2018 Updates - Neoplasms of the Lung

2018-2019 FCDS Educational Webcast Series
Steven Peace, CTR
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CDC & Florida DOH Attribution

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FLccSC LMS – CEU Quiz – FCDS IDEA

- 2017 - Florida Changed How FCDS Awards CEUs for FCDS Webcasts
- Attendees must take and pass a 3-5 question CEU Quiz to get CEUs
- CEU Awards are Restricted to Attendees with a FLccSC LMS Account
- The CEU Quiz will be posted to FLccSC 1-2 hours after the webcast ends
- Only registered FLccSC Users will be given access to the CEU Quiz
- Florida attendees must have a Florida FLccSC Account to take the Quiz
- South Carolina attendees must have a South Carolina FLccSC Account
- New FLccSC States will follow similar instructions for the CEU Quiz
- Attendees can attend any of the live webcasts without receiving CEUs
- Recorded Sessions are also available for non-FLccSC Users – No CEUs

Presentation Outline

- Overview of Neoplasms of the Lung
- Genetic, Clinical & Radiological Advances Since 2004
- 2015 WHO Classification of Lung Tumors
- 2018 ICD-0-3 Lung Histology Codes
- 2018 CAP Protocols for Lung
- Biomarkers and Genetics
- 2018 MP/H Lung Rules
- Anatomy of the Thorax – Lung & Pleura
- 2018 Anatomic Staging – SS2018 & AJCC TNM
- 2018 Non-Anatomic Site-Specific Data Items (SSDI)
- Lung Cancer Primary Treatment Options
- Importance of Text Documentation
- Practice Cases - Pending
- Questions
Figure 1. Trends in Age-adjusted Cancer Death Rates* by Site, Males, US, 1930-2015

*Age adjusted to the 2000 US standard population. 
Mortality rates for pancreatic and liver cancers are increasing.
Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancers of the liver, lung and bronchus, colon and rectum, and uterus are affected by these coding changes.

Figure 2. Trends in Age-adjusted Cancer Death Rates* by Site, Females, US, 1930-2015

*Age adjusted to the 2000 US standard population. 
Uterus refers to uterine cervix and uterine corpus combined. 
The mortality rates for liver cancer is increasing.
Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancers of the liver, lung and bronchus, colon and rectum, and uterus are affected by these coding changes.
United States Smoking Rates

The US Smoking Rate is at an All-Time Low

Cigarette smoking among US adults

- Health warning required
- Smiling banned on all domestic flights
- TV & radio ads illegal
- FDA approves nicotine gum
- California bans smoking in bars and restaurants

Percent who smoke

<table>
<thead>
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<th>Year</th>
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</tbody>
</table>

Data source: https://www.cdc.gov/tobacco/data_statistics/lates/trends/cig_smoking/ (US CDC)

ChartYourWorld.org

World Smoking Rates

Share of men who smoke, 2015

Men 15 and over who smoke any form of tobacco, including cigarettes, cigars, pipes or any other smoked tobacco products. Data include daily and non-daily or occasional smoking.

Source: World Bank – WDI

OurWorldInData.org/smoke.html • CC BY-SA
Dangerous Chemicals in All Tobacco

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

Association with Smoking
E-Cigarette Use

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

Source: United States Environmental Protection Agency (EPA)

Mesothelioma (just a mention)

Sources: http://www.mesothelioma.com and http://www.usaep.org
Genetic, Clinical & Radiological Advances Since 2004

- Imaging Advances (CT, PET, PET/CT, MRI, Ultrasound) have led to improved staging
- Lung Cancer Screening – low dose CT scan (LDCT) for high risk patients
- Immunohistochemistry: sputum, FNA, Gene Expression Analysis, Next Generation Genetics
- Genetics: EGFR, KRAS, MET, LKB1, BRAF, PIK3CA, ALK, RET, and ROS1
- The seminal discovery that epidermal growth factor receptor (EGFR) activating mutations are putative drivers and predict response to EGFR tyrosine kinase inhibitors (TKIs) in patients with NSCLC paved the way for development of targeted therapeutics based on molecular testing.
- Immune checkpoint inhibition in lung cancer – PD-L1 Inhibitors (nivolumab)
- Treatment Advances – Chemotherapy, Biologicals, Gene Targets, Immunotherapy
2015 WHO Classification of Lung Tumors

State of the Art: Concise Review

The 2015 World Health Organization Classification of Lung Tumors
Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification

William D. Travis, MD, (*) Elisabeth Brambilla, MD, ¶ Andrew G. Nicholson, MD, ¶ Yoshiki Yatabe, MD, ¶ John H. M. Austin, MD, ¶ Mary Beth Besseley, MD, ¶ Lucian R. Chirieac, MD, ¶ Sanja Dacic, MD, ¶* Edwin Duhig, MD, ¶ Douglas B. Flieder, MD, ¶ Kim Geisenger, MD, ¶ Fred R. Hirsch, MD, ¶* Yutaka Ishikawa, MD, ¶¶ Keith M. Kerr, MD, ¶¶ Masayuki Yokoyama, MD, ¶¶ Giuseppe Felicioni, MD, ¶¶¶ Charles A. Powell, MD, ¶¶¶ Mung Sound Fu, MD, ¶¶¶ and Ignacio Wainberg, MD, ¶¶¶ On Behalf of the WHO Panel

Abstract: The 2015 World Health Organization (WHO) Classification of Tumors of the Lung, Pleura, Thymus and Heart has just been published with numerous important changes from the 2004 WHO classification. The most significant changes in this edition involve (1) use of immunohistochemistry throughout the classification, (2) a new emphasis on genetic studies in particular, integration of molecular testing to help personalize treatment strategies for advanced lung cancer patients, (3) a new classification for small biopsies and visible tumors similar to that proposed in the 2011 Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society classification, (4) a completely different approach to lymphadenocarcinomas or proposed by the 2011 Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society classification, (5) restricting the diagnosis of large cell carcinomas only to exicted tumors that lack any clear morphologic or immunohistochemical differentiation with reclassification of the remaining tumors.
2015 WHO Classification of Tumours of Lung, Pleura, Thymus & Heart, 4th ed.

