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

University of Torino Lecture
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Past-Chair,
IASLC Staging and Prognostic Factors Committee
Content of this presentation

- Background and database
- Innovations in the 8th edition
- Implications for clinical practice
- Summary
- Conclusions
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- Background and database
  - Innovations in the 8th edition
  - Implications for clinical practice
- Summary
- Conclusions
# History of lung cancer TNM

<table>
<thead>
<tr>
<th>Year</th>
<th>Event or Edition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1943-1952</td>
<td>Pierre Denoix presented the TNM</td>
</tr>
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<tr>
<td>1968</td>
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</tr>
<tr>
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<tr>
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</tr>
<tr>
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</tr>
<tr>
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</tr>
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</tr>
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</tr>
<tr>
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<td>5th edition UICC and AJCC TNM</td>
</tr>
<tr>
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</tr>
<tr>
<td>2009</td>
<td>7th edition UICC and AJCC TNM</td>
</tr>
<tr>
<td>2016</td>
<td>8th edition UICC and AJCC TNM</td>
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<td>-----------</td>
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<td>2016</td>
<td>8th edition UICC and AJCC TNM</td>
</tr>
</tbody>
</table>

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
Based on 5,319 cases, the 5th–6th TNM staging is described as:

- Relatively small database from a single centre
- Not truly international
- Surgically orientated

Dr. Clifton F. Mountain, 1924-2007

International Workshop on Intrathoracic Staging

28th - 29th October 1996

Sponsored by International Association for the study of Lung Cancer
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

Recommendations submitted to the AJCC

Recommendations submitted to the UICC

Recommendations accepted by AJCC & UICC

Global implementation

National TNM committees

UICC literature watch

Adapted from Goldstraw P.

Dr. Leslie Sobin
Database for the 8th edition

<table>
<thead>
<tr>
<th>Region</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>46,560</td>
<td>49</td>
</tr>
<tr>
<td>Asia</td>
<td>41,705</td>
<td>44</td>
</tr>
<tr>
<td>North America</td>
<td>4,660</td>
<td>5</td>
</tr>
<tr>
<td>Australia</td>
<td>1,593</td>
<td>1.7</td>
</tr>
<tr>
<td>South America</td>
<td>190</td>
<td>0.3</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>94,708</td>
<td>100</td>
</tr>
</tbody>
</table>

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

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

- **Chemotherapy**: 21.1%
  - **Radiotherapy**: 57.7%
  - Surgery: 9.3%
  - Tri-modality: 4.4%
  - Chemo+RT: 1.5%
  - Chemo+Surg: 4.7%
# Elements of the classification of anatomic extent of lung cancer

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

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


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

<table>
<thead>
<tr>
<th>Descriptor</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\leq 1$ cm</td>
<td>T1a</td>
</tr>
<tr>
<td>&gt;1-2 cm</td>
<td>T1b</td>
</tr>
<tr>
<td>&gt;2-3 cm</td>
<td>T1c</td>
</tr>
<tr>
<td>&gt;3-4 cm</td>
<td>T2a</td>
</tr>
<tr>
<td>&gt;4-5 cm</td>
<td>T2b</td>
</tr>
<tr>
<td>&gt;5-7 cm</td>
<td>T3</td>
</tr>
<tr>
<td>&gt;7 cm</td>
<td>T4</td>
</tr>
<tr>
<td>Bronchus $&lt; 2$ cm</td>
<td>T2</td>
</tr>
<tr>
<td>Total atelectasis</td>
<td>T2</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>T4</td>
</tr>
</tbody>
</table>

New T categories

Tis (AIS)

T1mi

Clinical size: size of solid component

Pathologic size: size of invasive component

The T component
Size measurement in part-solid non-mucinous ADK


Courtesy of Dr. H. Asamura
The T component
Measurement of tumour size

IASLC recommendation for the measurement of tumour size:

Lung window

The N component

静脈両側の拡張と外科手術との相関

渡越恒夫

前項の観点から、静脈両側の拡張と外科手術との相関について考察する。

1. 静脈の拡張
   - 静脈の拡張は、外傷や感染、静脈瘤などの原因により発症する。
   - 静脈の拡張は、手術前の状態を観察するのに有用である。

2. 外科手術の重要性
   - 外科手術は、静脈の拡張に対処するための重要な手段である。
   - 手術の前後で静脈の拡張の状態を観察することが重要である。

参考文献

The amount of nodal disease has prognostic impact.

Upfront resection for single station cN2 will be discussed.

Prognosis refinement.

Better stratification.

Quantification of nodal disease

Pathological - any R

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

The M component: M1a

Prognosis for the different M1a descriptors is similar.

