La classification TNM du cancer bronchique: ce qui va changer en 2016

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Déclaration

- Absence de conflits d'intérêts commerciaux avec le sujet abordé

Bases historiques

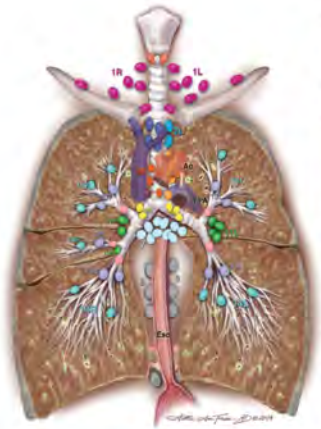
- 1946 : Denoix invente le TNM
- 1968 : 1ère édition du manuel de l'UICC (classification TNM des tumeurs malignes)
- 1973 : AJC : classification TNM basée sur la banque de données de Mountain
- 1974 : 2ème édition du manuel intégrant la classification de Mountain
- 1997 : 5ème édition toujours basée sur les données de Mountain
- 2002 : 6ème édition inchangée pour le cancer du poumon
- 2009 : 7ème édition (proposée par l'IASLC Staging Project)
- 2016 : 8ème édition (proposée par l'IASLC Staging and Prognostic factors committee)

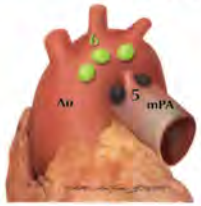
Classification TNM actuelle (7e édition)

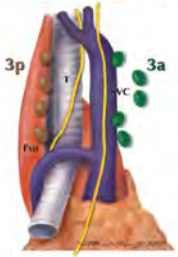
Les changements

Descripteur T/M (6ème édition)	**Changement T/M**	**N0**	**N1**	**N2**	**N3**
T1 (≤ 2 cm)	**T1a**	IA	IIA	IIIA	IIIB
T1 (>2 – 3 cm)	**T1b**	IA	IIA	IIIA	IIIB
T2 (>3 – 5 cm)	**T2a**	IB	**IIA**	IIIA	IIIB
T2 (>5 – 7cm)	**T2b**	**IIA**	IIB	IIIA	IIIB
T2 (≥ 7 cm)	**T3**	**IIB**	**IIIA**	IIIA	IIIB
T3 par invasion		IIB	IIIA	IIIA	IIIB
T4 (nodule même lobe)		**IIB**	**IIIA**	IIIA	IIIB
T4 par extension	**T4**	**IIIA**	**IIIA**	IIIB	IIIB
M1 (nodule pulmonaire ipsilatéral)		**IIIA**	**IIIA**	**IIIB**	**IIIB**
T4 (atteinte pleurale)	**M1a**	**IV**	**IV**	**IV**	**IV**
M1 (nodule pulmonaire controlatéral)		IV	IV	IV	IV
M1 (métastase à distance)	**M1b**	IV	IV	IV	IV

Nouvelle carte ganglionnaire







Supraclavicular zone
- 1 Low cervical, supraclavicular, and sternal notch nodes

SUPERIOR MEDIASTINAL NODES

Upper zone
- 2R Upper Paratracheal (right)
- 2L Upper Paratracheal (left)
- 3a Prevascular
- 3p Retrotracheal
- 4R Lower Paratracheal (right)
- 4L Lower Paratracheal (left)

AORTIC NODES

AP zone
- 5 Subaortic
- 6 Para-aortic (ascending aorta or phrenic)

INFERIOR MEDIASTINAL NODES

Subcarinal zone
- 7 Subcarinal

Lower zone
- 8 Paraesophageal (below carina)
- 9 Pulmonary ligament

N1 NODES

Hilar/Interlobar zone
- 10 Hilar
- 11 Interlobar

Peripheral zone
- 12 Lobar
- 13 Segmental
- 14 Subsegmental

FIGURE 3. The International Association for the Study of Lung Cancer (IASLC) lymph node map, including the proposed grouping of lymph node stations into "zones" for the purposes of prognostic analyses.

Les nouvelles données

Base de données

IASLC Staging Committee Article

The IASLC Lung Cancer Staging Project: The New Database to Inform the Eighth Edition of the TNM Classification of Lung Cancer

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Abstract: The analyses of the retrospective database of the International Association for the Study of Lung Cancer (IASLC), consisting of more than 81,000 evaluable patients diagnosed with lung cancer between 1990 and 2000, formed the basis of recommendations to the Union for International Cancer Control and the

Key Words: Lung cancer, Lung cancer databases, Lung cancer staging, Nonsmall cell lung cancer, Small cell lung cancer, TNM classification.

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EDC: 4667 / 94.708

TABLE 2. Number of Cases Submitted by Each Data Source, by Continent

Region	Data Source	EDC Source	N
Asia	EDC	Guangdong General Hospital, China	739
		Shanghai Lung Tumor Clinical Medical Center, China	51
	Japan 1999		13,344
	Japan 2002		14,695
	Japan 2004		10,889
	South Korea		1,987
Australia	EDC	Peter MacCallum Cancer Centre	4
	Prince Charles		229
	Sydney		1,360
Europe	Belgrade, Serbia		88
	Denmark		33,949
	EDC	Athens School of Medicine, Greece	39
		Clinical Center of Serbia, Serbia	40
		GCCB-S, Spain	2,362
		L'Institut Mutualiste Montsouris, France	120
		Military Medical Academy, Serbia	20
		Antwerp University Hospital, Multidisciplinary Oncological Centre Antwerp (MOCA), Belgium	195
		University Hospital Ghent, Belgium	85
		University of Torino, Italy	4
	Norway		2,354
	Turkey		7,304
North and South America	EDC	Alexander Fleming Institute, Argentina	6
		Clinica y Maternidad Suizo Argentina, Argentina	3
		Fundación Clínica Valle del Lili, Colombia	2
		Good Samaritan Hospital, USA	10
		Hospital Británico de Buenos Aires, Argentina	68
		Hospital Universitario Austral, Argentina	46
		Hospital Universitario-Fundación Favaloro, Argentina	36
		Hospital de Rehabilitación Respiratoria, Argentina	14
		Mayo Clinic Rochester, USA	47
		New York University Langone Medical Center and Cancer Center, USA	688
		Penrose Cancer Center, USA	73
		University of Sao Paulo Medical School, Brazil	15
	MDACC, USA		2,415
	MSKCC, USA		1,427
Global Total			94,708

GCCB-S, Grupo Cooperativo de Carcinoma Broncogénico de la Sociedad Española de Neumología y Cirugía Torácica; NYU, New York University; MDACC, M. D. Anderson Cancer Center; MSKCC, Memorial Sloan-Kettering Cancer Center.

TABLE 3. Number of Cases Submitted to the Database, With Exclusions and the Numbers Remaining for Analysis

Submitted	94,708
Excluded	17,552
Carcinoids	745
Other or unknown histology	5,986
Outside 1999–2010 timeframe	525
Incomplete survival data	938
Incomplete stage information	9,286
Multiple synchronous tumors	72
Included in initial analyses	77,156
NSCLC	70,967
SCLC	6,189

TABLE 4. Number of Cases Analyzed by Type of Data Source

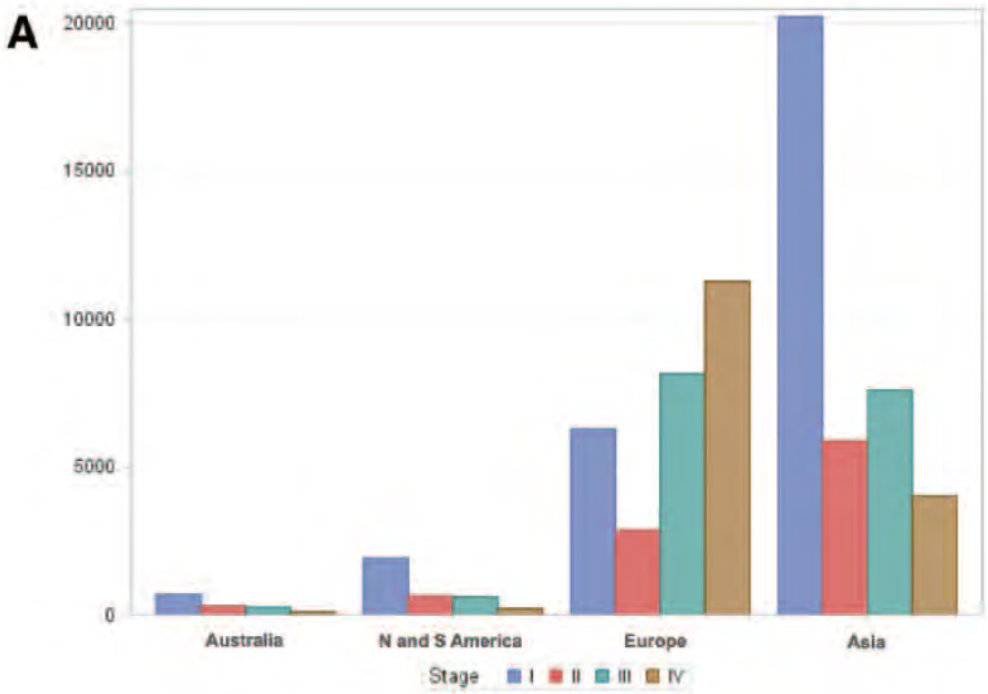
	Other	EDC	Total
Data source type			
Consortium	41,548	2,089	43,637
Registry	26,122		26,122
Surgical series	5,373	592	5,965
Institutional series		1,185	1,185
Institutional registry	208		208
Unknown		39	39
Total	73,251	3,905	77,156

Consortium: group of institutions where all individuals diagnosed with lung cancer are registered. Registry: all individuals diagnosed with lung cancer in a defined region, including those diagnosed at death. Surgical series: all individuals diagnosed with lung cancer and treated by a particular surgeon or unit. Institutional series: same as consortium, but in a single institution; may be limited to a specific treatment specialty or specialties. Institutional registry: all individuals diagnosed with lung cancer and admitted to a particular institution are registered.

