Ted Bloch Lecture:
PET/CT Evaluation of Pulmonary Nodules

SNMMI SW 2019

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- Chair, Nuclear Medicine
- Mayo Clinic, Rochester MN
Disclosures

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  • Novartis/AAA/Endocyte
  • GE
  • Ipsen
  • MedTrace
  • Pfizer
  • Alnylam
  • Medtronic
Educational Objectives

1. Identify the role of PET/CT in evaluation of Pulmonary Nodules
2. Use pulmonary nodule descriptions which promote uniformity in terminology
3. Assess pitfalls in imaging
4. Propose how to adequately report pulmonary nodules to provide the best information requesting physicians
General Outline

- Solitary Pulmonary Nodule (SPN)
- Primary Thoracic Malignancies
- Staging
- Therapy follow-up
Lung Nodules: When is PET/CT useful?

- Diagnostic W/U
  - Cancer vs non-cancer
  - Cancer of unknown origin
  - Prognosis
  - Staging
  - Directing biopsy
- Therapy Monitoring
- Restaging
- Surveillance for Recurrence
Solitary Pulmonary Nodule (SPN)

- Indeterminate lung lesion < 30 mm mean diameter surrounded by normal lung
  - Round, solid, non-spiculated, non-calcified, no metastasis or history of cancer.

Francis et al. 2011
Wahidi et al. 2007
Solitary Pulmonary Nodule (SPN)

- Measure mean diameter on axial
  - Longest
  - Orthogonal
- < 3 cm = nodule
- < 3 cm = mass
Calcified Pulmonary Nodule

- Granuloma
  - Central
- Hamartoma (benign)
  - Popcorn
  - May contain fat
  - Mayo grow slowly
- Indeterminate
  - Eccentric (not central)
Solitary Pulmonary Nodule (SPN)

- Cancer vs. non-cancer
Solitary Pulmonary Nodule (SPN)

- Cancer vs. non-cancer
  - Sensitivity 80-100%
  - Specificity 40-100% - wide range

Francis et. al. 2011
Wahidi et al. 2007
Solitary Pulmonary Nodule (SPN)

• Cancer vs. non-cancer

• Meta-analysis:
  • Sensitivity 95%
  • Specificity 75%

Behzadi et. al. 2009
Wahidi et al. 2007
Solitary Pulmonary Nodule (SPN)
Cancer vs. granulomatous infection

**Round solid nodule, stable for 2 years = Benign**
Pulmonary Nodule Pitfalls

• False positive (Granulomatous)
  • Infection**
  • Fungal

Daniels et. al. 2007
Lung Nodule and Adenopathy
Fleischner Guidelines Do Not Apply

<table>
<thead>
<tr>
<th>Nodule Type</th>
<th>Management Recommendations</th>
<th>Additional Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solitary pure GGNs ≤5 mm</td>
<td>No CT follow-up required</td>
<td>Obtain contiguous 1-mm-thick sections to confirm that nodule is truly a pure GGN</td>
</tr>
<tr>
<td>Solitary pure GGNs &gt;5 mm</td>
<td>Initial follow-up CT at 3 months to confirm persistence then annual surveillance CT for a minimum of 3 years</td>
<td>FGD/PET is of limited value, potentially misleading, and therefore not recommended</td>
</tr>
<tr>
<td>Solitary part-solid nodules</td>
<td>Initial follow-up CT at 3 months to confirm persistence. If persistent and solid component &lt;5 mm, then yearly surveillance CT for a minimum of 3 years. If persistent and solid component ≥5 mm, then biopsy or surgical resection</td>
<td>Consider PET/CT for part-solid nodules ≥10 mm</td>
</tr>
<tr>
<td>Multiple sub-solid nodules</td>
<td>Obtain follow-up CT at 2 and 4 years</td>
<td>Consider alternate causes for multiple GGNs ≥5 mm</td>
</tr>
<tr>
<td>Pure GGNs ≤5 mm without a dominant lesion</td>
<td>Initial follow-up CT at 3 months to confirm persistence then annual surveillance CT for a minimum of 3 years</td>
<td>FGD/PET is of limited value, potentially misleading, and therefore not recommended</td>
</tr>
<tr>
<td>Dominant nodule(s) with part-solid or solid component</td>
<td>Initial follow-up CT at 3 months to confirm persistence. If persistent, biopsy or surgical resection is recommended, especially for lesions with &gt;5 mm solid component</td>
<td>Consider lung-sparing surgery for patients with dominant lesion(s) suspicious for lung cancer</td>
</tr>
</tbody>
</table>
Flip-Flop Fungus Sign: Draining Node Hotter than Nodule

