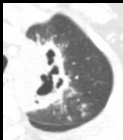


Lung Cancer Update

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DEPARTMENT OF
RADIOLOGY
University of Wisconsin
School of Medicine and Public Health

CHESTRAD 2023

A Case Review and Lecture Series
Saturday 15th July - Sunday 16th July - Monday 17th July
27 CPD Points

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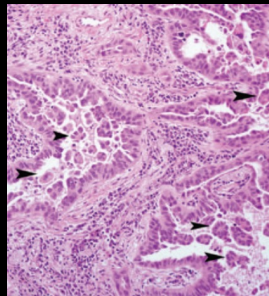
Objectives

- List common histopathologic types of lung cancer
- Define role of imaging in the TNM8 staging of lung cancer
- Highlight changes from TNM7 and describe shortcomings of TNM8

2

Lung Cancer Types

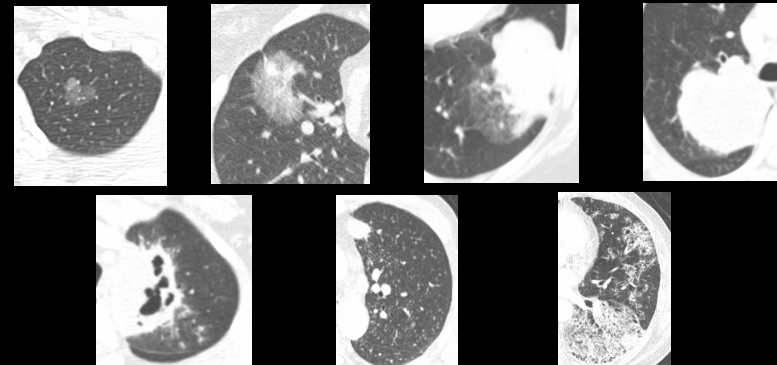
- Adenocarcinoma
- Squamous cell carcinoma
- Neuroendocrine tumors
 - Carcinoid tumor
 - Large cell neuroendocrine carcinoma
 - Small cell carcinoma
- Other rare subtypes



J Thorac Oncol. 2015 Sep;10(9):1243-1260.

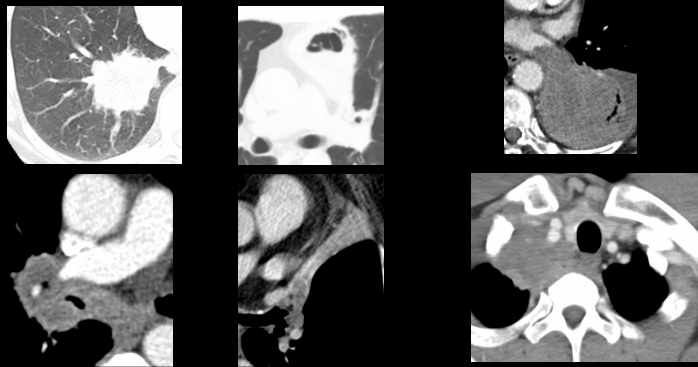
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Adenocarcinoma



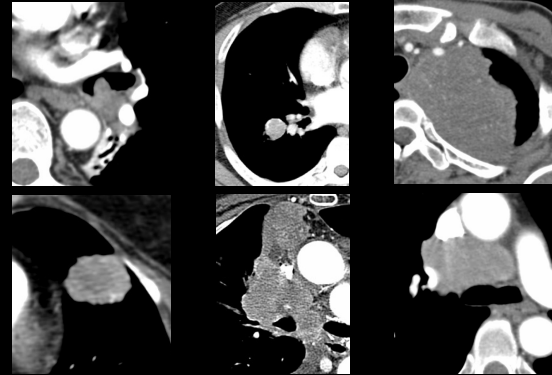
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Squamous Cell Carcinoma