TABLE 5. Comparison of Basic Elements of the Two IASLC Databases Used for Informing the seventh Edition and the eighth Edition of the TNM Classification of Lung Cancer

Element	Database for the seventh Edition	Database for the eighth Edition
Period of diagnosis	1990 to 2000	1999 to 2010
Total patients submitted	100,869	94,708
Geographical origin		
Europe	58,701 (58%)	46,560 (49%)
North America	21,130 (21%)	4,660 (5%)
Asia	11,622 (11.5%)	41,705 (44%)
Australia	9,416 (9.3%)	1,593 (1.7%)
South America	0	190 (0.3%)
Patients excluded	19,374 (19%)	17,552 (18%)
Patients included for analyses	81,495	77,154
NSCLC	68,463 (84%)	70,967 (92%)
SCLC	13,032 (16%)	6,189 (8%)
Treatment modalities		
Surgery alone	41%	57.7%
Radiotherapy + surgery	5%	1.5%
Chemotherapy + surgery	4%	21.1%
Chemotherapy alone	23%	9.3%
Radiotherapy alone	11%	1.5%
Chemotherapy + radiotherapy	12%	4.7%
Trimodality	3%	4.4%

CBNPC


A
20000
15000
10000
5000
0
Australia
N and S America
Europe
Asia
Stage I II III IV

CBPC

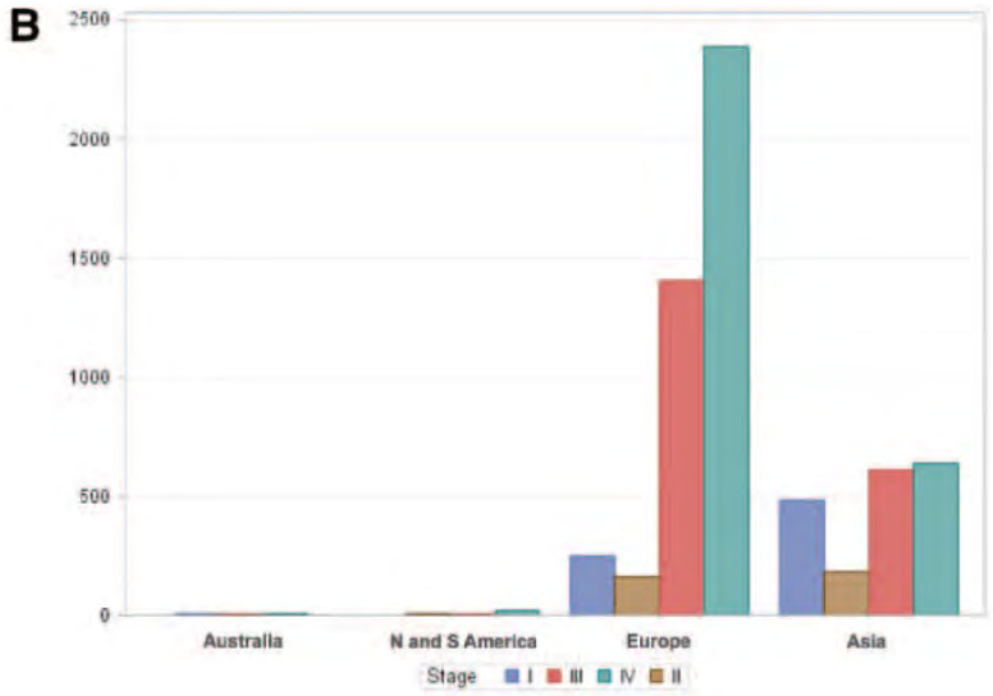

B
2500
2000
1500
1000
500
0
Australia
N and S America
Europe
Asia
Stage I III IV II

TABLE 6. Nonanatomical Elements Collected in the New Phase of the IASLC Lung Cancer Staging Project

Patient-related elements	Age
	Sex
	Race
	Smoking history
	Weight loss
	Zubrod performance status
	Comorbidity index
	Laboratory analyses: LDH, hemoglobin, calcium, alkaline phosphatase, sodium, leukocyte count, neutrophil count, platelets, albumin
	Lung function tests: FVC and % of predicted; FEV1 and % of predicted
	Weight
	Height
Tumor-related elements	SUVmax for T and for N
	Lobar, bronchial location of primary tumor
	Differentiation grade
	Histological type
	Vascular invasion
	Lymphatic invasion
	Pleural lavage cytology
	Tumor markers in those centers that have the possibility to determine them
Environment-related elements	Method of detection: symptoms, screening, incidental
	Treatment
	Residual tumor after treatment
	Geographic area: continent, country of origin

LDH: lactate-dehydrogenase; FVC: forced vital capacity; FEV1: forced expiratory volume in 1 second; SUVmax: maximum standardized uptake value; T: primary tumor; N: lymph nodes

T

IASLC STAGING COMMITTEE ARTICLE

The IASLC Lung Cancer Staging Project

Proposals for the Revisions of the T Descriptors in the Forthcoming Eighth Edition of the TNM Classification for Lung Cancer

Ramón Rami-Porta, MD, FETCS, Vanessa Bolejack, MPH,† John Crowley, PhD,† David Ball, MD, FRANZCR,‡ Jhingook Kim, MD,§ Gustavo Lyons, MD,‖ Thomas Rice, MD,¶ Kenji Suzuki, MD,# Charles F. Thomas Jr, MD,** William D. Travis, MD,†† and Yi-Long Wu, MD,‡‡ on behalf of the IASLC Staging and Prognostic Factors Committee, Advisory Boards and Participating Institutions§§*

(*J Thorac Oncol.* 2015;10: 990–1003)

TABLE 1. Number of M0 Non–Small-Cell Lung Cancer Cases Passing Initial Screening[a]

	N0					Any N				
	Total	**T1**	**T2**	**T3**	**T4**	**Total**	**T1**	**T2**	**T3**	**T4**
Clinically staged										
Total	30,102	17,430	9498	2357	817	40,263	19,182	14,394	4380	2307
Analyzed	10,230	6436	2926	719	149	13,012	7100	4239	1305	368
Clinically staged, surgically managed										
Total	29,153	17,248	9200	2178	527	36,697	18,807	13,253	3664	973
Analyzed	10,084	6416	2873	682	113	12,449	7022	4049	1167	113
Clinically staged, nonsurgically managed										
Total	949	182	298	179	290	3566	375	1141	716	1334
Analyzed	146	20	53	37	36	563	78	190	138	157
Pathologically staged										
Total	26,722	12,857	10,510	2780	575	36,830	14,954	15,973	4756	1147
Analyzed	22,257	11,559	8411	2108	179	30,018	13,368	12,628	3620	402

[a]Criteria for T descriptor analysis: cases must have known tumor size, at least one T descriptor supporting the assigned T category, and no T descriptors suggesting a higher T category.

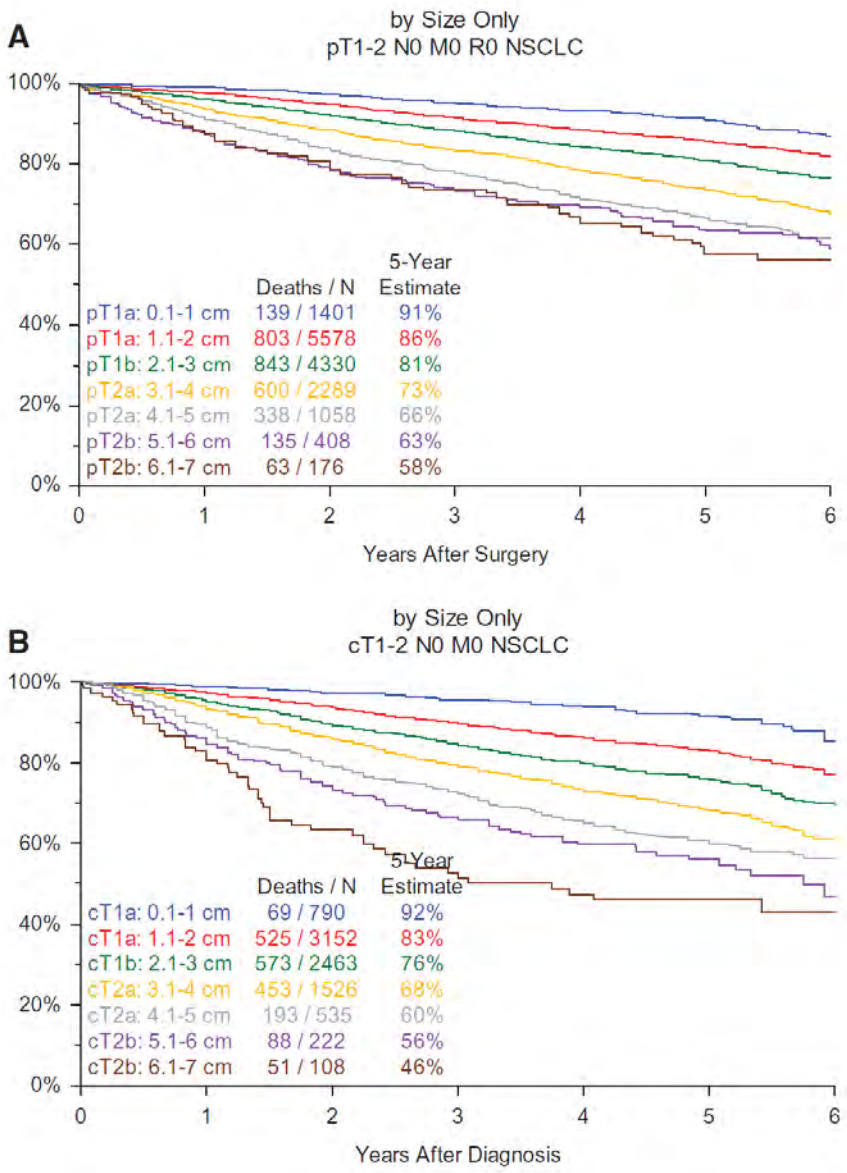


FIGURE 1. *A*, Survival of pathologically staged T1–T2 N0R0 tumors according to size only, at 1-cm intervals. *B*, Survival of clinically staged T1–T2 N0 tumors according to size only, at 1-cm intervals.

