Basics of PET/CT Imaging

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Objectives

• Basic PET imaging
• Evaluating the therapeutic response
• Evaluating the big 5
  ➡ Lymphoma
  ➡ Breast
  ➡ Lung
  ➡ Colon
  ➡ Head and Neck

Objectives

• … and the little 5
  • melanoma
  • gynecologic malignancies
  • neuroendocrine
  • esophageal
  • Other GI

Basic PET imaging

F-18 FDG

• Fluorine 18-fluorodeoxyglucose (F-18 FDG)
• FDG = Glucose Analog
• Main radiotracer in PET imaging
  • Half life 109 minutes (Tc-99m 6 hours)
  • F-18 cleared rapidly cleared through kidneys
  • Excreted through the kidneys

PET/CT

• PET Basics
  • Malignant cells
  • have enhanced glucose metabolism compared to non-malignant cells (malignant cells love sugar)
  • Have enhanced glucose transporters
PET basics

• What is the difference between glucose and F-18 FDG?
  - Glucose and F-18 FDG both are metabolized by malignant cells
  - Glucose enters the Krebs cycle and metabolizes
  - F-18 FDG does not enter the Krebs cycle

Patient preparation

• correct patient preparation is vital to obtain maximum diagnostic yield
• Goal: to maximize uptake in pathologic tissues and minimize physiologic activity

Patient preparation

• NPO for 6 hours prior
• Patient DONT’s
  - low carbs
  - no caffeine, candy or cigarettes
  - no exercise
  - NPO 6 hours prior to exam
  - Diabetic patients
    - perform study in afternoon
    - no insulin or eating 6 hours prior to exam
    - no exam if glucose > 200
  - Usual meds taken day of exam

PET scan timing

• Post biopsy - 1 week
• Post chemotherapy or post surgery
• 4-6 weeks
• Post-radiation or radio-immunotherapy
• 8-12 weeks
• Bone marrow stimulating agent -
• Can persist for up to 4 weeks

PET / CT protocol

• PET
  - 60 minute uptake following injection of radio tracer
  - Scanned from skull vertex (or skull base) to proximal femurs
  - lower extremities included for T-cell lymphomas or melanoma
• CT
  - Oral, IV contrast not given unless specifically ordered
The PET/CT scan

Evaluating therapeutic response

**SUV**
- Standard Uptake Value measurements depend on several factors:
  - standardizes uptake from patient to patient
    - tracer activity in tissue injected dose/pt. weight
  - nonetheless, variability from different manufacturers and even similar models
  - significant changes in body habitus -
    - eg - large patient with significant weight loss in 6 months has a repeat scan
    - SUV tends to be higher
  - 2.5 SUV serves as a very general cut-off between benign and malignant

**FDG PET for evaluating treatment**
- Treatment strategies are evolving and response assessment is needed
- PET/CT plays an increasing role in monitoring therapy
  - Complete metabolic Response - no residual activity
  - Partial metabolic response - improved; 25% decrease in SUV
  - Stable metabolic disease - no change; within 25% change in SUV
  - Progressive metabolic disease -
    - significant increase in activity of > 25% OR
    - new metastasis

**history of Lymphoma**
- initial staging
- 4 months later

The big 5
- Lymphoma
- Breast Cancer
- Lung Cancer
- Colon Cancer
- Head and Neck cancer
Lymphoma

- Hodgkins and Non-hodgkins
  - Age distributions
    - Hodgkins - bimodal - teens/20’s and elderly
    - Non-Hodgkins - increases with age

Lymphoma

- FDG avidity in Lymphoma
  - Hodgkins - typically FDG avid
  - Non-Hodgkins - variable
    - diffuse large B-cell - high
    - Marginal Zone (MALT) - variable
    - Mantle Cell - low

<table>
<thead>
<tr>
<th>Subtype</th>
<th>FDG Up take</th>
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<tbody>
<tr>
<td>B-cell NHL†</td>
<td>High</td>
</tr>
<tr>
<td>Diffuse large B-cell lymphoma</td>
<td>High</td>
</tr>
<tr>
<td>Burkitt lymphoma</td>
<td>High</td>
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<tr>
<td>Large cell anaplastic lymphoma</td>
<td>Low to moderate</td>
</tr>
<tr>
<td>Follicular lymphoma (grade 3)</td>
<td>Low to moderate</td>
</tr>
<tr>
<td>Follicular lymphoma (grades 1 and 2)</td>
<td>Low to moderate</td>
</tr>
<tr>
<td>Mantle cell lymphoma</td>
<td>Low to moderate</td>
</tr>
<tr>
<td>Marginal zone lymphoma (MALT)</td>
<td>None to high</td>
</tr>
<tr>
<td>Small lymphocytic lymphoma</td>
<td>None to low</td>
</tr>
</tbody>
</table>

