Dosimetry of particle beams with ultra-high pulse dose rates (in the context of VHEE)

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Very High Energy Electron Radiotherapy Workshop (VHEE’2020), 5-7 October 2020
Outline

- Background/Motivation
- Interest in UHPDR RT
- Recap on dosimetry
- Challenges of dosimetry of UHPDR beams
- First results
  - Calorimetry & ionization chamber dosimetry in UHPDR VHEE beams
- Conclusions
Motivation

- >360,000 new cancer cases/yr (70% rise over the next 2 decades)
- Radiotherapy is the most cost-effective methods responsible for ca. 50% of cancer survivals

How can we increase efficacy of RT?
- Improved the 3D dose conformation (thanks to major technological advances)
- Use of radiosensitizers/radioprotectors
- Application of different beam modalities
- UHDRP...
Why are we interested in UHPDR RT?

- First UDR studies – 1960s

- subcutaneous lymphoma
- delivery: 10 pulses (1 us) in 90 ms with 1.5 Gy/pulse

\[
\text{Pulmonary fibrosis [%]} \quad \text{# of weeks after exposure}
\]

\[1.8 \text{ Gy/min} \quad \gamma\text{-rays}
\]

\[4.5 \text{ MeV e-beam} \quad 3600 \text{ Gy/min}
\]

Favaudon, et al. Sci Transl Med 2014; 6

- Conv. (5 Gy/min)
- FLASH (300 Gy/s)

36 WEEKS POST-RT

normal appearance of skin

necrotic lesions

Vozenin et al., Clin Cancer Res 25 (2019) 35

\[\text{FLASH!}
\]


TCP

FLASH NTCP

Probability of response

Dose
Most of the studies performed using electron beams accelerated by modified clinical LINAC or dedicated electron accelerators (E < 20 MeV)

DRAWBACKS

- Limitations of clinical electrons
- High relative surface dose
- Shallow penetration/short range
- Range straggling (no Bragg peak)
- High penumbra
- Bulging effect
- Spread of beam in air (why we have cones)

**Limitations of electron beams due to energy** – what happens if the electron energy is increased??
What happens if the electron energy is increased (100+ MeV)?

- Increases depth of penetration
- No range straggling if beam penetrates through patient
- Ability to control position electromagnetically
  - Scanning beams more easily done than heavy particles
  - Speed of electromagnetic scanning allows for ~100X more beams delivered in the same time as photons
- Lower beam spread and reduced bulging effect

While maintaining some low energy characteristics
- Can produce pencil beams
- Less costly than heavy particles
- High surface dose
Advantages of VHEE RT

VHEE unlike X-ray photons maintain electronic equilibrium in tissues with varying densities.

Perturbation of dose, - consequence - under or over dosage of tissue.

Credit: C. DesRosiers

Treatment planning for radiotherapy with very high-energy electron beams and comparison of VHEE and VMAT plans

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(Received 22 December 2014; revised 7 April 2015; accepted for publication 12 April 2015; published 29 April 2015)

Very high-energy electron (VHEE) beams in radiation therapy: Treatment plan comparison between VHEE, VMAT, and PPBS

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VHEE plan vs VMAT plan (H&N case)

- VHEE can achieve superior dose distributions (vs photons), can provide **better sparing of organs at risk** and enable **dose escalation** to the tumour

### Summary of irradiation parameters and outcomes for *in vivo* studies investigating the FLASH effect

<table>
<thead>
<tr>
<th>Model</th>
<th>Assay</th>
<th>Dose rate (Gy/Hz)</th>
<th>Pulse rate (Hz)</th>
<th>Modality of radiation</th>
</tr>
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<tbody>
<tr>
<td>Zebrafish embryo (6)</td>
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<td>1.3-1.5</td>
<td>10-12</td>
<td>Electron</td>
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<td>Fish length, survival, and rate of oedema</td>
<td>1</td>
<td>0-43</td>
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<td>Whole body irradiation of mice (6)</td>
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<td>Early skin reaction score 1</td>
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**Normal tissues**

**Tumour tissues**

**Tumor size and T-cell infiltration**

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<td>Survival and tumor growth delay</td>
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<td>15-28</td>
<td>Electron</td>
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<tr>
<td>Thoric irradiation of orthotopic engrafted mouse lung carcinoma TC-1 Lue-in mice (13)</td>
<td>Number of tumors, tumor weights</td>
<td>1</td>
<td>12-16</td>
<td>Electron</td>
</tr>
<tr>
<td>Abdominal irradiation of mice (17)</td>
<td>Survival</td>
<td>1</td>
<td>10-25</td>
<td>Electron</td>
</tr>
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<td>Local irradiation of subcutaneous engrafted human breast cancer HEC-124A and head and neck carcinoma HEP-2 in nude mice (17)</td>
<td>Local irradiation of subcutaneous engrafted US7 human glioblastoma in nude mice (6)</td>
<td>1</td>
<td>10-30</td>
<td>Electron</td>
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**Review of FLASH studies** *(Wilson et al. Frontiers in Oncology 2020)*
FLASH – a biological effect

- **NOT defined** by physical beam parameters
- **BUT** it is **dependent** on beam parameters

How FLASH effect is influenced by:
- Mean dose-rate (averaged on the irradiation duration)?
- Dose-per-pulse?
- Dose rate in the pulse?
- Temporal beam structures?

....What about dosimetry?

