Developments in proton radiography and real-time PET at KVI-CART

Ikechi Ozoemelam
Tackling range uncertainties

- Treatment with charged particles offers precise dose distribution
- Due to range uncertainties, deviations between planned and delivered dose may occur
- Solutions:
  - Better patient model ➔ DECT and Proton radiography
Tackling range uncertainties

- Treatment with charged particles offers precise dose distribution
- Due to range uncertainties, deviations between planned and delivered dose may occur

Solutions:
- Better patient model → DECT and Proton radiography
- Visualization of beam trajectory → Range verification using secondary emissions such as annihilation photons (PET)

<table>
<thead>
<tr>
<th>Positron emitter</th>
<th>$T_{1/2}$ min</th>
</tr>
</thead>
<tbody>
<tr>
<td>O-15</td>
<td>2.0</td>
</tr>
<tr>
<td>C-11</td>
<td>20.4</td>
</tr>
<tr>
<td>P-30</td>
<td>2.5</td>
</tr>
<tr>
<td>K-38$^g$</td>
<td>7.6</td>
</tr>
</tbody>
</table>
Proton tomography (pCT) provides 3D measured RSP images. However, its clinical implementation is difficult.

Proton radiography (pRG) is simpler and easier to implement in clinic than pCT.

Combine pRG with 3D RSP predictions based on 3D X-ray imaging techniques.
Proton radiography in proton therapy

Proton radiography (pRG) + X-ray techniques

- Proton imaging along one single direction
- 2D projection of measured RSPs
- Comparison of 2D projections
- Correction and optimization of X-ray-based RSP predictions

- X-ray-based RSP predictions
- 2D projection of X-ray-predicted RSPs

Slides from Francesco Olivari and Emiel van der Graaf
pRG setup at KVI

Slides from Francesco Olivari and Emiel van der Graaf
pRG setup at KVI

pRG Setup at KVI-CART

Phantom

Scintillator screen

CCD Camera

Mirror

Slides from Francesco Olivari and Emiel van der Graaf
PET implementation strategies

Beam-on

In-room

Offline

figure from Zhu X and El Fakhri G, Theranostics 3 (2013) 731
PET implementation strategies

figure from Zhu X and El Fakhri G, Theranostics 3 (2013) 731
PET implementation strategies

figure from Zhu X and El Fakhri G, Theranostics 3 (2013) 731

Beam-on PET is attractive

- Maximum number of counts
- Minimal biological washout
- Faster feedback (almost real time)
  ➔ Fast trigger for corrective actions

short-lived nuclides are needed
(\(T_{1/2} = \text{ms to s}\))

- Acquisition time
- Biological Washout
Measurements at the KVI-CART

Beam-on PET using short-lived PET nuclides during particle therapy

1. Production yield measurements

- Identify potential short-lived positron emitters for monitoring treatment
- Measure the yield of these nuclides
- Assess the relevance of these nuclides in typical irradiation scenarios
Measurements at the KVI-CART

Beam-on PET using short-lived PET nuclides during particle therapy

1. Production yield measurements
   - Identify potential short-lived positron emitters for monitoring treatment
   - Measure the yield of these nuclides
   - Assess the relevance of these nuclides in typical irradiation scenarios

2. Imaging Experiments on phantoms
   - Proof of concept experiments on range verification
   - Precision in clinical irradiation scenarios
Measurements at the KVI-CART

Beam-on PET using short-lived PET nuclides during particle therapy

1. Production yield measurements
   - Identify potential short-lived positron emitters for monitoring treatment
   - Measure the yield of these nuclides
   - Assess the relevance of these nuclides in typical irradiation scenarios

2. Imaging Experiments on phantoms
   - Proof of concept experiments on range verification
   - Precision in clinical irradiation scenarios

3. Clinical Implementation
   - Experiments in more complicated phantoms and patients
   - Integration into clinical workflow
Production yield measurement

Experiment at the AGOR irradiation facility of the KVI-CART

Irradiation:
- 55 MeV protons
- 50 MeV/u $^4$He & 59 MeV/u $^3$He beams

*Similar range in water (22 mm)*

- Pulsed beam delivery
- Number of ions calibrated with a paddle scintillator

Targets:
- Water
- Graphite
- Calcium
- Phosphorus

Detector: NaI detector

Target - Detector - Beam - BIM


Production of short-lived nuclides: Protons

Consider the most weighted distal layer spot with $10^8$ protons on adipose

732 PET counts with a PET system with 3% sensitivity

Irradiation pulse period $\rightarrow$ 30 ms on and 60 ms off

<table>
<thead>
<tr>
<th>Target</th>
<th>Production (nuclei per 55 MeV proton)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graphite</td>
<td>$4.46 \times 10^{-4}$</td>
</tr>
<tr>
<td>PMMA</td>
<td>$2.44 \times 10^{-4}$</td>
</tr>
<tr>
<td>Adipose tissue</td>
<td>$2.44 \times 10^{-4}$</td>
</tr>
</tbody>
</table>
Production of short-lived nuclides: Helium

