Indiana University Health

Very High Energy Electrons Rationale for therapy and FLASH potential

AAPM Annual Meeting 2021, Virtual

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1

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

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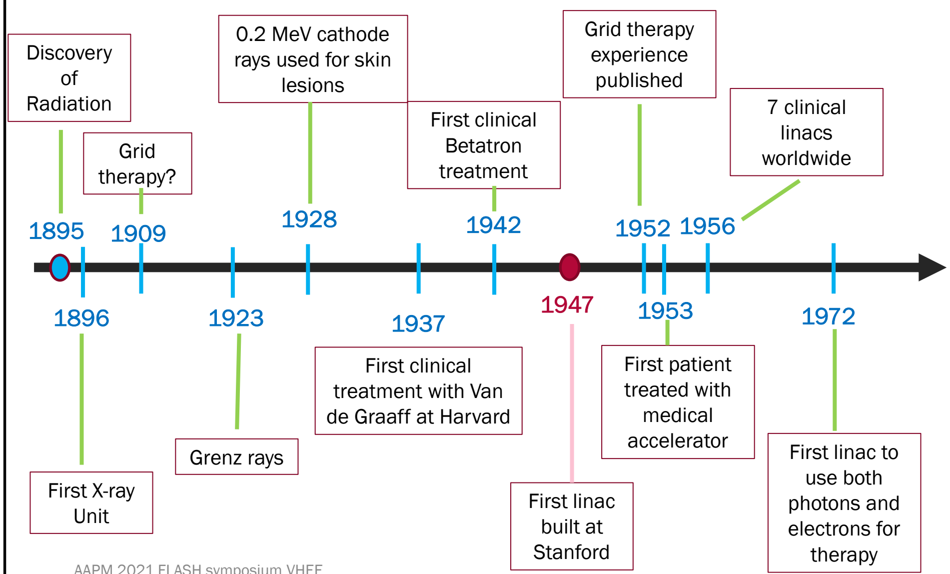
2

History I



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3

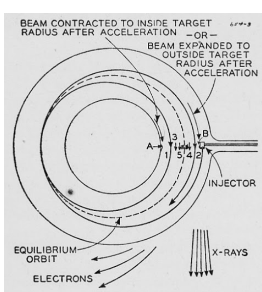
Skaggs, 1948 – focus on the development of "high" energy electron therapy

Development of the Betatron for Electron Therapy[1]

L. S. SKAGGS, Ph.D.,[2] G. M. ALMY, Ph.D.,[3] D. W. KERST, Ph.D.,[3] and L. H. LANZL[3]

With an Introduction on

The Therapeutic Principles of Fast Electrons



equal to that of water. The edge of the film was coincident with that edge of the presdwood blocks which faced the beam, and the plane of the film was approximately parallel to the beam. Figure 9 shows the resulting exposure of the film by a 13-Mev. beam of electrons. The extreme penetration of the beam was 6 cm., which is in agreement with the theoretical predictions. This theory predicts 14.5 cm. penetration for a 30-Mev. beam and 17.0 cm. for 35 Mev. The depth dose has not yet been measured, but from theory we expect in general a slight increase of ionization from the surface to a point near the end of the range and then a sharp decrease to practically zero ionization. This has actually been observed in a qualitative way by one of us (Kerst) using the scattered spray of electrons from an x-ray producing target.

Newell showed at the Carman lecture[1] for electrons of various voltages, in every case giving up much more energy close to the end of the range. Now, with the betatron, we have cathode rays at twenty or thirty million volts, a penetration of up to 13 or 14 cm. in tissue, which ought to reach almost any malignant lesion provided the beam is properly directed.

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"

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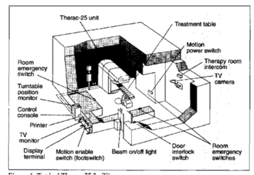
Image from: http://lampes-et-tubes.info/xr/xr033.php?l=e

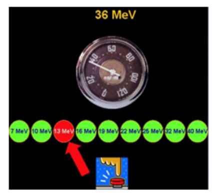
4

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



https://www.bir.org.uk/media/63754/bir_errors_2012_h_porter.pdf
https://www.iaea.org/resources/rpop/health-professionals/radiotherapy/accident-prevention/equipment-malfunction

