

Protocol for the Examination of Resection Specimens from Patients with Primary Non-Small Cell Carcinoma, Small Cell Carcinoma, or Carcinoid Tumor of the Lung

Version: 5.1.0.0

Protocol Posting Date: September 2025

CAP Laboratory Accreditation Program Protocol Required Use Date: June 2026

The changes included in this current protocol version affect accreditation requirements. The new deadline for implementing this protocol version is reflected in the above accreditation date.

For accreditation purposes, this protocol should be used for the following procedures AND tumor types:

Procedure	Description
Resection	Includes pneumonectomy, lobectomy, segmentectomy, and wedge resection
Tumor Type	Description
Carcinoma	Includes non-small cell carcinoma, small cell carcinoma, and carcinoid tumor of the lung

This protocol is NOT required for accreditation purposes for the following:

Procedure	
Biopsy	
Primary resection specimen with no residual cancer (e.g., following neoadjuvant therapy)	
Cytologic specimens	

The following tumor types should NOT be reported using this protocol:

Tumor Type
Mesothelioma (consider the Diffuse Pleural Mesothelioma protocol)
Lymphoma (consider the Precursor and Mature Lymphoid Malignancies protocol)
Sarcoma (consider the Soft Tissue protocol)

Version Contributors

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Glossary:

Author: Expert who is a current member of the Cancer Committee, or an expert designated by the chair of the Cancer Committee. **Expert Contributors:** Includes members of other CAP committees or external subject matter experts who contribute to the current version of the protocol.

^{*} Denotes primary author.

Accreditation Requirements

Synoptic reporting with core and conditional data elements for designated specimen types* is required for accreditation.

- Data elements designated as core must be reported.
- Data elements designated as conditional only need to be reported if applicable.
- Data elements designated as <u>optional</u> are identified with "+". Although not required for accreditation, they may be considered for reporting.

This protocol is not required for recurrent or metastatic tumors resected at a different time than the primary tumor. This protocol is also not required for pathology reviews performed at a second institution (i.e., second opinion and referrals to another institution).

Full accreditation requirements can be found on the CAP website under <u>Accreditation Checklists</u>. A list of core and conditional data elements can be found in the Summary of Required Elements under Resources on the CAP Cancer Protocols <u>website</u>.

*Includes definitive primary cancer resection and pediatric biopsy tumor types.

Synoptic Reporting

All core and conditionally required data elements outlined on the surgical case summary from this cancer protocol must be displayed in synoptic report format. Synoptic format is defined as:

- Data element: followed by its answer (response), outline format without the paired Data element: Response format is NOT considered synoptic.
- The data element should be represented in the report as it is listed in the case summary. The response for any data element may be modified from those listed in the case summary, including "Cannot be determined" if appropriate.
- Each diagnostic parameter pair (Data element: Response) is listed on a separate line or in a tabular format to achieve visual separation. The following exceptions are allowed to be listed on one line:
 - o Anatomic site or specimen, laterality, and procedure
 - Pathologic Stage Classification (pTNM) elements
 - Negative margins, as long as all negative margins are specifically enumerated where applicable
- The synoptic portion of the report can appear in the diagnosis section of the pathology report, at the end of the report or in a separate section, but all Data element: Responses must be listed together in one location
- Organizations and pathologists may choose to list the required elements in any order, use
 additional methods in order to enhance or achieve visual separation, or add optional items within
 the synoptic report. The report may have required elements in a summary format elsewhere in
 the report IN ADDITION TO but not as replacement for the synoptic report i.e., all required
 elements must be in the synoptic portion of the report in the format defined above.

Summary of Changes

v 5.1.0.0

- Invasive Tumor Size and Size of In Situ Carcinoma in Centimeters (cm) made conditionally reported
- eCP only metadata updates to Number of Intrapulmonary Lymph Nodes (within the same lobe), Number of Intrapulmonary Lymph Nodes (in different lobes), and Number of Distant Metastases

Reporting Template
Protocol Posting Date: September 2025
Select a single response unless otherwise indicated.
CASE SUMMARY: (LUNG)
Standard(s): AJCC 9
SPECIMEN
Synchronous Tumors (required if morphologically distinct unrelated multiple primary tumors are
present)
Not applicable
Morphologically distinct tumors that are considered to represent separate primary lung cancers should have separate synoptic
reports
Present#
Total Number of Primary Tumors:
Specimen ID(s):
Cannot be determined
Due and true (and not all that apply)
Procedure (select all that apply)
Wedge resection
Segmentectomy
Lobectomy
Completion lobectomy
Sleeve lobectomy
Bilobectomy
Pneumonectomy
Major airway resection (specify):
Adjacent structures (specify):
Other (specified
Not specified
On a simon Lateur lite.
Specimen Laterality
Right
Left
Not specified
TUMOR
TUMOR
Tumor Focality (Note A)
Single focus Separate tumor nodules (metastases) in same lobe (pT3)
+Number of Intrapulmonary Metastases:
Separate tumor nodules (metastases) in different ipsilateral lobe (pT4)
+Number of Intrapulmonary Metastases:
Separate tumor podules (metastases) in a contralateral lobe (nM1a)