**Highlights**

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

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Small Biopsy and Cytology Specimens

<table>
<thead>
<tr>
<th>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*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small Biopsy/Cytology Terminology/Criteria</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
</tr>
<tr>
<td>NSCC with NE morphology and positive NE markers, possible LCNEC</td>
</tr>
<tr>
<td>NSCC with NE morphology</td>
</tr>
<tr>
<td>If negative NE markers comment: This is a NSCC where LCNEC is suspected, but stains failed to demonstrate NE differentiation.</td>
</tr>
<tr>
<td>Morphologic squamous cell and adenocarcinoma patterns present: NSCC, NOS</td>
</tr>
<tr>
<td>Comment that adenocarcinoma and squamous components are present and this could represent adenosquamous carcinoma.</td>
</tr>
<tr>
<td>Morphologic squamous cell or adenocarcinoma patterns not present but immunostains favor separate glandular and adenocarcinoma components: NSCC, NOS</td>
</tr>
<tr>
<td>Specify the results of the immunohistochemical stains and the interpretation and comment this could represent adenosquamous carcinoma.</td>
</tr>
<tr>
<td>NSCC with spindle cell and/or giant cell carcinoma (mention if adenocarcinoma or squamous carcinoma are present)</td>
</tr>
</tbody>
</table>

*Modified from the articles by Travis et al.1,2,3
LCNCEC, large cell neuroendocrine carcinoma; NOS, not otherwise specified; NSCC, non-small cell carcinoma; NE, neuroendocrine; WHO, World Health Organization.
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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### TABLE 4. Adenocarcinoma In Situ

<table>
<thead>
<tr>
<th>Diagnostic criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>A small tumor ≤3 cm²</td>
</tr>
<tr>
<td>A solitary adenocarcinoma</td>
</tr>
<tr>
<td>Pure lepidic growth</td>
</tr>
<tr>
<td>No stromal, vascular or pleural invasion</td>
</tr>
<tr>
<td>No pattern of invasive adenocarcinoma (such as acinar, papillary, micropapillary, solid, colloid, enteric, fetal or invasive mucinous adenocarcinoma)</td>
</tr>
<tr>
<td>No spread through air spaces</td>
</tr>
<tr>
<td>Cell type mostly nonmucinous (type II pneumocytes or Clara cells), rarely may be mucinous (tall columnar cells with basal nuclei and abundant cytoplasmic mucus, sometimes resembling goblet cells)</td>
</tr>
<tr>
<td>Nuclear atypia is absent or inconspicuous</td>
</tr>
<tr>
<td>Septal widening with sclerosis/elastosis is common, particularly in nonmucinous adenocarcinoma in situ</td>
</tr>
</tbody>
</table>

*Modified from the articles by Travis et al. [1,31]*

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### TABLE 5. Minimally Invasive Adenocarcinoma

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

*Modified from the articles by Travis et al. [1,21]*

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

Acinar pattern is characterized by glandular formation.

Cribriform pattern shows distinctive holes in between the cancer cells - Swiss cheese.
Squamous Cell Carcinoma &
Large Cell Carcinoma

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

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

Neuroendocrine Tumors

- Classified Similar to the GI Track Neuroendocrine Tumors

- NOW INCLUDES
  - Carcinoid Tumor of Lung – low grade neuroendocrine tumor
  - Small Cell Lung Carcinoma – Ki67 confirmation for high grade SCLC
  - Large Cell Carcinoma Not Elsewhere Classified

- Mitotic Count used to differentiate low/high grade
2018 ICD-0-3 Lung Histology Codes

- 8013/3 – Combined Large Cell Neuroendocrine Carcinoma (C34._, C37.9)
- 8023/3 – NUT Carcinoma (C30.0, C31.9, C34._)
- 8140/3 – Minimally Invasive Adenocarcinoma, NOS (C34._)
- 8144/3 – Enteric Adenocarcinoma (C34.0, C67._, C66.9, C68._)
- 8250/2 – Adenocarcinoma in situ, non-mucinous (C34._)
- 8250/3 – Lepidic Adenocarcinoma (C34._)
- 8250/3 – Lepidic Predominant Adenocarcinoma (C34._)
- 8253/2 – Adenocarcinoma in situ, mucinous (C34._)
- 8253/3 – Invasive Mucinous Adenocarcinoma (C34._)
- 8254/3 – Mixed Invasive Mucinous and Non-Mucinous Adenocarcinoma (C34._)
- 8256/3 – Minimally Invasive Adenocarcinoma, Non-Mucinous (C34._)
- 8257/3 – Minimally Invasive Adenocarcinoma, Mucinous (C34._)
- 8265/3 – Micropapillary Adenocarcinoma (C34._)
- 8265/3 – Micropapillary Carcinoma, NOS (C18._, C19.9, C20.9, C34._)
- 8551/3 – Acinar Adenocarcinoma (C34._)
- 8842/3 – Pulmonary Myxoid Sarcoma with EWSR1-CREB1 translocation (C34._)

2018 Grade Coding for Lung Cancer

- **Clinical Grade** - the grade of a solid primary tumor before any treatment. Treatment may include surgical resection, systemic therapy, radiation therapy, or neoadjuvant therapy. **NOTE:** All surgical procedures are not treatment, e.g. TURB and endoscopic biopsies.

- **Pathological Grade** - the grade of a solid primary tumor that has been surgically resected and for which no neoadjuvant therapy was administered. If AJCC pathological staging is being assigned, the tumor must have met the surgical resection requirements in the AJCC manual. This may include the grade from the clinical workup, as all information from diagnosis (clinical staging) through the surgical resection is used for pathological staging.

- **Post-Therapy Grade** - the grade of a solid primary tumor that has been resected following neoadjuvant therapy. If AJCC post-therapy staging is being assigned, the tumor must have met the surgical resection requirements for yp in the AJCC manual. Neoadjuvant therapy must meet guidelines or standards, and not be that given for variable or unconventional reasons as noted in the AJCC manual.
2018 Grade Coding for Lung Cancer

2018 CAP Protocols for Lung
LUNG: Molecular/Genetic Biomarkers
EGFR, KRAS, MET, LKB1, BRAF, PIK3CA, ALK, RET, and ROS1

- Over half of lung adenocarcinomas contain one of a number of identifiable genetic alterations; some of these can be targeted by a specific therapeutic inhibitor that is either approved by the Food and Drug Administration (FDA) or in clinical trials.
- The National Comprehensive Cancer Network (NCCN) recommends testing for EGFR mutations and ALK rearrangements in all patients with recurrent or metastatic lung adenocarcinomas in order to guide therapy.
- The College of American Pathologists (CAP), International Association for the Study of Lung Cancer (IASLC), and Association for Molecular Pathology (AMP) have prepared a joint guideline that provides a detailed description of the patient and specimen requirements and acceptable testing designs and strategies for the detection of these alterations; details are beyond the scope of this document.