5

Neuroendocrine Tumors



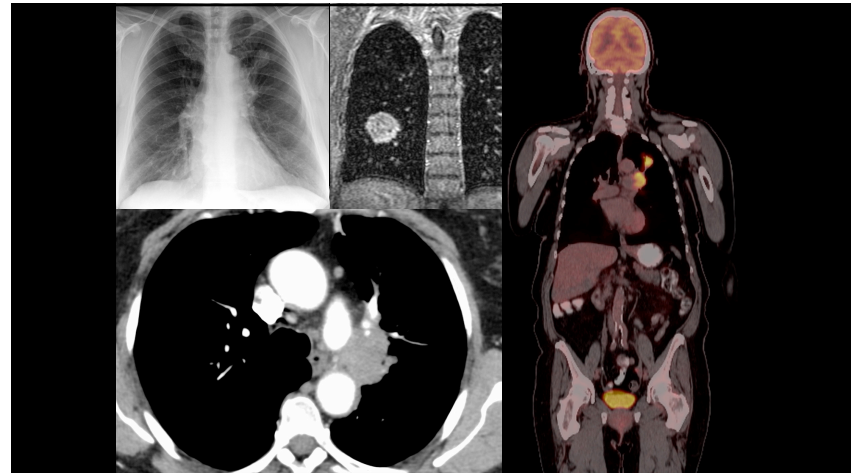
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Role of Imaging

- Screening
- Diagnosis
- Staging
- Surveillance
- Complications



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Imaging Modalities

Modality	Screening	Diagnosis	Staging	Surveillance	Complications
Radiography		+			+
CT	+++	+++	+++	+++	+++
MRI		+	++		++
US		+	++		++
PET/CT			+++		

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Diagnosis



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Importance of Staging

- Guides treatment
- Assess results of treatment
- Better defines prognosis
- Establishes nomenclature to improve communication and research

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Current Staging System

- 8th Edition of TNM staging system (AJCC/UICC)
 - (T)umor
 - (N)ode
 - (M)etastasis
 - Based on approximately 95,000 patients

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Methods for Staging

- History and physical examination
- Laboratory testing
- Imaging
- Tissue sampling

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Methods for Staging

- Chest CT
 - Usually establishes likely diagnosis of lung cancer
 - Depicts local and regional extent of tumor
 - Suggests alternate diagnosis

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Methods for Staging

- FDG PET/CT
 - Guides lymph node sampling
 - Occult metastases
 - Avoid unnecessary surgery

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Methods for Staging

- Brain MRI
 - Superior to CT for detecting metastases
 - Improved outcomes with early detection of brain metastases

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Methods for Staging

• Alternatives

- Abdomen CT and bone scan if PET not available
- Head CT if MRI not available

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Imaging Modalities

Modality	T	N	M
Radiography	+	+	+
CT	+++	++	++
MRI	++	++	+++
US	+	++	++
PET/CT	+	++	+++

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Date of origin: 2005
Last revised: 2013

American College of Radiology ACR Appropriateness Criteria®

Clinical Condition: Non-invasive Clinical Staging of Bronchogenic Carcinoma
Variant 1: Non-small-cell lung carcinoma.

Diagnostic Procedure	Rating	Comments	RRL*
CT chest without IV contrast	9	Through adrenal glands.	☐☐☐☐
CT chest with IV contrast	9	Through adrenal glands. See text. There are pros and cons to the use of IV contrast. There is no strong scientific evidence to support the use of IV contrast.	☐☐☐☐
FDG-PET/CT skull base to mid-thigh	9	If a diagnostic chest CT has not yet been performed, obtain FDG-PET skull base to mid-thigh and CT chest with or without contrast. Can only be staged more ground glass nodule.	☐☐☐☐☐
MRI head without and with IV contrast	7	If neurological symptoms are present or asymptomatic with adenocarcinoma histology greater than 3 cm in size or mediastinal adenopathy.	○
MRI head without IV contrast	5	If gadolinium contraindicated.	○
X-ray chest	5	May be useful as a baseline comparison to help detect complications of therapy and other non-tumor related disease in follow-up.	☐
CT abdomen with IV contrast	5		☐☐☐☐
CT head with IV contrast	5	If MRI is contraindicated and neurological symptoms are present.	☐☐☐☐
Tc-99m bone scan whole body	5	Not necessary if PET has been done.	☐☐☐☐
CT head without IV contrast	3		☐☐☐☐
MRI chest without and with IV contrast	3	Useful for evaluating chest wall invasion, cardiac invasion, and for local staging of superior sulcus tumors.	○
MRI chest without IV contrast	2	Useful for evaluating chest wall invasion, cardiac invasion, and for local staging of superior sulcus tumors. If gadolinium contraindicated.	○
CT abdomen without IV contrast	1		☐☐☐☐
CT abdomen without and with IV contrast	1		☐☐☐☐☐
CT head without and with IV contrast	1		☐☐☐☐
CT chest without and with IV contrast	1	Through adrenal glands.	☐☐☐☐

