18F-FDG-PET/CT in Cancer Treatment: Indications and Results in 2008

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1.1M+ scans at 1700+ sites in 2005
>90% of all new purchased scanners are PET/CT
90-95% of PET imaging is for cancer

Current costs/financial issues:
- Baseline $200K for new PET facility (room renovation, hot lab, radiation safety equipment)
- $1.5M for new PET scanner
- $1.7-2.5M for new PET/CT scanner
- Personnel
- Tracer costs
- Reimbursement issues (DRA)

Roles of PET/CT in Cancer Treatment
- Diagnosis
- Staging
- Predict tumor behavior
- Geographic tumor delineation
- Treatment response
- Surveillance
- Restaging

Current CMS-Approved Cancer Sites for PET/CT Staging & Restaging
- Breast
- Cervix
- Colorectal
- Esophagus
- Head and Neck
- Lymphoma
- Non-Small Cell Lung
- Melanoma
- Sarcoma
- Thyroid

http://www.cms.gov/coverage
CMS-Approved Cancer Sites/Indications for NOPR Enrollment

- Pancreas
- Ovarian
- Small Cell Lung
- Multiple Myeloma
- Unknown Primary
- Additional indications for CMS-approved sites
  - Lymphoma response assessment
  - NSCLC/H&N response assessment
  - Brain/Cervix restaging

Overview

- Site-by-site summary of accepted or evolving indications for FDG-PET/CT (orange = not CMS-approved)
- Current head and neck cancer FDG-PET/CT practice, with case examples
- Future directions

http://www.cms.gov/coverage

Breast Cancer

- Staging of high risk disease
  - Nodal staging
- Characterization of bone lesions
- Staging recurrent disease
- Response to chemotherapy

Breast Cancer—Axillary Staging


Breast Cancer—PET vs. SLNB


Breast Cancer—Bone Lesions


Cervix Cancer

- Staging of high risk disease
  - Nodal staging

- Staging recurrent disease

- Radiation treatment planning
Cervix Cancer


Colorectal Cancer

- Staging of rectal disease
  - Nodal staging
- Staging of non-liver metastases
  - Patient selection for liver surgery
- Staging recurrent disease
- Radiation treatment planning
- Response to chemotherapy

Rectal Cancer—Nodal Staging/XRT Planning

Bass M, et. al. *IJROBP* 70:1423-26 [2008]

Colorectal Cancer—Extrahepatic Staging

Occult Colorectal Cancer


Esophageal Cancer

• Staging of distant disease

• Response to preoperative therapy
  – Needs to be done with endoscopic UTS
  – Timing remains key issue

Esophageal Cancer

Upfront DM Staging Preop Restaging


Esophageal Cancer—Early Response

Esophageal Cancer—Residual vs. Inflammation


Non-Small Cell Lung Cancer

- Diagnose solitary pulmonary nodules
- Mediastinal and distant staging
  - Preoperative assessment (Ph III data)
- Staging recurrent disease
- Radiation treatment planning
  - One Ph II series
- Response to chemotherapy

Solitary Pulmonary Nodule

PET vs. CT

PET/CT


Non-Small Cell Lung Cancer—XRT Planning

Hong R, et. al. / IJROBP 67:720-26 [2007]
Faria S, et. al. / IJROBP 70:1035-38 [2008]
Non-Small Cell Lung Cancer—Ph III Data

ACOSOG Z0050


PLUS Trial


Lymphoma

- Characterize post-chemotherapy mass
- Response to chemotherapy
  - FDG-PET is formal part of IWG guidelines
- Staging recurrent disease

Lymphoma—IWG Response Criteria

- Staging of nodes and distant disease
- Staging recurrent disease


Sarcoma

- Staging of distant disease
  - Complements MRI and bone scanning
  - Inferior to spiral CT for lung assessment
- Clarification of CT/MRI findings
  - Fixation devices, post-operative scarring
- Staging recurrent disease
- Tumor grading/prognosis
- Response to chemotherapy

