2018 Updates for Neoplasms of the Lung

2018 SSDI Fields

2017-2018 FCDS Educational Webcast Series

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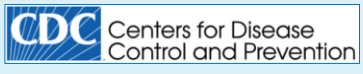
November 16, 2017

1

CDC & Florida DOH Attribution

"We acknowledge the Centers for Disease Control and Prevention, for its support of the Florida Cancer Data System, and the printing and distribution of the materials for the 2017-2018 FCDS Webcast Series under cooperative agreement 1NU58DP006350 awarded to the Florida Department of Health. The findings and conclusions in this series are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention".

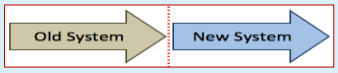


FCDS would also like to acknowledge the Florida Department of Health for its support of the Florida Cancer Data System, including the development, printing and distribution of materials for the 2017-2018 FCDS Webcast Series under state contract CODJU. The findings and conclusions in this series are those of the author(s) and do not necessarily represent the official position of the Florida Department of Health.

2

FLccSC LMS – CEU Quiz –FCDS IDEA

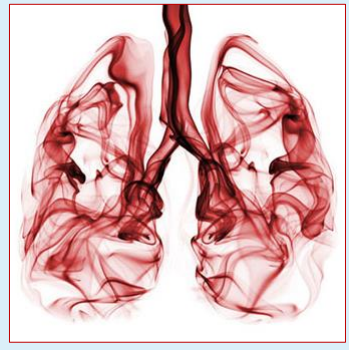
- Florida has changed how we track webcast attendance
- Florida has changed how we award CEUs for our webcast series
- Attendees must take and pass a 3-5 question CEU Quiz to be awarded CEUs
- Only registered FLccSC Users will be given access to the CEU Quiz
- Florida attendees must have a Florida FLccSC Account & pass the quiz to get CEUs
- South Carolina attendees must have a South Carolina FLccSC Account & pass the quiz to get CEUs
- Other Attendees can attend the live webcasts but cannot receive CEUs for attendance at this time
- Please remember this is a new system with new requirements - some still being worked out
- The CEU Quiz should be available about an hour after the webcast ends



3

Presentation Outline

- Overview of Neoplasms of the Lung
- FCDS Lung Audits – 2014/2015 Diagnosis
- Anatomy of the Thorax – Lung & Pleura
- WHO Neoplasms of the Lung – 4th edition
- 2018 ICD-O-3 Lung Histology Codes
- 2018 MPH Lung Rules – *Pending*
- 2018 Anatomic Staging – SS2018 – *Pending*
- 2018 Anatomic Staging – AJCC TNM 8th edition
- 2018 Non-Anatomic Site-Specific Data Items (SSDI)
- Importance of Text Documentation
- Practice Cases - *Pending*
- Questions



4

Overview

Figure 3. Leading Sites of New Cancer Cases and Deaths – 2017 Estimates

Estimated New Cases

Male			Female		
Prostate	161,360	19%	Breast	252,710	30%
Lung & bronchus	116,990	14%	Lung & bronchus	105,510	12%
Colon & rectum	71,420	9%	Colon & rectum	64,010	8%
Urinary bladder	60,490	7%	Uterine corpus	61,380	7%
Melanoma of the skin	52,170	6%	Thyroid	42,470	5%
Kidney & renal pelvis	40,610	5%	Melanoma of the skin	34,940	4%
Non-Hodgkin lymphoma	40,080	5%	Non-Hodgkin lymphoma	32,160	4%
Leukemia	36,290	4%	Leukemia	25,840	3%
Oral cavity & pharynx	35,720	4%	Pancreas	25,700	3%
Liver & intrahepatic bile duct	29,200	3%	Kidney & renal pelvis	23,380	3%
All sites	836,150	100%	All sites	852,630	100%

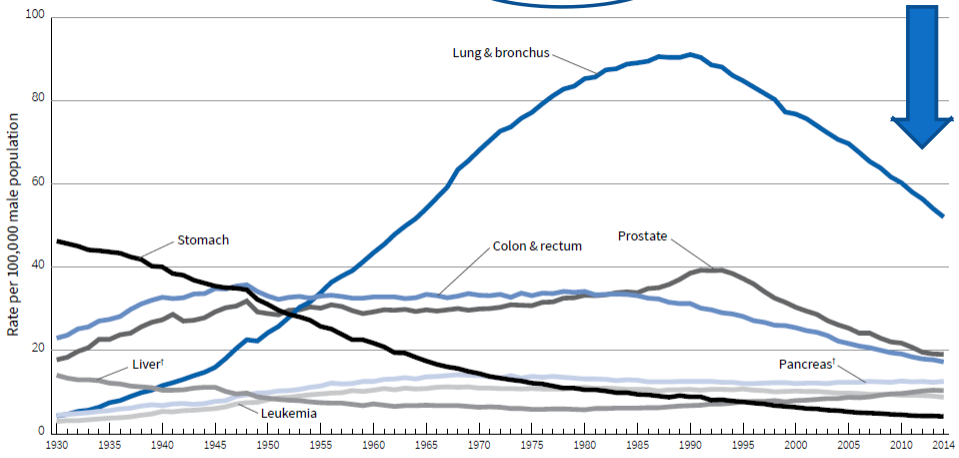
Estimated Deaths

Male			Female		
Lung & bronchus	84,590	27%	Lung & bronchus	71,280	25%
Colon & rectum	27,150	9%	Breast	40,610	14%
Prostate	26,730	8%	Colon & rectum	23,110	8%
Pancreas	22,300	7%	Pancreas	20,790	7%
Liver & intrahepatic bile duct	19,610	6%	Ovary	14,080	5%
Leukemia	14,300	4%	Uterine corpus	10,920	4%
Esophagus	12,720	4%	Leukemia	10,200	4%
Urinary bladder	12,240	4%	Liver & intrahepatic bile duct	9,310	3%
Non-Hodgkin lymphoma	11,450	4%	Non-Hodgkin lymphoma	8,690	3%
Brain & other nervous system	9,620	3%	Brain & other nervous system	7,080	3%
All sites	318,420	100%	All sites	282,500	100%

Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

5

Figure 1. Trends in Age-adjusted Cancer Death Rates* by Site, Males, US, 1930-2014

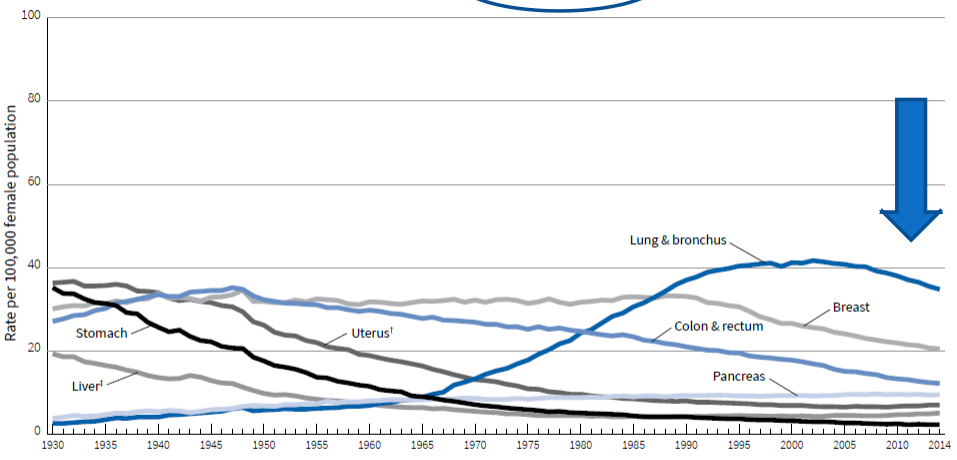


*Per 100,000, age adjusted to the 2000 US standard population. †Mortality rates for pancreatic and liver cancers are increasing.

Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancers of the liver, lung and bronchus, uterus, and colon and rectum are affected by these coding changes.

Source: US Mortality Volumes 1930 to 1959 and US Mortality Data 1960 to 2014, National Center for Health Statistics, Centers for Disease Control and Prevention.