### Table 11F: Major genetic changes in lung cancer

<table>
<thead>
<tr>
<th>Alterations</th>
<th>Small cell carcinoma (%)</th>
<th>Adenocarcinoma (%)</th>
<th>Squamous cell carcinoma (%)</th>
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<tbody>
<tr>
<td>Mutation</td>
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<tr>
<td>EGFR</td>
<td>0</td>
<td>&lt;5</td>
<td>0</td>
</tr>
<tr>
<td>KRAS</td>
<td>0</td>
<td>&lt;5</td>
<td>0</td>
</tr>
<tr>
<td>MET</td>
<td>&lt;1</td>
<td>15-20</td>
<td>&lt;5</td>
</tr>
<tr>
<td>RET</td>
<td>0</td>
<td>&lt;5</td>
<td>0</td>
</tr>
<tr>
<td>ROS1</td>
<td>0</td>
<td>&lt;1</td>
<td>0</td>
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<tr>
<td>Amplification</td>
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<tr>
<td>EGFR</td>
<td>&lt;1</td>
<td>5-10</td>
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<td>KRAS</td>
<td>&lt;1</td>
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<td>MET</td>
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<tr>
<td>RET</td>
<td>&lt;1</td>
<td>5-10</td>
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</tr>
<tr>
<td>ROS1</td>
<td>&lt;1</td>
<td>5-10</td>
<td>10</td>
</tr>
</tbody>
</table>

Source: WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart, 2015 and Lung Cancer Foundation of America
Biomarkers & Genetic Abnormalities

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

- Class of Antineoplastic Agents for NSCLC – Immunotherapy
  - BRAF V600E – Tafinlar/Dabrafenib
  - BRAF V600E – Mekinist (Trametinib)
  - ROS1 – Xalkori (Crizotinib)

- Class of Antineoplastic Agents for NSCLC – Immunotherapy
  - PD-1 – Keytruda/Pembrolizumab
  - PD-L1 – Tecentriq/Atezolizumab

- Treatment Targets for NSCLC – Angiogenesis Inhibitors & Targets
  - Bevacizumab (Avastin)
  - VEGF Receptor Ramucirumab (Cyramza)

- Maintenance Therapy for NSCLC – Chemotherapy
  - Alimta/Pemetrexed - stable disease, partial/complete response s/p Platinum
Biomarkers & Genetic Abnormalities

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

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

2018 Lung MP/H Rules
2018 Lung MP/H Rules

- Tumor, mass, tumor mass, lesion, neoplasm, nodule
- The terms tumor, mass, tumor mass, lesion, neoplasm and nodule are **not** used in a **standard manner** in clinical diagnoses, scans, or consults. **Disregard** the terms **unless** there is a **physician’s statement** that the term is **malignant/cancer**
- These terms are used **ONLY** to **determine** multiple **primaries**
- **Do not** use these terms for **casefinding** or **determining**

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2018 Lung MP/H Rules

- NSCLC needs further testing to determine if tumor is squamous or adenocarcinoma
- Non-small cell carcinoma **8046**; a broad category which includes all histologies in Table 3 **except** for small cell carcinoma/neuroendocrine tumors (NET Tumors) **8041** and all subtypes
- **Major Changes to Classification of Adenocarcinoma of Lung**
  - **Pathologists to Discontinue Use** of Term “bronchiolo-alveolar carcinoma” or “BAC”
  - **New Preferred Term** is “mucinous adenocarcinoma”
  - **New Histology Codes** for “mucinous adenocarcinoma” of the lung – **not same as colon**
  - **Recognition of non-invasive (in-situ) and minimally invasive neoplasms of the lung**
  - **New Histology Codes and Behaviors** for “in-situ”, “minimally invasive”, “acinar”, “lepidic” and “micropapillary” adenocarcinoma of lung – use for Lung Only
  - **In-situ Tumors** may be further described by architecture – acinar, lepidic, cribriform
  - **Multifocal or multiple discrete foci tumors** are often present in lepidic adenocarcinoma, minimally invasive adenocarcinoma, and adenocarcinoma in-situ
  - **Multiple foci may be referred to as ground-glass or lepidic in appearance on imaging**
Component is not equivalent to subtype/variant.
Component is only coded when the pathologist specifies the component as a second carcinoma.
Component is not equivalent to subtype/variant.
Component is only coded when the pathologist specifies the component as a second carcinoma.

2018 Lung MP/H Rules
MP Rules that Use Table 3 – How to Use Table 3

Table 3: Specific Histologies, NOS, and Subtype/Variants

Rule M5 - Abstract multiple primaries 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 carcinomas 8040 or any non-small cell carcinomas subtypes/variants.

Note 1: See Table 3 in Equivalent Terms and Definitions for terms and codes for small cell carcinoma and all of the subtypes/variants.

Note 2: With the exception of small cell neuroendocrine carcinomas, all other histologies listed in Table 3 in Equivalent Terms and Definitions are non-small cell carcinomas.

Note 3: It is irrelevant when the tumors are in the ipsilateral (same) lung or are bilateral (both lungs).

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

Note: The tumors may be subtype/variants of the same or different NOS histologies.

Same NOS: Colloid adenocarcinoma 8460/3 and papillary adenocarcinoma 8250/3 are both subtypes of adenocarcinoma NOS 8140/3 but are distinct different histologies. Abstract multiple primaries.

Different NOS: Krasmuting squamous cell carcinoma 8071/3 is a subtype of squamous cell carcinoma NOS 8070; typical carcinoid 8240/3 is a subtype of small cell/neuroendocrine tumors (NET Tumors) 8041/3. They are distinctly different histologies. Abstract multiple primaries.

Component is not equivalent to subtype/variant.
Component is only coded when the pathologist specifies the component as a second carcinoma.
2018 Lung MP/H Rules

