Applications of Very High Energy Electrons (50-250 MeV) for radiotherapy

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CLIC WORKSHOP 2017

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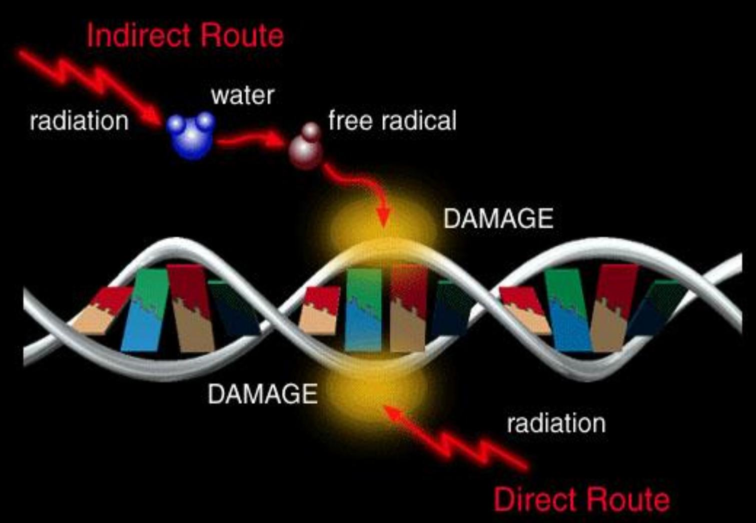
Outline

- Radiotherapy of deep-seated tumours
- Current state of radiotherapy
- **VHEE** – a new cancer treatment modality
- Requirements of VHEE radiotherapy technology
- **Potential benefits of VHEE** over extant radiotherapy methods
- **Experiment at CALIFES (now CLEAR) in Dec 2016**

Radiotherapy of deep-seated tumours

Aims of Radiotherapy:

- Irradiate tumour with sufficient dose to **arrest cancer growth**
- **Avoid complications** and minimise damage to surrounding tissue

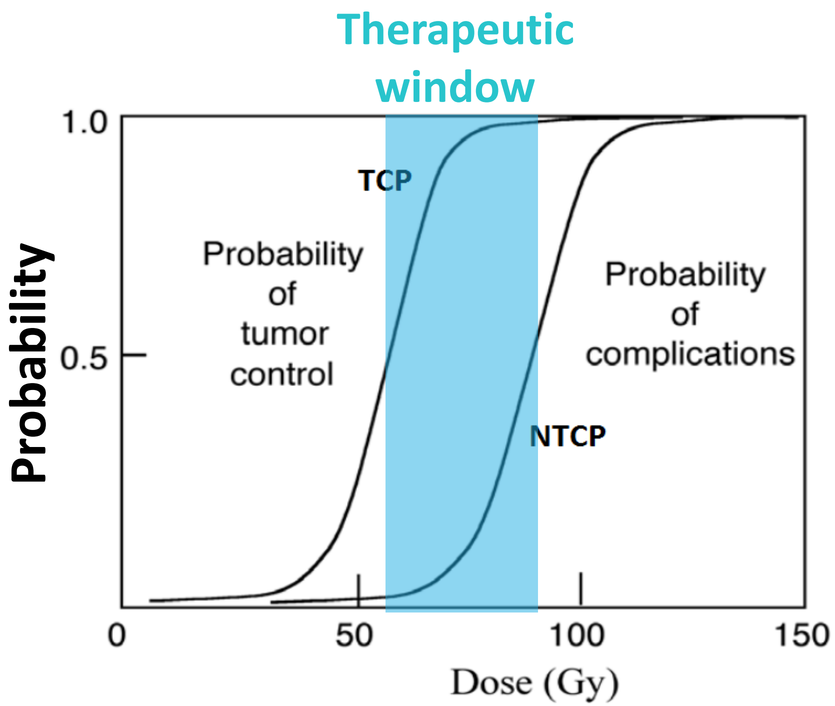


http://www.windows2universe.org/earth/Life/cell_radiation_damage.html

As radiation passes through tissue damage can be induced **directly** or **indirectly** by producing free radicals around DNA

DNA damage is induced via

- single and double-DNA strand breaks
- DNA cross-linking

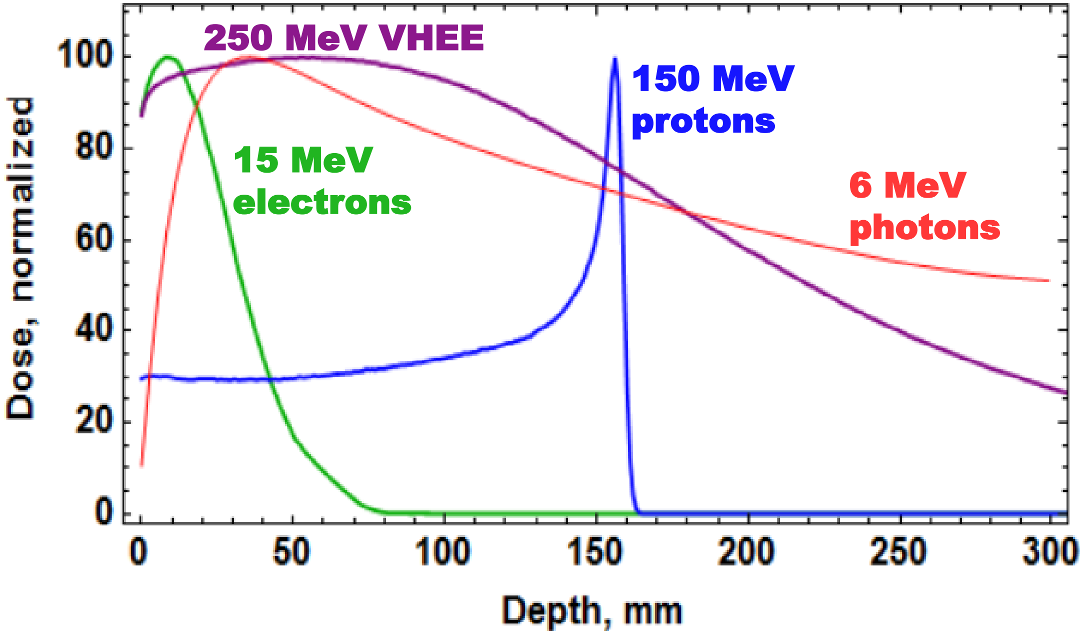


- Tumour and healthy tissue reaction to radiation described by the **tumour control probability (TCP) and normal tissue complication probability (NTCP)**
- Healthy cells on average have more effective DNA repair mechanisms than cancerous cells
- **Therapeutic window:** maximizing TCP / NTCP ratio.

Radiotherapy of deep-seated tumours

Essential for deep-seated tumour radiotherapy:

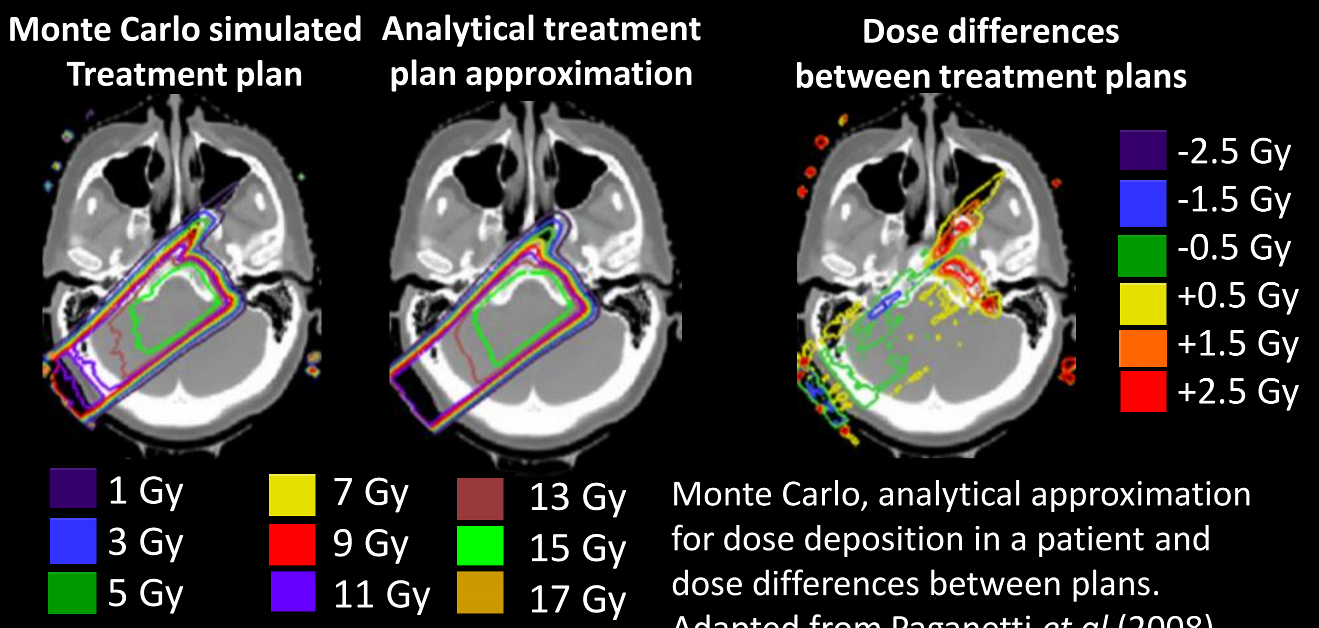
- Dose reach (10 – 30 cm depth in tissue)
- Conformal and reliable dose delivery



Dose profiles for various particle beams in water (beam widths $r = 0.5$ cm)

Reliability of treatment proton therapy plans for brain tumour radiotherapy

- Dosimetry properties of beams are most commonly studied using Monte Carlo based particle tracking codes such as ***GEANT4.***
- In clinical settings faster analytical algorithms are used to create for treatment planning.



Monte Carlo, analytical approximation for dose deposition in a patient and dose differences between plans. Adapted from Paganetti *et al* (2008).

