IASLC

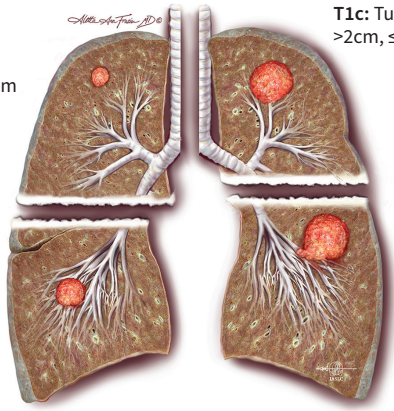
INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

Lung Cancer T Classification–9th Edition

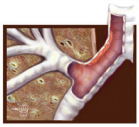
T1a, T1b T1c

T1a: Tumor ≤1cm

T1b: Tumor >1cm, ≤2cm



T1c: Tumor >2cm, ≤3cm



Superficial spreading tumor of any size with its invasive component limited to the bronchial wall, which may extend proximal to the main bronchus, is T1

Tumor ≤3cm; without endobronchial extension proximal to the lobar bronchus

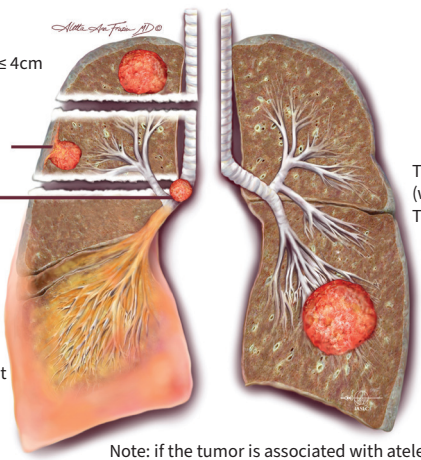
T2a T2b

Tumor > 3cm, ≤ 4cm

Tumor ≤ 4cm, invasion of the visceral pleura

Tumor involves main bronchus, regardless of distance from carina but without carinal involvement

Associated atelectasis or obstructive pneumonitis that extends to the hilar region, either involving part of the lung or the entire lung



Tumor > 4cm, ≤ 5cm (with or without other T2 descriptors)

Note: if the tumor is associated with atelectasis or pneumonitis, it is T2a if lesion ≤ 4cm or if tumor size cannot be measured; it is T2b if lesion > 4cm, ≤ 5cm.

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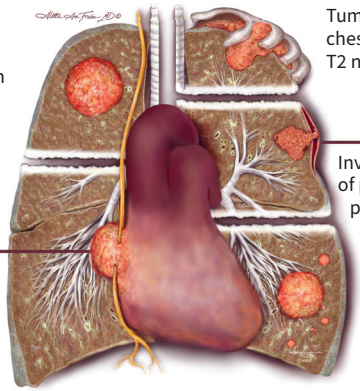
Lung Cancer T Classification–9th Edition

T3

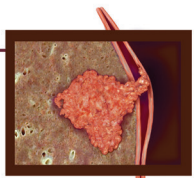


Tumor > 5cm, ≤ 7cm

Invasion of the azygos vein, phrenic nerve, or pericardium

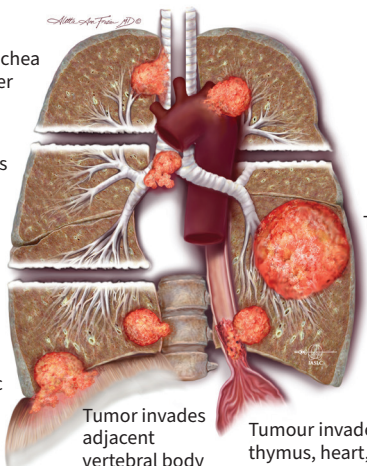
Tumor invades parietal pleura or chest wall or invades thoracic T1, T2 nerve roots, or stellate ganglion

Invasion of parietal pleura



Separate tumor nodule(s) in the lobe of the primary

T4



Tumor invades trachea and/or SVC or other great vessel

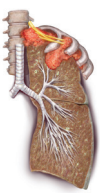
Tumor involves carina

Diaphragmatic invasion

Tumor invades adjacent vertebral body

Tumour invades mediastinum, thymus, heart, vagus nerve, recurrent laryngeal nerve, esophagus or diaphragm

Tumor that invades subclavian vessels, vertebral body, lamina, spinal canal, cervical nerve roots, or brachial plexus



Tumor > 7cm

Tumor accompanied by ipsilateral, separate tumor nodules, different lobe

Van Schil PE, Asamura H, Nishimura KK, et al. The IASLC lung cancer staging project: Proposals for the revisions of the T descriptors in the forthcoming ninth edition of the TNM classification for lung cancer. *J Thorac Oncol*. 2024; 19(5):749-765.

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INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

Lung Cancer N Classification–9th Edition

N0

No regional lymph node metastases

N1

Metastasis in ipsilateral intrapulmonary/ peribronchial/ hilar lymph node(s), including nodal involvement by direct extension

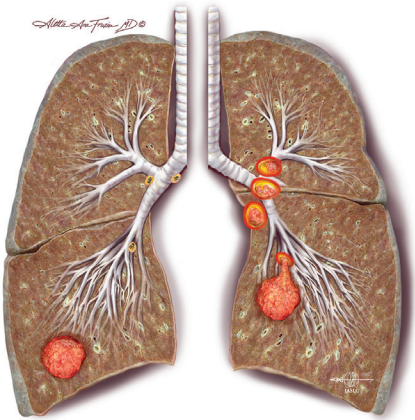

Figure. Courtesy of International Association for the Study of Lung Cancer. Permission must be requested and granted before photocopying or reproducing this material for distribution. Copyright ©2024 Aletta Ann Frazier, MD.

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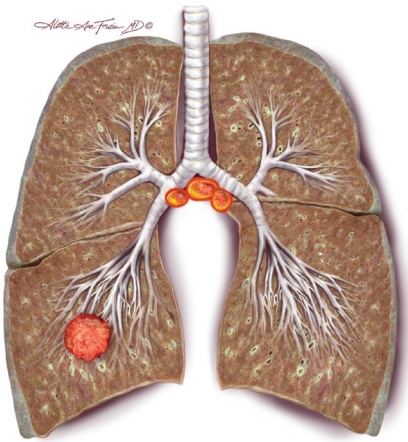
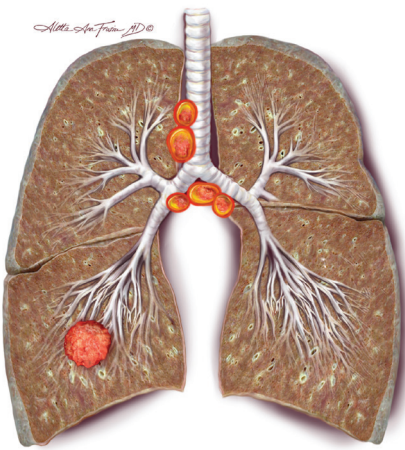
Lung Cancer N Classification–9th Edition

N2a



Metastasis to single ipsilateral mediastinal or subcarinal lymph node station

N2b



Metastasis to multiple ipsilateral mediastinal and/or subcarinal lymph node stations

Huang J, Osarogiagbon RU, Giroux DJ, et al. The International Association for the Study of Lung Cancer staging project for lung cancer: Proposals for the revision of the N descriptors in the forthcoming ninth edition of the TNM classification for lung cancer. *J Thorac Oncol*. 2024; 19(5):766-785.

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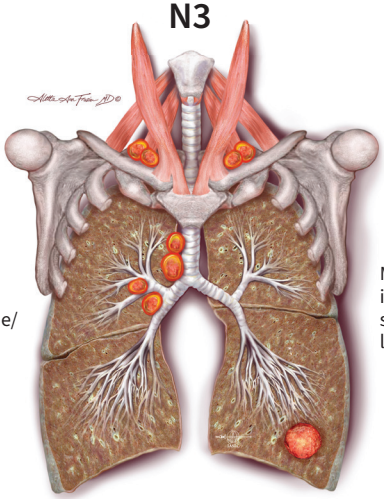
Lung Cancer N, M Classification–9th Edition

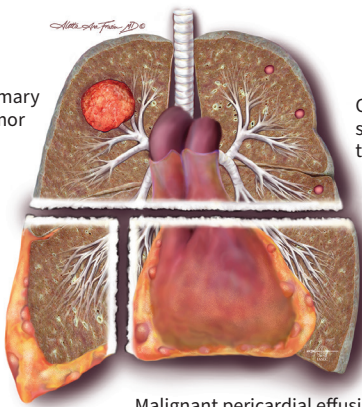
N3



Metastasis in contralateral hilar/ mediastinal/scalene/ supraclavicular lymph node(s)

Metastasis in ipsilateral scalene/ supraclavicular lymph node(s)

M1a



Primary tumor

Contralateral, separate tumor nodule(s)

Malignant pleural effusion/ nodule(s)

Malignant pericardial effusion/nodule(s)

Note: when the pleural (pericardial) effusions are negative after multiple microscopic examinations, and the fluid is non-bloody and not an exudate, they should be excluded as a staging descriptor.

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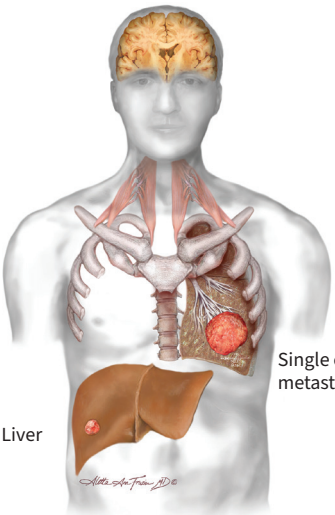
Lung Cancer M Classification–9th Edition

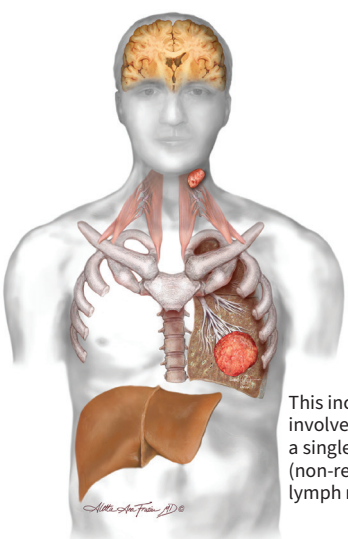
M1b



Single extrathoracic metastasis

Liver

M1b



This includes involvement of a single distant (non-regional) lymph node

Fong KM, Rosenthal A, Giroux DJ, et al. The International Association for the Study of Lung Cancer staging project for lung cancer: Proposals for the revision of the M descriptors in the forthcoming ninth edition of the TNM classification of lung cancer. *J Thorac Oncol*. 2024; 19(5):786-802.