+Number of Distant Metastases:
Multifocal tumor nodules of similar histology type not considered intrapulmonary metastases or too
numerous for separate synoptic reports (e.g. multiple ground-glass/lepidic nodules or carcinoid tumors)
(use m suffix)
+Number of Tumor Nodules
Specify number:
Other (specify):
Cannot be determined:
Pneumonic-type adenocarcinoma
Cannot be determined
Tumor Site (select all that apply)
Upper lobe of lung:
Middle lobe of lung:
Lower lobe of lung:
Bronchus, main:
Bronchus intermedius:
Bronchus, lobar (specify):
Other (specify):
Not specified
Invasive Tumor Size# (required only if present) # Invasive tumor size equals total tumor size for all tumor types other than invasive non-mucinous adenocarcinoma with lepidic component. For invasive non-mucinous adenocarcinoma with lepidic component, invasive tumor size equals the size of the invasive (non-lepidic) component. Not applicable
Greatest dimension in Centimeters (cm): cm
+Additional Dimension in Centimeters (cm): x cm
Cannot be determined (explain):
Total Tumor Size## (required only if invasive non-mucinous adenocarcinoma with lepidic component is present) ## For invasive non-mucinous adenocarcinomas with lepidic component, total tumor equals the size of the non-mucinous adenocarcinoma including the invasive and the lepidic components. Not applicable Greatest dimension in Centimeters (cm): cm +Additional Dimension in Centimeters (cm): x cm +Percentage of Total Tumor Size that is Invasive Specify percentage: % Other (specify): Cannot be determined
Cannot be determined (explain):

___ Mucoepidermoid carcinoma

Size of In Situ Carcinoma in Centimeters (cm) (required only if applicable):
cm
Histologia Tura (Nata C)
Histologic Type (Note C)
Adenocarcinoma in situ (AIS), non-mucinous
Adenocarcinoma in situ (AIS), mucinous
Minimally invasive adenocarcinoma, non-mucinous
Minimally invasive adenocarcinoma, mucinous
Invasive lepidic adenocarcinoma
Invasive acinar adenocarcinoma
Invasive papillary adenocarcinoma
Invasive micropapillary adenocarcinoma
Invasive solid adenocarcinoma
Invasive mucinous adenocarcinoma
Mixed invasive mucinous and non-mucinous adenocarcinoma
Colloid adenocarcinoma
Fetal adenocarcinoma
Enteric-type adenocarcinoma
Squamous cell carcinoma in situ (SCIS)
Invasive squamous cell carcinoma, keratinizing
Invasive squamous cell carcinoma, non-keratinizing
Invasive squamous cell carcinoma, basaloid
Lymphoepithelial carcinoma
Large cell carcinoma
Adenosquamous carcinoma
Pleomorphic carcinoma
Histologic Component(s) Present (may include percentages) (select all that apply)
Spindle cell carcinoma:
Giant cell carcinoma:
Adenocarcinoma:
Squamous cell carcinoma:
Large cell carcinoma:
Other (specify):
Pulmonary blastoma
Percentage of Fetal Adenocarcinoma Component : %
Percentage of Primitive Mesenchymal Stromal Component: %
Carcinosarcoma
Percentage of Non-small Cell Carcinoma Component: %
Specify Histologic Type(s):
Percentage of Sarcomatous Component: %
Specify Histologic Type(s):
NUT carcinoma
Thoracic SMARCA4-deficient undifferentiated tumor
Adenoid cystic carcinoma
Epithelial-myoepithelial carcinoma

Hyalinizing clear cell carcinoma
Myoepithelial carcinoma
Typical carcinoid / Neuroendocrine tumor, grade 1
Atypical carcinoid / Neuroendocrine tumor, grade 2
Carcinoid tumor, NOS / Neuroendocrine tumor, NOS
Small cell carcinoma
Combined small cell carcinoma (small cell carcinoma and non-small cell component) (specify type of
non-small cell component):
Large cell neuroendocrine carcinoma
Combined large cell neuroendocrine carcinoma (LCNEC and other non-small cell component)
(specify other type of non-small cell component):
Carcinoma, type cannot be determined:
Non-small cell carcinoma, subtype cannot be determined:
Other histologic type not listed (specify):
No viable tumor present (explain):
+Histologic Type Comment:
Histologic Patterns (may include percentages in 5% increments totaling 100%) (applicable to non-
mucinous adenocarcinomas only) (select all that apply)
Not applicable
Acinar:
Papillary:
Lepidic:
Solid:
Micropapillary:
Complex glands (cribriform and fused glands):
Other (specify):
+Histologic Grade# (Note D)
High-grade patterns in invasive non-mucinous adenocarcinoma include solid, micropapillary, cribriform, and fused
glands patterns.
G1, well-differentiated (includes invasive lepidic adenocarcinoma with less than 20% high-grade
pattern; typical carcinoid tumor)
G2, moderately differentiated (includes invasive acinar and papillary adenocarcinoma with less than
20% high-grade pattern; atypical carcinoid tumor)
G3, poorly differentiated (includes invasive non-mucinous adenocarcinoma with equal to or greater
than 20% high-grade pattern)
G4, undifferentiated (includes small cell carcinoma; large cell carcinoma)
Other (specify):
GX, cannot be assessed:
Not applicable:
Spread Through Air Spaces (STAS) (Note <u>C</u>)
Not identified

Present
Cannot be determined:
Not applicable:
Not applicable.
Visceral Pleura Invasion (Note E)
Not identified
Present
Cannot be determined:
Other (specify):
Direct Invasion of Other Structures (Note F)
Not applicable (no other structures present)
Not identified
Present
Involved Other Structures (select all that apply)
Adjacent lobe of lung
Parietal pleura
Chest wall
Select all that apply
Fibroadipose tissue
Skeletal muscle
Rib(s):
Cannot be determined (explain):
Main bronchus (up to but not including the carina)
Associated with atelectasis or obstructive pneumonitis extending to the hilar regions, involvin
either part of or all of the entire lung
Hilar soft tissues
Phrenic nerve
Parietal pericardium
Visceral pericardium (epicardium)
Azygos vein
Cervical nerve roots
Thoracic nerve roots
Brachial plexus (trunks, divisions, cords, or terminal nerves)
Stellate ganglion
Diaphragm
Heart
Great vessels (aorta, superior / inferior vena cava, intrapericardial pulmonary arteries / veins)
Supra-aortic arteries
Brachiocephalic vein
Subclavian vessels
Thymus
Trachea
Carina
Recurrent laryngeal nerve
Vagus nerve
Esophagus

