VOLUMI CLINICI NELL'IRRADIAZIONE DELLE NEOPLASIE BRONCOGENE

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CLINICAL TARGET VOLUME DEFINITION

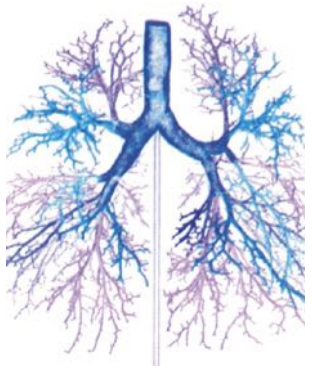
A. Radiological Anatomy

- Normal structures, Pitfalls and Nodal Stations

B. Non-Small Cell Lung Cancer

- Locally Advanced Disease

C. Small Cell Lung Cancer



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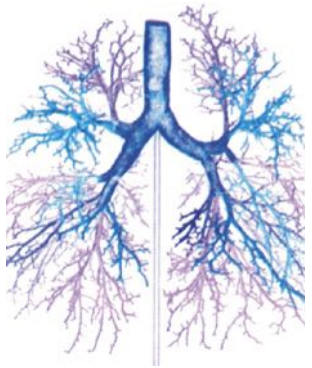
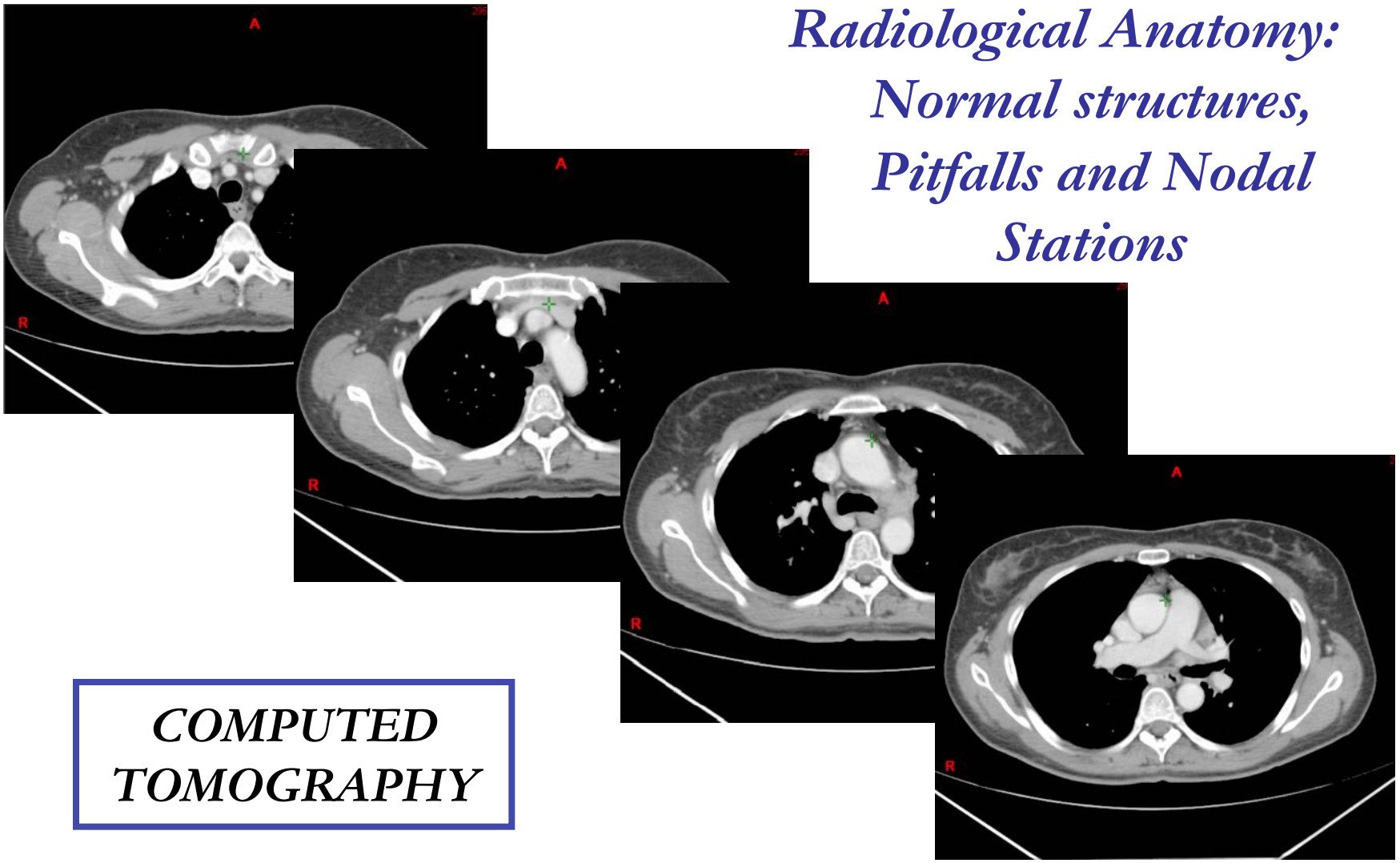


Radiological Anatomy: Normal structures, Pitfalls and Nodal Stations



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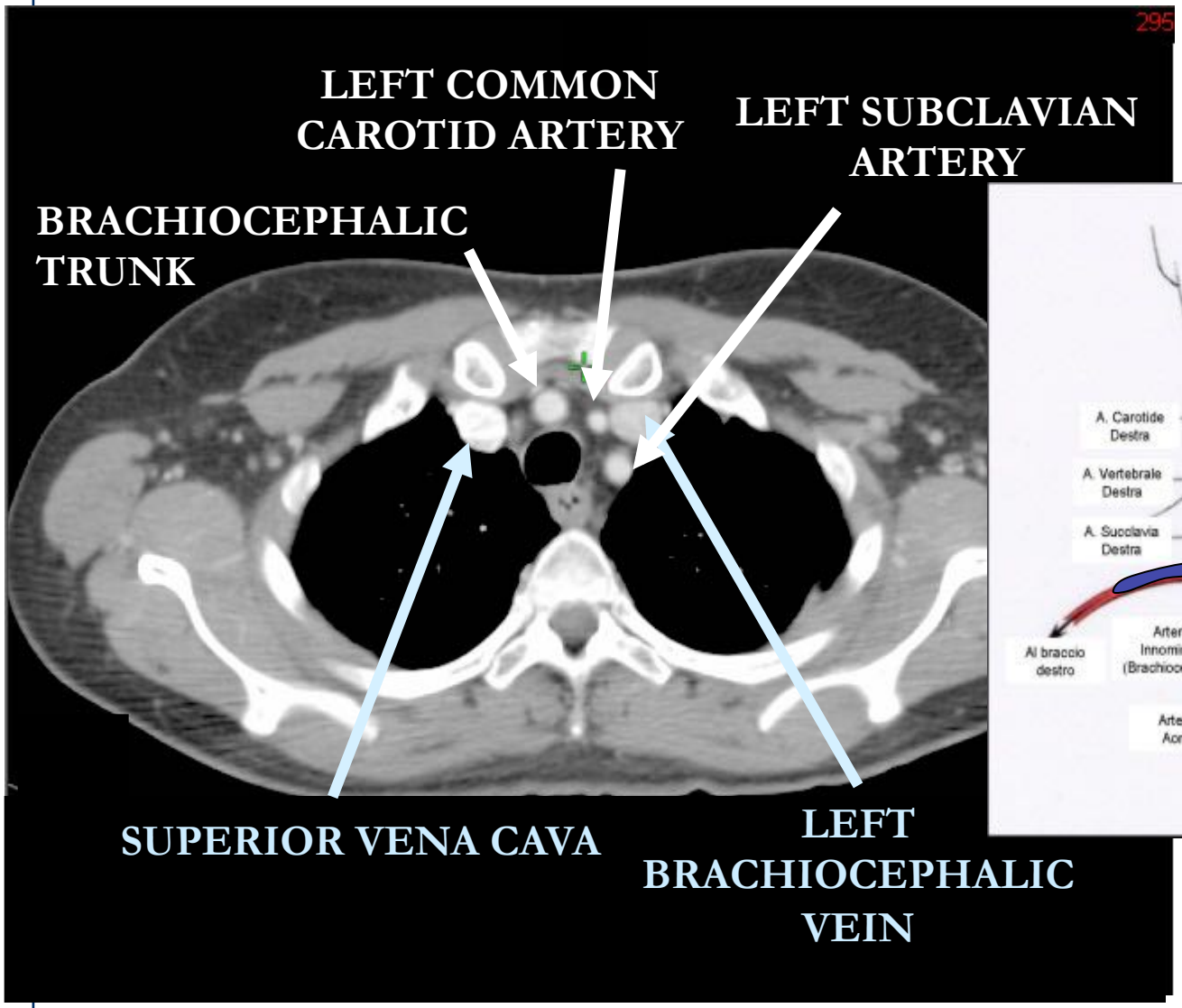
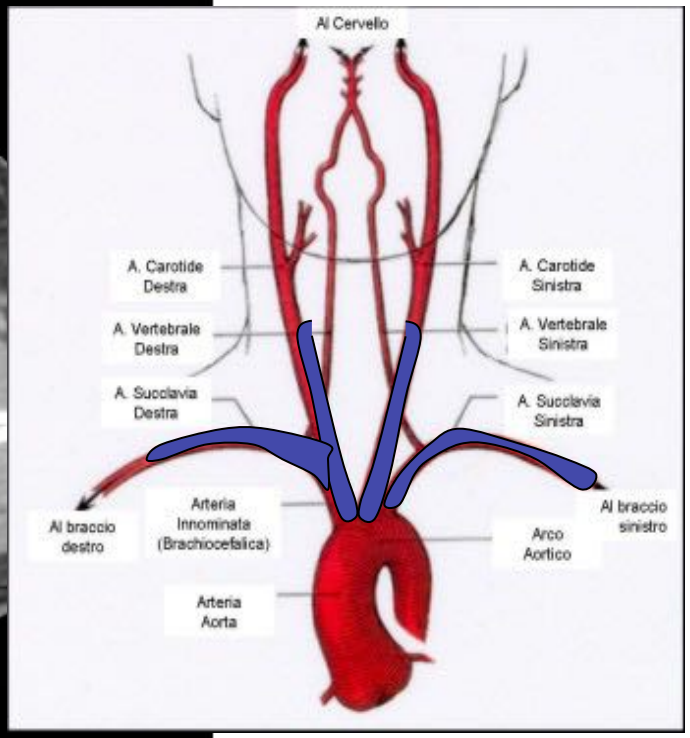
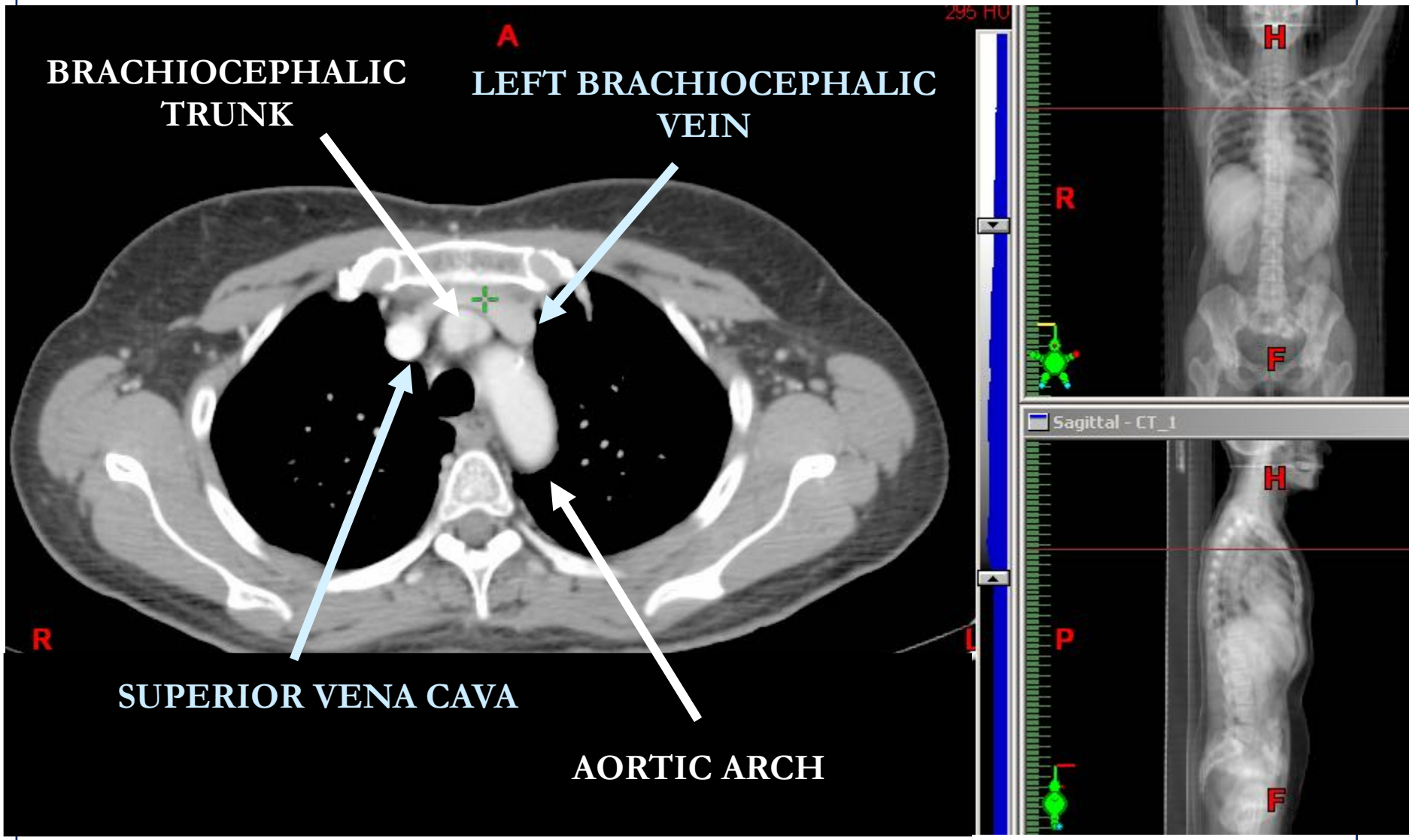
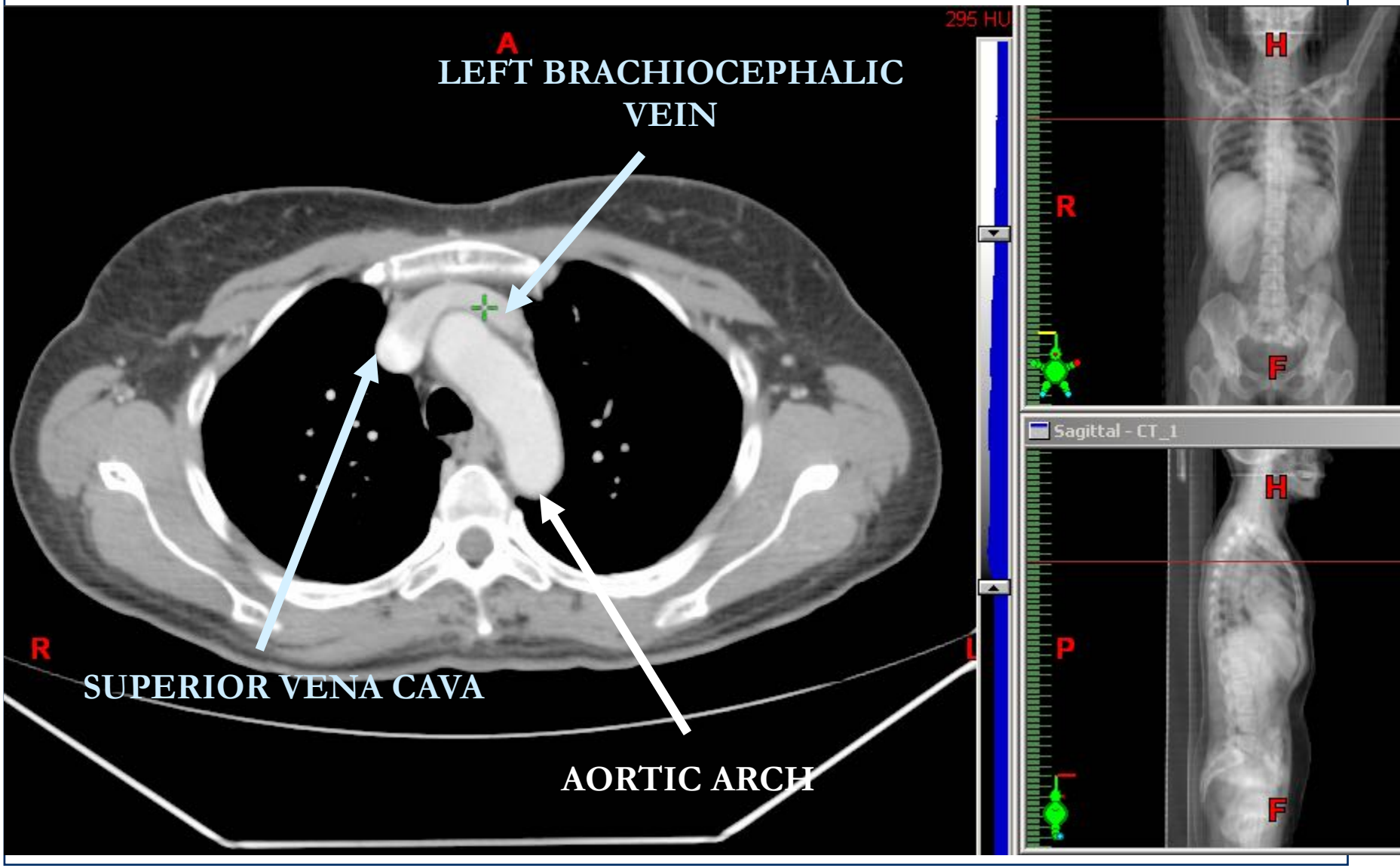
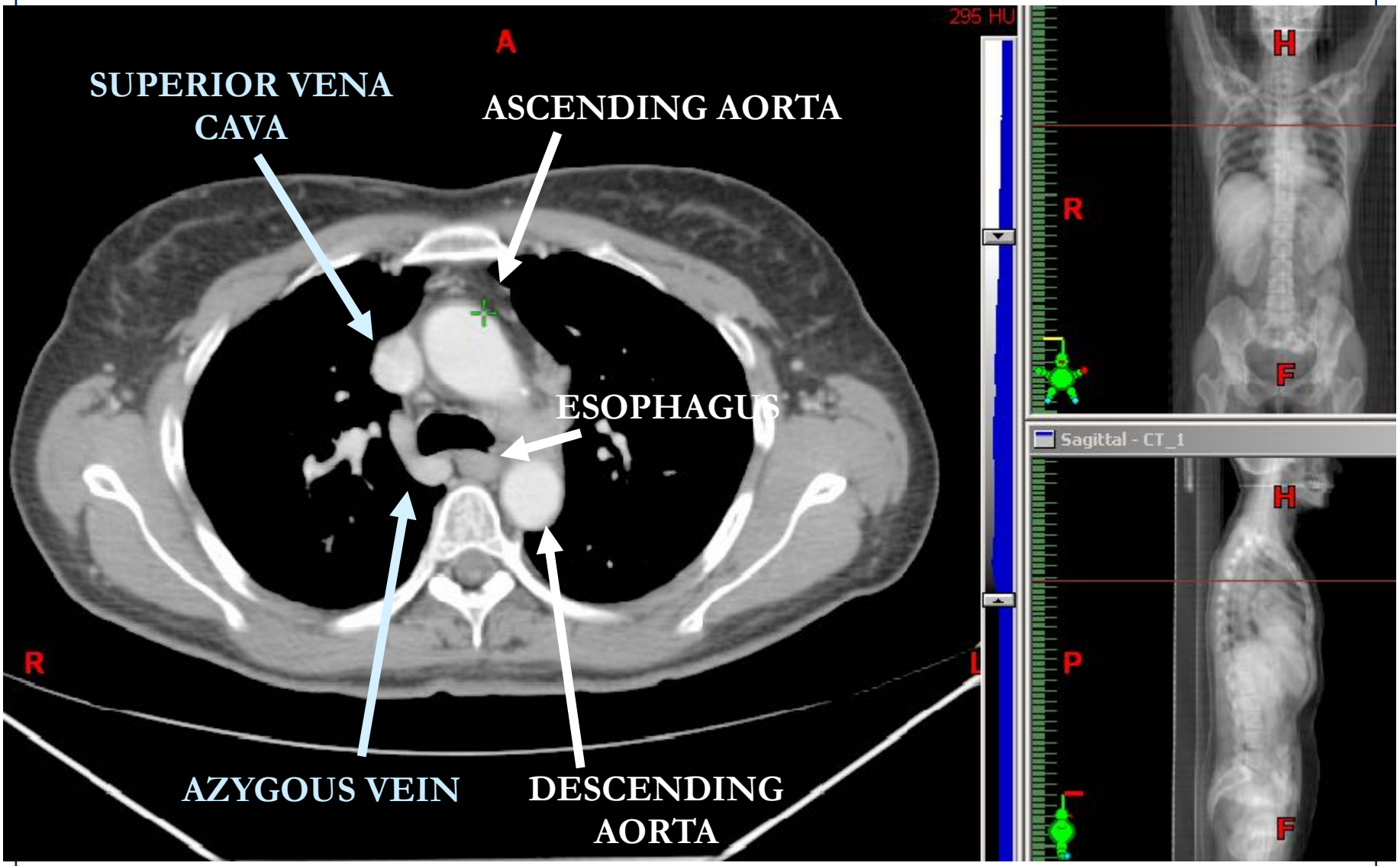




