Lung cancer heavy ion therapy
CMOS tracking device

iWoRiD presentation – June 2023

Lévana GESSON
PhD student
Under the supervision of
Marie VANSTALLE and Uli WEBER
01. Lung cancer heavy ion therapy treatment
Lung cancer heavy ion therapy treatment

Cancer

Number of new cases in 2020

- Breast (12.5%)
- Lung (12.2%)
- Colorectum (10.7%)
- Prostate (7.8%)
- Stomach (6%)
- Liver (5%)
- Other cancer (42.5%)

Number of deaths in 2020

- Lung (18.2%)
- Colorectum (9.5%)
- Liver (8.4%)
- Stomach (7.8%)
- Breast (6.9%)
- Oesophagus (5.9%)
- Pancreas (4.7%)
- Other cancer (39.1%)

Data source: Globocan 2020
Graph production: Global Cancer Observatory (http://gco.iarc.fr)

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- Cervix uteri (3.3%)
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Lung cancer heavy ion therapy treatment
State of art

**Lung cancer**
- One of most prevalent diagnosed cancer worldwide
- 22% overall mortality rate

**Non-small cell lung cancer**
- 80% of lung cancer diagnoses
- 5-year survival rate of 26%
- Stage III and above: tumor size 3-7cm

**Treatment**
- Photon therapy: 20% 5-year overall survival
- Carbon ion radiation therapy: 42% 5-year survival

**Limits of CIRT on NSCLC**
- Individual differences
- Respiratory movement
- No adequate sample size to study
- Cost (facility 140 millions; treatment 50 000)

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Lung cancer heavy ion therapy treatment
State of art

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3. 5-year survival rate of 26%
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3. Photon therapy: 20% 5-year overall survival
4. Carbon ion radiation therapy: 42% 5-year survival

4. Individual differences
5. Respiratory movement
6. No adequate sample size to study
7. Cost (facility 140 millions; treatment 50 000)
Lung cancer heavy ion therapy treatment
State of art

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Lung cancer heavy ion therapy treatment

Breathing movement

Pencil motion on similar time scale as intra-fractional tumor motion -> interplay effect

Motion effects
- Dose deterioration
- Delivered dose shift of 10-15% (1-5mm)
Lung cancer heavy ion therapy treatment

Breathing movement

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Dose distribution of heavy ions for lung tumor treatment planned at the end of inhale. [8]

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02. Monitoring with secondary particles
Monitoring with secondary particles
CMOS protons detection

How can we improve the lung cancer treatment focusing on the breathing movement problematic?

Collaboration between IPHC / GSI

Monitoring using the secondary protons produced during carbon ion treatment

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Monitoring with secondary particles
CMOS protons detection

How can we improve the lung cancer treatment focusing on the breathing movement problematic?

Collaboration between IPHC / GSI
Monitoring using the secondary protons produced during carbon ion treatment

- 928 rows x 960 columns
- Pixel size 20.7 μm
- 50 μm thickness + 14 μm epitaxial layer
- Readout time 186.5 μs (~ 5 kHz frame rate)
- Spatial resolution 10 μm

Measurements at MIT clinic, Marburg Germany

CMOS Mimosa-28 (IPHC)

Figure – Cluster map and projection for $^{12}$C beam of 326 MeV
Monitoring with secondary particles
MIT experiment

Carbon ion Beam (Scanning pencil beam)

Target: PMMA cylinder inside foam on moving table

CMOS trackers

Secondary protons

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Monitoring with secondary particles

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Secondary protons

CMOS trackers

Clusters

10°
20°

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Monitoring with secondary particles
MIT experiment

Carbon ion Beam
(Scanning pencil beam)

Target: PMMA cylinder inside foam on moving table

Secondary protons

Vertex (Production point)

Reconstructed track

CMOS trackers

Clusters

10°

20°

10°

20°

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Monitoring with secondary particles
MIT experiment

STIVI algorithm
*Developed by C. Finck and CA. Reidel*

Carbon ion
Beam (Scanning pencil beam)

Target: PMMA cylinder inside foam on moving table

Secondary protons

Vertex (Production point)

