

How VIII Edition TNM Affects Lung Cancer Management

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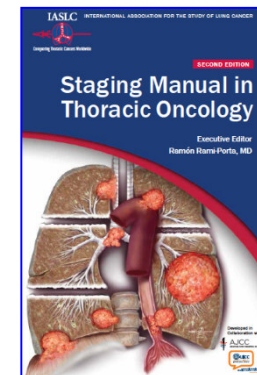
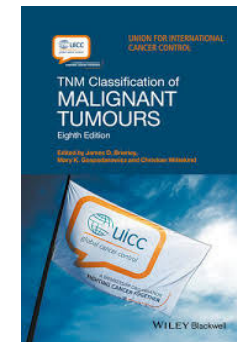
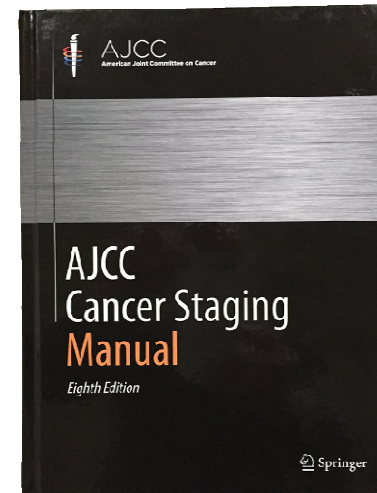


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**No conflicts of interest
to declare**

Content

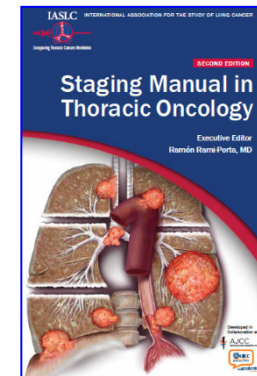
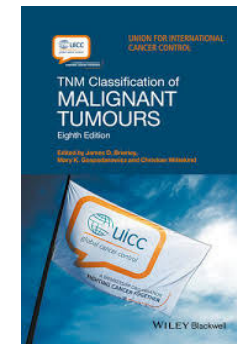
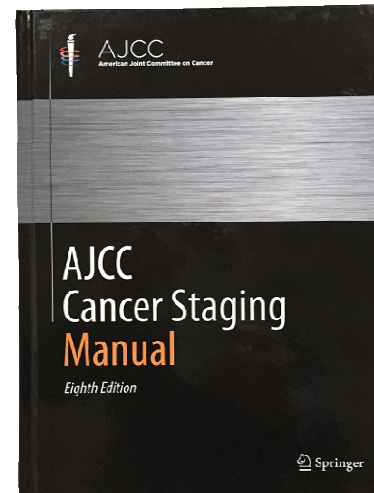
1. Database for the 8th edition
2. Innovations and clinical implications
3. Towards the 9th edition
4. Summary
5. Conclusions



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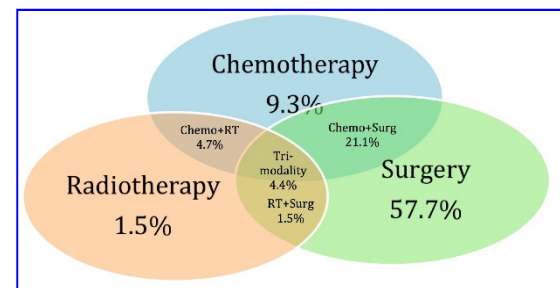
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DATABASE FOR THE 8TH EDITION

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	Number of cases
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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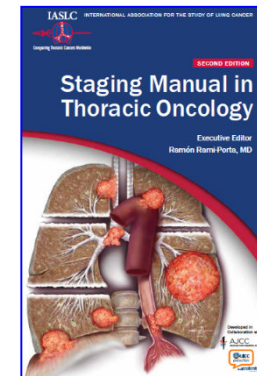
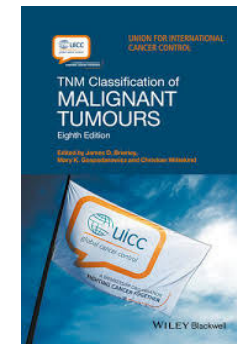
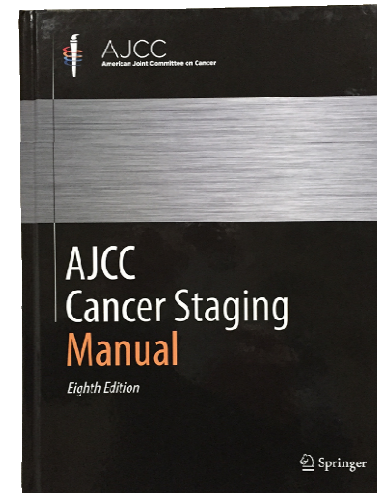
IASLC Staging and Prognostic Factors Committee 2009-2016. Vienna 2016