Vertebral body	
Lamina	
Spinal canal	
 ·	es not listed above) (specify):
Cannot be determined (explain):	
Treatment Effect (Note G)	
No known presurgical therapy	
Not identified	
Present	
Percentage of Residual Viable Tumor	
Specify percentage:	%
Other (specify):	
Cannot be determined:	
+Percentage of Necrosis	
Specify percentage:	%
Other (specify):	
Cannot be determined:	_
+Percentage of Stroma (includes fibro	sis and inflammation)
Specify percentage:	•
Other (specify):	
Cannot be determined:	
+Inflammation	
Mild	
Moderate	
Severe	
Cannot be determined:	
Lymphatic and / or Vascular Invasion (No	ote <u>H</u>)
Not identified	
Present	
Select all that apply	
Lymphatic invasion present	
Arterial invasion present	
Venous invasion present	
Other (specify):	_
Cannot be determined:	
+Tumor Comment:	
MARGINS (Note !)	
Margin Status for Invasive Tumor	
All margins negative for invasive tumor	
Closest Margin(s) to Invasive Tumor (s	

Bronchial:
Vascular:
Parenchymal:
Chest wall margin:
Other attached tissue margin(s) (specify):
Cannot be determined (explain):
Distance from Invasive Tumor to Closest Margin
Specify in Centimeters (cm).
Exact distance: cm
Greater than: cm
At least: cm
Less than: cm
Other (specify):
Cannot be determined:
Not applicable:
Invasive tumor present at margin
Margin(s) Involved by Invasive Tumor (select all that apply)
Bronchial:
Select all that apply
+ Tumor involves bronchial mucosa
+ Tumor in submucosal lymphatics
+ Tumor in peribronchial soft tissue
Vascular:
Parenchymal:
Other attached tissue margin(s) (specify):
Cannot be determined (explain):
Other (specify):
Cannot be determined (explain):
Not applicable:
Margin Status for Non-Invasive Tumor (select all that apply)
All margins negative for non-invasive tumor
Carcinoma in situ present at bronchial margin:
Carcinoma in situ present at parenchymal margin:
Lepidic component of invasive carcinoma present at parenchymal margin:
Other (specify):
Cannot be determined (explain):
Not applicable:
+Margin Comment:
· margin comment.
DECIONAL LYMPH NODES
REGIONAL LYMPH NODES
Lymph Node(s) from Prior Procedures
No known prior lymph node sampling performed

Not included	
Included	
Prior Lymph Node Procedure(s) Included (describe and specify case ID):	
Thor Lymph Hode i rocedure(s) meladed (describe and specify ease ib).	
Regional Lymph Node Status	
Not applicable (no regional lymph nodes submitted or found)	
Regional lymph nodes present	
All regional lymph nodes negative for tumor	
Tumor present in regional lymph node(s)	
Number of Lymph Nodes with Tumor	
Exact number (specify):	
At least (specify):	
Other (specify):	
Cannot be determined (explain):	
Nodal Site(s) with Tumor (select all that apply)	
Right Nodal Stations Involved	
1R: Low cervical, supraclavicular, scalene and sternal notch	
2R: Upper paratracheal	
4R: Lower paratracheal	
8R: Para-esophageal (below carina)	
9R: Pulmonary ligament	
10R: Hilar	
11R: Interlobar	
12R-14R: Intrapulmonary	
Select all that apply	
+ 12R: Lobar	
+ 13R: Segmental	
+ 14R: Subsegmental	
Other right node(s) (specify):	
Central Nodal Stations Involved	
3a: Pre-vascular	
3p: Retrotracheal	
7: Subcarinal	
Other central node(s) (specify):	
Left Nodal Stations Involved	
1L: Low cervical, supraclavicular, scalene and sternal notch	
2L: Upper paratracheal	
4L: Lower paratracheal	
5: Subaortic / aortopulmonary (AP) / AP window	
6: Para-aortic (ascending aorta or phrenic)	
8L: Para-esophageal (below carina)	
9L: Pulmonary ligament	
10L: Hilar	
11L: Interlobar	
12L-14L: Intrapulmonary	
Select all that apply	
+ 12L: Lobar	

+ 13L: Segmental	
+ 14L: Subsegmental	
Other left node(s) (specify):	
Cannot be determined:	
+Extranodal Extension (Note <u>J</u>)	
Not identified	
Present	
Cannot be determined:	
+Size of Largest Metastatic Deposit (specify in Millimeters):	mm
Other (specify):	
Cannot be determined (explain):	
Number of Lymph Nodes Examined	
Exact number (specify):	
At least (specify):	
Other (specify):	
Cannot be determined (explain):	
Nodal Site(s) Examined (select all that apply)	
Right Nodal Stations Examined	
1R: Low cervical, supraclavicular, scalene and sternal notch	
2R: Upper paratracheal	
4R: Lower paratracheal	
8R: Para-esophageal (below carina)	
9R: Pulmonary ligament	
10R: Hilar	
11R: Interlobar	
12R-14R: Intrapulmonary	
Select all that apply	
+12R: Lobar	
+ 13R: Segmental + 14R: Subsegmental	
Other right node(s) (specify):	
Central Nodal Stations Examined	
3a: Pre-vascular	
3p: Retrotracheal	
7: Subcarinal	
Other central node(s) (specify):	
Left Nodal Stations Examined	
1L: Low cervical, supraclavicular, scalene and sternal notch	
2L: Upper paratracheal	
4L: Lower paratracheal	
5: Subaortic / aortopulmonary (AP) / AP window	
6: Para-aortic (ascending aorta or phrenic)	
8L: Para-esophageal (below carina)	
9L: Pulmonary ligament	
10L: Hilar	
11L: Interlobar	
12L-14L: Intrapulmonary	

