VHEE Dosimetry Research Program at NPL

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Medical Radiation Science
National Physical Laboratory
Hampton Road, TW 11 0LW
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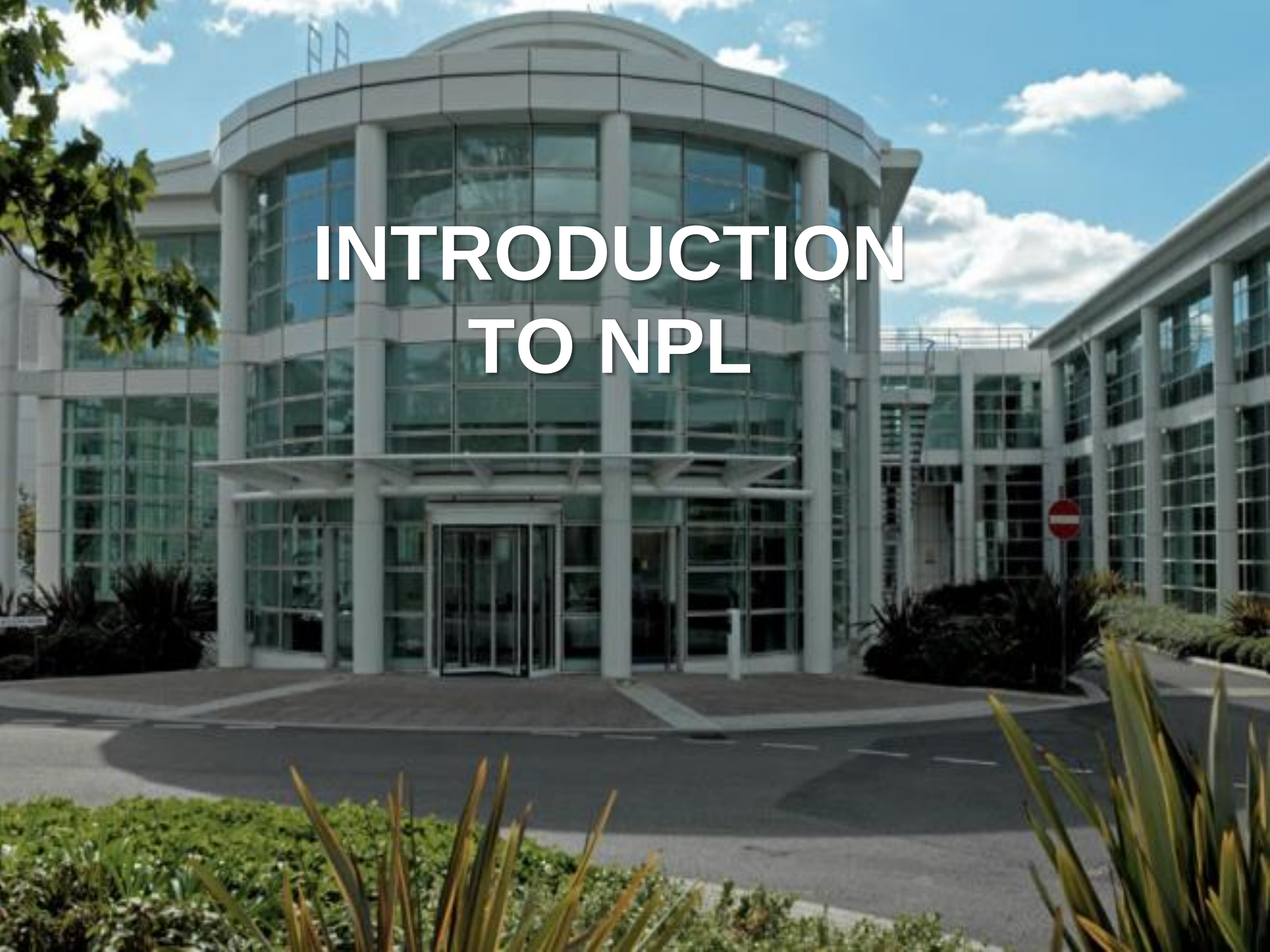
PRAE International Workshop, 8-10 October 2018

INTRODUCTION TO NPL



The National Physical Laboratory

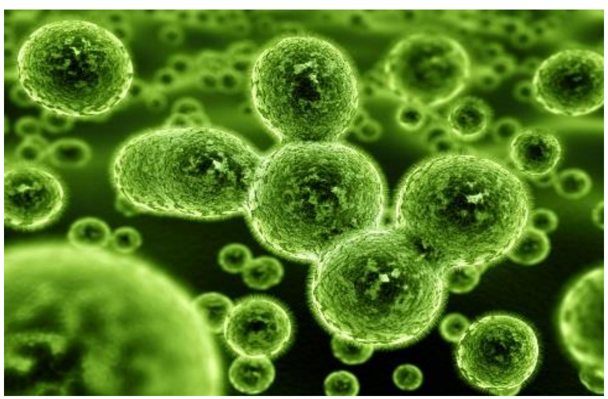
- The UK's National Metrology Institute
- Public Corporation owned by BEIS
  Strategic Partnership with Universities of Surrey and Strathclyde
- ~750 staff plus ~200 visiting researchers/year
- Partner with 80+ Universities and 200+ other organisations
- Connect with 2,500 businesses

Our Sectors

Digital

Environment & Energy

Life Sciences & Medical



Advanced Manufacturing

What do we do?

- Develop, maintain & disseminate internationally recognised measurement standards
- Collaborative R&D to solve address todays and anticipate tomorrows measurement challenges
- Provide access to our facilities and expertise through our products and services

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Instrumentation

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Calibration and Measurement Services

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Training

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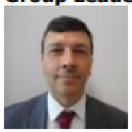
Consultancy

Co-Head of Department (with Ian Severn) for the 4 Groups below: Rebecca Nutbrown 

36 members of staff
17 students
3 guest workers
5 joined appointments

Biometrology

Group Leader: Florent Crepineau



Science Area Leader: Max Ryadnov

Andrea Briones (HRS)
Ines Camacho (HRS)
Emiliana De Santis (HRS)
Nilofar Faruqui (HRS)
Paula Gomez (RS)
Smita Gunnoo (HRS)
Kate Hammond (RS)
Alex Jones (PRS)
Ibolya Kepiro (HRS)
Helen Lewis (HRS)
Isabel Moraes (PRS)
Brunello Nardone (HRS)
James Noble (SRS)
Tristan Oliver Kwan(RS)
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Stephanie Rey (HRS)
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Russell Buckley-Taylor
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Alastair Davey
Marcus Eales
Conor Lanphere
Hannah MacDonald
Anna Munro (PhD)
Henry Sawczyc
Georgina Benn
Caoimhe Canavan
Chloe Chung
Edeline D'Souza (PhD)
Marcus Fletcher (PhD)
Andrea Longatti
Irene Marzuoli
Eveliny Nery (PhD)
William Whitehouse