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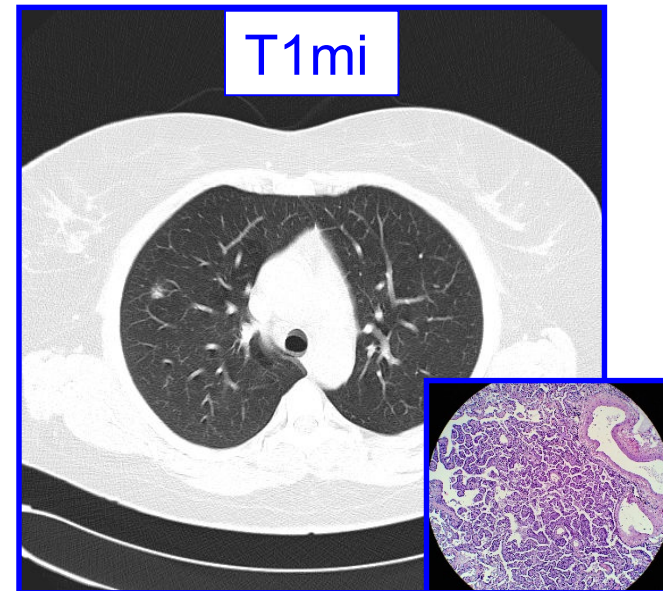
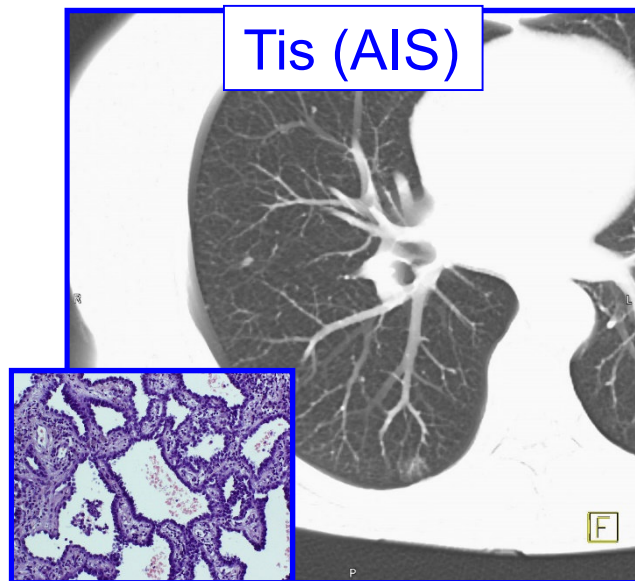
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Newcomers into the system



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

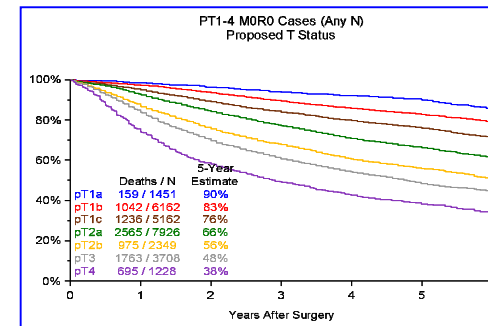
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New T categories based on tumour size and other descriptors

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

Descriptor	Category
Bronchus < 2 cm	T2
Total atelectasis	T2
Diaphragm	T4

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

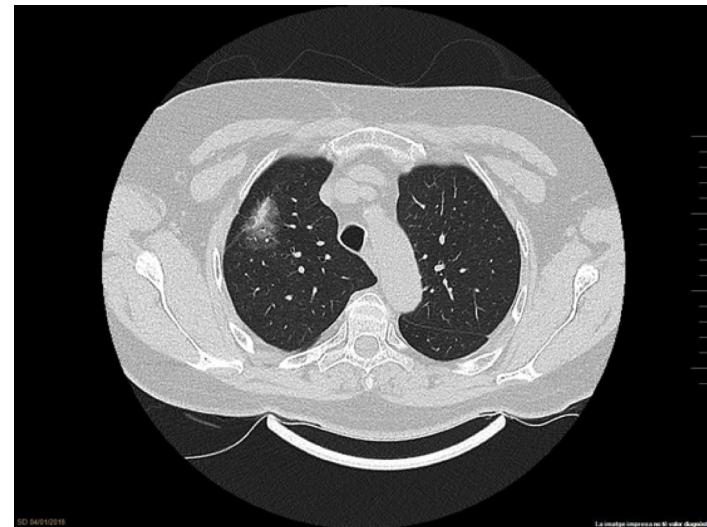


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Size of part-solid non-mucinous adenocarcinoma

Clinical size:
size of **solid component**

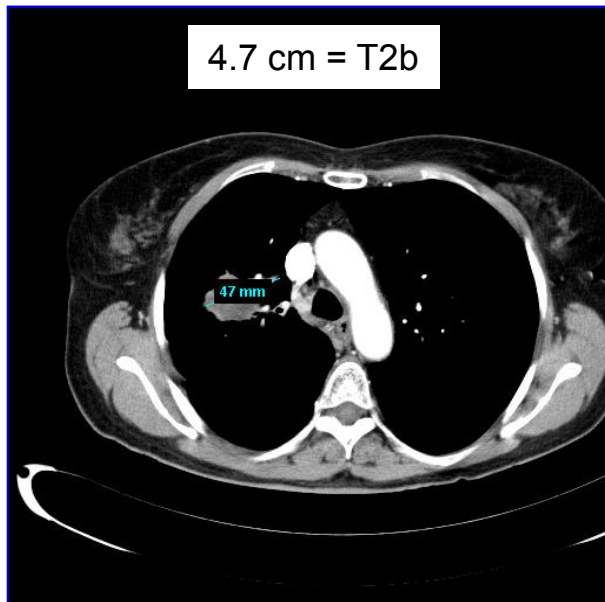
Pathologic size:
size of **invasive component**