Hodgkins disease

- Nodal or extranodal type
  - Nodal mature type
  - Micromucosa lymphoma
  - Lymphocytic predominant type
    - Lymphocytic predominance type
  - Follicular lymphoma
  - Extramedullary hematopoietic lymphoma
  - Periphera T-cell lymphoma
  - Anaplastic large cell lymphoma
  - Classical Hodgkin lymphoma
  - MALT lymphoma
  - Burkitt lymphoma
  - Peripheral T-cell lymphoma
  - Anaplastic large cell lymphoma
  - Classical Hodgkin lymphoma
  - MALT lymphoma
  - Burkitt lymphoma

14 y/o with Hodgkins Lymphoma
Lymphoma and FDG avidity
- FDG uptake determined by many factors
  - histologic features (HL vs. NHL)
  - grade (indolent vs aggressive)
  - viable tumor cell fraction
  - tumor cell proliferation
  - upregulation of glucose receptors
  - presence of hypoxia
- there can be considerable differences between lesions of same histology and tumor grades

PET/CT in Lymphoma
- Indications
  - staging with FDG avid potentially curable lymphoma
    - diffuse B-cell
    - hodgkin disease
  - Not indicated
    - incurable
    - non-FDG-avid, variable activity or indolent subtypes
    - grade 1 Follicular, marginal cell, mantle cell

Nodal involvement
- most common in Hodgkin and Non-Hodgkin lymphoma
- most common extra-nodal sites of NHL
  - stomach
  - skin
  - small bowel
- but, almost any organ has been documented to have lymphomatous involvement

75 y/o with recent dx of NHL
- bilateral femoral involvement
- no known BMSA or chemotherapy
- Marrow involvement indicates stage IV disease

Lymphoma - recent completion of chemotx
- Recent completion of chemotx
- persistent mass present on CT
- physiologic activity seen on PET
- Mass shows no activity, representing treated disease
extra-nodal NHL

Nasopharyngeal activity

Diffuse bone marrow involvement

skin lesion

Lymphoma caveats

- Bone Marrow involvement indicates a worse prognosis
- Residual activity in patients that have recently completed chemotherapy means poorer prognosis
- The greater the activity, the worse the prognosis

Breast Cancer
PET and Breast Cancer Diagnosis

- Detection of breast masses
- Sensitivity: 88%, Specificity: 80%
- Dependent on tumor size
- Sensitive for breast lesions > 1 cm
- Sensitivity markedly increases for large lesions
- ANY INCIDENTAL LESION IN THE BREAST THAT IS FDG AVID REQUIRES ADDITIONAL WORK-UP
- Mammo, US, Breast MRI

Staging

- PET/CT useful in staging when:
  - Advanced disease is suspected
  - 80-95% sensitive in detecting distant mets
  - Patient 'high risk'
  - Tumor is T3 (> 5 cm) or T4 (direct extension to the chest wall and/or skin)
  - Tumor is medial / upper breast
  - Higher risk for internal mammary/supraclavicular lymph node spread

Staging - nodal

- Axillary staging
  - PET/CT is not a substitute for axillary nodal dissection in early stage cancer
  - Not sensitive enough to detect positive axillary LN
  - False negative LN
    - Smaller (< 5 mm)
    - Fewer LN present
  - PET/CT best when LN are numerous

72 y/o female diagnosed one month prior

- No treatment yet
- Large breast mass with axillary and retroclavicular
- Tumor extends to skin surface
- Bone mets to sacrum

same patient

- Numerous pulmonary nodules not detected by PET
- PET sensitivity is 1 cm
- Stage IV breast cancer

same patient w pulmonary mets
Restaging

- Risk of recurrence greatest in 1st 5 years after treatment
- Pt. Educated on symptoms
  - New lumps
  - Bone, chest or abdominal pain
  - Persistent headaches
- Breast MRI not recommended for routine surveillance

49 y/o with breast CA

- Diagnosed initially 6 years prior
- Recurrence 2 years prior
- Bilateral mastectomy
- Normal PET scan

same patient 1 year later

- Extensive mets
  - Liver
  - Bone
  - Brain
  - Nodes

same patient 18 months later

- Resolution of bone lesions in lumbar spine and sacrum
- New lesions seen in bones and liver
- Progression of disease

RM - disease progression

2009  2010  2012

33 y/o with breast CA diagnosed 2 years prior

- Pt s/p lumpectomy and radiation and chemotx
- Masses found on recent PET/CT
- Breast MRI and US
- Breast CA recurrence
one year later

• TRAM flap reconstruction of the left breast
• New hypermetabolic mass in left breast

Breast CA recurrence in the reconstructed breast

Lung Cancer

• PET/CT is used in management of non-small Cell lung cancer
  • Detection
  • Staging
  • Re-staging

