Florida Statewide Cancer Registry
Florida Cancer Data System

2021-2022 FCDS Educational Webcast Series

2022 Lung: Recent Updates and How to Use Current Abstracting Resources for Cases

Steven Peace, CTR

January 20, 2022

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

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CDC & Florida DOH Attribution

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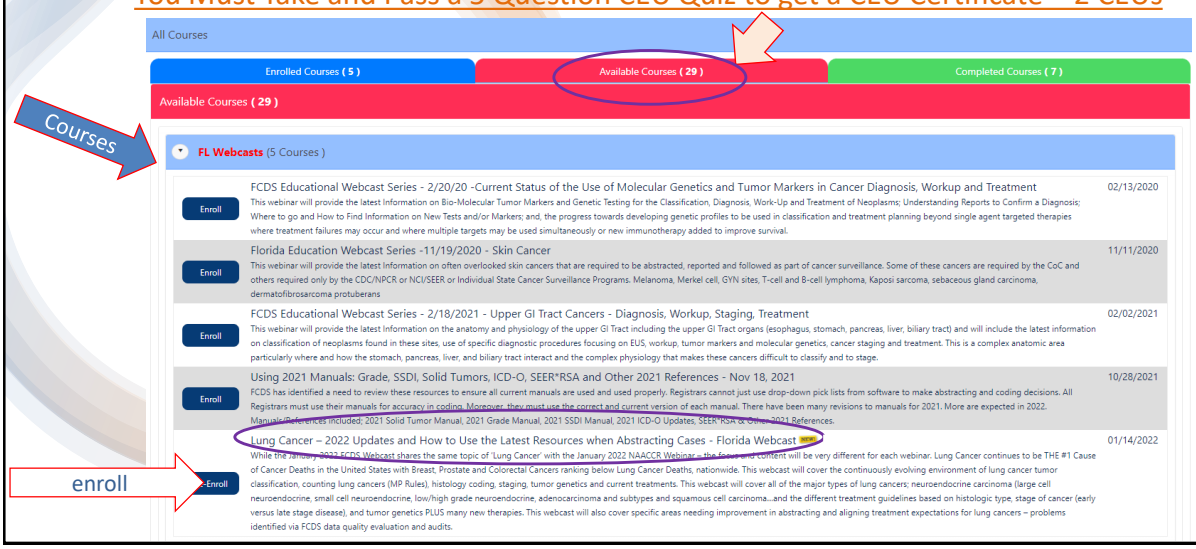
FLccSC and CEU Certificate

You Must Take and Pass a 5 Question CEU Quiz to get a CEU Certificate – 2 CEUs



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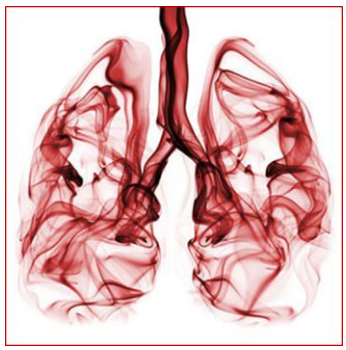
2022 Lung Outline

- Introduction to Neoplasms of the Lung
- 2021 Statistics for Lung Cancers
- Risk Factors – Signs & Symptoms
- Anatomy of the Lung and Thorax
- Screening Guidelines, Diagnostic Workup, and Lab Tests
- Biological Tumor Markers, Single and Multi-Gene Testing
- 2022 Lung Solid Tumor Rules – Histology – no new rules
- 2022 Lung ICD-O-3.2 – Review Histology – no new codes
- 2022 Lung NSCLC/NET/NEC Grade Coding Rules – no new rules
- 2022 Lung NSCLC/NET/NEC Site-Specific Data Items – no new SSDI
- 2022 Staging for Lung – SS2018 Focus (T & N for TNM)
- 2022 NCCN Treatment Guidelines for NSCLC Lung
- 2022 NCCN Treatment Guidelines for Neuroendocrine Lung
- Text Documentation for Lung Cancers
- Miscellaneous Notes – Impact of Covid-19
- Presentation References
- Questions



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Introduction to Neoplasms of the Lung and Cancer Statistics

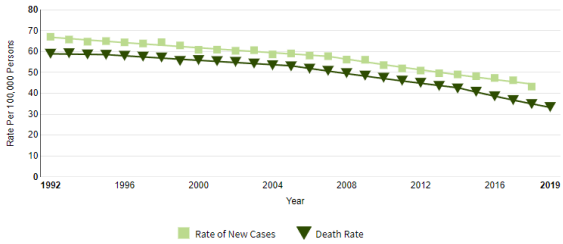
At a Glance

Estimated New Cases in 2021	235,760
% of All New Cancer Cases	12.4%
Estimated Deaths in 2021	131,880
% of All Cancer Deaths	21.7%

5-Year Relative Survival

21.7%

2011–2017



New cases come from SEER 13. Deaths come from U.S. Mortality.
All Races, Both Sexes. Rates are Age-Adjusted.
Modeled trend lines were calculated from the underlying rates using the Joinpoint Trend Analysis Software.

New cases are also referred to as incident cases in other publications. Rates of new cases are also referred to as incidence rates.

https://seer.cancer.gov/statfacts/html/lungb.html

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Introduction to Neoplasms of the Lung

Figure 3. Leading Sites of New Cancer Cases and Deaths – 2021 Estimates

Estimated New Cases

Male			Female		
Prostate	248,530	26%	Breast	281,550	30%
Lung & bronchus	119,100	12%	Lung & bronchus	116,660	13%
Colon & rectum	79,520	8%	Colon & rectum	59,060	6%
Urinary bladder	64,280	7%	Uterine corpus	66,570	7%
Melanoma of the skin	62,260	6%	Melanoma of the skin	43,850	5%
Kidney & renal pelvis	48,780	5%	Non-Hodgkin lymphoma	35,930	4%
Non-Hodgkin lymphoma	45,630	5%	Thyroid	32,130	3%
Oral cavity & pharynx	38,800	4%	Pancreas	28,480	3%
Leukemia	35,530	4%	Kidney & renal pelvis	27,300	3%
Pancreas	31,950	3%	Leukemia	25,560	3%
All sites	970,250		All sites	927,910	

Estimated Deaths

Male			Female		
Lung & bronchus	69,410	22%	Lung & bronchus	62,470	22%
Prostate	34,130	11%	Breast	43,600	15%
Colon & rectum	26,520	9%	Colon & rectum	24,460	8%
Pancreas	25,270	8%	Pancreas	22,950	8%
Liver & intrahepatic bile duct	20,300	6%	Ovary	13,770	5%
Leukemia	13,900	4%	Uterine corpus	12,940	4%
Esophagus	12,410	4%	Liver & intrahepatic bile duct	9,930	3%
Urinary bladder	12,260	4%	Leukemia	9,760	3%
Non-Hodgkin lymphoma	12,170	4%	Non-Hodgkin lymphoma	8,550	3%
Brain & other nervous system	10,500	3%	Brain & other nervous system	8,100	3%
All sites	319,420		All sites	289,150	

Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

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2021 Cancer Facts and Figures, American Cancer Society

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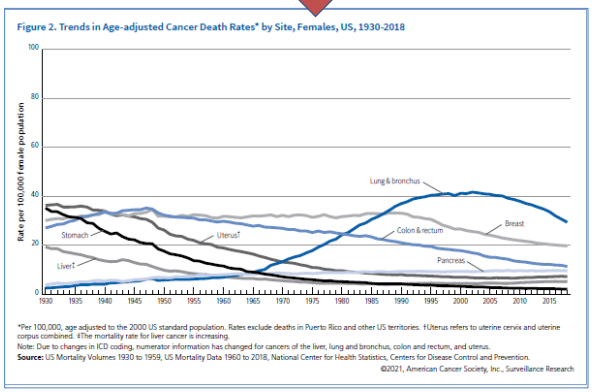
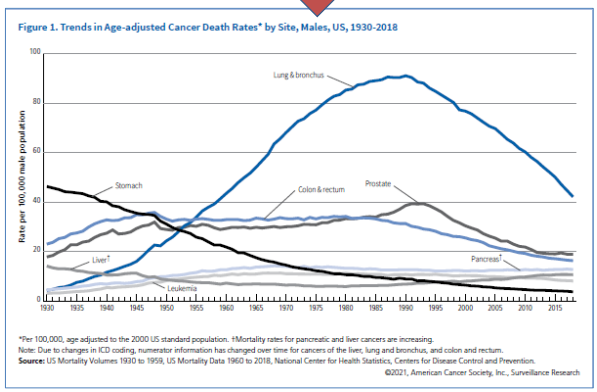
Introduction to Neoplasms of the Lung





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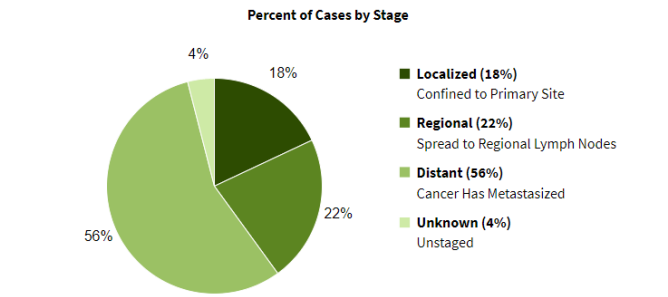
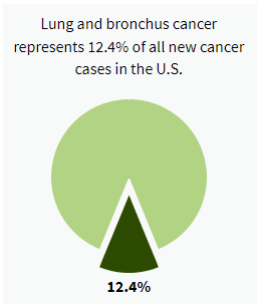
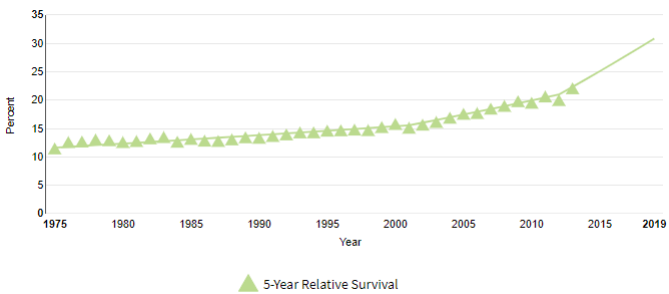
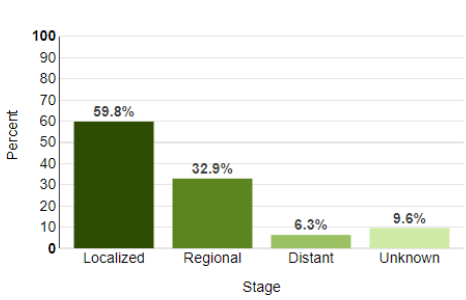
More Statistics









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SEER Cancer Statistics – Statistics At a Glance - USCS

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Risk Factors – Signs & Symptoms

Symptoms often do not appear until the cancer has spread.

- Difficulty breathing—might include wheezing, shortness of breath, or 'stridor' (a harsh sound with each breath)
- Cough that doesn't go away or gets worse
- Coughing up blood or rust-colored sputum (hemoptysis)
- Chest pain worse with breathing, coughing or laughing
- Arm or should pain with or without chest pain
- Recurring pneumonia or bronchitis
- Headaches or seizures
- Hoarseness
- Weight loss
- Loss of appetite
- Bone pain
- Swelling of the face or neck
- Upper eyelid drooping
- Fatigue

Risk Factors

- Tobacco Smoke
  - Cigarettes (packs/day – small cell lung cancer)
  - Light Cigarettes carry same risk as regular cigarettes
  - Menthol Cigarettes increase risk more – inhale deeply
  - Secondhand Smoke
  - Cigars and Pipes
- Radon Exposure (10% of deaths from lung cancer)
- Asbestos Exposure
- Workplace Carcinogens
  - Uranium Exposure
  - Inhaled Chemicals – see
  - Diesel Exhaust
- Beta Carotene Supplements
- Arsenic in Drinking Water
- Radiation to Lungs
- Air Pollution (5% of deaths from lung cancer)
- E-cigarettes (pending)
- Marijuana (pending)
- Talc and Talcum Powder (pending)

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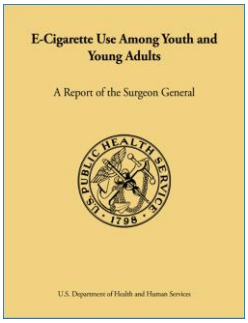
Risk Factors – Signs & Symptoms



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.

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Risk Factors – Signs & Symptoms

- Chronic H. pylori Infection – stomach bacteria
- Antimony Trioxide – flame retardant in plastics
- 6 Haloacetic Acids or HAAs – water treatment systems and water disinfectant byproducts
  - Bromochloroacetic acid (BCA)
  - Bromodichloroacetic acid (BDCA)
  - Chlorodibromoacetic acid (CDBA)
  - Dibromoacetic acid (DBA)
  - Dichloroacetic acid (DCA)
  - Tribromoacetic acid (TBA)

Official Citation: NTP (National Toxicology Program). 2021. Report on Carcinogens, Fifteenth Edition.; Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Service. https://ntp.niehs.nih.gov/go/roc15 (EndNote XML). DOI: https://doi.org/10.22427/NTP-OTHER-1003

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Aflatoxins
Alcoholic Beverage Consumption
4-Aminobiphenyl
Analgesic Mixtures Containing Phenacetin (see Phenacetin and Analgesic Mixtures Containing Phenacetin
Aristolochic Acids
Arsenic and Inorganic Arsenic Compounds
Asbestos
Azathioprine
Benzene
Benzidine (see Benzidine and Dyes Metabolized to Benzidine)
Beryllium and Beryllium Compounds
Bis(chloromethyl) Ether and Technical-Grade Chloromethyl Methyl Ether
1,3-Butadiene
1,4-Butanediol Dimethanesulfonate
Cadmium and Cadmium Compounds
Chlorambucil
1-(2-Chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea (see Nitrosourea Chemotherapeutic Agents)
Chromium Hexavalent Compounds
Coal Tars and Coal-Tar Pitches
Coke-Oven Emissions
Cyclophosphamide
Cyclosporin A
Diethylstilbestrol
Dyes Metabolized to Benzidine (Benzidine Dye Class) (see Benzidine and Dyes Metabolized to Benzidine)
Epstein-Barr Virus (see Viruses: Eight Listings)
Erionite
Estrogens, Steroidal
Ethylene Oxide
Formaldehyde
***Helicobacter pylori* (Chronic Infection)**

Hepatitis B Virus (see Viruses: Eight Listings)
Hepatitis C Virus (see Viruses: Eight Listings)
Human Immunodeficiency Virus Type 1 (see Viruses: Eight Listings)
Human Papillomaviruses: Some Genital-Mucosal Types (see Viruses: Eight Listings)
Human T-Cell Lymphotrophic Virus Type 1 (see Viruses: Eight Listings)
Kaposi Sarcoma–Associated Herpesvirus (see Viruses: Eight Listings)
Melphalan
Merkel Cell Polyomavirus (see Viruses: Eight Listings)
Methoxsalen with Ultraviolet A Therapy
Mineral Oils: Untreated and Mildly Treated
Mustard Gas
2-Naphthylamine
Neutrons (see Ionizing Radiation)
Nickel Compounds (see Nickel Compounds and Metallic Nickel)
Radon (see Ionizing Radiation)
Silica, Crystalline (Respirable Size)
Solar Radiation (see Ultraviolet Radiation Related Exposures)
Soots
Strong Inorganic Acid Mists Containing Sulfuric Acid
Sunlamps or Sunbeds, Exposure to (see Ultraviolet Radiation Related Exposures)
Tamoxifen
2,3,7,8-Tetrachlorodibenzo-*p*-dioxin
Thiotepa
Thorium Dioxide (see Ionizing Radiation)
Tobacco Smoke, Environmental (see Tobacco-Related Exposures)
Tobacco Smoking (see Tobacco-Related Exposures)
Tobacco, Smokeless (see Tobacco-Related Exposures)
o-Toluidine
Trichloroethylene
Ultraviolet Radiation, Broad-Spectrum (see Ultraviolet Radiation Related Exposures)
Vinyl Chloride (see Vinyl Halides [selected])
Wood Dust
X-Radiation and Gamma Radiation (see Ionizing Radiation)

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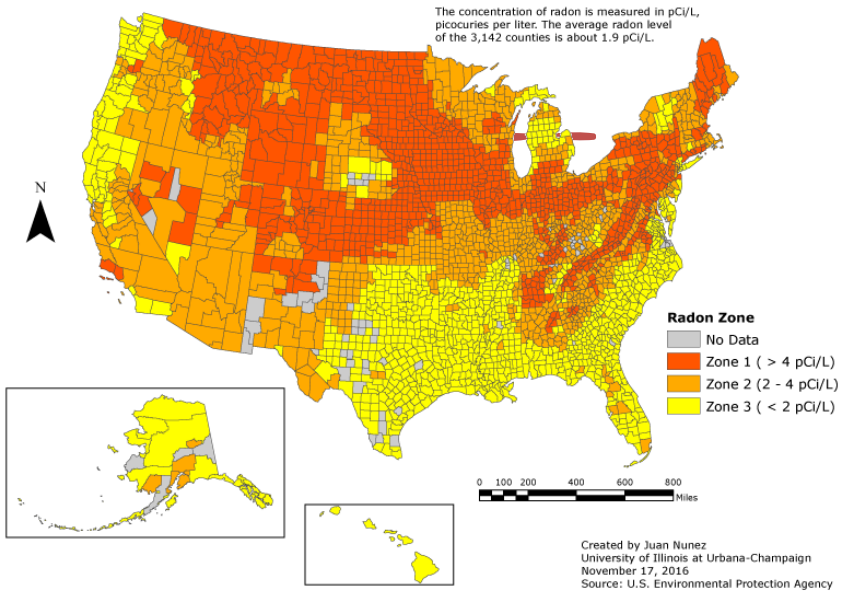
Indoor Radon Levels and Zones per U.S. County



By Jcnunez227 - Own work, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=53250357

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NIH Study Illuminates Origins of Lung Cancer in Never Smokers National Cancer Institute

- 10% to 20% of people who develop lung cancer have never smoked.
- Lung cancer in never smokers occurs more frequently in women.
- Lung cancer in never smokers occurs at an earlier age than in smokers.

