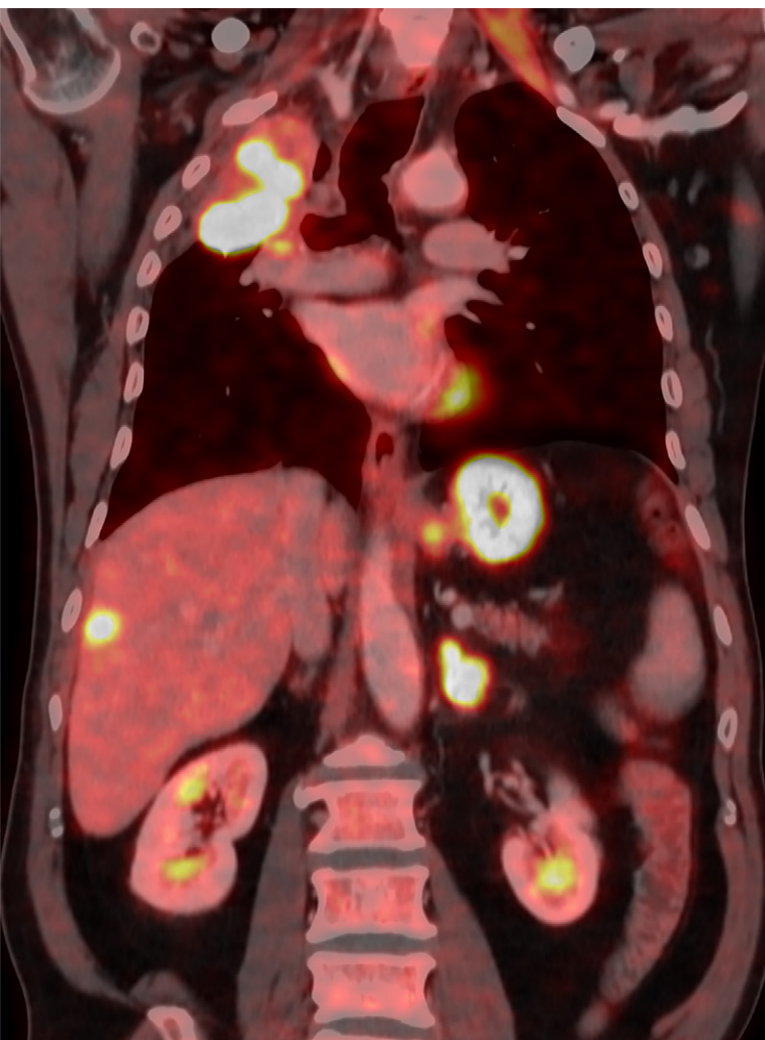


# Proposed Ninth Edition TNM Staging System for Lung Cancer: Guide for Radiologists

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Lung cancer continues to be the primary cause of cancer-related deaths globally. Precise staging is imperative for the development of successful treatment approaches and improvement of patient outcomes. Traditionally, lung cancer staging has depended on the TNM staging system, and the International Association for the Study of Lung Cancer (IASLC) has recently recommended modifications. The updated classification for the ninth edition of the TNM staging system (TNM-9), slated to take effect in January 2025, is derived from a thorough analysis of a newly established large international database of lung cancer cases compiled by the IASLC. Proposed changes in TNM-9 include the following: (a) The mediastinal nodal category (N2) was split into single-station (N2a) and multiple-station (N2b) subcategories, and (b) multiple extrathoracic metastatic lesions (M1c) were split into single organ system (M1c1) and multiple organ systems (M1c2) subcategories. Considering these revisions, adjustments have been made to the established stage groups. In terms of pathologic nodal staging, patients in the post-neoadjuvant ypN category demonstrated worse prognosis than those in the similar non-neoadjuvant pN category. Understanding the fundamental changes introduced in TNM-9 enables radiologists to precisely determine the clinical stage of lung cancer and enhance therapeutic approaches.

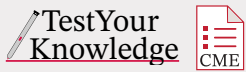
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## Introduction

Lung cancer is the leading cause of cancer-related deaths worldwide, accounting for the highest mortality rates among both men and women (1). How disease in patients with newly diagnosed lung cancer is treated depends on staging. Stage classification is the cornerstone to optimize patient stratification and predict survival. However, it is only one of the prognostic factors considered when selecting a therapeutic approach. Other factors such as performance status, medical comorbidities, tumor histologic features, and molecular analysis also affect prognosis and determine therapy. By stratify-

ing patients into similar universal groups, stage classification provides a consistent description of the anatomic extent of the tumor in a patient cohort, which allows comparison of one treatment to another. Stage classification relies on an agreed-on nomenclature of the anatomic extent of the cancer. Clear and consistent communication is vital for selecting a treatment strategy, especially in multidisciplinary discussions, in alignment with clinical trial data to predict outcomes after treatment (2).

The staging system describes the extent of the primary tumor as T, regional lymph node involvement as N, and distant



**RadioGraphics 2024; 44(12):e240057**  
<https://doi.org/10.1148/rg.240057>

**Content Code:** CH

**Abbreviations:** CRAB = Cancer Research and Biostatistics, FDG = fluorine 18 fluorodeoxyglucose, IASLC = International Association for the Study of Lung Cancer, NSCLC = non-small-cell lung cancer, TNM-9 = TNM staging system ninth edition

## TEACHING POINTS

- The N2 category includes metastasis in ipsilateral mediastinal and/or subcarinal lymph nodes. In TNM-9, the N2 category is split into single-station (N2a) and multiple-station (N2b) involvement.
- This new N2 subset is based on the number of IASLC lymph node stations and not the number of lymph nodes because node enumeration is not reliable.
- For patients who have undergone neoadjuvant therapy, the prognosis for each ypN category is worse compared with a similar pathologic N category in patients who did not undergo neoadjuvant therapy.
- In TNM-9, the multiple extrathoracic metastatic lesions (M1c) are split into single organ system (M1c1) and multiple organ systems (M1c2) subcategories.
- It is important for radiologists to identify multifocal lung adenocarcinoma with ground-glass features because the staging and patient treatment are different from those for pulmonary metastatic disease.

metastatic disease as M categories. A guiding principle is that any revision of this system should not only be based on statistically significant outcomes data but also have clinical significance while not making the TNM system overly complicated—all toward the goal that the system could be easily applied globally. The system should be consistently applied to both clinical staging and pathologic staging. Clinical staging, designated by the prefix “c” (c-stage or cTNM), involves all available information that reflects the anatomic extent of a tumor before the initiation of treatment. Clinical staging relies heavily on imaging, but it is not limited to imaging studies. Other data in clinical staging include patients’ symptoms and results of physical examination, endoscopy, biopsies, and surgical exploration. Because imaging is the main component of clinical staging, familiarity with the nuances and clinical implications of the updates in staging is essential to provide detailed yet succinct effective interpretations. Pathologic staging, designated by the prefix “p” (p-stage or pTNM), includes all available information from a surgical resection (or attempted resection), supplemented with all available information from clinical staging.

Updates in TNM staging are necessary for optimizing tailored patient therapy, particularly in patients with lung cancer, because the field has rapidly evolved with respect to detection, the use of minimally invasive surgical techniques, high-precision-dose radiation therapy, and the emergence of targeted therapy and immunotherapy (3).

The ninth edition of the TNM staging system (TNM-9), slated to take effect in January 2025, is based on the International Association for the Study of Lung Cancer (IASLC) database and is formally defined by the Union for International

Cancer Control and the American Joint Committee on Cancer. Although IASLC’s ninth edition database has a similar number of evaluable lung cancer cases as the seventh and eighth editions (TNM-7 and TNM-8), with more than 100 000 patients (4), the collected data have much greater granularity to address the limitations of TNM-8, which include the lack of quantification of nodal metastatic burden, lack of granularity within the M1c category, and exclusion of patients who have undergone neoadjuvant therapy from staging evaluation (5). *Neoadjuvant* refers to treatment given as a first step to shrink the tumor before the main treatment, usually surgery. In terms of the staging assessments, the prefix “y” indicates restaging and pertains to patients who have received neoadjuvant therapy. Analysis of this new database showed significant differences in survival between patients within subgroups of the N2 and M1c categories and a worse prognosis for patients with ypN disease (pathologic N after neoadjuvant therapy) than for those with pN (pathologic N without neoadjuvant therapy) disease (6). General recommendations for modification of these descriptors and overall stage groups have been published (3), with more supporting literature yet to be published. The aim of this article is to review the proposals for TNM-9 staging for lung cancer with an emphasis on clinical staging as it pertains to imaging interpretation.

## T Descriptor: Unchanged

The T descriptor delineates distinct attributes of the primary neoplasm, encompassing factors such as tumor measurements and the extent of local invasion (Table 1). Because TNM-8 introduced profound changes to the T descriptor, the goal of the analysis of TNM-9 revisions was to validate the T descriptors of TNM-8 and assess whether further changes were necessary. Analysis from the new database supported no change for T descriptors from TNM-8 (7). Because a major part of T staging relies on tumor size, and each 1-cm increment from 1 cm to 5 cm worsens the prognosis, care should be taken to optimize the acquisition of CT images and to perform accurate tumor measurements. For CT evaluation of the T descriptor, lung window settings with a sharp filter are used and images should be contiguous with a section thickness of 1 mm or less (8). This decreases partial averaging and facilitates accurate measurements and characterization of nodule type, whether solid, part-solid, or pure ground glass. For staging purposes, the long-axis diameter of the solid primary tumor is recorded, whether in the axial, sagittal, or coronal planes. For staging of the part-solid primary tumor, the clinical T descriptor is determined by the longest diameter of the solid component because it correlates better with the invasive component of the tumor at pathologic evaluation. In addition, recording the overall diameter (including the ground-glass component) will enable future evaluation to assess if this parameter affects prognosis (8).

