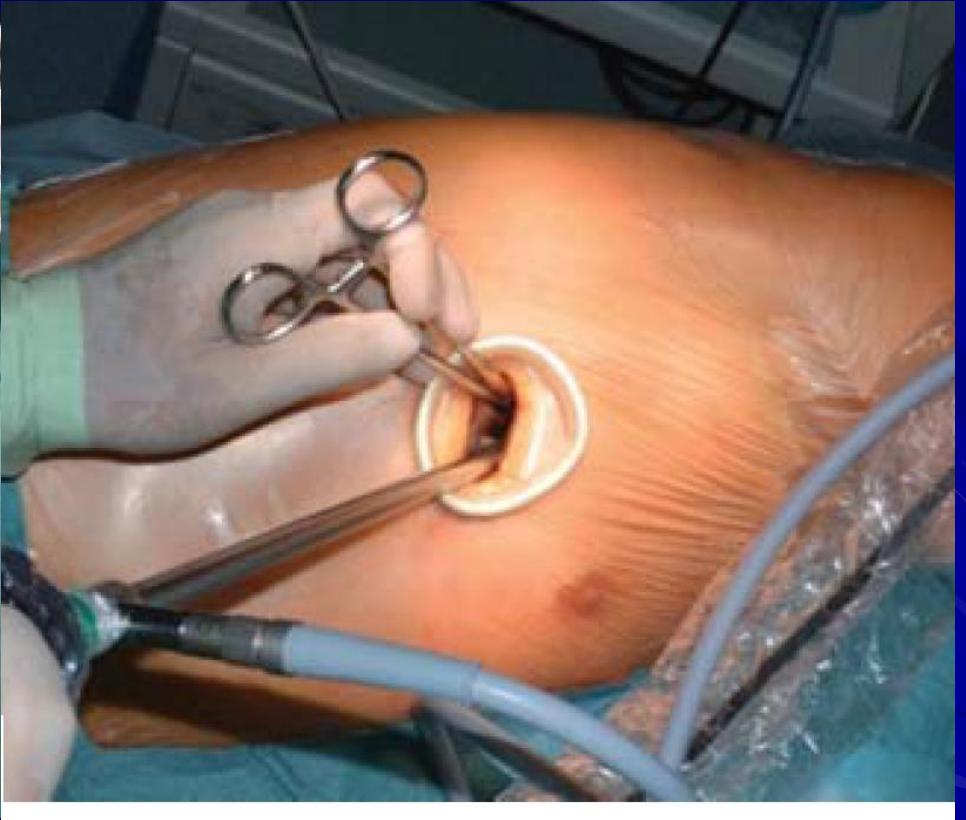
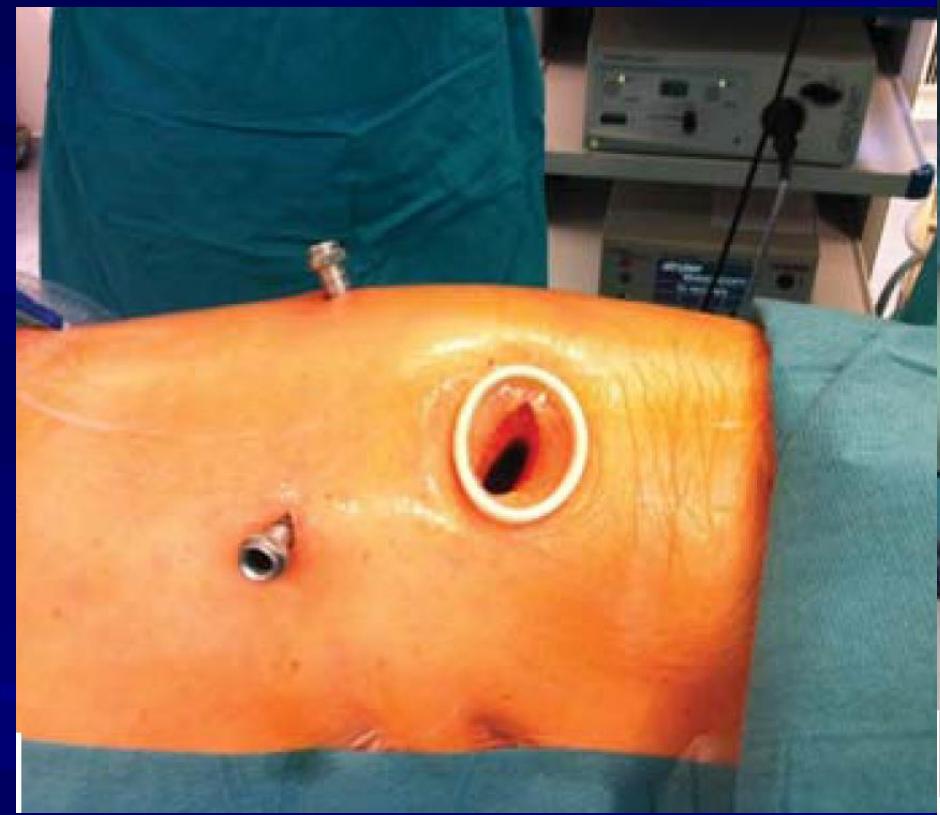
- (Wedge resection)
- (Atypical resection)
- (Segmentectomy)
- Lobectomy
- Bi-lobectomy
- Pneumonectomy (PNO)
- Pleuro-pneumonectomiy (mesothelioma)
- Ultra-radical resections (e.g.carina resection)
- Mediastinal lymph node dissection



