Pencil Beam Scanning (PBS) in Radiotherapy of Malignant Lymphomas

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PTC Prague, Czech Rep.
Why proton beam therapy

Why protons?
- Have Bragg peak and they stop in the tissue
- Radiobiological effectiveness is similar

Bragg’s peak is energy-dependent. This energy can be precisely regulated.

Better dose distribution in the body

Boron's peak is energy-dependent. This energy can be precisely regulated.

Dose 40-50%

Photons 60 Gy

2,400 X-rays of the skull

Protons 40% dose
Proton therapy technology

- First clinical use – 1953
- Technology sophisticated from 2011
Pencil beam scanning

Technology available from 2011

A fundamental change in proton technology

- Better dose distribution

![Diagram of pencil beam scanning](image)

- Intensity Modulated Beam
- Pair of Quads
- Scanning Magnets
- Fast
- Slow
- Vacuum Chamber
- Beam monitor
Equipment

Proton beam
- Cyclotron IBA Proteus 5
- 230 MeV nominal beam energy

IGRT
- Verisuite
- VisionRT
- Robotic couch
- DynR

Imaging
- 2x MRI
- 2x CT
- PET/CT

Clinical oncology

Urology

ORL

Cooperation with:
- Czech and Slovakia comprehensive cancer centers
- Charles University, Czech Technical University, Academy of Science
Malignant lymphomas

1) Comprehensive and extensive target volumes

2) Young patients

3) High curability rate

4) Late and very late effects of photon techniques

- Cardiotoxicity - RIHD
- Ischemic heart disease
- Pneumotoxicity
- Secondary cancer

3D CRT – heart dose!
IMRT - lung dose, breast dose!

Better tool – PBS(?)

Schellong et al., 2010; Hull et al., 2003; Heidenreich et al., 2003; Brusamolino et al., 2006; Harbron et al., 2013
Hahn E. described 44 cardiac events in 125 HL patients. Risk was correlated with heart dose and heart vessels dose.

Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer

- Population study
- 2,168 women
- Treatment 1958-2001
- Heart Dmean = 4.7 Gy

Risk increases with 7.4% per Gy

Without threshold.
Malignant lymphomas
Secondary malignancies

- Cellai et al. IJROBP (2001) described 14.9% incidence of SM in 20 years.

In a lifetime approximately 42 of 100 people will be diagnosed with cancer. Approximately one cancer (star) per 100 people could result from a single exposure to 0.1 Sv of low-LET radiation above background.
Cardiotoxicity and secondary malignancies are significant complications of radiotherapy of lymphomas

- Probability is dose-dependent
- Proton radiation can significantly reduce doses to the heart and integral dose
Which malignant lymphomas?

Maximum utilization of proton beam features:
- Sharp dose gradient
- Stopping at a defined depth
- Significant reduction of dose

Significant dosimetric benefit
- Hodgkin lymphoma/NHL
- Mediastinal forms
- Residual mediastinal mass

Women, 25 years old, Hodgkin lymphoma st. IIBE
Residual PET + mediastinal
Malignant Lymphomas

PROTON THERAPY FOR THE MANAGEMENT OF HODGKIN AND NON-HODGKIN LYMPHOMAS INVOLVING THE MEDIASTINUM: GUIDELINES FROM THE INTERNATIONAL LYMPHOMA RADIATION ONCOLOGY GROUP (ILROG)

Problem - movement
## Effects of movement

### Criteria gamma 3mm, 3%

<table>
<thead>
<tr>
<th></th>
<th>$\gamma&lt;1$ [%]</th>
<th>$\gamma&lt;1.5$ [%]</th>
<th>Average gamma</th>
<th>Max gamma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gating</strong></td>
<td>98.56</td>
<td>100</td>
<td>0.39</td>
<td>1.27</td>
</tr>
<tr>
<td><strong>Without gating</strong></td>
<td>67.88</td>
<td>88.52</td>
<td>0.76</td>
<td>2.00</td>
</tr>
</tbody>
</table>
Motion management

- Repainting: Movement up to 1 cm!
- Gating: Movement still present!
- Tumor tracking: Promising, but technology still not available!
- Deep inspiration breathhold: Stopping of movement, possible solution
Motion management - DIBH – Dyn‘R
Reproducibility