Table 3: Specific Histologies, NOS, and Subtype/variants

<table>
<thead>
<tr>
<th>Specific or NOS Histology Term and Code</th>
<th>Synonym of Specific or NOS</th>
<th>Subtype/variant of NOS and Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma 8140</td>
<td>Adenocarcinoma NOS</td>
<td>Acinar adenocarcinoma</td>
</tr>
<tr>
<td></td>
<td>Adenocarcinoma in situ</td>
<td>Adenocarcinoma (for lung only)</td>
</tr>
<tr>
<td></td>
<td>8140/2</td>
<td>8551*</td>
</tr>
<tr>
<td></td>
<td>Adenocarcinoma invasive</td>
<td>Adenocystic/adenocystic carcinoma</td>
</tr>
<tr>
<td></td>
<td>8140/3</td>
<td>8200</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Collard adenocarcinoma 8480</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fetal adenocarcinoma 8333</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lepidic adenocarcinoma/</td>
</tr>
<tr>
<td></td>
<td></td>
<td>adenocarcinoma, lepidic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>predominant 8250.3*</td>
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<tr>
<td></td>
<td></td>
<td>Mucinous carcinoma/adenocarcinoma</td>
</tr>
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<td></td>
<td></td>
<td>(for lung only) 8255.2*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>invasive 8255.3*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>minimally invasive 8257.3*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>microinvasive 8257.3*</td>
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<tr>
<td></td>
<td></td>
<td>preinvasive 8253.2</td>
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<td></td>
<td></td>
<td>Micropapillary adenocarcinoma/carcinoma 8265</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mucinous adenocarcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(for lung only) 8250.2*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>invasive 8256.3*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>minimally invasive 8256.3*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>preinvasive 8250.2*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Papillary adenocarcinoma 8260</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Polymorphous intermediate type</td>
</tr>
<tr>
<td></td>
<td></td>
<td>adenocarcinoma/enteric adenocarcinoma 8144</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Solid adenocarcinoma 8230</td>
</tr>
</tbody>
</table>

Rule M9: Abstract a single primary when there are simultaneous multiple tumors.
- In both lungs 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)

Note 2: NOS and subtypes/variants are:
- Adenocarcinoma 8140 and a subtype/variant of adenocarcinoma
- Mucinous adenocarcinoma and a subtype/variant of mucinous adenocarcinoma
- Non-small cell carcinoma 8046 and a subtype/variant of non-small cell carcinoma
- Sarcoma 8800 and a subtype/variant of sarcoma
- Small cell neuroendocrine tumor/NET 8841 and a subtype/variant of small cell neuroendocrine tumor/NET
- Squamous cell carcinoma 8070 and a subtype/variant of squamous cell carcinoma

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 pathologist states unequivocally that the tumors are 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.
# 2018 Lung MP/H Rules

## Table 2: Specific Histologies, NOS, and Subtype/Variants

<table>
<thead>
<tr>
<th>Specific or NOS Histology Term and Code</th>
<th>Synonym of Specific or NOS</th>
<th>Subtype/variant of NOS and Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small cell carcinoma/neuroendocrine tumors (NET Tumors) 8041</td>
<td>Reserve cell carcinoma</td>
<td>Atypical carcinoid 8249</td>
</tr>
<tr>
<td>Large cell carcinoma with neuroendocrine differentiation, lacks NE morphology and is coded as large cell carcinoma, not large cell neuroendocrine carcinoma</td>
<td>Round cell carcinoma</td>
<td>Combined small cell carcinoma 8045</td>
</tr>
<tr>
<td>Spindle cell carcinoma 8032</td>
<td>SCLC</td>
<td>Large cell neuroendocrine carcinoma/combined large cell neuroendocrine carcinoma 8013</td>
</tr>
<tr>
<td>Squamous cell carcinoma 8070</td>
<td>Small cell carcinoma NOS</td>
<td>Typical carcinoid 8240</td>
</tr>
<tr>
<td>Squamous cell carcinoma NOS</td>
<td>Small cell neuroendocrine carcinoma</td>
<td></td>
</tr>
<tr>
<td>Basaloid carcinomabasaloid squamous cell carcinoma 8083</td>
<td>Squamous cell carcinoma in situ 8070/2</td>
<td>Keratinizing squamous cell carcinoma 8071</td>
</tr>
<tr>
<td>Keratinizing squamous cell carcinoma 8071</td>
<td>Basaloid cell carcinoma</td>
<td>Non-keratinizing carcinoma 8072</td>
</tr>
</tbody>
</table>

## Table 2: Combination/Mixed Histology Codes

**Instructions:**
1. Compare the terms in the diagnosis (pathology, cytology, radiographic, clinical) to the terms in Column 1.
2. When the terms match, use the combination code listed in Column 2.
3. The last row in the table is a “last resort” code: adenocarcinoma mixed subtypes 8255.

**Note 1:** Do not use Table 2 in the following situations:
- For tumors with both invasive and in situ behavior, The Histology Rules instruct to code the invasive histology.
- When one of the histologies is described as differentiation or features
- When the terms are a NOS and a subtype/variant of that NOS, See the Histology Rules for instructions on coding a NOS and a subtype/variant in a single tumor or multiple tumors abstracted as a single primary.

**Note 2:** Some combinations can be either in situ or invasive; others are limited to a /2 or /3 behavior code.
- When a code is limited to in situ, /2 will be added to the code (both components are in situ)
- When a code is limited to invasive, /3 will be added to the code (both components are invasive)

**Note 3:** This table is not a complete listing of histology combinations.

Column 1 lists the required terms for the combination code.
Column 2 lists the combination term and code for histologies in Column 1.
### Component is not equivalent to subtype/variant.

Component is only coded when the pathologist specifies the component as a second carcinoma.
2018 Lung MP/H Rules

Rule M11 Abstract multiple primaries4 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.
  o 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 (SMEs) and the CoC site physician teams reviewed and approved these rules. Many of the CoC site teams physicians were also authors, co-authors, or editors of the AJCC Staging Manual.

Note 5: Lymph node involvement is recorded in staging criteria.

Rule M12 Abstract a single primary4 (the invasive) when an invasive tumor is diagnosed less than or equal to 60 days after an in situ tumor in the same lung.

Rule M13 Abstract multiple primaries4 when an invasive tumor occurs more than 60 days after an in situ tumor in the same lung.

The priority list is used for single primaries (including multiple tumors abstracted as a single primary)

This is a hierarchical list of source documentation.

1. Biomarkers
2. Tissue or pathology report (in priority order)
   A. Addendum(s) and/or comment(s)
   B. Final diagnosis
3. CAP protocol
   Note 1: Addendums and comments on the pathology report are given a high priority because they often contain information about molecular testing, genetic testing, and/or special stains which give a more specific diagnosis.
   Note 2: The pathologist’s diagnosis from the pathology report is always reliable, so the final diagnosis is the second priority.
   Note 3: The CAP protocol is a checklist which:
     • Provides guidelines for collecting the essential data elements for complete reporting of malignant tumors and optimal patient care.
     • Allows physicians to check multiple histologies
     Note: The CAP protocol must be documented in one location. Most frequently, in the:
       • The pathology final diagnosis
       • Addendum to the path report
4. Cytology (Fine needle biopsy, pleural fluid)
   Note 1: Code the behavior 3.
2018 Lung MP/H Rules

- Only **code features** when there is a **specific code** for the NOS with features in **Table 3** in the Equivalent Terms and Definitions, **ICD-O** and all **updates**.