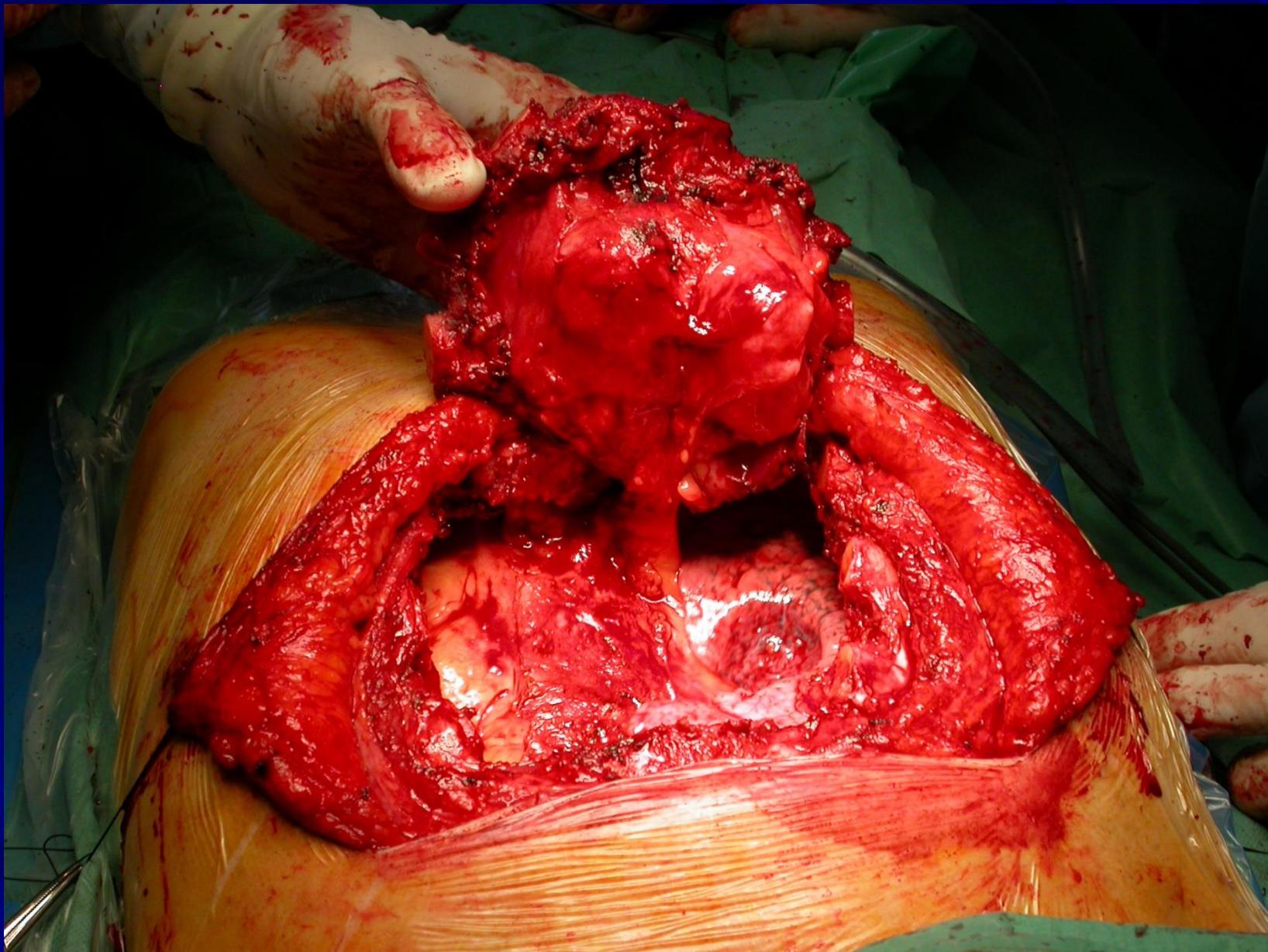
Courtesy of dr. Rényi-Vámos and dr. Agócs

Video Assisted ThoracoScopy (VATS)

