COLLEGE of AMERICAN PATHOLOGISTS

Protocol for the Examination of Specimens From Patients With Primary Non-Small Cell Carcinoma, Small Cell Carcinoma, or Carcinoid Tumor of the Lung

Based on AJCC/UICC TNM, 7th edition
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Procedure
• Resection

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The College of American Pathologists offers these protocols to assist pathologists in providing clinically useful and relevant information when reporting results of surgical specimen examinations of surgical specimens. The College regards the reporting elements in the "Surgical Pathology Cancer Case Summary" portion of the protocols as essential elements of the pathology report. However, the manner in which these elements are reported is at the discretion of each specific pathologist, taking into account clinician preferences, institutional policies, and individual practice.

The College developed these protocols as an educational tool to assist pathologists in the useful reporting of relevant information. It did not issue the protocols for use in litigation, reimbursement, or other contexts. Nevertheless, the College recognizes that the protocols might be used by hospitals, attorneys, payers, and others. Indeed, effective January 1, 2004, the Commission on Cancer of the American College of Surgeons mandated the use of the required data elements of the protocols as part of its Cancer Program Standards for Approved Cancer Programs. Therefore, it becomes even more important for pathologists to familiarize themselves with these documents. At the same time, the College cautions that use of the protocols other than for their intended educational purpose may involve additional considerations that are beyond the scope of this document.

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CAP Lung Protocol Revision History

Version Code
The definition of the version code can be found at www.cap.org/cancerprotocols.

Version: Lung 3.3.0.0

Summary of Changes
The following changes have been made since the June 2012 release.

Resection

Tumor Site
"Mainstem bronchus" was added, as follows:

Tumor Site
___ Upper lobe
___ Middle lobe
___ Lower lobe
___ Mainstem bronchus
___ Other(s) (specify): _____
___ Not specified

Histologic Type
Bronchioloalveolar carcinoma elements were deleted, and adenocarcinoma elements were updated, as follows:

…
___ Adenocarcinoma
___ Adenocarcinoma, lepidic predominant
___ Adenocarcinoma, acinar predominant
___ Adenocarcinoma, papillary predominant
___ Adenocarcinoma, solid predominant
___ Adenocarcinoma, micropapillary predominant
___ Minimally invasive adenocarcinoma
___ Adenocarcinoma in situ
___ Mucinous adenocarcinoma
___ Fetal adenocarcinoma
___ Enteric adenocarcinoma
…

Histologic Grade
This reporting element was changed from required to optional.

Margins
Specific reporting elements for "Parietal Pleural Margin" and "Chest Wall Margin" were deleted. Added "required only if applicable" to "Other Attached Tissue Margin" and deleted "Not applicable," as follows:

Other Attached Tissue Margin (required only if applicable)
Specify margin: _____
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
___ Involved by invasive carcinoma

Treatment Effect
Added "required only if applicable."

Lymph-Vascular Invasion
"Select all that apply" was added, and optional subelements were added under "Present," as follows:

Lymph-Vascular Invasion (select all that apply)
___ Not identified
___ Present
    + ___ Lymphatic
    + ___ Arterial
    + ___ Venous
___ Indeterminate

Ancillary Studies
All reporting elements were deleted, and the following note was added:
Note: For reporting cancer biomarker testing results, the CAP Lung Biomarker Template should be used.
Pending biomarker studies should be listed in the Comments section of this report.

Explanatory Notes

B. Histologic Type
The second sentence of the first paragraph was replaced with the following:
The International Association for the Study of Lung Cancer (IASLC)/American Thoracic Society (ATS)/European Respiratory Society (ERS) multidisciplinary classification of adenocarcinoma, published in 2011, is recommended for classification of adenocarcinomas.[6,7]

In the first sentence of the second paragraph, "bronchiolalveolar carcinoma" was replaced with "adenocarcinoma in situ," and the following sentence was added at the end of the paragraph:
The diagnoses of adenocarcinoma in situ and minimally invasive adenocarcinoma should only be made on solitary lesions of 3 cm diameter or less.