*Relative
Radiation Level

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T Stage

- Tumor size
- Local invasion
- Endobronchial location
- Presence of separate tumor nodules

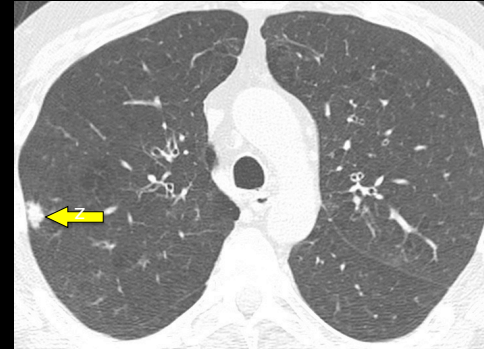
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T1

- Surrounded by lung or visceral pleura
- Invasion distal to lobar bronchus
- Size
 - ≤ 1 cm (T1a)
 - > 1 cm but ≤ 2 cm (T1b)
 - > 2 cm but ≤ 3 cm (T1c)

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T1b: > 1 but ≤ 2 cm



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T1c: > 2 cm but ≤ 3 cm



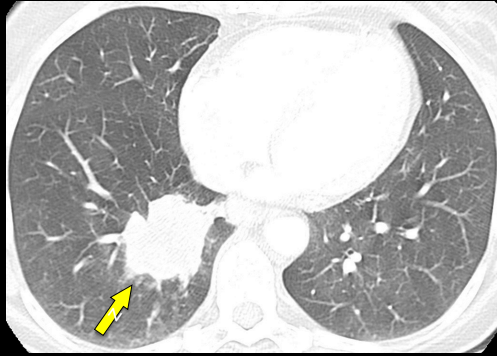
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T2

- Local invasion of visceral pleura
- Atelectasis to hilum
- Involves **main bronchus** but not carina
- Size
 - > 3 cm and ≤ 4 cm (T2a)
 - > 4 cm and ≤ 5 cm (T2b)

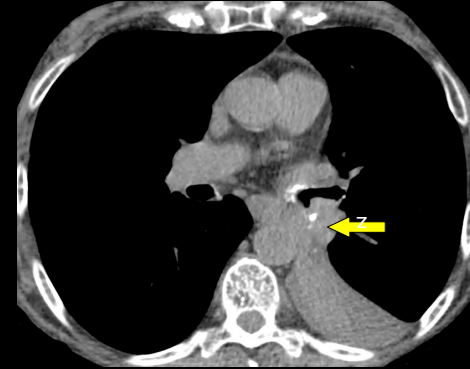
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T2b: >4 cm but ≤5 cm



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T2: Lobar Obstruction



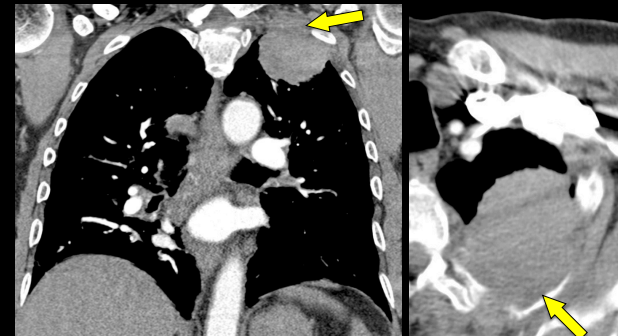
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T3

- Local invasion of chest wall, pericardium, or phrenic nerve
- Separate tumor nodule(s) in same lobe
- Size >5 cm but ≤7 cm

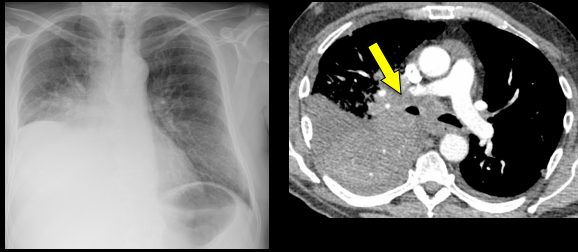
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T3: Chest Wall Invasion