TABLE 2. Results of Univariate Analyses of Survival of Pathologically Staged T1–T3 N0M0R0 Cases According to Tumor Size and T2 and T3 Descriptors

		Survival from Surgery	
Variable	**n/N (%)**	**HR (95% CI)**	***P* value**
Other histology vs. adeno	7064/21,122 (33)	2.19 (2.07, 2.32)	<0.001
Squamous vs. other	5237/21,122 (25)	1.96 (1.85, 2.07)	<0.001
Age ≥ 60 vs. <60	16,070/21,014 (76)	2.29 (2.11, 2.49)	<0.001
Male vs. female	12,457/20,995 (59)	1.86 (1.75, 1.98)	<0.001
Americas vs. Asia	1873/21,123 (9)	1.79 (1.64,1.97)	<0.001
Europe/Australia vs. Asia	2361/21,123 (11)	2.61 (2.43,2.80)	<0.001
Size >2 vs. ≤2 cm	12,970/21,123 (61)	1.50 (1.39,1.62)	<0.001
Size >3 vs. >2–3 cm	7163/21,123 (34)	1.59 (1.47,1.70)	<0.001
Size >5 vs. >3–5 cm	1925/21,123 (9)	1.45 (1.31,1.59)	<0.001
Size >7 vs. >5–7 cm	606/21,123 (3)	1.45 (1.26,1.67)	<0.001
Size >1 vs. ≤1 cm	19,623/21,122 (93)	2.68 (2.28, 3.14)	<0.001
Size >4 vs. ≤4 cm	3669/21,122 (17)	2.43 (2.28, 2.58)	<0.001
Size >6 vs. ≤6 cm	1041/21,122 (5)	2.79 (2.55, 3.06)	<0.001
Multiple pT2 descriptors vs. other pT2, pT3	1817/9952 (18)	1.17 (1.07, 1.27)	<0.001
pT3 vs. pT1-2	1882/21,122 (9)	2.63 (2.44, 2.83)	<0.001
pT2 main bronchus >2 cm vs. all others	67/19,013 (0)	1.53 (0.98, 2.37)	0.059
pT3 main bronchus <2 cm vs. all others	24/19,013 (0)	1.82 (0.91, 3.64)	0.091
pT2 atelectasis vs. all others	161/11,869 (1)	1.98 (1.51, 2.61)	<0.001
pT3 atelectasis vs. all others	8/11,869 (0)	3.06 (0.76, 12.24)	0.114
pT2 visceral pleura PL1 vs. PL0	2690/15,685 (17)	1.74 (1.60,1.89)	<0.001
pT2 visceral pleura PL2 vs. PL0	813/15,685 (5)	2.23 (1.97,2.54)	<0.001
pT2 3–5 cm size only vs. pT1, pT2 ≤ 3 cm	3320/21,123 (16)	1.79 (1.66,1.93)	<0.001
pT2 3–5 cm plus other descriptor vs. pT1, pT2 ≤ 3 cm	1362/21,123 (6)	2.22 (2.01,2.46)	<0.001
pT2 5–7 cm size only vs. pT1, pT2 ≤ 3 cm	586/21,123 (3)	2.59 (2.25,2.99)	<0.001
pT2 5–7 cm plus other descriptor vs. pT1, pT2 ≤3 cm	450/21,123 (2)	2.85 (2.46,3.31)	<0.001
pT3 Single descriptor vs. pT1, pT2 ≤ 3 cm	1556/21,123 (7)	3.20 (2.94,3.49)	<0.001
pT3 Multiple pT3 descriptors vs. pT1, pT2 ≤ 3 cm	326/21,123 (2)	4.27 (3.66,4.99)	<0.001

The *p* value from Wald χ^2 test in Cox Regression.
HR, hazard ratio; 95% CI, 95% confidence interval; n, number with descriptor; N, number evaluated; %, percent with descriptor.

TABLE 3. Multivariate Survival Analyses of Proposed 1-cm Cutpoints in Pathologically Staged T1 Tumors

		Survival from Surgery	
Variable	**n/N (%)**	**HR (95% CI)**	***P* Value**
Age ≥60 vs. <60	12,554/16,644 (75)	2.06 (1.87,2.28)	<0.001
Americas vs. Asia	1559/16,644 (9)	2.24 (2.01,2.50)	<0.001
Europe/Australia vs. Asia	1647/16,644 (10)	2.58 (2.36,2.83)	<0.001
Male vs. female	9371/16,644 (56)	1.70 (1.57,1.83)	<0.001
Other histology vs. adeno	4759/16,644 (29)	1.47 (1.31,1.65)	<0.001
Squamous vs. other	3473/16,644 (21)	0.98 (0.87,1.10)	0.685
T1a >1–2 vs.<1 cm	5462/16,644 (33)	1.45 (1.21,1.74)	<0.001
T1b >2–3 vs.<1 cm	4230/16,644 (25)	1.82 (1.52,2.18)	<0.001
T2a <3 vs. <1 cm	5611/16,644 (34)	2.43 (2.04,2.90)	<0.001

Each size increment distinguishes between risk groups. A comparison of T2a less than 3 cm (T2a by descriptors other than size) versus larger T1 cases (T1b > 2–3 cm, not shown in table) indicates that T2a cases are appropriately in a higher risk category ($p < 0.001$). p value from Wald χ^2 test in Cox regression.

HR, hazard ratio; 95% CI, 95% confidence interval; n, number with descriptor; N, number evaluated, %=percent with descriptor.

T1

The subclassification of T1 into
T1a: tumor 1 cm or less in greatest dimension,
T1b: tumor more than 1 cm but not more than 2 cm in greatest dimension, and
T1c: tumor more than 2 cm but not more than 3 cm in greatest dimension;

TABLE 4. Survival Comparisons of Pathologically Staged T2–T4 Tumors >4–5 cm, >5–7 cm, and >7 cm in Greatest Dimension

			Survival from Surgery	
	Variable	**n/N (%)**	**HR (95% CI)**	***P* Value**
Univariate	Other histology vs. adeno	4357/10,028 (43)	1.61 (1.50, 1.73)	<0.001
	Squamous vs. other	3318/10,028 (33)	1.45 (1.35, 1.56)	<0.001
	Age ≥60 vs. <60	7934/9987 (79)	1.94 (1.76, 2.15)	<0.001
	Male vs. female	6599/9967 (66)	1.53 (1.41, 1.65)	<0.001
	Americas vs. Asia	762/10,028 (8)	1.24 (1.09, 1.42)	0.001
	Europe/Australia vs. Asia	1439/10,028 (14)	1.90 (1.74, 2.07)	<0.001
	Proposed T2b 4–5 cm vs. all others	1480/10,028 (15)	1.10 (1.00, 1.21)	0.046
	Proposed T3 5–7 cm vs. all others	1417/10,028 (14)	1.48 (1.35, 1.62)	<0.001
	Other T3 (excluding >7 cm) vs. all others	828/10,028 (8)	1.30 (1.16, 1.46)	<0.001
	Proposed T4 (including T3 > 7 cm) vs. all others	761/10,028 (8)	2.14 (1.92, 2.38)	<0.001
Multivariate	Other histology vs. adeno	4312/9940 (43)	1.28 (1.14, 1.43)	<0.001
	Squamous vs. other	3281/9940 (33)	0.92 (0.82, 1.03)	0.165
	Age ≥60 vs. <60	7891/9940 (79)	1.95 (1.76, 2.16)	<0.001
	Male vs. female	6581/9940 (66)	1.46 (1.35, 1.59)	<0.001
	Americas vs. Asia	761/9940 (8)	1.45 (1.27, 1.66)	<0.001
	Europe/Australia vs. Asia	1428/9940 (14)	1.82 (1.66, 1.99)	<0.001
	Proposed T2b 4–5 cm vs. T2 3–4 cm	1467/9940 (15)	1.27 (1.15, 1.41)	<0.001
	Proposed T3 5–7 cm vs. T2 3–4 cm	1409/9940 (14)	1.59 (1.44, 1.76)	<0.001
	Other T3 (excluding >7 cm) vs. T2 3–4 cm	821/9940 (8)	1.62 (1.43, 1.83)	<0.001
	Proposed T4 (Including T3>7 cm) vs. T2 3–4 cm	757/9940 (8)	2.24 (2.00, 2.52)	<0.001

Specific comparisons not shown in table: when survival of tumors greater than 5 to 7 cm is compared with that of tumors greater than 4 to 5 cm, the p value is 0.0002, indicating survival is significantly different for these groups. When survival of T3 tumors (excluding those >7 cm) is compared with that of tumors greater than 5 to 7 cm, the p value is 0.821, indicating survival is similar between these groups; p value from Wald χ^2 test in Cox regression.

HR, hazard ratio; 95% CI, 95% confidence interval; n, number with descriptor; N, number evaluated; %, percent with descriptor.

T2

The subclassification of T2 into
T2a: tumor more than 3 cm but not more than 4 cm in greatest dimension and
T2b: tumor more than 4 cm but not more than 5 cm in greatest dimension;

TABLE 5. Multivariate Survival Analyses of Pathologically Staged pT2-3 Tumors Based on Their Endobronchial Location

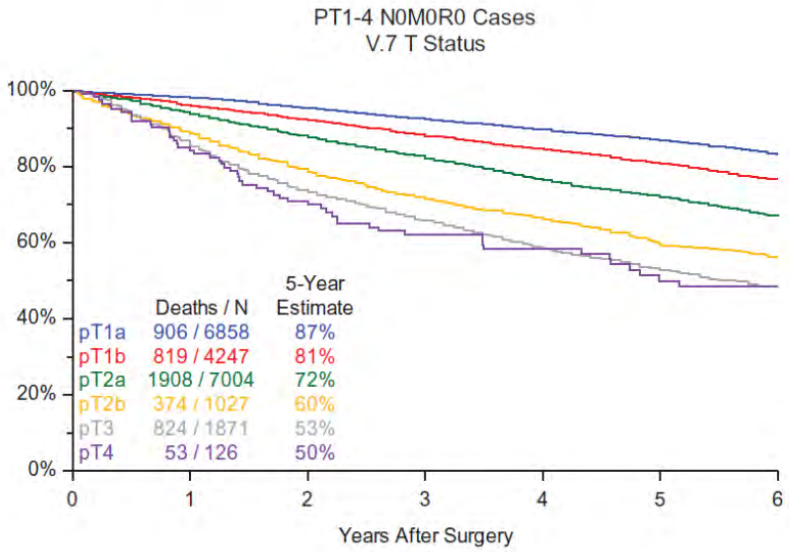
Multivariate Results Variable	n/N (%)	Survival from Surgery	
		HR (95% CI)	*P* Value
Other histology vs. adenocarcinoma	3725/8807 (42)	1.42 (1.26, 1.60)	<0.001
Squamous vs. other	2868/8807 (33)	0.88 (0.78, 1.00)	0.045
Age ≥ 60 vs. <60	7031/8807 (80)	1.96 (1.76, 2.20)	<0.001
Male vs. female	5807/8807 (66)	1.45 (1.33, 1.58)	<0.001
Americas vs. Asia	234/8807 (3)	1.74 (1.39, 2.18)	<0.001
Europe vs. Asia	1031/8807 (12)	1.98 (1.78, 2.21)	<0.001
Size >2 vs. ≤ 2 cm	7640/8807 (87)	1.28 (1.09, 1.50)	0.002
Size >3 vs. 2 to ≤3 cm	6230/8807 (71)	1.09 (0.97, 1.22)	0.133
Size >5 vs. 3 to ≤5 cm	1571/8807 (18)	1.33 (1.20, 1.48)	<0.001
Size >7 vs. 5 to ≤7 cm	467/8807 (5)	0.99 (0.83, 1.19)	0.953
pT2 main bronchus >2 cm from carina vs. pT2 without invasion	67/8807 (1)	1.08 (0.69, 1.69)	0.725
pT3 main bronchus <2 cm from carina vs. pT2 without invasion	24/8807 (0)	1.03 (0.51, 2.06)	0.937
pT3 other than main bronchus vs. pT2, pT3 with invasion of main bronchus	1304/8807 (15)	1.56 (1.39, 1.76)	<0.001

p value from Wald χ^2 test in Cox regression.
HR, hazard ratio; 95% CI, 95% confidence interval; n, number with descriptor; N, number evaluated; %, percent with descriptor.