Current radiotherapy methods:

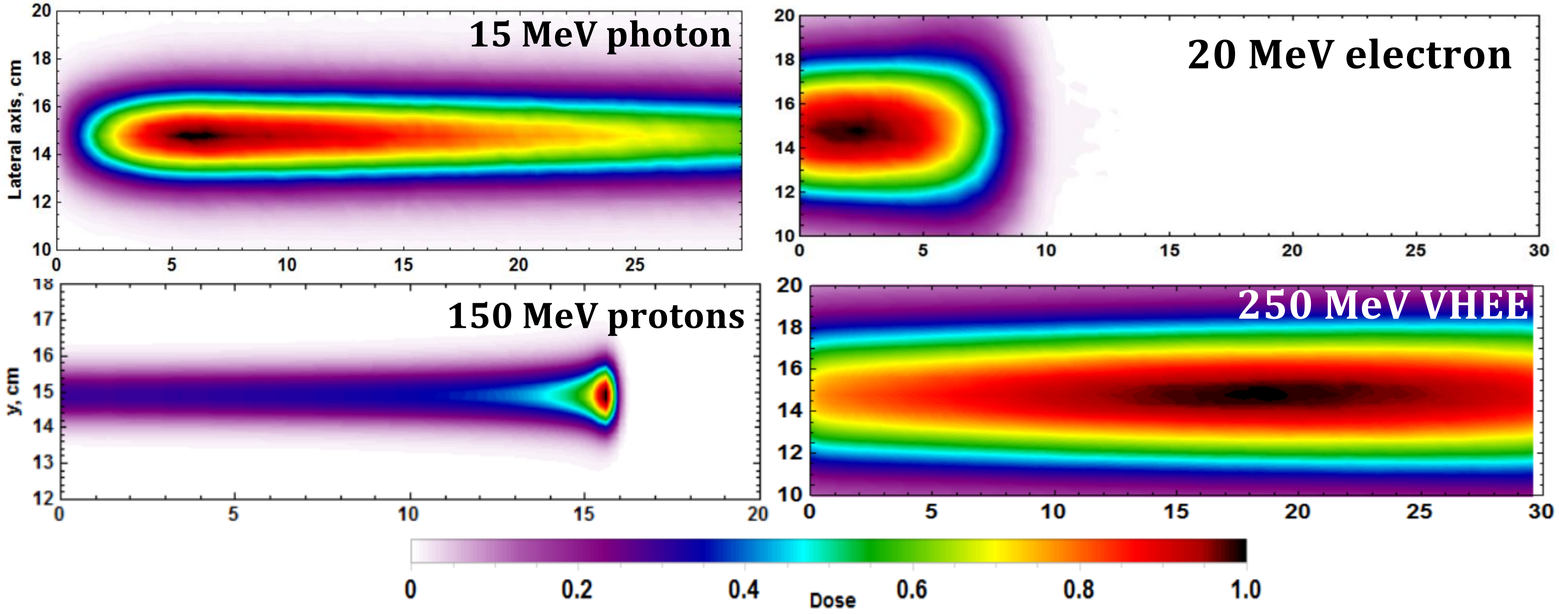
- 6 - 18 MV photons
- 5 - 20 MeV electrons
- 50 - 300 MeV/u hadrons (protons, Carbon-12)

Current radiotherapy methods

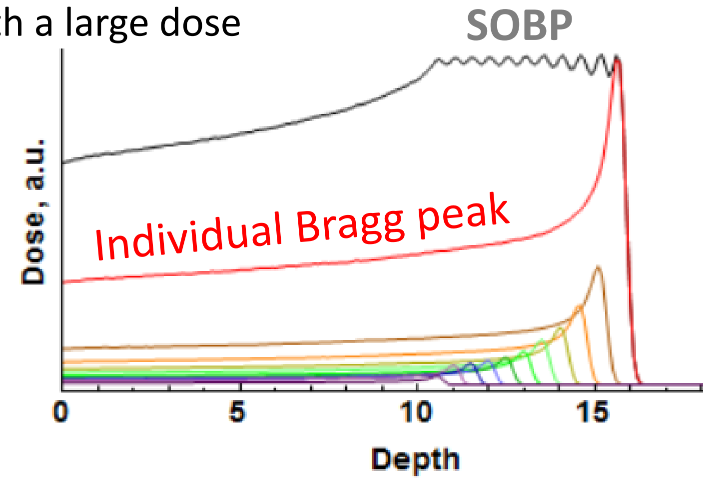
Gamma / X-ray photon radiotherapy
6 – 18 MeV
- The ***most commonly and widely used*** radiation therapy today
- Peak dose deposited close to the skin surface
- ***Multiple-angle irradiation*** used in order to optimize the treatment plan for deep-seated tumours
- ***Dose build-up*** after low-density fields

Low-energy electron radiotherapy
5 – 20 MeV
- Often used in radiotherapy for treating ***superficial tumours*** and skin cancers
- Electrons in this energy range have a ***well-defined cut-off point*** few centimetres deep in tissue after which the dose drops rapidly
- Cannot be used for deep-seated tumours

Hadron therapy (protons, heavy ions)
100 – 300 MeV/u
- ***High cost*** and ***limited availability***
- ***Assigned only in complex cases*** – e.g. paediatric tumours and adult tumours near sensitive structures such as the brain and the spinal cord
- ***Well-defined finite range*** in matter
- ***Spread-out Bragg peaks (SOBP)*** often used, formed by superposition of several suitably weighted Bragg peaks to cover a wider volume – inevitably raising entrance dose
- Clinicians indicate depth of Bragg peak is ***particularly sensitive to inhomogeneities*** in the medium – potential to irradiate healthy tissue with a large dose



Dose maps of various particle beams in water

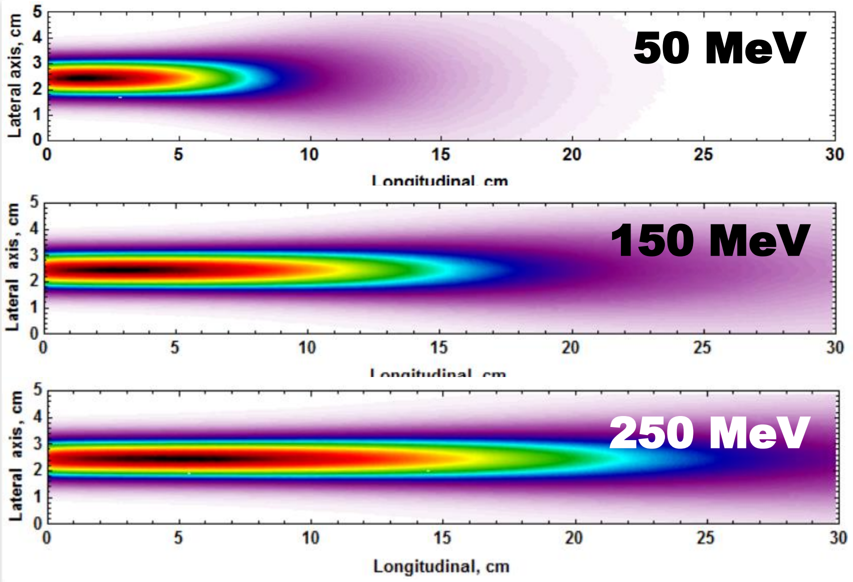


Spread out Bragg peak and single Bragg peak contributions

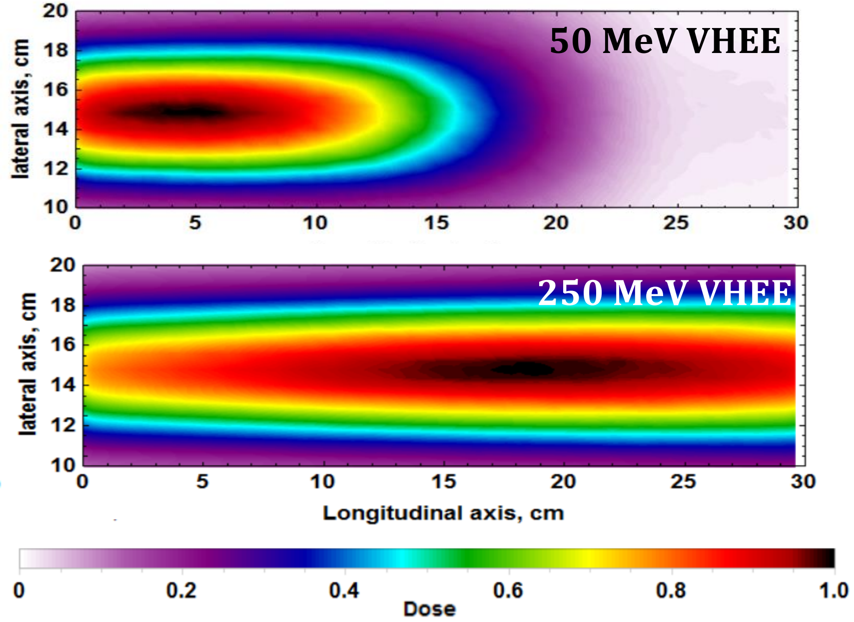
Why VHEE?