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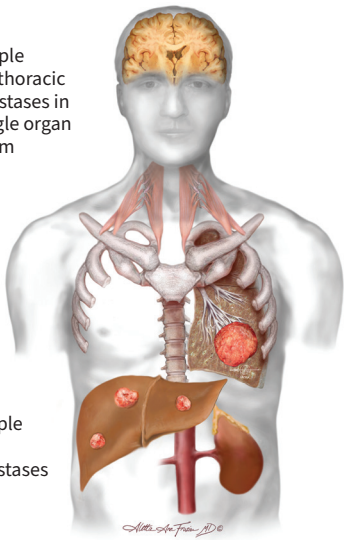
Lung Cancer M Classification–9th Edition

M1c1

Multiple extrathoracic metastases in a single organ system



Multiple liver metastases

An organ system denotes all sites of an organ that is distributed in the body (e.g. the skeletal system, skin, extrathoracic lymphatic system) or of a paired organ (e.g. adrenal, kidney)

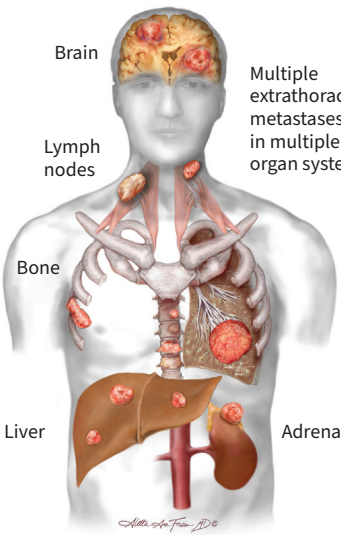
M1c2

Brain

Lymph nodes

Bone

Liver



Multiple extrathoracic metastases in multiple organ systems

Adrenal

Fong KM, Rosenthal A, Giroux DJ, et al. The International Association for the Study of Lung Cancer staging project for lung cancer: Proposals for the revision of the M descriptors in the forthcoming ninth edition of the TNM classification of lung cancer. *J Thorac Oncol*. 2024; 19(5):786-802.

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INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

Lung TNM Definitions–9th Edition

T: Primary tumor	
Tx	Primary tumor cannot be assessed[a]
T0	No evidence of primary tumor
Tis	Carcinoma in situ[b]
T1	Tumor surrounded by lung or visceral pleura, or in a lobar or more peripheral bronchus[c]
T1mi	Minimally invasive adenocarcinoma[d]
T1a	Tumor ≤1 cm in greatest dimension
T1b	Tumor >1 cm but ≤2 cm in greatest dimension
T1c	Tumor >2 cm but ≤3 cm in greatest dimension
T2	Tumor with any of the following features:
T2a	• tumor >3 cm but ≤4 cm in greatest dimension; • invades visceral pleura; • invades an adjacent lobe; • involves main bronchus (up to but not including the carina) or is associated with atelectasis or obstructive pneumonitis extending to the hilar region, involving either part of or the entire lung
T2b	Tumor >4 cm but ≤5 cm in greatest dimension
T3	Tumor with any of the following features: • tumor >5 cm but ≤7 cm in greatest dimension; • invades parietal pleura or chest wall; • invades pericardium, phrenic nerve, or azygos vein;[e] • invades thoracic nerve roots (i.e. T1, T2) or stellate ganglion; • separate tumor nodule(s) in the same lobe as the primary
T4	Tumor with any of the following features: • tumor >7 cm in greatest dimension; • invades mediastinum, thymus, trachea, carina, recurrent laryngeal nerve, vagus nerve, esophagus or diaphragm; • invades heart, great vessels (aorta, superior/inferior vena cava, intrapericardial pulmonary arteries/veins), supra-aortic arteries, or brachiocephalic veins; • invades subclavian vessels, vertebral body, lamina, spinal canal, cervical nerve roots, or brachial plexus (i.e. trunks, divisions, cords, or terminal nerves); • separate tumor nodule(s) in a different ipsilateral lobe than that of the primary

N: Regional Lymph Nodes	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar and/or intrapulmonary lymph nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
	N2a – Single N2 station involvement
	N2b – Multiple N2 station involvement
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene or supraclavicular lymph node(s)

M: Distant Metastasis	
M0	No distant metastasis
M1	Distant metastasis
M1a	Tumor with pleural or pericardial nodules or malignant pleural or pericardial effusions, separate tumor nodule(s) in a contralateral lobe
M1b	Single extrathoracic metastasis in a single organ system
M1c	Multiple extrathoracic metastases
M1c1	Multiple extrathoracic metastases in a single organ system
M1c2	Multiple extrathoracic metastases in multiple organ systems

[a] This includes tumors proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy.

[b] This includes adenocarcinoma in situ – Tis (AIS) – and squamous cell carcinoma in situ – Tis (SCIS).

[c] The uncommon superficial spreading tumor of any size with its invasive component limited to the bronchial wall, which may extend proximal to the main bronchus, is also classified as T1a.

[d] Solitary adenocarcinoma (not more than 3 cm in greatest dimension), with a predominantly lepidic pattern and not more than 5 mm invasion in greatest dimension.

[e] 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.

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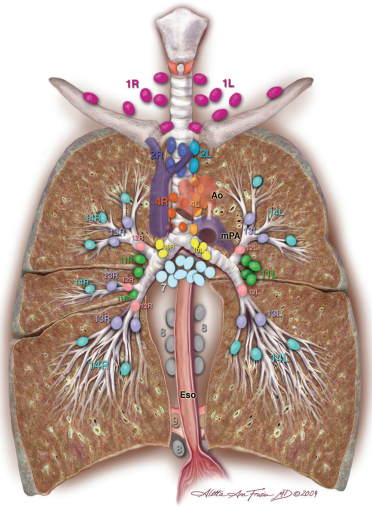
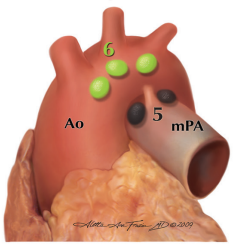
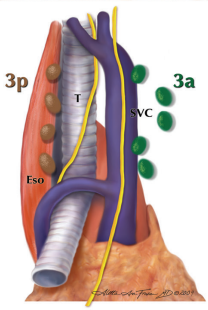
Nodal Chart–9th Edition







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

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INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

IASLC Nodal Definitions–9th Edition

#1 (Left/Right) Low 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
#L1 and #R1 limited by the midline of the trachea.

#2 (Left/Right) Upper paratracheal nodes

2R: Upper border: Apex of lung and pleural space and, in the midline, the upper border of the manubrium
Lower border: Intersection of caudal margin of innominate vein with the trachea
2L: Upper border: Apex of the lung and pleural space and, in the midline, the upper border of the manubrium
Lower border: Superior border of the aortic arch
As for #4, in #2 the oncologic midline is along the left lateral border of the trachea.

#3 Pre-vascular and retrotracheal nodes

3a: Prevascular – On the right
Upper border: Apex of chest
Lower border: Level of carina
Anterior border: Posterior aspect of sternum
Posterior border: Anterior border of superior vena cava
3a: Prevascular – On the left
Upper border: Apex of chest
Lower border: Level of carina
Anterior border: Posterior aspect of sternum
Posterior border: Left carotid artery
3p: Retrotracheal
Upper border: Apex of chest
Lower border: Carina

#4 (Left/Right) Lower paratracheal nodes

4R: Includes right paratracheal nodes, and pretracheal nodes extending to the left lateral border of trachea
Upper border: Intersection of caudal margin of innominate vein with the trachea
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

#5 Subaortic (aorto-pulmonary window)

Subaortic lymph nodes lateral to the ligamentum arteriosum
Upper border: The lower border of the aortic arch
Lower border: Upper rim of the left main pulmonary artery

#6 Para-aortic nodes (ascending aorta or phrenic)

Lymph nodes anterior and lateral to the ascending aorta and aortic arch
Upper border: A line tangential to the upper border of the aortic arch
Lower border: The lower border of the aortic arch

#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

#8 (Left/Right) Para-esophageal 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

#9 (Left/Right) Pulmonary ligament nodes

Nodes lying within the pulmonary ligament
Upper border: The inferior pulmonary vein
Lower border: The diaphragm

#10 (Left/Right) Hilar nodes

Includes 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

#11 Interlobar nodes

Between the origin of the lobar bronchi
***#11s:** Between the upper lobe bronchus and bronchus intermedius on the right
***#11i:** Between the middle and lower lobe bronchi on the right
*optional sub-categories

#12 Lobar nodes

Adjacent to the lobar bronchi

#13 Segmental nodes

Adjacent to the segmental bronchi

#14 Sub-segmental nodes

Adjacent to the subsegmental bronchi

Rusch VW, Asamura H, Watanabe H, et al. The IASLC lung cancer staging project: A proposal for a new international lymph node map in the forthcoming seventh edition of the TNM classification for lung cancer. *J Thorac Oncol*. 2009;4:568-577.

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INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

Lung Cancer TNM Stages–9th Edition

Stage Groups of the 9th Edition of the Tumor, Node, Metastasis (TNM) Classification of Lung Cancer

9th Edition TNM Descriptors and Stages

T/M	Categories and Descriptors	N0	N1	N2		N3
				N2a	N2b	
T1	T1a ≤1 cm	IA1	IIA	IIB	IIIA	IIIB
	T1b >1 to ≤2 cm	IA2	IIA	IIB	IIIA	IIIB
	T1c >2 to ≤3 cm	IA3	IIA	IIB	IIIA	IIIB
T2	T2a Visceral pleura / central invasion	IB	IIB	IIIA	IIIB	IIIB
	T2a >3 to ≤4 cm	IB	IIB	IIIA	IIIB	IIIB
	T2b >4 to ≤5 cm	IIA	IIB	IIIA	IIIB	IIIB
T3	T3 >5 to ≤7 cm	IIB	IIIA	IIIA	IIIB	IIIC
	T3 Invasion	IIB	IIIA	IIIA	IIIB	IIIC
	T3 Same lobe separate tumor nodules	IIB	IIIA	IIIA	IIIB	IIIC
T4	T4 >7 cm	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 Invasion	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 Ipsilateral separate tumor nodules	IIIA	IIIA	IIIB	IIIB	IIIC
M1	M1a Contralateral tumor nodules	IVA	IVA	IVA	IVA	IVA
	M1a Pleural / pericardial effusion, nodules	IVA	IVA	IVA	IVA	IVA
	M1b Single extrathoracic metastasis	IVA	IVA	IVA	IVA	IVA
	M1c1 Multiple metastases in 1 organ system	IVB	IVB	IVB	IVB	IVB
	M1c2 Multiple metastases in >1 organ systems	IVB	IVB	IVB	IVB	IVB

1. Asamura H, Nishimura KK, Giroux DJ, et al. IASLC lung cancer staging project: The new database to inform revisions in the ninth edition of the TNM classification of lung cancer. *J Thorac Oncol*. 2023;18(5):564-575.
2. Van Schil PE, Asamura H, Nishimura KK, et al. The IASLC lung cancer staging project: Proposals for the revisions of the T descriptors in the forthcoming ninth edition of the TNM classification for lung cancer. *J Thorac Oncol*. 2024; 19(5):749-765.
3. Huang J, Osarogiagbon RU, Giroux DJ, et al. The International Association for the Study of Lung Cancer staging project for lung cancer: Proposals for the revision of the N descriptors in the forthcoming ninth edition of the TNM classification for lung cancer. *J Thorac Oncol*. 2024; 19(5):766-785.
4. Rusch VW, Asamura H, Watanabe H, et al. The IASLC lung cancer staging project: A proposal for a new international lymph node map in the forthcoming seventh edition of the TNM classification for lung cancer. *J Thorac Oncol*. 2009;4:568-577.
5. Fong KM, Rosenthal A, Giroux DJ, et al. The International Association for the Study of Lung Cancer staging project for lung cancer: Proposals for the revision of the M descriptors in the forthcoming ninth edition of the TNM classification of lung cancer. *J Thorac Oncol*. 2024; 19(5):786-802.
6. Rami-Porta R, Nishimura KK, Giroux DJ, et al. The International Association for the Study of Lung Cancer lung cancer staging project: Proposals for revision of the TNM stage groups in the forthcoming (ninth) edition of the TNM classification for lung cancer. *J Thorac Oncol*. 2024; 19(7):1007-1027.