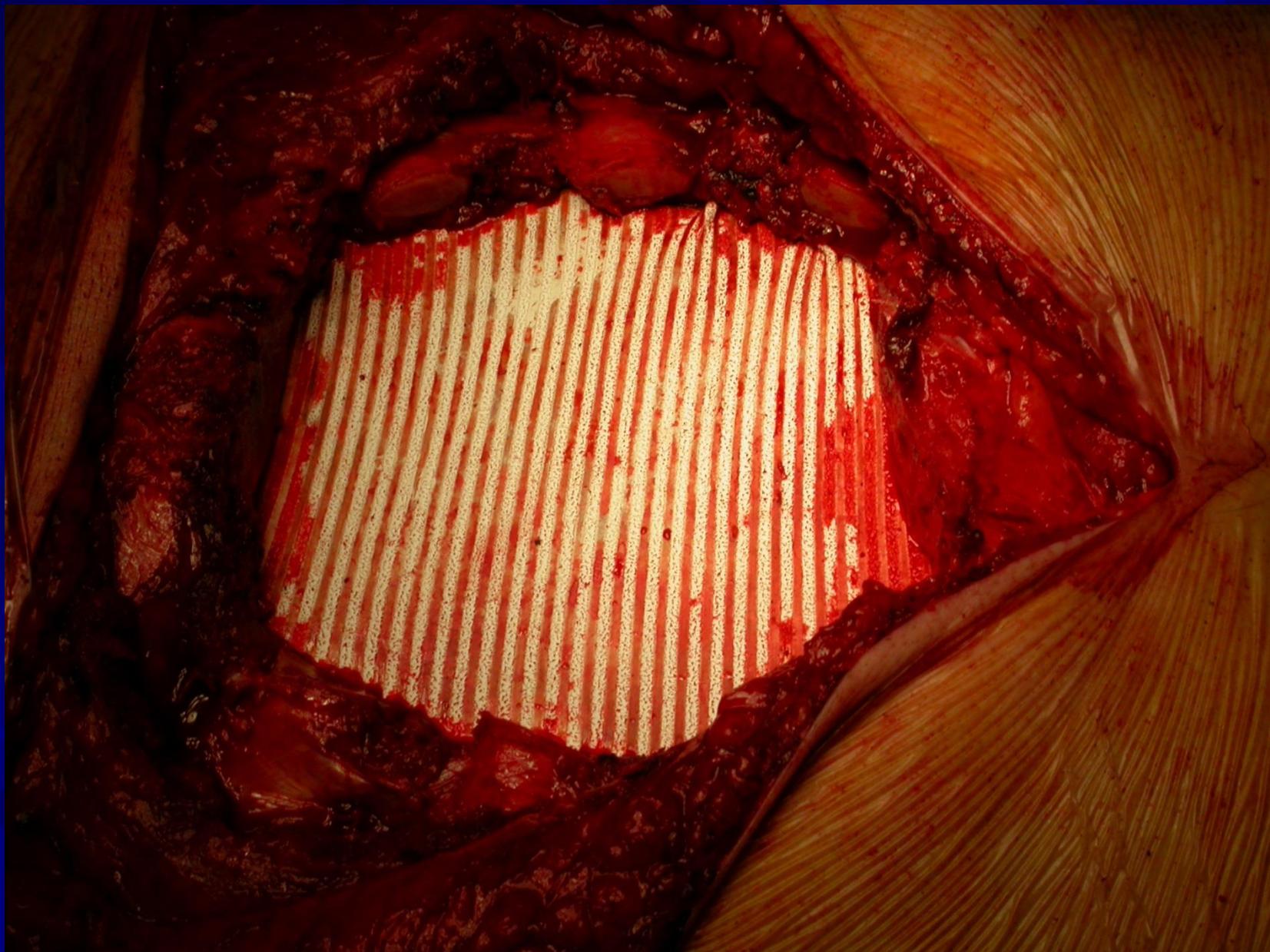




Courtesy of dr. Rényi-Vámos



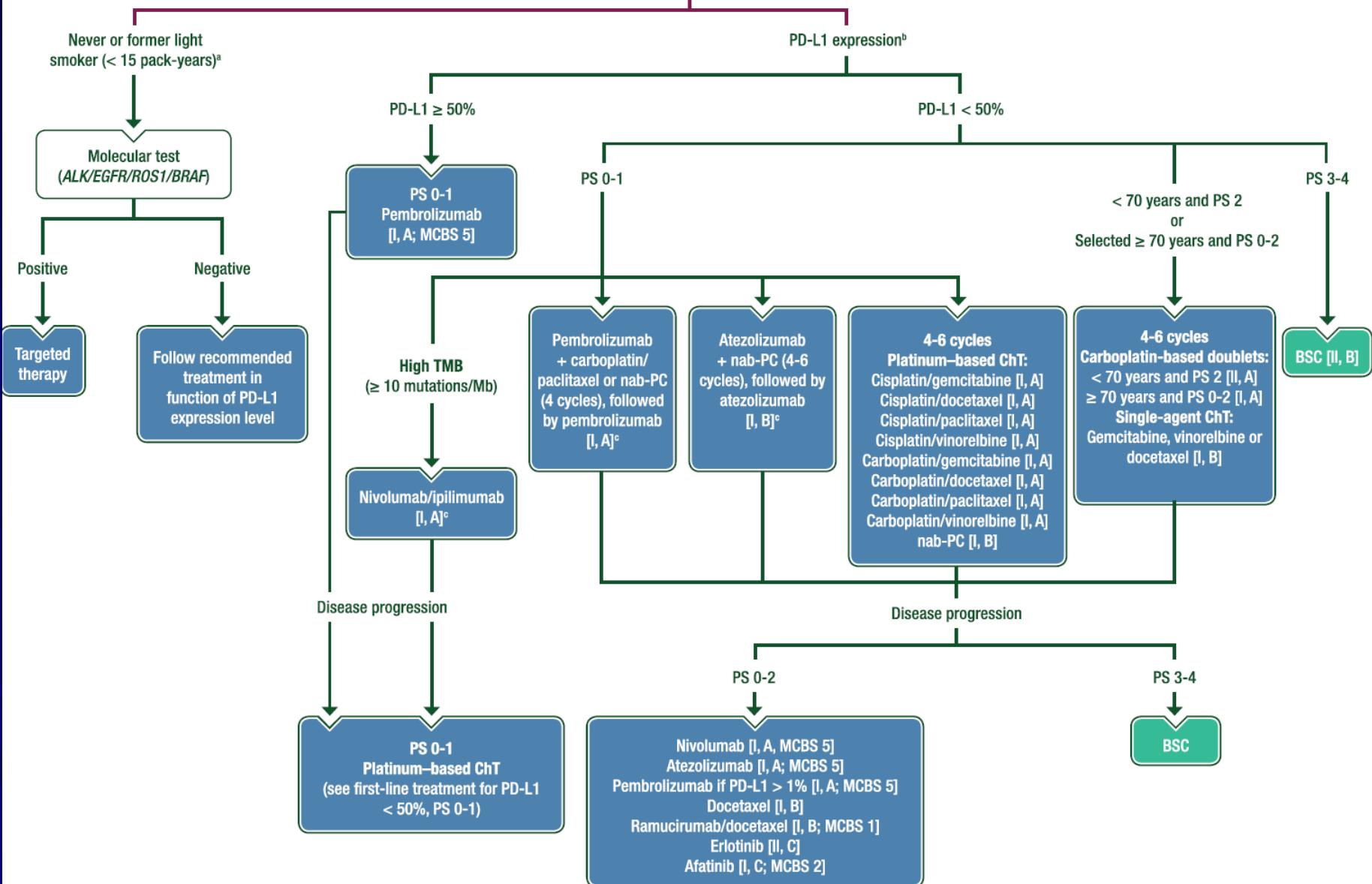
Courtesy of dr. Agócs



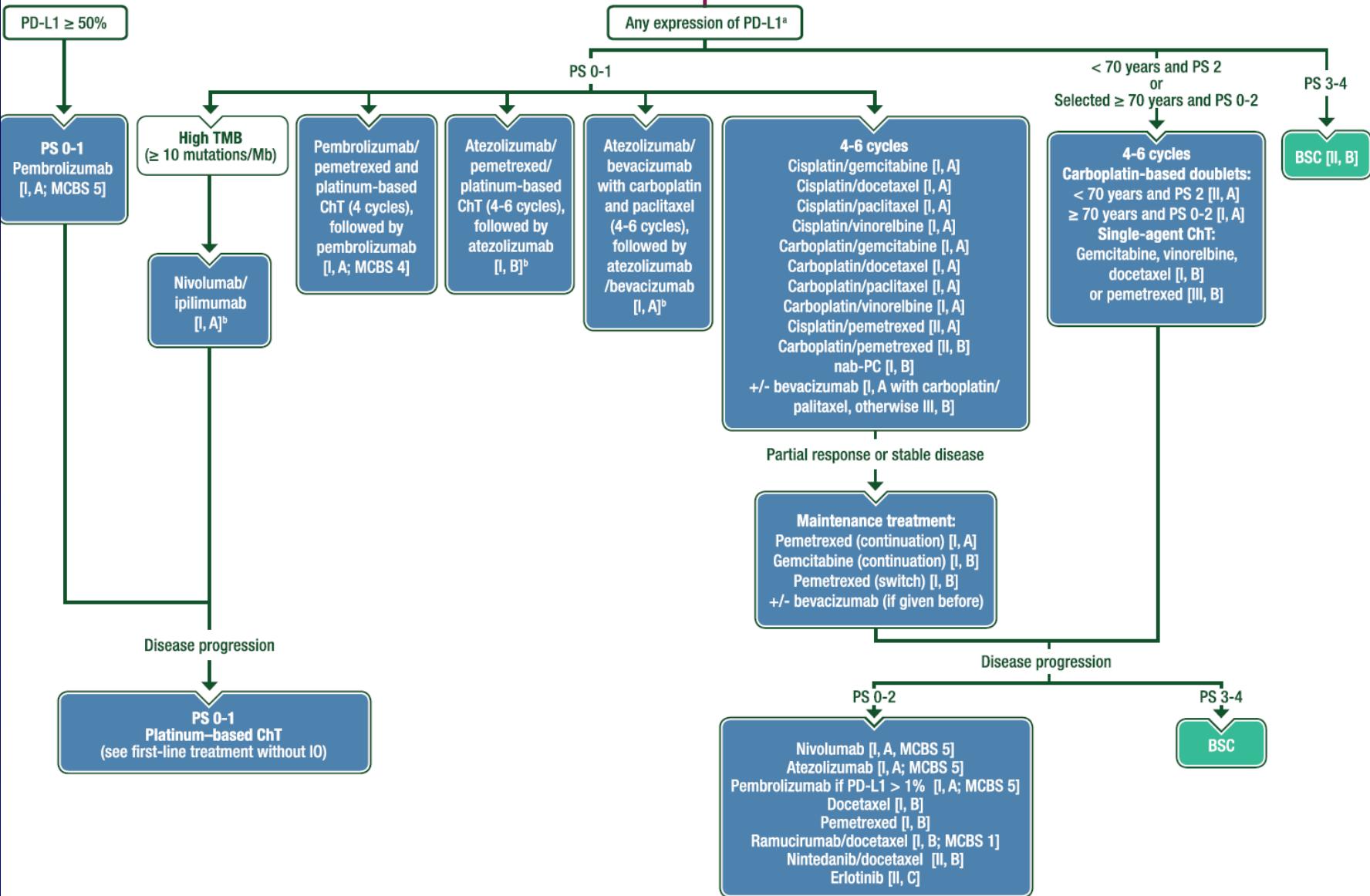
Pharmaceutical therapy

- 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: platina-etoposid, ECO, hycamtin