- Rapid advances in compact high-gradient (> 100 MV/m) accelerator technology in recent years
  - CLIC (> 100 MV/m)
  - NLC (~70MV/m),
  - W-band (> 200MV/m)*
- Superior dose deposition properties compared to MV photons
- High dose-reach in tissue
- High dose rate (compared to photons)
- More reliable beam delivery around inhomogeneous media
- Better sparing of surrounding healthy tissue
- Particle steering

*V. Dolgashev, HG2016

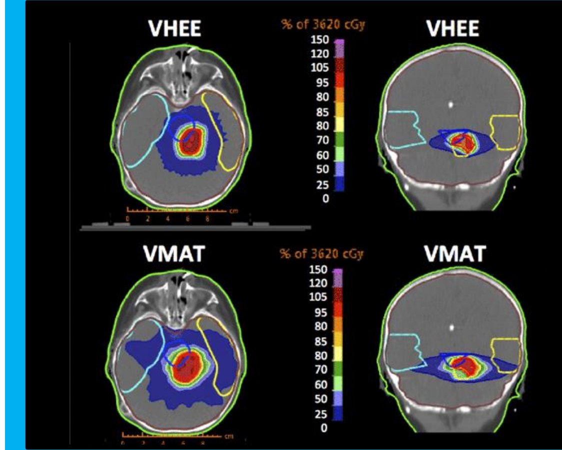


Dose maps of narrow ($\sigma = 5\text{mm}$) VHEE beams in water

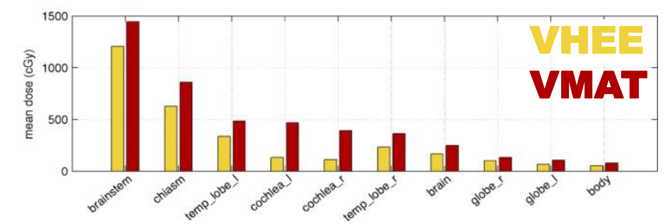


Dose maps of wide ($\sigma = 20\text{mm}$) VHEE beams in water

- **Clinical studies by M. Bazalova-Carter *et al.* (2015) have compared 100 MeV VHEE** with conventional **(6 and 15 MV) VMAT** (Volumetric Modulated Arc Therapy) photon radiotherapy plans
- ***Pediatric brain tumour, lung*** and ***prostate cases***
- VHEE therapy plan showed a **decrease of dose** up to **70%** in surrounding organs-at-risk (OARs)
- ***VHEE plan was found to be more conformal than VMAT plan***



Brain tumour dose maps for 100 MeV VHEE and 6 MV volumetric modulated arc photon therapy (VMAT) .



Absorbed dose histograms for surrounding organs-at-risk.

M. Bazalova-Carter *et al*, «Treatment planning for radiotherapy with very high-energy electron beams and comparison of VHEE and VMAT plans», Medical Physics, vol. 42(5), **2015**.

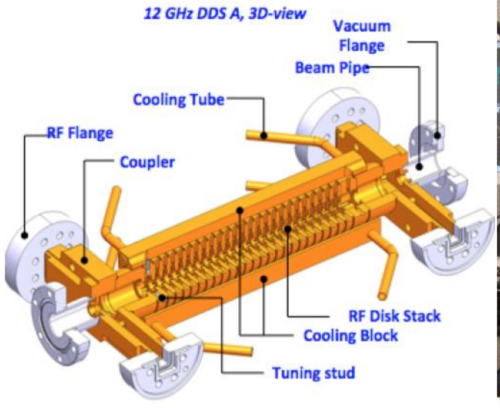
Accelerator design requirements

Essential factors for VHEE radiotherapy:

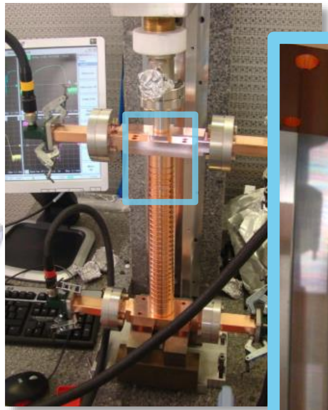
- Compactness in order to fit into current radiotherapy facilities (4– 10 meters long)
- Reliable dose delivery for long periods of time (hospital working hours)
- Large area irradiation (transverse field sizes above $> 1 \times 1\ \text{cm}^2$)

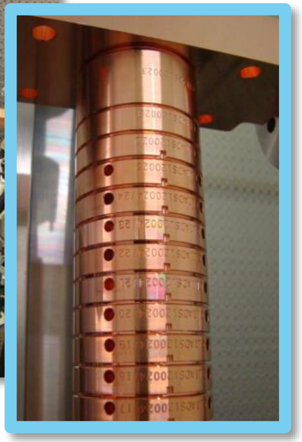
- **CLIC technology with suitable modifications could be readily applicable to VHEE radiotherapy machine design!**

In collaboration with CERN's CLIC group and KEK's X-band group and the University of Manchester's Accelerator group, a **CLIC DDS (Damped-Detuned Structure)** was designed, fabricated and tested, and it will provide an accelerating gradient $\sim\mathbf{100\ MeV/m}$



CAD of DDS prototype

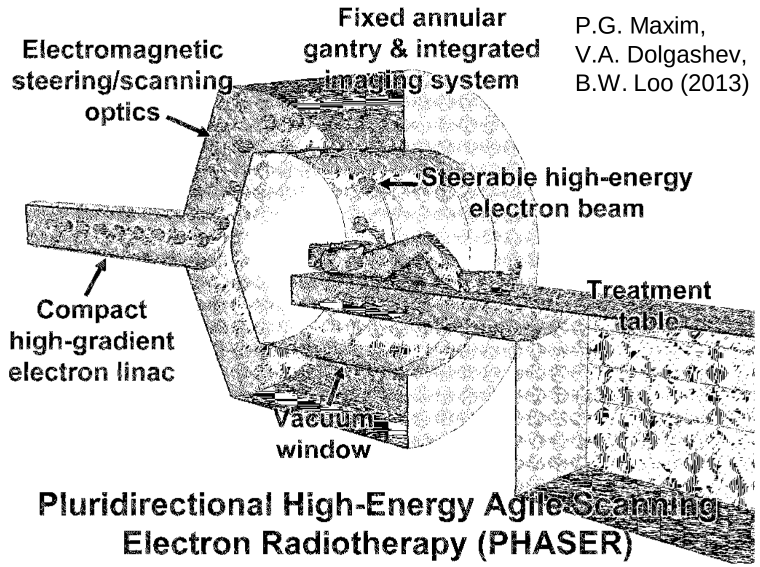




CLIC DDS 100 MV/m design. With suitable modifications potentially suitable for VHEE radiotherapy treatment machine.

VHEE therapy system patent

- Radiotherapy system patented and proposed by of **P.G. Maxim, V.A. Dolgashev, B.W. Loo** in **2013** comprises of:
  - ***compact high-gradient VHEE accelerator*** and delivery system
  - ***fixed annular gantry*** around the patient
  - beam-steering system
- ***Large number of access angles*** by having multiple fixed beam lines (10-30) arrayed around patient
- Few moving parts
- Delivery of dose sufficiently fast to potentially '***freeze' physiologic motion***



P.G. Maxim, V.A. Dolgashev, B.W. Loo (2013)

Proposed and patented VHEE radiation therapy delivery system.

VHEE therapy system patent
P.G. Maxim, V.A. Dolgashev, B.W. Loo (2013)
(U.S. patent 8,618,521)

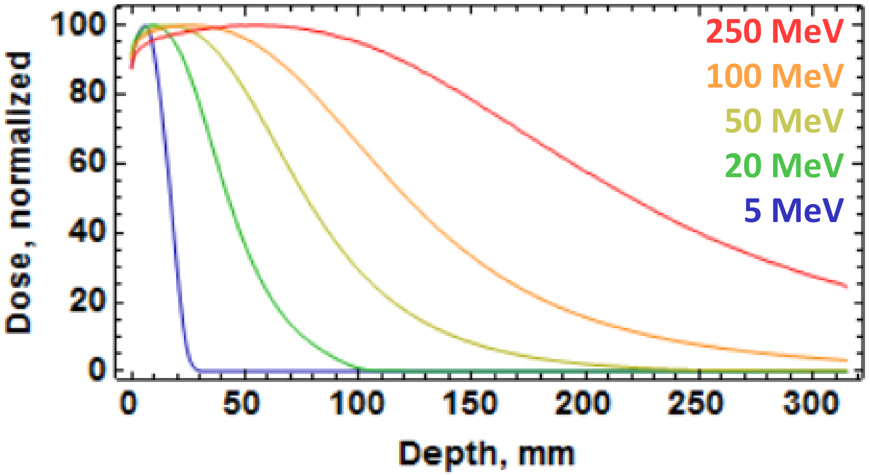
Unique beam characteristics of VHEE beams

We conducted several VHEE beam simulations in **GEANT4 and a follow-up experiments with CALIFES**:

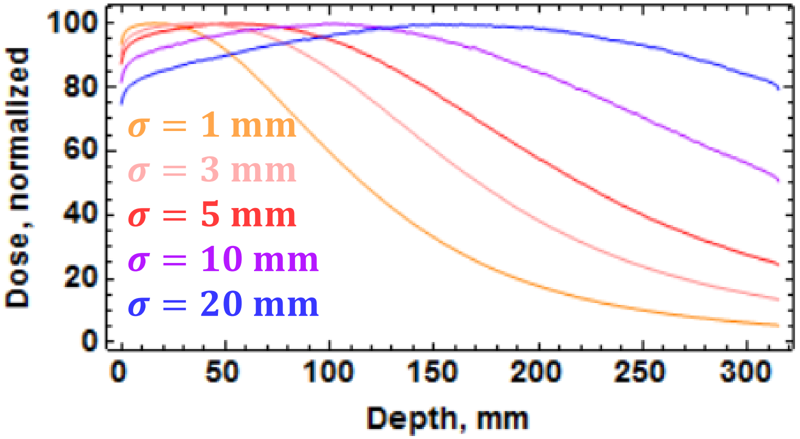
- **Longitudinal and transverse dose profiles** of 50 – 250 MeV VHEE beams
- **Effects of inhomogeneities** – embedded air cavity in a water phantom
- **Focussed VHEE beams**

250 MeV electron beams can sufficiently penetrate tissue up to **20-25 cm** – ideal for deep-seated tumour irradiation in non-obese patients

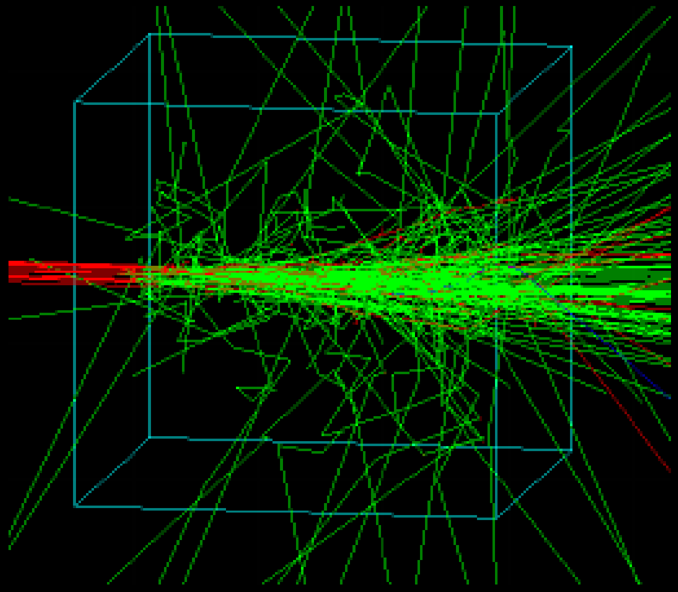
$\sigma = 5$ mm, various energies

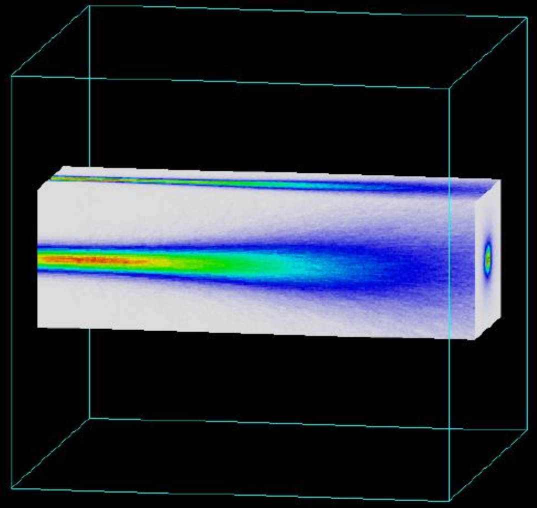


E = 250 MeV, various sigma



Electron dose profiles in water dependence on energy and beam width.

