“The Importance of PET/CT in Human Health”

Homer A. Macapinlac, M.D.
Learning objectives

• Provide an overview of the impact of PET/CT imaging on the management of patients and its impact on health care expenditures.

• Review the current use of PET/CT in the multi-disciplinary care of oncology patients, with emphasis on its utility in adaptive therapeutic strategies.
Summary

• FDG PET/CT impacts the management of patients in nearly all solid tumors.
• In USA, reduction in reimbursement of FDG PET/CT, reduced utilization and its cost remains low compared to total cost of care
• Novel tracers approval requires large randomized trials to prove survival benefit.
78-y-old man with NSCCa of the lung.

(A) Large isodense mass seen on CT.

(B) PET scan shows a hypermetabolic rim of increased FDG uptake, with necrotic center.

(C) Fused image shows good alignment of 2 modalities. Lymph node in mediastinum (arrow) also demonstrated increased FDG uptake.
Global Cancer Problem

- 14.1 million cancer cases and 8.2 million cancer deaths occurred in 2012 worldwide.
- Economically developing world account for:
  - 56% of the cases
  - 64% of the deaths
- By 2030: 21.7 million cancer cases per year
  - 13 million cancer deaths
  - 60-70% of cases in developing world
Global Cancer Facts

- Lung cancer most common in men globally
- Prostate ca most common in developed countries
- Breast ca is most common type among women
  - 1.7 m new, 0.5 m deaths
  - Lung ca is most common cause of death in women surpassing breast ca in dev’ed countries
- 23% of ca due to infection in developing countries (vs 7%)
  - Vaccination, treatment, behavioral change
- Tobacco: 6 m deaths/yr
- Hep B vaccination, Cervical Ca screening are best buys
Multi-Disciplinary Care
From Modality to Disease Based Practice

- Radiology/Fluoroscopy
- CT
- MRI
- Nuclear Medicine
- Ultrasound
- Interventional

- Thoracic Oncology
- GI Oncology
- Pediatric Oncology
- Breast Oncology
- GU Oncology
- Etc...
Clinical Importance of PET/CT is to provide an imaging consultation!

• Answer the most important question.
  – Is cancer present or absent?
  – Direct or avoid biopsy?
  – Triage the management!

• In a patient who finished treatment for cancer
  – NED (follow conservatively)
  – Recurrence (Direct biopsy then decide therapy)

• In a patient undergoing multimodality therapy
  – Same, better or worse?
National Oncologic PET Registry Results

Overall Impact on Patient Management
  – Diagnosis, Staging, Restaging, Recurrence
  – Data on 22,975 scans from May 8, 2006 – May 7, 2007

Treatment Monitoring
  – *Cancer* 2009:115:410-18

Impact on Patient Management for by Cancer Type
  – Staging, Restaging, Recurrence (proven cancer type)
  – Data on 40,863 scans from May 8, 2006 – May 7, 2008
<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Initial Treatment Strategy (formerly “diagnosis” &amp; “staging”)</th>
<th>Subsequent Treatment Strategy (formerly “restaging” and “monitoring response to treatment”)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>Cover</td>
<td>Cover</td>
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<tr>
<td>Esophagus</td>
<td>Cover</td>
<td>Cover</td>
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<tr>
<td>Head and Neck (not thyroid or CNS)</td>
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<td>Cover</td>
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<tr>
<td>Lymphoma</td>
<td>Cover</td>
<td>Cover</td>
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<tr>
<td>Non-small cell lung</td>
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<td>Cover</td>
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<tr>
<td>Ovary</td>
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<td>Cover</td>
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<tr>
<td>Brain</td>
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<td>Cover</td>
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<tr>
<td>Cervix</td>
<td>Cover with exceptions *</td>
<td>Cover</td>
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<tr>
<td>Small cell lung</td>
<td>Cover</td>
<td>Cover</td>
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<tr>
<td>Soft tissue sarcoma</td>
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<td>Cover</td>
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<tr>
<td>Pancreas</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Testes</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Prostate</td>
<td>Non-cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Thyroid</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Breast (male and female)</td>
<td>Cover with exceptions *</td>
<td>Cover</td>
</tr>
<tr>
<td>Melanoma</td>
<td>Cover with exceptions *</td>
<td>Cover</td>
</tr>
<tr>
<td>All other solid tumors</td>
<td>Cover with exceptions *</td>
<td>Cover</td>
</tr>
<tr>
<td>Myeloma</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>All other cancers not listed</td>
<td>Cover</td>
<td>Cover</td>
</tr>
</tbody>
</table>
CMS Covered Indications for FDG PET

