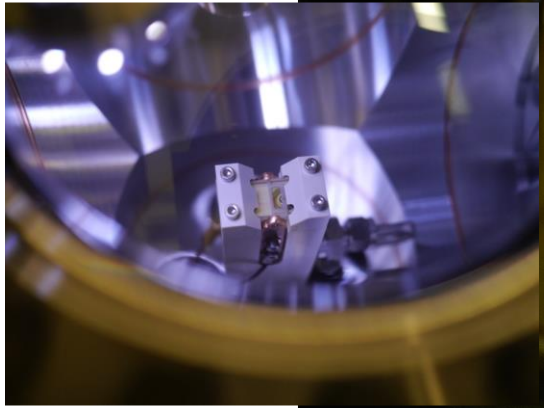
Uniform beam delivery and real time dosimetry for FLASH radiotherapy applications

R. Corsini

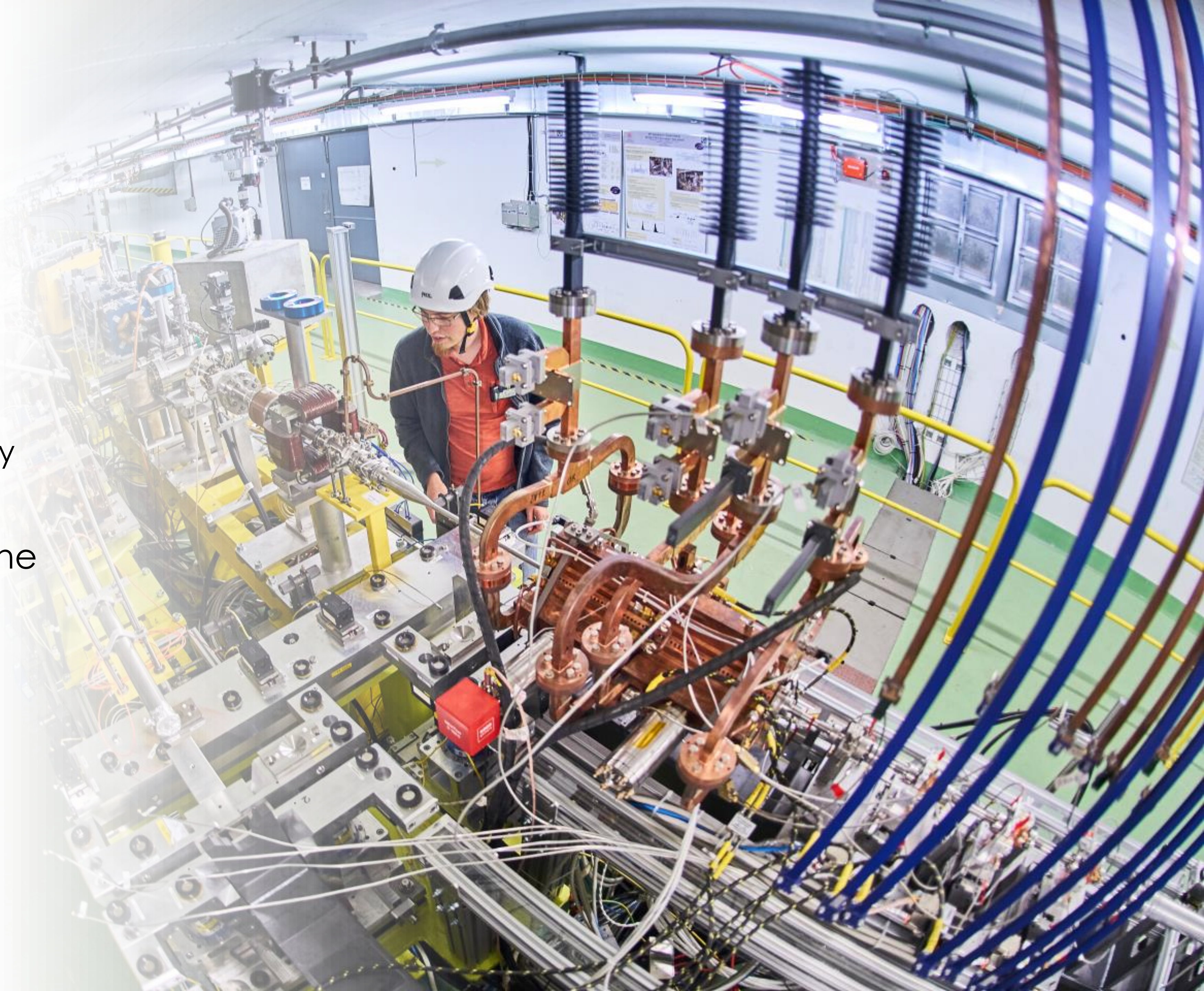
for

C. Robertson,
J. Bateman
and for the
CLEAR team



Talk outline

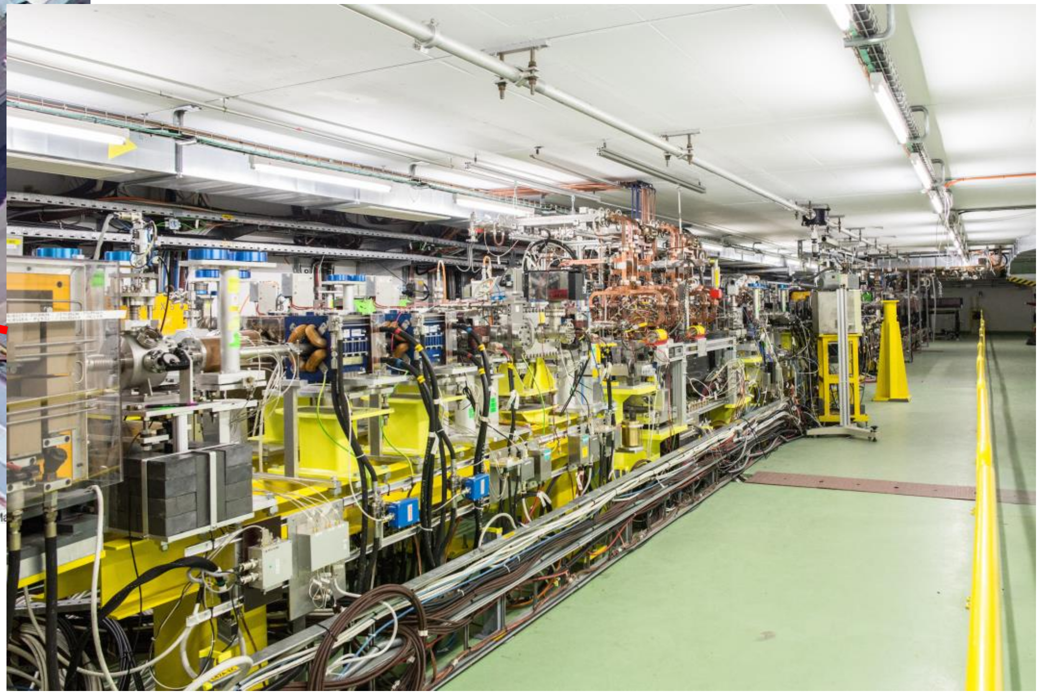
- Introduction:
  the CLEAR facility
- Background:
  - VHEE/FLASH radiotherapy
  - VHEE/FLASH at CLEAR
- Uniform beam delivery – the double scatterer system
- Real time dosimetry



From the CLIC Test Facility to CLEAR

CLIC Test Facility (CTF3) - completed its experimental program in 2016

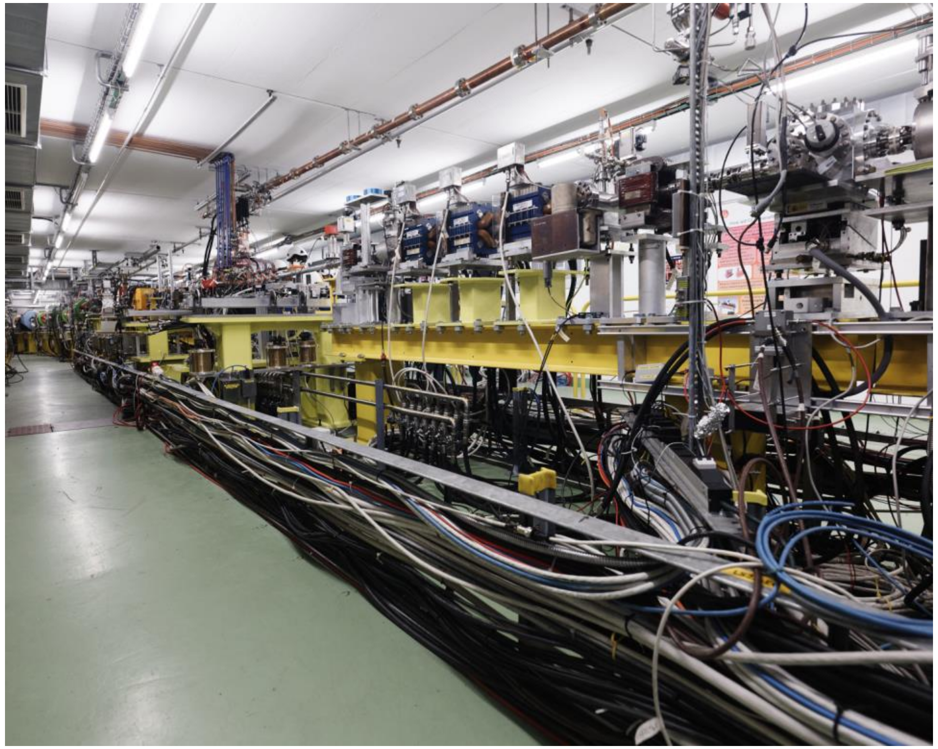
Proposal to reuse the CLEX area and the CALIFES e- linac for accelerator R&D



