Revisions to the TNM Staging of Lung Cancer: Rationale, Significance, and Clinical Application[1]

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Lung cancer remains the leading cause of cancer-related mortality worldwide. To formulate effective treatment strategies and optimize patient outcomes, accurate staging is essential. Lung cancer staging has traditionally relied on a TNM staging system, for which the International Association for the Study of Lung Cancer (IASLC) has recently proposed changes. The revised classification for this eighth edition of the TNM staging system (TNM-8) is based on detailed analysis of a new large international database of lung cancer cases assembled by the IASLC for the purposes of this project. Fundamental changes incorporated into TNM-8 include *(a)* modifications to the T classification on the basis of 1-cm increments in tumor size; *(b)* grouping of lung cancers that result in partial or complete lung atelectasis or pneumonitis; *(c)* grouping of tumors with involvement of a main bronchus irrespective of distance from the carina; *(d)* reassignment of diaphragmatic invasion in terms of T classification; *(e)* elimination of mediastinal pleural invasion from the T classification; and *(f)* subdivision of the M classification into different descriptors on the basis of the number and site of extrathoracic metastases. In response to these revisions, established stage groups have been modified, and others have been created. In addition, recommendations for classifying patterns of disease that result in multiple sites of pulmonary involvement, including multiple primary lung cancers, lung cancers with separate tumor nodules, multiple ground-glass/lepidic lesions, and consolidation, as well as recommendations for lesion measurement, are addressed. Understanding the key revisions introduced in TNM-8 allows radiologists to accurately stage patients with lung cancer and optimize therapy.

Abbreviations: FDG = fluorine 18 fluorodeoxyglucose, IASLC = International Association for the Study of Lung Cancer, NSCLC = non–small cell lung carcinoma, pN = pathologic lymph node, SCLC = small cell lung carcinoma, TNM-7 = seventh edition of the TNM staging system, TNM-8 = eighth edition of the TNM staging system

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SA-CME LEARNING OBJECTIVES

After completing this journal-based SA-CME activity, participants will be able to:

- Describe the rationale and methodology for the development of TNM-8 for lung cancer.
- Describe the T, N, and M descriptors and stage groups in TNM-8.
- Discuss how to use the classification and staging systems to properly characterize and stage lung cancers with multiple pulmonary sites of involvement.

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Introduction

Lung cancer remains the leading cause of cancer-related mortality worldwide, with an estimated 222 500 new cases diagnosed and 155 870 deaths expected from the disease in 2017 (1). Staging plays an important role in the management of patients and is based on groupings of patients with similar clinical outcomes. The TNM staging system is the established, uniform method of staging lung cancer and depends primarily on the anatomic extent of disease. The seventh edition of the TNM staging system (TNM-7) has been used in clinical practice since its publication in 2009. TNM-7 introduced key revisions that were based on the analysis of an international database organized by the International Association for the Study of Lung Cancer (IASLC) as part of the IASLC Lung Cancer Staging Project (2,3). Important changes included the addition of small cell lung carcinoma (SCLC) and bronchopulmonary carcinoid to the TNM staging system, revisions to the T and M descriptors on the basis of significant differences in 5-year survival between patients with different disease features, and revisions to several stage groups.

TEACHING POINTS

- The analysis demonstrated significant separation of T1 lesions from T2 lesions on the basis of a size threshold of 3 cm, as well as a progressive reduction in patient survival for each 1-cm cut point (≤1 cm; >1 cm to 2 cm; >2 cm to 3 cm; >3 cm to 4 cm; >4 cm to 5 cm; >5 cm to 6 cm; >6 cm to 7 cm; and >7 cm). Statistical analyses evaluating the significance of pathologic tumor size controlled for age, gender, cell type, and geographic region demonstrated that the difference in survival was significant for all tumor size cut points.
- Analysis of the new database demonstrated that partial atelectasis or pneumonitis aligns with other T2 descriptors in terms of 5-year survival; however, patients with complete atelectasis or pneumonitis demonstrated better survival than those with other T3 descriptors. Therefore, in TNM-8, partial and complete forms of lung atelectasis and pneumonitis are grouped together as T2 lesions.
- Analysis of the new database demonstrated that the current nomenclature for the N classification results in consistent separation of prognostically distinct groups, and no changes were made to this category. Thus, N0 is defined as the absence of regional lymph node involvement; N1 includes metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary lymph nodes, including involvement by direct extension; N2 includes metastasis in ipsilateral mediastinal and/or subcarinal lymph nodes; and N3 includes metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph nodes.
- In TNM-8, intrathoracic metastasis retains the M1a designation, but the extrathoracic metastasis group has been split into M1b (single extrathoracic metastasis in a single distant organ) and M1c (multiple extrathoracic metastases in one or more distant organs) on the basis of differences in patient survival.
- The IASLC recommends that all tumors should be measured and the measurement reported in centimeters with millimeter increments. At multidetector CT, solid and nonsolid lesions should be measured on the image demonstrating the greatest average tumor dimension, regardless of the plane (axial, sagittal, or coronal). Part-solid lesions should be measured on the image or images demonstrating the largest average tumor diameter and the largest diameter of the solid component. Although long-axis and short-axis measurements may be recorded for all lesions, only the longest diameter for solid and nonsolid lesions and the longest diameter of the solid component for part-solid lesions should be used for staging purposes.

One of the most important limitations of the original IASLC Lung Cancer Staging Project was the retrospective nature of the database. To inform the eighth edition of the TNM staging system (TNM-8), an international consortium led by the IASLC resulted in the collection of new lung cancer cases and the creation of a large database (4). Analysis of this new database by the IASLC Staging and Prognostic Factors Committee showed significant differences in survival between patients with different T and M classifications, and recommendations for further modification of individual descriptors and overall stage groups have been published (5–7). In addition, a subcommittee of the IASLC Staging and Prognostic Factors Committee investigated patterns of disease that result in multiple sites of pulmonary involvement, including multiple primary lung cancers, lung cancers with separate tumor nodules, multiple ground-glass/lepidic lesions, and consolidation, and has issued recommendations regarding the staging of cancer in patients with such features (8). As the role of imaging in the clinical evaluation and staging of lung cancer continues to evolve, radiologists must understand the foundation and potential implications of TNM-8.

In this article, we present the rationale and methodology of the IASLC in producing TNM-8, specific revisions to the T and M classifications and stage groups, and new recommendations regarding the staging of disease with multiple sites of pulmonary involvement and the measurement of tumors. The recommendation that non–small cell lung carcinoma (NSCLC), SCLC, and bronchopulmonary carcinoid be staged with the TNM system is maintained in TNM-8.

Development and Methodology of TNM-8

General Considerations

TNM-7 incorporated several key changes to individual descriptors and overall stage groups on the basis of the analysis of a large lung cancer database as part of the IASLC Lung Cancer Staging Project. Despite these advances, several descriptors could not be validated.

For the creation of TNM-8 and to potentially overcome some of the limitations of the original retrospective database, the IASLC assembled a new database with retrospective and prospective clinical information. This database included data on 94 708 new cases of lung cancer diagnosed between 1999 and 2010 collected from 35 sources in 16 countries, 4667 of which were submitted through an online electronic data capture system stored at Cancer Research and Biostatistics in Seattle, Wash (4). Of these cases, 17 552 with an unknown or different histologic type and incomplete stage information were excluded, leaving 77 156 patients (70 967 with NSCLC and 6189 with SCLC) with clinical and pathologic staging information for analysis. Clinical staging involves the utilization of tools such as the findings from physical examination, laboratory tests, and imaging to determine the stage before surgery, whereas pathologic staging involves information informed by surgical findings and histopathologic evaluation of resected specimens. Various subsets of this database were investigated to determine appropriate T, N, and M descriptors and stage groups. Detailed information regarding the methodology is provided in Table 1.

Table 1: Development and Methodology of TNM-8

Variable	Methodology
Tumor (T)	33 115 patients with NSCLC fulfilled initial inclusion criteria for analysis: *(a)* absence of metastatic disease (M0), *(b)* complete clinical (c) or pathologic (p) staging information, *(c)* documented tumor size, and *(d)* sufficiently detailed T descriptors to support the assigned classification: 13 012 with sufficient clinical stage information, 12 449 of which underwent surgical resection. 30 018 with complete pathologic stage information, 28 150 of which underwent complete resection. Patients with induction therapy were excluded. Survival was measured from the date of diagnosis for clinically staged cases and the date of surgery for pathologically staged cases. Overall survival was evaluated by using the Kaplan-Meier method, and prognostic groups were assessed by using Cox proportional hazards regression analysis. Specific threshold measurements for tumor size established in TNM-7 were reevaluated and the data analyzed to determine possible additional size increments that could be used clinically. Cases with more than one positive descriptor within a T category were assessed separately from those with only one positive descriptor to evaluate the effect of individual T descriptors. Multivariate Cox regression analysis adjusted for patient age and gender, tumor histologic type, and geographic region was performed; and specific T descriptors were identified for possible reclassification on the basis of differences in survival when compared with other descriptors in the same or an adjacent category.
Lymph node (N)	38 910 patients with NSCLC had clinical lymph node (cN) information available, and 31 426 patients with NSCLC had pathologic lymph node (pN) information available. Most data (23 012 cases) were submitted from Japan and primarily used the Naruke lymph node map to determine the location of lymph nodes and establish overall lymph node status; for other regions, the Mountain-Dressler modification of the American Thoracic Society lymph node map was used. Because the IASLC lymph node map was published in 2009, it was not used with any meaningful frequency in the new database. Survival was calculated by using the Kaplan-Meier method; and prognostic groups were assessed by using Cox regression analysis adjusted for patient age and gender, histologic type of the tumor, and geographic region. For the purposes of the analyses, cN and pN classifications were used for survival regardless of the T classification and within the different T categories. In addition, the effect of the number of involved lymph node stations was evaluated: In the new database, information regarding the number of involved lymph nodes was not included outside the cases submitted through the electronic data capture system.
Metastasis (M)	2411 cases of NSCLC with unresected M1 disease were available for analysis: 1059 cases were submitted to Cancer Research and Biostatistics through the electronic data capture system. 1296 cases were from the Turkish Thoracic Society. 56 cases were from an institutional registry at Prince Charles Hospital (Brisbane, Australia). Final analyses were restricted to the cases from the electronic data capture system because they included all of the specific data points necessary for evaluation. The statistical methodology used for the analysis of the M classification was similar to that used for the analysis of the T and the N classifications, and prognosis was assessed by using Cox proportional hazards regression analysis.
Stage groups	The analysis of stage groups included cases with a confirmed histologic diagnosis of NSCLC and complete stage information. Candidate proposals for overall TNM stage groups were developed in conjunction with proposed revisions to the T and M classifications. After the proposed T and M revisions were applied to a training dataset, candidate stage groups were developed; and overall survival was assessed by using clinical, pathologic, and best stage information. Survival was measured from the date of diagnosis for clinically staged tumors and from the date of surgery for pathologically staged tumors and was calculated by using the Kaplan-Meier method.