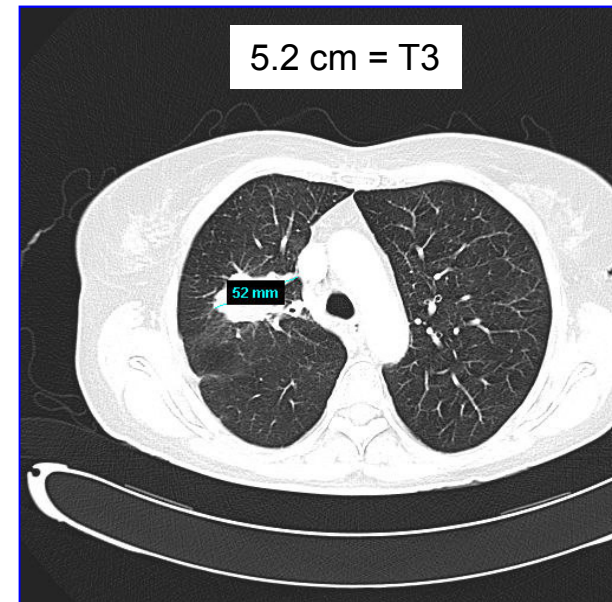
Travis W et al. J Thorac Oncol 2016; 11: 1204-1223.

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Measurement of solid tumour size



**Lung
window**



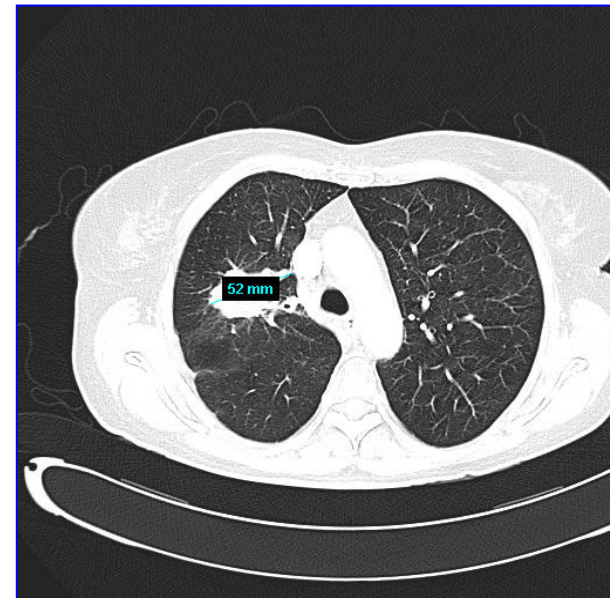
Travis W et al. J Thorac Oncol 2016; 11: 1204-1223.

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Measurement of tumour size after induction therapy

Multiply the percentage of viable cells by the total tumour size

In this case there was complete pathologic response. So,
 $0\% \times 52\text{mm} = 0$. **ypT0**

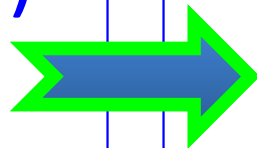


Travis W et al. J Thorac Oncol 2016; 11: 1204-1223.

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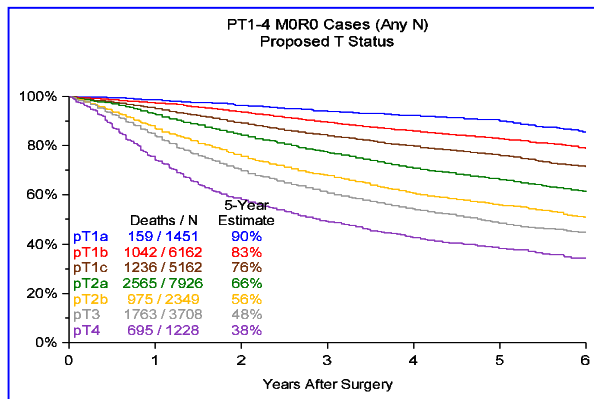
Management implications (I)

- Tis (AIS)
- Tis (SCIS)
- T1mi
- T1a



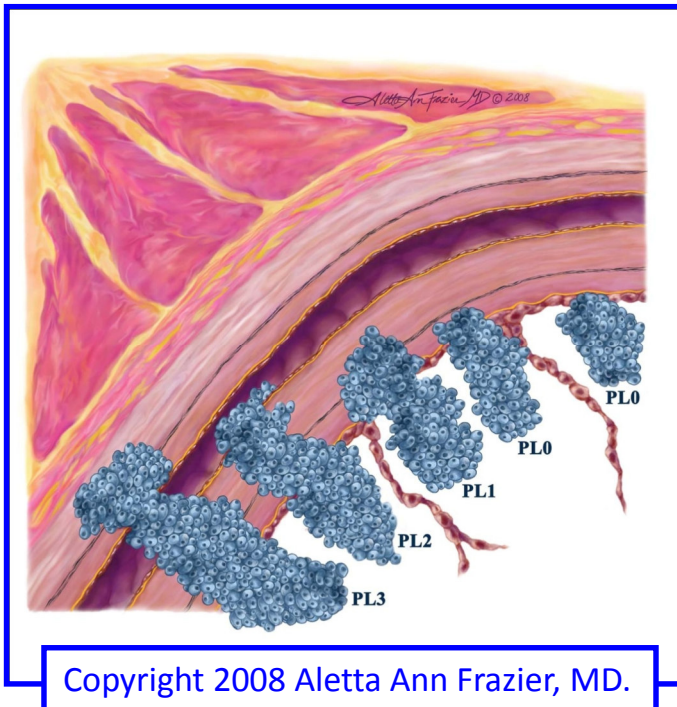
- Increased awareness
- Study therapeutic options
 - Sublobar resections
 - Systematic nodal dissection
 - Stereotactic radiotherapy
 - Radiofrequency ablation
- Tumour biology: growth, density, SUVmax, molecular profile, genetic signatures