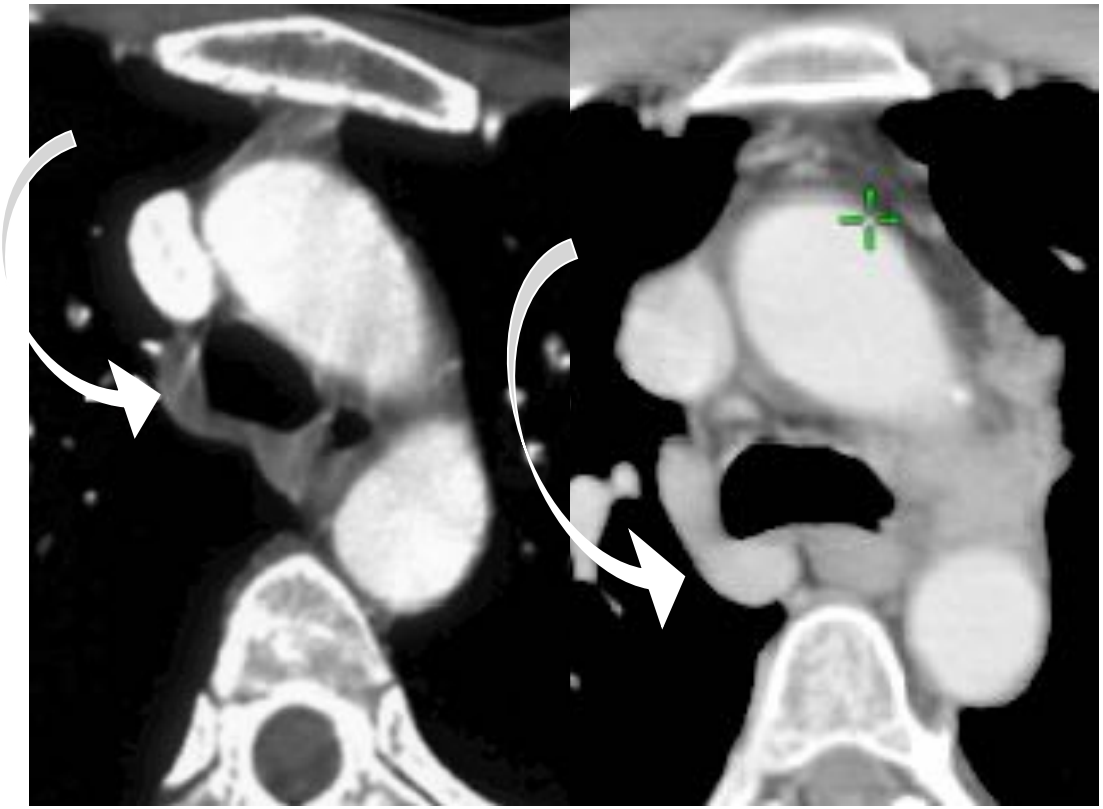

BRACHIOCEPHALIC TRUNK
LEFT BRACHIOCEPHALIC VEIN
SUPERIOR VENA CAVA
AORTIC ARCH
A
R
H
F
Sagittal - CT_1
P


295 HU
A
LEFT BRACHIOCEPHALIC VEIN
SUPERIOR VENA CAVA
AORTIC ARCH
R
L
H
R
F
Sagittal - CT_1
H
P
F


296 HU
A
SUPERIOR VENA CAVA
ASCENDING AORTA
ESOPHAGUS
AZYGOUS VEIN
DESCENDING AORTA
R
L
H
R
F
Sagittal - CT_1
H
P
F

DIAGNOSTIC PITFALLS IN THORAX ANATOMY

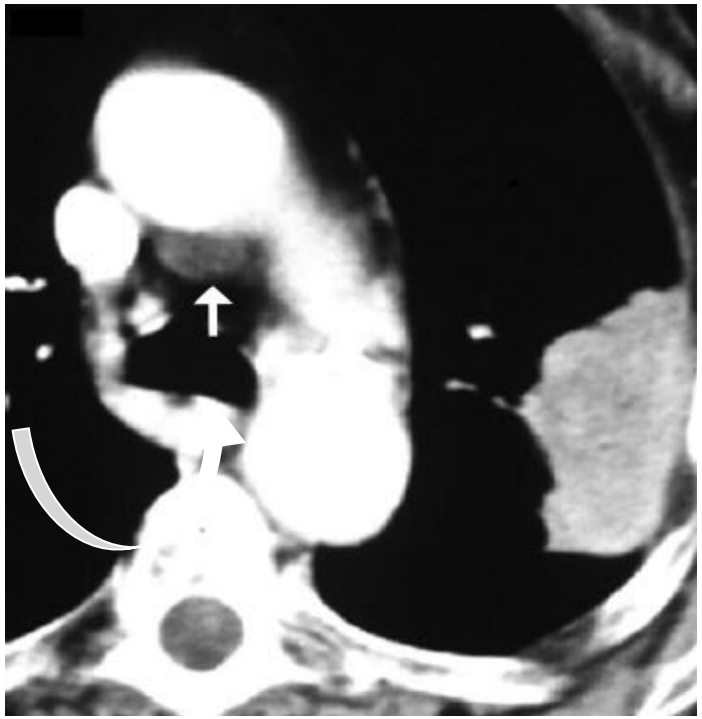
AZYGOUS VEIN

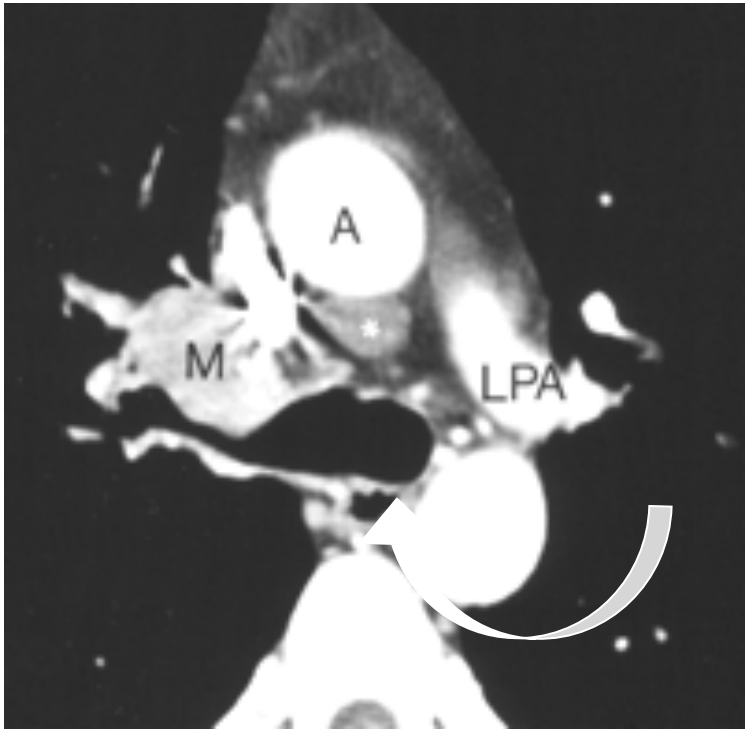


Roy and Wells, Cancer Imaging (2006) 6, 116–123

DIAGNOSTIC PITFALLS IN THORAX ANATOMY

Superior Aortic Recess





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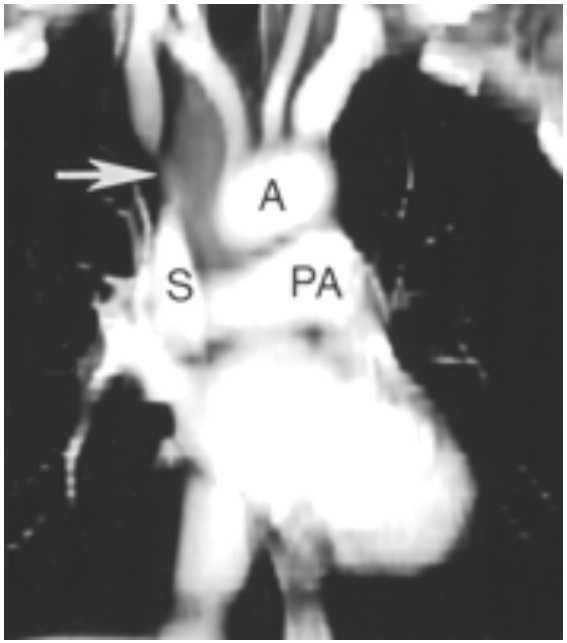
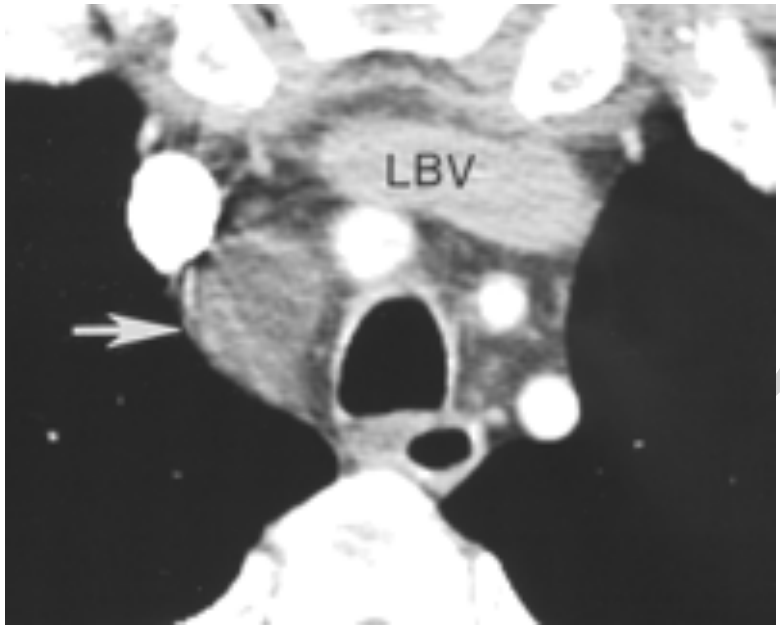
Truong, AJR 2012

DIAGNOSTIC PITFALLS IN THORAX ANATOMY

Superior Aortic Recess: at level of left brachiocephalic vein (LBV) shows cephalad extension of superior aortic recess adjacent to trachea; This is "high-riding"(CRESTA) variant





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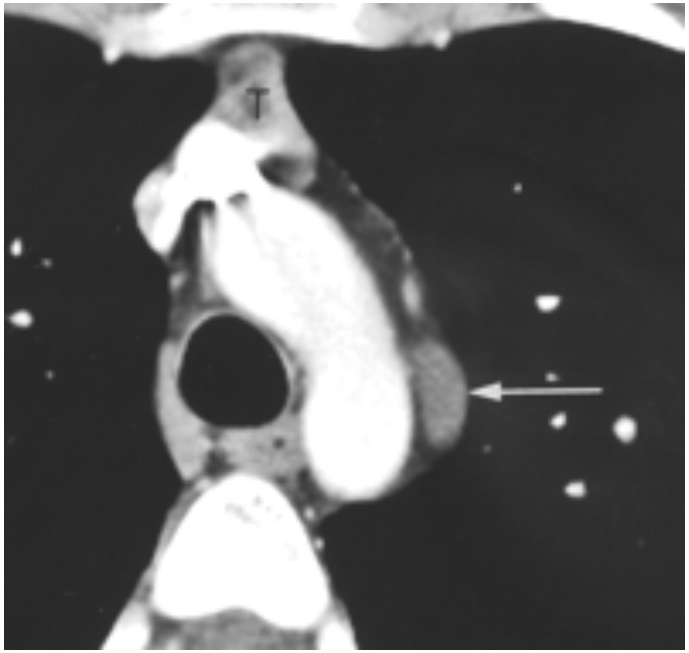
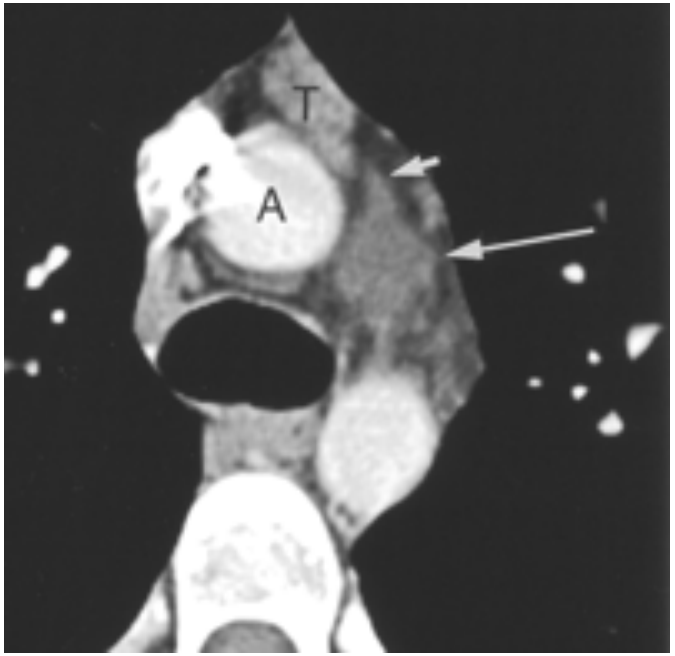
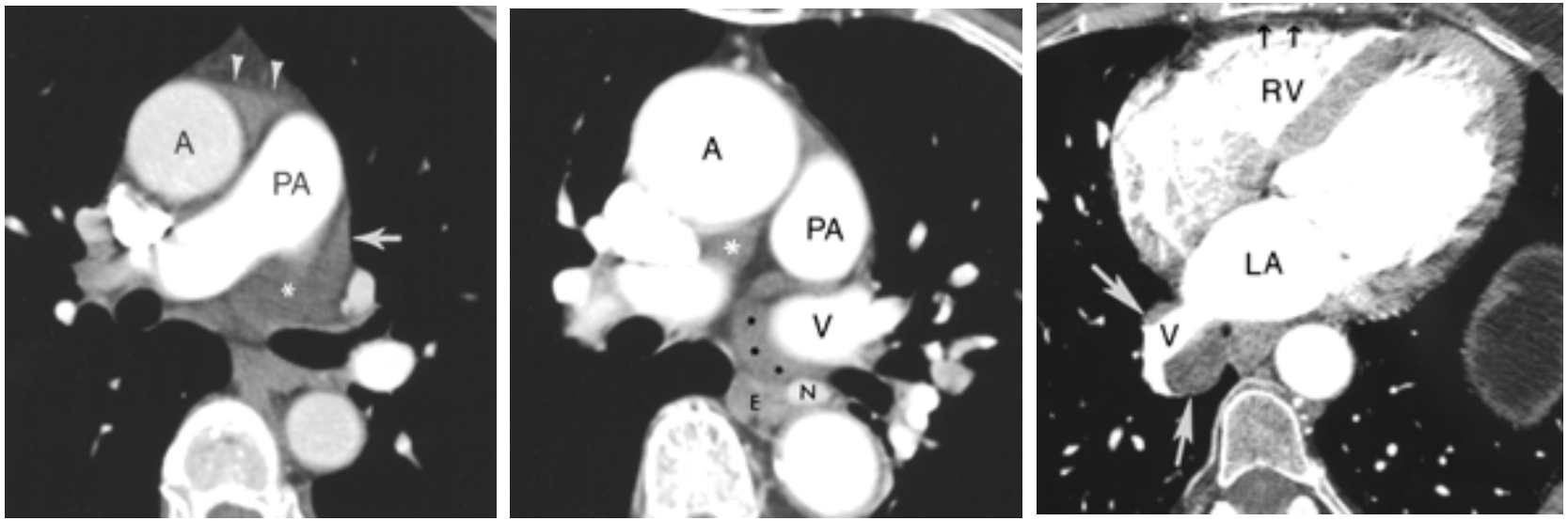




Truong, AJR 2012

DIAGNOSTIC PITFALLS IN THORAX ANATOMY

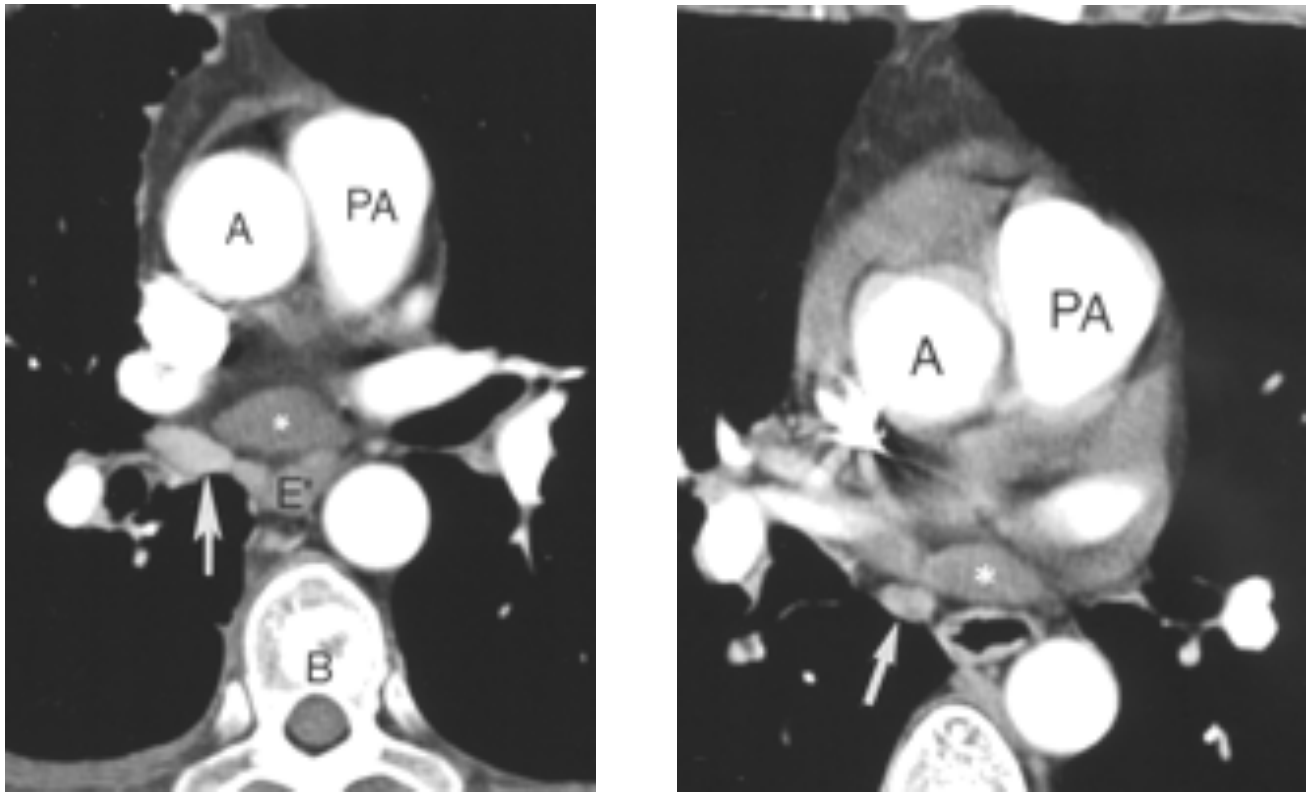
Left pulmonic recess, Left pulmonary venous recess and Serosal sleeve



Truong, AJR 2012

DIAGNOSTIC PITFALLS IN THORAX ANATOMY

Note difference in attenuation between fluid in oblique sinus and adjacent mediastinal lymph nodes



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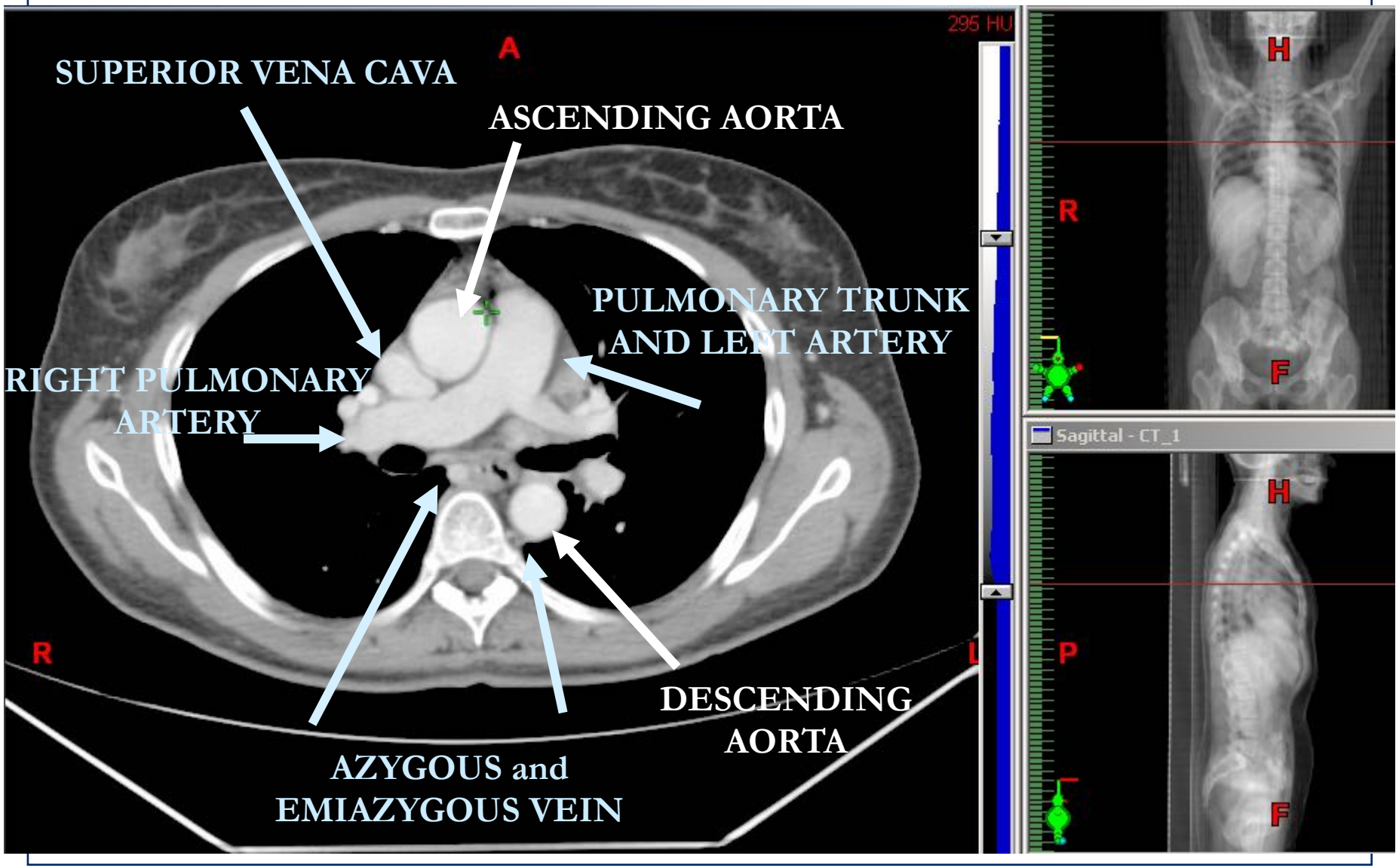
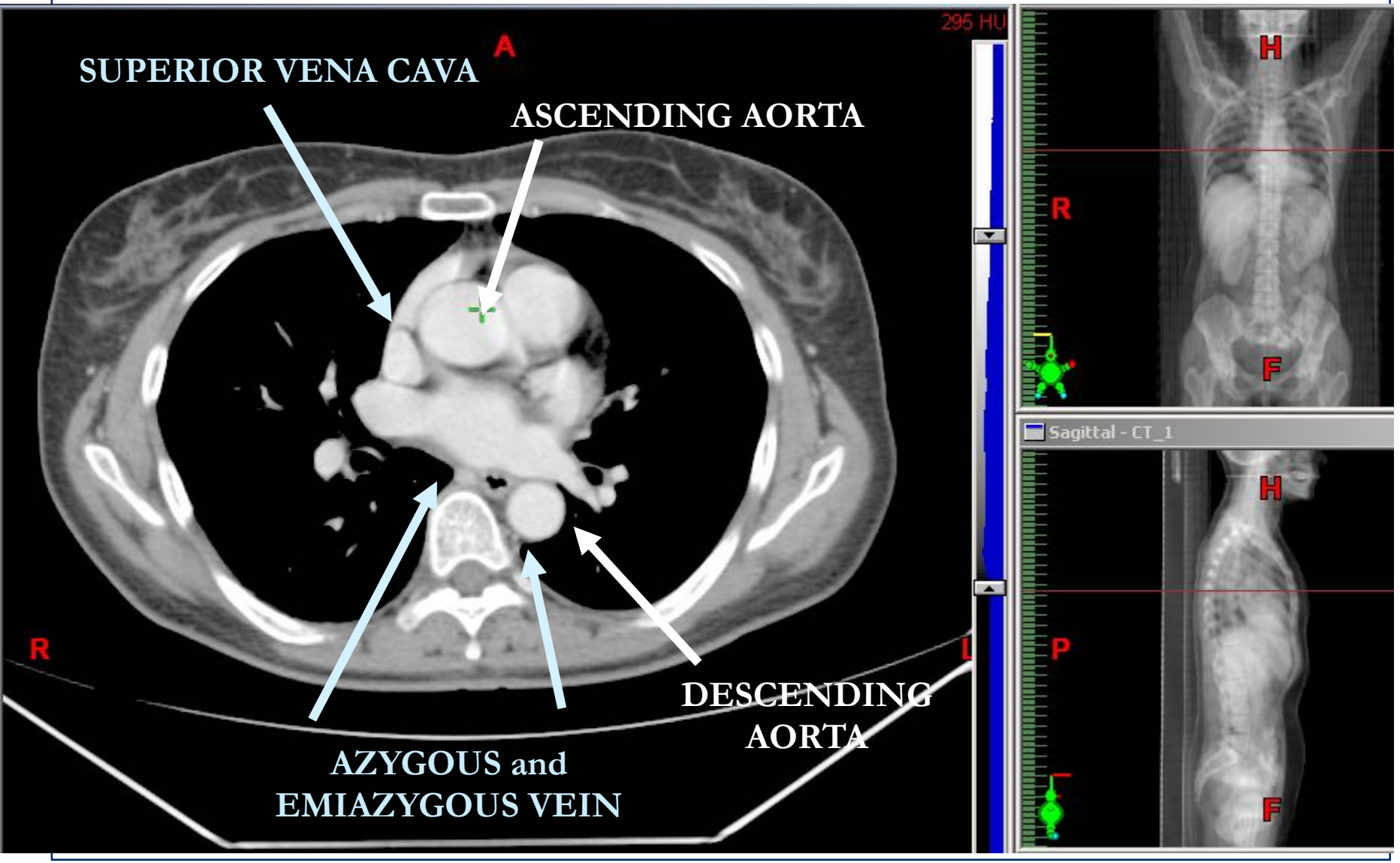

295 HU
A
SUPERIOR VENA CAVA
ASCENDING AORTA
PULMONARY TRUNK
AND LEFT ARTERY
RIGHT PULMONARY
ARTERY
R
L
DESCENDING
AORTA
AZYGOUS and
EMIAZYGOUS VEIN
H
R
F
Sagittal - CT_1
H
P
F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ASCENDING AORTA
R
L
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H
R
F
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H
P
F

CT-BASED DEFINITION OF THORACIC LYMPH NODE STATIONS: AN ATLAS FROM THE UNIVERSITY OF MICHIGAN

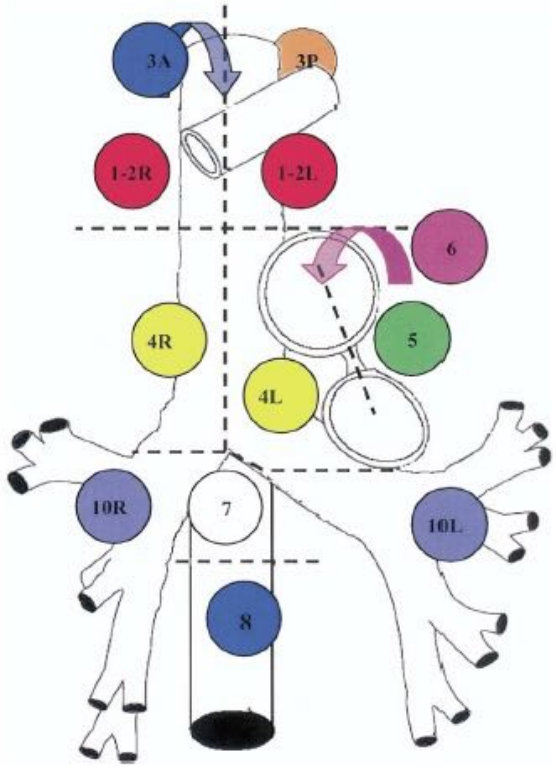

Table 1. Mountain and Dresler classification system

Station	Description
1R: highest mediastinal nodes	Nodes lying above horizontal line at upper rim of bracheocephalic (left innominate) vein where it ascends to left, crossing in front of trachea at its midline
2R and 2L: upper paratracheal nodes	Nodes lying above horizontal line drawn tangential to upper margin of aortic arch and below inferior boundary of station 1 nodes
3: prevascular nodes and retrotracheal nodes	Prevascular and retrotracheal nodes may be designed 3A and 3P; midline nodes are considered to be ipsilateral
4R and 4L: right and left lower paratracheal nodes	Lower paratracheal nodes on right lie to right of midline of trachea between horizontal line drawn tangential to upper margin of aortic arch and line extending across right main bronchus, and contained within mediastinal pleural envelope; lower paratracheal nodes on left lie to left of midline of trachea between horizontal line drawn tangential to upper margin of aortic arch and line extending across left main bronchus at level of upper margin of left upper lobe bronchus, medial to ligamentum arteriosum and contained within mediastinal pleural envelope
5: subaortic (aortic–pulmonary window)	Subaortic nodes are lateral to ligamentum arteriosum or aorta or left pulmonary artery and proximal to first branch of left pulmonary artery and lie within mediastinum pleural envelope
6: paraaortic nodes	Nodes lying anterior and lateral to ascending aorta and aortic arch or inominate artery beneath line tangential to upper margin of aortic arch
7: subcarinal nodes	Nodes lying caudal to carina of trachea but not associated with lower lobe bronchi or arteries within lung
8: paraeosphageal nodes	Nodes lying adjacent to wall of esophagus and to right or left of midline, excluding subcarinal nodes
10: hilar nodes	Proximal lobar nodes, distal to mediastinal pleural reflection and nodes adjacent to bronchus intermedius on right; radiographically, hilar shadow may be created by enlargement of both hilar and interlobar nodes
11: interlobar nodes	Nodes lying between lobar bronchi