Figure 2. Trends in Age-adjusted Cancer Death Rates* by Site, Females, US, 1930-2014

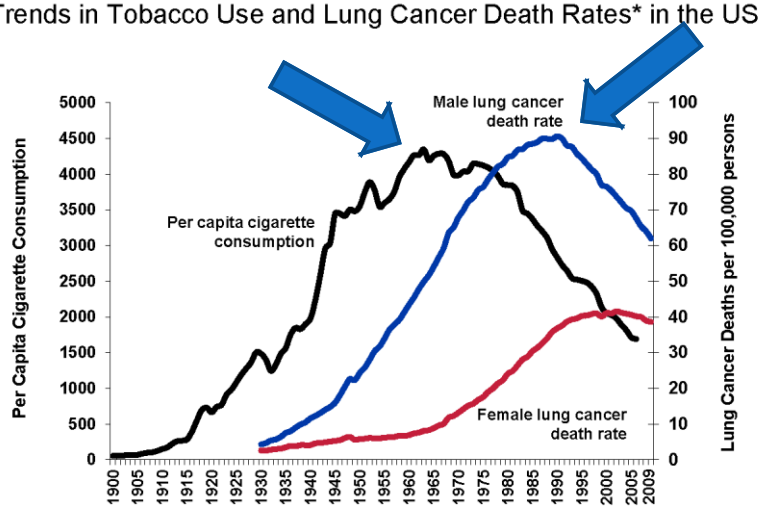


*Per 100,000, age adjusted to the 2000 US standard population. †Uterus refers to uterine cervix and uterine corpus combined. ‡The mortality rate for liver cancer is increasing.

Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancer of the liver, lung and bronchus, uterus, and colon and rectum are affected by these coding changes.

Source: US Mortality Volumes 1930 to 1959, US Mortality Data 1960 to 2014, National Center for Health Statistics, Centers for Disease Control and Prevention.

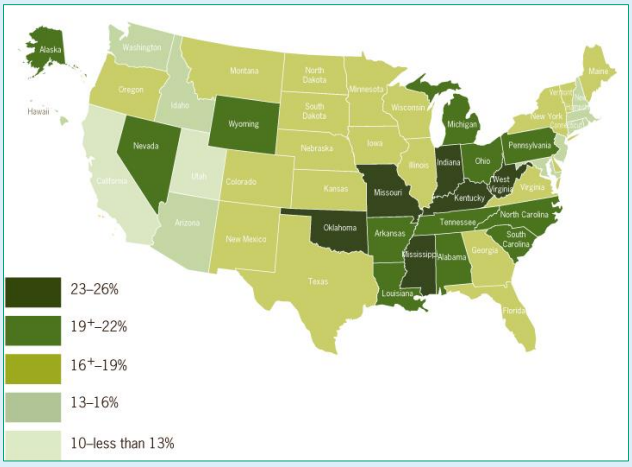
Trends in Tobacco Use and Lung Cancer Death Rates* in the US



*Age-adjusted to 2000 US standard population.

Source: Death rates: US Mortality Data, 1960-2009, US Mortality Volumes, 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention. Cigarette consumption: US Department of Agriculture, 1900-2007.

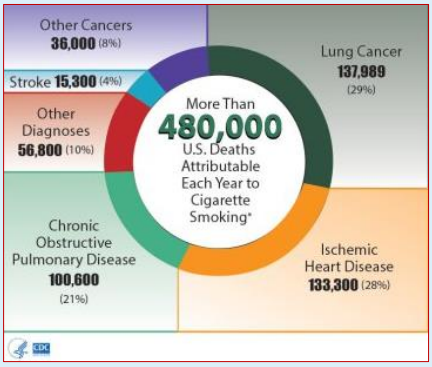
U.S. Adult Smoking Rates

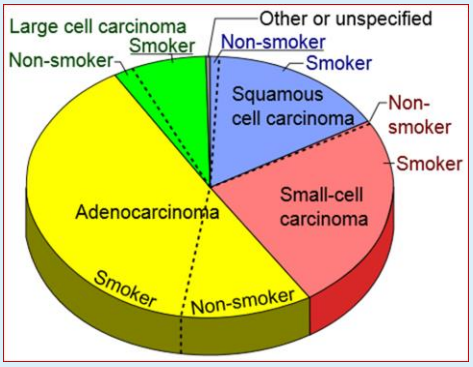


Adult Smoking Rates - http://www.cdc.gov

Dangerous Chemicals in All Tobacco

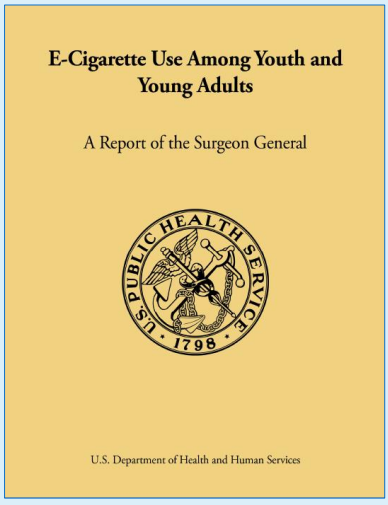
Association with Smoking



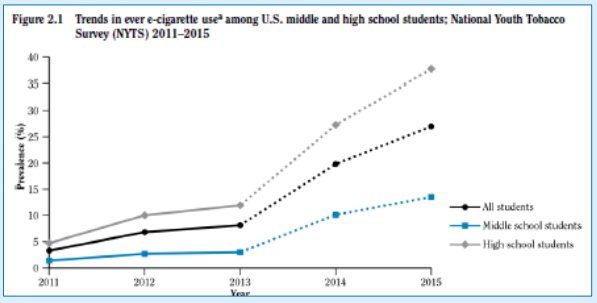


Kenfield SA, Wei EK, Stampfer MJ, Rosner BA, Colditz GA (2008), Tobacco Control 17 (3): 198-204

E-Cigarette Use



Florida Registrars
Code E-Cigarettes in Field
✓ Tobacco Use, NOS



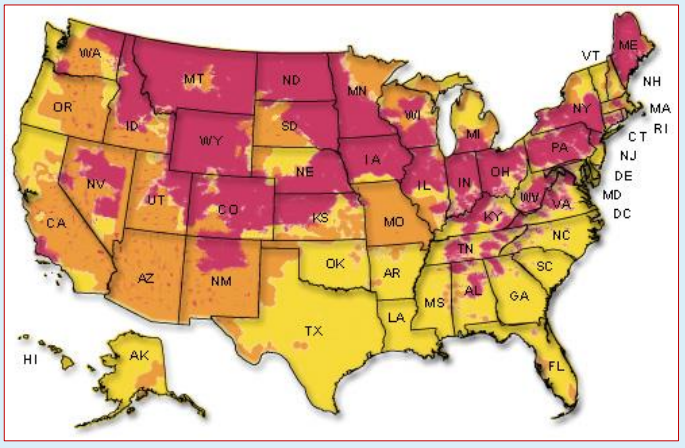
U.S. Department of Health and Human Services. E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2016.

E-Cigarette Use

- E-cigarettes have only been readily available in the United States since 2006. As a result, there's limited research on their health risks.
- Question Remains: Are e-cigarettes safer than smoking?
- People who use e-cigarettes while still smoking do not reduce the levels of toxic chemicals they were exposed to. And, a large number of e-cigarette users do still smoke.
- "The full benefit of using e-cigarettes is from completely stopping smoking," says Shahab. "Any health benefits come from dramatic reductions in these chemicals, and we're not seeing this in people that use both e-cigarettes and combustible cigarettes."
- And although this study found significantly lower levels of these substances in vapers than smokers, the chemicals are still there.
- Does this study confirm that e-cigarettes are safer than smoking. Concerns remain…
- Why? E-cigarettes do not contain tobacco. Instead, they carry a nicotine-containing liquid which is heated into a vapour and breathed in. The nicotine satisfies the cravings associated with a smoking addiction, but doesn't cause cancer…or does it?