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5

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

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

Image from: https://www.pinterest.com/jmjewison24/red-headed-stepchild/

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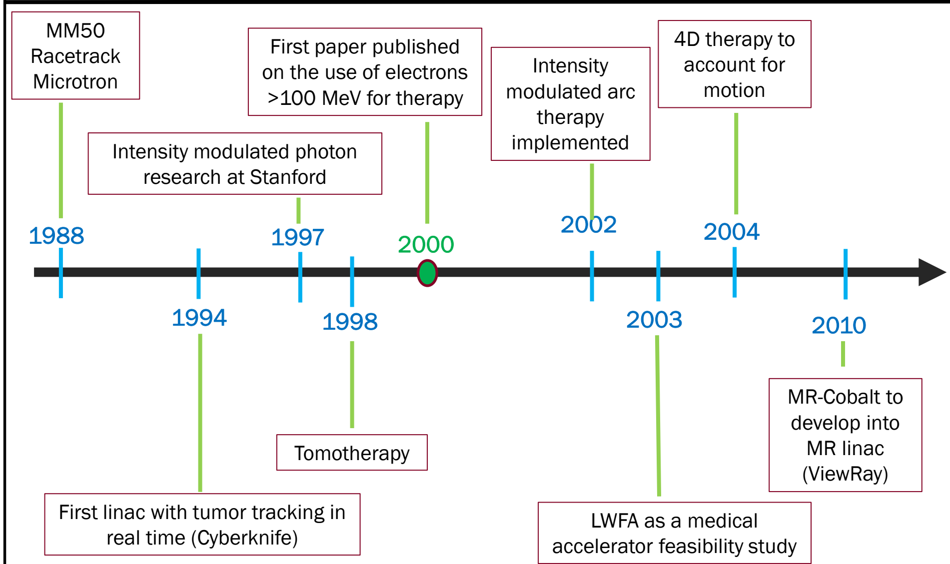
6

History II



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7

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

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8

VHEE Penumbra

HEALTH

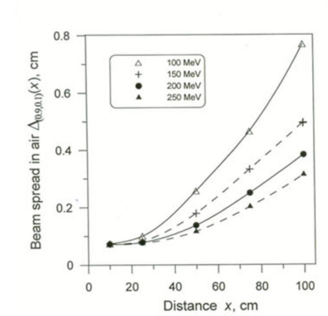
TABLE II. The penumbra, $P_{80/20}$, at phantom surface and at half the depth of R_{85} for different energy settings.

Energy (MeV)	$R_{85/2}$ (mm)	Penumbra at surface	Penumbra at $R_{85/2}$
10	18	12.0	16.0
15	28	7.5	13.3
30	47	4.4	11.5
50	59	2.9	8.6

From Karlsson, et al

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

Penumbra less impactful as # beams increases



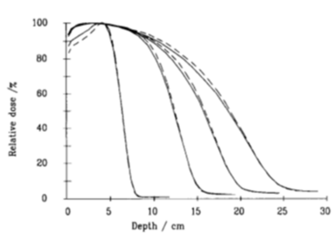
From DesRosiers, et al

9

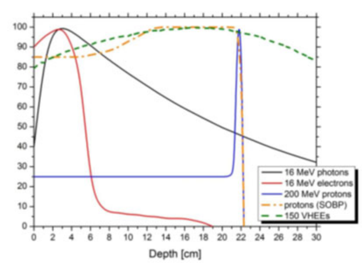
VHEE other characteristics

HEALTH

PDD

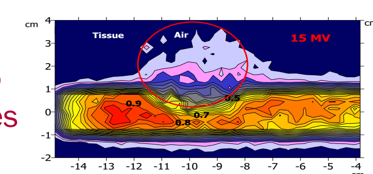


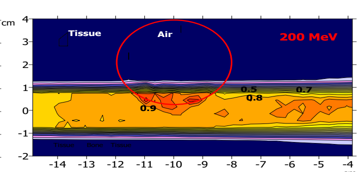
MM50 Racetrack Microtron
From Karlsson, et al



From Subiel, et al

Insensitivity to heterogeneities





10

History III

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

11

FLASH dominant R&D

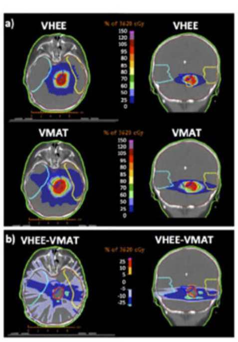
- Electrons
  - Most well established and consistent effect at low energies (<10 MeV)
  - First patient treated
  - VHEE
- Photons
  - Not a lot of studies, one negative
  - High dose rate challenge
- Particles

12

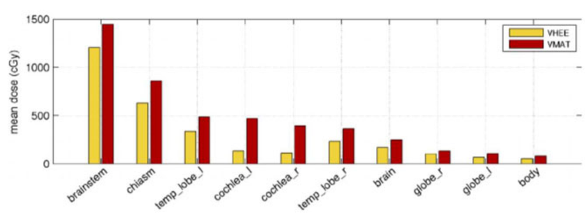
FLASH R&D

Even without enhanced dosimetric effect, high dose rates are advantageous because speed of treatment reduces motion effects for all modalities.