T1 tumors are 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (ie, not in the main bronchus). T1 tumors are categorized into three subgroups based on 1-cm increments: T1a nodules are 1 cm or smaller, T1b tumors measure more than 1 cm but less than or equal to 2 cm, and T1c lesions measure more than 2 cm but less

Table 1: Ninth Edition TNM Staging System: Primary Tumor Characteristics

Classification	Description
Tx	Tumor in sputum and/or bronchial washing but not assessed with imaging or bronchoscopy
T0	No evidence of tumor
Tis	Carcinoma in situ (squamous or adenocarcinoma)
T1	Tumor ≤3 cm, surrounded by lung and/or visceral pleura, not involving main bronchus
T1a (mi)	Minimally invasive adenocarcinoma
T1a	Tumor ≤1 cm or superficial spreading tumor in the central airways (tumor of any size but with its invasive component confined to the tracheal or bronchial wall)
T1b	Tumor >1 cm to ≤2 cm
T1c	Tumor >2 cm to ≤3 cm
T2	Tumor >3 cm to ≤5 cm or involvement of the main bronchus without the carina, regardless of distance from the carina or invasion of visceral pleural or atelectasis or postobstructive pneumonitis extending to the hilum
T2a	Tumor >3 cm to ≤4 cm
T2b	Tumor >4 cm to ≤5 cm
T3	Tumor >5 cm to ≤7 cm or tumor of any size that involves the chest wall, the pericardium, the phrenic nerve, or one or more satellite tumor nodules in the same lobe
T4	Tumor >7 cm or any tumor with invasion of mediastinum, diaphragm, heart, great vessels, recurrent laryngeal nerve, carina, trachea, esophagus, spine, or brachial plexus or separate tumor nodule(s) in different lobe of ipsilateral lung

Source.—Reference 6.

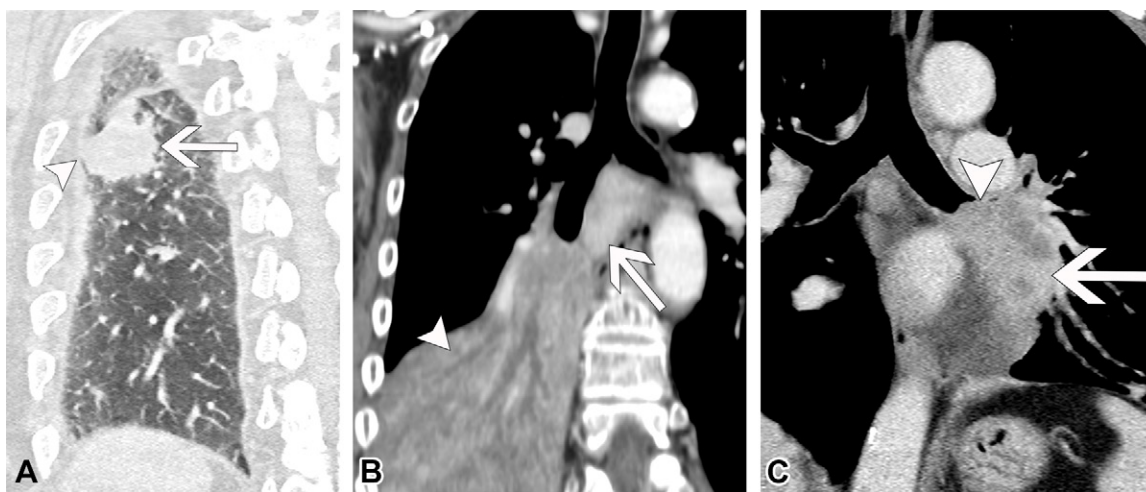


**Figure 1.** T1 lung cancer in three patients. **(A)** Axial unenhanced chest CT image (lung window) in a 76-year-old man shows a right-upper-lobe part-solid adenocarcinoma (arrows). The overall diameter (between arrows) is 1.5 cm, with the solid component (arrowhead) measuring only 0.4 cm, consistent with a clinical T descriptor of T1(mi). In part-solid nodules, because the solid component better correlates with the invasive carcinoma, the solid component is used for the staging whereas the overall diameter is only recorded. **(B)** Axial unenhanced chest CT image (lung window) in a 74-year-old woman shows a part-solid adenocarcinoma (arrows) in the right lower lobe, with an overall diameter of 4.5 cm (between arrows) and a solid component (arrowhead) measuring 1.5 cm, compatible with a clinical T descriptor of T1b. **(C)** Coronal reconstruction image of an unenhanced chest CT scan (lung window) in a 61-year-old woman shows a right-upper-lobe solid adenocarcinoma (arrow) measuring 2.4 cm, compatible with stage T1c.

than or equal to 3 cm (Fig1). The uncommon superficial spreading tumor 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 (9). Carcinoma in situ, a histologic descriptor, is classified as Tis, which applies to both squamous carcinoma (Tis[SCIS]) and adenocarcinoma (Tis[AIS]). Tis usually appears at CT as pure ground-glass opacity measuring 3 cm or less (8). Minimally invasive adenocarcinomas are designated as T1 (mi) if the invasive component is 5 mm or less and the noninvasive lepidic component is 3 cm or less (10). At CT,

T1 (mi) tumors typically appear as part-solid nodules with a total size of 3 cm or less and a solid component of 5 mm or less, but minimally invasive adenocarcinomas may be found histologically in pure ground-glass nodules and even, in rare cases, in solid nodules (8). Although the solid component observed on CT scans correlates with the invasive nature of minimally invasive adenocarcinoma, CT should not be viewed as a replacement for histologic evaluation for the invasive component during pathologic examination, because pure ground-glass nodules are sometimes found to be fully invasive (11).





**Figure 2.** T2 lung cancer in three patients. **(A)** Coronal reconstruction image from an unenhanced chest CT scan (lung window) in a 69-year-old man with non-small-cell lung cancer (NSCLC) shows a mass (arrow) in the superior segment of the right lower lobe that measured 3.5 cm and involved the visceral pleura (arrowhead) and was histologically confirmed after surgery, compatible with stage T2a. **(B)** Coronal reconstruction image from a contrast-enhanced chest CT scan (soft-tissue window) in a 74-year-old woman with NSCLC shows a nonmeasurable right lung central mass (arrow) involving the right-lower-lobe bronchus and causing right-lower-lobe atelectasis (arrowhead), compatible with stage T2a. **(C)** Coronal reconstruction image from a contrast-enhanced chest CT scan (soft-tissue window) in a 71-year-old woman with NSCLC shows a left lung central mass (arrow) measuring 4.2 cm, invading the hilum and the left main bronchus (arrowhead) without involving the carina, compatible with stage T2b.

T2 tumors are categorized into two subgroups: T2a tumors, which measure more than 3 cm but less than or equal to 4 cm, and T2b lesions, which measure more than 4 cm but less than or equal to 5 cm (Fig 2). The size of the lesion is determined by the longest diameter, and nonmeasurable lesions are classified as T2a. T2 descriptors include involvement of the main bronchus without involving the carina, invasion of the visceral pleura, and association with atelectasis or obstructive pneumonitis extending to the hilum (9).

T3 tumors measure more than 5 cm but are less than or equal to 7 cm. T3 may also be used to describe tumors of any size that exhibit specific anatomic features such as involvement of the chest wall, pericardium, phrenic nerve, or satellite tumor nodules within the same lobe as that of the primary tumor (Fig 3). Within the T3 descriptors, patients with a pathologic T3 descriptor (pT3) due to chest wall and/or parietal pleural invasion have worse overall survival than patients with pT3 due to tumor size or separate lung nodules. However, this difference in survival was not present for patients with clinically staged disease. Because of the inconsistency, it was decided that there was insufficient evidence to change the chest wall portion of the T3 descriptor. The discrepancy between the clinical and pathologic staging of the parietal pleura and chest wall invasion was thought to be due to the low sensitivity of CT for identifying parietal pleural involvement and sometimes even chest wall involvement (7).