Fusion of two DIBH CT scans (HL, IS RT)
Robustness of deep inspiration

- 3 patients - CT in the upper or lower part of deep inspiration

- Comparison of differences in WET for 5 points for each CT series
- Calculation in Python
**PET/CT check of dose distribution**

“Virtual” dose distribution

- Activation of tissue
- PET/CT immediately after fraction (in 10 min)
- Spatial control
- Detection of activation outside of the target volume

“In vivo” dose control
Clinical experiences at PTC Prague

- 2013 - 2014 – 4D CT and repainting
- 2015 – DIBH (in combination with repainting, if necessary)
Proton Radiotherapy for Mediastinal Hodgkin Lymphoma: Single Institution Experience

Dědečková et al., 10th ISHL, Cologne, 2016
Characteristics of patient group (n=35)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males/Females [pts.]</td>
<td>10/25</td>
</tr>
<tr>
<td>Age at the time of RT median [years]</td>
<td>27 (13-59)</td>
</tr>
<tr>
<td>RT volume [pts.]</td>
<td></td>
</tr>
<tr>
<td>Involved field</td>
<td>9</td>
</tr>
<tr>
<td>Residual disease</td>
<td>11</td>
</tr>
<tr>
<td>Involved site</td>
<td>15</td>
</tr>
<tr>
<td>Follow-up median [months]</td>
<td>9.9 (2.6-36.4)</td>
</tr>
<tr>
<td>RT on PET neg/PET positive disease [pts.]</td>
<td>25/10</td>
</tr>
<tr>
<td>RT in DIBH/FB [pts.]</td>
<td>17/18</td>
</tr>
<tr>
<td>Median dose [GyE]</td>
<td>30 (19.8-44)</td>
</tr>
</tbody>
</table>

All patients were irradiated via pencil beam scanning (PBS) technique

Dědečková et al., 10th ISHL, Cologne, 2016
## Dosimetric parameters (n=35)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV volume [cm³]</td>
<td>1,207.6 (442.8-2,252.8)</td>
</tr>
<tr>
<td>Heart Dmean [Gy]</td>
<td>6.6 (0.9-20.7)</td>
</tr>
<tr>
<td>Lungs bilat. Dmean [Gy]</td>
<td>4.9 (2.4-9.2)</td>
</tr>
<tr>
<td>Lungs bilat. V5 [%]</td>
<td>30 (12-59.8)</td>
</tr>
<tr>
<td>Lungs bilat. V20 [%]</td>
<td>22.3 (7.9-44.8)</td>
</tr>
<tr>
<td>L mammary gland Dmean [Gy]</td>
<td>1.3 (0-6.8)</td>
</tr>
<tr>
<td>R mammary gland Dmean [Gy]</td>
<td>0.9 (0-2.5)</td>
</tr>
<tr>
<td>L mammary gland V4 [%]</td>
<td>11.6 (1.4-48.2)</td>
</tr>
<tr>
<td>R mammary gland V4 [%]</td>
<td>10.2 (1.7-19.4)</td>
</tr>
<tr>
<td>Oesophageus Dmean [Gy]</td>
<td>17.3 (0-30.8)</td>
</tr>
<tr>
<td>Spinal Cord Dmax 2% [Gy]</td>
<td>5.2 (0-21)</td>
</tr>
</tbody>
</table>

Dědečková et al., 10th ISHL, Cologne, 2016
Acute toxicity (CTCAE v4.0)

- Pharyngeal mucositis
  - grade 2: 9%
  - grade 1: 63%

- Leucopenia
  - grade 3: 3%
  - grade 2: 6%

- Radiodermatitis
  - grade 2: 3%
  - grade 1: 40%

- Pleuritic pain
  - grade 1: 3%

NO CASE of radiation pneumonitis or Lhermittés syndrome

NO PATIENT required growth factors or hemosubstitution during RT

Dědečková et al., 10th ISHL, Cologne, 2016
Treatment results

**Time to relaps (Kaplan Meier)**

- 35 patients (100%) achieved **local control**
- 2 pts (6%) **progressed out of the target** volume (distal regions)
- 34 pts (97%) are in **complete remission** (1 pt after alo-SCT)
- 1 pt (3%) has **progressive disease** on salvage therapy