C. Histologic Grade
The following was added: There is no well-established system for grading of squamous cell carcinoma or adenocarcinoma of the lung. Several systems have been proposed utilizing architectural pattern, nuclear grade, and mitotic rate. The architectural pattern of adenocarcinoma shows prognostic reproducibility and may be utilized. In this system, lepidic pattern is classified as G1, acinar and papillary patterns as G2, and micropapillary, solid, and mucinous patterns as G3.[6]

K. Ancillary Studies
This note was deleted.

References
References #6 and 7 were added, and the remaining references renumbered accordingly. References #28 to 35 were deleted.

Surgical Pathology Cancer Case Summary

Protocol web posting date: October 2013

LUNG: Resection

Select a single response unless otherwise indicated.

Specimen
___ Lung
___ Lobe(s) of lung (specify): _____
___ Bronchus (specify): _____
___ Other (specify): _____
___ Not specified

Procedure
___ Major airway resection
___ Wedge resection
___ Segmentectomy
___ Lobectomy
___ Bilobectomy
___ Pneumonectomy
___ Other (specify): _____
___ Not specified

Specimen Integrity
___ Intact
___ Disrupted
___ Indeterminate

Specimen Laterality
___ Right
___ Left
___ Not specified

Tumor Site (select all that apply)
___ Upper lobe
___ Middle lobe
___ Lower lobe
___ Mainstem bronchus
___ Other(s) (specify): _____
___ Not specified

Tumor Size
Greatest dimension: ___ cm
+ Additional dimensions: ___ x ___ cm
___ Cannot be determined

Tumor Focality (Note A)

___ Unifocal
___ Separate tumor nodules in same lobe
___ Separate tumor nodules in different lobes (specify sites): _____
___ Synchronous carcinomas (specify sites): _____
___ Cannot be determined

Histologic Type (Note B)

___ Carcinoma, type cannot be determined
___ Non-small cell carcinoma, subtype cannot be determined
___ Small cell carcinoma
___ Combined small cell carcinoma (small cell carcinoma and non-small cell component) (specify type of non-small cell carcinoma component: _____)
___ Squamous cell carcinoma
___ Squamous cell carcinoma, papillary variant
___ Squamous cell carcinoma, clear cell variant
___ Squamous cell carcinoma, small cell variant
___ Squamous cell carcinoma, basaloid variant
___ Adenocarcinoma
___ Adenocarcinoma, lepidic predominant
___ Adenocarcinoma, acinar predominant
___ Adenocarcinoma, papillary predominant
___ Adenocarcinoma, solid predominant
___ Adenocarcinoma, micropapillary predominant
___ Minimally invasive adenocarcinoma
___ Adenocarcinoma in situ
___ Mucinous adenocarcinoma
___ Fetal adenocarcinoma
___ Enteric adenocarcinoma
___ Large cell carcinoma
___ Large cell neuroendocrine carcinoma
___ Combined large cell neuroendocrine carcinoma (specify type of other non-small cell carcinoma component: _____)
___ Basaloid carcinoma
___ Lymphoepithelioma-like carcinoma
___ Clear cell carcinoma
___ Large cell carcinoma with rhabdoid phenotype
___ Adenosquamous carcinoma
___ Sarcomatoid carcinoma
___ Pleomorphic carcinoma
___ Spindle cell carcinoma
___ Giant cell carcinoma
___ Carcinosarcoma
___ Pulmonary blastoma
___ Typical carcinoid tumor
___ Atypical carcinoid tumor
___ Mucoepidermoid carcinoma
___ Adenoid cystic carcinoma
___ Epithelial-myoepithelial carcinoma
___ Other (specify): _____

+ Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

+ Histologic Grade (Note C)