Melanoma

- Staging of nodes and distant disease
- Staging recurrent disease

Sarcoma—Promise and Pitfalls

Head and Neck Cancer

“Dose Sculpting” to Avoid Normal Tissues

Cumulative IMRT Adoption

Locoregional Control of Oropharyngeal Carcinoma

<table>
<thead>
<tr>
<th>Conventional</th>
<th>IMRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>70-90% T1-2</td>
<td>92%</td>
</tr>
<tr>
<td>30-70% T3-4</td>
<td>87-94%</td>
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### Salivary Recovery After IMRT

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean</th>
<th>N</th>
<th>Mean</th>
<th>Wilcoxon Rank Sum</th>
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<tbody>
<tr>
<td>3D XRT</td>
<td>12</td>
<td>0.33</td>
<td>11</td>
<td>0.43</td>
<td>$P = 0.43$</td>
</tr>
<tr>
<td>IMRT</td>
<td>38</td>
<td>0.49</td>
<td>20</td>
<td>0.82</td>
<td>$P = 0.002$</td>
</tr>
</tbody>
</table>


### “Dysphagia Structures”

Chao K, et. al. (eds.) *Practical Essentials of IMRT, 2nd Edition* [2005]

### H&N CT for Target Delineation

Chao K, et. al. (eds.) *Practical Essentials of IMRT, 2nd Edition* [2005]
**IMRT Dose Prescriptions**

- 70 Gy/35 fx
- 63 Gy/35 fx
- 56 Gy/35 fx

**CT Target Delineation**

Chao K, et. al. (eds.) *Practical Essentials of IMRT, 2nd Edition* [2005]

**MR Fusion for Target Delineation**

**How Could PET/CT Help XRT?**

- **Tumor localization**
  - Enlarge/reduce/confirm primary tumor target
  - Enlarge/reduce/confirm neck coverage
- **Treatment selection**
  - Locoregional and whole body staging
  - Biological characterization
- **Response assessment**
  - Need for neck dissection
H&N FDG-PET Staging—Early Data

- 90-100% primary lesions visualized

- Neck Staging
  - Sensitivity: 74-91%
  - Specificity: 88-98%
  - Negative Predictive Value: 88-99%

- cN0 neck staging accuracy?


H&N FDG-PET Staging—Meta-Analysis

- 32 series, 1236 cases with neck dissection path
  - All series pre-2005 studied PET alone

- Validated FDG-PET for neck staging
  - Sensitivity: 79% [CI = 72-85%]
  - Specificity: 86% [CI = 83-89%]
  - Outperformed CT head-to-head

- Not effective for staging cN0 patients


H&N FDG-PET Whole Body Staging

- 33 scans in 35 consecutive pts

- 7 pts (21%) FDG+ distant disease
  - 4 pts with lung/liver/bone mets
  - 3 pts with secondary cancers

- FDG-PET provided higher yield staging
  - CT missed 2/3 mediastinal mets
  - CT missed distant disease in 2/7 patients


PET/CT GTV Delineation
**IMRT Guided by PET/CT Staging**

Based on CT only

Based on PET/CT


**FMISO-PET/CT—Dose Painting by Numbers**


**PET/CT Challenges—GTV Registration**


**PET/CT Challenges—GTV Thresholding**

Burri RJ, et. al. *IJROBP* 71:682-88 [2008]
Primary H&N Tumor SUV & Outcomes

- U Iowa (85 pts/retrospective)
  - 98-100% NPV at primary and neck if FDG-PET negative after IMRT
  - Limited primary tumor specificity

- Stanford (103 pts/retrospective)
  - 96-97% NPV overall
  - Scanning >1 month post XRT improved sensitivity and NPV

- What is the optimal timing for post XRT PET imaging?

\[ p = 0.017 \]