Medical Radiation Physics

Nathalia Almeida Costa (HRS)
Ilias Billas (HRS)
Matthew Cashmore (HRS)
Daniel Deidda (HRS)
Ana Denis-Bacelar (SRS)
Alexandros Douralis (RS)
Andrew Fenwick (HRS)
Kelley Ferreira (HRS)
Warda Heetun (ARS)
Mohammad Hussein (SRS)
Andrew Robinson (PRS)
David Shipley (SRS)
Ileana Silvestre Patallo (HRS)

Consultant:
Vere Smyth

Students:
Aaron Axford
Nicholas Bates
Becky King
Arkadiusz Wojtasik
Kate Baxter
Hannah Cook
Sophia Pells

Guest Worker:
Yunuen Cervantes Espinosa - *International Secondment Scheme*

Joint Appointments:
Phil Evans
Jill Wevrett
Matt Hall

Medical Radiation Science

Graham Bass (SRS)
Catharine Clark (PRS)
Gavin Cox (RS)
David Crossley (SRS)
Simon Duane (PRS)
Clare Gouldstone (HRS)
Michael Homer (HRS)
Martin Kelly (HRS)
Nigel Lee (HRS)
Ana Monica Lourenco (HRS)
James Manning (HRS)
David Maughan (HRS)
William Norwood-Grundy (RS)
Hugo Palmans (PRS)
Francesco Romano (SRS)
Thorsten Sander (SRS)
Peter Sharpe (PRS)
Giuseppe Schettino (PRS)
Anna Subiel (HRS)
Russell Thomas (SRS)
Nathaniel Woodall (ARS)

Students:
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Matt Bolt (PhD)
Chris Green
Michael McManus (PhD)
Emily Russell (PhD)
Esther Baer (PhD)
Sam Flynn (PhD)
Edward Lovelock
Kathryn Polin (PhD)
Gabrielle Wishart (PhD)

Guest Worker:
Charles-Antoine Collins-Fekete

Joint Appointment:
Prof Andrew Nisbet
Tony Price

Ultrasound & Underwater Acoustics

Group Leader: Stuart Kitney

Science Area Leader: **Bajram Zeqiri**

Commercial Engagement Leader:
Mark Hodnett

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Nicole Anstey (RS)
Christian Baker (HRS)
Nick Crawford (HRS)
Chris Dilley (RS)
Chris Fury (HRS)
Robert Goddard (RS)
Gary Hayman (HRS)
Mark Hodnett (PRS)
Aoife Ivory (HRS)
Nicholas Lucas (HRS)
Sam Masterman (ARS)
Piero Miloro (SRS)
Rob Patterson (ARS)Srinath Rajagopal (SRS)
Stephen Robinson (PRS)
David Sinden (SRS)
Dan Sarno (HRS)
Maria Theodorou (HRS)
Lian sheng Wang (SRS)
Jake Ward (SRS)
Bajram Zeqiri (NPLF)

Student:
Marina Bakaric
Piers Turner EngD
Alberto Sanchez-Pastor Gomez

Some research activities

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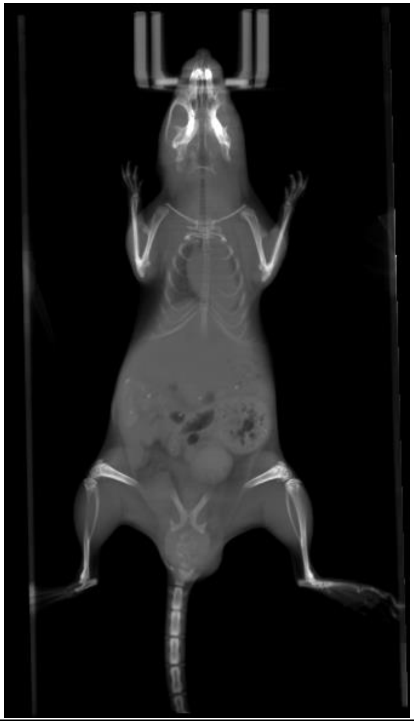
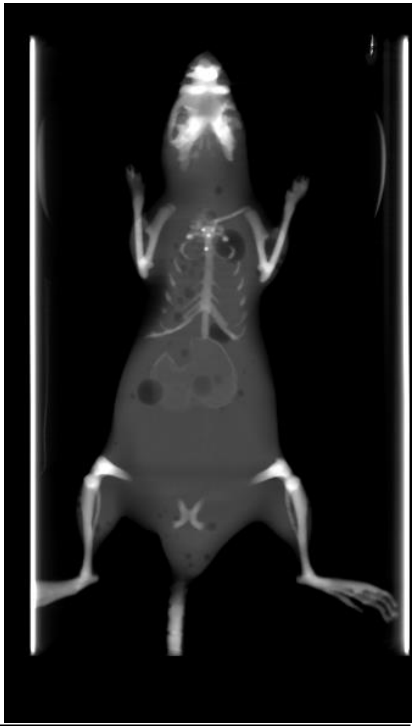
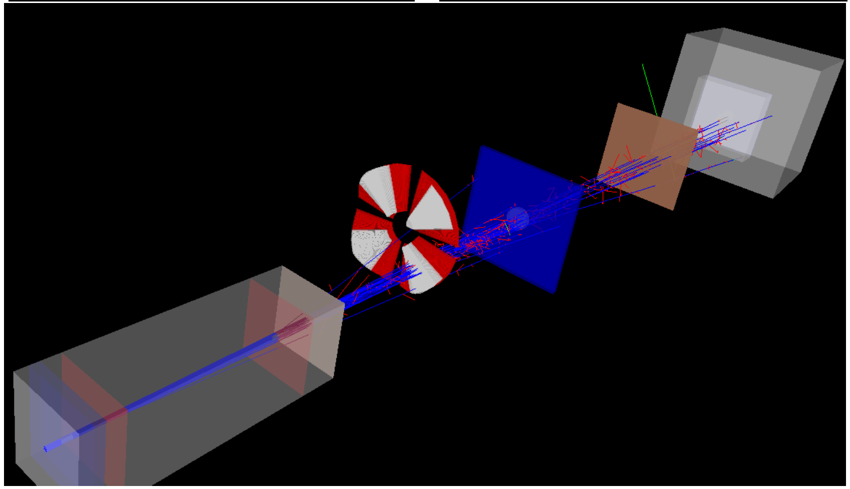
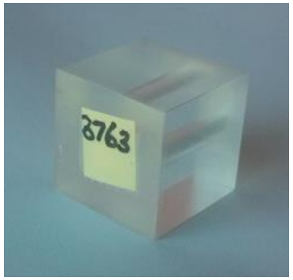
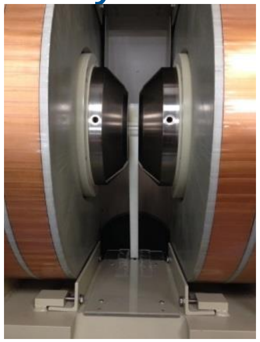
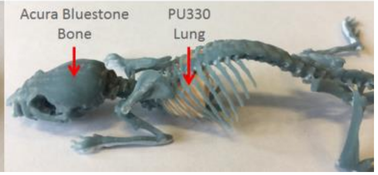
- Radiation dosimetry for
  - *Protons & light ion radiotherapy*
  - *MRI guided radiotherapy*
  - *Small & composite fields & FFF*
  - *Molecular radiotherapy*
  - *Electronic brachytherapy*
  - *Ultrashort pulses/VHEEs*
- Definition of new quantities to better define radiation damage
- Radiobiology for new modalities
- Phantom development for dosimetry and medical Imaging

