10th European Conference Perspectives in Lung Cancer.

Brussels, March 2009.

The 7th Edition of TNM in Lung Cancer.

Imperial College London

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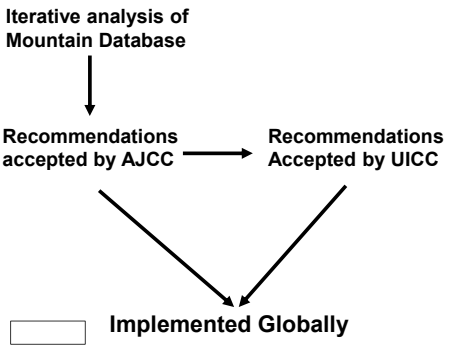
Process for revision: 1973-2002.



"Mountain" Revisions 1973 – 2002.

No attempt at Internal or External Validation!

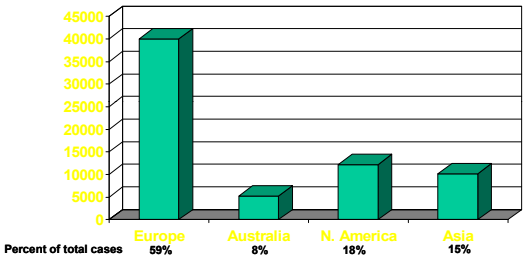
The IASLC International Database 1990 – 2000.

Total cases submitted	**100,869**
Excluded from current analysis	**19,854**
Outside of 1990-2000 time frame	**5,443**
Incomplete survival data	**1,505**
Unknown histology	**2,468**
Incomplete stage information	**7,720**
Recurrent cases and other (e.g not known if recurrent vs. newly diagnosed, occult tumours)	**1,603**
Carcinoids, sarcomas and other histologies	**1,115**
Included in analyses	**81,015**
SCLC (and mixed SCLC/NSCLC)	**13,290**
NSCLC (basis for IASLC recommendations for 7th Edition)	**67,725**

IASLC Staging Project

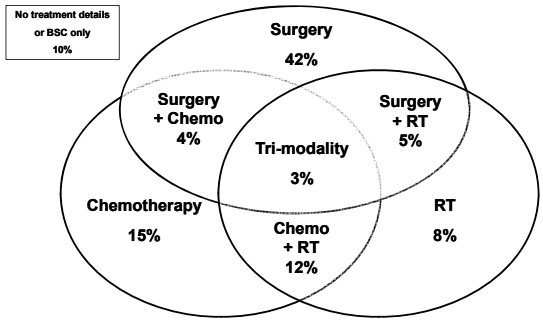
Distribution by Continent

67,725 Non-Small Cell Cases



IASLC Staging Project

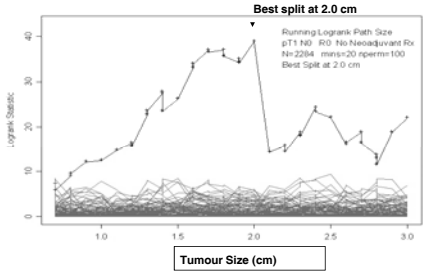
Treatment Modalities – 67,725 NSCLC.



Validation and Methodology.

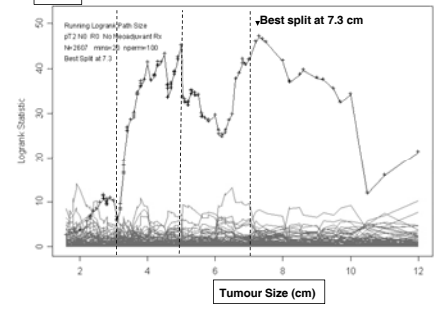
- **Exploratory analyses tested for relevance in clinical/evaluative and post-surgical/pathological data.**
- **All T recommendations explored within various Nodal and Residual combinations/permutations.**
- **Internal validation by comparing results by type of data source and geographical regions (supplemented in T size cut points and TNM stage groupings by random split into training and validation subsets).**
- **External validation for all recommendations comparing "best stage" against SEER 1998-2000, and literature search.**

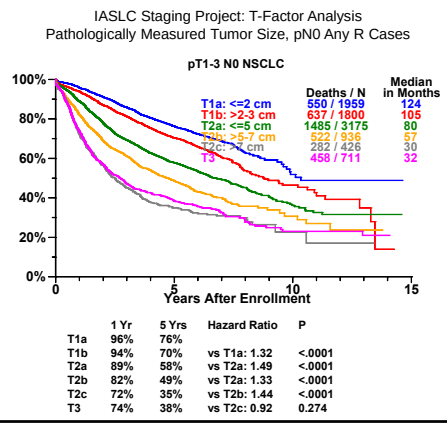
IASLC Staging Project: T-Factor Analysis
Pathologically Measured Tumor Size, pT1 N0 R0 Cases, Learning Set



"Running logrank:" A running logrank statistic is calculated and plotted on the Y-axis for each possible split point based on pathologically measured tumour size (X-axis). The blue lines show logrank statistics calculated on 100 random permutations of the data. The black line shows logrank statistics for the actual data.

