



De nieuwe anatomische afbakening van de mediastinale lymfeklieren

Peroperatieve N staging

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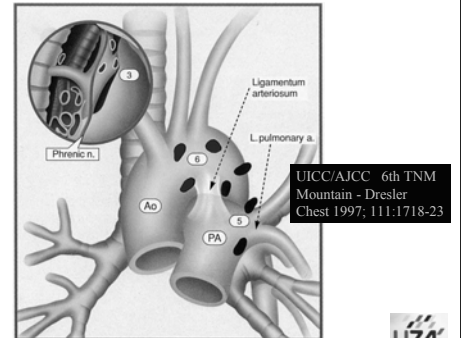
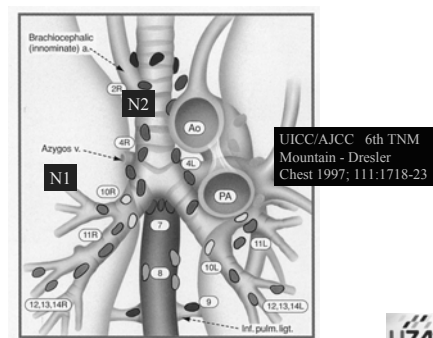
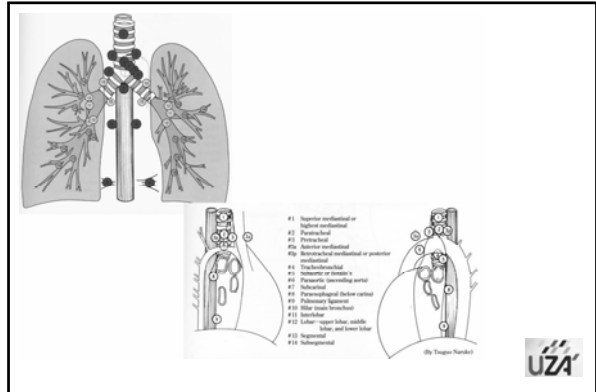
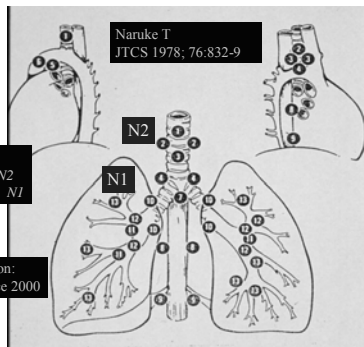
TOGA symposium, 23 oktober 2009



LN mapping and staging

Lymph node mapping
7th edition TNM classification 2010

Peroperative staging



Superior Mediastinal Nodes

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

Aortic Nodes

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

Inferior Mediastinal Nodes

- 7 Subcarinal
- 8 Paraspinal (below carina)
- 9 Pulmonary Ligament

N₂ Nodes

- 10 Hilar
- 11 Interlobar
- 12 Lobar
- 13 Segmental
- 14 Subsegmental

Upper zone (R)

AP zone (L)

Subcarinal zone

Lower zone

Hilar zone

Peripheral zone

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

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Supraclavicular zone

- 1 Low cervical, supraclavicular, and sternal notch nodes

Superior Mediastinal Nodes

Upper zone

- 2R Upper Paratracheal (right)
- 2L Upper Paratracheal (left)
- 3R Pre-vascular
- 3L Retrotracheal
- 4R Lower Paratracheal (right)
- 4L Lower Paratracheal (left)

Aortic Nodes

AP zone

- 5 Subcarinal
- 6 Para-aortic (ascending aorta or phrenic)

Inferior Mediastinal Nodes

Subcarinal zone

- 7 Subcarinal

Lower zone

- 8 Paraspinal (below carina)
- 9 Pulmonary Ligament

N₂ Nodes

Hilar/Interlobar zone

- 10 Hilar
- 11 Interlobar

Peripheral zone

- 12 Lobar
- 13 Segmental
- 14 Subsegmental

Best of both worlds: East – West Surgery - Radiology

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

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

UZA

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

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Superior Mediastinal Nodes

Upper zone

- 2R Upper Paratracheal (right)
- 2L Upper Paratracheal (left)