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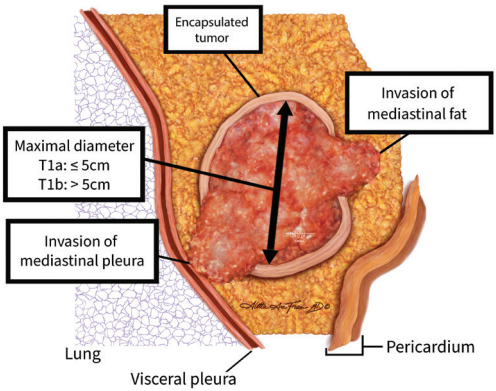
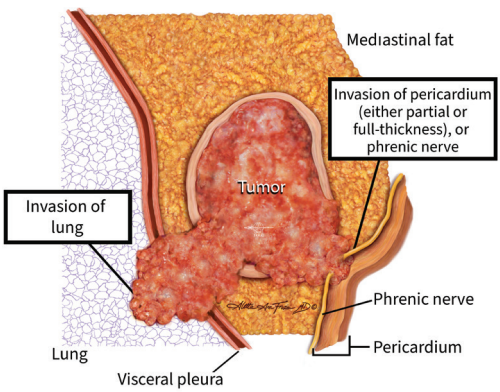
Funding support for the 9th Edition of the IASLC Staging Project was generously provided by AstraZeneca

Thymic Epithelial Tumors T Classification–9th Edition

T1

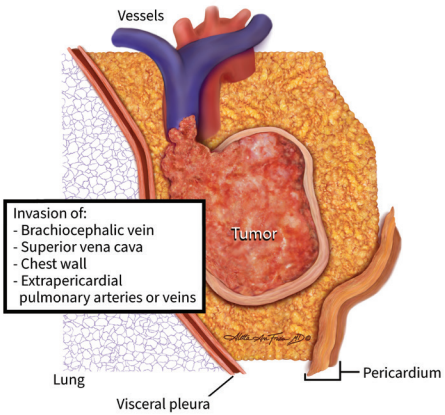


T2

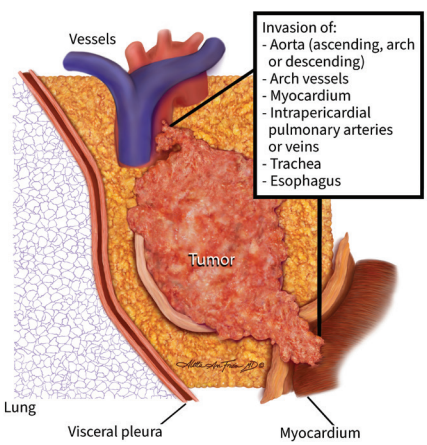


Thymic Epithelial Tumors T Classification–9th Edition

T3



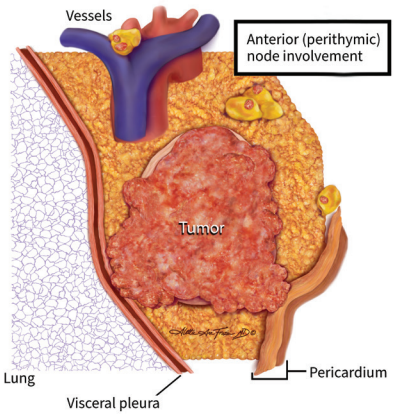
T4



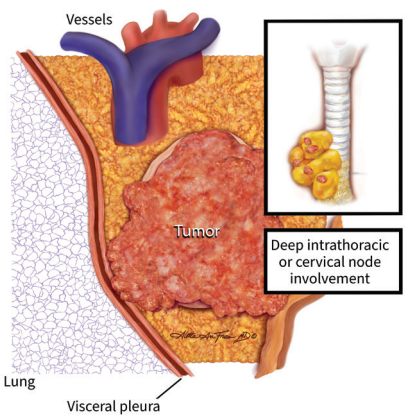
Okumura M, Marino M, Cilento V, et al. The International Association for the Study of Lung Cancer thymic epithelial tumor staging project: Proposal for the T component for the forthcoming ninth edition of the TNM classification of malignant tumors. *J Thorac Oncol*. 2023;18(12):1638-1654.

Thymic Epithelial Tumors N Classification–9th Edition

N1



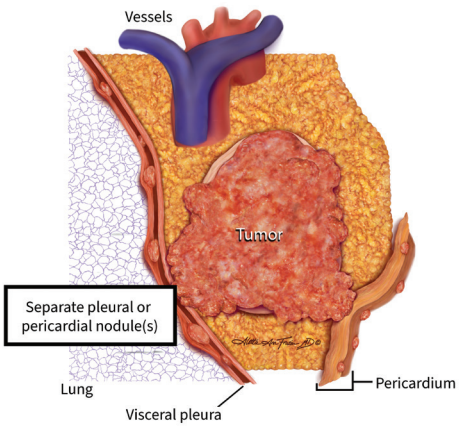
N2



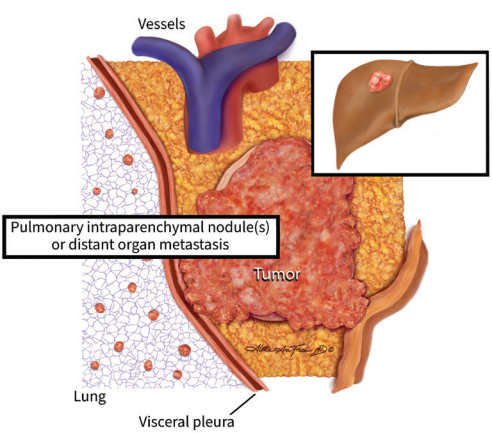
Fang W, Girard N, Cilento V, et al. The International Association for the Study of Lung Cancer thymic epithelial tumors staging project: Proposals for the N and the M components for the forthcoming ninth edition of the TNM classification of malignant tumors. *J Thorac Oncol*. 2023;19(1):52-70.

Thymic Epithelial Tumors M Classification–9th Edition

M1a



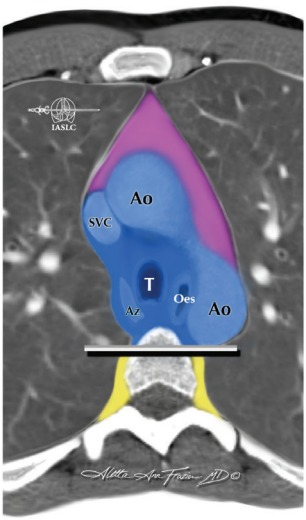
M1b



Fang W, Girard N, Cilento V, et al. The International Association for the Study of Lung Cancer thymic epithelial tumors staging project: Proposals for the N and the M components for the forthcoming ninth edition of the TNM classification of malignant tumors. *J Thorac Oncol*. 2023;19(1):52-70.

ITMIG Mediastinal Compartments

Axial #1



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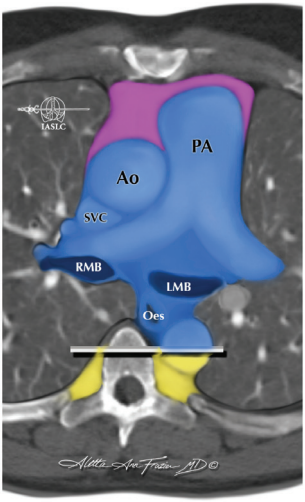


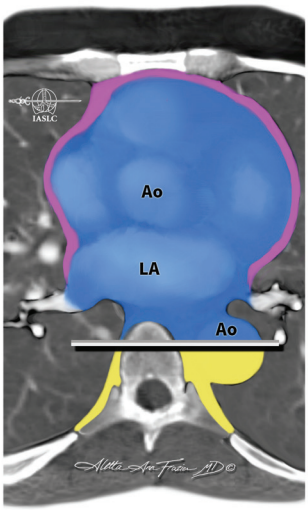
Prevascular compartment
Visceral compartment
Paravertebral compartment
Visceral-paravertebral boundary

Ao: aorta
PA: pulmonary artery
SVC: superior vena cava
T: trachea
Az: azygos vein
Oes: esophagus
RMB: right main bronchus
LMB: left main bronchus
LA: left atrium
RV: right ventricle

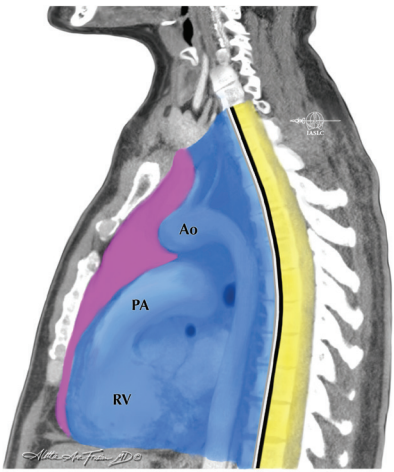
ITMIG: International Thymic Malignancy Interest Group.

ITMIG Mediastinal Compartments

Axial #3



Sagittal



Prevascular compartment
Visceral compartment
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Carter B, Tomiyama N, Bhora F et al. A Modern Definition of Mediastinal Compartments. *J Thorac Oncol*. 2014; 9(9): S97-S101.

ITMIG: International Thymic Malignancy Interest Group.

IASLC

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

Thymic Epithelial Tumor TNM Definitions–9th Edition

T category	Descriptor*
T1	A tumor that is limited to the thymus with or without encapsulation, directly invades into the mediastinal fat only or directly invades the mediastinal pleura but does not involve any other mediastinal structure. T1 is subdivided into 1. T1a (5 cm or less in its greatest dimension) 2. T1b (larger than 5 cm in its greatest dimension) irrespective of mediastinal pleura (MP) invasion. *Level 1 structures—thymus, anterior mediastinal fat, mediastinal pleura*
T2	Tumor directly invades the pericardium (either partial or full-thickness), or the lung or the phrenic nerve. *Level 2 structures—pericardium, lung, phrenic nerve*
T3	Tumor directly invades any of the following: 1) Brachiocephalic vein, 2) Superior vena cava, 3) Chest wall or 4) Extrapericardial pulmonary arteries or veins. *Level 3 structures—brachiocephalic vein, SVC, chest wall, hilar pulmonary vessels*
T4	Tumor directly invades any of the following: 1) Aorta (ascending, arch, or descending), 2) Arch vessels, 3) Intrapericardial pulmonary artery or veins, 4) Myocardium, 5) Trachea, or 6) Esophagus. *Level 4 structures—aorta (ascending, arch, or descending], arch vessels, intrapericardial pulmonary artery or veins, myocardium, trachea, esophagus)*

*T categories are defined by "levels" of invasion; they reflect the highest degree of invasion regardless of how many other (lower level) structures are invaded.

N category	Descriptor*
N0	No nodal involvement
N1	Anterior (perithymic) nodes
N2	Deep intrathoracic or cervical nodes

* Involvement must be pathologically proven in pathologic staging.

TNM, tumor, node, metastasis.

M category	Descriptor
M0	No metastatic pleural, pericardial, or distant sites
M1	Distant metastasis
M1a	Separate pleural or pericardial nodule(s)
M1b	Pulmonary intraparenchymal nodule or distant organ metastasis*

*Involvement of non-regional lymph nodes is staged as M1b.