+ ___ Not applicable
+ ___ GX: Cannot be assessed
+ ___ G1: Well differentiated
+ ___ G2: Moderately differentiated
+ ___ G3: Poorly differentiated
+ ___ G4: Undifferentiated
+ ___ Other (specify): _____

Visceral Pleura Invasion (Note D)

___ Not identified
___ Present
___ Indeterminate

Tumor Extension (select all that apply) (Note E)

___ Not applicable
___ Not identified
___ Superficial spreading tumor with invasive component limited to bronchial wall
___ Tumor involves main bronchus 2 cm or more distal to the carina
___ Parietal pleura
___ Chest wall
  + Specify involved structure(s): _____
___ Diaphragm
___ Mediastinal pleura
___ Phrenic nerve
___ Parietal pericardium
___ Tumor in the main bronchus less than 2 cm distal to the carina but does not involve the carina
___ Mediastinum
  + Specify involved structure(s): _____
___ Heart
___ Great vessels
___ Trachea
___ Esophagus
___ Vertebral body
___ Carina
___ Other (specify): _____

Margins (select all that apply) (Note F)

If all margins uninvolved by invasive carcinoma:
  Distance of invasive carcinoma from closest margin: ___ mm
  Specify margin: _____

<u>Bronchial Margin</u>

___ Not applicable
___ Cannot be assessed
___ Uninvolved by invasive carcinoma and carcinoma in situ
___ Involved by invasive carcinoma
___ Involved by carcinoma in situ

Vascular Margin
___ Not applicable
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
___ Involved by invasive carcinoma

Parenchymal Margin
___ Not applicable
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
___ Involved by invasive carcinoma

Other Attached Tissue Margin (required only if applicable)
Specify margin: _____
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
___ Involved by invasive carcinoma

Treatment Effect (required only if applicable) (Note G)
___ Cannot be determined
___ Greater than 10% residual viable tumor
___ Less than 10% residual viable tumor

+ Tumor Associated Atelectasis or Obstructive Pneumonitis (Note H)
+ ___ Extends to the hilar region but does not involve entire lung
+ ___ Involves entire lung

Lymph-Vascular Invasion (select all that apply) (Note I)
___ Not identified
___ Present
    + ___ Lymphatic
    + ___ Arterial
    + ___ Venous
___ Indeterminate

+ Lymph Nodes (Note J)
+ Extranodal extension
+ ___ Not identified
+ ___ Present

Pathologic Staging (pTNM) (Note J)

TNM Descriptors (required only if applicable) (select all that apply)
___ m (multiple primary tumors)
___ r (recurrent)
___ y (posttreatment)

Primary Tumor (pT)
___ pTX: Cannot be assessed, or tumor proven by presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
___ pT0: No evidence of primary tumor
___ pTis: Carcinoma in situ

___ pT1a: Tumor 2 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); or
Superficial spreading tumor of any size with its invasive component limited to the bronchial wall, which may extend proximally to the main bronchus

___ pT1b: Tumor greater than 2 cm, but 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)

___ pT2a: Tumor greater than 3 cm, but 5 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); or
Tumor 5 cm or less in greatest dimension with any of the following features of extent: involves main bronchus, 2 cm or more distal to the carina; invades the visceral pleura; associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung

___ pT2b: Tumor greater than 5 cm, but 7 cm or less in greatest dimension

___ pT3: Tumor greater than 7 cm in greatest dimension; or
Tumor of any size that directly invades any of the following: parietal plural chest wall (including superior sulcus tumors), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium; or
Tumor of any size in the main bronchus less than 2 cm distal to the carina but without involvement of the carina; or
Tumor of any size associated with atelectasis or obstructive pneumonitis of the entire lung; or
Tumors of any size with separate tumor nodule(s) in same lobe

___ pT4: Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina; or
Tumor of any size with separate tumor nodule(s) in a different lobe of ipsilateral lung (Note A)