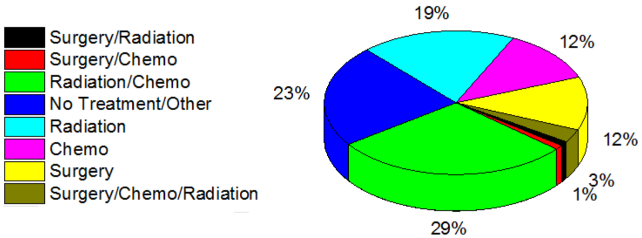




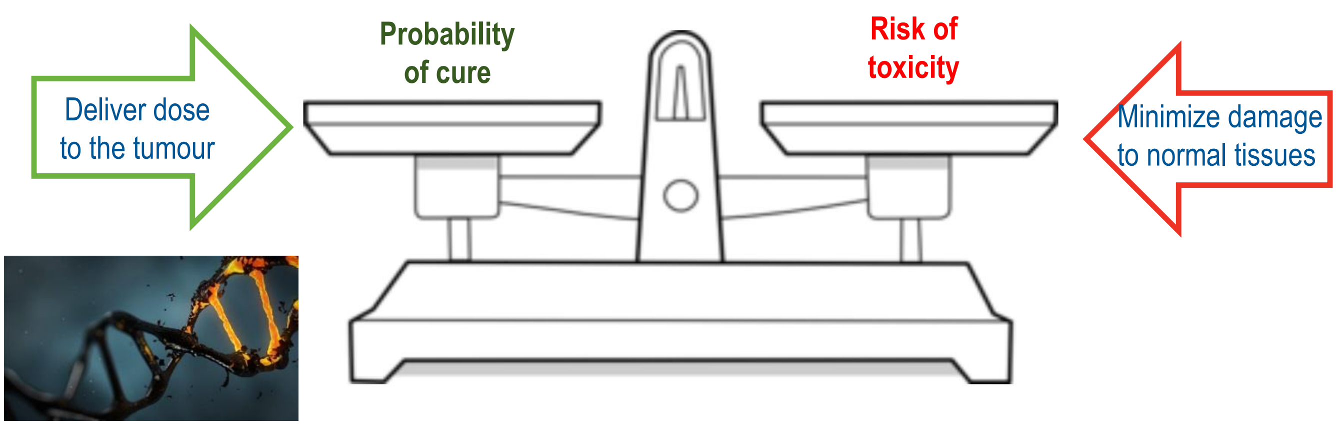
Radiation Therapy (RT) - overview

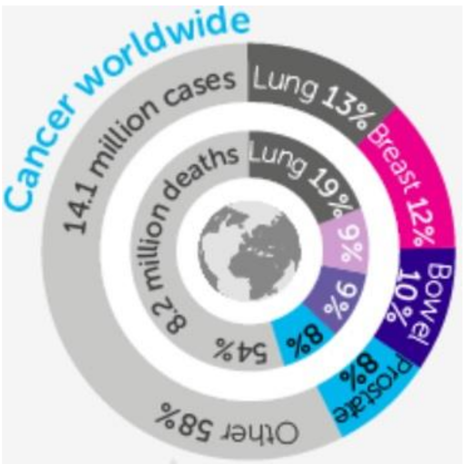
- 360,000 new cancer cases/yr (70% rise over the next 2 decades)
- Worldwide : over 15, 000, 000
- Radiotherapy is the most cost-effective methods responsible for ca. **50% of cancer survivals**



The importance of dosimetry:

- Successful radiotherapy depends on delivering the correct dose to the treatment volume and sparing surrounding healthy tissues

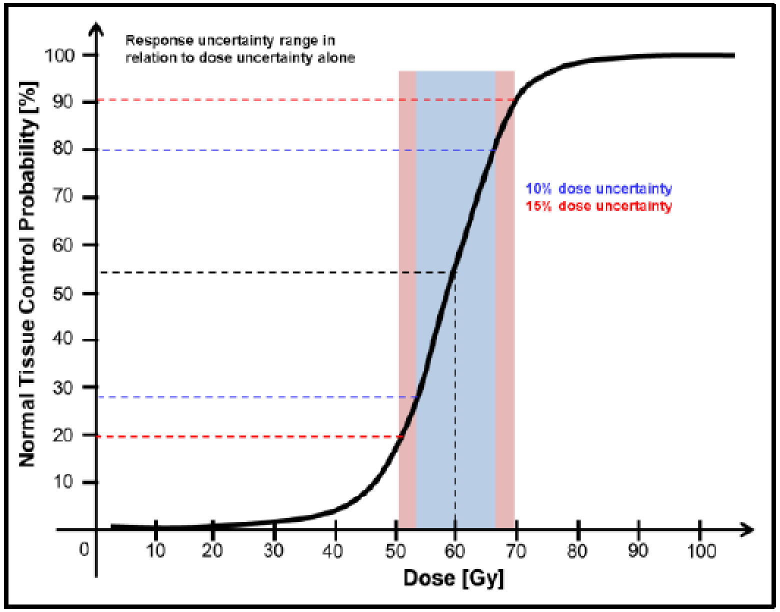




- Dose delivered to the tumour should be within **5%** of the prescribed dose

Status of dosimetry in radiobiology

- in clinical studies dose uncertainties are ~3%
- radiobiological experiments are affected by large dose uncertainties: **tens%!!!**
- dosimetry in radiobiology research **is often inadequate**



