Very High Energy Electrons ( >100 MeV) in Radiation Therapy

What? Are you nuts? We don’t even like 20 MeV very much!

Colleen DesRosiers
06/14/2017
“Imagination is more important than knowledge.”

Albert Einstein, Ph.D.
Introduction

Very High Energy Electrons (VHEE)
The idea...

Best treatment available in radiation therapy using photons (linac based):

• IMRT
• VMAT

- Specialty units
  • Cyberknife
  • Tomotherapy
  • View Ray
  • Gamma Knife/ Perfexion

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Limitations for photons

- Photons are not charged – cannot be “scanned”

- Modulated treatment delivery relies heavily on mechanical motion!!
  - Mechanical motion is slow – inefficient
    - Interplay effects with patient motion
    - Patient throughput
  - Precision – width of MLC
Alternatives to photon therapy

- Brachytherapy
- Electrons
- Heavy particles
Brachytherapy limitations

- Accessibility to target
- Proximity to radiation source
- Control of dose distribution
Electron beam therapy limitations

- Depth of target
- High surface dose
- High penumbra (scattering in air)
- Bulging effect
Heavy Particle therapy limitations

• **Cost**
  - *Facility*
  - *treatment*

• **Sensitivity to patient/target motion**
Depth Dose curves

Depth Distribution - Various Modalities

- Photons
- Electrons
- Protons (BP)
- Protons (SOBP)

Relative Dose vs. Depth
The optimum therapy characteristics

- **Optimum dose distribution**
  1. *Heavy particles (SOBP) for depth dose*
  2. *Small beams – high modulation*
  3. *Large number of beam directions*

- **Quickest treatment delivery**
  - *Reduce motion effects*
  - *Patient throughput*
  - *Electromagnetically (or otherwise approaching speed of light) scanned*

- **Cost competitive with photon beams**
Consideration of electron beams

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??

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Thought experiment…

What will happen if the energy of the electrons 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*

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Courtesy of the imagination of Lech Papiez, PhD, 1998
Thought experiment… (continued)

While maintaining some low energy characteristics

- *Can produce pencil beams*
- *High surface dose*
- *Less costly than heavy particles*

Courtesy of the imagination of Lech Papiez, Ph.D., 1998
Materials and Methods 1

Indiana University
Oak Ridge National Laboratory
Initial VHEE experiments

- Monte Carlo simulations with PENELOPE
- Physical measurements at Oak Ridge National Laboratory electron linear accelerator (ORELA)
  - Solid water
  - Gaf-Chromatic film
  - 150 MeV
  - Estimated 100 Gy dose
Monte Carlo comparison with measured

ORELA facility
Varian Linear accelerator
Accelerator structure length = 17 meters

DesRosiers, Moskvin, Papiez, 2000
PENELOPE data

Electron Beams of 200 MeV in Water Phantom

Radius 5 cm

Radius 1 cm
Depth distribution various modalities

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Angular spread of VHEE

The relationship between electron energy, spread of beam in air and distance

DesRosiers, Moskvin, Papiez, 2000
Monte Carlo simulation results comparing 15 MV photon distribution to 200 MeV electron beams

DesRosiers, Moskvin, Papiez, 2000
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Lung phantom MC study

Comparison of 6 MV, 15 MV, 200 MeV in RPC Lung phantom

Given same target dose coverage, VHEE shows some reduced normal tissue dose

<table>
<thead>
<tr>
<th>Tissue Structure</th>
<th>VHEE Relative dose</th>
<th>6 MV Relative dose</th>
<th>15 MV Relative Dose</th>
<th>VHEE/6MV</th>
<th>VHEE/15MV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung Lt</td>
<td>1.1%</td>
<td>1.4%</td>
<td>1.4%</td>
<td>0.800</td>
<td>0.754</td>
</tr>
<tr>
<td>Lung Rt</td>
<td>13.7%</td>
<td>14.3%</td>
<td>15.8%</td>
<td>0.963</td>
<td>0.869</td>
</tr>
<tr>
<td>Heart</td>
<td>7.4%</td>
<td>7.2%</td>
<td>8.3%</td>
<td>1.034</td>
<td>0.888</td>
</tr>
<tr>
<td>Spinal Cord</td>
<td>0.9%</td>
<td>1.1%</td>
<td>1.1%</td>
<td>0.87</td>
<td>0.895</td>
</tr>
<tr>
<td>Body</td>
<td>3.3%</td>
<td>3.7%</td>
<td>3.7%</td>
<td>0.911</td>
<td>0.896</td>
</tr>
</tbody>
</table>