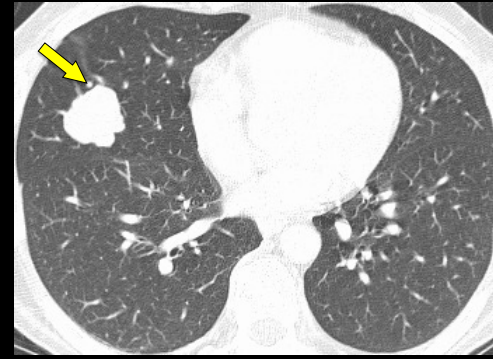
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T3: Phrenic Nerve Invasion



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T3: Tumor Nodule Same Lobe



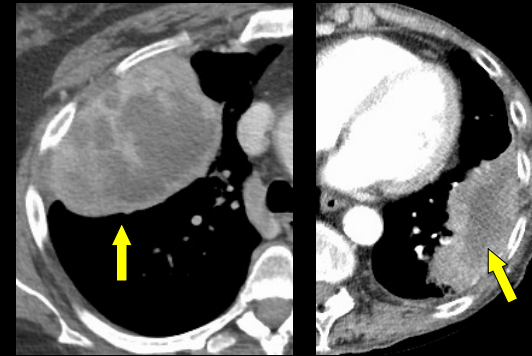
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T4

- Local invasion
 - Mediastinum
 - Diaphragm
 - Carina or trachea
 - Heart or great vessels
 - Esophagus
 - Recurrent laryngeal nerve
 - Vertebral body
- Separate tumor nodule(s) in same lung
- Size >7 cm

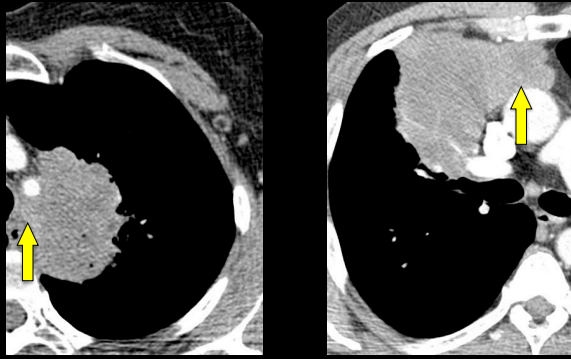
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T4: >7 cm



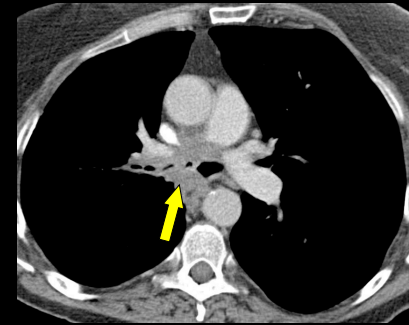
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T4: Mediastinal Invasion



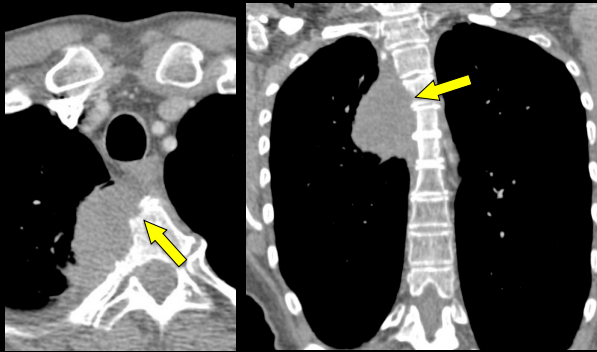
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T4: Carinal Invasion



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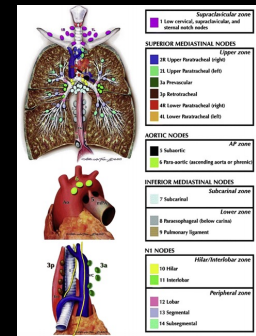
T4: Vertebral Body Invasion



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N Stage

- Lymph node station involvement
- Guided by CT and PET findings
- CT: short axis > 10 mm
- PET: FDG avidity



