The 8th Edition of the TNM Classification for Lung Cancer

Background, Innovations and Implications for Clinical Practice

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Content of this presentation

- Background and database
- Innovations in the 8th edition
- Implications for clinical practice
- Summary
- Conclusions

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History of lung cancer TNM

Year	Event or Edition
1943-1952	Pierre Denoix presented the TNM
1960-1967	TNM brochures by the UICC; lung cancer was included in 1966
1968	1st edition UICC TNM
1975	2nd edition UICC TNM
1977	1st edition AJCC TNM
1978	3rd edition UICC TNM, revised 1982
1983	2nd edition AJCC TNM
1987	4th edition UICC TNM
1988	3rd edition AJCC TNM
1992	4th edition AJCC TNM
1997	5th edition UICC and AJCC TNM
2002	6th edition UICC and AJCC TNM
2009	7th edition UICC and AJCC TNM
2016	8th edition UICC and AJCC TNM

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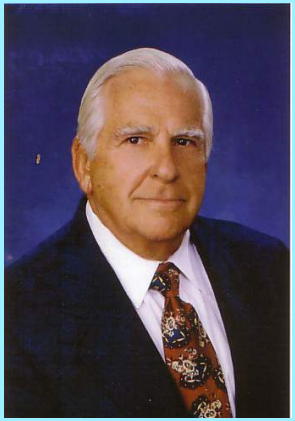
Mountain's database

IASLC database

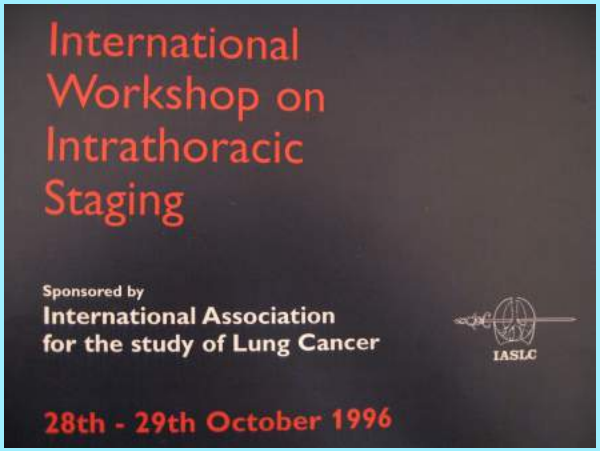
History of lung cancer TNM

- Pierre Denoix, 1912-1990
- Surgical oncologist
- Institut Gustave-Roussy, Paris
- Proposed TNM system between 1943 and 1952



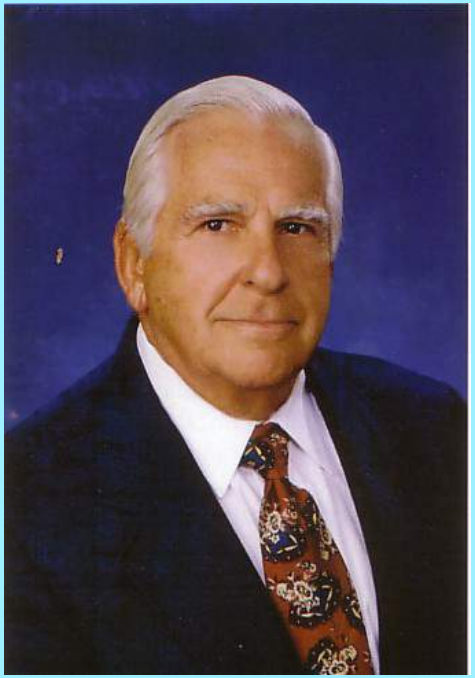
- Clifton F. Mountain, 1924-2007
- Thoracic surgeon
- MD Anderson Cancer Center
- His database informed the 2nd to 6th TNMs

- Peter Goldstraw
- Thoracic surgeon
- Royal Brompton Hospital, London
- Promoter of IASLC database
- IASLC database informed 7th and 8th TNMs



5th – 6th TNM: 1997-2002

- based in 5,319 cases
- relatively small database from a single centre
- not truly international
- surgically orientated



Dr. Clifton F. Mountain
1924-2007

IASLC Staging Projects

7th edition

- 1996: idea
- 1998: Committee
- 1990-2000: databases
- 2001: finances, CRAB
- 2002: dataset
- 2002-2005: data registry
- 2006-2009: publications
- 2010: 7th edition

8th edition

- 2008-9: other tumours
- 2009: prospective phase & new dataset
- 2009-2013: registry of new cases (1999-2010)
- 2013-2014: data analyses
- 2015-2016: publications
- **2017: 8th edition**

Prof. Peter Goldstraw

Process for TNM revision 2002 onwards

Recommendations from IASLC

UICC literature watch

Recommendations submitted to the AJCC

Recommendations submitted to the UICC

National TNM committees

Recommendations accepted by AJCC & UICC

Global implementation

Dr. Leslie Sobin

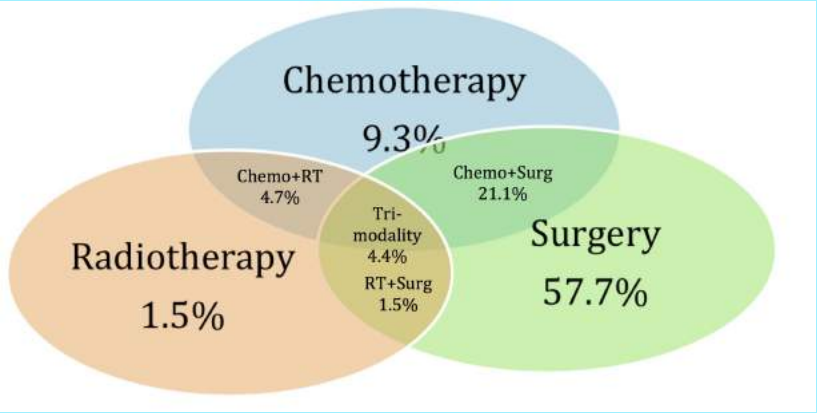
Adapted from Goldstraw P.

IASLC Staging and Prognostic Factors Committee

Vienna, 3rd December 2016

Database for the 8th edition

Region	Number	%
Europe	46,560	49
Asia	41,705	44
North America	4,660	5
Australia	1,593	1.7
South America	190	0.3
TOTAL	**94,708**	**100**



Type of data	Número de casos
Retrospective	73,251
Prospective	3,905
TOTAL	**77,156**

Rami-Porta R et al. J Thorac Oncol 2014; 9: 1618-1624

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Elements of the classification of anatomic extent of lung cancer

Components	Categories	Descriptors	Optional descriptors	Supplementary information	Site-specific rules
T	TX ……T4	Size, location, invaded structures, etc	Grade R L Pn V C	Instructions for homogeneous classification of situations not included in descriptors or optional descriptors	Several
N	NX …..N3	Presence, absence and location			6 nodes for pN0
M	M0….M1c	Presence, absence, location			None

Plus proposed classifications for testing: VPI, pT3a-b-c, N1a-b, N2a-b, cLy

T descriptors

- Tumour size
- Endobronchial location
- Atelectasis/pneumonitis
- Visceral pleura invasion
- Invasion of peripheral structures
- Invasion of central structures
- Separate tumour nodules in same lobe, same lung

24 descriptors

T component

- Pathologic populations
  - pT1-4 N0 M0 R0
  - pT1-4 any N M0 R0
  - pT1-4 any N M0 any R
- Clinical populations
  - cT1-4 N0 M0
  - cT1-4 any N M0

- Univariate and multivariate analyses
- Adjusted for histology, region, age and gender

T: results

- Size: every cm counts
- Tumour size as descriptor in all T categories
- VPI: no change
- T2 & T3 endobronchial: same prognosis
- T2 & T3 atelectasis: same prognosis
- T3 diaphragm has a T4 prognosis
- T3 mediastinal pleura, rarely used