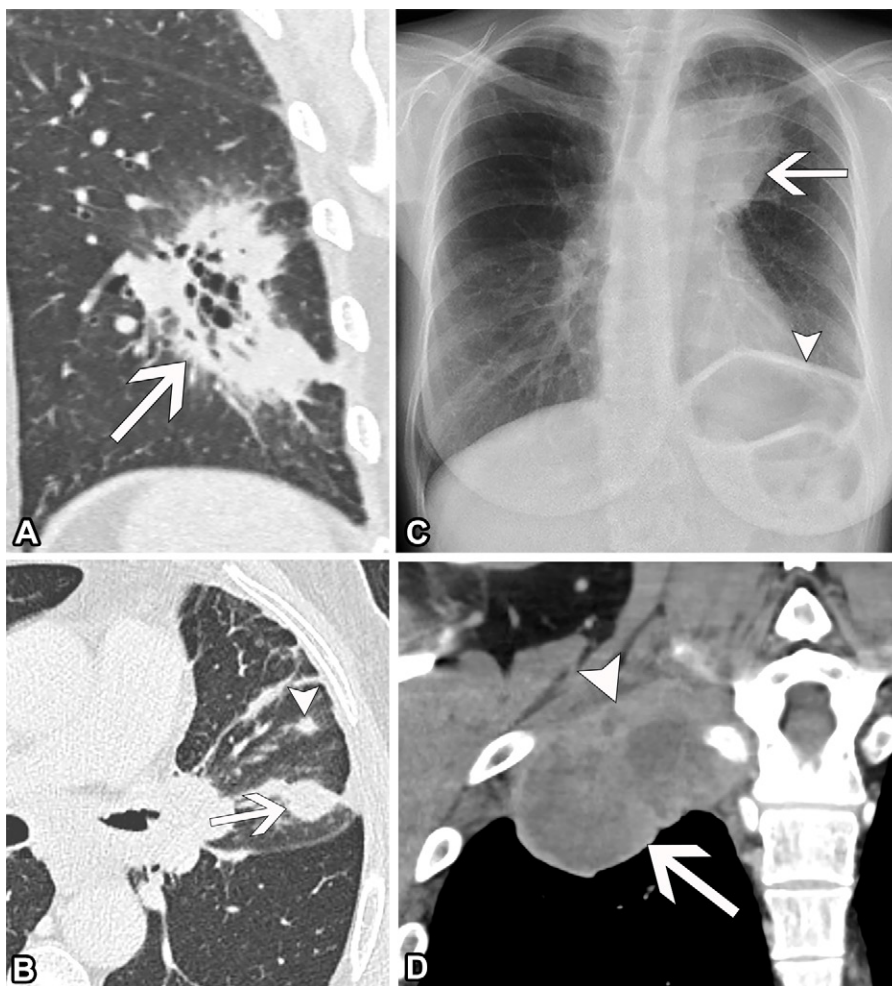
T4 tumors measure more than 7 cm or display specific anatomic characteristics such as invasion of the diaphragm, mediastinum, heart, great vessels, trachea, carina, recurrent laryngeal nerve, esophagus, vertebral body, or brachial plexus (superior branches C8 or above). Additional tumor nodules in the ipsilateral lung but in a different lobe than that of the

primary tumor are also a component of the T4 category (Fig 4). A superior sulcus tumor (ie, Pancoast tumor) is classified as T4 when there is clear involvement of C8 or superior nerve roots, cords of the brachial plexus, subclavian vessels, vertebral bodies, lamina, or spinal canal, whereas it is categorized as T3 if it involves the thoracic nerve roots only (ie, T1 or T2 nerve roots) (9,12).

### N Descriptor: New N2 Categories

Nodal disease is an important prognostic factor in lung cancer staging and has a pivotal role in determining treatment decisions. Historically, the classification of the N descriptor in lung cancer has been based on anatomic location and did not involve the quantification of affected lymph nodes. The anatomic location is reported using the IASLC lymph node map, with 14 different lymph node stations (13,14). When findings of an imaging study are interpreted for staging lung cancer, regional node stations should be referred to by their number according to the IASLC lymph node map rather than by their word description (Fig 5). Word node station descriptions differ from one radiologist or clinician to another, whereas the nodal station numbers are universally accepted. The use of nodal station numbers helps to ensure that sites of tissue sampling accurately correspond to specific nodal groups identified at imaging.

Analyses conducted from TNM-7 and TNM-8 indicated that the burden of nodal metastases at the hilar and mediastinal stations is linked to prognosis (15). This prognostic burden correlation is seen with use of the IASLC lymph node map, with use of a simplified zone system, and even with enumeration of lymph nodes, without assigning them an anatomic location (16). However, in TNM-9 it was decided to



**Figure 3.** T3 lung cancer in four patients. **(A)** Coronal reconstruction image from an unenhanced chest CT scan (lung window) in a 71-year-old woman with NSCLC shows a mass (arrow) in the left lower lobe measuring 5.8 cm at its greater plane dimension. **(B)** Axial unenhanced chest CT image (lung window) in a 68-year-old man with NSCLC shows the primary tumor (arrow) in the left upper lobe associated with a separate tumor nodule (arrowhead) in the same lobe. **(C)** Posteroanterior chest radiograph in a 62-year-old woman with NSCLC shows a mass (arrow) in the left upper lobe that involves the left phrenic nerve (not seen) causing elevation of the left hemidiaphragm (arrowhead) due to left phrenic nerve involvement. **(D)** Coronal reconstruction image from a contrast-enhanced chest CT scan (soft-tissue window) in a 46-year-old man with NSCLC shows a right superior sulcus tumor (arrow) involving the chest wall and first ribs (arrowhead) but without vertebral, spinal canal, or brachial plexus involvement.

continue using the nodal station system because there is no clear difference between station-level and zone-level analyses. Changing definitions of the anatomic location of nodes to zones would have imposed a major shift in the way nodes are recorded for staging, complicating matters unnecessarily.

It was also decided not to use nodal enumeration for staging purposes because enumerating lymph nodes is less reliable than anatomically locating lymph nodes. Counting lymph nodes at imaging is imprecise and therefore has no role in clinical staging. It is also inaccurate to count lymph nodes at pathologic staging because fragmentation of lymph nodes leads to overestimation of the number of lymph nodes, which can occur with sampling of lymph nodes before surgery, at surgical resection, and at specimen handling.

There are important nuances in assigning the N descriptor in clinical staging. Details of these nuances tailored to the radiologist have been elaborated (14). Of particular importance is what constitutes an ipsilateral or a contralateral lymph node with respect to the primary tumor. For this purpose, the left lateral wall of the trachea and not the midline serves as the boundary between the right and left paratracheal lymph nodes (node stations 2 and 4). In addition, when involved, the subcarinal lymph node (station 7) is considered ipsilateral to the primary tumor, whether the primary lung cancer is in the right or left lung. Thoracic lymph nodes not mentioned in the IASLC lymph node map including the internal mammary, an-

terior diaphragmatic, middle diaphragmatic, and intercostal lymph nodes are considered distant (M) metastatic disease and not regional lymph node involvement (N) (Fig 6).

The more robust database of TNM-9 allows better discrimination between categories and optimized stratification, with consideration of nodal metastatic burden (16). The new N classification for TNM-9 is presented in Table 2. The IASLC Staging and Prognostic Factors Committee recommends that the previous N0, N1, N2, and N3 descriptors be continued, with the addition of new subs descriptors to N2 (Fig 7) (16).

The N1 and N3 categories remain unchanged from TNM-8. The N1 category includes metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension (Fig 8). The N3 category comprises metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph nodes (Fig 9).

The N2 category includes metastasis in ipsilateral mediastinal and/or subcarinal lymph nodes. In TNM-9, the N2 category is split into single-station (N2a) and multiple-station (N2b) involvement. N2a disease (Fig 10) has a better prognosis than N2b disease (Fig 11) in both clinical and pathologic classifications, and the differences between all neighboring nodal subcategories are highly significant. The prognostic differences between N2a and N2b are robust and consistent across resection status, histologic type, T category, and



**Figure 4.** T4 lung cancer in six patients. **(A)** Axial unenhanced chest CT scan (lung window) in a 77-year-old woman with NSCLC shows a right-lower-lobe mass (arrow) associated with a separate tumor nodule (arrowhead) in the right middle lobe. **(B)** Coronal contrast-enhanced chest CT image (soft-tissue window) in a 57-year-old woman with NSCLC shows a large central mass (straight arrow) in the right lung invading the mediastinum (arrowhead) and the right hemidiaphragm (curved arrow). **(C)** Coronal reconstruction of a contrast-enhanced chest CT scan (soft-tissue window) in a 73-year-old woman with NSCLC shows a right-upper-lobe lung mass (arrow) invading the distal part of the trachea and the carina (arrowhead). **(D)** Sagittal reconstruction of a contrast-enhanced chest CT scan (soft-tissue window) in a 60-year-old woman with NSCLC shows a mass (arrow) involving both the right upper lobe and right lower lobe and protruding into the superior vena cava (arrowhead). **(E)** Axial contrast-enhanced chest CT image (soft-tissue window) in a 64-year-old woman with NSCLC shows left-lower-lobe lung cancer (straight arrow) invading the pericardium and the epicardial fat (curved arrow) as well as the left atrium (arrowhead). **(F)** Coronal reconstruction image of a contrast-enhanced chest CT scan (soft-tissue window) in a 63-year-old woman with NSCLC shows a left-upper-lobe superior sulcus tumor (arrow) invading the left brachial plexus (arrowhead) above the C8 level.

geographic region (16). The proposed N2 split into subsets also makes sense practically. Unlike N1 stations, which are difficult to distinguish in clinical staging, N2 nodes are readily distinguished with imaging and invasive clinical staging procedures. Separating the N2 category better quantifies the burden of disease because it has long been thought that single-station N2 disease has a better prognosis than multiple-station N2 disease (16). This new N2 subset is based on the number of IASLC lymph node stations and not the number of lymph nodes because node enumeration is not reliable.

