Latest developments in PET verification of proton therapy

Katia Parodi, Ph.D.

Heidelberg Ion Therapy Centre, Heidelberg, Germany

Previously: Massachusetts General Hospital and Harvard Medical School, Boston, USA and Research Center Dresden-Rossendorf, Dresden, Germany

51st AAPM Annual Meeting
Anaheim, July 27th, 2009
Overview

- The advantages and challenges of ion beam therapy
- PET verification of ion beam therapy
  - Motivation and principles
  - Implementations and clinical experiences
  - Technological and methodological improvements
- Conclusion and outlook
Range uncertainties issues in ion therapy

**Difference TP / delivery**
- Daily setup variations
- Internal organ motion
- **Anatomical / physiological changes**

**Dose calculation errors**
- Conversion CT numbers - ion range
- Inhomogeneities, metallic implants
- CT artifacts

After W. Enghardt, Oncoray Dresden
The principle of PET monitoring in ion therapy

By-product of irradiation
\((^{15}\text{O}, ^{11}\text{C}, ^{13}\text{N}...\)
with \(T_{1/2} \sim 2, 20 \text{ and } 10 \text{ min}\)

\(A(r) \neq D(r):\)
"Dose-guidance" and range verification from "surrogate,, PET?"

Measured activity compared with Monte Carlo calculation as for \(^{12}\text{C} \text{ therapy at GSI Darmstadt, Germany} (\text{Enghardt et al, NIMA 525, 2004})\)
Offline PET/CT after proton Tx @ MGH

Proton Irradiation... 14-20 min elapsed... Offline PET/CT

Passive beam delivery @ Francis H. Burr Proton Therapy Center

Only long-lived isotopes ($^{11}$C: $T_{1/2} \approx 20$ min
$^{15}$O: $T_{1/2} \approx 2$ min)

Full ring tomograph CT for co-registration

PET/CT @ MGH Radiology
**Calculation model of $\beta^+$-activation**

**FLUKA Monte Carlo code using**
- Field-specific beam source information from Geant4 modeling of the nozzle and beam modifiers *(Paganetti et al, MP 31, 2004)*
- Planning CT (segmented into 27 material) and same CT-range calibration curve as TPS *(Parodi et al MP 34, 2007, PMB 52, 2007)*
- Experimental cross-sections for $\beta^+$-emitter production
- Semi-empirical biological modeling *(Parodi et al IJROBP 2007)*
- Convolution with 3D Gaussian kernel (7-7.5 mm FWHM)

**Graphical Data**

*Data from IAEA Nuclear Data Section*

...and other reaction channels on N, O, Ca yielding, e.g., $^{13}$N, $^{38}$K, ...

*(Parodi et al, PMB 45, 2002, Parodi et al, PMB 52, 2007)*
The PET/CT clinical experience @ MGH

**Phantom studies**: achievable mm-accurate range verification at ~ 2 Gy for $t_{\text{meas}} \sim 20 - 30$ min (Parodi et al Med Phys 2007, Knopf et al PMB 2008)

**Pilot study** (9 subjects: 3 paraspinal, 4 head, 1 sacrum, 1 eye) followed by

**larger study** (14 subjects: 8 head, 3 paraspinal, 1 sacrum, 2 prostate)

- 1 – 2 (3) fields for a typical total dose of ~ 2 GyE
- Same immobilization device at treatment / imaging site
- Post-treatment CT followed by 30 min list mode PET acquisition
- Rigid co-registration of TP-CT and PET-CT
The PET/CT clinical experience @ MGH

- Patients undergoing 1 post-treatment PET/CT (repeated scan in 2 cases)

<table>
<thead>
<tr>
<th>Area</th>
<th># of patients</th>
<th># of patients that received 1 field</th>
<th># of patients that received 2 (or 3) fields</th>
<th>Dose per field [GyE]</th>
</tr>
</thead>
<tbody>
<tr>
<td>head</td>
<td>12</td>
<td>3</td>
<td>8 (1)</td>
<td>0.9-3</td>
</tr>
<tr>
<td>eye</td>
<td>1</td>
<td>1</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>C-spine</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>0.6-2.5</td>
</tr>
<tr>
<td>T-spine</td>
<td>1</td>
<td></td>
<td>1</td>
<td>1.8</td>
</tr>
<tr>
<td>L-spine</td>
<td>2</td>
<td>2</td>
<td></td>
<td>0.9-2</td>
</tr>
<tr>
<td>sacrum</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1-2</td>
</tr>
<tr>
<td>prostate</td>
<td>2</td>
<td>2</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>23</strong></td>
<td><strong>9</strong></td>
<td><strong>13 (1)</strong></td>
<td><strong>0.6-10</strong></td>
</tr>
</tbody>
</table>

*Parodi et al, IJROBP 68, 2007; Knopf et al, PMB 54, 2009*
The clinical PET/CT study @ MGH (skull base tumour)

Clival Chordoma
Field 1: 0.87 Gy, $\Delta T_1 \sim 26$ min
Field 2: 0.87 Gy, $\Delta T_2 \sim 16$ min
PET $t_{\text{meas}} = 30$ min