A genomic analysis of lung cancer in people with no history of smoking has found that a majority of these tumors arise from the accumulation of mutations caused by natural processes in the body.

"What we're seeing is that there are different subtypes of lung cancer in never smokers that have distinct molecular characteristics and evolutionary processes."

"This analysis shows that there is heterogeneity, or diversity, in lung cancers in never smokers.",

Researchers used whole-genome sequencing to characterize three molecular subtypes of lung cancer in people who had never smoked. Credit: National Cancer Institute

NCI's Division of Cancer Epidemiology and Genetics

Zhang T, Joubert P, Ansari-Pour N, et al. Genomic and evolutionary classification of lung cancer in never smokers. Nature Genetics. Sept 6, 2021. DOI: 10.1038/s41588-021-00920-0.

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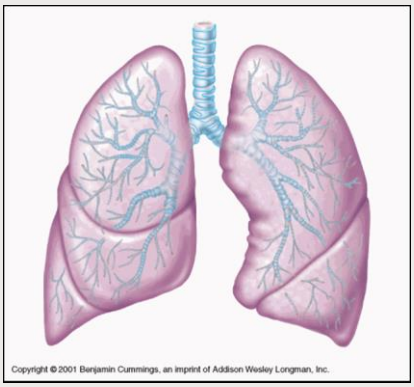
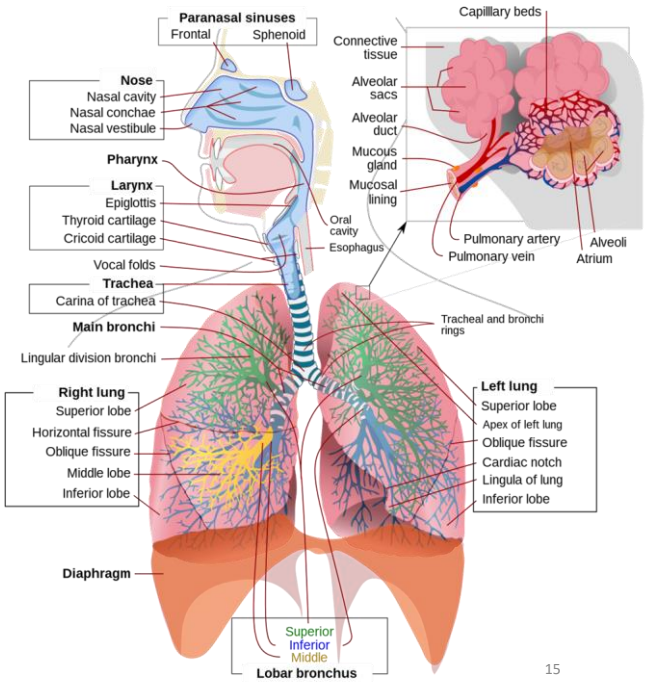
Anatomy of the Lung





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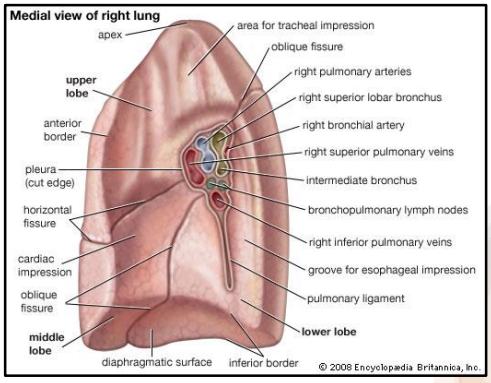
Anatomy of the Lung

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

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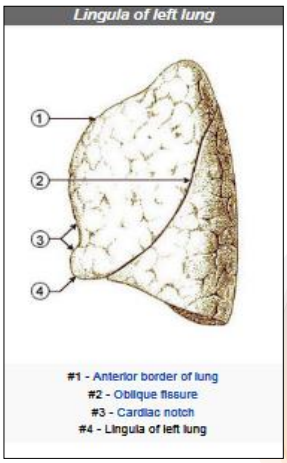
Anatomy of the Lung

- 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

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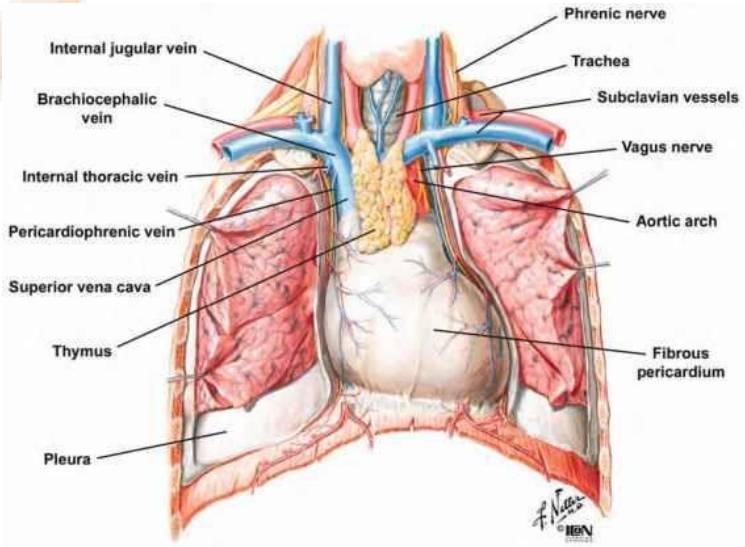
Anatomy of the Lung



https://www.pinterest.com/pin/357402920421732388/ - http://www.guwsmedical.info

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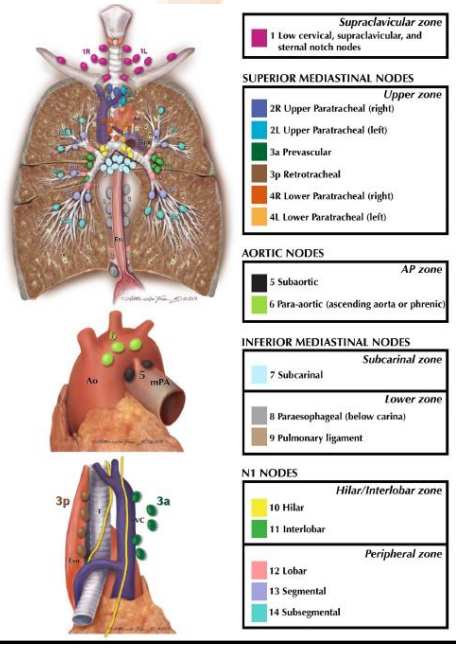
Anatomy of the Lung



- **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 and N Category Codes 19

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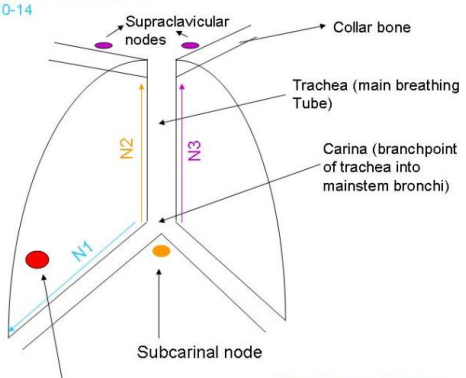
Anatomy of the Lung

N1 Nodes (blue arrow): Nodes distal to the carina
- "Double digit nodes" = #s 10-14
- 10 = Hilar nodes
- 11 = Interlobar nodes
- 12 = Lobar nodes
- 13 = Segmental nodes
- 14 = Subsegmental nodes

N2 Nodes (orange arrow): Same side in mediastinum plus aortic nodes (not shown) and subcarinal nodes
- Same side "Single digit nodes" = # 2-6
- 2= Upper paratracheal nodes
- 3= prevascular nodes and retrotracheal nodes
- 4=Lower paratracheal nodes
- 5=Subaortic (not shown)
- 6=Para-aortic
- 7=Subcarinal
- 8 = paraesophageal
- 9=pulmonary ligament



Source: http://cancergrace.org/lung/files/2010/04/simplified-staging.jpg 20

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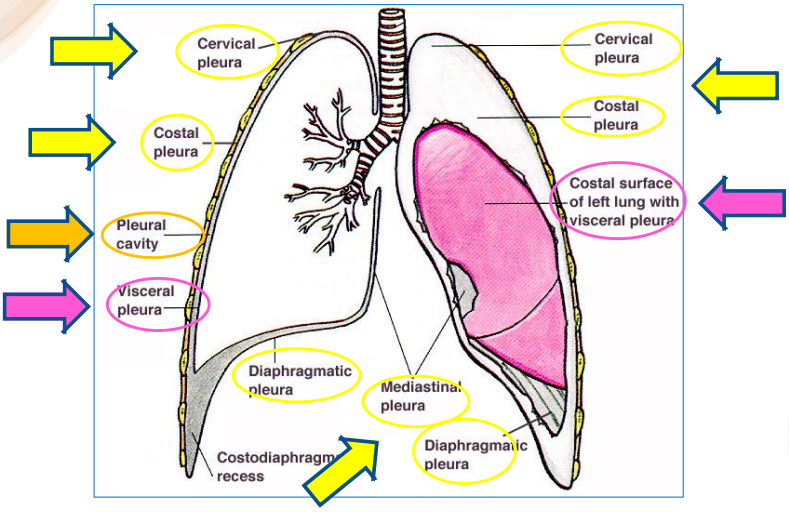
Anatomy of the Lung



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

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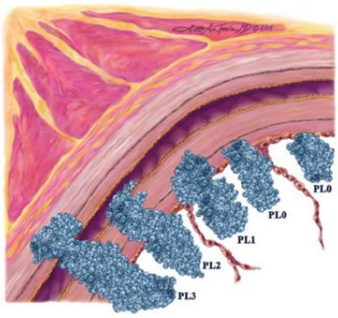
Anatomy of the Lung

Pleural Invasion Classification

Modified Hammar Classification of visceral pleural invasion (VPI)



Visceral Pleural Invasion: Pathologic Criteria and Use of Elastic Stains
Proposal for the 7th Edition of the TNM Classification for Lung Cancer

(*J Thorac Oncol.* 2008;3: 1384–1390)

- PL0
  - Tumor within the subpleural lung parenchyma or
  - Invading superficially into the pleural connective tissue beneath the elastic layer

PL0

T2 (visceral)

- PL1 : beyond the elastic layer
- PL2 : invade to the pleural surface

PL1 & PL2

T3 (parietal)

- PL3 : invade into any component of the parietal pleura

PL3

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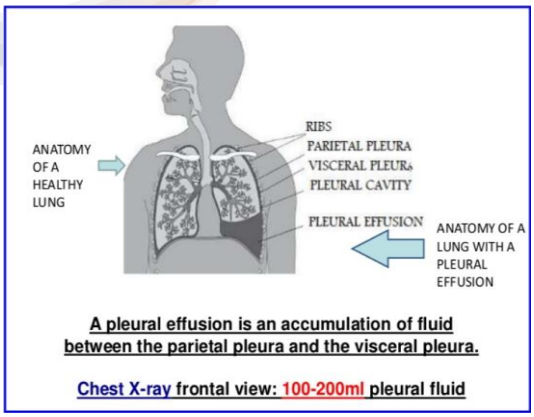
Anatomy of the Lung



Source: www.slideshare.net/pleuraleffusion/drmahesh

Note 8: Most pleural and pericardial effusions with lung cancer are due to tumor. In a few patients, however, multiple cytopathological examinations of pleural and/or 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 element.

2 Regional by direct extension only

- Atelectasis/obstructive pneumonitis
  - Extends to hilar region, involving part or all of lung
- Blood vessel(s) (major)
  - Aorta
  - Azygos vein
  - Pulmonary artery or vein
  - Superior vena cava (SVC syndrome)
- Brachial plexus
- Carina from lung
- Chest wall (thoracic wall)
- Compression of esophagus or trachea not specified as direct extension
- Diaphragm (separate lesion-see code 7)
- Esophagus
- Mediastinum, extrapulmonary or NOS
- Nerve(s)
  - Cervical sympathetic (Horner's syndrome)
  - Recurrent laryngeal (vocal cord paralysis)
  - Vagus
- Pancoast tumor (superior sulcus syndrome), NOS
- Parietal pericardium
- Parietal pleura
- Pericardium, NOS
- Phrenic nerve
- Pleura, NOS
- Pulmonary ligament
- Separate tumor nodule(s) in the same lobe as the primary
- Visceral pleura invasion (PL1, PL2, PL3, or NOS)
- Trachea

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Anatomy of the Lung - Terminology

- 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*

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Screening Guidelines, Diagnostic Workup, and Lab Tests

US Preventive Services Task Force (USPSTF), the American Cancer Society, the American Academy of Family Physicians (AAFP), and the American College of Chest Physicians.

Recommend yearly lung cancer screening with LDCT scans for people who:

- ✓ **Are 50 to 80 years old and in fairly good health, *and***
- ✓ **Currently smoke or have quit in the past 15 years, *and***
- ✓ **Have at least a 20 pack-year smoking history. This is the number of packs of cigarettes per day multiplied by the number of years smoked. For example, someone who smoked 2 packs a day for 10 years [2 x 10 = 20] has 20 pack-years of smoking, as does a person who smoked 1 pack a day for 20 years [1 x 20 = 20]**

it's important that people who are going to be screened:

Receive counseling to quit smoking if they currently smoke, ***and***

Have been told by their doctor about the possible benefits, limits, and harms of screening with LDCT scans, ***and***

Can go to a center that has experience in lung cancer screening and treatment.

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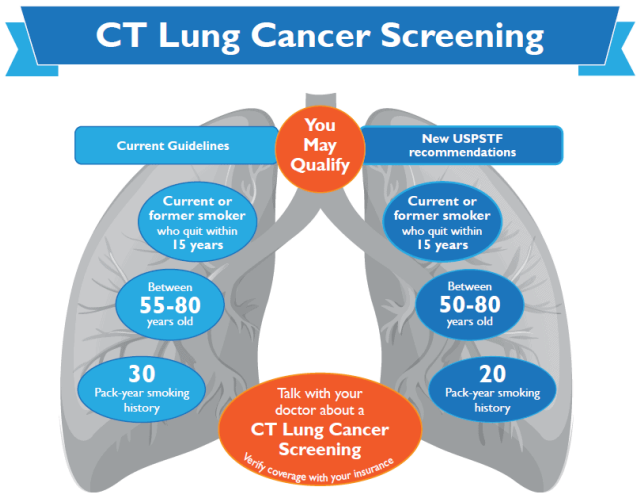
Low Dose Helical (Spiral) CT Scan of Lung



DESIGNATED Lung Cancer Screening Center AMERICAN COLLEGE OF RADIOLOGY

DESIGNATED Lung Cancer Screening Center AMERICAN COLLEGE OF RADIOLOGY

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Increasing Adherence to CT Lung Cancer Screening Programs

Despite the conclusive evidence for the effectiveness of Lung Cancer Screening from the US National Lung Screening Trial (NLST), national data indicate low uptake (≤4%) in the United States.

Other countries like the UK achieve higher uptake rates of more than 50%...comparable to breast & colon screening

It remains an important challenge to ensure acceptance by the target population and adherence to initial as well as subsequent rounds of screening to ensure the success of Lung Cancer Screening Programs across the United States.

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Diagnostic Workup

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

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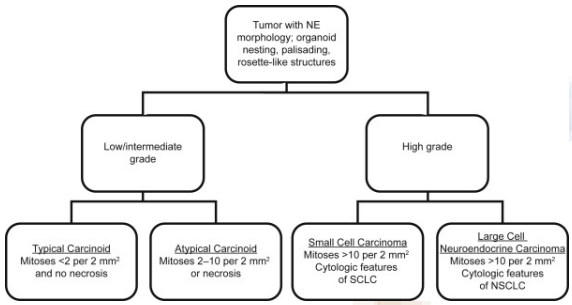
Diagnostic Workup – Tumor Classification

Pulmonary Neuroendocrine Tumors

- Carcinoid Tumor - 8240
- Atypical Carcinoid Tumor - 8249
- Low Grade Neuroendocrine Carcinoma - 8240
- Small Cell (Neuroendocrine) Carcinoma - 8041
- Large Cell (Neuroendocrine) Carcinoma - 8013
- High Grade Neuroendocrine Carcinoma – 8246
- Poorly Differentiated Neuroendocrine Carcinoma - 8246



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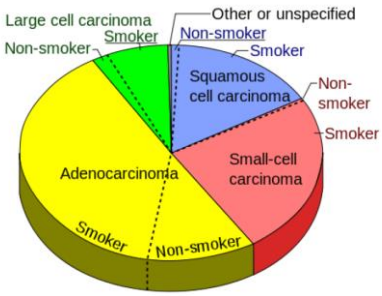
Diagnostic Workup – Tumor Classification

Non-Small Cell Carcinoma of the Lung - NSCLC



- Adenocarcinoma (55%)
  - Mucinous Adenocarcinoma
  - Microinvasive Adenocarcinoma
  - Micropapillary Adenocarcinoma
  - Minimally Invasive Adenocarcinoma
  - Non-Mucinous Adenocarcinoma
    - Acinar predominant
    - Lepidic Predominant
    - Papillary Predominant
    - Solid Predominant
- Squamous Cell Carcinoma (20%)
- Large Cell Carcinoma (5%)
- NSCLC, NOS

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Diagnostic Workup – Tumor Classification

Reclassification of Bronchoalveolar Carcinoma (BAC)

A. Mucinous carcinoma/adenocarcinoma
- 8253/3 when
  - Behavior unknown/not documented (use staging form
  - Invasive
- 8257/3 when
  - Microinvasive
  - Minimally invasive
- 8253/2 when
  - Preinvasive
  - In situ

B. Non-mucinous carcinoma/adenocarcinoma
- 8256/3 when
  - Microinvasive
  - Minimally invasive
- 8250/2 when
  - Preinvasive
  - In situ

C. Adenocarcinomas (CAP Terminology) Adenocarcinoma, acinar predominant 8551
- Adenocarcinoma, lepidic predominant 8250
- Adenocarcinoma, micropapillary predominant 8265
- Adenocarcinoma, papillary predominant 8260
- Adenocarcinoma, solid predominant 8230

Note: Previously, only **invasive** /3 codes were available for mucinous adenocarcinoma of the lung. It has been recognized that not all lung cancers are invasive /3 so new codes were implemented.

