De nieuwe anatomische afbakening van de mediastinale lymfeklieren

Peroperatieve N stagering

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UZ Antwerpen

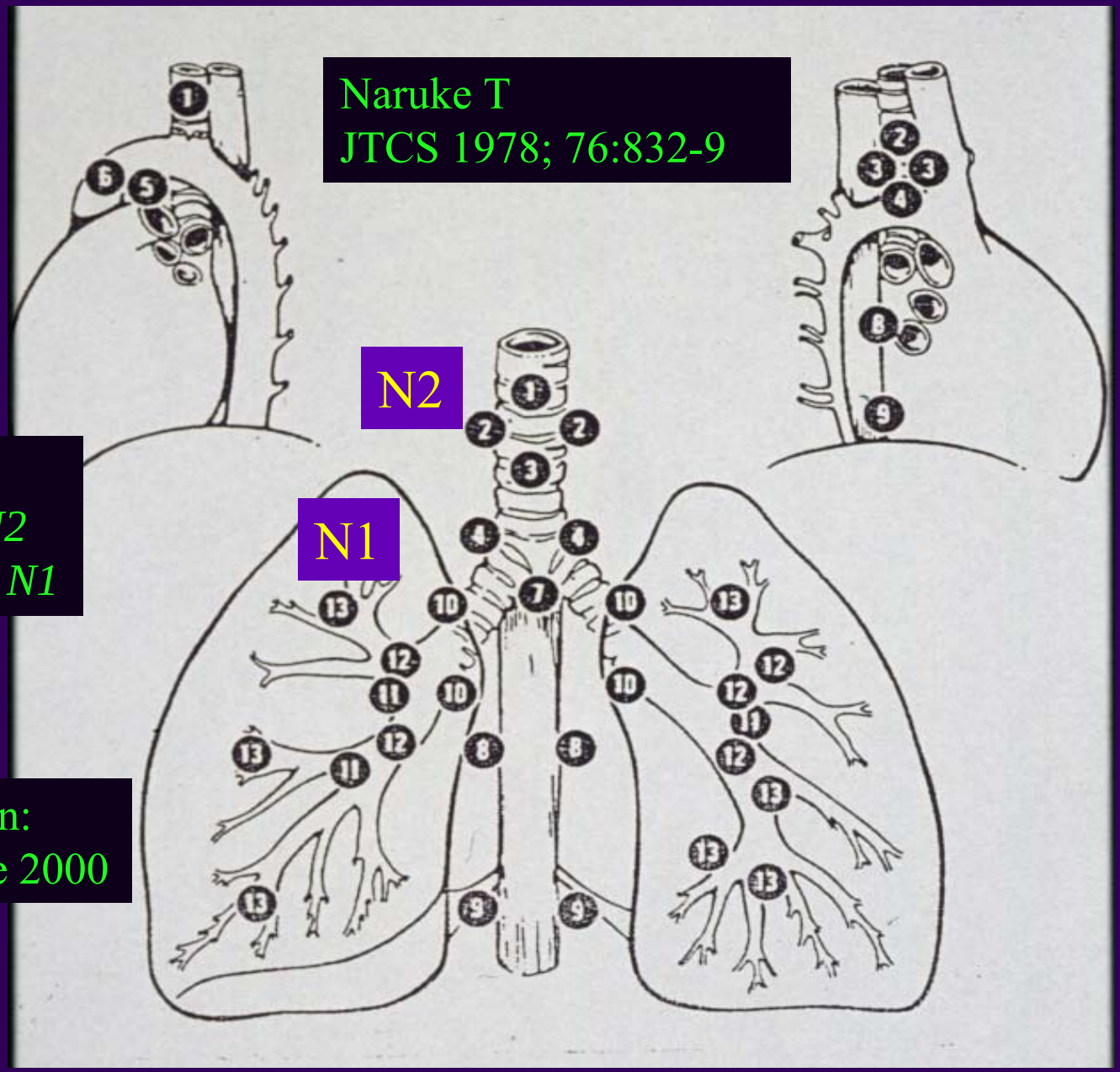
TOGA symposium, 23 oktober 2009

LN mapping and staging

Lymph node mapping

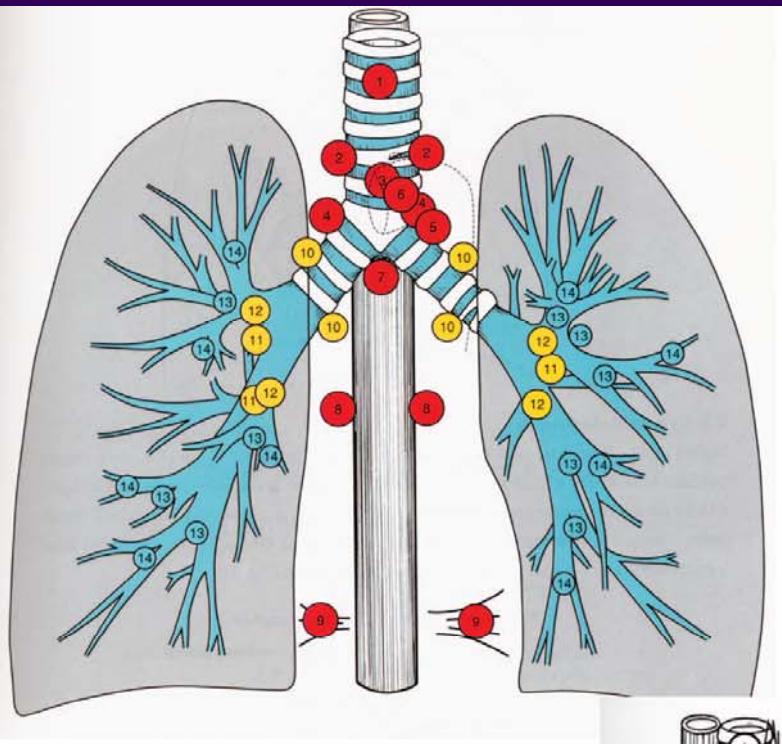
7th edition TNM classification 2010

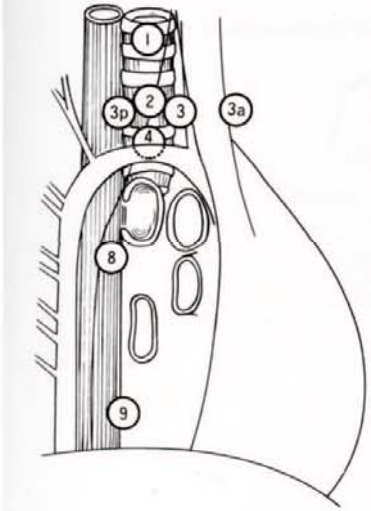
Peroperative staging



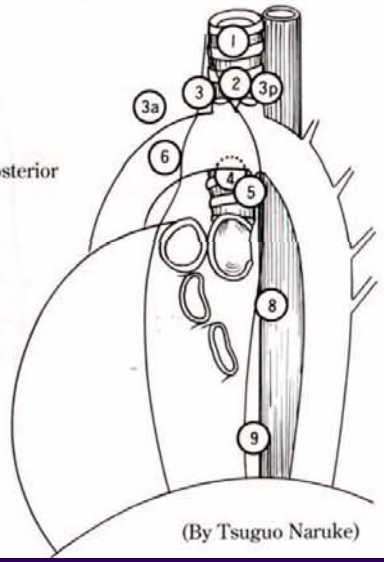
14 LN stations
single digit N2
double digits N1

