The 8th Edition of the TNM Classification for Lung Cancer Background, Innovations and Implications for Clinical Practice

> University of Torino Lecture 28th June 2017 Torino, Italy

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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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1987	4th edition UICC TNM			
1988	3rd edition AJCC TNM	Mountain's		
1992	4th edition AJCC TNM	database		
1997	5th edition UICC and AJCC TNM			
2002	6th edition UICC and AJCC TNM			
2009	7th edition UICC and AJCC TNM	IASLC		
2016	8th edition UICC and AJCC TNM	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

International Workshop on Intrathoracic Staging

Sponsored by International Association for the study of Lung Cancer

28th - 29th October 1996

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

Process for TNM revision 2002 onwards



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 descriptor S	Supplementary information	Site- specific rules
Т	TXT4	Size, location, invaded structures, etc	Grade R L Pn V	Instructions for homogeneous classification of situations not included in	Several
Ν	NXN3	Presence, absence and location	C	descriptors or optional descriptors	6 nodes for pN0
Μ	M0M1c	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</td <td>T1a</td>	T1a
>1-2 cm	T1b
>2-3 cm	T1c
>3-4 cm	T2a
>4-5 cm	T2b
>5-7 cm	Т3
>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



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-











Tsuguo Naruke 1934-2006 WEALSWALD T.D.

脑がんの拡大進展と外科手術との相関

(前半说年3月28日使任)

目264.477-181-88(188 50(68889) 成毛 哲 夫

E.

前かんの知道の一トは「メバビ協・出行性・社 当性・周辺性に大当されるが、外科手術の時点に ないてはこれら対後難に異会する、対応の言いら のはされた市場時であり、進行何では話用子が重要 する。

これらの記録を切除の対象とする外科技にとつ て、ランド的解除は手板手指に適適した問題であ り、曲行道解和掛は手板手指にっては説明であ して声音な研できた、構造地気軽については説明が して声言な研できた、構造地気軽については説明が して声しいが、切除地の道氏酵素の円分が、気管 支路内に酸率されたがく相談の完成がであとしか考 とちれぬ証明を調整する。近年、曲物法管定時内 に酸油酸物の成功がかった。そうので、これの可 整整は否定できないが、臨床の装置では関なるの ということができょう、施設を振行する差 の使用のも可想的にだめであらうか、試試感に 開着の点なしにによって、予想にあのあることを 感じるからである。

私たちは、今まで、肺がんに対する肺炎肺素式 を塗め、振動能であれ感素が除てあれ、細胞の空 離野を行なうことを原因としてきた、その結果? アリ酸脂肪の対策については、学教的最差に大きい 効果のあることを詰めている声、並行して行な つた為竹家族の感謝においてはまだ確認な対策が 得られていない。

ここでは、平根時の時間が展開と認知部につい て、ドメイロ転移・形も組織の血管接触(血管物 転換の意識地向子として)がよび結婚目前(構成 転換の意識として)を並行がにしらべ、時から相 数の提供を転訪れば低しようとした。

研究対象と方法 国立がんたンター用配において、(900年を月上 91960年10月までに新鮮した原発性新いた時間1 1999の5ち、ジン・2015時、原原原源に用しては 100月(Table 1)、直営経験については167回を 対象とした。

GBBBは Hare Nice で回販にに取っの問題を 加え、問題の形成、大きさ、位定、原見気管支を 確認し、さらに気管支寄湯、粘酸を信息して内損 的にバー支援の有縁・提供を構造する。最低学的 には、肥富の創稿分類、肥齢付から起取の点管後 開の有机、肥富に式提する計測、気管支防病、お よび残時和減を提供してバール達然の場相を検討し

作科病理学上の分類は主に服務学会委員会の説

Table I. Medc of Opitation

Fig. 1.

 Diagram deconstrating the time of lymph anderi (2) Separity multiatume, (2) Funtaselevi (3) Pre-strue urchait, (3) Tancheshomalani, (3) Pre-strue urchait, (4) Structure, (3) Industriat, (2) Functional (3) Structure, (3) Industriat, (3) Functional (3) Distribution Regiment, (11) Indus broaches, (13) Segmental breaches.



 Disgram demonstrating dis site of lymph motes on size right motionization.



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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



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

M₁a M1b M₁c

Stage groupings

	NO	N1	N2	N3	M1a	M1b	M1c
					any N	any N	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
T 3	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



	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%

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



	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

CENTRA ATTACAT

The IASLE Lung Cancer Staging Project: Summary of Processis for Revisions of the Classification of Lung Cancers with Multiple Pulmonary Stes of Involvement in the Forthcoming Eighth Edition of the TNM Classification

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Frank C. Determed, HD, "* William A. Franklin, HD," Andrew G. Hicharan Miceles Chard, HD," Diagte A Anarderg, HD, "William D. Train, HD," Reser J. Huzzane, HD, "Exits H, Hanan, HD," Janaka S. Daragtan, HD," Lynn T. Tomour, HD, "Valente M. Rusch, M.D," House Assesse, HD," Banda Rand-Harta, MD,"" on behalf of the MSLC Staguy and Propositics Consistery Advancy loands, and the Mittigle Rokenwary Ster, Molignay,

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The IASLE Lung Cancer Staging Project: Background 1. 1000 Data and Proposals for the Classification of Lung Cancer with Separate Tumor Nodules in the Forthcoming Eighth Edition of the TNW Classification for Lung Cancer

Frank C. Detterbeck, HD, ** Marena Indejack, MH, * Douglas A. Armiteg, HD,* John Carriery, R.D." Jacobs S. Dorlington House Grand, HD,' Rith H. Hanon, H CINEKA ARTON

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Frank C. Detterbeck

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

- 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

Clinical data



Cancers with multiple lesions

- 1. Multiple primary tumours:
 - One TNM for each tumour
- 2. Separate tumour nodules:
 - T3, T4, M1a

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

- 3. Multiple adenos with GGO/lepidic features:
 - Highest T (#/m) N M
- 4. Pneumonic type adenocarcinoma:
 - T3, T4, M1a

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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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James D. Brierley Mary K. Gospodarowicz Christian Wittekind









AS C-INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

18TH WORLD CONFERENCE **ON LUNG CANCER**

OCTOBER 15-18, 2017 YOKOHAMA, JAPAN

SAVE THE DATE! October 15-18, 2017 | Yokohama, Japan

TOKYO

CONFERENCE CO-PRESIDENTS

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Professor and Chief Division of Hematology/Oncology **Department** of Medicine Samsung Medical Center Sungkyunkwan University YOKOHAMA **School of Medicine** Seoul, KOREAI.HOUR FLIGH

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OSAKA

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