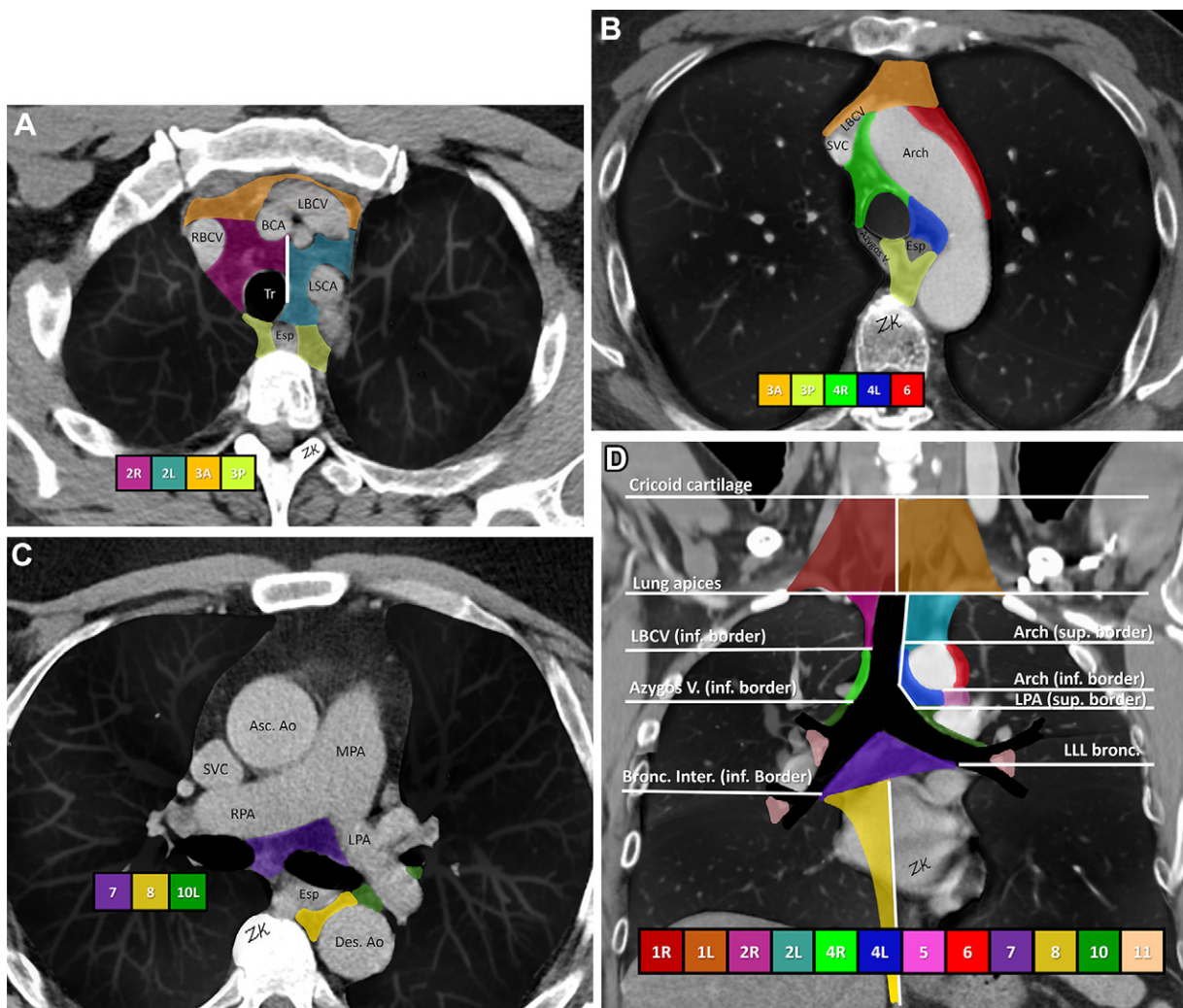
The N0 to N3 descriptors for both clinical and pathologic N staging refer to distinct prognostic groups. The proposed N categories of TNM-9 maintain the prognostic discriminatory capacity in patients who received neoadjuvant therapy, including a robust difference between single- versus multiple-station ypN2 disease. However, stage for stage, for patients who have undergone neoadjuvant therapy, the prognosis for each ypN category is worse compared with a similar pathologic N category in patients who did not undergo neoadjuvant therapy.

Patients who received neoadjuvant therapy and had negative nodes at resection (ypN0) had worse survival outcomes than those with pN0 disease at resection who did not receive neoadjuvant therapy first (16). The same worse prognosis occurs with other N categories and subcategories. The necessity for precise ypN disease characterization is increasing in clinical practice, driven by the prognostic power of ypN descriptors and the increasing adoption of advanced neoadjuvant targeted therapies and immunotherapies. These developments substantially affect the survival outcomes of distinct biomarker-defined subgroups among patients with lung cancer (17).

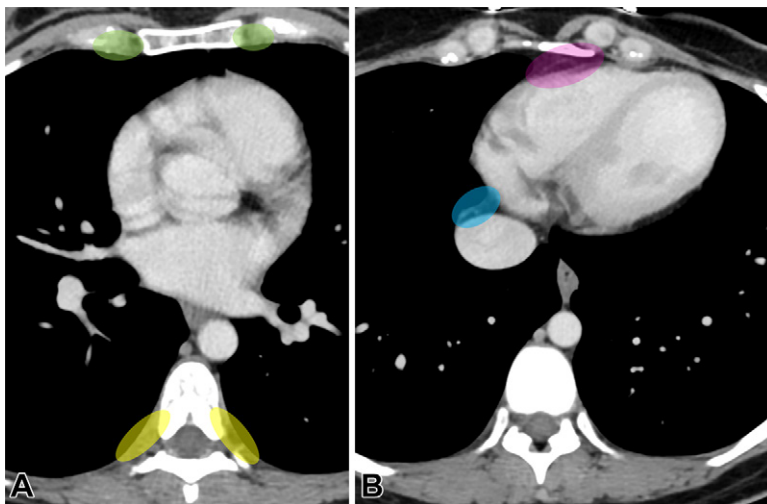
### M Descriptor: New M1c Categories

Therapy for patients with M1 disease has rapidly evolved since TNM-8 was published, particularly the concept of oligometastatic disease as an entity with specific curative options. Advanced methods of local ablative therapies for primary tumors and metastatic lesions (eg, stereotactic body radiation therapy), in combination with targeted therapy or immunotherapy, have





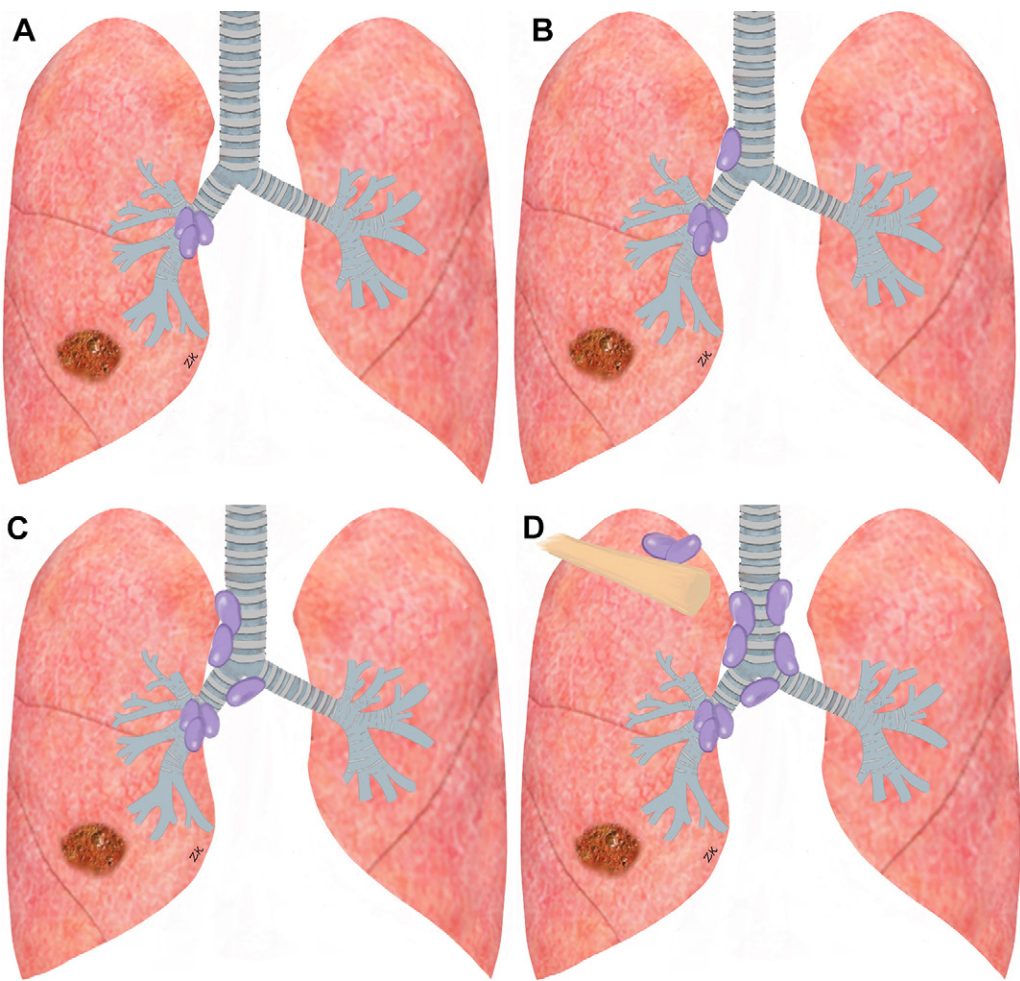
**Figure 5.** Illustrations of the IASLC lymph node map with anatomic definitions on chest CT images in axial (**A–C**) and coronal (**D**) views. The left lateral wall of the trachea, not the midline, serves as the boundary between stations 2R and 2L (white line in **A**) or as demonstrated between stations 4R and 4L (**B**). Arch = aortic arch, Asc. Ao = ascending aorta, Azygos V. = azygos vein, BCA = brachiocephalic artery, Bronc. Inter. = bronchus intermedius, Des. Ao = descending aorta, Esp = esophagus, LBCV = left brachiocephalic vein, LLL bronc = left lower lobe bronchus, LPA = left pulmonary artery, LSCA = left subclavian artery, MPA = main pulmonary artery, RBCV = right brachiocephalic vein, RPA = right pulmonary artery, SVC = superior vena cava, Tr = trachea.