Special Considerations

One of the most important limitations of the previous editions of the TNM staging system for lung cancer has been the lack of guidance regarding cancers with multiple sites of pulmonary involvement, including multiple primary lung cancers, lung cancers with separate tumor nodules, multiple ground-glass/lepidic lesions, and consolidation. It has been well documented that there is marked variability in the classification of these different patterns of disease by experts in the field and that these groups demonstrate significant differences in biologic behavior in terms of survival and recurrence patterns (8–10). For instance, although separate primary lung cancers have long been recognized by the TNM staging system, no clear guideline has been provided regarding how this diagnosis should be established (8). Although specific terminology with regard to what constitutes a separate tumor nodule was included in TNM-7, there is considerable variability in how this information has been interpreted (9,10).

A subcommittee of the IASLC Staging and Prognostic Factors Committee evaluated the relevant literature of 1995–2015 and included their expert opinion to describe distinct patterns of disease, formulate criteria to categorize lung cancer with multiple pulmonary sites of involvement, and indicate how the TNM classification system can be applied to each disease pattern. A cohort of cases with information regarding separate tumor nodules was available in the new database; however, the numbers of cases representing the other disease patterns (such as multiple ground-glass/lepidic lesions and pneumonic-type adenocarcinoma) were insufficient for formal analysis. Nevertheless, recommendations were made on the basis of the available data.

Staging of SCLC

It was first recommended that SCLC be staged with the TNM system with the release of TNM-7, and the results of subsequent studies have demonstrated the efficacy of this staging application (11,12). Survival analyses were performed for SCLC cases obtained from 1999 through 2010 with clinical and pathologic staging information. Patient prognosis was compared with TNM-7 as validation and was evaluated in relation to the proposed changes to the T and M classifications in TNM-8. A total of 5002 retrospective cases were available for evaluation, of which 4848 were clinically staged, 582 were pathologically staged, and 428 were both clinically and pathologically staged. Of the 4848 patients with clinical staging information, 577 (12%) were treated surgically. Most nonsurgical patients were treated with chemotherapy, with or without radiation therapy, and 1% of patients received supportive care.

Changes in TNM-8

On the basis of the analyses described in the previous sections, revisions to the T and M classifications were constructed, and candidate proposals for TNM stage groups were developed. For TNM-8, the TNM descriptors are listed in Table 2 (7), and the stage groups are listed in Table 3 (7).

T Classification

The T classification indicates specific characteristics of the primary neoplasm and includes features such as size, the presence and extent of local tumor invasion, and the presence and location of separate tumor nodules. Analysis of the new database by using these established characteristics demonstrated significant differences in the 5-year survival of patients with various features.

Tumor Size.—Information regarding tumor size was available for a large number of cases in the new database, and survival statistics were calculated for those patients with completely resected tumors of various sizes (Table 4) (5). The analysis demonstrated significant separation of T1 lesions from T2 lesions on the basis of a size threshold of 3 cm, as well as a progressive reduction in patient survival for each 1-cm cut point (≤1 cm; >1 cm to 2 cm; >2 cm to 3 cm; >3 cm to 4 cm; >4 cm to 5 cm; >5 cm to 6 cm; >6 cm to 7 cm; and >7 cm). Statistical analyses evaluating the significance of pathologic tumor size controlled for age, gender, cell type, and geographic region demonstrated that the difference in survival was significant for all tumor size cut points. Therefore, T1 tumors are subdivided into three groups at 1-cm thresholds: T1a nodules measuring 1 cm or less, T1b tumors measuring more than 1 cm and less than or equal to 2 cm, and T1c lesions measuring more than 2 cm and less than or equal to 3 cm (Fig 1). Similarly, T2 tumors have been subdivided into two groups: T2a tumors measuring more than 3 cm and less than or equal to 4 cm, and T2b lesions measuring more than 4 cm and less than or equal to 5 cm (Fig 2). In TNM-8, tumors measuring more than 5 cm and less than or equal to 7 cm have been reclassified as T3 lesions (Fig 3), and tumors measuring more than 7 cm have been reclassified as T4 tumors (Fig 4). The new size thresholds introduced in TNM-8 can be easily applied in clinical practice and maintain compatibility with the size descriptors established in TNM-7.

Involvement of Main Bronchi.—In TNM-7, involvement by lung cancer of a main bronchus 2

Table 2: TNM Descriptors for TNM-8

Descriptor	Definition
T descriptor	
TX	Primary tumor cannot be assessed or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized with imaging or bronchoscopy
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor ≤ 3 cm in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus
T1a	Tumor ≤ 1 cm in greatest dimension
T1b	Tumor > 1 cm but ≤ 2 cm in greatest dimension
T1c	Tumor > 2 cm but ≤ 3 cm in greatest dimension
T2 descriptor	
T2	Tumor > 3 cm but ≤ 5 cm or tumor with any of the following features: involvement of a main bronchus regardless of the distance from the carina; invasion of the visceral pleura; associated with partial or complete lung atelectasis or pneumonitis
T2a	Tumor > 3 cm but ≤ 4 cm in greatest dimension
T2b	Tumor > 4 cm but ≤ 5 cm in greatest dimension
T3	Tumor > 5 cm but ≤ 7 cm in greatest dimension or one that directly invades any of the following structures: parietal pleura, chest wall (including superior sulcus tumors), phrenic nerve, parietal pericardium; or separate tumor nodule or nodules in the same lobe
T4	Tumor measuring >7 cm in greatest dimension that invades any of the following structures: mediastinum, diaphragm, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina; or separate tumor nodule or nodules in a different lobe of the same lung
N descriptor	
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 nodes
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph nodes
M descriptor	
M0	No distant metastasis
M1	Distant metastasis
M1a	Separate tumor nodule or nodules in contralateral lung; malignant pleural effusion or pleural thickening or nodules or masses; malignant pericardial effusion or pericardial thickening or nodules or masses
M1b	Single distant (extrathoracic) metastasis in a single organ
M1c	Multiple distant (extrathoracic) metastases in a single organ or multiple organs

Source.—Reference 7.

cm or more from the carina was classified as T2 disease, and more proximal involvement was classified as T3 disease. Analysis of the new database demonstrated that involvement of a main bronchus 2 cm or more from the carina is appropriate as a T2 descriptor in that the survival of patients with this feature is similar to that of patients with other T2 descriptors. However, involvement of a main bronchus less than 2 cm from the carina, but without direct invasion of the carina, is associated with better survival than that for patients with other T3 descriptors and therefore should be downstaged to T2. Multivariate analysis revealed that involvement of a main bronchus, regardless of the distance from the carina, does not increase risk after adjusting for tumor size. Therefore, lesions involving a main bronchus, regardless of the distance from the carina, have been grouped together as T2 lesions (Fig 5).

Atelectasis or Pneumonitis of the Lung.—In TNM-7, partial atelectasis or pneumonitis (of a lung lobe) was classified as T2 disease, and atelectasis or pneumonitis of an entire lung was

Table 3: Stage Groups for TNM-8

Stage	Tumor	Node	Metastasis
Occult carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA1	T1a(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

Source.—Reference 7.
*mi = minimally invasive.

Table 4: Five-year Survival of Patients according to the T Classification for Pathologically and Clinically Staged Tumors in TNM-8

	Five-year Survival of Patients (%)	
T Descriptor	Pathologically Staged Tumors	Clinically Staged Tumors
T1a	92	92
T1b	86	83
T1c	81	76
T2a	74	67
T2b	65	60
T3	57	52
T4	47	38

Source.—Reference 5.

classified as T3 disease. Analysis of the new database demonstrated that partial atelectasis or pneumonitis aligns with other T2 descriptors in terms of 5-year survival; however, patients with complete atelectasis or pneumonitis demonstrated better survival than those with other T3 descriptors. Therefore, in TNM-8, partial and complete forms of lung atelectasis and pneumonitis are grouped together as T2 lesions (Fig 6).

Diaphragmatic Invasion.—In TNM-7, invasion of the diaphragm by lung cancer was classified as T3 disease. Analysis of the new database demonstrated worse 5-year survival of patients with this feature than that of patients with other T3 tumors but similar to the 5-year survival of patients with T4 lesions. Therefore, diaphragmatic invasion is reclassified as T4 disease in TNM-8 (Fig 7).

Involvement of the Mediastinal Pleura.—In TNM-7, involvement of the mediastinal pleura was classified as T3 disease. Analysis of the new database demonstrated that patients with lung cancers that show this feature have a better prognosis than patients with other T3 lesions, although this characteristic was represented by a relatively small number of cases. The committee also noted that the designation of mediastinal pleura invasion was rarely used as a descriptor in clinical staging, because it can be difficult to determine. In clinical practice, mediastinal pleura invasion can be considered if the lesion directly contacts the mediastinum. However, when other findings suggestive of invasion are present, the tumor has typically already extended beyond the mediastinal pleura and invaded the mediastinum, a finding that remains classified as T4 disease. At pathologic staging, the discovery of isolated mediastinal pleura invasion in the absence of invasion of additional mediastinal structures is rare. Therefore, mediastinal pleural invasion has been eliminated from the T classification in TNM-8.