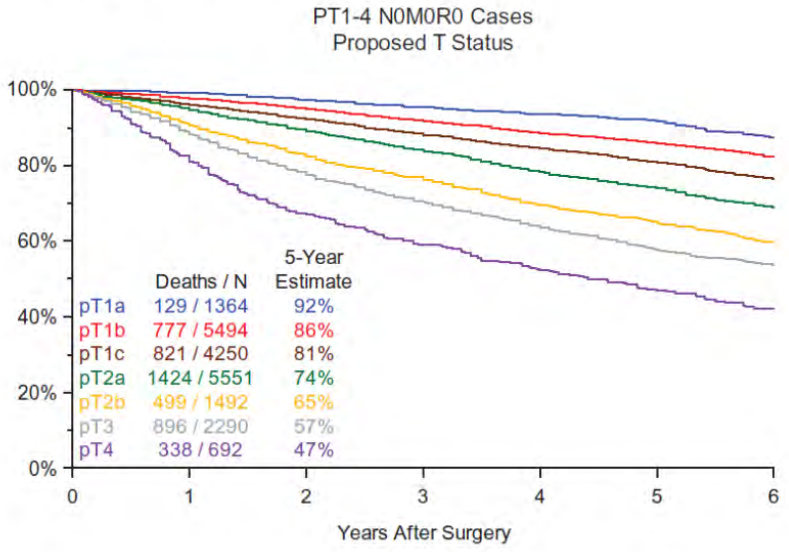
Autres

- T2 tumors greater than 5 and less than or equal to 7 cm were reclassified as T3
- T3 tumors greater than 7 cm reclassified as T4
- T2 and T3 tumors so classified by endobronchial location combined as T2
- invasion of the diaphragm reclassified as T4

A 7th Edition T Categories



Proposed T Categories



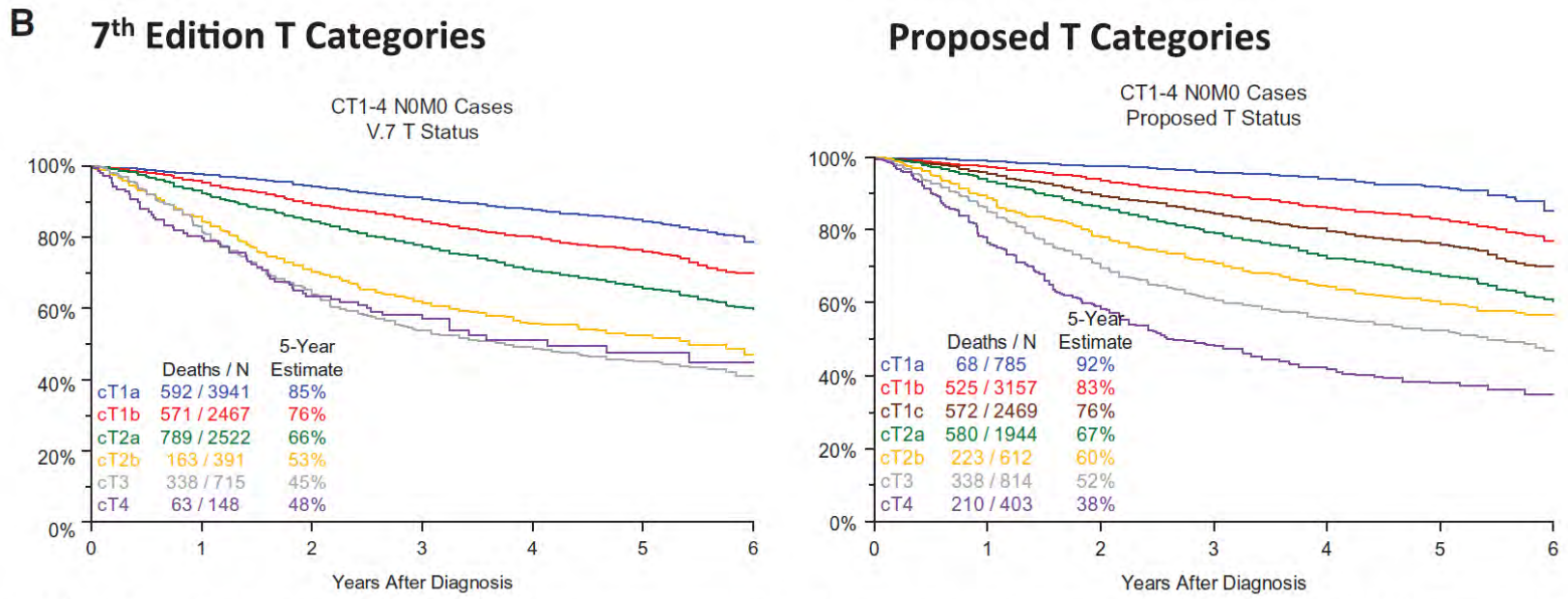


FIGURE 2. *A*, Survival according to 7th edition and proposed T categories for pathologically staged T1–T4 N0M0R0 tumors. *B*, Survival according to 7th edition and proposed T categories for clinically staged T1–T4 N0M0 tumors.

TABLE 8. Survival Comparisons of Clinically Staged Tumors According to the T Categories of the 7th Edition and to the Proposed T Categories for the 8th Edition

7th Edition Categories					Proposed Categories				
Contrast	**Estimate**	**Lower Limit**	**Upper Limit**	***P* value**	**Contrast**	**Estimate**	**Lower Limit**	**Upper Limit**	***P* value**
T1a vs. T1b	1.5534	1.3844	1.7430	<0.0001	T1a vs. T1b	1.8380	1.4274	2.3668	<0.0001
T1b vs. T2a	1.3518	1.2126	1.5070	<0.0001	T1b vs. T1c	1.4165	1.2580	1.5949	<0.0001
T2a vs. T2b	1.4465	1.2202	1.7149	<0.0001	T1c vs. T2a	1.2967	1.1543	1.4567	<0.0001
T2b vs. T3	1.2804	1.0613	1.5449	0.0098	T2a vs. T2b	1.2038	1.0309	1.4056	0.0190
T3 vs. T4	0.8851	0.6726	1.1648	0.3836	T2b vs. T3	1.3031	1.0996	1.5443	0.0022
					T3 vs. T4	1.4542	1.2221	1.7305	<0.0001

M

STATE OF THE ART: CONCISE REVIEW

The IASLC Lung Cancer Staging Project

Proposals for the Revision of the M Descriptors in the Forthcoming Eighth Edition of the TNM Classification of Lung Cancer

Wilfried E.E. Eberhardt, MD, Alan Mitchell, MSc,† John Crowley, PhD,† Haruhiko Kondo, MD,‡ Young Tae Kim, MD,§ Andrew Turrisi III, MD,‖ Peter Goldstraw, MBChB,¶ and Ramon Rami-Porta, MD,#** On behalf of the International Association for the Study of Lung Cancer Staging and Prognostic Factors Committee, Advisory Board Members, and Participating Institutions††*

(*J Thorac Oncol.* 2015;10: 1515–1522)

TABLE 1. Subject Counts by Data Source and 7th edition M Category

			7th Edition M Category	
Database Type	**Country**	**Institution**	**M1a**	**M1b**
EDC	Argentina	Hospital Británico de Buenos Aires	2	4
		Hospital Universitario Austral	2	2
		Hospital Universitario-Fundación Favalor		7
		Hospital de Rehabilitación Respiratoria	3	1
	Australia	Peter MacCallum Cancer Institute		2
	Belgium	University Hospital Antwerp	15	51
		University Hospital Ghent	6	18
	Brazil	University of Sao Paulo Medical School		2
	China	Guangdong General Hospital	83	188
	France	L'Institut Mutualiste Montsouris	3	5
	Greece	Athens School of Medicine	6	15
	Spain	Complejo Hospitalario de Ourense	41	83
		Complejo Hospitalario La Mancha Centro	9	31
		Fundación Jiménez Díaz	18	45
		Htal. de la Plana Vila-Real	12	28
		Htal. General Universitario de Valencia	1	
		Htal. General Universitario Gregorio Mar	1	
		Htal. General Universitario de Albacete	14	42
		Htal. Meixoeiro	3	26
		Htal. Nuestra Señora de Sonsoles	2	8
		Htal. San Pedro Alcántara	12	24
		Htal. Severo Ochoa	10	13
		Htal. Sierrallana, Sección de Neumologia	9	23
		Htal. Universitari Joan XXIII	13	10
		Htal. Universitario Central de Asturias	6	5
		Htal. Universitario La Fe	12	28
		Htal. Universitario de Canarias	10	15
		Htal. de Sagunto		4
	United States	Mayo Clinic Rochester		13
		NYU Langone Medical Center and Cancer Center	29	37
		Penrose Cancer Center	2	5
Subtotal—EDC cases by 7th edition M category			324	735
Subtotal—EDC cases			1059	
Consortium	Turkey	Turkish Thoracic Society	81	1215
Institutional registry	Australia	Prince Charles Hospital	2	54
Subtotal—All institutions by 7th edition M category			407	2004
Total			2411	

EDC, electronic data capture.

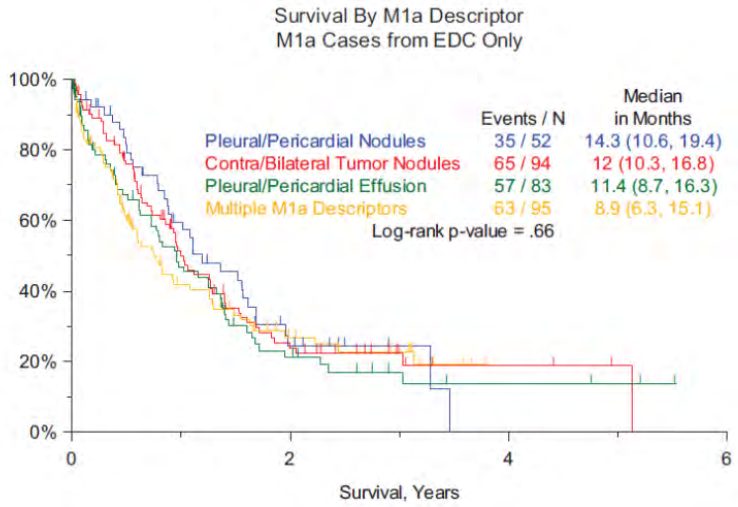


FIGURE 1. Prognostic impact of M1a descriptors.

