RadioGraphics

Lung Cancer Staging Essentials: The New TNM Staging System and Potential Imaging Pitfalls[1]

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CME FEATURE

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LEARNING OBJECTIVES FOR TEST 1

After reading this article and taking the test, the reader will be able to:

- Identify the correct TNM stage of a lung cancer on the basis of its radiologic appearance.
- Discuss the revisions in the new 7th edition of the TNM staging system for lung cancer and identify the important differences from the 6th edition.
- Describe the most commonly encountered pitfalls in lung cancer staging.

Lung cancer is the leading cause of cancer-related deaths worldwide, with a dismal 5-year survival rate of 15%. The TNM (tumor-node-metastasis) classification system for lung cancer is a vital guide for determining treatment and prognosis. Despite the importance of accuracy in lung cancer staging, however, correct staging remains a challenging task for many radiologists. The new 7th edition of the TNM classification system features a number of revisions, including subdivision of tumor categories on the basis of size, differentiation between local intrathoracic and distant metastatic disease, recategorization of malignant pleural or pericardial disease from stage III to stage IV, reclassification of separate tumor nodules in the same lung and lobe as the primary tumor from T4 to T3, and reclassification of separate tumor nodules in the same lung but not the same lobe as the primary tumor from M1 to T4. Radiologists must understand the details set forth in the TNM classification system and be familiar with the changes in the 7th edition, which attempts to better correlate disease with prognostic value and treatment strategy. By recognizing the relevant radiologic appearances of lung cancer, understanding the appropriateness of staging disease with the TNM classification system, and being familiar with potential imaging pitfalls, radiologists can make a significant contribution to treatment and outcome in patients with lung cancer.

Abbreviations: FDG = 2-[fluorine-18]fluoro-2-deoxy-D-glucose, IASLC = International Association for the Study of Lung Cancer

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Supraclavicular	Scalene	Mediastinal: Contra-	Mediastinal: Ipsi-	Subcarinal	Hilar: Contra-	Hilar: Ipsi-	Peribronchial (ipsilateral)	Lymph Node (N)
								Stage IV (Metastatic: M1a or M1b, any T, any N)
+	+	+			+			N3 Stage IIIB
–	–	–	+ &/ +		–			N2 Stage IIIA
–	–	–	–	–	–	+ &/ +		N1 Stage IIA / Stage IIB
–	–	–	–	–	–	–	–	N0 Stage IA / Stage IB / Stage IIA / Stage IIB

Metastatic (M):

M1a:
Local intrathoracic spread:
- Malignant pleural/pericardial effusion
- Separate tumor nodule(s) in the contralateral lung

M1b:
Disseminated (extrathoracic) disease:
Liver, bone, brain, adrenal gland, etc.

Primary Tumor (T)	T1a	T1b	T2a	T2b	T3	T4
a. Size	≤2cm	>2cm but ≤3cm	>3cm but ≤5cm	>5cm but ≤7cm	>7cm	Any
b. Endobronchial location	No invasion proximal to lobar bronchus		Main bronchus (≥2cm distal to the carina)		Main bronchus (<2cm distal to the carina)	–
c. Local Invasion	Surrounded by lung or visceral pleura		Visceral pleura		Chest wall/diaphragm/ mediastinal pleura/ parietal pericardium	Mediastinum/trachea/heart/ great vessels/esophagus/ vertebral body/carina
d. Other			Atelectasis/obstructive pneumonitis that extends to the hilar region but does not involve the entire lung		Atelectasis/obstructive pneumonitis of entire lung; separate tumor nodule(s) in ipsilateral primary tumor lobe	Separate tumor nodule(s) within the ipsilateral lung but different lobe as the primary mass

Figure 1. Chart illustrates the descriptors from the 7th edition of the TNM staging system for lung cancer.

Introduction

Lung cancer is the leading cause of cancer-related deaths in the United States, with a 5-year survival rate of only 15% (1). Lung cancer is classified as either non–small cell or small cell lung cancer, with the former accounting for 87% of all lung cancers (1).

The descriptors of the internationally used TNM (tumor-node-metastasis) classification system for staging various cancers include the size of and the degree of locoregional invasion by the primary tumor (T), the extent of regional lymph node involvement (N), and the presence or absence of intrathoracic or distant metastases (M). The goal of such a classification system is to assist clinicians in planning treatment, determining prognosis, evaluating treatment results, and facilitating information exchange between multiple centers (2).

The International Association for the Study of Lung Cancer (IASLC) serves as the primary source of recommendations for lung cancer staging revisions recognized by the International Union Against Cancer (UICC) (3). The much-anticipated 7th edition of the TNM staging system for lung cancer incorporates several proposed revisions to better align TNM staging with prognosis and, in some cases, with treatment (3–5), on the basis of evidence from a significantly larger worldwide database that has been subjected to extensive validation (6).

In this article, we discuss and illustrate each descriptor of the TNM staging system and present the changes within each subsection of the new 7th edition of the TNM system. In addition, we discuss common pitfalls in lung cancer staging (nodal metastatic drainage patterns, incidental pulmonary nodules, mediastinal adenopathy, metastatic disease, chest wall and pleural invasion, and pleural-pericardial metastasis) and the relative merits of 2-[fluorine-18]fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET), magnetic resonance (MR) imaging, and computed tomography (CT) in this setting. We also briefly discuss staging-based treatment regimens.

Figure 1 shows the descriptors from the 7th edition of the TNM staging system for lung cancer (in a manner similar to Lababede et al [7]), whereas Table 1 compares and contrasts the 6th and 7th editions, with rationale given for the revisions in the newer edition (2–5,7–9).

Table 1
Comparison of the 6th and 7th Editions of the TNM Staging System for Lung Cancer

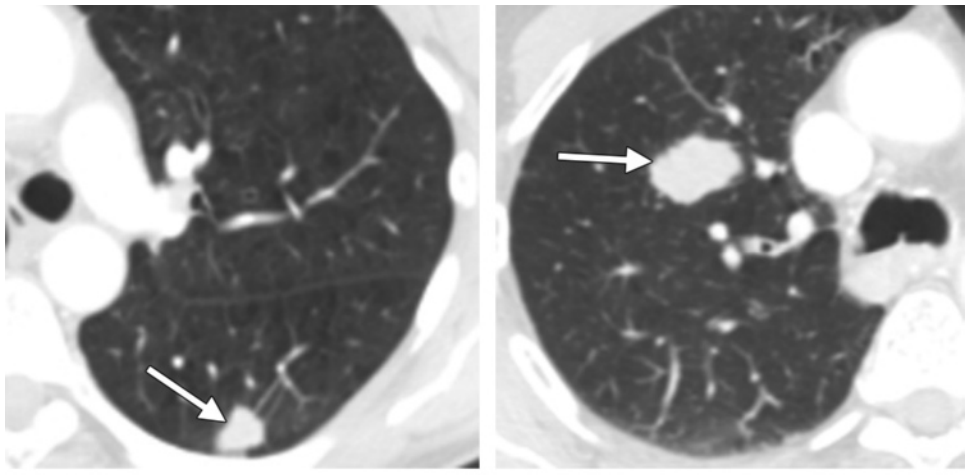
Category	6th Edition	7th Edition	Reason for Revision*
Tumor			
Size	T1: ≤3 cm	T1a: ≤2 cm	5-year survival rate = 77%
		T1b: >2 cm but ≤3 cm	5-year survival rate = 71%
	T2: >3 cm	T2a: >3 cm but ≤5 cm	5-year survival rate = 58%
	. . .	T2b: >5 cm but ≤7 cm	5-year survival rate = 49%
	. . .	T3: >7 cm	5-year survival rate = 35%
Tumor nodule(s) separate from primary mass			
Same lung and lobe as primary mass	T4	T3	5-year survival rate = 28% (similar to that for T3 and better than that for T4)
Same lung but not same lobe as primary mass	M1	T4	5-year survival rate = 22% (similar to that for T4)
Contralateral lung	M1	M1a	5-year survival rate = 3% (consistent with that for other intrathoracic metastatic disease)
Node			
Lymph node map	Lymph node staging primarily from the MD-ATS (Mountain-Dresler–American Thoracic Society) map	New IASLC lymph node map published (Fig 7)	New IASLC map reconciles differences between earlier lymph node maps and provides new descriptions of the nodal anatomy with respect to anatomic borders to ensure accurate localization of lymph nodes (cf Table 3)
Malignant pleural or pericardial effusion	T4	M1a	5-year survival rate = 2% (similar to that for tumors in the intrathoracic metastatic category, compared with a 5-year survival rate of 15% in other patients with T4 tumors
Metastasis			
Metastatic disease	M0: absent	M0: absent	. . .
	M1: present	M1a: local thoracic metastatic disease	Additional nodules in the contralateral lung (M1a) result in a median survival time of 10 months and a 1-year survival rate of 45%
		M1b: distant or extrathoracic metastatic disease	Extrathoracic metastases result in a median survival time of 6 months and a 1-year survival rate of 22%

*Sources.—References 4–7.