Management implications (II)



- 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

Visceral pleura invasion



PL0:	----
PL1 & PL2:	T2
PL3:	T3

Elastic stains are recommended to identify visceral pleura invasion

Travis WD et al. J Thorac Oncol 2008; 3: 1384-1390

Importance of elastic stains

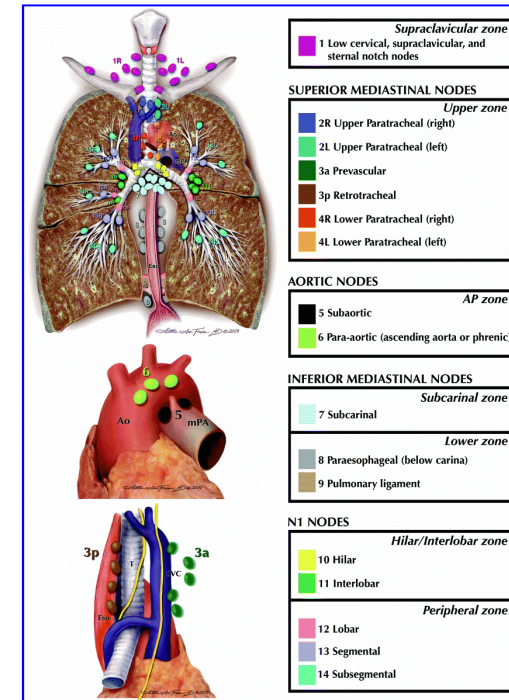
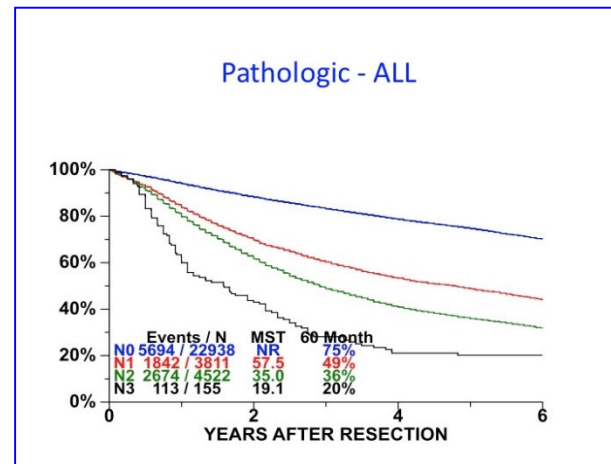
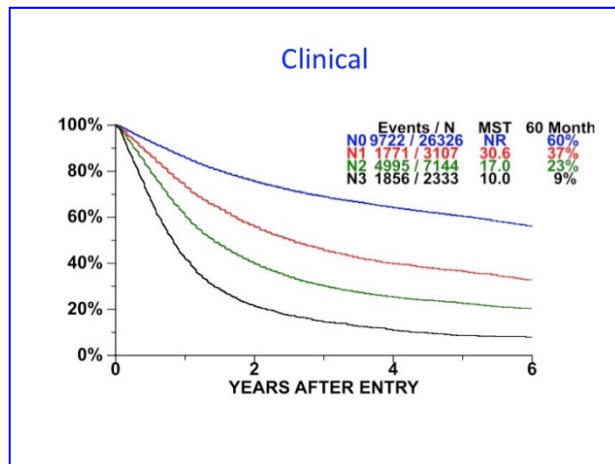
Apparent Stage I	# of cases	VPI, n (%) Elastic stains
Adenocarcinoma	46	8 (17%)
BAC	15	0 (0%)
Squamous	31	8 (26%)
Large cell	7	2 (29%)
Adenosquamous	1	1 (100%)
Total	100	19 (19%)

Use of elastic stains: 49 pathologists: never 25 (51%), some times 14 (29%) , always 10 (20%)