anatomical description:
English version since 2000

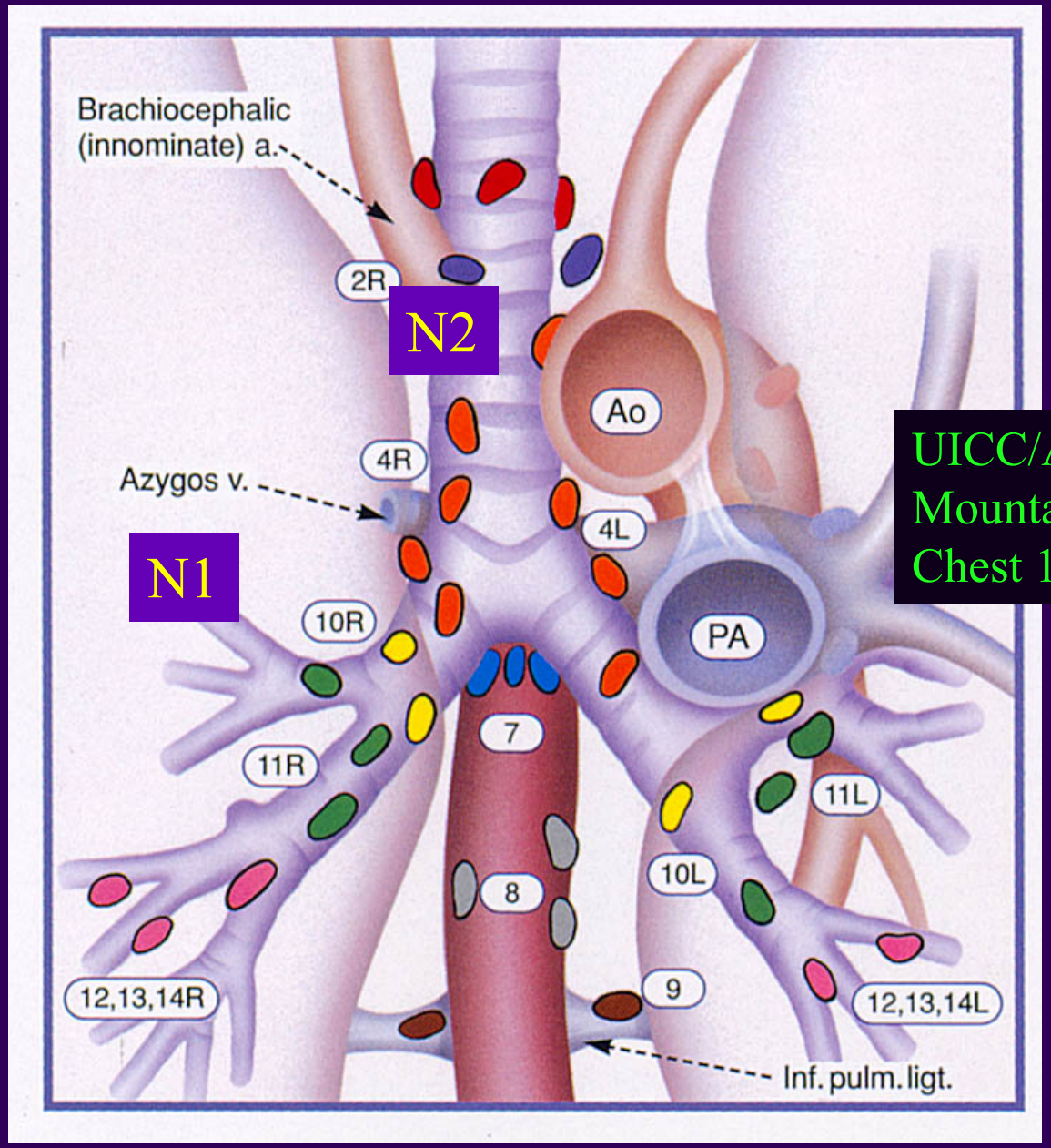




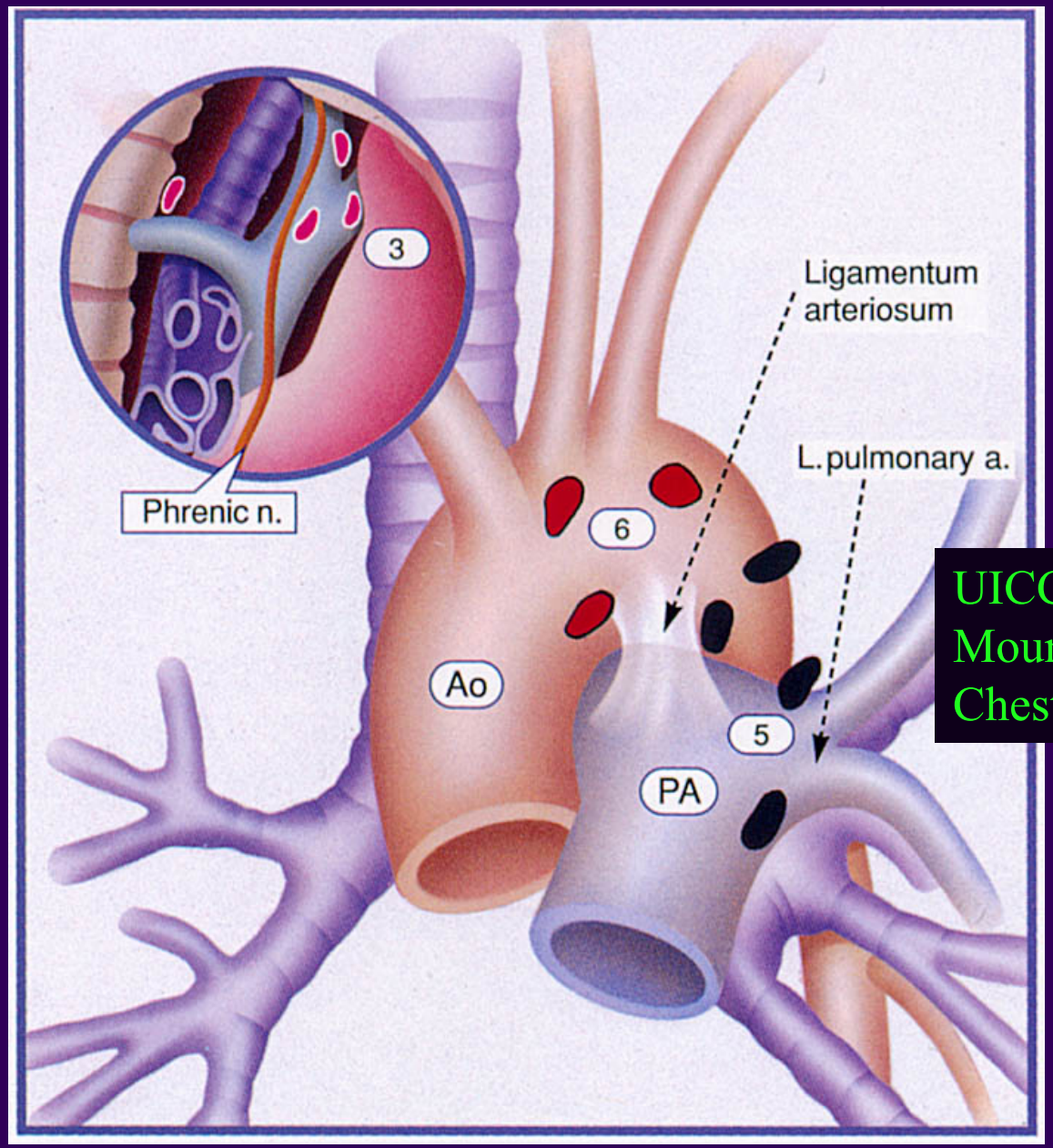
#1 Superior mediastinal or highest mediastinal
#2 Paratracheal
#3 Pretracheal
#3a Anterior mediastinal
#3p Retrotracheal mediastinal or posterior mediastinal
#4 Tracheobronchial
#5 Subaortic or Botallo's
#6 Paraaortic (ascending aorta)
#7 Subcarinal
#8 Paraesophageal (below carina)
#9 Pulmonary ligament
#10 Hilar (main bronchus)
#11 Interlobar
#12 Lobar···upper lobar, middle lobar, and lower lobar
#13 Segmental
#14 Subsegmental



(By Tsuguo Naruke)