TNM, tumor, node, metastasis

Thymic Epithelial Tumors TNM Stages–9th Edition

Thymic Epithelial Tumor Stage Groups – 9th Edition

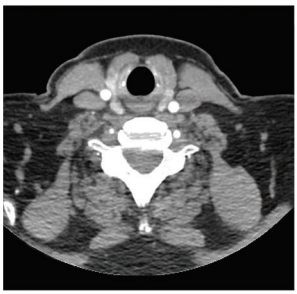
Stage	T category	N category	M category
I	T1a-b	N0	M0
II	T2	N0	M0
IIIA	T3	N0	M0
IIIB	T4	N0	M0
IVA	T any T any	N1 N0,N1	M0 M1a
IVB	T any T any	N2 N any	M0, M1a M1b

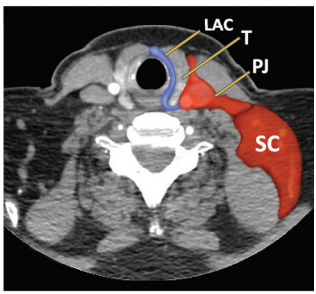
Note: any invasion must be histologically confirmed for pathologic stage

TNM, tumor, node, metastasis

1. Okumura M, Marino M, Cilento V, et al. The International Association for the Study of Lung Cancer thymic epithelial tumor staging project: Proposal for the T component for the forthcoming (ninth) edition of the TNM classification of malignant tumors. *J Thorac Oncol*. 2023;18(12):1638-1654.
2. Fang W, Girard N, Cilento V, et al. The International Association for the Study of Lung Cancer thymic epithelial tumors staging project: Proposals for the N and the M components for the forthcoming (ninth) edition of the TNM classification of malignant tumors. *J Thorac Oncol*. 2023;19(1):52-70.
3. Ruffini E, Huang J, Cilento V. The International Association for the Study of Lung Cancer thymic epithelial tumors staging project: Proposal for a stage classification for the forthcoming (ninth) edition of the TNM classification of malignant tumors. *J Thorac Oncol*. 2023;18(12):1655-1671
4. Marom EM, Fang V, Ruffini E. The International Association for the Study of Lung Cancer thymic epithelial tumor staging project: A re-assessment of the International Thymic Malignancy Interest Group/International Association for the Study of Lung Cancer lymph node map for thymic epithelial tumors for the forthcoming ninth edition of the TNM classification of malignant tumors. *J Thorac Oncol*. 2023;18(12):1672-1688.
5. Bhora FY, Chen DJ, Detterbeck FC. The ITMIG/IASLC Thymic Epithelial Tumors Staging Project: A Proposed Lymph Node Map for Thymic Epithelial Tumors in the Forthcoming 8th Edition of the TNM Classification of Malignant Tumors. *J Thorac Oncol*. 2014;9(9Suppl 2): S88-S96.
6. Rusch V, Asamura H, Watanabe H. The IASLC lung cancer staging project: A proposal for a new international lymph node map in the forthcoming seventh edition of the TNM classification for lung cancer. *J Thorac Oncol*. 2009;4(5):568-577.

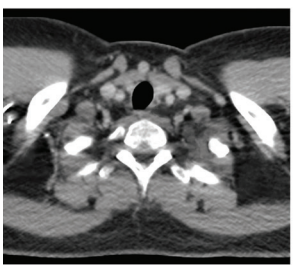
ITMIG/IASLC Lymph Node Map

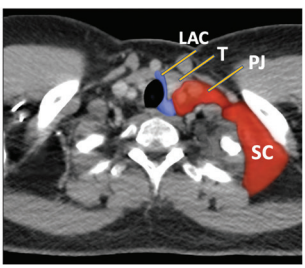


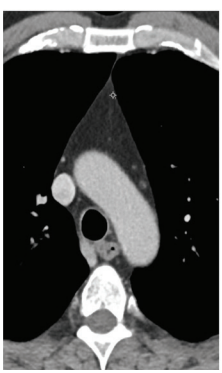


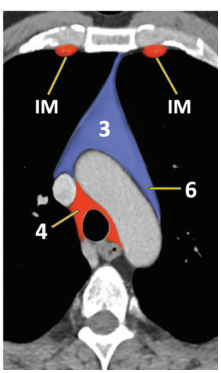
Lower Neck/Cricoid Cartilage Level
Figure 1. Lymph node levels at the lower neck, below the level of the cricoid cartilage. N1 region (blue) and N2 region (red). LAC, low anterior cervical region; PJ, peri-jugular region; SC, supraclavicular region; T, thyroid

Lower Neck/ Mid Trachea Level
Figure 2. Lymph node levels at the lower neck, mid trachea level. N1 region (blue) and N2 region (red). LAC, low anterior cervical region; PJ, peri-jugular region; SC, supraclavicular region; T, thyroid



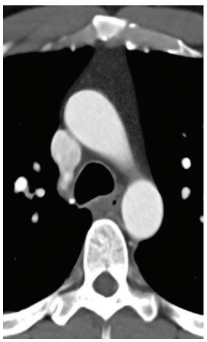


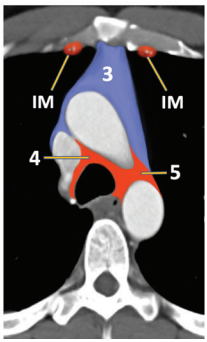




Aortic Arch Level
Figure 3. Shaded lymph node groups at the level of the aortic arch. N1 region (blue) and N2 region (red). IM, internal mammary node group. Numbers 3, 4, 6 refer to IASLC node map used for lung cancer.

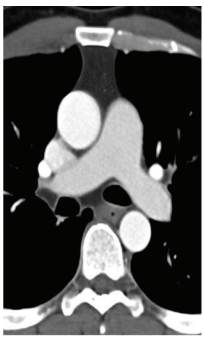
ITMIG/IASLC Lymph Node Map

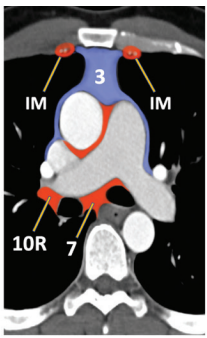


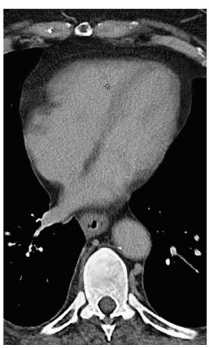


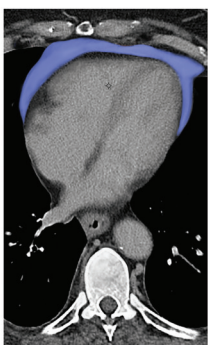
Aorto-Pulmonary Window Level
Figure 4. Shaded lymph node groups at the level of the aorto-pulmonary window. N1 region (blue) and N2 region (red). IM, internal mammary node group. Numbers 3, 4, 5 refer to IASLC node map used for lung cancer.

Main Pulmonary Artery Level
Figure 5. Shaded lymph node groups at the level of the main pulmonary artery. N1 region (blue) and N2 region (red). IM, internal mammary node group. Numbers 3, 7, 10R refer to IASLC node map used for lung cancer.









Lower Chest (base of the heart) Level
Figure 6. Native and shaded CT in the Lower chest demonstrating the anterior (perithymic) region (N1)(blue).

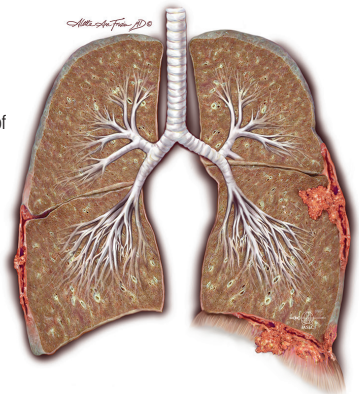
Marom EM, Fang V, Ruff ini E. The International Association for the Study of Lung Cancer thymic epithelial tumor staging project: A re-assessment of the International Thymic Malignancy Interest Group/International Association for the Study of Lung Cancer lymph node map for thymic epithelial tumors for the forthcoming ninth edition of the TNM classification of malignant tumors. *J Thorac Oncol*. 2023;18(12):1672-1688.

IASLC

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

Pleural Mesothelioma T Classification–9th Edition

T1 T2



CLINICAL T (cT)
cT1: Tumor limited to the ipsilateral pleura with **Psum[a] ≤12mm** with no involvement of the fissure (**Fmax[b] ≤5mm**)

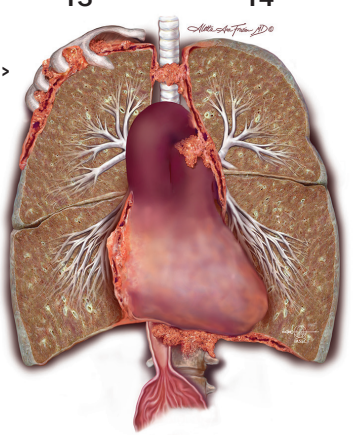
PATHOLOGICAL T (pT)
pT1: Tumor limited to the ipsilateral pleura with no involvement of the fissure

cT2: Tumor involving the ipsilateral pleura with **Psum[a] ≤12mm** and with any of the following:
- involvement of the fissure (**Fmax[b] >5mm**)
- mediastinal fat invasion
- solitary area of chest wall soft tissue invasion;

or
Tumor involving the ipsilateral pleura with **Psum[a] >12mm but ≤30mm**, with or without:
- involvement of the fissure (**Fmax[b] >5mm**)
- mediastinal fat invasion
- solitary area of chest wall soft tissue invasion

pT2: Tumor involving the ipsilateral pleura and with any of the following:
- involvement of the fissure
- ipsilateral lung parenchyma invasion
- diaphragm (non-transmural) invasion

T3 T4



cT3: Tumor involving the ipsilateral pleura with **Psum[a] > 30 mm**; with or without:
- involvement of the fissure (**Fmax[b] >5mm**)
- mediastinal fat invasion
- solitary area of chest wall soft tissue invasion

pT3: Tumor limited to the ipsilateral pleura (with or without fissure involvement) and with invasion of any of the following:
- mediastinal fat
- surface of pericardium
- endothoracic fascia
- solitary area of chest wall soft tissue

cT4: Tumor with invasion of any of the following (**any Psum[a]**):
- chest wall bony invasion (rib)
- mediastinal organs (heart, spine, esophagus, trachea, great vessels)
- diffuse chest wall invasion
- direct tumor extension through the diaphragm or pericardium
- direct extension to the contralateral pleura
- presence of malignant pericardial effusion

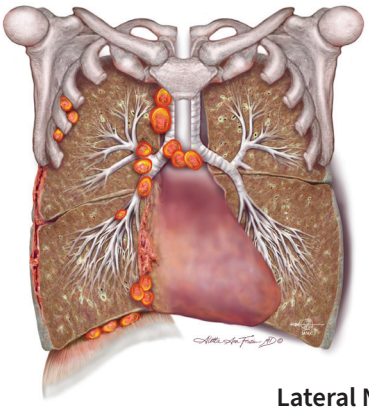
pT4: Tumor with invasion of any of the following:
- chest wall bony invasion (rib)
- mediastinal organs (heart, spine esophagus, trachea, great vessels)
- diffuse chest wall invasion
- transmural invasion of the diaphragm or pericardium
- direct extension to the contralateral pleura
- presence of malignant pericardial effusion

Gill RR, Nowak AK, Giroux DJ, et al. The International Association for the Study of Lung Cancer mesothelioma staging project: Proposals for revisions of the "T" descriptors in the forthcoming ninth edition of the TNM classification for pleural mesothelioma. *J Thorac Oncol*. 2024;S1556-0864.