<table>
<thead>
<tr>
<th>Total observed</th>
<th>Total failed</th>
<th>Total censored</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td>2</td>
<td>33</td>
</tr>
</tbody>
</table>

Dědečková et al., 10th ISHL, Cologne, 2016
Summary on protons for mediastinal Hodgkin lymphoma

- Promising and safe option for a majority of patients

- Low acute toxicity profile and a potential to decrease the risk of significant late toxicity

- Should be considered in all HL patients indicated for mediastinal RT (first of all, young patients with long life expectancy) or re-irradiation
Case 1 – Mediastinal Hodgkin Lymphoma

<table>
<thead>
<tr>
<th>Organ at risk</th>
<th>Parameter</th>
<th>Dose Gy</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>Dmean</td>
<td>27.85</td>
</tr>
<tr>
<td>Lung (R+L)</td>
<td>Dmean</td>
<td>4.96</td>
</tr>
<tr>
<td>Heart</td>
<td>Dmean</td>
<td>3.17</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>Dmax</td>
<td>1.7</td>
</tr>
<tr>
<td>Breast R</td>
<td>Dmean</td>
<td>1.61</td>
</tr>
<tr>
<td>Breast L</td>
<td>Dmean</td>
<td>1.17</td>
</tr>
</tbody>
</table>

Standard case – significant reduction of heart dose, lung dose, reduction of breast dose
Case 2 – Mediastinal Hodgkin Lymphoma

<table>
<thead>
<tr>
<th>Organ at risk</th>
<th>Parameter</th>
<th>Dose Gy</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>Dmean</td>
<td>28.32</td>
</tr>
<tr>
<td>Lung (R+L)</td>
<td>Dmean</td>
<td>5.26</td>
</tr>
<tr>
<td>Heart</td>
<td>Dmean</td>
<td>5.8</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>Dmax</td>
<td>13.8</td>
</tr>
<tr>
<td>Esophageus</td>
<td>Dmean</td>
<td>13.15</td>
</tr>
</tbody>
</table>

Most suitable case for protons — significant reduction of heart dose, lung dose
Case 3 – Subdiaphragmatical Non-Hodgkin Lymphoma

Organ at risk | Parameter | Dose Gy |
--- | --- | --- |
PTV | Dmean | 33.5 |
Liver | Dmean | 6.42 |
Kidney R | Dmean | 8.85 |
Kidney L | Dmean | 3.57 |
Spinal cord | Dmax | 26.6 |

Feasible with protons — significant reduction of liver, kidney, abdominal cavity dose
Case 4 – Mediastinal Non-Hodgkin Lymphoma, highly pretreated

<table>
<thead>
<tr>
<th>Organ at risk</th>
<th>Parameter</th>
<th>Dose Gy</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>Dmean</td>
<td>37.25</td>
</tr>
<tr>
<td>Lung (R+L)</td>
<td>Dmean</td>
<td>8.74</td>
</tr>
<tr>
<td>Heart</td>
<td>Dmean</td>
<td>15.5</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>Dmax</td>
<td>0.05</td>
</tr>
<tr>
<td>Esophageus</td>
<td>Dmean</td>
<td>17.2</td>
</tr>
</tbody>
</table>

Refractory, bulky mediastinal disease – almost impossible to treat to such doses with photons. Probably CR after allo-SCT.
Case 5 – Non-Hodgkin Lymphoma, highly pretreated, pleural involvement

<table>
<thead>
<tr>
<th>Organ at risk</th>
<th>Parameter</th>
<th>Dose Gy</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>Dmean</td>
<td></td>
</tr>
<tr>
<td>Lung (R+L)</td>
<td>Dmean</td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>Dmean</td>
<td></td>
</tr>
<tr>
<td>Spinal cord</td>
<td>Dmax</td>
<td></td>
</tr>
<tr>
<td>Esophagus</td>
<td>Dmean</td>
<td></td>
</tr>
</tbody>
</table>

Refractory disease, pleural involvement, after TBI – considered like palliative treatment, 3 years after CR
Conclusion

- Adaptive radiotherapy with PBS for Head and neck cancer is feasible approach with low toxicity rate and promising effectivity.

- PBS radiotherapy with gating in DIBH is feasible approach for malignant lymphomas with significantly better dosimetry than photon radiotherapy.
Thank you for attention!