• The Flip-Flop Fungus Sign represents a “Flip-Flop” of the ratio of activity expected with primary lung cancer
Acute
Subacute
Early
Chronic
Fungal Infection Lung Cancer

Flip-Flop Fungus Sign

• *Fungal Serology*
  • Negative
  • CT in 3 mo
  • Positive
  • Biopsy
Pulmonary Nodule Pitfalls

- False positive (Granulomatous)
  - Infection**
    - Fungal
  - Inflammation
    - Sarcoidosis
    - Wegner’s/GPA
    - Organizing pneumonia
    - Rheumatoid

Daniels et. al. 2007
Solitary Pulmonary Nodule (SPN)

Inflammatory nodules can mimic cancer

- Fluctuate in growth
- Wax and wane
- Different sites behave differently
Pulmonary Nodule Pitfalls

- Sarcoidosis
Pulmonary Nodule Pitfalls

• Sarcoidosis
Pulmonary Nodule Pitfalls

- Wegener’s granulomatosis - GPA
Pulmonary Nodule Pitfalls

• Cryptogenic organizing pneumonia
Rheumatoid Nodule vs Lung Cancer

1. ≥ 4 nodules
2. Peripheral location
3. Cavitation
4. Satellite nodules
5. Smooth border
6. Subpleural rind

At least 3
Sen: 77%
Spec: 92%

1. Low activity
   - $\text{SUV}_{\text{max}} = 2.7 \leq 2$
2. No avid nodes

Koslow et al 2019
Pulmonary Nodule Pitfalls

- Rheumatoid Nodule

Koslow et al 2019
Pulmonary Nodule Pitfalls

• Rheumatoid Nodule

Koslow et al 2019
# Systemic Patterns Suggest Inflammatory Diagnosis

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Common Areas of Activity</th>
<th>Less Common Areas of Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granulomatous infections</td>
<td>Lung nodules, draining nodes</td>
<td>Diffuse lung activity, diffuse nodal activity, focal spleen and liver, bone</td>
</tr>
<tr>
<td>Giant cell arteritis</td>
<td>Circumferential great vessel walls</td>
<td>...</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>Hilar and mediastinal nodes, perihilar and upper lung nodules</td>
<td>Extraparenchymal nodes, skeletal foci, diffuse of focal spleen and liver, perineural, meningeal</td>
</tr>
<tr>
<td>Fibrosing mediastinitis</td>
<td>Infiltrative perihilar and mediastinal</td>
<td>...</td>
</tr>
<tr>
<td>IgG4-related disease</td>
<td>Pancreas, lung nodules, lymph nodes, salivary glands, prostate</td>
<td>Infiltrative retroperitoneum, kidneys, orbits, bile ducts, thymus, meninges, aorta</td>
</tr>
<tr>
<td>Organizing pneumonia</td>
<td>Lung nodules, draining nodes</td>
<td>...</td>
</tr>
<tr>
<td>Granulomatosis with polyangiitis (Wegener)</td>
<td>Lung nodules, draining nodes, renal, brain, nasal, sinuses and Eustachian tubes, central airways</td>
<td>Orbits, eyes, synovium of joints, skin, pericardium,</td>
</tr>
<tr>
<td>Histiocytic processes (eg, Erdheim-Chester disease)</td>
<td>Long bone diaphysis, infiltrative retroperitoneum and mediastinum</td>
<td>Pituitary glands, orbits, lungs</td>
</tr>
</tbody>
</table>