IASLC

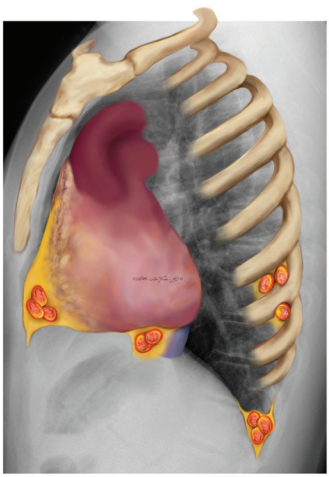
INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

Pleural Mesothelioma N Classification–9th Edition



N1

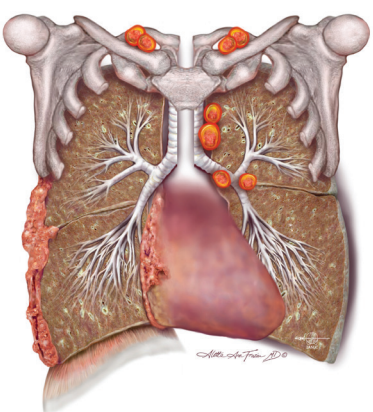
Metastases to ipsilateral intrathoracic lymph nodes (includes ipsilateral bronchopulmonary, hilar, subcarinal, paratracheal, aortopulmonary, para-esophageal, peridiaphragmatic, pericardial fat pad, intercostal, and internal mammary nodes)



Lateral N1

Nodal groups

- Anterior pericardial fat pad
- Fat pad adjacent to IVC
- Posterior intercostal nodes
- Posterior costophrenic angle



N2

Metastases in the contralateral mediastinal, ipsilateral or contralateral supraclavicular lymph nodes

Billè AR, Ripley RT, Giroux DJ, et al. Proposals for the N descriptors in the forthcoming 9th edition of the TNM classification for pleural mesothelioma. *J Thorac Oncol*. in press 2024.

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INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

Pleural Mesothelioma TNM Definitions–9th Edition

Primary Tumor (T)		
Category	**Clinical T (cT)**	**Pathologic T (pT)**
Tx	Tumor cannot be assessed	
T0	No tumor is present	
T1	Tumor limited to the ipsilateral pleura with Psum[a] ≤12 mm with no involvement of the fissure (Fmax[b] ≤5 mm)	Tumor limited to the ipsilateral pleura with no involvement of the fissure
T2	Tumor involving the ipsilateral pleura with Psum[a] ≤12 mm and with any of the following: • Involvement of the fissure (Fmax[b] >5 mm) • Mediastinal fat invasion • Solitary area of chest wall soft tissue invasion or Tumor involving the ipsilateral pleura with Psum[a] >12 mm but ≤30 mm, with or without: • Involvement of the fissure (Fmax[b] >5 mm) • Mediastinal fat invasion • Solitary area of chest wall soft tissue invasion	Tumor involving the ipsilateral pleura and with any of the following: • Involvement of the fissure • Ipsilateral lung parenchyma invasion • Diaphragm (non-transmural) invasion
T3	Tumor involving the ipsilateral pleura with Psum[a] >30 mm; with or without: • Involvement of the fissure (Fmax[b]>5mm) • Mediastinal fat invasion • Solitary area of chest wall soft tissue invasion	Tumor limited to the ipsilateral pleura (with or without fissure involvement) and with invasion of any of the following: • Mediastinal fat • Surface of pericardium • Endothoracic fascia • Solitary area of chest wall soft tissue
Category	**Clinical T (cT)**	**Pathologic T (pT)**
T4	Tumor with invasion of any of the following (any Psum[a]): • Chest wall bony invasion (rib) • Mediastinal organs (heart, spine, esophagus, trachea, great vessels) • Diffuse chest wall invasion • Direct tumor extension through the diaphragm or pericardium • Direct extension to the contralateral pleura • Presence of malignant pericardial effusion	Tumor with invasion of any of the following: • Chest wall bony invasion (rib) • Mediastinal organs (heart, spine esophagus, trachea, great vessels) • Diffuse chest wall invasion • Transmural invasion of the diaphragm or pericardium • Direct extension to the contralateral pleura • Presence of malignant pericardial effusion

[a] Psum = pmax1 + pmax2 + pmax3 (sum of 3 measurements of maximal pleural thickness measured on axial images along the chest wall or mediastinum in each of the three divisions of the chest – upper, middle and lower divided by two lines; one at the top of the aortic arch and the second drawn at the top of the left atrium)

[b] Fmax = maximal thickness of pleural tumor along the fissures measured on sagittal images

IASLC

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

Pleural Mesothelioma TNM Definitions–9th Edition

N Category	Clinical (cN) and pathologic (pN) N descriptors
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastases to ipsilateral intrathoracic lymph nodes (includes ipsilateral broncho-pulmonary, hilar, subcarinal, paratracheal, aortopulmonary, para-esophageal, peridia-phragmatic, pericardial fat pad, intercostal, and internal mammary nodes)
N2	Metastases to contralateral lymph nodes. Metastases to ipsilateral or contralateral supraclavicular lymph nodes

M Category	Clinical M descriptor (cM)
M0	No distant metastasis
M1	Distant metastasis present

Pleural Mesothelioma TNM Stages–9th Edition

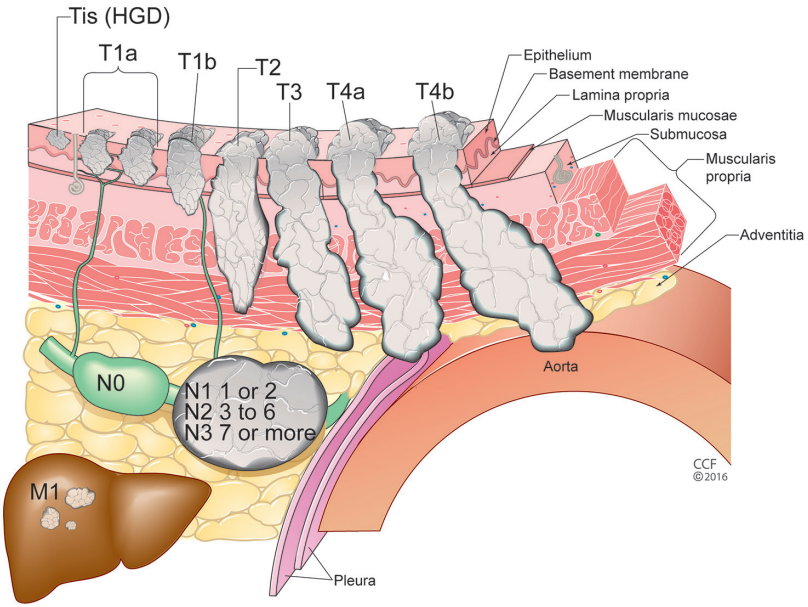
	N0	N1	N2
T1	I	II	IIIA
T2	II	IIIA	IIIA
T3	IIIA	IIIA	IIIA
T4	IIIB	IIIB	IIIB
M1	IV	IV	IV

1. Wolf AS, Eisele M, Giroux DJ, et al. The International Association for the Study of Lung Cancer pleural mesothelioma staging project: Expanded database to inform revisions in the ninth edition of the TNM classification of pleural mesothelioma. *J Thorac Oncol*. 2024;S1556-0864.
2. Gill RR, Nowak AK, Giroux DJ, et al. The International Association for the Study of Lung Cancer mesothelioma staging project: Proposals for revisions of the "T" descriptors in the forthcoming ninth edition of the TNM classification for pleural mesothelioma. *J Thorac Oncol*. 2024;S1556-0864.
3. Bille AR, Ripley RT, Giroux DJ, et al. Proposals for the N descriptors in the forthcoming 9th edition of the TNM classification for pleural mesothelioma. *J Thorac Oncol*. in press 2024.
4. Kindler HL, Rosenthal A, Giroux DJ, et al. The IASLC Mesothelioma staging project: Proposals for the M descriptors in the forthcoming ninth edition the TNM classification for pleural mesothelioma. *J Thorac Oncol*., in press 2024.
5. Nowak AK, Giroux DJ, Eisele M, et al. The IASLC Pleural Mesothelioma Staging Project: Proposal for revision of the TNM stage groupings in the forthcoming ninth edition of the TNM classification for pleural mesothelioma. *J Thorac Oncol*, in press 2024.

IASLC

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

Cancer of the Esophagus and Esophagogastric Junction 9th Edition



Ninth edition TNM categories. T is categorized as Tis: high-grade dysplasia; T1: cancer invades lamina propria, muscularis mucosae, or submucosa and is subcategorized into T1a (cancer invades lamina propria or muscularis mucosae) and T1b (cancer invades submucosa); T2: cancer invades muscularis propria; T3: cancer invades adventitia; T4, cancer invades local structures and is subcategorized as T4a: cancer invades adjacent structures such as pleura, pericardium, azygos vein, diaphragm, or peritoneum and T4b: cancer invades major adjacent structures such as aorta, vertebral body, or trachea. N is categorized as N0: no regional lymph node metastasis; N1, regional lymph node metastases involving 1 to 2 nodes; N2, regional lymph node metastases involving 3 to 6 nodes; and N3, regional lymph node metastases involving 7 or more nodes. M is categorized as M0: no distant metastasis; and M1: distant metastasis.

1. AJCC Cancer Staging Manual. 8th ed. Amin MB, Edge S, Greene FL, et al., eds. New York: Springer, 2017.
2. TNM Classification of Malignant Tumours, 8th Edition. Brierley JD, Gospodarowicz MK, Wittekind C, eds. London: Wiley, 2016.
3. Rice TW, Ishwarran H, Ferguson MK, et al. Cancer of the esophagus and esophageal junction: An 8th edition staging primer. *J Thorac Oncol*. 2016; 12(1):36-42.

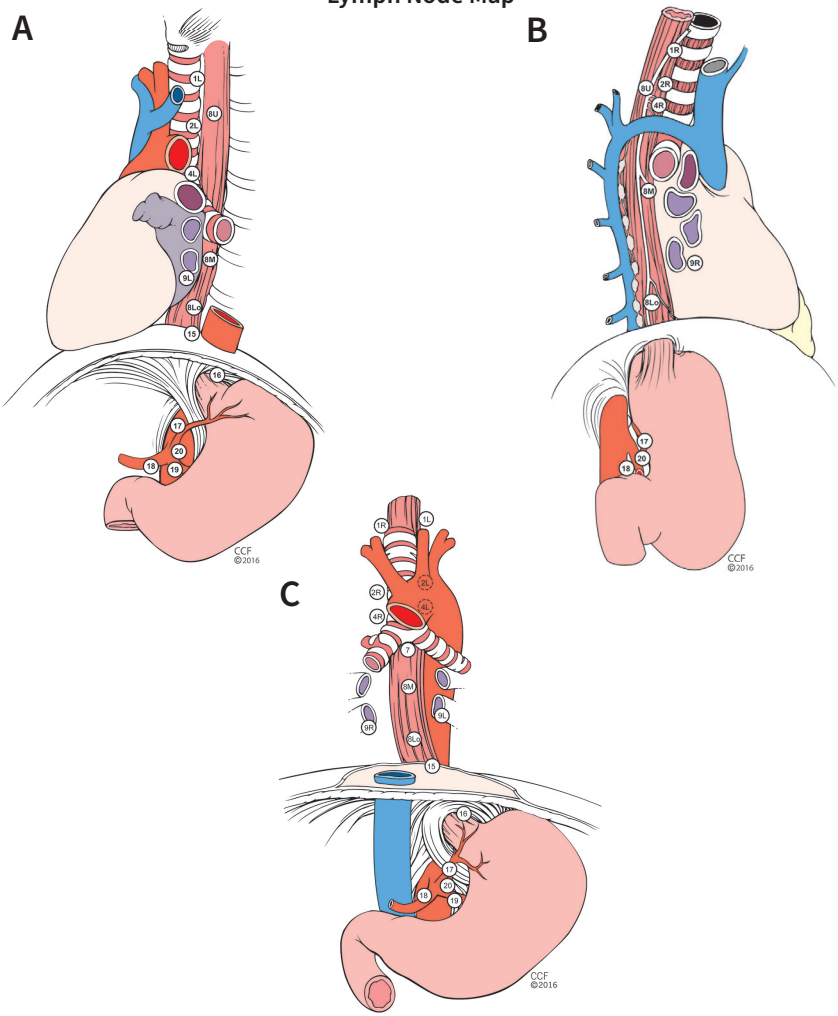
TNM Definitions

T Category	Descriptor
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ/high-grade dysplasia
T1	Tumor invades lamina propria, muscularis mucosa, or submucosa
T1a	Tumor invades lamina propria or muscularis mucosa
T1b	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades adventitia
T4	Tumor invades adjacent structures
T4a	Tumor invades pleura, pericardium, azygos vein, diaphragm, or peritoneum (resectable)
T4b	Tumor invades other adjacent structures such as aorta, vertebral body, or trachea (non-resectable)