N Classification

The lymph node (N) classification is determined by the presence or absence of intrathoracic lymph node involvement. In contrast to primary lung cancer, the short-axis diameter is typically used for lymph node measurement. Several lymph node maps have been developed and used by health care providers for staging lung cancer, including the Naruke lymph node map, the Mountain-Dressler modification of the American Thoracic Society lymph node map, and, more recently, the IASLC lymph node map. The IASLC map assigns lymph nodes to seven specific zones: supraclavicular, upper, aorticopulmonary, subcarinal, lower, hilar/interlobar, and peripheral zones (13). However, a detailed description of the IASLC lymph node map is beyond the scope of this article.

Analysis of the new database demonstrated that the current nomenclature for the N classification

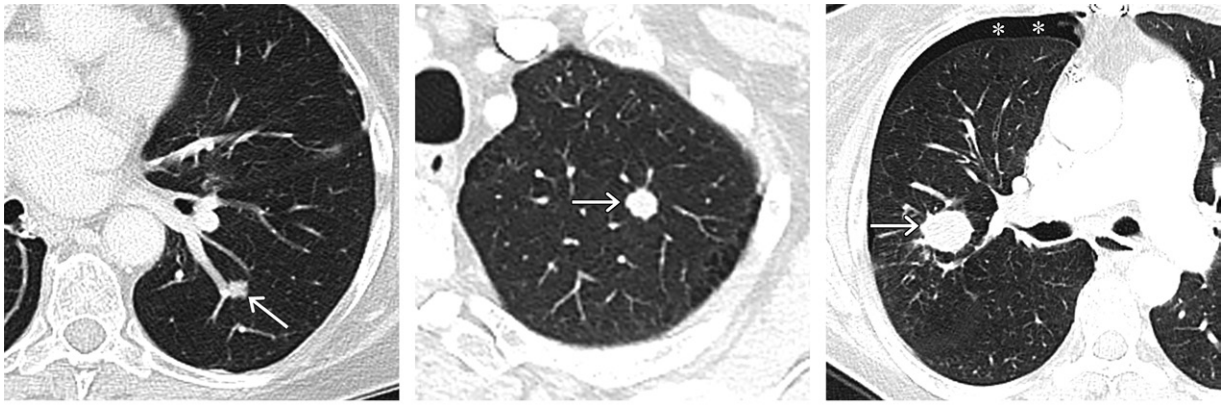
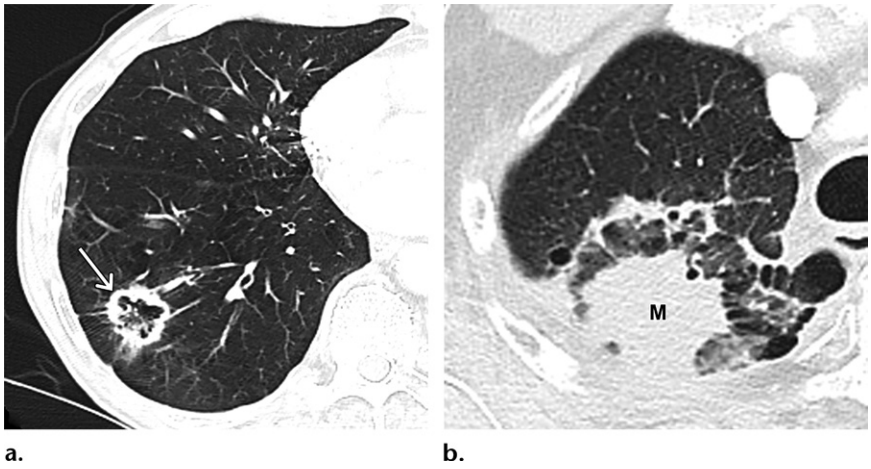


Figure 1. T1 tumor size. Axial contrast material–enhanced multidetector CT images of three different patients with NSCLC show the subdivisions of T1 lung cancers on the basis of 1-cm thresholds. **(a)** Image of a 69-year-old woman shows a T1a lesion (arrow); T1a lesions measure 1 cm or less. **(b)** Image of a 78-year-old man shows a T1b nodule (arrow); T1b nodules measure more than 1 cm and less than or equal to 2 cm. **(c)** Image of a 54-year-old woman shows a T1c tumor (arrow); T1c tumors measure more than 2 cm and less than or equal to 3 cm. Note the small pneumothorax (*) after CT-guided core needle biopsy.

Figure 2. T2 tumor size. Axial contrast-enhanced multidetector CT images of two different patients with NSCLC show the subdivisions of T2 tumors on the basis of 1-cm cut points. **(a)** Image of a 70-year-old man shows a T2a tumor (arrow); T2a tumors measure more than 3 cm and less than or equal to 4 cm. **(b)** Image of a 68-year-old woman shows a T2b mass *(M)*; T2b lesions measure more than 4 cm and less than or equal to 5 cm.



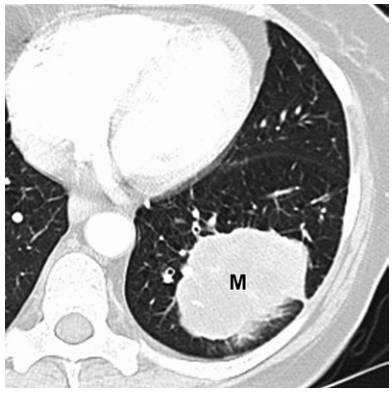


Figure 3. T3 tumor size. Axial contrast-enhanced multidetector CT image of a 68-year-old woman with NSCLC at the level of the ventricles shows a 6.6-cm mass *(M)* in the left lower lobe, a finding compatible with a T3 lesion in TNM-8. Analysis of the new database demonstrated that tumors measuring more than 5 cm and less than or equal to 7 cm are well aligned with other T3 descriptors in TNM-8.

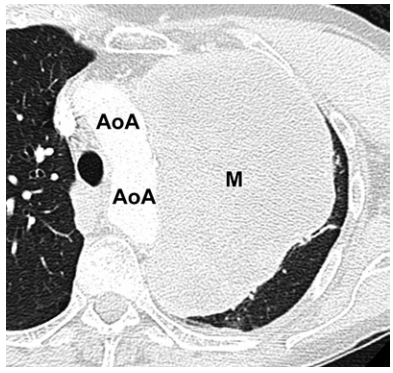


Figure 4. T4 tumor size. Axial contrast-enhanced multidetector CT image of a 71-year-old woman with NSCLC at the level of the aortic arch *(AoA)* shows a large mass *(M)* in the left upper lobe, a finding compatible with a T4 lesion in TNM-8. Analysis of the new database demonstrated that tumors measuring more than 7 cm are well aligned with other T4 descriptors in TNM-8.

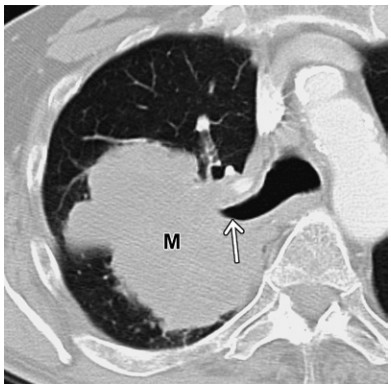
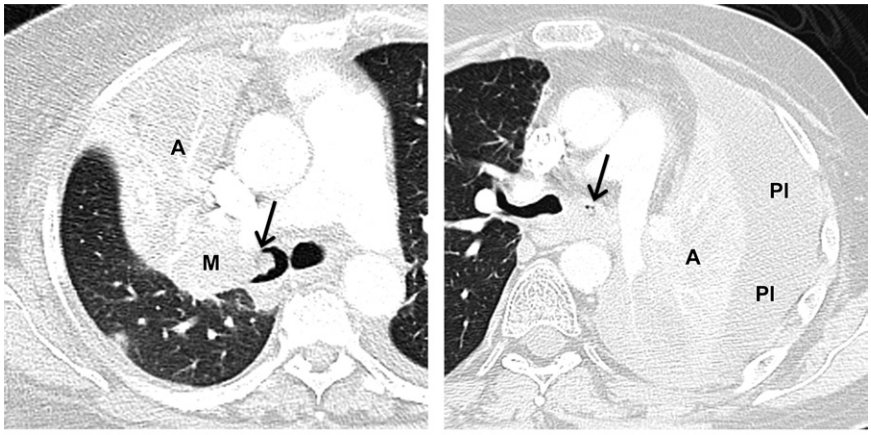
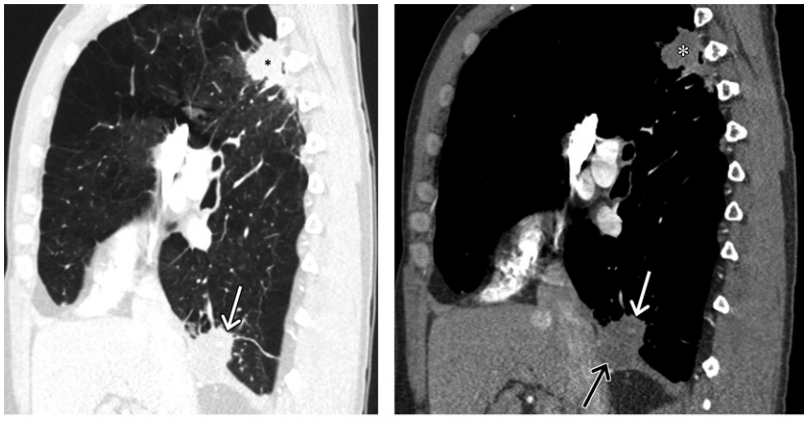


Figure 5. Tumor involvement of main bronchi. Axial contrast-enhanced multidetector CT image of a 73-year-old man with NSCLC at the level of the right main bronchus shows a right upper lobe mass *(M)* invading the proximal right main bronchus (arrow). Analysis of the database revealed that involvement of a main bronchus, regardless of the distance from the carina, does not increase risk after adjusting for tumor size, and these lesions are grouped together as a T2 descriptor in TNM-8. It is important to note that in this case, the size of the primary tumor would upstage the T classification to T4.