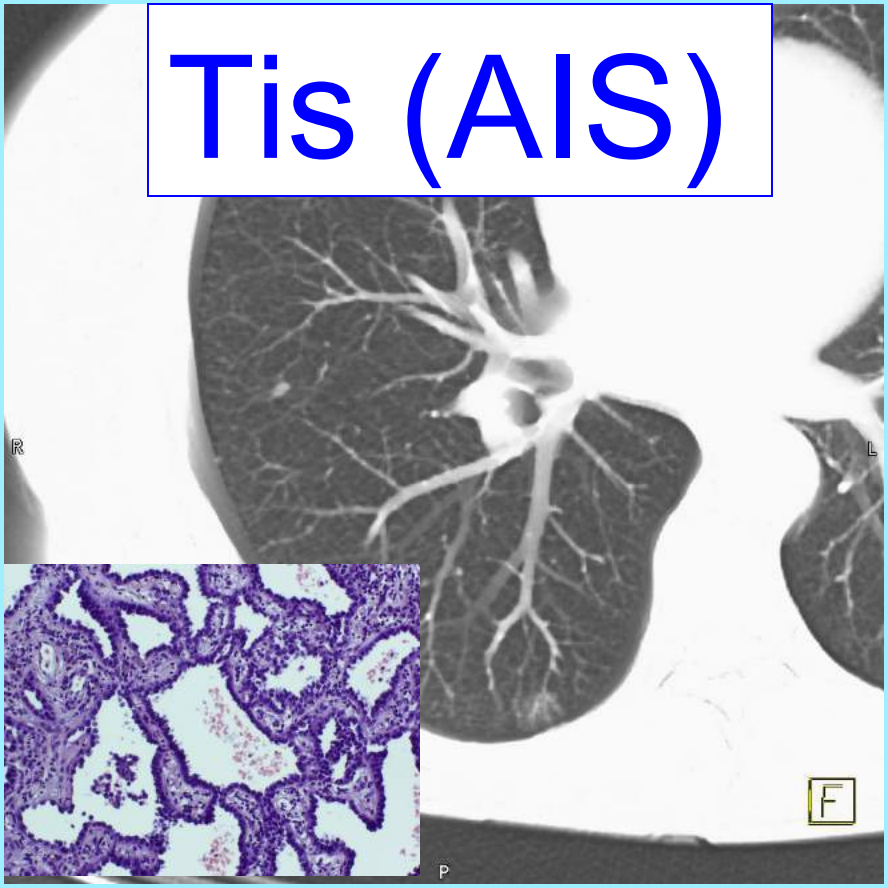
The T component

Descriptor	Category
</= 1 cm	T1a
>1-2 cm	T1b
>2-3 cm	T1c
>3-4 cm	T2a
>4-5 cm	T2b
>5-7 cm	T3
>7 cm	T4
Bronchus < 2 cm	T2
Total atelectasis	T2
Diaphragm	T4

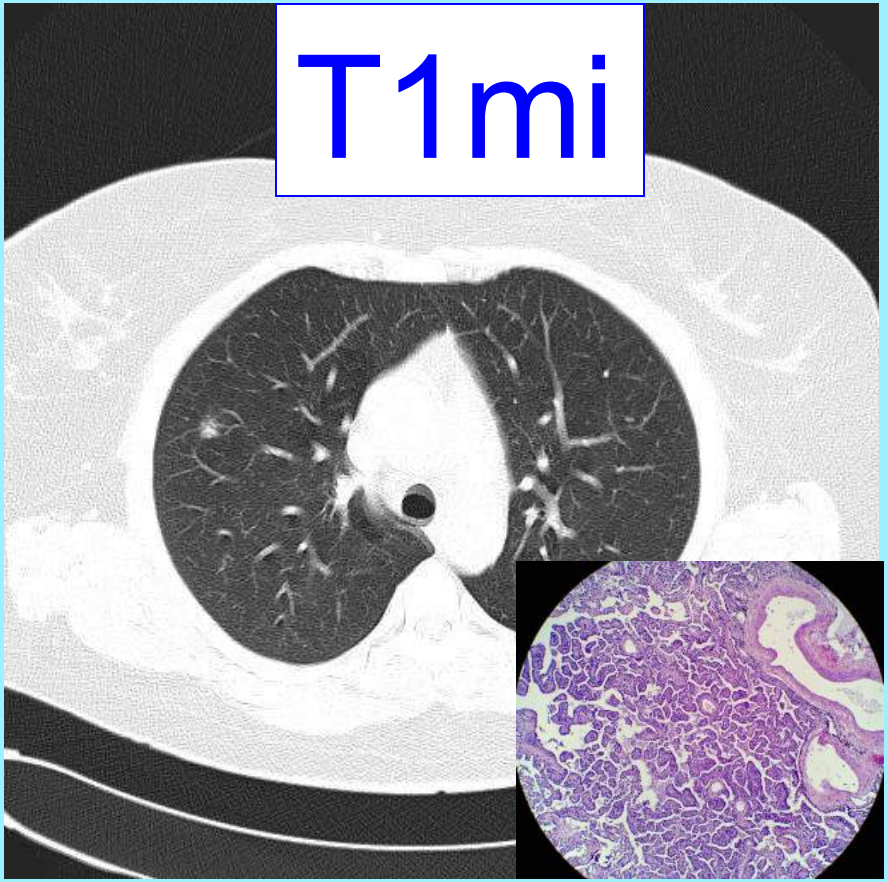
Rami-Porta R et al. J Thorac Oncol 2015; 10: 990-1003.

New T categories

Tis (AIS)



T1mi



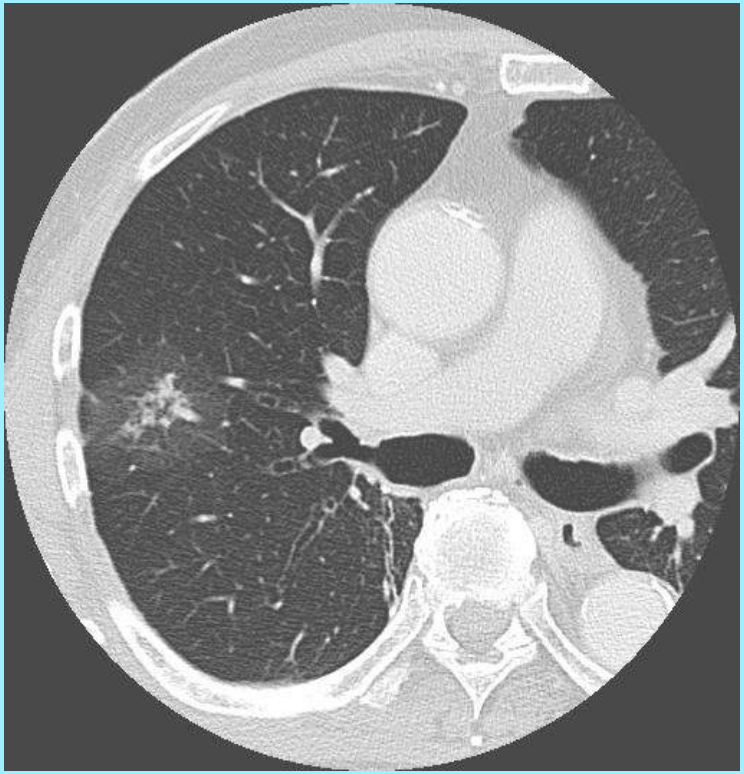
Travis W et al. J Thorac Oncol 2016; 11: 1204-1223.

