New Guidelines for the Classification and Staging of Lung Cancer: TNM Descriptor and Classification Changes in the 8th Edition.

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AIMS

- To make the audience aware of the imminent revision of the TNM Classification for Lung Cancer.
- To describe the changes in T and M categories and descriptors, and resultant TNM Stage Groupings.
- To explain the data and analysis supporting these changes.
- To engender discussions within the MDT as to how these changes can be accommodated.
- To initiate discussions within the MDT as to the possible impact of these changes on management.

SUMMARY

The 7th edition of the TNM classification was published in 2009 (1) and enacted in January 2010 (2;3). It was novel in that it was entirely based upon the proposals emanating from the International Association for the Study of Lung Cancer (IASLC) Lung Cancer Staging Project (4). The success of this project has encouraged the IASLC to expand its remit for the forthcoming 8th edition of the TNM to the classification of other thoracic malignancies, those of the thymus and pleura, and involvement in the dissemination of proposals for the classification of cancers of the oesophagus and oesophagogastric junction.

In preparation for the 8th edition of the TNM classification for lung cancer the IASLC and their statistical partners at Cancer Research And Biostatistics (CRAB) established a new data base (5). This collected data on another 94,708 cases of lung cancer diagnosed between 1999 and 2010, treated by all modalities of care, donated by 35 institutions in 16 countries around the globe. After exclusions 77,156 remained for analysis, 70,967 cases of non-small cell lung cancer (NSCLC) and 6,189 cases of small-cell lung cancer (SCLC). Analysis of the cases of NSCLC has allowed proposals to be formulated for revisions to the T, N and M descriptors and categories, and the resultant TNM Stage groupings.

The proposals the T descriptors have been published (6). Size continues to be an important determinant and will become a descriptor for all of the T categories from T1 to T4 inclusive. The T size cut points of the 7th edition will be retained, vis 2, 3, 5 and 7 cms, and new cut points at 1 and 4 cms have been proposed. As a result new T categories have been created and others have been re-assigned. In addition tumours invading the diaphragm have been reclassified as T4 and tumours extending within 2 cms of the carina, but without invasion of the carina itself, or those tumours associated with collapse or consolidation of the whole lung have been down-staged to T2. The resultant T categories are shown in Table 1 along with the proposals for N and M categories.

It is recommended that the N categories of the 7th edition be retained. Exploratory analysis of surgically resected, pathologically classified cases has suggested that the prognostic significance of the anatomic location of involved nodes can be augmented if combined with the number of involved

nodes in N1 and N2 locations and the use of this sub-classification has been proposed for testing in the 8th edition (7).

The proposals for the M classification retain the existing category of M1a (8). The category of M1b has been re-assigned to describe a form of extremely limited "oligometastatic" cases in which there is a single metastatic deposit in one distant organ. A new category of M1c has therefore emerged to describe the commoner situation in which there are multiple metastases in one or more distant sites. The resultant T N M Stage groupings, derived from recursive partitioning and amalgamation analyses were refined by the committee by study of their statistical features and clinical relevance (9)and are shown in Table 2.

As in the 7th edition the IASLC Staging and Prognostic Factors Committee have attempted to resolve some issues in which data is limited by review of the literature and by consensus. These include how one should assess tumour size in the small tumours of mixed density increasing common when evaluation CT screen detected cancers. The committee's recommendation is that it should be the solid element on imaging, or the invasive component on pathological examination which should be measured to determine T size (10). In a series of articles the committee has given advice as to how one should classify the various scenarios in which multiple tumours are discovered in the lung(s) (11-14).

The IASLC has submitted all of these proposals to the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC), the 2 bodies that regulate the TNM classification for all tumour sites globally. The 8th edition is due to be published this Autumn. The IASLC will have extensive educational products available to attendees at the 17th World Conference on Lung Cancer, to be held in Vienna from the 4th to the 7th of December 2016.

Table 1. Proposed T, N and M descriptors for the 8th edition of TNM for Lung Cancer (changes to the 7th edition are highlighted in bold and underlined).

T - Primary Tumour

- 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].

- **T1(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**   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** **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 - Regional Lymph Node Involvement.

- 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 - Distant Metastasis.

- 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.**

Notes

1. The uncommon superficial spreading tumour of any size with its invasive component limited to the bronchial wall, which may extend proximal to the main bronchus, is also classified as T1a.
2. Solitary adenocarcinoma, $\leq$ 3 cm in size, with a predominately lepidic pattern and $\leq$ 5mm invasion in any one focus.
3. T2 tumours with these features are classified T2a if 4 cm or less in greatest dimension or if size cannot be determined, and T2b if greater than 4 cm but not larger than 5 cm in greatest dimension.
4. Most pleural (pericardial) effusions with lung cancer are due to tumour. In a few patients, however, multiple microscopic examinations of pleural (pericardial) fluid are negative for tumour, and the fluid is non-bloody and is not an exudate. Where these elements and clinical judgement dictate that the effusion is not related to the tumour, the effusion should be excluded as a staging descriptor.
5. This includes involvement of a single distant (non-regional) lymph node.