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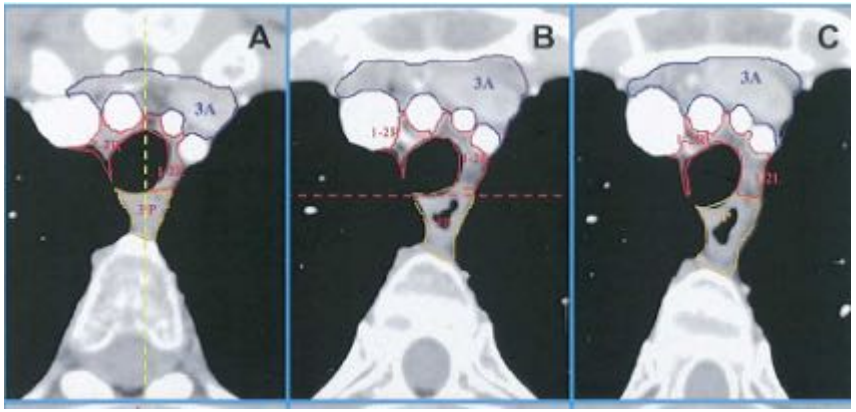
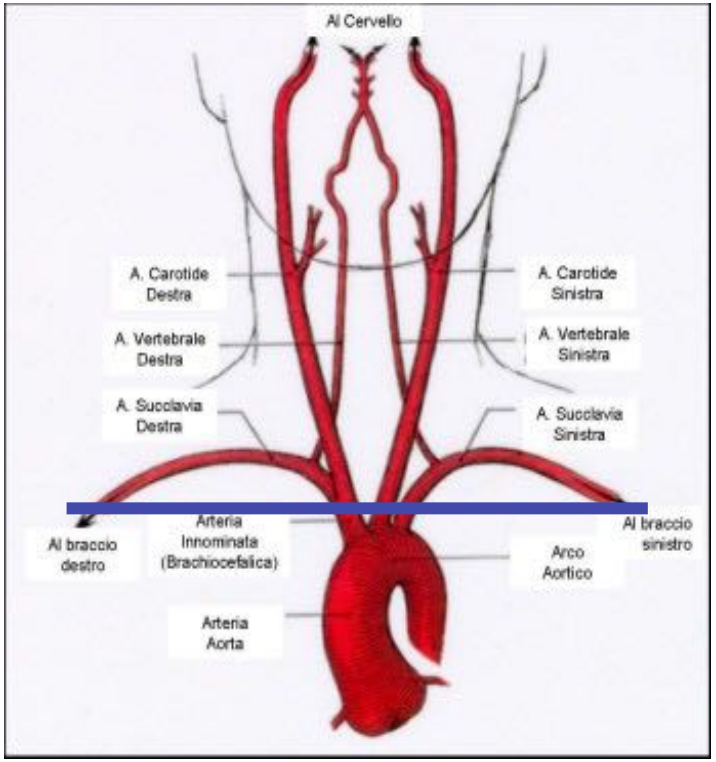


Nodal stations 1-2R, 1-2L, 3A and 3P



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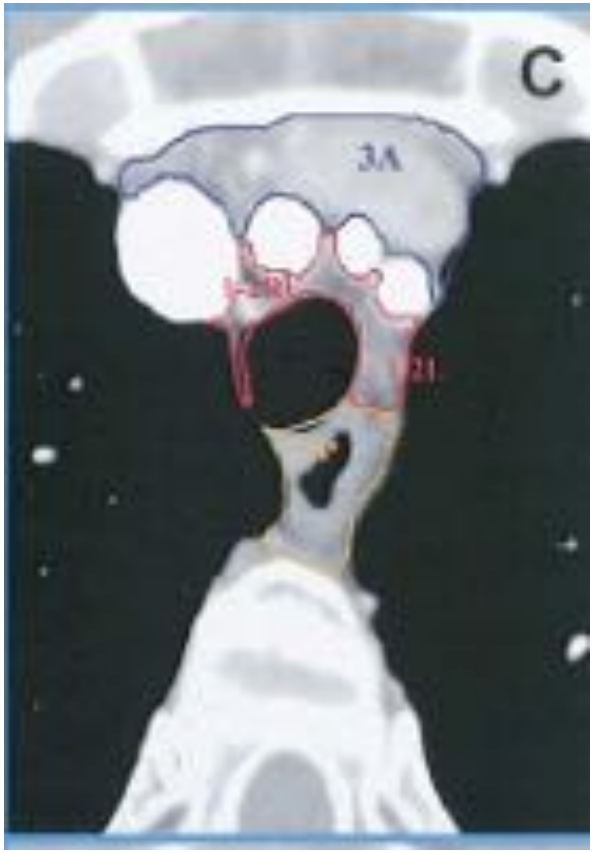
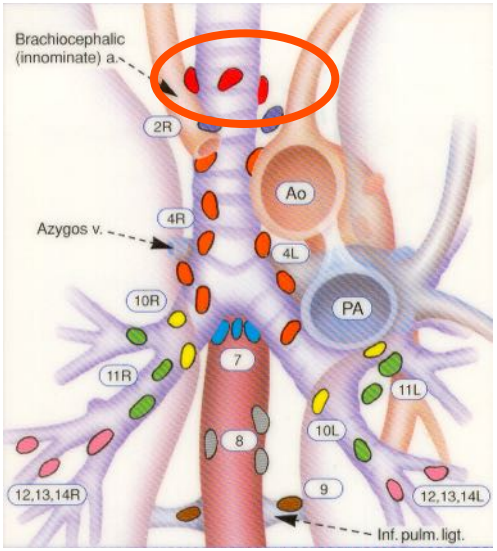
PATHOLOGICAL NODAL STATIONS

American Toracic Society of Surgery (ATS),1997





2R-2L. Upper Paratracheal Nodes

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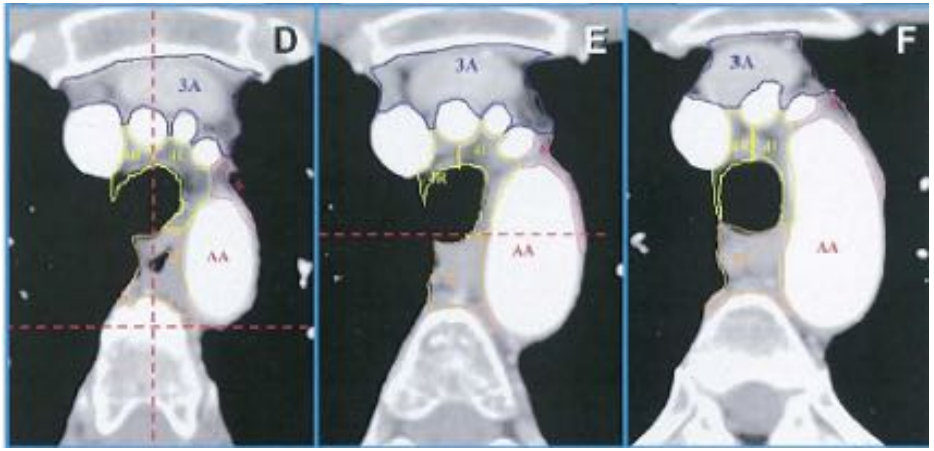
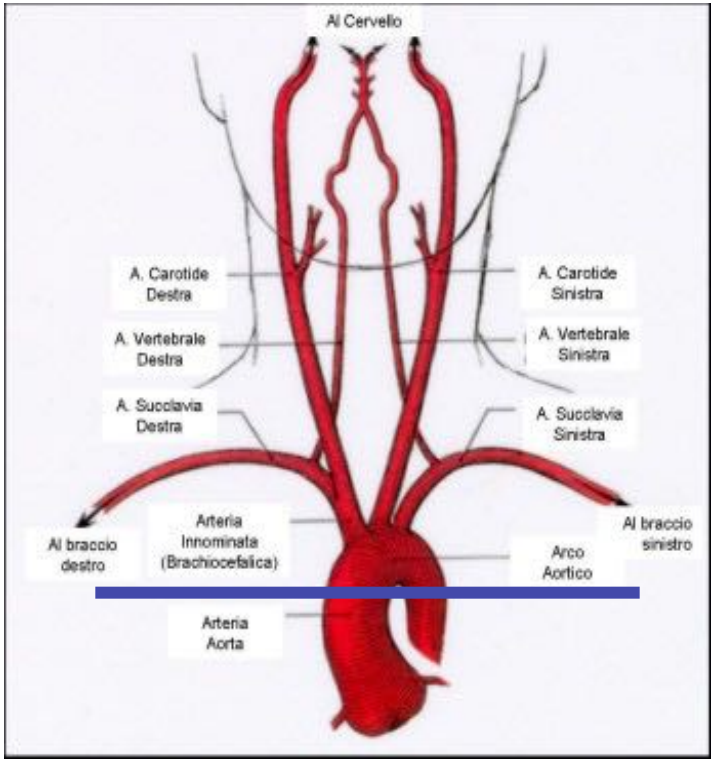


Nodal stations 4R, 4L, 3A and 3P



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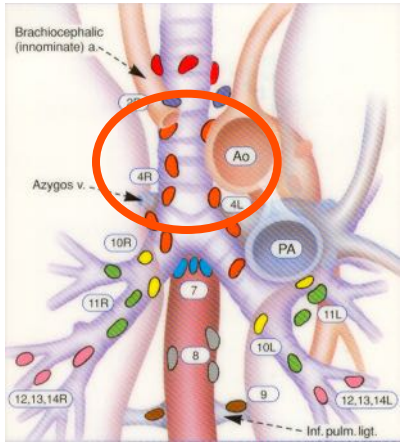

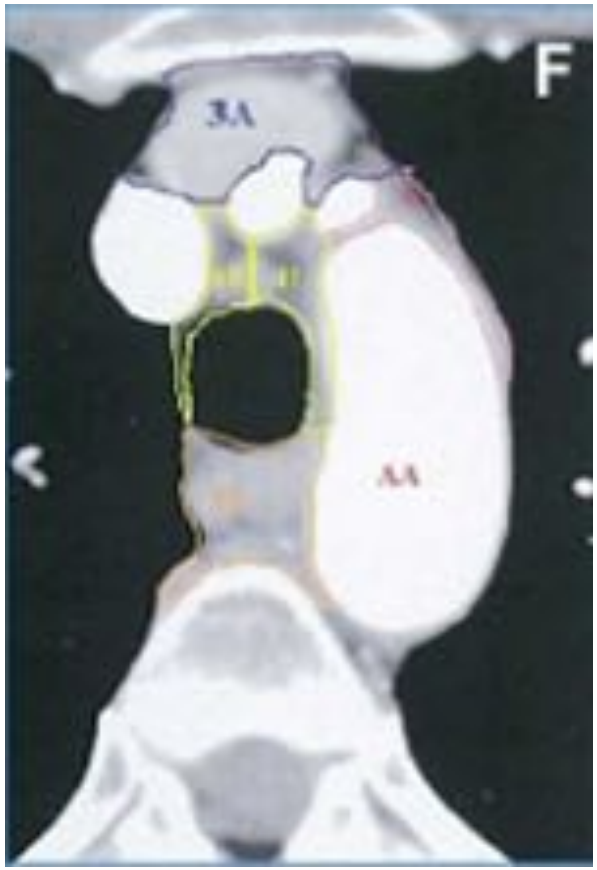

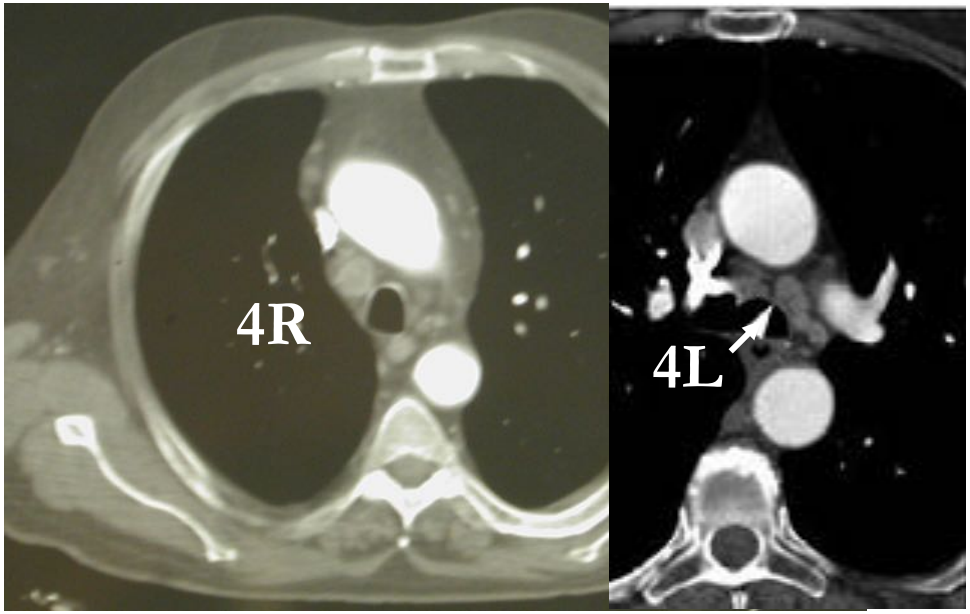

4R-4L. Lower Paratracheal Nodes

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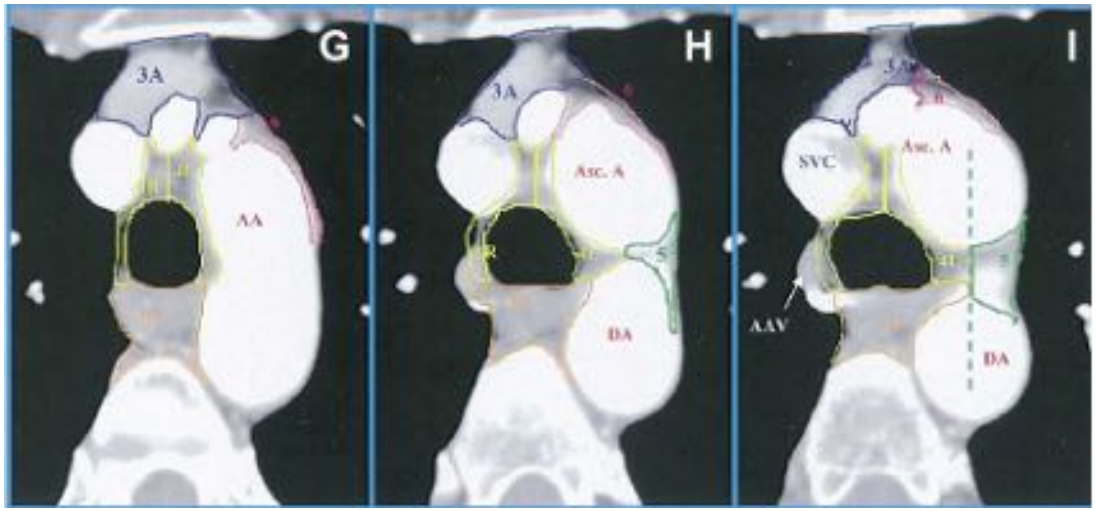
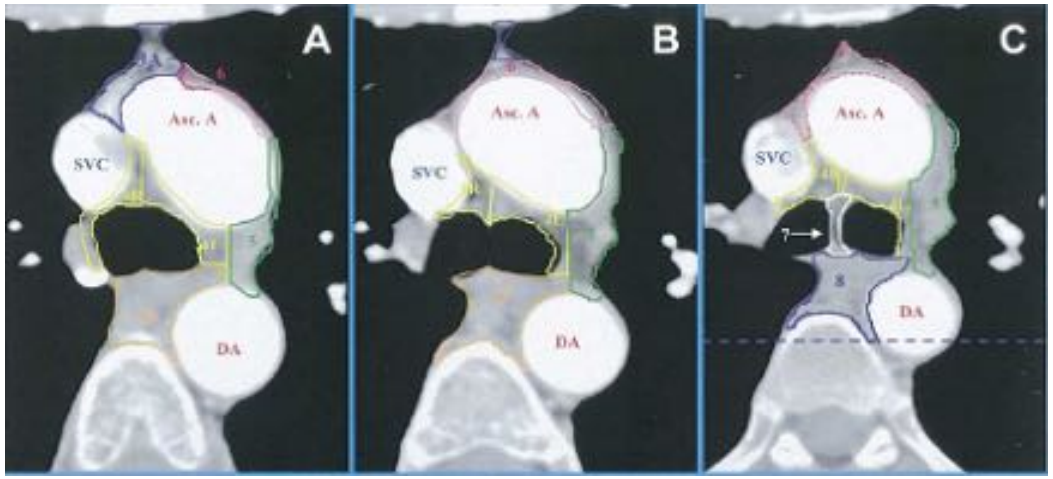


Nodal stations 3A, 4R, 4L,

5 and 6



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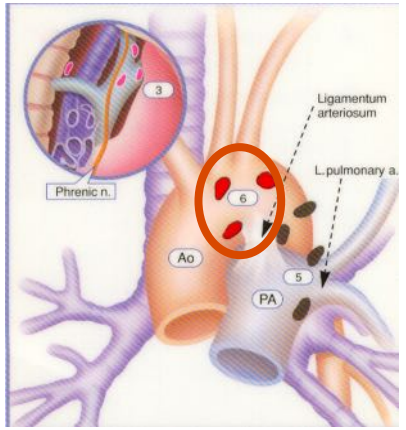

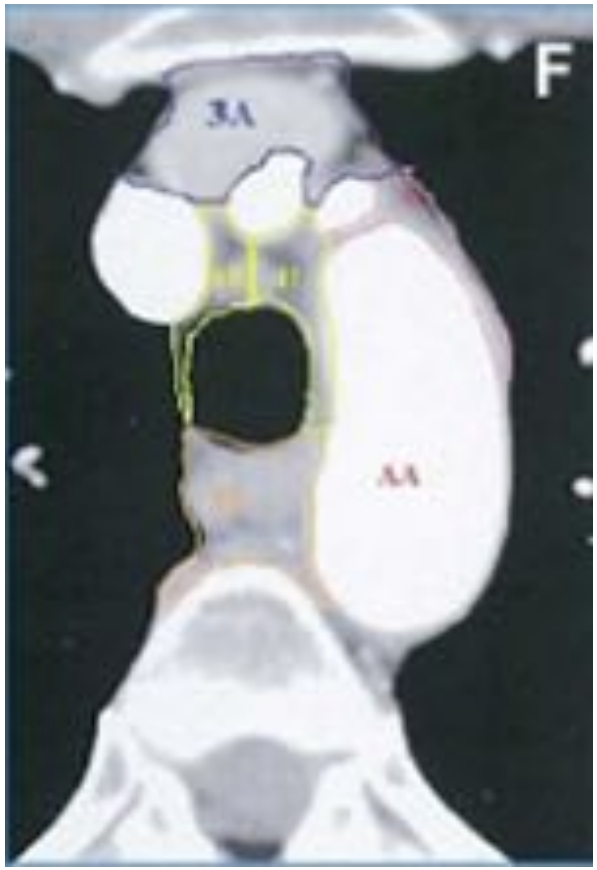

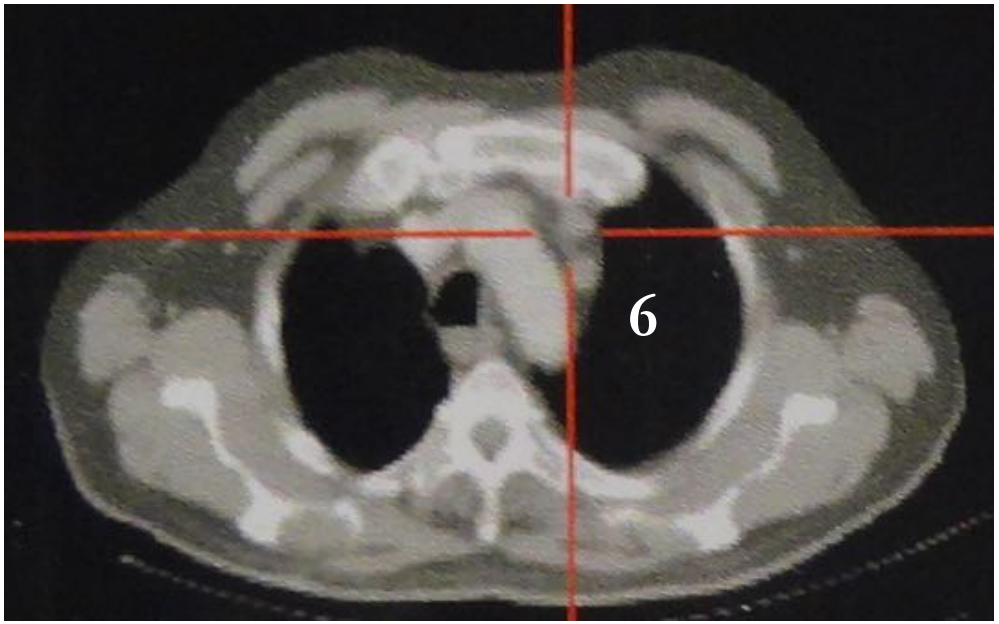

6. Paraortic Nodes

PATHOLOGICAL NODAL STATIONS

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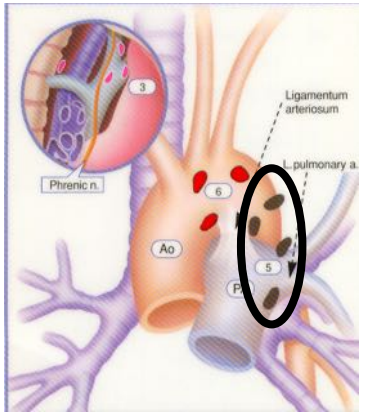

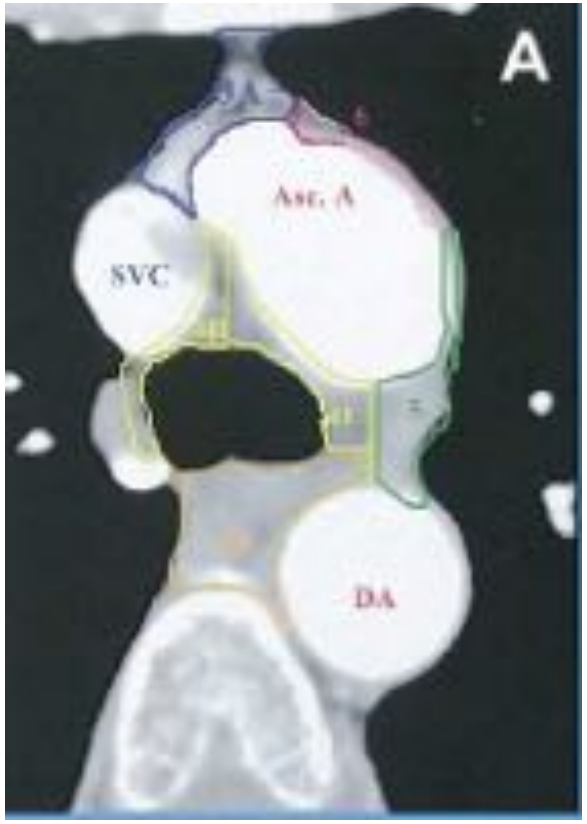

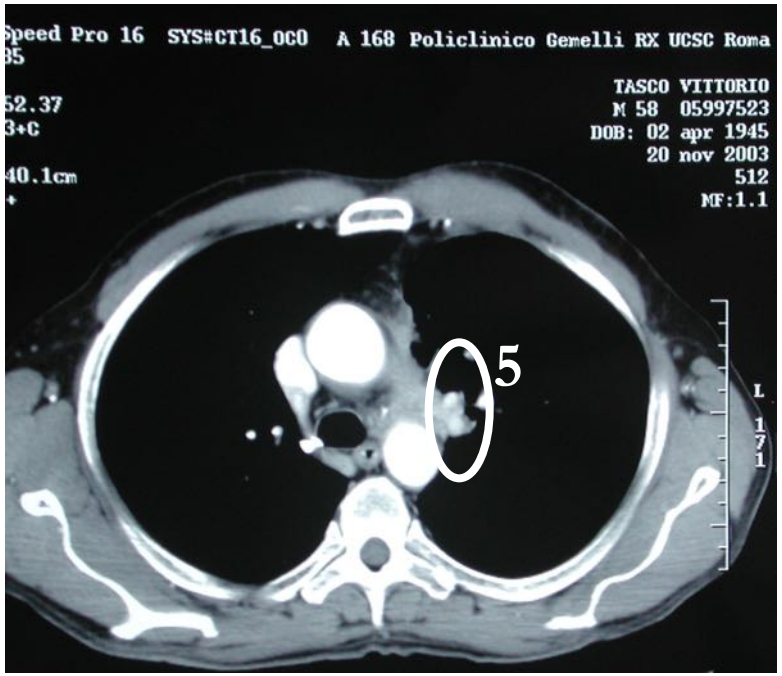

5. Aortic-pulmonary window

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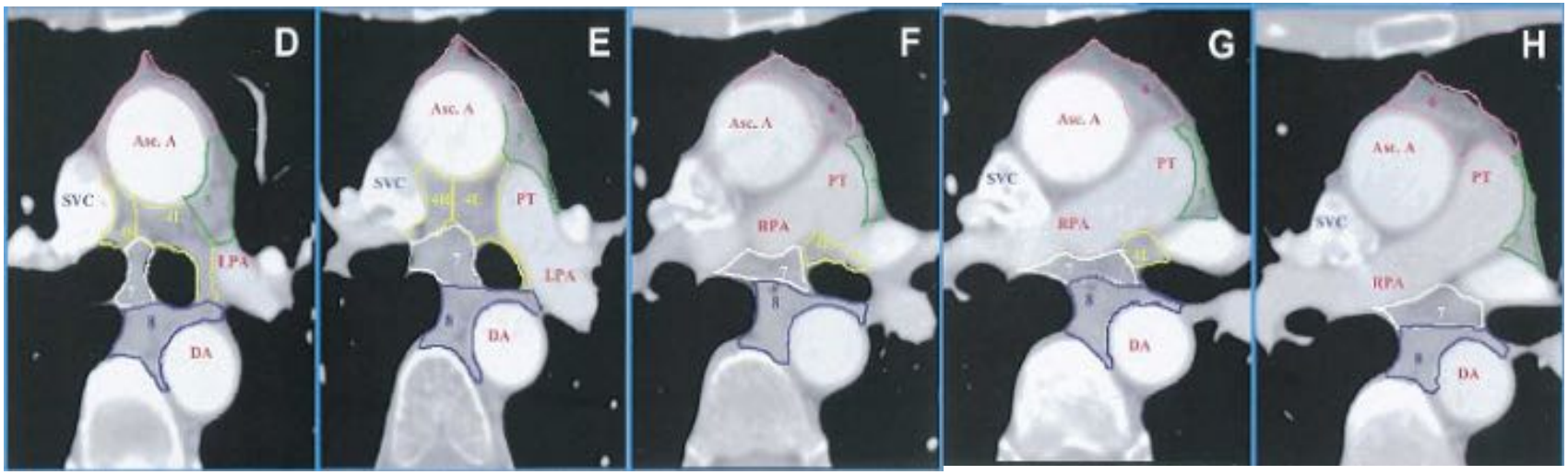