**Figure 6.** Normal CT images with overlays illustrate the regions where nonregional thoracic lymph node involvement may be seen, in rare cases. (**A**) Axial CT image obtained at the level of the left atrium shows the internal mammary (green areas) and intercostal (yellow areas) regions. (**B**) Axial CT image obtained at the level of the base of the heart shows the anterior diaphragmatic (pink area) and middle diaphragmatic (blue area) regions. Lymph node metastasis in regions not described in the regional IASLC lymph node map, such as axillary lymph nodes or the lymph node regions demonstrated in these images, are classified as distant metastases (M1).

Table 2: Ninth Edition TNM Staging System: Regional Lymph Node Characteristics	
Classification	Description
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)
N2a	Single N2 station involvement
N2b	Multiple N2 station involvement
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

Source.—Reference 6.



**Figure 7.** Illustrations show the N classification of the TNM-9 staging system for lung cancer. **(A)** N1 is unchanged: ipsilateral peribronchial, hilar, and/or intrapulmonary metastatic lymph nodes. **(B)** N2a classification is new: single-station ipsilateral mediastinal and/or subcarinal metastatic lymph nodes. This illustration shows one metastatic lymph node in the 4R station and several N1 lymph nodes in the ipsilateral hilum. **(C)** N2b classification is new: multistation ipsilateral mediastinal and/or subcarinal metastatic lymph nodes. This illustration shows two metastatic lymph nodes in station 4R and one lymph node in station 7. **(D)** N3 is unchanged: contralateral mediastinal/hilar or low-cervical/supraclavicular metastatic lymph nodes. Lymph nodes in this illustration that constitute N3 are the contralateral 4L lymph nodes and the ipsilateral supraclavicular 1R lymph nodes. The new N2 subset dividing N2 into N2a and N2b is based on the number of IASLC lymph node stations and not the number of lymph nodes because node enumeration is not reliable.

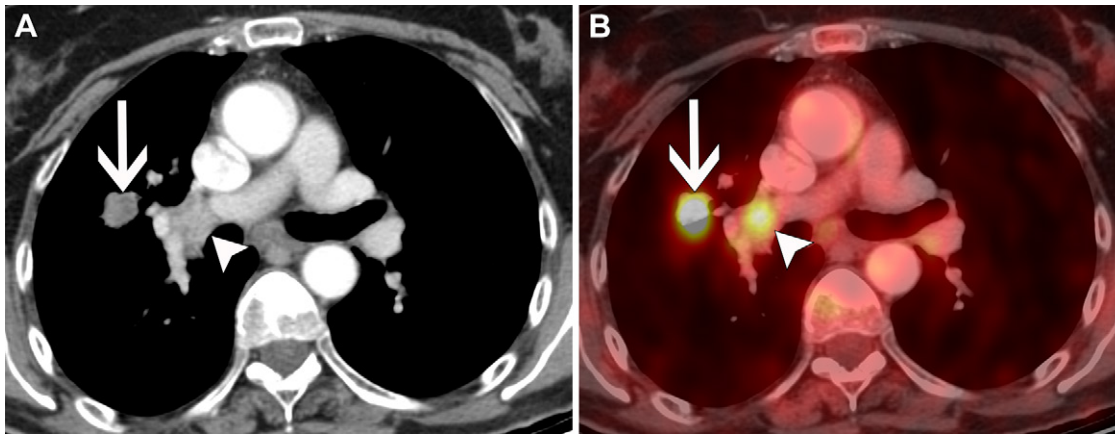
emerged (18). Whole-body staging with fluorine 18 fluorodeoxyglucose (FDG) PET/CT is widely used, even when metastatic disease is known, because therapy may differ according to the metastatic burden. Assessments using the TNM-9 database revealed that a higher quantity of metastatic lesions was associated with a poorer prognosis (18). Because this correlation appears to be a continuum, and adjustment for confounders was not possible, no specific lesion number was deemed appropriate for stage classification. Among patients with multiple me-

tastases, a worse prognosis was seen when a greater number of organ systems were involved. The new M classification for TNM-9 is presented in Table 3. The IASLC Staging and Prognostic Factors Committee recommends that the previous M0, M1a, M1b, and M1c descriptors be continued, with the addition of new subsets to the M1c descriptor (Fig 12).

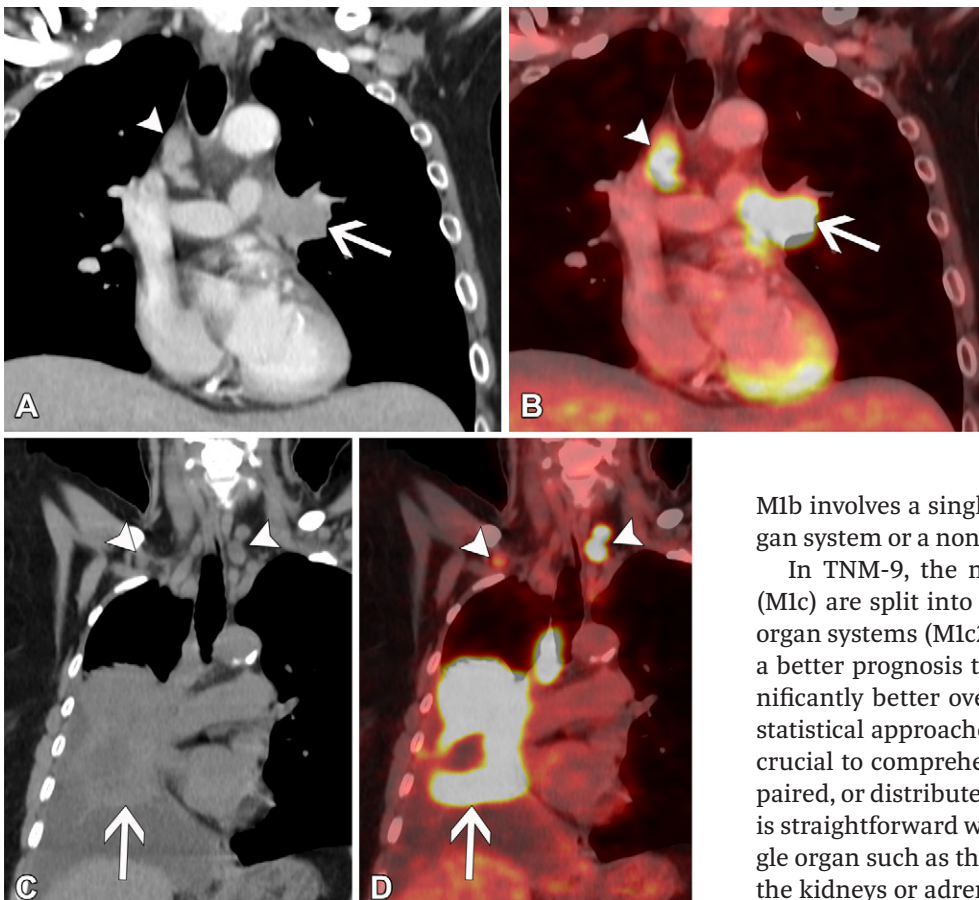
M1a and M1b categories remain unchanged from TNM-8. The M1a category includes one or more separate contralateral tumor nodules (pleural or pericardial metastasis) (Fig 13).



**Figure 8.** N1 disease in a 54-year-old man with NSCLC. **(A)** Axial contrast-enhanced chest CT image (soft-tissue window) shows the right-upper-lobe primary tumor (arrow) with a single metastatic N1 lymph node in the right hilar 10R station (arrowhead). **(B)** Axial fused fluorodeoxyglucose (FDG) PET/CT image at the same level as in **A** shows that the lymph node (arrowhead) is FDG avid, similar to the primary tumor (arrow).

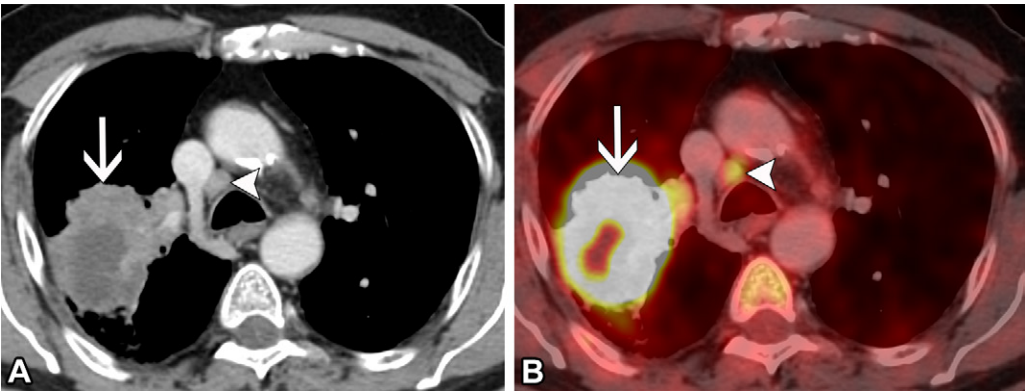


**Figure 9.** N3 disease in two different patients. **(A, B)** Coronal reconstruction of a contrast-enhanced chest CT scan (soft-tissue window) **(A)** in a 63-year-old woman with NSCLC shows a left-upper-lobe primary mass (arrow) that directly involves the left hilum, with metastatic N3 lymph nodes in the contralateral 4R station (arrowhead). Coronal fused FDG PET/CT image **(B)** at the same level as that in **A** shows that the lymph nodes (arrowhead) are FDG avid, similar to the primary tumor (arrow). **(C, D)** Coronal reconstruction of an unenhanced chest CT scan (soft-tissue window) **(C)** in a 58-year-old man with NSCLC shows a right-lower-lobe primary mass involving the right hilum (arrow), with metastatic N3 bilateral low-cervical lymph nodes at the 1R and 1L stations (arrowheads). Coronal fused FDG PET/CT image **(D)** at the same level as that in **C** shows that the lymph nodes (arrowheads) are FDG avid, similar to the primary tumor (arrow). For supraclavicular lymph node (station 1) involvement, both ipsilateral and contralateral lymph node involvement is considered N3 disease.