TNM Descriptors

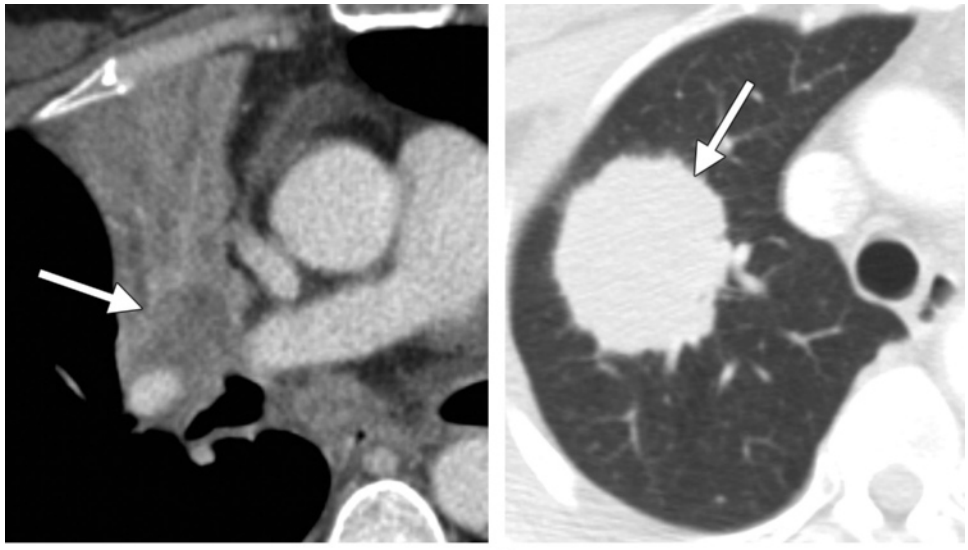
Tumor

The degree of primary tumor spread is represented by the T descriptor, which provides details regarding tumor size, local invasion, endobronchial location, and presence of separate tumor nodules. The T1 and T2 categories include subcategorization of size with new T1a, T1b, T2a, and T2b subdescriptors.

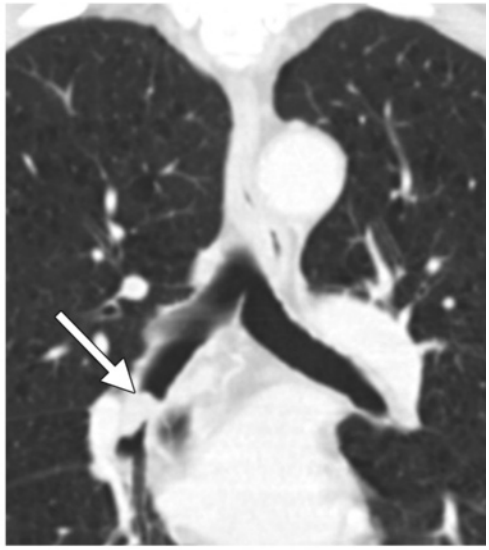


a. b.

Figure 2. Stage T1 tumors. **(a)** Chest CT scan shows a left lower lobe nodule (arrow) measuring less than 2 cm in size, a finding that is consistent with a stage T1a tumor (≤2 cm). **(b)** Chest CT scan obtained in a different patient shows a right upper lobe nodule (arrow) measuring 2.9 cm in size, a finding that is consistent with a stage T1b tumor (>2 cm but ≤3 cm).



a. b.



c.

Figure 3. Stage T2 tumors. **(a)** Chest CT scan shows a centrally located lung nodule (arrow) causing airway obstruction, with atelectasis or postobstructive pneumonia that does not, however, involve the entire lung. **(b)** Chest CT scan obtained in a different patient shows a mass in the right lung (arrow) measuring 4.8 cm, a finding that is consistent with a stage T2a tumor (>3 cm but ≤5 cm). **(c)** Coronal chest CT scan obtained in a third patient shows a nodule in the bronchus intermedius (arrow). The nodule is 4 cm from the carina (an endobronchial lesion > 2 cm from the carina is considered stage T2). At histopathologic analysis, the nodule proved to be a squamous cell carcinoma.

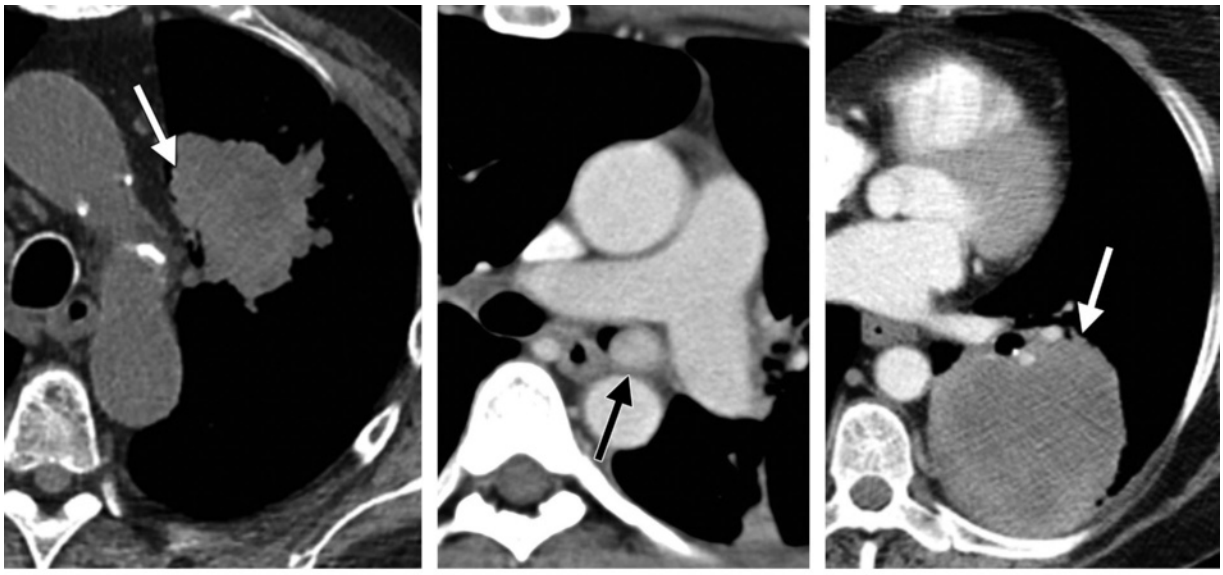


Figure 4. Stage T3 tumors. **(a)** Chest CT scan shows an irregular mass in the left upper lobe with suspicious local extension to the mediastinal pleura (arrow), a finding that was subsequently confirmed at surgery and histopathologic analysis. **(b)** Chest CT scan obtained in a different patient shows an endobronchial mass (arrow) less than 2 cm from the carina. Pathologic analysis confirmed malignant carcinoid tumor, which can be staged using the 7th edition of the TNM staging system. **(c)** Chest CT scan obtained in a third patient shows a left lower lobe mass over 7 cm in diameter (arrow).

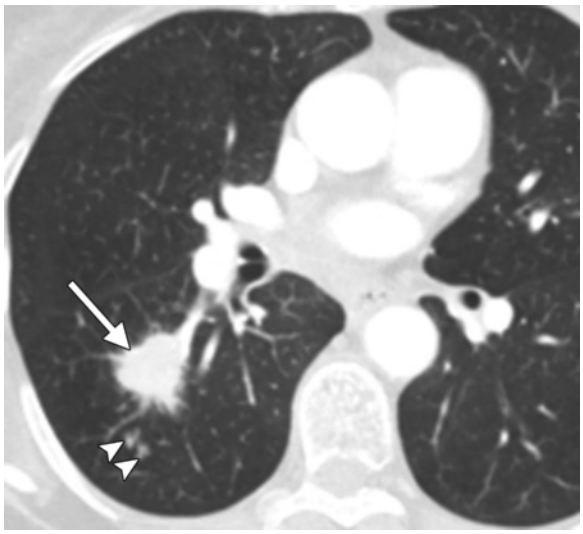


Figure 5. Stage T3 tumors. Chest CT scan shows a primary mass (arrow) with satellite nodules (arrowheads) in the right lower lobe. This is considered stage T3 disease in the 7th edition (stage T4 disease in the 6th edition).