Nodal stations 4R, 4L, 5, 7 and 8

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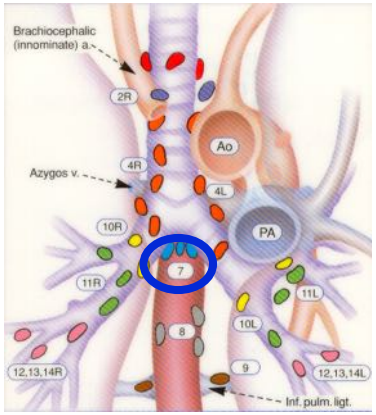

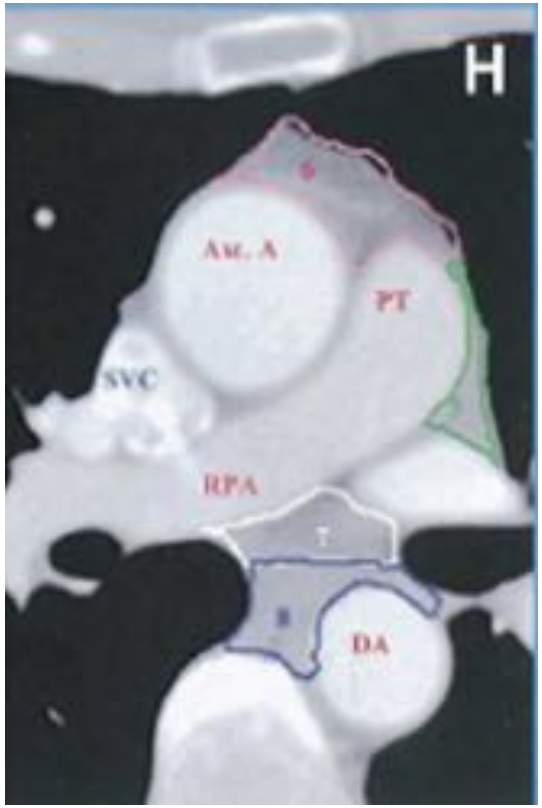

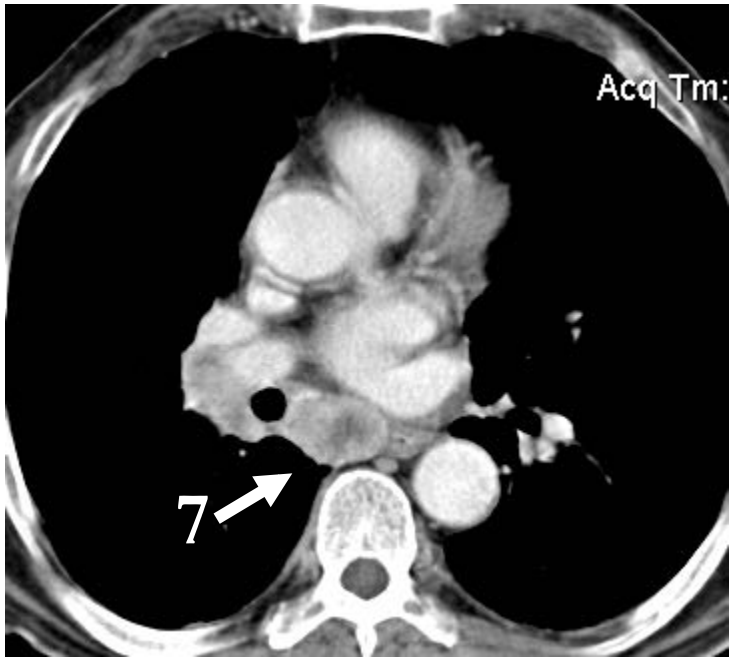

7. Subcarinal Nodes

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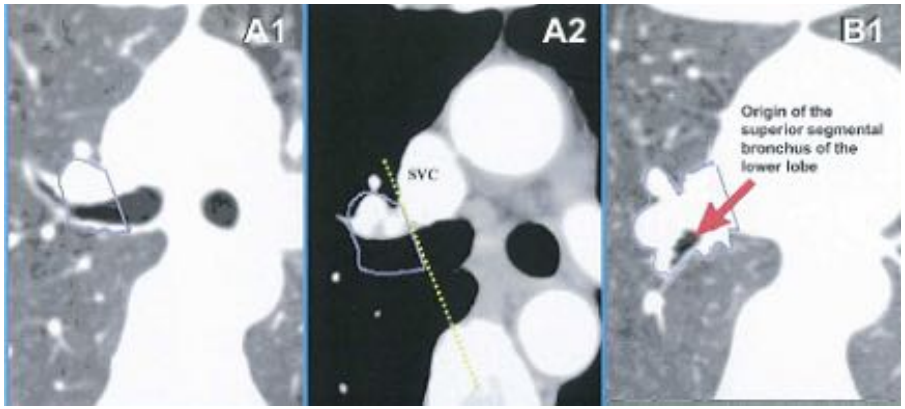
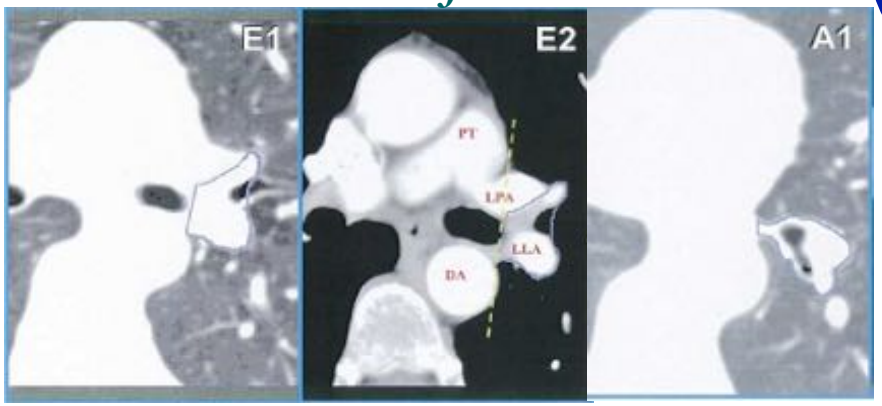
Stations 10 and 11R: ***Right hilar nodes limits***

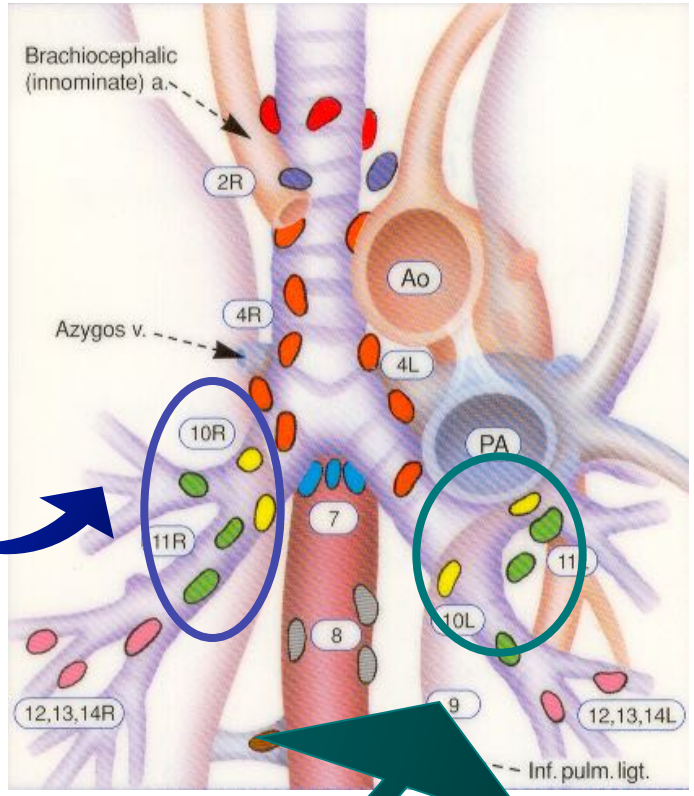


UPPER MEDIAL INFERIOR

Stations 10 and 11L: ***Left hilar nodes limits***



UPPER MEDIAL INFERIOR



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PATHOLOGICAL NODAL STATIONS

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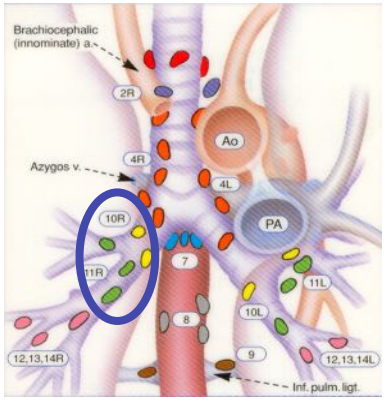
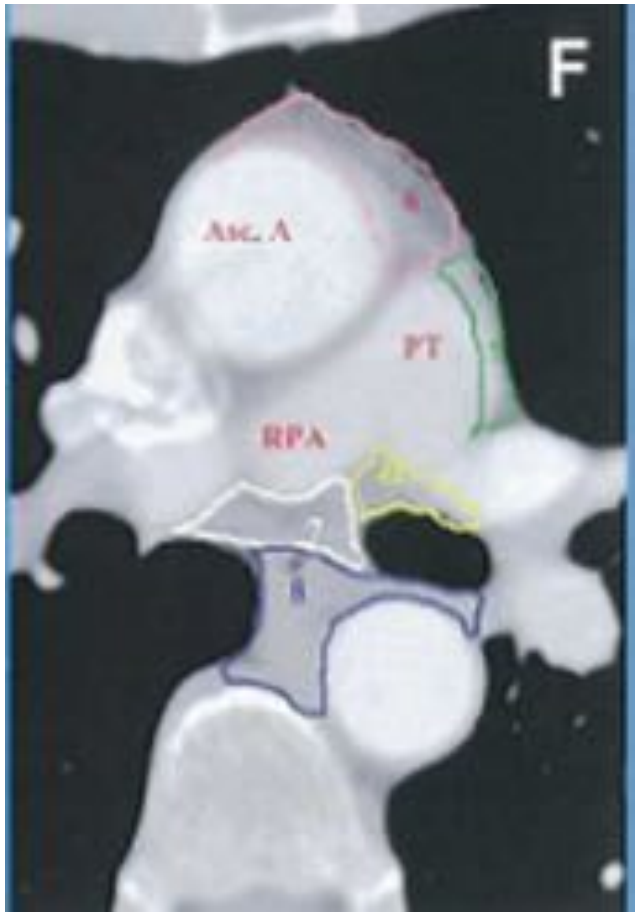
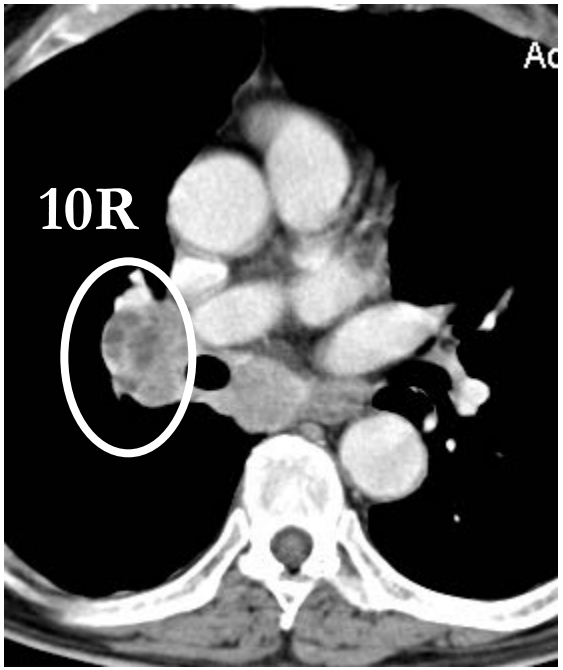






10R-10L. Hilar Nodes

CLINICAL TARGET VOLUME DEFINITION

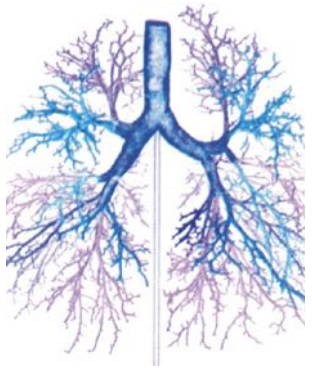
A. Radiological Anatomy

- Normal structures, Pitfalls and Nodal Stations

B. Non-Small Cell Lung Cancer

- ***Locally Advanced Disease***

C. Small Cell Lung Cancer



Locally Advanced Non-Small Cell Lung Cancer

CLINICAL TARGET VOLUME DEFINITION is a CRUCIAL POINT in curative radiotherapy because

- OVERESTIMATION may increase TOXICITY
- UNDERESTIMATION will result in local RECURRENCE

TARGET VOLUME DEFINITION IN L.A. NSCLC:

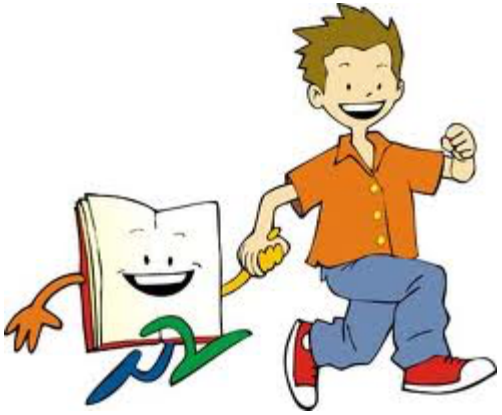
"A LESSON LEARNED FROM LOCAL RECURRENCES"

RECURRENCE SITE

APPROPRIATENESS OF TARGET DELINEATION

TARGET VOLUME DEFINITION IN L.A. NSCLC:

"A LESSON LEARNED FROM LOCAL RECURRENCES"



SITE OF LOCAL FAILURE :

- LOW RISK AREAS OF RELAPSE

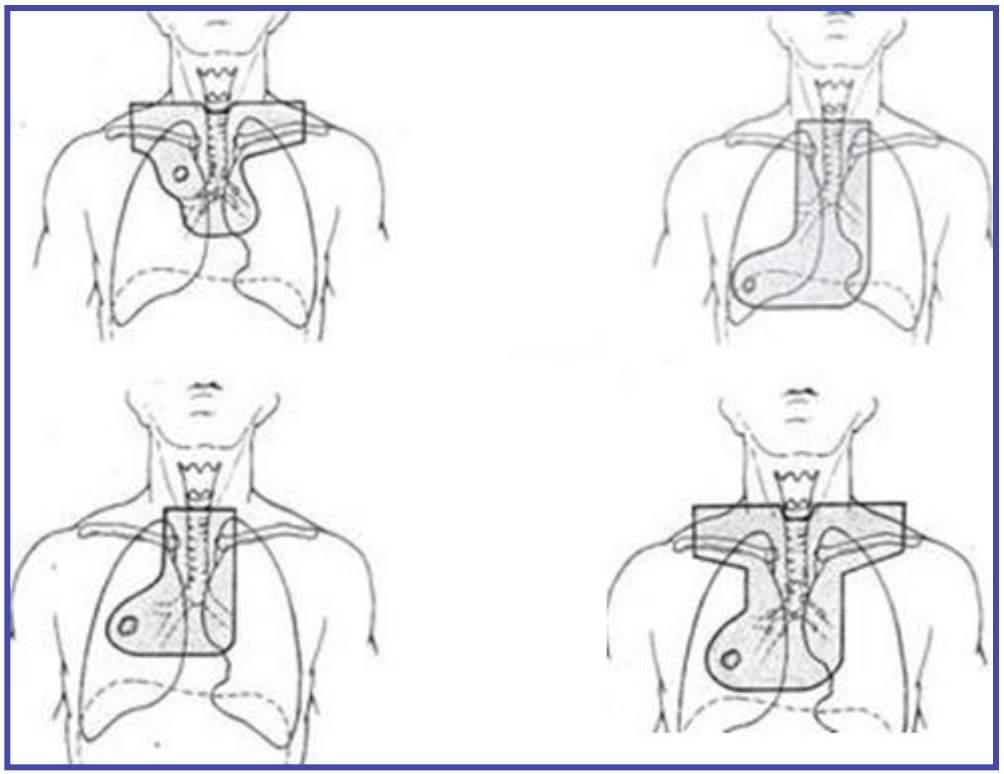
- HIGH RISK AREAS OF RELAPSE

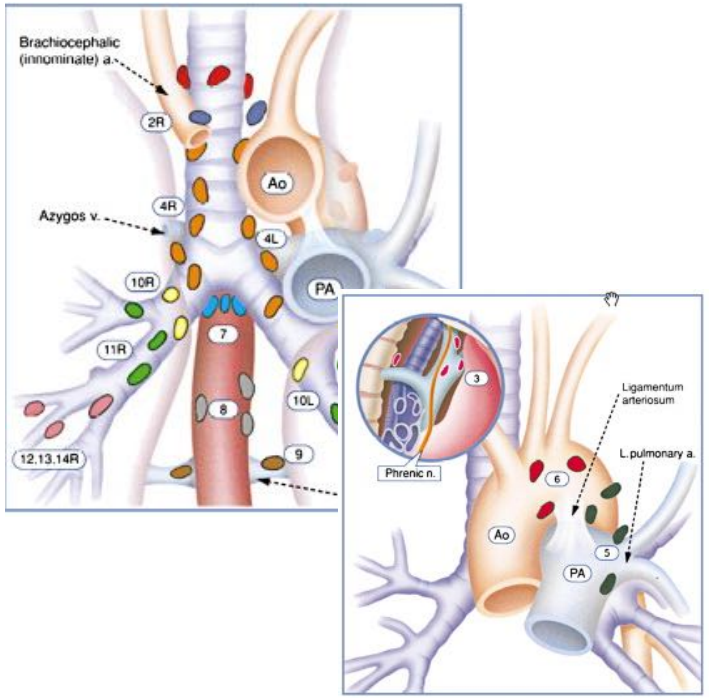
De Ruysscher, Radiot Oncol 2011

SITE OF LOCAL FAILURE :

- *LOW RISK AREAS OF RELAPSE:*

ELECTIVE NODAL IRRADIATION (ENI)

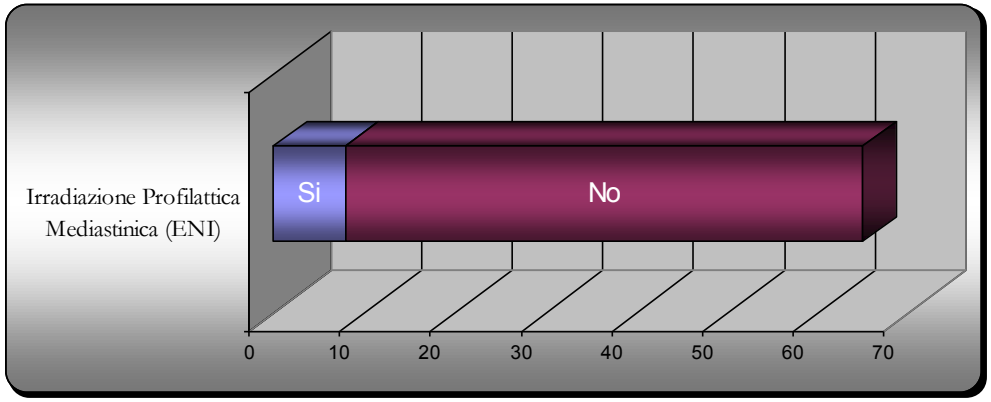




GRUPPO POLMONE 2009-2010

PROGETTO R.E.S.P.I.RO

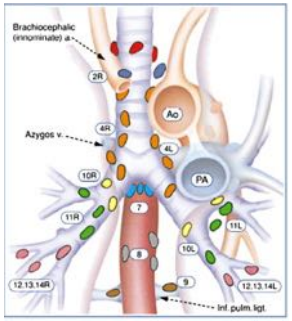
Ricerca E Survey Polmonare In Radioterapia Oncologica



No ENI in 88% of respondent centres

Ramella S, Maranzano E,Tumori, 98: 66-78, 2012

EDITORIAL



The phase III trial

"*strikes at the heart of the dilemma*"

Schild S, 2008

Yuan S et al. "***A Randomized study of IFI vs ENI***" Am JCO 2007

200 patients, inoperable stage III, concurrent chemoradiation

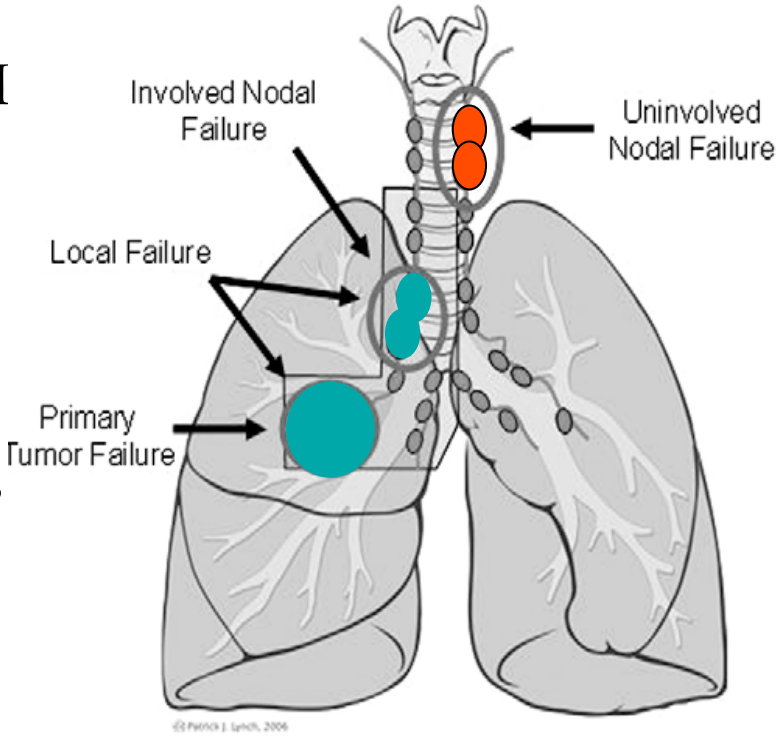
		5y LC	Pneumo	2y-SVV	5y-SVV
ENI	60-64Gy	36%	29%	25.6%	18.3%
IFI*	68-74Gy	51%, *p=0.03*	17%, *p=0.04*	39.4%, *p=0.048*	25.1%

EDITORIAL

ELECTIVE NODAL IRRADIATION (ENI) DOESN'T APPEAR TO PROVIDE A CLEAR BENEFIT FOR PATIENTS WITH UNRESECTABLE NON–SMALL-CELL LUNG CANCER (NSCLC)

An argument against the use of ENI and in favour of Involved Field Radiotherapy

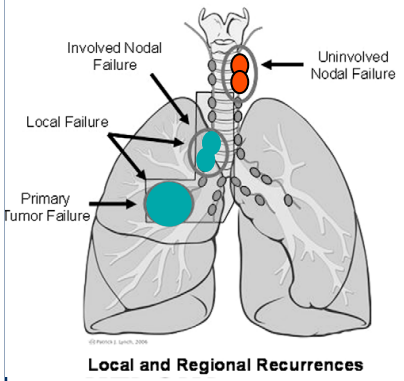
Failure in nodal region that are ***clinically uninvolved***



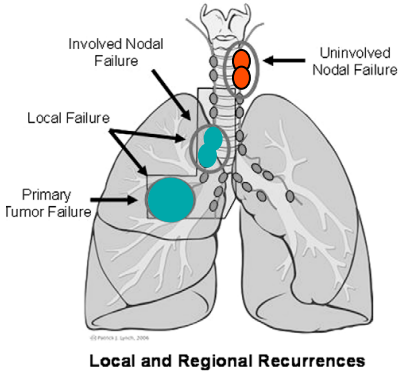
Local and Regional Recurrences

Schild S, Int J Radiat Oncol Biol Phys 2008

SITE OF LOCAL FAILURE : LOW RISK AREAS



ISOLATED NODAL RECURRENCE



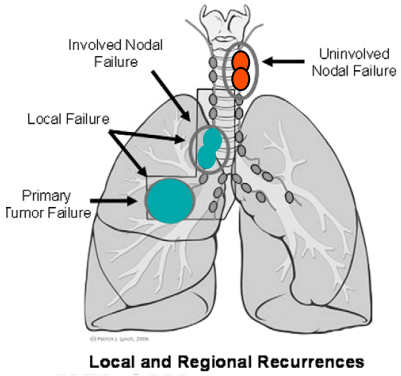
REPORT FROM THE INTERNATIONAL ATOMIC ENERGY AGENCY (IAEA) CONSULTANTS' MEETING ON ELECTIVE NODAL IRRADIATION IN LUNG CANCER: NON–SMALL-CELL LUNG CANCER (NSCLC)

Reference	Number of patients	LN target volume using CT and/or ^{18}FDG PET	ENI yes/no	ENI dose (Gy)	% isolated LN failure
Graham M., *et al.*, 1995†	179	LN ≥1 cm	No		8%
Kong FM., *et al.*, 2005*	106	LN ≥1 cm (pre-chemotherapy)	No		6%
Rosenzweig K., *et al.*, 2001*	171	LN ≥1.5 cm	No	-	6.4%
Senan S., *et al.*, 2002*	50	LN ≥1 cm N2 and T4N0	Yes	50	0

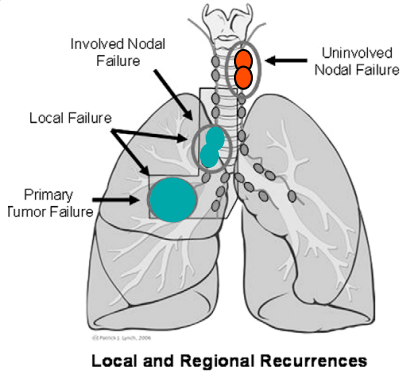
TC-BASED TARGET VOLUME

Belderbos, Int. J. Radiat Oncol Biol. Phys., 72: 335–342, 2008

SITE OF LOCAL FAILURE : LOW RISK AREAS



ISOLATED NODAL RECURRENCE



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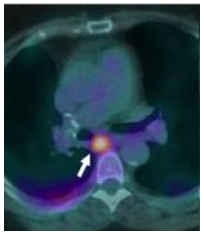
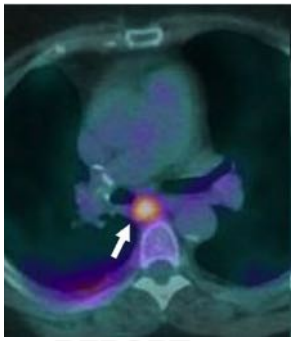