1-2 mm agreement for position of distal max. and 50 % fall-off in bony structures
The clinical PET/CT study @ MGH (c‘nt)

**Good reproducibility repeated PET/CT scans (2 H&N cases)**

<table>
<thead>
<tr>
<th>Bq/ml</th>
<th>First scan</th>
<th>Second scan</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Meas PET</td>
<td>MC PET</td>
</tr>
<tr>
<td></td>
<td>Meas PET</td>
<td>MC PET</td>
</tr>
</tbody>
</table>

**Challenges for abdominopelvic and ocular sites**

- Biological washout, motion and co-registration issues
- Uncertainties of CT-based modeling due to overlapping HU domains

*Knopf et al, PMB 54, 2009, Parodi et al, IJROBP 68, 2007*
Towards better imaging strategies

Reducing delay time $\Delta T$ and scan time $t_{\text{meas}}$...

Offline current situation
$\Delta T = 20$ min
PET $t_{\text{meas}} = 30$ min
Total decays: $1.1 \times 10^7$

Offline nearby scanner
$\Delta T = 5$ min
PET $t_{\text{meas}} = 30$ min
Total decays: $2.7 \times 10^7$

In-beam dedicated
$\Delta T = 0$
PET $t_{\text{meas}} = 100$ s
(60s beam-on with 100% recovery + 40s decay)
Total decays: $2.4 \times 10^7$

Parodi et al, IJROBP 71, 2008
Novel PET systems for in-room imaging (I)

Mobile PET scanner (PhotoDetection Systems Inc) @ MGH

- ≈ Same treatment position and reduced delay irradiation-imaging
- Already benchmarked against offline PET/CT in phantom experiments
  (see poster A. Knopf SU-FF-J-129)

- Clinical investigation ongoing

http://www.photodetection.com
Analytical modeling for in-room imaging

Extend to short-lived emitters a proposed fast analytical approach deriving the PET signal directly from the planned Dose (PET = filter * Dose)

MC-PET (offline PET scan)  Analytically filtered dose

Parodi and Bortfeld, PMB 2006; Parodi et al, AAPM 2006

Attanasi et al, Talk TH-D-303A-3
Novel PET systems for in-room imaging (II)

*Dual-head scanner mounted on rotating gantry at NCC Kashiwa, Japan*

- Distance between two opposing detector heads of 30 - 100 cm
- Icentric rotating of 0 - 360 deg.
- Position resolution of 1.6-2.1 mm FWHM
- Detection area of $164.8 \times 167.0$ mm$^2$
Novel PET systems for in-room imaging (II)

**Planar imaging starting immediately after end of irradiation**

\[ A(r) \neq D(r): \text{Measured daily activity compared to reference activity (reproducibility check)} \]

- 50 patients of H&N, Liver, Lung, Prostate and Brain (2007/10 - )
- Daily measurement of the PET image of every irradiation field for a proton treatment
- Measured PET images of 1000 or more (50 patients)

*Courtesy of T. Nishio, NCC Kashiwa*
Clinical implementation and experience @ NCC

First treatment day

Planned dose
2.5 GyE

Measured activity
(200s)

Second treatment day

comparing

Courtesy of T. Nishio, NCC Kashiwa, accepted for publication in IJROBP
Clinical implementation and experience @ NCC

First treatment day

Planned dose
2.5 GyE

Measured activity
(200s)

N-th treatment day

Dose distribution changed

Comparing

Re-planning

Courtesy of T. Nishio, NCC Kashiwa, accepted for publication in IJROBP
Change of activity in treatment period

121MeV/SSOBP90/G10deg./B20deg. /2.5GyEpfx.: (a) dose distribution

Activity distribution (delivery dose): (b) 2.5 GyE, (c) 10 GyE, (d) 17.5 GyE, (e) 32.5 GyE, (f) depth profile

Courtesy of T. Nishio, NCC Kashiwa, accepted for publication in IJROBP
Change of activity in treatment period

\[ \Delta R_{\text{max}}(\text{plan(b)} - \text{plan(a)}) \leq \begin{cases} -21.1 \text{ mmWEl} : \text{port1} \\ -15.0 \text{ mmWEl} : \text{port2} \\ -17.2 \text{ mmWEl} : \text{port3} \end{cases} \]

GTV: 184[cc] ↓ 125[cc]

Courtesy of T. Nishio, NCC Kashiwa, accepted for publication in IJROBP
The issue of moving organs

Detrimental effect of motion not only on imaging BUT also on dose delivery

Sensitivity of ion therapy to density variations is increased in the presence of intra-fractional organ movement, e.g., due to respiration

Motion is accounted for using special motion-compensated beam delivery strategies like gating or beam tracking

Feasibility and potential of time-resolved 4D PET verification
Ion beam tracking
at GSI Germany