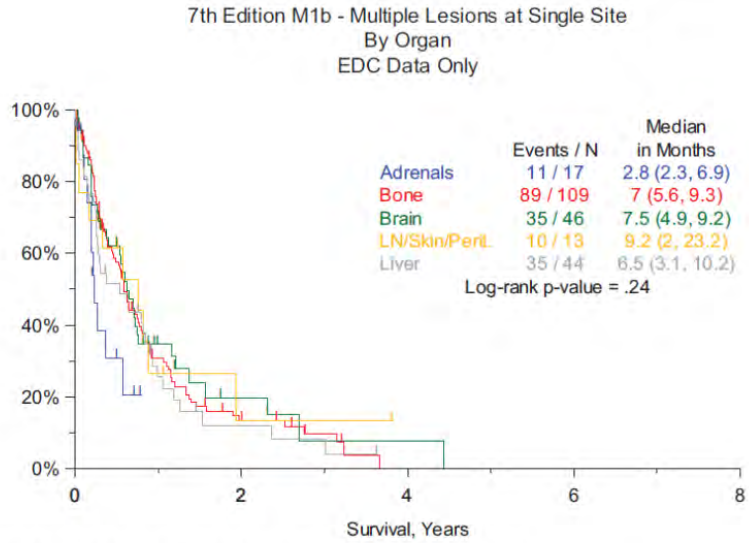


FIGURE 3. Multiple lesions at single site by organ.

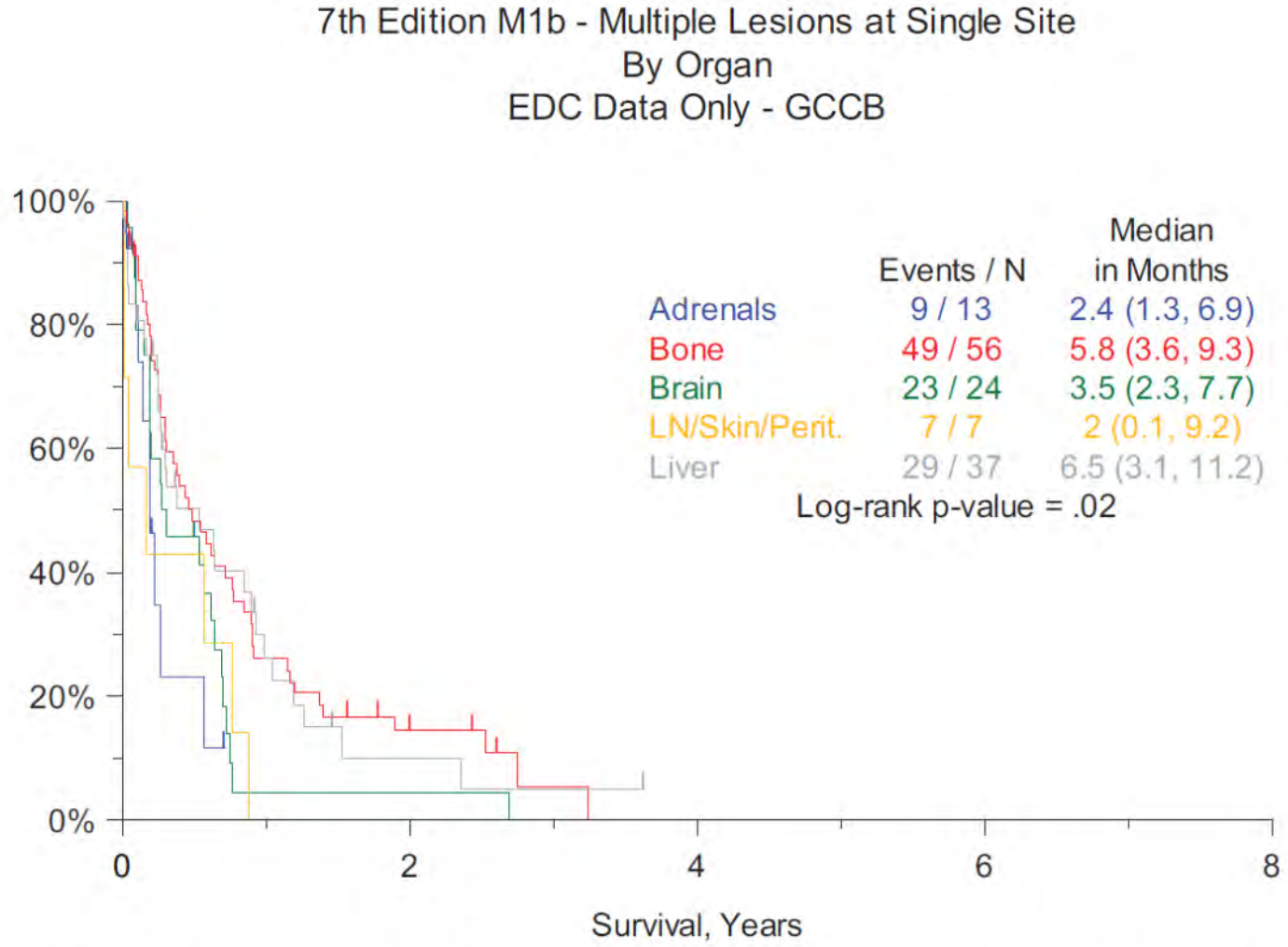


FIGURE 6. Multiple lesions at single site by organ—GCCB.

TABLE 3. Prognostic Impact of Single and Multiple Metastatic Lesions in a Single Organ versus Multiple Metastatic Sites

		Overall Survival		
Proposed Category	**Variable**	**n/N (%)**	**HR (95% CI)**	***P* Value**
M1a	M1a	324/1025 (32)	Reference level	
M1b	M1b, single organ/lesion	225/1025 (22)	1.11 (0.91, 1.36)	0.308
M1c	M1b, single organ/multiple lesions	229/1025 (22)	1.63 (1.34, 1.99)	<0.001
	M1b, multiple organs	247/1025 (24)	1.85 (1.52, 2.24)	<0.001

P value from score χ^2 test in Cox regression.
HR, hazard ratio; 95% CI, 95% confidence interval.

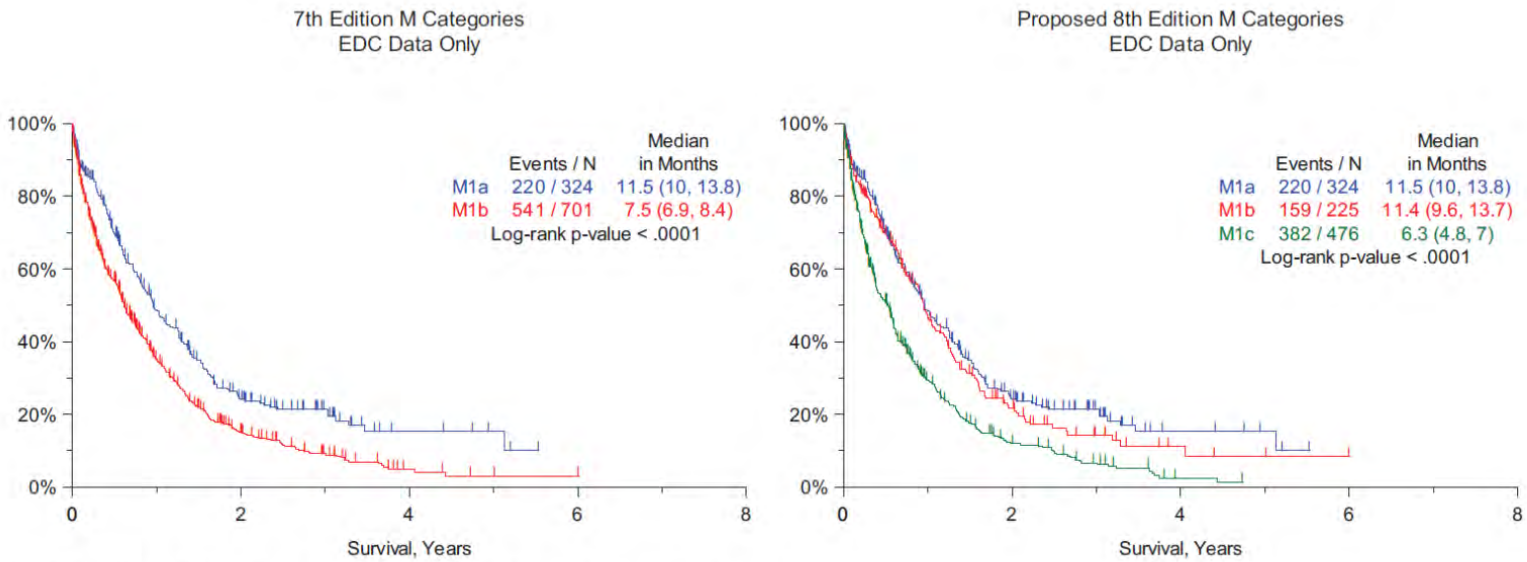


FIGURE 8. The 7th edition and proposed 8th edition M categories.

Recommandations

1. Maintain the use of the current M1a category, including any of the following descriptors: (a) pleural/pericardial effusion, (b) contralateral/bilateral tumor nodules, (c) pleural/pericardial nodules, and (d) multiple M1a descriptors.
2. Reclassify the current M1b category for patients with a single metastatic lesion in a single organ site, for example: (a) brain, (b) liver, (c) bone, (d) distant lymph node/skin/peritoneum, and (e) adrenal gland. Categorization of localization of single lesions in a single organ should be prospectively tested based on the individually involved organ.
3. Introduce the new M1c category for patients with (a) multiple lesions in a single organ or (b) multiple lesions in multiple organs. Comparable with the data now available for the influence of tumor volume in the T descriptors,[2] it is recommended to prospectively register in detail (a) the number of metastatic lesions and (b) the number of involved organs.