a. **b.**

Figure 6. Atelectasis or pneumonitis in two different patients. **(a)** Axial contrast-enhanced multidetector CT image of a 59-year-old woman with NSCLC below the level of the carina shows a right perihilar obstructing mass *(M)* extending into the proximal right main bronchus (arrow), resulting in atelectasis *(A)* of the right upper lobe. **(b)** Axial contrast-enhanced multidetector CT image of a 42-year-old man with NSCLC at the level of the left pulmonary artery shows a mass (arrow) obstructing the left main bronchus and resulting in complete atelectasis *(A)* of the left lung. A left pleural effusion *(Pl)* is also depicted. Analysis of the new database demonstrated better survival of patients with complete atelectasis or pneumonitis than those with other T3 descriptors; and in TNM-8, partial and complete lung atelectasis or pneumonitis are grouped together as a T2 descriptor.



a. **b.**

Figure 7. Diaphragmatic invasion. Axial contrast-enhanced multidetector CT images (**a**, lung window; **b**, soft-tissue window) of a 67-year-old man with NSCLC show a mass (white arrow) in the right lower lobe invading the right hemidiaphragm (black arrow on **b**). A separate pulmonary lesion (*) is depicted more cephalad in the right lung. Analysis of the new database demonstrated that the 5-year survival of patients with diaphragmatic invasion was worse than that of patients with other T3 lesions defined by other descriptors but was similar to that of patients with T4 tumors. Therefore, diaphragmatic invasion has been reclassified as T4 disease in TNM-8.

results in consistent separation of prognostically distinct groups, and no changes were made to this category (14). Thus, N0 is defined as the absence of regional lymph node involvement; N1 includes metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary lymph nodes, including involvement by direct extension; N2 includes metastasis in ipsilateral mediastinal

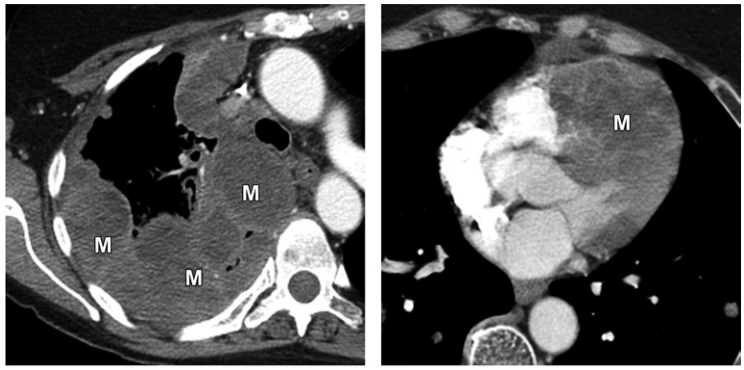


Figure 8. Intrathoracic metastases in two different patients. **(a)** Axial contrast-enhanced multidetector CT image of the right hemithorax of a 59-year-old woman with NSCLC (NSCLC not shown) shows extensive pleural thickening and numerous pleural masses *(M),* findings consistent with M1a disease. **(b)** Axial contrast-enhanced multidetector CT image of the heart of a 62-year-old man with NSCLC (NSCLC not shown) shows a heterogeneous mass *(M)* that involves the right ventricle and interventricular septum and is compatible with cardiac metastasis.

and/or subcarinal lymph nodes; and N3 includes metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph nodes (Table 2).

The prognostic effect of the number of lymph node stations involved and the potential effect of skip metastases were also investigated. To evaluate the effect of lymph node stations, pN staging was subdivided into several groups, where the letter *a* denoted single lymph node station involvement and the letter *b* denoted multiple lymph node station involvement within an N category: single pN1 station (pN1a) and multiple pN1 stations (pN1b); and single pN2 station (pN2a) and multiple pN2 stations (pN2b). The survival curves of the pN1b and pN2a groups showed overlap and no difference in survival, whereas the survival differences between the pN1a and pN1b groups and between the pN2a and pN2b groups were significant. Nevertheless, this information was derived from pathologic staging only, and validation in the clinical dataset could not be performed.

To investigate the potential effect of skip metastases, pN2a was divided into the following components, in which a designation ending in the numeral *1* indicated the presence of skip metastases and a designation ending in the numeral *2* indicated the absence of skip metastases (eg, involvement of contiguous lymph node stations): single pN2 with skip (no pN1 involvement, pN2a1); and single pN2 without skip (pN1 and pN2 involvement, pN2a2).

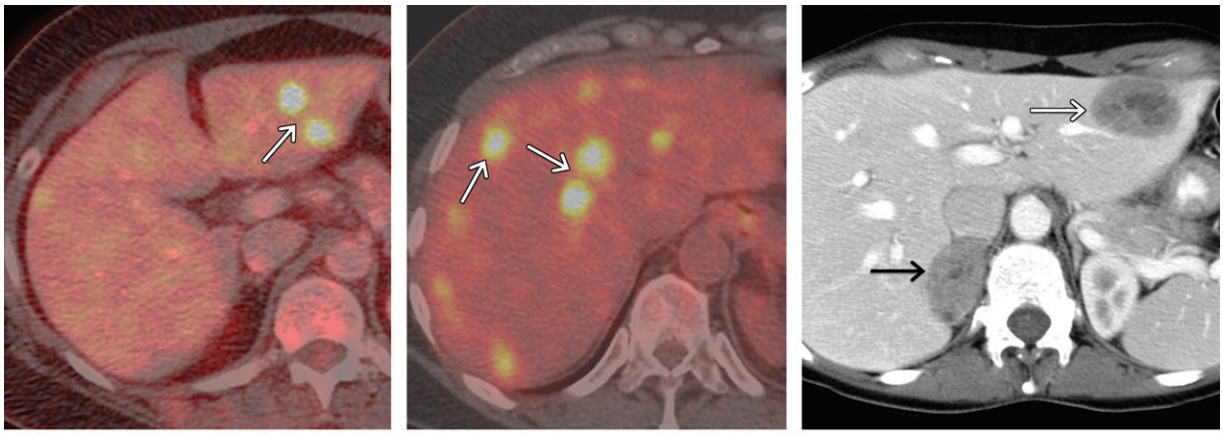
Patients with pN2a1 disease showed better survival than those with pN1b disease; however, this difference was not significant. The differences in survival were significant between the pN2a1 and pN2a2 groups ($P = .0007$ for R0, and $P = .0002$ for any R) and between the pN2a2 and pN2b groups ($P = .0028$ for R0, and $P = .0117$ for any R); however, there was no significant difference between pN1b and pN2a1. Thus, the prognosis for patients with pN2a1 disease without lymph node involvement in the N1 region (skip metastasis) was close to the prognosis for patients with pN1b disease without lymph node involvement in the N2 region.

The IASLC recommends that the IASLC lymph node map should be used to describe regional lymph node involvement and that the following information should be recorded: *(a)* lymph node station and/or location (N1, N2, or N3), *(b)* the number of lymph node stations involved (pN1a, pN2a, pN1b, or pN2b), and *(c)* the presence or absence of skip metastasis (pN2a1 or pN2a2).

M Classification

In TNM-7, the division of metastatic disease into M1a and M1b components for intrathoracic and extrathoracic metastases, respectively, represented one of the most important changes introduced. In the analysis of the new lung cancer database, the survival of patients with a single metastatic lesion in one extrathoracic organ (median survival, 6.3 months) was similar to that of patients with M1a disease (median survival, 11.5 months) but better than the survival of those with multiple metastatic lesions or metastases in multiple extrathoracic organs (median survival, 6.3 months). In TNM-8, intrathoracic metastasis retains the M1a designation (Fig 8), but the extrathoracic metastasis group has been split into M1b (single extrathoracic metastasis in a single distant organ) and M1c (multiple extrathoracic metastases in one or more distant organs) on the basis of differences in patient survival (6) (Fig 9).

In the results of prior work, investigators have suggested that there are important prognostic differences between patients with a single metastasis and those with multiple metastases or multiple sites of involvement, such as the brain, adrenal glands, or bone (15–21). However, a clear consensus on this topic has not been achieved owing to several limitations, including the retrospective nature of much of this work, the differences in the individual definitions of oligometastatic disease, and variations in local treatment plans. The IASLC recommends that radiologists should document the following features at staging examinations: *(a)* the number of metastatic lesions, *(b)* the diameter of individual metastatic lesions, and *(c)* the number of involved organs.



a. b. c.

Figure 9. Distant (extrathoracic) metastases in three different patients. **(a)** Axial fused image of combined fluorine 18 fluorodeoxyglucose (FDG) positron emission tomography (PET) and CT (PET/CT) of a 63-year-old man with NSCLC (NSCLC not shown) shows two foci of increased FDG uptake (arrow) in the left hepatic lobe that are concerning for metastases. The results of histopathologic examination of the specimen from ultrasound-guided biopsy helped confirm metastatic disease. **(b)** Axial fused FDG PET/CT image of a 58-year-old man with NSCLC (NSCLC not shown) shows numerous foci of increased FDG uptake (arrows) throughout the liver, findings consistent with metastases. **(c)** Axial contrast-enhanced multidetector CT image of a 42-year-old woman with NSCLC (NSCLC not shown) shows hepatic (white arrow) and right adrenal (black arrow) metastases. TNM-8 recognizes differences in survival on the basis of both the location and the number of metastases. Therefore, distant metastatic disease (formerly M1b) has been split into M1b (solitary metastasis in a single organ) and M1c (multiple metastases in a single organ or multiple organs).

Revisions to the Stage Classification

Numerous changes to individual T and M descriptors in TNM-8 have resulted in important modifications to the stage classification, including the editing of existing stage groups and the creation of several new stage groups (7) (Table 3). For example, the separation of T1 lung cancers into T1a, T1b, and T1c components on the basis of 1-cm and 2-cm thresholds has resulted in the creation of three new stages—IA1, IA2, and IA3, respectively—to describe these tumors in the absence of lymph node involvement and metastatic disease. In addition, a new stage group, stage IIIC, has been created to include locally advanced T3 and T4 lung cancers associated with N3 disease but without metastasis, which reflects their relatively worse prognosis compared with that for stage IIIB. Changes have been made to stage IV on the basis of the location and extent of metastatic disease. For instance, intrathoracic metastatic disease, including contralateral tumor nodules, pleural or pericardial spread, and myocardial or cardiac metastasis, remains classified as stage IVA; however, a single metastasis to a single organ (M1b disease) is now considered stage IVA, and multiple distant metastases in a single organ or multiple organs (M1c disease) are now considered stage IVB.