J Thorac Oncol. 2009;4(5):568-577

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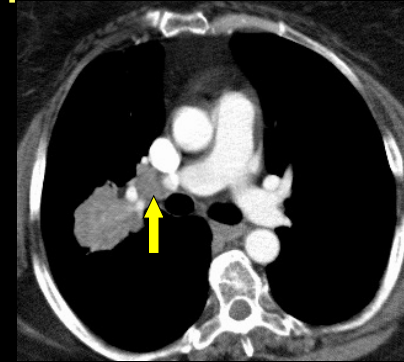
N Stage

- N1: *ipsilateral* hilar or intrapulmonary
- N2: *ipsilateral* mediastinal*
- N3: *contralateral* mediastinal or hilar, *ipsilateral or contralateral* supraclavicular or scalene

*Subcarinal nodes are considered *ipsilateral*

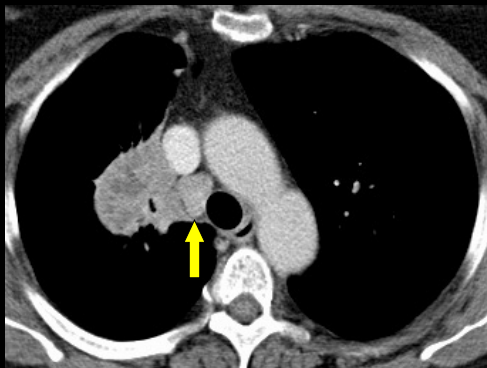
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N1: Ipsilateral Hilar Node



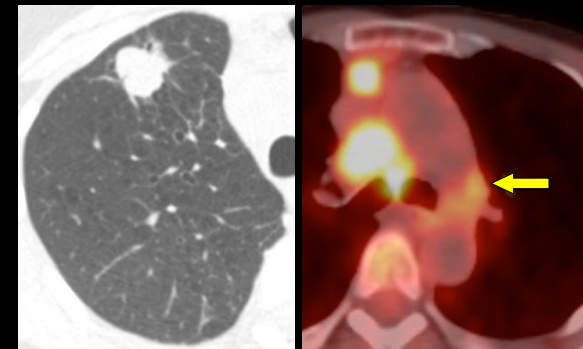
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N2: Ipsilateral Mediastinal Node



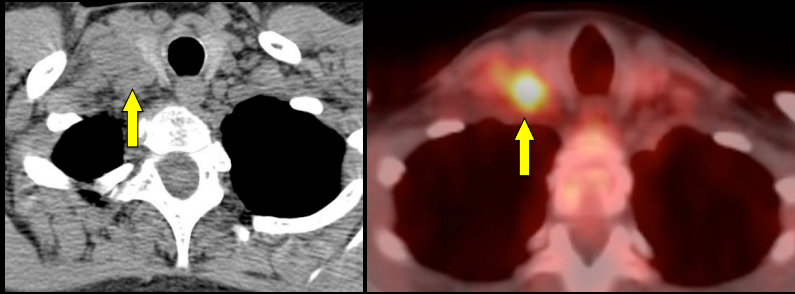
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N3: Contralateral Mediastinal



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N3: Scalene



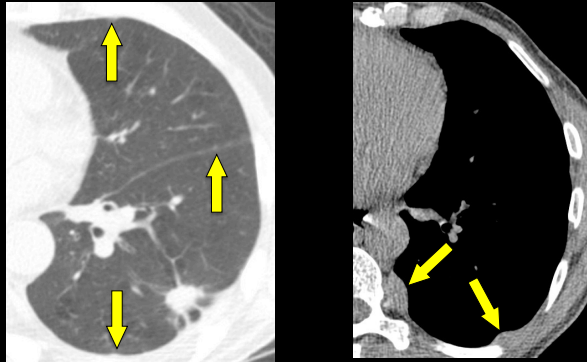
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M Stage

- M1a
 - Malignant pleural or pericardial effusion
 - Pleural or pericardial metastases
 - Metastasis to contralateral lung
- M1b
 - Single extrathoracic metastasis
- M1c
 - Multiple extrathoracic metastases

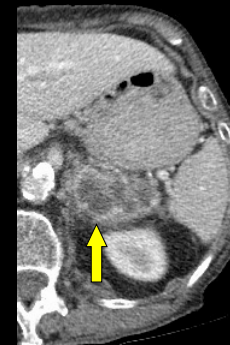
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M1a: Pleural Metastases