Courtesy of C. Cawthorne

ICRU Report 24 (1976): *a change of 7-10% in dose to target volume results in significant change in the TCP* → dose delivered to the tumour should be within **5%** of the prescribed dose

Workshop held at NIST in 2011 (organized by NCI, NIAD & NIST)

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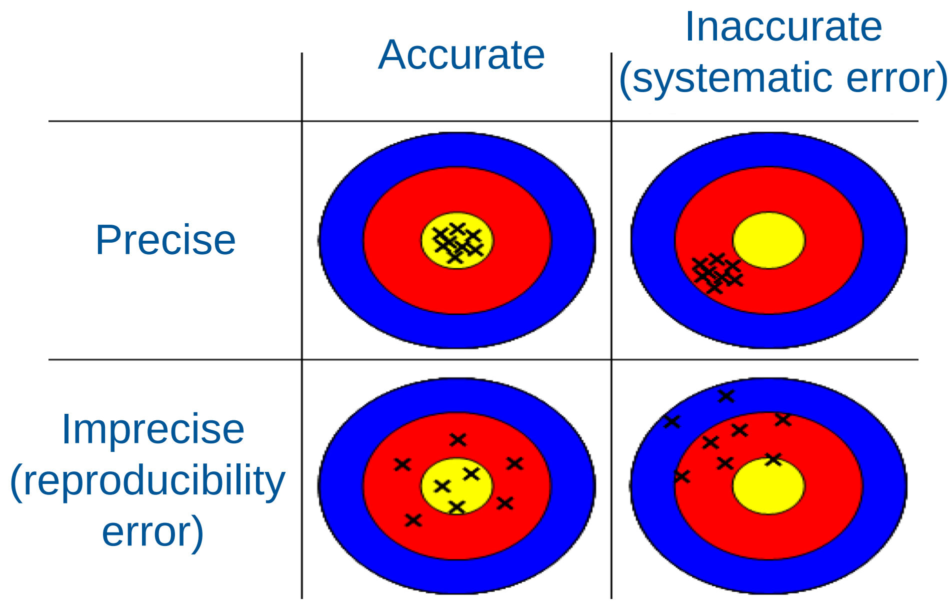
Volume 118 (2013) http://dx.doi.org/10.6028/jres.118.021
Journal of Research of the National Institute of Standards and Technology

The Importance of Dosimetry Standardization in Radiobiology

Marc Desrosiers[1], Larry DeWerd[2], James Deye[3], Patricia Lindsay[4], Mark K. Murphy[5], Michael Mitch[1], Francesca Macchiarini[6], Strahinja Stojadinovic[7], and Helen Stone[3]

Category	Item	% of articles
Absolute Dosimetry/ Calibration	Standards/Guides Used	7
	Detector Type Used	3
Determination of Dose	Dosimetry Method	37
	Uncertainty in Dose	4
Radiation Source Specification	Detector Type Used	28
	Radioisotope	86
	kV, Filtration, HVL	50
Details of the Irradiation	Animal/Cell Type	100
	Dose Details	100
	Field Size and Shape	0
	Geometry of Fields	24
	Animal Containment	100

Precision and accuracy of dose



- Precision refers to reproducibility of measurement and accuracy to the proximity of measurement result to the true value

- Inaccurate dose → invalid conclusions (?)

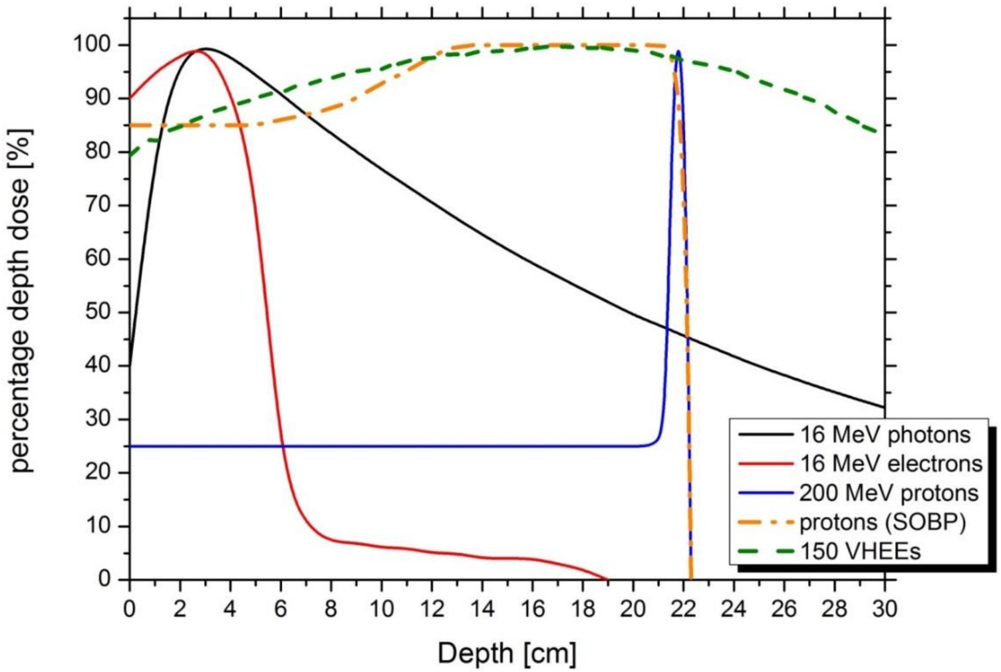
↓

response not correctly linked to a relevant biological radiation interaction

Given the size of the error in the biological contribution, it is important that the <u>physical errors are minimized</u>

Standard Laboratories can enable **<u>accurate and traceable dosimetr</u>**y to support radiotherapy treatments

Current state-of-the art RT



DRAWBACKS

- X-rays

Large dose deposition outside tumour volume

- Electrons (<22 MeV)

Used solely for treatment of superficial tumours

- Protons & heavy ions

£££!!! Still lack of clinical evidence of proton RT superiority over photon treatment for several cancer cases, RANGE UNCERTAINTIES

How about VHEE (electrons >50 MeV)?