The T component

Size measurement in part-solid non-mucinous ADK

Clinical size:
size of
solid component

Pathologic size:
size of
invasive component

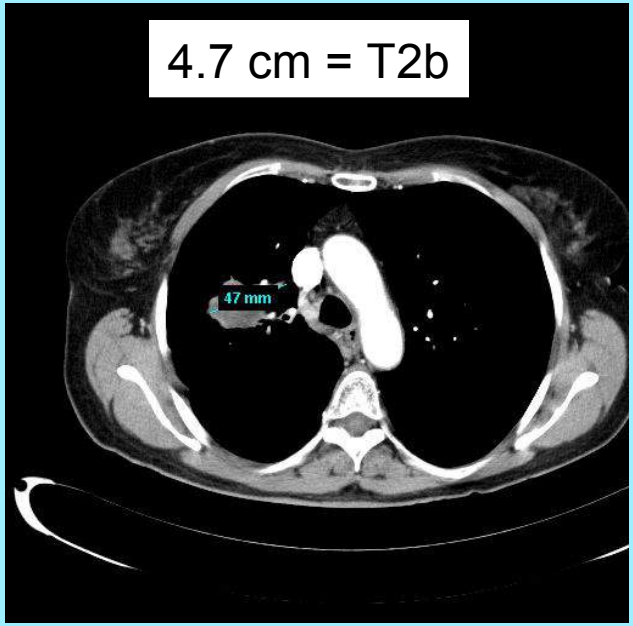


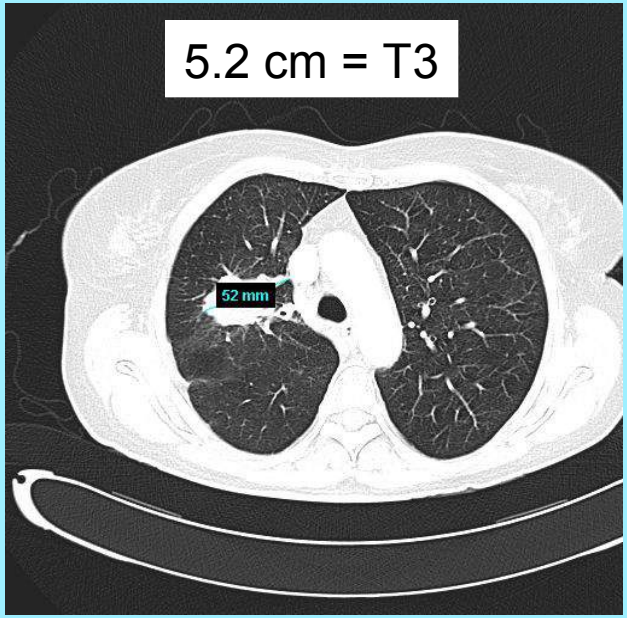
Courtesy of Dr. H. Asamura

Travis W et al. J Thorac Oncol 2016; 11: 1204-1223.

The T component

Measurement of tumour size



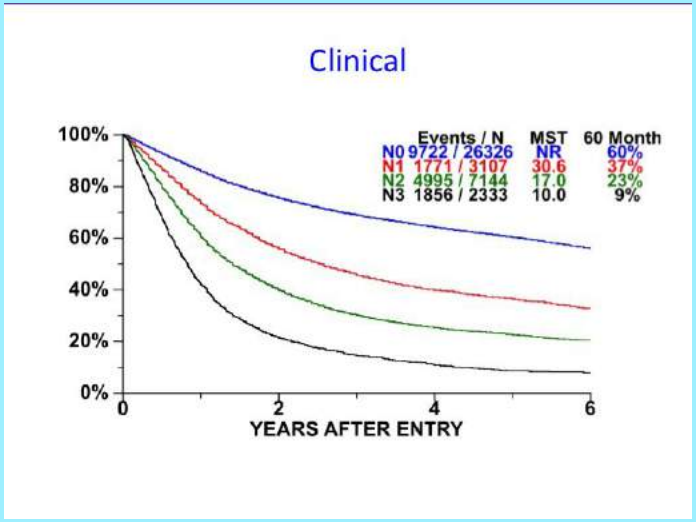


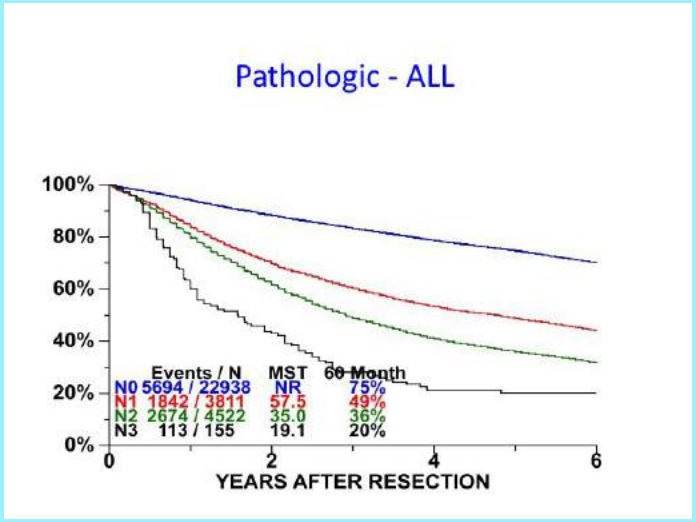
IASLC recommendation for the measurement of tumour size:

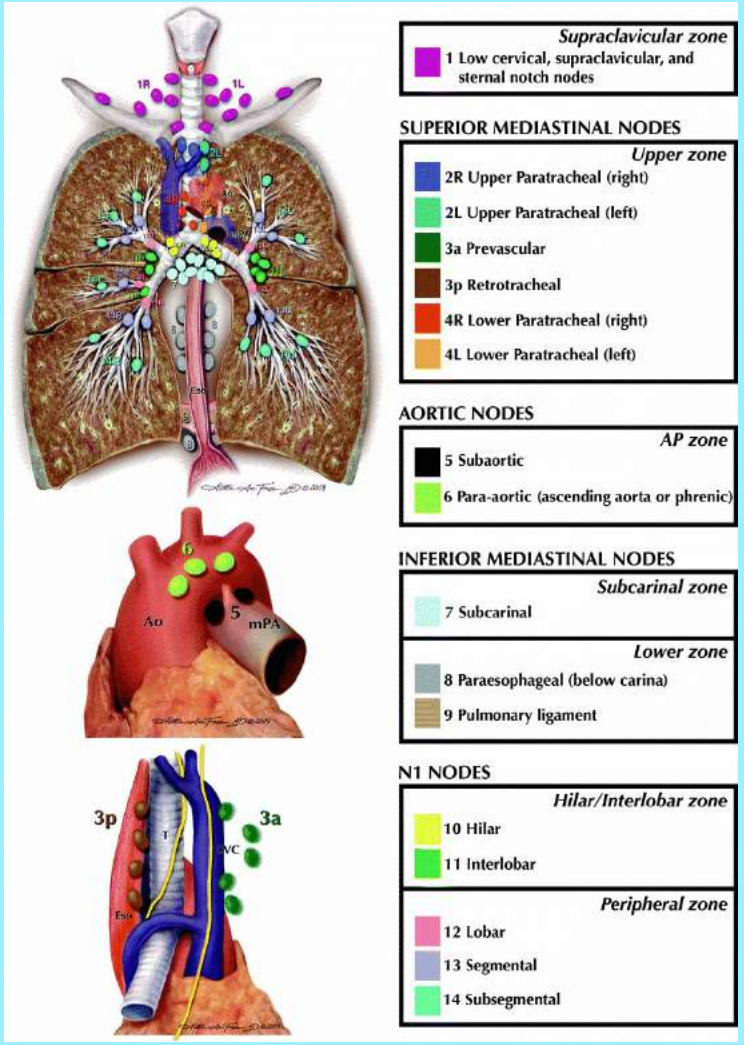
Lung window

Travis W et al. J Thorac Oncol 2016; 11: 1204-1223.