Taube JM et al. Am J Surg Pathol 2007; 31: 953-956

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The N component

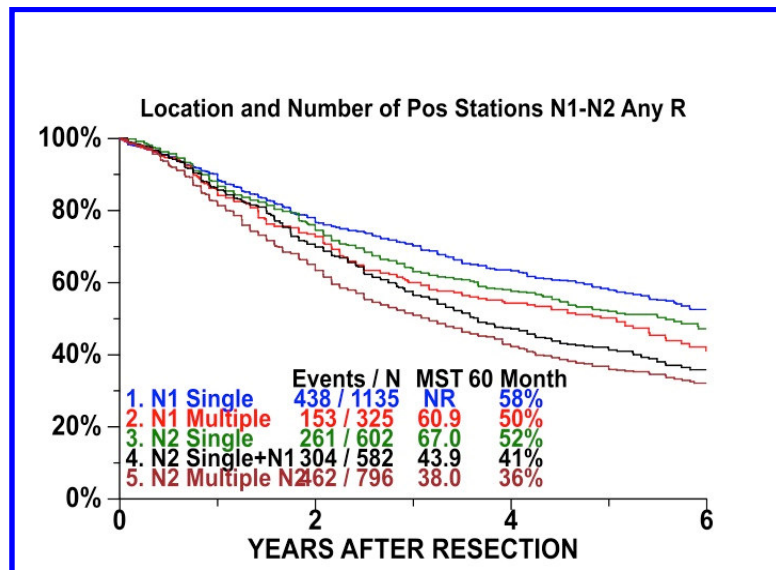


Asamura H et al. J Thorac Oncol 2015; 10: 1675-84.

Rusch V et al. J Thorac Oncol 2009; 4: 568-577.

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Quantification of nodal disease



N1 Single = N1a

N1 Multiple = N1b

N2 Single N2 (“skip mets”) = N2a1

N2 Single N2 + N1 = N2a2

N2 Multiple N2 = N2b

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

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Management implications (III)

N1 Single = N1a

N1 Multiple = N1b

N2 Single N2 (“skip mets”) = N2a1

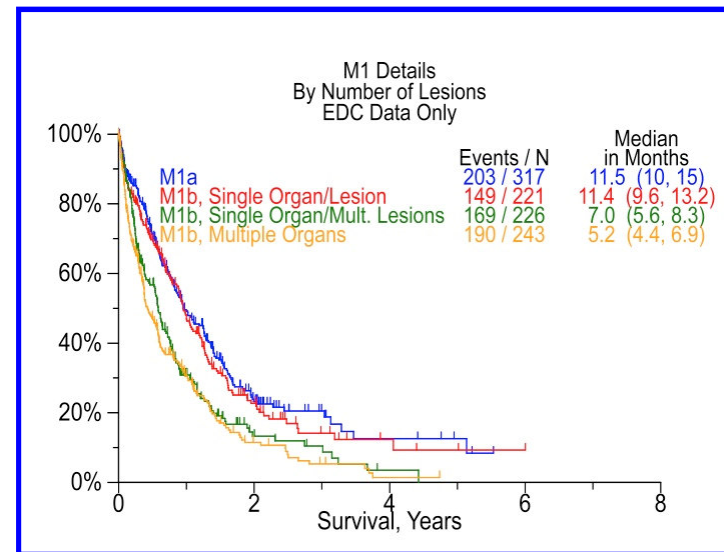
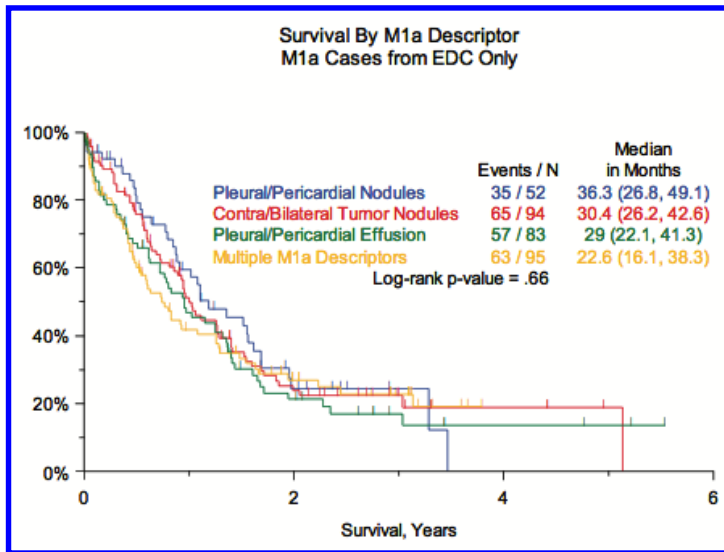
N2 Single N2 + N1 = N2a2

N2 Multiple N2 = N2b

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

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

The M component



M1a
M1b
M1c
M1c

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

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Management implications (IV)

M1a

M1b

M1c

M1c

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

Prognostic impact of M descriptors of the 8th edition of TNM classification of lung cancer

J Thorac Dis 2017;9(3):685-691

Margarida Dias, Ana Antunes, Sérgio Campinha, Sara Conde, Ana Barroso

Pulmonology Department, Gaia/Espinho Hospital Center, Vila Nova de Gaia, Portugal

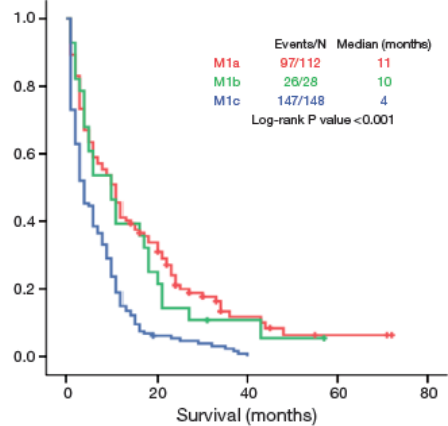


Figure 3 Overall survival according to different M1 categories.