Concept first proposed by DesRosiers *et.al* (in 2000)

Advantages of VHEE RT

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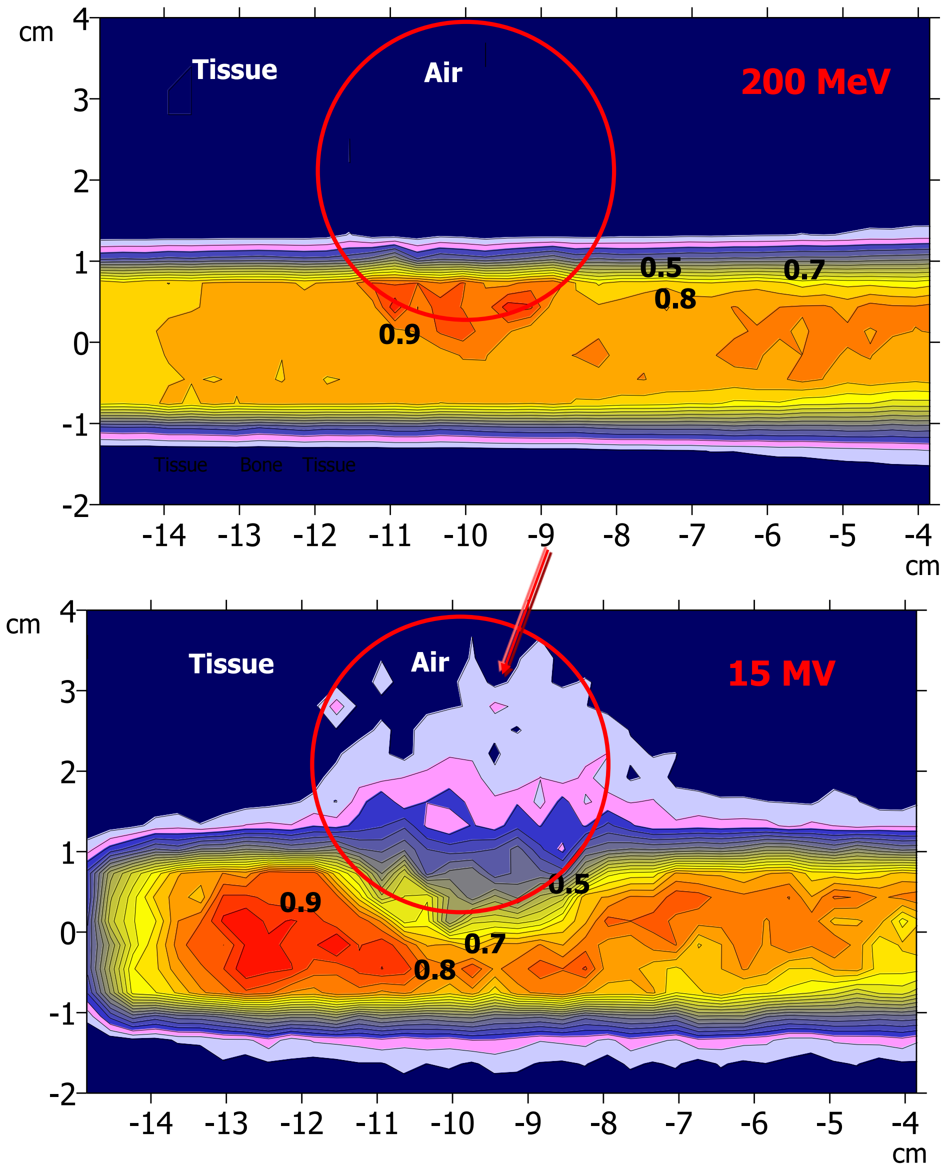
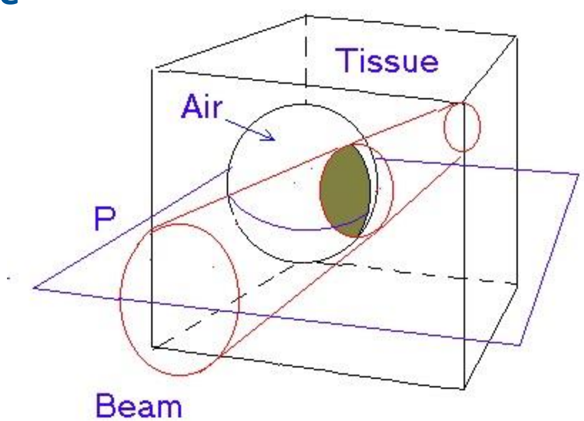


VHEE unlike X-ray photons maintain electronic equilibrium in tissues with varying densities

VHEE

conventional RT photons

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



DesRosiers *et al.*, Proceedings of the SPIE, Vol. 6881, (2008)

Very High Energy Electron (VHEE) beams

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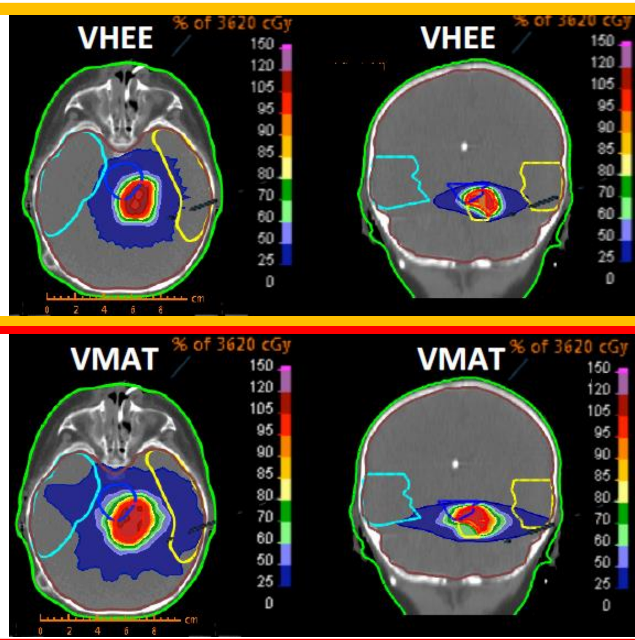
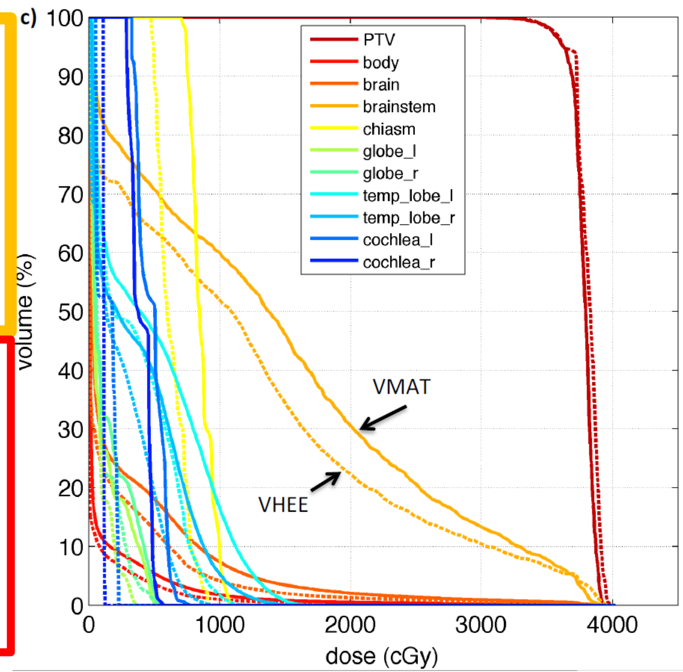
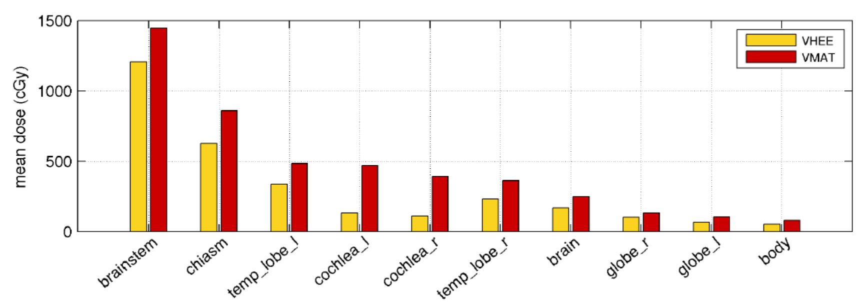
- VHEE can achieve superior dose distributions (vs photons), can provide **better sparing of organs at risk** and enable **dose escalation** to the tumour