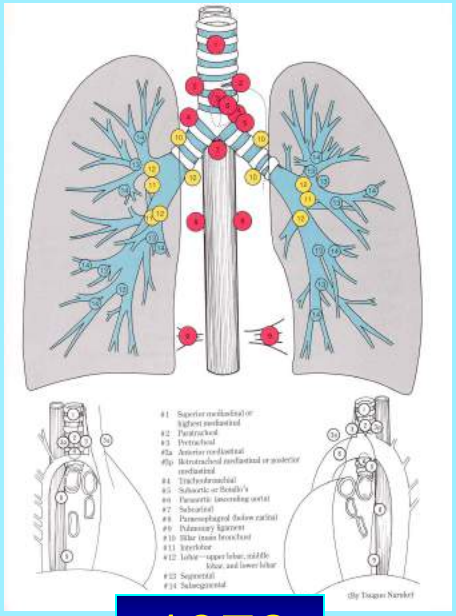
The N component



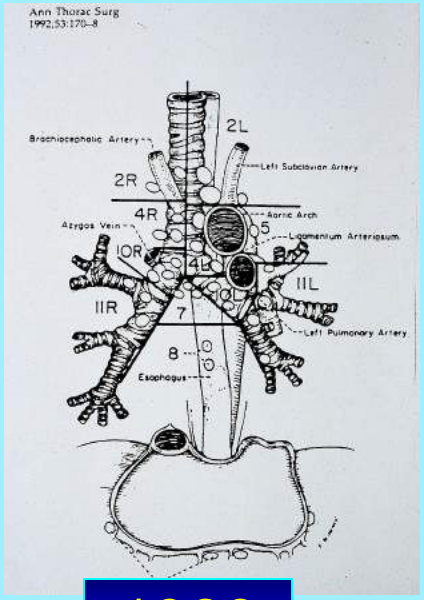




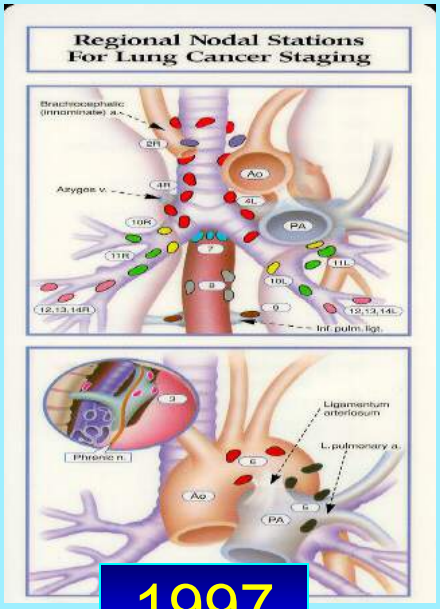
Asamura H et al. J Thorac Oncol 2015; 10: 1675-84.---Rusch V et al. J Thorac Oncol 2009; 4: 568-577



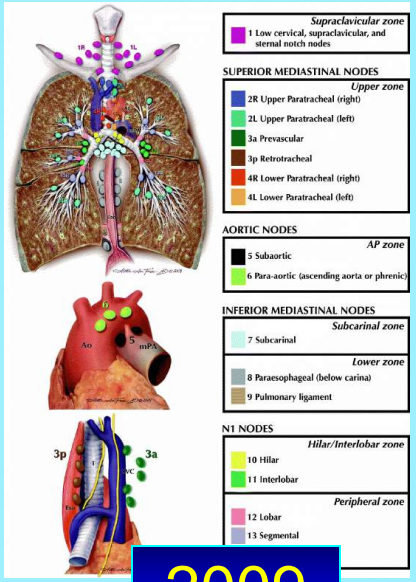
1978



1983



1997



2009

Tsuguo Naruke
1934-2006

肺がんの拡大進展と外科手術との相関

成毛 韓夫

肺がんの転移ルートはリンパ行性・血行性・経気性・隣接性に大別されるが，外科手術の時点においてはこれらが複雑に混在する．病期の古いものはそれが当然であり，血行例では肺門子が重要である．

これらの症例を切除の対象とする外科医にとって，リンパ節転移は手術手技に直結した問題であり，血行進展転移は予後を左右する重要因子として年月を経てきた．経気性転移については証明がむずかしいが，切除後の遺残肺葉の再発が，気管支断内に播種されたがん細胞に起因するという考えられる症例を経験する．近年，細胞診管支鏡内に腫瘍移植の成功が報告されているので，これの可能性は否定できないが，臨床の経験では稀なものということができよう．隣接転移は，肺門近傍の腫瘍が胸壁を侵す症例を代表とするが，腫瘍が胸膜腔に近接するか，これをわずかに突破する程度の症例のもつ意味はどうであろうか，胸膜腔に関連のあるなしによって，予後に差のあることを感じるからである．

私たちは，今まで，肺がんに対する肺切除術式を変め，肺葉切であれ肺全摘であれ，肺門の全廓清を行なうことを原則としてきた．その結果リンパ節転移の対策については，手術的根治に大きい効果のあることを認めているが，血行して行なった血行転移の症例においてはまだ確実な対策が得られていない．

ここでは，手術時の胸腔内病理と切除術について，リンパ節転移・がん組織の血管侵襲（血行性転移の重要因子として）および肺膜浸潤（隣接転移の温床として）を主体的にしらべ，肺がん転移の進展を総括的に把握しようとした．

研究対象と方法

国立がんセンター病院において，1962年5月より1966年12月までに経験した原発性肺がん切除184例のうち，リンパ節転移・胸膜浸潤に関しては100例（Table 1），血管侵襲については167例を対象とした．

Table 1. Mode of Operation

Resection	100cases
Pneumonectomy	23
Radical	21
Palliative	2
Lobectomy	61
Radical	59*
Palliative	11**

* 1 Case, Bi-segmentectomy
** 2 Cases, Segmentectomy

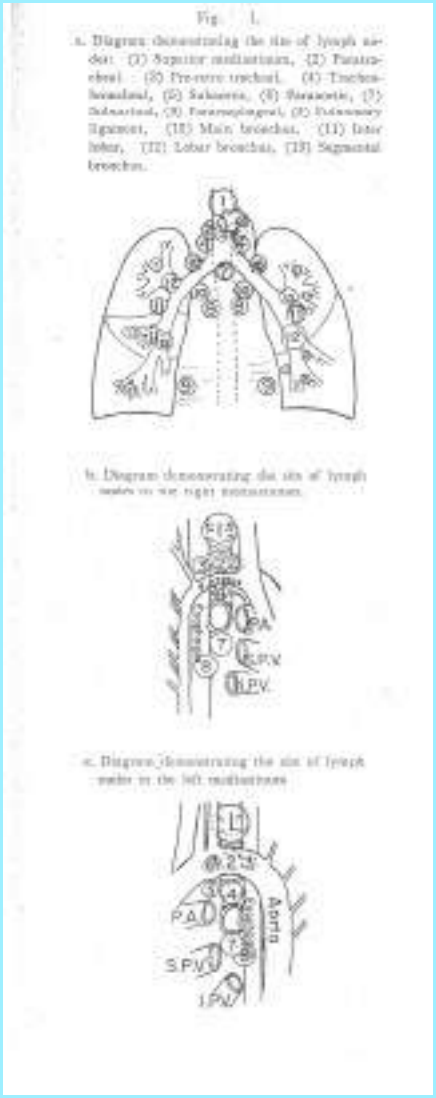


Fig. 1.

a. Diagram demonstrating the site of lymph nodes: (1) Superior mediastinum, (2) Paratracheal, (3) Pre-retro tracheal, (4) Tracheobronchial, (5) Subaortic, (6) Paraaortic, (7) Subaortal, (8) Paraesophageal, (9) Pulmonary ligament, (10) Main bronchus, (11) Intralobar, (12) Lobar bronchus, (13) Segmental bronchus.