CLEAR is a user facility at CERN, running in parallel with the main CERN accelerator complex, with the primary goal of enhancing and complementing the existing accelerator R&D and testing capabilities at CERN

Approved December 2016

The CERN Linear Electron Accelerator for Research (CLEAR)

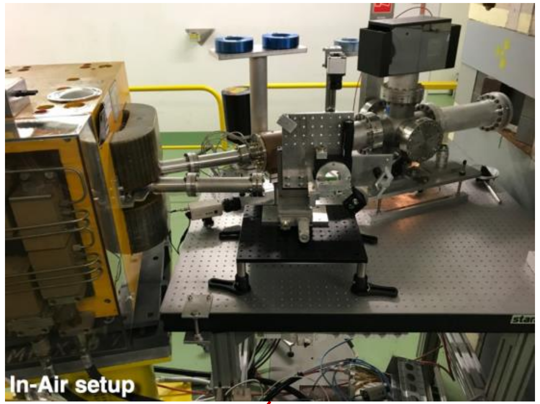


CLEAR is composed by a 200 MeV electron linac followed by a 20 m experimental beamline, and it is operated at CERN from 2017 as a multi-purpose user facility.

Scientific and strategic goals:

- Providing a test facility at CERN with high availability, easy access and high quality e- beams.
  - Performing R&D on accelerator components, including beam instrumentation prototyping and high gradient RF technology
  - Providing an irradiation facility with high-energy electrons, e.g. for testing electronic components in collaboration with ESA or for **medical purposes(VHEE/FLASH)**
  - Performing R&D on novel accelerating techniques – electron driven plasma and THz acceleration.
- Maintaining CERN and European expertise for electron linacs linked to future collider studies
- Using CLEAR as a training infrastructure for the next generation of accelerator scientists and engineers.

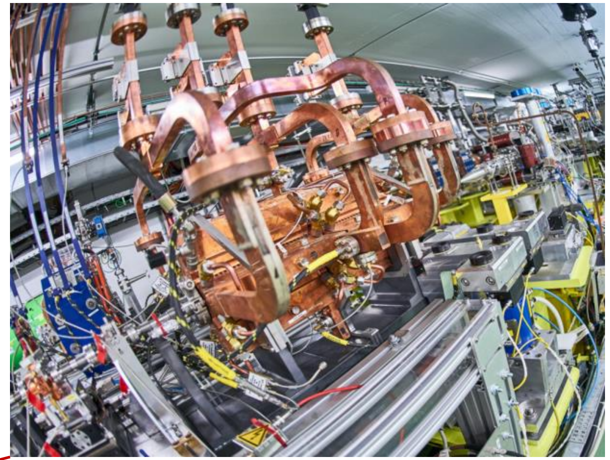
CLEAR provides electron beams for a large and varied range of experiments