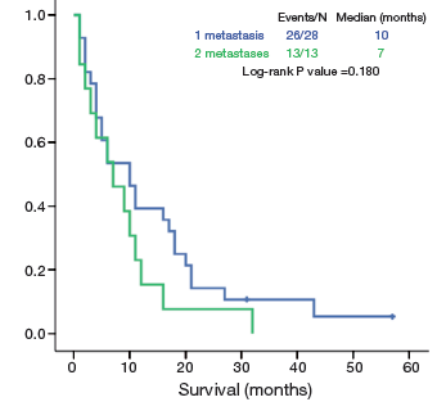


Figure 4 Overall survival of patients with a single metastasis versus patients with two metastases in a single organ.

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Stage grouping

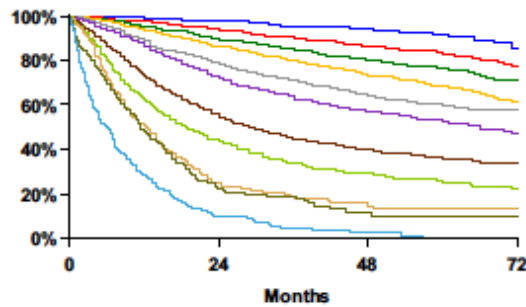
	N0	N1	N2	N3	M1a any N	M1b any N	M1c any N
T1a	IA1	IIB	IIIA	IIIB	IVA	IVA	IVB
T1b	IA2	IIB	IIIA	IIIB	IVA	IVA	IVB
T1c	IA3	IIB	IIIA	IIIB	IVA	IVA	IVB
T2a	IB	IIB	IIIA	IIIB	IVA	IVA	IVB
T2b	IIA	IIB	IIIA	IIIB	IVA	IVA	IVB
T3	IIB	IIIA	IIIB	IIIC	IVA	IVA	IVB
T4	IIIA	IIIA	IIIB	IIIC	IVA	IVA	IVB

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

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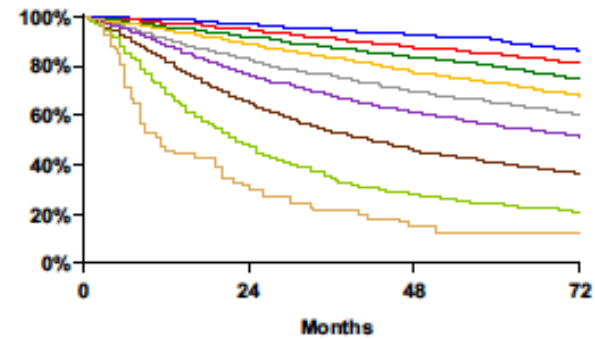
8th edition stage grouping

Clinical



Proposed	Events / N	MST	24 Month	60 Month
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%

Pathologic



Proposed	Events / N	MST	24 Month	60 Month
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%

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

Does a change in stage mean a change in therapy?

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Does a change in stage mean a change in therapy?

Should the 7th Edition of the Lung Cancer Stage Classification System Change Treatment Algorithms in Non-small Cell Lung Cancer?

Daniel J. Boffa, MD, Frank C. Detterbeck, MD,* Erica J. Smith, MPH,† Ramon Rami-Porta, MD,‡
John Crowley, PhD,§ Daniel Zelterman, PhD,¶ Lynn Tanoue, MD,|| Anthony W. Kim, MD,*
and Peter Goldstraw, MB, FRCS***

Introduction: Approximately 10 to 15% of non-small cell lung cancer patients will be assigned a stage classification according to the 7th

Key Words: Lung cancer, Staging, Treatment.

(J Thorac Oncol. 2010;5: 1779–1783)

Ann Surg Oncol (2011) 18:1–3
DOI 10.1245/s10434-010-1427-z

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

EDITORIAL

Reacting to Changes in Staging Designations in the 7th Edition of the AJCC Staging Manual

Daniel J. Boffa, MD¹ and Frederick L. Greene, MD²

¹Department of Thoracic Surgery, Yale University School of Medicine, New Haven, CT; ²Department of General Surgery, Carolinas Medical Center, Charlotte, NC

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Lung cancers with multiple lesions

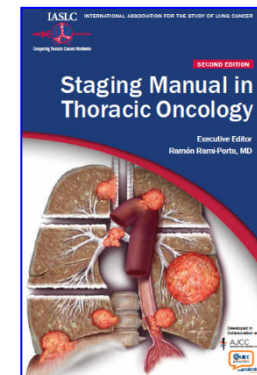
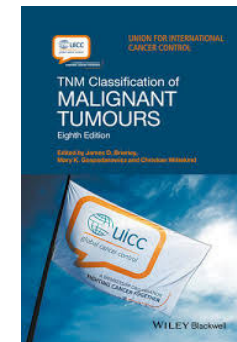
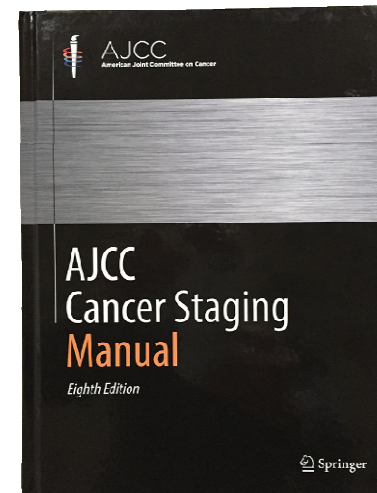
1. Multiple primary tumours:
 - **One TNM for each tumour**
2. Separate tumour nodules:
 - **T3, T4, M1a**
3. Multiple adenos with GGO/lepidic features:
 - **Highest T (#/m) N M**
4. Pneumonic type adenocarcinoma:
 - **T3, T4, M1a**