VHEE

state of the art X-ray treatment



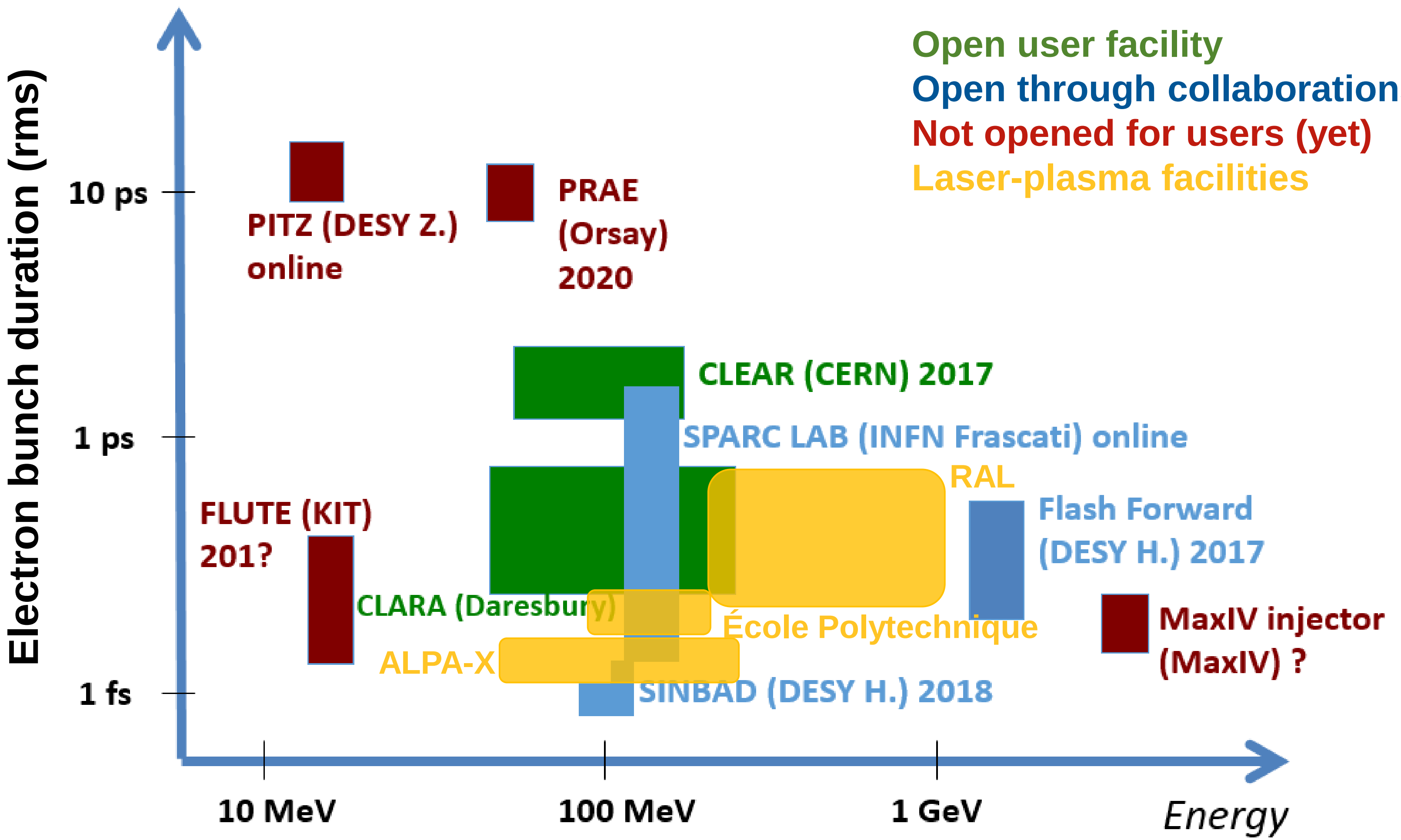




Bazalova et al., Med.Phys. 42 (2015)

Present and planned European electron test beams

not complete



Adapted from E.Aldi

source: https://goo.gl/sn4dqP

VHEE – unusual beams

- Energies exceeding beam energies in conventional RT
- Very short nature of electron pulse duration:
  - pico- (10e-12)
  - femto- (10e-15)

  } second

Conventional RT e-beam

↓

micro (10e-6) second

↓

Dosimetric challenge

Dosimetry – brief overview

- Dosimetry – measurement of dose
- "Dose" – abbreviation of "absorbed dose" quantity

