Positron Emission Tomography for Radiation Treatment

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Outline: Part 1

• Physics of PET and PET-CT
• Oncology Imaging with FDG PET
• PET and Radiation Treatment Planning
• Summary

Work supported in part by research grants from North Carolina Baptist Hospital, Varian Medical Systems, and GE Healthcare

Positron Annihilation

511 keV γ

• Coincidence detection of two 0.511 MeV photons
• Annihilation radiation from positron-electron pair
• Photon directions at 180° at annihilation point—different from decay point
• Range of positron
• Positron emitters with biological compatibility
• Low Z (typically), proton rich, short half lives
• "Local" production with a cyclotron

Physics of PET and PET-CT

• CE-Imaging: The Physics and Technology of Radionuclide Imaging – III
  Wednesday, 7:30:00 AM - 9:25:00 AM, Room: L100J
  – 7:30 AM WE-SAMS-L100J-1 Basic Physics of PET and PET/CT - F. Fahey
  – 8:25 AM WE-SAMS-L100J-2 PET/CT Performance Evaluation Techniques and Quality Assurance - B. Kemp

• PET-CT Workshop
  Wednesday, 4:00:00 PM - 5:30:00 PM, Room: L100E
  WE-E-L100E-1 PET-CT Workshop - PET/CT Scanners Offering From Different Manufacturers - J. Anderson, O. Mawlawi, M. Georgiou
PET Radionuclides

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Half-Life</th>
<th>&quot;run&quot; speed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluorine 18 (18F)</td>
<td>110 min</td>
<td>fast</td>
</tr>
<tr>
<td>Carbon 11 (11C)</td>
<td>20 min</td>
<td>fast</td>
</tr>
<tr>
<td>Nitrogen 13 (13N)</td>
<td>10 min</td>
<td>fast</td>
</tr>
<tr>
<td>Oxygen 15 (15O)</td>
<td>122 sec</td>
<td>fast</td>
</tr>
<tr>
<td>Rubidium 82 (82Ru)</td>
<td>75 sec</td>
<td>very fast</td>
</tr>
</tbody>
</table>

With and Without Attenuation Correction

Phantom with 'normal' uptake except left lung that has an small spherical 'hot tumor'.

Non-corrected PET
CT-attenuated corrected
Cs-attenuated corrected

With
Without

FDG PET Imaging

PET Imaging
- Activity distribution is imaged
  - Physiology, function, biology
- Complementary to (~anatomic) CT and MR
- Increased sensitivity compared to CT alone
- Most indications approved for reimbursement are oncology

PET Imaging in Oncology
- Diagnosis – less common
- Staging - yes
- Target Definition
  - Radiation treatment
  - Other "targeted" therapy
- Re-staging – yes
- Treatment Evaluation

2-[18F]-fluoro-2-deoxy-D-glucose (FDG)

- 18F-FDG is most common tracer
- Malignant tissues may have increased glycolysis and increased FDG uptake
- FDG-PET images are maps of glucose metabolism – non-specific imaging
- Difficulties with small tumors (< 3 – 10 mm diameter)
- Use increasing – 200 PET-CT scanners in 2 years*
- PET-CT hybrid scanners: registration solved

PET and Radiation Treatment Planning

- Main contribution – Staging: Target Localization
  - Very important: stage determines treatment approach
  - Binary results: presence/absence of disease, metastasis
- Dramatic differences possible
  - Treatment mode: radio, chemo, beamo (EG Shaw)
    - none, one, all three? 10-30% NSCLC patients stage changes
  - Radiation treatment fields: ie, inclusion of nodes
    - Estimation – better coverage of target with PET in 30 – 60% of patients receiving definitive radiation treatment*

**FDG PET and Staging, Localization**

Change in stage before and after PET-CT

<table>
<thead>
<tr>
<th>Pre-PET/CT stage</th>
<th>No. patients</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>Upstage ratio</th>
<th>Downstage ratio</th>
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</thead>
<tbody>
<tr>
<td>I</td>
<td>1</td>
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<td>1</td>
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<tr>
<td>II</td>
<td>5</td>
<td>5</td>
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<td>5</td>
<td>5</td>
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<td>5</td>
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<tr>
<td>III</td>
<td>10</td>
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</tr>
</tbody>
</table>

Impact on size of PTV: CT vs PET/CT

- Relative changes ranged from 0.40 to 1.86
- In 5 of 23 cases, new FDG nodes detected that increased PTV