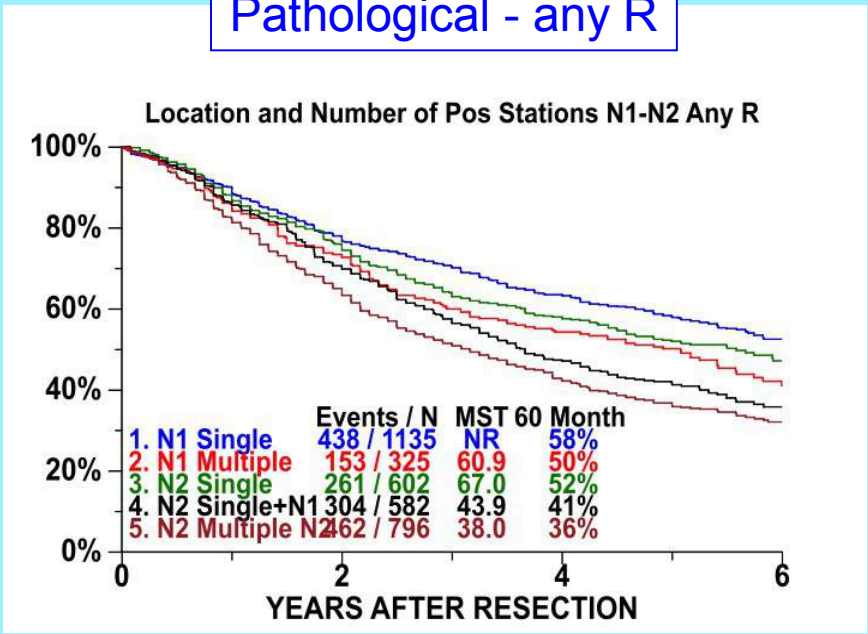
b. Diagram demonstrating the site of lymph nodes on the right mediastinum.

c. Diagram demonstrating the site of lymph nodes on the left mediastinum.

Naruke T. Nippon Kyobu Geka Gakkai Zasshi 1967; 68: 1607-21.

Quantification of nodal disease

Pathological - any R



N1 Single = N1a
N1 Multiple = N1b
N2 Single N2 (“skip mets”) = N2a1
N2 Single N2 + N1 = N2a2
N2 Multiple N2 = N2b

- The amount of nodal disease has prognostic impact
- Upfront resection for single station cN2 will be discussed
- Prognosis refinement
- Better stratification

Asamura H et al. J Thorac Oncol 2015; 10: 1675-84

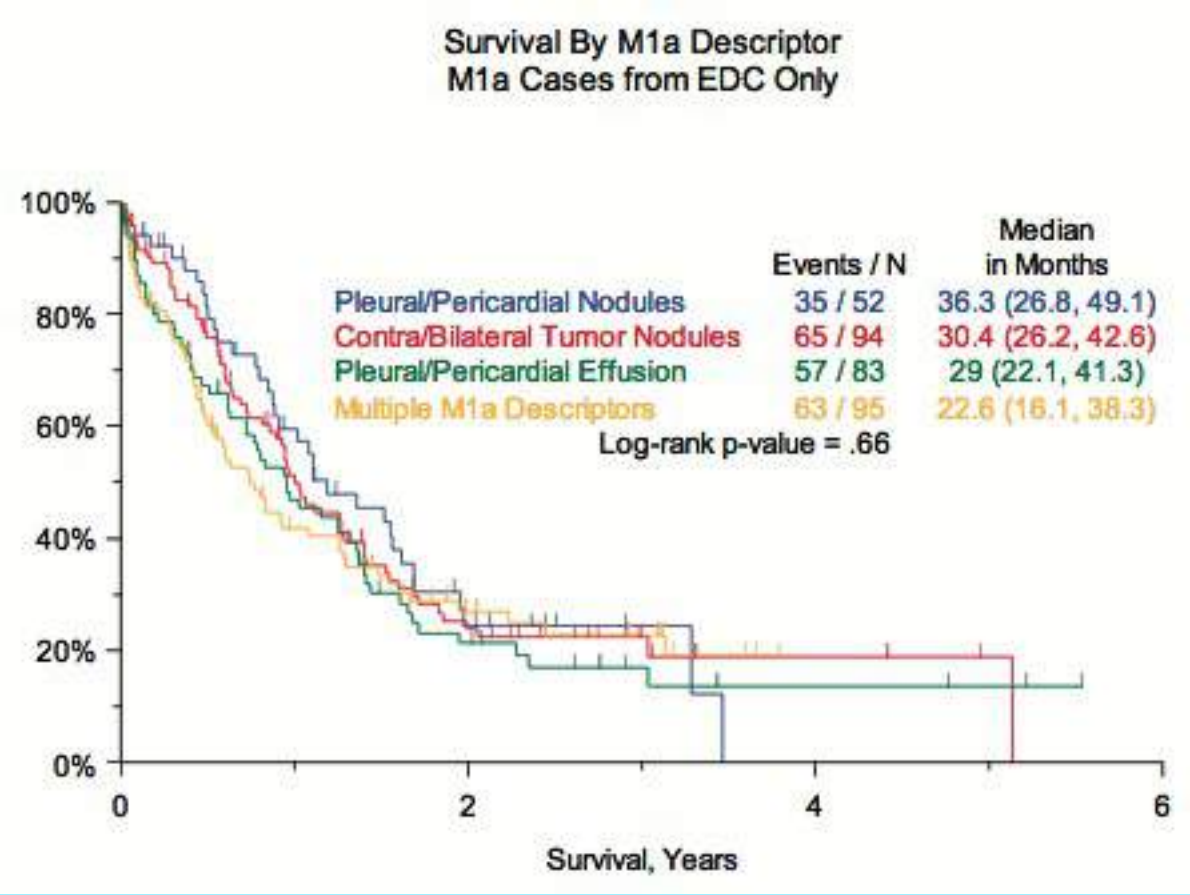
N: proposed recommendations

- To keep the present descriptors as they are
- To propose new descriptors pN1a, pN1b, pN2a1, pN2a2, pN2b, pN3 for prospective testing:
  - pN1a: involvement of single pN1 nodal station
  - pN1b: involvement of multiple pN1 nodal stations
  - pN2a1: involvement of single pN2 nodal station without pN1 (skip pN2)
  - pN2a2: involvement of single pN2 nodal station with pN1
  - pN2b: involvement of multiple pN2 nodal stations
  - pN3: as it is

Asamura H et al. J Thorac Oncol 2015; 10: 1675-1684.