13

Radon Gas



http://pillartopost.com/epa

14

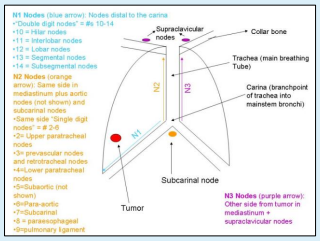
FCDS Lung Audits – 2014/2015 Diagnosis

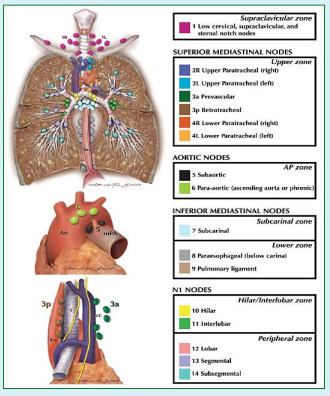
- Clarify the Difference between Atelectasis, Obstructive Pneumonitis, Consolidation, and (Malignant/Non-Malignant) Pleural Effusion
  - *Atelectasis/Pneumothorax = Complete or Partially Collapsed Lung*
  - *Pneumonitis - inflammation of the walls of the alveoli in the lungs, often caused by a virus.*
  - *Obstructive Pneumonitis – pneumonitis resulting in bronchial obstruction*
  - *Consolidation - a region of lung tissue that has filled with liquid or blood or pus instead of air*
  - *Pleural Effusion/Hemothorax - a buildup of extra fluid in the space between the lungs and the chest wall.*
    - Most pleural effusions are hemorrhagic or bloody which indicates malignant pleural effusion without even looking at cytology
    - Any pleural effusion in lung cancer is deemed "malignant" and must be proven "negative" x 2-3 cytology examinations
    - When pleural effusion described as "minimal" or "small" it may not be 'treated' as with involvement – still code as malignant pleural effusion for consistency in staging cases
  - *Primary Tumor Extension to either Pleura is not the same as pleural effusion*

15

FCDS Lung Audits – 2014/2015 Diagnosis

- Tumor Size 000 (no evidence of primary tumor) vs. 999 (unk)
- Several Regional Lymph Node Issues
- N1, N2 and N3 are ALL "regional lymph nodes"





Source: International Association for the Study of Lung Cancer, 2008

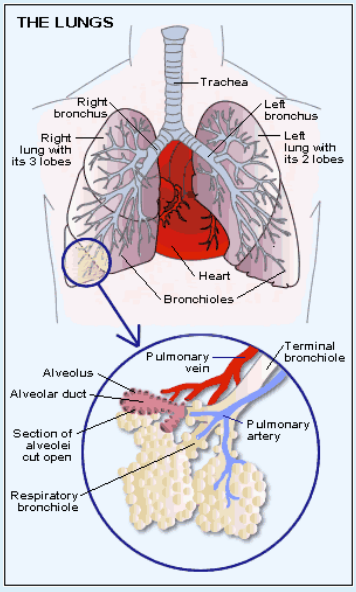
- Must look at whether hilar or mediastinal nodes – do not treat as same
- Coding FNA of Regional Lymph Node in Scope of Reg Lymph Node Surgery
- Coding Regional Lymph Nodes Examined / Regional Lymph Nodes Positive
- Disconnect between Surgery of Primary Site Code 30 versus 33 and "regional" node definitions – often code 33 is for mediastinal node removal

16

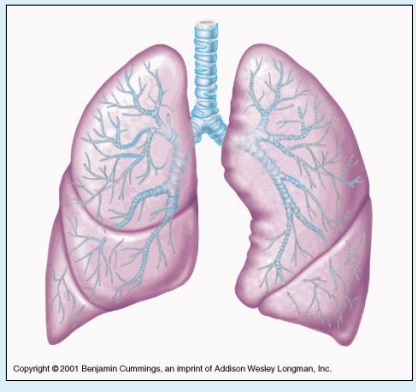
Lung Anatomy

17

http://www.omnimedicalsearch.com/conditions-diseases/images/lung-cancer.jpg



Lung Anatomy



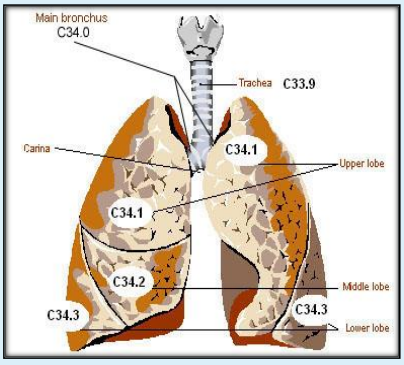
http://www.damav.com/mare/lung/

http://legacy.owensboro.kctcs.edu

18

Lung Anatomy

C34.0 Main bronchus
C34.1 Upper lobe, lung
C34.2 Middle lobe, lung
(right lung only)
C34.3 Lower lobe, lung
C34.8 Overlapping lesion
C34.9 Lung, NOS



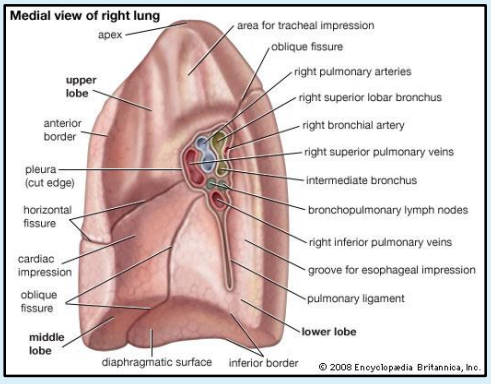
Source: SEER Training: ICD-O-3 Site Codes

19

Lung Anatomy

The hilum is the space in each lung where the bronchus and blood vessels enter the lung.

The apex is the rounded area at the top of each lung.

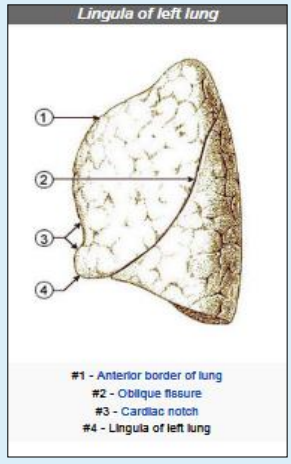


Source: 2008 Encyclopedia Britannica, Inc. on-line

20

Lung Anatomy

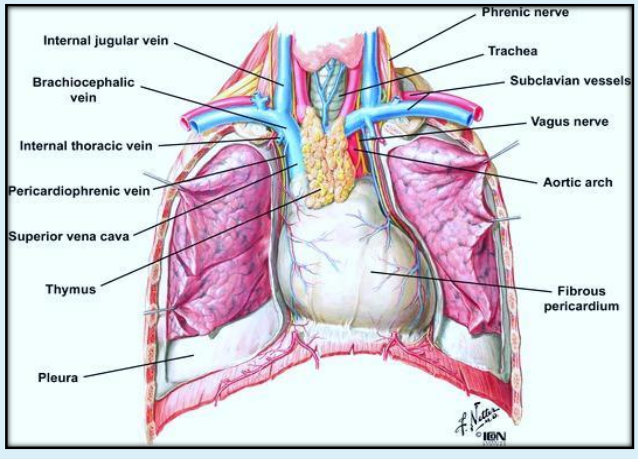
The lingula, found only in the left lung, is a projection of the upper lobe of the left lung thought to be a remnant of an ancient middle lobe of the left lung.



Source: SEER Training: ICD-O-3 Site Codes

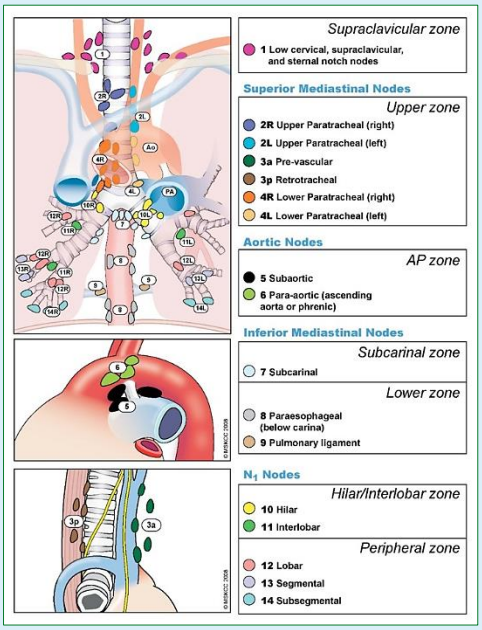
21

Lung Anatomy



Source: Springer Images. Figure adapted from Atlas of Human Anatomy, 2nd ed. Contents of the superior and middle mediastinum. http://www.springerimages.com/Images/MedicineAndPublicHealth/1-10.1007_978-1-60327-372-5_4-9

22



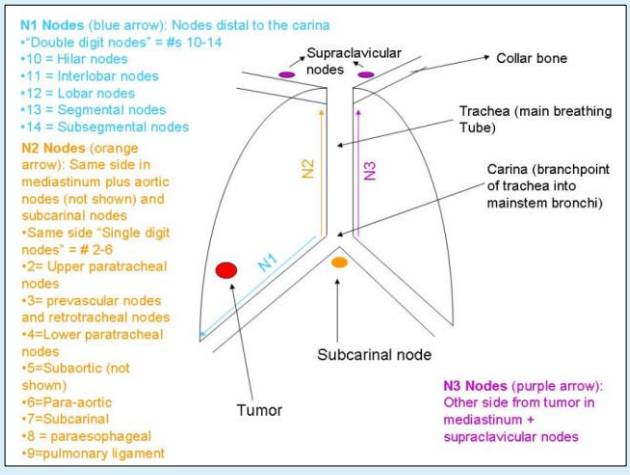
Lung Anatomy

- **NX** Regional lymph nodes cannot be assessed
- **N0** No regional lymph node metastases
- **N1** Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
- **N2** Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
- **N3** Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