UICC/AJCC 6th TNM
Mountain - Dresler
Chest 1997; 111:1718-23



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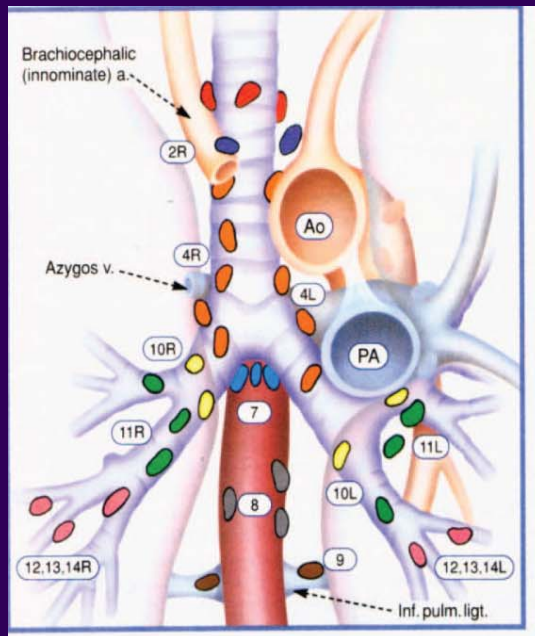
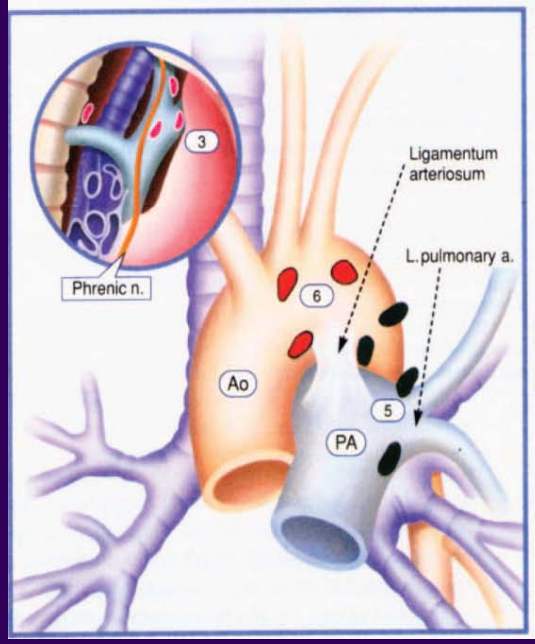




Superior Mediastinal Nodes

- 1 Highest Mediastinal
- 2 Upper Paratracheal
- 3 Pre-vascular and Retrotracheal
- 4 Lower Paratracheal (including Azygos Nodes)

Upper zone (R)

N_2 = single digit, ipsilateral
N_3 = single digit, contralateral or supraclavicular

Aortic Nodes

- 5 Subaortic (A-P window)
- 6 Para-aortic (ascending aorta or phrenic)

AP zone (L)