PET-BASED TARGET VOLUME

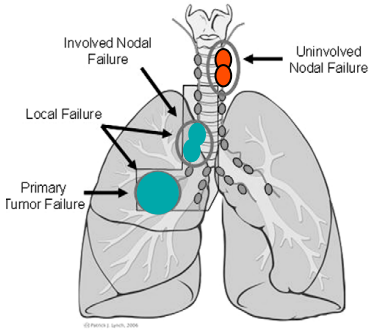
Belderbos, Int. J. Radiat Oncol Biol. Phys., 72: 335–342, 2008

SITE OF LOCAL FAILURE : LOW RISK AREAS



REPORT

ISOLATED NODAL RECURRENCE



Local and Regional Recurrences

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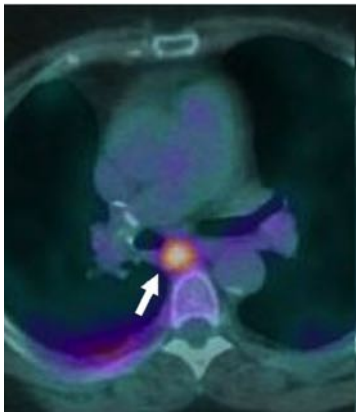
Senan S., *et al.*, 2002*	50	LN ≥1 cm N2 and T4N0 tumors: ipsilateral hilus included	Yes	50	0
De Ruysscher D., *et al.*, 2005†	44	PET + LN only	No	-	2 %
Belderbos J., *et al.*, 2006†	67	PET + LN only	No	-	3 %
Rosenzweig K., *et al.*, 2007*	524	LN ≥1.5 cm and in 314 patients PET + LN also	No		6.1%

TC

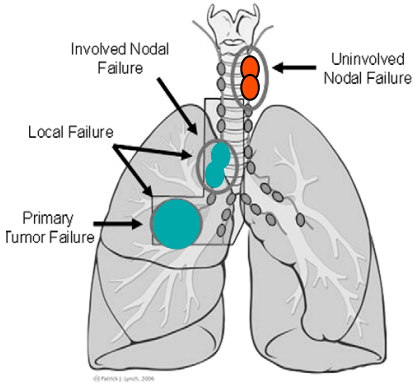
PET

Belderbos, Int. J. Radiat Oncol Biol. Phys., 72: 335–342, 2008

SITE OF LOCAL FAILURE : LOW RISK AREAS

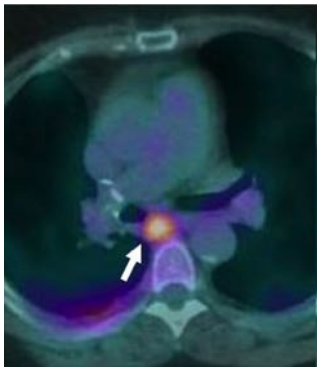


ISOLATED NODAL RECURRENCE



Local and Regional Recurrences

Sulman, Radiation Oncology 2009	PET	115	1,7%
Fernandes, Radiother and Oncology 2010	PET	48	4.3%
Fleckenstein, Int J Radiat Oncol Biol Phys 2011	PET	33	4%
Bradley, Int J Radiat Oncol Biol Phys 2012	PET	47	2%



IMPACT OF FDG/PET ON RADIOTHERAPY PLANNING IN PATIENTS WITH NSCLC

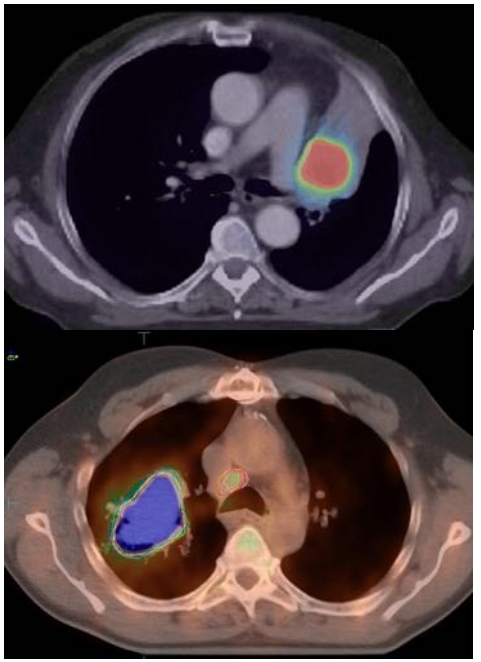
Author	Number of patients	Fusion method	Impact on radiation planning
Nestle (1)	34	Visual	35%
Kiffer (2)	15	Visual	47%
Vanuystel (3)	73	Software	67%
Munley (4)	35	Visual	34%
Brianzoni (5)	24	Hardware	50%
Kalff (6)	105	Visual	50%
MacManus (7)	102	Visual	67%
Mah (8)	30	Software	40%
Giraud (9)	11	Software	45%
Erdi (10)	11	Software	100%
Bradley (11)	26	Software	58%
Deniaud-Alexandre (12)	92	Visual	49%
Faria (13)	32	Hardware	56%

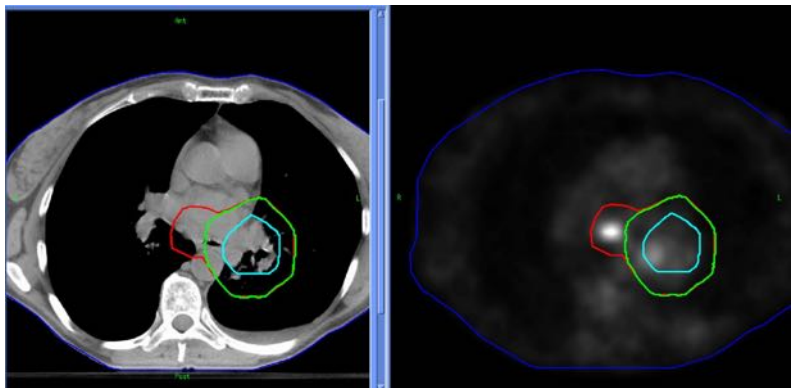
D. De Ruysscher, Lung Cancer *75 (2012) 141– 145*

TARGET VOLUME DEFINITION:

ROLE OF FDG/PET IN LUNG CANCER

- Differentiation of tumour from atelectasis
- More reproducible counturing
- Change of treatment intent or target volume:
  - Distant metastasis staging
  - ***Definition of the mediastinal extent***

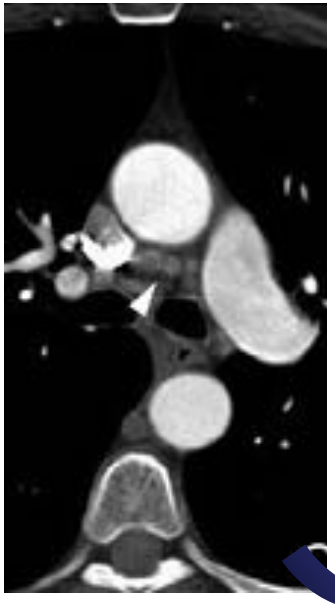




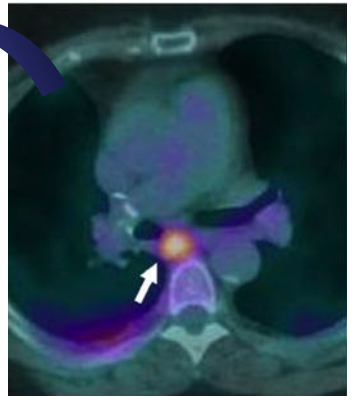
Greco, Lung Cancer 2007

TARGET VOLUME DEFINITION: A CRUCIAL POINT

Definition of the mediastinal extent



	Sensitivity	*Specificity*
TC	57%	82%



	Sensitivity	*Specificity*
PET	85%	90%

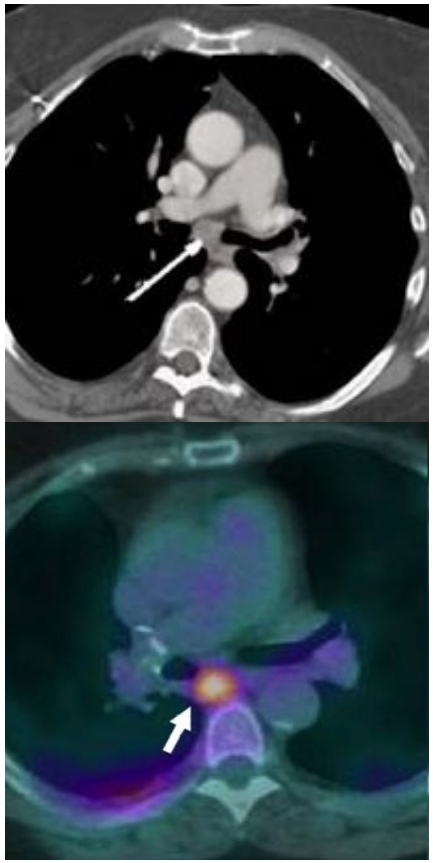
Toloza, Chest 2003
Gould, Annals Int Med 2003

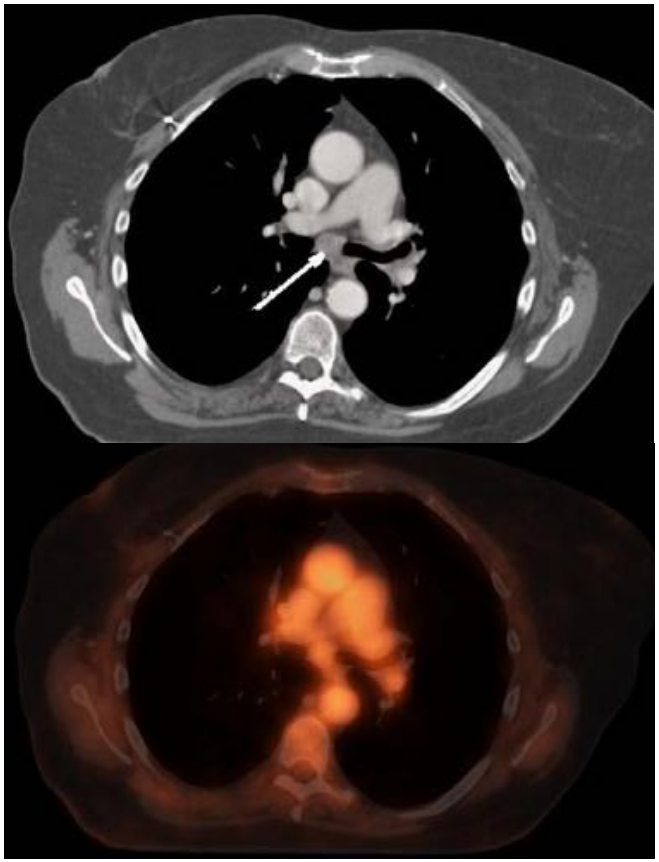
1. FDG PET ACCURACY on CT ENLARGED LYMPH

SENSITIVITY 91%

TC+

PET+



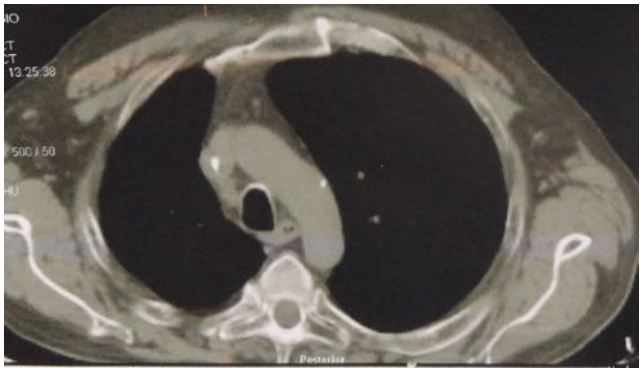


Hellwing, Nuklearmedizin 2009

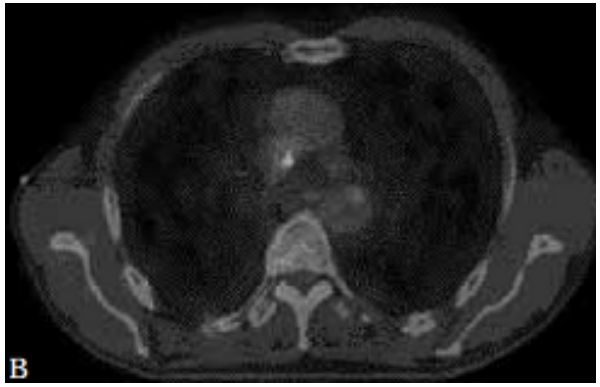
2. FDG PET ACCURACY on CT NORMAL LYMPH

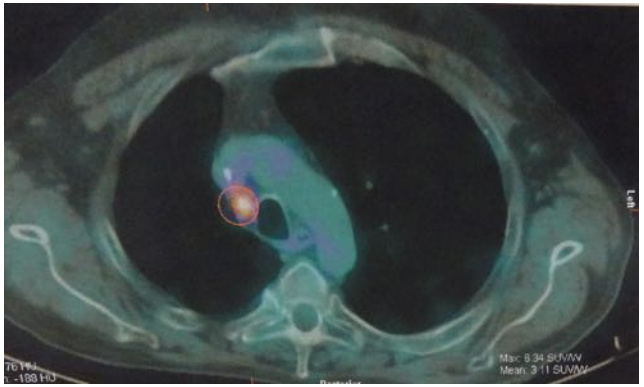
SPECIFICITY 94%

TC+



PET+





Hellwing, Nuklearmedizin 2009

TARGET VOLUME DEFINITION: A CRUCIAL POINT

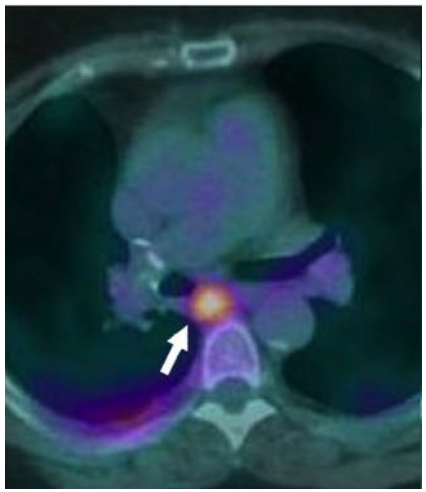
	Sensitivity	***Specificity***
TC	57%	82%
PET	85%	90%
Mediastinoscopy	78%	100%

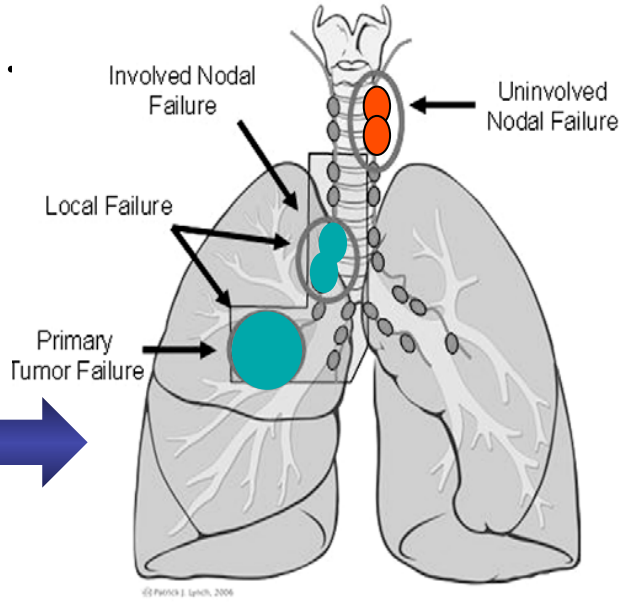
"Unlike PET-scans, mediastinoscopy does not survey all potentially involved nodes; PET very high negative predictive value"

De Ruysscher, Lung Cancer 2012, Toloza, Chest 2003, Gould, Annals Int Med 2003

ISOLATED NODAL RECURRENCE *from* INVOLVED FILED RADIOTHERAPY

AT THIS POINT ……





Local and Regional Recurrences

ISOLATED NODAL RECURRENCE from INVOLVED FILED RADIOTHERAPY

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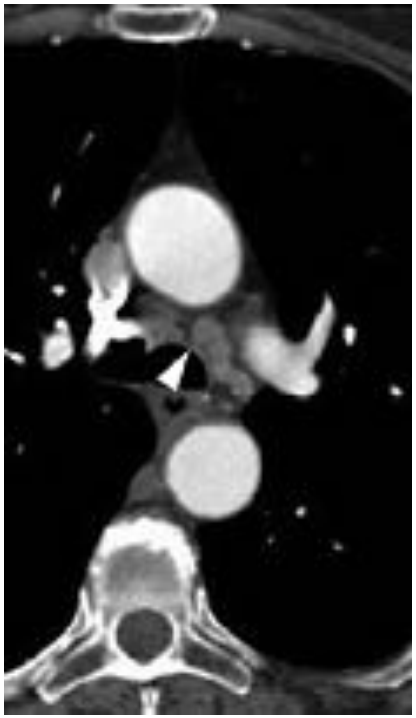
TARGET DEFINITION METHODOLOGY

TARGET DEFINITION: METHODS AND MATERIALS

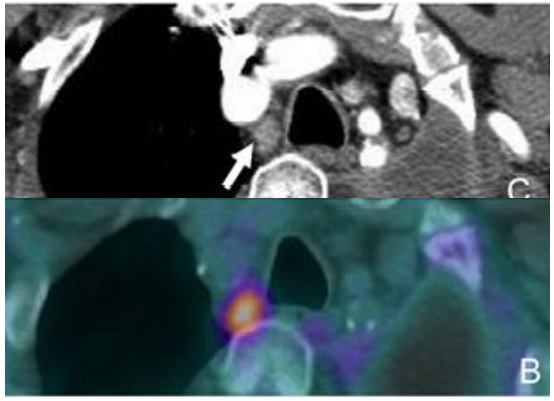
GTV N= THE INVOLVED LYMPH NODES

CT short axis >1cm



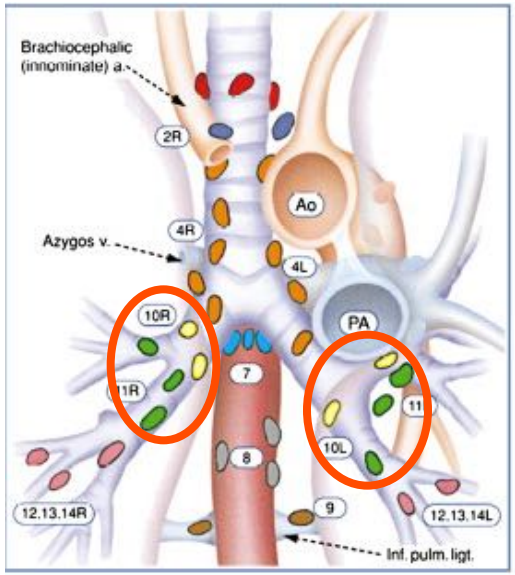
+

PET+ nodes



+

Hilar regions



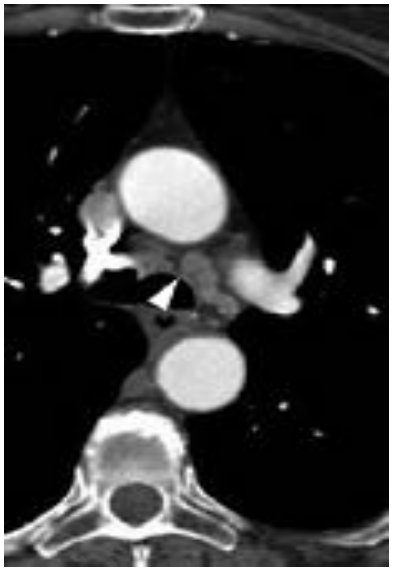
Fernandes, Radiot and Oncology 2010

TARGET DEFINITION: METHODS AND MATERIALS

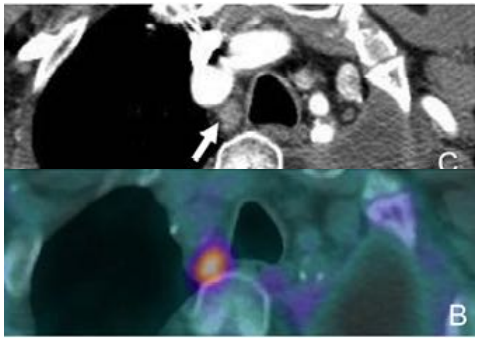
GTV N=

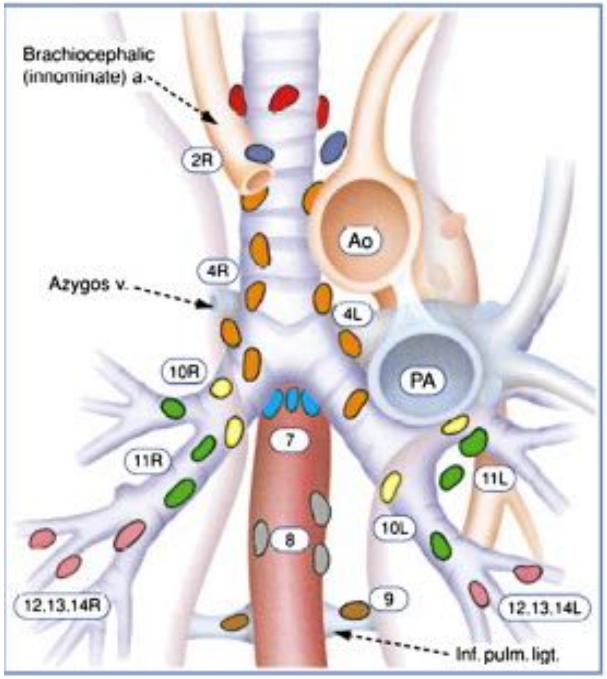
For the right mid lobe or right lower lobe, left lingular, or left lowe lobe lesion, if a mediastinal lymph node was involved, the IPSILATERAL HILAR and SUBCARINAL lymph nodes were treated.

CT short axis >1cm



PET+ nodes





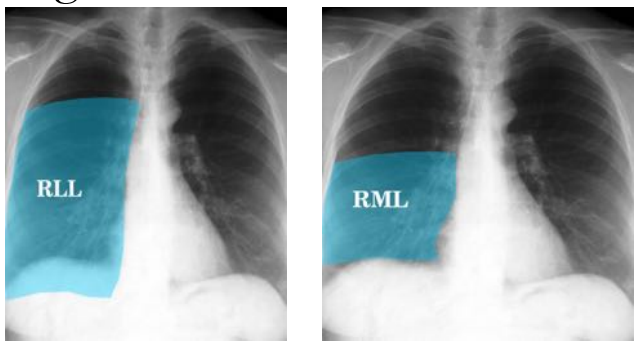
Sulman, Komaki, et al. Radiat Oncol 2009

TARGET DEFINITION: METHODS AND MATERIALS

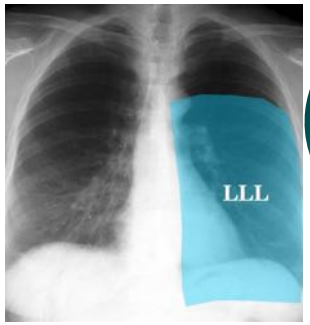
GTV N=

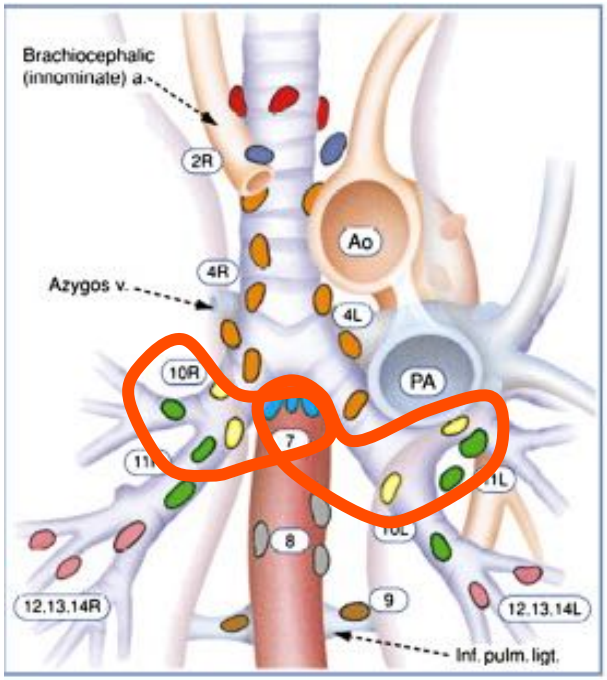
For the right mid lobe or right lower lobe, left lingular, or left lowe lobe lesion, if a mediastinal lymph node was involved, the IPSILATERAL HILAR and SUBCARINAL lymph nodes were treated.

Right medium and lower lobes



Left lower lobe



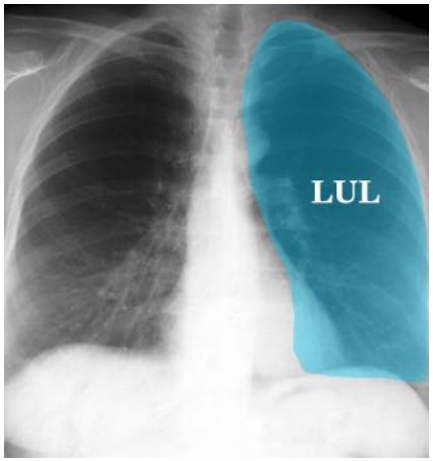


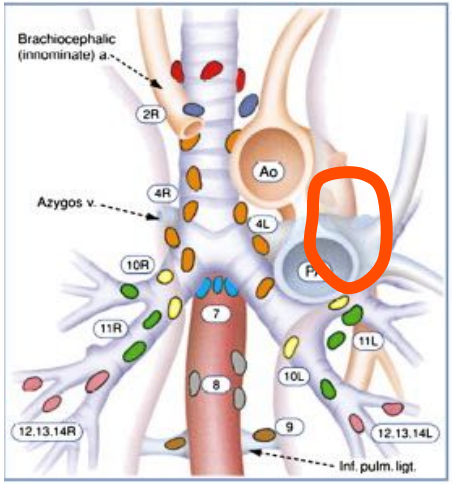
Sulman, Komaki, et al. Radiat Oncol 2009

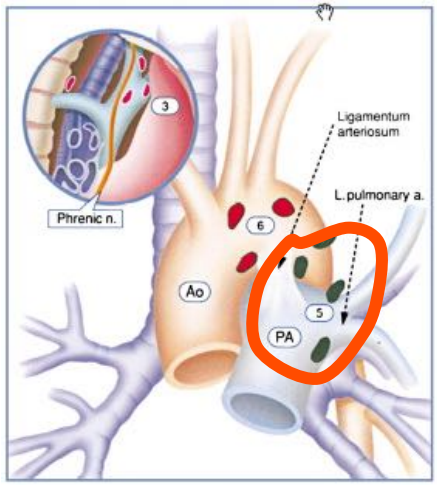
TARGET DEFINITION: METHODS AND MATERIALS

GTV N=

For a left upper lobe lesion, the AORTO-PULMONARY WINDOW lymph node were treated if there was mediastinal lymph node involvement







Sulman, Komaki, Radiat Oncol 2009

TARGET DEFINITION: METHODS AND MATERIALS

GTV N= THE INVOLVED LYMPH NODES

FROM *"ELECTIVE"* NODAL IRRADIATION TO *"SELECTIVE"* NODAL IRRADIATION

UNSOLVED QUESTION:

Fernandes, Radiot and Oncology 2010

Most patients (88%) received either concurrent or sequential CT.