DesRosiers, et al, ASTRO annual meeting, 2008
Review of literature
• Treatment planning papers
  – Schuller, et al. (2017)

• Conclusions
  – Developed treatment planning system with VHEE pencil beams by linking EGSnrc Monte Carlo with research version of Ray Station
  – Demonstrate equivalent or superior dose distributions as compared with 6 MV and 15 MV VMAT
  – Demonstrate some improvement compared with protons
Pediatric brain treatment

VHEE specifications
- 100 MeV beams
- 36 beams
- 1mm beam diameters
- 2 mm spacing between beams
- 9200 beamlets total

VMAT specifications
- 6 MV photons
- Clinically used plan

Reprinted with permission, Bazalova-Carter, et al., MedPhys
Lung and Prostate comparisons

The 100 MeV VHEE lung plan resulted in mean dose decrease to all OARs by up to 27% for the same target coverage compared to the clinical 6 MV flattening filter-free (FFF) VMAT plan.

The 100 MeV prostate plan resulted in 3% mean dose increase to the penile bulb and the urethra, but all other OAR mean doses were lower compared to the 15 MV VMAT plan.

Reprinted with permission, Bazalova-Carter, et al., MedPhys
Rapid dose delivery can be achieved using current linacs (>100 Gy/s) – how?

• Fewer electrons needed to produce the same dose as photons
• Efficiency of x-ray production low (6%)

Why is this important?
- Allows for a large number of treatment beams to be treated
- Patient/target motion effects are reduced or eliminated

Bazalova-Carter, et al., MedPhys
Equipment Design
Methods for producing VHEE

- Linear accelerators
- Microtrons
- Laser Plasma
Linear accelerator

- Electron gun produces microsecond pulses
- Length of tube proportional to beam energy

Linac accelerator structure = 15 – 20 meters long!!
Microtron

Electrons produced in microsecond pulses typically

Accelerated by applied magnetic field

Racetrack microtron for 150 MeV design proposed by Washio, et al. (non-medical application)

Highest energy medical microtron MM50 at University of Michigan, 50 MeV

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Figure 4.11 from Khan, The Physics of Radiation Therapy, 4th edition
A new type of medical accelerator

*Laser Wakefield Plasma Accelerator* (LWFA)

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What is laser plasma acceleration?

Plasma acceleration is a technique for accelerating charged particles using an electric field associated with electron plasma wave or other high-gradient plasma structures.

Plasma = ionized gas
Some FAQs about Laser plasma technology

- Who first introduced the technology?
  - *Introduced by Tajima & Dawson, UCLA in 1979*

- What is the pulse frequency?
  - *Ultrashort laser pulses (femtosecond = $10^{-15}$ sec)*

- What kind of a laser is used?
  - *Titanium sapphire crystal laser (Terawatt = $10^{12}$ W)*

- Helium plasma

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An intense electromagnetic pulse can create a wake of plasma oscillations through the action of the nonlinear ponderomotive force. Electrons trapped in the wake can be accelerated to high energy. Existing glass lasers of power density $10^{18}$ W/cm$^2$ shone on plasmas of densities $10^{18}$ cm$^{-3}$ can yield GeV of electron energy per centimeter of acceleration distance. This acceleration mechanism is demonstrated through computer simulation. Applications to accelerators and pulsers are examined.
Laser propagating in underdense plasma generates plasma waves

Plasma waves are just like waves formed behind a boat

Electrons can surf the electric field of the wave’s wake and can be accelerated up to hundreds GeV/m

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• Intense laser pulse drives the wakefield
• Plasma bubbles (dark blue circles) are formed (contains positive and negative ions)
• Electrons are expelled by laser and encircle plasma bubbles
• Electrons form a density spike and will be injected into the bubble when a threshold level is reached, producing further acceleration

LWFA are typically built on a “table top”

University of Strathclyde, Glasgow, UK

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Laser plasma (LWFA) comparison with linear accelerators (Linac)

- Plasma can handle much heavier energy flow, less prone to structural failure
- More efficient accelerator
  - Linac: 10 MeV/meter
  - LWFA: GeV/cm = 100,000X more efficient than a linac
- Pulse width
  - Linac: 10^{-6} seconds
  - LWFA: 10^{-15} seconds
- Electrons may be positioned electromagnetically or by controlling laser position
## Methods of acceleration comparison