In addition to the creation of new stage groups, further modifications have been made to established stages. These changes are the result of one or more modifications to specific descriptors. For instance, all T1 subdivisions associated with N1 disease have shifted from stage IIA to IIB. Reassignment of diaphragmatic invasion to T4 is associated with various changes. For example, when present with N0 disease, diaphragmatic invasion shifts from stage IIB to IIIA. In some instances, changes to the T and M classifications may affect the stage group assigned to a specific case. For example, the reclassification of tumors measuring more than 5 cm from T2b to T3 means that these lesions are assigned to a higher stage group regardless of the N classification. When present with N0 and N1 disease, such lung cancers shift from stage IIA to IIB and from stage IIB to IIIA, respectively, because of the change in the T classification; when these tumors are associated with N2 or N3 disease, the stage group changes from stage IIIA to IIIB and from stage IIIB to IIIC, respectively.

Special Considerations

Lung Cancer with Multiple Sites of Pulmonary Involvement

The subcommittee of the IASLC Staging and Prognostic Factors Committee identified four distinct patterns of disease in cases of lung cancer characterized by multiple sites of pulmonary involvement: *(a)* multiple primary lung cancers, *(b)* lung cancers with separate tumor nodules, *(c)* multiple ground-glass/lepidic lesions, and *(d)* consolidation (8). Discussed herein are the criteria to categorize lung cancer with multiple pulmonary sites of involvement and the application of the staging system to each pattern (Table 5) (8).

Multiple Primary Lung Cancers.—Investigators have demonstrated that the demographics, clinical

Table 5: Lung Cancer with Multiple Pulmonary Sites of Involvement: Patterns of Disease and TNM Classification

Parameter	Multiple Primary Lung Cancers	Lung Cancer with Separate Tumor Nodule(s)	Multiple Ground-glass/ Lepidic Lesions	Consolidation
Description	Unrelated primary malignancies	Primary lung cancer with a related tumor nodule	Multiple separate tumors with some similarities	Single lung cancer with diffuse involvement of lungs
Imaging features	Two (or more) separate lesions with imaging characteristics of lung cancer	"Classic" appearance of lung cancer and separate solid nodule(s)	Multiple nonsolid and/or part-solid lesions	Multiple areas of consolidation and ground-glass opacities
Pathologic features	Different histologic type or different morphologic features	Distinct lesions with the same morphologic features	Adenocarcinomas with prominent lepidic component; typically, varying degrees of adenocarcinoma in situ, minimally invasive adenocarcinoma, and lepidic-predominant adenocarcinoma	Same histologic features; most are invasive mucinous adenocarcinoma
TNM classification	Separate clinical and pathologic staging for each lung cancer	Location of a separate tumor nodule relative to the primary lung cancer determines T3, T4, or M1a; single N and M for all lesions	T is based on highest T lesion with (#/m);* single N and M for all lesions	T is based on size and location: T3 if in a single lobe, and T4 or M1a if in different ipsilateral or contralateral lobes; single N and M for all lesions

Source.—Reference 8.
*Multifocal adenocarcinoma should be classified by the T category of the lesion with the highest-level T descriptor and by the number of lesions (#)—or simply "(m)" for multiple—indicated in parentheses.

outcomes, and recurrence patterns of patients with multiple primary lung cancers are similar to those of patients with single lung cancers when stratified on the basis of histologic subtype and overall clinical stage (8). The criteria developed to distinguish separate primary lung cancers from related tumor foci when two lesions are identified include both clinical and pathologic findings. Some cases may be identified on the basis of a few features, whereas others may incorporate several features. Factors for the radiologist to consider include the presence and completeness of prior imaging, current imaging, and histopathologic findings obtained at biopsy or surgical resection. The subcommittee recommends that the decision to classify two (or more) lung lesions as synchronous primary cancers or two foci of a single lung cancer should be based on multidisciplinary opinion that incorporates clinical, imaging, and histopathologic findings (8,22) (Fig 10).

The IASLC recommends that in the setting of two (or more) separate primary lung cancers, each malignancy should be staged separately within the TNM staging system, each being assigned distinct descriptors and a distinct overall stage group. This recommendation extends to both synchronous and metachronous lung cancers regardless of location, as well as synchronous primary lung cancers that are recognized clinically or those recognized only at histopathologic examination.

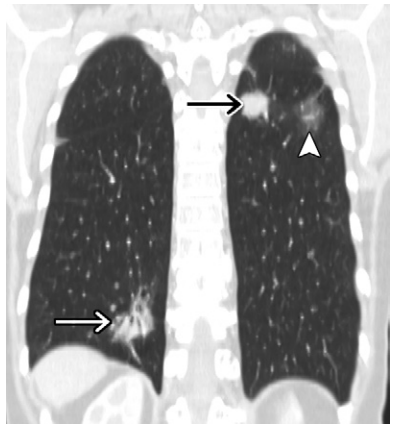
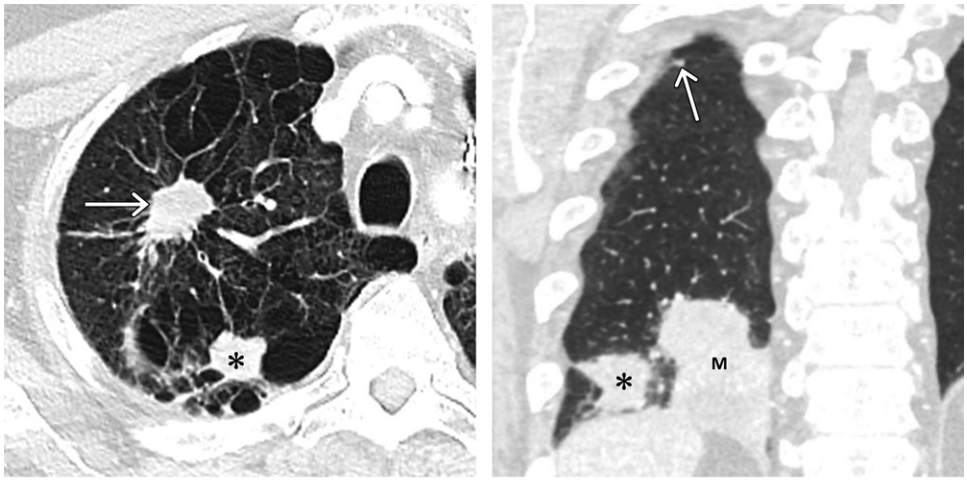
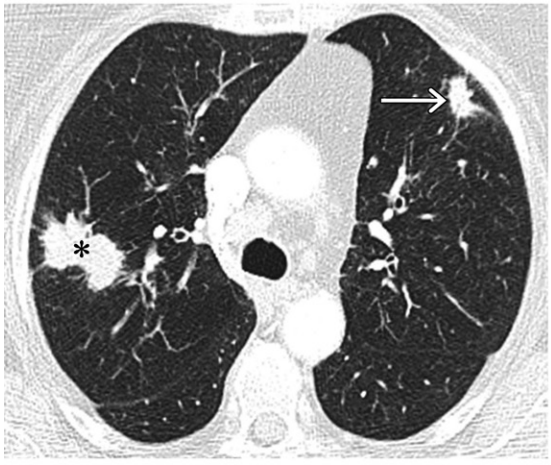


Figure 10. Multiple primary lung cancers. Coronal nonenhanced multidetector CT image of a 48-year-old woman with multiple primary lung cancers shows multiple lesions, including a part-solid nodule (white arrow) in the right lower lobe and a solid nodule (black arrow) and a nonsolid nodule (arrowhead) in the left upper lobe, all of which represent primary lung cancers with different histologic subtypes. In many cases, differentiation between different primary lung cancers and lung cancers with metastases can be difficult, and the IASLC recommends that patients with multiple lung lesions should be assessed by a multidisciplinary tumor board.

Figure 11. Lung cancers with separate tumor nodules in three different patients. **(a)** Axial contrast-enhanced multidetector CT image of a 73-year-old man with NSCLC shows a solid nodule with irregular margins (arrow) in the right upper lobe, which represents the primary lung cancer, as well as a separate tumor nodule (*) in the same lobe. These findings represent T3 disease. **(b)** Coronal contrast-enhanced multidetector CT image of the right hemithorax of a 66-year-old man with NSCLC shows a right lower lobe mass *(M)* and an adjacent tumor nodule (*), as well as a smaller tumor nodule (arrow) in the right upper lobe. These findings represent T4 disease. **(c)** Axial contrast-enhanced multidetector CT image of a 65-year-old woman with NSCLC shows an irregular nodule (*) in the right upper lobe representing the primary lung cancer, as well as a separate tumor nodule (arrow) in the left upper lobe. These findings represent M1a disease, and the findings at histopathologic examination of the specimen from biopsy of the left upper lobe nodule helped confirm metastatic disease.



a. b.



c.

Tumor Nodules.—Patients may present with a primary lung cancer and one or more separate tumor nodules, all of which correspond to the same histologic subtype of cancer. These separate nodules tend to behave similarly to solitary lung cancers, although the clinical outcomes are slightly worse and can be affected by the specific treatment plan (8,23). The criteria developed to categorize two lung lesions as a primary lung cancer and a separate tumor nodule include both clinical and histopathologic findings. In general, the presence of a lung cancer with a separate tumor nodule should be suspected when there is a lesion demonstrating the "classic" appearance of lung cancer (ie, a solid spiculated lesion) and when one (or more) solid separate lung nodules are identified. The lesions may be presumed to be separate (metastatic) tumor nodules through clinical staging or proved through pathologic staging after comprehensive histopathologic assessment.