2R ↓ intersection caudal margin innominate vein with trachea
2L ↓ superior border aortic arch
oncological midline

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

UZA

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

3a 3p 4R 4L 5 6

UZA

3a ≠ 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

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Proposed changes LN stations - zones

5 lateral to ligamentum arteriosum
4L medial

Aortic Nodes
 ● 5 Subcarinal
 ○ 6 Para-aortic (ascending aorta or phrenic)

AP zone

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

UZA

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

Inferior Mediastinal Nodes
 Subcarinal zone
 ○ 7 Subcarinal
 Lower zone
 ● 8 Pretracheal (below carina)
 ● 9 Pulmonary ligament

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

UZA

oncological midline

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

7 grotere regio !

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

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Proposed changes LN stations - zones

N2 Nodes
 Hilal/Interlobar zone
 ○ 10 Hilal
 ○ 11 Interlobar
 Peripheral zone
 ● 12 Lobar
 ● 13 Segmental
 ● 14 Subsegmental

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

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

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Deaths / N in Months
 N1a 446 / 798 52 (45,62)
 N1b 110 / 173 31 (27,46)
 N2a 491 / 740 35 (31,39)
 N2b 220 / 281 19 (17,23)

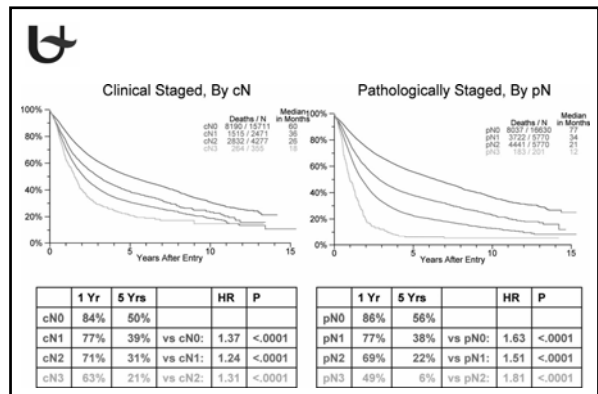
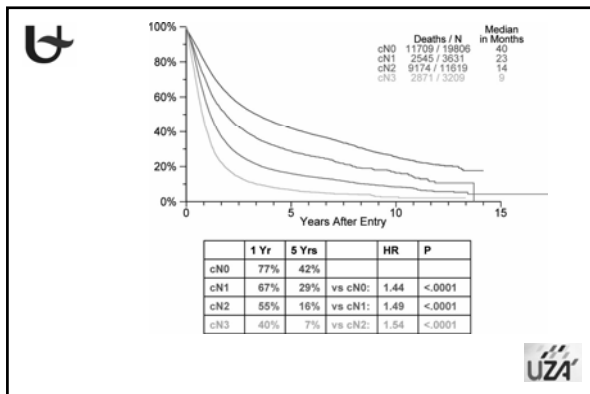
N1a single N1 zone
 N1b multiple N1 zones
 N2a single N2 zone
 N2b multiple N2 zones

	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

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

UZA



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 8)
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. CRTT)
- 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	p = .004
MLND	186	41	59 %	57.5	

- 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.	p < .0001
MLS	264	32	

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



Surgical - pathologic N1

- N1 : heterogeneous group
- 1174 pts NSCLC : N0 50 % N1 22 % N2 28 %
- 5 - year survival N1 : 47.5 %
 - intralobar N1 (level 12,13) 53.6 %
 - extralobar, hilar N1 (10,11) 38.5 % p=0.001
- intralobar N1 ≅ N0
- extralobar N1 ≅ N2, single station

Riquet M. Prognostic significance of surgical - pathologic N1 disease in NSCLC. Ann Thorac Surg 1999; 67: 1572-76





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

