Objectives

- Review electron therapy history
- Understand >100 MeV electrons, (VHEE) in historical context
- Describe equipment and current state for clinical availability of VHEE
- Discuss FLASH considerations
- Examine potential role for electrons in FLASH
  - Clinically available energies (below 30 MeV)
  - VHEE
History I

Discovery of Radiation
1895

0.2 MeV cathode rays used for skin lesions
1909

First X-ray Unit
1896

First clinical treatment with Van de Graaff at Harvard
1923

First linac built at Stanford
1947

First clinical Betatron treatment
1928

First patient treated with medical accelerator
1952

Grid therapy experience published
1942

First linac to use both photons and electrons for therapy
1956

7 clinical linacs worldwide

Grenz rays


Skaggs, 1948 – focus on the development of “high” energy electron therapy

Penetration of a 35 MeV electron = 17 cm

“Now, with the betatron, we have cathode rays...which out to reach almost any malignant lesion provided this beam is properly directed”
Electron accidents

• 1966 – 3 patients overdosed, Hammersmith Hospital
  Playfair, Spiers & Smithers report implicates photons more likely to underdose, electrons more likely to overdose

• 1990 – Spain – CGR accelerator
  • Energy selector mechanism failed resulting in up to 9X overdose
  • 27 patients overdosed, 15 patients died

• 1985-87 – US and Canada – Therac 25, AEC
  • Electron beams delivered with X-ray parameters
  • 6 overdoses
    • patient described intense electric shock, ran out of room screaming
    • 3 patients died from radiation injury

Was a perception created that electrons are less safe than photons?

Did this perception halt the further development of electrons in radiation therapy?
History II

- MM50 Racetrack Microtron
- First paper published on the use of electrons >100 MeV for therapy
- Intensity modulated arc therapy implemented
- 4D therapy to account for motion
- 1988
- 1994
- 1997
- 2000
- 2002
- 2004
- First linac with tumor tracking in real time (Cyberknife)
- Tomotherapy
- LWFA as a medical accelerator feasibility study

VHEE (>100 MeV)

- Potential advantages over other modalities
  - Clinical Electrons (<30 MeV)
    - Can reach deep seated tumors
    - Less penumbra
  - Photons
    - Less sensitive to inhomogeneities
    - Position can be controlled (scanning) resulting in reduced treatment times and finer IMRT
  - Protons/heavy particles
    - Less sensitive to inhomogeneities
    - Easier to position
    - Less expensive
VHEE Penumbra

<table>
<thead>
<tr>
<th>Energy (MeV)</th>
<th>Penumbra at $R_{0.5}$ (mm)</th>
<th>Penumbra at $R_{10}$ (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>18</td>
<td>12.0</td>
</tr>
<tr>
<td>15</td>
<td>28</td>
<td>7.5</td>
</tr>
<tr>
<td>30</td>
<td>47</td>
<td>4.4</td>
</tr>
<tr>
<td>50</td>
<td>59</td>
<td>2.9</td>
</tr>
</tbody>
</table>

From Karlsson, et al

VHEE penumbra
- better than clinical electrons
- worse than clinical photons

Penumbra less impactful as # beams increases

From DesRosiers, et al

VHEE other characteristics

PDD

MM50 Racetrack Microtron
From Karlsson, et al

From Subiel, et al

Insensitivity to heterogeneities
History III

- **2013 - present**: compact linear accelerator development (PHASER, etc.)
- **2014 - present**: FLASH, ongoing radiation biology experiments
- **2015 – present**: Grid therapy in FLASH era

FLASH dominant R&D

- **Electrons**
  - Most well established and consistent effect at low energies (<10 MeV)
  - First patient treated
  - VHEE
- **Photons**
  - Not a lot of studies, one negative
  - High dose rate challenge
- **Particles**
Even without enhanced dosimetric effect, high dose rates are advantageous because speed of treatment reduces motion effects for all modalities.