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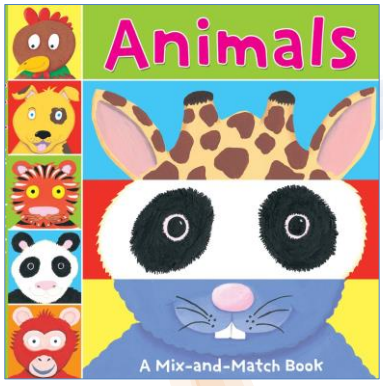
Diagnostic Workup – Tumor Classification

Mixed Tumors of the Lung

- Adenosquamous Carcinoma - 8560
- Sarcomatoid Carcinoma (Giant Cell and Spindle Cell) - 8033
- Epithelial-Myoepithelial Carcinoma - 8562
- Combined Large Cell Neuroendocrine Carcinoma - 8013
- Mixed Invasive Mucinous and Non-Mucinous Carcinoma - 8254
- Combined Small Cell Carcinoma - 8045
- Squamous Cell Carcinoma, Large Cell, Nonkeratinizing - 8072
- Squamous Cell Carcinoma, Small Cell, Nonkeratinizing - 8073
- Squamous Cell Carcinoma, Sarcomatoid - 8074
- Squamous Cell Carcinoma, Spindle Cell - 8075
- Adenocarcinoma with Mixed Subtypes - 8255



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Biological Tumor Markers, Single and Multi-Gene Testing

Updates to the NCCN Guidelines for Non–Small Cell Lung Cancer (NSCLC) for 2021 include recommendations for biomarker testing in all appropriate patients with newly diagnosed advanced lung cancer, including squamous cell lung cancer. When a targetable genetic alteration is detected, the NCCN Guidelines recommend treatment with a first-line therapy targeted to that alteration. The guidelines contain new information on use of adjuvant treatment with osimertinib for resected early-stage *EGFR*-mutated NSCLC. New targeted agents are now recommended for the treatment of *ALK* rearrangements, *RET* alterations, *MET* exon 14 skipping mutations in patients with advanced NSCLC; and new immunotherapy agents are recommended for advanced NSCLC without a driver oncogene.

J Natl Compr Canc Netw 2021;19(5.5):610–613
doi: 10.6004/jnccn.2021.5020

The guidelines recommend considering testing in stage IV squamous cell lung cancer as quickly as possible upon diagnosis, because it is not possible to exclude an adenocarcinoma component in a biopsy, and studies show that approximately 5% to 10% of tumors with squamous cell histology harbor targetable mutations when considered across all targetable alterations

Another change in the guidelines is a strong push toward testing in resectable stage IB–IIIA NSCLC. The ADAURA trial found that the third-generation EGFR tyrosine kinase inhibitor (TKI) osimertinib improved 3-year disease-free survival in stage IB–III, EGFR-positive NSCLC.4 “This study galvanized the push for earlier testing in NSCLC,” Dr. Aisner stated.

The 2021 NCCN Guidelines now list osimertinib as an option for adjuvant therapy in patients with resectable stage IIB–IIIA or high-risk stage IB–IIA NSCLC harboring EGFR mutations who received previous adjuvant chemotherapy or are ineligible to receive platinum-based chemotherapy.

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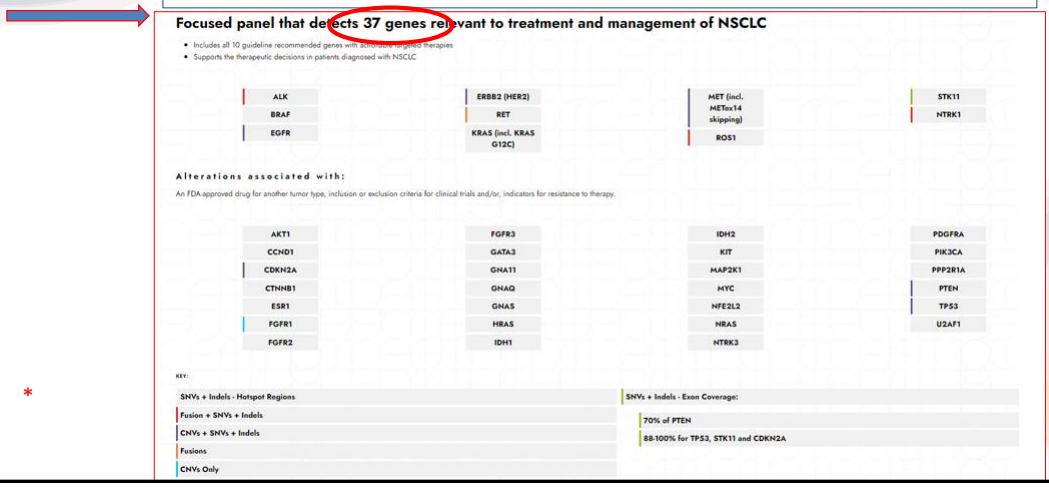
Multi-Gene Testing/Liquid Biopsy

NEO GENOMICS - InVisionFirst®-Lung is an NGS-based liquid biopsy test that detects actionable genes relevant to the treatment and management of advanced non-small cell lung cancer (NSCLC)
Liquid biopsy and tissue-based analysis are complementary approaches for molecular testing for biomarker assessment. A recent consensus statement from the International Association for the Study of Lung Cancer (IASLC, June 2021) discusses the innate limitations to tissue-based testing related to inadequate or insufficient tissue, challenging biopsy locations and turnaround time for rapid treatment decisions and state liquid biopsy is an acceptable initial approach for biomarker evaluation at time of diagnosis, as well as for monitoring the efficacy of targeted therapies[1].



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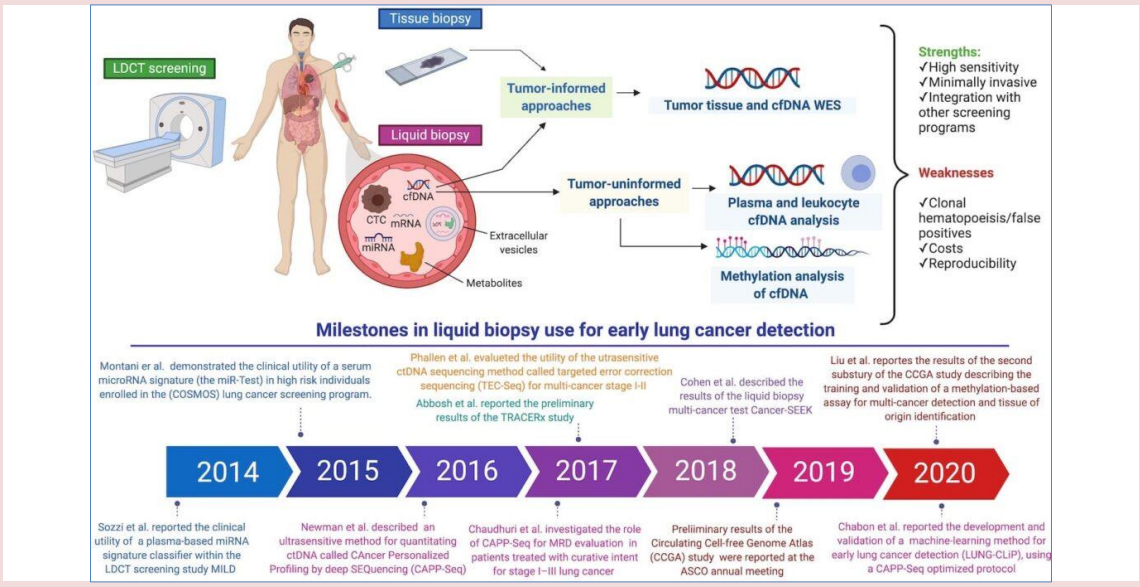

https://cancerworld.net/liquid-biopsy-for-early-cancer-moves-closer/

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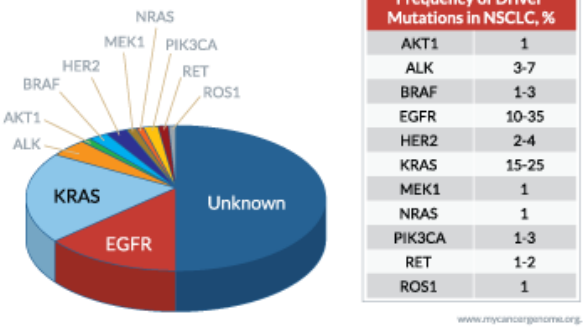
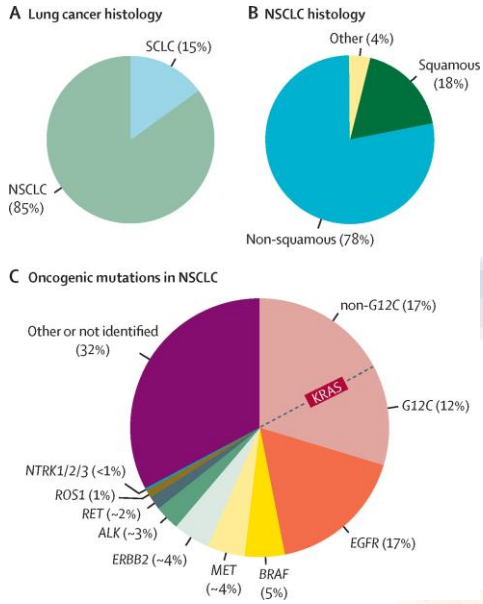
Biological Tumor Markers, Single and Multi-Gene Testing



Frequency of Driver Mutations in NSCLC, %	
AKT1	1
ALK	3-7
BRAF	1-3
EGFR	10-35
HER2	2-4
KRAS	15-25
MEK1	1
NRAS	1
PIK3CA	1-3
RET	1-2
ROS1	1



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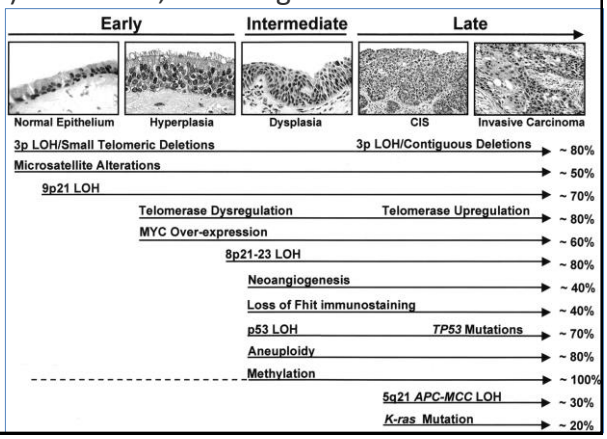
Biological Tumor Markers, Single and Multi-Gene Testing

- Characteristics that can be targeted with currently available treatments:
  - Anaplastic Lymphoma Kinase (ALK) gene rearrangement
  - Epidermal Growth Factor Receptor (EGFR) mutations, including EGFR exon 20
  - BRAF V600E mutation
  - KRAS mutation
  - MET mutation
  - NTRK gene rearrangement
  - RET mutation
  - ROS1 gene rearrangement
  - T790M mutation
- Immunotherapies (test for PD-L1)



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Biological Tumor Markers, Single and Multi-Gene Testing

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.

Table 1. Treatment Options for Patients Without Driver Oncogenes

PD-L1 Expression	Treatment Options[a]
High (≥50%, TC_3/IC_3)	Pembrolizumab Atezolizumab
Low (TPS >1%)	Pembrolizumab (category 2B)
Any (squamous)	Carboplatin, paclitaxel, pembrolizumab Ipilimumab/Nivolumab Carboplatin, paclitaxel, ipilimumab/nivolumab
Any (nonsquamous)	Carboplatin, pemetrexed, pembrolizumab Carboplatin, paclitaxel, bevacizumab, atezolizumab Carboplatin, nab-paclitaxel, atezolizumab Ipilimumab/Nivolumab Carboplatin, pemetrexed, ipilimumab/nivolumab

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Biological Tumor Markers, Single and Multi-Gene Testing

KRAS
+Mutational Analysis
___ No KRAS mutation detected
___ Mutation(s) identified
___ KRAS:p.G12C
___ KRAS:p.G12D
___ KRAS:p.G12V
___ KRAS:p.G12S
___ KRAS:p.G12A
___ KRAS:p.G12R
___ KRAS:p.G13D
___ KRAS:p.G13C
___ KRAS:p.Q61L
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Interpretation (select all that apply)
___ A KRAS mutation is identified which is associated with resistance to tyrosine kinase inhibitor therapy
___ A KRAS mutation is identified which is associated with response to specific inhibitors

EGFR
+Mutational Analysis
___ No EGFR mutation detected
___ Mutation(s) identified
___ EGFR:p.G719X
___ EGFR Exon 19 deletion (specify if known): _____
___ EGFR Exon 20 insertion (specify if known): _____
___ EGFR:p.S768I
___ EGFR:p.T790M
___ EGFR:p.L858R
___ EGFR:p.L861Q
___ Other (specify): _____
___ Cannot be determined (explain): _____

+EGFR L858R by Immunohistochemistry (clone 43B2)
___ Negative
___ Positive
___ Equivocal (explain): _____

+EGFR Exon 19 Deletion (E746_A750del) (clone 6B6)
___ Negative
___ Positive

MET
+Mutational Analysis
___ No MET mutation detected
___ Mutation(s) identified
___ MET:p.D963_splice mutation
___ MET:p.D1010N
___ MET:p.D1010_splice mutation
___ MET exon 14 deletion
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Copy Number Analysis
___ No MET amplification detected
___ MET amplification identified
___ Specify Copy Number: _____
___ Specify Ratio to Centromere 7: _____
___ Cannot be determined (explain): _____

+Interpretation (select all that apply)
___ A MET alteration is present which is associated with response to MET tyrosine kinase inhibitors
___ MET amplification is present which is associated with response to MET tyrosine kinase inhibitors

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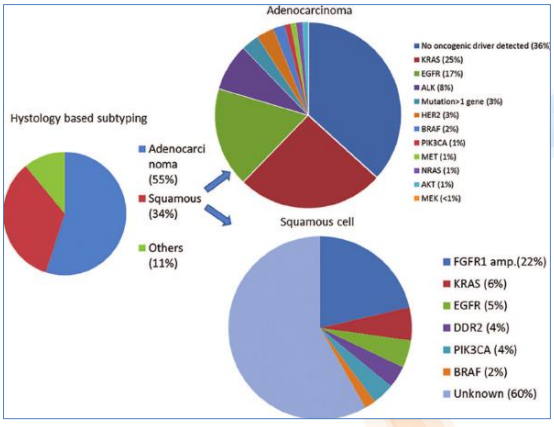
Biological Tumor Markers, Single and Multi-Gene Testing

- 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 (in trials for early stage disease, also)

  - ALK – Opdivo/Nivolumab
  - ALK – Xalkori/Crizotinib
  - ALK – Zykadia/Ceritinib
  - ALK – Alecensa/Alectinib
  - ALK – Alunbrig/Brigatinib
  - ALK - Lorlatinib



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Biological Tumor Markers, Single and Multi-Gene Testing

- 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/Nivolumab/ipilimumab
- 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

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Biological Tumor Markers, Single and Multi-Gene Testing

- 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
  - MET – Tepotinib
  - MET – Capmatinib
  - RET – Selpercatinib
  - RET - Pralsetinib
  - 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

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Biological Tumor Markers, Single and Multi-Gene Testing
NCCN Guidelines - Lung

TESTING RESULTS[ll,mm]

EGFR mutation positive (eg, *exon 19* deletion or *L858R*)	NSCL-20
EGFR exon 20 insertion mutation positive	NSCL-23
KRAS G12C mutation positive	NSCL-24
ALK rearrangement positive	NSCL-25
ROS1 rearrangement positive	NSCL-28
BRAF V600E mutation positive	NSCL-29
NTRK1/2/3 gene fusion positive	NSCL-30
METex14 skipping mutation positive	NSCL-31
RET rearrangement positive	NSCL-32
PD-L1 ≥50% and negative for actionable molecular markers above	NSCL-33
PD-L1 ≥1%–49% and negative for actionable molecular markers above	NSCL-34
PD-L1 <1% and negative for actionable molecular markers above	NSCL-35

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Biological Tumor Markers, Single and Multi-Gene Testing
NCCN Guidelines - Lung

***EGFR* Mutation Positive**
(eg, *exon 19* deletion or *L858R*)
- First-line therapy
  - Afatinib[1]
  - Erlotinib[2]
  - Dacomitinib[3]
  - Gefitinib[4,5]
  - Osimertinib[6]
  - Erlotinib + ramucirumab[7]
  - Erlotinib + bevacizumab* (nonsquamous)[8]
- Subsequent therapy
  - Osimertinib[9]