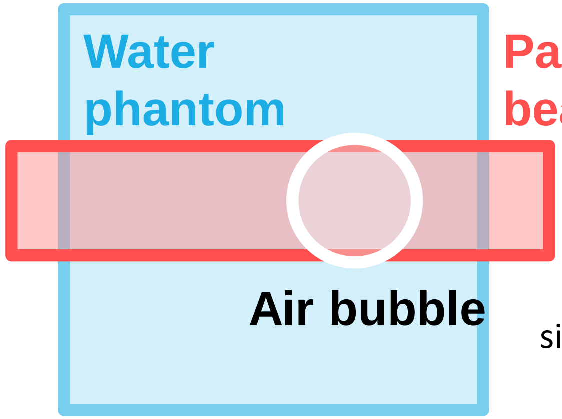




VHEE beam simulation particle tracks and dose deposition projection map in GEANT4.

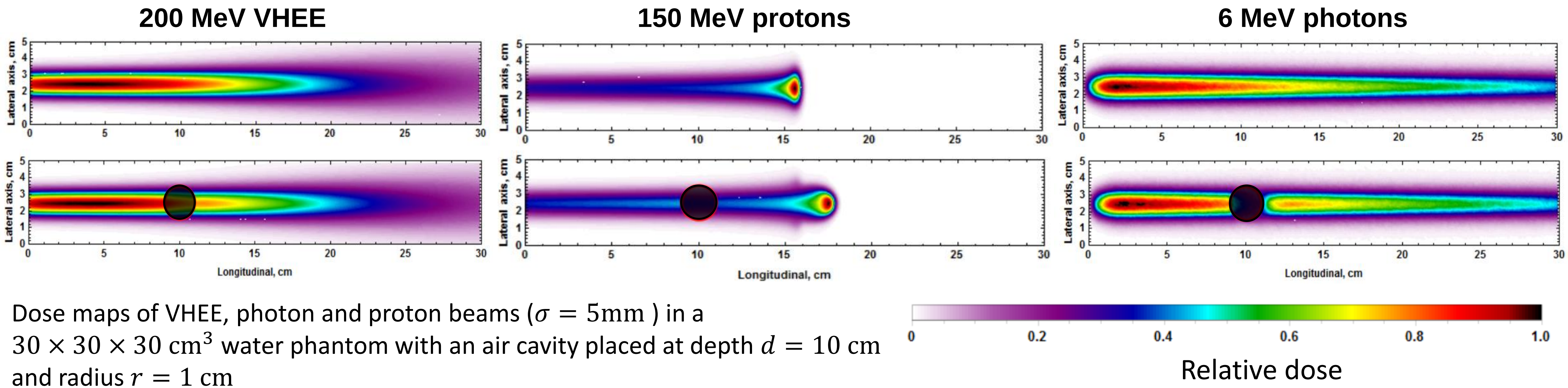
Effects of inhomogeneities on dose

- **Protons:** Shift in Bragg peak position (~diameter of embedded air cavity) – results in large dose deposition in healthy tissue!
- **Photons:** Dose build-up after the air cavity for photons
- **VHEE: relatively insensitive to intervening low-density media (dose difference range $\sim 0.3\%$) – precise and reliable dose delivery to cancerous tissue**



Schematic of simulation set-up in GEANT4

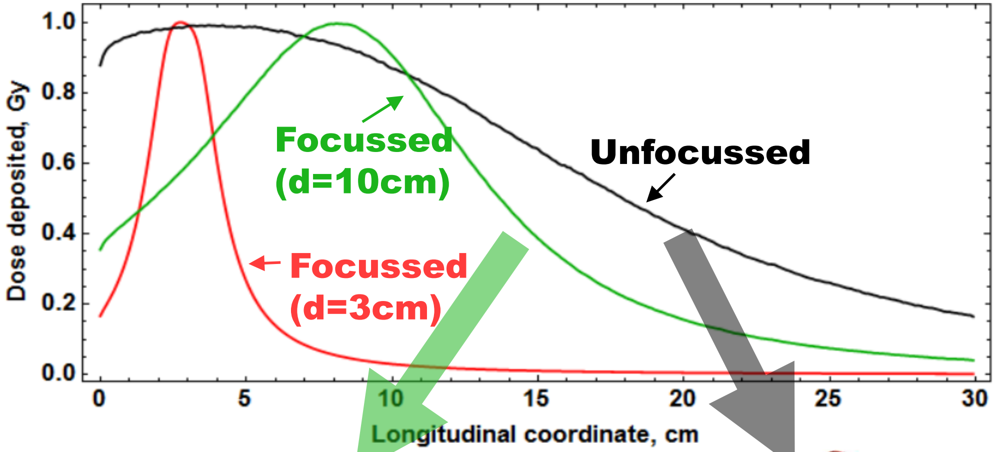
We came to these conclusions from discussions with clinicians at Christie Hospital (Manchester)



Dose maps of VHEE, photon and proton beams ($\sigma = 5\text{mm}$) in a $30 \times 30 \times 30\ \text{cm}^3$ water phantom with an air cavity placed at depth $d = 10\ \text{cm}$ and radius $r = 1\ \text{cm}$

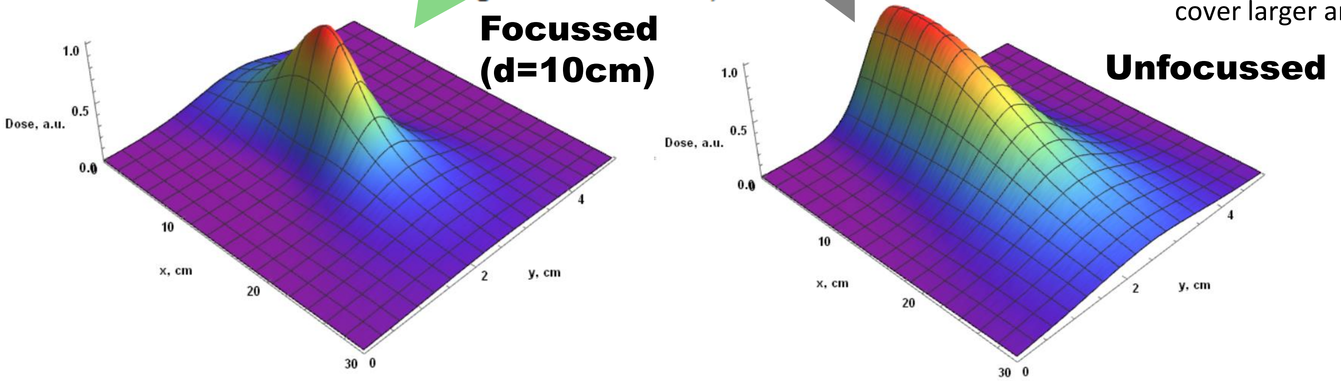
Dose Delivery With Focussed Electron Beams

- **Our recent simulation studies indicate focussed VHEE can achieve better dose deposition than proton beams**
- Focussed VHEE beams **reduce entrance dose**
- **Increased dose rate** to cancerous tissue