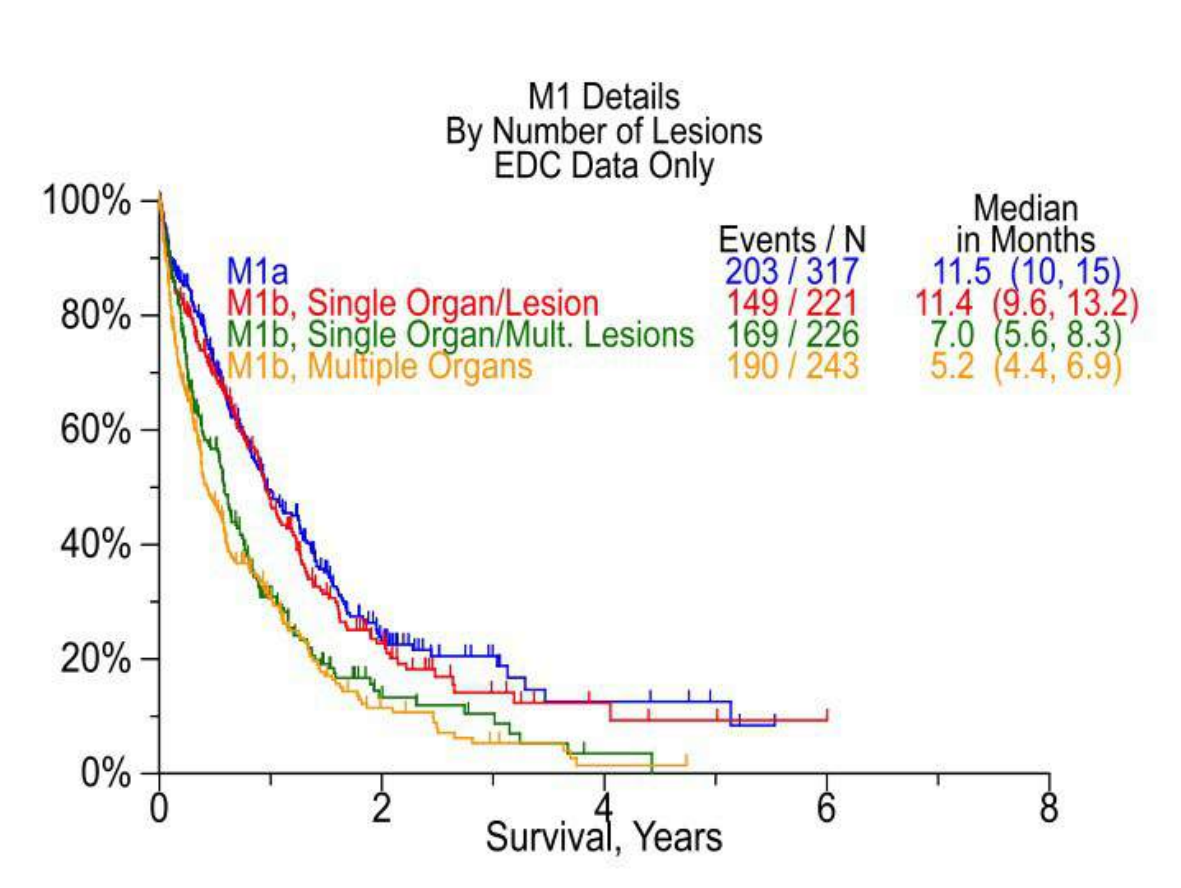
The M component: M1a

Prognosis for the different M1a descriptors is similar.



Eberhardt W et al. J Thorac Oncol 2015; 10: 1515-1522.

The M component: M1b



M1a

M1b

M1c

M1c

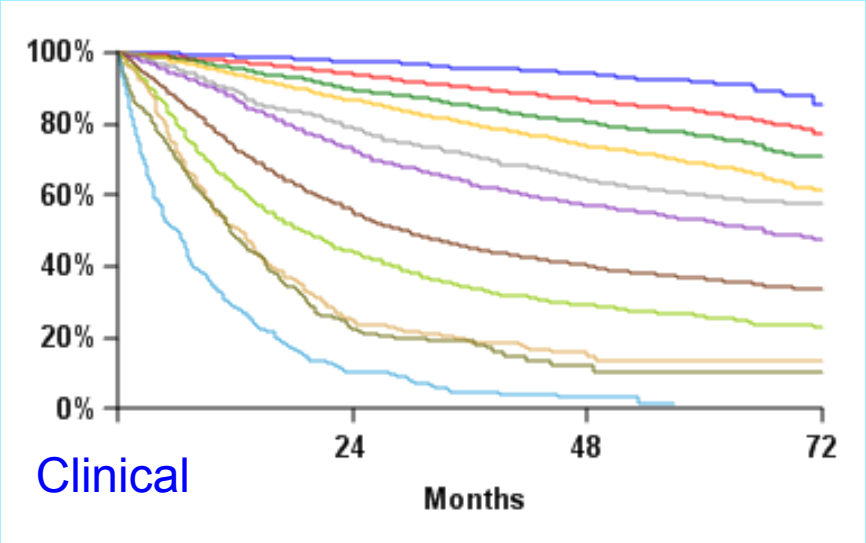
Eberhardt W et al. J Thorac Oncol 2015; 10: 1515-1522.

Stage groupings

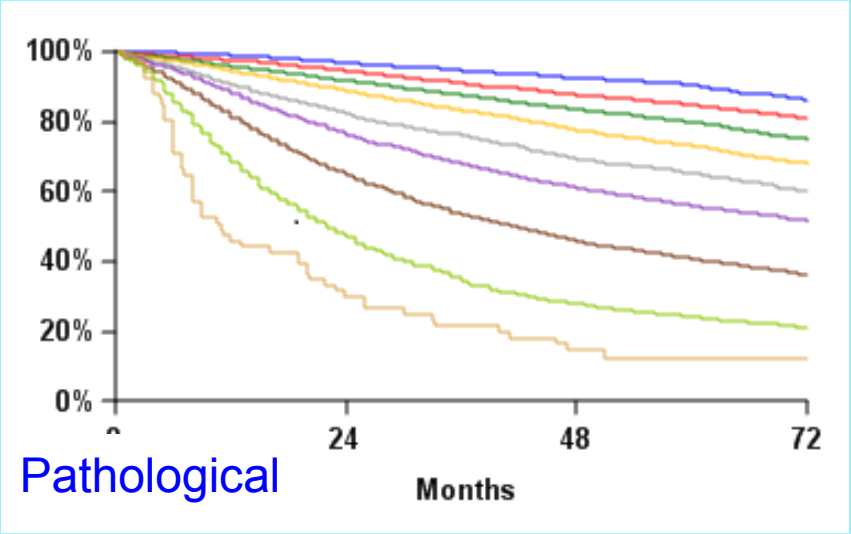
	N0	N1	N2	N3	M1a any N	M1b any N	M1c any N
T1a	IA1	IIB	IIIA	IIIB	IVA	IVA	IVB
T1b	IA2	IIB	IIIA	IIIB	IVA	IVA	IVB
T1c	IA3	IIB	IIIA	IIIB	IVA	IVA	IVB
T2a	IB	IIB	IIIA	IIIB	IVA	IVA	IVB
T2b	IIA	IIB	IIIA	IIIB	IVA	IVA	IVB
T3	IIB	IIIA	IIIB	IIIC	IVA	IVA	IVB
T4	IIIA	IIIA	IIIB	IIIC	IVA	IVA	IVB

Goldstraw P et al. J Thorac Oncol 2016; 11: 39-51.

Stage grouping for the 8th edition



Goldstraw P et al. J Thorac Oncol 2016; 11: 39-51.



	Events/N	MST	24 months	60 months
IA1	68/781	NR	97%	92%
IA2	505/3105	NR	94%	83%
IA3	546/2417	NR	90%	77%
IB	560/1928	NR	87%	68%
IIA	215/585	NR	79%	60%
IIB	605/1453	66.0	72%	53%
IIIA	2052/3200	29.3	55%	36%
IIIB	1551/2140	19.0	44%	26%
IIIC	831/986	12.6	24%	13%
IVA	336/484	11.5	23%	10%
IVB	328/398	6.0	10%	0%

	Events/N	MST	24 months	60 months
IA1	139/1389	NR	97%	90%
IA2	823/5633	NR	94%	85%
IA3	875/4401	NR	92%	80%
IB	1618/6095	NR	89%	73%
IIA	556/1638	NR	82%	65%
IIB	2175/5226	NR	76%	56%
IIIA	3219/5756	41.9	65%	41%
IIIB	1215/1729	22.0	47%	24%
IIIC	55/69	11.0	30%	12%

Cancers with multiple lesions

Multiplicity of lesions is defined by DISEASE PATTERN

1. Second primary lung cancers
2. Separate tumour nodules
3. Multiple adenocarcinomas with GG/ lepidic features
4. Pneumonic type adenocarcinoma