• Three (3) FDG-PET scans will be nationally covered for oncologic indications when used to guide subsequent physician management of anti-tumor strategy after initial anticancer therapy.

• Additional scans will be permitted at MAC or MA Plan Contractor discretion.
Medical Imaging: Decline in Utilization and Spending

• Past decade imaging expenditures rose at a much faster rate than other medical services
• lower payments by CMS, Radiology benefit managers (RBM), Clinic decision support (CDS)
• Maturation of advanced imaging techniques
• Patient radiation safety awareness
• Appropriateness Criteria and Clinical Utilization Guidelines
Fig. 4 Annual percentage changes in Medicare Part B program spending per enrollee for medical imaging. Source: Medicare Part B (fee-for-service) Physician/Supplier Procedure Summary data files. DRA = Deficit Reduction Act of 2005.

Martey S. Dodoo, Richard Duszak Jr, Danny R. Hughes

Trends in the Utilization of Medical Imaging From 2003 to 2011: Clinical Encounters Offer a Complementary Patient-Centered Focus

http://dx.doi.org/10.1016/j.jacr.2013.02.023
USA Clinical PET/CT 2014

• 1.62 million/yr – 13% net decrease from 2011 *
  – (81.2 million CT’s, 7% higher than 2013)
  – PET-10k (1981), 20k (1991), 2011 (1.9 million)
• 2,350 sites using fixed or mobile PET, PET/CT or PET/MR*
• 95% radiopharmaceuticals – outside supplier
  – FDG: 96%, Rubidium 2%
• 94% of all PET studies in 2012 were for cancer:
  – Dx 19%, staging 38%, Rx plan 13%, follow-up 30%
  – Top indications: lung, lymphoma, breast, colon
  – Neurology and cardiology = 6% of procedures

*IMV's 2014 PET Imaging Market Summary Report (http://www.imvinfo.com)
Section of PET
Total Number of Scans – 19000
FY14 Distribution

- Lymphoma: 30%
- Other: 21%
- NSCLC: 15%
- Breast: 9%
- H&N: 7%
- Melanoma: 6%
- Esophageal: 5%
- Colorectal: 4%
- Gyn Malignancies: 2%
- Thyroid: 1%
- Brain: 0%
Cost to outcomes issue

• FDG PET reimbursement has gone down (50%)
  – 1.5% of the total costs of cancer care
  – Appropriate use can reduce cost of cancer care

• CMS, won’t reimburse new radiotracers because there have not been large enough clinical trials to show that the tracer changes management of patients or improves outcomes. Do they live longer? Prove it.

J Nucl Med 2011; 52:86S–92S
Hodgkin’s Lymphoma: Initial and subsequent treatment strategies

• Before: CXR, CECT, Ga67, RNCA, MR
  – Subsequent repeat everything at end of Rx
• Current: FDG PET/CT, (Lugano), CECT (non FDG avid)
  – Subsequent: FDG PET/CT end of Rx
  – Mid cycle (Deauville Criteria)
• Change: FDG PET/CT replaced Ga67, CECT
  • Biopsy Deauville 4-5: (+) refractory, (-) short interval PET 3-6 months for up to 12 months until Deauville 1-2.
  • less CECT, MR for brain/spine, Less RNCA (US), CXR
• Practice change: early response assessment, change management, predict outcome
Lugano Classification: Initial evaluation and staging of HL and NHL patients

- FDG PET/CT is the standard for FDG-avid lymphomas, CT is for non-avid histology.
- Modified Ann Arbor terminology for anatomic distribution of disease. A/B suffixes for HL.
- If PET-CT is done, BM biopsy is not indicated for HL/DLBCL. Biopsy if PET (-) or discordant.
- Treatment based on limited (I & II, non-bulky) or advanced (III or IV) disease.