Other Lung Cancers

• Small cell Lung Cancer
  • Intensely positive with PET
  • But, usually metastatic at time of diagnosis
  • Treatment is palliative
  • Carcinoid / Neuroendocrine
    • can be moderate to low activity (2-4 SUV)
    • Why is carcinoid not FDG avid?
  • Mesothelioma
    • Intensely positive on PET
  • Bronchioalveolar Carcinoma
    • only 50% positive — SUV ranges from 1.5 to 3.5

Lung Cancer Detection

• all lung CA FDG avid
• Size of the nodule determines detection, regardless of the histologic type
  • > 1cm - PET reliable at detection
  • 7-10 mm - PET is usually reliable
  • <7 mm - PET not reliable
• SUV of primary nodule may be proportionate to the aggressiveness of the cancer
Recent Dx of Lung CA

S Sign of Golden

Solitary Pulmonary nodule

- When should PET be used?
  - indeterminate nodule seen on CT
  - Clinician needs to assess likelihood of malignancy
    - patients age
    - smoking history
    - history of other malignancy
  - Radiologist assess SPN
    - density, calcifications, growth, margins, size, satellite nodules

PET imaging of SPN

- If high risk, then should proceed to biopsy
- PET CT should be performed when:
  - indeterminate findings in a difficult to biopsy nodule
  - patient is averse to biopsy
  - discordant clinical/radiologic findings
    - low risk patient / suspicious imaging
    - high risk patient / benign appearing nodule

Hx of Panic attacks

PET detects unexpected distant metastasis in 10-20% of lung cancer cases

- PET has poor sensitivity when compared to MRI in detecting brain metastasis
  - MRI is performed when patient is symptomatic
- PET performs well for adrenal metastasis
- PET is comparable to bone scan for osseous metastasis

2.5 or not 2.5

- old school thinking of SUV of pulmonary nodules
  - > 2.5 malignant
  - < 2.5 benign
- Study from Japan in 2006
  - if using 2.5 as cut off
    - 37% called benign were malignant
    - 11% were malignant with SUV < 1.6
    - no visible activity - 0% malignant (100% sensitive, 63% specific)
    - lower the activity, less likely to be malignant

Distant metastasis
Bone metastasis
- Bone scan may not be best
- theoretically
  - sclerotic lesions - bone scan better
  - lytic lesions - PET scan better
- reality - PET detects both well

Pleural disease
- mesothelioma and metastasis are intensely FDG avid
- activity within pleural effusion-
  - 90% accuracy of being malignant effusion
- Benign conditions that are FDG avid
  - asbestosis
  - post-radiation inflammation
  - infection/inflammatory

Hx of SOB
59 y/o female presents for restaging
- Currently receiving chemotherapy
- Patchy distribution related to mets
- Pleural distribution bilaterally
- Dx: mesothelioma

same patient
Metastatic breast cancer
With metastatic and pleural involvement

Mesothelioma vs. Pleural mets
Colon Cancer

Colon CA

- PET used to stage and re-stage colon carcinomas
- Challenge is in determining tumor recurrence.
  - post-surgical fibrosis
  - radiation changes -
    - may have to wait 6 months effectively differentiated radiation changes from residual tumor
    - 3 months typical

Colon CA

- Routes of spread
  - local
  - liver
  - abdominal LN
  - lung

hx of colon cancer

Head and Neck Cancer

Indications of PET/Ct

- Detecting and Localizing unknown primary malignancies
- Staging - regional nodes or distant metastasis
- Restaging
  - following treatment
- Directing biopsies
- many head and neck cancers are squamous cell carcinoma and usually FDG avid
Floor of mouth cancer

Unknown primary tumors
- typical scenario
- pt presents with neck mass
- biopsy positive for SCCa
- no mucosal lesion found on physical exam
- PET can be used to direct biopsy

PET guides biopsy to the base of the right tongue - positive for SCC

Little 5
- Melanoma
- Gynecologic Malignancies
- Neuroendocrine
- Esophageal and Gastric
- Other GI (hepatic, biliary, pancreatic)

Melanoma
- Accounts for 1-2% of cancer deaths/yr
- Stage I and II - negative lymph nodes
- Stage III - positive LN metastasis
- Stage IV - distant metastasis
- Poor prognosis remains in those with metastatic disease
Melanoma

- Prognostic factors
  - number and size of lesions
- Surgical excision of metastatic LN remains the only effective tx for cure.
- Melanoma can metastasize to any organ.