The new lung cancer database included a cohort of patients (3.5%) with primary lung cancers and separate tumor nodules, most of which were single nodules of the same histologic subtype as the primary malignancy (7). Analysis of these cases demonstrated a progressive decrease in survival on the basis of increasing distance from the primary lung cancer (Fig 11). For instance, survival was better for patients with tumor nodules in the same lobe as the primary lung cancer, compared

with those with nodules in a different ipsilateral lobe or the contralateral lung. Among patients with pathologic staging, survival of patients with tumor nodules in the same lobe as the primary tumor (classified as T3 in TNM-7) was similar to that of patients with other T3 tumors. In addition, survival of patients with tumor nodules in the same lung as the primary tumor but in a different lobe (classified as T4 in TNM-7) was similar to survival of patients with other T4 tumors. Among patients with clinical staging, survival of patients with tumor nodules in the contralateral lung relative to the primary lung cancer was similar to that of patients with other M1a descriptors. However, it should be noted that the analysis suggested that survival was primarily affected by treatment, and there was no significant difference in overall survival by separate tumor nodule location among patients managed only surgically or among those managed nonsurgically (8,23). Patients who were treated surgically experienced better overall survival. Other factors such as tumor nodule size could not be assessed because of the small number of cases in the database. Thus, the classification scheme introduced in TNM-7 is maintained in TNM-8 and should be applied regardless of whether lymph node or extrathoracic metastases are present.

Multiple Ground-glass/Lepidic Lesions.—Lung cancers manifesting as multiple pulmonary lesions with ground-glass or lepidic features are associated with various demographics, excellent patient outcomes, and infrequent recurrences (8,24). At multidetector CT, these tumors appear as subsolid lesions, either nonsolid lesions (pure ground-glass lesions) or part-solid lesions (ground-glass and solid components). Pathologically, these lesions represent lepidic-predominant adenocarcinoma, minimally invasive adenocarcinoma, or adenocarcinoma in situ, with or without other subtypes of adenocarcinoma as lesser components (25). The solid and ground-glass components identified at multidetector CT correspond to invasive and lepidic patterns, respectively (8,26). Although these lesions are typically considered separate tumors with an in situ or invasive component that has arisen from a predominant noninvasive component, the findings from clonality studies in which these neoplasms are compared have produced conflicting results.

Compared with other patterns of lung cancer, adenocarcinomas manifesting as subsolid lesions tend to have a lower propensity for lymph node involvement or metastatic spread, have a greater propensity for developing additional subsolid lung cancers, and are more likely to behave in an indolent manner (25). Although the demographics are variable, affected patients are often women and nonsmokers (8,25). It should be noted that almost all cases of multifocal lung cancer represent adenocarcinoma.

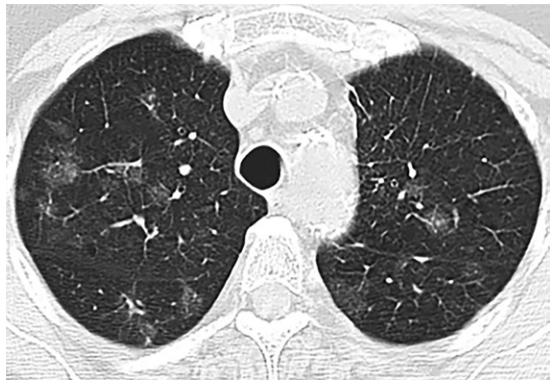
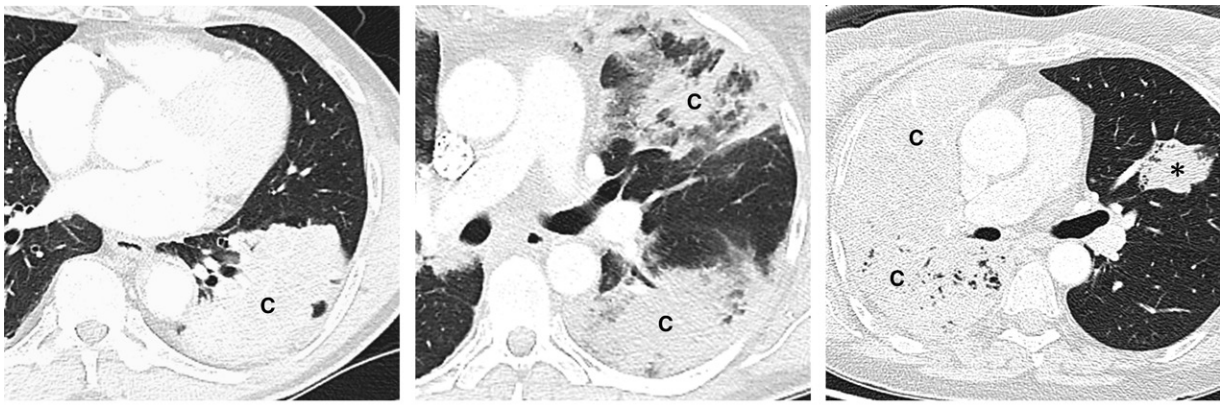


Figure 12. Multiple ground-glass/lepidic lesions (multifocal adenocarcinoma). Axial nonenhanced multidetector CT image of a 52-year-old woman with multifocal lung adenocarcinoma shows approximately 16 ground-glass nodules bilaterally, the largest of which is in the right upper lobe and measures approximately 2.2 cm in focal diameter. In the setting of multiple ground-glass lesions or lepidic tumors, the IASLC recommends use of the dominant lesion for T staging purposes. In this case, 2.2 cm corresponds to a T1c lesion, and the overall descriptor can be listed as either T1c(16) or T1c(m).

The criteria developed to categorize lesions as multiple ground-glass/lepidic lesions (multifocal adenocarcinoma) include both clinical and pathologic findings. The IASLC recommends that tumors should be classified as multifocal adenocarcinoma if a malignant subsolid nodule is present (regardless of whether it is suspected at clinical staging or histopathologically proven) and if other nodules with ground-glass features are identified (regardless of whether tissue sampling has been performed to evaluate the other nodules; if sampling has been performed, lesions may be classified as lepidic-predominant adenocarcinoma, minimally invasive adenocarcinoma, or adenocarcinoma in situ) (25). This definition also includes cases in which a subsolid lesion with a 50% or greater solid (invasive) component appears to have arisen from a ground-glass nodule (or a lepidic background) and other ground-glass nodules are present. The designation of multifocal lung adenocarcinoma should not be applied to patients with multiple ground-glass nodules likely representing benign or preneoplastic lesions such as atypical adenomatous hyperplasia.

Multifocal adenocarcinoma should be classified by the T category of the lesion with the highest-level T descriptor and by the number of lesions (#)—or simply "(m)" for multiple—indicated in parentheses (Fig 12). The lesion size is determined by the largest diameter of the solid component measured on multidetector CT images or the largest diameter of the invasive



a. b. c.

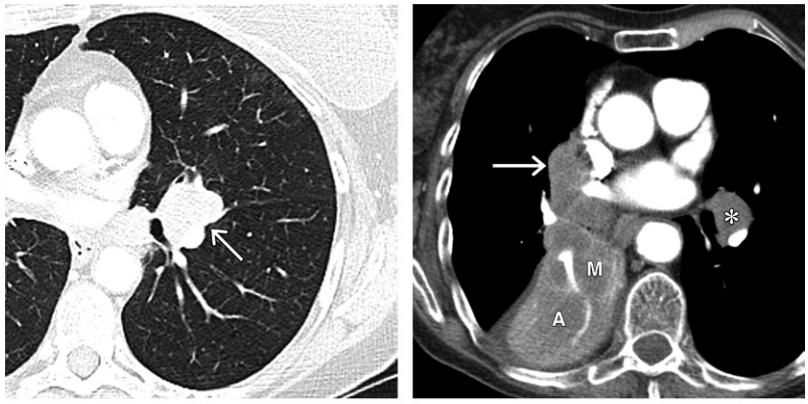
Figure 13. Lung cancer manifesting as consolidation in three different patients. **(a)** Axial contrast-enhanced multidetector CT image of the left hemithorax of a 76-year-old woman undergoing evaluation of nonresolving pneumonia shows consolidation *(C)* in the left lower lobe. The findings at histopathologic examination of the specimen from biopsy disclosed adenocarcinoma. Because this lesion is limited to the left lower lobe, it is designated as T3 disease. **(b)** Axial contrast-enhanced multidetector CT image of the left hemithorax of a 49-year-old woman with multifocal adenocarcinoma shows multiple areas of consolidation *(C)* in the left lung. Because these lesions are depicted in both lobes of the left lung, they are classified as T4 disease. **(c)** Axial contrast-enhanced multidetector CT image of a 53-year-old woman with multifocal adenocarcinoma shows consolidation *(C)* of the entire right lung and focal consolidation (*) in the left upper lobe. Because these areas of consolidation are depicted in both lungs, they are classified as M1a disease.

component at histologic examination. Adenocarcinoma in situ and minimally invasive adenocarcinoma should be designated as Tis and T1a(mi), respectively (26). The T(#/m) multifocal classification should be used regardless of whether these lesions are suspected solely on the basis of imaging or are pathologically proven and regardless of whether the lesions are in the same lobe or in different ipsilateral or contralateral lobes. The N and M categories that apply to all of the tumor foci collectively should be used.

Consolidation.—Another pattern of disease includes lung cancer manifesting as diffuse consolidation or a "pneumonic type" of lung adenocarcinoma that occurs without proximal bronchial obstruction (27–29). On multidetector CT images, these lesions appear as areas of consolidation and ground-glass opacities. The criteria developed to categorize lesions as pneumonic-type lung adenocarcinoma include both clinical and pathologic findings. These lesions manifest as a consolidative pattern on multidetector CT images, in the absence of an obstructed bronchus; that consolidative pattern may be confined to a particular region (segment or lobe), may affect multiple regions (appearing confluent or separate), or may involve the lung in a diffuse manner. These tumors manifest as a combination of areas of consolidation and ground-glass opacities with ill-defined margins owing to the infiltrative nature. Air bronchograms are frequently identified. Most pneumonic-type lung cancers are invasive mucinous adenocarcinomas; the rest are mixed or nonmucinous adenocarcinomas (8,25). Although these patients may have extensive pulmonary involvement, lymph node involvement and metastatic disease are uncommon at presentation (30–32). Progression is typically slow, but the overall survival is worse compared with that of patients with multifocal ground-glass/lepidic lesions.