Inferior Mediastinal Nodes

- 7 Subcarinal

Subcarinal zone

- 8 Paraesophageal (below carina)
- 9 Pulmonary Ligament

Lower zone

N_1 Nodes

- 10 Hilar
- 11 Interlobar

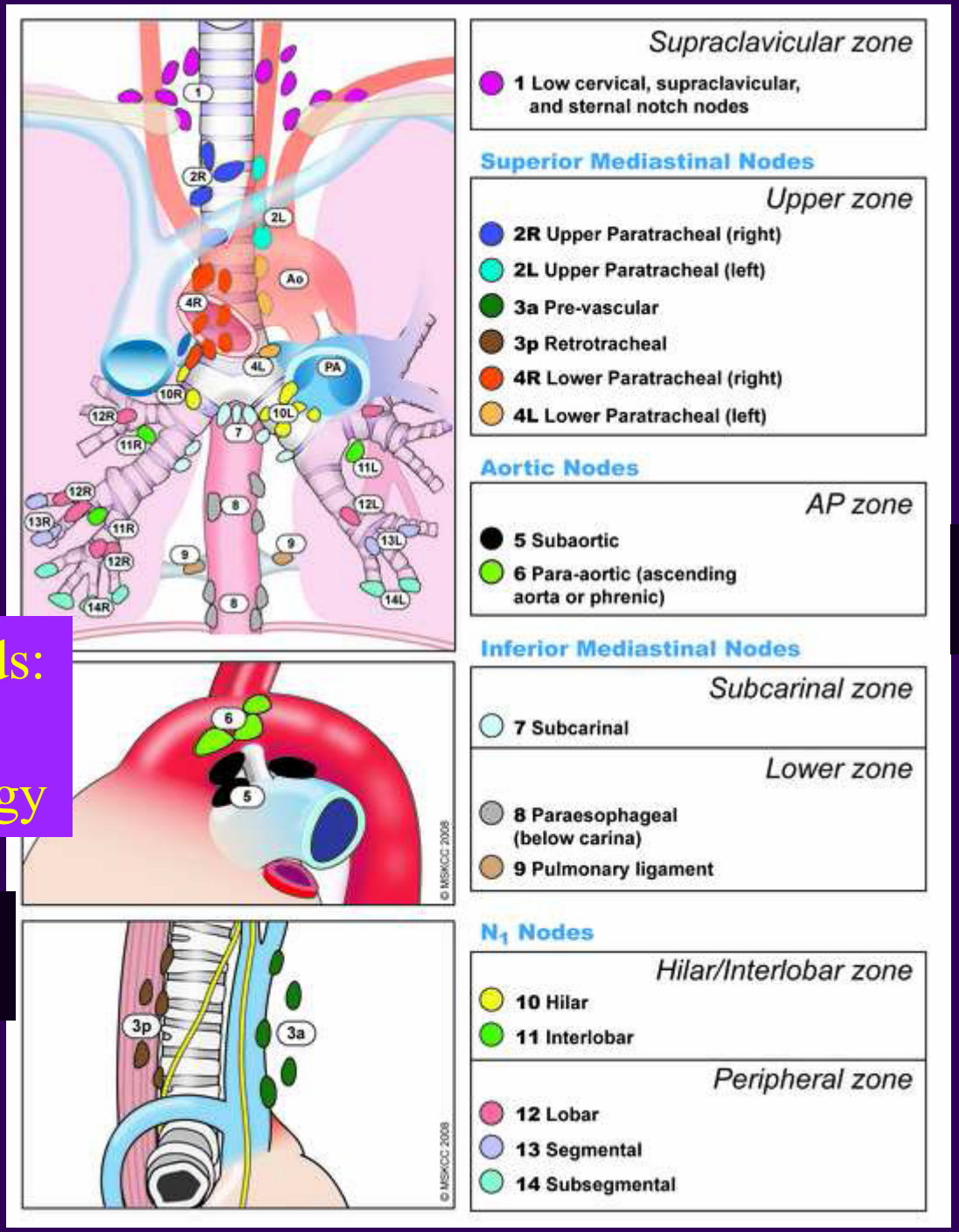
Hilar zone

- 12 Lobar
- 13 Segmental
- 14 Subsegmental

Peripheral zone

Proposed changes N factor: zones

Rusch V et al.
J Thorac Oncol
2007; 2:603-12



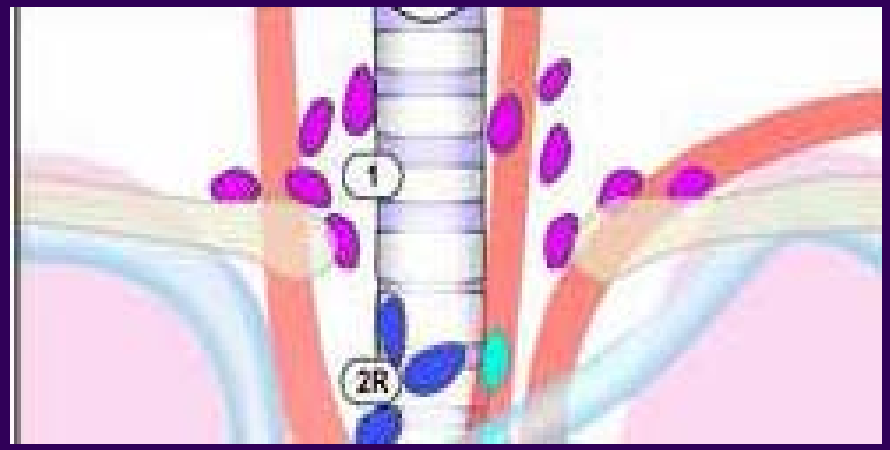
Proposed changes N factor: zones

Rusch V. J Thorac Oncol 2009; 4:568-77

Best of both worlds: East – West Surgery - Radiology

Van Schil P. J Thorac Oncol 2009; 4:561-2

Proposed changes LN stations - zones



Supraclavicular zone

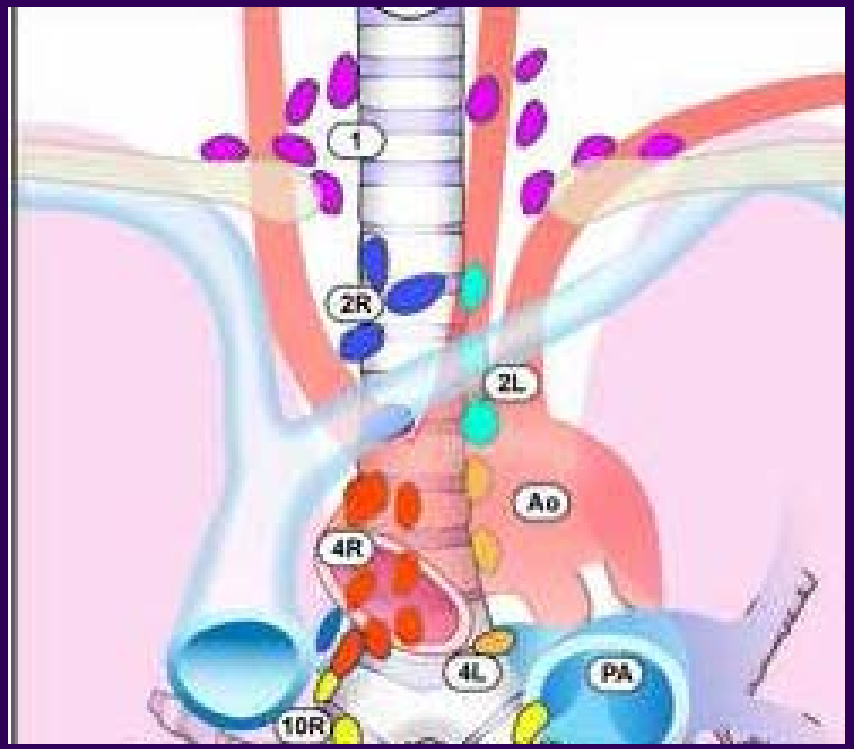
1 Low cervical, supraclavicular, and sternal notch nodes

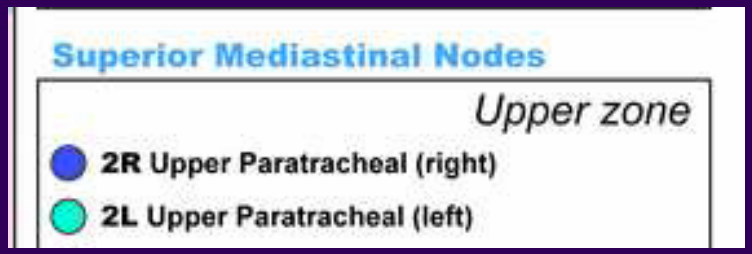
↑ lower margin cricoid
↓ clavicles, ↑ manubrium

N3 !

Rusch V. J Thorac Oncol 2009; 4:568-77

Proposed changes LN stations - zones



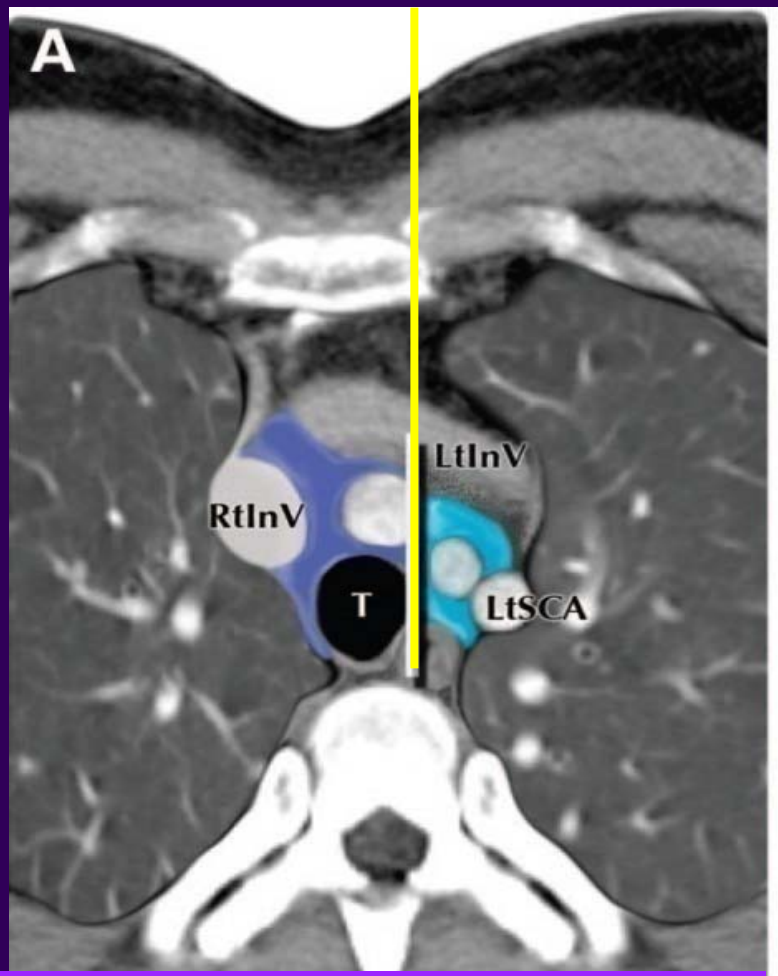


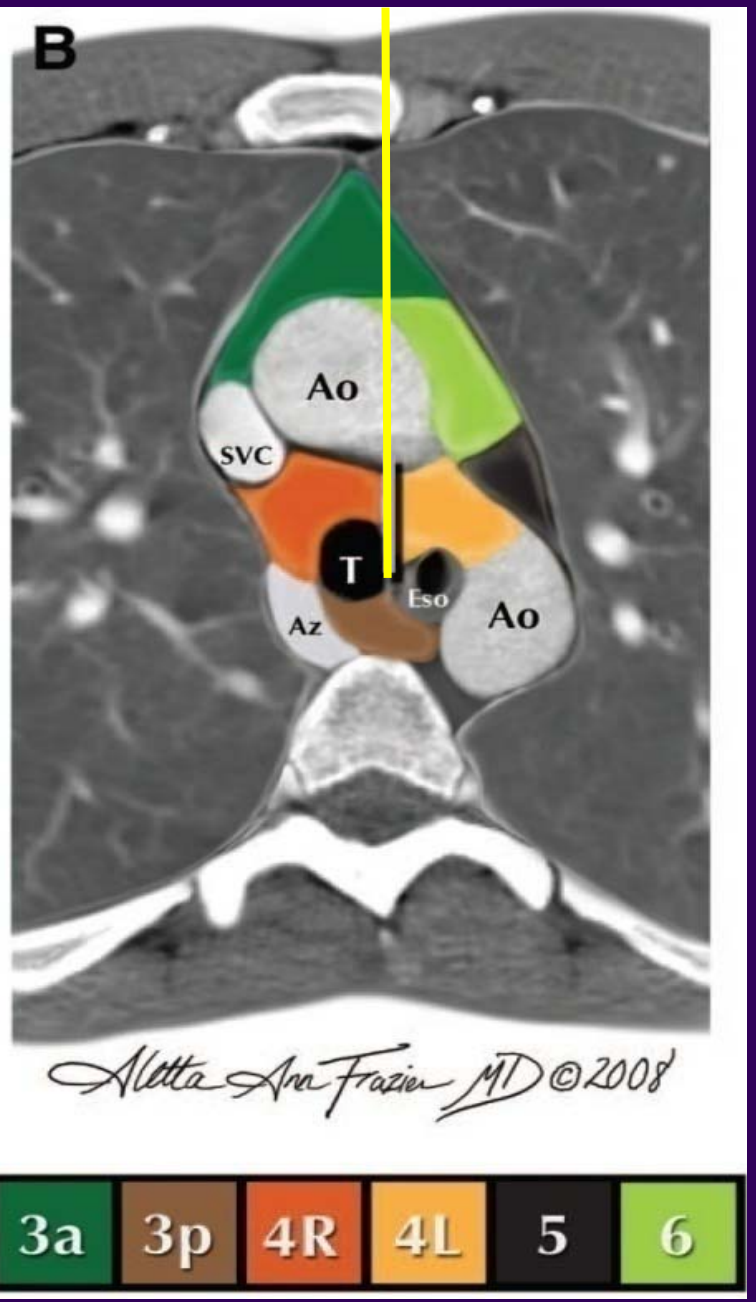
2R ↓ intersection caudal margin innominate vein with trachea