Component is not equivalent to subtype/variant.
Component is only coded when the pathologist specifies the component as a second carcinoma

Anatomy of the Thorax – Lung & Pleura

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

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

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

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

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

Source: 2008 Encyclopedia Britannica, Inc. on-line

Lung Anatomy

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

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

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

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

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastases

N1 Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension

N2 Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)

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


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

A pleural effusion is an accumulation of fluid between the parietal pleura and the visceral pleura.

*Chest X-ray* frontal view: 100-200ml pleural fluid

Source: www.slideshare.net/pleuraleffusion/drmahesh
Pleura Anatomy


2018 Anatomic Staging – SS2018

SUMMARY STAGE 2018
GENERAL CODING INSTRUCTIONS
AUGUST 2018

Effective with cases diagnosed January 1, 2018 and Beyond

Prepared by
The Quality, Strategy and Improvement Branch
National Cancer Institute
National Institutes of Health
U.S. Department of Health and Human Services

Editors
Evelyn L. B. Miller, M.D., M.S.
Catherine Kief, M.D.
Sara E. Kief, M.D.

SUMMARY STAGE 2018 (STS2018) Coding Instructions

LUNG

Note 1: The following codes were added:

- 1421:24 – Carcinoma of bronchus, T1-2, N0, M0
- 1436:12 – Carcinoma of bronchus, T3-4, N0, M0

Note 2: The following codes were revised:

- 1421:1 – Carcinoma of bronchus, T1, N0, M0
- 1436:4 – Carcinoma of bronchus, T2, N0, M0
- 1421:2 – Carcinoma of bronchus, T3, N0, M0

Note 3: Category “Other” was revised to “Other primary,” as per the AJCC 8th edition coding manual.

Note 4: Tumor is defined as a mass, geographic, or diffuse, or mass with indeterminate features.

Note 5: Staging criteria are based on the AJCC 8th edition.

Note 6: Staging criteria are based on the AJCC 8th edition.

Note 7: Tumor is defined as a mass, geographic, or diffuse, or mass with indeterminate features.

Note 8: Tumor is defined as a mass, geographic, or diffuse, or mass with indeterminate features.

Note 9: Tumor is defined as a mass, geographic, or diffuse, or mass with indeterminate features.

Note 10: Tumor is defined as a mass, geographic, or diffuse, or mass with indeterminate features.

Note 11: Tumor is defined as a mass, geographic, or diffuse, or mass with indeterminate features.

Note 12: Tumor is defined as a mass, geographic, or diffuse, or mass with indeterminate features.

Note 13: Tumor is defined as a mass, geographic, or diffuse, or mass with indeterminate features.

Note 14: Tumor is defined as a mass, geographic, or diffuse, or mass with indeterminate features.
Cancer Staging Basics

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

- Incorporate SSDI Required for Staging for all cases.

Criteria Used to Stage Lung Cancer

- **What To Look For & Document When Reviewing Lung Cancer Cases**
  - Physical Exam – paraneoplastic syndrome, nerve or vessel obstruction
    - CT Chest – tumor location, tumor size, nodes, pleural effusion
    - CT Abdomen – liver or adrenal mets
    - CT/MRI Brain – brain mets
  - Pathology Report(s) – Resection of Primary and Nodal Status
    - Pathology Report(s) – Extension to/thru visceral pleura
    - Pathology Report(s) – Extension to parietal pleura
    - Cytology Report(s) – Pleural Fluid (blood/exudate)
  - Genetic Abnormalities – EGFR, KRAS, BRAF, ALK, ROS1, MET, RET, PDL-1, HER2
Lung Cancer – SS2018
Stage Criteria & Staging Notes

Stage Criteria & Staging Notes

1. Localized (not localized, NOS)
   • Adenocarcinoma in situ (AIS): adenocarcinoma with post lobular pattern, less than or equal to 3 cm in greatest dimension
   • Squamous cell carcinomas (SCC)

2. Regional by direct extension only
   • Atelectasis/obstructive pneumonitis
     o Extends to lobe region, involving part or all of lobe
   • Blood vessel(s) (major)
     o Aorta
   • Pulmonary artery or vein
   • Superior vena cava (SVC) syndrome
   • Carcinoma from lung
   • Compression of esophagus or trachea not specified as direct extension
   • Diaphragm (separate lesion—see code 7)
   • Esophagus
   • Main stem bronchus less than 2.0 cm from carina
   • Mediastinum, extrapleural, or NOS
   • Nerve(s)
     o Brachial plexus (Cain’s syndrome)
     o Recurrent laryngeal (cardiac paralysis)
     o Vagus
   • Pleural tumor (pleural effusion without tumor), NOS
   • Patient perforation
   • Patient pleural
   • Pericardium, NOS
   • Pleural space
   • Pleura, NOS
   • Pulmonary ligament
   • Separate tumor node(s) in the same lobe as the primary
   • Visceral pleura
   • Trachea

Note 3: "Atelectasis" is not the same thing as "obstructive pneumonitis" and should be coded as such.

Note 4: Atelectasis is the failure of the lung to expand (inflate) completely. This may be due to a blockage, a tumor, general anesthesia, pneumothorax or other lung diseases. Atelectasis is often a collapsed lung.

For staging purposes, a patient must present with an obstructing tumor (code 2).

Specific information about visceral pleural invasion (FL1 or FL2) or parietal pleural invasion (PL1) are coded as regional (code 2). Elastic layer involvement has prognostic significance for lung cancer.

Note 5: Specific information about visceral pleural invasion (FL1 or FL2) or parietal pleural invasion (PL1) are coded as regional (code 2). Elastic layer involvement has prognostic significance for lung cancer.
Lung Cancer – SS2018
Stage Criteria & Staging Notes

Regional lymph node(s) involved only
- **IPSLATERAL nodes only**
  - Bronchial
  - Carinal (bronchocarinal) (bronchial bifurcation)
  - Hilum (bronchopulmonary) (peripheral lobes) (bronchopulmonary root)
  - Interlobar
    - Lobar
    - Segmental
    - Subsegmental
  - Mediastinal, NOS
    - Aortic (above diaphragm), NOS
    - Esophagus, NOS
  - Pericardial, NOS
  - Paratracheal (left, right, upper, low, NOS)
  - Retracheal

- Post-paratracheal
- Pericardial
- Pericarlar
- Paratracheal, NOS
- Azygos (lower paratracheal)
- Pretracheal, NOS
- Regional lymph node(s), NOS
- Lymph node(s), NOS