Sulman, Komaki, Radiat Oncol 2009

47% received induction and 53% concurrent chemotherapy.

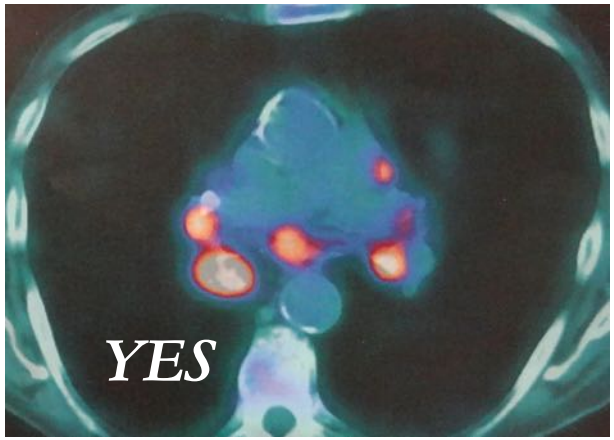
In case of sequential chemo, it was NOT specified if volume was delineated on PRE- or POST- chemotherapy CT

TARGET DEFINITION: METHODS AND MATERIALS

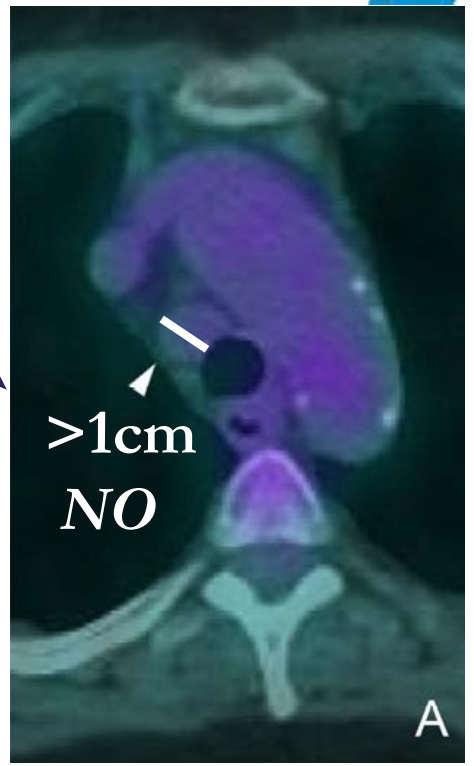
CTV N=

ALL PET-POSITIVE lymph node

PET+ NODES



PET-NEG NODES

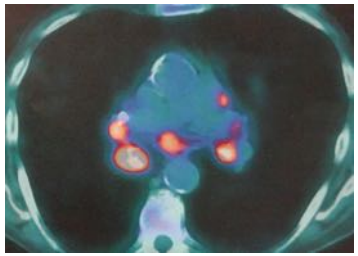


Fleckenstein, Int J Radiat Oncol Biol Phys 2011

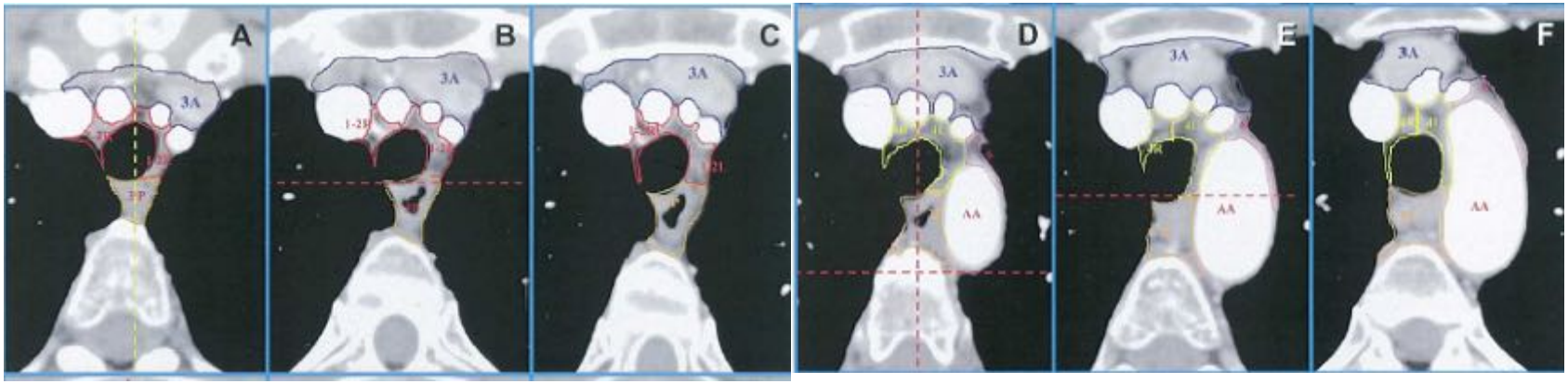
TARGET DEFINITION: METHODS AND MATERIALS

CTV N=

- **All PET-positive** lymph node ***REGIONS***

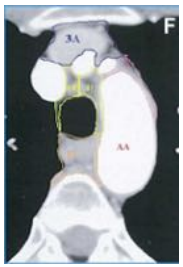


- Thus, all American Joint Committee of Cancer **LYMPH NODE REGIONS**



Fleckenstein, Int J Radiat Oncol Biol Phys 2011

TARGET DEFINITION: METHODS AND MATERIALS



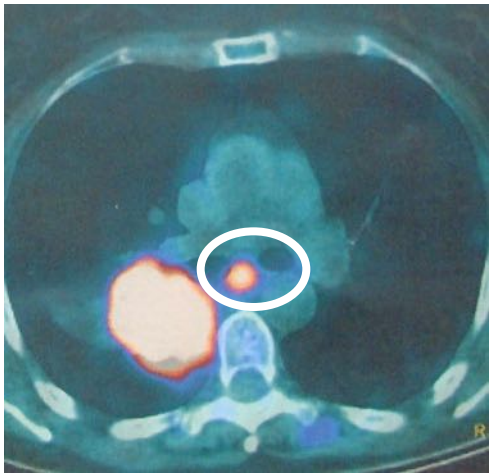
CTV N=

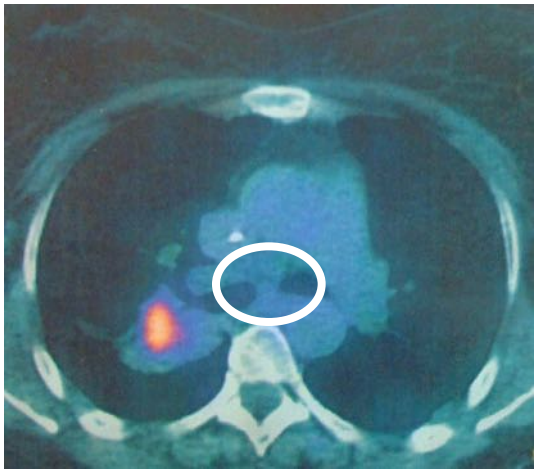
- All and only PET-positive lymph nodes REGIONS
- Induction chemotherapy

GTV was delineated on the **POSTCHEMO** scan.

•If the primary tumor or a pathologic lymph node station reached a **COMPLETE RESPONSE** after chemo, this site was in the GTV.

PET/ CTPRE-CHEMO





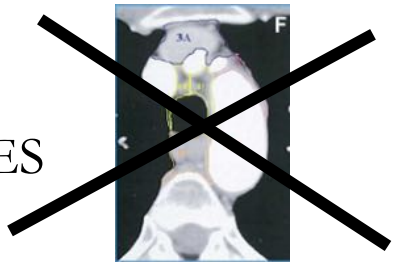
PET/ CTPOST-CHEMO

De Ruysscher Int J Radiat Oncol Biol Phys 2005

TARGET DEFINITION: METHODS AND MATERIALS

CTV N=

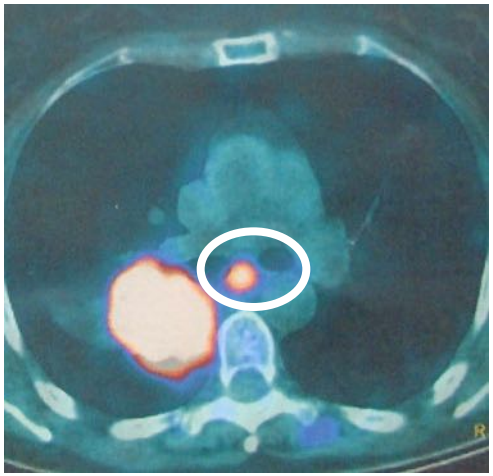
- All and only PET-positive LYMPH NODES
- Induction chemotherapy

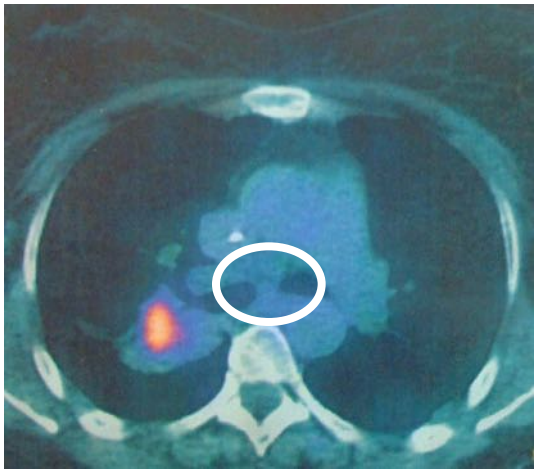


•If the primary tumor or a pathologic lymph node station reached a COMPLETE RESPONSE after chemo, this site was in the GTV.

GTV was delineated on the POST-CHEMO scan.

PET/ CTPRE-CHEMO



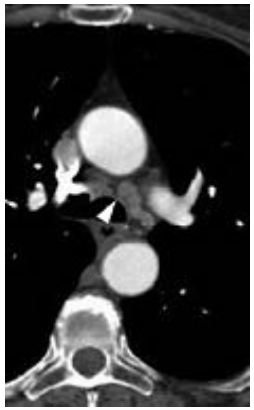


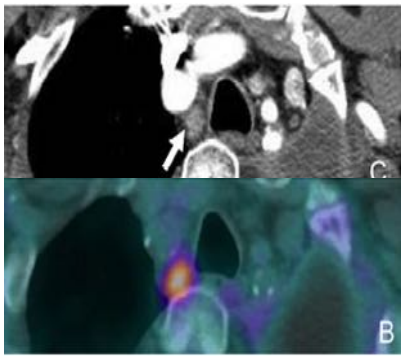
PET/ CTPOST-CHEMO

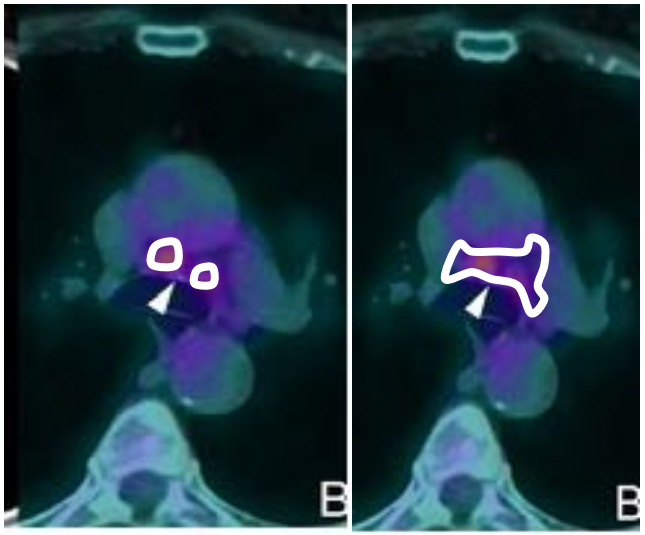
Belderbos, Int J Radiat Oncol Biol Phys 2006

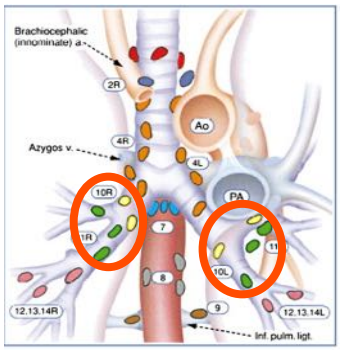
TARGET DEFINITION: METHODS AND MATERIALS

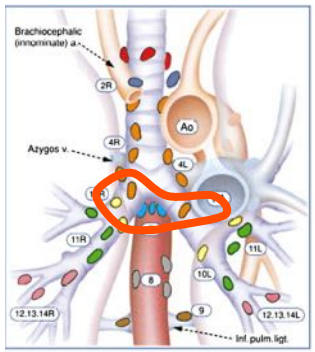
CTV N





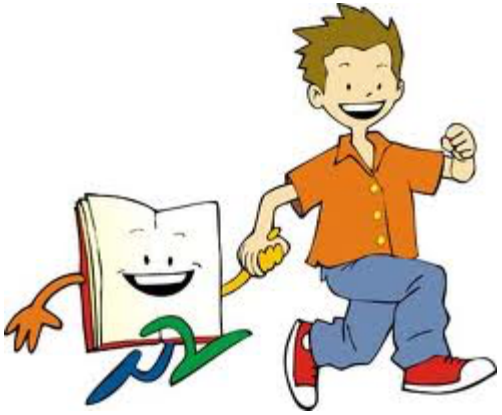






TARGET VOLUME DEFINITION IN L.A. NSCLC:

"A LESSON LEARNED FROM LOCAL RECURRENCES"



SITE OF LOCAL FAILURE :

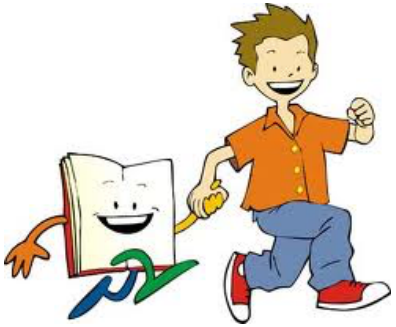
- LOW RISK AREAS OF RELAPSE

- HIGH RISK AREAS OF RELAPSE

De Ruysscher, Radiot Oncol 2011

TARGET VOLUME DEFINITION IN L.A. NSCLC:

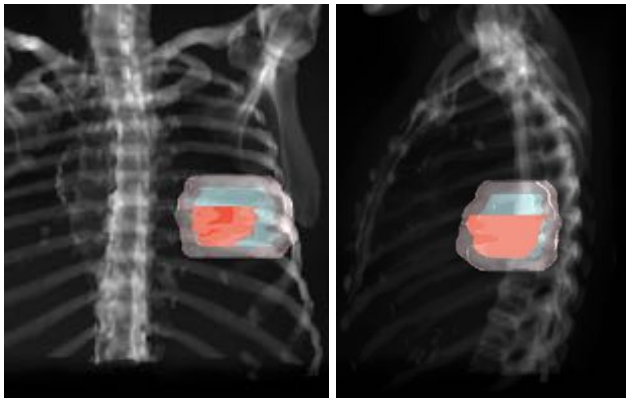
"A LESSON LEARNED FROM LOCAL RECURRENCES"



SITE OF LOCAL FAILURE :

HIGH RISK AREAS OF RELAPSE

SUBVOLUMES OF PRIMARY TUMOR

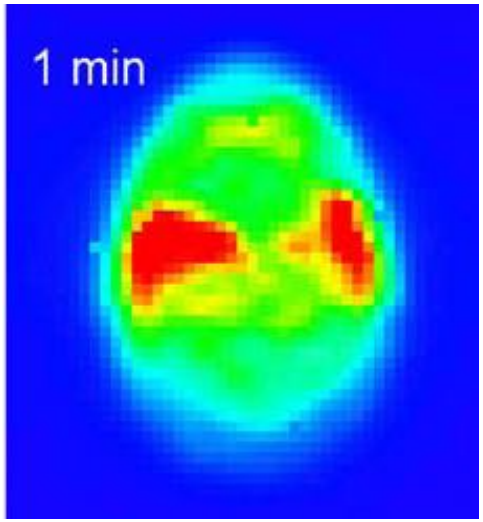


De Ruysscher, Radiot Oncol 2011

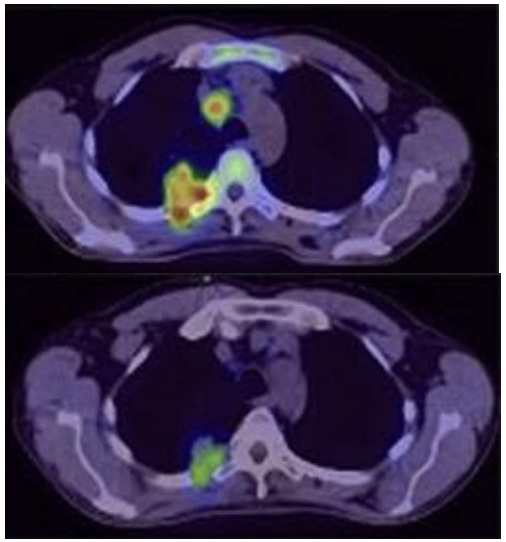
TARGET VOLUME DEFINITION IN L.A. NSCLC:

SUBVOLUMES OF PRIMARY TUMOR

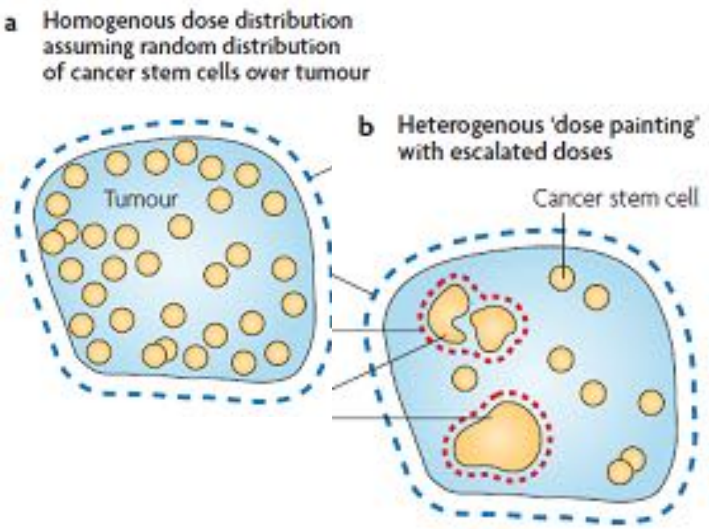
- Hypoxia
- Proliferation
- Stem cells



The 18F-MISO images



The 18F-FLT PET/CT images



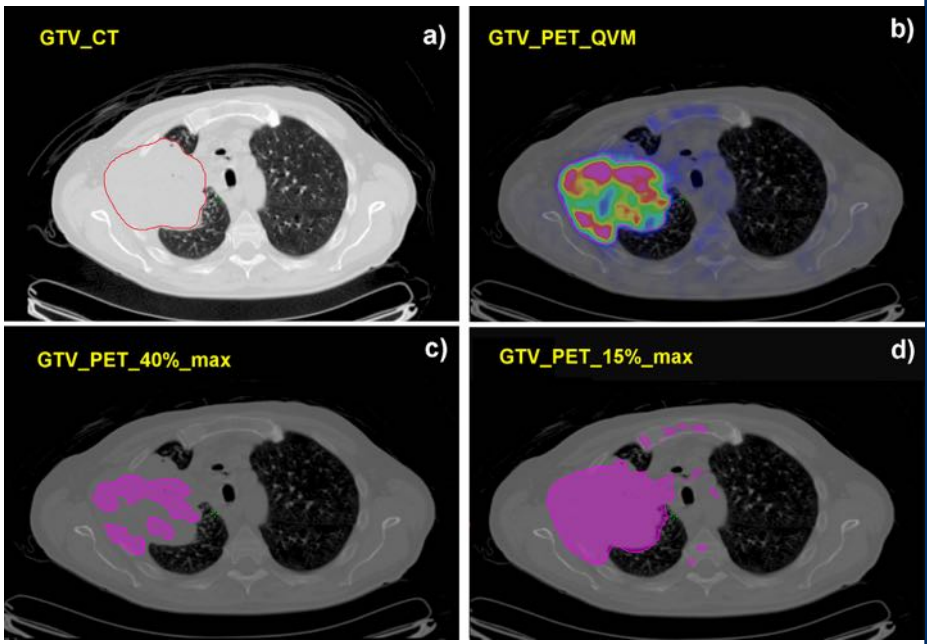
Padhani, Eur Radiol (2007) 17: 861–872
Baumann, Nature reviews. Cancer 2008
Everitt, Int. J. Rad Oncol Biol Phys, 75:1098–1104, 2009

TARGET VOLUME DEFINITION IN L.A. NSCLC:

SUBVOLUMES OF PRIMARY TUMOR

FDG PET- based counturing methods

- Visual GTV
- SUVmax2.5
- %SUVmax (15%, 40%..)
- Source-to-background ratio
- Gradient-based method



Shirai, Int Journ of mol imaging 2012

TARGET VOLUME DEFINITION IN L.A. NSCLC:

SUBVOLUMES OF PRIMARY TUMOR

EDITORIAL

FDG-PET IN RADIOTHERAPY TREATMENT PLANNING: PANDORA'S BOX?

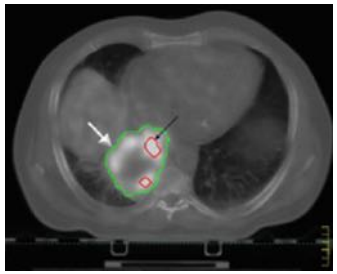
ARNOLD C. PAULINO, M.D., AND PETER A. S. JOHNSTONE, M.D.

PANDORA'S BOX

Paulino Int. J. Radiation Oncology Biol. Phys., Vol. 59, No. 1, pp. 4–5, 2004

TARGET VOLUME DEFINITION IN L.A. NSCLC:

SUBVOLUMES OF PRIMARY TUMOR



PET- imaging

PANDORA'S BOX

"A LESSON LEARNED FROM LOCAL RECURRENCES"

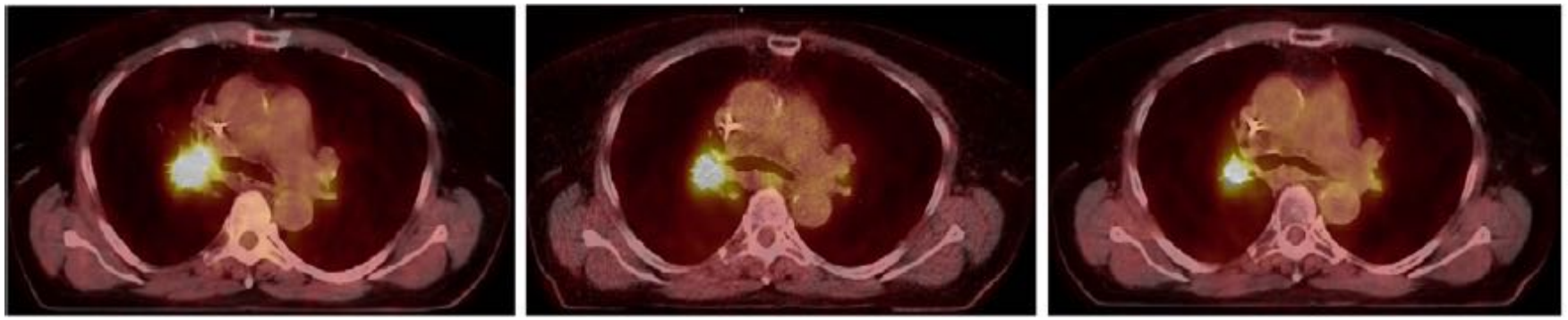
Nestle, Radiotherapy and Oncology 81 (2006) 209–225

Is pre-therapeutical FDG-PET/CT capable to detect high risk tumor subvolumes responsible for local failure in non-small cell lung cancer?

LOCOREGIONAL RELAPSE: *WHERE*

PET/CT

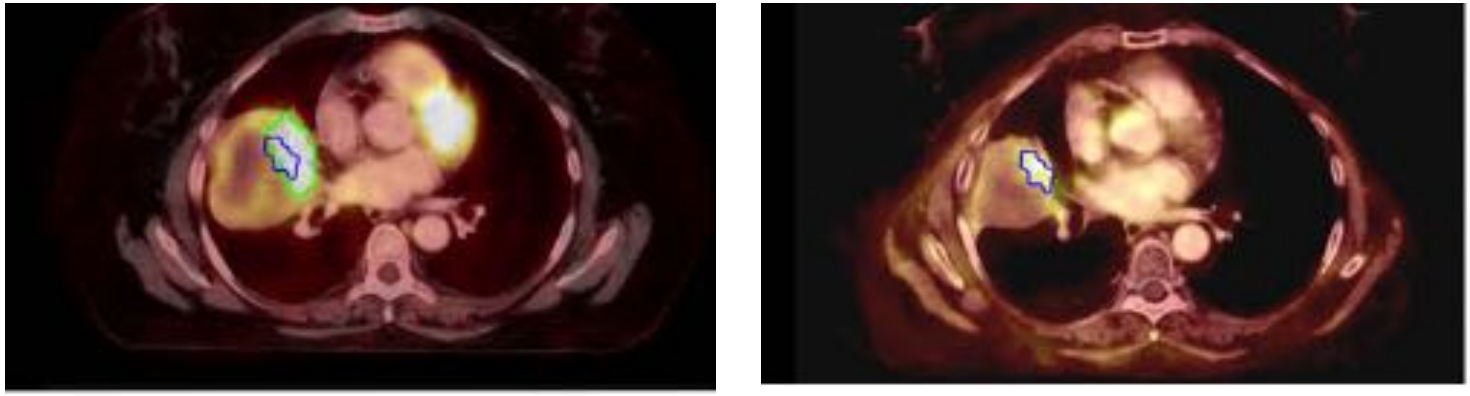
BEFORE RT *DURING RT* *AFTER RT*



Tumor recurrence were localized mostly in the ***MOST ACTIVE ONES*** of pre-therapeutically metabolic regions.