Select all that apply
+ 12L: Lobar
+ 13L: Segmental
+ 14L: Subsegmental
Other left node(s) (specify):
Cannot be determined:
Paris and Lamanh Nada Occurrent
+Regional Lymph Node Comment:
DISTANT METASTASIS
Distant Site(s) Involved, if applicable (select all that apply)
Not applicable
Separate tumor nodule(s) in contralateral lobe:
Pleural nodule(s):
Pericardial nodule(s):
Malignant pleural effusion:
Malignant pericardial effusion:
Single extrathoracic metastasis in one organ (including a single nonregional lymph node):
Multiple extrathoracic metastases in a single organ:
Multiple extrathoracic metastasis in multiple organs:
Other (specify):
Cannot be determined:
pTNM CLASSIFICATION (AJCC Version 9) (Note J)
Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report
is issued. As per the AJCC (Chapter 1, 8th Ed.) it is the managing physician's responsibility to establish the final pathologic stage based upon all pertinent information, including but potentially not limited to this pathology report.
Modified Classification (required only if applicable) (select all that apply)
Not applicable
y (post-neoadjuvant therapy)
r (recurrence)
pT Category
pT not assigned (cannot be determined based on available pathological information)
pT0: No evidence of primary tumor
pTis: Carcinoma in situ; or Squamous cell carcinoma in situ (SCIS); or Adenocarcinoma in situ (AIS)
adenocarcinoma with pure lepidic pattern, less than or equal to 3 cm in greatest dimension
pT1: Tumor is less than or equal to 3 cm in greatest dimension surrounded by lung or visceral pleura, or in a lobar or more
peripheral bronchus
pT1mi: Minimally invasive adenocarcinoma: adenocarcinoma (less than or equal to 3 cm in greatest
dimension) with a predominantly lepidic pattern and less than or equal to 5 mm invasion in greatest
dimension
pT1a: Tumor less than or equal to 1 cm in greatest dimension OR Tumor of any size whose invasive

component is limited to the bronchial wall and may extend proximal to the main bronchus (this is an
uncommon superficial, spreading tumor) pT1b: Tumor greater than 1 cm but less than or equal to 2 cm in greatest dimension
 ·
pT1c: Tumor greater than 2 cm but less than or equal to 3 cm in greatest dimension
pT1 (subgroup cannot be determined)
pT2: Tumor greater than 3 cm but less than or equal to 5 cm in greatest dimension OR tumor less than or equal to 4 cm with one or more of the following features: Invades visceral pleura; or Invades an adjacent lobe; or Involves main bronchus (up to but not including the carina) or associated with atelectasis or obstructive pneumonitis, extending to the hilar regions, involving either part of
or the entire lung pT2a: Tumor greater than 3 cm but less than or equal to 4 cm in greatest dimension OR Tumor less
than or equal to 4 cm in greatest dimension with one or more of the following features: Invades
visceral pleura; or Invades an adjacent lobe; or Involves main bronchus (up to but not including the
carina) or associated with atelectasis or obstructive pneumonitis, extending to the hilar regions,
involving either part of or the entire lung
pT2b: Tumor greater than 4 cm but less than or equal to 5 cm in greatest dimension with or without
any of the following features: Invades visceral pleura; or Invades an adjacent lobe; or Involves main
bronchus (up to but not including the carina) or associated with atelectasis or obstructive pneumonitis
extending to the hilar regions, involving either part of or the entire lung
pT2 (subgroup cannot be determined)
pT3: Tumor greater than 5 cm but less than or equal to 7 cm in greatest dimension OR Tumor less
than or equal to 7 cm with one or more of the following features: Invades parietal pleura or chest wall
or Invades pericardium, phrenic nerve or azygos vein (although these structures lie within the
mediastinum, the degree of mediastinal penetration by the tumor needed to invade these structures
is not counted as T4); or Invades thoracic nerve roots (i.e., T1, T2) or stellate ganglion; or Separate
tumor nodule(s) in the same lobe as the primary
pT4: Tumor greater than 7 cm in greatest dimension OR Tumor of any size with one or more of the
following features: Invades mediastinum (except structures listed in T3), thymus, trachea, carina,
recurrent laryngeal nerve, vagus nerve, esophagus or diaphragm; or Invades heart, great vessels
(aorta, superior / inferior vena cava, intrapericardial pulmonary arteries / veins), supra-aortic arteries
or brachiocephalic veins; or Invades subclavian vessels, vertebral body, lamina, spinal canal, cervica
nerve roots or brachial plexus (i.e., trunks, divisions, cords or terminal nerves); or Separate tumor
nodule(s) in a different ipsilateral lobe than that of the primary
T Suffix (required only if applicable)
The suffix m (or a specific number) should only be used in the setting of multifocal ground-glass / lepidic nodules that histologically
present as adenocarcinomas with prominent lepidic component or multifocal tumors of same histologic type that are too numerous for individual separate synoptic report and that are not better classified as intrapulmonary metastases (e.g. numerous carcinoid
tumors). Multiple primary lung cancers showing different histologic type or different morphology based on comprehensive histologic
subtyping are better staged as independent tumors without m suffix.
Not applicable
(m) multiple primary synchronous tumors in a single organ
pN Category
pN not assigned (no nodes submitted or found)
pN not assigned (no nodes submitted of locald) pN not assigned (cannot be determined based on available pathological information)
pN0: No tumor involvement of regional lymph node(s)
pN1: Tumor involvement of ipsilateral peribronchial and / or ipsilateral hilar and / or ipsilateral
prv1. Turnor involvement or ipsilateral perioronicitial and / or ipsilateral fillal and / or ipsilateral