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L. Hancock, VHEE2020, CERN

M. Bazalova-Carter et al

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Grid therapy -1952

- Spatially fractionated beam
- High dose delivery/high dose rates
- Reduced normal tissue toxicity
- FLASH effect? (Eling, et al.)
- VHEE suitable for grid therapy
  - Pencil beams
  - *Easily scanned*
  - *Easily positioned*

Grid therapy (eHGRT)
Martinez-Rovira, et al. 2015

![Proton grid therapy](From Martinez-Rovira, et al., 2015)

**Fig. 8:** 2D depth dose distributions in eHGRT (energy: 150 MeV, grid size: 3000 x 3000 μm², etc: 5500 μm; field size: 2 x 2 cm²). The spatial fractionation of the dose is observed in the healthy tissue, while the tumor profits from a more homogeneous dose distribution.

**Table 1.** Penumbra values at several depths for the several techniques considered: xGRT, eHGRT (150 MeV), and pORT.

<table>
<thead>
<tr>
<th>Depth (cm)</th>
<th>xGRT (μm)</th>
<th>eHGRT (μm)</th>
<th>pORT (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>61 ± 2</td>
<td>311 ± 7</td>
<td>492 ± 25</td>
</tr>
<tr>
<td>3</td>
<td>62 ± 2</td>
<td>985 ± 20</td>
<td>588 ± 29</td>
</tr>
<tr>
<td>5</td>
<td>63 ± 2</td>
<td>1826 ± 37</td>
<td>920 ± 46</td>
</tr>
<tr>
<td>7</td>
<td>62 ± 2</td>
<td>2213 ± 45</td>
<td>1343 ± 67</td>
</tr>
</tbody>
</table>
Equipment Design for VHEE

- Betatron
  - Max energy ~100 MeV
  - Insufficient dose rate, cannot produce FLASH
- Racetrack microtron (Scanditronix)
  - Clinical 50 MeV electron accelerator
  - 100 MeV electron accelerator
- Linear accelerator – compact design (PHASER)
- Laser Wakefield Accelerator (LWFA)
  - 200 MeV acceleration in 1 mm

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Equipment – LWFA at LOA


Flacco, A. VHEE2020 Workshop, CERN

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Compact linear accelerator advancements

• Aim to design VHEE to fit in existing linac vaults
• Distributed RF coupling and cryogenic copper
  – Produces 150 MV/meter
  – SLAC “DRAGON” achieves with similar RF power as current linacs
• Inverse Compton Source
  – 80 MeV/m
• X band pulse compressor

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Equipment - CERN

VHEE dose delivery in phantom

CERN VHEE 2020 Workshop, Nanni, Wuensch
Equipment – SLAC/PHASER

Next-generation linear accelerator

Ultra-rapid "FLASH" RT: New biology
FLASH RT preclinical biology experiments at Stanford

CERN VHEE 2020 Workshop, Loo, Maxim

Equipment Tsinghua

CERN VHEE 2020 Workshop, Shi
Institutions developing VHEE
partial list, many are collaborators

- CERN
- Lausanne University
- SLAC
- Tsinghua University
- University of Strathclyde
- Manchester University Cockcroft Institute
- ELBE Center, Dresden
- Sapienza, University of Rome

Dosimetry challenges

- Ion chambers - recombination
  - Plane parallel chambers (PTW Roos)
- Film
  - Gaf chromic, EBT3
  - Radiographic unsuitable due to limited dose range
- Calorimetry
- Monte Carlo
- Polymer gels? OSLDs? Diodes? Alanine?
The case for VHEE

• Not considering FLASH effect...
  – Dosimetric advantages
    • High spatial resolution IMRT due to scanned pencil beam
    • Fast delivery due to scanning
      – Minimizes motion
      – Allows better for multiple beams
  – Inhomogeneities
  – Cost advantages
    • Likely to be comparable to standard medical accelerator
    – Compact accelerator designs

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The case for VHEE (cont.)

• Considering FLASH...
  – Well established with electrons
  – Technology available currently (if it can be done with photons, it can be done hundreds of times easier with electrons)
  – Cost

To learn more about VHEE visit, VHEE2020 Workshop CERN
https://indico.cern.ch/event/939012/timetable/?view=standard

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It all starts with an idea…

Lech Papiez, PhD
March 12, 1950 – April 15, 2016

I ❤ ELECTRONS