***EGFR exon 20* insertion mutation positive**
- Subsequent therapy
  - Amivantamab-vmjw[10]
  - Mobocertinib[11]

***KRAS G12C* mutation positive**
- Subsequent therapy
  - Sotorasib[12]

***ALK* Rearrangement Positive**
- First-line therapy
  - Alectinib[13,14]
  - Brigatinib[15]
  - Ceritinib[16]
  - Crizotinib[13,17]
  - Lorlatinib[18]
- Subsequent therapy
  - Alectinib[19,20]
  - Brigatinib[22]
  - Ceritinib[23]
  - Lorlatinib[24]

***ROS1* Rearrangement Positive**
- First-line therapy
  - Ceritinib[24]
  - Crizotinib[25]
  - Entrectinib[26]
- Subsequent therapy
  - Lorlatinib[27]
  - Entrectinib[26]

***BRAF* V600E Mutation Positive**
- First-line therapy
  - Dabrafenib/trametinib[28]
- Subsequent therapy
  - Dabrafenib/trametinib[29,30]

***NTRK1/2/3* Gene Fusion Positive**
- First-line/Subsequent therapy
  - Larotrectinib[31]
  - Entrectinib[32]

***MET* Exon 14 Skipping Mutation**
- First-line therapy/Subsequent therapy
  - Capmatinib[33]
  - Crizotinib[34]
  - Tepotinib[35]

***RET* Rearrangement Positive**
- First-line therapy/Subsequent therapy
  - Selpercatinib[36]
  - Pralsetinib[37]
  - Cabozantinib[38,39]
  - Vandetanib[40]

PD-L1 ≥1%
- First-line therapy**
  - Pembrolizumab[41-43]
  - (Carboplatin or cisplatin)/pemetrexed/pembrolizumab (nonsquamous)[44]
  - Carboplatin/paclitaxel/bevacizumab*/atezolizumab (nonsquamous)[45]
  - Carboplatin/(paclitaxel or albumin-bound paclitaxel)/pembrolizumab (squamous)[46]
  - Carboplatin/albumin-bound paclitaxel/atezolizumab (nonsquamous)[47]
  - Nivolumab/ipilimumab[48]
  - Nivolumab/ipilimumab/pemetrexed/(carboplatin or cisplatin) (nonsquamous)[49]
  - Nivolumab/ipilimumab/paclitaxel/carboplatin (squamous)[49]

PD-L1 ≥50% (in addition to above)
- First-line therapy**
  - Atezolizumab[50]
  - Cemiplimab-rwlc[51]

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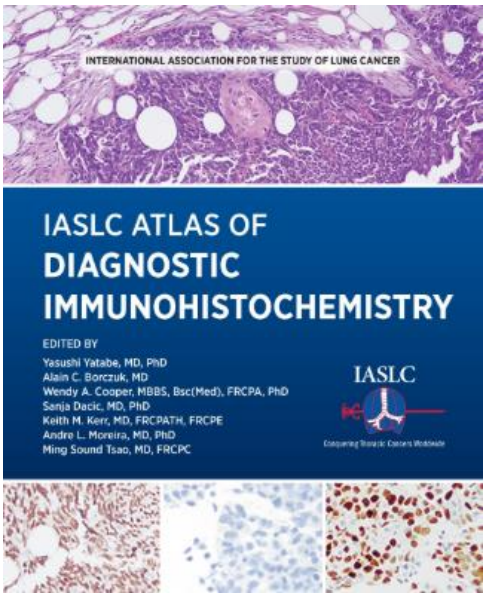
IASLC Atlas of Diagnostic Immunohistochemistry

- Immunohistochemistry (IHC) is a cornerstone of pathologic diagnosis, by far the most widely used ancillary technique to assist with the identification and classification of disease.
- For the last 30 years, pathologists have harnessed this powerful technology to transform the way we make diagnoses across the spectrum of pathologic medicine but especially in tumor pathology. Histochemical techniques and electron microscopy still have their place, but IHC is the go-to technique to answer a problem.
- It is very clear that in order to render the best and most accurate diagnosis for our patients with thoracic malignancy, pathologists must understand how IHC works, how to use it, when to use it, and how to appropriately interpret the results of the assays performed. In this atlas, members of the Pathology Committee of the International Association for the Study of Lung Cancer have provided a succinct but comprehensive review of many aspects of IHC that are relevant to thoracic tumor diagnosis, building on a review article published in the Journal of Thoracic Oncology (Yatabe et al 2019). We very much hope that readers will find this atlas a useful tool to aid their work.



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IASLC Atlas of Diagnostic Immunohistochemistry

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2022 Updates Lung All Manuals

- NAACCR 2022 Implementation Guidelines
- V22 NAACCR Data Standards and Data Dictionary
- NAACCR XML Dictionaries
- NAACCR V22 Edits Metafile (including Changes Spreadsheet)
- SEER Program Coding and Staging Manual (includes Summary of Changes)
- Commission on Cancer STORE Manual
- Site Specific Data Items (SSDI) and Grade Manual v2.1 (includes change log)
- AJCC Cancer Staging System
- SEER RSA (EOD, Summary Stage, SSDI's, Grade) v2.1 (includes summary of changes)
- Summary Stage 2018 (includes revision history)
- Extent of Disease (EOD) 2018 (includes change log)
- Solid Tumor Rules (includes summary and changes)
- ICD O 3.2 (includes new codes, coding guidelines, and changes)
- SEER Site/Histology Validation List
- Hematopoietic Manual and Database (see revision history on the left)

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2022 Lung Solid Tumor Rules

Lung Multiple Primary Rules
C340-C343, C348, C349
(Excludes lymphoma and leukemia M9590 – M9992 and Kaposi sarcoma M9140)

Single Tumor

Rule M2 Abstract a **single primary**[i] when there is a **single tumor.**
Note 1: A single tumor is always a single primary.
Note 2: The tumor may overlap onto or extend into adjacent/contiguous site or subsites.
Note 3: The tumor may have in situ and invasive components.
Note 4: The tumor may have two or more histologic components.

This is the end of instructions for Single Tumor

[i] **Prepare one abstract. Use the histology coding rules to assign the appropriate histology code.**

Multiple Tumors

Note: Multiple tumors may be a single primary or multiple primaries.

Rule M3 Abstract **multiple primaries**[ii] when there are **separate, non-contiguous** tumors in sites with ICD-O **site** codes that differ at the second C**X**xx and/or third character Cx**X**x.
Note: When **codes differ** at the second or third characters, the tumors are in **different** primary **sites.**

Rule M4 Abstract **multiple primaries**[ii] when the patient has a subsequent tumor after being **clinically disease-free** for greater than **three years** after the original diagnosis or last recurrence.
Note 1: **Clinically** disease-free means that there was **no evidence** of recurrence in the same lung on follow-up.
- Scans are NED

Note 2: When there is a recurrence less than or equal to three years of diagnosis, the "**clock**" starts over. The time interval is calculated from the **date of last recurrence.** In other words, the patient must have been disease-free for greater than three years from the date of the last recurrence.
Note 3: When it is **unknown/not documented** whether the patient had a recurrence, use **date of diagnosis** to compute the time interval.
Note 4: The physician may state this is a **recurrence**, meaning the patient had a previous lung tumor and now has another lung site tumor. **Follow the rules**; do not attempt to interpret the physician's statement.

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2022 Lung Solid Tumor Rules

Rule M5 Abstract **multiple primaries**[ii] when there is **at least one** tumor that is **small cell** carcinoma **8041** or any small cell subtypes/variants and another tumor that is **non-small cell** carcinoma **8046** or any non-small cell carcinoma subtypes/variants.

Note 1: Small cell carcinoma and non-small cell carcinoma are the two major classifications/divisions for lung cancer.
- See Table 3 in Equivalent Terms and Definitions for terms and codes for small cell carcinoma and all of the subtypes/variants
- With the exception of small cell/neuroendocrine carcinoma and sarcomas, **all other histologies** listed in **Table 3** in Equivalent Terms and Definitions are **non-small cell** carcinoma

Note 2: It is **irrelevant** whether the tumors are in the **ipsilateral** (same) lung or are **bilateral** (both lungs).

Rule M6 Abstract **multiple primaries**[ii] when separate/non-contiguous tumors are two or more **different subtypes/variants** in Column 3, Table 3 in the Equivalent Terms and Definitions. Timing is irrelevant.

Note 1: The tumors may be subtypes/variants of the **same** or **different** NOS histologies.
- **Same NOS:** Colloid adenocarcinoma 8480/3 and lepidic adenocarcinoma 8250/3 are both subtypes of adenocarcinoma NOS 8140/3 but are distinctly different histologies. Abstract multiple primaries.
- **Different NOS:** Keratinizing squamous cell carcinoma 8071/3 is a subtype of squamous cell carcinoma NOS 8070; Lepidic adenocarcinoma 8250/3 is a subtype of adenocarcinoma 8140/3. They are distinctly different histologies. Abstract multiple primaries.

Note 2: The tumors may be different **behaviors:** Acinar adenocarcinoma 8551/3 and mucinous carcinoma, in situ 8253/2 are both subtypes of adenocarcinoma NOS 8140/3 but are distinctly different histologies. Abstract multiple primaries.

Rule M7 Abstract a **single primary**[i] when synchronous, separate/non-contiguous tumors **in the same lung** are on **the same row** in Table 3 in the Equivalent Terms and Definitions.

Note 1: Tumors must be **in the same lung.**

Note 2: The same row means the tumors are:
- The same histology (same four-digit ICD-O code) **OR**
- One is the preferred term (column 1) and the other is a synonym for the preferred term (column 2) **OR**
- A NOS (column 1/column 2) and the other is a subtype/variant of that NOS (column 3)

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2022 Lung Solid Tumor Rules

Rule M8 Abstract **multiple primaries**[ii] when separate/non-contiguous tumors are:
- On different rows in Table 3 in the Equivalent Terms and Definitions
- A combination code in Table 2 and a code from Table 3

Note 3: Timing is irrelevant. Tumors may be synchronous or non-synchronous.

Note 4: Each row in the table is a distinctly different histology.

Example 1: In 2018, the patient has non-mucinous adenocarcinoma **8250/3**. Patient returns in 2019 with large cell carcinoma **8012/3**. These histologies are on different rows in Table 3. Abstract two primaries.

Example 2: In 2017, patient had epithelial-myoepithelial carcinoma **8562** (combination code from Table 2). In 2020, the patient returned with a myoepithelial carcinoma **8982** in the same lung (histology from Table 3). Abstract two primaries.

Rule M9 Abstract a **single primary**[i] when there are **simultaneous multiple** tumors:
- In **both** lungs (multiple in right and multiple in left) **OR**
- In the **same** lung **OR**
- **Single** tumor in one lung; **multiple** tumors in **contralateral** lung

Note 1: Tumors may be combinations of:
- In situ and invasive **OR**
- NOS and subtype/variant (See Table 3 in the Equivalent Terms and Definitions)
- Cancer NOS **8000** or carcinoma NOS **8010** and any other histology

Note 2: Examples of NOS and subtypes/variants include:
- Adenocarcinoma **8140** and a subtype/variant of adenocarcinoma
- Squamous cell carcinoma **8070** and a subtype/variant of squamous cell carcinoma
- NSCLC **8046** and a subtype/variant of NSCLC
- Carcinoma NOS **8010** and adenocarcinoma

Note 3: Code multiple primaries only when there is **proof** that one of the tumors is a different histology. Proof is any one of the following:
- Pathology from a biopsy or resection proves tumors are different histologies
- Attending, oncologist, or pulmonologist state unequivocally that the tumors are different primaries
  - **Unequivocal** means that **no words** such as "**probable**" are used in the statement. Terms which are on the "ambiguous terms" list such as "probable" cannot be used to prove different primaries.

Note 4: When there are multiple tumors in one or both lungs, the physician usually biopsies only one mass/tumor. They treat the patient based on that single biopsy, assuming all of the masses/tumors are the same histology.

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2022 Lung Solid Tumor Rules

Note 5: Multiple tumors in the same lung, or both lungs, or single tumor in one lung and multiple tumors in the contralateral lung must be diagnosed **simultaneously (same time) to apply this rule. Refer to the rules when multiple tumors are not diagnosed simultaneously.**

Rule M10 Abstract a **single primary**[i] when an **in situ** tumor is diagnosed **after** an **invasive** tumor **AND** tumors occur in the same lung.
Note 1: The rules are **hierarchical**. Only use this rule when none of the previous rules apply.
Note 2: The tumors may be a **NOS** and a **subtype/variant** of that NOS. See Table 3 in the Equivalent Terms and Definitions for listings of NOS and subtype/variants.
Note 3: The **in situ** is recorded as a **recurrence** for those registrars who collect recurrence data.

Rule M11 Abstract **multiple primaries**[ii] when there is a **single** tumor in **each lung** (one tumor in the right lung and one tumor in the left lung).
Note 1: The only **exception** is when there is **proof** that one tumor is **metastatic**. Proof is any one of the following:
- Tissue from both tumors is compared and the pathologic diagnoses definitively says one tumor is metastatic
- Attending physician, oncologist, or pulmonologist state unequivocally that the tumor in the contralateral lung is metastatic
  - Unequivocal means that no words such as "probably possibly, most likely, etc." are used in the statement. Terms which are on the "ambiguous terms" list make the statement equivocal (cannot be used to prove metastases)

Note 2: Lung **metastases usually** present as multiple tumors/masses. A single tumor in each lung is unlikely to be a single primary (e.g. metastatic to the contralateral lung).
Note 3: The term "**bilateral**" **is not** a synonym for a **single primary**. It is simply a statement that there are tumors in both lungs.
Note 4: This rule is based on **long-term epidemiologic studies** of multiple primaries. The specialty medical experts (SME) and the CoC site physician teams reviewed and approved these rules. Many of the CoC site team physicians were also authors, co-authors, or editors of the AJCC Staging Manual.
Note 5: Lymph node involvement is recorded in staging criteria.
Note 6: Tumors do **not** need to be diagnosed at the same time (simultaneous or synchronous).

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2022 Lung Solid Tumor Rules

Rule M12 Abstract a **single primary**[i] (the invasive) when an **invasive** tumor is diagnosed **less than or equal to 60** days **after** an **in situ** tumor in the same lung.
Note 1: The rules are **hierarchical.** Only use this rule when none of the previous rules apply.
Note 2: The tumors may be a **NOS** and a **subtype/variant** of that NOS.
Note 3: When the case has been abstracted, **change behavior** code on original abstract from /2 to /3.
Note 4: Do **not** change **date of diagnosis**.
Note 5: If the case has already been submitted to the central registry, **report** all changes.
Note 6: The physician may **stage both** tumors because staging and determining multiple primaries are done for different reasons. Staging determines which treatment would be most effective. Determining multiple primaries is done to stabilize the data for the study of epidemiology (long-term studies done on incidence, mortality, and causation of a disease with the goal of reducing or eliminating that disease).
Note 7: See the **CoC** and **SEER** manuals for **instructions** on coding **other data items** such as Date of Diagnosis, Accession Year and Sequence Number.

Rule M13 Abstract **multiple primaries**[ii] when an **invasive** tumor occurs **more than 60** days after an **in situ** tumor in the same lung.
Note 1: The rules are **hierarchical**. Only use this rule when none of the previous rules apply.
Note 2: Abstract **both** the invasive and in situ tumors.
Note 3: Abstract as multiple primaries even if **physician states** the invasive tumor is disease **recurrence** or **progression.**
Note 4: This rule is based on long-term epidemiologic studies of recurrence intervals. The specialty medical experts (SMEs) reviewed and approved these rules. Many of the SMEs were also authors, co-authors, or editors of the AJCC Staging Manual.

Rule M14 Abstract a **single primary**[i] when none of the previous rules apply.
Note: Use this rule as a last resort. Please confirm that you have not overlooked an applicable rule.

This is the end of instructions for Multiple Tumors

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2021 Lung cancer ICD-O-3.2 Updates 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.

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2021 Lung cancer ICD-O-3.2 Updates Adenocarcinoma and BAC Revisions

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.