**FDG PET and Radiation Treatment**

Change in PTV and prescribed dose

<table>
<thead>
<tr>
<th>Patient no. and Department</th>
<th>PET/PET-CT PTV (cm³)</th>
<th>PET/PET-CT PTV (cm³)</th>
<th>Management changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Medical School</td>
<td>T6506 (3D)</td>
<td>T6506 (3D)</td>
<td>Increase in PTV to ensure primary tumor is contained</td>
</tr>
<tr>
<td>2 University Hospital</td>
<td>T6506 (3D)</td>
<td>T6506 (3D)</td>
<td>Increase in prescribed dose to account for PET detected FDG nodes</td>
</tr>
<tr>
<td>3 Hospital</td>
<td>T6506 (3D)</td>
<td>T6506 (3D)</td>
<td>Increase in prescribed dose to account for PET detected FDG nodes</td>
</tr>
<tr>
<td>4 Total</td>
<td>T6506 (3D)</td>
<td>T6506 (3D)</td>
<td>Increase in prescribed dose to account for PET detected FDG nodes</td>
</tr>
<tr>
<td>5 Clinical</td>
<td>T6506 (3D)</td>
<td>T6506 (3D)</td>
<td>Increase in prescribed dose to account for PET detected FDG nodes</td>
</tr>
<tr>
<td>6 Tumor</td>
<td>T6506 (3D)</td>
<td>T6506 (3D)</td>
<td>Increase in prescribed dose to account for PET detected FDG nodes</td>
</tr>
</tbody>
</table>

PET may decrease target volumes vs CT

Changes in target outline translate to reduced treatment field size

GTV: CT vs PET-CT

Use of PET-CT may reduce GTV/CTV

GTV-CT  GTV-PET-CT


Ex: FDG-PET increased the target volume

Pre-PET: RLL lesion with right paratracheal node
Post-PET: RLL lesion with right paratracheal, subcarinal, and hilar lymphadenopathy (some < 1 cm on CT)
GTV increased to encompass these nodal regions.

Courtesy of K Mah, Univ Toronto, Sunnybrook

Impact of PET-CT on RT Volume Delineation Using Combined PET-CT Scanner: Wash U Group

• Prospective study: 26 NSCLC patients
  – 8/26 (31%) PET changed staging
  – Of 24 still planned radically
    • In 3, PET/CT reduced volume compared to CT alone due to atelectasis
    • In 10, PET/CT increased volume as unsuspected nodal disease was detected
    • In 1, new separate tumor focus was found in same lung
  – Overall PET/CT resulted in alterations in radiation planning in over 50% of patients by comparison to CT alone.

Bradley, J et al. IRROP 51, 2004

Process: PET in Radiation Treatment

• Cancer diagnosis → biopsy, imaging
• Treatment position, immobilization
• PET imaging in treatment position
• Expert image review
• Image transfer – DICOM, other?
• Image registration (if needed)
• Target localization and definition
• Treatment planning
**PET-CT Simulator**
- Adjacent control, scanner, inject-wait, lab, and toilet
- 1/8 in Pb; control, scanner
- 1/2 in Pb; inject-wait, toilet
- Isotope prep near on-site
- CT, PET-CT operation is quality – future additional QA testing
- Shared Virtual Simulation
- Laser marking system
- Automated PACS archive, selective push to TPS
- Normal access security

**Target Definition**
- Qualitative: Expert clinical review
  - Visual, inclusion of clinical history and data
  - Above background
- Quantitative: Voxel intensity values
  - 40-50% of peak intensity (above background?)
  - Standardized Uptake Value (SUV) of ROI
    - SUV > 2.5 indicates positive for cancer
  - Region determined by PET, extent by CT

**Radiation Treatment Planning with PET**
**Target Definition**
Same patient image: different window and level!

**The Digital Contour**
A Threshold Process

Depending on image window and level setting, target volume can change by 50%. Also:
- SUV not a part of DICOM data
- SUV utility unclear
The Digital Contour
A Threshold Process

Standardized Uptake Value (SUV)
- Semi-quantitative measure of glucose metabolism
- Essentially: Average voxel value within an ROI
  - normalized by activity and body weight
- Relative to an individual patient
  - Malignancy vs benign
  - Tumor grade
  - Treatment response
  - Prognosis (?) – biological models

SUV Limitations
- Semi-quantitative measure of glucose metabolism
- Definition of the ROI (CT? self-referencing), and its location over time (ie, scan to scan)
- Tumor heterogeneity: necrosis, variable grade
- Tumor volume changes with time
- Small tumors difficult to image (size → resolution)
- Glucose load?
  Consensus? Quantification of FDG uptake?

PET-Based Targeting – H/N
K Greven, PI
- 7 methods

Unpublished: Lawrence, Greven, Bourland, et al. 2007
Target Definition: “a mess” (R Jeraj)

Device QA
Geometric Phantoms

Target Definition: “a mess”

Device QA
Geometric Phantoms

GTV-CT and GTV-PET
Other Issue: Inter-observer Variation

PET
CT

From: Caldewell, Mah, Vong, et al., IJROBP 51(4):923-931, 2004
Acknowledgements

- Work supported in part by research grants from North Carolina Baptist Hospital, Varian Medical Systems, and GE Healthcare
- Kathy Mah, University of Toronto, Sunnybrook
- Sasa Matic, Washington University in St. Louis
- Assen Kirov, Memorial Sloan Kettering, NY, NY

Summary: Part 1

- Physics of PET and PET-CT
- PET in oncology: Staging → Treatment Path
- PET and Radiation Treatment Planning
  - Localization of regions to be treated
  - Targeting, contour delineation, with limits

Robert Jeraj, PhD
PET in Treatment Assessment