intrapulmonary lymph node station(s), including involvement by direct extension pN2: Tumor involvement of ipsilateral mediastinal nodal station(s) and / or subcarinal lymph node station	
pN2a: Tumor involvement of a single ipsilateral mediastinal nodal station or of the subcarinal nodal station	
pN2b: Tumor involvement of multiple ipsilateral mediastinal nodal stations with or without	
involvement of the subcarinal nodal station	
pN2 (subgroup cannot be determined)	
pN3: Tumor involvement of contralateral mediastinal, contralateral hilar, ipsilateral / contralateral scalene, or ipsilateral / contralateral supraclavicular lymph node station(s)	
N Suffix (required only if applicable) (select all that apply)	
Not applicable	
(sn) Sentinel node procedure	
(f) FNA or core needle biopsy	
pM Category (required only if confirmed pathologically)	
Not applicable - pM cannot be determined from the submitted specimen(s)	
pM1: Microscopic confirmation of distant metastasis # Most pleural (pericardial) effusions with lung cancer are a result of the tumor. In a few patients, however, multiple microscopic	
examinations of pleural (pericardial) fluid are negative for tumor, and the fluid is non-bloody and not an exudate. If these elements	;
$and\ clinical\ judgment\ dictate\ that\ the\ effusion\ is\ not\ related\ to\ the\ tumor,\ the\ effusion\ should\ be\ excluded\ as\ a\ staging\ descriptor.$	
pM1a: Microscopic confirmation of metastasis in pleural or pericardial nodules, and / or malignant	
pleural or pericardial effusions, and / or separate tumor nodule(s) in a contralateral lobe#	
pM1b: Microscopic confirmation of single extrathoracic metastasis in a single organ system (including invalidation of single parameters).	ηg
involvement of a single non-regional node) pM1c: Microscopic confirmation of multiple extrathoracic metastases in a single or multiple organ system(s)	
pM1c1: Microscopic confirmation of multiple extrathoracic metastases in a single of multiple organ system(s)	٢
example, the skeleton is considered one organ. Several metastases in a single bone or several	
metastases in several bones are classified as M1c1.)	
pM1c2: Microscopic confirmation of multiple extrathoracic metastases in multiple organ systems	
pM1c (subgroup cannot be determined)	
pM1 (subgroup cannot be determined)	
ADDITIONAL FINDINGS	
+Additional Findings (select all that apply)	
None identified	
Atypical adenomatous hyperplasia:	
Tumorlets:	
Squamous dysplasia	
Diffuse neuroendocrine hyperplasia	
Biopsy site changes	
Granulomatous inflammation (specify necrotizing or non-necrotizing if discernible): Post-obstructive changes	
Fibrosis (specify pattern if discernable):	
Emphysema	
——————————————————————————————————————	

CAP Approved	Lung_5.1.0.0. REL_CAPCP
Other (specify):	
SPECIAL STUDIES	

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

COMMENTS	
Comment(s):	

Explanatory Notes

A. Tumor Focality

When more than one tumor nodule is identified in resection specimens, it is important to attempt distinction of synchronous primary tumors from a tumor with intrapulmonary metastasis. These scenarios have different prognoses and are staged differently. Multiple tumor nodules of different histologic types (e.g., one squamous cell carcinoma and one adenocarcinoma) are considered synchronous primaries and should be recorded as such in the pathology report with an individual TNM category assigned to each tumor. In such cases, required reporting elements should be recorded for each primary tumor, and this is most easily achieved by issuing two synoptic reports (one for each of the cancers). For lung adenocarcinomas, comprehensive histologic assessment has been proposed for the distinction of synchronous primaries from separate tumor nodules (intrapulmonary metastasis). Other pathologic criteria for distinguishing synchronous primary lung adenocarcinomas from separate tumor nodules (intrapulmonary metastasis) that are not based strictly on histologic assessment (e.g., assessing similarity of breakpoints using comparative genomic hybridization) are detailed in the 8th edition of the AJCC staging manual.

Multifocal lung adenocarcinoma with lepidic features is the designation applied to multiple discrete foci of lepidic-predominant adenocarcinoma (LPA), minimally invasive adenocarcinoma (MIA), or adenocarcinoma in situ (AIS) with or without other subtypes of adenocarcinoma as lesser components that manifest on computed tomography (CT) as multiple subsolid (either pure ground glass or part solid) nodules. This designation applies whether a detailed histologic assessment shows a matching or different appearance among the tumor foci. Data suggest that in most cases, the multiple lesions represent synchronous primary tumors. Assignment of T category in these cases is based on the highest T lesion, followed by the suffix "m", indicating multiplicity, or the number of tumors in parentheses (e.g., T1b(m) or T1b(2)) (Table 1). It should be noted that foci of atypical adenomatous hyperplasia (AAH) are not counted for the purpose of TNM classification.

In some patients, adenocarcinoma manifests radiographically as diffuse consolidation, which has been designated as "pneumonic-type" lung adenocarcinoma. Such imaging findings typically correspond pathologically to invasive mucinous adenocarcinoma, but mixed mucinous and non-mucinous patterns may also be seen. Invasive mucinous adenocarcinoma often exhibits lepidic-predominant growth, but robust sampling usually discloses invasive foci. Occasionally, invasive mucinous adenocarcinoma shows a heterogeneous mixture of other growth patterns. To qualify as pneumonic-type adenocarcinoma, tumor should be diffusely distributed throughout a region(s) of lung, as opposed to forming discrete single or multiple well-demarcated nodules or masses.