Stage T1.—Tumors less than or equal to 2 cm in maximum diameter are stage T1a tumors; those larger than 2 cm but smaller than or equal to 3 cm are stage T1b tumors (Fig 2).

Tumors surrounded by lung or visceral pleura and endobronchial lesions without invasion proximal to a lobar bronchus are still considered stage T1 tumors as in the earlier edition.

Stage T2.—Tumors larger than 3 cm but smaller than or equal to 5 cm are stage T2a tumors (Fig 3a); those larger than 5 cm but smaller than or equal to 7 cm are stage T2b tumors.

Tumors with local invasion of the visceral pleura alone, with possible atelectasis and obstructive pneumonitis extending to the hilar region but not involving the entire lung, are considered stage T2 tumors. Endobronchial lesions more than 2 cm distal to the carina also belong in this category (Fig 3b, 3c).

Stage T3.—Tumors larger than 7 cm are now considered stage T3 tumors (Fig 4c). Separate tumor nodules in the same lobe as the primary lesion are now in the T3 category as well (Fig 5).

Endobronchial lesions less than 2 cm distal to the carina (Fig 4b); tumors with local invasion of the chest wall, diaphragm, mediastinal pleura, and parietal pericardium; superior sulcus

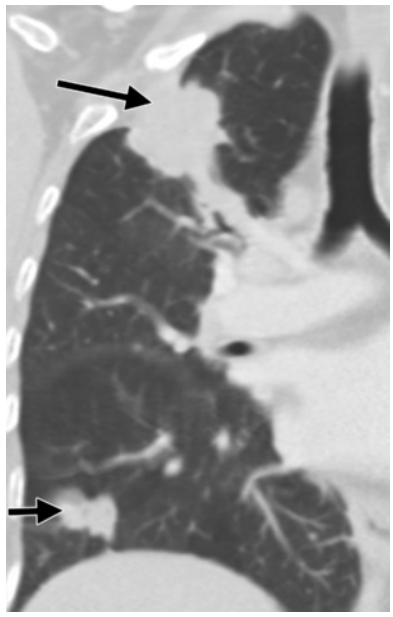


Figure 6. Stage T4 tumors. Chest CT scan shows a primary lung tumor in the right upper lobe (long arrow) with a smaller separate nodule in the right lower lobe (short arrow). In the 7th edition, this is considered stage T4 disease (stage M1 [metastatic] disease in the 6th edition).

tumors; and tumors with atelectasis and obstructive pneumonitis affecting the entire lung are still considered stage T3 neoplasms.

Stage T4.—Stage T4 tumors include separate tumor nodules in the same lung but not in the same lobe as the primary lesion, which were previously considered metastatic (M1) (Fig 6). In addition, the presence of a malignant pleural effusion, pleural dissemination, or pericardial disease now constitutes metastatic disease (M1a) and is no longer in the T category (3).

However, tumors of any size that demonstrate local invasion of the mediastinum or carina, trachea, heart, great vessels, esophagus, or vertebral bodies are still considered stage T4 tumors (Fig 7).

The 7th edition of the TNM staging system includes several changes to the T category (4).

Teaching Point

1. There are several new size criteria subcategories. The new tumor size limits of 2, 3, 5, and 7 cm (to differentiate between stages T1a, T1b, T2a, T2b, and T3) are markedly different from those in the 6th edition, in which only a single size limit of 3 cm is used for differentiation between T1 and T2 tumors.

Teaching Point

2. Because of statistically significant findings of survival rates, stage T4 disease is downgraded to stage T3 when satellite nodules are present in the same lobe as the primary lesion, and stage M1 disease is downgraded to stage T4 when nodules are present in the same lung but not the same lobe as the primary lesion.

Teaching Point

3. The presence of malignant pleural effusion, pleural dissemination, or pericardial disease is now considered metastatic disease—specifically, stage M1a for local intrathoracic disease—rather than stage T4 disease.

Node

Lymph nodes measuring 1 cm or more in the short axis are considered significant in size and suspicious for metastatic disease, although the predictive accuracy of this criterion is limited (10,11).

Teaching Point

Although the IASLC proposed a new lymph node map that reconciles the differences between the previous nodal maps and provides detailed anatomic and zonal definitions for all lymph node stations (Fig 8, Table 2), there are no changes to the N descriptors in the 7th edition of the TNM staging system. This retention

Figure 8. Drawings and chart illustrate the new IASLC lymph node map, which reconciles differences between earlier nodal maps including the Naruke and MD-ATS (Mountain-Dresler–American Thoracic Society) maps. The new nodal station numbers and names are shown, including the grouping of stations into "zones" for future prognostic analyses. *Ao* = aorta, *AP* = anteroposterior, *Eso* = esophagus, *mPA* = main pulmonary artery, *SVC* = superior vena cava, *T* = trachea. (Reprinted, with permission, from reference 8.)

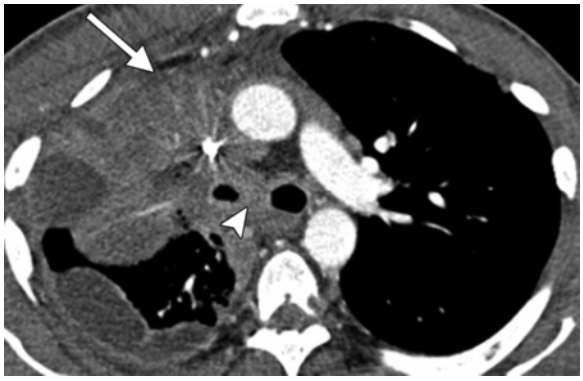
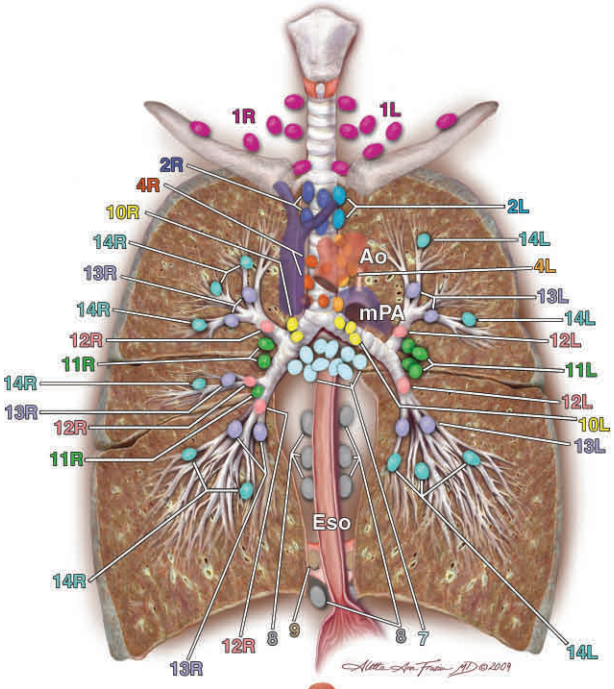
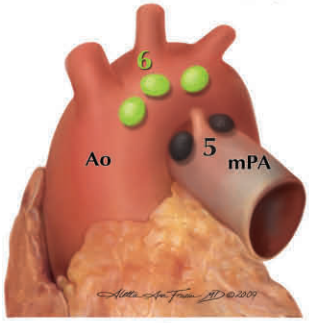
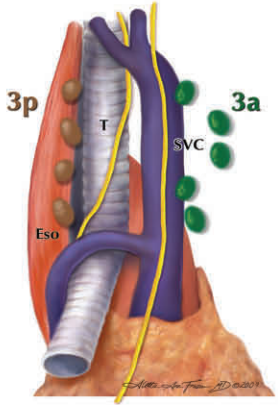


Figure 7. Stage T4 tumors. Chest CT scan shows a right upper lobe mass (arrow) with mediastinal and carinal invasion, ipsilateral loculated pleural effusion, and thickening and enhancement of the pleura. Note the tumor encasement and resultant narrowing of the right main-stem bronchus (arrowhead). The pleural thickening and enhancement, although nonspecific, are suggestive of metastatic pleural disease. In the 7th edition, proved pleural carcinomatosis is considered stage M1a disease (stage T4 in the 6th edition).