Detterbeck F et al. J Thorac Oncol 2016; 11: 639-650

Lung cancers with multiple lesions

Frank C. Detterbeck

The IASLC Lung Cancer Staging Project: Summary of Proposals for Revisions of the Classification of Lung Cancers with Multiple Pulmonary Sites of Involvement in the Forthcoming Eighth Edition of the TNM Classification

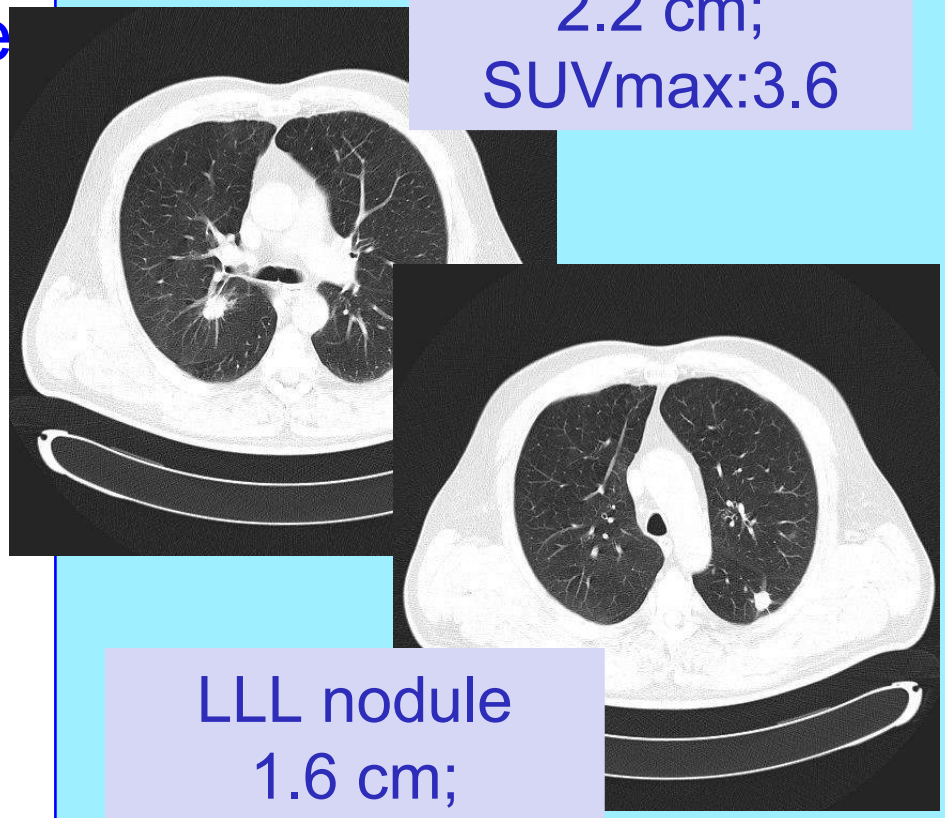
The IASLC Lung Cancer Staging Project: Background Data and Proposals for the Classification of Lung Cancer with Separate Tumor Nodules in the Forthcoming Eighth Edition of the TNM Classification for Lung Cancer

The IASLC Lung Cancer Staging Project: Background Data and Proposals for the Application of TNM Staging Rules to Lung Cancer Presenting as Multiple Nodules with Ground Glass or Lepidic Features or a Pneumonic Type of Involvement in the Forthcoming Eighth Edition of the TNM Classification

Second primary tumours

Clinical data

- Different histologic type
- Different radiographic appearance
- Different metabolic features
- Different biomarkers
- Different growth rate
- No nodal involvement or M1



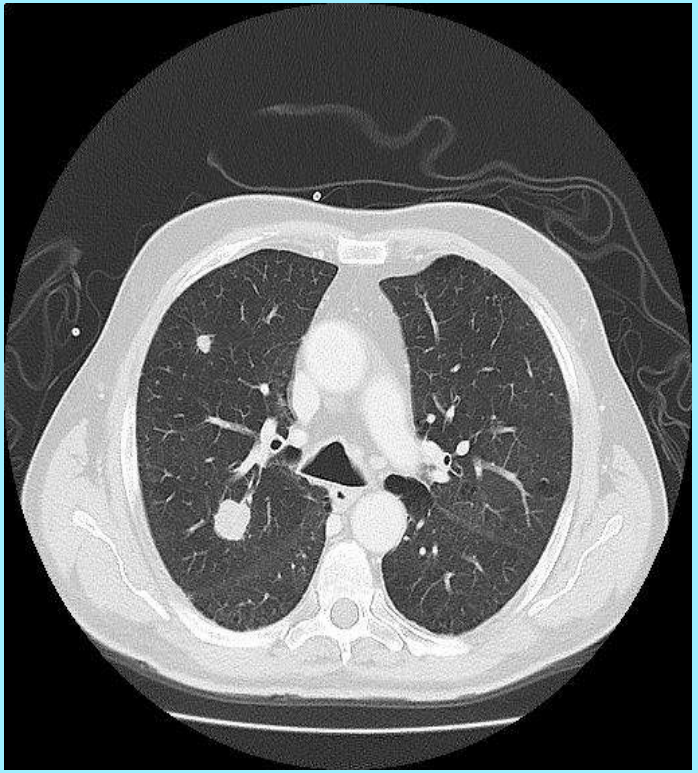
RUL nodule
2.2 cm;
SUVmax:3.6

LLL nodule
1.6 cm;
SUVmax:1.8

Separate tumour nodules

- One typical solid lung cancer
- One or more separate solid nodules with similar CT features, with pressumed or confirmed same histologic type
- Thought NOT to be synchronous tumours
- WITHOUT GG features

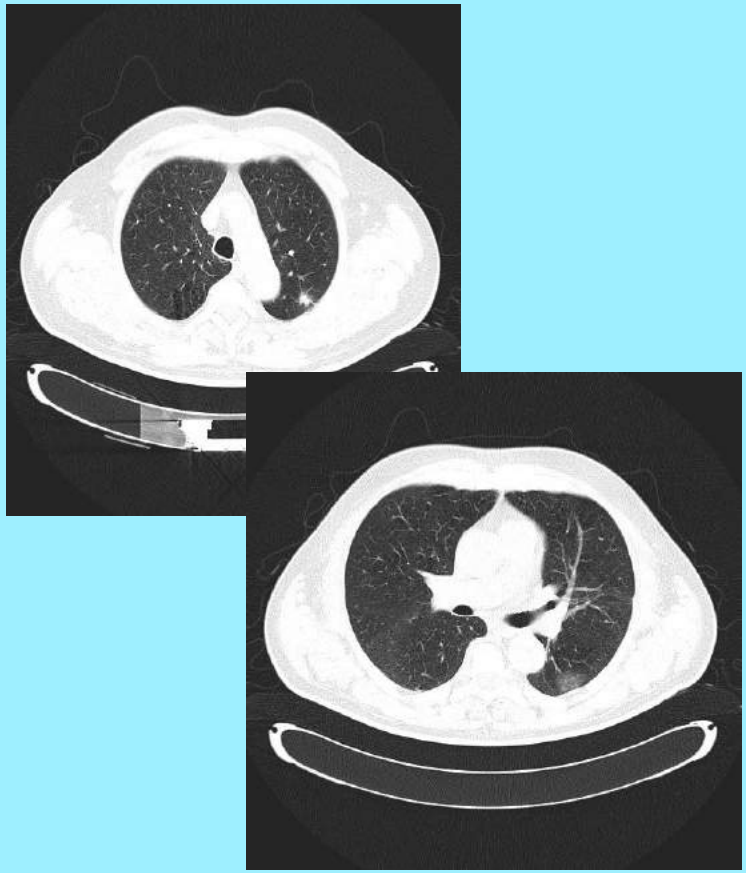
Clinical data



Multiple adenocarcinomas with GG/lepidic features

- Multiple sub-solid nodules (pure or part-solid) with at least one suspected (or proven) to be cancer
- With or without biopsy
- It applies to AIS, MIA and LPA
- GGOs <5cm suggestive of AAH do not count for TNM