Johnson et al 2015
Systemic IgG-4RD Pattern

Johnson et al 2015
Pulmonary Nodule Pitfalls

- False negative
  - Carcinoid
    - up to 85% FN

Erasmus et al. 1998
Pulmonary Nodule Pitfalls

• False negative
  • Carcinoid
  • Controversial
  • often positive

Daniels et. al. 2007
Pulmonary Nodule Pitfalls

- Carcinoid -> Ga68 DOTATATE
Pulmonary Nodule Pitfalls
Pulmonary Nodule Pitfalls

- Carcinoid -> Ga68 DOTATATE
Pulmonary Nodule Pitfalls

- *Carcinoid -> Ga68 DOTATATE*
- More sensitive than Octreotide SPECT/CT
Pulmonary Nodule Pitfalls

• False negative
  • Adenocarcinoma
    • Low grade
    • GGO +/-
    • *Slow growth*

• Old Grannies
  Don’t grow!

“No FDG Avid Cancer”
Solitary Pulmonary Nodule (SPN)

• Size of solid nodule
  • > 30 mm diameter (is a mass)
    • Likely cancer based on CT alone
  • < 10 mm diameter
    • Decreased NPV of PET
  • PET resolution (i.e. 2D -> 3D -> TOF)
    • Improves NPV of small nodules

Behzadi et. al. 2009
Solitary Pulmonary Nodule (SPN)

- Size of solid nodule (Scanner – Cancer type)
  - < 10 mm diameter
    - PET imaging resolution is an issue
      - SUV underestimates true metabolism
    - PET negative
      - “Too small to properly evaluate by PET”
  - PET positive
    - “Worrisome for cancer”
Improving Software Reconstruction

PL

TOF

3D

SUVm 3.86

SUVm 1.83

SUVm 1.58

5 mm

Johnson et al 2015
<table>
<thead>
<tr>
<th>4 mm</th>
<th>BPL</th>
<th>TOF</th>
<th>non-TOF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.6</td>
<td>0.9</td>
<td>0.8</td>
<td>Misregistered</td>
</tr>
</tbody>
</table>
Silicon Photomultipliers

25 mm LYSO crystals

Silicon Photomultiplier SSD

Photomultiplier Tube
Solitary Pulmonary Nodule (SPN)

- PET positive vs. negative
  - SUVmax 2.5 “cut-off”
    - Not recommended
  - Correlate to internal controls
    - Recommended
  - < SUVmax of liver
    - Likely benign
  - < SUVmax of blood pool
    - Very likely benign
  - Old Granny

Behzadi et. al. 2009
Typical CT features of Adenocarcinoma

- **Solid**
  - Invasive Adenocarcinoma
    - (mucinous can mimic)

- **Partsolid**
  - Minimally invasive to Invasive

- **Pure Ground-glass**
  - Atypical adenomatous hyperplasia to In-situ

Subsolid
Adenocarcinoma

• Ground glass, part-solid or solid
  • Solid
    • PET/CT helpful (SPN)
  • Ground glass opacity
    • PET/CT usually not helpful
      • Hot GGO is often infectious/inflammatory
      • Cold GGO could still be cancer

Hasegawa et. al. 2000
Exception That Makes The Rule

Brinjikji et al 2015
Adenocarcinoma

- Ground glass, part-solid or solid
  - Solid
    - PET/CT helpful (SPN)
  - Ground glass opacity
    - PET/CT usually not helpful
      - Hot GGO is often infectious/inflammatory
      - Cold GGO could still be cancer
  - Part-solid
    - PET/CT may be helpful

Hasegawa et. al. 2000
Part-solid Nodule

- When is PET/CT helpful?
  - Stable on CT 1-3 months
  - Solid component at least 10 mm

Okada et. al. 2011

2 months later
Part-solid nodule

- Stable part-solid nodule
  - PET negative
- New part-solid nodules
  - PET positive

1 week later

Reactive nodes
Infection

Adenocarcinoma
Infection

Okada et al. 2011
Part-solid nodule

- Serial CT for Diagnosis of Adenocarcinoma
- FDG PET/CT for Prognosis and Staging
- “No FDG Avid Cancer” – Don’t say this!!!
- Non-FDG avid nodule = can treat or follow

1 week later

Okada et. al. 2011
T-staging: Multifocal Adenocarcinoma

Multifocal adenocarcinoma represents multiple partially sub-solid lesions.