FDG-PET Response Assessment

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  - 98-100% NPV at primary and neck if FDG-PET negative after IMRT
  - Limited primary tumor specificity

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MDACC H&N PET/CT Trial—Prospective Response Assessment

- 59 patients → 6 responders (A)
- 52 patients → 72 clinically evaluated
  - 16 neck dissections
  - 2 lymph *primary or salvage*
  - 4 primary failures
  - 4 primary and nodal failures
  - 6 responders
  - 0 non-responders
  - 80 responders
  - 2 non-responders

Mueller B, et. al. Submitted

MDACC H&N PET/CT Trial—Pre-XRT vs. Post-XRT SUV

- Pre-treatment
- Post-treatment

\[ p < 0.001 \]

Moeller B, et. al.
MDACC H&N PET/CT Trial—
Restaging Accuracy

Moeller B, et. al. Submitted

MDACC H&N PET/CT Trial—
“Risk-Stratified” PET-CT Assessment

High Risk
- HPV-negative
  - OR -
- Non-OP primary
  - OR -
- Tobacco user

Low Risk
- HPV-positive
  - OR -
- OP primary
  - AND -
- Tobacco non-user

Schwartz D, Macapinlac H, Weber R

J Natl Cancer Inst 100:688-9 [2008]

SUV Standardization Issues

- PET instrumentation/reconstruction parameter standards
- ROI delineation standards
- Partial volume/attenuation correction standards
- Time of SUV determination relative to injection
- Body mass/plasma glucose SUV corrections
- Patient/disease stage selection issues
- PET/CT central review/QA process?

**PET/CT—Settling Into a Mature Niche**

- Refinement of PET/CT Tumor Localization
  - What will be our gold standard?

- Refinement of PET/CT’s Diagnostic Role
  - Interactions with other tests
  - Interactions with other clinical risk factors
  - Individualize targeted therapy?

- Does PET/CT truly improve treatment results?

**H&N Case Examples**

**“Useful” FDG-PET/CT GTV**
- Stage III Tonsil CA

**“Equivocal” FDG-PET/CT GTV**
- Stage III Base of Tongue CA
“Equivocal” FDG-PET/CT N Staging

- Stage II High Grade True Vocal Cord CA
  
  
  SUV = 3.1

Mixed False +/- True + Staging

- Stage III Tonsil CA and…

Incidental Thyroid Screening

- Stage IVa Tonsil CA and…

Incidental Parotid/Lung Screening

- Stage III Larynx CA and…
Incidental H&N Primary

- Follow-up for resected Stage II lung adenocarcinoma

Future Directions

- Phase III trial comparing chemoXRT +/− C225 EGFR blockade
- First treatment Phase III with PET/CT outcomes (NCI/CMS/FDA)
  - Post-treatment neck response staging accuracy
  - Pretreatment chemoXRT primary tumor and nodal SUV_{max} & outcomes
  - Post hoc PET/CT image processing analysis

RTOG 0522

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National Oncologic PET Registry

- Prospective collection of clinical/imaging data for candidate indications, in exchange for CMS reimbursement
- Opened in 2006
- Pilot publication
  - 22,975 cases from 1,178 centers
  - PET/CT altered management in 36.5% of cases

Hillner B, et. al. *J Clin Oncol* [2008]
**Novel Non-FDG Tracers**

- **Amino Acids**
  - O-(2-18F-fluoroethyl)-L-tyrosine (FET)
  - L-3-[18F]-fluoro-L-phenylalanine (FDOPA)
  - 3,4-dihydroxy-L-3-[18F]-fluoro-L-phenylalanine (FDOPA)

- **Lipids**
  - 18F-fluorocholine (FCH)
  - 18F-fluoroacetate

- 18F-16α-17β-fluoroestradiol (FES)
- 3’-deoxy-3’-18F-fluorothymidine (FLT)
- 18F-fluoromisonodazole (FMISO)

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MDACC H&N SPORE
VA MERIT