Supraclavicular zone
- 1 Low cervical, supraclavicular, and sternal notch nodes

SUPERIOR MEDIASTINAL NODES

Upper zone
- 2R Upper Paratracheal (right)
- 2L Upper Paratracheal (left)
- 3a Prevascular
- 3p Retrotracheal
- 4R Lower Paratracheal (right)
- 4L Lower Paratracheal (left)

AORTIC NODES

AP zone
- 5 Subaortic
- 6 Para-aortic (ascending aorta or phrenic)

INFERIOR MEDIASTINAL NODES

Subcarinal zone
- 7 Subcarinal

Lower zone
- 8 Paraesophageal (below carina)
- 9 Pulmonary ligament

N1 NODES

Hilar/Interlobar zone
- 10 Hilar
- 11 Interlobar

Peripheral zone
- 12 Lobar
- 13 Segmental
- 14 Subsegmental

Table 2
IASLC Anatomic Definitions for Lymph Node Stations

Location of Involved Lymph Nodes, Anatomic Definitions	Upper Border	Lower Border	Other Borders
	Station Number 1		
Low cervical, supraclavicular, sternal notch: 1R = right-sided, 1L = left-sided	Lower margin of the cricoid cartilage	Clavicles bilaterally; in the midline, upper border of the manubrium	Border between 1R and 1L = midline trachea
	Station Number 2		
Upper paratracheal:			
2R = right-sided	Apex of the right lung and the pleural space; in the midline, upper border of the manubrium	Intersection of the caudal margin of the innominate vein and the trachea	Includes nodes extending to the left lateral border of the trachea
2L = left-sided	Apex of the right lung and the pleural space; in the midline, upper border of the manubrium	Superior border of the aortic arch	. . .
	Station Number 3		
Prevascular and retrotracheal:			
3a = prevascular	Apex of the chest	Carina	Anterior border = posterior aspect of the sternum
3p = retrotracheal	Apex of the chest	Carina	Right posterior border = anterior border of the superior vena cava, left posterior border = left carotid artery
	Station Number 4		
Lower paratracheal:			
4R = right paratracheal and pretracheal nodes	Intersection of the caudal margin of the innominate vein and the trachea	Lower border of the azygos vein	Includes nodes extending to the left lateral border of the trachea
4L = nodes to the left of the left lateral border of the trachea, medial to the ligamentum arteriosum	Upper margin of the aortic arch	Upper rim of the left main pulmonary artery	. . .
	Station Number 5		
Subaortic (aortopulmonary window): Subaortic lymph nodes lateral to the ligamentum arteriosum	Lower border of the aortic arch	Upper rim of the left main pulmonary artery	. . .
	Station Number 6		
Paraaortic (ascending aorta or diaphragm): Lymph nodes anterior and lateral to the ascending aorta and aortic arch	Line tangential to the upper border of the aortic arch	Lower border of the aortic arch	. . .

(continued)

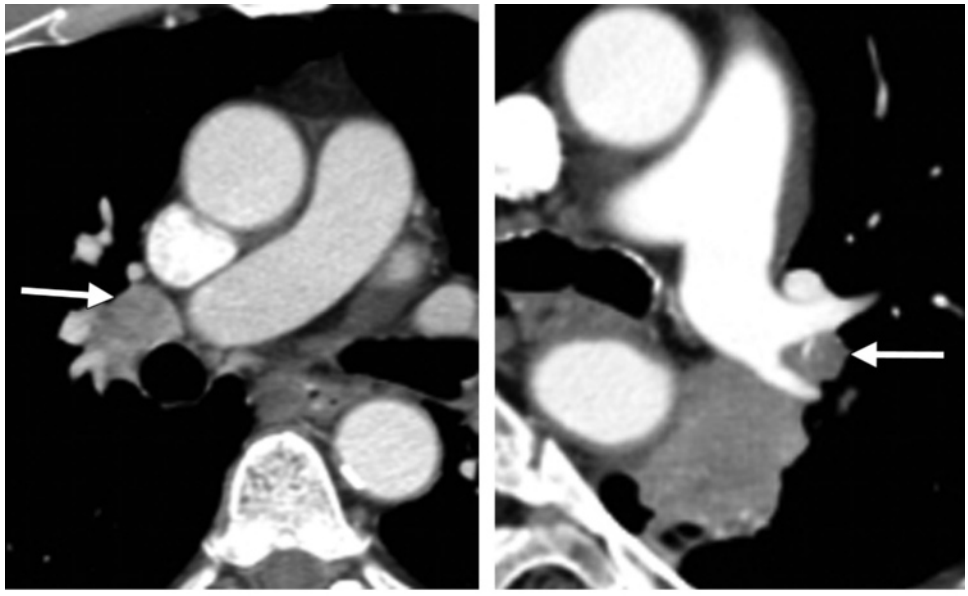
Table 2
IASLC Anatomic Definitions for Lymph Node Stations *(continued)*

Location of Involved Lymph Nodes, Anatomic Definitions	Upper Border	Lower Border	Other Borders
	Station Number 7		
Subcarinal	Carina of the trachea	7R = lower border of the bronchus intermedius, 7L = upper border of the lower lobe bronchus	. . .
	Station Number 8		
Paraesophaeal (below carina): Nodes lying adjacent to the esophageal wall and to the right or left of midline, excluding subcarinal nodes	Lower border of the bronchus intermedius (right), upper border of the lower lobe bronchus (left)	Diaphragm	. . .
	Station Number 9		
Pulmonary ligament: Nodes lying within the pulmonary ligament	Inferior pulmonary vein	Diaphragm	. . .
	Station Number 10		
Hilar: Nodes immediately adjacent to the mainstem bronchus and hilar vessels, including the proximal pulmonary veins and main pulmonary artery	Lower rim of the azygous vein (right), upper rim of the pulmonary artery (left)	Interlobar region	. . .
	Station Number 11		
Interlobar: Between the origin of the lobar bronchi (11s = between the upper lobe bronchus and the bronchus intermedius on the right, 11i = between the middle and lower lobe bronchi on the right)	. . .	. . .	. . .
	Station Number 12		
Lobar: Adjacent to the lobar bronchi	. . .	. . .	. . .
	Station Number 13		
Segmental: Adjacent to the segmental bronchi	. . .	. . .	. . .
	Station Number 14		
Subsegmental: Adjacent to the subsegmental bronchi	. . .	. . .	. . .

Sources.—References 7 and 8.
Note.—3a = 3 (anterior), 3p = 3 (posterior), 11i = 11 (inferior), 11s = 11 (superior).

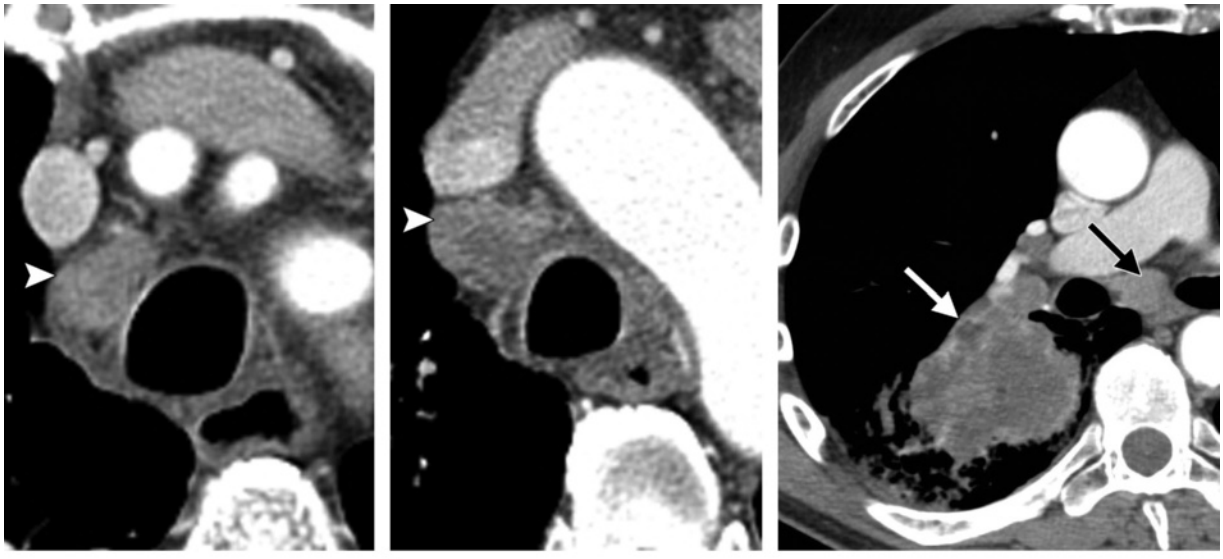
of the earlier descriptors is due to the difficulty of obtaining large patient samples with precise lymph node staging that could be analyzed across each T stage to obtain statistically valid results (8).