In-air test stand

Testing ground for beam diagnostics R&D and THz radiation studies

Irradiation for medical and other applications

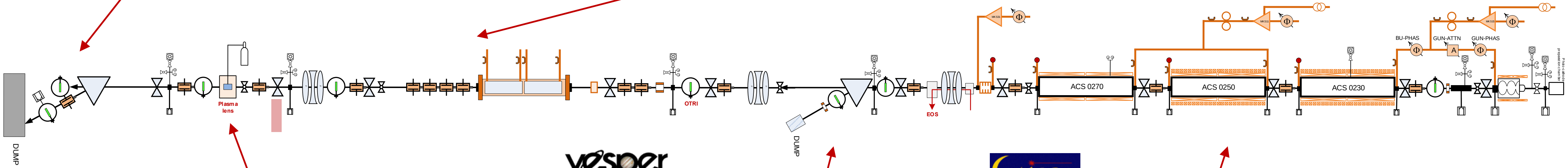


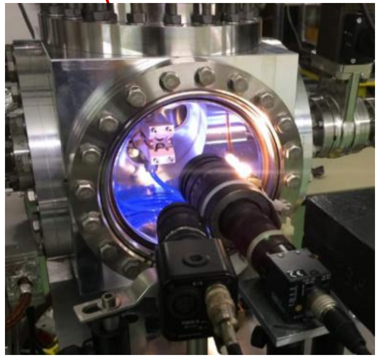
CLIC Test-Stand

High-gradient and linear collider R&D

+ *Beam instrumentation area*

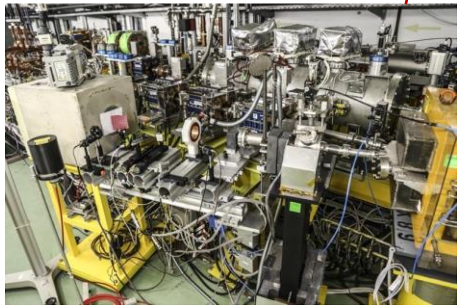
CERN Linear Electron Accelerator for Research