The size of diffuse pneumonic-type adenocarcinomas, as well as miliary forms of adenocarcinoma, is often difficult to measure. When a single tumor area is present, it is categorized according to standard TNM criteria. Multiple tumor areas are categorized according to the extent of lobar involvement: T3 when limited to a single lobe, T4 when there is involvement of other ipsilateral lobe, and M1a is used to indicate the presence of contralateral lung involvement. 3

In the setting of multiple lung cancers other than adenocarcinoma, pathologists may use the suffix m for multiple tumors of same histology as long as those tumors are not better considered intrapulmonary metastases. In this situation, AJCC suggests assigning the T category based on the size of the largest tumor nodule and using the m suffix to indicate an increased tumor burden.

Table 1. Schematic Summary of Disease Patterns and TNM Classification of Patients with Lung Cancer with Multiple Pulmonary Sites of Involvement

	Second Primary	Multifocal	Pneumonic-type	Separate
	Lung Cancer	GG/L Nodules	Adenocarcinoma	Tumor Nodule
Imaging features	Two or more distinct masses with imaging characteristic of lung cancer (e.g., spiculated)	Multiple ground- glass or part-solid nodules	Patchy areas of ground glass and consolidation	Typical lung cancer (e.g., solid, spiculated) with separate solid nodule
Pathological features	Different histotype or different morphology based on comprehensive histologic assessment	Adenocarcinomas with prominent lepidic component (typically varying degrees of AIS, MIA, LPA)	Same histology throughout (most often invasive mucinous adenocarcinoma)	Distinct masses with the same morphologic features based on comprehensive histologic assessment
TNM classification	Separate cTNM and pTNM for each cancer	T based on highest T lesion, with (#/m) indicating multiplicity; single N and M	T based on size or T3 if in single lobe, T4 or M1a if in different ipsilateral or contralateral lobes; single N and M	Location of separate nodule relative to primary site determines whether T3, T4, or M1a; single N and M
Conceptual view	Unrelated tumors	Separate tumors, albeit with similarities	Single tumor, diffuse pulmonary involvement	Single tumor with intrapulmonary metastasis

AIS, adenocarcinoma in situ; GG/L, ground-glass/lepidic; LPA, lepidic-predominant adenocarcinoma; MIA, minimally invasive adenocarcinoma. From AJCC Cancer Staging Manual, 8th edition. Used with permission.

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B. Tumor Size

Based on data showing prognosis correlates with invasive size in non-mucinous adenocarcinomas with lepidic and invasive components, the AJCC has adopted a rule that for non-mucinous adenocarcinomas with a lepidic component, only the size of the invasive component is used to assign T category.

1.2,3,4,5 This rule aligns with the recommendation previously set forth by the Union for International Cancer Control (UICC) of using invasive size for T descriptor size. This rule does not apply to other histologic types of lung cancer, including invasive mucinous lung adenocarcinoma. Data available to establish Version 9 TNM categories were insufficient to analyze the eighth-edition proposal to distinguish invasive from non-invasive tumor size in part-solid and part-lepidic non-mucinous lung adenocarcinomas. Therefore, reporting both invasive size and total tumor size of these tumors remains important for validation of this concept.

The invasive component to be measured in non-mucinous adenocarcinomas with a lepidic component includes any histologic subtype other than a lepidic pattern (i.e., acinar, papillary, micropapillary, and/or solid) and/or tumor cells infiltrating myofibroblastic stroma. In tumors where the invasive component is not a single discrete measurable focus, estimating the percentage of the total tumor that is invasive and then multiplying by the total tumor size to estimate invasive tumor size is recommended.

- 1. AJCC Version 9 Tumors of the Lung Cancer Staging System. Copyright 2024 American College of Surgeons.
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C. 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. Although acceptable in small biopsies, a designation of non-small cell lung carcinoma is not acceptable in resection specimens.

Lung carcinomas should be adequately sampled in order to ensure defining features are satisfactorily represented in the sections examined histologically and the presence or absence of invasion can be thoroughly assessed. The WHO defines invasion in adenocarcinoma as: (1) any histologic subtype other than a lepidic pattern (i.e., acinar, papillary, micropapillary, and/or solid), (2) tumor cells infiltrating myofibroblastic stroma, (3) vascular or pleural invasion, or (4) spread through air spaces (STAS).¹

STAS is defined as micropapillary clusters, solid nests or single cells of tumor extending beyond the edge of the tumor into the air spaces of the surrounding lung parenchyma. Studies and meta-analyses have shown STAS to be an independent prognostic factor in the major histologic types of lung cancer and increased incidence of recurrence in tumors that have undergone limited resection (e.g., segmentectomy, wedge resection). STAS should not be incorporated into the measurement of tumor size.

For cases in which a diagnosis of adenocarcinoma in situ (AIS) or minimally invasive adenocarcinoma (MIA) is being considered, the lesion must be entirely submitted for histopathologic examination. A diagnosis of MIA is applied to a lepidic-predominant tumor ≤ 3 cm in size with an invasive component measuring ≤ 0.5 cm provided it does not exhibit any of the following: (1) tumor invades lymphatics, blood vessels or pleura, (2) tumor necrosis is present, (3) STAS is present. Tumors ≤ 3 cm with ≤ 0.5 cm of invasion exhibiting 1 or more of these exclusionary features are classified as lepidic-predominant adenocarcinoma. A diagnosis of AIS or MIA should only be made on solitary lesions ≤ 3 cm in diameter. Specimens showing only AIS are categorized as Tis (AIS). MIA is classified as T1mi. ≤ 3

For the uncommon occurrence of a lepidic-predominant tumor >3.0 cm with either no invasion or ≤0.5 cm of invasion, it is recommended that such tumors be classified as lepidic-predominant adenocarcinoma and categorized as pT1a, as there is insufficient data to conclude they have the same prognostic features as ≤3.0 cm tumors meeting criteria for AIS or MIA.³

Classification of adenocarcinomas by predominant histologic pattern can be useful for assessing pathologic grade and distinguishing separate independent tumors from intrapulmonary metastases. The WHO recommends classifying invasive non-mucinous adenocarcinomas according to the predominant

subtype and specifying non-predominant subtypes semi-quantitatively in 5% increments. In poorly differentiated cases, immunohistochemistry can greatly aid in classification. This is particularly useful in making a diagnosis of solid-type adenocarcinoma or nonkeratinizing squamous cell carcinoma.