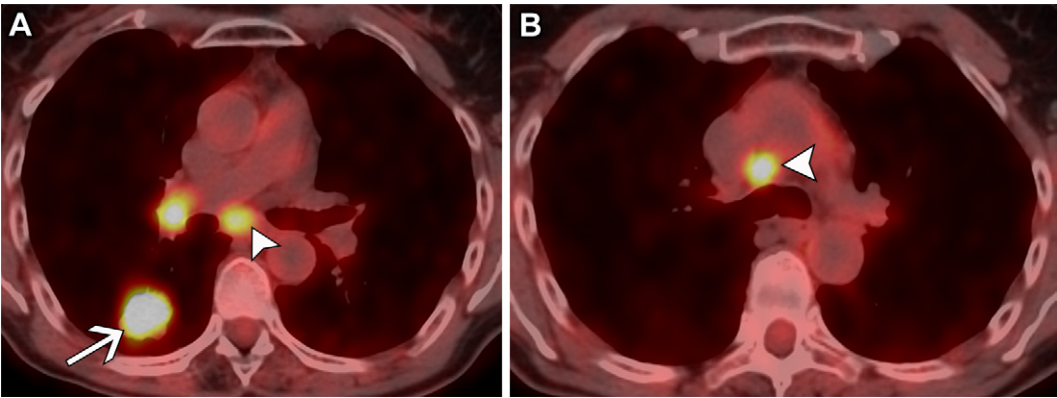


M1b involves a single extrathoracic metastasis in a single organ system or a nonregional metastatic lymph node (Fig 14).

In TNM-9, the multiple extrathoracic metastatic lesions (M1c) are split into single organ system (M1c1) and multiple organ systems (M1c2) subcategories. M1c1 disease (Fig 15) has a better prognosis than M1c2 disease does (Fig 16). This significantly better overall survival is consistent across several statistical approaches and multiple subset analyses (18). It is crucial to comprehend that an organ system can be solitary, paired, or distributed diffusely throughout the body (18). This is straightforward when the area of concern is a localized single organ such as the brain or the liver. Paired organs such as the kidneys or adrenal glands represent one organ system. A diffuse system, such as the skeleton, is also considered one



**Figure 10.** N2a disease in a 65-year-old man with NSCLC. **(A)** Axial contrast-enhanced chest CT image (soft-tissue window) shows the right-upper-lobe primary mass (arrow) with a single-station metastatic N2 lymph node in the ipsilateral paratracheal 4R station (arrowhead). **(B)** Axial fused FDG PET/CT image at the same level as in **A** shows that the lymph node (arrowhead) is FDG avid, similar to the primary tumor (arrow).



**Figure 11.** N2b disease in a 53-year-old woman with NSCLC. Axial fused FDG PET/CT images at different levels show an FDG-avid mass in the right lower lobe (arrow in **A**) with multiple-station metastatic FDG-avid N2 lymph nodes in ipsilateral 4R and 7 stations (arrowhead).

Table 3: Ninth Edition TNM Staging System: Distant Metastases Characteristics		
Classification		Description
M0	No distant metastasis	
M1	Distant metastasis	
M1a	Malignant pleural or pericardial effusion or pleural or pericardial nodules or separate tumor nodule(s) in a contralateral lobe	
M1b	Single extrathoracic metastasis in a single organ system	
M1c	Multiple extrathoracic metastases	
M1c1	Metastases in a single organ system	
M1c2	Metastases in multiple organ systems	

Source.—Reference 6.

Note.— The M1c1 definition should be applied to an organ system, regardless of whether the organ is solitary, paired, or diffuse throughout the body.

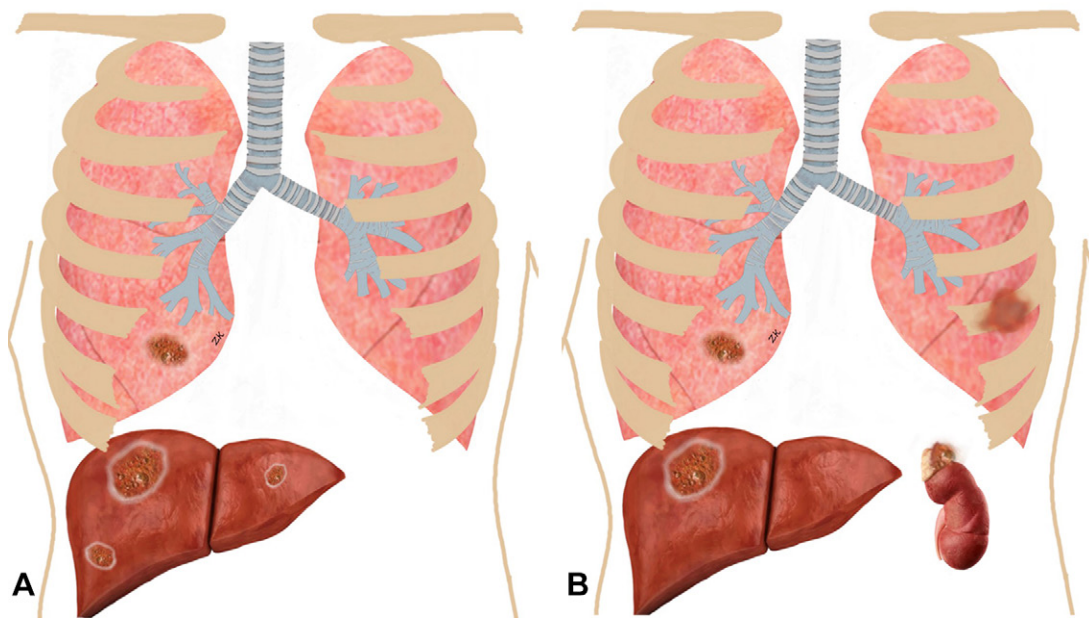
organ system (18). Awareness of this nuance in TNM-9 allows radiologists to carefully document distant metastatic spread, thus providing the elements needed for the M classification, leading to precise stage determination. Depending on the metastatic tumor burden, accurate staging may result in different treatment plans.

**Special Entities: Multifocal Lung Adenocarcinoma with Ground-Glass or Lepidic Features and Pneumonic-Type Adenocarcinoma**

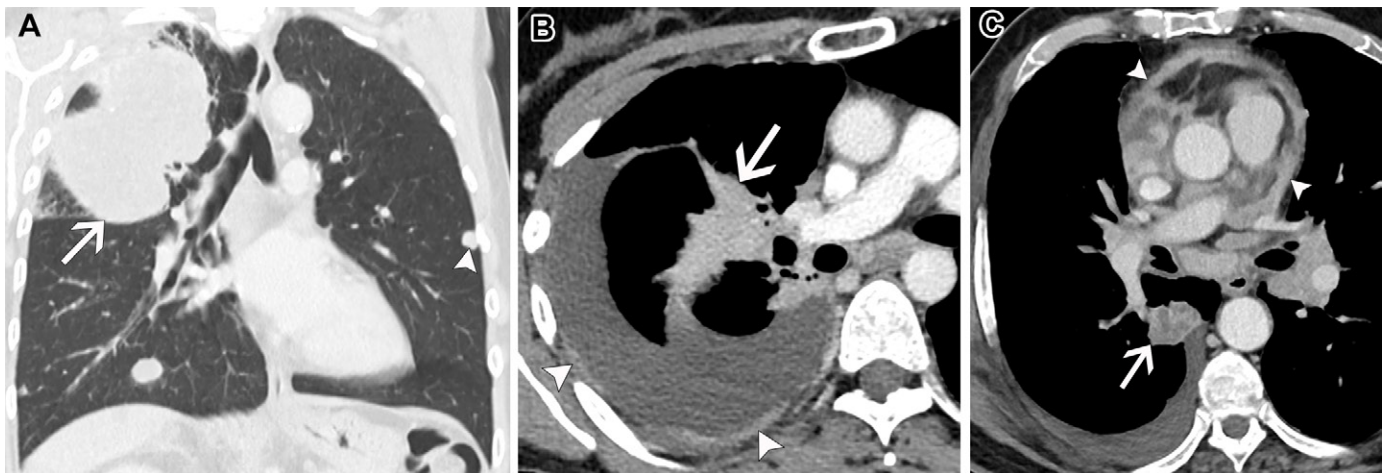
The TNM-8 staging system for lung cancer was the first to address lung cancers that manifest as multiple discrete nodules

of lung cancer that show ground-glass or lepidic features. It was also the first to address pneumonic-type lung adenocarcinoma, manifesting as an infiltrate or consolidation involving a large region of the lung. The staging applied to these two forms of lung cancer remains unchanged in TNM-9. The rationale for applying different TNM staging rules to these two entities is that they exhibit different biologic behavior, including survival and recurrence patterns (19,20). These forms of lung cancer should be distinguished from the more common pulmonary metastatic disease, which typically manifests as separate solid nodules, which are assigned a staging descriptor according to their location, whether in the same lobe (T3)





**Figure 12.** Illustrations show the new M1c classifications in the ninth edition of the TNM lung cancer staging system. **(A)** M1c1 disease is multiple extrathoracic metastases in a single organ system. **(B)** M1c2 is multiple extrathoracic metastases in multiple organ systems.