N Category	Descriptor
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1 - 2 regional lymph nodes
N2	Metastasis in 3 - 6 regional lymph nodes
N3	Metastasis in 7 or more regional lymph nodes

M Category	Descriptor
M0	No distant metastasis
M1	Distant metastasis

Lymph Node Map

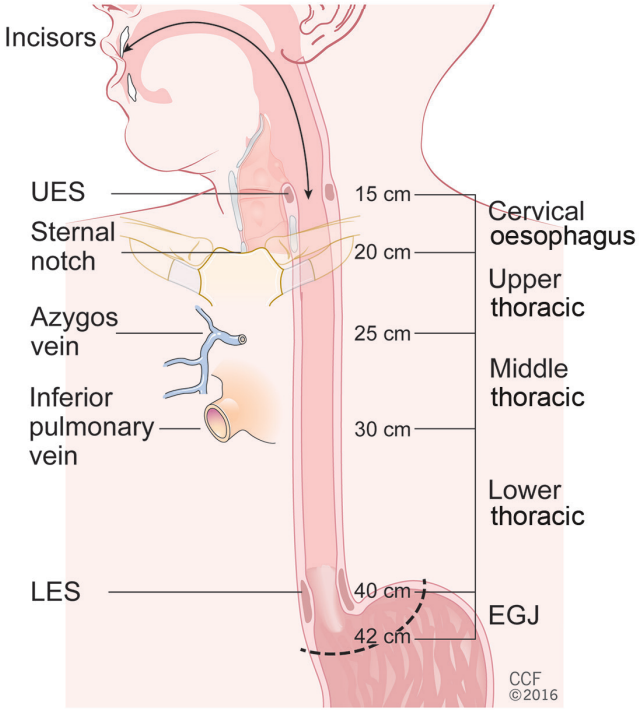


Lymph Node Legend

Regional lymph node stations for staging esophageal cancer from left (A), right (B), and anterior (C). 1R: Right lower cervical paratracheal nodes, between the supraclavicular paratracheal space and apex of the lung. 1L: Left lower cervical paratracheal nodes, between the supraclavicular paratracheal space and apex of the lung. 2R: Right upper paratracheal nodes, between the intersection of the caudal margin of the brachiocephalic artery with the trachea and apex of the lung. 2L: Left upper paratracheal nodes, between the top of the aortic arch and apex of the lung. 4R: Right lower paratracheal nodes, between the intersection of the caudal margin of the brachio cephalic artery with the trachea and cephalic border of the azygos vein. 4L: Left lower paratracheal nodes, between the top of the aortic arch and the carina. 7: Subcarinal nodes, caudal to the carina of the trachea. 8U: Upper thoracic paraesophageal lymph nodes, from the apex of the lung to the tracheal bifurcation. 8M: Middle thoracic paraesophageal lymph nodes, from the tracheal bifurcation to the caudal margin of the inferior pulmonary vein. 8Lo: Lower thoracic paraesophageal lymph nodes, from the caudal margin of the inferior pulmonary vein esophagogastric junction. 9R: Pulmonary ligament nodes, within the right inferior pulmonary ligament. 9L: Pulmonary ligament nodes, within the left inferior pulmonary ligament. 15: Diaphragmatic nodes, lying on the dome of the diaphragm and adjacent to or behind its crura. 16: Paracardial nodes, immediately adjacent to the gastroesophageal junction. 17: Left gastric nodes, along the course of the left gastric artery. 18: Common hepatic nodes, immediately on the proximal common hepatic artery. 19: Splenic nodes, immediately on the proximal splenic artery. 20: Celiac nodes, at the base of the celiac artery. Cervical periesophageal level VI and level VII lymph nodes are named as per the head and neck map.

1. AJCC Cancer Staging Manual. 8th ed. Amin MB, Edge S, Greene FL, et al., eds. New York: Springer, 2017.
2. TNM Classification of Malignant Tumours, 8th Edition. Brierley JD, Gospodarowicz MK, Wittekind C, eds. London: Wiley, 2016.
3. Rice TW, Ishwarran H, Ferguson MK, et al. Cancer of the esophagus and esophageal junction: An 8th edition staging primer. *J Thorac Oncol*. 2016; 12(1):36-42.

Location of Esophageal Cancer Primary Site



Exact measurements depend on body size and height. Location of cancer primary site is defined by cancer epicenter. Cancers involving the esophagogastric junction (EGJ) that have their epicenter within the proximal 2 cm of the cardia (Siewert types I/II) are to be staged as esophageal cancers. Cancers whose epicenter is more than 2 cm distal from the EGJ, even if the EGJ is involved, will be staged using the stomach cancer TNM and stage groups.

Key: LES, lower esophageal sphincter; UES, upper esophageal sphincter.

Rice TW, Ishwarran H, Ferguson MK, et al. Cancer of the esophagus and esophageal junction: An 8th edition staging primer. *J Thorac Oncol*. 2016; 12(1):36-42.

Clinical Stage Groups (cTNM)

Clinical Stage for Squamous Cell Carcinoma of the Esophagus and the Esophagogastric Junction (cTNM)			
Stage 0	Tis	N0	M0
Stage I	T1	N0, N1	M0
Stage II	T2	N0, N1	M0
	T3	N0	M0
Stage III	T1, T2	N2	M0
	T3	N1, N2	M0
Stage IVA	T4a, T4b	N0, N1, N2	M0
	Any T	N3	M0
Stage IVB	Any T	Any N	M1

Clinical Stage for Adenocarcinoma of the Esophagus and the Esophagogastric Junction (cTNM)			
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T1	N1	M0
Stage IIB	T2	N0	M0
Stage III	T2	N1	M0
	T3, T4a	N0, N1	M0
Stage IVA	T1-T4a	N2	M0
	T4b	N0, N1, N2	M0
	Any T	N3	M0
Stage IVB	Any T	Any N	M1

1. Rice TW, Ishwaran H, Blackstone EH, et al. Recommendations for clinical staging (cTNM) of cancer of the esophagus and esophagogastric junction for the 8th edition AJCC/UICC staging manuals. *Dis Esophagus*. 2016;7:913-19.
2. Rice TW, Apperson-Hansen C, DiPaola LM, et al. Worldwide Esophageal Cancer Collaboration: Clinical staging data. *Dis Esophagus*. 2016;7:707-14.
3. Rice TW, Ishwarran H, Ferguson MK, et al. Cancer of the esophagus and esophageal junction: An 8th edition staging primer. *J Thorac Oncol*. 2016; 12(1):36-42.

Pathologic Stage Groups (pTNM)

Pathologic Stage for Cancers of the Esophagus and the Esophagogastric Junction (pTNM)			
Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage IIA	T2	N0	M0
Stage IIB	T1	N1	M0
	T3	N0	M0
Stage IIIA	T1	N2	M0
	T2	N1	M0
Stage IIIB	T2	N2	M0
	T3	N1, N2	M0
	T4a	N0, N1	M0
Stage IVA	T4a	N2	M0
	T4b	Any N	M0
	AnyT	T3	M0
Stage IVB	AnyT	Any N	M1

Pathologic stage is similar for both squamous cell carcinoma and adenocarcinoma.

Rice TW, Ishwaran H, Hofstetter WL, et al. Recommendations for pathologic staging (pTNM) of cancer of the esophagus and esophagogastric junction for the 8th edition AJCC/UICC staging manuals. *Dis Esophagus*. 2016;7:897-905.

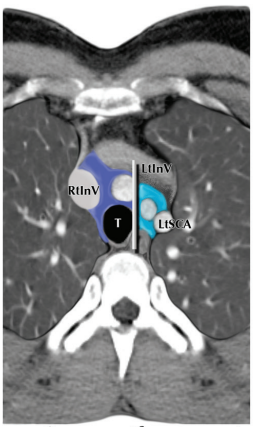
Postneoadjuvant Pathologic Stage Groups (ypTNM)

Pathologic Stage After Neoadjuvant Therapy for Cancers of the Esophagus and the Esophagogastric Junction (ypTNM)			
Stage	**T**	**N**	**M**
Stage I	T0-2	N0	M0
Stage II	T3	N0	M0
Stage IIIA	T0-2	N1	M0
Stage IIIB	T3	N1	M0
	T0-3	N2	M0
	T4a	N0	M0
Stage IVA	T4a	N1-2	M0
	T4a	NX	M0
	T4b	N0-2	M0
	Any T	N3	M0
Stage IVB	Any T	Any N	M1

ypStage is also identical for both histopathologic cell types.

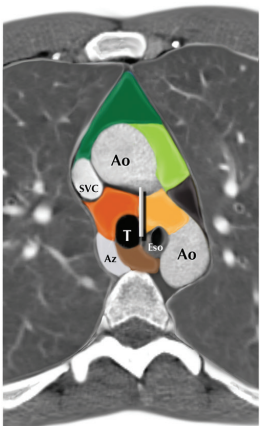
Rice TW, Ishwaran H, Kelsen DP, et al. Recommendations for neoadjuvant pathologic staging (ypTNM) of cancer of the esophagus and esophagogastric junction for the 8th edition AJCC/UICC staging manuals. *Dis Esophagus*. 2016;29(8):906-912.

Axial #1



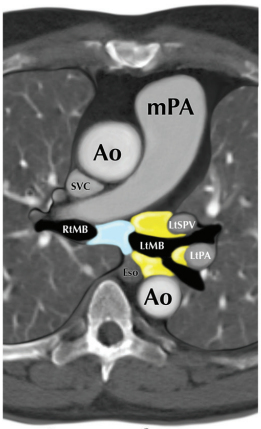
2R 2L

Axial #2



3a 3p 4R 4L 5 6

Axial #3



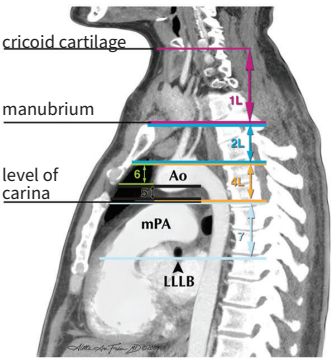
7 10

Abbreviations:

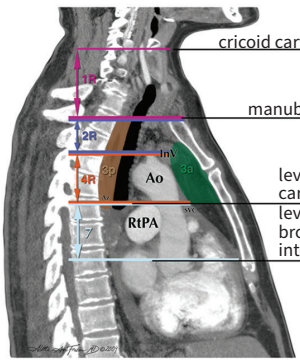
Ao– aorta
Az – azygos vein
Eso – esophagus
InV – innominate vein
LLLB – left lower lobe bronchus
LtInV – left innominate vein
LtMB – left mainstem bronchus
LtPA – left pulmonary artery
LtSCA – left subclavian artery
LtSPV – left superior pulmonary vein
mPA – main pulmonary artery
RtInV – right innominate vein
RtMB – right mainstem bronchus
RtPA – right pulmonary artery
LtPA – left pulmonary artery
SVC – superior vena cava
T – trachea

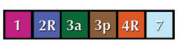
Rusch VW, Asamura H, Watanabe H, Giroux DJ, Rami-Porta R, Goldstraw P. The IASLC lung cancer staging project. A proposal for a new international lymph node map in the forthcoming seventh edition of the TNM classification for lung cancer. *J Thorac Oncol.* 2009; 4: 568-577.

