Ion-beam imaging

as a tool in ion-beam therapy –

based on the technology of

silicon pixel detectors

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and M. Martisikova (DKFZ)
Outline

- Ion-beam therapy (IBT) & the motivation for ion-beam imaging in IBT

- Ion-beam imaging
  - Basic principle & advantages
  - Possible clinical applications

- Our research on helium-beam radiography\(_{(\alphaRAD)}\) with Timepix
  - Why exactly helium ions? Theory
  - Findings of pRAD and \(\alpha\text{RAD}\) measurements
  - Pros and cons of the detection system
  - Outlook
Ion-beam therapy
Advantage and challenge

F. Albertini, A. Bolsi, T. Lomax (PSI)
Jäkel 2012, Ion Beam Therapy
Ed: Linz

- Important to detect any uncertainty on the treatment day
  - like anatomical changes or
  - uncertainties on material composition on the ion’s path: relative stopping power (RSP) based on x-ray CT
  \[ \delta \text{RSP} = \pm 3 \% \]
Ion-beam imaging: iRad/iCT
Basic principle and advantages

**Range Beam Radiography measurement:**

- **X-Ray:**
  - Flux of photons (a.u.)
  - Position in depth (a.u.)

- **Direct information on** $WET = \int_{entr}^{exit} RSP(z) \, dz$:
  - No error-prone conversion from photon-imaging (x-ray) to behavior of ions

- **Low radiation exposure:**
  - 10 times less than for x-ray @ same density/WET resolution [8]

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Ion-beam imaging
possible applications

- **Planning iCT @ day of planning**
  Would be perfect, but:
  - fast rotation of ion beam around the patient
  - time consuming (valuable treatment beam time)

- **iRad @ day of treatment**

 verification of 2D WET-map from the planning CT in treatment position!

\[
\text{WET}_{\text{meas}} = \text{WET}_{\text{CT}}
\]

4He @ high energy

Proton radiography for QA:
Schneider et al., 2004; MedPhys 22(4)
Why exactly helium ions? Theory

• Multiple Scattering (MCS)
  reduced by a factor of 2 for \( ^4\text{He} \) w.r.t. \( ^1\text{H} \)
  → Better spatial resolution

• Energy loss straggling
  \( \sigma_S/S \) reduced by a factor of 2 for \( ^4\text{He} \) w.r.t. \( ^1\text{H} \)
  → Better contrast-to-noise r.

• Energy loss
  Increased by a factor of 4
  → Increased dose

more detailed in:
How do we perform αRAD?

- **dE-measurements w/ high accuracy**
  \[ \frac{\delta dE}{dE} < 3.2 \%; \quad \frac{4 \text{ MeV}}{\text{mm}} < \frac{dE}{dx} < 21 \frac{\text{MeV}}{\text{mm}} \]

- **Most likely path**
  - MLP: Schulte et al., 2008, Med.Phys. 35(11)
  - Collins Fekete et al., 2015, PMB 60(13)
  - Timepix: Llopart et al., 2007, NIM A 581(1-2), equi. purchased from ADVACAM
  - dE meas.: Gehrke et al., 2017, JINST 12 P04025
Findings of αRAD and pRAD measurements

- **Suppression of secondary-ion background** is crucial for αRAD.

  - Gain of CNR: > 2.5!
  - All ions
  
  - 4He only
  
  - + accurate dE meas.
  
  => WET resolution of 0.6 %
  
  @ clinical dose level (300 µGy)

- αRAD provides 55 % better SR than pRAD, w/o any disadvantages in terms of imaging dose or CNR.

  - Comparison of pRad/αRad: Gehrke et al., 2018, PMB 63 035037
Pros & Cons of the detection system + Outlook

+ High WET resolution (<0.6 %) @ clinical doses for dE meas. in the steep gradient of the Bragg Peak

+ Concept of energy-painted αRAD could provide
  - thin & light-weight detection systems
  - fragmentation within the det. system

- Low WET resolution (>3 %) in regions of shallow gradients (>2 cm from BP) less of a problem for residual E meas.

Outlook: tailoring initial energy to different small WET regions

Gain of CNR: > 2.5!
Acknowledgements

Talk by Laura Ghesquiere @ 2:40 pm:
Ion-range monitoring by sec. ions

Images: C. Amato, L. Ghesquiere, R. Felix-Bautista, T. Gehrke, M. Martisikova
Why exactly helium ions? Theory

- **Multiple Scattering (MCS)**
  - Reduced by a factor of 2 for $^4$He w.r.t. $^1$H
  - Better spatial resolution

- **Energy loss straggling**
  - Reduced by a factor of 2
  - Better contrast-to-noise ratio

- Energy loss
  - Increased by a factor of 4
  - Increased dose

More detailed in:
How do we perform it?
Detector technology (II)

Energy(ToT)-mode for dE-measurement (after x-ray calibration [Jakubek 2011, NIMA 633(1), pS262])

@ **full depletion**: too high dE/px ($\gtrsim 1.6 \text{ MeV}$)
$\rightarrow$ strong saturation effects (volcano)

@ **partial depletion** $\rightarrow$ good results:
$\frac{\delta dE}{dE} < 7 \%$, up to $57 \frac{\text{MeV}}{\text{mm}}$.