The M component: M1b

M1 Details
By Number of Lesions
EDC Data Only

M1a, Single Organ/Lesion
M1b, Single Organ/Mult. Lesions
M1b, Multiple Organs

Events / N
203 / 317
149 / 221
169 / 226
190 / 243

Median in Months
11.5 (10, 15)
11.4 (9.6, 13.2)
7.0 (5.6, 8.3)
5.2 (4.4, 6.9)

Survival, Years
### Stage groupings

<table>
<thead>
<tr>
<th>T1a</th>
<th>IA1</th>
<th>IIB</th>
<th>IIIA</th>
<th>IIIB</th>
<th>IVA</th>
<th>IVA</th>
<th>IVB</th>
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</thead>
<tbody>
<tr>
<td>T1b</td>
<td>IA2</td>
<td>IIB</td>
<td>IIIA</td>
<td>IIIB</td>
<td>IVA</td>
<td>IVA</td>
<td>IVB</td>
</tr>
<tr>
<td>T1c</td>
<td>IA3</td>
<td>IIB</td>
<td>IIIA</td>
<td>IIIB</td>
<td>IVA</td>
<td>IVA</td>
<td>IVB</td>
</tr>
<tr>
<td>T2a</td>
<td>IB</td>
<td>IIB</td>
<td>IIIA</td>
<td>IIIB</td>
<td>IVA</td>
<td>IVA</td>
<td>IVB</td>
</tr>
<tr>
<td>T2b</td>
<td>IIA</td>
<td>IIB</td>
<td>IIIA</td>
<td>IIIB</td>
<td>IVA</td>
<td>IVA</td>
<td>IVB</td>
</tr>
<tr>
<td>T3</td>
<td>IIIB</td>
<td>IIIA</td>
<td>IIIB</td>
<td>IIIC</td>
<td>IVA</td>
<td>IVA</td>
<td>IVB</td>
</tr>
<tr>
<td>T4</td>
<td>IIIA</td>
<td>IIIA</td>
<td>IIIB</td>
<td>IIIC</td>
<td>IVA</td>
<td>IVA</td>
<td>IVB</td>
</tr>
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</table>

### Stage grouping for the 8th edition

**Clinical**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Events/N</th>
<th>MST</th>
<th>24 months</th>
<th>60 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA1</td>
<td>68/781</td>
<td>NR</td>
<td>97%</td>
<td>92%</td>
</tr>
<tr>
<td>IA2</td>
<td>505/3105</td>
<td>NR</td>
<td>94%</td>
<td>83%</td>
</tr>
<tr>
<td>IA3</td>
<td>546/2417</td>
<td>NR</td>
<td>90%</td>
<td>77%</td>
</tr>
<tr>
<td>IB</td>
<td>680/1928</td>
<td>NR</td>
<td>87%</td>
<td>68%</td>
</tr>
<tr>
<td>IIA</td>
<td>215/585</td>
<td>NR</td>
<td>79%</td>
<td>60%</td>
</tr>
<tr>
<td>IIB</td>
<td>605/1453</td>
<td>66.0</td>
<td>72%</td>
<td>53%</td>
</tr>
<tr>
<td>IIIA</td>
<td>2052/3200</td>
<td>29.3</td>
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<td>36%</td>
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<tr>
<td>IIIB</td>
<td>1551/2140</td>
<td>19.0</td>
<td>44%</td>
<td>26%</td>
</tr>
<tr>
<td>IIIC</td>
<td>831/986</td>
<td>12.6</td>
<td>24%</td>
<td>13%</td>
</tr>
<tr>
<td>IVA</td>
<td>336/484</td>
<td>11.5</td>
<td>23%</td>
<td>10%</td>
</tr>
<tr>
<td>IVB</td>
<td>328/398</td>
<td>6.0</td>
<td>10%</td>
<td>0%</td>
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</table>

**Pathological**

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

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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

Lung cancers with multiple lesions
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 presumed or confirmed same histologic type
- Thought NOT to be synchronous tumours
- WITHOUT GG features
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
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
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
• 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
Content of this presentation

• Background and database
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• Conclusions
Summary

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

• Background and database
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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

<table>
<thead>
<tr>
<th>Nomenclature</th>
<th>Taxonomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exchange of information</td>
<td>Prognostic estimation</td>
</tr>
<tr>
<td>Therapeutic indications</td>
<td>Quality control of health care</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical practice</th>
<th>Stratification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evaluation of therapy</td>
<td>Identification of subgroups</td>
</tr>
</tbody>
</table>
SAVE THE DATE!
October 15–18, 2017 | Yokohama, Japan

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