Lugano Classification: Response assessment of HL and NHL patients

- PET-CT is to be used to assess response in FDG-avid histologies using the 5-point scale; CT is preferred for low or variable FDG avidity.
- Complete metabolic response is considered a complete remission even with persistent mass.
- PR requires a decrease > 50% in sum of the product of perpendicular diameters of up to six representative nodes or extranodal lesions.

Lugano Classification: Response assessment of HL and NHL patients

• PD on CT criteria requires only increase in the perpendicular diameters of single node ≥ 50%.
• Surveillance scans after remission discouraged particularly for HL and DLBCL; repeat scans may be considered in cases of equivocal findings after treatment.
• Judicious use of follow-up scans considered in indolent lymphomas with residual intra-abdominal or retroperitoneal disease.
15 year old female
Nodular sclerosing HL stage IIB

Baseline

6 weeks post-tx
15 year old female
NSHL stage IIB

Baseline
6 weeks post-tx
15 year old female
NSHL stage IIB

Baseline 6 weeks post-tx
# Deauville PET Criteria

<table>
<thead>
<tr>
<th>SCORE</th>
<th>PET/CT SCAN RESULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NO UPTAKE ABOVE BACKGROUND</td>
</tr>
<tr>
<td>2</td>
<td>UPTAKE ≤ MEDIASTINUM</td>
</tr>
<tr>
<td>3</td>
<td>UPTAKE &gt; MEDIASTINUM BUT &lt; LIVER</td>
</tr>
<tr>
<td>4*</td>
<td>UPTAKE MODERATELY INCREASED COMPARED TO THE LIVER AT ANY SITE</td>
</tr>
<tr>
<td>5*</td>
<td>UPTAKE MARKEDLY INCREASED COMPARED TO THE LIVER AT ANY SITE</td>
</tr>
<tr>
<td>X</td>
<td>NEW AREAS OF UPTAKE UNLIKELY RELATED TO LYMPHOMA</td>
</tr>
</tbody>
</table>

The prognostic value of interim PET scan in patients with classical Hodgkin lymphoma.

- The prognostic value of interim FDG PET was evaluated after 2 cycles of ABVD in classical HL patients (n = 229), based on Deauville criteria.

- 3 NM MD’s blinded for clinical information except for initial PET
  - Unanimous agreement for final interpretation in 95% of cases

- 3-year PFS in PET2-negative vs. PET2-positive
  - early stage non-bulky disease 95·9% vs. 76·9% (P < 0·0018)
  - bulky stage II disease 83·3% vs. 20·0% (P = 0·017)
  - advanced stage IPS ≤2 77·0% vs. 30·0% (P < 0·001)
  - advanced stage IPS ≥3 71·0% vs. 44·4%(P = 0·155)

- The outcome after positive PET2 was better than previously reported. The results from non-randomized studies of PET2-guided therapy would be valuable with careful interpretation.

Br J Haematol. 2014 Apr;165(1):112-6
Results of a Trial of PET-Directed Therapy for Early-Stage Hodgkin’s Lymphoma

- RAPID was designed to determine whether patients with clinical stage IA or stage IIA Hodgkin’s lymphoma and negative PET findings after three cycles of ABVD require consolidation radiotherapy.

- The results of this study did not show the noninferiority of the strategy of no further treatment after chemotherapy with regard to progression-free survival.

- Nevertheless, patients in this study with early-stage Hodgkin’s lymphoma and negative PET findings after three cycles of ABVD had a very good prognosis either with or without consolidation radiotherapy.
Follicular Lymphoma

4 cycles R-CHOP

2 cycles R-ESHAP

2 cycles R-hyperCVAD
34 year old woman relapsed DLBCL
small bowel bx

CD19 CAR T cell Rx
Summary

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