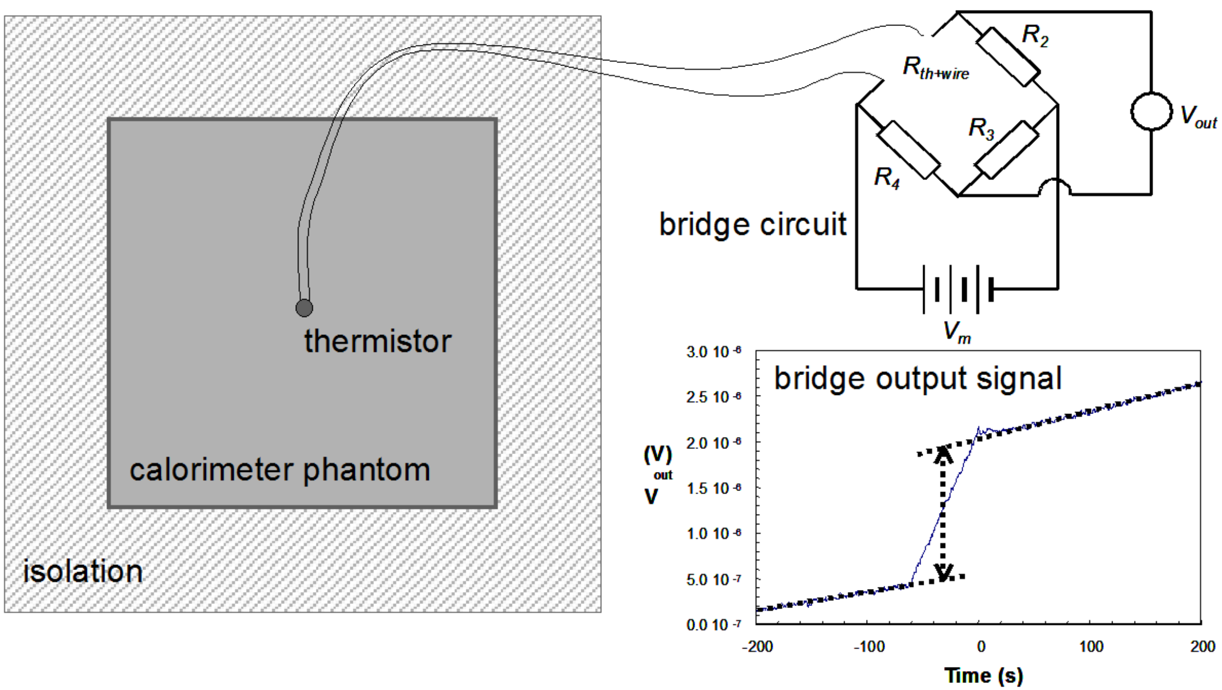
- Primary standard devices:
  1) detectors measuring absorbed dose
  2) detectors measuring ionizations
  3) detectors quantifying # of radicals formed in a medium

- Calorimetry: Principle of operation

Calorimetry

$$D_{med} = c_{med} \cdot \Delta T \cdot \frac{1}{1-h}$$

Material	ρ (kg m^{-3})	c (J kg^{-1} K^{-1})	k (J s^{-1} m^{-1} K^{-1})	α (m^2 s^{-1})	ΔT/D (mK Gy^{-1})
Water	998	4180	0.602	1.44×10^{-7}	0.24
Graphite	1770	725	135	1.05×10^{-4}	1.4



Quest for accurate VHEE dosimetry

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- Lack of standard VHEE beams
- Calorimetry (only NMIs have this capability)
- Ionometry (gold standard in RT dosimetry)
- Alanine
- Films

Test of dose-rate dependence of ionization chambers with ultrashort VHEE beams

VHEE – unusual beams

- Energies exceeding beam energies in conventional RT
- Very short nature of electron pulse duration:
  - pico- (10e-12)
  - femto- (10e-15)

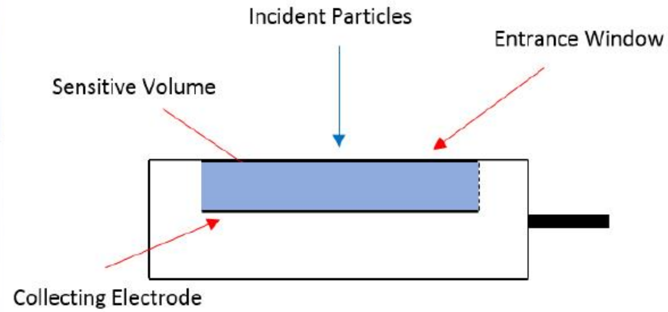
  } second

Conventional RT e-beam

micro (10e-6) second

Dosimetric challenge
for dose rate-dependent detectors

Ionometry – principles of operation



PTW Roos® chamber

- Ionometry: the measurement of the number of ionizations in substance
- The number of ionizations are used as a measure of the radiation dose
- High voltage applies between electrodes
- Air ionized, electrons emitted from the atoms
- The electrons move to the positive electrode
- Current induced
- An electrometer then count the number of total (+/-) charges Q
- Q is proportional with the dose to the air volume

Michael McManus' PhD project

Types of Ion Recombination

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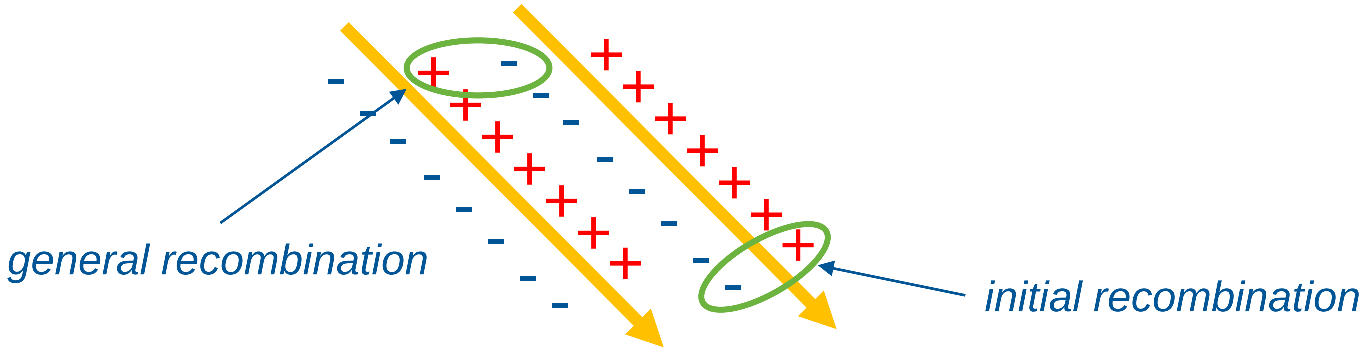
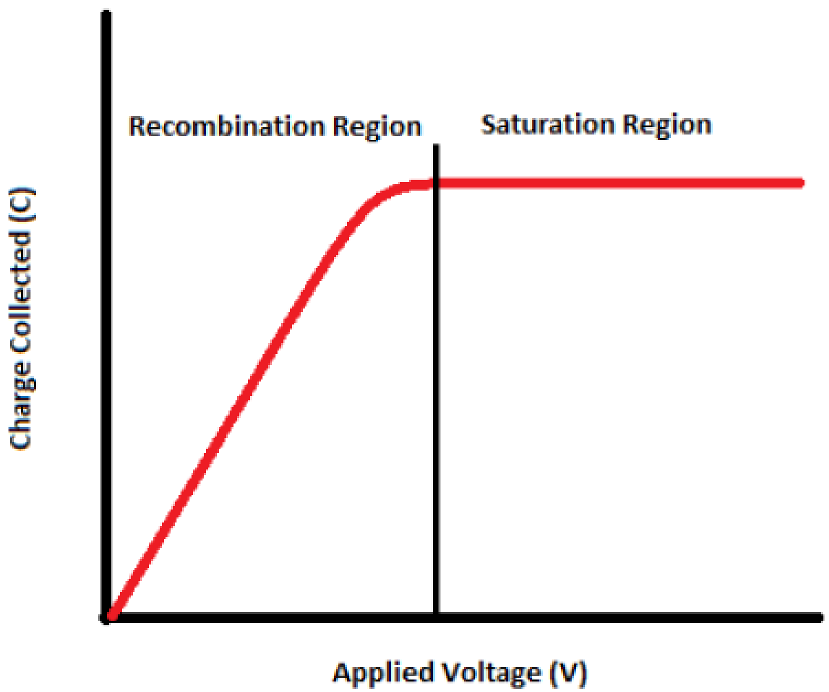