Stage N1.—Lymph nodes in the hilar, interlobar, lobar, segmental, and subsegmental regions are considered stage N1 disease (Fig 9).



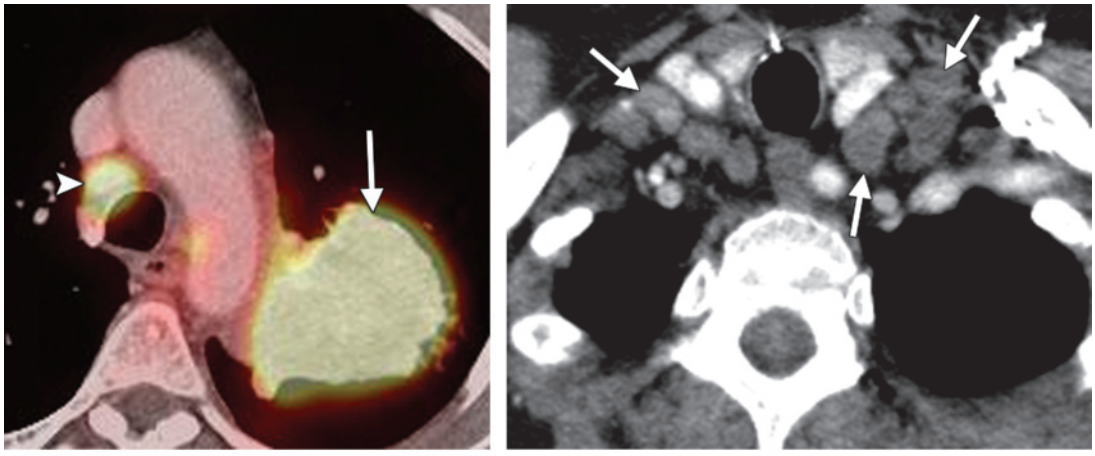
a. b.

Figure 9. Stage N1 lymph nodes. **(a)** Chest CT scan obtained in a patient with right-sided lung cancer shows an enlarged right hilar lymph node (level 10) (arrow) measuring 15 mm in the short axis. **(b)** Chest CT scan obtained in a different patient shows a left lower lobe mass and an ipsilateral enlarged interlobar lymph node (level 11) (arrow) measuring 11 mm in the short axis.



a. b. c.

Figure 10. Stage N2 lymph nodes. **(a)** Chest CT scan shows an enlarged (1.6-cm) right upper paratracheal lymph node (level 2) (arrowhead). **(b)** Chest CT scan obtained in a different patient shows an enlarged (1.5-cm) right lower paratracheal lymph node (level 4) (arrowhead). Like the lymph node in **a,** it is clearly to the right of the new border proposed by the IASLC (ie, the left lateral border of the trachea). **(c)** Chest CT scan obtained in a third patient shows a right lower lobe mass (white arrow) with an enlarged (1.6-cm) subcarinal lymph node (level 7) (black arrow).



a. b.

Figure 11. Stage N3 lymph nodes. **(a)** Axial PET/CT image of the chest shows a primary mass in the left lung (arrow) and a right lower paratracheal lymph node (arrowhead), both of which demonstrate intense radiotracer uptake. Metastatic involvement of the lymph node was confirmed at mediastinoscopic resection. **(b)** Chest CT scan obtained at the lung apex in a different patient shows enlarged bilateral supraclavicular lymph nodes (arrows). Metastatic involvement was confirmed at excisional biopsy.

Stage N2.—Lymph nodes in the ipsilateral mediastinum are considered stage N2 disease. Affected anatomic regions include the upper paratracheal, prevascular and retrotracheal, lower paratracheal, subcarinal, paraesophageal, and pulmonary ligament regions (Fig 10).

Stage N3.—Lymph nodes on the side opposite the primary tumor, and all significantly large lymph nodes in the ipsilateral or contralateral supraclavicular or scalene regions, are considered stage N3 disease (Fig 11).

The new nodal map proposed by the IASLC (Fig 8) (8) includes several major changes.

1. Anatomically distinct descriptions are provided for all lymph node stations, with the upper and lower anatomic borders described in particular detail (Table 2).

2. Supraclavicular and sternal notch lymph nodes, which were not previously considered to constitute a lymph node station, are categorized as level 1 nodes.

3. The boundary between the right- and left-sided level 2 and level 4 (upper and lower paratracheal) nodes is reset to the left lateral wall of the trachea due to lymphatic drainage patterns. The arbitrary midline division of the trachea created by the American Thoracic Society is eliminated.

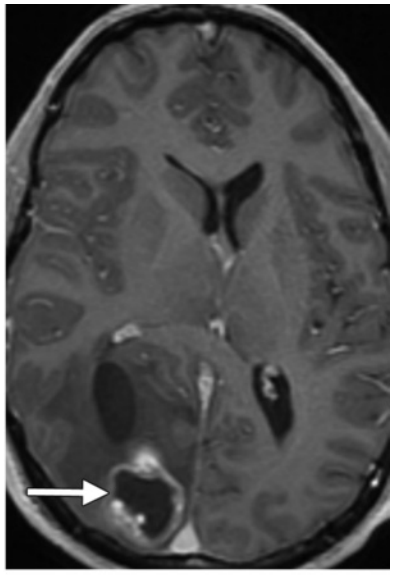
4. Certain lymph node stations are grouped into zones (Fig 8) for future prognostic analyses and do not represent current standard nomenclature.

Metastases

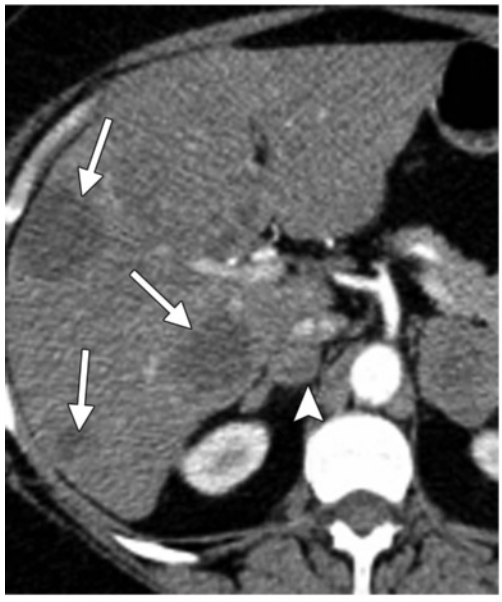
Nearly one-half of newly diagnosed lung cancers already demonstrate metastases within the lung, brain, liver, adrenal gland, and osseous structures (Figs 12, 13). Any metastatic disease is automatically designated stage IV disease and, with a few exceptions, is surgically unresectable.

Because of differences in prognosis, the M category is now subcategorized into intrathoracic metastasis (M1a) and extrathoracic metastasis (M1b), with the former having a better prognosis (5).

Stage M1a disease includes malignant pleural effusions, pleural dissemination, pericardial disease, and pulmonary nodules in the contralateral



a.



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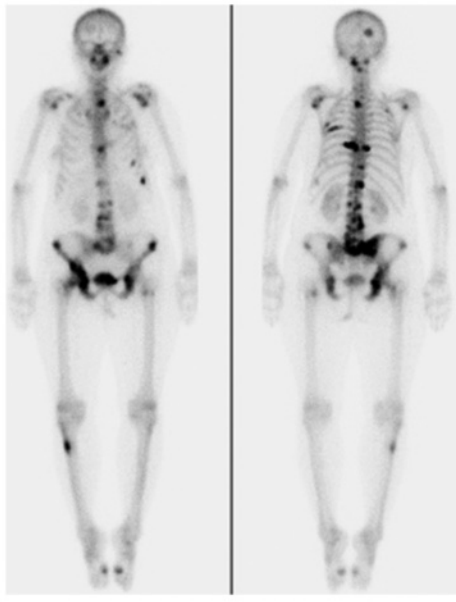


c.