MIMOSA23: $\frac{\delta dE}{dE} < 59 \%$; $1 \frac{\text{MeV}}{\text{mm}} < \frac{dE}{dx} < 4 \frac{\text{MeV}}{\text{mm}}$, (w/o 2 outliers)

DynAMITe: $\frac{\delta dE}{dE} < 23 \%$; $2 \frac{\text{MeV}}{\text{mm}} < \frac{dE}{dx} < 12 \frac{\text{MeV}}{\text{mm}}$

[Pettersen et al 2017, NIMA 860; Price et al 2015, JINST 10, P05013]
Timepix enables single ion detection with information about:

- energy loss

### Graph

- Measured
- Simulated (nominal)
- Recalibrated

**Nominal Energy (MeV/u):**
- 50.57
- 71.73
- 143.52
- 220.51

**Formulae:**
- Linear fit: \( y = ax + b; \ a = 0.71, \ b = -0.06; \ R^2 = 0.997 \)
- Recalibrated:
  \[ y_{\text{rec}} = \frac{1}{a} y_{\text{meas}} - \frac{b}{a} \]

**References:**
Ion identification & tracking

- Unambiguous separation between primary and secondary ions

Identification
Ion identification & tracking
αRADS quantitatively improve

Spatial resolution improvement to:
MTF$_{10\%}$ = 1.2 lp/mm  cf. MTF$_{CT,1mm}$ = \( \frac{1}{2D_{sample}} \)

= 0.5 lp/mm

Gain of CNR: > 2.5!

WET resolution ~1 % at clinical dose levels + clinically useful spatial resolution
Ion Tracking Challenge

Bragg Curve

$^4\text{He}$ \quad \sim \text{168 MeV/u}

Plastic

$160 \text{ mm}$ \quad $159 \text{ mm}$

$3 \times \text{Timepix}$

$\text{MTF}_{10\%} = 0.2 \text{ lp/mm}$

$\text{MTF}_{10\%} = 1.3 \text{ lp/mm}$
Comparison between pRad and αRad

Examples of images

<table>
<thead>
<tr>
<th>Air gap:</th>
<th>CSP</th>
<th>APR</th>
</tr>
</thead>
<tbody>
<tr>
<td>@ 0 mm</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
</tr>
<tr>
<td>@ 80 mm</td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
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</tbody>
</table>

Comparison between pRad and αRad

Results

- **αRad improves SR** compared to pRad on average by 55%.
  \[ MTF_{10\%,\text{avg}} = 0.46 \text{ lp/mm (worst case: 0.31 lp/mm)} \] @ phantom’s WET≈190 mm.

- \( \text{CNR}_{\alpha\text{Rad}} = \text{CNR}_{p\text{Rad}} \) @ the same clinical doses.
~300 µGy: problem of **sparse images for carbon ions**

6x higher dose: **benefit for SR with disadvantages for CNR**
Back up
Safety clearance w.r.t. SR & DOSE – idea

\[ \sigma_x^2(z_0, z_1) = Z_p^2 E_0^2 \left( 1 + 0.038 \ln \left( \frac{z_1 - z_0}{X_0} \right) \right)^2 \int_{z_0}^{z_1} \frac{(z_1 - z)^2 \beta^2(z)c^2p^2(z)}{X_0} \, dz \]

- **Idea:** push the low-\(\beta\) region out of object & rear tracker.

- **New set-up**

Carlo Amato, Master thesis, University of Pisa 2017
If required, **SRs up to \(~0.7\) lp/mm** can be achieved with the TPX-based system. The decrease in CNR (increase in dose) might be tolerable for certain situations.

Carlo Amato, Master thesis, University of Pisa 2017
Back up
Acquisition time (currently **5-6 min**)

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Technology</td>
<td>250 nm, CMOS</td>
<td>130 nm CMOS</td>
</tr>
<tr>
<td>Transistors/px</td>
<td>~550</td>
<td>~2600</td>
</tr>
<tr>
<td>ToA res.</td>
<td>10 ns</td>
<td>1.56 ns</td>
</tr>
<tr>
<td>ToA &amp; ToT</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>Bits per Pixel</td>
<td>14</td>
<td>48</td>
</tr>
<tr>
<td>Data-driven or full frame</td>
<td>Only ff</td>
<td>dd or ff</td>
</tr>
<tr>
<td>0-suppressed read-out</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>Dead time per px (for (our readout systems)</td>
<td>&gt;= 9000 µs</td>
<td>&gt;=0.01 µs</td>
</tr>
<tr>
<td>Output bandwidth</td>
<td>&lt;= 3.2 Gbps</td>
<td>&lt;=5.2 Gbps</td>
</tr>
</tbody>
</table>

Acquisition times for radiographs < 1 s possible with TPX3!
Outlook  
- WET range

- **Challenge:** WET range w/ high resolution: ~2 cm
- Conceivable approach: scan with adaptive energy + 2 dE-det. layers

8x11 ROIs of 14x14 mm, First ROI @ (-106,-219.6)  

WET calc. with matrad based on CT-scan of Alderson head phantom
Scalable due to tech. of edgeless silicon sensors

Accessed on: 05.12.2018
Back-up

overshoots

second.

prim.

already stopping due to straggling

overlaps

rel. no of clusters

cluster size (px)

cluster signal (a.u.)
image reconstruction algorithm

air gap: @ 0 mm @ 80 mm @ 0 mm @ 80 mm

CSP

APR


Ion Tracking (front and back)
Method – assessment of spat. res.

\[ \alpha = 2.9^\circ \]
\[ \Delta x = \tan(\alpha) \times 0.22 = 0.011 \text{ mm} \]
How do we perform it?
Detector technology (I)

Utilization of the very **handy, semiconductor based** Timepix detector

- Sensor: 300 µm Si
- Pixel pitch: 55 µm
- 1.4 cm x 1.4 cm, 3-side buttable
- Each of the 65k pixels operable in 2 modes:
  - ToA (100 ns) OR
  - ToT (THL @ 5 keV, res. of 2 keV)
- Full-frame readout (100-3400 fps) ➔ 300-9000 µs dead time per pixel