Sagittal Left

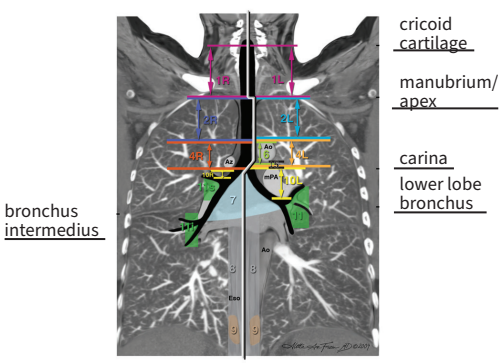


Sagittal Right





Coronal



Abbreviations:

Ao– aorta
Az – azygos vein
Eso – esophagus
InV – innominate vein
LLLB – left lower lobe bronchus
LtInV – left innominate vein
LtMB – left mainstem bronchus
LtPA – left pulmonary artery
LtSCA – left subclavian artery
LtSPV – left superior pulmonary vein
mPA – main pulmonary artery
RtInV – right innominate vein
RtMB – right mainstem bronchus
RtPA – right pulmonary artery
LtPA – left pulmonary artery
SVC – superior vena cava
T – trachea

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2021 WHO Classification
Lung Adenocarcinoma in Resected Specimens

Invasive Non-Mucinous Lung Adenocarcinoma

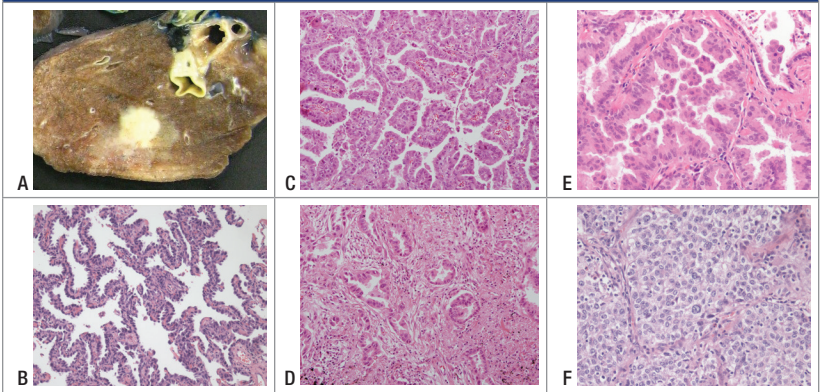

Figure 1. A. Macroscopic image of a subpleural tumour showing a solid component superiorly corresponding to invasive adenocarcinoma and a more ill-defined component inferiorly corresponding to a lepidic/non-invasive component. B. Lepidic pattern adenocarcinoma. C. Papillary pattern with central fibrovascular cores. D. Acinar Pattern. E. Micropapillary pattern lacking fibrovascular cores. F. Solid pattern.

Table 1. Grading of resected early-stage invasive non-mucinous lung adenocarcinoma based on histological patterns.

Grade	Differentiation	Patterns
1	Well differentiated	Lepidic-predominant with no or < 20% high-grade pattern
2	Moderately differentiated	Acinar or papillary-predominant with no or < 20% high-grade pattern
3	Poor differentiated	Any tumour with ≥ 20% high-grade pattern (solid, micropapillary, cribriform, or complex glandular pattern[a])

[a]Fused glands or single cells infiltrating in a desmoplastic stroma.

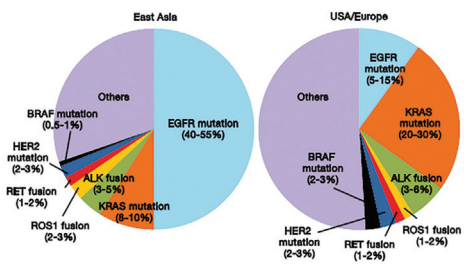

Figure 2. Pie chart showing the proportion of oncogenic driver mutations nonmucinous adenocarcinoma of the lung from eastern Asia and USA/Europe.

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2021 WHO Classification
Lung Adenocarcinoma in Resected Specimens

Adenocarcinoma *In Situ*

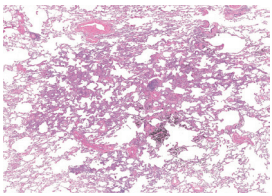

Figure 3. A circumscribed proliferation of malignant cells along the existing alveolar framework without invasive growth.

Diagnostic Features of Adenocarcinoma *In Situ*

- A small localized tumour (≤ 30 mm)
- Pure lepidic growth
- No stromal, vascular, or pleural invasion
- No pattern of invasive adenocarcinoma (e.g. acinar, papillary, micropapillary, solid, colloid, enteric, fetal, or invasive mucinous adenocarcinoma)
- No spread through airspaces
- Cell type mostly non-mucinous (type II pneumocytes or club cells) but very rarely may be mucinous (tall columnar cells with basal nuclei and abundant cytoplasmic mucin, sometimes resembling goblet cells)
- Nuclear atypia is inconspicuous
- Septal widening with sclerosis/elastosis is common, particularly in non-mucinous adenocarcinoma *in situ*.

Minimally Invasive Adenocarcinoma

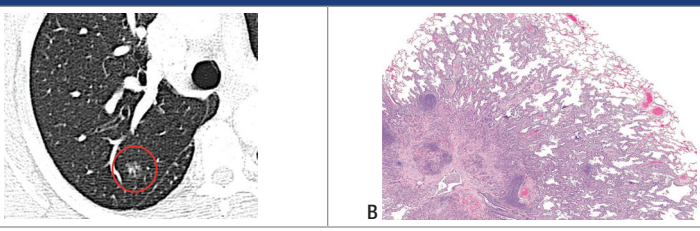

Figure 4. A. CT scan showing part-solid nodule (circle) that is mostly ground-glass, with a small solid component measuring < 5 mm B. Microscopically a lepidic-predominant tumour with a total size <30 mm and an invasive area of 4mm. The tumour mostly shows a lepidic pattern of growth (top and right), with a nodule of invasive adenocarcinoma (bottom left).

Invasive Mucinous Adenocarcinoma

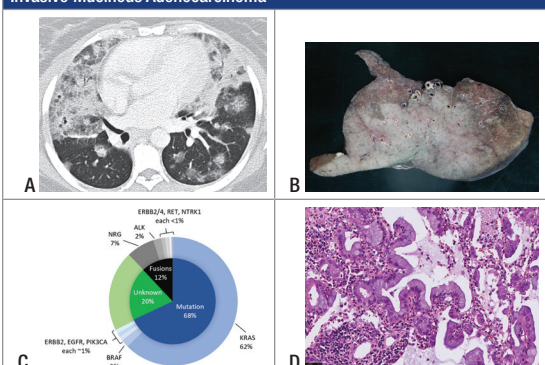

Figure 5.

A. CT showing diffuse bilateral airspace and ground-glass opacity with nodular components.

B. Macroscopic image shows a poorly defined tumour with a soft mucoid appearance.

C. Pie chart of molecular alterations in invasive mucinous adenocarcinomas.

D. Microscopically invasive mucinous adenocarcinoma shows columnar cells with abundant apical intracytoplasmic mucin and small basally oriented nuclei with minimal cytological atypia growing.

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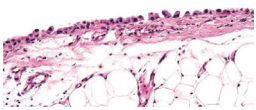
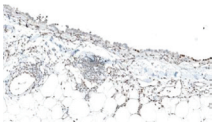
2021 WHO Classification
Mesothelioma

Mesothelioma *in situ*

A preinvasive single-layer surface proliferation of neoplastic mesothelial cells.



Mesothelioma *in situ*

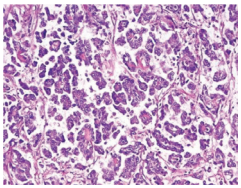


BAP1 loss

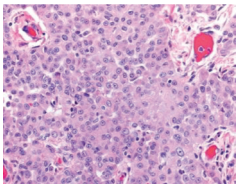
- No thoracopic or imaging evidence of tumor
- History of recurrent pleural effusions
- Loss of BAP1 and/or MTAP by IHC and/or CDKN2A homozygous deletion by FISH

Diffuse Mesothelioma

Diffuse plural thickening by a malignant neoplasm with epithelioid, sarcomatoid, or biphasic histology



Tubulopapillary growth



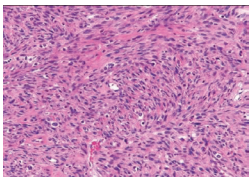
Solid growth

Diffuse epithelioid mesothelioma:

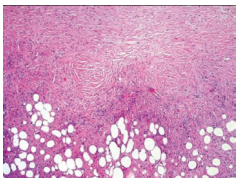
- May appear cytologically bland or show marked atypia
- A variety of architectural patterns, cytologic and stromal features may occur, some with prognostic significance
- Epithelioid mesothelioma should also be graded

Diffuse sarcomatoid mesothelioma:

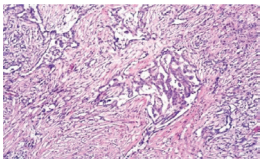
- Characterized by spindle cells arranged in fasicles or in haphazard patterns.
- Desmoplastic mesothelioma is characterized by spindled cells with minimal atypia arranged in a patternless pattern in dense hyalinized stroma



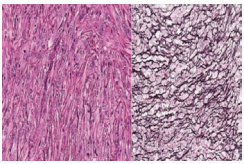
Sarcomatoid mesothelioma



Desmoplastic mesothelioma



Biphasic mesothelioma with epithelioid and sarcomatoid components



Transitional morphology shows features in between epithelioid and sarcomatoid. Reticulin stains (right) show fibers surrounding each cell as opposed to groups of cells as in epithelioid mesothelioma, may be helpful in some cases.

Diffuse biphasic mesothelioma:

- Composed of both epithelioid and sarcomatoid morphology;
- ≥ 10% of each component should be present in resection specimens.
- Areas of transitional morphology should be considered sarcomatoid

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2021 WHO Classification
Diffuse Pleural Mesothelioma

Histological Classification of Diffuse Pleural Mesothelioma

Type	Description	Patterns/features	Favorable	Unfavorable	Reporting
Epithelioid mesothelioma	Composed of round epithelioid cells, usually with cohesive architecture, but single cells within a fibrous stroma may also be seen	Architectural patterns: Tubulopapillary Trabecular Adenomatoid Solid Micropapillary Cytological features: Rhabdoid Deciduoid[a] Small cell[a] Clear cell[a] Signet ring[a] Lymphohistiocytoid Pleomorphic Stromal features: Myxoid	Architectural patterns: Tubulopapillary Trabecular Adenomatoid Cytological features: Lymphohistiocytoid Low nuclear grade[a] Stromal features: Myxoid (if predominant, i.e. when ≥ 50% of tumor with < 50% solid pattern contains myxoid stroma)	Architectural patterns: Solid (≥ 50%) Micropapillary Cytological features: Rhabdoid Pleomorphic Low nuclear grade[b] Necrosis: (included in grading)	Grade (high or low), architectural patterns present (and in definitive resection specimens such as EPD and EPP, percentages of each pattern; for all other specimens, indicate "with ... patterns/features")
Sarcomatoid mesothelioma, including desmoplastic pattern	Composed of elongated/spindle cells (> 2 times longer than wide) arranged in solid sheets or within a fibrous stroma	Cytological features: Lymphohistiocytoid Transitional Pleomorphic Stromal features: Desmoplastic With heterologous differentiation	Cytological features: Lymphohistiocytoid	Cytological features: Transitional	
Biphasic mesothelioma	Showing both epithelioid and sarcomatoid components (in definitive resection specimens, namely EPD and EPP, ≥ 10% of each component is required for diagnosis); for smaller samples, including biopsy and cytology specimens, the diagnosis of biphasic mesothelioma can be rendered regardless of percentages of each component present				Percentage of each component should be reported regardless of specimen type