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2021 Lung cancer ICD-O-3.2 Updates
Squamous Cell Carcinoma/Large Cell Carcinoma

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

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2021 Lung cancer ICD-O-3.2 Updates
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 Neuroendocrine Carcinoma – Ki67 confirms high grade SCLC*
  - *Large Cell Neuroendocrine Carcinoma Not Elsewhere Classified*
- Mitotic Count/Ki67 used to differentiate low/high grade

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2021 Lung cancer ICD-O-3.2 Updates
Reclassified Histologic Types in Lung Cancer

- 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

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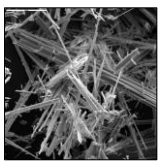
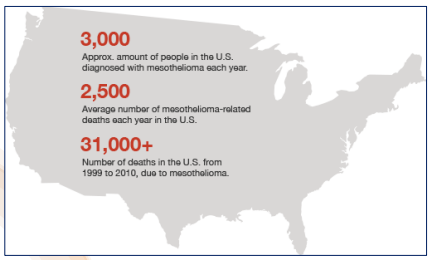
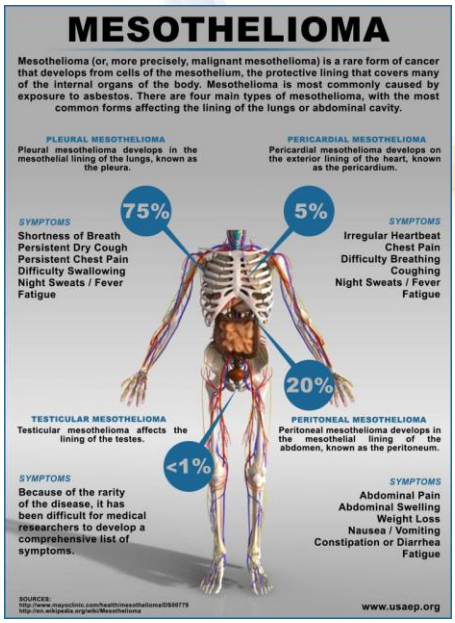
Mesothelioma
(just a mention)







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

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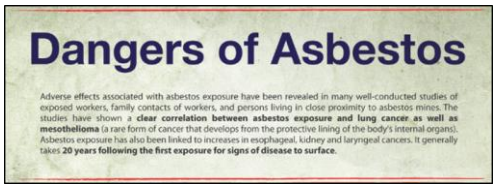
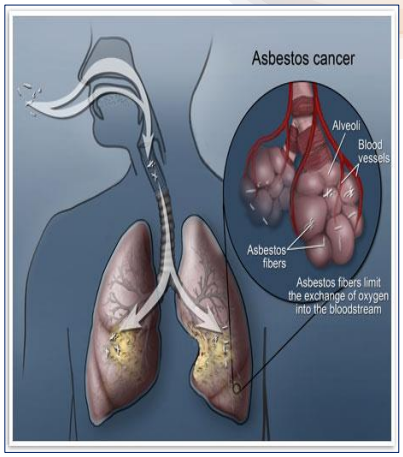


Asbestos

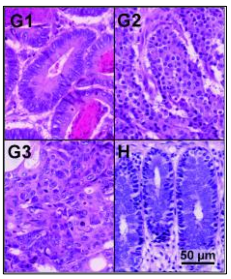


http://www.mesothelioma.com/asbestos-cancer

2021 Lung – All Histologies Grade Coding Rules

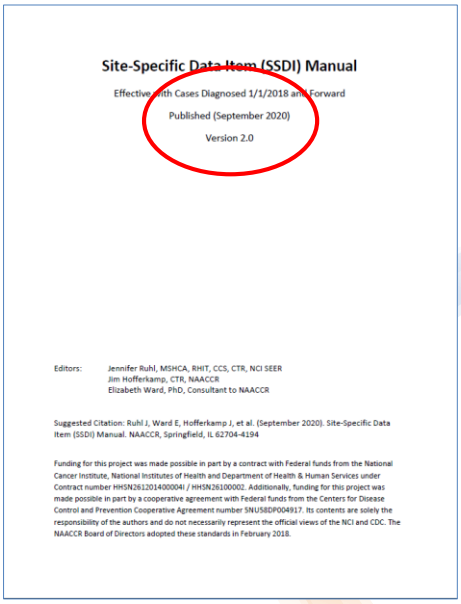
Code	Grade Description
1	G1: Well differentiated
2	G2: Moderately differentiated
3	G3: Poorly differentiated
4	G4: Undifferentiated
9	Grade cannot be assessed (GX); Unknown

Code	Grade Description
1	G1: Mitotic count (per 10 HPF) less than 2 AND Ki-67 index (%) less than 3
2	G2: Mitotic count (per 10 HPF) equal 2-20 OR Ki-67 index (%) equal 3-20
3	G3: Mitotic count (per 10 HPF) greater than 20 OR Ki-67 index (%) greater than 20
A	Well differentiated
B	Moderately differentiated
C	Poorly differentiated
D	Undifferentiated, anaplastic
9	Grade cannot be assessed (GX); Unknown



2021 Lung & Pleura Site-Specific Data Items

- None Used to Assign Lung Stage Group
  - Separate Tumor Nodules
  - Visceral and Parietal Pleural Invasion
  - ALK Rearrangement
  - EGFR Mutational Analysis
  - Pleural Effusion
- None Used to Assign Mesothelioma Group
  - Pleural Effusion
- NONE REQUIRED BY FCDS AT THIS TIME



Site-Specific Data Item (SSDI) Manual

Effective with Cases Diagnosed 1/1/2018 and Forward

Published (September 2020)

Version 2.0

Editors: Jennifer Ruhl, MSHCA, RHIT, CCS, CTR, NCI SEER
Jim Hofferkamp, CTR, NAACCR
Elizabeth Ward, PhD, Consultant to NAACCR

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2021 Staging for Lung Cancer – Summary Stage

STAGE AT DIAGNOSIS – NOT STAGE AFTER TREATMENT – NEOADJUVANT OR ANY OTHER

- 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**

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REMINDER: Anatomy of the Lung - Terminology

- 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*

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2021 Staging for Lung Cancer – Summary Stage

There are Real World Reasons Why Staging is Confusing for Lung Cancers

Comparison of the Descriptors in the Eighth Edition of the TNM Classification of Lung Cancer Compared with the Seventh Edition*

Descriptor	7th Edition T/N/M	8th Edition T/N/M
T component		
0 cm (pure lepidic adenocarcinoma ≤3 cm in 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		
Metastasis within the thoracic cavity	M1a	M1a
Single extrathoracic metastasis	M1b	M1b
Multiple extrathoracic metastasis	M1b	M1c

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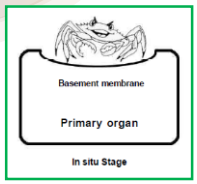
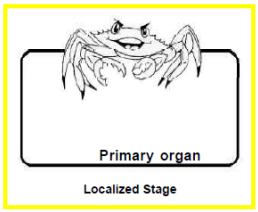
2021 Staging for Lung Cancer – Summary Stage

STAGE AT DIAGNOSIS – NOT STAGE AFTER TREATMENT – NEOADJUVANT OR ANY OTHER





0 In situ, intraepithelial, noninvasive

- Adenocarcinoma in situ (AIS): adenocarcinoma with pure lepidic pattern, less than or equal to 3 cm in greatest dimension
- Squamous cell carcinoma in situ (SCIS)

1 Localized only (localized, NOS)

- Adjacent ipsilateral lobe
- Confined to carina, NOS
- Confined to hilus
- Confined to lung, NOS
- Main stem bronchus, NOS (without involvement of the carina)
  - ~~Including extension from other part of lung~~

See T2

- Minimally invasive adenocarcinoma
  - Adenocarcinoma tumor WITH predominantly lepidic pattern (AIS) measuring less than or equal to 3 cm in greatest dimension
    - WITH invasive component measuring less than or equal to 5 mm in greatest dimension
- Superficial tumor, WITH invasive component limited to bronchial wall
  - WITH or WITHOUT proximal extension to main stem bronchus

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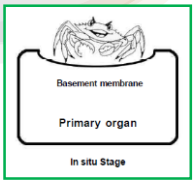
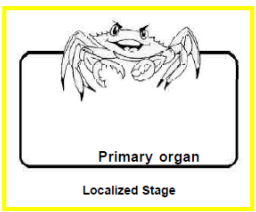
2021 Staging for Lung Cancer – Summary Stage

STAGE AT DIAGNOSIS – NOT STAGE AFTER TREATMENT – NEOADJUVANT OR ANY OTHER





Tis		Carcinoma *in situ* Squamous cell carcinoma *in situ* (SCIS) Adenocarcinoma *in situ* (AIS): adenocarcinoma with pure lepidic pattern, ≤3 cm in greatest dimension
T1		Tumor ≤3 cm in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus)
	T1mi	Minimally invasive adenocarcinoma: adenocarcinoma (≤3 cm in greatest dimension) with a predominantly lepidic pattern and ≤5 mm invasion in greatest dimension
	T1a	Tumor ≤1 cm in greatest dimension. A superficial, spreading tumor of any size whose invasive component is limited to the bronchial wall and may extend proximal to the main bronchus also is classified as T1a, but these tumors are uncommon.
	T1b	Tumor >1 cm but ≤2 cm in greatest dimension
	T1c	Tumor >2 cm but ≤3 cm in greatest dimension
T2		Tumor >3 cm but ≤5 cm ~~or having any of the following features: (1) Involves the main bronchus, regardless of distance to the carina, but without involvement of the carina; (2) Invades visceral pleura (PL1 or PL2); (3) Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, involving part or all of the lung~~
	T2a	Tumor >3 cm but ≤4 cm in greatest dimension
	T2b	Tumor >4 cm but ≤5 cm in greatest dimension

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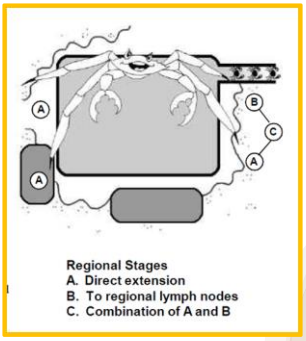
2021 Staging for Lung Cancer – Summary Stage

STAGE AT DIAGNOSIS – NOT STAGE AFTER TREATMENT – NEOADJUVANT OR ANY OTHER

2 Regional by direct extension only

- Atelectasis/obstructive pneumonitis
  - Extends to hilar region, involving part or all of lung
- Blood vessel(s) (major)
  - Aorta
  - Azygos vein
  - Pulmonary artery or vein
  - Superior vena cava (SVC syndrome)
- Brachial plexus
- Carina from lung
- Chest wall (thoracic wall)
- Compression of esophagus or trachea not specified as direct extension
- Diaphragm (separate lesion-see code 7)
- Esophagus
- Mediastinum, extrapulmonary or NOS
- Nerve(s)
  - Cervical sympathetic (Horner's syndrome)
  - Recurrent laryngeal (vocal cord paralysis)
  - Vagus
- Pancoast tumor (superior sulcus syndrome), NOS
- Parietal pericardium
- Parietal pleura
- Pericardium, NOS
- Phrenic nerve
- Pleura, NOS
- Pulmonary ligament
- Separate tumor nodule(s) in the same lobe as the primary
- Visceral pleura invasion (PL1, PL2, PL3, or NOS)
- Trachea



Regional Stages
A. Direct extension
B. To regional lymph nodes
C. Combination of A and B

T2		~~Tumor >3 cm but ≤5 cm~~ or having any of the following features: (1) ~~Involves the main bronchus, regardless of distance to the carina, but without involvement of the carina~~; (2) Invades visceral pleura (PL1 or PL2); (3) Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, involving part or all of the lung
	T2a	~~Tumor >3 cm but ≤4 cm in greatest dimension~~
	T2b	~~Tumor >4 cm but ≤5 cm in greatest dimension~~

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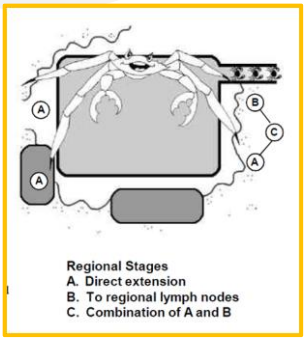
2021 Staging for Lung Cancer – Summary Stage

STAGE AT DIAGNOSIS – NOT STAGE AFTER TREATMENT – NEOADJUVANT OR ANY OTHER



Regional Stages
A. Direct extension
B. To regional lymph nodes
C. Combination of A and B

T2		~~Tumor >3 cm but ≤5 cm or~~ having any of the following features: (1) ~~Involves the main bronchus, regardless of distance to the carina, but without involvement of the carina;~~ (2) Invades visceral pleura (PL1 or PL2); (3) Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, involving part or all of the lung
	T2a	~~Tumor >3 cm but ≤4 cm in greatest dimension~~
	T2b	~~Tumor >4 cm but ≤5 cm in greatest dimension~~
T3		Tumor >5 cm but ≤7 cm in greatest dimension or directly invading any of the following: parietal pleura (PL3), chest wall (including superior sulcus tumors), phrenic nerve, parietal pericardium; or separate tumor nodule(s) in the same lobe as the primary
T4		~~Tumor >7 cm or tumor of any size invading one or more of the following: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina, separate tumor nodule(s) in an ipsilateral lobe different from that of the primary~~

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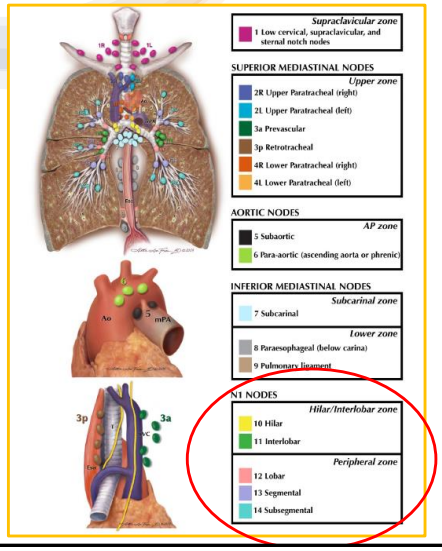
2021 Staging for Lung Cancer – Summary Stage

STAGE AT DIAGNOSIS – NOT STAGE AFTER TREATMENT – NEOADJUVANT OR ANY OTHER



3 Regional lymph node(s) involved only

- IPSILATERAL nodes only
  - Bronchial
  - Carinal (tracheobronchial) (tracheal bifurcation)
  - Hilar (bronchopulmonary) (proximal lobar) (pulmonary root)
  - Intrapulmonary
    - Interlobar
    - Lobar
    - Segmental
    - Subsegmental
  - Mediastinal, NOS
    - Anterior
    - Aortic (above diaphragm), NOS
      - Peri/para-aortic, NOS
        - Ascending aorta (phrenic)
      - Subaortic (aortic-pulmonary window)
    - Inferior mediastinal
      - Paraesophageal
      - Pulmonary ligament
      - Subcarinal
    - Posterior (tracheoesophageal)
    - Superior mediastinal
      - Paratracheal (left, right, upper, low, NOS)
      - Prevascular
      - Retrotracheal
  - Peri/parabronchial
  - Periesophageal
  - Pericardial
  - Peritracheal, NOS
    - Azygos (lower peritracheal)
  - Precarinal
  - Pretracheal, NOS
  - Regional lymph node(s), NOS
    - Lymph node(s), NOS

DISTANT NODES

N3 Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

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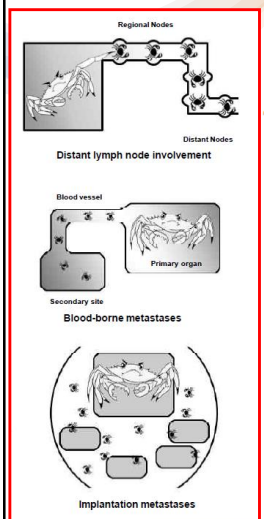
2021 Staging for Lung Cancer – Summary Stage

STAGE AT DIAGNOSIS – NOT STAGE AFTER TREATMENT – NEOADJUVANT OR ANY OTHER



N3 Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

7 Distant site(s)/lymph node(s) involved

- Distant site(s) (including further contiguous extension)
  - Abdominal organs
  - Adjacent rib
  - Contralateral lung/main stem bronchus
  - Contralateral main stem bronchus
  - Heart
  - Inferior vena cava
  - Neural foramina
  - Pericardial nodules or pleural effusion (malignant) (ipsilateral, contralateral, bilateral, NOS)
  - Pleural tumor foci or nodules on ipsilateral lung (separate from direct extension) or contralateral lung
  - Rib
  - Separate tumor nodule(s) in contralateral lung
  - Separate tumor nodule(s) in a different ipsilateral lobe
  - Skeletal muscle
  - Skin of chest
  - Sternum
  - Vertebra(e) (vertebral body)
  - Visceral pericardium

M1a Separate tumor nodule(s) in a contralateral lobe; tumor with pleural or pericardial nodules or malignant pleural or pericardial effusion[a]

M1b Single extrathoracic metastasis in a single organ (including involvement of a single nonregional node)

M1c Multiple extrathoracic metastases in a single organ or in multiple organs

- Distant lymph node(s), NOS
  - IPSILATERAL or CONTRALATERAL
    - Low cervical
    - Proximal root
    - Scalene (inferior deep cervical)
    - Sternal notch
    - Supraclavicular (transverse cervical)
  - CONTRALATERAL/BILATERAL nodes
    - Bronchial
    - Cervical
    - Hilar (bronchopulmonary) (proximal lobar) (pulmonary root)
    - Mediastinal
      - Anterior
      - Aortic (above diaphragm), NOS
        - Peri/para-aortic, NOS
          - Ascending aorta (phrenic)
        - Subaortic (aortic-pulmonary window)
      - Inferior mediastinal
        - Paraesophageal
        - Pulmonary ligament
        - Subcarinal
    - Periesophageal
    - Posterior (tracheoesophageal)
    - Pretracheal
    - Superior mediastinal
      - Paratracheal (left, right, upper, low, NOS)
      - Prevascular
      - Retrotracheal
- Distant metastasis, NOS
  - Carcinomatosis
  - Distant metastasis WITH or WITHOUT distant lymph node(s)

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2021 Staging for Lung Cancer – Summary Stage

STAGE AT DIAGNOSIS – NOT STAGE AFTER TREATMENT – NEOADJUVANT OR ANY OTHER

Veterans Administration Lung Study Group's (VALG) Staging Classification for Small Cell Lung Cancer

(AJCC TNM Uses Same Criteria as NSCLC)

Round Hole – Square Peg

- **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) - cancer is confined to an area that is small enough to be treated with radiation therapy in one "port" or one treatment area. Only about 1 out of 3 people with SCLC have limited stage cancer when it is first found.
- **Extensive-Stage:** AJCC (8th edition) Stage IV and most T3-T4 - cancers that have spread widely throughout the lung, to the other lung, to lymph nodes on the other side of the chest, or to other parts of the body