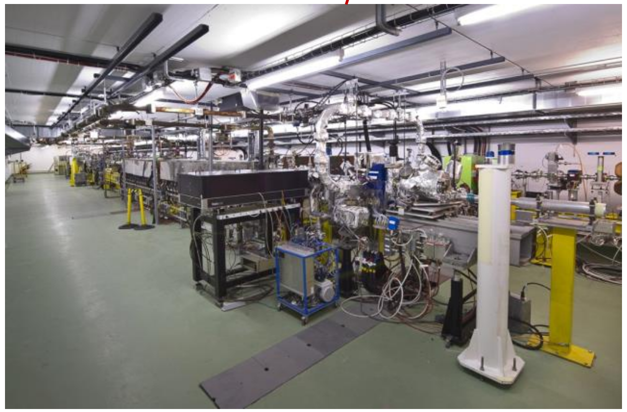
The Plasma Lens Experiment

Novel concepts of plasma-based focusing and acceleration



VESPER

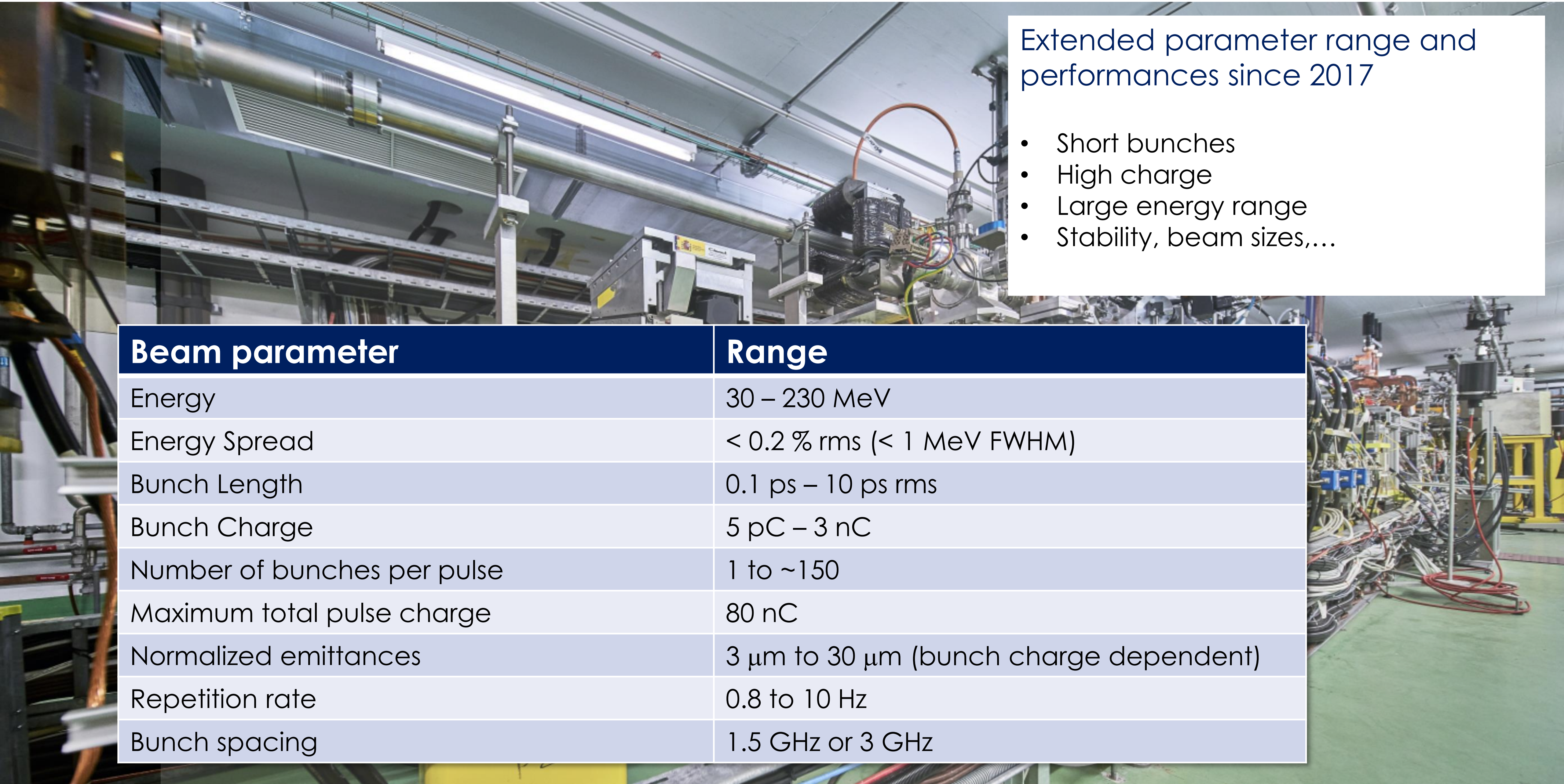
Beam irradiation facility for studies on radiation damage of electronics and medical applications



CALIFES electron linac

Flexible accelerator providing 200 MeV electron beams to all CLEAR users

CLEAR Beam Parameters



Extended parameter range and performances since 2017

- Short bunches
- High charge
- Large energy range
- Stability, beam sizes,…

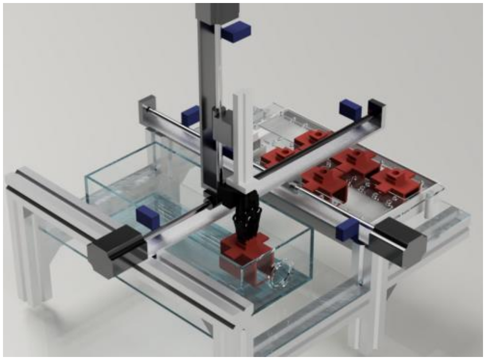
Beam parameter	Range
Energy	30 – 230 MeV
Energy Spread	< 0.2 % rms (< 1 MeV FWHM)
Bunch Length	0.1 ps – 10 ps rms
Bunch Charge	5 pC – 3 nC
Number of bunches per pulse	1 to ~150
Maximum total pulse charge	80 nC
Normalized emittances	3 μm to 30 μm (bunch charge dependent)
Repetition rate	0.8 to 10 Hz
Bunch spacing	1.5 GHz or 3 GHz

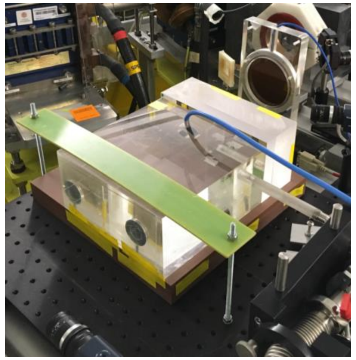
BACKGROUND - VHEE and FLASH Radiotherapy

The potential use of very high-energy electron beams (VHEE, 50-250 MeV) for Radio Therapy (RT) recently gained interest, since electrons at these energies can travel deep into the patient.