<u>Regional Lymph Nodes (pN)</u>

___ pNX: Cannot be assessed

___ pN0: No regional lymph node metastasis

___ pN1: Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes, and intrapulmonary nodes, including involvement by direct extension

___ pN2: Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)

___ pN3: Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

___ No nodes submitted or found

Number of Lymph Nodes Examined

Specify: ____

___ Number cannot be determined (Note J) (explain): _____

Number of Lymph Nodes Involved

Specify: ____

___ Number cannot be determined (Note J) (explain): _____

If lymph node(s) involved, specify involved nodal station(s): _____

+ Data elements preceded by this symbol are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

Distant Metastasis (pM)
___ Not applicable
___ pM1: Distant metastasis
+ Specify site(s), if known: _____
___ pM1a: Separate tumor nodule(s) in contralateral lung; tumor with pleural nodules or malignant pleural (or pericardial) effusion (Note A)
___ pM1b: Distant metastases (in extrathoracic organs)

+ Additional Pathologic Findings (select all that apply)
+ ___ None identified
+ ___ Atypical adenomatous hyperplasia
+ ___ Squamous dysplasia
+ ___ Metaplasia (specify type): _____
+ ___ Diffuse neuroendocrine hyperplasia
+ ___ Inflammation (specify type): _____
+ ___ Emphysema
+ ___ Other (specify): _____

+ Ancillary Studies
Note: For reporting cancer biomarker testing results, the CAP Lung Biomarker Template should be used. Pending biomarker studies should be listed in the Comments section of this report.

+ Comment(s)

Explanatory Notes

A. Tumor Focality

There is evidence that patients with multiple tumor nodules of similar histology in the same lobe have markedly better survival than patients with tumors that meet the American Joint Committee on Cancer (AJCC) 7th edition TNM classification criteria for T4 (ie, invasion of mediastinal structures), and, in fact, their survival is similar to patients categorized as T3 in the AJCC 6th edition. For this reason, the presence of grossly recognizable multiple tumor nodules of similar histology in the same lobe are to be categorized as T3.[1] Survival among patients with multiple tumor nodule(s) of similar histology in ipsilateral separate lobes is similar to patients classified as T4, and therefore such tumors are to be categorized as T4.[1,2] However, if separate tumors that are of similar histology in different segments, lobes, or lungs show an origin from carcinoma in situ, no carcinoma in lymphatics common to both tumors, and no extrapulmonary metastases at the time of diagnosis, they should be categorized as synchronous primary carcinomas and staged independently.[3] Physically distinct and separate tumors of different histologic types are generally considered separate synchronous primaries and are staged separately.[1-3] In such cases, the highest T category is reported, followed in parentheses by multiplicity or number of tumors (eg, T2(m) or T2(5)).

B. Histologic Type

For consistency in reporting, the histologic classification published by the World Health Organization (WHO) for tumors of the lung, including carcinoids, is recommended.[4,5] The International Association for the Study of Lung Cancer (IASLC)/American Thoracic Society (ATS)/European Respiratory Society (ERS) multidisciplinary classification of adenocarcinoma, published in 2011, is recommended for classification of adenocarcinomas.[6,7] This protocol does not preclude the use of other systems of classification of histologic types.[8]

The diagnosis of adenocarcinoma in situ requires exclusion of stromal, vascular, and pleural invasion—a requirement that demands that the tumor be evaluated histologically in its entirety.[4] It is therefore recommended that a definitive diagnosis of bronchioloalveolar adenocarcinoma not be made on specimens in which the tumor is incompletely represented. The diagnoses of adenocarcinoma in situ and minimally invasive adenocarcinoma should only be made on solitary lesions of 3 cm diameter or less.