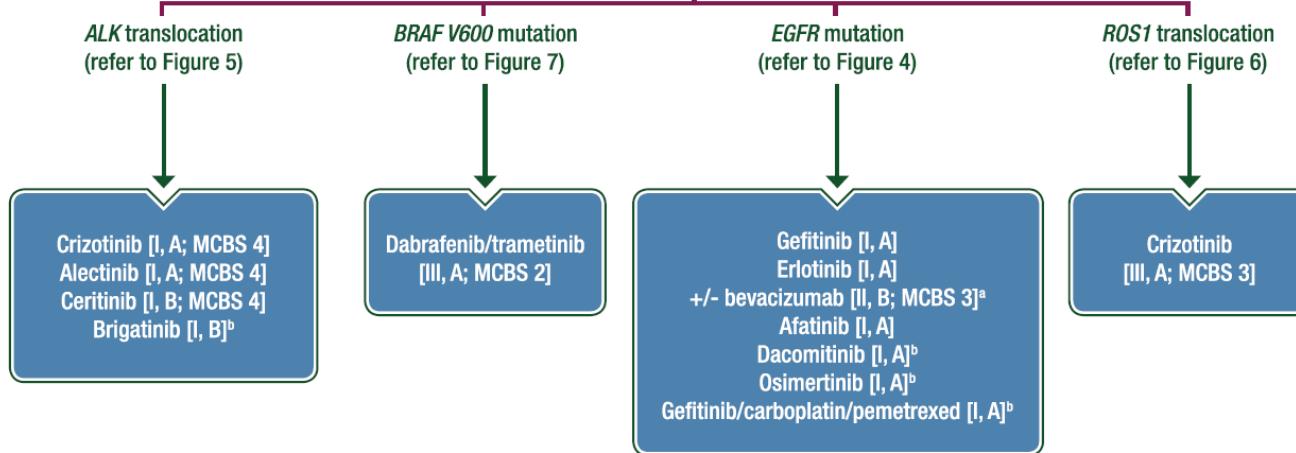
Stage IV SCC



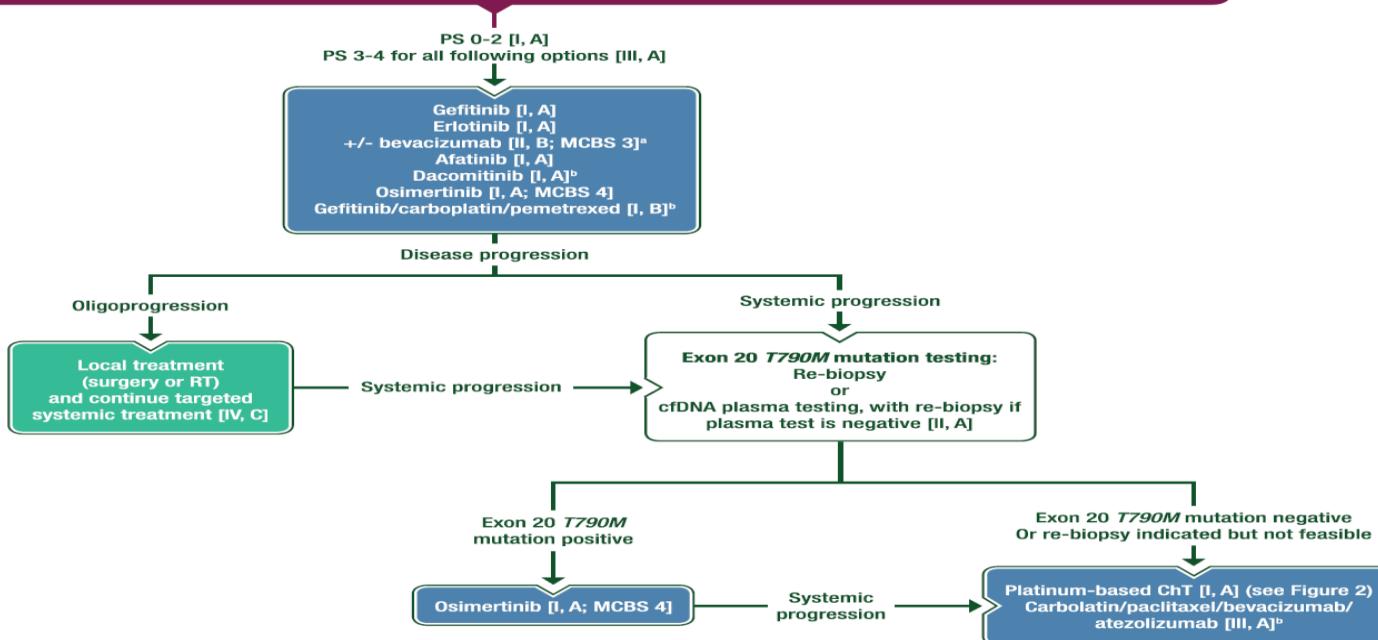
Stage IV NSCC: Molecular tests negative (ALK/BRAF/EGFR/ROS1)