2L ↓ superior border aortic arch

oncological midline

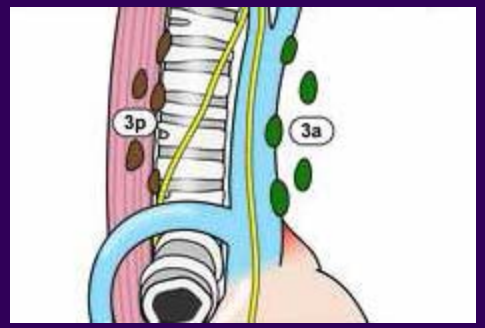
Rusch V. J Thorac Oncol 2009; 4:568-77

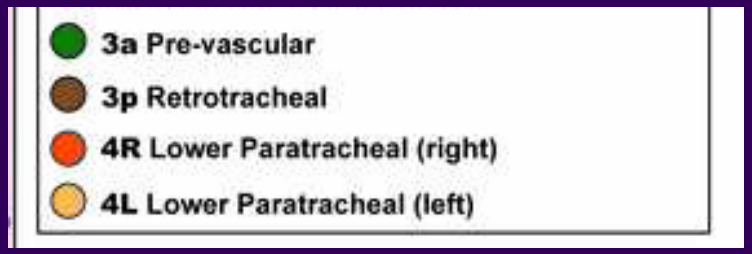




Oncological midline:
at L side of trachea!
tumour R +2R = N2
tumour L +2R = N3

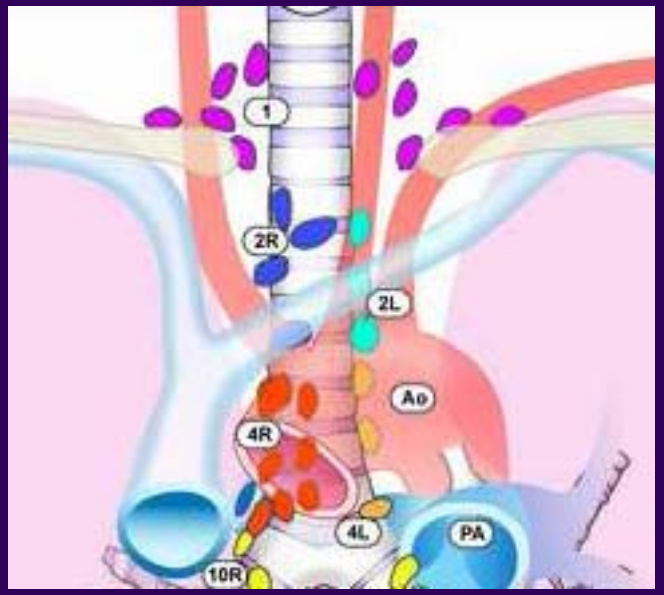
Proposed changes LN stations - zones





3 ≠ pretracheal !
4 ≠ tracheobronchial

3a-p: anatomically distinct



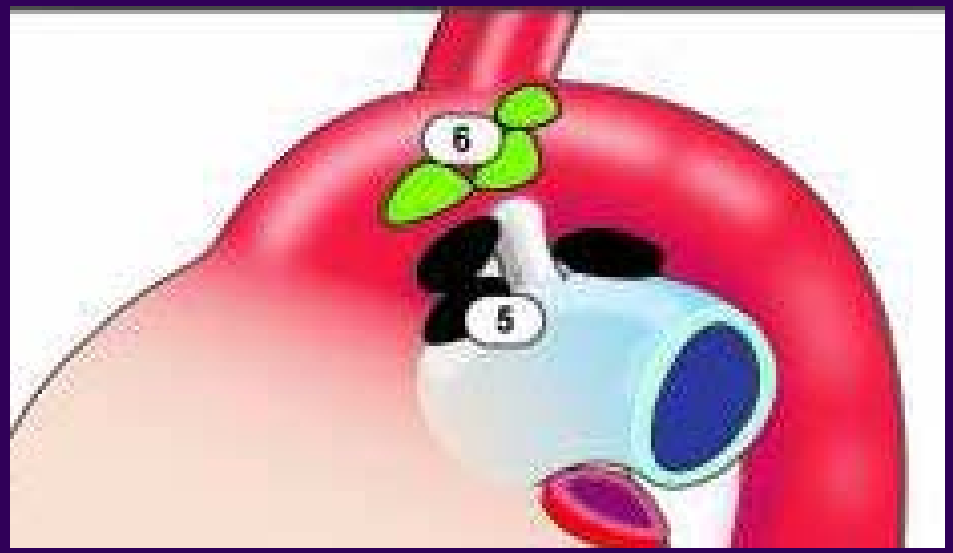
4R ↓ lower border of azygos vein
4L ↓ upper rim of L main PA

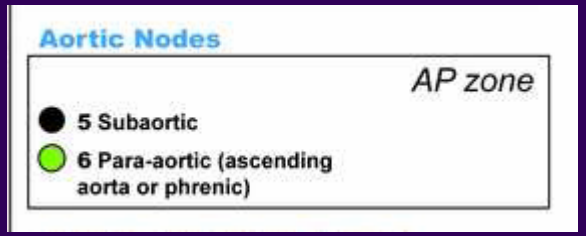
10 R+L ↓ interlobar region

mediastinoscopy: N1 nodes L+R !