Bert et al, Med Phys 2007
Bert and Rietzel, Radiat Oncol 2007

Amplitude of sensor signal

Laterally compensated beam goes through different absorber thickness

Laterally compensated beam goes through different absorber thickness

depth compensation with wedge

3cm (peak2peak)
~3s period

PMMA target

Absorber

wedge system

beam energy

lateral position

Compensation

TCS

4DTP

scanner magnets

beam

Δx

Δy

Δz

HEIDELBERG IONENSTRAHL-THERAPIE ZENTRUM

Heidelberger Ionenstrahl-Therapie Zentrum

Laterally compensated beam goes through different absorber thickness

→ depth compensation with wedge
4D in-beam PET experiment @ GSI

Parodi et al, Med. Phys, in press

The data acquisition

- ~6min irradiation
- ~25min decay
- ~18min decay

<table>
<thead>
<tr>
<th>In-beam</th>
<th>Offline (I)</th>
<th>Offline (II)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moving phantom</td>
<td>Static phantom</td>
<td></td>
</tr>
</tbody>
</table>

(static in ref. meas.)

PET detected events

Amplitude of sensor signal

Time correlation between PET acquisition and motion track, both synchronized with pulsed irradiation
Results: 2D images

Signal recovery implementing phase-resolved 4D reconstruction co-registered to a reference phase

Parodi et al, Med. Phys., In press

Standard 3D reco, no Phase sorting

4D reco + co-registration
Results: signal recovery in motion direction

**Proof-of-principle** of 4D in-beam PET verification of ion tracking

Larger experimental campaign at GSI Darmstadt in collaboration with Forschungszentrum Rossendorf, GSI and HIT is ongoing (next experiment in August 2009!) and further activities are planned in the framework of a recently approved European project.
Conclusion and outlook I

- Ion beam therapy is rapidly spreading worldwide
- Full clinical exploitation of its promise
  - In-vivo imaging of “surrogate” signal, e.g., from escaping secondary radiation to infer information on the primary dose delivery
  - Reliable computational tools for accurate modeling of the “surrogate” signal and the dose deposition
- PET is a mature imaging technique for in-vivo treatment verification
- Ongoing research on technological / methodological improvements to enable optimal quality assurance of ion beam therapy
Conclusion and outlook II

- "In-beam" PET implementation would be method of choice but is technological challenging due to the need of
  - Dedicated, expensive instrumentation (industrial partners?)
  - Dedicated data acquisition solutions to suppress noise form background radiation ($\gamma$, $n$, $p$, …) during “beam-on” time
  

- Exploitation of “background” is being currently explored and could represent very promising complementary (or alternative) imaging.

See Next Talk...

---

In-beam PET @ pulsed beam

Measured background radiation timely correlated to beam micropulses (measured with GSO crystal at 90° from $^{12}$C beam @ GSI)

Parodi et al, NIMA 2004
Acknowledgements

A. Ferrari, F. Sommerer, CERN Geneva, Switzerland
Th. Haberer, J. Debus, HIT Heidelberg, Germany
W. Enghardt, K. Laube, FZD Dresden-Rossendorf, Germany
C. Bert, N. Saito, N. Chaudhri, GSI Darmstadt, Germany
E. Rietzel, SIEMENS, Germany
T. Nishio, NCC Kashiwa, Japan

The moving target team @ GSI is partly funded by Siemens Particle Therapy

PTCOG 48
28 September - 03 October 2009
Heidelberg Convention Center
http://www.ptcog-meeting.de

Thank you for your attention
Results: depth profiles

β⁺-activity depth-profiles for 4D reco., uncorrected reco. and static ref.

Depth 90% falloff (mm)

- 4D PET In–beam + Offline (I): 14.2 ± 0.3
- Static PET In–beam + Offline (I): 14.2 ± 0.3
- 3D PET (no 4D reco) In–beam + Offline (I): 14.3 ± 0.8
Results: dependence on statistics
Investigation of optimal imaging strategy

- Calculate $\beta^+$-yield for $p$ irradiation
- Model activity build-up / decay during and after irradiation
- Include biological decay
Number of detectable “physical” decays
(base of skull case, 1 Gy)

<table>
<thead>
<tr>
<th></th>
<th>In-beam ( (\text{t}<em>{\text{meas}} \approx \text{t}</em>{\text{irradiation}}) )</th>
<th>Offline ( (\text{t}_{\text{meas}} = 30\text{min}, \Delta t = 5\text{min}) )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>proton beam</strong></td>
<td><img src="image1.png" alt="Graph" /></td>
<td><img src="image2.png" alt="Graph" /></td>
</tr>
<tr>
<td><strong>carbon beam</strong></td>
<td><img src="image3.png" alt="Graph" /></td>
<td><img src="image4.png" alt="Graph" /></td>
</tr>
</tbody>
</table>

Parodi et al, IJROBP 71, 2008
In-beam PET for $^{12}$C ion therapy @ GSI

FZ Dresden-Rossendorf

For every treatment fraction (typically 20 d @ 1Gy)

Planned dose

MC calculated $\beta^+$-Activity

Measured $\beta^+$-Activity

Verification of
- Beam range
- Lateral position

In case of deviation
- Timely reaction

Enghardt et al, NIMA 525, 2004