**Treatment of multifocal adenocarcinoma is guided by the presence of worrisome lesions, while balancing optimal lung preservation.**

- **Staging**
- T-stage by largest nodule with (m) designating multifocality.
- Each nodule is considered an independent primary.

- **Treatment**
- Save lung tissue
- Treat bad actors
- Prevent metastatic disease
- Watch for transformation to higher grade
Machine Learning Tools - CANARY

FDG PET adds to prognosis

Bartholmai et al 2015
Primary Lung Cancer

• Pathologic or presumed diagnosis based on CT
• Role of PET/CT?
  • Prognosis
    • Standard uptake value (SUV)
    • Metabolic tumor volume (MTV)
    • Total lesion glycolysis (TLG)
• Staging
  • Upstaged (7-26%)
  • Downstaged (6-17%)
• Directing biopsy

Maziak et. al. 2009
Heo et. al. 2011
Kalff et. al. 2001
Liao et. al. 2012
Volumetric Evaluation

SUVmax: 16.1
MTV: 1,018 cm³
TLG: 6,210
Stage: IIIA
Grade: Poorly Differentiated
Type: Sq. Cell
Age: 59
Sex: Female

SUVmax: 18.1
MTV: 18 cm³
TLG: 90
Stage: IIIB
Grade: Poorly Differentiated
Type: Sq. Cell
Age: 59
Sex: Female

Johnson et al 2015
Volumetric Evaluation

Davison et al 2013
T-staging: Atelectasis or pneumonitis

Any degree of atelectasis or pneumonitis is now considered stage T2.
• No longer a distinction between segmental versus entire lung involvement

PET/CT can be helpful to determine how much of the consolidated lung is tumor (1) versus true atelectasis (2).

<table>
<thead>
<tr>
<th>TMM 7</th>
<th>TMM 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2  Associated atelectasis or obstructive</td>
<td>Associated atelectasis or obstructive</td>
</tr>
<tr>
<td>pneumonitis extends to the hilar region but does not involve entire lung</td>
<td>pneumonitis extends to the hilar region and involves all or part of the lung</td>
</tr>
<tr>
<td>T3  Associated atelectasis or obstructive</td>
<td>No longer a descriptor (see T2)</td>
</tr>
<tr>
<td>pneumonitis of the entire lung</td>
<td></td>
</tr>
</tbody>
</table>
T-staging: Invasion

Local tumor invasion can be very difficult to evaluate and may require a multimodality approach to ensure adequate surgical planning.

**Teaching point**

MRI can be a useful modality to determine local tumor invasion.

CT best demonstrates local bony and gross soft tissue invasion. Mediastinal invasion was indeterminate based on the above CT.

PET/CT is not an appropriate modality to determine local invasion, as blooming artifact creates false positive results.

MRI allows for evaluation of tissue planes surrounding the tumor to determine areas of invasion, which was not observed on this exam.

The patient was able to undergo resection as the MRI demonstrated no mediastinal invasion.
T-staging: Invasion

At most centers, T3 disease is considered potentially operable, while T4 is non-surgical.

**TNM 8**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>T3</strong></td>
<td>Invades parietal pleura, chest wall, phrenic nerve, mediastinal pleura or parietal pericardium</td>
</tr>
<tr>
<td><strong>T4</strong></td>
<td>Invasion of the diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body</td>
</tr>
</tbody>
</table>

**Phrenic nerve invasion:** surgical

**Tracheal invasion:** non-surgical

**Recurrent laryngeal nerve invasion:** non-surgical

Recurrent laryngeal nerve invasion results in paralysis of the ipsilateral vocal cord. The contralateral vocal cord will compensate, resulting in **increased FDG-uptake**.