N

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The IASLC Lung Cancer Staging Project: Proposals for the Revision of the N Descriptors in the Forthcoming Eighth Edition of the TNM Classification for Lung Cancer

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Table 1. Origin of the data for clinical nodal (cN) categories

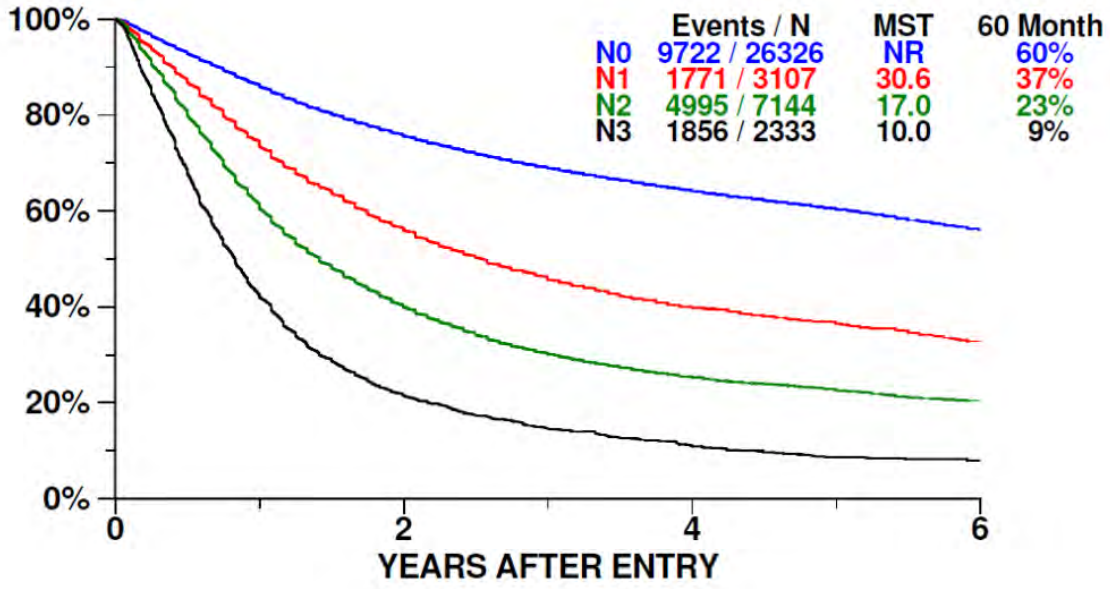
Data source	Clinical N				Total	Follow-up (months)		
	N0	N1	N2	N3		Min	Median	Max
Denmark	6435	845	2690	1390	11360	4	27	124
EDC	1243	182	402	277	2104	<1	22	125
Japan 1999	8497	918	1540	79	11034	1	66	83
Japan 2002	450	200	725	391	1766	1	16	87
Japan 2004	8501	683	985	43	10212	1	62	88
MSKCC	535	97	198	31	861	1	80	122
Prince Charles	88	13	24	6	131	28	34	39
Sydney	14	1	3	0	18	49	59	98
TurkeyG	563	168	577	116	1424	<1	65	73
Total	26326	3107	7144	2333	38910	<1	61	125

Table 2.Origin of the data for pathological nodal (pN) categories

Data source	Pathological N				Total	Follow-up (months)		
	N0	N1	N2	N3		Min	Median	Max
Belgrade	10	54	24	0	88	6	42	70
EDC	1002	218	189	21	1430	<1	23	125
Japan 1999	7717	1296	1855	100	10968	1	66	83
Japan 2002	2994	386	401	11	3792	1	73	90
Japan 2004	6662	726	1296	19	8703	1	62	77
Korea	933	270	222	1	1426	60	87	139
MDACC	1233	260	212	0	1705	<1	42	120
MSKCC	451	74	60	1	586	1	79	110
Norway	1193	369	145	1	1708	8	55	96
Sydney	743	158	118	1	1020	<1	69	139
Total	22938	3811	4522	155	31426	<1	64	139

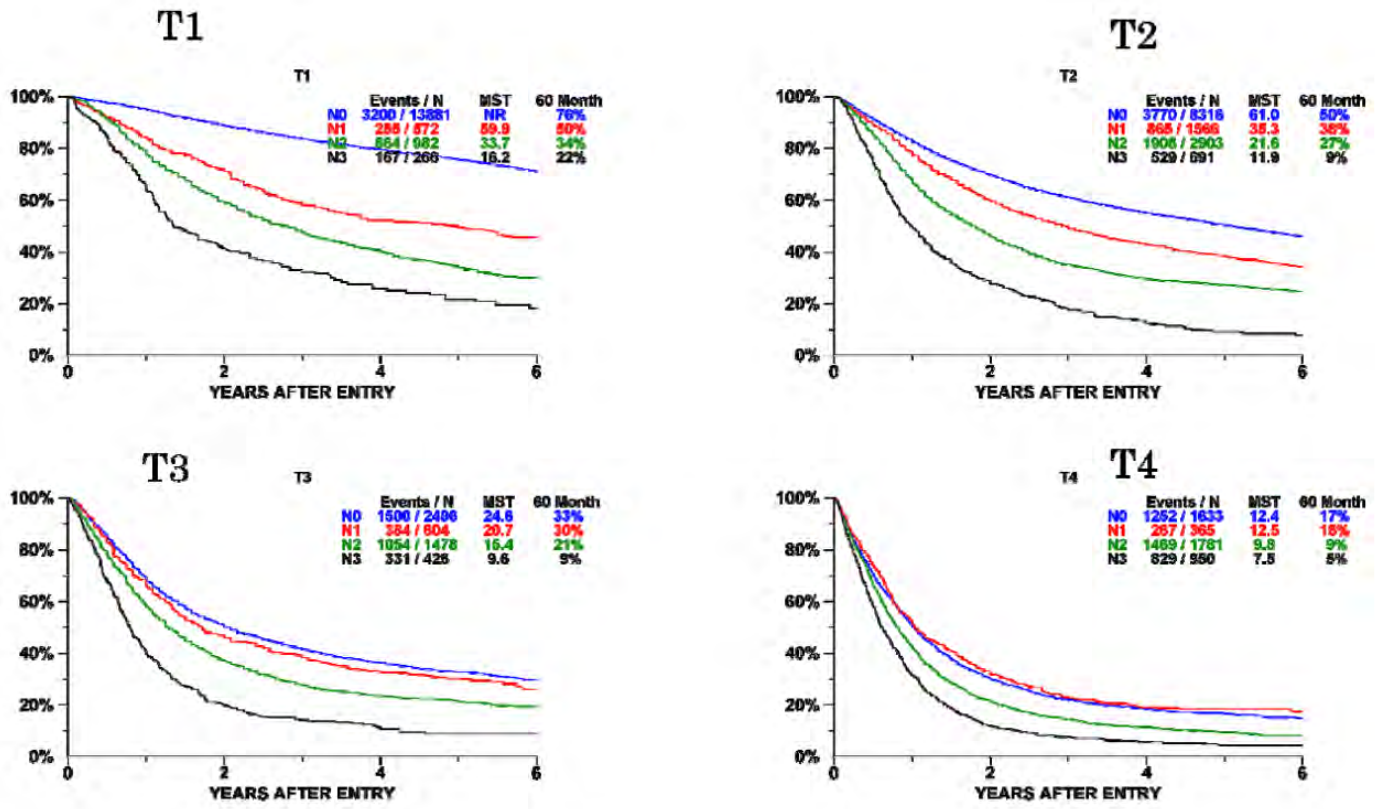
cN

Figure 1.


Events / N
MST
60 Month
N0 9722 / 26326 NR 60%
N1 1771 / 3107 30.6 37%
N2 4995 / 7144 17.0 23%
N3 1856 / 2333 10.0 9%
100%
80%
60%
40%
20%
0%
0
2
4
6
YEARS AFTER ENTRY

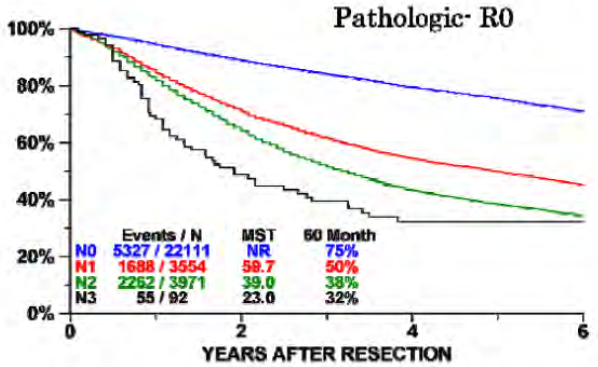
cN selon T

Figure 2.

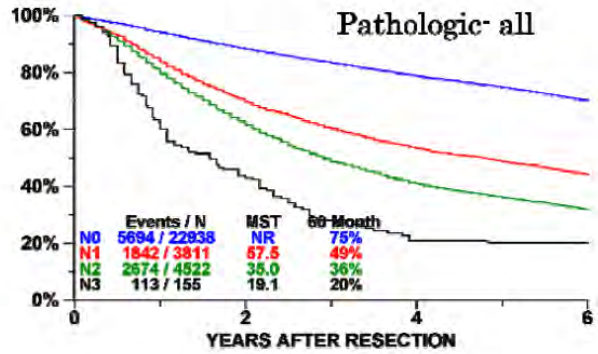


pN

Figure 3.



N0 vs N1 vs N2 vs N3 Comparisons Adjusted for Histology (adeno vs others), Sex, Age 60+, and Region. (Cox PH regression on R0 cases)		
comparison	HR	P
N1 vs N0	2.13	<0.0001
N2 vs N1	1.65	<0.0001
N3 vs N2	1.56	.0012

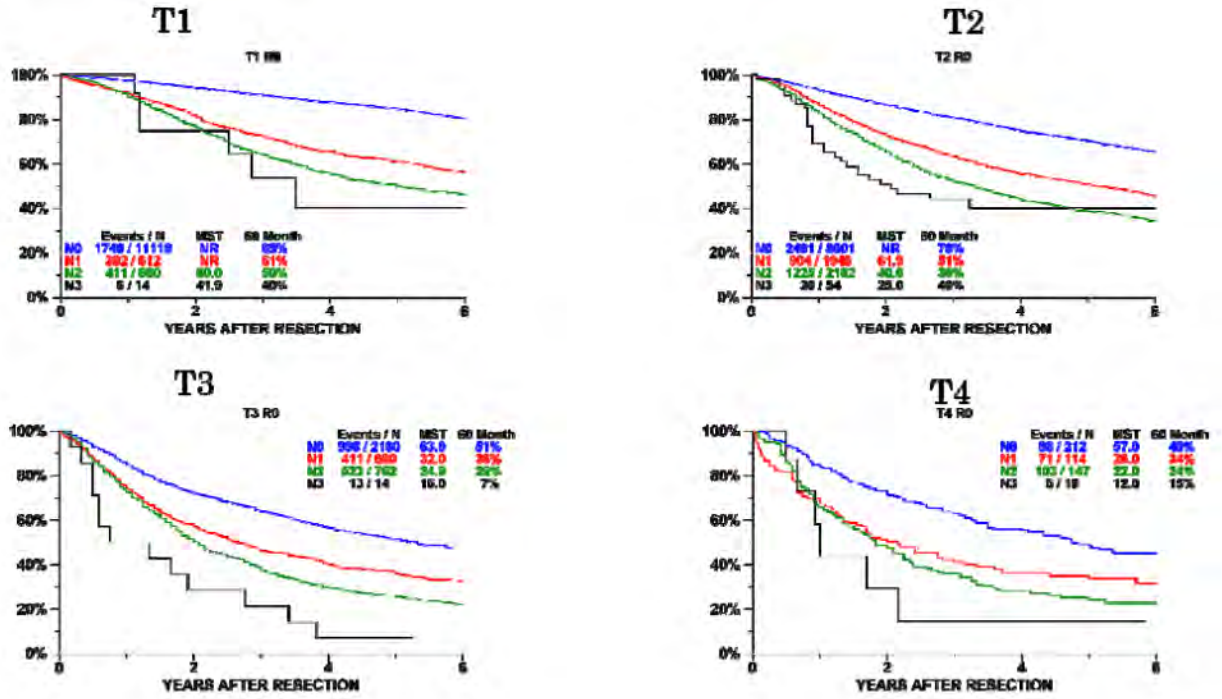


N0 vs N1 vs N2 vs N3 Comparisons Adjusted for Histology (adeno vs others), Sex, Age 60+, R0 resection, and Region. (Cox PH regression on all cases)		
comparison	HR	P
N1 vs N0	2.10	<0.0001
N2 vs N1	1.63	<0.0001
N3 vs N2	1.66	<0.0001

1

pN selon T (R0)

Figure 4.