Abramyuk, Radiot Oncol 2009; 91: 399-404

Identification of residual metabolic-active areas within individual NSCLC tumours using a pre-radiotherapy ^{18}Fluorodeoxyglucose-PET-CT scan



The ***HOTSPOT*** within the residual area (90%SUV) was completely ***WHITIN THE GTV*** (OF=100%).

Aerts, Radiotherapy and Oncology 2009; 91: 386-392

STABILITY OF ^{18}F-DEOXYGLUCOSE UPTAKE LOCATIONS WITHIN TUMOR DURING RADIOTHERAPY FOR NSCLC: A PROSPECTIVE STUDY

Green lines indicate 60% of maximal standardized uptake value (SUV_{max}) threshold.

RESULT 1

The ***LOCATION*** of the high FDG uptake patterns within the tumor during RT remained ***STABLE***.

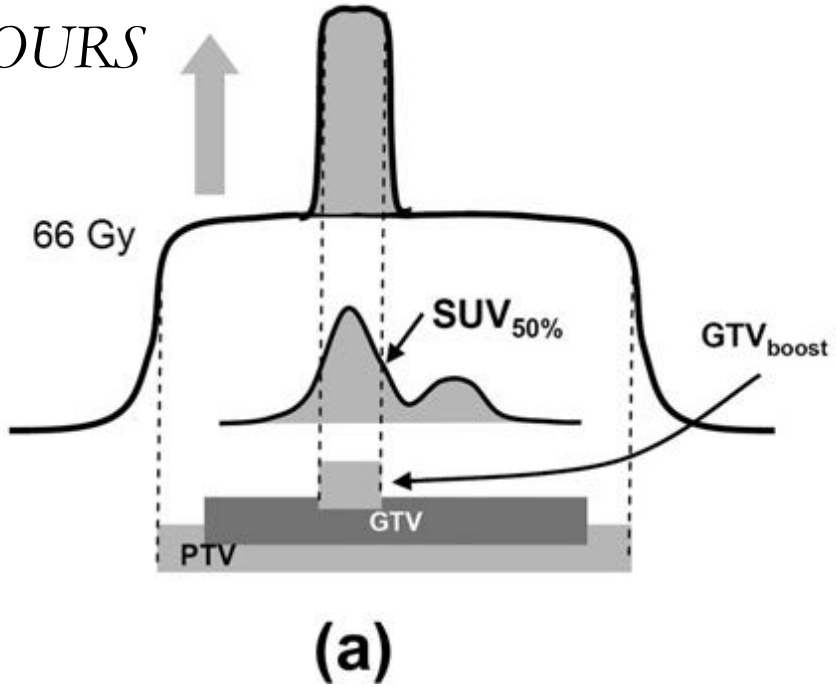
Aerts, Int J Radiat Oncol Biol Phys 2008

DOSE PAINTING

"Locally boosting the tumor to increase local control based on functional imaging." Two approaches can be distinguished:

- *DOSE PAINTING BY CONTOURS*

  Boost volume is created based on certain threshold. The voxel with values BELOW this threshold are considered to be at low risk for recurrence and the voxel with value ABOVE this threshold are considered to be at high risk.



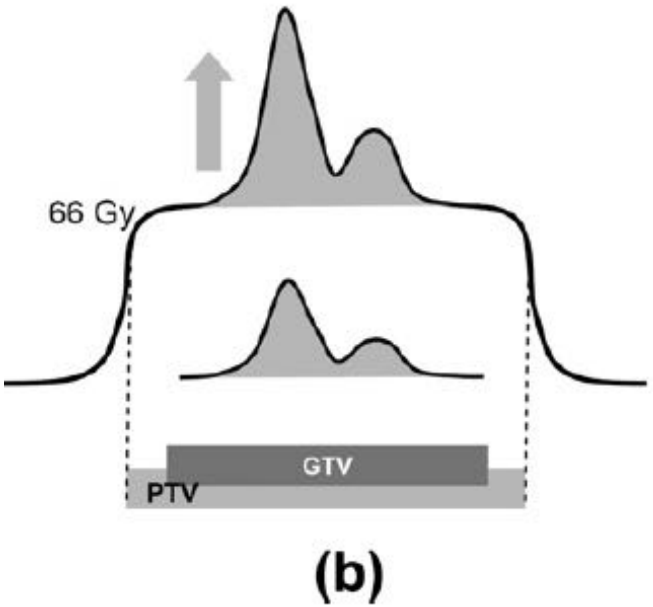
Maijer, Radiotherapy and Oncology 2011; Chao KS, Int J Radiat Oncol Biol Phys 2001
Madani I, Int J Radiat Oncol Biol Phys 2006; De Ruysscher D, Radiother Oncol 2011

DOSE PAINTING

"Locally boosting the tumor to increase local control based on functional imaging." Two approaches can be distinguished:

- *DOSE PAINTING BY NUMBERS*

A continuously increasing relationship is assumed between the voxel intensity of the functional imageset in question and the risk of local recurrence in that voxel.



Maijer, Radiotherapy and Oncology 2011; Chao KS, Int J Radiat Oncol Biol Phys 2001
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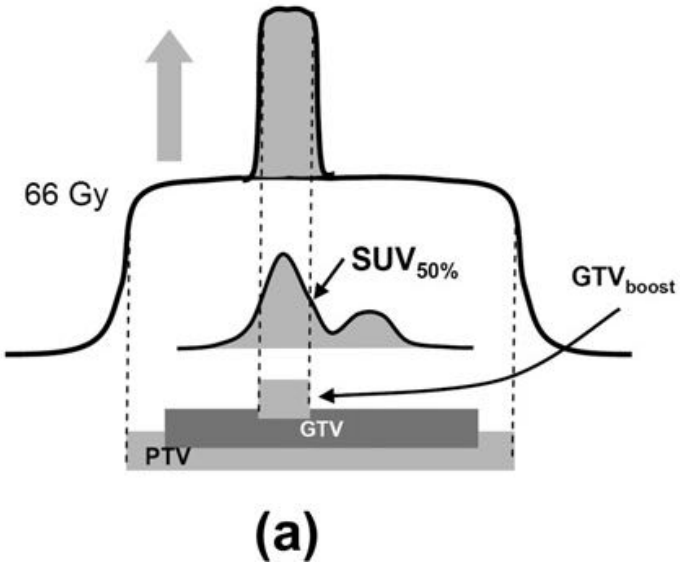
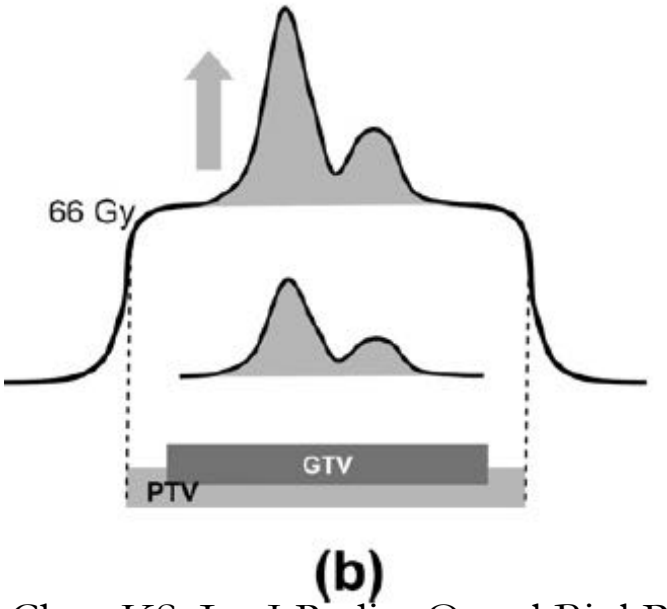


DOSE PAINTING BY NUMBERS



Maijer, Radiotherapy and Oncology 2011; Chao KS, Int J Radiat Oncol Biol Phys 2001
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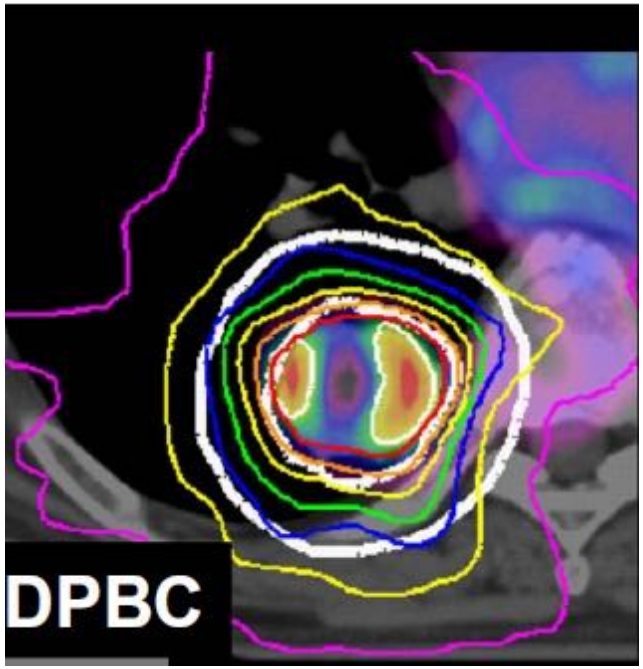
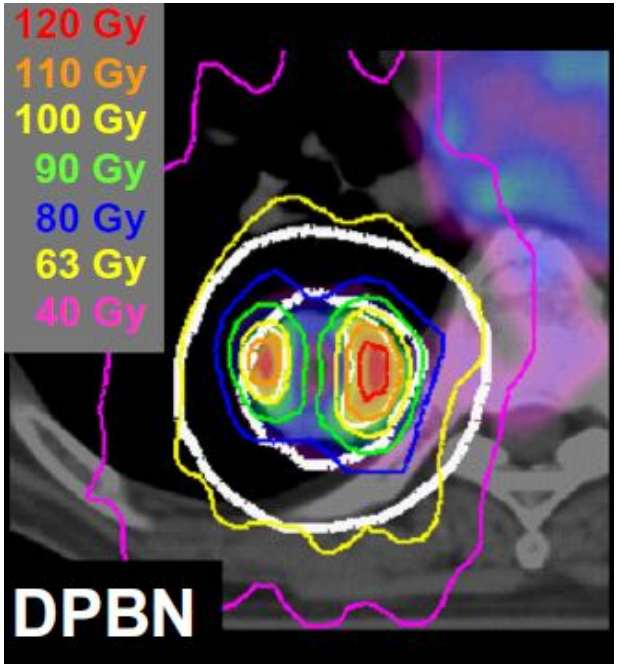
DOSE PAINTING

DOSE PAINTING BY CONTOURS

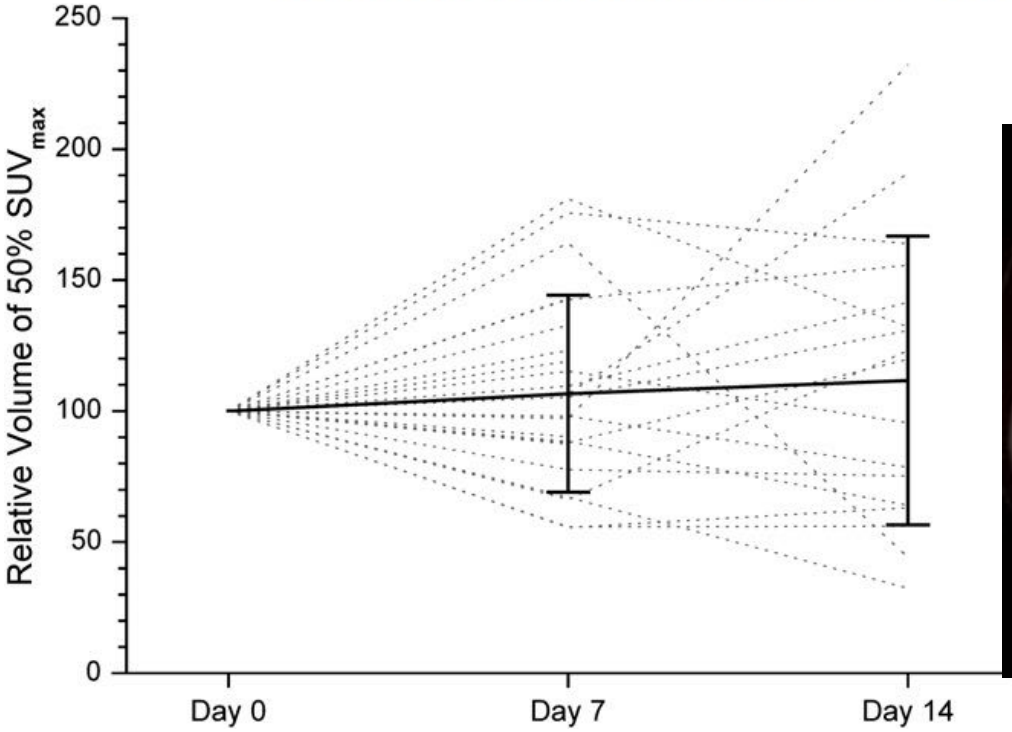


DOSE PAINTING BY NUMBERS



Maijer, Radiotherapy and Oncology 2011; 100: 396-401

STABILITY OF ^{18}F-DEOXYGLUCOSE UPTAKE LOCATIONS WITHIN TUMOR DURING RADIOTHERAPY FOR NSCLC: A PROSPECTIVE STUDY



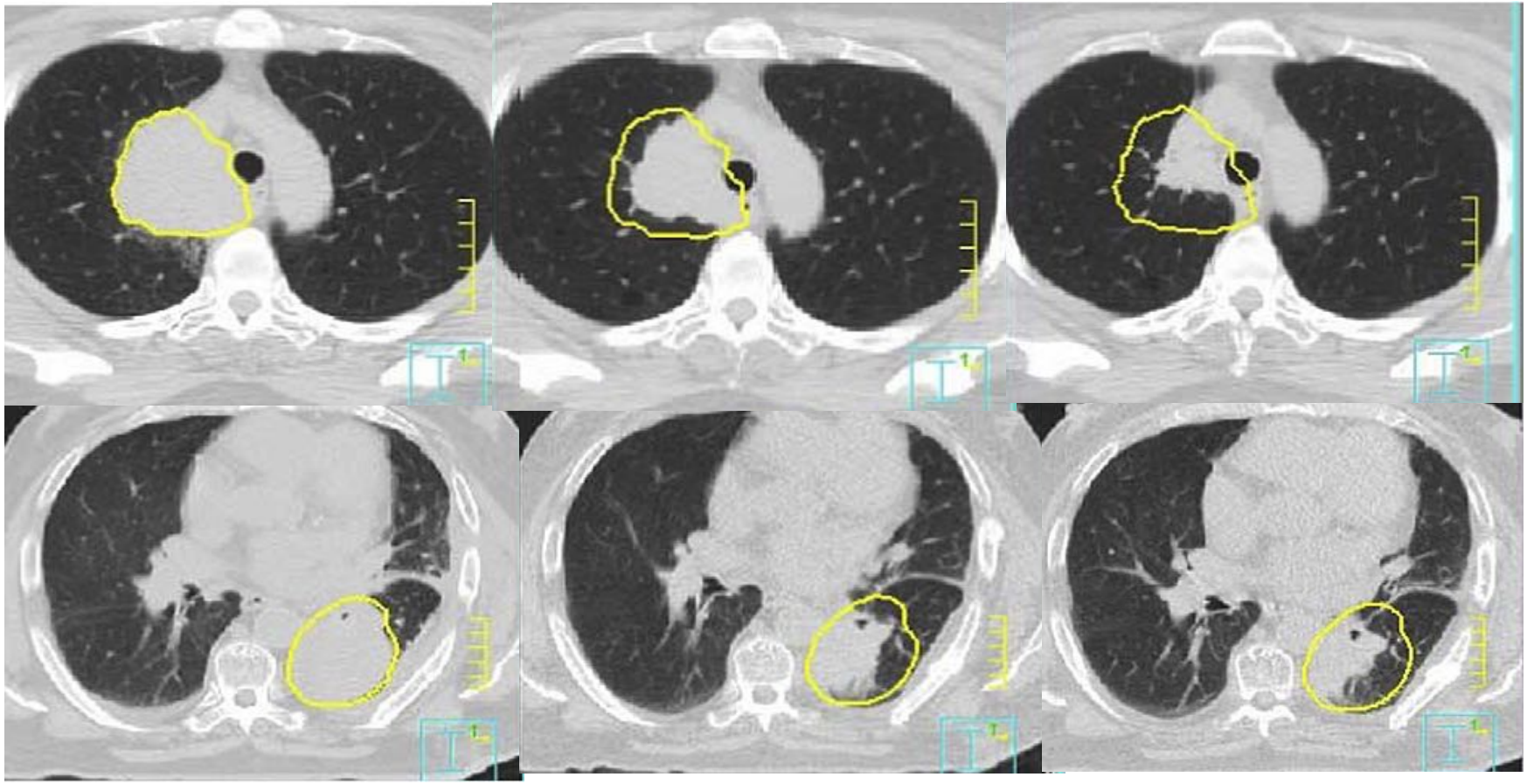
RESULT 2

The ***VOLUME*** of the Volume 50% SUV ***VARIED MARKEDLY*** (at Day 0, the volume of the 60% zone was 16.8 ± 20.3 cm3).

Aerts, Int J Radiat Oncol Biol Phys 2008

TARGET VOLUME DEFINITION IN L.A. NSCLC:

ADAPTIVE RADIOTHERAPY



Fox J, Ford E, Redmond K, Int. J. Radiation Oncology Biol. Phys., 74(2) pp. 341–348, 2009

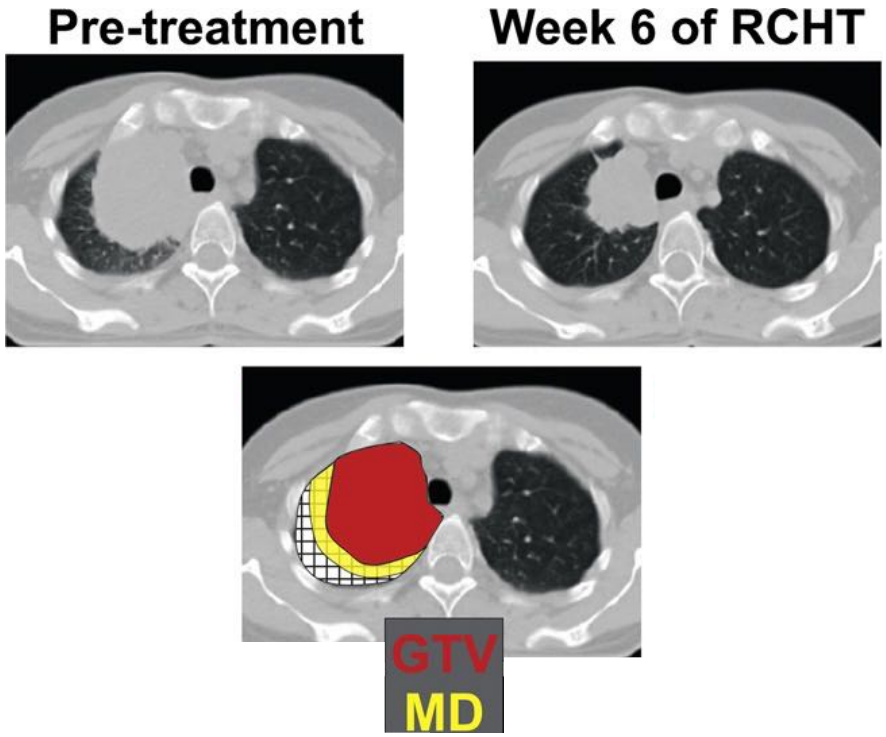
TARGET VOLUME DEFINITION IN L.A. NSCLC:

ADAPTIVE RADIOTHERAPY

	N° pts	*RT delivery*	*Initial volume Median (range) cc*	*GTV % Reduction*	*% reduction per fraction*
Lim 2009	31	3DCRT	63.9 (3.4-421.8) (*primitive tumor: T*)	40.2% @30Gy 51.1% @45-66Gy	1.65 (0.82-2.49)
Fox 2009	22	3DCRT	81.72 (7.37-16.35) *(primitive tumor: T)*	24.7% 44.3%	NR
Kupelian 2005	10	TOMO	5.9-737.2	NR	1.2 (0.6-2.3)
Siker 2006	25	TOMO	NR	29 (4.5-80)	NR
Woodford 2007	17	TOMO	127+/-115 (SD)	38% (12-87)	0.79 (0.24-1.65)
Trodella 2012	***18***	***3DCRT***	***186.6 (32.7-532.7) (CTV:T+N)***	***47.9% (29.8-82.5) Mean dose 36Gy***	***2.55(1.28-4.98)***

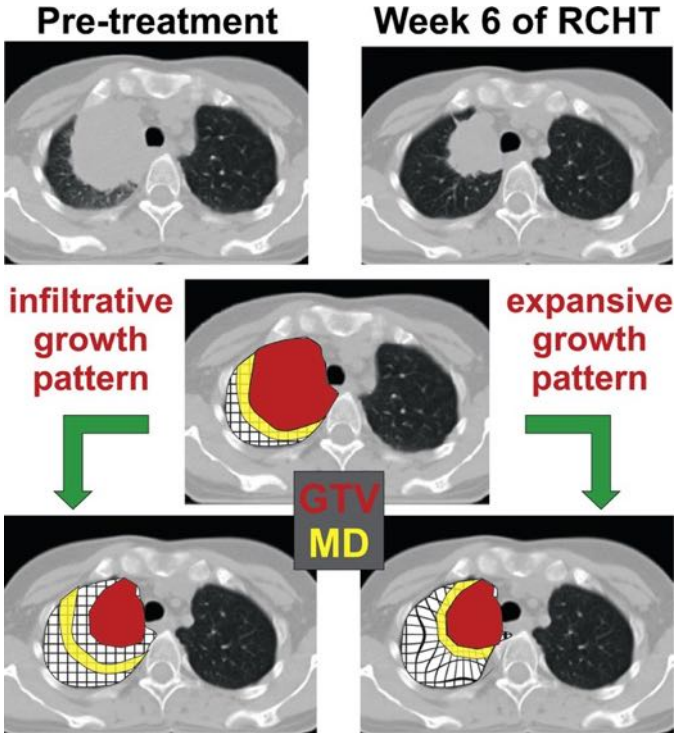
TARGET VOLUME DEFINITION IN L.A. NSCLC:

ADAPTIVE RADIOTHERAPY



TARGET VOLUME DEFINITION IN L.A. NSCLC:

ADAPTIVE RADIOTHERAPY

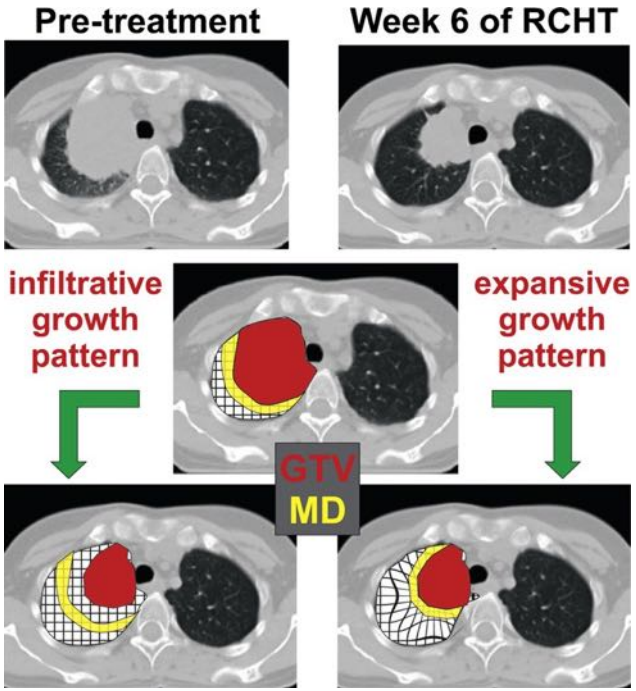


Dose distributions to the volumes of suspect MD were simulated for a scenario with synchronous shrinkage of the MD and GTV and for a scenario of a stationary MD despite GTV shrinkage; simulations were performed using deformable image registration.
TCP calculations considering doses to the GTV and MD were performed.

Guckenberger, Int J Rad Oncol Biol Phys, 81:e275–e282, 2011

TARGET VOLUME DEFINITION IN L.A. NSCLC:

ADAPTIVE RADIOTHERAPY



"Adaptation of radiotherapy to the shrinking GTV ***DID NOT COMPROMISE*** dose coverage of volumes of suspect ***MICROSCOPIC DISEASE*** and has the potential to increase TCP by >40% compared with radiotherapy planning without ART."

Guckenberger, Int J Rad Oncol Biol Phys, 81:e275–e282, 2011

TARGET VOLUME DEFINITION IN L.A. NSCLC:

MICROSCOPIC DISEASE EXTENSION (MDE)

Giraud 2000: GTV+ 6-8mm (SCC vs ADK)

GTV-CT OVERESTIMATES GTV-PATH

Van Loon 2012	by 6.6mm
Grills 2007	by 5.8mm

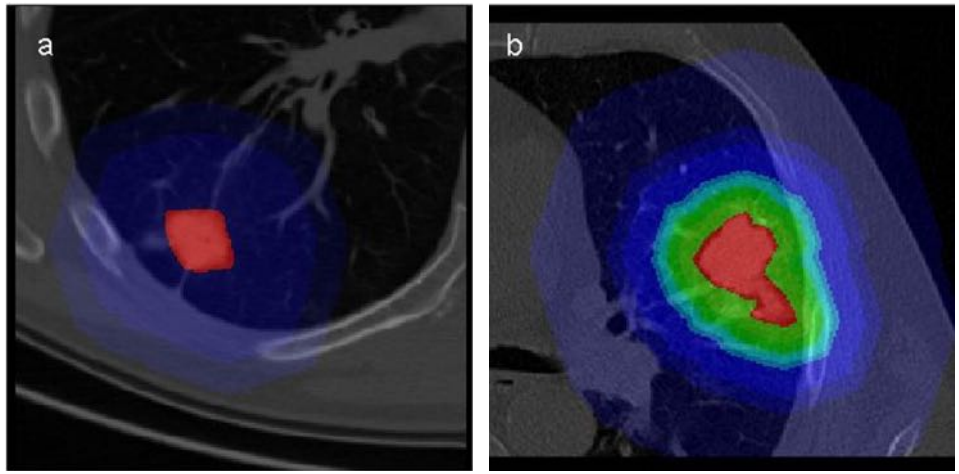
For 3DCRT a CTV margin of 3 mm is sufficient to obtain an MDE-specific control probability of 90%.