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D. Histopathologic Grade

The predominant histological pattern of non-mucinous adenocarcinomas is associated with prognosis with lepidic-predominant tumors having the best prognosis, acinar and papillary-predominant tumors having an intermediate prognosis, and solid-predominant and micropapillary-predominant tumors having the worst prognosis. A recent study by the International Association for the Study of Lung Cancer (IASLC) Pathology Committee found that a combination of predominant and worst histological pattern improves prediction of patient outcome. The following grading scheme was recommended for resected early-stage non-mucinous lung adenocarcinoma.

IASLC Histopathologic Grading Scheme for Non-mucinous Lung Adenocarcinoma:

- Grade 1 (G1): Well-differentiated (lepidic-predominant with no or < 20% high-grade pattern)
- Grade 2 (G2): Moderately differentiated (acinar or papillary-predominant with no or < 20% high-grade pattern)
- Grade 3 (G3): Poorly differentiated (any tumor with ≥ 20% high-grade pattern (i.e., solid, micropapillary, cribriform, or complex glandular pattern).

Note: A complex glandular pattern is defined by fused glands or single cells infiltrating in a desmoplastic stroma.

Neuroendocrine tumors continue to be classified based on their diagnostic criteria as low-grade (typical carcinoid/neuroendocrine tumor, grade 1), intermediate-grade (atypical carcinoid/neuroendocrine tumor, grade 2) and neuroendocrine carcinoma (large cell carcinoma and small cell carcinoma).²

Use of the above grading schemes is required for non-mucinous adenocarcinomas and neuroendocrine tumors. There is currently no established grading scheme for invasive mucinous adenocarcinoma or squamous cell carcinoma of the lung.²

For other tumors, the four-tiered grading scheme for lung cancer (shown below) has been put forth by the American Joint Committee on Cancer (AJCC) may be used. 1.3

AJCC Histopathologic Grading Scheme:³

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

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- AJCC Version 9 Tumors of the Lung Cancer Staging System. Copyright 2024 American College of Surgeons.

E. Visceral Pleural Invasion

The presence of visceral pleural invasion by tumors ≤ 3 cm changes the T category from pT1 to pT2a. Studies have shown that tumors ≤ 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. 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 1). To qualify for visceral pleural invasion, tumor cells must have crossed the thickest visceral pleural elastic layer, which is usually the outermost (external) elastic layer in the visceral pleura (the layer closest to the visceral pleural mesothelial-lined surface). In many patients, a thinner, sometimes discontinuous, elastic layer (internal visceral pleural elastic layer) can be appreciated closer to the lung parenchyma. Penetration of tumor through this thinner, variably discontinuous internal (i.e., closer to the lung parenchyma)) elastic layer does not qualify as visceral pleura invasion. The pleural elastic layers can be difficult to appreciate in hematoxylin-eosin stains. Elastic stains may facilitate the assessment of visceral pleural invasion.

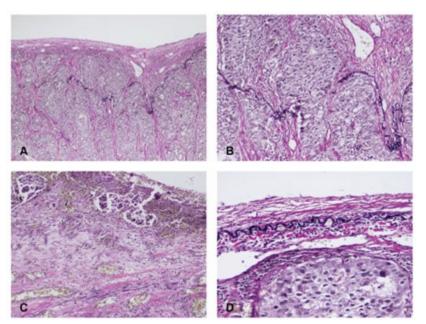


Figure 1. Types of visceral pleural invasion. Staining for elastin (e.g., elastic-Van Gieson [EVG] stain) can aid in detection of visceral pleural invasion where it is indeterminate by hematoxylin-eosin (H&E) stain. A and B. Visceral pleural invasion is present when a tumor penetrates beyond the thick (external) 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 T2a. 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 direct invasion across a fissure or directly if the fissure is incomplete into an adjacent ipsilateral lobe should be classified as T2a unless the size of the tumor or other criteria that would dictate a higher T category are met.

Z

Pleural tumor nodules, including same lobe visceral pleural nodules, separate from the primary tumor (non-contiguous) should be categorized as M1a.¹

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F. Direct Invasion of Other Structures

Lung tumors sometimes exhibit direct invasion of structures surrounding the lung parenchyma in which the arise. Direct hilar fat/soft tissue invasion without evidence of direct extension into other structures that would meet a higher T designation is categorized as T2a. Occasionally, lung cancer specimens consist of en bloc resections that incorporate extrapulmonary structures directly invaded by tumor. Accurate assessment of such specimens might require carefully study of the operative note and preoperative imaging, or communication with the surgeon regarding the nature and location of any attached extrapulmonary structures.

According to the AJCC, direct invasion of the parietal pleura is categorized as T3, as is direct invasion of the chest wall (including the superior sulcus). Although parietal pleural invasion appears to portend a worse prognosis within the pT3 category than an intralobar metastasis, evidence was insufficient to classify it as pT4 in Version 9 of the TNM Classification for Lung Cancer. Specifying the chest wall structures directly invaded by tumor (e.g., intercostal muscle[s], rib[s], pectoralis muscle, latissimus muscle, serratus muscle) can facilitate patient management. Direct phrenic nerve and parietal pericardial invasion are also categorized as T3. Tumor extension into the visceral pericardium (epicardium) is categorized as T4.

Direct invasion of central thoracic structures, including the heart, great vessels, mediastinum, trachea, recurrent laryngeal nerve, esophagus, vertebral body, and carina is considered T4. Direct invasion of the diaphragm is also categorized as T4.