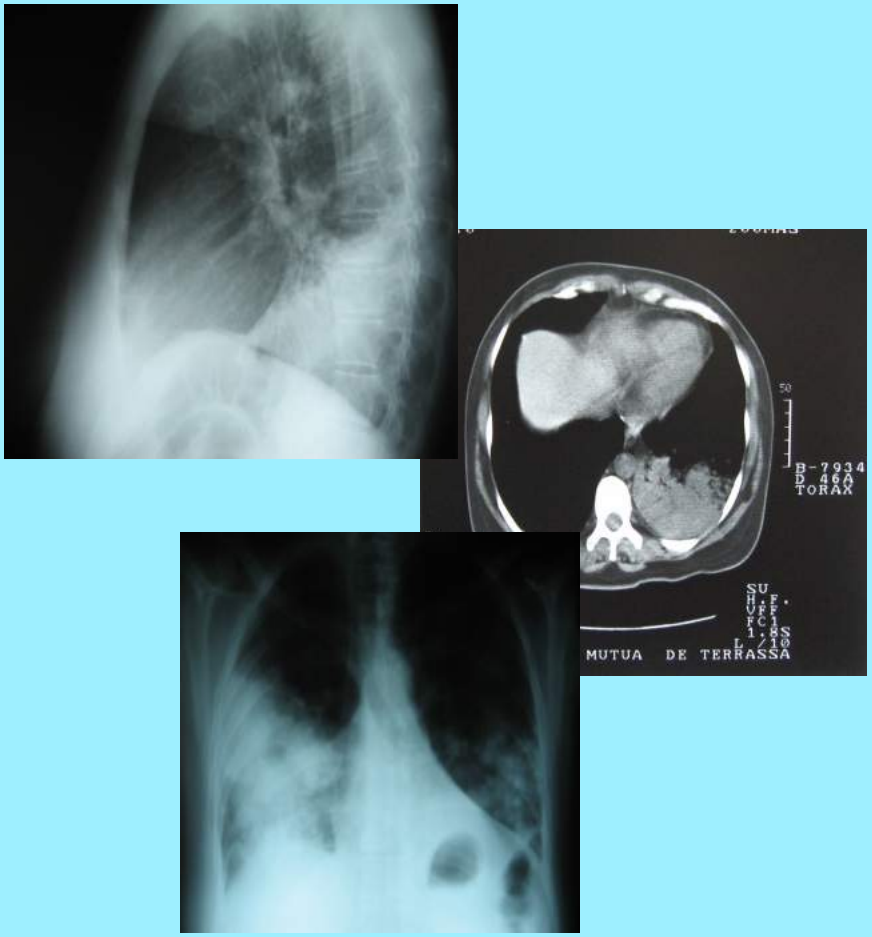
Clinical data



Pneumonic type adenocarcinomas

Clinical data

- Single or multiple areas of infiltrates or consolidation
- One lobe, one or both lungs
- GG, consolidation or both
- With or without biopsy
- NO discrete GG nodules
- NO pneumonia or atelectasis



Cancers with multiple lesions

1. Multiple primary tumours:
   - **One TNM for each tumour**
2. Separate tumour nodules:
   - **T3, T4, M1a**
3. Multiple adenos with GGO/lepidic features:
   - **Highest T (#/m) N M**
4. Pneumonic type adenocarcinoma:
   - **T3, T4, M1a**

Detterbeck F et al.
J Thorac Oncol
2016; 11 (5):
639-650
651-665
666-680
681-692

Content of this presentation

- Background and database
- Innovations in the 8th edition
- **Implications for clinical practice**
- Summary
- Conclusions

Implications for clinical practice: T

- Every cm counts; careful follow-up
- Accurate tumour size measurement, important
- Worse prognosis of larger tumours
- Better prognosis for endobronchial location and total atelectasis and pneumonitis
- Prognosis refinement
- Better stratification for clinical trials

Implications for clinical practice: N

- The amount of nodal disease has prognostic impact
- Important to quantify nodal disease both at clinical and pathologic staging
- Upfront resection for single station cN2 will be discussed
- Prognosis refinement
- Better stratification

Implications for clinical practice: M

- Number of M1s is more important than their location
- M1b: baseline definition of oligometastases and oligoprogression
- Prognosis refinement
- Better stratification

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Summary

- More relevance to tumour size
- Reclassification of some T descriptors
- Validation of present N descriptors
- Acknowlegment of relevance of quantification of nodal disease
- Three metastatic groups
- More stages for better prognostic stratification
- More recommendations for uniform staging

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Conclusions

The innovations in the 8th edition of the TNM classification of lung cancer:

- increase our capacity to refine prognosis
- improve tumour stratification in future trials
- prompt future research
- facilitate homogeneous tumour classification and collection of prospective data
- they should be used from **1st January 2017**

Objectives of tumour staging

Nomenclature	Taxonomy
	Exchange of information
Clinical practice	Prognostic estimation
	Therapeutic indications
	Quality control of health care
Clinical trials	Stratification
	Evaluation of therapy
	Identification of subgroups

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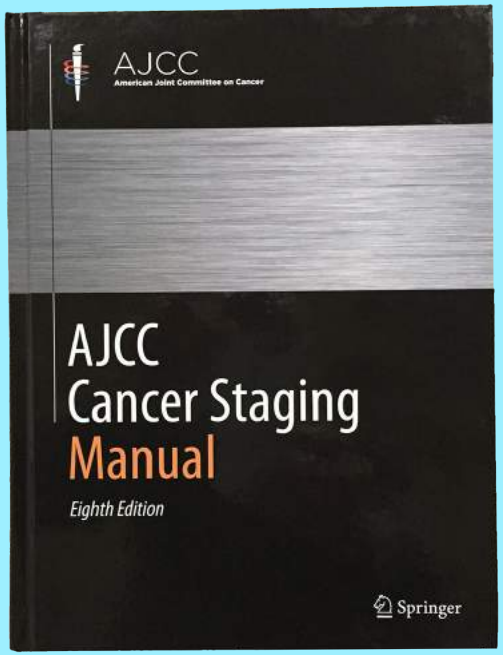

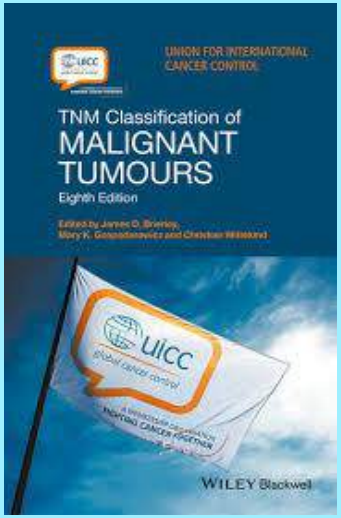

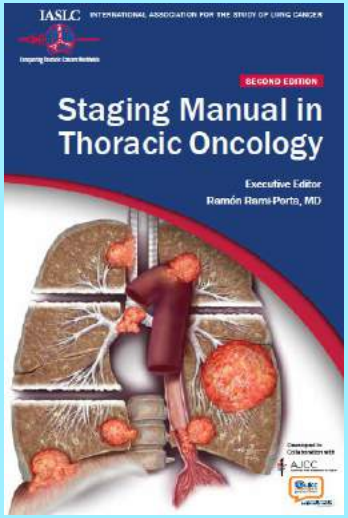

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18TH WORLD CONFERENCE ON LUNG CANCER

OCTOBER 15–18, 2017 . YOKOHAMA, JAPAN

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October 15–18, 2017 | Yokohama, Japan

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