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



Stage IV lung carcinoma with *EGFR*-activating mutation

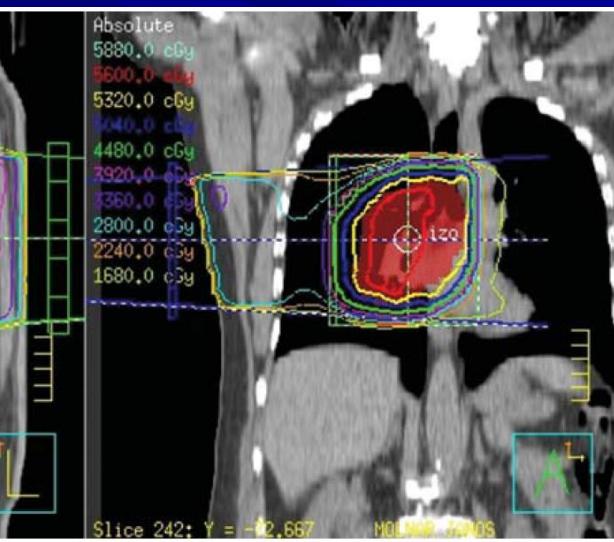
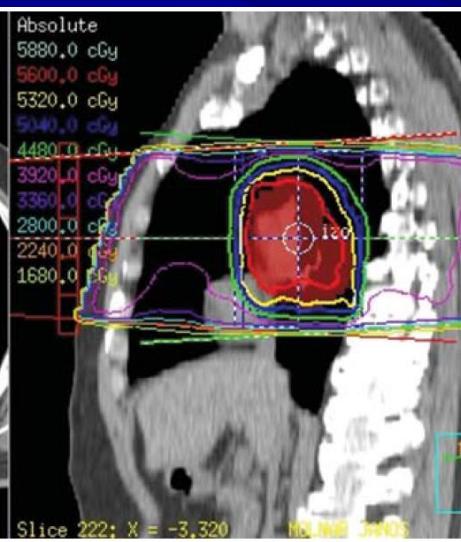
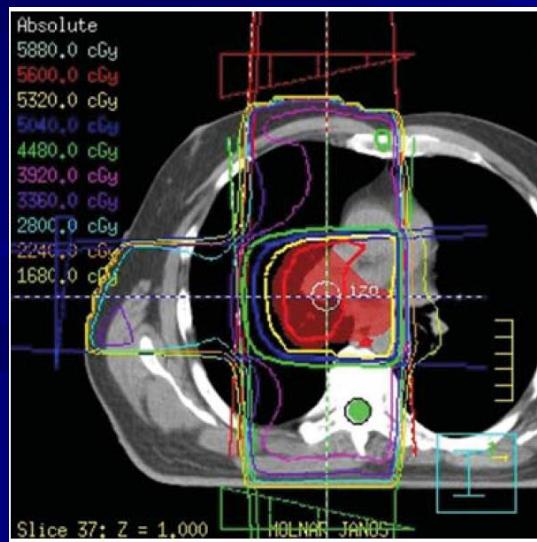
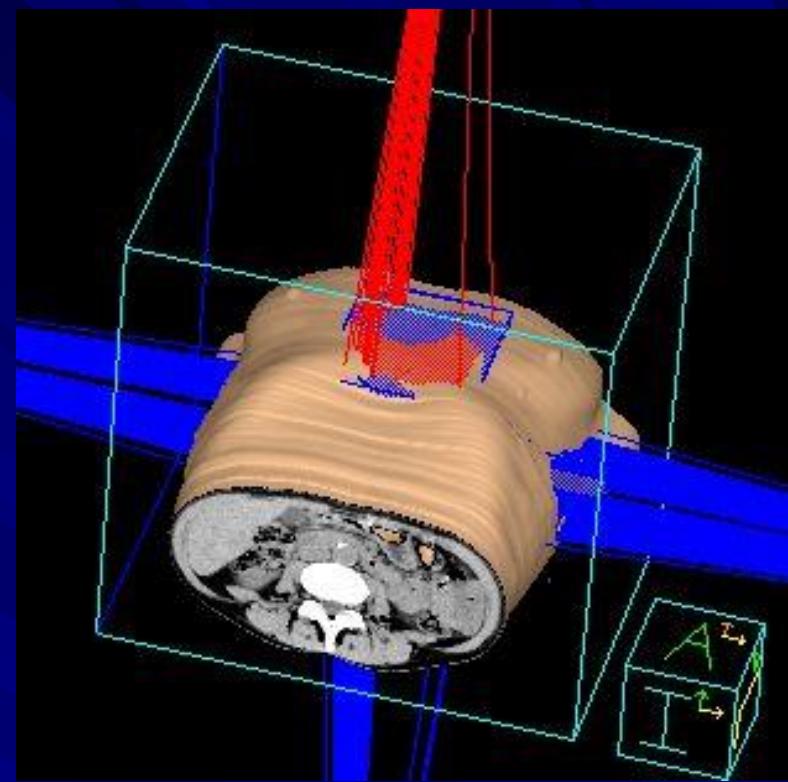
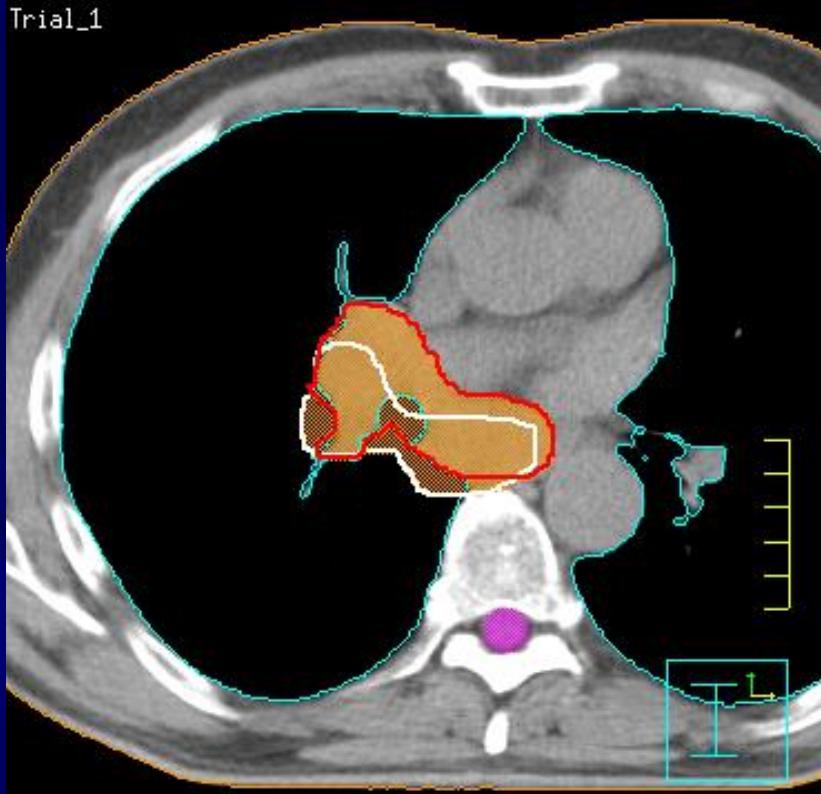