Figure 12. Metastatic disease as seen at conventional imaging. **(a)** Axial contrast material–enhanced T1-weighted MR image of the brain obtained in a patient with known primary lung cancer shows a ring-enhancing lesion with surrounding edema in the right occipital pole (arrow), a finding that is consistent with metastasis. **(b)** Abdominal CT scan obtained in a different patient shows multiple enhancing hepatic masses (arrows) and a right adrenal mass (arrowhead), findings that are consistent with metastatic disease. **(c)** Technetium-99m methylene diphosphonate nuclear bone scintigrams obtained in a third patient with lung cancer show multifocal areas of abnormal radiotracer uptake in the axial and appendicular skeleton, findings that are consistent with metastases.

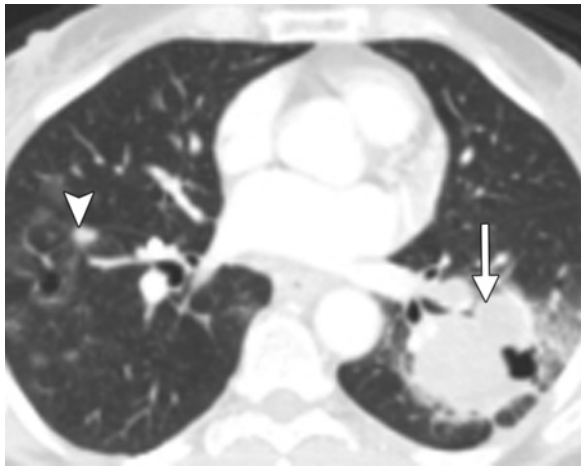


Figure 13. Separate tumor nodules. Chest CT scan shows a primary mass in the left lung (arrow) with a separate nodule in the right lung (arrowhead). This is stage M1a disease according to the 7th edition (stage M1 in the 6th edition) and involves intrathoracic spread rather than spread to distant extrathoracic sites.

Table 3
Stage Groupings in the 6th and 7th Editions of the TNM Staging System for Lung Cancer

Stage	6th Edition	7th Edition
IA	T1, N0, M0	T1a–T1b, N0, M0
IB	T2, N0, M0	T2a, N0, M0
IIA	T1, N1, M0	T1a–T1b, N1, M0
		T2a, N1, M0
		T2b, N0, M0
IIB	T2, N1, M0	**T2b, N1**, M0
	T3, N0, M0	T3, N0, M0
IIIA	T3, N1, M0	T1–T2, N2, M0
	T1–T3, N2, M0	T3, N1–N2, M0
		T4, N0–N1, M0
IIIB	T4, N0–N2, M0	**T4, N2**, M0
	T1–T4, N3, M0	T1–T4, N3, M0
IV	T1–T4, N0–N3, M1	T1–T4, N0–N3, M1a–M1b

Note.—Important changes are shown in boldface (3).

lung (Fig 13). Again, the addition of malignant pleural or pericardial disease to the M category is new. Stage M1b disease involves spread to the liver, adrenal gland, brain, bone, and other locations away from the chest (Fig 12).

The 7th edition of the TNM staging system includes some changes to the M category (5).

Teaching Point

1. Metastatic (M1) disease is subcategorized into M1a (intrathoracic spread) and M1b (disseminated disease involving extrathoracic spread) categories.

2. Malignant pericardial and pleural diseases are now considered to be metastatic (M1a) disease, rather than stage T4 disease.

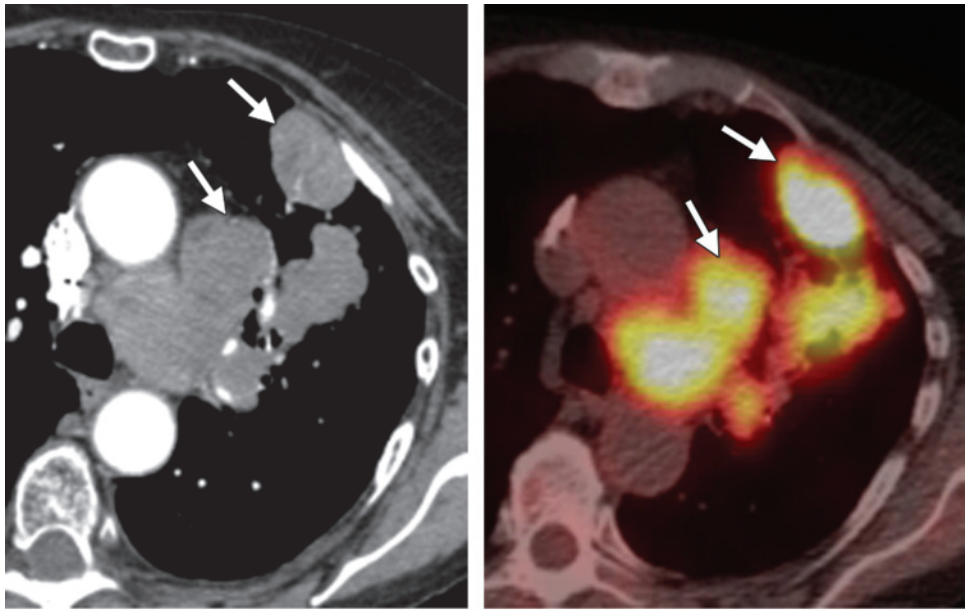
Synthesis in the TNM Classification System

Synthesizing the many possible combinations of T, N, and M descriptors into their appropriate stage groupings is crucial. Table 3 compares the stage groupings in the 6th edition with those in the 7th edition. Several changes have been made in an attempt to better align the stage groupings with prognosis and treatment (2,3). Most important, T2(a) N1 is stage IIA (rather than IIB) disease, and T4 N0 or N1 is stage IIIA (rather than IIIB) disease. These changes would be expected to influence treatment and to have prognostic value.

Small Cell Lung Cancer

Small cell lung cancer accounts for 15% of all lung cancers and is notorious for its rapid growth rate and its early dissemination to regional lymph nodes and distant sites (12). Approximately two-thirds of patients have extensive disease with hematogenous metastatic disease at the time of presentation, and only chemotherapy is suitable for these patients. Patients with tumors limited to one hemithorax, regional lymph node metastases involving hilar, ipsilateral, or contralateral mediastinal and supraclavicular nodes, and ipsilateral pleural effusion (regardless of whether cytologic findings are positive or negative) are treated with chemotherapy and radiation therapy (13).

Although the TNM descriptors are not commonly used in clinical practice for staging small cell lung cancer, current recommendations state that the 7th edition of the TNM staging system for non–small cell lung cancer can and should also be applied to small cell lung cancer, since increasing stage correlates with decreased survival times in patients with these tumors as well, thereby proving the usefulness of this criterion in determining prognosis. On the basis of the descriptors of the 7th edition of the TNM system,



a. b.

Figure 14. Small cell lung cancer. Chest CT scan **(a)** and corresponding PET/CT image **(b)** show a mass in the left lung (top arrow) with intense radiotracer uptake on the PET/CT image. The mass proved to be small cell lung cancer at pathologic analysis. Note the confluent ipsilateral prevascular (bottom arrow) and left paratracheal lymphadenopathy (N2), which shows intense uptake as well. The 7th edition of the TNM staging system can also be used for staging small cell lung cancer.

Vallières et al (12) have reported 5-year survival rates in patients with small cell lung cancer as follows: 56%, 57%, 38%, 40%, 12%, and 0% for patients with stage IA, IB, IIA, IIB, IIIA, and IIIB disease, respectively (Fig 14).

Carcinoid Tumor

Malignant carcinoid tumors represent only 1%–2% of all resected lung cancers and are relatively rare. The TNM staging system has not applied to carcinoid tumors in the past, although the 7th edition recommends their inclusion because all three descriptors are helpful in predicting prognosis (Fig 4). The estimated 5-year survival rates for patients with stage I, II, III, and IV bronchopulmonary carcinoid tumors were 93%, 85%, 75%, and 57%, respectively (14).