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

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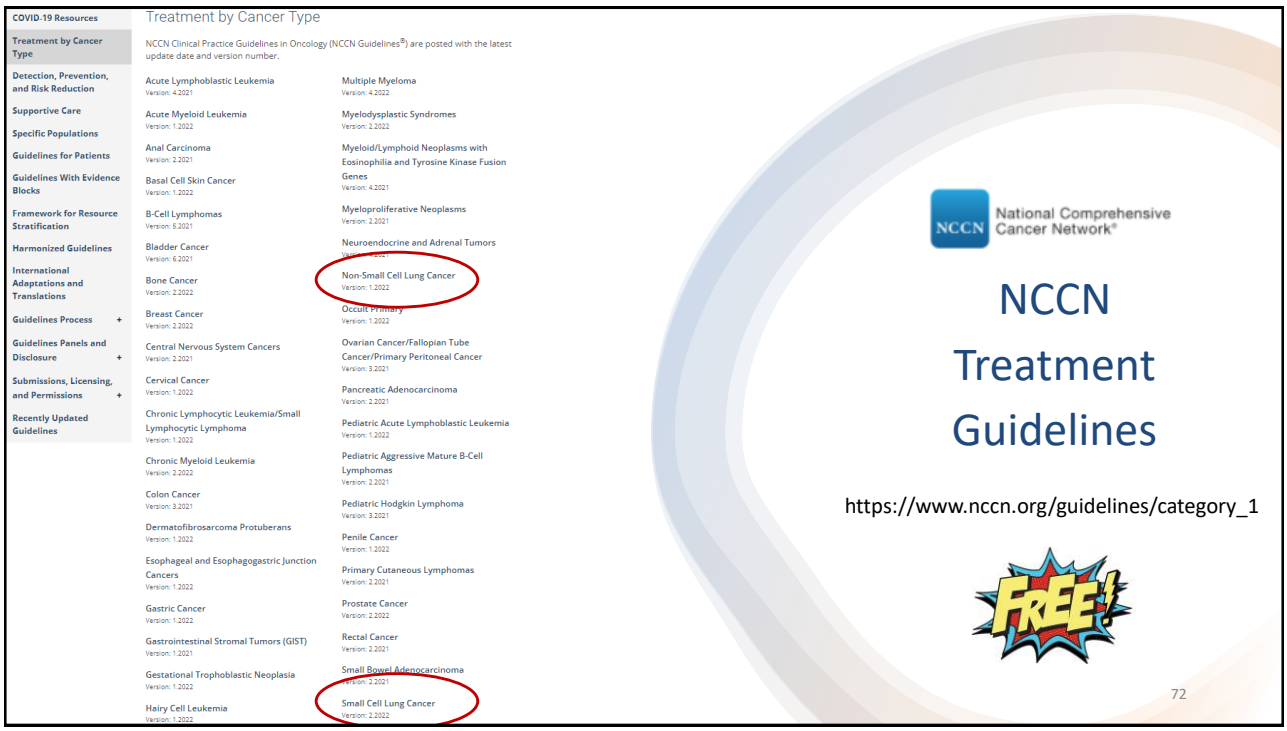

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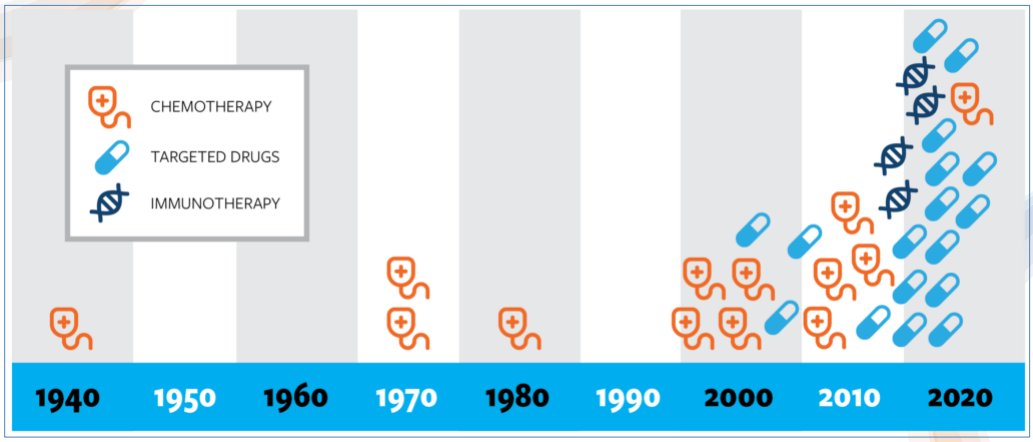
History of Lung Cancer Treatment Advances



Lung Cancer Research Foundation - https://www.lungcancerresearchfoundation.org

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FDA Approvals Timeline for Anti-Neoplastic Agents for Lung

1940s	2006-2015	2015-2020
Mechlorethamine Hydrochloride	Bevacizumab	Nivolumab
	Topotecan Hydrochloride	Pembrolizumab
1970s	Pemetrexed Disodium	Osimertinib
Methotrexate	Crizotinib	Alectinib
Doxorubicin Hydrochloride	Paclitaxel Albumin Formulation	Necitumumab
	Afatinib Dimaleate	Durvalumab
1980s	Ramucirumab	Dabrafenib
Cisplatin	Ceritinib	Brigatinib
		Trametinib
1995-2005		Atezolizumab
Etoposide		Lorlatinib
Gemcitabine Hydrochloride		Dacomitinib
Docetaxel		Afatinib
Carboplatin		Larotrectinib
Gefitinib		Entrectinib
Erlotinib		Selpercatinib
		Capmatinib

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FDA Approvals Timeline for Anti-Neoplastic Agents for Lung

FDA NEWS RELEASE

FDA Approves First Targeted Therapy for Lung Cancer Mutation Previously Considered Resistant to Drug Therapy

For Immediate Release:

May 28, 2021

Today, the U.S. Food and Drug Administration approved Lumakras (sotorasib) as the first treatment for adult patients with non-small cell lung cancer whose tumors have a specific type of genetic mutation called KRAS G12C and who have received at least one prior systemic therapy. This is the first approved targeted therapy for tumors with any KRAS mutation, which accounts for approximately 25% of mutations in non-small cell lung cancers. KRAS G12C mutations represent about 13% of mutations in non-small cell lung cancers.

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IMPORTANT – FCDS MISSING FIRST COURSE TX MANY EARLY LUNG CANCERS WITH NO TREATMENT

- FCDS Researchers and Data Users have recently identified a problem with reporting first course treatment for early lung cancers. Patients diagnosed on imaging only – no referral for surgery.
- No Surgery – No Radiation Therapy – No Molecular Genetic Testing Orders – What is Going On Here?
- These patients with Stage I or Stage II Lung Cancer MUST be getting Treatment Somewhere
- Changes in Abstracting habits and increased use of multi-facility abstracting pools for multi-center network reporting where registrars just copy and paste the whole abstract…and do not add any new info about why the patient came to each and every facility.
- Each Facility Encounter provides some level of care – document care from each center.
- Are registrars or contractors not getting or gaining access to all admissions?
- Are registrars or contractors not reading all admissions/encounters/charts from other facilities in network?
- Are registrars just missing the treatment or recommendations for first course of treatment / referrals?
- Are registrars not coding recommended therapy .. recommended by docs not recommended by you.
- Are registrars missing referrals to other cancer centers?
- FCDS will design a follow back audit to find missing TX for early stage lung cancers at ALL Facilities

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Types of Surgery for Lung Cancer

Radiofrequency ablation (RFA) might be considered for some people with small lung tumors that are near the outer edge of the lungs, especially if they can't tolerate surgery. RFA uses high-energy radio waves to heat the tumor. A thin, needle-like probe is put through the skin and moved in until the tip is in the tumor. Once the tip is in place, an electric current is passed through the probe, which heats the tumor and destroys the cancer cells.

Video-assisted thoracic surgery (VATS), also called thoracoscopy, is used to treat early-stage lung cancers. It uses smaller incisions, typically has a shorter hospital stay and fewer complications than a thoracotomy. Most experts recommend that only early-stage tumors of the lung be treated this way. The cure rate after this surgery seems to be the same as with surgery done with a larger incision.

Robotically-assisted thoracic surgery (RATS) In this approach, the thoracoscopy is done using a robotic system. The surgeon sits at a control panel in the operating room and moves robotic arms to operate through several small incisions in the patient's chest. RATS is similar to VATS in terms of less pain, blood loss, and recovery time.

Segmentectomy or wedge resection: In these surgeries, only part of a lobe is removed. This approach might be used if a person doesn't have enough normal lung function to withstand removing the whole lobe.

Lobectomy: The lungs are made up of 5 lobes (3 on the right and 2 on the left). In this surgery, the entire lobe containing the tumor(s) is removed. If it can be done, this is often the preferred type of operation for NSCLC.

Sleeve resection: This operation may be used to treat some cancers in large airways in the lungs. If you think of the large airway with a tumor as similar to the sleeve of a shirt with a stain a few inches above the wrist, the sleeve resection would be like cutting across the sleeve (airway) above and below the stain (tumor) and then sewing the cuff back onto the shortened sleeve. A surgeon may be able to do this operation instead of a pneumonectomy to preserve more lung function.

Pneumonectomy: This surgery removes an entire lung. Used when tumor is close to the center of the chest.

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Surgery Codes - Lung C340–C349

(Except for M9732, 9741-9742, 9761-9809, 9820, 9826, 9831-9834, 9840-9920, 9931-9993)

Codes

00 None; no surgery of primary site; autopsy ONLY

19 Local tumor destruction or excision, NOS
Unknown whether a specimen was sent to pathology for surgical events coded 19 (used principally for cases diagnosed prior to January 1, 2003)

15 Local tumor destruction, NOS
12 Laser ablation or cryosurgery
13 Electrocautery; fulguration (includes use of hot forceps for tumor destruction)
No specimen sent to pathology from surgical events 12-13 and 15

[***SEER Note:*** Assign code 15 for radiofrequency ablation (RFA)]

20 Excision or resection of less than one lobe, NOS
23 Excision, NOS
24 Laser excision
25 Bronchial sleeve resection ONLY
21 Wedge resection
22 Segmental resection, including lingulectomy
Specimen sent to pathology from surgical events 20–25

30 Resection of [at least one] lobe or bilobectomy, but less than the whole lung (partial pneumonectomy, NOS)
33 Lobectomy WITH mediastinal lymph node dissection
The lymph node dissection should also be coded under *Scope of Regional Lymph Node Surgery* (NAACCR Item # 1292).

[***SEER Note:*** Assign code 30 when lymph node dissection is not performed, but lymph nodes are obtained as part of the lobectomy specimen]

45 Lobe or bilobectomy extended, NOS
46 WITH chest wall
47 WITH pericardium
48 WITH diaphragm

55 Pneumonectomy, NOS
[***SEER Note:*** Code 55 includes the following procedures: complete pneumonectomy, sleeve pneumonectomy, standard pneumonectomy, total pneumonectomy, resection of whole lung]

56 WITH mediastinal lymph node dissection (radical pneumonectomy)
The lymph node dissection should also be coded under *Scope of Regional Lymph Node Surgery* (NAACCR Item # 1292).

65 Extended pneumonectomy
66 Extended pneumonectomy plus pleura or diaphragm

70 Extended radical pneumonectomy
The lymph node dissection should also be coded under *Scope of Regional Lymph Node Surgery* (NAACCR Item # 1292).
[***SEER Note:*** An extended radical pneumonectomy is a radical pneumonectomy (including removal of mediastinal nodes) and the removal of other tissues or nodes]

80 Resection of lung, NOS

90 Surgery, NOS

99 Unknown if surgery performed; death certificate ONLY

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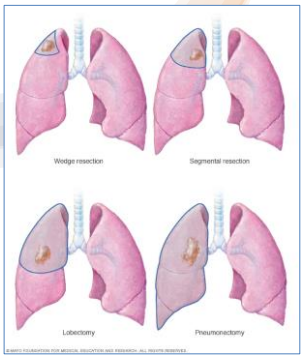
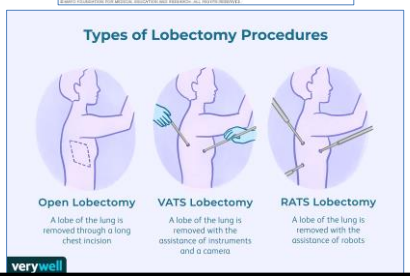
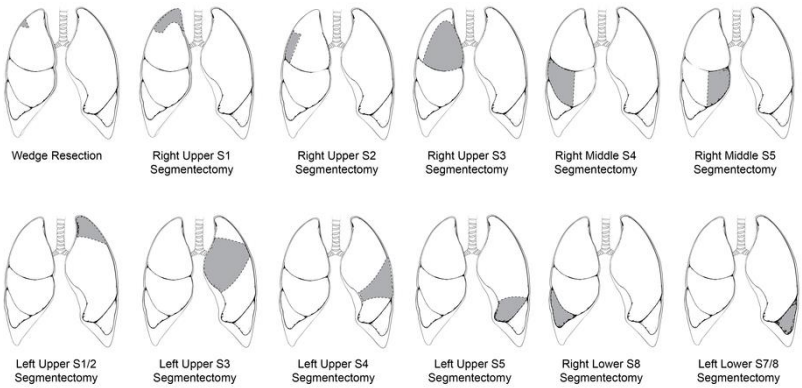
Surgical Procedures - Lung Cancer Treatment







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2021 NCCN Treatment Guidelines for Lung NSCLC

PATHOLOGIC DIAGNOSIS OF NSCLC → **INITIAL EVALUATION**

NSCLC →
- Pathology review[a]
- H&P (include performance status + weight loss)[b]
- CT chest and upper abdomen with contrast, including adrenals
- CBC, platelets
- Chemistry profile
- Smoking cessation advice, counseling, and pharmacotherapy
  - Use the 5 A's Framework: Ask, Advise, Assess, Assist, Arrange http://www.ahrq.gov/clinic/tobacco/5steps.htm
- Integrate palliative care[c] (See NCCN Guidelines for Palliative Care)
- For tools to aid in the optimal assessment and management of older adults, see the NCCN Guidelines for Older Adult Oncology

CLINICAL STAGE

Stage IA, peripheral[d] (T1abc, N0)	See Pretreatment Evaluation (NSCL-2)
Stage IB, peripheral[d] (T2a, N0); Stage I, central[d] (T1abc–T2a, N0); Stage II (T1abc–T2ab, N1; T2b, N0); Stage IIB (T3, N0)[e]; Stage IIIA (T3, N1)	See Pretreatment Evaluation (NSCL-3)
Stage IIB[f] (T3 invasion, N0); Stage IIIA[f] (T4 extension, N0–1; T3, N1; T4, N0–1)	See Pretreatment Evaluation (NSCL-5)
Stage IIIA[f] (T1–2, N2); Stage IIIB (T3, N2)	See Pretreatment Evaluation (NSCL-8)
Separate pulmonary nodule(s) (Stage IIB, IIIA, IV)	See Pretreatment Evaluation (NSCL-8)
Multiple lung cancers	See Treatment (NSCL-10)
Stage IIIB[f] (T1–2, N3); Stage IIIC (T3, N3)	See Pretreatment Evaluation (NSCL-12)
Stage IIIB[f] (T4, N2); Stage IIIC (T4, N3)	See Pretreatment Evaluation (NSCL-13)
Stage IVA (M1a)[c] (pleural or pericardial effusion)	See Pretreatment Evaluation (NSCL-13)
Stage IVA (M1b)[c]	See Pretreatment Evaluation (NSCL-14)
Stage IVB (M1c)[c] disseminated metastases	See Systemic Therapy (NSCL-18)

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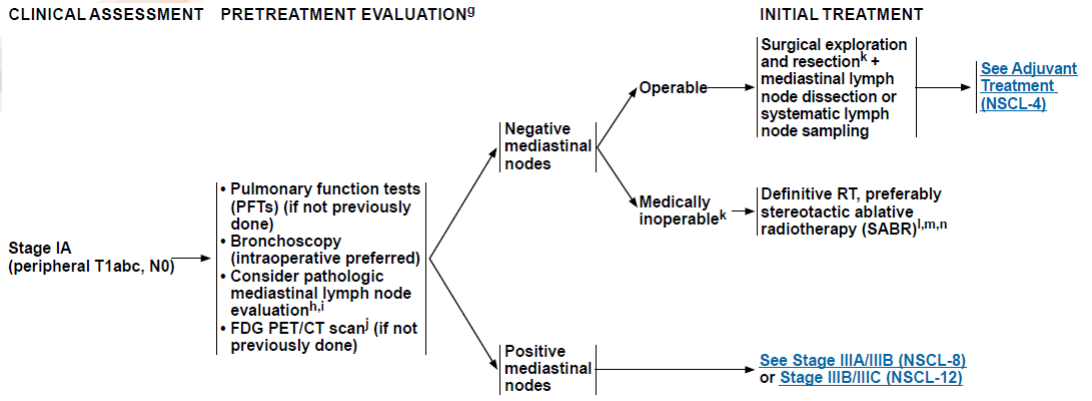
2021 NCCN Treatment Guidelines for Lung NSCLC



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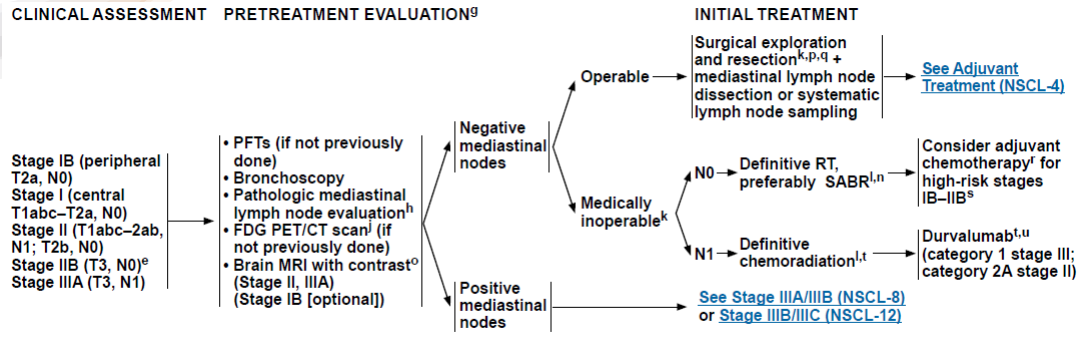
2021 NCCN Treatment Guidelines – Lung NSCLC