Giraud P, Int J Radiat Oncol Biol Phys 2000;48:1015–1024
Van Loon, Int J Radiat Oncol Biol Phys 2012;82:448–456
Grills IS, Int J Radiat Oncol Biol Phys 2007;69:334–341
Siedschlag, Radiotherapy and Oncology 100 (2011) 344–350

MICROSCOPIC DISEASE EXTENSION (MDE)

MDE does not occur in all patients: ***50% patients***

LOW RISK OF MDE



HIGH RISK OF MDE

Variable	MDE absent: Mean ± SD	MDE present: Mean ± SD	UVA: *p* value	MVA: *p* value
GTV_{CT} (cm^3)	22.9 ± 11.4	61 ± 21.1	0.14	0.03
CT mean (Hounsfield units)	−237 ± 22.8	−164 ± 24.1	0.04	0.03
CT Circularity	0.78 ± 0.02	0.71 ± 0.03	0.10	NS
SUV_{max}	9.7 ± 4.9	11.7 ± 1.4	0.28	NS
GTV_{PET} (cm^3)	9.8 ± 3.1	24.6 ± 5.7	0.04	NS
Tumor type (% with adenocarcinoma)	58 %	35 %	0.18	NS
Age (years)	58.4 ± 11.4	62.6 ± 11.4	0.29	NS

Van Loon, Int J Radiat Oncol Biol Phys 2012;82:448–456

CLINICAL TARGET VOLUME DEFINITION

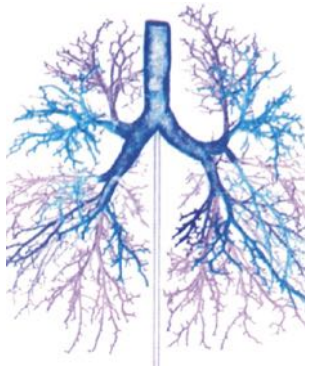
A. Radiological Anatomy

- Normal structures, Pitfalls and Nodal Stations

B. Non-Small Cell Lung Cancer

- Locally Advanced Disease

C. Small Cell Lung Cancer



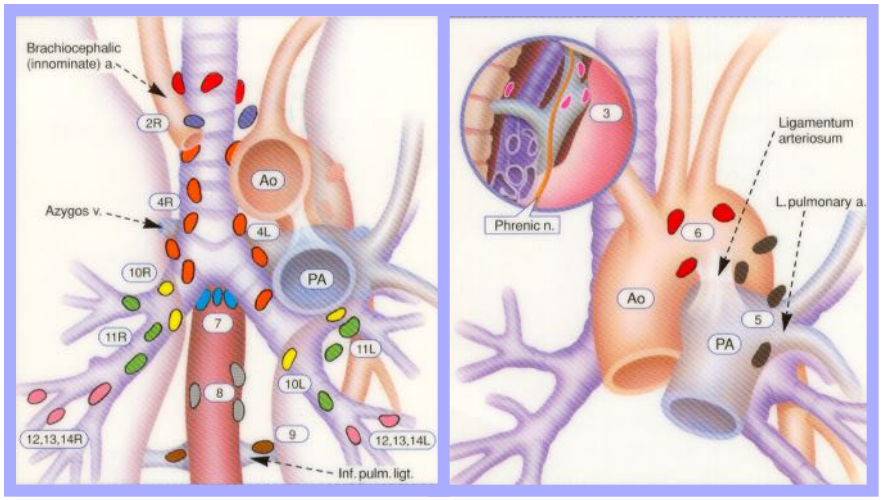
TARGET VOLUME DEFINITION IN L.A. NSCLC:

SMALL CELL LUNG CANCER

Controversy exist among radiation oncologist regarding the most effective way to define "***Cancer Target***"

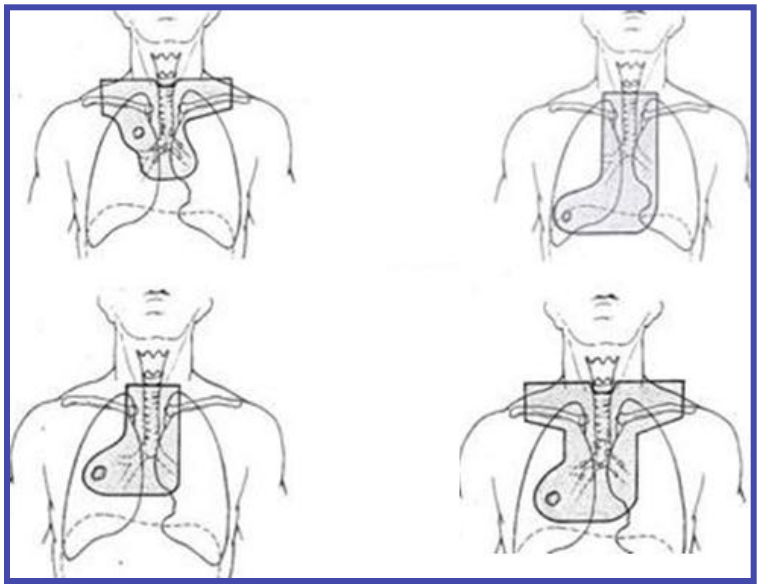
This is especially true with MEDIASTINAL lymph node irradiation…..

ENI vs INVOLVED



SMALL CELL LUNG CANCER: ENI vs no-ENI

- *466 patients*
- *2D planning*
- *No platinum-based* chemo



CHEMO → Partial Response / Complete Response

SWOG-Phase III
Kies MS, et al. J. Clin. Oncol. 1987

SMALL CELL LUNG CANCER: ENI vs no-ENI

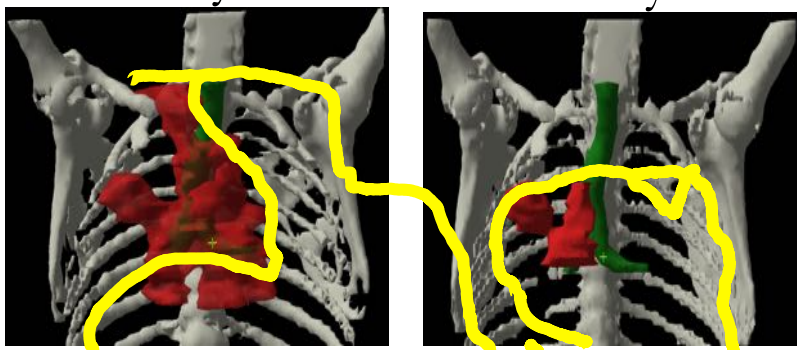
LOCAL RELAPSE

PR

Radiotherapy

30 Gy

30 Gy

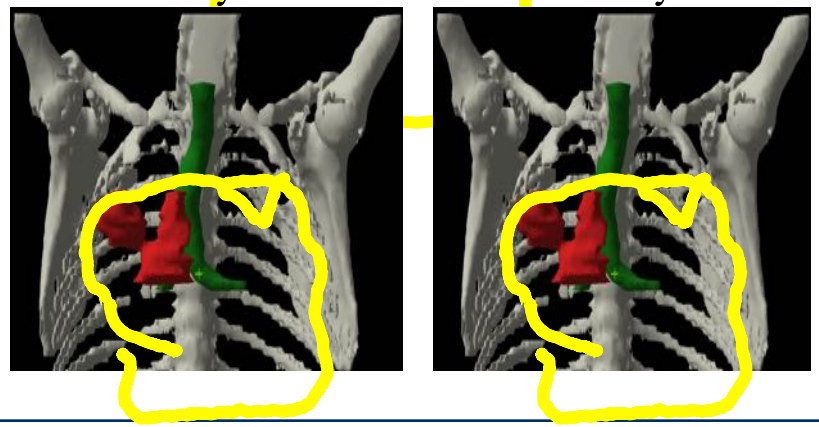


→ 32%

Radiotherapy

30 Gy

30 Gy



→ 28%

p=NS

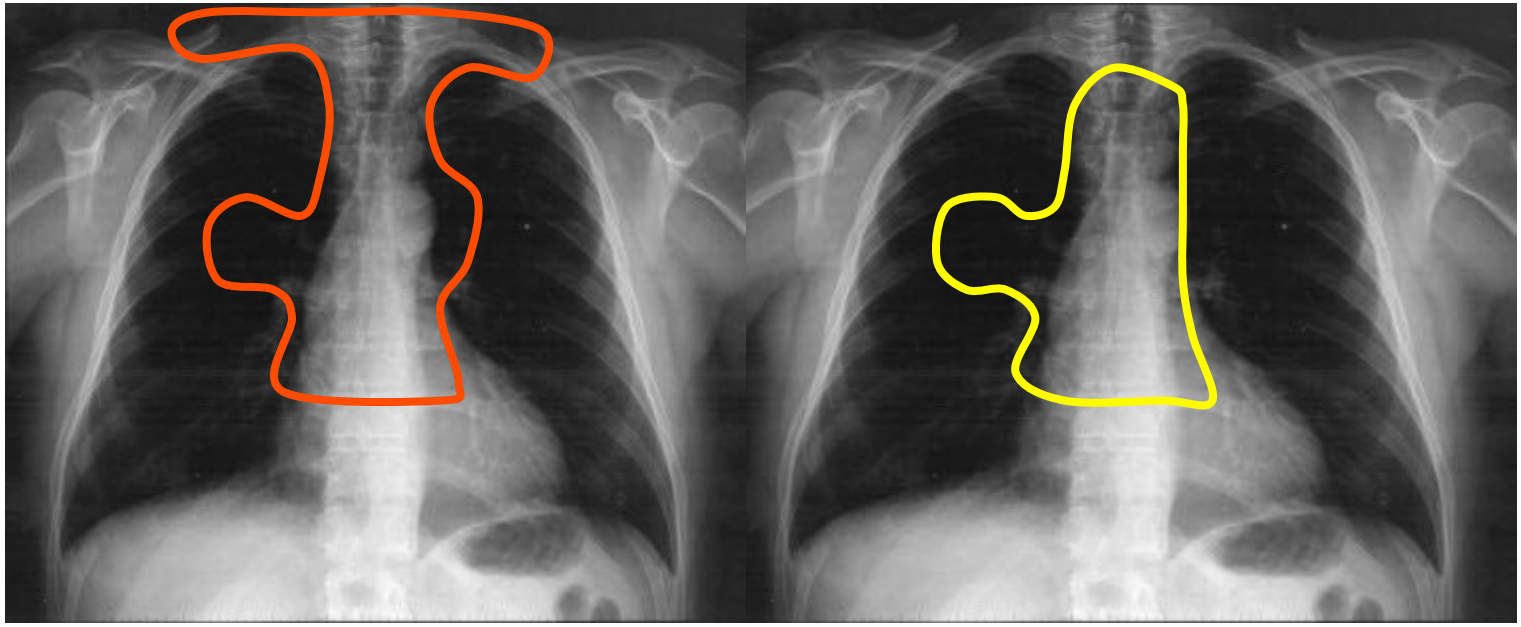
SWOG-Phase III

Kies MS, et al. J. Clin. Oncol. 1987

TWICE-DAILY COMPARED WITH ONCE-DAILY THORACIC RADIOTHERAPY IN LIMITED SMALL-CELL LUNG CANCER TREATED CONCURRENTLY WITH CISPLATIN AND ETOPOSIDE

GTV: tumor defined by CT scanning, included full mediastinum and ipsilateral hilum but no supraclavicular fossae

From ENI to not ENI

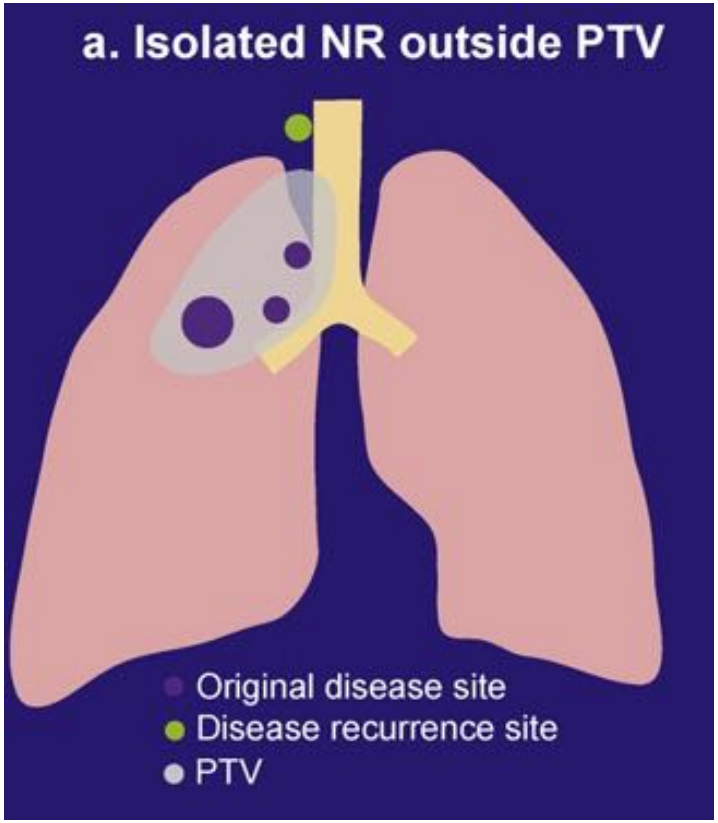


Turrisi A, N Engl J Med 1999;340:265-71
George R. Simon, Chest. 2003;123:259S-271S

SMALL CELL LUNG CANCER: ENI vs no-ENI

MODERN STUDIES:

Liengswangwong et al. J. Clin. Oncol. 1994;12:496±502. Mayo Clinic	100%In field recurrence
Brodin O,et al. Acta Oncol. 1990;29:739±746	86%In field recurrence

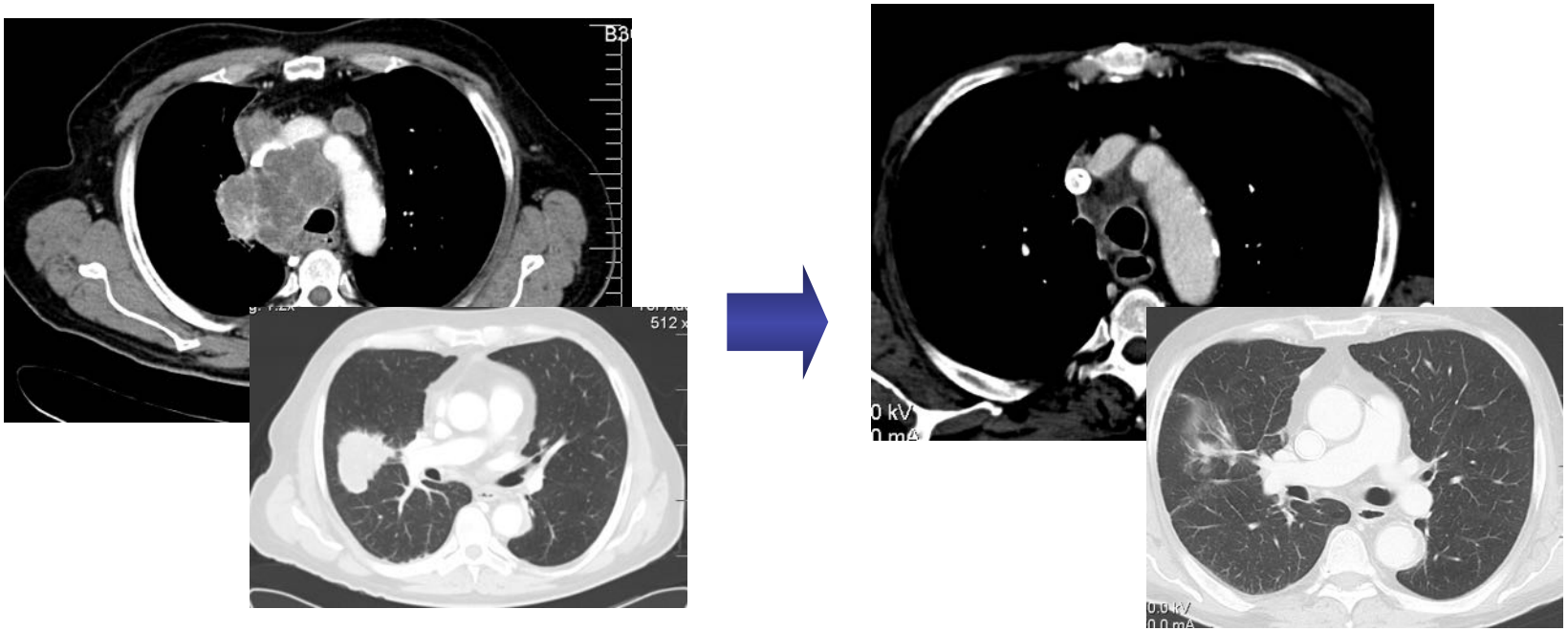


NO OUT-FIELD RECURRENCES

SMALL CELL LUNG CANCER:

In 2004 a new approach….

GTV: **RESIDUAL** lung tumor after induction CHT and with involved limph node **REGIONS** both pre and post CHT

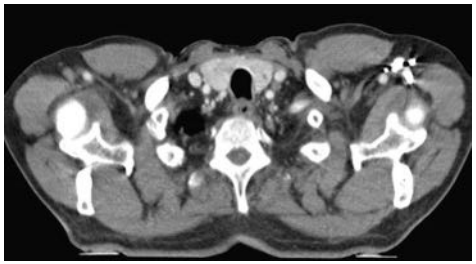


CT-BASED IMAGING

Bogart JA, CALGB, Int J Radiat Oncol Biol Phys 2004;59:460–468.

SMALL CELL LUNG CANCER:

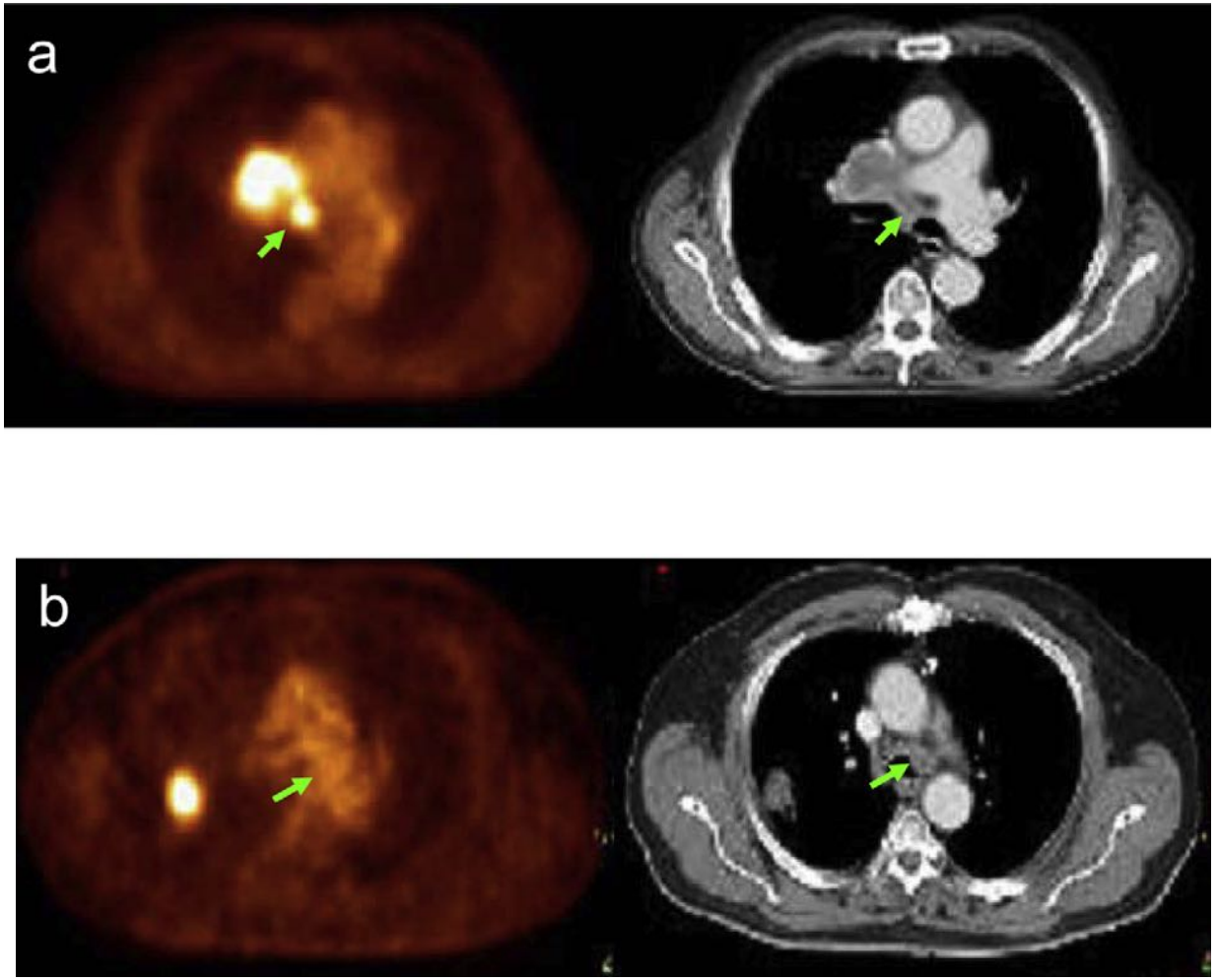
CT-BASED IMAGING



De Ruysscher Radioth Oncol 2006	"The omission of elective nodal irradiation on the basis of CT scans in patients with LD-SCLC resulted in a **HIGHER THAN EXPECTED** rate of isolated nodal failures (***11%***) in the ipsilateral supraclavicular fossa."
Giuliani Radioth Oncol 2012	"We recommend that **ADJACENT** elective nodal volumes be included in patients who are staged and planned on CT alone. The **EXTENT** of pre-chemotherapy disease should also be carefully considered in RT."

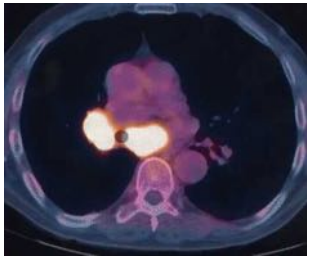
SMALL CELL LUNG CANCER: ENI vs no-ENI

PET IMAGING
improved definition of clinically involved vs uninvolved nodes

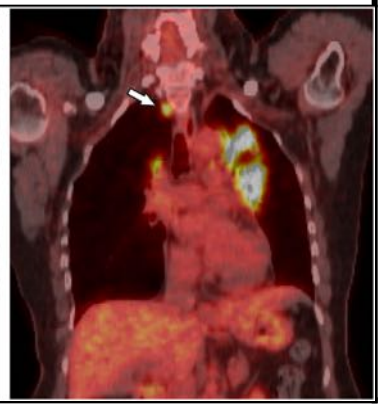


SMALL CELL LUNG CANCER:

PET-BASED IMAGING



Van Loon Int J Radiot Oncol Biol Phys 2010	T: POST-CHEMO VOLUME N: PRE-CHEMO STATIONS "In the present study, with **SELECTIVE NODAL IRRADIATION** based on PET, isolated nodal recurrences occurred in **3%** of patients"
Shirvani Int J Radiot Oncol Biol Phys 2012	"Involved-field RT using **IMRT guided by PET-CT**. Isolated nodal failure **1,6**%"



CLINICAL TARGET VOLUME DEFINITION

Take Home Messages (1)

Knowledge of normal radiological anatomy (normal structures, pitfalls and nodal stations) is the prerequisite for target delineation

The introduction of FDG-PET in Lung Cancer (NSCLC and SCLC) improved target delineation and reduced isolated nodal recurrences

CLINICAL TARGET VOLUME DEFINITION

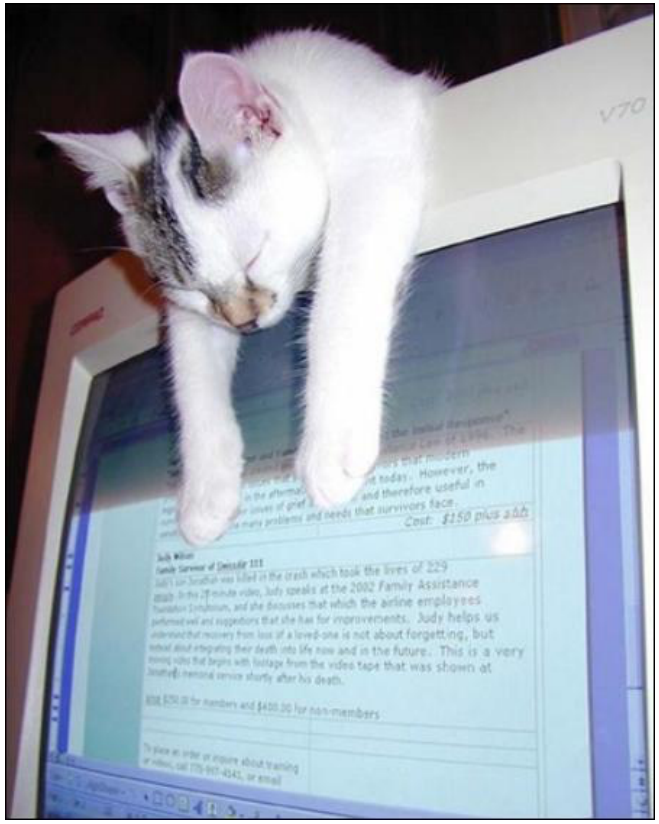
Take Home Messages (2)

In L.A. NSCLC the role of ENI is not recommended

Particular attention should be given to the counturing methodology.

Recent evidences suggest that high risk areas of recurrence are subvolumes among the GTV.

In SCLC elective mediastinum irradiation could be omitted if patient is primary staged with FDG-PET.



Thank you !