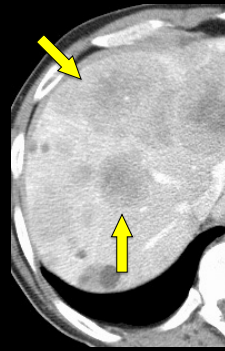
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M1b: Single Extrathoracic Metastasis



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M1c: Multiple Extrathoracic Metastases



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Composite Stage

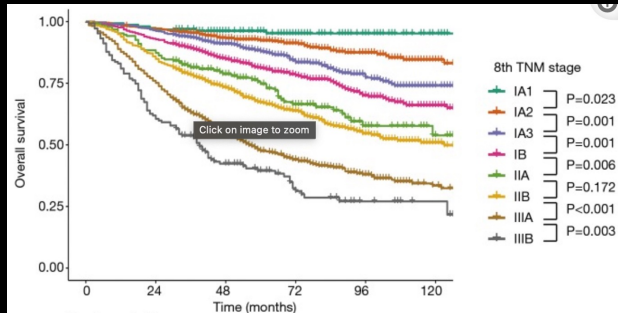
TABLE 5 Lung Cancer Stage Grouping (Eighth Edition)

T/M	Label	N0	N1	N2	N3
T1	T1a ≤2	IA1	IIB	IIIA	IIIB
	T1b >1-2	IA2	IIB	IIIA	IIIB
	T1c >2-3	IA3	IIB	IIIA	IIIB
T2	T2a Cont, Visc Pl	IB	IIB	IIIA	IIIB
	T2a >3-4	IB	IIB	IIIA	IIIB
	T2b >4-5	IIA	IIB	IIIA	IIIB
T3	T3 >5-7	IIB	IIIA	IIIB	IIIC
	T3 Inv	IIB	IIIA	IIIB	IIIC
	T3 Satell	IIB	IIIA	IIIB	IIIC
T4	T4 >7	IIIA	IIIA	IIIB	IIIC
	T4 Inv	IIIA	IIIA	IIIB	IIIC
	T4 Ispt Nod	IIIA	IIIA	IIIB	IIIC
M1	M1a Contr Nod	IVA	IVA	IVA	IVA
	M1a Pt Dissem	IVA	IVA	IVA	IVA
	M1b Single	IVA	IVA	IVA	IVA
	M1c Multi	IVB	IVB	IVB	IVB

Chest 2017;151(1)193-203

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Survival by Stage



Yun JK et al. J Thorac Dis. 2019

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Multiple Primary Lung Cancers

- Incidence 1.5%-2.0% per patient year
- Most same histology
 - Genetic predisposition
 - Environmental exposures

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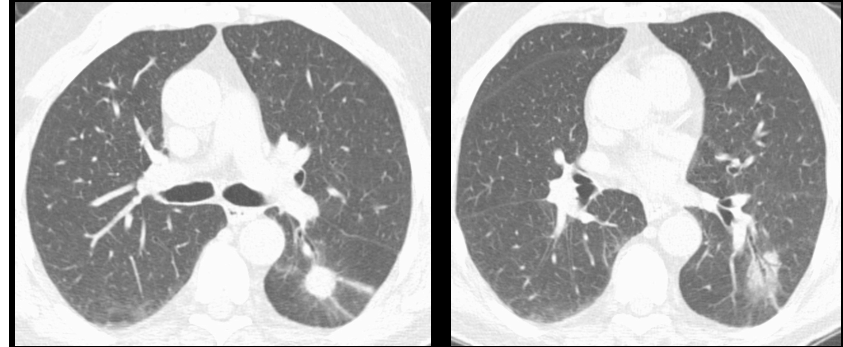
Complex Patterns

	Second Primary Lung Cancer	Multifocal GG/L Nodules	Pneumonic-Type of Adenocarcinoma	Separate Tumor Nodule
Imaging Features	Two or more distinct masses with imaging characteristic of lung cancer (eg, spiculated)	Multiple ground glass or part-solid nodules	Patchy areas of ground glass and consolidation	Typical lung cancer (eg, solid, spiculated) with separate solid nodule
Pathologic Features	Different histotype or different morphology by 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 morphology by 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 ipsi- or contralateral lobes; single N and M	Location of separate nodule relative to primary site determines if 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