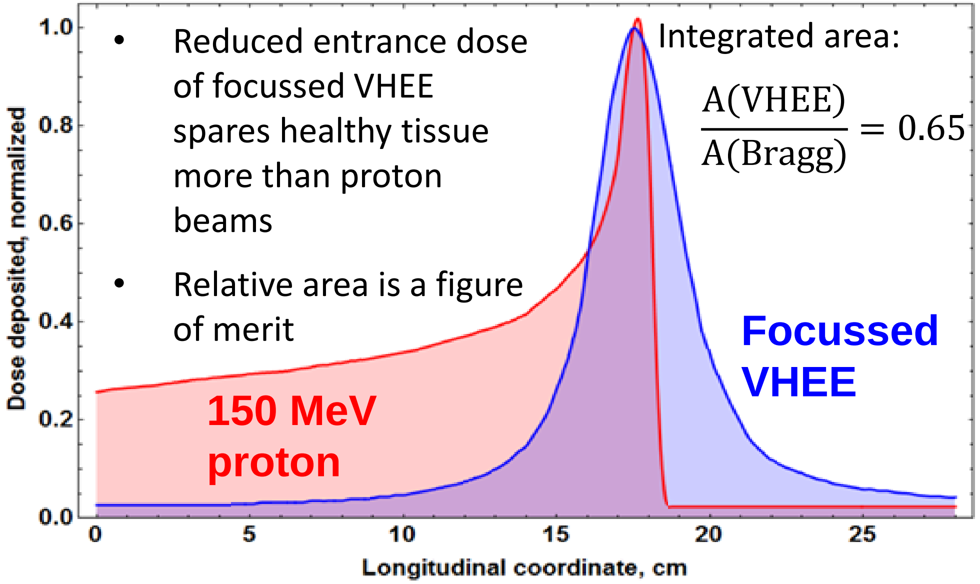


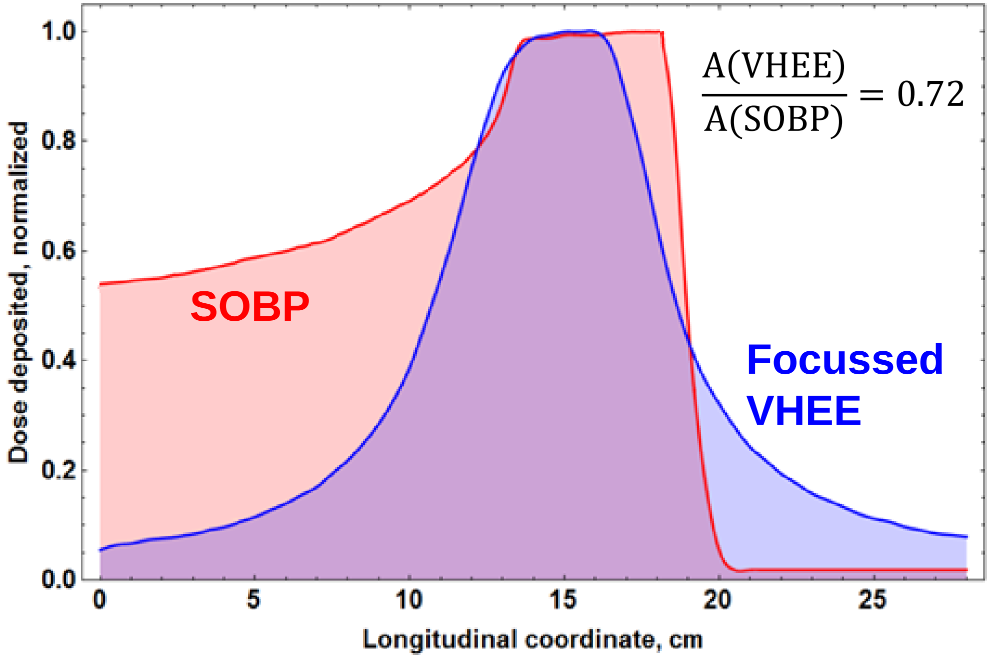
Focused and unfocused beam simulations with 200 MeV VHEE

In patient treatment a superposition of several peaks – Spread-out Bragg Peak (SOBP) – is used to cover larger areas.



Dose maps for VHEE beams in water: focussed (left) and unfocused (right)

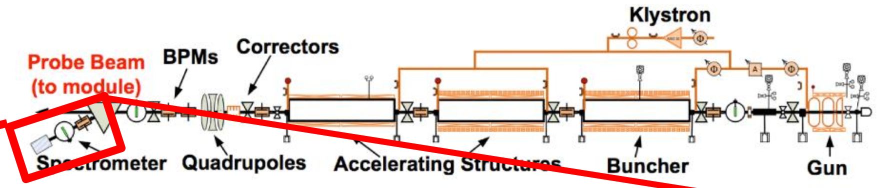




Strongly focussed wide ($r = 5 - 10$ cm) VHEE beams compared with mono-energetic and spread-out Bragg peaks

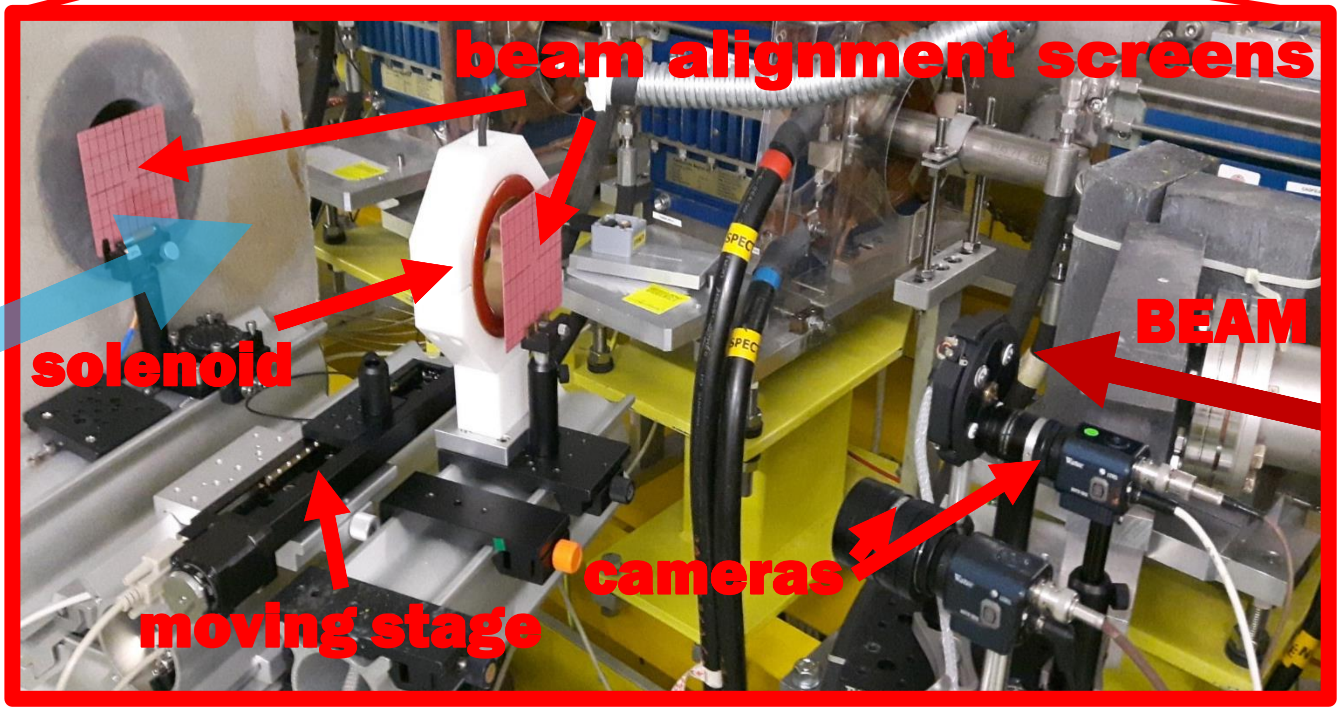
Experiments at CALIFES (now **CLEAR)** facility, **Dec 2016, with 200 MeV electron beams**

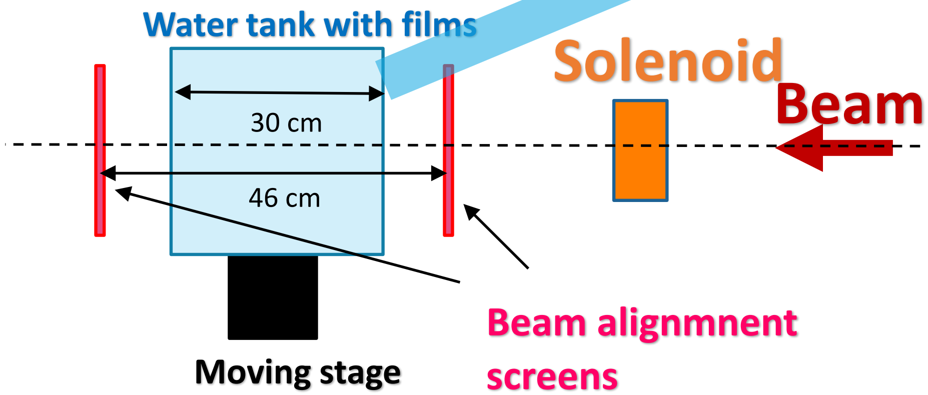
Beam dosimetry experiments with radiosensitive films planned with the new CLEAR facility at CERN .



CALIFES facility Parameters:

Beam parameter (end of linac)	Value range
Energy	197 MeV
Energy spread	**< 0.5 MeV FWHM**
Bunch charge	0.5 nC
Train length	**50 bunches**
Beam spot size	**1 mm**
Charge Jitter	**≈ 20 %**
Relative energy spread	1 %





- *100 bunches of 50 pC/shot spaced by ~1 sec. at 8 cm distance corresponds to 100 Gy.*

Experiment at CALIFES (CERN), Dec 2016

- Dose characteristics of VHEE beams through water were investigated at CALIFES facility with 200 MeV beam
- Dose dependancy on heterogeneities was investigated
- Results were compared with GEANT4 simulations

Longitudinal dose profile measurement in water

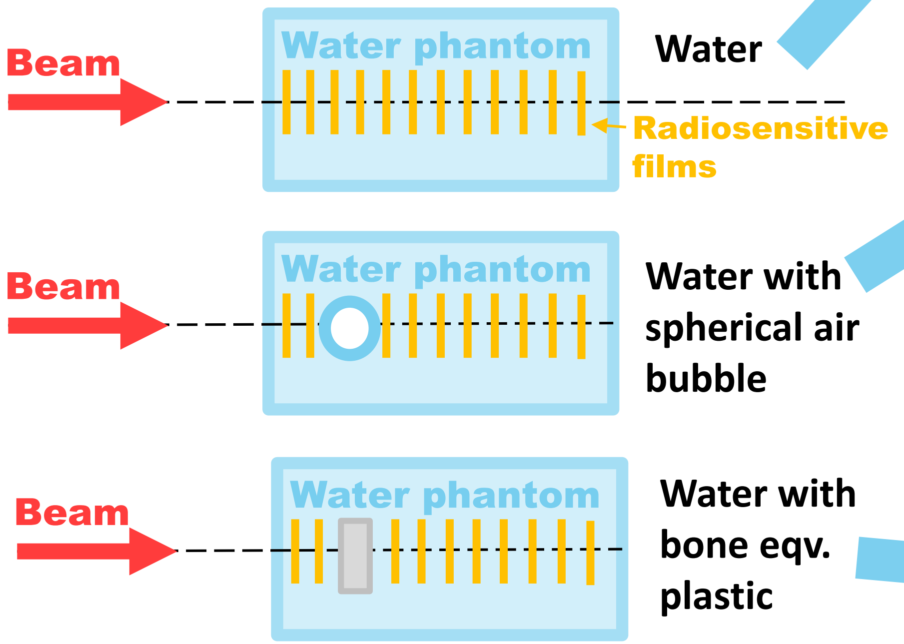
Air geometries:

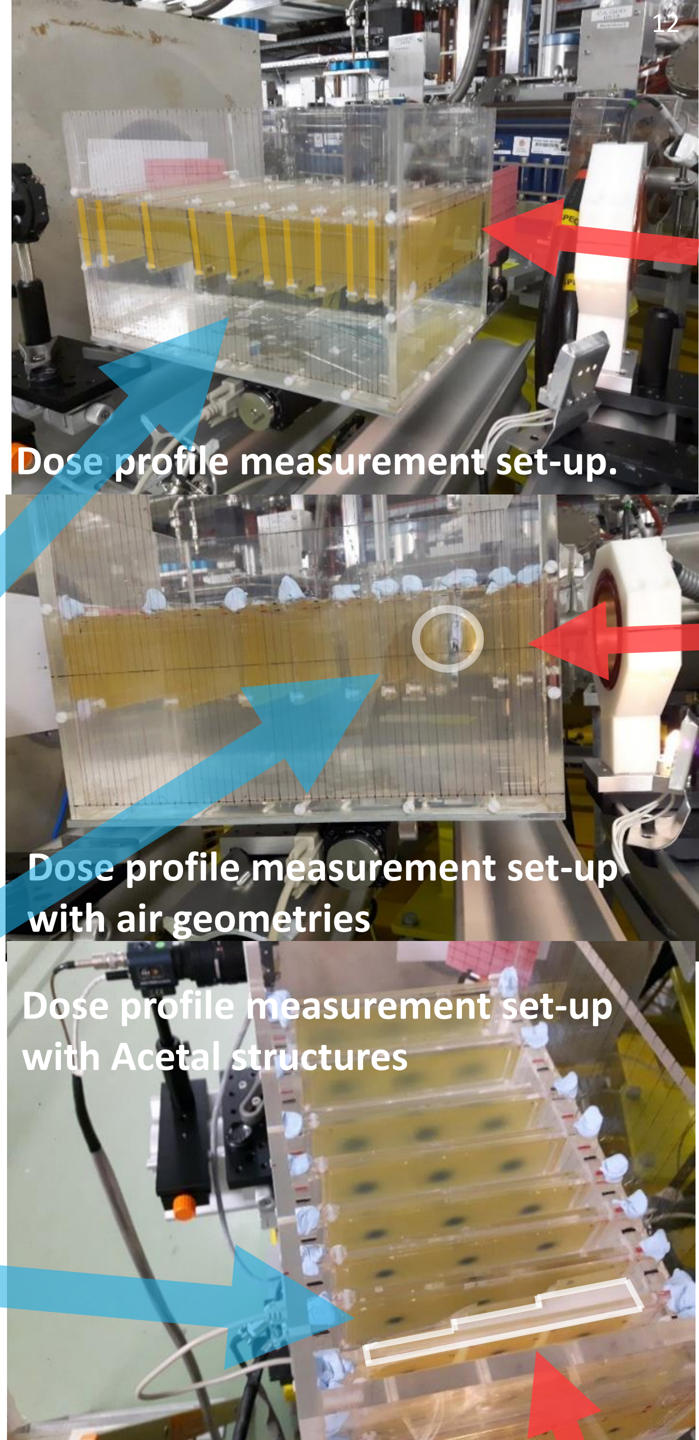
- **rectangular (15 mm thick)**
- **spherical (r = 20 mm)**

Acetal geometries

- **5, 10, 15 mm thick plastic ($\rho = 1.45\,\mathrm{kg/m^3}$)**

Dose depth profile in water



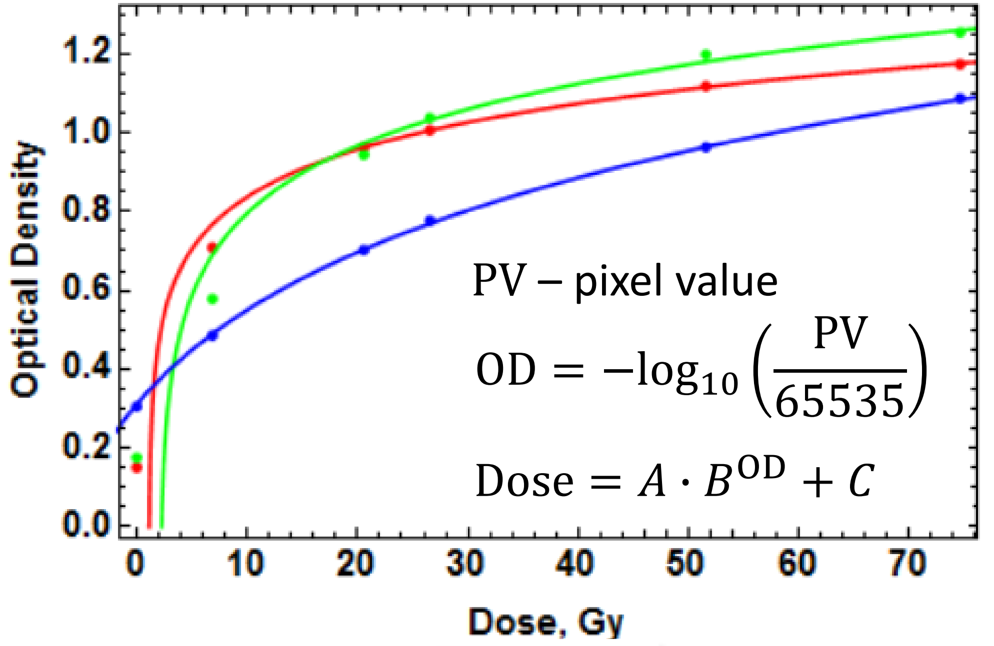


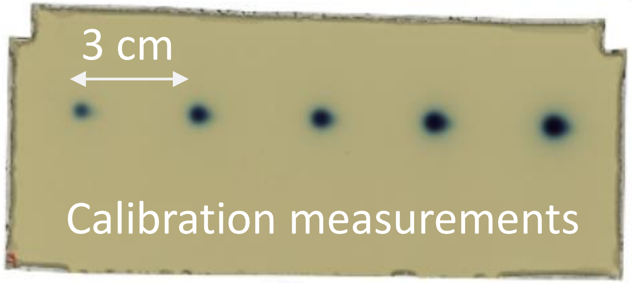
Dose profiles of VHEE

Two dimensional dose profiles obtained at various depths.

Taking the maxima at each depth we can compare that to simulated depth dose profiles.

CALIBRATION

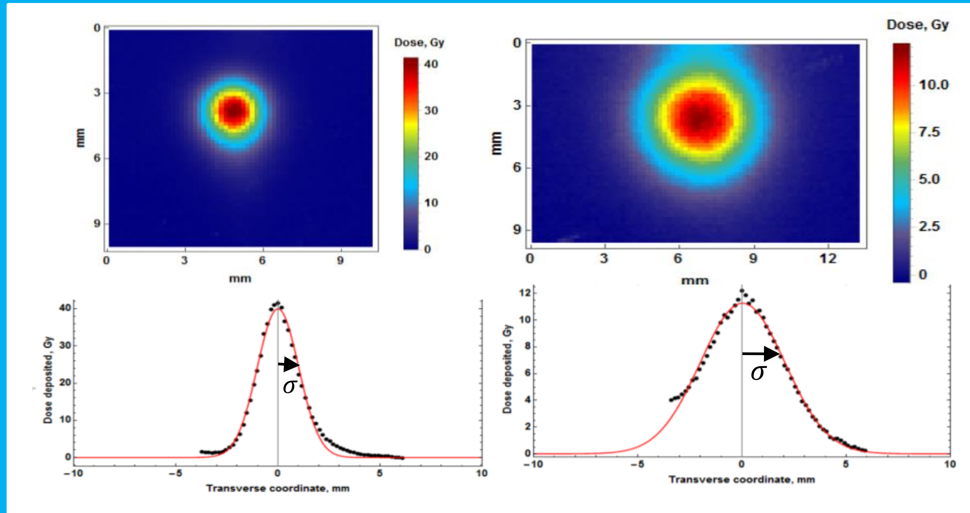




Dose calibration curves for EBT3 film in 3 cm depth in water.

DIVERGENCE MEASUREMENT

At tank surface | At tank back surface



Dose maps and transverse dose profiles of divergence measurement 32 cm apart.