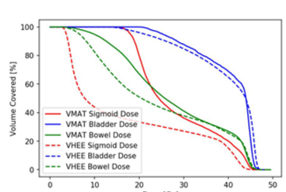
Treatment planning VHEE

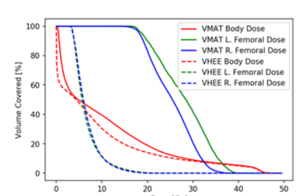


L. Hancock, VHEE2020, CERN



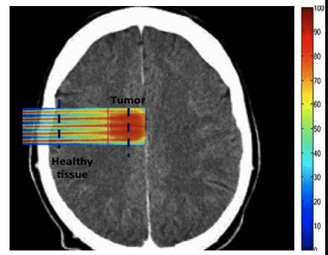
M. Bazalova-Carter et al





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*



Proton grid therapy
From Martinez-Rovira, et al., 2015

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

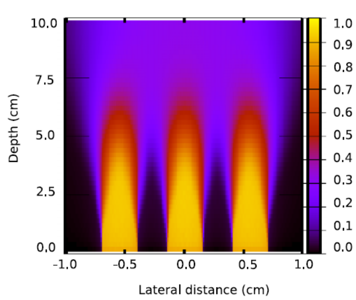


FIG. 8. 2D depth dose distributions in eHGRT (energy: 150 MeV; grid size: $3000 \times 3000\ \mu m^2$; ctc: $5500\ \mu m$; field size: $2 \times 2\ cm^2$). The spatial fractionation of the dose is observed in the healthy tissue, while the tumor profits from a more homogeneous dose distribution.

TABLE I. Penumbra values at several depths for the several techniques considered: xGRT, eHGRT (150 MeV), and pGRT.

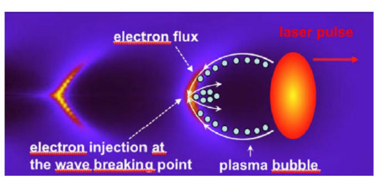
	Penumbra (μm)		
Depth (cm)	xGRT	eHGRT	pGRT
1	61 ± 2	311 ± 7	492 ± 25
3	62 ± 2	985 ± 20	588 ± 29
5	63 ± 2	1826 ± 37	920 ± 46
7	62 ± 2	2213 ± 45	1343 ± 67

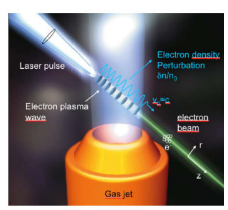
Equipment Design for VHEE

- 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

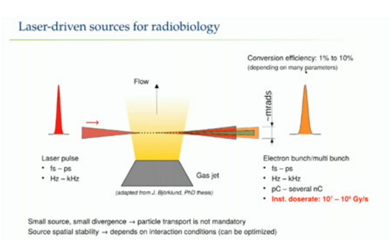
17

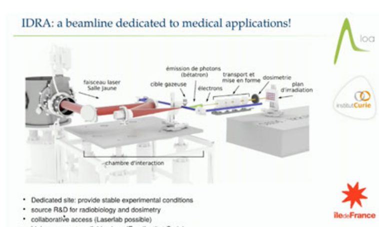
Equipment – LWFA at LOA





V. Malka et al. "Ultra-short electron beams based spatio-temporal ra Mutation Research 704 (2010) 142–151, Figures 1, 3 and text





Flacco, A. VHEE2020 Workshop, CERN

18

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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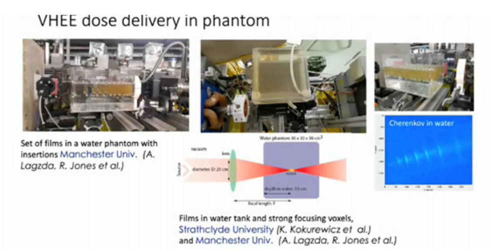
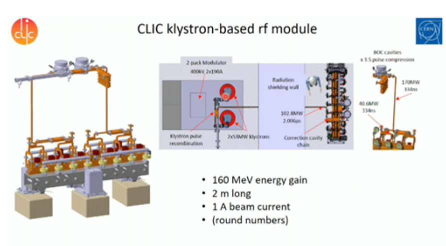
19