Recommendations

1. The use of the N descriptors described in the 7th edition of TNM for Lung Cancer should be carried forward, without changes into the 8th edition.
2. Additional analyses suggest that the combination of location of metastatic nodes, nN (single station versus multiple stations), and absence versus presence of skip metastasis as pN0, pN1a, pN1b, pN2a1, pN2a2, and pN2b may give a more accurate prognosis. This classification requires prospective evaluation before being considered for future revisions of the TNM staging system for lung cancer.
3. The IASLC Nodal map and anatomical definitions[8] should be used to describe regional lymph node involvement for lung cancer

Les changements proposés à la classification

T1

- Tx — Primary tumour cannot be assessed, or tumour proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy.
- T0 — No evidence of primary tumour.
- Tis — Carcinoma in situ
- T1 — Tumour 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e. not in the main bronchus)[1].
- **T1a(mi) Minimally invasive adenocarcinoma[2].**
- **T1a Tumour 1 cm or less in greatest dimension[1].**
- **T1b Tumour more than 1 cm but not more than 2 cm in greatest dimension[1].**
- **T1c Tumour more than 2 cm but not more than 3 cm in greatest dimension[1].**

T2

T2 Tumour more than 3cm **but not more than 5 cm**; or tumour with any of the following features[3]:

- Involves main bronchus regardless of distance from the carina, but without involvement of the carina.

- Invades visceral pleura.

- Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, involving part or all of the lung.

T2a **Tumour more than 3 cm but not more than 4 cm in greatest dimension.**

T2b **Tumour more than 4 cm but not more than 5 cm in greatest dimension.**

T3 – T4

T3 **Tumour more than 5 cm but not more than 7 cm in greatest dimension**, or directly invades any of the following structures: chest wall (including parietal pleura and superior sulcus tumours), phrenic nerve, parietal pericardium; or associated with separate tumour nodule(s) in the same lobe as the primary.

T4 **Tumour more than 7 cm in greatest dimension,** or invades any of the following structures: **diaphragm,** mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, oesophagus, vertebral body, carina; or associated with separate tumour nodule(s) in a different ipsilateral lobe to that of the primary.

N

- Nx Regional lymph nodes cannot be assessed.
- N0 No regional lymph node metastasis.
- N1 Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension.
- N2 Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s).
- N3 Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s).

M

- M0 — No distant metastasis.
- M1 — Distant metastasis present.
  - M1a — Separate tumour nodule(s) in a contralateral lobe; tumour with pleural or pericardial nodule(s) or malignant pleural or pericardial effusion[4].
  - **M1b — Single extrathoracic metastasis[5].**
  - **M1c — Multiple extrathoracic metastases in one or several organs.**

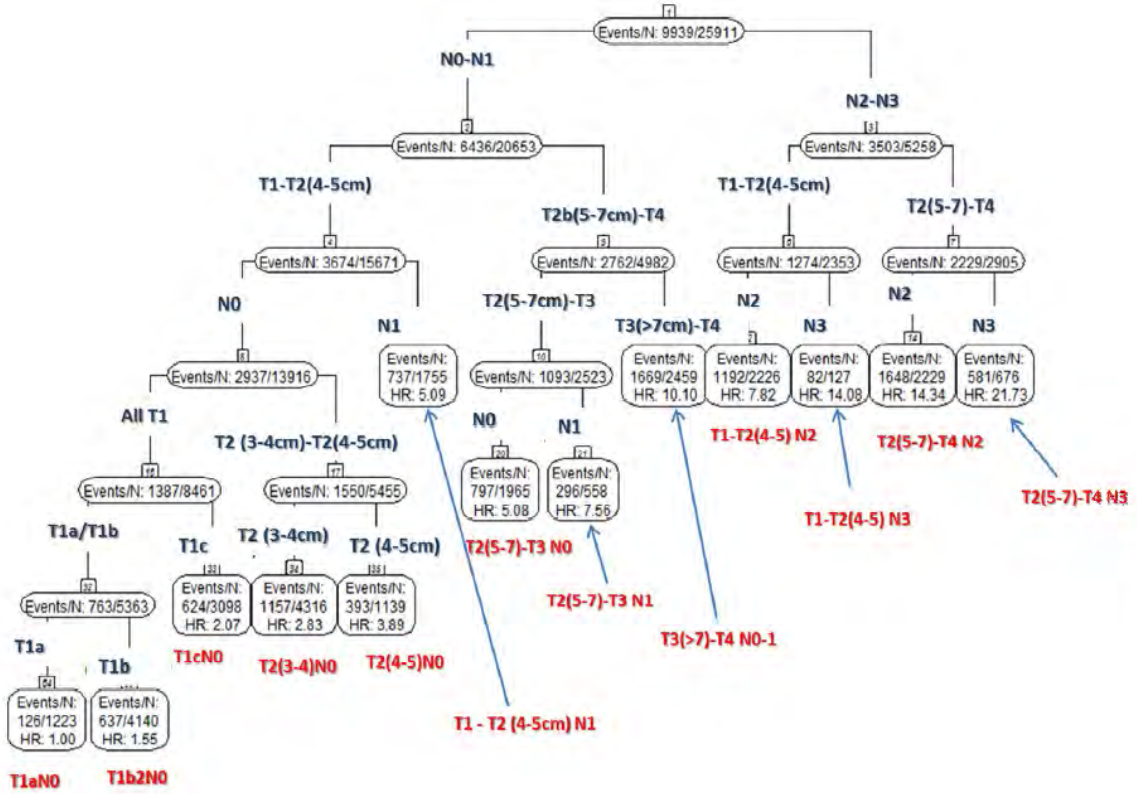


Figure 1. Recursive partitioning and amalgamation-generated survival tree based on best stage for 25,911 M0 training set cases. T and N categories are modelled as order variables. Stratified hazard ratios are given relative to the left-most terminal node, T1aN0.

Les changements proposés

Descripteur T/M (7ème édition)	**Changement T/M**	**N0**	**N1**	**N2**	**N3**
T1 (≤ 1 cm)	**T1a**	**IA1** (IA)	**IIB** (IIA)	IIIA	IIIB
T1 (>1 – 2 cm)	**T1b**	**IA2** (IA)	**IIB** (IIA)	IIIA	IIIB
T1 (>2 – 3 cm)	**T1c**	**IA3** (IA)	**IIB** (IIA)	IIIA	IIIB
T2 (>3 – 4 cm)	**T2a**	IB	**IIB** (IIA)	IIIA	IIIB
T2 (>4 – 5 cm)	**T2b**	**IIA** (IB)	**IIB** (IIA)	IIIA	IIIB
T2 (>5 – 7cm)	**T3**	**IIB** (IIA)	**IIIA** (IIB)	**IIIB** (IIIA)	**IIIC** (IIIB)
T3 avec envahissement de structures	**T3**	IIB	IIIA	**IIIB** (IIIA)	**IIIC** (IIIB)
T3 endobronchique atélectasie >3 – 4 cm	**T2a**	**IB** (IIB)	**IIB** (IIIA)	IIIA	IIIB
T3 endobronchique atélectasie >4 – 5 cm	**T2b**	**IIA** (IIB)	**IIB** (IIIA)	IIIA	IIIB
T3 (≥ 7 cm)	**T4**	**IIIA** (IIB)	IIIA	**IIIB** (IIIA)	**IIIC** (IIIB)
T3 diaphragme	**T4**	**IIIA** (IIB)	IIIA	**IIIB** (IIIA)	**IIIC** (IIIB)
T4	T4	IIIA	IIIA	IIIB	**IIIC** (IIIB)
M1a	**M1a**	**IVA** (IV)	**IVA** (IV)	**IVA** (IV)	**IVA** (IV)
M1b lésion unique	**M1b**	**IVA** (IV)	**IVA** (IV)	**IVA** (IV)	**IVA** (IV)
M1c lésions multiples	**M1c**	**IVB** (IV)	**IVB** (IV)	**IVB** (IV)	**IVB** (IV)

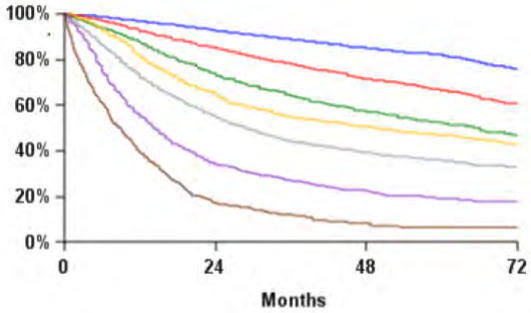
Table 5. Sample sizes for TNM subsets providing the basis for proposed changes, best stage.