Rusch V. J Thorac Oncol 2009; 4:568-77

Proposed changes LN stations - zones

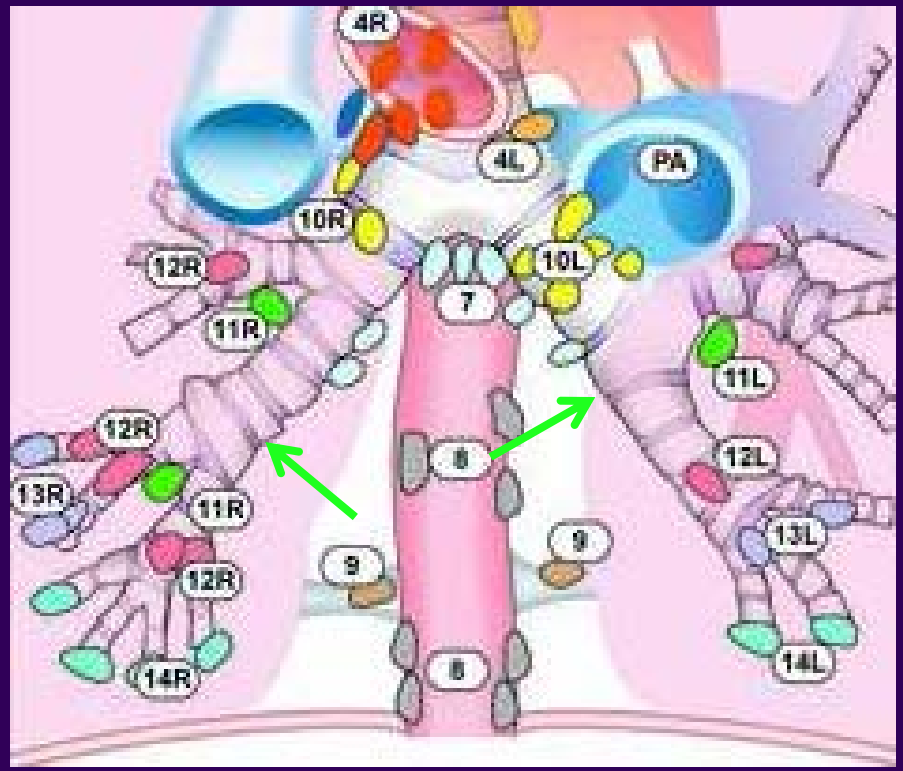


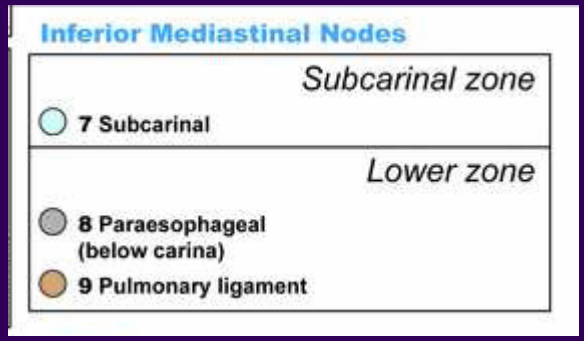


5 lateral to ligamentum arteriosum
4L medial

Rusch V. J Thorac Oncol 2009; 4:568-77

Proposed changes LN stations - zones





7 ↑ carina of trachea

↓ L ↑ border LLL bronchus

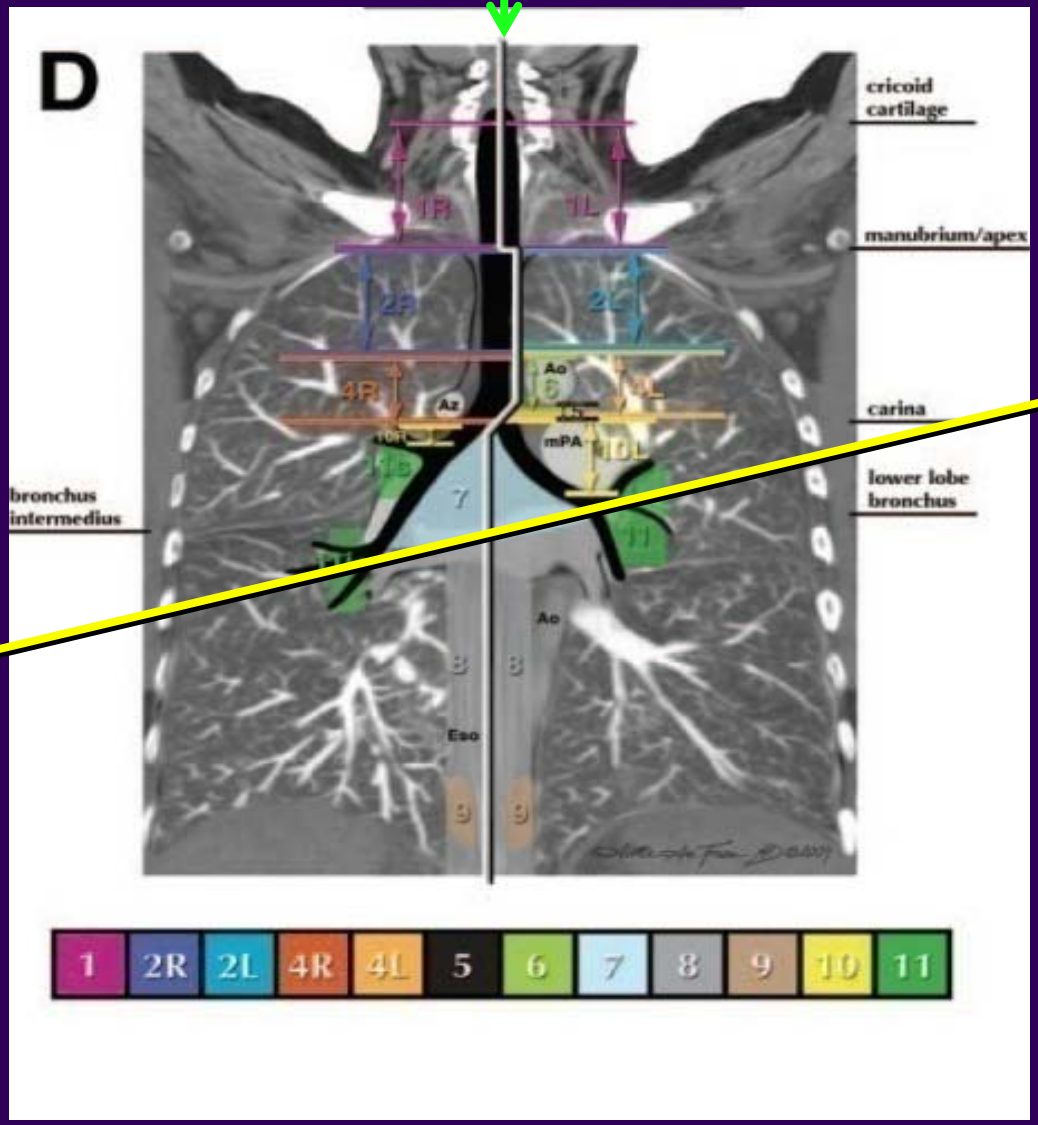
R ↓ border of bronchus intermedius

10 R+L ↓ interlobar region

main bronchus	medial 7	N2
	lateral 10, 11	N1

Rusch V. J Thorac Oncol 2009; 4:568-77

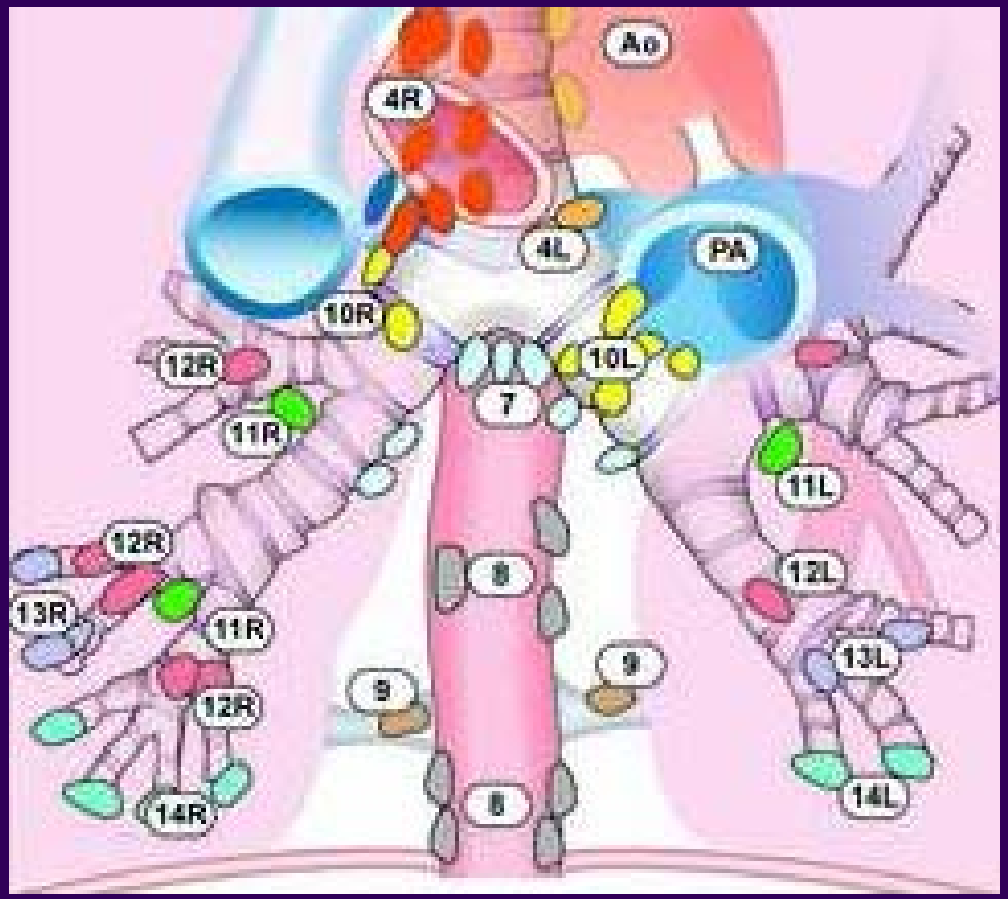
oncological midline



7 ↑ carina of trachea
↓ L ↑ border LLL bronchus
R ↓ border of bronchus intermedius

7 grotere regio !