Teaching point

Thorough evaluation of tumor invasion is important as this determines patient operability.
T-staging: Two different primaries

Separate TNM staging for each primary lung cancer.

**Teaching point**

Staging of two separate primary lung malignancies requires individual TNM evaluation.

Two synchronous primary lung cancers result in a IA3 squamous cell carcinoma and a IIIA poorly differentiated NCSLC.

**Survival**

<table>
<thead>
<tr>
<th></th>
<th>IA3</th>
<th>IIIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 mo</td>
<td>90%</td>
<td>55%</td>
</tr>
<tr>
<td>60 mo</td>
<td>77%</td>
<td>36%</td>
</tr>
</tbody>
</table>

FDG-avid station 10L and 11L adenopathy.
T-staging: Pancoast tumors

Represent approximately 3-5% of all lung cancers

Characterization Criteria

- Invades the parietal pleura
- Causes pain secondary to invasion:
  - Muscles
  - Upper ribs
  - Thoracic vertebral bodies
  - Subclavian vessels
  - Inferior aspect of the brachial plexus
  - C7-T2 nerve roots
  - Hand and arm pain
  - Upper end of thoracic sympathetic chain
  - Stellate ganglion

Staging

<table>
<thead>
<tr>
<th>T3</th>
<th>Invades parietal pleura, chest wall or sympathetic chain</th>
</tr>
</thead>
<tbody>
<tr>
<td>T4</td>
<td>Invasion of the brachial plexus, vertebral body or vascular structures</td>
</tr>
</tbody>
</table>

Pancoast Syndrome

C8-T2 brachial plexus invasion results in radiating pain within the upper extremity, as well as weakness and atrophy of the intrinsic muscles of the hand.

Horner’s Syndrome

Invasion of the thoracic sympathetic chain and stellate ganglion results in ipsilateral ptosis, miosis and anhidrosis.

Teaching point

Hand pain in the setting of an apical lung cancer is highly concerning for brachial plexus involvement.
Teaching point

Resection of the brachial plexus in a Pancoast tumor can result in a non-functioning arm and must be avoided if possible.

**CT**
- Bone invasion
- Thoracic inlet invasion

**PET/CT**
- Initial staging
- Treatment strategy

MRI/MRA
- Brachial plexus
- Vertebral column
- Vascular structures

**Survival (IIIA)**

<table>
<thead>
<tr>
<th></th>
<th>24 mo</th>
<th>60 mo</th>
</tr>
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<tbody>
<tr>
<td>TNM 7</td>
<td>55%</td>
<td>36%</td>
</tr>
<tr>
<td>TNM 8</td>
<td>55%</td>
<td>36%</td>
</tr>
</tbody>
</table>

MRI is the best modality to assess for brachial plexus involvement.
PET/MR for Pancoast Tumors
Lung Cancer Lymph Node Metastases

• During initial diagnostic work-up
  • PET: 85% sens & 90% spec
  • CT: 61% sens & 79% spec
  • PET/CT: ~ 90% NPV

• Micro-metastases
  • CT will miss
  • PET & needle biopsy can also miss

• Infection/Inflammation

Gould et. al. 2003
In general, patients with stage N3 disease are considered surgically unresectable. Accurate nodal station identification is necessary to create a map for lymph node biopsy and determine potential surgical candidates.

**TNM 7 and TNM 8**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nx</td>
<td>Regional lymph nodes unable to be assessed.</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastases.</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including direct extension.</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in ipsilateral mediastinal and/or subcarinal lymph nodes.</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral/contralateral scalene or supraclavicular lymph nodes.</td>
</tr>
</tbody>
</table>

- **Station 1**: non-surgical
- **Station 7**: surgical
- **Station 4R/10R**: surgical
- **Station 4R**: contralateral non-surgical

**Non-surgical**
Non-small Cell Lung Cancer Staging

• *Non-surgical =
  • Contralateral mediastinal node
  • Supraclavicular node
  • Malignant pleural effusion
  • Distant metastasis
    • Brain, bone, liver, adrenal
Lung Cancer Distant Metastases