Bronchioloalveolar Carcinoma

Bronchioloalveolar carcinoma is a type of adenocarcinoma that typically shows a lepidic growth pattern without surrounding stromal or vascular invasion. At radiology, the presence of a pure ground-glass nodule, a nodule or mass with air bronchogram, or persistent masslike consolidation despite treatment with antibiotics should suggest the diagnosis. Although bronchioloalveolar carcinoma is more commonly associated with a high rate of false-negative findings at FDG PET, its staging is similar to that of other subtypes of non–small cell lung cancer. Pure bronchioloalveolar carcinoma reportedly accounts for approximately 5% of all non–small cell lung cancer tumors (15).

Staging Pitfalls

Nodal Metastatic Drainage Patterns

After draining to ipsilateral hilar lymph nodes, tumors from the right upper lobe drain to the right paratracheal nodes, those from the left upper lobe drain to the peri- and subaortic lymph nodes, and those from the middle and lower lobes drain to the subcarinal nodes. However, direct drainage to the mediastinal lymph nodes without drainage to the hilar and interlobar nodes sometimes occurs. This phenomenon, known as skip metastasis, most frequently involves tumors in the upper lobe and those with the histologic features of adenocarcinoma (8).

Incidental Pulmonary Nodules

In the 16%–28% of cases in which a lung cancer patient presents with other lung nodules, a diagnostic dilemma exists in determining whether these nodules represent metastases from the

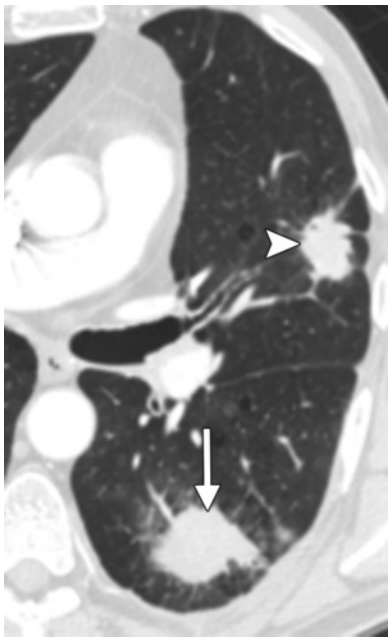


Figure 15. Second primary lung tumors. Chest CT scan shows synchronous but widely separated lung tumors. The pathology report on the pneumonectomy specimen revealed the upper lobe lesion (arrowhead) to be a poorly differentiated squamous cell carcinoma, and the lower lobe lesion (arrow) to be a moderately differentiated squamous cell carcinoma. The pathologist wrote, "The two carcinomas are physically distant from one another, show substantial morphologic differences, and are judged to be separate synchronous primaries."

primary tumor, multiple primary non–small cell lung cancer tumors (synchronous or metachronous), or benign lesions (16). Kim et al (16) reported that 96% of these separate nodules, all less than 10 mm in size, were of benign etiology, but recommended that the presence of these small nodules should not preclude surgical resection. Yuan et al (17) reported that coexisting small nodules were more likely to be malignant when located in the same lobe as the primary tumor. The presence of separate nodules in the same lobe does not in itself preclude resection by means of lobectomy in patients with primary lung cancer (18).

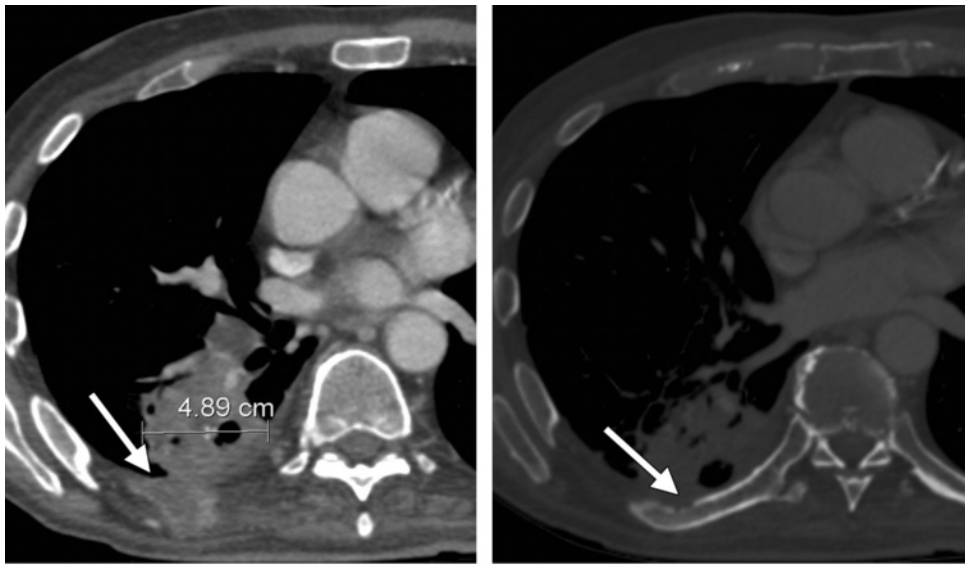
Second primary lung tumors such as synchronous (Fig 15) and metachronous tumors have been found in 1%–10% of cases and have a favorable prognosis compared with metastatic nodules (19). In the study by Yuan et al (17), synchronous tumors were more likely located in other lobes of the ipsilateral lung or in the contralateral lung.

The differentiation between synchronous multiple primary non–small cell lung cancer and pulmonary metastases is difficult. According to Martini and Melamed (20), synchronous tumors are present at the same time but are separate and have different histologic features. If the two tumors have similar histologic features, to be considered independent primary tumors, they must be located in different lungs, lobes, or segments; they must have no common lymphatic vessels; and no distinct metastases may be present. If these criteria are not met, the two tumors are considered to represent a primary tumor with metastatic disease. When second primary lung cancers are present, restaging may be necessary to identify all cases in which surgical resection is viable, with the intent to cure whenever possible (19,21,22).

Mediastinal Adenopathy

Compared with invasive mediastinal staging methods such as mediastinoscopy, CT and MR imaging lack the sensitivity and specificity for accurate mediastinal nodal staging in patients with non–small cell lung cancer (23–25). Some specific challenges include the presence of metastatic disease in normal-sized nodes (<1 cm in the short axis), increased difficulty in identifying disease in certain nodal stations, enlarged nodes that are simply hyperplastic or reactive in etiology, or the presence of obstructive pneumonitis or atelectasis (23,26–28).

FDG PET is a helpful tool in identifying mediastinal lymph node malignancy, with a sensitivity and specificity of 79% and 91%, respectively (compared with 60% and 77%, respectively, for CT) (29–31). PET has a negative predictive value of 98.4% in evaluating for mediastinal lymph nodes (32,33). FDG PET scans can be positive for large lymph nodes due to a reactive etiology, whereas they may be falsely negative for small (subcentimeter) metastatic lymph nodes. Therefore, mediastinoscopy remains the standard of reference, with a sensitivity of 80% and a specificity of 100% (32). It is important to differentiate



a. b.

Figure 16. Chest wall and pleural invasion. Chest CT scans obtained with a soft-tissue window **(a)** and a bone window **(b)** show a right upper lobe mass measuring 4.9 cm in diameter, with a chest wall mass (arrow in **a**) and associated bone destruction of the adjacent posterior rib (arrow in **b**). These findings are definitive for chest wall invasion.

N2 (at least stage IIIA) from N3 (at least stage IIIB) disease, since the latter is considered to be surgically unresectable. Furthermore, integrated PET/CT is the best noninvasive method for detecting nodal metastasis, since it provides spatially matched morphologic and functional data (34). Compared with mediastinoscopic and surgical staging, the accuracy of PET and PET/CT in lymph node staging was 56% and 78%, respectively (35).