Proposed changes LN stations - zones



N_1 Nodes

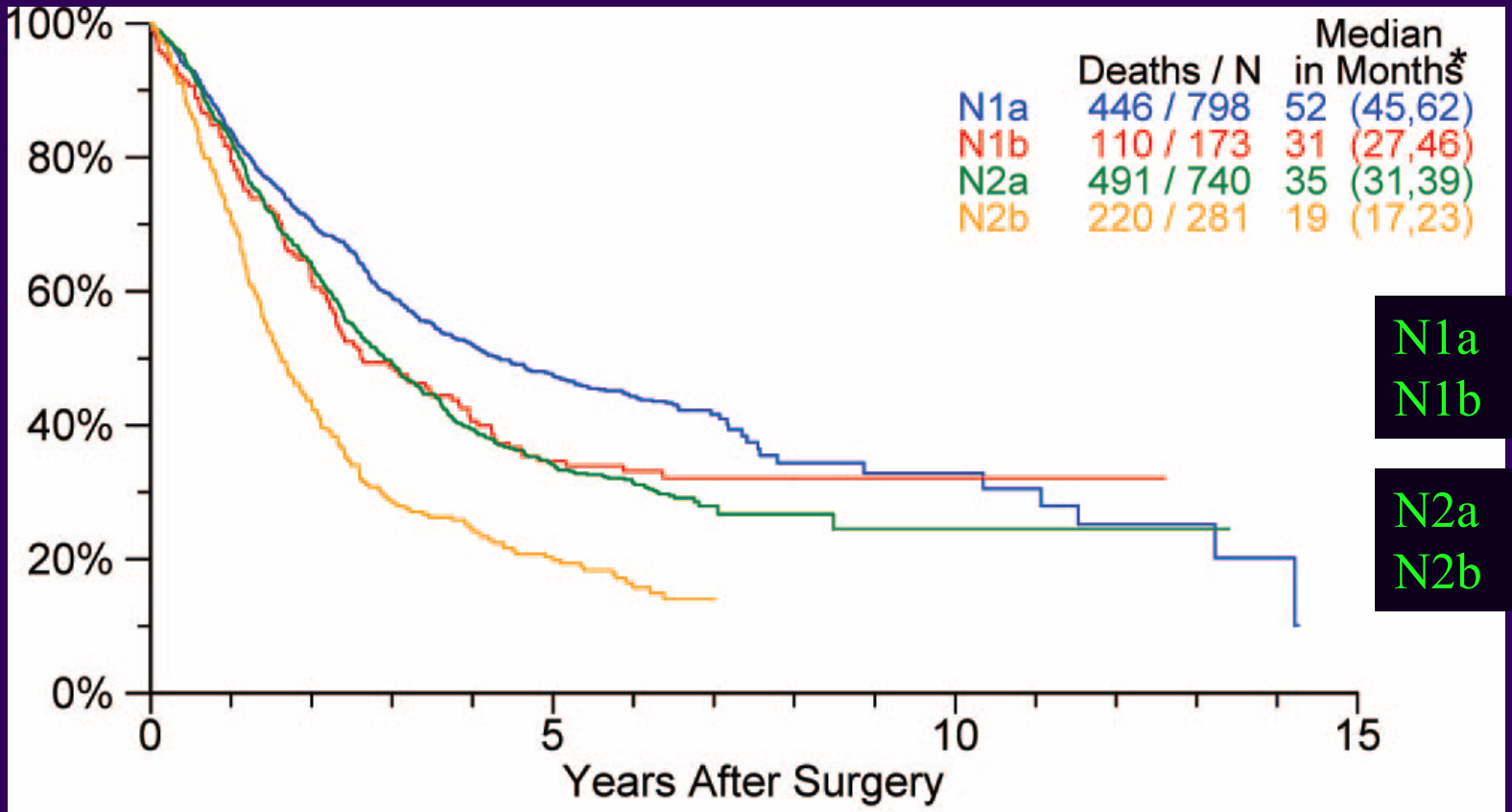
Hilar/Interlobar zone

- **10** Hilar
- **11** Interlobar

Peripheral zone

- **12** Lobar
- **13** Segmental
- **14** Subsegmental

Rusch V. J Thorac Oncol 2009; 4:568-77



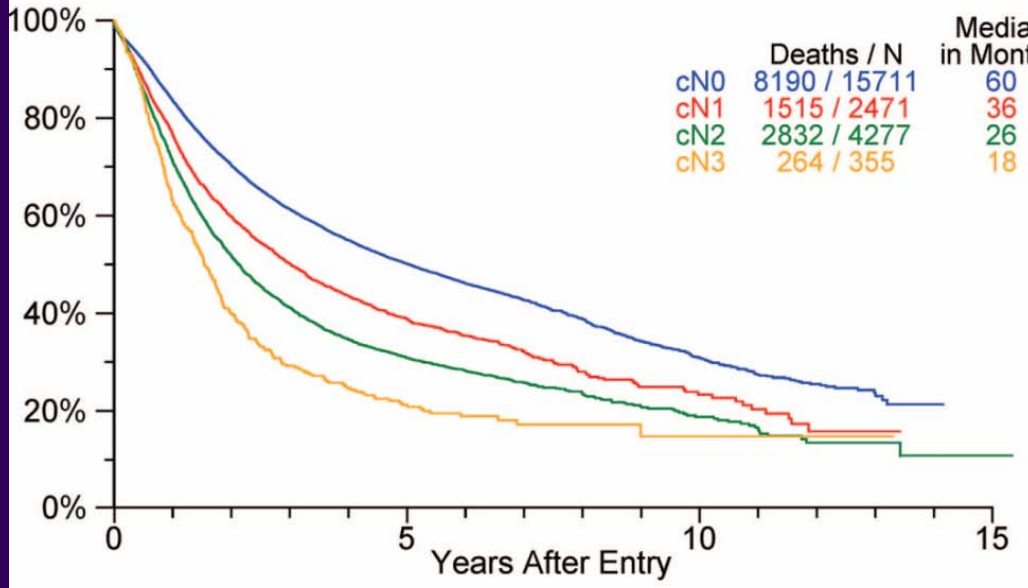
N1a single N1 zone
N1b multiple N1 zones

N2a single N2 zone
N2b multiple N2 zones

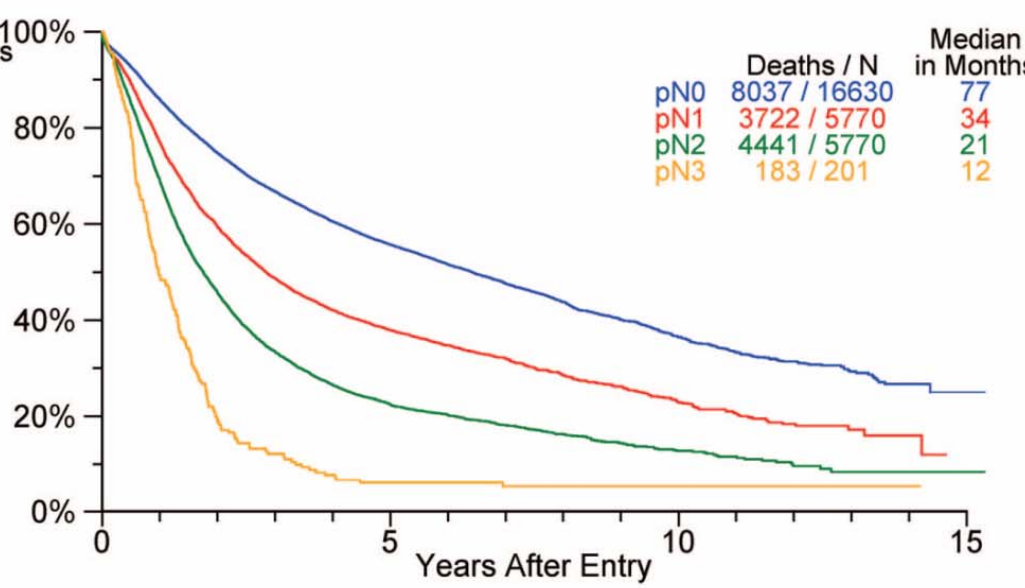
	1 Yr	5 Yrs		HR	P
N1a	86%	48%			
N1b	79%	35%	vs N1a:	1.32	<.0090
N2a	83%	34%	vs N1b:	1.04	0.7137
N2b	71%	20%	vs N2a:	1.65	<.0001

*estimates of median survival, followed by 95% confidence intervals in parentheses

Clinical Staged, By cN



Pathologically Staged, By pN



	1 Yr	5 Yrs		HR	P
cN0	84%	50%			
cN1	77%	39%	vs cN0:	1.37	<.0001
cN2	71%	31%	vs cN1:	1.24	<.0001
cN3	63%	21%	vs cN2:	1.31	<.0001

	1 Yr	5 Yrs		HR	P
pN0	86%	56%			
pN1	77%	38%	vs pN0:	1.63	<.0001
pN2	69%	22%	vs pN1:	1.51	<.0001
pN3	49%	6%	vs pN2:	1.81	<.0001

LN mapping and staging

Lymph node mapping

7th edition TNM classification 2010

Peroperative staging

COMPLETE RESECTION

- **R0 : no residual tumor**
- **R1 : microscopic residual tumor**
- **R2 : macroscopic residual tumor**

IASLC : Complete Resection Subcommittee

Complete resection R0

- free resection margins proved microscopically

  bronchial, venous, arterial stumps, peribronchial soft tissue, any peripheral margin near tumor or of additionally resected tissue
- systematic or lobe-specific systematic nodal dissection :

  ≥ 6 nodal stations (3 mediastinal)
- no extracapsular extension in nodes removed separately or at the margin of the lung specimen
- highest mediastinal lymph node must be negative

Rami-Porta R et al. Complete resection in lung cancer surgery : proposed definition. Lung Cancer 2005; 49:25-33

IASLC : Complete Resection Subcommittee

Incomplete resection R1 - R2

- tumor involvement of resection margins
- extracapsular extension in nodes removed separately or at the margin of the lung specimen
- + nodes that were not removed

  R2 if recognized by surgeon
- + cytology of pleural or pericardial effusions

Rami-Porta R et al. Complete resection in lung cancer surgery : proposed definition. Lung Cancer 2005; 49:25-33

IASLC : Complete Resection Subcommittee
Uncertain resection Rx

Resection margins free of disease microscopically but one of the following applies :