Reconstructed track

CMOS trackers

Clusters

Hits

STIVI algorithm
*Developed by C. Finck and CA. Reidel*
Monitoring with secondary particles
MIT experiment results

- Full clinical treatment plan
  - Sphere of 50mm of diameter
  - Plan of 2 Gy
  - 2.5 min

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- Monitoring with secondary particles
- MIT experiment results

- Full clinical treatment plan
  - Sphere of 50mm of diameter
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- Carbon ion Beam
  (Scanning pencil beam)

Moving target
Static centered target

Number of vertex

Vertex position along the beam axis (μm)

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Monitoring with secondary particles
MIT experiment results

- Full clinical treatment plan
  - Sphere of 50mm of diameter
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Monitoring with secondary particles

<table>
<thead>
<tr>
<th>Foam</th>
<th>PPMA Target</th>
</tr>
</thead>
</table>

Number of vertex

- Moving target
- Static centered target

Differences in proton distribution observable with the CMOS trackers
We can deduce from distributions if treatment plan delivered as planned

- Carbon ion Beam
  (Scanning pencil beam)
Monitoring with secondary particles
MIT experiment results

**Full clinical treatment plan**
- Sphere of 50mm of diameter
- Plan of 2 Gy
- 2.5 min

<table>
<thead>
<tr>
<th></th>
<th>Static</th>
<th>Moving</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vertex X vs Y</strong></td>
<td><img src="image1" alt="Static plot" /></td>
<td><img src="image2" alt="Moving plot" /></td>
</tr>
<tr>
<td><strong>Vertex X vs Z</strong></td>
<td><img src="image3" alt="Static plot" /></td>
<td><img src="image4" alt="Moving plot" /></td>
</tr>
<tr>
<td><strong>Vertex Y vs Z</strong></td>
<td><img src="image5" alt="Static plot" /></td>
<td><img src="image6" alt="Moving plot" /></td>
</tr>
</tbody>
</table>

Claire-Anne Reidel
preliminary plots
Monitoring with secondary particles
CMOS tracking device

Real time monitoring of:
- Beam position
- Movement of high density-gradients areas

Using these data for better control of the treatment:
- Improve 4D treatment plans and reduce margins

Software and interfaces for the Front-End:
- Real time visualization
- Interfaces for interlock, gating
- Interfaces for beam control
Monitoring with secondary particles
CMOS tracking device

MC simulation on a clinical case with GATE (Geant4 based) on patient 4D-CT

CMOS device optimization:
- dimension, shape, number
- Time of response
- ADC

Digital hardware:
- Data transfer and digital pre-processing on sensor

Algorithms for fast processing of data:
- Deep learning for clustering, tracking
- GPU/FPGA
Conclusion

Breathing movement induce dose shift and deterioration
Conclusion

Breathing movement induce dose shift and deterioration

Monitoring using secondary protons

Lung cancer heavy ion therapy
Conclusion

Breathing movement induce dose shift and deterioration

Monitoring using secondary protons

CMOS tracking device to reconstruct protons’ vertex distribution

Lung cancer heavy ion therapy
Conclusion

- Breathing movement induce dose shift and deterioration
- Monitoring using secondary protons
- CMOS tracking device to reconstruct protons’ vertex distribution
- Clinical application concept
References

[1] Nymus 3D animations – part of the Demcon group
[9] University of Iowa health care - https://www.youtube.com/watch?v=nZO44EicYO4
Back-up
Heavy ions compared to photons
- high LET (linear energy transfer)
- high RBE (relative biological effectiveness)
- low OER (oxygen enhancement ratio)
- high mortality rate of tumor cells
- good activator of antitumor immunity
- more efficient to prevent angiogenesis and metastasis
Lung cancer heavy ion therapy CMOS tracking device
State of art

Combine CIRT with imaging techniques (PET/4D-CT)

Adjuvant chemotherapy drugs

Improve combination of CIRT with immunotherapy

Improvement needed for treatment planning and dose calculation because of lung movement