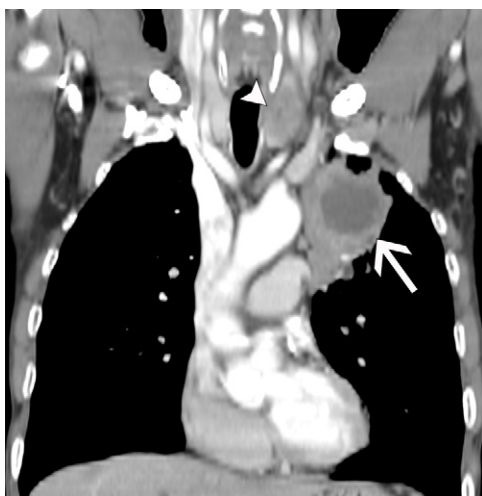
**Figure 13.** M1a metastatic disease in three patients. **(A)** Coronal contrast-enhanced chest CT image (lung window) in a 59-year-old woman with NSCLC shows a right-upper-lobe primary mass (arrow), with an additional tumor nodule in the left lower lobe (arrowhead); another metastasis is seen in the right lower lobe. **(B)** Axial contrast-enhanced chest CT image (soft-tissue window) in a 63-year-old man with NSCLC shows a right-upper-lobe primary mass (arrow) involving the right hilum, associated with right pleural metastases (arrowheads) causing a pleural effusion. **(C)** Axial contrast-enhanced chest CT image (soft-tissue window) in a 75-year-old man with NSCLC shows a right-lower-lobe mass (arrow) associated with pericardial metastasis encasing the pericardium (arrowheads).

as the primary lung cancer, in the ipsilateral lung in a different lobe as the primary lung cancer (T4), or in the contralateral lung (M1a).

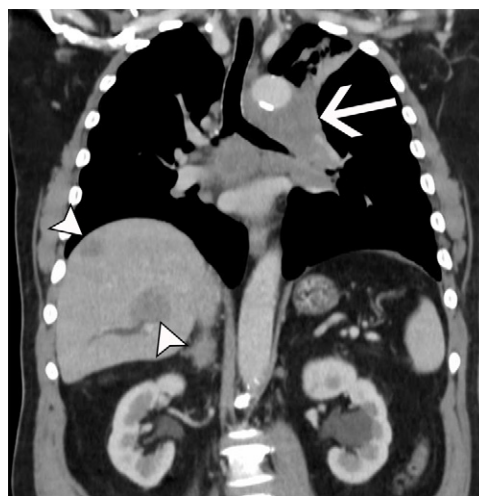
Multifocal ground-glass or lepidic adenocarcinoma consists of a primary subsolid (usually part-solid) adenocarcinoma and multiple separate subsolid (comprising part-solid and pure ground-glass) lung nodules. These separate discrete subsolid nodules may be in the same lobe as the primary ipsilateral lung, the contralateral lung, or both (19,20). These additional nodules correspond to adenocarcinoma in situ, minimally invasive adenocarcinoma, or lepidic-predominant adenocarcinoma (19,20). They are hypothesized to be differ-

ent primary lung cancers in different stages of development. In the clonality studies that were performed in this entity, 71%–83% of those nodules studied were indeed of a different clone, but such studies are few (19). These additional nodules do not need to be biopsied, and staging is applied using the accepted clinical criteria (Table 4). In terms of clinical staging, the highest T descriptor is provided by the dominant nodule. The number of subsolid lesions in both lungs is counted and designated with a number sign (#) in the T descriptor or a lower case “m” for “multiple” in parenthesis, with a single N and M for all tumors (highest T[#/m]NM) (Fig 17). A key feature of staging is to not count the small ground-glass nodules

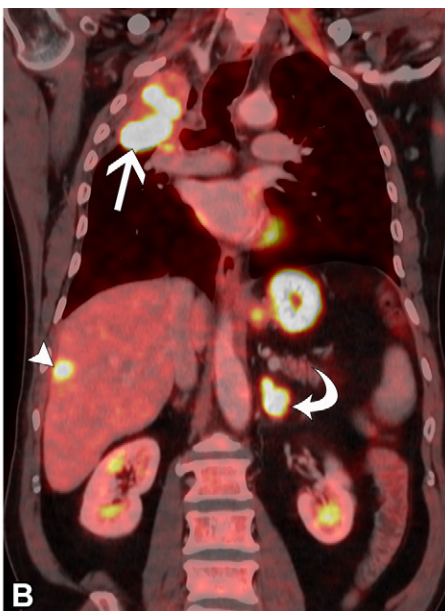




**Figure 14.** M1b metastatic disease in a 61-year-old man with NSCLC. Coronal reconstruction of a contrast-enhanced chest CT scan (soft-tissue window) shows the left-upper-lobe primary mass (arrow) with a single histologically proven metastasis in the left lobe of the thyroid gland (arrowhead).



**Figure 15.** M1c1 metastatic disease in a 64-year-old man with NSCLC. Coronal reconstruction of a contrast-enhanced chest CT scan (soft-tissue window) shows a left-upper-lobe mass (arrow) invading the mediastinum with multiple metastases solely in the liver (arrowheads).



**Figure 16.** M1c2 metastatic disease in a 65-year-old man with NSCLC. **(A)** Coronal reconstruction of a contrast-enhanced chest CT scan (soft-tissue window) shows the right-upper-lobe primary mass (straight arrow) invading the mediastinum with a metastasis in the liver (arrowhead) and in the left adrenal gland (curved arrow). **(B)** Coronal fused FDG PET/CT image at the same level shows that the metastases (arrowhead and curved arrow) are FDG avid, similar to the primary tumor (straight arrow).

that measure up to 5 mm because these are thought to represent atypical adenomatous hyperplasia, a precursor to lung adenocarcinoma. It is important for radiologists to identify multifocal lung adenocarcinoma with ground-glass features because the staging and patient treatment are different from those for pulmonary metastatic disease. These patients have much longer overall survival time and differ in patterns of progression. Distant recurrence is unusual, whereas local recurrence and the appearance of new primary lung lesions are more common (19). Consequently, treatment in patients with this entity involves limiting the amount of lung resected; the rest of the nodules are monitored with serial imaging and not resected, thus preserving as much lung as possible (19).

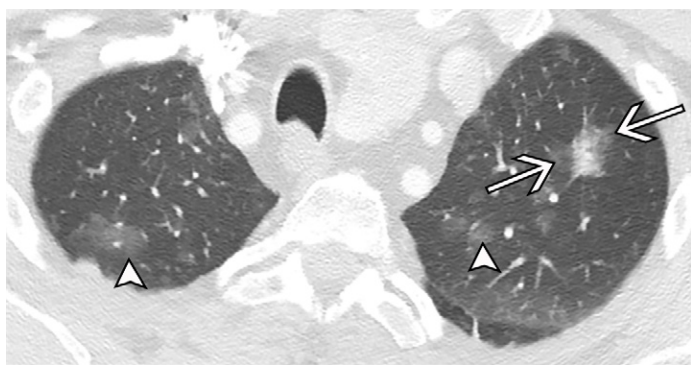
The pneumonic-type adenocarcinoma, a rare type of presentation, was also addressed in TNM-8, and staging of this tumor remains unchanged in TNM-9 (19). At CT, these tumors appear as consolidation with or without additional consolidative or ground-glass opacities, either confined to a segment or lobe or spread diffusely in the lungs. At histologic evaluation, these tumors have a growth pattern with lepidic features, predominantly but typically showing invasive mucinous tumor foci (20). It is often difficult to measure the size of the primary tumor accurately in pneumonic-type adenocarcinoma because of its indistinct borders and propensity for what appears as aerogenous spread. Thus, in terms of staging, the pneumonic-type adenocarcinoma is classified as T3 when it

**Table 4: Clinical Criteria for the Diagnosis of Multifocal Ground-Glass or Lepidic Lung Adenocarcinoma**

Multiple subsolid nodules (pure ground-glass or part solid), with at least one nodule suspected (or proven) to be cancer
Applies regardless of whether a biopsy of the nodules has been performed
Applies if the other nodules are found by biopsy to be AIS, MIA, or LPA
Applies if a nodule has become >50% solid but is judged to have arisen from a GGN, provided that there are other subsolid nodules
GGN lesions <5 mm or lesions suspected to be AAH are not counted

Source.—Reference 19.

Note.—AAH = atypical adenomatous hyperplasia, AIS = adenocarcinoma in situ, GGN = ground-glass nodule, LPA = lepidic-predominant adenocarcinoma, MIA = minimally invasive adenocarcinoma.