TABLE 8. Proposed Stage Groupings for 8th edition of TNM for Lung Cancer (changes to the 7th edition are highlighted in bold and underlined).

Occult carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA1	**T1(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**

REFERENCES

1. Goldstraw P. IASLC Staging Manual in Thoracic Oncology. 1st ed. Florida, USA: EditorialRx Press; 2009.
2. Sobin LH, Gospodarowicz MK, Wittekind C. UICC TNM Classification of Malignant Tumours. 7th ed. New York: Wiley-Liss; 2009.
3. Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. AJCC Cancer Staging Manual. 7th ed. New York: Springer; 2009.
4. Goldstraw P, Crowley J, IASLC International Staging Project. The IASLC International Staging Project on Lung Cancer. Journal of Thoracic Oncology 1, 281-286. 2006.
5. Rami-Porta R, Bolejack V, Giroux DJ, Chansky K, Crowley J, Asamura H, et al. The IASLC Lung Cancer Staging Project: The new database to inform the eigth edition of the TNM classification of lung cancer. J Thorac Oncol 2014;9:1618-24.
6. Rami-Porta R, Bolejack V, Crowley J, Ball D, Kim J, Lyons G, et al. 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. J Thorac Oncol 10, 990-1003. 2015.
7. Asamura H, Chansky K, Crowley J, Goldstraw P, Rusch VW, Vansteenkiste J, et al. 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. J Thorac Oncol 10, 1675-1684. 2015.
8. Eberhardt WEE, Mitchell A, Crowley J, Kondo H, Kim YT, Turrisi A, et al. The IASLC Lung Cancer Staging Project: Proposals for the Revision of the M Descriptors in the Forthcoming (8th) Edition of the TNM Classification of Lung Cancer. J Thorac Oncol 10, 1515-1522. 2015.
9. Goldstraw P, Chansky K, Crowley J, Rami-Porta R, Asamura H, Eberhardt WEE, et al. The IASLC Lung Cancer Staging Project: proposals for the revision of the TNM stage groupings in the forthcoming (eighth) edition of the TNM classification for lung cancer. J Thorac Oncol 11, 39-51. 2016.
10. Travis WD, Asamura H, Bankier A, Detterbeck F, Goo JM, MacMahon H, et al. The IASLC Lung Cancer Staging Project: Proposals for Coding T Categories for Subsolid nodules and Assessment of Tumor Size in Part-Solid Tumors in the Forthcoming Eigth Edition of the TNM Classification of Lung Cancer. J Thorac Oncol. In press 2016.
11. Detterbeck FC, Franklin WA, Nicholson AG, Girard N, Arenberg DA, Travis WD, et al. The IASLC Lung Cancer Staging Project: Background Data and Proposed Criteria to Distinguish Separate Primary Lung Cancers from Metastatic Foci in Patients with Two Lung Tumors in the Forthcoming Eigth Edition of the TNM Classification for Lung Cancer. J Thorac Oncol 11, 651-665. 2016.
12. Detterbeck FC, Marom EM, Arenberg DA, Franklin WA, Nicholson AG, Travis WD, et al. The IASLC Lung Cancer Staging Project: Background Data and Proposals for the Application of TNM Staging Rules to Lung Cancer Presenting with Ground Glass or Lepidic Features or a Pneumonic Type of Involvement in the Forthcoming Eigth Edition of the TNM Classification. J Thorac Oncol 11, 666-680. 2016.
13. Detterbeck FC, Bolejack V, Arenberg DA, Crowley J, Donington JS, Franklin WA, et al. The IASLC Lung Cancer Staging Project: Background Data and Proposals for the Classification of Lung Cancer with Separate Tumor Nodules oin the Forthcoming Eigth Editon of the TNM Classification for Lung Cancer. J Thorac Oncol 11, 681-692. 2016.
14. Detterbeck FC, Nicholson AG, Franklin WA, Marom EM, Travis WD, Girard N, et al. The IASLC Lung Cancer Staging Project: Summary of Proposals for Revisions of the Classification of Lung Cancers with Multiple Pulmonary Sites of Involvement in the Forthcoming Eight Edition of the TNM Classification. J Thorac Oncol 11, 639-650. 2016.