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

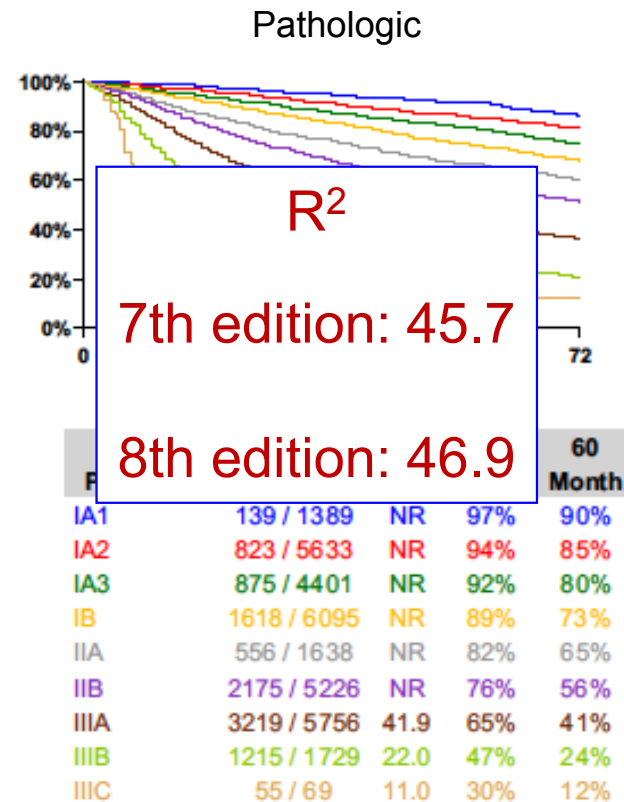
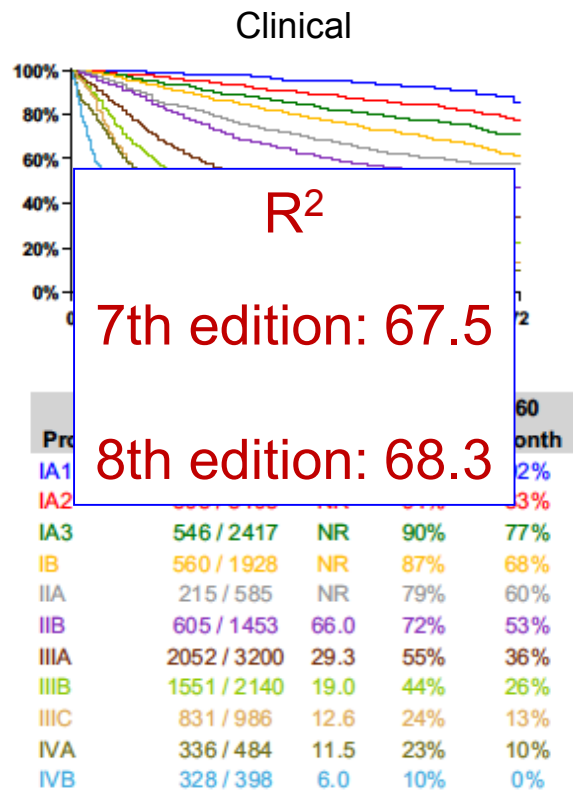
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8th edition stage grouping



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

For the 9th edition...

DO NOT expect:

M1a: Separate tumour nodule(s) in a contralateral lobe;
tumour with pleural or pericardial nodules or
malignant pleural or pericardial effusions and **EGFR**
status

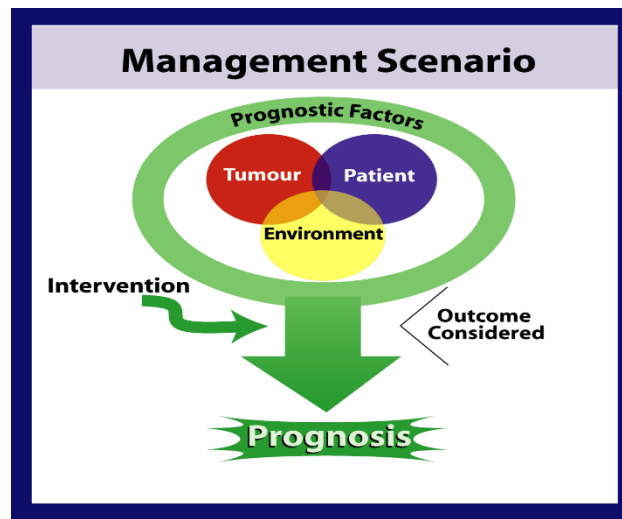
*

This would be **mixing** different parameters

For the 9th edition...