IASLC Staging Project: T-Factor Analysis
Pathologically Measured Tumor Size, pT2 N0 R0 Cases, Learning Set





Summary of Changes to T Descriptors.

- **T1 sub-classified:**
  - **T1a tumours ≤ 2 cms.**
  - **T1b tumours > 2 cms and ≤ 3 cms.**
- **T2 sub-classified:**
  - **T2a tumours > 3cms and ≤ 5cms.**
  - **T2b tumours > 5 cms and ≤ 7 cms.**
- **Reclassify T2 tumours > 7 cms as T3.**
- **Reclassify T4 tumours due to additional tumour nodules in the primary lobe as T3.**
- **Reclassify T4 tumours due to malignant pleural effusion as M1, create M1a category.**

Summary of Changes to N & M Descriptors.

- **Retain current N classification.**
- **Reclassify M1 due to additional tumour nodules in other ipsilateral lobe(s) as T4.**
- **Reclassify M1 due to additional tumour nodules in the contralateral lung as M1a.**
- **Reclassify M1 due to distant metastases as M1b.**

Revised TNM Subgroups As Suggested by RPA on 17,726 "Best Stage" Cases

☐ = Change in Classification

T and M		N0	N1	N2	N3
UICC6 and Descriptor	New T/M	Stg	Stg	Stg	Stg
T1 (<=2cm)	T1a	IA	IIA	IIIA	IIIB
T1 (>2 – 3 cm)	T1b	IA	IIA	IIIA	IIIB
T2(<=5cm)	T2a	IB	IIA IIB	IIIA	IIIB
T2 (>5-7cm)	T2b	IIA IB	IIB	IIIA	IIIB
T2 (>7cm))	T3	IIB IB	IIIA IIB	IIIA	IIIB
T3 invasion		IIB	IIIA	IIIA	IIIB
T4 (same lobe nodules)		IIB IIIB	IIIA IIIB	IIIA IIIB	IIIB
T4 (extension)	T4	IIIA IIIB	IIIA IIIB	IIIB	IIIB
M1 (ipsilateral lung)		IIIA IV	IIIA IV	IIIB IV	IIIB IV
T4 (pleural effusion)	M1a	IV IIIB	IV IIIB	IV IIIB	IV IIIB
M1 (contralateral lung)		IV	IV	IV	IV
M1 (distant)	M1b	IV	IV	IV	IV

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T1 (>2 – 3 cm)	T1b	IA	IIA	IIIA	IIIB
T2(<=5cm)	T2a	IB	IIA IIB	IIIA	IIIB
T2 (>5-7cm)	T2b	IIA IB	IIB	IIIA	IIIB
T2 (>7cm))	T3	IIB IB	IIIA IIB	IIIA	IIIB
T3 invasion		IIB	IIIA	IIIA	IIIB
T4 (same lobe nodules)		IIB IIIB	IIIA IIIB	IIIA IIIB	IIIB
T4 (extension)	T4	IIIA IIIB	IIIA IIIB	IIIB	IIIB
M1 (ipsilateral lung)		IIIA IV	IIIA IV	IIIB IV	IIIB IV
T4 (pleural effusion)	M1a	IV IIIB	IV IIIB	IV IIIB	IV IIIB
M1 (contralateral lung)		IV	IV	IV	IV
M1 (distant)	M1b	IV	IV	IV	IV

Additional Recommendations:

- **Role of TNM in SCLC confirmed.**
- **TNM relevant in Carcinoid Tumours.**
- **A New International Nodal Chart agreed,**
  - **Incorporating concept of "Nodal Zones".**
- **A uniform definition of "Visceral Pleural Invasion" has been agreed.**
- **Additional Prognostic Factors studied:**
  - **SUV_{max} on initial PET scan.**
  - **PS, Age, Sex, Laboratory variables.**
  - **Biological Markers.**

What is Next?

We have finalised the prospective data set, are developing a web-based system for data collection, have obtained funding for the next cycle and are selecting database partners.

We hope that colleagues in Europe will continue to support this phase of the project.

Look out for !

- **UICC / AJCC 7th Edition "mid" 2009.**
- **Further publications in JTO.**
- **IASLC: Staging Manual and Staging Handbook in Thoracic Oncology, new Atlas, CT diagrams.**
- **IASLC laminates and posters, including Nodal Chart.**
- **Electronic resources for IASLC members, including PowerPoint material.**

Publications available without subscription.

www.jto.org

Latest publication:

Proposals for the inclusion of Broncho-Pulmonary Carcinoids, Travis WD et al.

Journal of Thoracic Oncology 2008: 3 ; 1213 – 1223.