- Potential advantages of VHEE RT:
  - Depth – dose profile for electrons better than X-rays
  - Charged particles can be focused and steered (not possible with X-rays)
  - Electron beams rather unsensitive to tissue inhomogeneities
  - Electron accelerators comparatively more compact, simpler and cheaper than proton/ion machines
- This last advantage is now even more true given the recent advancements on high-gradient acceleration (CLIC technology)
- Ultra-high dose rate radiation delivery (above 100 Gy/s) showed normal tissue sparing, without compromising tumor control (FLASH effect). Electron linacs can relatively easily reach the high beam currents needed for FLASH treatment of large fields.

More and more existing electron linac facilities are now being intensively used to investigate VHEE/FLASH RT





VHEE/FLASH RT studies at the CLEAR facility (CERN)

Facility	Applications
ARES	Accel. components, Diagnostics R&D Medical: VHEE RT, Electron CT Acceleration: ACHIP [29]
CLARA	Accel. components, Diagnostics R&D Medical: VHEE RT Acceleration: DWA, (P/L)WFA, THz
CLEAR	High gradient acceleration, plasma lens Radiation damage, Diagnostics R&D Medical: VHEE & FLASH RT
FLUTE	Diagnostics R&D, THz Experiments Medical: FLASH RT, Detectors Machine Learning
PITZ	Min. beam emittance developments THz source development Medical: FLASH RT & dosimetry
SPARC_LAB	Acceleration: PWFA, LWFA Radiation sources: FEL, THz, betatron

From: D. Angal-Kalinin et al., Electron beam test facilities for novel applications, Proc. IPAC '23

BACKGROUND - The FLASH effect

- FLASH is a biological effect, in which the fast delivery of radiation (in the so-called Ultra High Dose Rate – UHDR regime) destroys cancerous cells while sparing healthy surrounding tissues.
- Observed for the first time (actually, rediscovered) in 2014: mice tumours were irradiated with short pulses (≤200 ms) at UHDR (≥100 Gy/s).
- The FLASH effect has been observed so far with protons, gamma and low energy electrons.
- Electrons hold the higher potential for UHDR over large fields, with comparatively cheap and compact installations.
- Very High Energy Electrons (VHEE, >50 MeV) are needed to treat deep seated tumours.

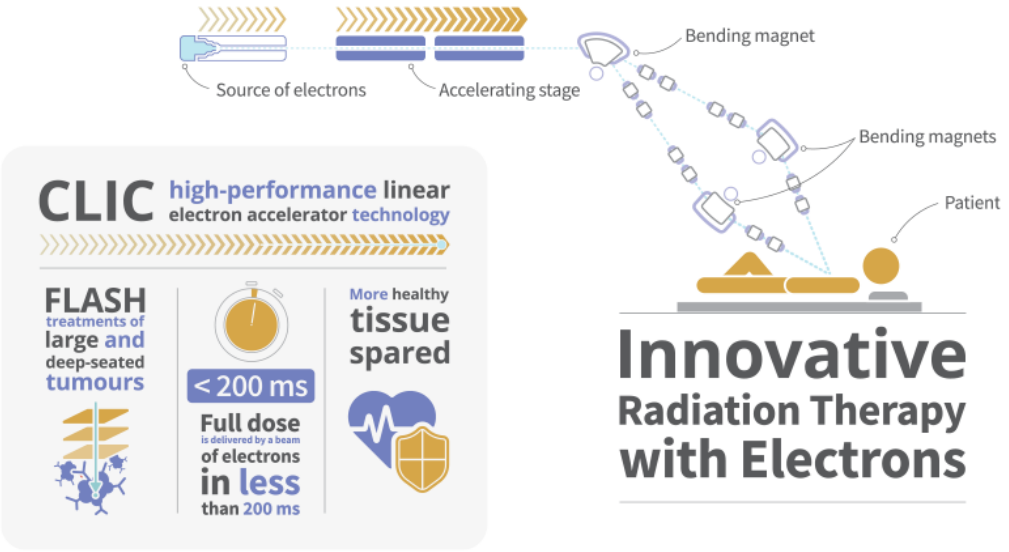
CERN, CHUV and now THERYQ are actively collaborating on the realization of a clinical facility for the treatment of large, deep-seated tumors by a VHEE beam in FLASH conditions

The target is a facility that:

- Uses 100 MeV-range electrons and optimized dose delivery.
- Is compact enough to fit on a typical hospital campus.