IASLC lymph node map from Memorial Sloan-Kettering Cancer Center, 2009

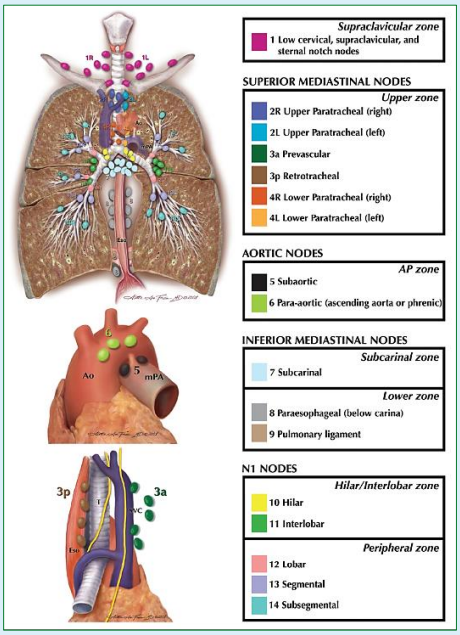
23

Lung Anatomy



Source: http://cancergrace.org/lung/files/2010/04/simplified-staging.jpg

24



Lung Anatomy

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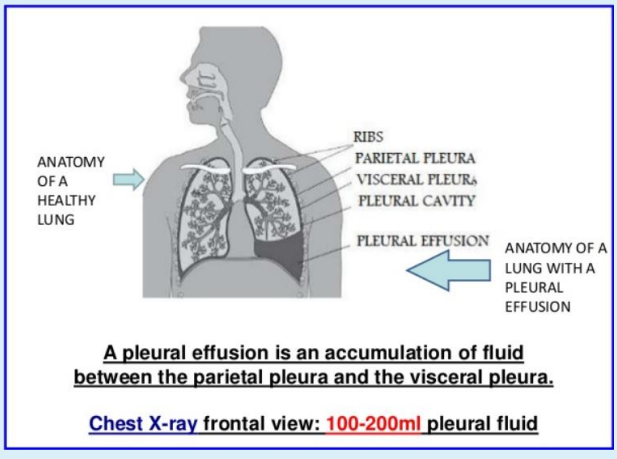
IASLC lymph node map - WHO Classification of Tumours of the Lung, 2015

25

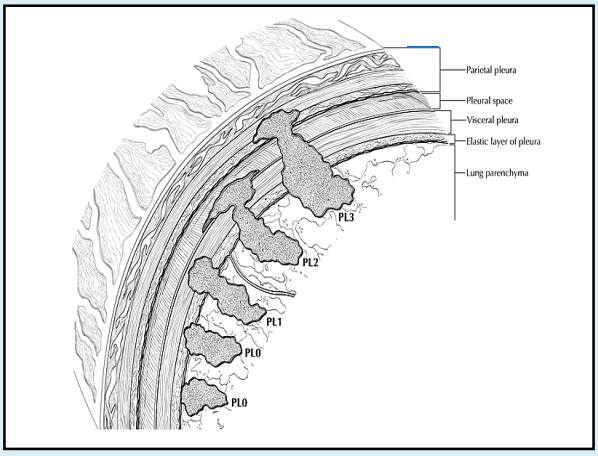
Lung Anatomy



Source: www.slideshare.net/pleuraleffusion/drmahesh

26

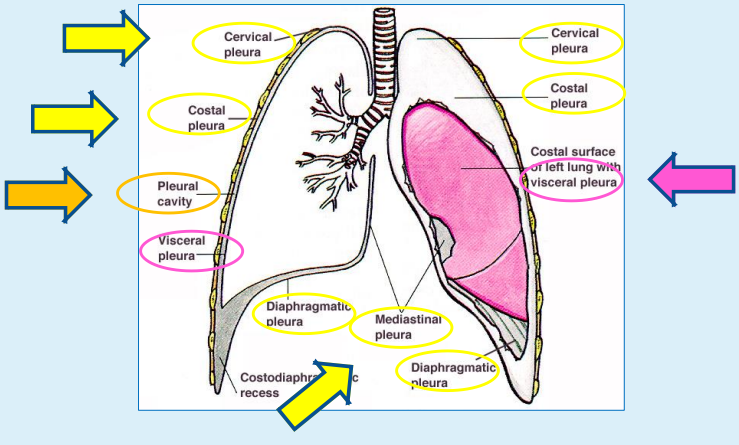
Lung Anatomy



Collaborative Stage Data Collection System, Part I Section II – Lab Tests, Tumor Markers, SSFs

27

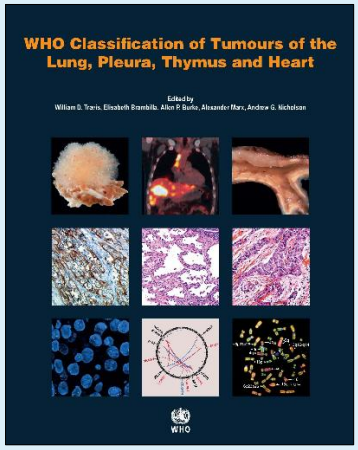
Pleura Anatomy



Source: http://www.depure.org/learning-further-about-anatomy-of-lung/basic-anatomy-of-lung/

28

2015 WHO Classification of Tumours of Lung, Pleura, Thymus & Heart, 4th ed.



Highlights

- Multi-Disciplinary Correlation
- Invasive Neoplasm classified according to predominant subtype
- Stop Using the Term "BAC" and "bronchio-alveolar carcinoma"
- Replace BAC with 5 new adenocarcinoma subtypes
  - Add "in situ" classification
  - Add "minimally invasive"
- Add genetic test/markers
  - EGFR, Alk, KRAS, TTF-1, p40
- SCC with minor changes

29

Small Biopsy and Cytology Specimens

TABLE 3. Diagnostic Terminology for Small Biopsy/Cytology Compared with the 2015 WHO Terms in Resection Specimens with Small Cell Carcinoma, LCNEC, Adenosquamous Carcinoma, and Sarcomatoid Carcinoma[a]

Small Biopsy/Cytology Terminology/Criteria	2015 WHO Classification in Resections
Small cell carcinoma	Small cell carcinoma
NSCC with NE morphology and positive NE markers, possible LCNEC	LCNEC
NSCC with NE morphology If negative NE markers comment: This is a NSCC where LCNEC is suspected, but stains failed to demonstrate NE differentiation.	Large cell carcinoma with NE morphology (LCNEM)
Morphologic squamous cell and adenocarcinoma patterns present: NSCC, NOS Comment that adenocarcinoma and squamous components are present and this could represent adenosquamous carcinoma.	Adenosquamous carcinoma (if both components ≥10%)
Morphologic squamous cell or adenocarcinoma patterns not present but immunostains favor separate glandular and adenocarcinoma components: NSCC, NOS Specify the results of the immunohistochemical stains and the interpretation and comment this could represent adenosquamous carcinoma.	Adenocarcinoma, squamous cell carcinoma, adenosquamous carcinoma or large cell carcinoma with unclear immunohistochemical features
NSCC with spindle cell and/or giant cell carcinoma (mention if adenocarcinoma or squamous carcinoma are present)	Pleomorphic, spindle cell, and/or giant cell carcinoma

[a]Modified from the articles by Travis et al.[1,7,11]
LCNEC, large cell neuroendocrine carcinoma; NOS, not otherwise specified; NSCC, non–small cell carcinoma; NE, neuroendocrine; WHO, World Health Organization.

30

Adenocarcinoma and BAC Changes

TABLE 4. Adenocarcinoma In Situ[a]

Diagnostic criteria

- A small tumor ≤3 cm[a]
- A solitary adenocarcinoma
- Pure lepidic growth
- No stromal, vascular or pleural invasion
- No pattern of invasive adenocarcinoma (such as acinar, papillary, micropapillary, solid, colloid, enteric, fetal or invasive mucinous adenocarcinoma).
- No spread through air spaces
- Cell type mostly nonmucinous (type II pneumocytes or Clara cells), rarely may be mucinous (tall columnar cells with basal nuclei and abundant cytoplasmic mucin, sometimes resembling goblet cells).
- Nuclear atypia is absent or inconspicuous
- Septal widening with sclerosis/elastosis is common, particularly in nonmucinous adenocarcinoma in situ

[a]Modified from the articles by Travis et al.[1,7,11]

In the 2015 WHO classification, the term "predominant" is not listed in the name for the major adenocarcinoma subtypes as it was in the 2011 classification.