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G. Treatment Effect

For patients who have received neoadjuvant chemotherapy, immunotherapy and/or radiation therapy before surgical resection, quantifying the extent of therapy-induced tumor regression provides prognostically relevant information. 1.2 Measuring residual tumor size in patients with a partial response

can be challenging, as there are often discontinuous clusters of viable tumor at the peripheral edges of an irregular area of treatment-related necrosis. The IASLC recently published multidisciplinary recommendations for the pathologic assessment of lung cancer resection specimens after neoadjuvant therapy. To evaluate treatment effect, the resection specimen should be sectioned in the plane that shows the maximum dimension of the tumor bed and its relationship to structures relevant for determining pT category and margin status. Three-dimensional size of the tumor bed and an estimated percentage of gross necrosis should be recorded. Tumor beds up to 3.0 cm may be submitted entirely for microscopic examination. For larger tumors, the IASLC recommends complete sampling of an entire cross-section of tumor bed with mapping of each section to a gross photograph. The percentages of viable tumor, stromal tissue (i.e., fibrosis and inflammation) and necrosis (in increments of 10% totaling 100%) should be determined based on review of all microscopic sections of tumor bed. If a component amounts to less than 5%, an estimate of single percentages should be recorded. This approach to evaluating residual tumor refines that suggested by the AJCC of multiplying the percentage of the mass that is composed of viable tumor by the size of the total mass to estimate post-neoadjuvant tumor size. A "y" prefix is applied to the TNM classification in resections following multimodality therapy (see Note J). If no viable tumor is identified on resection, ypT0 is the appropriate designation.

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H. Lymphatic and/or Vascular Invasion

There are data showing lymphatic invasion by tumor represents an unfavorable prognostic finding, but studies on the role of large vessel invasion have produced somewhat conflicting results. 1.2 The presence of lymphovascular invasion is exclusionary of adenocarcinoma in situ (AIS) and minimally invasive adenocarcinoma (MIA). Angiolymphatic invasion does not alter the pT and pN classifications or the TNM stage grouping.

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I. 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 that contain extrapulmonary structures as part of the specimen have additional margins (e.g., parietal pleura, chest wall), which should be designated by the surgeon for appropriate handling. Note that the visceral pleura is not a surgical margin.

J. pTNM Classification

The TNM staging system of the AJCC and the UICC is recommended for both non-small cell lung cancer and small cell lung cancer. Typical 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 clinical stage information modified/refined by operative findings and pathological evaluation of the resected specimen. The pTNM classification is applicable when surgery is performed before adjuvant systemic or radiation therapy is initiated. 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.

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.

<u>The "m" suffix</u> can indicate the presence of multiple ground-glass/lepidic adenocarcinomas or be used to indicate increased tumor burden of multifocal tumors of same histologic type that are too numerous for individual separate synoptic reports. It is recorded in parentheses: pT(m) (see Note A).

The "y" prefix indicates those cases in which classification is performed during or following initial multimodality therapy (i.e., 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 (i.e., before initiation of neoadjuvant therapy) (see Note G).

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

T Category Considerations

Version 9 of the TNM classification for lung cancer maintains the eighth-edition T descriptors.²

Although obstructive pneumonitis associated with tumor is sometimes seen histologically, accurate assessment of tumor-associated obstructive pneumonitis as well as atelectasis requires integration of clinical and radiographic information. Atelectasis and obstructive pneumonitis recognized by pathology only should not be used for TNM staging.

N Category Considerations

Lymph node metastases are an adverse prognostic factor, the extent of which is dependent on the location and number of the involved lymph node stations. The involved lymph node stations should be recorded according to the International Association for the Study of Lung Cancer (IASLC) lymph node map. Given the nature of the procedure, lymph nodes obtained by mediastinoscopy are often received fragmented, and it may not be possible to distinguish a single fragmented lymph node from fragments of multiple lymph nodes. For this reason, only if the actual number of nodes is known or provided should it be quantified. Otherwise, it is permissible to report the sites of nodal metastases without specifying the number involved.

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. 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.

The anatomic classification of regional lymph nodes proposed by the IASLC is shown below. A complete description of the anatomic limits of each nodal station can be found in the AJCC Staging Manual.

1

- Station 1 Lower cervical, supraclavicular, and sternal notch nodes
- Station 2 Upper paratracheal nodes
- Station 3 Prevascular and retrotracheal nodes
- Station 4 Lower paratracheal nodes
- Station 5 Subaortic nodes (aorto-pulmonary window)
- Station 6 Paraaortic nodes (ascending aorta or phrenic)
- Station 7 Subcarinal nodes
- Station 8 Paraesophageal nodes (below carina)
- Station 9 Pulmonary ligament nodes
- Station 10 Hilar nodes
- Station 11 Interlobar nodes
- Station 12 Lobar nodes
- Station 13 Segmental nodes
- Station 14 Subsegmental nodes

Metastasis to nonregional lymph nodes (i.e., lymph nodes that are not included in the IASLC lymph node map) are assigned to the M1b or M1c category depending or whether single or multiple metastases are present.

M Category Considerations

With respect to this protocol, reporting a pM designation is required only if metastasis is pathologically confirmed in the specimen(s) being examined. The designation pMX should not be used.

In addition to malignant pleural effusion, malignant pericardial effusion, as well as separate tumor nodule(s) in a contralateral lobe are categorized as M1a. Visceral or parietal ipsilateral pleural tumor nodules and pericardial tumor nodules that are not in direct continuity with the primary lung tumor are also categorized as M1a. A single extrathoracic metastasis in a single organ system is categorized as M1b. Multiple extrathoracic metastases are categorized as M1c1 when they occur in a single organ system and M1c2 when they occur in multiple organ systems.

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