Grading of Epithelial Mesothelioma

Nuclear grade:

Nuclear atypia score: _____ 1 for mild, 2 for moderate, 3 for severe

Miotic count score: _____ 1 for low (≤1 mitosis/2mm^2), 2 for intermediate (2-4 mitoses/2mm^2), 3 for high (≥ 5 mitoses/2mm^2)

Sum: _____ 2 or 3 = nuclear grade I, 4 or 5 = nuclear grade II, 6 = nuclear grade III

Necrosis: present/absent

Overall tumor grade:

Low grade = nuclear grades I and II without necrosis

High grade = nuclear grades II with necrosis, nuclear grade III with or without necrosis

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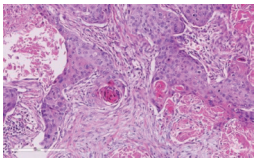
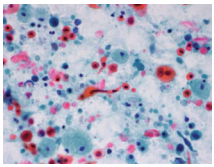
2021 WHO Classification
Squamous Cell Carcinoma (SQCC)

A malignant epithelial tumour characterized by the presence of keratinization, intercellular bridges, or immunohistochemical markers of squamous cell differentiation



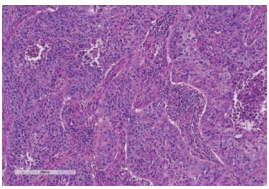
Keratinization with pearl formation



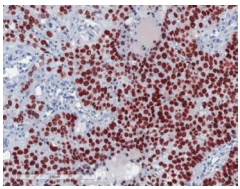
Keratinizing tumor cells (cytology)

Keratinizing squamous cell carcinoma with formation of keratin pearls (left) and on cytology specimen showing isolated malignant cells with bizarrely shaped tadpole-appearance and keratinized cytoplasm (right).

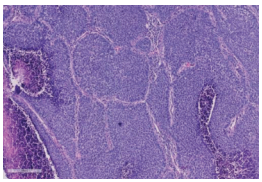
Non-keratinizing squamous cell carcinoma with tumor cells growing in solid pattern (left), no keratinization and diffuse strongly positive nuclear p40 staining by immunohistochemistry (right).



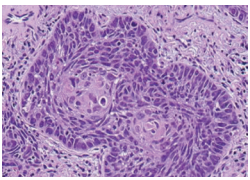
Carcinoma with solid growth pattern



P40 immunostain



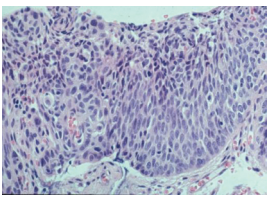
Solid carcinoma with lobular pattern



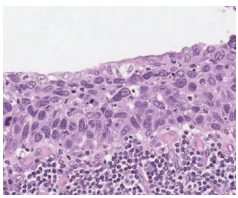
Intercellular bridges

Basaloid squamous cell carcinoma with cells showing scant cytoplasm, lobular growth pattern and peripheral palisading (left), and diffuse p40 staining by immunohistochemistry. Abrupt keratinization and intercellular bridges may be seen (right).

Squamous dysplasia (left) **and carcinonoma *in situ*** (right) are pre-invasive lesions of squamous cell carcinoma arising in the bronchial epithelium. They show a continuum of morphologically recognizable neoplastic histological changes associated with accumulation of somatic genetic alterations



Severe dysplasia



Squamous carcinoma *in situ*

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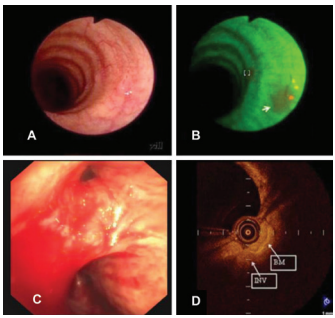
Squamous Dysplasia and Carcinoma-*In Situ*



Squamous cell carcinoma *in situ*.

White-light reflective bronchoscopy (A) and autofluorescence bronchoscopy (B) of a squamous cell carcinoma *in situ* with microinvasion in the trachea. There was no light abnormality on the white-light reflectance bronchoscopy examination. A plaque-like lesion on white-light reflectance bronchoscopy (C) and optical coherence tomography (D) showing invasion of the tumor through the basal membrane.

Diagnostic Criteria for Squamous Dysplasia and Squamous Carcinoma *in Situ*

Abnormality	Thickness	Cell Size	Maturation/Orientation	Nuclei
Mild dysplasia	Mildly increased	Mildly increased Mild anisocytosis and pleomorphism	Continuous progression of maturation from base to luminal surface Basilar zone expanded, with cellular crowding in the lower third of epithelium Distinct intermediate (prickle cell) zone present Superficial flattening of epithelial cells	Mild variation of N:C ratio Finely granular chromatin Minimal angulation Nucleoli inconspicuous or absent Nuclei vertically oriented in lower third Mitoses absent or very rare
Moderate dysplasia	Moderately increased	Mildly increased Cells often small May have moderate anisocytosis and pleomorphism	Partial progression of maturation from base to luminal surface Basilar zone expanded, with cellular crowding in the lower two thirds of epithelium Intermediate zone confined to upper third of epithelium Superficial flattening of epithelial cells	Moderate variation of N:C ratio Finely granular chromatin Angulations, grooves, and lobulations present Nucleoli inconspicuous or absent Nuclei vertically oriented in lower two thirds Mitotic figures present in lower third
Severe dysplasia	Markedly increased	Markedly increased May have marked anisocytosis and pleomorphism	Little progression of maturation from base to luminal surface Basilar zone expanded, with cellular crowding well into the upper third of epithelium Intermediate zone greatly attenuated Superficial flattening of epithelial cells	N:C ratio often high and variable Chromatin coarse and uneven Nuclear angulations and folding prominent Nucleoli frequently present and conspicuous Nuclei vertically oriented in lower two thirds Mitotic figures present in lower two thirds
Carcinoma *in situ*	May or may not be increased	May be markedly increased May have marked anisocytosis and pleomorphism	No progression of maturation from base to luminal surface; epithelium can be inverted, with little change in appearance Basilar zone expanded, with cellular crowding throughout the epithelium Intermediate zone absent Surface flattening confined to the most superficial cells	N:C ratio often high and variable Chromatin coarse and uneven Nuclear angulations and folding prominent Nucleoli may be present or inconspicuous No consistent orientation of nuclei in relation to epithelial surface Mitotic figures present through full thickness

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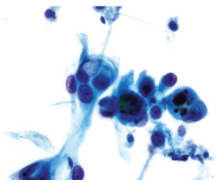
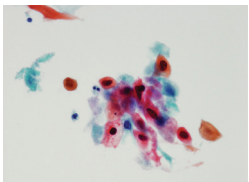
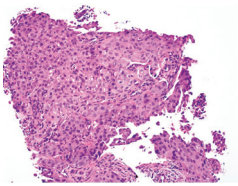
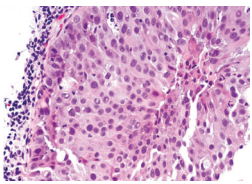
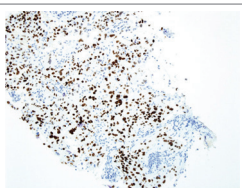
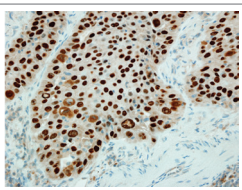
2021 WHO Classification
Small Biopsy and Cytology Samples

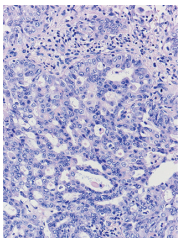
A. Adenocarcinoma (ADC) Cytology	A. Squamous Cell Carcinoma (SQCC) Cytology
	
B. Nonsmall Cell Carcinoma (NSCC), Favor ADC	**B. NSCC, Favor SQCC**
	
C. TTF-1	**C. P40**
	
a) Cytology shows cluster of tumor cells around a small lumen with focal intracytoplasmic mucin, (b) NSCC, favor ADC; solid but no glandular pattern, (c) TTF-1 is positive	a) Cytology shows pleomorphic and keratinized tumor cells including a tadpole cell, (b) NSCC favor squamous cell carcinoma (c) P40 is positive (TTF-1 was negative)

General Principles

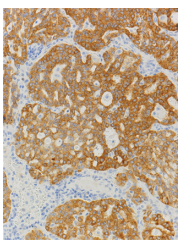
- Minimize stains to maximize tissue for molecular testing
- Cut tissue block as sparingly as possible
- Obtain unstained slides for molecular at time of cutting block for IHC
- Use limited panel of IHC (i.e TTF-1 and P40): reduces NSCC-NOS from ~40% to <10%.
- Molecular testing, if clinically appropriate, can be performed on remaining tissue

ALK Rearranged Adenocarcinoma

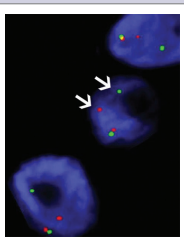
A) Cribriform Pattern



B) ALK IHC



C) ALK FISH



Travis WD, Brambilla E, Burke AP, Marx A, Nicholson AG. WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart. Lyon: IARC; 2015."

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Terminology and Criteria for Common Lung Cancers in Small Biopsies and Cytology

Small Biopsy/Cytology Terminology	Morphology/Stains	2021 WHO Classification in Resection Specimens
Adenocarcinoma (describe identifiable patterns present)	Morphological adenocarcinoma patterns clearly present	Adenocarcinoma (Predominant pattern) Lepidic, Acinar, Papillary, Solid, Micropapillary
Adenocarcinoma with lepidic pattern (if pure, add note: an invasive component cannot be excluded)		Lepidic (nonmucinous) Minimally invasive adenocarcinoma, adenocarcinoma *in situ* or an invasive adenocarcinoma with a lepidic component
Invasive mucinous adenocarcinoma (describe patterns present; if pure lepidic pattern, use term mucinous adenocarcinoma with lepidic pattern		Invasive mucinous adenocarcinoma
Adenocarcinoma with colloid features		Colloid adenocarcinoma
Adenocarcinoma with fetal features		Fetal adenocarcinoma
Adenocarcinoma with enteric features		Enteric adenocarcinoma
Non-small cell carcinoma, favor adenocarcinoma	Morphologic adenocarcinoma patterns not present, but supported by special stains, i.e. +TTF-1	Adenocarcinoma (solid pattern may be just one component of the tumor)[b]
Squamous cell carcinoma	Morphologic squamous cell patterns clearly present	Small cell carcinoma
Non-small cell carcinoma, favor squamous cell carcinoma	Morphologic squamous cell patterns not present, but supported by stains i.e. +p40	Squamous cell carcinoma, (nonkeratinizing pattern may be just one component of the tumor)
Non-small cell carcinoma, not otherwise specified NSCC-NOS	No clear adenocarcinoma, squamous or neuroendocrine morphology or staining pattern	Large cell carcinoma
Small cell carcinoma		Small cell carcinoma
Non-small cell carcinoma with neuroendocrine (NE) morphology and positive NE markers, possible LCNEC		Large cell neuroendocrine carcinoma (LCNEC)
Morphologic squamous cell and adenocarcinoma patterns present: Non-small cell carcinoma, NOS, (comment that adenocarcinoma and squamous components are present and this could represent adenosquamous carcinoma).		Adenosquamous carcinoma