C. Histopathologic Grade (G)

To standardize histologic grading, the following grading system is recommended.[4]

Grade X (GX): Cannot be assessed
Grade 1 (G1): Well differentiated
Grade 2 (G2): Moderately differentiated
Grade 3 (G3): Poorly differentiated
Grade 4 (G4): Undifferentiated

Undifferentiated (grade 4) is reserved for carcinomas that show minimal or no specific differentiation in routine histologic preparations. According to the definition of grading, a squamous cell carcinoma or an adenocarcinoma arising in the lung can be classified only as grade 1, grade 2, or grade 3, because by definition these tumors show squamous or glandular differentiation, respectively. If there are variations in the differentiation of a tumor, the least favorable variation is recorded as the grade, using grades 1 through 3. By definition, small cell and large cell carcinomas of the lung are assigned grade 4, because they are high-grade tumors with poor prognosis. There is no well-established system for grading of squamous cell carcinoma or adenocarcinoma of the lung. Several systems have been proposed utilizing architectural pattern, nuclear grade, and mitotic rate. The architectural pattern of adenocarcinoma shows prognostic reproducibility and may be utilized. In this system, lepidic pattern is

classified as G1, acinar and papillary patterns as G2, and micropapillary, solid, and mucinous patterns as G3.[6]

D. Visceral Pleural Invasion

The presence of visceral pleural invasion by tumors smaller than 3 cm changes the T category from pT1 to pT2 and increases the stage from IA to IB in patients with N0, M0 disease or stage IIA to IIB in patients with N1, M0 disease (M0 is defined as no distant metastasis).[1] Studies have shown that tumors smaller than 3 cm that penetrate beyond the elastic layer of the visceral pleura behave similarly to similar-size tumors that extend to the visceral pleural surface.[9,10] Visceral pleural invasion should therefore be considered present not only in tumors that extend to the visceral pleural surface, but also in tumors that penetrate beyond the elastic layer of the visceral pleura (Figure).[9-11] Elastic stains may aid in the assessment of visceral pleural invasion.[9,12]