- **Initial Recombination**
  - Recombination along a single charged particle track
  - Independent of dose and dose-rate.
  - More pronounced in highly ionising particles such as α particles.
- **General Recombination**
  - Recombination between separate charged particle tracks.
  - Directly dependent on charge density i.e. the number of ions produced per unit volume.
  - Dose-rate dependent.
- General recombination is likely to play a much larger role in recombination effect of ultra-short VHEEs.

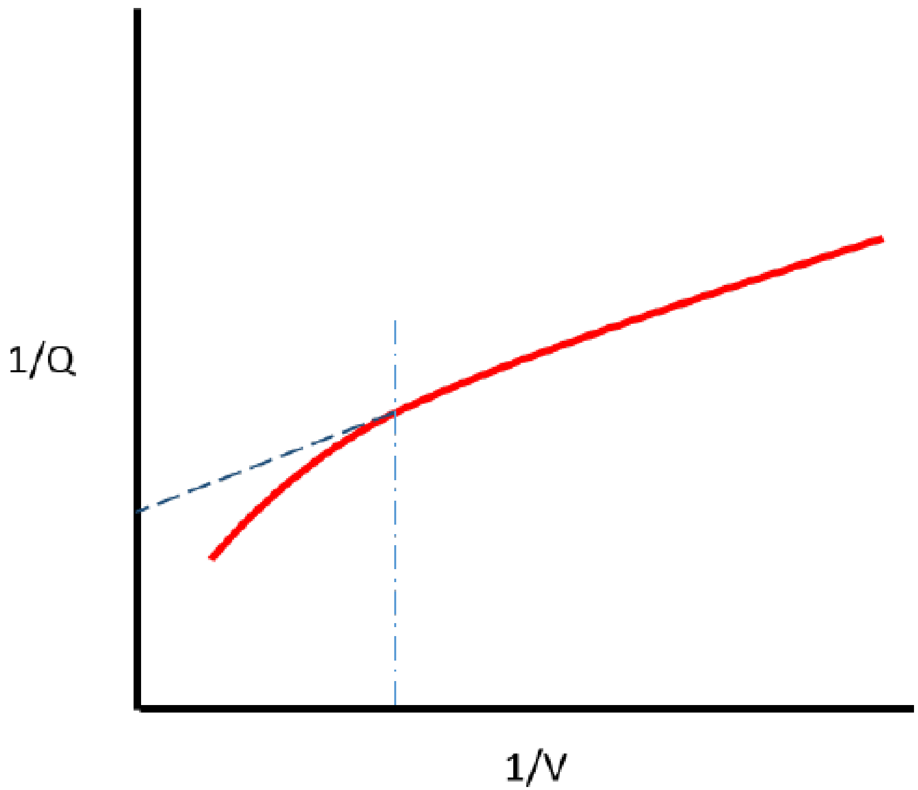
Ion Recombination



General saturation curve for ion chambers.

- In theory, if the voltage is increased above the saturation voltage, we should observe 100% charge collection.
- Not realistic due to the onset of electrical breakdown at high voltage and charge multiplication.
- Recombination will therefore always be present despite voltage.

Ion Recombination - Two-Voltage Analysis (TVA) Technique

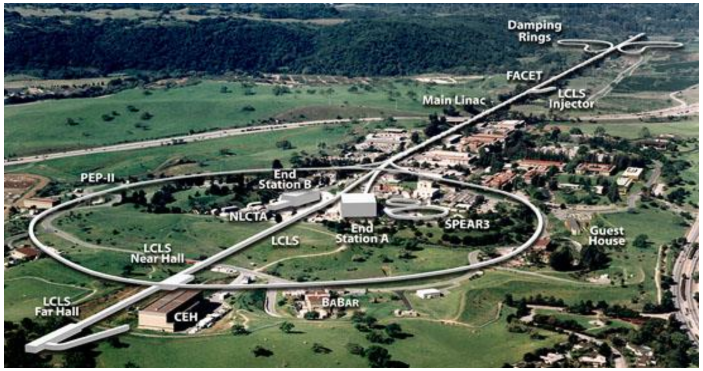


- Extrapolate the linear region of this plot to $V = \infty$ to determine the collection efficiency in Code of Practice for pulsed radiation from y-intercept.
- As collecting voltage increases, charge multiplication and other non-dosimetric artifacts cause a non-linear increase in charge collected.

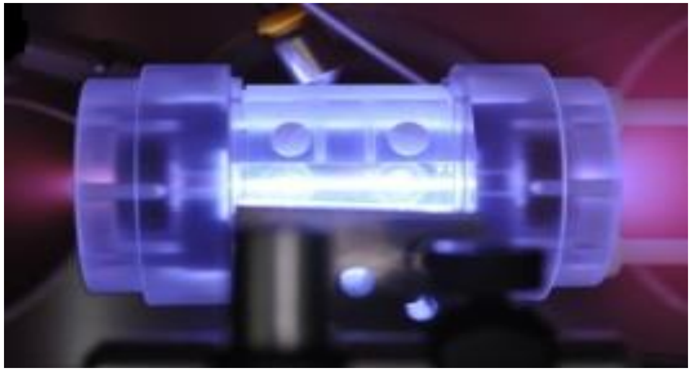
Generation of VHEE (future perspective)

1. Conventional accelerators (RF cavities); Limit ≈ **100 MV/m →** acceleration gradient limits maximum energy obtained

2. Laser-plasma accelerators: <u>compact, cheaper, higher acceleration gradient</u> ≈ **100 GV/m**



SLAC - **3,3 km**
50 GeV e-beam



Plasma capillary - **3 cm**
3 GeV e-beam

- Only **2 mm** of plasma required to accelerate beam to **150 MeV**!

Acknowledgements

National Physical Laboratory

NPL

Michael McManus

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Thank you for your attention

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