- Skin of chest
- Stomach
- Vertebral (vertebral body)
- Visceral pericardium

- **Distant (nonsentinal), NOS**
  - Ipsilateral or **CONTRALATERAL**
    - Lower cervical
      - Peripheral nerve
      - Perineural
      - Subcutaneous (anterior deep cervical)
      - Sternal sulci
      - Supraventricular (anterior chest)
  - **CONTRALATERAL/BILATERAL nodes**
    - Carinal
    - Dural (bronchopulmonary) (peripheral lobes) (bronchopulmonary root)
    - Mediastinal
      - Aortic (above diaphragm), NOS
      - Trachea (tracheal), NOS
      - Ascending aorta (aortic)
      - Hilum (bronchopulmonary window)
      - Inferior mediastinum
      - Paracardial
      - Pulmonary ligament
      - Subcarinal
      - Tracheoesophageal
      - Superior mediastinum
      - Paratracheal (left, right, upper, low, NOS)
      - Retracheal
      - Pretracheal

- **Distant metastasis, NOS**
  - Circumsternal
  - Distant metastasis WITH or WITHOUT distant lymph node(s)

4 Regional by BOTH direct extension AND regional lymph node(s)
- Codes (2) = (3)

7 Distant site(s)/lymph node(s) involved
- **Distant site(s)** (including further contiguous extension)
  - Abdominal organs
  - Adjacent rib
  - Chest wall (thoracic wall)
  - Common carotid artery or main branches
  - Contralateral main stem bronchus
  - Heart
  - Inferior vena cava
  - Neural foramen
  - Percutaneous needle or pleural effusion (subpulmonary) (quadrant, contralateral, bilateral, NOS)
  - Pleural mass or nodes on ipsilateral lung (separate from direct extension) or contralateral lung
  - Rib
  - Separate mass or node(s) in contralateral lung
  - Separate mass or node(s) in a different ipsilateral lobe
  - Skeletal muscle
FCDS Lung Audits – 2014/2015 Diagnosis

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

FCDS Lung Audits – 2014/2015 Diagnosis

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

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

Source: International Association for the Study of Lung Cancer, 2008
2018 Anatomic Staging – AJCC TNM 8th ed

AJCC Cancer Staging Manual

8th Edition

VOLUME 67 | NUMBER 2
MARCH/APRIL 2017


Ramlak Rami-Porta, MD; Hideto Asamura, MD; William D. Travis, MD; Valerie W. Rusch, MD

Abstract: The revision for the eighth edition of this tumor, node, and metastasis (TNM) classification of lung cancer was based on analyses of the International Association for the Study of Lung Cancer database, which included 77,136 available patients diagnosed with lung cancer from 1999 to 2010. Among tumor (T) descriptors, the following new tumor size groups were created: T1a, T1b, T1c, T2a, T2b, T2c, T2d, T3a, T3b, T3c, T4a, T4b, T4c, T4d, T4e. The T-stages were redefined to reflect adenocarcinoma in situ, minimally invasive adenocarcinoma (MIA), invasive adenocarcinoma, and large cell carcinoma. For the most part, the descriptors have been modified to more accurately reflect the biology of the tumors and their behavior.

Keywords: lung cancer, lung cancer staging, non-small cell lung cancer, regional lymph node metastasis, small cell lung cancer, stage grouping, TNM classification, minimally invasive adenocarcinoma.
2018 Anatomic Staging – AJCC TNM 8th ed

TABLE 9. Schematic Summary of Patterns of Disease and TNM Classification in Patients Who Have Lung Cancer With Multiple Pulmonary Sites of Involvement

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>SECOND PRIMARY LUNG CANCER</th>
<th>SEPARATE TUMOR NODULE (INTRAPULMONARY METASTASIS)</th>
<th>MULTIFOCAL GG/L NODULES</th>
<th>PNEUMONIC TYPE OF ADENOCARCINOMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging features</td>
<td>Two or more distinct masses with imaging characteristics of lung cancer (eg, spiculated)</td>
<td>Typical lung cancer (eg, solid, spiculated) with separate solid nodule</td>
<td>Multiple ground-glass or part-solid nodules</td>
<td>Patchy areas of ground glass and consolidation</td>
</tr>
<tr>
<td>Pathologic features</td>
<td>Different histotype or different morphology by comprehensive histologic assessment</td>
<td>Distinct masses with the same morphologic features by comprehensive histologic assessment</td>
<td>Adenocarcinoma with prominent lepidic component (typically varying degrees of AIS, MIA, IPA)</td>
<td>Same histologic features throughout (most often invasive mucinous adenocarcinoma)</td>
</tr>
<tr>
<td>TNM classification</td>
<td>Separate cTMM and pTMM for each cancer</td>
<td>Location of separate nodule relative to primary site determines if T3, T4 or M1a; T1, N1 and M</td>
<td>T based on highest T lesion with (MM) indicating multiplicity: Single N and M</td>
<td>T based on size or T3 if in single lobe, T4 or M1a if in different (pulmonary or contralateral lobe) single N and M</td>
</tr>
<tr>
<td>Conceptual view</td>
<td>Unrelated tumors</td>
<td>Single tumor, with intrapulmonary metastasis</td>
<td>Separate tumors, albeit with similarities</td>
<td>Single tumor, diffuse pulmonary involvement</td>
</tr>
</tbody>
</table>


Cancer Staging Basics

- There are three components to AJCC Cancer Stage and to assign Summary Stage 2018:
  - Where and how big the original mass or primary tumor is = T
  - Which nodes the cancer has spread to including how many positive = N
  - Whether the cancer has spread to 1 or more distant site(s) = M

- The T, N, and M information is joined to assign a Summary Stage and an AJCC “Stage Group” (now called Anatomic Stage/Prognostic Group with addition of genetic and bio-molecular tumor markers and other prognostic factors in the AJCC 8th edition)

  - All cancers must be assigned 2018 Summary Stage – SS2018
    - All cancers can be assigned clinical stage – verify histology inclusion for TNM Chapter
    - Surgically resected cancers can be assigned pathological stage – verify histology inclusion list
    - Patients completing pre-surgical chemo, radiation, or other therapy can be assigned post-treatment stage
Site/Histo = AJCC Schema + Schema ID

Site/Histo = AJCC Schema + Schema ID
Clinical Classification - cTNM

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

Pathologic Classification - pTNM

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

* “Pathologic staging depends on the proven anatomic extent of disease, whether or not the primary lesion has been completely removed. If a biopsied primary tumor technically cannot be removed...and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.”
Post-Neoadjuvant \( p \) Classification - \( ypTNM \)