- 10 ms decay contribution
- Difference in fit quality between $^{13}$O ($T_{1/2} = 8.6$ ms) and $^{12}$N ($T_{1/2} = 11$ ms) is insignificant: conclusions difficult
- Production of very short-lived component in both oxygen and carbon
- Production on oxygen and graphite with $^4$He is 2.1 and 2.8 times smaller than that with proton resp.
- Production on oxygen and graphite with $^3$He is 2.8 and 4.4 times larger than that with $^4$He resp.
- $5 \times 10^7$ $^4$He on adipose (considering differences in stopping power)
- 216 PET counts with a PET system with 3% sensitivity
Proof of concept study

Scanner sensitivity at the centre of FoV = 0.27%

Aggregation over several pulses

**MC Simulations**

- Large dual-panel scanner
- $1 \times 10^8$ protons = $5.5 \pm 1.1$ mm
- $5 \times 10^8$ protons = $5.2 \pm 0.5$ mm


Spotty Spot $^{12}$N imaging

Imaging Experiments with a larger scanner

Scanner Configuration
- Two 20 × 20 cm$^2$ Panels
- 32 detector blocks with 5408 LSO crystals
- Arrangement equivalent to 1/6 of a Siemens full ring scanner (panel separation of 25 cm much smaller than the diameter of a full ring scanner)

Target Configuration
- PMMA and Graphite Targets
- Considered target and range shifts (PMMA blocks)

Scanner sensitivity at the centre of FoV = 2.2%
Detector pulsing

- Modification of the PMT voltage dividers to enable PMT switching
- Synchronized with the beam pulsing
- 10 ms beam-on and 90 ms beam-off

PMT Signal of 1 block
Detector pulsing

- Modification of the PMT voltage dividers to enable PMT switching
- Synchronized with the beam pulsing
- 10 ms beam-on and 90 ms beam-off

PMT Signal of 1 block

2 → PMT
1 → Beam

300 µs
Spot-by-Spot imaging: Time Spectrum

```
end of irradiation
```

![Graph showing time spectrum with annotation for end of irradiation]
Spot-by-Spot imaging: Time Spectrum

end of irradiation

annihilation photon counts ms⁻¹

time [s]

annihilation photon counts ms⁻¹

time [ms]
Spot-by-Spot imaging: Time Spectrum

Before correction

First 50 pulses

\( T_{1/2} = 18.1 \pm 1.1 \text{ ms} \)

Correction factor

First 50 pulses

\( T_{1/2} = 11.2 \pm 0.2 \text{ ms} \)

After correction
Spot-by-Spot imaging: Image reconstruction

Corrections

1. Coincidence rate recovery

2. Scanner sensitivity

- Histogram of intersection of LOR with plane

- Two corrections were implemented
  - for recovery of coincidence rate after the detector is switched on
  - Scanner sensitivity.
Spot-by-Spot imaging: $^{12}$N Image

Developments in proton radiography and real-time PET at KVI-CART
Spot-by-Spot imaging: $^{12}$N Image

10$^8$ Protons

Beam

10$^9$ Protons

Early Image

Late Image

Developments in proton radiography and real-time PET at KVI-CART
Spot-by-Spot imaging: $^{12}\text{N}$ Image

 developments in proton radiography and real-time PET at KVI-CART
Summary and Outlook

- Proton radiography could be used to improve RSP derived from CT images.

- Beam-on PET is an attractive option to detect deviations between the intended and delivered dose during ion therapy.

- Short-lived positron emitters such as $^{12}\text{N}$ and $^{12}\text{N}/^{13}\text{O}$ dominate the PET counts early on into irradiation with protons and helium ions respectively.
New image-guided preclinical research facility

- dose delivery
  - PBS; scattering
  - protons; helium; carbon
  - shoot through; SOBP
  - spatial fractionation
  - very high dose rates
- imaging at irradiation position
  - CT + bioluminescence
- MC-based irradiation planning
- on-site animal accommodation + labspace

Slides from Sytze Brandenburg

funded by DUTCH CANCER SOCIETY
Open Access facility

- access based on scientific quality
  - evaluated by independent PAC

- user support by
  - EU-funded transnational access
    - ENSAR2 until March 2020
    - INSPIRE until March 2022
    - new proposal under evaluation for period until mid-2024

- ESA: Biological Effects of Space Radiation

- information: https://www.rug.nl/kvi-cart/research/facilities/agor/

- KVI-CART medical physics and the AGOR accelerator facility will be incorporated in the University Medical Center Groningen
Acknowledgement

• host institutions

• all colleagues at KVI-CART and UMCG