$\sigma = 1.01\ \mathrm{mm}$ $\sigma = 2.03\ \mathrm{mm}$

IMAGE ANALYSIS

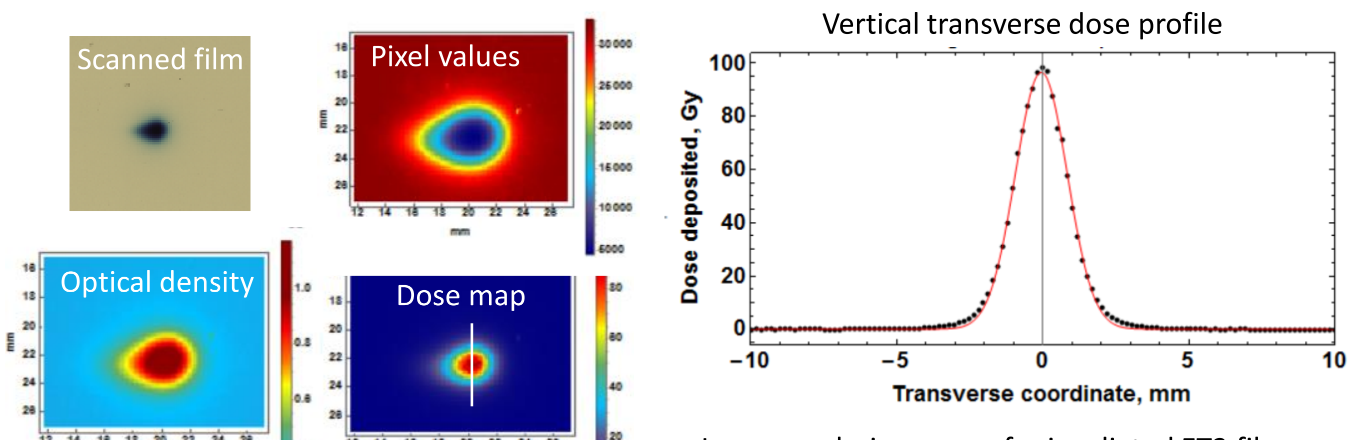
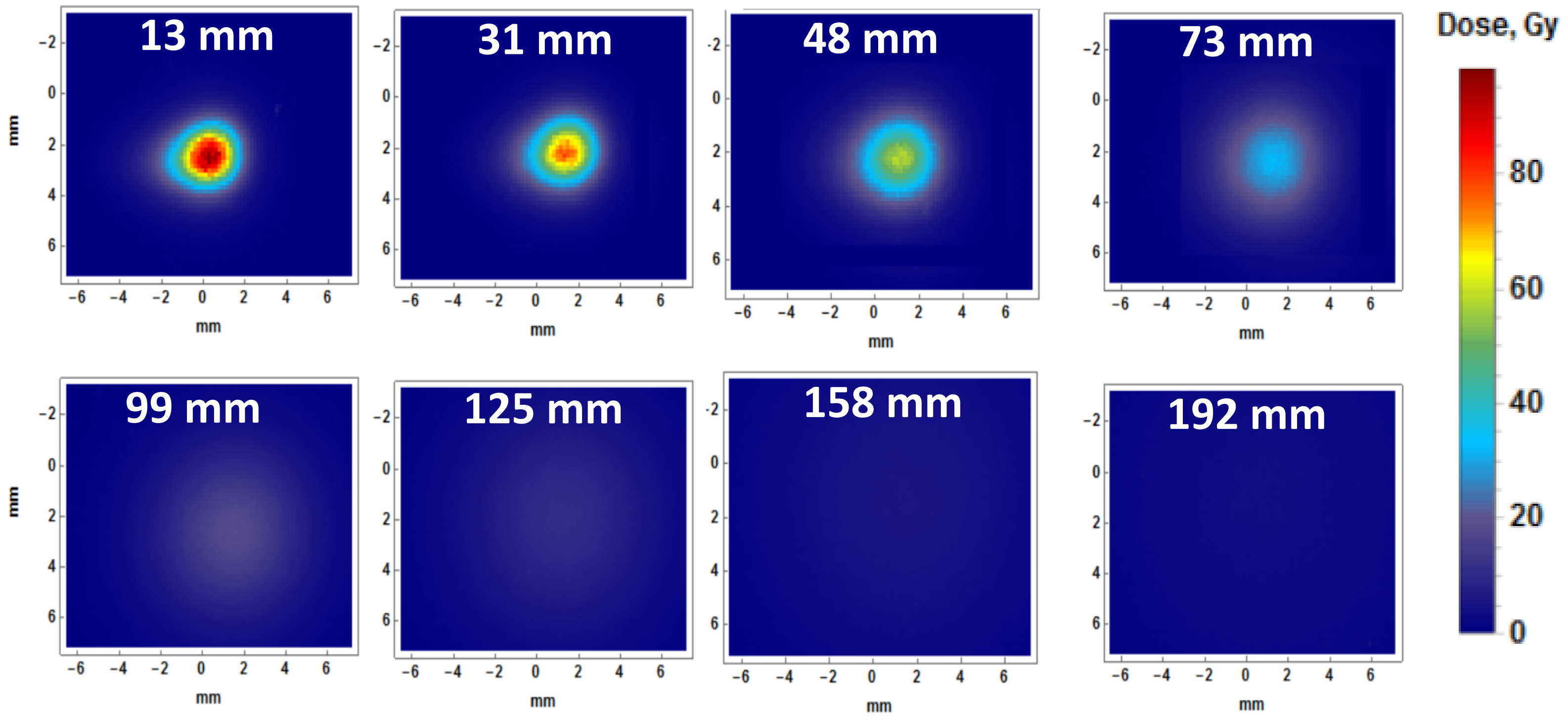


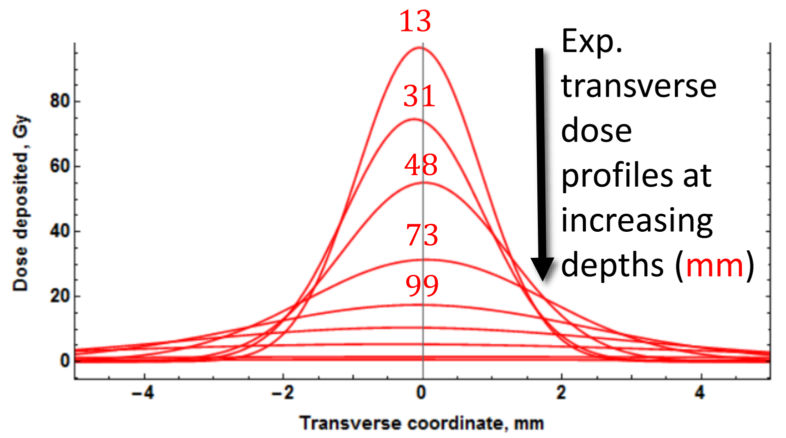
Image analysis process for irradiated ET3 films.

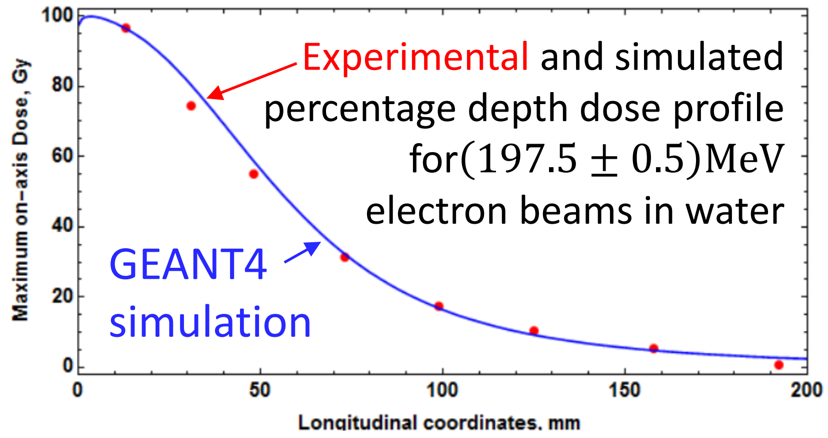
Dose profiles of VHEE

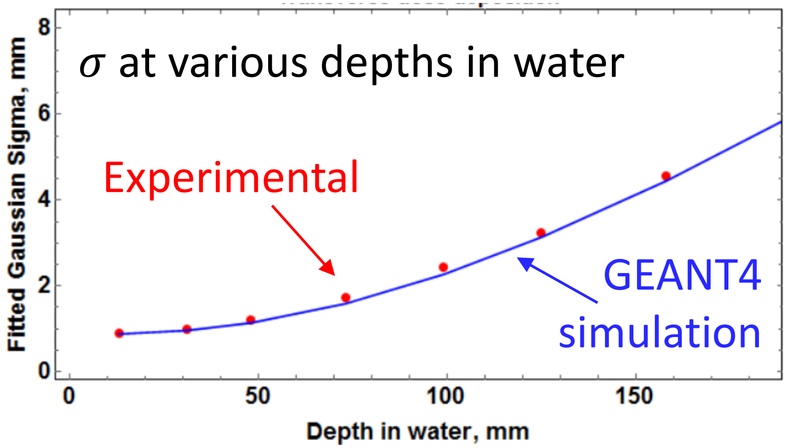
- Two dimensional dose profiles obtained at various depths
- Obtained percentage depth profiles and beam σ at various depths compared with GEANT4 simulation results
- Dose depth profiles and beam widths of various target geometries compared



Transverse dose maps of VHEE beams in water at given depths with entrance $\sigma = 1.01$ mm.