However, these tumors still should be classified according to the predominant subtype after evaluation of the tumor using comprehensive histologic subtyping.

While it is theoretically possible to have equal percentages of two prominent components, in practice, a single predominant component should be chosen.

31

Adenocarcinoma and BAC Changes

TABLE 5. Minimally Invasive Adenocarcinoma[a]

Diagnostic criteria

- A small tumor ≤3 cm
- A solitary adenocarcinoma
- Predominantly lepidic growth
- ≤0.5 cm invasive component in greatest dimension in any one focus
- Invasive component to be measured includes
  - Any histologic subtype other than a lepidic pattern (such as acinar, papillary, micropapillary, solid, colloid, fetal or invasive mucinous adenocarcinoma)
  - Tumor cells infiltrating myofibroblastic stroma
- Minimally invasive adenocarcinoma diagnosis is excluded if the tumor
  - Invades lymphatics. blood vessels, air spaces or pleura,
  - Contains tumor necrosis,
  - Spreads through air spaces
- The cell type mostly nonmucinous (type II pneumocytes or Clara cells), but rarely may be mucinous (tall columnar cells with basal nuclei and abundant cytoplasmic mucin, sometimes resembling goblet cells).

[a]Modified from the articles by Travis et al.[1,7,11]

Lepidic pattern is defined as a tumor composed of neoplastic cells lining the alveolar lining with no architectural disruption/complexity, and no lymphovascular and/or pleural invasion.

Acinar pattern is characterized by glandular formation.

Cribriform pattern shows distinctive holes in between the cancer cells - Swiss cheese.

32

Squamous Cell Carcinoma & Large Cell Carcinoma

- Squamous Cell - Similar to Head & Neck Nasopharyngeal Carcinoma Classification
  - *Basaloid*
  - *Keratinizing*
  - *Non-Keratinizing*

- Large Cell – cannot confirm this histology on small biopsy or cytology
  - *Must be surgically resected tumor*
  - *Most previous subtypes have been reclassified and now in different groups*
  - *Solid Adenocarcinoma – reclassification of large cell based on TTF-1*
  - *Non-Keratinizing Squamous Cell Carcinoma – reclassification based on p40*

33

Neuroendocrine Tumors

Table 1

Pathologic Criteria of Neuroendocrine Neoplasms of the Lung

	Typical Carcinoid	Atypical Carcinoid	Large-Cell Neuroendocrine Carcinoma	Small-Cell Lung Cancer
Light microscope morphology	Neuroendocrine morphology	Neuroendocrine morphology	Neuroendocrine morphology, positive immunohistochemical staining or neuroendocrine granules by electron microscopy, cytologic features of non–small-cell lung cancer	Smaller than lymphocytes, scant cytoplasm, finely granular nuclear chromatin, absent or faint nucleoli
Mitoses per 2 mm^2	< 2	≥ 2 and < 10 or coagulative necrosis	≥ 10	≥ 10
Necrosis	No	Often punctate	Often large zones	Frequent, large zones
Histologic grade	Low	Intermediate	High	High

Adapted from Hage et al [12]

- Classified Similar to the GI Track Neuroendocrine Tumors
- NOW INCLUDES
  - *Carcinoid Tumor of Lung – low grade neuroendocrine tumor*
  - *Small Cell Lung Carcinoma – Ki67 confirmation for high grade SCLC*
  - *Large Cell Carcinoma Not Elsewhere Classified*
- Mitotic Count used to differentiate low/high grade

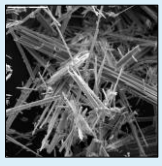
34

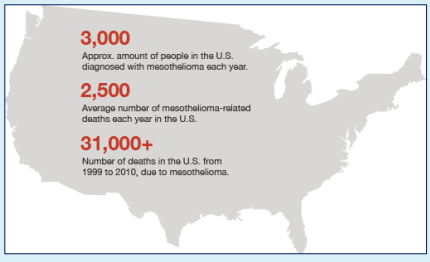
2018 ICD-O-3 Lung Histology Codes

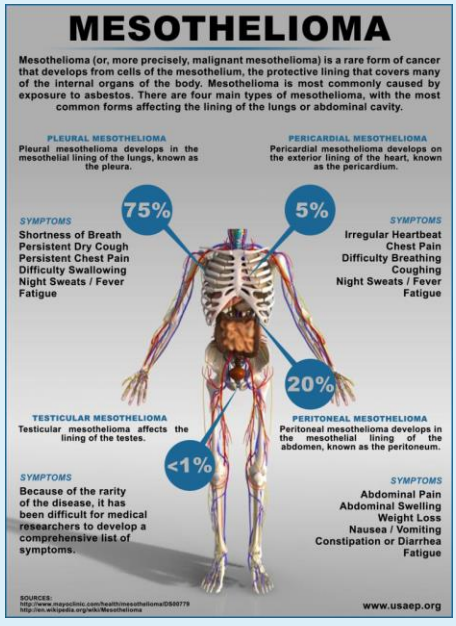
- 8013/3 – Lung Only – Combined Large Cell Neuroendocrine Carcinoma
- 8023/3 – Nasal Cavity, Sinus & Lung – NUT Carcinoma
- 8140/2 – Lung Only – Adenocarcinoma in situ, non-mucinous
- 8250/2 – Lung Only – Minimally invasive Adenocarcinoma, non-mucinous
- 8250/3 – Lung Only – Lepidic Adenocarcinoma
- 8250/3 – Lung Only – Lepidic Predominant Adenocarcinoma
- 8253/2 – Lung Only – Adenocarcinoma in situ, mucinous
- 8257/3 – Lung Only – Minimally Invasive Adenocarcinoma
- 8845/2 – Lung Only – Pulmonary Myxoid Sarcoma with EWESRq-CREB1 translocation
- 8551/3 – Lung Only – Acinar Adenocarcinoma
- 8253/3 – Lung Only – Invasive Mucinous Adenocarcinoma
- 8253/3 – Lung Only – Bronchiolo-Alveolar Mucinous Type
- 8254/3 – Lung Only – Mixed Invasive Mucinous and Non-Mucinous Adenocaricnoma
- 8254/3 – Lung Only – Bronchiolo-Alveolar, Mixed Mucinous and Non-Mucinous

35

Mesothelioma (just a mention)

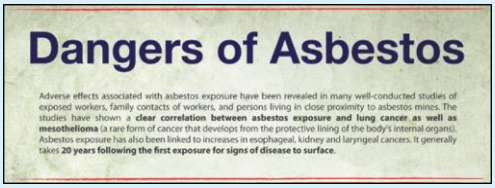




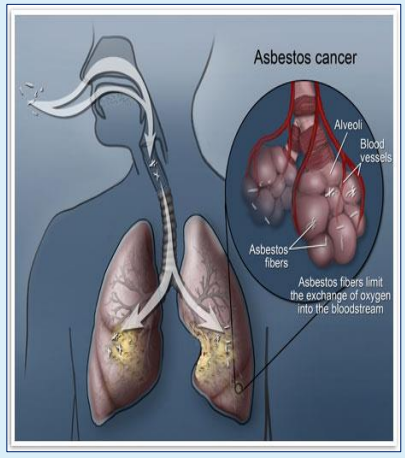


36

Sources: http://www.mesothelioma.com and http://www.usaep.org



Asbestos



http://www.mesothelioma.com/asbestos-cancer

37

Biomarkers & Genetic Abnormalities

Table 1.07 Major genetic changes in lung cancer

Alterations	Small cell carcinoma (%)	Adenocarcinoma (%)	Squamous cell carcinoma (%)
Mutation			
BRAF	0	< 5	0
EGFR Caucasian	< 1	10–20	< 1
Asian	< 5	35–45	< 5
ERBB2/HER2	0	< 5	0
KRAS Caucasian	< 1	15–35	< 5
Asian	< 1	5–10	< 5
PIK3CA	< 5	< 5	5–15
RB	> 90	5–15	5–15
TP53	> 90	30–40	50–80
Amplification			
EGFR	< 1	5–10	10
ERBB2/HER2	< 1	< 5	< 1
MET	< 1	< 5	< 5
MYC	20–30	5–10	5–10
FGFR1	< 1	< 5	15–25
Gene rearrangement			
ALK	0	5	< 1
RET	0	1–2	0
ROS1	0	1–2	0
NTRK1	0	< 1	0
NRG1	0	< 1	0