Metastatic Disease

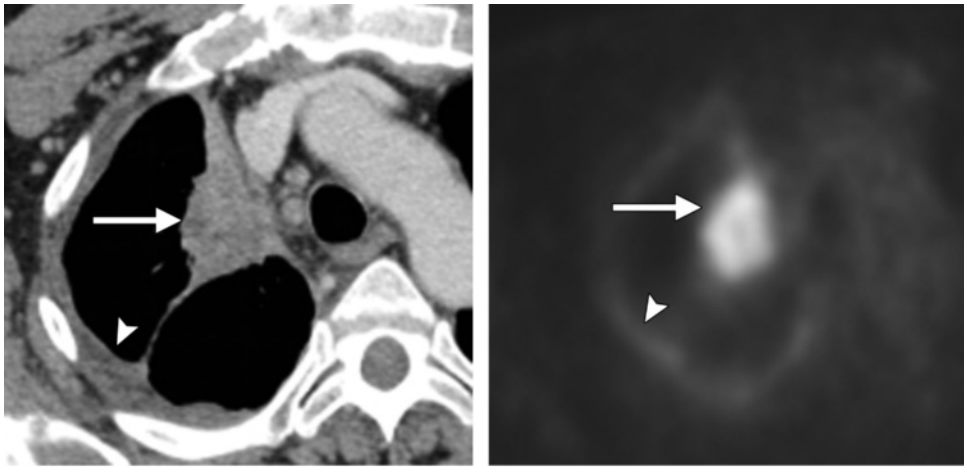
The overall accuracy of PET in staging metastatic disease is 94%, compared with 80% for conventional imaging. PET is superior to other imaging modalities such as CT and MR imaging in detecting metastatic disease to the adrenal gland, liver, and lung (25). Whole-body PET/CT has replaced traditional isotope bone scintigraphy in the assessment of osseous metastasis. It is important to note that conventional contrast-enhanced brain CT and MR imaging is the method of choice for the staging of brain tumors due to superior results in detecting brain metastasis compared with PET, which has a reported sensitivity of only 60% due to high glucose uptake in normal surrounding brain tissue (25,33). Nonetheless, a solitary distant metastatic focus in a patient with non–small cell lung cancer requires histopathologic confirmation, especially if doing so can mean the difference between surgical and nonsurgical treatment.

Chest Wall and Pleural Invasion

It is difficult to predict pleural involvement at CT, since contiguity of the neoplasm with the pleural surface is not necessarily equivalent to invasion (36). The main CT findings with higher positive predictive values for detecting pleural involvement are associated bone destruction or a chest wall mass (Fig 16). Other morphologic CT criteria, such as *(a)* extent of contact of the mass and its angle with the pleura and *(b)* the presence of a fat plane between the tumor and chest wall, are less helpful in the assessment of chest wall invasion, and further work-up is usually required in such cases (36).

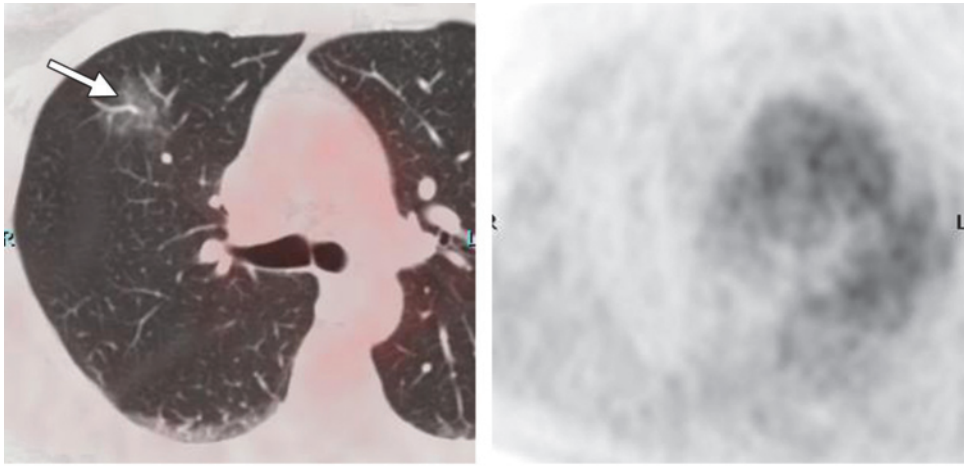
Pleural-Pericardial Metastasis

Pericardial effusion with enhancing nodules is highly suggestive of malignant involvement of the pericardium. Similarly, nodular and enhancing pleural thickening is suggestive of metastatic pleural disease (Fig 17). However, both CT and MR imaging findings are inconclusive for the determination of benign versus malignant pleural and pericardial disease. FDG PET has been shown to have a high sensitivity and negative predictive value in detecting pleural malignancy (37). Diagnostic thoracentesis is still essential in evaluating for the presence of malignant cells in lung cancer patients with a pleural effusion (33).



a. b.

Figure 17. Pleural metastasis. **(a)** Chest CT scan shows a right upper lobe mass (arrow) abutting the mediastinum, along with pleural thickening and effusion (arrowhead). **(b)** Axial FDG PET scan shows radiotracer uptake in the right upper lobe mass (arrow) and ipsilateral pleura (arrowhead). At thoracentesis, the pleural effusion proved to contain malignant adenocarcinoma cells from the primary tumor in the right upper lobe (cf **a**).



a. b.

Figure 18. Bronchioloalveolar carcinoma. **(a)** Axial chest PET/CT image shows a focal area of ground-glass attenuation in the right upper lobe (arrow) without architectural distortion of the lung parenchyma, a finding that was confirmed to be bronchioloalveolar carcinoma at pathologic analysis. **(b)** Axial FDG PET scan shows only normal physiologic cardiac uptake.

Limitations of PET

Negative PET findings in true lung cancer such as bronchioloalveolar carcinoma (Fig 18) and carcinoid tumor can be due to the biologic indolence of the tumor, technical limitations of PET, or lower overall tumor cell volume; however, such false-negative findings are usually suggestive of early-stage disease with a favorable prognosis (38–40). Because of their limited spatial resolution, PET scans can be falsely negative for pulmonary nodules or metastatic lymph nodes less than 1 cm in size (41,42). PET can also yield false-positive findings in the setting of inflammatory or infectious processes. Despite these limitations, any patient who is a potential surgical candidate should undergo PET/CT, the preferred noninvasive method for staging non–small cell lung cancer, since it improves preoperative staging and reduces the number of futile thoracotomies (34,43).

Staging-based Treatment Regimens

Early-stage disease, including stage IA, IB, IIA, IIB, and, in some cases, IIIA disease, is considered surgically resectable with a possible role for neoadjuvant or adjuvant chemotherapy and radiation therapy. Targeted therapy has also been approved for advanced disease (44). In patients with stage IIIB disease, surgical resection is considered impracticable, and chemotherapy–radiation therapy becomes the primary treatment (44,45). Patients with metastatic disease are considered to have stage IV disease and normally would not be surgical candidates, the main exceptions being patients with a solitary adrenal or brain metastatic focus. Long-term survival and improved quality of life after surgical resection have been demonstrated in a small percentage of such patients (46–49).

Conclusions

Radiologists must understand the details set forth in the TNM classification system and be familiar with the changes in the 7th edition, which attempts to better correlate disease with prognostic value and treatment strategy. By recognizing the relevant radiologic appearances of lung cancer, understanding the appropriateness of staging disease with the TNM classification system, and being familiar with potential imaging pitfalls, radiologists can make an important contribution to treatment and outcome in lung cancer patients.

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Lung Cancer Staging Essentials: The New TNM Staging System and Potential Imaging Pitfalls

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Page 1168
1. There are several new size criteria subcategories. The new tumor size limits of 2, 3, 5, and 7 cm (to differentiate between stages T1a, T1b, T2a, T2b, and T3) are markedly different from those in the 6th edition, in which only a single size limit of 3 cm is used for differentiation between T1 and T2 tumors.

Page 1168
2. Because of statistically significant findings of survival rates, stage T4 disease is downgraded to stage T3 when satellite nodules are present in the same lobe as the primary lesion, and stage M1 disease is downgraded to stage T4 when nodules are present in the same lung but not the same lobe as the primary lesion.

Page 1168
3. The presence of malignant pleural effusion, pleural dissemination, or pericardial disease is now considered metastatic disease—specifically, stage M1a for local intrathoracic disease—rather than stage T4 disease.

Page 1168 (Figure on page 1169, Table on pages 1170 and 1171)
Although the IASLC proposed a new lymph node map that reconciles the differences between the previous nodal maps and provides detailed anatomic and zonal definitions for all lymph node stations (Fig 8, Table 2), there are no changes to the N descriptors in the 7th edition of the TNM staging system.

Page 1175
1. Metastatic (M1) disease is subcategorized into M1a (intrathoracic spread) and M1b (disseminated disease involving extrathoracic spread) categories.