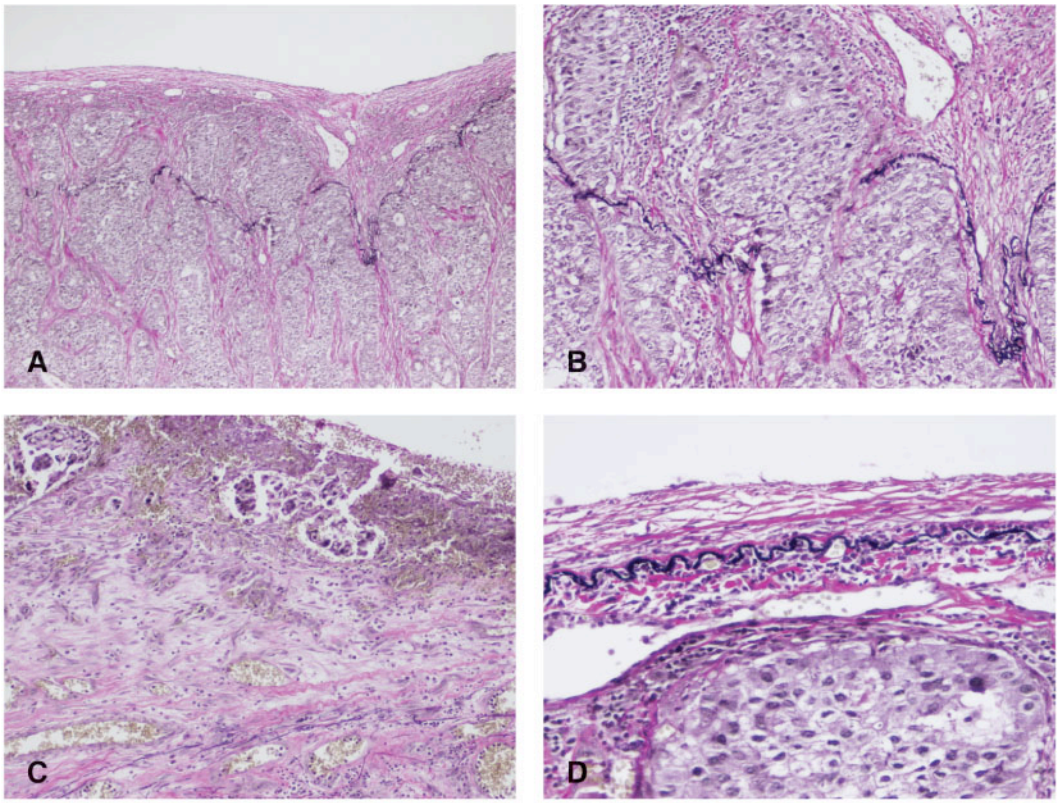

Figure. Types of visceral pleural invasion. Staining for elastin (eg, elastic-Van Gieson [EVG] stain) can aid in detection of visceral pleural invasion where it is indeterminate by hematoxylin-eosin (H&E) stain. A and B. Visceral pleural invasion is present when a tumor penetrates beyond the elastic layer of the visceral pleura (type PL1 pleural invasion) C. Tumor extension to the visceral pleural surface is also categorized as visceral pleural invasion (type PL2). Both types of visceral pleural invasion raise the T category of otherwise T1 tumors to T2. D. Visceral pleural invasion is categorized as absent in tumors that do not penetrate the visceral pleural elastic layer (type PL0). (Original magnifications x200 [A], x400 [B and C], x600 [D]).

Based on available data, a tumor with local invasion of another ipsilateral lobe without tumor on the visceral pleural surface should be classified as T2.[12]

Pleural tumor foci that are separate from direct pleural invasion should be categorized as M1a.[2]

E. Tumor Extension

According to the AJCC, direct invasion of the parietal pleura is categorized as T3, as is direct invasion of the chest wall.[13] Although not required, specifying the chest wall structures directly invaded by tumor (eg, intercostal muscle[s], rib[s], pectoralis muscle, latissimus muscle, serratus muscle) may facilitate patient management.

In addition to containing the heart and great vessels, the mediastinum includes the thymus and other structures between the lungs, direct invasion of any of which is considered T4.

Occasionally, lung cancer specimens consist of en bloc resections that incorporate other structures directly invaded by tumor that are not referred to in AJCC pathologic staging, but are discussed under the clinical staging section of the AJCC manual.[13] The T categories that correspond to direct invasion of these structures are summarized in the collaborative staging manual.[14] These should be reported under the "other" designation and include the following:

- Tumors with direct invasion of the phrenic nerve or brachial plexus (inferior branches or not otherwise specified) from the superior sulcus are categorized as T3.
- Superior sulcus tumors with encasement of subclavian vessels or unequivocal involvement of the superior branches of the brachial plexus are categorized as T4.
- Direct invasion of the visceral pericardium or cervical sympathetic, recurrent laryngeal, or vagus nerve(s) is considered T4.

F. Margins

Surgical margins represent sites that have either been cut or bluntly dissected by the surgeon to resect the specimen. The presence of tumor at a surgical margin is an important finding, because there is the potential for residual tumor remaining in the patient in the area surrounding a positive margin. Peripheral wedge resections contain a parenchymal margin, which is represented by the tissue at the staple line(s). Lobectomy and pneumonectomy specimens contain bronchial and vascular margins, and depending on the completeness of the interlobar fissures and other anatomic factors, may also contain parenchymal margins in the form of staple lines. En bloc resections in which extrapulmonary structures are part of the specimen contain additional margins (eg, parietal pleura, chest wall) that should be designated by the surgeon for appropriate handling. This includes cases in which the visceral pleura is adherent to the parietal pleura. Note that the visceral pleura is not a surgical margin.

G. Treatment Effect

For patients who have received neoadjuvant chemotherapy and/or radiation therapy before surgical resection, quantifying the extent of therapy-induced tumor regression provides prognostically relevant information.[15] A "y" prefix is applied to the TNM classification in such cases (see Note J).