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

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

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

---

**T Category**

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>SUBCATEGORY</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in a specimen of biopsied tissue from the primary tumor</td>
<td></td>
</tr>
<tr>
<td>T1a</td>
<td>No evidence of primary tumor</td>
<td></td>
</tr>
<tr>
<td>T1b</td>
<td>Carcinoma in situ</td>
<td></td>
</tr>
<tr>
<td>T1c</td>
<td>Tumor 3 cm or less in greatest dimension, surrounded by fat or visceral organ, with or without residual tumor in the lymph nodes</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>Tumor more than 3 cm but not more than 5 cm in greatest dimension, with or without residual tumor in the lymph nodes</td>
<td></td>
</tr>
<tr>
<td>T2a</td>
<td>Tumor 1 cm or less in greatest dimension</td>
<td></td>
</tr>
<tr>
<td>T2b</td>
<td>Tumor more than 1 cm but not more than 2 cm in greatest dimension</td>
<td></td>
</tr>
<tr>
<td>T2c</td>
<td>Tumor more than 2 cm but not more than 3 cm in greatest dimension</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>Tumor more than 3 cm but not more than 5 cm in greatest dimension, with or without residual tumor in the lymph nodes</td>
<td></td>
</tr>
<tr>
<td>T3a</td>
<td>Tumor more than 3 cm but not more than 5 cm in greatest dimension, with or without residual tumor in the lymph nodes</td>
<td></td>
</tr>
<tr>
<td>T3b</td>
<td>Tumor more than 5 cm in greatest dimension</td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>Tumor more than 5 cm in greatest dimension, with or without residual tumor in the lymph nodes</td>
<td></td>
</tr>
</tbody>
</table>

---

81

82

41
**T Category**

<table>
<thead>
<tr>
<th>cT</th>
<th>CT Image on HRCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0 cm</td>
</tr>
<tr>
<td>0.6-3 cm</td>
<td>3 cm</td>
</tr>
<tr>
<td>≥3.5 cm</td>
<td>≥3.5 cm/11</td>
</tr>
<tr>
<td>0.6-3 cm</td>
<td>3.5 cm/11</td>
</tr>
<tr>
<td>1.1-3 cm/12</td>
<td>1.1-3 cm/12</td>
</tr>
<tr>
<td>2.1-3 cm</td>
<td>2.1-3 cm</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Radial part</th>
<th>Total tumor size</th>
<th>Pathologic Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>pN0</td>
<td>pN0(i-)</td>
<td>pN0(i+)</td>
</tr>
<tr>
<td>pN0(mol-)</td>
<td>pN0(mol+)</td>
<td>pN0(mol+)</td>
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</tbody>
</table>

**N Category**

<table>
<thead>
<tr>
<th>pT</th>
<th>Invasive part</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0 cm</td>
</tr>
<tr>
<td>0.6-3 cm</td>
<td>3 cm</td>
</tr>
<tr>
<td>≥3.0 cm</td>
<td>≥3.0 cm/11</td>
</tr>
<tr>
<td>0.6-3 cm</td>
<td>3.0 cm/11</td>
</tr>
<tr>
<td>1.1-3 cm/12</td>
<td>1.1-3 cm/12</td>
</tr>
<tr>
<td>2.1-3 cm</td>
<td>2.1-3 cm</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Pathologic Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAH</td>
<td>pT1a</td>
</tr>
<tr>
<td>AIS</td>
<td>pT1b</td>
</tr>
<tr>
<td>MIA</td>
<td>pT1c</td>
</tr>
</tbody>
</table>

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

- pN0
- pN0(i-)
- pN0(i+)
- pN0(mol-)
- pN0(mol+)
Lung Anatomy

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

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

IASLC Staging Survival Tree
**M Category**

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

**Anatomic Stage/Prognostic Groups**

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

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>T1a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>A1</td>
<td>T1a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>A2</td>
<td>T1b</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>A3</td>
<td>T1c</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>B</td>
<td>T2a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IA</td>
<td>T2b</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIB</td>
<td>Tla, Tlbc</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>IIB</td>
<td>T2ab</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>IIB</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIA</td>
<td>Tla, Tlbc</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td>IIA</td>
<td>T2a, T2ab</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td>IIA</td>
<td>T2</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>IIA</td>
<td>T4</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIA</td>
<td>T4</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>IIA</td>
<td>T4</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td>IIA</td>
<td>T4</td>
<td>N1</td>
<td>M1a</td>
</tr>
<tr>
<td>IIA</td>
<td>T4</td>
<td>N1</td>
<td>M1b</td>
</tr>
<tr>
<td>IIA</td>
<td>T4</td>
<td>N1</td>
<td>M1c</td>
</tr>
</tbody>
</table>

Small Cell Lung Cancer VALG Stage

- **Veterans Administration Lung Study Group’s (VALG) Staging Classification for Small Cell Lung Cancer**

- **Limited-Stage**: AJCC (8th edition) Stage I-II (excludes most T3-T4 due to multiplicity of tumors in same lung – cannot radiate for local control)

- **Extensive-Stage**: AJCC (8th edition) Stage IV and most T3-T4

Still use AJCC TNM when can be more specific. But, most clinicians will refer to the VALG “limited” or “extensive” when assessing for treatment options, particularly for inclusion/exclusion of XRT to chest when T3-T4.
2018 Lung Site-Specific Data Items

- REQUIRED for Staging - NONE

- RECOMMENDED for Clinical Care – CoC Required
  - Separate Tumor Nodules
  - Visceral and Parietal Pleural Invasion

- Registry Data Collection Variables - SSDIs not yet defined
  - Resection Margins
  - Adequacy of Mediastinal Dissection
  - EGFR Mutation
  - ALK Gene Rearrangement
  - Symptoms
  - Weight Loss
  - Performance Status
  - Prophylactic Cranial Radiotherapy
  - LVI and Perineural Invasion
  - Type of Visceral Pleural Invasion – PL1 versus PL2
  - SUV of Primary Tumor

Lung Cancer Primary Treatment Options

- Appropriate treatment for lung cancer is based on whether the tumor is small cell (13%) or non-small cell (84%), as well as the stage and molecular characteristics of the cancer.

- For early-stage non-small cell lung cancers, surgery is the usual treatment, sometimes with chemotherapy, alone or in combination with radiation therapy.

- Advanced-stage non-small cell lung cancer is usually treated with chemotherapy, targeted drugs (or a combination of the two), or immunotherapy.