Chest 2017;151(1)193-203

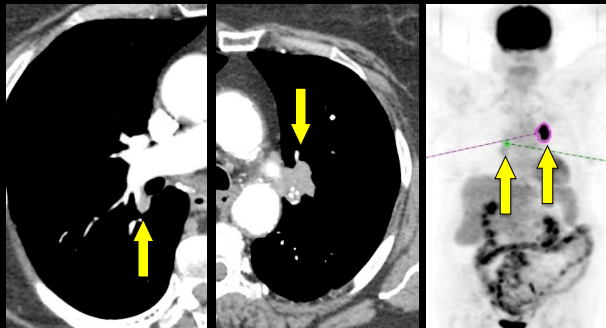
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Synchronous Primary



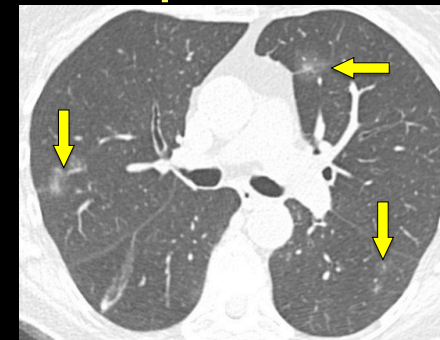
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Synchronous Primary



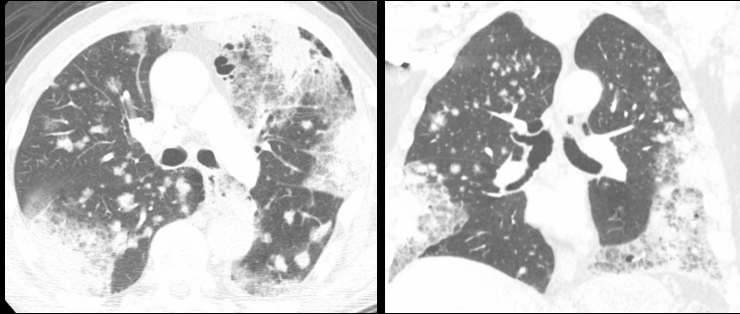
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Multiple GGNs



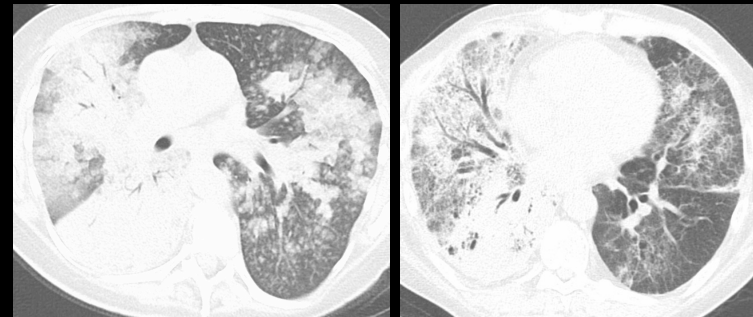
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“Pneumonic Type”



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“Pneumonic Type”



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Improvements

- TNM6 (2002)
 - 5319 surgically staged patients
 - Primarily from single site
- TNM7 (2009)
 - 68,463 NSCLC patients
 - 46 centers across 20 countries
 - Staged clinically, primarily from CT
 - TNM descriptors revised based on survival data

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Improvements

- TNM8 (2017)
 - Prospective database 70,967 NSCLC
 - Demographic data
 - Detailed pathologic detail
 - Molecular
 - Genetics
 - Margins
 - SUV_{max} from FDG PET/CT when available

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Shortcomings

- TNM8 (2017)
 - <5% patients had complete data
 - Increase in demographic skew
 - Shift toward surgical cases



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Shortcomings - Geography

Location	TNM 7	TNM 8
Asia	11.5%	44% (93% Japan)
North America	21%	5%
Australia	9.3%	1.7%
Europe	58%	49% (73% Denmark)
South America	-	0.3%

J Thorac Oncology 2014;9(11)1618-1624

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Shortcomings - Stage

Treatment	TNM 7	TNM 8
Surgery +/- chemo +/- radiotherapy	53%	85%
Chemotherapy	23%	9.3%
Radiotherapy	11%	1.5%
Chemotherapy + radiotherapy	12%	4.7%