Radiotherapy

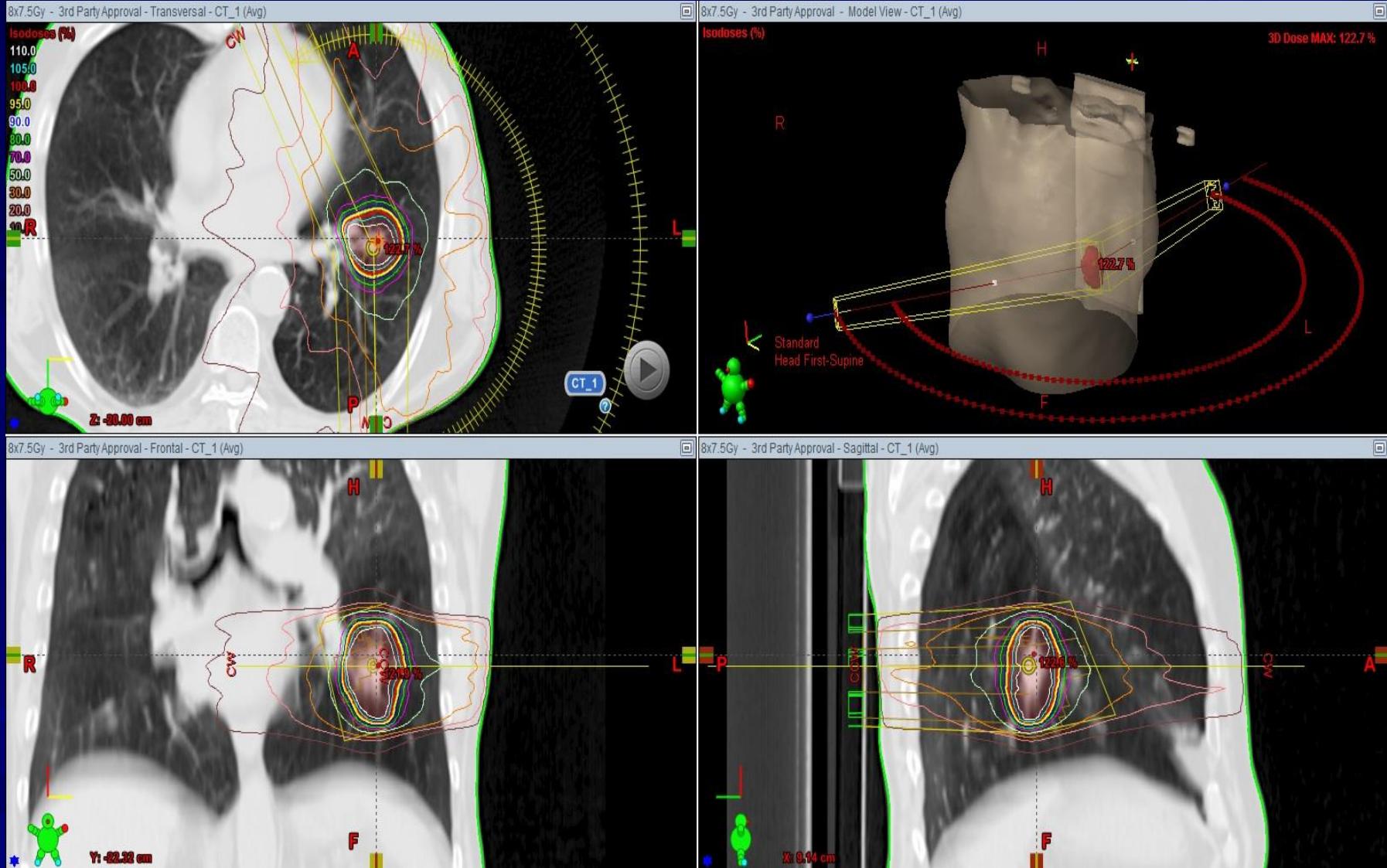
- External beam and brachytherapy
- High dose treatment
 - Always CT / PET-CT based treatment planning
high level QA, respiratory motion compensation
 - 3D conformal / IMRT, 60-70 Gy
 - SABRT: curative if surgery no feasible,
 $3 \times 20/5 \times 12 \text{ Gy}$
- Palliative treatment: simple technique, short treatment course
- Brachytherapy
 - Palliative, airway maintaining ($1 \times 10 \text{ Gy}$, $3 \times 8 \text{ Gy}$)