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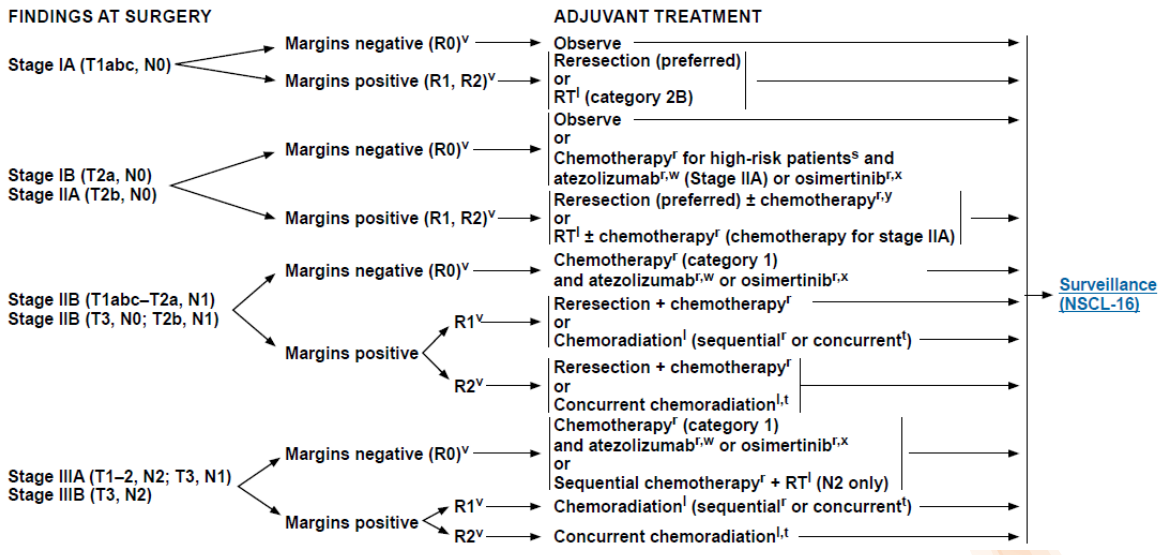
2021 NCCN Post-Surgical Treatment Guidelines – Lung NSCLC



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Biological Tumor Markers, Single and Multi-Gene Testing NCCN Guidelines - Lung

TESTING RESULTS[ll,mm]

EGFR mutation positive (eg, *exon 19* deletion or *L858R*)	NSCL-20
EGFR exon 20 insertion mutation positive	NSCL-23
KRAS G12C mutation positive	NSCL-24
ALK rearrangement positive	NSCL-25
ROS1 rearrangement positive	NSCL-28
BRAF V600E mutation positive	NSCL-29
NTRK1/2/3 gene fusion positive	NSCL-30
METex14 skipping mutation positive	NSCL-31
RET rearrangement positive	NSCL-32
PD-L1 ≥50% and negative for actionable molecular markers above	NSCL-33
PD-L1 ≥1%–49% and negative for actionable molecular markers above	NSCL-34
PD-L1 <1% and negative for actionable molecular markers above	NSCL-35

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Biological Tumor Markers, Single and Multi-Gene Testing
NCCN Guidelines - Lung

***EGFR* Mutation Positive**
(eg, *exon 19* deletion or *L858R*)
- First-line therapy
  - Afatinib[1]
  - Erlotinib[2]
  - Dacomitinib[3]
  - Gefitinib[4,5]
  - Osimertinib[6]
  - Erlotinib + ramucirumab[7]
  - Erlotinib + bevacizumab* (nonsquamous)[8]
- Subsequent therapy
  - Osimertinib[9]

***EGFR exon 20* insertion mutation positive**
- Subsequent therapy
  - Amivantamab-vmjw[10]
  - Mobocertinib[11]

***KRAS G12C* mutation positive**
- Subsequent therapy
  - Sotorasib[12]

***ALK* Rearrangement Positive**
- First-line therapy
  - Alectinib[13,14]
  - Brigatinib[15]
  - Ceritinib[16]
  - Crizotinib[13,17]
  - Lorlatinib[18]
- Subsequent therapy
  - Alectinib[19,20]
  - Brigatinib[22]
  - Ceritinib[23]
  - Lorlatinib[24]

***ROS1* Rearrangement Positive**
- First-line therapy
  - Ceritinib[24]
  - Crizotinib[25]
  - Entrectinib[26]
- Subsequent therapy
  - Lorlatinib[27]
  - Entrectinib[26]

***BRAF* V600E Mutation Positive**
- First-line therapy
  - Dabrafenib/trametinib[28]
- Subsequent therapy
  - Dabrafenib/trametinib[29,30]

***NTRK1/2/3* Gene Fusion Positive**
- First-line/Subsequent therapy
  - Larotrectinib[31]
  - Entrectinib[32]

***MET* Exon 14 Skipping Mutation**
- First-line therapy/Subsequent therapy
  - Capmatinib[33]
  - Crizotinib[34]
  - Tepotinib[35]

***RET* Rearrangement Positive**
- First-line therapy/Subsequent therapy
  - Selpercatinib[36]
  - Pralsetinib[37]
  - Cabozantinib[38,39]
  - Vandetanib[40]

PD-L1 ≥1%
- First-line therapy**
  - Pembrolizumab[41-43]
  - (Carboplatin or cisplatin)/pemetrexed/ pembrolizumab (nonsquamous)[44]
  - Carboplatin/paclitaxel/bevacizumab*/ atezolizumab (nonsquamous)[45]
  - Carboplatin/(paclitaxel or albumin-bound paclitaxel)/pembrolizumab (squamous)[46]
  - Carboplatin/albumin-bound paclitaxel/ atezolizumab (nonsquamous)[47]
  - Nivolumab/ipilimumab[48]
  - Nivolumab/ipilimumab/pemetrexed/ (carboplatin or cisplatin) (nonsquamous)[49]
  - Nivolumab/ipilimumab/paclitaxel/carboplatin (squamous)[49]

PD-L1 ≥50% (in addition to above)
- First-line therapy**
  - Atezolizumab[50]
  - Cemiplimab-rwlc[51]

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2021 NCCN Radiation Treatment Guidelines – Lung - NSCLC

PRINCIPLES OF RADIATION THERAPY

Table 2. Commonly Used Doses for SABR

Total Dose	# Fractions	Example Indications
25–34 Gy	1	Peripheral, small (<2 cm) tumors, esp. >1 cm from chest wall
45–60 Gy	3	Peripheral tumors and >1 cm from chest wall
48–50 Gy	4	Central or peripheral tumors <4–5 cm, especially <1 cm from chest wall
50–55 Gy	5	Central or peripheral tumors, especially <1 cm from chest wall
60–70 Gy	8–10	Central tumors

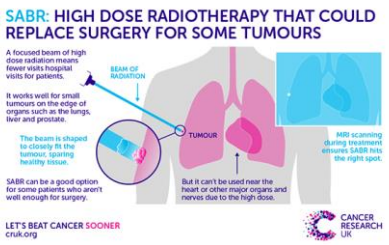

Table 3. Maximum Dose Constraints for SABR*

OAR/Regimen	1 Fraction	3 Fractions	4 Fractions	5 Fractions
Spinal cord	14 Gy	18 Gy (6 Gy/fx)	26 Gy (6.5 Gy/fx)	30 Gy (6 Gy/fx)
Esophagus	15.4 Gy	27 Gy (9 Gy/fx)	30 Gy (7.5 Gy/fx)	105% of PTV prescription^
Brachial plexus	17.5 Gy	24 Gy (8 Gy/fx)	27.2 Gy (6.8 Gy/fx)	32 Gy (6.4 Gy/fx)
Heart/ pericardium	22 Gy	30 Gy (10 Gy/fx)	34 Gy (8.5 Gy/fx)	105% of PTV prescription^
Great vessels	37 Gy	NS	49 Gy (12.25 Gy/fx)	105% of PTV prescription^
Trachea & proximal bronchi	20.2 Gy	30 Gy (10 Gy/fx)	34.8 Gy (8.7 Gy/fx)	105% of PTV prescription^
Rib	30 Gy	30 Gy (10 Gy/fx)	40 Gy (10 Gy/fx)	NS
Skin	26 Gy	24 Gy (8 Gy/fx)	36 Gy (9 Gy/fx)	32 Gy (6.4 Gy/fx)
Stomach	12.4 Gy	NS	27.2 Gy (6.8 Gy/fx)	NS

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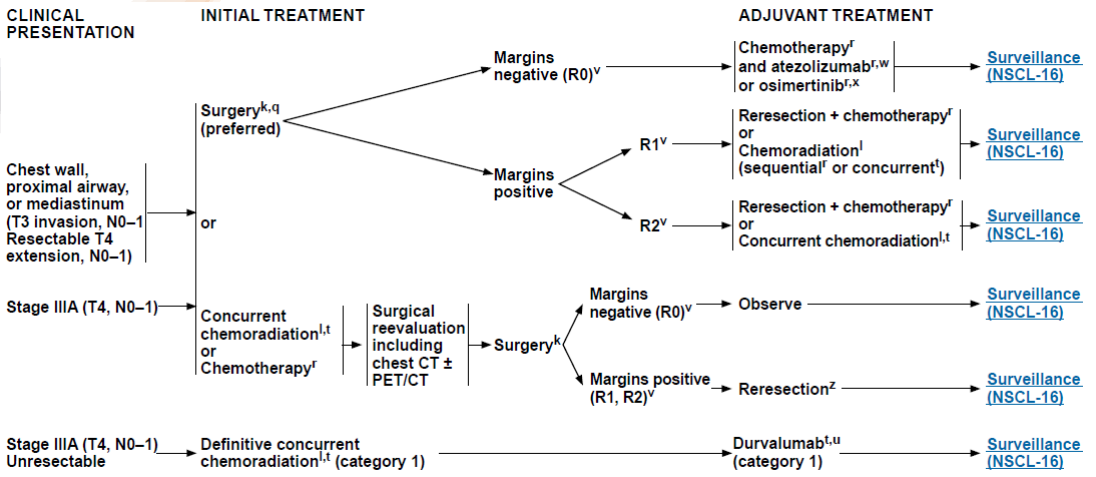
2021 NCCN Post-Surgical Treatment Guidelines – Lung NSCLC



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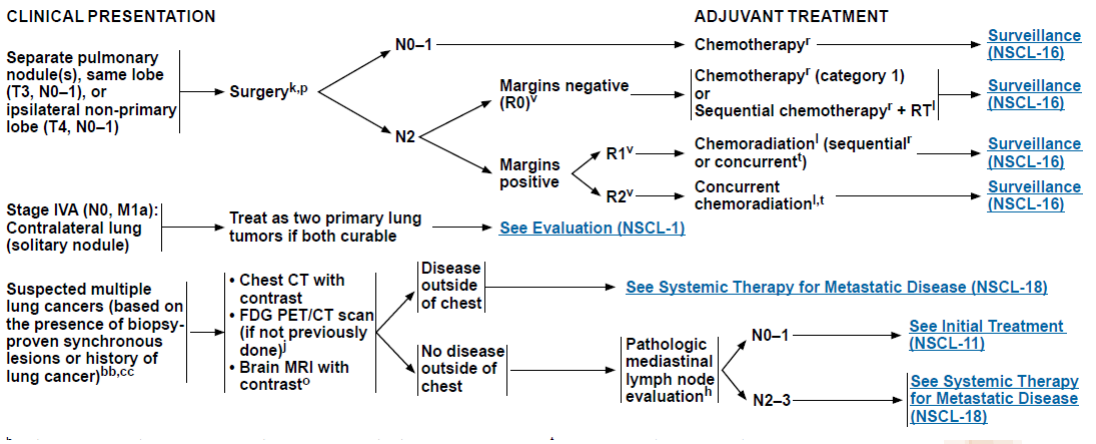
2021 NCCN Post-Surgical Treatment Guidelines – Lung NSCLC



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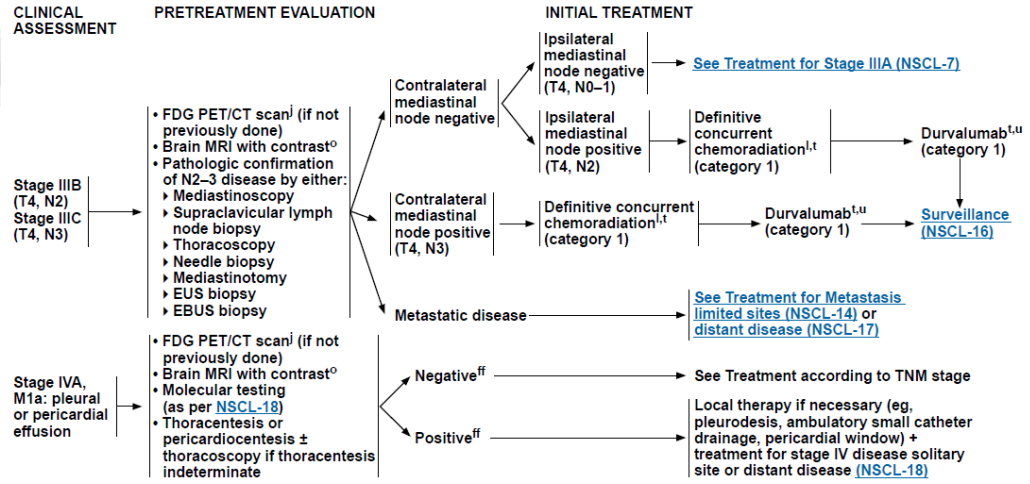
2021 NCCN Advanced/Metastatic Treatment Guidelines – Lung - NSCLC



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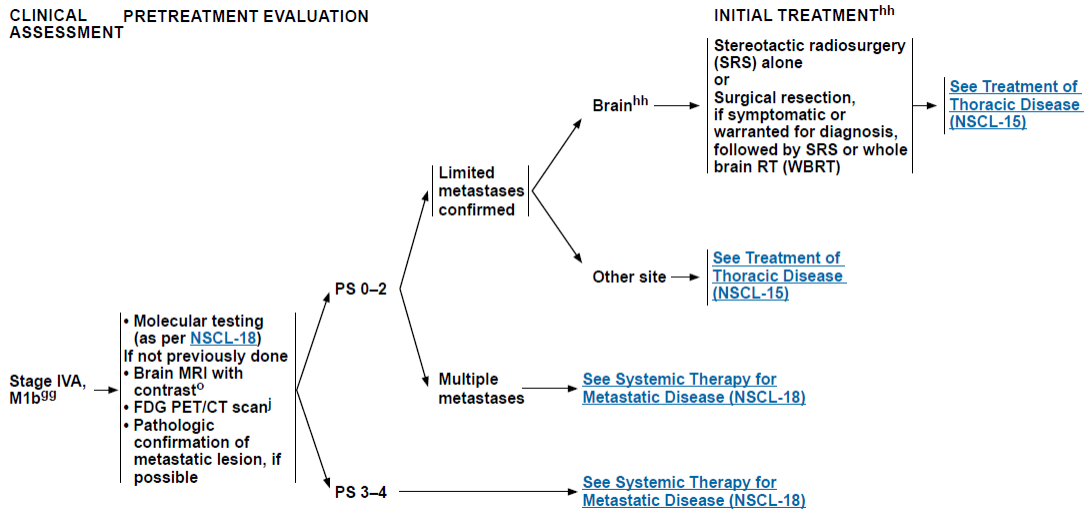
2021 NCCN Advanced/Metastatic Treatment Guidelines – Lung NSCLC



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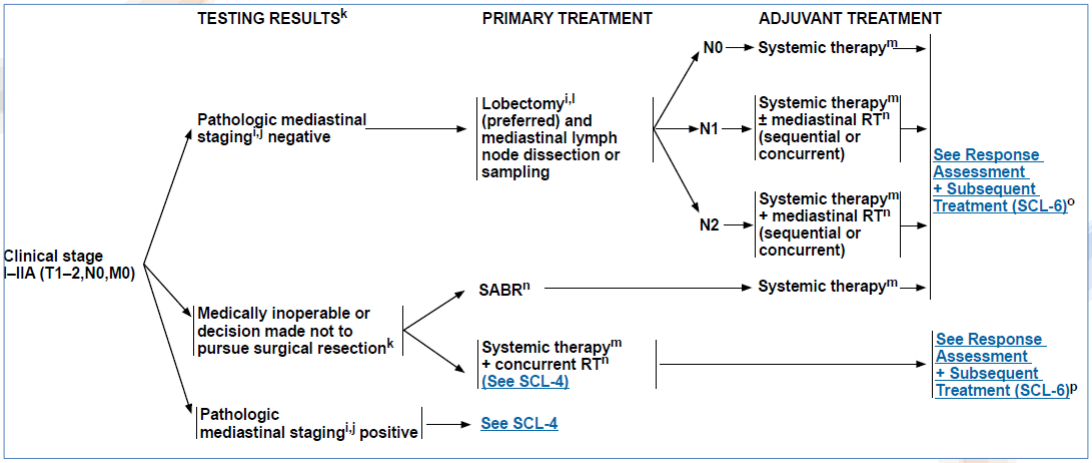
2021 NCCN Small Cell Lung Cancer Treatment Guidelines