The T classification depends on factors such as lesion size and the number of lobes involved. When a single area of tumor involvement is identified, the T classification is determined by the size of the lesion, with N and M classifications determined by lymph node involvement and metastatic disease (5,7). In TNM-8, multiple sites of lung tumor involvement are designated as T3 if they are confined to one lobe, T4 if they affect different lobes in the same lung, and M1a if they involve both lungs (Fig 13). When tumor is present within both lungs, the T classification is based on the appropriate T category for the lung with the greatest extent of tumor involvement. For tumor that is confined to a single lobe but is difficult to measure, the T3 descriptor should be assigned. The T4 descriptor should be assigned to disease in which there is extension of tumor into an adjacent lobe or there is a discrete separate area of involvement of an adjacent lobe. The N and M categories that apply to all of the tumor foci collectively should be used. This classification scheme should be used regardless of whether these lesions are suspected at imaging or pathologically proven, and a detailed histologic assessment is not required for pneumonic-type lung cancer.

The IASLC also recommends that this scheme should be used for the staging of miliary forms of adenocarcinoma, a pattern of lung disease characterized by numerous small pulmonary nodules scattered throughout the lung. In contrast to the



a. b.

Figure 14. SCLC in two different patients. **(a)** Axial contrast-enhanced multidetector CT image of the left hemithorax of a 67-year-old woman with SCLC shows a solid nodule in the left upper lobe (arrow) along the left interlobar fissure. The findings from histopathologic examination of the specimen from CT-guided core needle biopsy disclosed SCLC. **(b)** Axial contrast-enhanced multidetector CT image of a 61-year-old woman with SCLC shows a right infrahilar mass *(M)* resulting in complete atelectasis *(A)* of the right lower lobe, as well as ipsilateral mediastinal lymphadenopathy (arrow) and contralateral hilar lymphadenopathy (*). Staging of SCLC with the TNM system was introduced in TNM-7, and this recommendation is carried over into TNM-8. The TNM descriptors and overall stage for this patient were T2bN3M0 and stage IIIB, respectively.

diffuse form, which could potentially be measured, miliary disease is inherently difficult to measure, and a single lobe should be classified as T3 without regard to size.

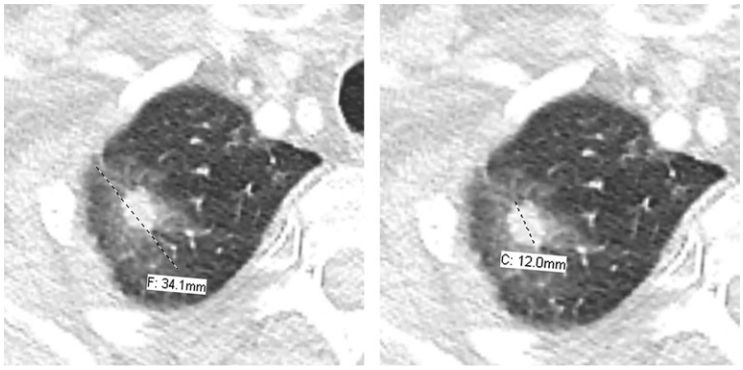
Staging of SCLC

The IASLC first recommended that the TNM staging system should be used to stage SCLC in 2009 with the publication of TNM-7. Before that time, early staging systems developed by the Veterans Administration Lung Study Group were used to divide SCLCs into two subgroups, limited-stage SCLC and extensive-stage SCLC, on the basis of the extent of disease and the feasibility of treatment with a single radiation portal. For example, limited-stage SCLC represents disease confined to one hemithorax, which may include local extension and ipsilateral or supraclavicular lymphadenopathy if disease can be included in a single radiation portal. Extensive-stage SCLC includes all other cases. In TNM-7, stages I to III correspond to limited-stage SCLC, and stage IV corresponds to extensive-stage SCLC (33). The TNM staging system has been shown to better differentiate stage-specific survival compared with the Veterans Administration Lung Study Group system, and the primary benefit of the TNM system is the identification of patients who may benefit from surgical resection (11,12).

The prognostic value of clinical and pathologic TNM staging in patients with SCLC was confirmed in the analysis of the new database, and the IASLC recommends its use for staging of these patients (Fig 14). Evaluation of patients with clinically staged M1b disease showed no significant survival difference between patients with either a single site or multiple sites of metastatic disease. However, a difference in survival between patients with single-site metastasis involving the brain and those with other sites of single or multiple-site metastases was identified at 12 months (36% vs 23% and 20%, respectively) (34). In addition, improved survival was seen in patients with a single site of metastasis and no pleural effusion, compared with patients who had either pleural effusions or multiple metastatic sites or both. The IASLC recommends that the subdivision of M descriptors into M1a, M1b, and M1c for NSCLC should also be used for SCLC. In addition, to inform future revisions of the TNM staging system, it is recommended that radiologists should record the following information regarding SCLC: *(a)* the number of extrathoracic metastatic sites, *(b)* the number of organs involved, *(c)* the diameter of individual metastatic sites, *(d)* the types of examinations and studies used for staging, and *(e)* whether patients with brain metastases are symptomatic or asymptomatic (34).

Tumor Measurement

The IASLC recommends that all tumors should be measured and the measurement reported in centimeters with millimeter increments. At multidetector CT, solid and nonsolid lesions should be measured on the image demonstrating the greatest average tumor dimension, regardless of the plane (axial, sagittal, or coronal). Part-solid lesions should be measured on the image or



a. **b.**

Figure 15. Measurement of part-solid lesions. Axial contrast-enhanced multidetector CT images of the right hemithorax of a 78-year-old woman show a part-solid nodule in the right upper lobe compatible with biopsy-proven invasive adenocarcinoma. **(a)** Image shows measurement of the entire lesion; the focal diameter *(F)* is 34.1 mm (dashed line). **(b)** Image shows measurement of the diameter of the solid component (C = 12.0 mm; dashed line). The IASLC recommends that the measurement of the solid component of part-solid lesions, representing the invasive component of the tumor, should be used to define its T classification. Investigators have demonstrated that this measurement better predicts prognosis than the overall tumor size in lepidic-predominant adenocarcinomas.

images demonstrating the largest average tumor diameter and the largest diameter of the solid component. Although long-axis and short-axis measurements may be recorded for all lesions, only the longest diameter for solid and nonsolid lesions and the longest diameter of the solid component for part-solid lesions should be used for staging purposes (5,8,26,35).

In the findings of several studies investigating the accuracy of lesion measurement with CT section thickness, investigators have demonstrated that lower section thickness resulted in less variability in measurement (36–39). Specifically, 1-mm sections result in the least amount of measurement variability, especially for lesions smaller than 10 mm and for those that demonstrate spiculation rather than smooth margins (36). In addition to minimizing partial volume averaging, thin sections allow optimal evaluation of morphologic features such as density, shape, and margin because of the enhanced spatial resolution.

The findings from studies evaluating the accuracy of lung nodule measurements obtained with different window settings have shown conflicting results. Some investigators suggest that mediastinal settings are more accurate, and others have shown greater accuracy with the use of lung window settings (26,40,41). In the results of several recent studies evaluating minimally invasive adenocarcinoma and small lung adenocarcinomas, investigators have suggested that measurements obtained by using lung windows are more similar to pathologic measurements and that the use of mediastinal windows may underestimate the size of the invasive component (42–44). Therefore, the IASLC recommends that lung or intermediate window settings should be used to detect and measure the solid components of subsolid nodules (Fig 15).

Several approaches have been proposed for the evaluation of part-solid lesions with several solid components. One proposal is similar to that for microinvasive breast cancer, in which the single largest focus of invasion is measured, and the other solid components are cataloged but not measured (45). Kadota et al (46) proposed a different approach for characterizing the invasive component of part-solid adenocarcinomas on histopathologic slides, in which all invasive components were measured and the sum expressed as a percentage of the overall tumor size. However, this approach has not been evaluated in the context of multidetector CT. Therefore, the IASLC recommends that the long-axis measurement of the largest solid component should be identified. If this measurement exceeds 5 mm, then invasion is likely.

Limitations

Although TNM-8 represents continued advancement from prior staging systems, several limitations persist. Although the database used for the updated staging project is large and includes lung cancer cases from around the world, it can be considered a convenience sample of available data (47). Specifically, geographic regions other than Europe and Asia and nonsurgically managed patients are underrepresented in the database (47). However, the results of both internal and external validation demonstrated the transportability of the data. For instance, TNM-8 has been externally validated against

the National Cancer Database in the United States, a database that principally includes nonsurgically managed patients.

Finally, although differences in survival have been demonstrated across the updated descriptors and stage groups, it is important to remember that many other elements are ultimately involved with prognosis, including patient-related factors (performance status, age, comorbidities), tumor-related factors (histologic subtype, grade), environment-related factors (access to care, quality of care), and treatment-related factors (treatment regimen, response to therapy) (47,48).

Conclusion

Revisions to the TNM staging system have been made on the basis of important differences in patient survival resulting from detailed analyses of a new large lung cancer database. Key changes include further modifications to the T and M classifications on the basis of 1-cm thresholds for the primary tumor; grouping of tumors resulting in atelectasis or pneumonitis of a lobe or an entire lung; grouping of tumors involving a main bronchus; reassignment of diaphragmatic invasion; elimination of mediastinal pleural invasion; and further subdivision of metastatic disease into descriptors that are based on the number and sites of metastases. These changes have resulted in modifications to stage groups, with new groups created and others modified. In addition, TNM-8 introduces new recommendations regarding the staging of lung cancers with multiple pulmonary sites of involvement and new guidelines for tumor measurement. Understanding the key revisions introduced in TNM-8 will allow radiologists to accurately stage lung cancer and optimize patient management.