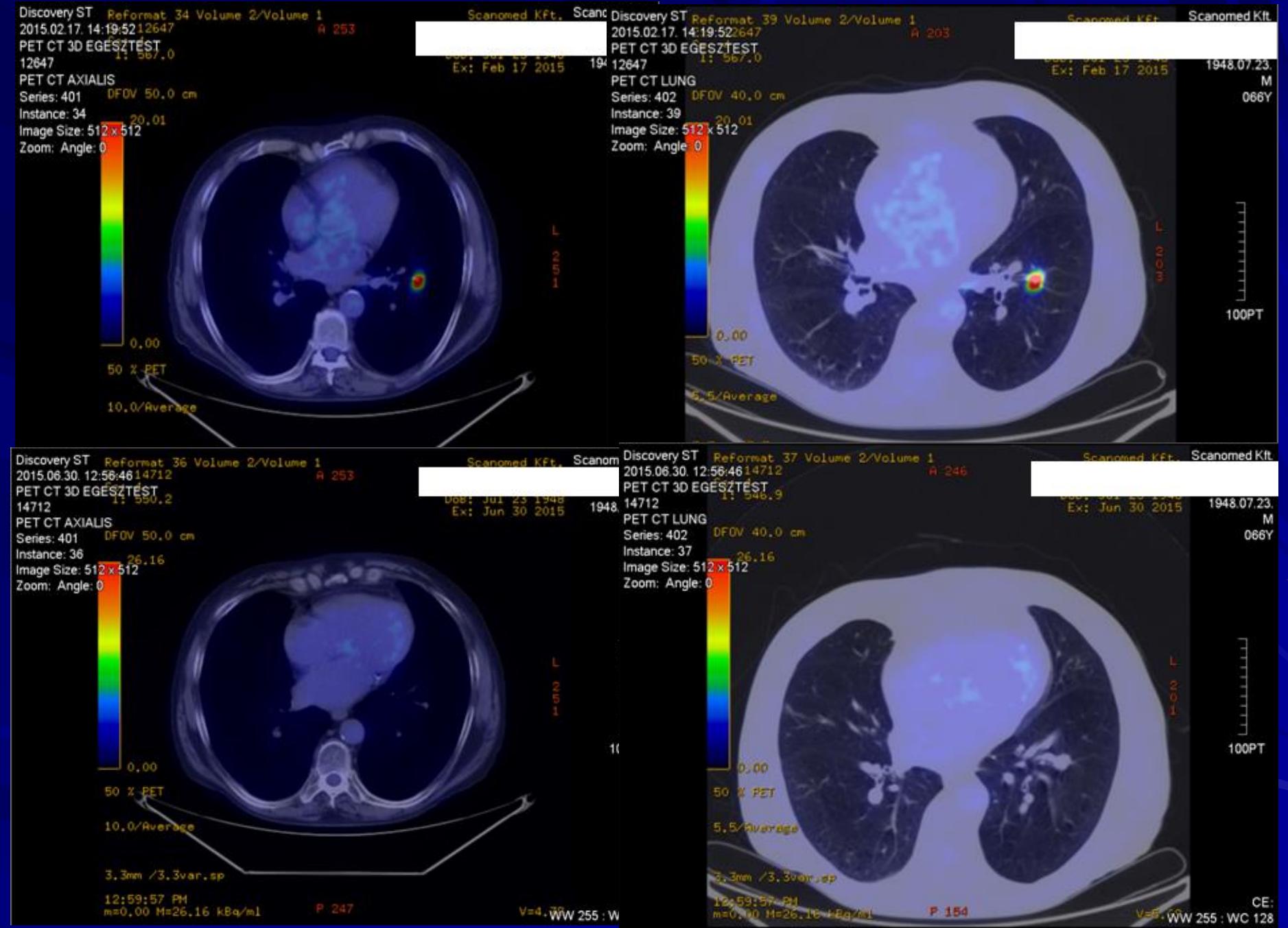


Trial_1





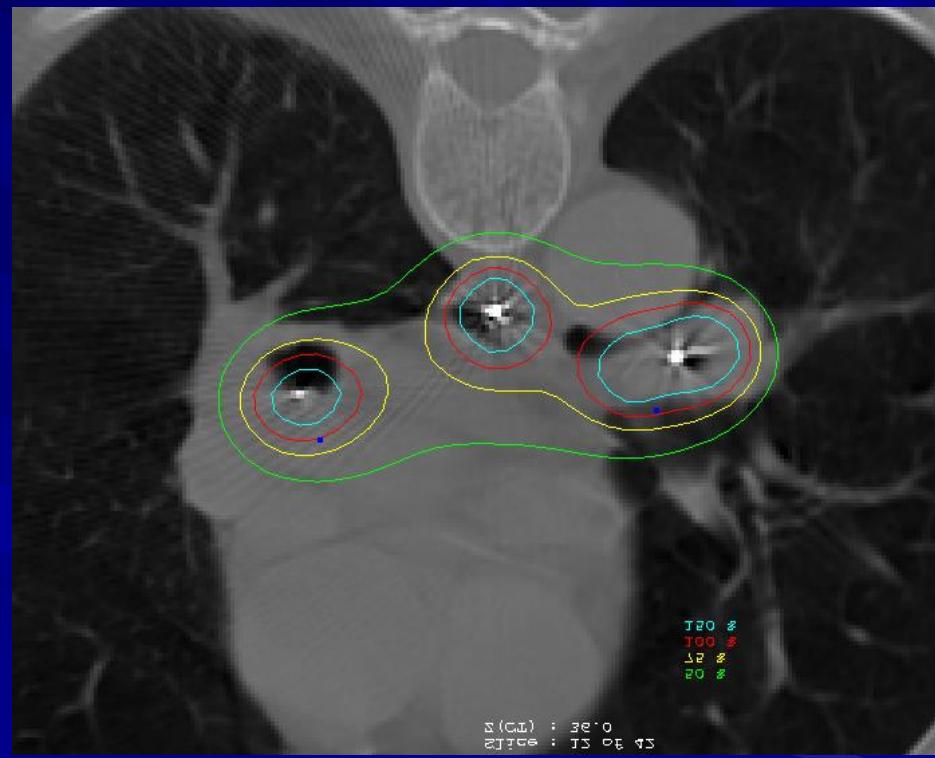
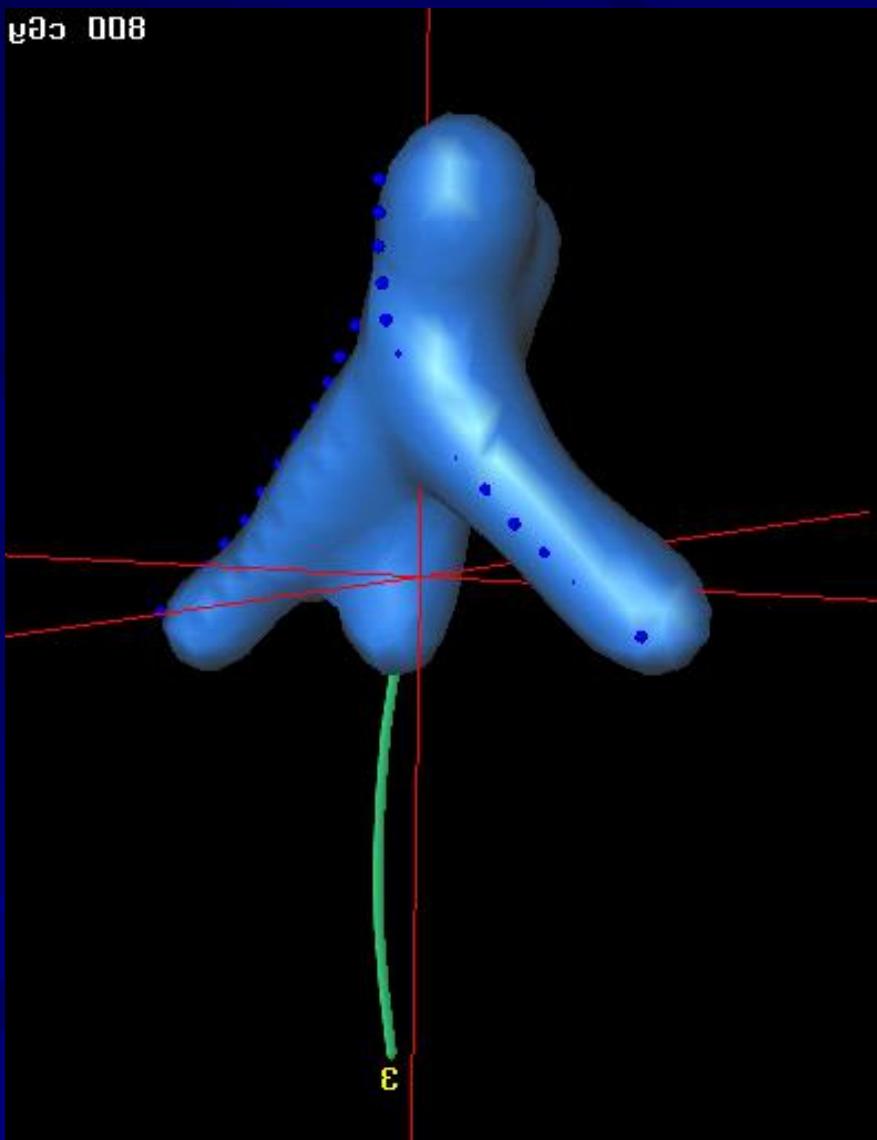