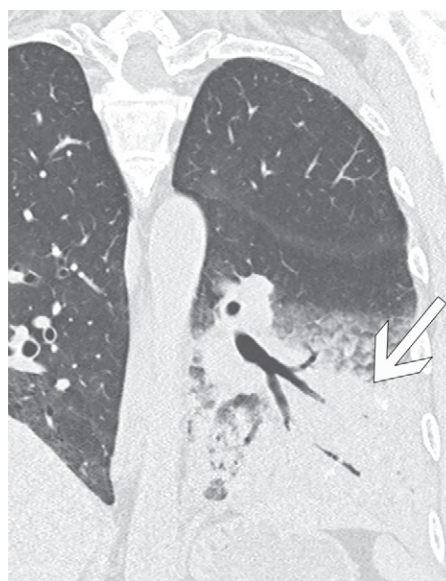


**Figure 17.** Multiple ground-glass or lepidic lesions (multifocal adenocarcinoma) in a 70-year-old man with NSCLC. Axial contrast-enhanced CT image (lung window) shows that the primary tumor is the leading nodule. The part-solid nodule in the left upper lobe (between arrows) has an overall diameter of 2.2 cm, and the solid component measures 1.2 cm; this would normally be described as a T1b lesion. However, there are numerous additional ground-glass nodules (arrowheads) in both lungs. For multiple ground-glass lesions or lepidic tumors, the IASLC advises using the dominant lesion for T staging. Because of the multiple additional ground-glass nodules, the overall descriptor is T1b(m), (with “m” for multiple). In counting the additional foci of ground-glass malignancy, only nodules larger than 5 mm are included because those with a diameter up to 5 mm are thought to represent atypical adenomatous hyperplasia, a precursor to lung adenocarcinoma.

involves one lobe (Fig 18), T4 when it involves one lung, and M1a when it involves both lungs, with a single N and M for all lesions (5,21). Despite the diffuse lung involvement, patients with this entity typically do not present with nodal or distant metastases. Survival after resection is worse than that in patients with multifocal lung adenocarcinoma with ground-glass or lepidic features (19).

### Revisions to the Stage Classification

The changes introduced in the TNM-9 staging system, particularly with the addition of the N2 subcategories, resulted in



**Figure 18.** Lung cancer manifesting as consolidation in a 57-year-old woman. Coronal reconstruction of an unenhanced chest CT (lung window) image shows consolidation in the left lower lobe (arrow). Histopathologic examination after biopsy revealed adenocarcinoma. Because the disease is limited to the left lower lobe, it was classified as T3 disease

changes in stage groupings (6). Patients with T1 disease and N1 are now classified as stage IIA (previously IIB), those with T1N2a disease are classified as stage IIB, and those with T1N2b disease are classified as stage IIIA. Patients with T2 and N2a are now classified as stage IIIA, whereas patients with T2N2b are classified as stage IIIB. On the other hand, changes in the M1c subcategories did not affect stage groupings, with both M1c1 and M1c2 disease staged as IVB. New stage grouping classification is presented in Table 5. Overall survival did not significantly change between stage groups in comparison with those in TNM-8 (6). Continued accrual of more detailed data using this revised stage classification will allow survival analyses and facilitate a sharper distinction between subsets within the current T, N, and M categories as well as the stage groupings. Future renditions of staging will involve decisions to balance the value of increasing complexity with implementation and whether the changes are clinically meaningful (22).

### Limitations, Unresolved Issues, and Future Directions

Although TNM-9 signifies progress compared with the previous versions of the staging system, limitations remain. With a large database, there is a trend toward increased granularity that leads to increased staging complexity. Staging classification fundamentally delineates specific cohorts of individual cases. However, any categorization in this spectrum remains inherently somewhat arbitrary (2). Stage classification is insufficient to address the myriad intricacies and determine the optimal treatment approach for an individual patient. Specifically, the proposals of TNM-9 did not address actionable

Table 5: Ninth Edition TNM Staging System: Stage Group Categories

T/M	Label	N0	N1	N2		N3
				N2a	N2b	
T1	T1a	IA1	IIA	IIB	IIIA	IIIB
	T1b	IA2	IIA	IIB	IIIA	IIIB
	T1c	IA3	IIA	IIB	IIIA	IIIB
T2	T2a	IB	IIB	IIIA	IIIB	IIIB
	T2b	IIA	IIB	IIIA	IIIB	IIIB
T3	...	IIB	IIIA	IIIB	IIIB	IIIC
T4	...	IIIA	IIIA	IIIB	IIIB	IIIC
M1	M1a	IVA	IVA	IVA	IVA	IVA
	M1b	IVA	IVA	IVA	IVA	IVA
	M1c1	IVB	IVB	IVB	IVB	IVB
	M1c2	IVB	IVB	IVB	IVB	IVB

Source.—Reference 6.

mutations. For these patients, targeted therapy or immunotherapy can contribute to significant survival benefits (18).

Despite these limitations, the anatomic staging system for patients with newly diagnosed lung cancer is robust, considering available prognostic information. TNM-9 is already available, and imaging interpretation is a key contributor to clinical staging. It is important for radiologists to understand the crucial points in the T, N, and M classifications, more so than the final stage group. Some of the nuances in the staging descriptors, such as the difference between T1b and T1c, can lead to a different therapeutic approach, without a substantial change in the overall stage classification. For example, in two recent randomized trials (23,24), sublobar resection, rather than lobectomy, was shown to be a valid treatment option for T1 lung cancers measuring 2 cm or smaller (23–25). The consistent nomenclature of staging classification to describe homogeneous groups of tumors, including tumor measurements, has many applications including evaluating therapy.

The data submitted to IASLC and Cancer Research and Biostatistics (CRAB) for the creation of the TNM-9 database were not sufficiently reliable to permit analysis of the TNM-8 proposal to use suspected invasive component size (solid component at CT) rather than total tumor size (overall size including the ground-glass component) for the T size descriptor for part-solid adenocarcinomas. A potential factor is the timing of the adoption of TNM-8 by the Union for International Cancer Control and the American Joint Committee on Cancer in 2017 (26,27). Because the cases included in the IASLC and CRAB database ranged from 2011 to 2019, most of them were submitted before the implementation of this updated tumor measurement definition (7). Because most of the submitted cases did not provide the total size in addition to the required measurements of the solid-invasive component, this point could not be analyzed, and the current recommendation is to use the solid component only for the T descriptor while also reporting the total size, with the ground-glass component in

the radiology report. Application of this principle in pathologic stage I to IIA nonmucinous lung adenocarcinomas may result in downstaging of 22% of tumors (28). In addition, the prognostic implication of lymphangitic carcinomatosis could not be evaluated because such data were sparse in the database. Data entry for the TNM database is usually performed by research assistants or clinicians using the radiology report. Awareness of the nuances of TNM-9 allows radiologists to provide accurate detailed descriptions for staging not only for individual patients but also for future staging renditions that will rely on these reports.

The reporting of multifocal lung adenocarcinoma with ground-glass features in the database was disappointing because only a few were documented in the database. Many of these cases rely heavily on clinical staging; most of these lesions are not resected or sampled until they progress. Radiologists must be aware of this entity in order to provide accurate interpretation. Use of consistent nomenclature in the radiology report allows oncologists and their research assistants to enter the data correctly to contribute to the TNM database.

In terms of future directions, TNM-9 did not address an infrequent presentation of patients with primary lung cancer featuring air lucency or cystic components, leaving unresolved the question of whether to assess the cystic or solid components for staging (29). Another area of study concerns patients who have received neoadjuvant therapy. Although overall survival was worse for all patients who underwent neoadjuvant treatment (ypT) compared with that for those who did not undergo induction therapy, sample sizes were small and the findings must be confirmed in larger patient populations (7).

Regarding the M component, metastatic tumor burden analysis using the size of the largest metastasis suggested a threshold of 1.2 cm. Although this threshold correlated with a statistically significant effect on overall survival, the sample size was too small for validation and generalizability (18). This issue remains for future staging revisions to resolve, it is hoped, with more cases in which metastatic lesion size is documented. For the definition of oligometastatic disease, multiple cutoff points including three, five, and seven extrathoracic metastatic lesions have been examined. Differences in survival suggest that there is a continuum of worsening prognosis with an increasing number of metastatic lesions (18). Another aspect not explored because of insufficient data involves determining whether there should be a cap on the number of metastatic lesions within a single organ system. This issue is important because the clinical care of patients with M1c1 disease may vary according to the number of lesions. Exploratory analysis results (18) indicated variations in prognosis among M1 subsets associated with different organs, particularly the brain, requiring further investigation for future revision.

Conclusion

Effective and precise communication of staging information helps to guide the decision-making process during multidisciplinary discussions. Together with other patient information, staging is the foundation to estimate prognosis and predict therapy outcome. One of the strengths of the TNM-9



staging system is that stage groupings for both clinical and pathologic staging maintained their statistical significance in determining prognosis. Because therapeutic treatment decisions are made with clinical staging before the availability of postsurgical pathologic staging, radiologists play a vital role in staging and patient care. A comprehensive understanding of the proposed updates of the TNM-9 staging classification system and the potential effect of staging on treatment options is key to providing accurate imaging interpretation.

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**Disclosures of conflicts of interest.**—Z.K. Consultant for Aidoc, member of Society of Thoracic Radiology education committee. M.T.T. Editorial board member and president-elect of the Society of Thoracic Radiology. E.M. Honoraria for lectures from AstraZenica, Boehringer Ingelheim, Dohme, Merck, and Sharp; president of the Society of Thoracic Radiology; past president of the International Thymic Malignancy Interest Group. All other authors, the editor, and the reviewers have disclosed no relevant relationships.

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