**The importance of dosimetry:**
- Successful radiotherapy depends on delivering the correct dose to the treatment volume and sparing surrounding healthy tissues

Are we able to perform accurate absorbed dose measurements with **UHPDR beams** with the level of accuracy required for clinical translations?
Recap on dosimetry

DETECTOR CATEGORIES

- Directly measure the quantity of absorbed dose (e.g. calorimeters)
- Measure ionisations (e.g. free-air chamber)
- Quantify in direct or indirect way the number of produced radicals (e.g. Fricke)

Radiation energy turns into heat

heat is tiny, but measurable

primary standards for absorbed dose are calorimeters
Calorimetry: principle

\[ D = c \cdot \Delta T \]

<table>
<thead>
<tr>
<th>Material</th>
<th>( c ) (J·kg(^{-1})·K(^{-1}))</th>
<th>( \Delta T/D ) (mK·Gy(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>water</td>
<td>4180</td>
<td>0.24</td>
</tr>
<tr>
<td>graphite</td>
<td>710</td>
<td>1.41</td>
</tr>
</tbody>
</table>
Calorimetry
Ion chamber
Challenges of dosimetry of UHPDR beams

Loss of collection efficiency in IC

Conventional (CONV.) vs. FLASH

- **Mean dose rate**: 0.05 Gy/s vs. 40-1000 Gy/s
- **Dose per pulse**: 0.3 mGy vs. 1-10 Gy
- **Dose in a pulse**: $10^2$ Gy/s vs. $10^6$ Gy/s
- **Delivery time**: few min vs. <1 s

NEW DOSIMETRY TOOLS & METHODS NEEDED

USE THE RIGHT TOOL FOR THE RIGHT JOB

Petersson et al., Med Phys 44 (2017) 1157
First experimental results: UHPDR VHEEs
First experimental results: UHPDR VHEEs

**OBJECTIVE:** To study ion collection efficiency as a function of dose-per-pulse at instantaneous dose rates $5.0 \times 10^6 – 3.1 \times 10^8$ Gy/s for VHEE beams (energies suitable for deep-seated tumours)

- **BEAM PARAMETERS:** 200 MeV, x and y $\sigma$ of 5 mm, $\Delta E$ between 0.25 and 6.5%
- **side-by-side measurements:** PTW Roos chamber and NPL’s graphite calorimeter
- **quantification of the recombination factor** $k_{s,abs}$ for the Roos chamber for a range of collecting voltages: 75 V – 600 V

---

**Nominal Beam Charge (nC/pulse) | Dw,cal (Gy/pulse) | ks,abs**

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<th>Dw,cal (Gy/pulse)</th>
<th>ks,abs</th>
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<td>0.05</td>
<td>0.03</td>
<td>1.3</td>
</tr>
<tr>
<td>0.2</td>
<td>0.20</td>
<td>3.41</td>
</tr>
<tr>
<td>0.25</td>
<td>0.14</td>
<td>2.46</td>
</tr>
<tr>
<td>1</td>
<td>0.67</td>
<td>6.00</td>
</tr>
<tr>
<td>2.2</td>
<td>1.25</td>
<td>8.80</td>
</tr>
<tr>
<td>3</td>
<td>1.95</td>
<td>11.96</td>
</tr>
<tr>
<td>4.5</td>
<td>2.63</td>
<td>14.99</td>
</tr>
<tr>
<td>6</td>
<td>3.66</td>
<td>18.94</td>
</tr>
<tr>
<td>7.5</td>
<td>4.12</td>
<td>19.54</td>
</tr>
<tr>
<td>9</td>
<td>4.56</td>
<td>21.38</td>
</tr>
<tr>
<td>10.5</td>
<td>5.26</td>
<td>22.99</td>
</tr>
</tbody>
</table>

$$k_{s,abs} = \frac{D_{w,cal}}{Mk_{pol}k_{TP}Q_0N_{D,w,Q_0}}$$

The test-stand at the CLEAR facility, with the calorimeter, ion chamber and monitor chamber placed along the beam line with the beam travelling from right to left.
Results cont.

- \( k_s \) up to 10 \((V = 200V) \) → collection eff. 10%
- \( k_s \) up to 4 \((V = 600V) \) → collection eff. 25%
- \( k_{s,abs} \) compared with \( k_{s,TVA} \) (two-voltage method)

- Available recombination models include Boag’s free-electron fraction models (Boag 1996)
- By optimising the free-electron fraction parameter in these equations, we were able to determine a best fit of our data.
- All analytical models of Boag and Di Martino show similar predictions of the recombination factor and estimations of the free electron fraction
- Analytical (Boag 1996, Di Martino 2005) and logistic (Petterson 2017) models tested
- The logistic model from Petersson shows the best fit to data over the whole dose-per-pulse range, however this model has no physical meaning and simply relies on two fitting constants \( \alpha \) and \( \beta \)
Conclusions & final statements

- Tools and methods established for dosimetry of conventional RT sources are not suitable for UHPDR beams (lack of primary standards, CoPs & reliable active dosimeters for real time dosimetry)

- Challenges of dosimetry for ultra-high pulse dose rate to be addressed within EMPIR UHDpulse project, which aims to provide metrological and validated tools will be provided to support accurate preclinical studies and to enable future clinical applications for UHPDR beams → Introduced by Andreas Schueller

- Plane-parallel Roos chamber exposed to UHPDR VHEE suffers from significant collection loses which cannot be described with available analytical ion recombination models

- Accurate absolute dosimetry is paramount in translational FLASH studies (given the uncertainties in biological response)
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- Michael McManus
- Francesco Romano
- Nigel Lee
- Hugo Palmans
- Wilfrid Farabolini
- Antonio Gilardi

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