EMERGING TARGETED AGENTS FOR PATIENTS WITH GENETIC ALTERATIONS

Genetic Alteration (ie, Driver event)	Available Targeted Agents with Activity Against Driver Event in Lung Cancer
BRAF V600E mutation*	vemurafenib[1] dabrafenib[2]
MET amplification	crizotinib[3,4]
ROS1 rearrangements	crizotinib[5]
HER2 mutations	trastuzumab[6] (category 2B) afatinib[7] (category 2B)
RET rearrangements	cabozantinib[8] (category 2B)

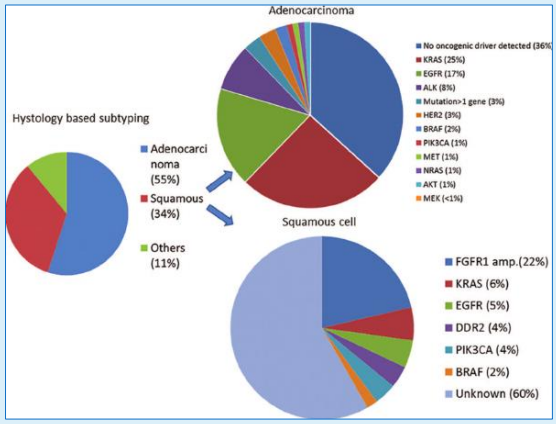
*Non-V600E mutations have variable kinase activity and response to these agents.

Source: WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart, 2015 and NCCN Guidelines NSCLCv7.2015

38

Biomarkers & Genetic Abnormalities

- Class of Antineoplastic Agents for NSCLC – Target Gene Therapy
  - *EGFR – Opdivo/Nivolumab*
  - *EGFR – Tarceva/Erlotinib*
  - *EGFR – Gilotrif/Afatinib*
  - *EGFR – Iressa/Gefitinib*
  - *EGFR – Portrazza/Necitumumab*
  - *EGFR T790M – Tagrisso/Osimertinib*
  - *ALK – Opdivo/Nivolumab*
  - *ALK – Xalkori/Crizotinib*
  - *ALK – Zykadia/Ceritinib*
  - *ALK – Alecensa/Alectinib*
  - *ALK – Alunbrig/Brigatinib*



39

Biomarkers & Genetic Abnormalities

- Class of Antineoplastic Agents for NSCLC – Target Gene Therapy
  - *BRAF V600E – Tafinlar/Dabrafenib)*
  - *BRAF V600E – Mekinist (Trametinib)*
  - *ROS1 – Xalkori (Crizotinib)*
- Class of Antineoplastic Agents for NSCLC – Immunotherapy
  - *PD-1 – Keytruda/Pembrolizumab*
  - *PD-L1 – Tecentriq/Atezolizumab*
- Treatment Targets for NSCLC – Angiogenesis Inhibitors & Targets
  - *Bevacizumab (Avastin)*
  - *VEGF Receptor Ramucirumab (Cyramza)*
- Maintenance Therapy for NSCLC – Chemotherapy
  - *Alimta/Pemetrexed - stable disease, partial/complete response s/p Platinum*

40

Biomarkers & Genetic Abnormalities

- Class of Antineoplastic Agents for NSCLC – Target Gene Therapy – Future
  - *HER2/ERBB2 – Trastuzumab – This is a protein not a mutant gene*
  - *MET – Crizotinib*
  - *MET – Cabozantinib*
  - *RET – Cabazantinib*
  - *RET – Vandetanib*
  - *RET – Alectinib*

- Class of Antineoplastic Agents for NSCLC – Future
  - *Molecular Testing – Next Generation Sequencing – Multiple Mutations 1 Test*
  - *FISH and IHC Improvements*
  - *Liquid Biopsy*
  - *Combination Trials*

41

Standard Chemotherapy

- Cisplatin
- Carboplatin
- Paclitaxel (Taxol)
- Nab-Paclitaxel (Abraxane)
- Docetaxel (Taxotere)
- Gemcitabine (Gemzar)
- Vinorelbine (Navelbine)
- Irinotecan (Camptosar)
- Etoposide (VP-16)
- Vinblastine
- Pemetrexed (Alimta)

42

What about Small Cell Lung Cancer?

- Standard Chemotherapy
  - *Cisplatin and etoposide*
  - *Carboplatin and etoposide*
  - *Cisplatin and irinotecan*
  - *Carboplatin and irinotecan*
- Radiation Therapy
  - *limited stage*
  - *post-chemo*
  - *brain mets*
  - *palliation*
- Surgery – rare for SCLC

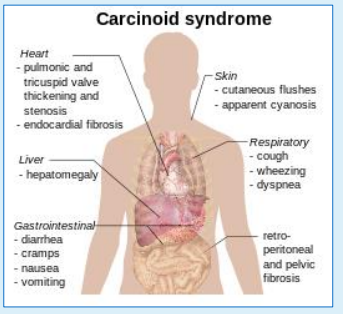
Grade	Traditional	ENETs, WHO	Moran *et al*
Low	Carcinoid Tumour	Neuro endocrine tumour, grade 1	Neuroendocrine carcinoma grade 1
Intermediate	Carcinoid Tumour	Neuro endocrine tumour grade 2	Neuroendocrine carcinoma grade2
High	Small cell carcinoma,	Neuroendocrine carcinoma grade 3, small cell carcinoma	Neuroendocrine carcinoma grade 3, small cell carcinoma
	Large cell neuroendocrine carcinoma	Neuroendocrine carcinoma grade 3, large cell neuroendocrine carcinoma	Neuroendocrine carcinoma grade 3, large cell neuroendocrine carcinoma

*Taken from North American Neuroendocrine Tumour Society guidelines, WHO: World Health Organization

43

What about Carcinoid Tumor of Lung?

- Standard Chemotherapy
  - *Streptozocin*
  - *Etoposide (VP-16)*
  - *Cisplatin*
  - *Carboplatin*
  - *Temozolomide*
  - *Cyclophosphamide (Cytoxan®)*
  - *5-fluorouracil (5-FU)*
  - *Doxorubicin (Adriamycin®)*
  - *Dacarbazine (DTIC)*



- Somatostatin Analogs – NOT TREATMENT FOR CANCER – treats symptoms of carcinoid syndrome
  - *Octreotide/Sandostatin*
  - *Lanreotide/Somatuline*
- *Alpha Interferon*
- Targeted Drugs – clinical trials – *Sunitinib/Sutent & Everolimus/Afinitor*

44

2018 MPH Lung Rules – *Pending*

45

2018 Anatomic Staging – SS2018 – *Pending*

46

Cancer Staging Basics

1. Where did the cancer start (primary site)?
2. Where did the cancer go (how far did it spread)?
3. How did the cancer get to the other organ or structure?
4. What is the SS2018 and AJCC TNM for this cancer?

➢ Incorporate SSDI Required for Staging for all cases.

47

Cancer Staging Basics

- There are three components to AJCC Cancer Stage and to assign Summary Stage 2018:
  - *Where and how big the original mass or primary tumor is = T*
  - *Which nodes the cancer has spread to including how many positive = N*
  - *Whether the cancer has spread to 1 or more distant site(s) = M*
- The T, N, and M information is joined to assign a Summary Stage and an AJCC "Stage Group" (now called **Anatomic Stage/Prognostic Group** with addition of genetic and bio-molecular tumor markers and other prognostic factors in the AJCC 8th edition)
  - **All cancers must be assigned a Summary Stage – SS2018**
  - **All cancers are assigned clinical stage – verify histology inclusion for TNM Chapter**
  - **Surgically resected cancers are assigned pathological stage – verify histology inclusion list**
  - **Patients completing pre-surgical chemo, radiation, or other therapy are assigned post-treatment stage**

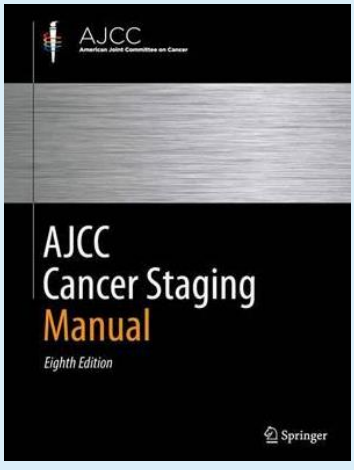
48

Criteria Used to Stage Lung Cancer

- <u>What To Look For & Document When Reviewing Lung Cancer Cases</u>
- Physical Exam – paraneoplastic syndrome, nerve or vessel obstruction
- CT Chest – tumor location, tumor size, nodes, pleural effusion
- CT Abdomen – liver or adrenal mets
- CT/MRI Brain – brain mets
- Pathology Report(s) – Resection of Primary and Nodal Status
- Pathology Report(s) – Extension to/thru visceral pleura
- Pathology Report(s) – Extension to parietal pleura
- Cytology Report(s) – Pleural Fluid (blood/exudate)
- Genetic Abnormalities – EGFR, KRAS, BRAF, ALK, ROS1, MET, RET, PDL-1, HER2