Equipment - CERN



Beam parameter	Range
Energy	60 – 220 MeV
Energy Spread	< 0.2 % rms (< 1 MeV FWHM)
Bunch Length	0.1 ps – 10 ps rms
Bunch Charge	5 pC – 3 nC
Number of bunches per pulse	1 to ~150
Maximum total pulse charge	30 nC
Normalized emittances	3 μm to 30 μm (bunch charge dependent)
Repetition rate	0.8 to 10 Hz
Bunch spacing	1.5 GHz (from Laser)



CERN VHEE 2020 Workshop, Nanni, Wuensch

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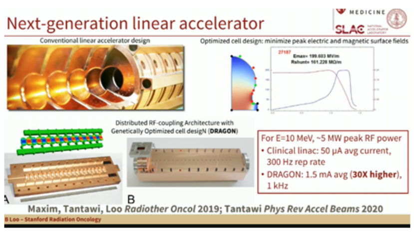
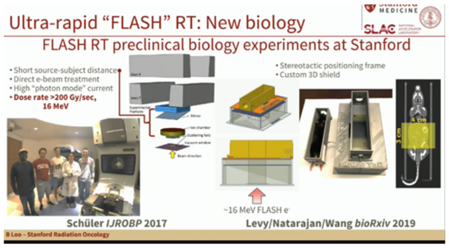
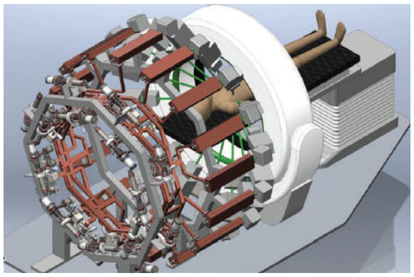
20

Equipment – SLAC/PHASER







CERN VHEE 2020 Workshop,
Loo, Maxim

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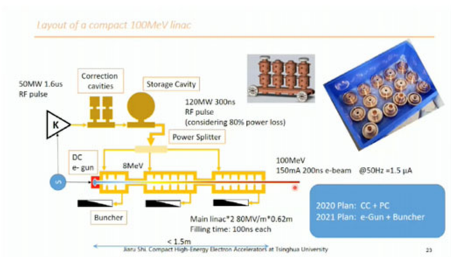
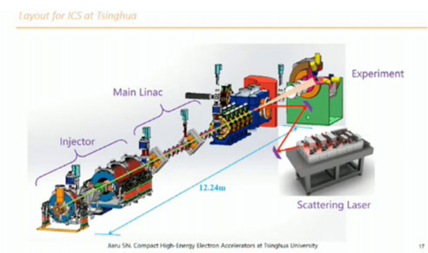
21

Equipment Tsinghua





CERN VHEE 2020 Workshop, Shi

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22

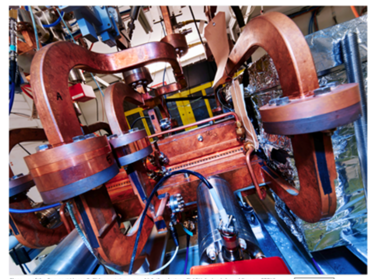
Institutions developing VHEE partial list, many are collaborators

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

CERN and Lausanne University Hospital collaborate on a pioneering new cancer radiotherapy facility

CERN and the Lausanne University Hospital (CHUV) are collaborating to develop the conceptual design of an innovative radiotherapy facility, used for cancer treatment

15 SEPTEMBER, 2020



Close-up of the Compact Linear Collider prototype, on which the electron FLASH design is based (Image: CERN) View on CDS

https://home.cern/news/news/knowledge-sharing/cern-and-lausanne-university-hospital-collaborate-pioneering-new-cancer

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23

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?

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24

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

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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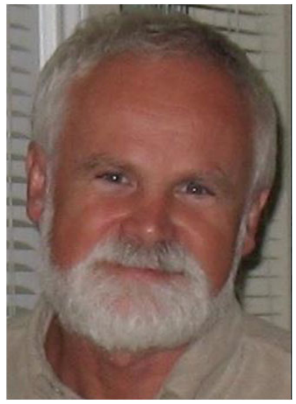
It all starts with an idea…



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

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31

I ♥ ELECTRONS

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32