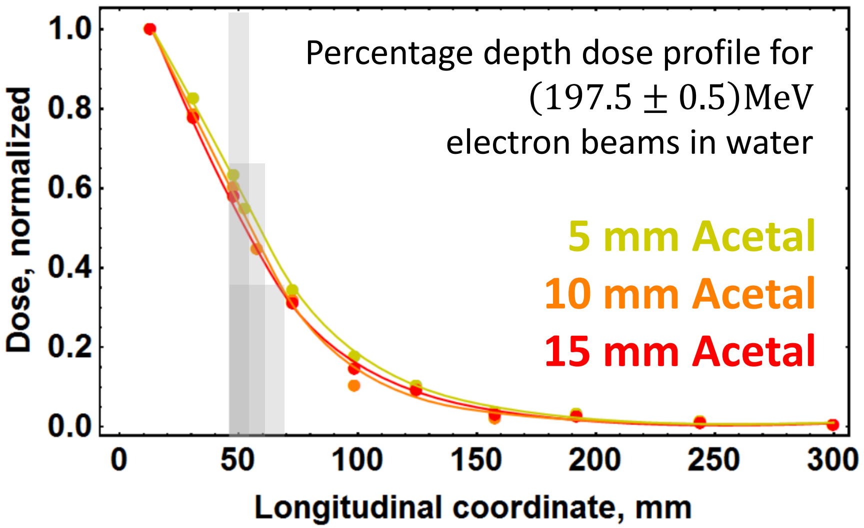


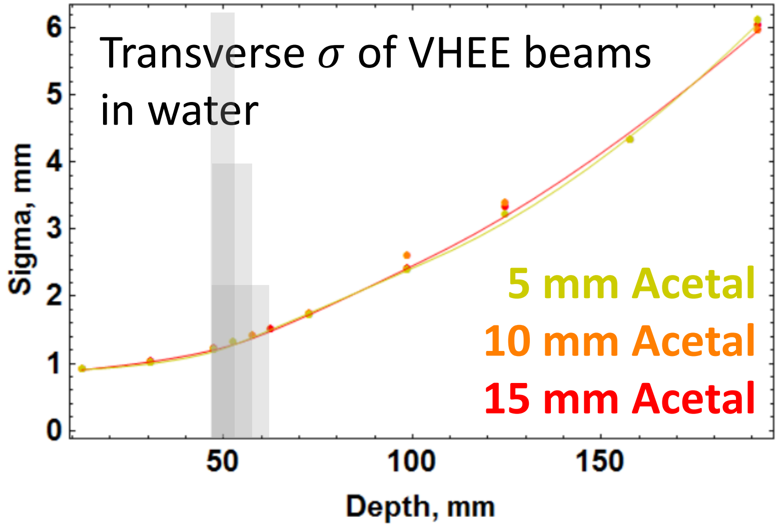


VHEE dose profiles - Bone geometries

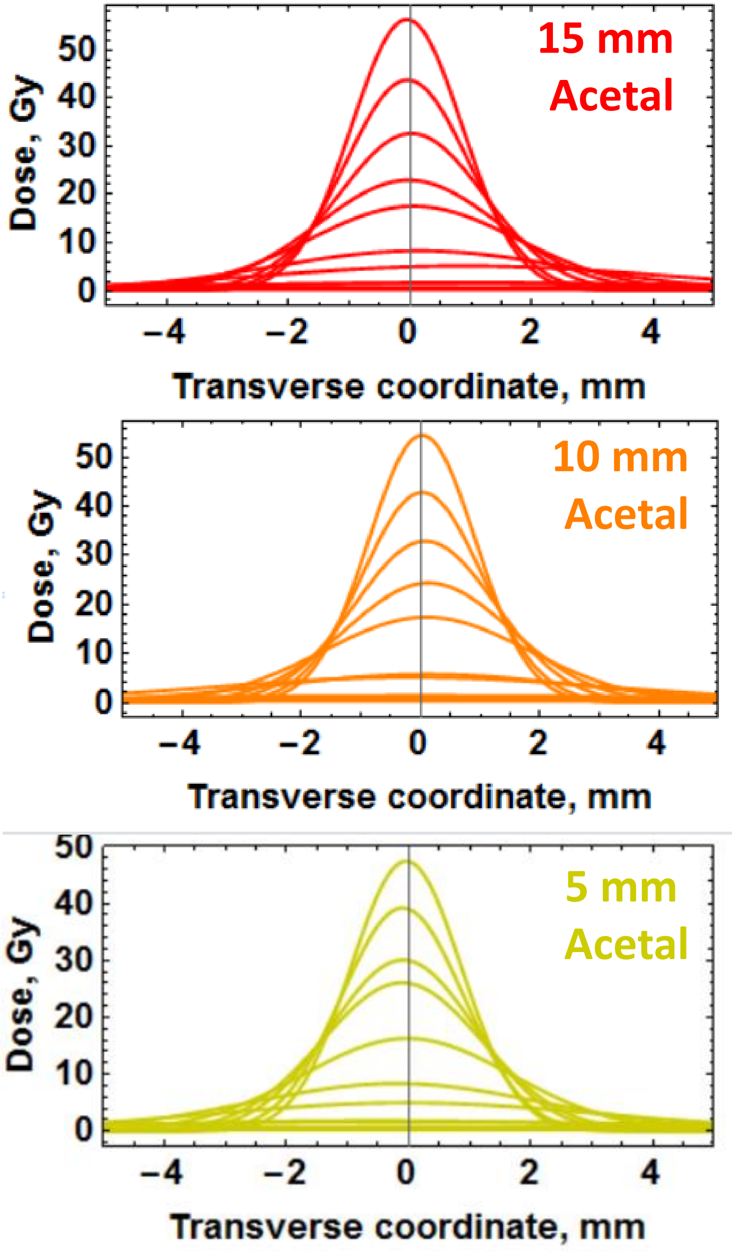
- Varied thicknesses (5, 10, 15 mm) of Acetal bone equivalent plastic ($\rho = 1.45\,\mathrm{kg/m^3}$) embedded at 5 cm depth

- Percentage dose depth (PDD) profiles and beamwidths were found to be relatively unaffected by increasing plastic thickness





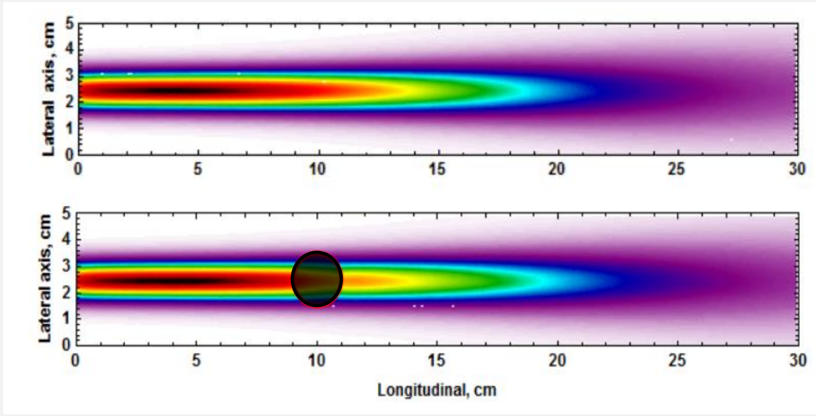
Transverse dose (D) profiles of VHEE beams at various depths in water



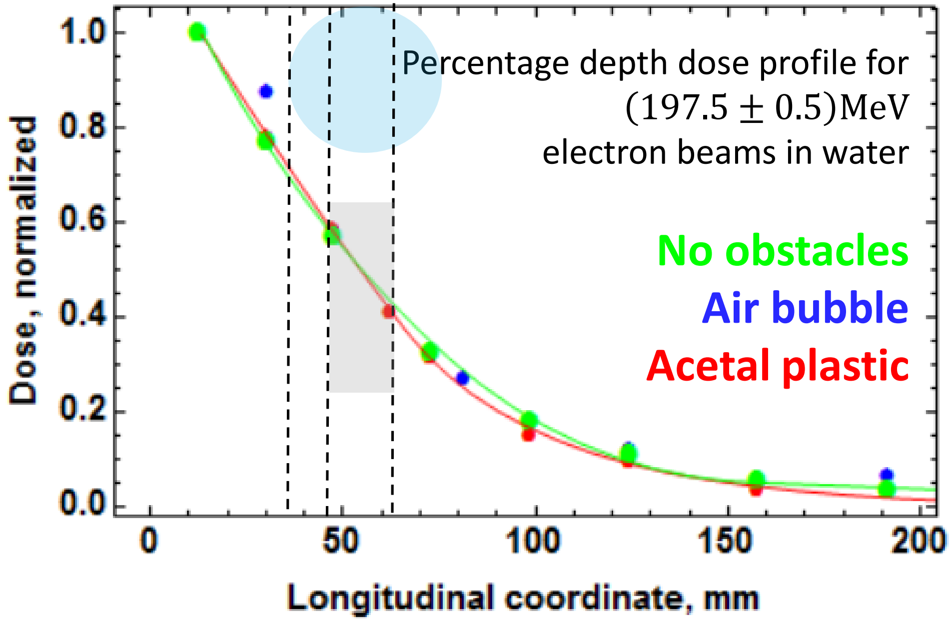
VHEE dose profiles - comparison

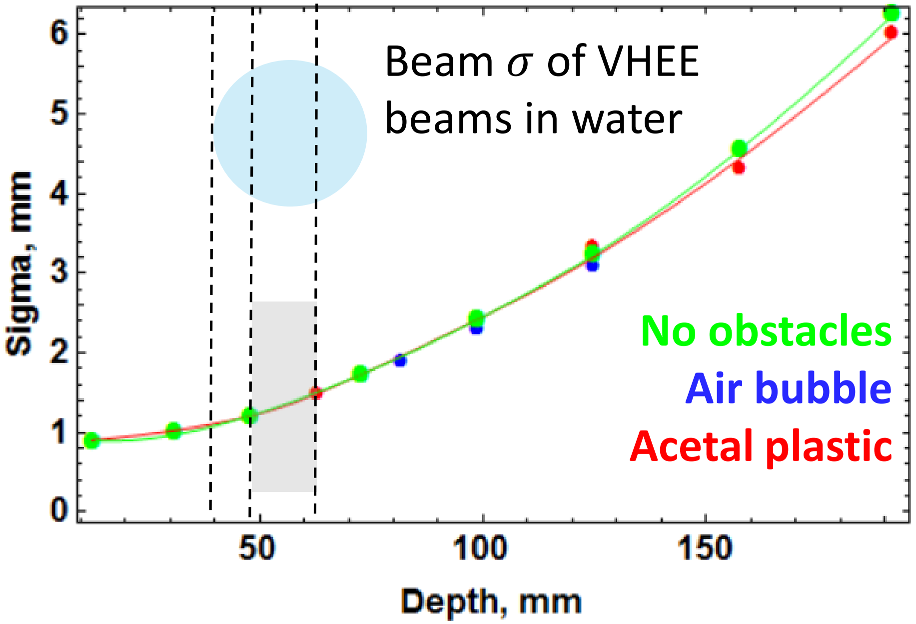
- Comparing all dosimetric VHEE beam characteristics in water with and without embedded air and bone structures
- Depth dose profiles almost unaffected (within borders of uncertainty) regardless of geometric setup of the target

200 MeV VHEE



Dose maps of VHEE beams in water with an embedded air cavity





Summary and Future Work

- VHEE is a recent and a rapidly developing area of radiotherapy
- Simulation studies have indicated several advantages of using VHEE beams for radiotherapy including:
  - improved dose deposition characteristics
  - increased dose rate
  - ease of beam steering and manipulation
- Availability of facilities such as CALIFES/CLEAR 200 – 250 MeV electron accelerator facility is an essential asset for studies with VHEE beams
- High-gradient X-band structures are a potential option for a compact VHEE radiotherapy machine
- A new linac design will be required with little to no azimuthally moving parts and multiple linacs surrounding the patient
- Recent simulation studies at CALIFES indicate that VHEE could be used as a reliable radiotherapy modality for deep-seated tumours
- VHEE'17 Very High Energy Electron Radiotherapy: Medical & Accelerator physics Aspects towards machine realisation workshop, 24-26 July, 2017 at Daresbury Laboratories – all are welcome!

We are very grateful for a strong collaboration:

Jim Clarke (Cockroft Institute)

Roberto Corsini (CERN)

Walter Wuensch (CERN)

MANCHESTER 1824
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TOWARDS A FUTURE WITHOUT CANCER

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