		N0		N1		N2		N3	
Seventh Edition Descriptor	**Proposed T/M**	**Overall Stage**	**Sample Size**	**Overall Stage**	**Sample Size**	**Overall Stage**	**Sample Size**	**Overall Stage**	**Sample Size**
T1 <=1cm	T1a	IA ->IA1	1765	IIA ->IIB	47	IIIA	59	IIIB	4
T1 >1-2cm	T1b	IA ->IA2	6127	IIA ->IIB	321	IIIA	444	IIIB	20
T1 >2-3cm	T1c	IA ->IA3	4606	IIA ->IIB	492	IIIA	596	IIIB	37
T2 >3-4cm	T2a	IB	6382	IIA ->IIB	1250	IIIA	1666	IIIB	89
T2 >4-5cm	T2b	IB ->IIA	1689	IIA ->IIB	497	IIIA	559	IIIB	35
T2 >5-7cm	T3	IIA ->IIB	1244	IIB ->IIIA	418	IIIA->IIIB	455	IIIB->IIIC	45
T3 structures	T3	IIB	1666	IIIA	432	IIIA->IIIB	736	IIIB->IIIC	55
T3 >7cm	T4	IIB ->IIIA	870	IIIA	316	IIIA->IIIB	320	IIIB->IIIC	33
T3 Diaphragm	T4	IIB ->IIIA	47	IIIA	16	IIIA->IIIB	22	IIIB->IIIC	0
T3 endobronchial location/atelect									
>3-4 cm	T2a	IIB ->IB	18	IIIA->IIB	18	IIIA	10	IIIB	1
>4-5cm	T2b	IIB ->IIA	11	IIIA->IIB	2	IIIA	9	IIIB	1
T4	T4	IIIA	1862	IIIA	538	IIIB	1770	IIIB->IIIC	893
M1a	M1a	IV ->IVA	62	IV ->IVA	11	IV ->IVA	100	IV ->IVA	145
M1b single lesion	M1b	IV ->IVA	38	IV ->IVA	13	IV ->IVA	68	IV ->IVA	74
M1b multiple lesions	M1c	IV ->IVB	59	IV ->IVB	18	IV ->IVB	128	IV ->IVB	191

Table 6. Cox proportional hazards regression model output for the seventh edition of TNM, and proposed 8th edition **clinical** stage groupings using the entire database available for the 8th edition. Adjusted for age (≥70), sex, and histology (adenocarcinoma vs. others). Stratified by type of database submission (registry vs. others).

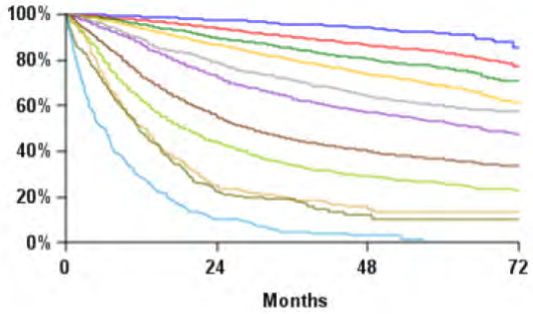
Comparison	Hazard Ratio		*P*	
	7th Edition	Proposed 8th Edition	7th Edition	Proposed 8th Edition
IA2 vs IA1	-	1.82	-	<.0001
IA3 vs IA2	-	1.40	-	<.0001
IB vs IA	1.75	-	<.0001	-
IB vs IA3	-	1.29	-	<.0001
IIA vs IB	1.57	1.30	<.0001	0.0012
IIB vs IIA	1.22	1.30	0.0046	0.0008
IIIA vs IIB	1.28	1.48	<.0001	<.0001
IIIB vs IIIA	1.57	1.38	<.0001	<.0001
IIIC vs IIIB	-	1.36	-	<.0001
IVA vs IIIC	-	1.75	-	<.0001
IVB vs IVA	-	1.91	-	<.0001
IV vs IIIB	2.61	-	<.0001	-

A.



	Events / N	MST	24 Month	60 Month
IA	1119 / 6303	NR	93%	82%
IB	768 / 2492	NR	85%	66%
IIA	424 / 1008	66.0	74%	52%
IIB	382 / 824	49.0	64%	47%
IIIA	2139 / 3344	29.0	55%	36%
IIIB	2101 / 2624	14.1	34%	19%
IV	664 / 882	8.8	17%	6%

B.



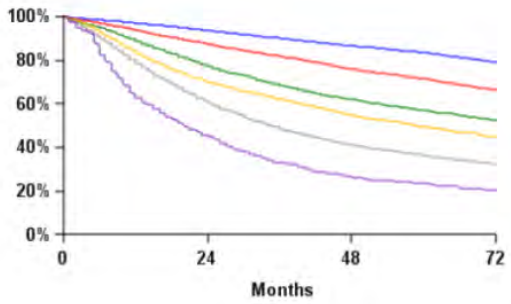
	Events / N	MST	24 Month	60 Month
IA1	68 / 781	NR	97%	92%
IA2	505 / 3105	NR	94%	83%
IA3	546 / 2417	NR	90%	77%
IB	560 / 1928	NR	87%	68%
IIA	215 / 585	NR	79%	60%
IIB	605 / 1453	66.0	72%	53%
IIIA	2052 / 3200	29.3	55%	36%
IIIB	1551 / 2140	19.0	44%	26%
IIIC	831 / 986	12.6	24%	13%
IVA	336 / 484	11.5	23%	10%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

Figure 2. Overall survival by clinical stage according to the 7th edition (A) and the proposed 8th edition (B) groupings using the entire database available for the 8th edition. MST = Median Survival Time. Survival is weighted by type of database submission: Registry versus Other.

Table 7. Cox proportional hazards regression model output for the seventh edition of TNM, and proposed 8th edition **pathologic** stage groupings using the entire database available for the 8th edition. Adjusted for age (≥70), sex, histology (adenocarcinoma vs. others), and type of database submission (registry vs. others).

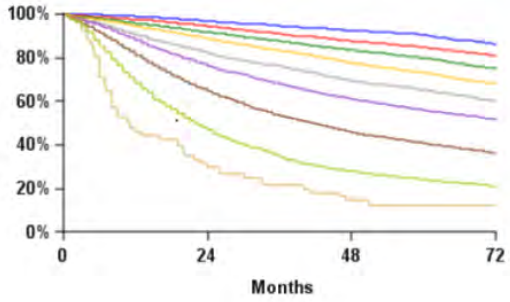
Comparison	Hazard Ratio		*P*	
	7th Edition	Proposed 8th Edition	7th Edition	Proposed 8th Edition
IA2 vs IA1	-	1.44	-	<.0001
IA3 vs IA2	-	1.31	-	<.0001
IB vs IA	1.68	-	<.0001	-
IB vs IA3	-	1.32	-	<.0001
IIA vs IB	1.66	1.29	<.0001	<.0001
IIB vs IIA	1.22	1.40	<.0001	<.0001
IIIA vs IIB	1.61	1.66	<.0001	<.0001
IIIB vs IIIA	1.58	1.67	<.0001	<.0001
IIIC vs IIIB	-	1.85	-	<.0001

A.



	Events / N	MST	24 Month	60 Month
IA	1837 / 11423	NR	94%	83%
IB	2168 / 7711	NR	87%	71%
IIA	1514 / 3702	NR	77%	57%
IIB	1325 / 2776	58.9	70%	49%
IIIA	3467 / 5818	35.0	61%	36%
IIIB	364 / 506	20.0	45%	23%

B.



	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%

Figure 3. Overall survival by pathologic stage according to the 7th edition (A) and the proposed 8th edition (B) groupings using the entire database available for the 8th edition. MST = Median Survival time. Survival is weighted by type of database submission: Registry versus Other.

Les changements proposés

Descripteur T/M (7ème édition)	**Changement T/M**	**N0**	**N1**	**N2**	**N3**
T1 (≤ 1 cm)	**T1a**	**IA1** (IA)	**IIB** (IIA)	IIIA	IIIB
T1 (>1 – 2 cm)	**T1b**	**IA2** (IA)	**IIB** (IIA)	IIIA	IIIB
T1 (>2 – 3 cm)	**T1c**	**IA3** (IA)	**IIB** (IIA)	IIIA	IIIB
T2 (>3 – 4 cm)	**T2a**	IB	**IIB** (IIA)	IIIA	IIIB
T2 (>4 – 5 cm)	**T2b**	**IIA** (IB)	**IIB** (IIA)	IIIA	IIIB
T2 (>5 – 7cm)	**T3**	**IIB** (IIA)	**IIIA** (IIB)	**IIIB** (IIIA)	**IIIC** (IIIB)
T3 avec envahissement de structures	**T3**	IIB	IIIA	**IIIB** (IIIA)	**IIIC** (IIIB)
T3 endobronchique atélectasie >3 – 4 cm	**T2a**	**IB** (IIB)	**IIB** (IIIA)	IIIA	IIIB
T3 endobronchique atélectasie >3 – 5 cm	**T2b**	**IIA** (IIB)	**IIB** (IIIA)	IIIA	IIIB
T3 (≥ 7 cm)	**T4**	**IIIA** (IIB)	IIIA	**IIIB** (IIIA)	**IIIC** (IIIB)
T3 diaphragme	**T4**	**IIIA** (IIB)	IIIA	**IIIB** (IIIA)	**IIIC** (IIIB)
T4	T4	IIIA	IIIA	IIIB	**IIIC** (IIIB)
M1a	**M1a**	**IVA** (IV)	**IVA** (IV)	**IVA** (IV)	**IVA** (IV)
M1b lésion unique	**M1b**	**IVA** (IV)	**IVA** (IV)	**IVA** (IV)	**IVA** (IV)
M1c lésions multiples	**M1c**	**IVB** (IV)	**IVB** (IV)	**IVB** (IV)	**IVB** (IV)

Les nouveaux stades proposés

Occult Carcinoma	Tx	N0	M0
Stage 0	Tis	N0	M0
Stage IA1	**Tia(mi)**	**N0**	**M0**
	T1a	**N0**	**M0**
Stage IA2	**T1b**	**N0**	**M0**
Stage IA3	**T1c**	**N0**	**M0**
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
Stage IIB	**T1a-c**	**N1**	**M0**
	T2a	**N1**	**M0**
	T2b	N1	M0
	T3	N0	M0
Stage IIIA	**T1a-c**	**N2**	**M0**
	T2a-b	N2	M0
	T3	N1	M0
	T4	N0	M0
	T4	N1	M0
Stage IIIB	**T1a-c**	**N3**	**M0**
	T2a-b	N3	M0
	T3	**N2**	**M0**
	T4	N2	M0
Stage IIIC	**T3**	**N3**	**M0**
	T4	**N3**	**M0**
Stage IVA	**Any T**	**Any N**	**M1a**
	Any T	**Any N**	**M1b**
Stage IVB	**Any T**	**Any N**	**M1c**

Les problèmes

Au niveau des données

- Échec du projet électronique
- Mauvaise répartition géographique
- Prédominance des stades chirurgicaux
- Très peu de stades IV proportionnellement
- …

Au niveau des analyses

- Manque de données pour de nombreux descripteurs
- Non prise en considération des types de bilan réalisés
- Traitements et facteurs génétiques non pris en compte sauf chirurgie
- Nouvelle carte ganglionnaire non analysée (concept de zones à valider)
- Facteurs pronostics : normes non définies
- …

Au niveau décisionnel

- De plus en plus compliqué
- Ne semble guère plus opérationnel

Conclusions

A l'UICC de décider !