- Brain
  - PET/CT is at best a poor screening exam
    - High background normal brain activity
    - Mets can be seen as low or high activity
    - Recommend MRI for any PET finding

- Bone (Sens & Spec: 90% & 98%)
  - PET/CT is excellent and may add to or even replace conventional imaging

- Adrenal (Sens & Spec: 93% & 90%)
  - PET/CT very helpful, but still may require biopsy

- Liver
  - PET/CT excellent, but less well studied

Bury et. al. 1998
Kumar et. al. 2004
M-staging: Adrenal nodules

NSCLC is the most common primary to develop adrenal metastases.
- The reported incidence of solitary adrenal metastases in NCSLC is 4%
- The reported prevalence of an adrenal incidentaloma is 4-10%

**Teaching point**

NSCLC is the most common primary to develop adrenal metastases, but benign adenomas remain more common.

---

**Imaging Characteristics**

**Adrenal adenoma CT criteria**
- Non-contrast: 100% specific
  - Internal density <10 HU
- Contrast: 92% specific
  - Absolute: >60% washout in 15 minutes
  - Relative: >40% washout in 15 minutes

**Adrenal adenoma MR criteria**
- Chemical shift:
  - Compare in/out phase imaging to determine lesion lipid content
  - Not applicable to lipid-poor lesions

**PET/CT criteria**
- Benign versus malignant disease
  - ≥ 1.0 cm in size
  - Less FDG avid than general blood pool

In the setting of NSCLC, current guidelines recommend biopsy of concerning adrenal masses to rule out benign adenoma, if imaging is non-diagnostic.

McClean et. al. 2001
CT: suspected M1 adrenal

Out of Phase MR
M-staging: Adrenal nodules

- Pathologic results will determine M0 versus M1b stage

Teaching point

If imaging cannot prove a solitary adrenal nodule is benign, a biopsy is recommended for further evaluation.
M-staging: Brain metastases

NSCLC is the most common primary to develop brain metastases.

**NCCN Guidelines (Screening MRI)**
- Stage T1 plus N1-2
- Stages T2-T4 regardless of N disease.
- Symptomatic patients

**Teaching point**
Screening contrast-enhanced MRI is recommended for symptomatic patients or newly-diagnosed NSCLC stages T1/N1-2 and T2-T4.
PET/MR for Advanced Lung Cancer
Post-therapy Follow-up

- Surgery
- Radiation
  - External Beam
  - Focused radiation
    - Intensity-Modulated Radiotherapy (IMRT)
    - Stereotactic Body Radiotherapy (SBRT)
- Chemotherapy
Follow-up Post Surgery

• Infection/aspiration/healing activity
• Reactive nodes common
• Cancer recurs where cancer was before
  • Compare to pre-op PET/CT
  • Focus on suture lines, hilum
Follow-up Post External Beam Radiation

- Wait > 3 weeks post therapy
- Focal and increasing activity is worrisome
- Diffuse or decreasing activity less worrisome
  - But may mask cancer
  - Symptomatic pneumonitis - steroids
- Infection common
- Reactive nodes common
- FDG activity before CT changes appear
Follow-up Post Focused Radiation

- Harder to differentiate residual/recurrent cancer
- Activity should be decreasing after ~ 1 month
- Expect focal activity for up to 6 months
- First PET/CT in 3-4 months is baseline only
  - Serial scans helpful
- Alternative: image 24-48 hours post-therapy
  - Before inflammatory FDG activity begins
  - After cells are killed (stunned?)
  - This approach is under investigation
Follow-up Post Focused Radiation

- Intensity-Modulated Radiotherapy (IMRT)

4 Month F/U = baseline
Follow-up Post Focused Radiation

- Stereotactic Body Radiotherapy (SBRT)

- 4 Month F/U, resolving pneumonitis on steroids

- 9 Month F/U = recurrence
Post Chemotherapy

• Therapy Monitoring
  • After 1-3 of 6 cycles
  • Scan 1-3 days before next cycle

• Restaging
  • 4-6 weeks after full therapy (6 cycles)

• Long-term surveillance
  • Compare to previous and initial pre-therapy PET/CT
Chemotherapy Monitoring