49

2018 Anatomic Staging – AJCC TNM 8th ed



DESCRIPTOR	SEVENTH EDITION	EIGHTH EDITION
T component		
0 cm (pure lepidic adenocarcinoma ≤3 cm total size)	T1a if ≤2 cm; T1b if >2-3 cm	Tis (AIS)
≤0.5 cm invasive size (lepidic predominant adenocarcinoma ≤3 cm total size)	T1a if ≤2 cm; T1b if >2-3 cm	T1mi
≤1 cm	T1a	T1a
>1-2 cm	T1a	T1b
>2-3 cm	T1b	T1c
>3-4 cm	T2a	T2a
>4-5 cm	T2a	T2b
>5-7 cm	T2b	T3
>7 cm	T3	T4
Bronchus <2 cm from carina	T3	T2
Total atelectasis/pneumonitis	T3	T2
Invasion of diaphragm	T3	T4
Invasion of mediastinal pleura	T3	-
N component		
No assessment, no involvement, or involvement of regional lymph nodes	NX, N0, N1, N2, N3	No change
M component		
Metastases within the thoracic cavity	M1a	M1a
Single extrathoracic metastasis	M1b	M1b
Multiple extrathoracic metastases	M1b	M1c

Abbreviations: AIS, adenocarcinoma in situ; mi, minimally invasive adenocarcinoma; Tis, tumor in situ.

50

Clinical Classification - cTNM

- Based on Evidence Acquired Before Any Treatment
  - *Physical Exam*
  - *Imaging (CT Scan, PET Scan)*
  - *Laboratory Tests*
  - *Thoracentesis*
  - *Endoscopy with ultrasound or biopsy (core/FNA)*
    - Bronchoscopy (EBUS)
    - Esophagoscopy (EUS)
    - Mediastinoscopy
    - Thoracoscopy (VATS without resection of primary tumor)
  - *Exploratory Thoracotomy*

51

Pathologic Classification - pTNM

- Includes Any Evidence Acquired Before Any Treatment PLUS
- Pathologic Assessment of Resected Primary Tumor (to highest pT) *
- Pathologic Assessment of Regional Lymph Nodes (to highest pN) *
- Isolated Tumor Cells (ITCs) in Lymph Node(s) are Classified N0 or M0
  - *pN0*
  - *pN0(i-)*
  - *pN0(i+)*
  - *pN0(mol-)*
  - *pN0(mol+)*
- pM can be either cM or pM when the T and/or N categories are valid

* *"Pathologic staging depends on the proven anatomic extent of disease, whether or not the primary lesion has been completely removed. If a biopsied primary tumor technically cannot be removed…and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer."*

52

Post-Neoadjuvant p Classification - ypTNM

- **Best Demonstrates Need for Accurate Clinical Stage** when the first cancer surgery follows radiation therapy, chemotherapy, hormones, immunologic agents meant to alter the tumor behavior, size, extension, lymph node status, etc. resulting in down-stage of disease at time of first surgery and with some current regimens showing no primary tumor and negative nodes at surgery.

- *Patient must have received planned presurgical therapy(s):*
  - *Radiation Therapy (any modality)*
  - *Chemotherapy*
  - *Hormone(s)*
  - *Biologic Agent (BRM/Immuno)*
  - *Combination of above*

- *Patient must have post-therapy excision of primary site and nodes sufficient to meet the criteria to assign AJCC Stage Pathologic Classification or pTNM.*

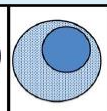
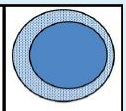
53

T Category

CATEGORY	SUBCATEGORY	DESCRIPTORS
T: Primary tumor		
TX		Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
T0		No evidence of primary tumor
Tis		Carcinoma in situ: • Tis (AIS): adenocarcinoma • Tis (SCIS): squamous cell carcinoma
T1		Tumor 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (ie, not in the main bronchus); 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
	T1mi	Minimally invasive adenocarcinoma
	T1a	Tumor 1 cm or less in greatest dimension
	T1b	Tumor more than 1 cm but not more than 2 cm in greatest dimension
	T1c	Tumor more than 2 cm but not more than 3 cm in greatest dimension
T2		Tumor more than 3 cm but not more than 5 cm; or tumor with *any* of the following features (T2 tumors with these features are classified T2a if 4 cm or less or if size cannot be determined and as T2b if greater than 4 cm but not larger than 5 cm): • Involves main bronchus regardless of distance to the carina, but without involving the carina • Invades visceral pleura • Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, either involving part of the lung or the entire lung
	T2a	Tumor more than 3 cm but not more than 4 cm in greatest dimension
	T2b	Tumor more than 4 cm but not more than 5 cm in greatest dimension
T3		Tumor more than 5 cm but not more than 7 cm in greatest dimension or one that directly invades any of the following: parietal pleura (PL3), chest wall (including superior sulcus tumors), phrenic nerve, parietal pericardium; or associated separate tumor nodule(s) in the same lobe as the primary
T4		Tumors more than 7 cm or one that invades any of the following: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina; separate tumor nodule(s) in a different ipsilateral lobe to that of the primary

54

T Category

cT*	CT image on HRCT						
	Solid part Total tumor size including GG Pathologic Differential Diagnosis	0 ≤0.5 cm AAH‡, AIS, MIA	0 cm 0.6-3.0 cm AIS, MIA, LPA	≤0.5 cm† ≤3.0 cm†† MIA, LPA, AIS	0.6-1.0 cm† 0.6-3.0 cm†† LPA, Invasive AD, MIA	1.1-2.0 cm † 1.1-3.0 cm†† LPA, Invasive AD	2.1-3.0 cm† 2.1-3.0 cm†† Invasive AD
	Clinical Stage*		cTis	cT1mi	cT1a	cT1b	cT1c
pT	Invasive part	0	0 cm	≤0.5 cm†	0.6-1.0 cm†	1.1-2.0 cm†	2.1-3.0 cm†
	Total tumor size including lepidic growth part	Usually ≤0.5 cm‡	≤3.0 cm	≤3.0 cm	0.6-3.0 cm††	1.1-3.0 cm††	2.1-3.0 cm††
	Pathology	AAH	AIS	MIA	Lepidic predominant AD or Invasive AD with lepidic component	Invasive AD with a lepidic component or lepidic predominant AD	Invasive AD with lepidic component
	Pathologic Stage		pTis	pT1mi	pT1a	pT1b	pT1c

55

FCDS Lung Audits – 2014/2015 Diagnosis

- Clarify the Difference between Atelectasis, Obstructive Pneumonitis, Consolidation, and (Malignant/Non-Malignant) Pleural Effusion
  - *Atelectasis/Pneumothorax = Complete or Partially Collapsed Lung*
  - *Pneumonitis - inflammation of the walls of the alveoli in the lungs, often caused by a virus.*
  - *Obstructive Pneumonitis – pneumonitis resulting in bronchial obstruction*
  - *Consolidation - a region of lung tissue that has filled with liquid or blood or pus instead of air*
  - *Pleural Effusion/Hemothorax - a buildup of extra fluid in the space between the lungs and the chest wall.*
    - Most pleural effusions are hemorrhagic or bloody which indicates malignant pleural effusion without even looking at cytology
    - Any pleural effusion in lung cancer is deemed "malignant" and must be proven "negative" x 2-3 cytology examinations
    - When pleural effusion described as "minimal" or "small" it may not be 'treated' as with involvement – still code as malignant pleural effusion for consistency in staging cases
  - *Primary Tumor Extension to either Pleura is not the same as pleural effusion*