H. Tumor Associated Atelectasis or Obstructive Pneumonitis

Although the presence and extent of obstructive pneumonitis associated with tumor can sometimes be determined in pneumonectomy specimens, accurate assessment of tumor-associated atelectasis or obstructive pneumonitis typically requires integration of radiographic information.[16]

I. Vascular/Lymphatic Invasion

There is data showing that lymphovascular invasion by tumor may represent an unfavorable prognostic finding.[17] Angiolymphatic invasion does not change the pT and pN classifications or the TNM stage grouping.

J. TNM and Stage Grouping

The TNM staging system of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) is recommended for non-small cell lung cancer.[13,18] Small cell lung

cancer has been more commonly classified according to a separate staging system as either "limited" or "extensive" disease, but based on analysis of the International Association for the Study of Lung Cancer (IASLC) database, TNM staging is also recommended for small cell lung cancer.[19,20] Carcinoid and atypical carcinoid tumors should also be classified according to the TNM Staging System.

By AJCC/UICC convention, the designation "T" refers to a primary tumor that has not been previously treated. The symbol "p" refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathologic staging is usually performed after surgical resection of the primary tumor. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumor has been completely removed. If a biopsied tumor is not resected for any reason (eg, when technically unfeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

T Category Considerations

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 classified as T1.[13]

Most pleural effusions with lung cancer are due to tumor. However, in a few patients, multiple cytopathologic examinations of pleural fluid are negative for tumor, the fluid is nonbloody and is not an exudate. Where these elements and clinical judgment dictate that the effusion is not related to the tumor, the effusion should be excluded as a staging element, and the tumor should be classified as T1, T2, or T3.[13]

Although pneumonectomy specimens allow assessment of tumor involvement of a main bronchus, determining the distance to the carina, which is necessary to accurately assign a T category for centrally located tumors, typically requires consultation with the surgeon, bronchoscopist, or radiologist.[21]

A number of other T category considerations are addressed above (see Notes A, D, E, and G).

N Category Considerations

Although extranodal extension of a positive mediastinal lymph node may represent an unfavorable prognostic finding, it does not change the pN classification or the TNM stage grouping.[22-25] Extranodal extension refers to the extension of metastatic intranodal tumor beyond the lymph node capsule into the surrounding tissue. Direct extension of a primary tumor into a nearby lymph node does not qualify as extranodal extension.

In certain situations, in particular when lymph nodes are obtained by mediastinoscopy, it may not be possible to ascertain the actual number of nodes submitted for evaluation (unless it is specified by the surgeon), as the pieces of tissue submitted may represent multiple discrete nodes or multiple fragments of a single node. If nodal involvement is identified in this setting, the lymph node station(s) (see below) involved, if known, should be reported.

The anatomic classification of regional lymph nodes proposed by the International Association for the Study of Lung Cancer (IASLC) is shown below, which reconciles differences between the Naruke and Mountain/Dresler lymph node maps.[13,26,27]

N2 Nodes

Station 1 Lower cervical, supraclavicular, and sternal notch nodes
Upper border: lower margin of cricoid cartilage
Lower border: clavicles bilaterally and, in the midline, the upper border of the manubrium, 1R designates right-sided nodes, 1L, left-sided nodes in this region

Station 2 Upper paratracheal nodes
2R: Upper border: apex of lung and pleural space
Lower border: intersection of caudal margin of innominate vein with the trachea
2L: Upper border: apex of the lung and pleural space
Lower border: superior border of the aortic arch

Station 3 Prevascular and retrotracheal nodes: 3A: prevascular; 3P: retrotracheal

Station 4 Lower paratracheal nodes:

4R: includes right paratracheal nodes, and pretracheal nodes extending to the left lateral border of trachea
Upper border: lower border of origin of innominate artery
Lower border: lower border of azygos vein
4L: includes nodes to the left of the left lateral border of the trachea, medial to the ligamentum arteriosum
Upper border: upper margin of the aortic arch
Lower border: upper rim of the left main pulmonary artery

Station 5 Subaortic nodes (aorto-pulmonary window): Subaortic nodes are lateral to the ligamentum arteriosum
Upper border: the lower border of the aortic arch
Lower border: upper rim of the left main pulmonary artery

Station 6 Para-aortic nodes (ascending aorta or phrenic): Nodes lying anterior and lateral to the ascending aorta and the aortic arch
Upper border: a line tangential to the upper border of the aortic arch
Lower border: the lower border of the aortic arch

Station 7 Subcarinal nodes
Upper border: the carina of the trachea
Lower border: the upper border of the lower lobe bronchus on the left; the lower border of the bronchus intermedius on the right

Station 8 Paraesophageal nodes (below carina): Nodes lying adjacent to the wall of the esophagus and to the right or left of the midline, excluding subcarinal nodes
Upper border: the upper border of the lower lobe bronchus on the left; the lower border of the bronchus intermedius on the right
Lower border: the diaphragm

Station 9 Pulmonary ligament nodes: Nodes lying within the pulmonary ligament
Upper border: the inferior pulmonary vein
Lower border: the diaphragm

N1 Nodes

Station 10 Hilar nodes: Nodes immediately adjacent to the mainstem bronchus and hilar vessels including the proximal portions of the pulmonary veins and main pulmonary artery
Upper border: the lower rim of the azygos vein on the right; upper rim of the pulmonary artery on the left
Lower border: interlobar region bilaterally

Station 11 Interlobar nodes: Nodes lying between the origin of the lobar bronchi

Optional notations for subcategories of Station 11:

11s	between the upper lobe bronchus and bronchus intermedius on the right
11i	between the middle and lower lobe bronchi on the right
Station 12	Lobar nodes: Nodes adjacent to the lobar bronchi
Station 13	Segmental nodes: Nodes adjacent to the segmental bronchi
Station 14	Subsegmental nodes: Nodes around the subsegmental bronchi

Isolated tumor cells (ITCs) are single tumor cells or small clusters of cells not more than 0.2 mm in greatest dimension detected on routine sections or more commonly by immunohistochemistry or molecular methods. ITCs in lymph nodes or at distant sites should be classified as N0 or M0, respectively.[13]

The following classification of ITCs may be used:

pN0(i-)	No regional lymph node metastasis histologically, negative morphological findings for ITC
pN0(i+)	No regional lymph node metastasis histologically, positive morphological findings for ITC
pN0(mol-)	No regional lymph node metastasis histologically, negative nonmorphological findings for ITC
pN0(mol+)	No regional lymph node metastasis histologically, positive nonmorphological findings for ITC

TNM Stage Groupings

Stage IA	T1a	N0	M0
	T1b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T1a	N1	M0
	T1b	N1	M0
	T2a	N1	M0
	T2b	N0	M0
Stage IIB	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a	N2	M0
	T1b	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1-2	M0
	T4	N0-1	M0
Stage IIIB	T1a	N3	M0
	T1b	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N3	M0
	T4	N2-3	M0
Stage IV	Any T	Any N	M1a or M1b

TNM Descriptors

For identification of special cases of TNM or pTNM classifications, the "m" suffix and "y," and "r" prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The "m" suffix indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM (see Note A).

The "y" prefix indicates those cases in which classification is performed during or following initial multimodality therapy (ie, neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and

radiation therapy). The cTNM or pTNM category is identified by a "y" prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The "y" categorization is not an estimate of tumor prior to multimodality therapy (ie, before initiation of neoadjuvant therapy) (see Note F).

The "r" prefix indicates a recurrent tumor when staged after a documented disease-free interval, and is identified by the "r" prefix: rTNM.

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