- After only 1-3 cycles
- Better prediction of long-term outcome than restaging PET/CT?
- Stop/switch ineffective therapy in mid course
- CT findings may be unchanged
Chemotherapy Monitoring
Better prediction of long-term outcomes

Monitoring
Restaging

# cancer cells

Good outcome

Poor outcome

PET detectable

Cycles of Chemo
Restaging Criteria (Hopkins)

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$^{18}$F-FDG uptake less than mediastinal blood pool consistent with complete metabolic response</td>
</tr>
<tr>
<td>2</td>
<td>Focal $^{18}$F-FDG uptake greater than mediastinal blood pool but less than liver, consistent with likely complete metabolic response</td>
</tr>
<tr>
<td>3</td>
<td>Diffuse $^{18}$F-FDG uptake greater than mediastinal blood pool or liver consistent with probable inflammation</td>
</tr>
<tr>
<td>4</td>
<td>Focal $^{18}$F-FDG uptake greater than liver consistent with likely residual disease</td>
</tr>
<tr>
<td>5</td>
<td>Focal and intense $^{18}$F-FDG uptake consistent with residual disease</td>
</tr>
</tbody>
</table>

Sheikhbahaei et al 2016
Restaging Criteria

Sheikhbahaei et al 2016

[Graph showing survival curves for PET positive and PET negative cases]
Restaging Criteria

Sheikhbahaei et al 2016
Surveillance

- Bad word!!!
  - CMS does not like “surveillance
- Scans after 1+3 still have benefit
  - 28% change clinical management
- Clinical suspicion
  - Labs
  - Symptoms
  - Imaging
- Interval Therapy

Marcus et al 2015
Pseudo-progression

- Programmed Cell Death
  - Drugs target PD-1 pathway (check-point)
- Multiple drugs now used in lung cancer
  - The “abs” (example - nivolumab)
- Can turn on immune system to kill cancer
  - Can look like progression on CT and PET
  - Peeks at 8 weeks post therapy
- Can turn on immune system to attach self
- Hard to differentiate on 1 follow-up scan
- Did the tumor change behavior?
- An immune response is GOOD!

Nishino et al 2016
Conclusions

- PET/CT useful for:
  - Cancer vs non-cancer
  - Prognosis
  - Staging
  - Directing biopsy
  - Therapy follow-up

- Know caveats, limitations, artifacts and pitfalls
Question 1

• A 1.5 cm part-solid lung nodule that has been stable for 2 years on CT and has FDG activity < blood pool
  A. Is very likely benign
  B. No longer needs to be followed with imaging
  C. Is an active infectious or inflammatory lesion
  D. May represent indolent adenocarcinoma
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Question 2

• A patient has biopsy proven squamous cell cancer in her left upper lobe. Which of the following features make surgery unlikely to lead to cure (a non-surgical candidate).
  A. Left hilar nodal metastasis (station 10L).
  B. Malignant cells in a left pleural effusion.
  C. Chest wall invasion including the third rib.
  D. Subcarinal metastasis (Station 7).
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Question 3

• Ga68-DOTATATE PET/CT is…
  A. Better than FDG PET/CT for non-small cell lung cancer
  B. More sensitive for carcinoid tumors than In11-octreotide SPECT/CT
  C. Widely available due to oversupply of Ga68
  D. Useful to predict response to I131-MIBG therapy
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Question 4

• A positive flip-flop fungus sign
  A. Is when a lung nodule is more FDG avid than the draining lymph nodes
  B. Together with a positive fungal serology, suggests a biopsy is required
  C. Suggests it is time for new flip-flops
  D. Suggests that testing fungal serologies followed by repeat CT may be an option
Question 4

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Question 5

• In patients with multifocal primary pulmonary adenocarcinoma
  A. Treatment is based solely on the most worrisome nodule
  B. Treatment is avoided because all of these patients do well
  C. Treatment is a balance between preserving lung function and treating the most worrisome lesions
  D. Treatment assumes that the lesions are mostly metastatic
Question 5

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