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References

1. American Cancer Society. Cancer facts & figures 2017. American Cancer Society website. https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2017.html. Accessed January 30, 2017.
2. Goldstraw P, Crowley J, Chansky K, et al. The IASLC Lung Cancer Staging Project: proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM classification of malignant tumours. J Thorac Oncol 2007;2(8):706–714.
3. Groome PA, Bolejack V, Crowley JJ, et al. The IASLC Lung Cancer Staging Project: validation of the proposals for revision of the T, N, and M descriptors and consequent stage groupings in the forthcoming (seventh) edition of the TNM classification of malignant tumours. J Thorac Oncol 2007;2(8):694–705.
4. Rami-Porta R, Bolejack V, Giroux DJ, et al. The IASLC Lung Cancer Staging Project: the new database to inform the eighth edition of the TNM classification of lung cancer. J Thorac Oncol 2014;9(11):1618–1624.
5. Rami-Porta R, Bolejack V, Crowley J, 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 2015;10(7):990–1003.
6. Eberhardt WE, Mitchell A, Crowley J, et al. 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. J Thorac Oncol 2015;10(11):1515–1522.
7. Goldstraw P, Chansky K, Crowley J, et al. The IASLC Lung Cancer Staging Project: proposals for revision of the TNM stage groupings in the forthcoming (eighth) edition of the TNM classification for lung cancer. J Thorac Oncol 2016;11(1):39–51.
8. Detterbeck FC, Nicholson AG, Franklin WA, 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 eighth edition of the TNM classification. J Thorac Oncol 2016;11(5):639–650.
9. Fonseca A, Detterbeck FC. How many names for a rose: inconsistent classification of multiple foci of lung cancer due to ambiguous rules. Lung Cancer 2014;85(1):7–11.
10. Homer RJ. Pathologists' staging of multiple foci of lung cancer: poor concordance in absence of dramatic histologic or molecular differences. Am J Clin Pathol 2015;143(5):701–706.
11. Ignatius Ou SH, Zell JA. The applicability of the proposed IASLC staging revisions to small cell lung cancer (SCLC) with comparison to the current UICC 6th TNM Edition. J Thorac Oncol 2009;4(3):300–310.
12. Kalemkerian GP, Akerley W, Bogner P, et al. Small cell lung cancer. J Natl Compr Canc Netw 2013;11(1):78–98.
13. Rusch VW, Asamura H, Watanabe H, et al. The IASLC Lung Cancer Staging Project: a proposal for a new international lymph node map in the forthcoming seventh edition of the TNM classification for lung cancer. J Thorac Oncol 2009;4(5):568–577.
14. Asamura H, Chansky K, Crowley J, et al. The International Association for the Study of Lung Cancer Lung Cancer Staging Project: proposals for the revision of the N descriptors in the forthcoming 8th edition of the TNM classification for lung cancer. J Thorac Oncol 2015;10(12):1675–1684.
15. Griffioen GH, Toguri D, Dahele M, et al. Radical treatment of synchronous oligometastatic non-small cell lung carcinoma (NSCLC): patient outcomes and prognostic factors. Lung Cancer 2013;82(1):95–102.
16. Gray PJ, Mak RH, Yeap BY, et al. Aggressive therapy for patients with non-small cell lung carcinoma and synchronous brain-only oligometastatic disease is associated with long-term survival. Lung Cancer 2014;85(2):239–244.
17. Tönnies M, Pfannschmidt J, Bauer TT, Kollmeier J, Tönnies S, Kaiser D. Metastasectomy for synchronous solitary non-small cell lung cancer metastases. Ann Thorac Surg 2014;98(1):249–256.
18. Congedo MT, Cesario A, Lococo F, et al. Surgery for oligometastatic non–small cell lung cancer: long-term results from a single center experience. J Thorac Cardiovasc Surg 2012;144(2):444–452.
19. Bonnette P, Puyo P, Gabriel C, et al. Surgical management of non-small cell lung cancer with synchronous brain metastases. Chest 2001;119(5):1469–1475.
20. Tanvetyanon T, Robinson LA, Schell MJ, et al. Outcomes of adrenalectomy for isolated synchronous versus metachronous adrenal metastases in non–small-cell lung cancer: a systematic review and pooled analysis. J Clin Oncol 2008;26(7):1142–1147.
21. De Ruysscher D, Wanders R, van Baardwijk A, et al. Radical treatment of non–small-cell lung cancer patients with synchronous oligometastases: long-term results of a prospective phase II trial (Nct01282450). J Thorac Oncol 2012;7(10):1547–1555.
22. Detterbeck FC, Franklin WA, Nicholson AG, 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 eighth edition of the TNM classification for lung cancer. J Thorac Oncol 2016;11(5):651–665.
23. Detterbeck FC, Bolejack V, Arenberg DA, et al. The IASLC Lung Cancer Staging Project: background data and proposals for the classification of lung cancer with separate tumor nodules in the forthcoming eighth edition of the TNM classification for lung cancer. J Thorac Oncol 2016;11(5):681–692.
24. Detterbeck FC, Marom EM, Arenberg DA, et al. The IASLC Lung Cancer Staging Project: background data and proposals for the application of TNM staging rules to lung cancer presenting as multiple nodules with ground glass or lepidic features or a pneumonic type of involvement in the forthcoming eighth edition of the TNM classification. J Thorac Oncol 2016;11(5):666–680.
25. Travis WD, Brambilla E, Noguchi M, et al. International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society international multidisciplinary classification of lung adenocarcinoma. J Thorac Oncol 2011;6(2):244–285.
26. Travis WD, Asamura H, Bankier AA, 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 eighth edition of the TNM classification of lung cancer. J Thorac Oncol 2016;11(8):1204–1223.
27. Wislez M, Massiani MA, Milleron B, et al. Clinical characteristics of pneumonic-type adenocarcinoma of the lung. Chest 2003;123(6):1868–1877.
28. Akira M, Atagi S, Kawahara M, Iuchi K, Johkoh T. High-resolution CT findings of diffuse bronchioloalveolar carcinoma in 38 patients. AJR Am J Roentgenol 1999;173(6):1623–1629.
29. Battafarano RJ, Meyers BF, Guthrie TJ, Cooper JD, Patterson GA. Surgical resection of multifocal non-small cell lung cancer is associated with prolonged survival. Ann Thorac Surg 2002;74(4):988–993; discussion 993–994.
30. Barlesi F, Doddoli C, Gimenez C, et al. Bronchioloalveolar carcinoma: myths and realities in the surgical management. Eur J Cardiothorac Surg 2003;24(1):159–164.
31. de Perrot M, Chernenko S, Waddell TK, et al. Role of lung transplantation in the treatment of bronchogenic carcinomas for patients with end-stage pulmonary disease. J Clin Oncol 2004;22(21):4351–4356.
32. Ahmad U, Wang Z, Bryant AS, et al. Outcomes for lung transplantation for lung cancer in the United Network for Organ Sharing Registry. Ann Thorac Surg 2012;94(3):935–940; discussion 940–941.
33. Shepherd FA, Crowley J, Van Houtte P, et al. The International Association for the Study of Lung Cancer Lung Cancer Staging Project: proposals regarding the clinical staging of small cell lung cancer in the forthcoming (seventh) edition of the tumor, node, metastasis classification for lung cancer. J Thorac Oncol 2007;2(12):1067–1077.
34. Nicholson AG, Chansky K, Crowley J, et al. The International Association for the Study of Lung Cancer Lung Cancer Staging Project: proposals for the revision of the clinical and pathologic staging of small cell lung cancer in the forthcoming eighth edition of the TNM classification for lung cancer. J Thorac Oncol 2016;11(3):300–311.
35. de Groot PM, Carter BW, Betancourt Cuellar SL, Erasmus JJ. Staging of lung cancer. Clin Chest Med 2015;36(2):179–196, vii–viii.
36. Petrou M, Quint LE, Nan B, Baker LH. Pulmonary nodule volumetric measurement variability as a function of CT slice thickness and nodule morphology. AJR Am J Roentgenol 2007;188(2):306–312.
37. Goo JM, Tongdee T, Tongdee R, Yeo K, Hildebolt CF, Bae KT. Volumetric measurement of synthetic lung nodules with multi–detector row CT: effect of various image reconstruction parameters and segmentation thresholds on measurement accuracy. Radiology 2005;235(3):850–856.
38. Ravenel JG, Leue WM, Nietert PJ, Miller JV, Taylor KK, Silvestri GA. Pulmonary nodule volume: effects of reconstruction parameters on automated measurements—a phantom study. Radiology 2008;247(2):400–408.
39. Wang Y, de Bock GH, van Klaveren RJ, et al. Volumetric measurement of pulmonary nodules at low-dose chest CT: effect of reconstruction setting on measurement variability. Eur Radiol 2010;20(5):1180–1187.
40. Revel MP, Bissery A, Bienvenu M, Aycard L, Lefort C, Frija G. Are two-dimensional CT measurements of small noncalcified pulmonary nodules reliable? Radiology 2004;231(2):453–458.
41. Naidich DP, Bankier AA, MacMahon H, et al. Recommendations for the management of subsolid pulmonary nodules detected at CT: a statement from the Fleischner Society. Radiology 2013;266(1):304–317.
42. Son JY, Lee HY, Lee KS, et al. Quantitative CT analysis of pulmonary ground-glass opacity nodules for the distinction of invasive adenocarcinoma from pre-invasive or minimally invasive adenocarcinoma. PLoS One 2014;9(8):e104066. http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0104066. Published August 7, 2014.
43. Lee KH, Goo JM, Park SJ, et al. Correlation between the size of the solid component on thin-section CT and the invasive component on pathology in small lung adenocarcinomas manifesting as ground-glass nodules. J Thorac Oncol 2014;9(1):74–82.
44. Lee SM, Goo JM, Lee KH, Chung DH, Koh J, Park CM. CT findings of minimally invasive adenocarcinoma (MIA) of the lung and comparison of solid portion measurement methods at CT in 52 patients. Eur Radiol 2015;25(8):2318–2325.
45. Hayes DF, Allred C, Anderson BO, et al. In: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A, eds. AJCC cancer staging manual. 7th ed. New York, NY: Springer, 2010; 345–377.
46. Kadota K, Villena-Vargas J, Yoshizawa A, et al. Prognostic significance of adenocarcinoma in situ, minimally invasive adenocarcinoma, and nonmucinous lepidic predominant invasive adenocarcinoma of the lung in patients with stage I disease. Am J Surg Pathol 2014;38(4):448–460.
47. Detterbeck FC, Boffa DJ, Kim AW, Tanoue LT. The eighth edition lung cancer stage classification. Chest 2017;151(1):193–203.
48. Detterbeck F. Stage classification and prediction of prognosis: difference between accountants and speculators. J Thorac Oncol 2013;8(7):820–822.