56

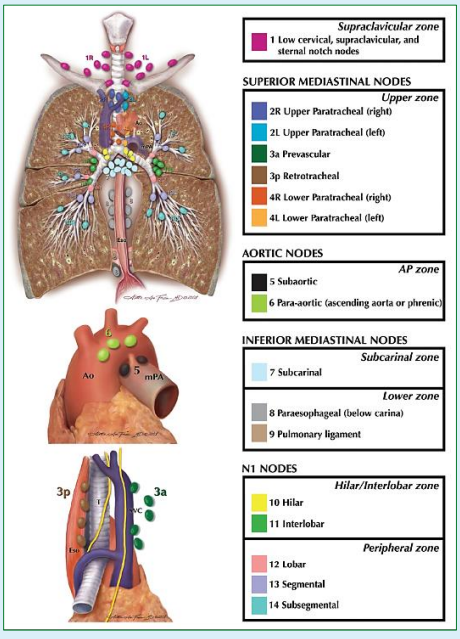
N Category

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 lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral, or contralateral scalene, or supraclavicular lymph node(s)

Isolated Tumor Cells (ITCs) in Lymph Node(s) are Classified N0 or M0

- pN0
- pN0(i-)
- pN0(i+)
- pN0(mol-)
- pN0(mol+)

57



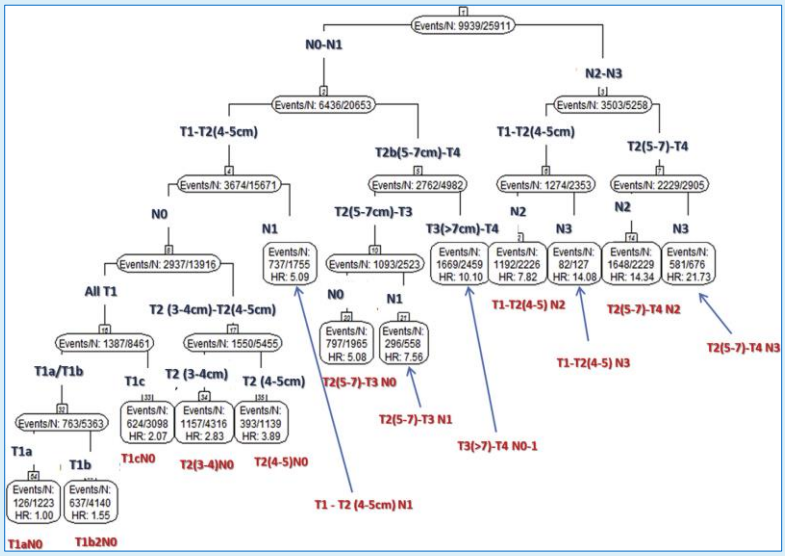
Lung Anatomy

- **NX** Regional lymph nodes cannot be assessed
- **N0** No regional lymph node metastases
- **N1** Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
- **N2** Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
- **N3** Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

IASLC lymph node map - WHO Classification of Tumours of the Lung, 2015

58

IASLC Staging Survival Tree



M Category

M: Distant metastasis		
M0		No distant metastasis
M1		Distant metastasis
	M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural nodules or malignant pleural or pericardial effusion; most pleural (pericardial) effusions with lung cancer are due to tumor; in a few patients, however, multiple microscopic examinations of pleural (pericardial) fluid are negative for tumor, and the fluid is nonbloody and is not an exudate; where these elements and clinical judgment dictate that the effusion is not related to the tumor, the effusion should be excluded as a staging descriptor
	M1b	Single extrathoracic metastasis in a single organ and involvement of a single distant (nonregional) node
	M1c	Multiple extrathoracic metastases in one or several organs

Anatomic Stage/Prognostic Groups

- Stage IA is now divided into IA1, IA2, and IA3 for T1a, T1b, and T1cN0M0 tumors
- ALL N1 disease is stage IIB except for T3-T4N1M0 tumors, which are stage IIIA
- New Stage IIIC is created for T3-T4N3M0 tumors
- Stage IV is divided into IVA (M1a and M1b) and IVB (M1c)

61

Anatomic Stage/Prognostic Groups

STAGE	T	N	M
Occult carcinoma	TX	N0	M0
0	Tis	N0	M0
IA1	T1mi	N0	M0
	T1a	N0	M0
IA2	T1b	N0	M0
IA3	T1c	N0	M0
IB	T2a	N0	M0
IIA	T2b	N0	M0
IIB	T1a,b,c	N1	M0
	T2a,b	N1	M0
	T3	N0	M0
IIIA	T1a,b,c	N2	M0
	T2a, b	N2	M0
	T3	N1	M0
	T4	N0	M0
	T4	N1	M0
IIIB	T1a,b,c	N3	M0
	T2a,b	N3	M0
	T3	N2	M0
	T4	N2	M0
IIIC	T3	N3	M0
	T4	N3	M0
IVA	Any T	Any N	M1a
	Any T	Any N	M1b
IVB	Any T	Any N	M1c

62

Small Cell Lung Cancer VALG Stage

- **Veterans Administration Lung Study Group's (VALG)** Staging Classification for Small Cell Lung Cancer
- **Limited-Stage:** AJCC (8th edition) Stage I-III (excludes most T3-T4 due to multiplicity of tumors in same lung – cannot radiate for local control)
- **Extensive-Stage:** AJCC (8th edition) Stage IV and most T3-T4

Still use AJCC TNM when can be more specific. But, most clinicians will refer to the VALG "limited" or "extensive" when assessing for treatment options, particularly for inclusion/exclusion of XRT to chest when T3-T4.

63

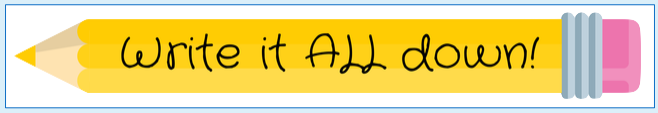
2018 Lung Site-Specific Data Items

- **REQUIRED for Staging – NONE**
- RECOMMENDED for Clinical Care – Not Yet Approved or Fully Defined
  - *Resection Margins*
  - *Adequacy of Mediastinal Dissection*
  - *EGFR Mutation*
  - *ALK Gene Rearrangement*
  - *Symptoms*
  - *Weight Loss*
  - *Performance Status*
  - *Prophylactic Cranial Radiotherapy*
  - *LVI and Perineural Invasion*
  - *Type of Visceral Pleural Invasion – PL1 versus PL2*
  - *SUV of Primary Tumor*

64

Text Documentation

- Dates
- CT Scans
- Screening
- Tumor Size – clinical and pathological
- Nodal Status – clinical and pathological
- All Metastatic Sites
- Results of Genetic Profile – what is positive and what marker studies were performed
- Specific Agents for Chemotherapy
- Specific Agents for Targeted Therapies
- Radiation Fields and Dosage



- ALL Surgical Procedures to Primary Site
- ALL Surgical Procedures to Lymph Nodes
- Caution: Do not code Surgery to Other Regional or Distant Sites unless cancer-related.
- When assigning post-treatment stage be very cautious that patient meets criteria for *yp.*
- *This year we do not collect yc – perhaps next yr*

65

PRACTICE CASES

Practice Cases

- We will not include Histology Coding Practice Cases until we can confirm with MPH.
- We will not include Staging Practice Cases until we can confirm with AJCC & SS2018.
- We hope that by mid-2018 we can provide a selection of practice cases from multiple sites and histologies for registrars to code number of primaries (MPH), histology (MPH) and to stage cases using Summary Stage 2018 and AJCC Cancer Staging, 8th ed.
- The July FCDS Annual Conference will focus heavily on new standards and practice.

67

References and Resources

- *WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart, 4th edition;* World Health Organization, IARC, Lyon 2015
- *The 2015 World Health Organization Classification of Lung Tumors; Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification*; Journal of Thoracic Oncology ® • Volume 10, Number 9, September 2015
- *Biomarker Testing of Specimens from Patients with NSCLC*, CAP, June 2016
- *AJCC Cancer Staging Manual, 8th edition;* American Joint Committee on Cancer,2017
- *Lung Cancer—Major Changes in the American Joint Committee on Cancer Eighth Edition Cancer Staging Manual;* CA Cancer J Clin; 2017;67:138–155. VC 2017 American Cancer Society.
- *The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer*, dx.doi.org/10.1016/j.jtho.2015.09.009; Journal of Thoracic Oncology Vol. 11 No. 1: 39-51
- *E-Cigarette Use Among Youth and Young Adults*; *A Report of the Surgeon General*; DHHS, 2016
- Shahab, L., et al. (2017). *Nicotine, Carcinogen, and Toxin Exposure in Long-Term E-Cigarette and Nicotine Replacement Therapy Users*. Annals of Internal Medicine. DOI: 10.7326/M16-1107
- NCCN Guidelines – Lung Cancer Screening, Non-Small Cell Lung Cancer, Small Cell Lung Cancer

68

Questions