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Linac</th>
<th>Microtron</th>
<th>Cyclotron</th>
<th>Laser plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pulse size</strong></td>
<td>$10^{-6}$ sec</td>
<td>$10^{-6}$ sec</td>
<td>$10^{-8}$ sec</td>
<td>$10^{-15}$ seconds</td>
</tr>
<tr>
<td><strong>Charge per pulse</strong></td>
<td>$10^{11}$ electrons</td>
<td>$10^{11}$ electrons</td>
<td>700 protons</td>
<td>$10^7$ electrons</td>
</tr>
<tr>
<td><strong>Instantaneous charge rate</strong></td>
<td>0.016 A</td>
<td>0.01 A – 1.6x10^4 A</td>
<td>11 nA</td>
<td>1.6x10^3 A</td>
</tr>
</tbody>
</table>
Energy deposition

- Low LET
  - Spurs = 4 nm (2x DNA diameter), 100 eV, 3 ion pairs, 95% energy deposition with photons

- High LET
  - Blob = 7 nm, 100-500 eV, 12 ion pairs, neutrons and alpha

- Will the nature of the energy deposition be impacted by the intense electric fields?
Materials and Methods 2

University of Strathclyde Experiment
Glasgow, Scotland
2011-2014

Experiment supported by Clarian Values Fund VFR 273
VHEE (> 100 MeV)

- Initial experiments using VHEE have been carried out using the ALPHA-X laser-plasma wakefield accelerator beam line at the University of Strathclyde, Glasgow, UK.

- The purpose of this investigation is to use Monte Carlo simulations to compare with characterization of the interaction of the VHEE beam using a BANG3Pro polymer gel dosimeter dosimeter.

- MC simulations do not account for spatial/temporal effects.
Bang gel dosimetry

- BANG® gels are muscle-tissue-equivalent chemical dosimeters
- Optical density per unit length is proportional to radiation dose
- Dose response is based on radiation-induced polymerization of monomers which are dispersed in the gel

MGS Research
Bang gel experiment layout

Schematic for experiment layout

Photo of actual experiment
LET sensitive gel dosimetry

- Dependent on the method employed in the reading of the optical density of the gels

- Theory
  - High LET radiations produce “blobs” which scatter light mostly in the forward direction
  - Low LET radiation produce “spurs” which scatter light isotropically

Results from these experiments indicate that VHEE behave more like heavy particles producing molecular scattering favoring the forward direction
Spatio temporal radiation biomedicine

- Femtolysis (Gauduela et al) femto second radiolysis
  - Mutagenic DNA lesions
  - Cell signalling
  - Genomic instability
  - Apoptosis
  - Microenvironment
  - Bystander effects

- Calls for “intensive development of ultra short laser technologies and advanced high time resolved spectroscopic methods” for the purpose of observing “short lived nonequilibrium radical trajectories” on the “molecular motion scale”
The treatment of cancerous tumors using lasers offers the potential to significantly downscale the size and the cost of proton therapy infrastructures. This could lead to high dissemination in hospitals, as compared to more conventional systems based on RF acceleration that require the construction of large infrastructures.
United States Patent Application Publication
Loo et al.

Pub. No.: US 2013/0231516 A1
Pub. Date: Sep. 5, 2013

PLURIDIRECTIONAL VERY HIGH ELECTRON ENERGY RADIATION THERAPY SYSTEMS AND PROCESSES

Fixed annular gantry & integrated imaging system
Steerable high-energy electron beam
Vacuum window

Pluridirectional High-Energy Agile Scanning Electron Radiotherapy (PHASER)
Summary

- VHEE for radiotherapy
  - Somewhere between photons and heavy particles
  - Finest IMRT
  - Quick treatment delivery
  - Low cost
- May offer improved dose distributions in brain, lung and prostate as compared with photon beams
- VHEE using LWFA may offer unique dosimetric benefits due to intense electron fluence
  - Comparable to heavy particles?
- Groups at Laboratoire d’Optique and SLAC working towards medical applications LWFA
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• Xu et al, Performance of a commercial optical CT scanner and polymer gel dosimeters for 3D dose verification. Med. Phys 31 (11), pp.3024-3033
Questions?:

*Boldly stolen from Bartlett, et al. AAMD presentation 2017*