- Small cell lung cancer is usually treated with chemotherapy, alone or combined with radiation; a large percentage of patients on this regimen experience remission, although the cancer often returns.
Standard Chemotherapy

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

Targeted Therapies

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

■ Class of Antineoplastic Agents for NSCLC – Target Gene Therapy
  - BRAF V600E – Tafinlar/Dabrafenib
  - BRAF V600E – Mekinist (Trametinib)
  - ROS1 – Xalkori (Crizotinib)

■ Class of Antineoplastic Agents for NSCLC – Immunotherapy
  - PD-1 – Keytruda/Pembrolizumab
  - PD-L1 – Tecentriq/Atezolizumab

■ Treatment Targets for NSCLC – Angiogenesis Inhibitors & Targets
  - Bevacizumab (Avastin)
  - VEGF Receptor Ramucirumab (Cyramza)

■ Maintenance Therapy for NSCLC – Chemotherapy
  - Alimta/Pemetrexed - stable disease, partial/complete response s/p Platinum

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

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

<table>
<thead>
<tr>
<th>EGFRmut</th>
<th>ALK rearrangement</th>
<th>ROS1 rearrangement</th>
<th>PD-L1 expression level</th>
<th>PD-L1 expression level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Targetable driver mutation present?</td>
<td>Yes</td>
<td>Measurable benefit with immunotherapy</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PD-L1 ≥ 50%</td>
<td>PD-L1 &lt; 50%</td>
</tr>
</tbody>
</table>

**Treatment: 1st line**
- **Standard Chemotherapy**
  - Cisplatin and etoposide
  - Carboplatin and etoposide
  - Cisplatin and irinotecan
  - Carboplatin and irinotecan

**2nd line**
- Osimertinib or<br>Platinum doublet with pembrolizumab or bevacizumab
- Pembrolizumab or<br>Platinum doublet with pembrolizumab
- Carboplatin and<br>Immune checkpoint inhibitor
- Docetaxel and<br>Bevacizumab or<br>Immune checkpoint inhibitor
- Docetaxel and<br>Ramucirumab or<br>Immune checkpoint inhibitor

**3rd line**
- Platinum doublet with pembrolizumab or bevacizumab
- Pembrolizumab or<br>Platinum doublet with pembrolizumab
- Carboplatin and<br>Immune checkpoint inhibitor
- Docetaxel and<br>Ramucirumab or<br>Immune checkpoint inhibitor

Consider clinical trial options from time of diagnosis and throughout treatment.

Abbreviations: PD-L1, programmed cell death 1 ligand 1; EGFRmut, EGFR mutated.

- Carboplatin/pembrolizumab is also FDA approved in this setting.
- Pembrolizumab use requires PD-L1 > 1%.

---

What about Small Cell Lung Cancer?

- **Standard Chemotherapy**
  - Cisplatin and etoposide
  - Carboplatin and etoposide
  - Cisplatin and irinotecan
  - Carboplatin and irinotecan

- **Radiation Therapy**
  - limited stage
  - post-chemo
  - brain mets
  - palliation

- **Surgery** – rare for SCLC

---

<table>
<thead>
<tr>
<th>Grade</th>
<th>Traditional</th>
<th>ENETs, WHO</th>
<th>Moran et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Carcinoid</td>
<td>Neuro endocrine carcinoma, grade 1</td>
<td>Neuroendocrine carcinoma, grade 1</td>
</tr>
<tr>
<td>Intermediate</td>
<td>Carcinoid</td>
<td>Neuro endocrine tumour, grade 2</td>
<td>Neuroendocrine carcinoma, grade 2</td>
</tr>
<tr>
<td>High</td>
<td>Carcinoid tumour, grade 3, small cell carcinoma</td>
<td>Neuroendocrine carcinoma, grade 3, small cell carcinoma</td>
<td>Neuroendocrine carcinoma, grade 3, small cell carcinoma</td>
</tr>
<tr>
<td></td>
<td>Small cell carcinoma</td>
<td>Neuroendocrine carcinoma, grade 3, large cell neuroendocrine carcinoma</td>
<td>Neuroendocrine carcinoma, grade 3, large cell neuroendocrine carcinoma</td>
</tr>
</tbody>
</table>

*Taken from North American Neuroendocrine Tumour Society guidelines, WHO: World Health Organization*
What about Carcinoid Tumor of Lung?

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

- Somatostatin Analogs – NOT TREATMENT FOR CANCER – treats symptoms of carcinoid syndrome
  - Octreotide/Sandostatin
  - Lanreotide/Somatuline

- Alpha Interferon

- Targeted Drugs – clinical trials – Sunitinib/Sutent & Everolimus/Afinitor

Text Documentation

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

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

- We will not include Histology Coding Practice Cases until we can confirm with MPH.

- We will not include Staging Practice Cases until we can confirm with AJCC & SS2018.

- We hope that by late 2018 we can provide a selection of practice cases from multiple sites and histologies for registrars to code number of primaries (MP/H Rules), histology and behavior (ICD-O-3 Codes and MP/H Rules) and to stage cases using SS2018 - Summary Stage 2018 with references to AJCC Cancer Staging, 8th ed and 2018 Site-Specific Data Items.
References and Resources

- WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart, 4th edition; World Health Organization, IARC, Lyon 2015
- The 2015 World Health Organization Classification of Lung Tumors; Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification; Journal of Thoracic Oncology • Volume 10, Number 9, September 2015
- Biomarker Testing of Specimens from Patients with NSCLC, CAP, June 2016
- AJCC Cancer Staging Manual, 8th edition; American Joint Committee on Cancer, 2017
- E-Cigarette Use Among Youth and Young Adults; A Report of the Surgeon General; DHHS, 2016
- NCCN Guidelines – Lung Cancer Screening, Non-Small Cell Lung Cancer, Small Cell Lung Cancer

References and Resources

- Perspectives in Lung Cancer Imaging, T Henzler, Journal of Thoracic Oncology Vol. 12 No. 1S
- Genetics of Non-Small Cell Lung Cancer, M Markman, K Vaux, emedicine@MedScape, April 10, 2018
- Lung Cancer Foundation of America - https://lcfamerica.org/research-grants/therapies/available-targeted-therapies/
- AJCC Histology and Topography Code Supplement, 8th edition, 2018
- College of American Pathologists – CAP Protocol Lung and Biomarkers Lung
- 2018 Multiple Primary and Histology Coding Rules - Lung
- ICD-O-3 Updates, NAACCR, Springfield, IL 2018
- Site-Specific Data Items Manual, NAACCR, Springfield, IL 2018
- Updated Molecular Testing Guideline for the Selection of Lung Cancer Patients for Treatment With Targeted Tyrosine Kinase Inhibitors – CAP, IASLC, AMP
Questions