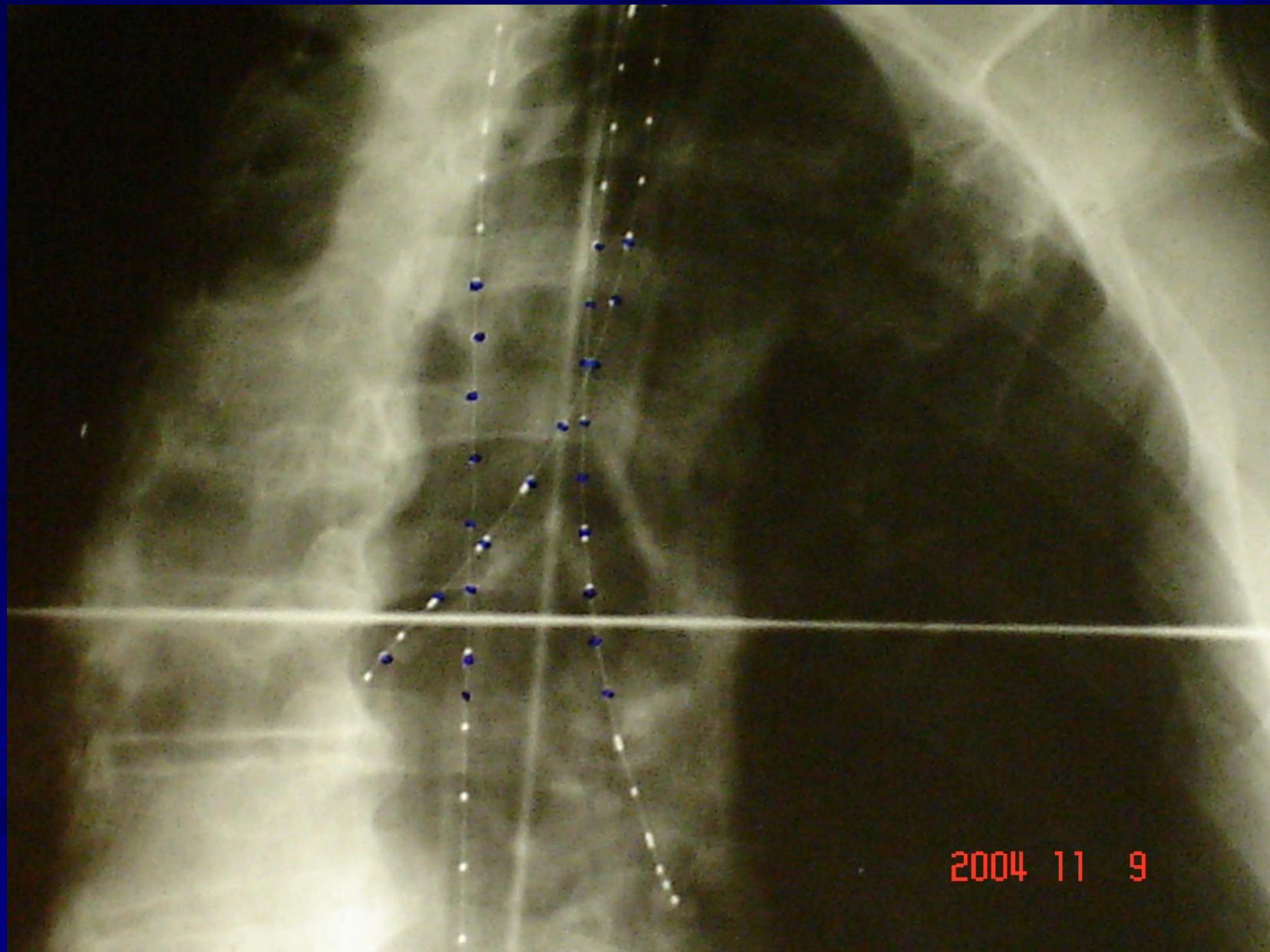




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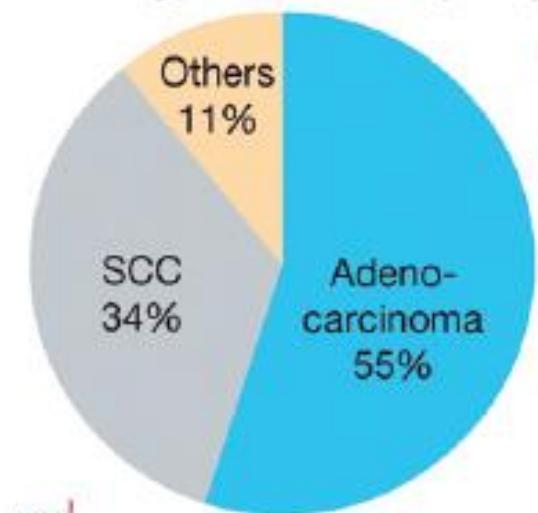
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5-year survival by histology and extension

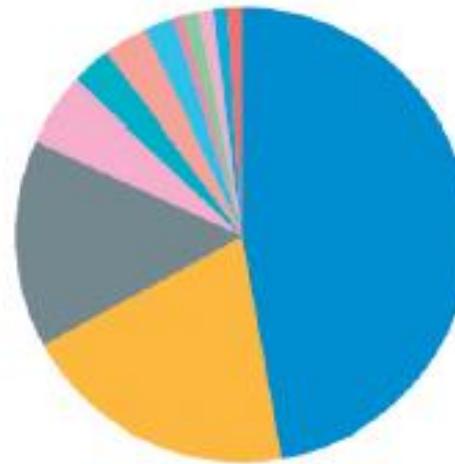
Histology	All stage	Local	Regional	Mets
All histology	13.9	39.6	14.4	1.5
Squamous cell cc.	15.4	34.3	14.9	1.5
Adenocarcinoma	16.6	49.9	16.1	1.5
Bronchioalveolar cc.	42.1	65.1	31.8	4.2
Papillaris adenocc.	23.7	57.4	25.8	5.4
Adenosquamous cc.	21.6	49.6	19.1	2.2
SCLC	4.6	12.3	7.5	1.4
Large cell cc.	11.4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

NSCLC
as one
disease

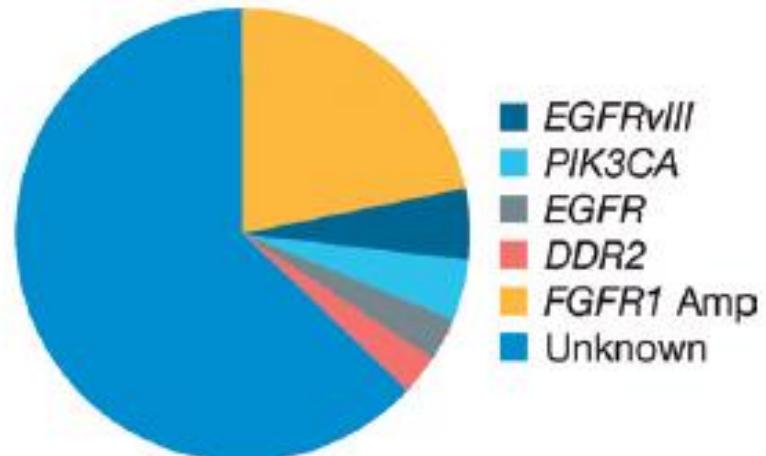
Histology-based subtyping



Adenocarcinoma



SCC



Understanding Disease