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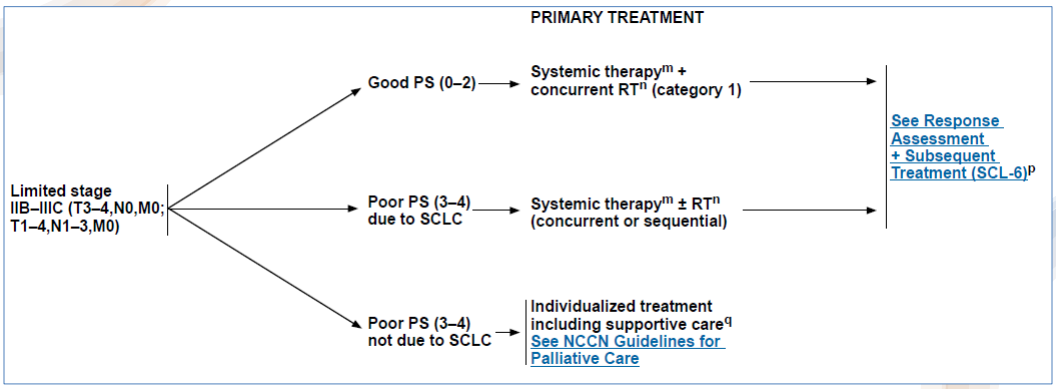
2021 NCCN Small Cell Lung Cancer Treatment Guidelines



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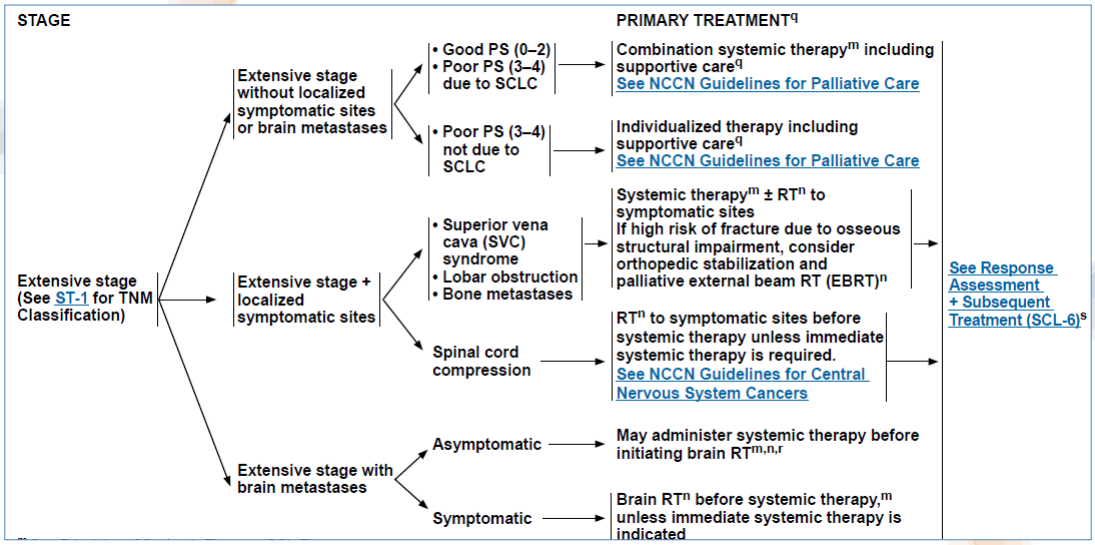
2021 NCCN Small Cell Lung Cancer Treatment Guidelines



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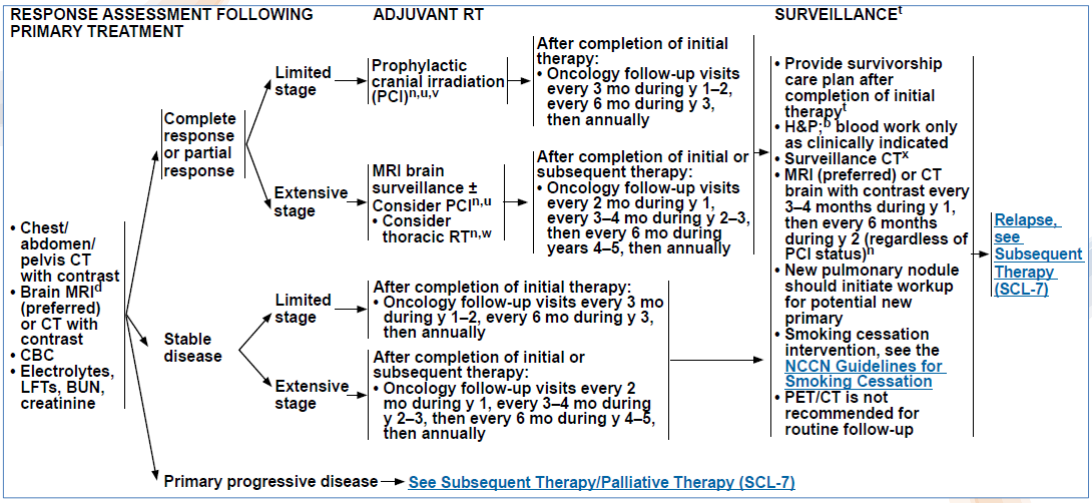
2021 NCCN Small Cell Lung Cancer Treatment Guidelines



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TEXT DOCUMENTATION

LUNG

National Cancer Registrars Association

INFORMATIONAL ABSTRACT

A Guide to Determining What Text to Incl

The abstract is the basis of all registry functions. It is a tool used to hel stage and to aid cancer research; therefore, the abstract must be compl information needed to provide a concise analysis of the patient's diseas treatment.

To assist registrars in preparing abstracts, NCRA's Education Committe of informational abstracts. These site-specific abstracts provide an outl determining what text to include. The outline has a specific sequence d efficiency and includes eight sections: Physical Exam/History; X-Rays/S Diagnostic Procedures; Pathology; Primary Site; Histology; and Treatm resources is located at the end of each informational abstract. The sou noted in the various sections below are not inclusive, but they are the r need to do additional research to complete the abstract.

When using the informational abstract, follow the outline and strive to sections. Be concise by using phrases, not sentences. Make sure to use disease process and the specific cancer site and to use NAACCR Stand When the abstract is completed, review thoroughly to ensure accuracy.

PHYSICAL EXAM/HISTORY

Include:

- **Demographics:** Age, gender, race and ethnicity of the patient.
- **Chief Complaint:** What brought the patient to the doctor? Often it is a persistent cough, which may be productive, hemoptysis, chest pain or a combination of symptoms. It may be a routine chest x-ray that shows an abnormality.
- **History:** Personal history of any cancer, family history of cancer, alcohol history, exposure to environmental carcinogens such as asbestos or radon and exposure to second-hand smoke, tobacco history.
- **Physical Examination:** Date of the exam, place of exam, and documentation of information pertinent to the lung cancer such as diminished breath sounds, palpable lymphadenopathy. If there are no significant physical findings, it is acceptable to say PE neg.
- **Comorbidities:** Only text to the specific abstracted. Age ma ultimate treatment

Where to Find Inform exam look for HTN (hy (coronary artery disea obstructive pulmonary

Example: 2-15-18 Fac months hx of progress tightness, now w/ wor weakness & weight los CXR revealed pneumo to ED for further eval LN in Lt supraclav regi bilat lung bases w/ lt Remainder neg.

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X-RAYS/SCOPES/SCANS

Include:

- **X-rays and Scans:** pertinent to the diagnosis of cancer and metastases,
- Document tumor size and/or extension.
- Each exam dated and listed in chronological order.
- Most commonly these will include a chest x-ray and a CT of the chest.
- Other studies may be done to rule out metastases and may include a bone scan, an MRI of the brain, a CT of the abdomen and pelvis, a PET/CT to look for separate tumor nodules, etc.
- Endobronchial ultrasou navigational bronchosc used to eval adenopath bx mediastinoscopy to resectability.

Example: 2-15-18 Facility in LUL. 2-18-18 CT chest extending to pleural surfa cm mass in Lt supraclav nodal met. 3-1-18 WBBS, 3-15-18 PET/CT 3 cm hyp mass in L supraclav regio Findings concerning for p with nodal mets.

LABS

There are no pertinent lab tests for lung ca.

DIAGNOSTIC PROCEDURES (Includes SCOPES and OPERATIVE

For any of the diagnostic procedures – procedures that detect the cancer, it – include the date, name of procedure, and a brief description of the find

Include:

- **Bronchoscopy:** To determine if there are endobronchial lesions.
- **Mediastinoscopy:** To determine whether there needs to be a resection of the primary.
- **Surgical Resection:** List the method of entering such as thoracotomy or video-assisted thoracoscopic surgery (VATS) and the findings, to include the tumor, pertinent po findings that may impac Document what was re lymph nodes, if any, we

Example: 4-1-18 Facility M Carina normal. No endobr 18 Facility M: CTguided b

PATHOLOGY

Include:

Results of biopsies and surgical resection, if any, in chronological order. Te coding of clinical, pathologic, and post-therapy grade.

- (OPTIONAL) EGFR, ROS-1, and ALK/KRAS tests if applicable/performed at your facility.

Example: 4-1-18 Bronch w brushings – atypical cells (squamous cell carcinoma bx Lt supraclav LN – mets primary lung origin. 4-4-1 Poorly Diff SqCC.

PRIMARY SITE

Include:

Primary site, including subsite & laterality for paired sites. See STORE and the Solid Tumor Manual for further clarifications on coding Primary Site and Laterality.

Example: Lung Left Upper

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LUNG

HISTOLOGY

Include:

Histology of the primary site including the morphology, and the behavior.

Example: Squamous Cell Carcinoma, poorly-differentiated 8070/3

TREATMENT

Include:

All treatment given in chronological order, along with documentation to support all treatment-related fields when treatment was given.

- **Surgery:** Date(s) of surgical procedure and surgical approach such as endoscopic, open, robotic. Significant findings as dictated by the treating provider.
- If the surgeon does not give any significant findings, it is acceptable to say "no significant findings."
- **Text:** To support if treatment was refused/ contraindicated/not given if applicable.

Example: 4-15/5-30-18 @ Facility M: 5040 cGy to Lt lung, mediastinal, and Lt Supraclav LNs w/ 6 MV IMRT (28 fx).

6-2-18-7-9-18 @ Facility M: Carboplatin, etoposide, 6 cycles.

RESOURCES

NAACCR Standard Abbreviations:
naaccr.org/Applications/ContentReader/?c=17

Evidence Based Treatment by Stage Guidelines:
www.nccn.org/professionals/physician_gls/f_guidelines.asp
The NCCN Guidelines are most frequently used for treatment and are also used for information on diagnostic workup.

NCI Physician's Data Query (PDQ): www.cancer.gov/cancertopics/pdq

Solid Tumor Rules: seer.cancer.gov/tools/solidtumor/

Multiple Primary & Histology Coding Rules:
Labs/TestsNCI: Understanding Lab Tests/Test Values:
www.cancer.gov/cancertopics/factsheet/detection/laboratory-tests

Site Specific Data Items:
www.naaccr.org/SSDI/SSDI-Manual.pdf?v=1527608547

NAACCR Grade Coding Instructions:
www.naaccr.org/SSDI/Grade-Manual.pdf

Site Specific Surgery Codes: STORE Manual, Appendix B
www.facs.org/quality-programs/cancer/ncdb/registrymanuals/oocmanuals

Radiation Treatment: CTR Guide to Coding Radiation in the STORE:
www.facs.org/-/media/files/quality-programs/cancer/ncdb/case_studies_coding_radiation_treatment.ashx

Systemic Treatment: Chemotherapy/Immunotherapy/Hormone/Other

SEER Rx Antineoplastic Drugs Database: seer.cancer.gov/tools/seerrx/

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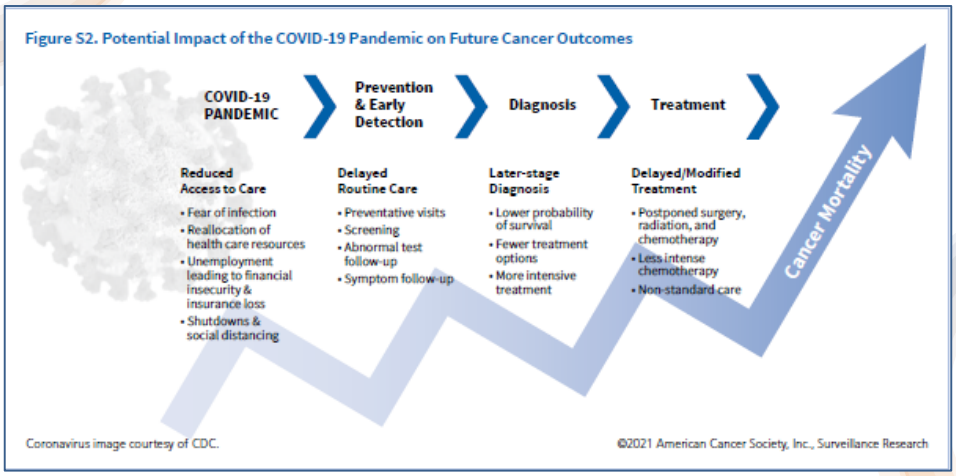
Miscellaneous Notes



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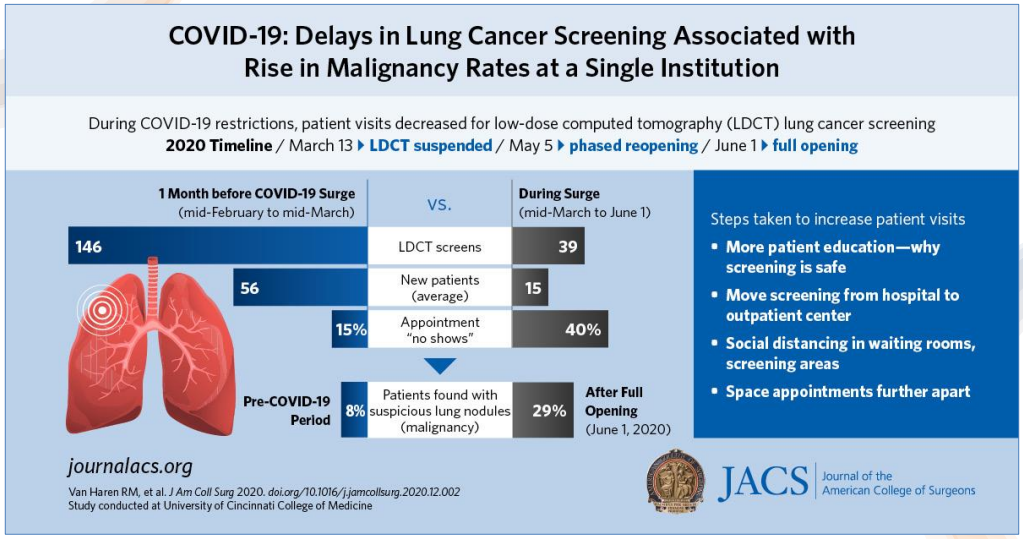
Miscellaneous Notes



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- National Cancer Institute: PDQ Lung and Drugs Approved for Lung Cancer: https://www.cancer.gov/about-cancer/treatment/drugs/lung#1
- Increasing Adherence to CT Lung Cancer Screening Programs: IASLC: 2022: https://www.iaslc.org/iaslc-news/ilcn/increasing-adherence-ct-lung-cancer-screening-programs
- IASLC Atlas of Diagnostic Immunochemistry: IASLC: ISBN: 978-1-940488-07-3; IASLC, Denver, CO; www.iaslc.org
- IASLC 2009 Nodal Map: IASLC Lung Cancer Staging Project: Rusch et al., J Thorac Oncol 2009; IASLC, Denver, CO: www.iaslc.org
- Lung Cancer: Pulmonary Neuroendocrine Tumors; Memorial Sloan Kettering Cancer Center;2022; https://www.mskcc.org/cancer-care/types/lung/types/pulmonary-neuroendocrine-tumors
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- Protocol for Examination of Resection Specimens from Patients with Primary Non-Small Cell Carcinoma, Small Cell Carcinoma, or Carcinoid Tumor of the Lung: College of American Pathologists, Version 4.2.0.1, http://www.cap.org/cancerprotocols, 2021
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- Lung Cancer Genomic Testing (EGFR, KRAS, ALK); Memorial Sloan Kettering Cancer Center; 2022; https://www.mskcc.org/cancer-care/types/lung/diagnosis/genetic-testing
- FDA Approvals in Lung Cancer Treatment: Lung Cancer Research Foundation: https://www.lungcancerresearchfoundation.org/research/why-research/treatment-advances/
- Informational Abstract: Lung Cancer: National Cancer Registrars Association; www.CancerRegistryEducation.org
- American Lung Association: What Are the Types of Lung Cancer Treatment: https://www.lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer/treatment/types-of-treatment
- NIH study illuminates origins of lung cancer in never smokers was originally published by the National Cancer Institute; Zhang T, Joubert P, Ansari-Pour N, et al. Genomic and Evolutionary Classification of Lung Cancer in Never Smokers. Nature Genetics. Sept 6, 2021. DOI: 10.1038/s41588-021-00920-0.
- Lung Cancer Treatment: RadiologyInfo.org: https://www.radiologyinfo.org/en/info/lung-cancer-therapy
- Covid-19 and Lung Cancer: IASLC; Evolving Standards of Care: Dec 10, 2021; https://www.iaslc.org/iaslc-news/ilcn/covid-19-and-lung-cancer\
- SEER Coding Guidelines – Lung
- Solid Tumor Manual, Lung Chapter
- Site-Specific Surgery Codes – Lung 2021
- Summary Stage Manual

Questions

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