But TNM can be **combined** with other parameters
to build

PROGNOSTIC GROUPS



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For the 9th edition...

TNM + Clinical factors + Molecular + Etc.



PROGNOSTIC GROUPS

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IASLC Lung Cancer Staging Project: 9th Edition Database Implementation in Electronic Data Capture System



BiomarkersTab:

Genetic Biomarkers

Copy Number Alteration (CNA) Biomarkers

Protein Alterations

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IASLC Lung Cancer Staging Project: 9th Edition Database Biomarkers Section

Genetic Biomarkers

Genetic Biomarkers for this Subject

Date Assessed	Type of Sample	Total mutational burden	Gene	Platform	DNA Variant
12-JUN-2017	Biopsy		ASXL1	Sanger	
13-JUN-2017	Plasma	55			
15-JUN-2017	Plasma		FGFR4	FISH	FGFR4 Mutation

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IASLC Lung Cancer Staging Project: 9th Edition Database

Biomarkers Section

Copy Number Alterations

CNA Biomarkers for this Subject

CNA	Date Assessed	Type of Sample	Platform	Average Gene Copy Number
CCND1 11q13 AMP	12-JUN-2017	Biopsy	OncoScan	42
FOXA1 14q21.1 AMP	15-JUN-2017	Plasma	FISH	38

CNA	Date Assessed	Genotype	Average Gene: Centromere Ratio	Centromere Copy Number
CCND1 11q13 AMP	12-JUN-2017	Homozygous	19.27%	40
FOXA1 14q21.1 AMP	15-JUN-2017	Heterozygous	24.65%	24

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IASLC Lung Cancer Staging Project: 9th Edition Database Biomarkers Section

Protein Alterations

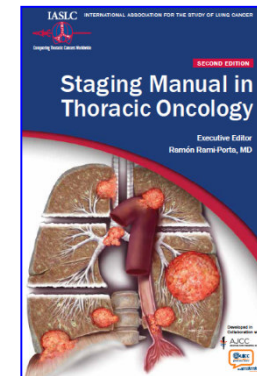
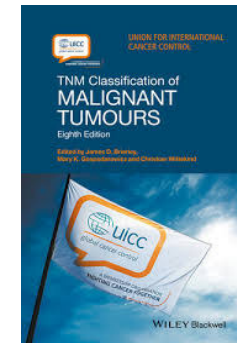
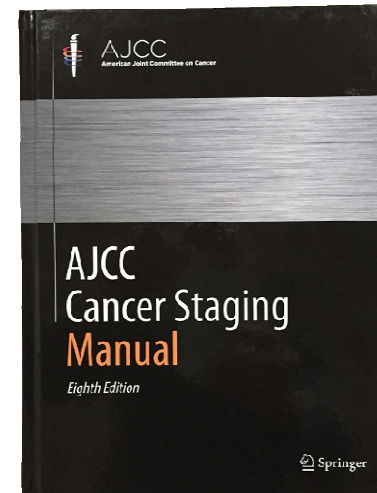
Protein Alterations for this Subject

Protein	Date Assessed	Type of Sample	Platform	Antibody	% Tumor Cells	% Immune Cells	H-Score
PD-L1	12-JUN-2017	Biopsy	Mass Spectrometry	DAKO 28-8	36	45	121
ALK	15-JUN-2017	Plasma	IHC	Dako ALK1	32	42	181

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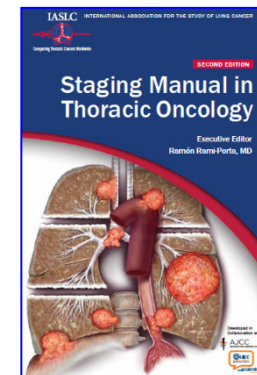
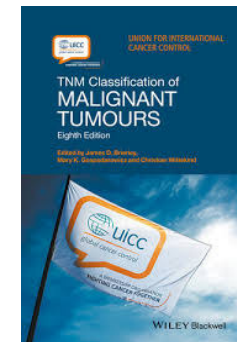
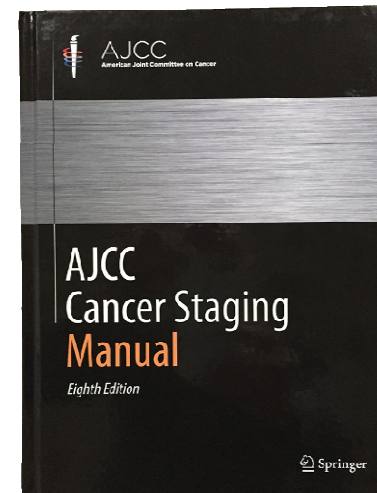
Summary

- More relevance to tumour size
- Reclassification of some T descriptors
- Validation of present N descriptors
- Acknowledgement of relevance of quantification of nodal disease
- Three metastatic groups
- More stages for better prognostic stratification
- More recommendations for uniform staging
- TNM as an important component of prognostic groups in 9th ed.

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Conclusions

- The 8th edition TNM for lung cancer implies changes in management, but not necessarily in treatment
- New tumours, relevance of tumour size, quantification of nodal disease, and number of extrathoracic metastases require precise determination and strict assessment
- The 9th edition may increase our capacity for a more individualized prognosis

IASLC



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