J Thorac Oncology 2014;9(11)1618-1624

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Shortcomings - Imaging

- TNM7 - many patients did not undergo FDG PET/CT
- TNM8
 - Many Japanese patients likely did not undergo FDG PET/CT
 - Earlier stage
 - Submitted 1999, 2002, 2004 (limited availability)

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Shortcomings - Imaging

- TNM8
 - FDG PET/CT data not recorded
 - Value of PET not well represented in current TNM
 - MRI not included
 - Evolution of TNM often slower than imaging advances

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Shortcomings - T

- Central airways
 - T2 vs. T4 (carinal involvement)
 - Ex: T2N0M0 within 1 mm from carina likely not resectable (stage IB or IIA)
- Limited T4 - impact of recent advances in surgical technique not addressed
 - Vertebral involvement
 - Central vascular

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Shortcomings - T

- Visceral pleural invasion
 - Pathologic definition not standardized
 - Problematic on CT and other imaging



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Shortcomings - T

- Identifying primary site challenging
 - Multiple nodules or masses
 - Coexistent peripheral and central infiltrating disease



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Shortcomings - T

- T and M interdependence
- 15 mm RUL nodule (T1bN0M0)
 - 8-mm tumor nodule same lobe → T3N0M0
 - 8-mm tumor nodule same lung → T4N0M0
 - 8-mm tumor nodule other lung → T1bN0M1a
- Separate primaries
 - T1bN0M0 and T1aN0M0

Radiol Clin N Am 2018;56(1)419-435

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Shortcomings - T

- Multiple lesions
 - Separate primary vs. metastasis
 - Open to radiologic interpretation
 - Increased number in TNM8 but no change in survival – suggests selective reporting
 - Radiologic reported 1.7% vs. pathologically reported 3.5%
 - Lack of database information precludes assessing impact

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Shortcomings - T

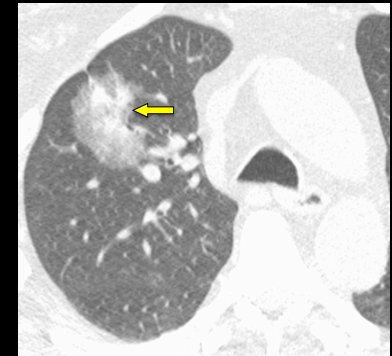
- Subsolid lesions
 - Slower growth rates
 - Imaging characteristics of most TNM8 lesions not captured
 - May underestimate survival in patients with more indolent lesions



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Shortcomings - T

- Subsolid lesions
 - Slower growth rates
 - Imaging characteristics of most TNM8 lesions not captured
 - May underestimate survival in patients with more indolent lesions



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Shortcomings - T

- Lymphangitic carcinomatosis not addressed
 - T3 if nodular
 - M1a if associated pleural involvement
 - Typically associated with advanced disease but can occur locally with early-stage disease



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Shortcomings - N

- Heterogeneity of N2 disease
 - Single N2 station
 - Skip lesions (single N2 but no N1)
- Undefined sites
 - Axillary
 - Internal mammary
 - Lower cervical
 - Upper abdominal

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Shortcomings - M

- Impact of FDG PET/CT
- Choice of brain imaging
 - CT vs. MRI
 - Variable recommendations
- Variability in biopsy and imaging

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Shortcomings - M

- Retrospective analysis of 12395 patients with lung cancer
- 1994-1998 (no PET)
- 1999-2004 (PET)
- Stage shift from III-IV with improved survival in both groups



Chee KG et al. Arch Intern Med 2008

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Bottom Line

- TNM8 overrepresents surgically resected disease and underrepresents chemotherapy treated cases
- Survival for earlier stage disease increased compared to TNM7
- Survival for advanced stage disease (especially IIIB) worsened

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TMN 9

- Expected in 2024
- Robust dataset
- Should better reflect current practices
 - FDG PET/CT
 - Brain MRI
 - Mediastinal staging

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Summary

- Imaging is central to lung cancer diagnosis and staging
- Staging impact on prognosis is likely more important for early-stage disease
- Molecular and biologic profiles become more important for advanced disease

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