Reducing technology / hospitalization / examination cost
Figure - DRBE and dose-averaged linear energy transfer (LETD) maps for intensity modulated particle therapy (IMPT) versus spot-scanning hadron arc (SHArc). (a) Case A: optimization with target (T) and normal tissue (NT) constraints. (b) Case B: clinical-like scenario with planning target volume (PTV)/organs at risk (OAR) optimization. Both cases were conducted using 3 clinical ion beams (p, 4He, and 12C ions). Line profiles, dose volume histogram (DVH), and dose-averaged linear energy transfer volume histogram (LETDVH) are provided for intercomparison of SHArc plans (bottom panels). (c) Angular-fluence maps for SHArc-p, SHArc-He, and SHArc-C plans in cases A (top) and B (bottom) [16]
Overview

Treatment plan

Imaging
Define tumoral/targeted volume

Treatment planning System (TPS)

Monitoring with secondary protons

Treatment

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**Figure** - DRBE and dose-averaged linear energy transfer (LETD) maps for intensity modulated particle therapy (IMPT) versus spot-scanning hadron arc (SHArc). (a) Case A: optimization with target (T) and normal tissue (NT) constraints. (b) Case B: clinical-like scenario with planning target volume (PTV)/organs at risk (OAR) optimization. Both cases were conducted using 3 clinical ion beams (p, 4He, and 12C ions). Line profiles, dose volume histogram (DVH), and dose-averaged linear energy transfer volume histogram (LETDVH) are provided for intercomparison of SHArc plans (bottom panels). (c) Angular-fluence maps for SHArc-p, SHArc-He, and SHArc-C plans in cases A (top) and B (bottom) [16]
General and scientific context

**LET 3/3**

**Figure** - DRBE and dose-averaged linear energy transfer (LETD) maps for intensity modulated particle therapy (IMPT) versus spot-scanning hadron arc (SHArc). (a) Case A: optimization with target (T) and normal tissue (NT) constraints. (b) Case B: clinical-like scenario with planning target volume (PTV)/organs at risk (OAR) optimization. Both cases were conducted using 3 clinical ion beams (p, 4He, and 12C ions). Line profiles, dose volume histogram (DVH), and dose-averaged linear energy transfer volume histogram (LETDVH) are provided for intercomparison of SHArc plans (bottom panels). (c) Angular-fluence maps for SHArc-p, SHArc-He, and SHArc-C plans in cases A (top) and B (bottom) [16]

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Lung cancer heavy ion therapy CMOS tracking device

GATE simulation

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Monitoring with secondary particles
GATE simulation

Gate simulation on human phantom with a Carbon ion beam 170 MeV/u

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Lung cancer heavy ion therapy treatment
Radiotherapy

X-ray Therapy

Delivered target dose
Required dose

Carbons

X-rays

Depth in Water (mm)

Relative Dose

[1]

[2]

[3]

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Lung cancer heavy ion therapy treatment
Radiotherapy

Proton Therapy

Delivered target dose

Required dose

![Graph showing dose distribution with different types of radiation](image1.png)

- [1] Photon 21 MeV
- [2] $^{12}$C 270 MeV/u

Carbons

X-rays

[1] [2] [3]
Lung cancer heavy ion therapy treatment

Radiotherapy

Proton Therapy

Heavy ion
- Less damage to surrounding tissue
- Lower scattering of the beam
- Higher biological effect
- But dose after Bragg peak

[1]

Carbons

X-rays

[2]

Heavy ion therapy using beams of heavy ions such as carbon ions can offer several advantages over traditional radiotherapy with X-rays. These include:

- **Less damage to surrounding tissue**
  - By reducing the scattering of the beam, heavy ions can deliver a more focused dose to the tumor, minimizing damage to healthy tissue.

- **Lower scattering of the beam**
  - Heavy ions have a more defined path through tissue compared to lighter ions or X-rays, resulting in less scattering and better localization of the dose.

- **Higher biological effect**
  - Heavy ions can penetrate deeper into tissue and cause more localized damage to cancer cells, potentially improving treatment efficacy.

- **But dose after Bragg peak**
  - While heavy ion therapy can offer significant benefits, the dose distribution can also result in a peak dose at a certain depth, which may need careful planning to ensure optimal tumor control.

[1] [2] [3]