Melanoma and PET

- Excellent modality for staging disease
- Indications
  - tumor thickness > 4mm and high risk for metastasis
- Limitations of PET
  - Brain metastasis
  - small size of tumor
  - necrotic masses
  - slow growing tumors

Gynecologic Malignancies

Ovarian carcinoma

Early detection

- No single modality has proven reliable or cost effective
- CA-125
- Pelvic / transvaginal US
- Pre-menopausal
  - Most ovarian masses are benign and followed until regression
- Post menopausal
  - Ovarian masses more likely to be malignant

Ovarian Carcinoma

PET/CT screening

- No systematic studies for ovarian cancer detection
- High radiation burden, cost
- What about the incidentally noted ovarian uptake?
  - Must be followed
  - Pre-menopausal
  - Physiologic activity in functional lesions
  - Post menopausal patients is always more concerning
Detection

- Detection of ovarian cancer by PET is frequently an unexpected finding
- Any activity in the adnexa in a postmenopausal patient worrisome for cancer!!

Recent diagnosis of breast cancer

- Minimal uptake in left breast from recent biopsy
- Activity noted in right adnexal region
- BRCA positive

Recent diagnosis of breast cancer

Dx: ovarian carcinoma

Routes of spread - lymphatic

- Lymphatic
  - Ovarian veins  para-aortic LN
  - Broad ligament  pelvic LN
  - Round ligament  inguinal LN

ovarian CA - sister mary joseph nodule

In 1928, sister Mary Joseph said to Dr. Mayo while doing rounds on patients:

Sir, I have been noting this umbilical node in most of our cancer patients!

Excellent observation, sister. I am going to publish a paper on this!

http://medicalmemories4u.blogspot.com
NW - 67 y/o with abdominal pain
- Extensive peritoneal activity
- Similar in appearance to ovarian carcinoma
- Omentum and bowel serosa involved

NW - same patient

NW - same patient

Fallopian tube carcinoma
- Least common gynecologic malignancy
- 4 per 1,000,000
- 1/3 of patients have breast CA
- CA-125 elevated

Fallopian tube p tx

History of vaginal CA
- Vaginal CA
- Rare
- Spreads usually through direct local invasion
- Activity confined to left vaginal wall
- Vaginal involvement usually due to metastases from other GU CA

Fallopian tube carcinoma
Neuroendocrine tumors (NET)
- Heterogenous group of relatively uncommon neoplasms
- Originate from neuroendocrine cells
- Histologically diverse
- Clinical challenge in diagnosing:
  - Variable clinical manifestations
  - Slow growth

Neuroendocrine tumors (NET)
- Clinically
  - Functional - release of amines
    - Diarrhea, flushing, pain, asthma
  - Non-functional
    - Symptoms relate to mass effect from the tumor
    - Depending on anatomic site, metastasis may have already occurred

Neuroendocrine tumors
- Most common sites
  - Gastro-entero-pancreatic (GEP)
  - Bronchi/lungs
- Less common
  - Skin
  - Adrenal glands
  - Thyroid

Neuroendocrine tumors (in the lung)
- All arise from Kulchitsky cells of bronchial mucosa
- Aggressiveness depends on mitotic activity
- Most aggressive - SCLC
- Least aggressive - Carcinoid
Merkel Cell carcinoma
- neuroendocrine tumor of the skin
- similar to melanoma
- can be aggressive
- seen with sun exposure in light skinned individuals
- variable activity on PET FDG

Esophageal and Gastric cancers

Esophageal Cancer
- re-staging
  - PET good for assessing response to radiation therapy and resection
  - Recurrence
    - surgical bed
    - distally in liver, lung and bone

Esophageal Ca
- Esophageal CA diagnosis
  - High affinity to all types of esophageal CA
  - False negatives are due to small size of tumor
  - Caveat: distal esophageal activity prevalent in esophagitis, GERD, hiatal hernia

Stomach Cancer
- FDG accumulates in gastric mucosa
- small lesion detection is difficult, therefore assessing primary CA is of limited value
- better at assessing regional spread of disease
Other GI

Hepatic Malignancy
- Liver normally demonstrates heterogenous activity
- makes small lesion detection difficult
- HCC detection = 1/degree of tumor differentiation
- well differentiated —> low activity
- however, once detected, useful in evaluating distant mets
- Hepatic adenoma —> FDG avid

Pancreatic Cancer
- staging better assessed with CT or MRI
- subtle findings such as vascular invasion cannot be detected
- can be helpful in
  - assessing distant mets
  - differentiating pancreatic CA vs. pancreatitis

Cholangiocarcinoma
- nodule type —> 80% detection
- infiltrative type —> 20% detection
- false positive —> inflammation from biliary obstruction

Conclusion
- PET/CT scanning revolutionized oncologic imaging
- Breast, Lymphoma, and Lung Cancers are most frequently imaged malignancies
- PET scan is dependent on glucose receptors, but other factors also determine scan quality
- Many pitfalls exist and are critical in understanding prior to interpretation