- **less rigorous LN evaluation**
- **intracapsular involvement highest mediastinal node extracapsular = R2**
- **bronchial margin : ca. in situ**
- **+ pleural lavage cytology R1 cy+**

Rami-Porta R et al. Complete resection in lung cancer surgery : proposed definition. Lung Cancer 2005; 49:25-33

Systematic nodal dissection

- dissection of mediastinal, hilar and lobar LN
  in a systematic fashion
- 240 pts cT1-3 N0-1 NSCLC
- 3 % expl. thoracotomy - 20 % N2 disease
- skip metastases : 34 % N2 disease
- no subgroup 0 % incidence of N2 metastases

Graham A. Systematic nodal dissection in the intrathoracic staging of patients with NSCLC. J Thorac Cardiovasc Surg 1999; 117:246-51

Systematic nodal dissection

- peripheral tumors < 2 cm. : 24 % LN mets
- necessary for accurate staging NSCLC
- gold standard for mediastinal staging
- confusion : radical lymphadenectomy
  lymph node sampling
- R : 4,2 7,8,9 L : 5,6,4 7,8,9

Graham A. Systematic nodal dissection in the intrathoracic staging of patients with NSCLC. J Thorac Cardiovasc Surg 1999; 117:246-51

Lobe-specific systematic nodal dissection

- dissection of intrapulmonary (lobar, interlobar, segmental) and hilar LN + ≥ 3 mediastinal LN stations:

RUL – RML	7 + (2R or 4R or
RLL	7 + 4R + (8 or 9)
LUL	5, 6, 7
LLL	7, 8, 9

- LN specimen : ≥ 6 LN : 3 hilar, intrapulmonary
  3 mediastinal (station 7)

Rami-Porta R et al. Complete resection in lung cancer surgery : proposed definition. Lung Cancer 2005; 49:25-33

Accuracy PET - CT scanning anno 2009

- 200 patients operated lung cancer
- PET-CT followed by staging mediastinoscopy and resection, if appropriate
- PET-CT

correct staging	99 pts	49.5 %
under-staged	59	29.5 %
over-staged	42	21 %

- superior mediastinal nodes not correctly staged in 19 %

Carnochan FM, Walker WS. Eur J Cardiothorac Surg 2009; 35:781

Sampling *vs* lymph node dissection

- **ECOG 3590 : randomized prospective trial of adjuvant therapy in patients with completely resected stages II and IIIA NSCLC (adjuvant RT vs. CTRT)**
- **stratification, *nonrandomized* comparison (n=373):**

  SS systematic sampling

  MLND complete mediastinal lymph node dissection (complete removal of all lymph nodes)

Keller SM. Mediastinal lymph node dissection improves survival in patients with stages II and IIIA NSCLC. Ann Thorac Surg 2000; 70:358-66

Sampling *vs* lymph node dissection

	n	N1	N2	MST	
SS	187	40	60 %	29.2 mos	
MLND	186	41	59 %	57.5	p = .004

- SS as efficacious as MLND in staging pts. NSCLC
- MLND identifies more levels of N2 disease
- MLND improved survival with *right* NSCLC ↔ SS

Keller SM. Ann Thorac Surg 2000; 70:358-66

Sampling *vs* lymph node dissection

- randomized trial (532 pts)
- lung resection with systematic nodal dissection – SND vs mediastinal LN sampling - MLS

	n	MST	
SND	268	43 mos.	
MLS	264	32	p < .0001

Wu Y. A randomized trial of systematic nodal dissection in resectable NSCLC. Lung Cancer 2002; 36:1- 6

Sampling *vs* lymph node dissection

5-ys	stage I	II	IIIA
SND	82.2	32	27 %
MLS	57.5	27	6.2 %
	p = .02	.05	.0009

multivariate analysis : LN dissection
stage (pTNM)
tumor size
n LN metastases

Wu Y. Lung Cancer 2002; 36:1-6

Sampling *vs* lymph node dissection

ACOSOG Z0030: randomized trial sampling ↔ lymphadenectomy

- 1111 pts included; lobectomy 75%, pneumonectomy 4%
- † 2.0% LN sampling 0.76% LN dissection
- LN dissection: ↑ median operative time, chest tube drainage
- no Δ median hospitalization (6 days); survival data...

Allen MS et al. Ann Thorac Surg 2006; 81:1013

Guidelines peroperative LN staging

- systematic nodal dissection recommended
  - R en bloc 2-4R, en bloc 7-9, 3a and 3p when present
  - L 4L, 5, 6, en bloc 7-9
- lobe-specific *always station 7, at least 6 nodal stations N1+2*

RUL-RML	2R, 4R, 7	LUL	5, 6, 7
RLL	4R, 7, 8, 9	LLL	7, 8, 9

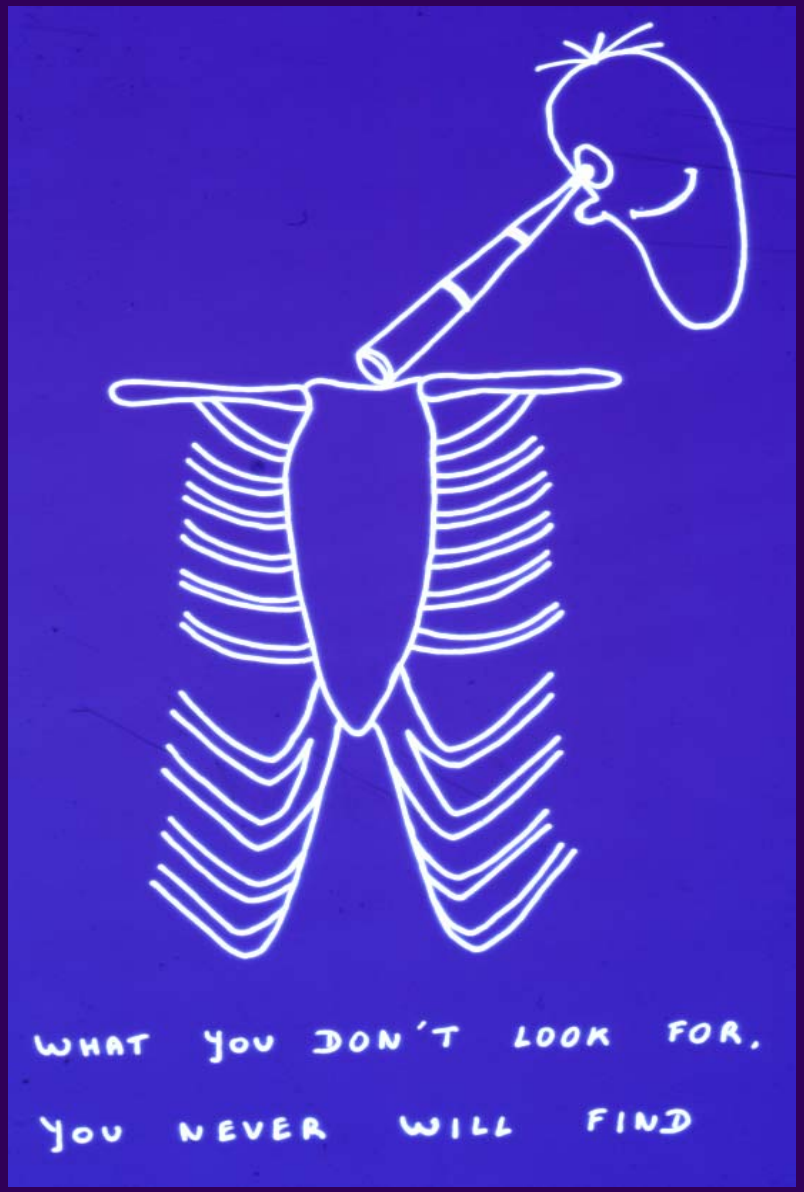
- induction therapy: same recommendation, technically more difficult
- high-risk patients: node assessment may be minimized

Lardinois D, De Leyn P, Van Schil P et al. ESTS guidelines for intraoperative LN staging in NSCLC. Eur J Cardiothorac Surg 2006; 30:787-92

Lymph node staging

AIM = COMPLETE RESECTION

- 7th edition TNM LN staging
  - anatomical boundaries, nodal zones, N1-N2
  - oncological midline: L side trachea
- mediastinoscopy: N1 nodes !
- peroperative staging : T and N factor, surgical stage
  - systematic nodal dissection gold standard
  - lobe-specific nodal dissection: minimum 6 stations


WHAT YOU DON'T LOOK FOR.
YOU NEVER WILL FIND