The collaboration demonstrated that the facility is feasible and are now finalizing the details of its technical implementation aiming at first clinical tests in 1-2 years

If successful, the facility may open the way for many future VHEE/FLASH facilities



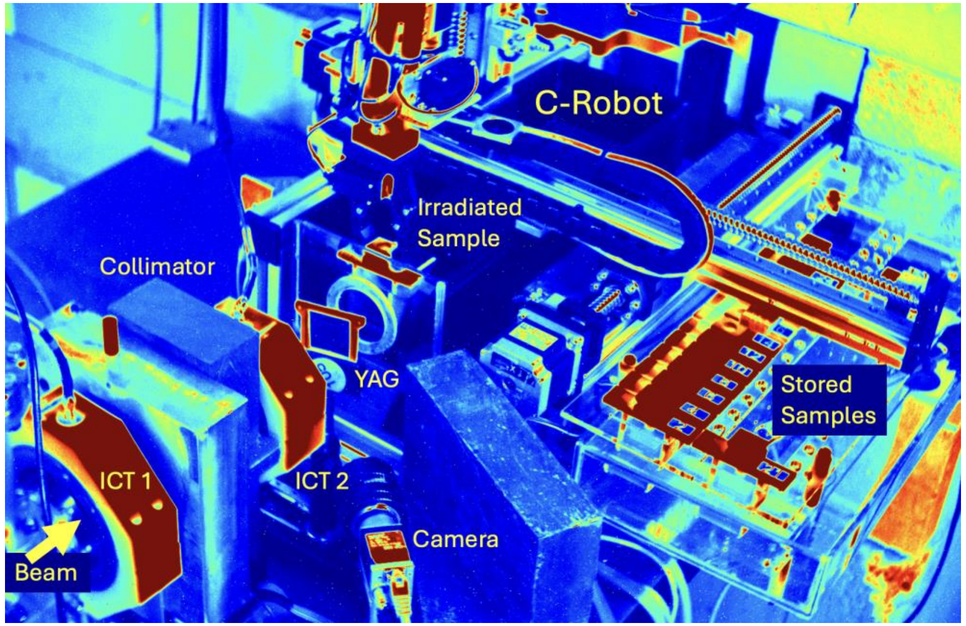
CLEAR is today at the forefront of VHEE/FLASH experimental research

Methods, Dosimetry and Beam Delivery Techniques

The CLEAR team has developed in the last years methods and tools dedicated to VHEE and FLASH studies, including dosimetry techniques, sample handling, and beam delivery.

- Radiochromic films are the main dosimetry tool used routinely in CLEAR. Detailed procedures for handling and exploiting the films were developed and validated in order to ensure a reliable dosimetry.
- The development of a robotic system (the C-Robot) allowed for remote handling of a large number of samples and is fundamental to avoid frequent accesses to the accelerator hall.
- A double scattering system for uniform beam delivery was studied and is now been routinely used.
- Methods for active dosimetry were also developed in CLEAR.

Typical experimental set-up used in CLEAR for chemistry and biological irradiation experiments.



Chemistry and biological studies

Several irradiation experiments were performed in the last two years in collaboration with external institutes, with the aim to clarify the mechanisms at the root of the FLASH effect, comparing the effects of UHDR with conventional dose rates on controlled samples.

(See https://clear.cern/content/publications)

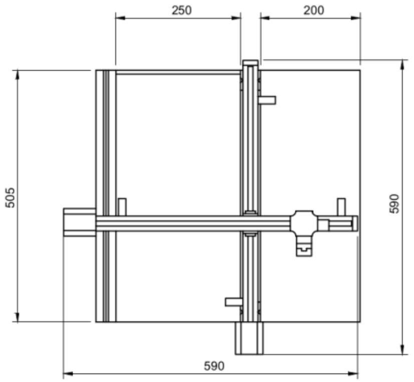
The CLEAR-Robot

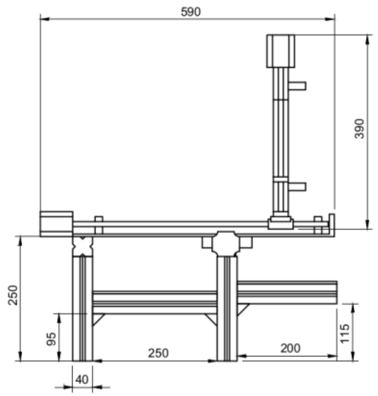
In order to facilitate the precise control of samples for multiple irradiations, the CLEAR-Robot (C-Robot) was designed and built by members of the CLEAR Operation Team.

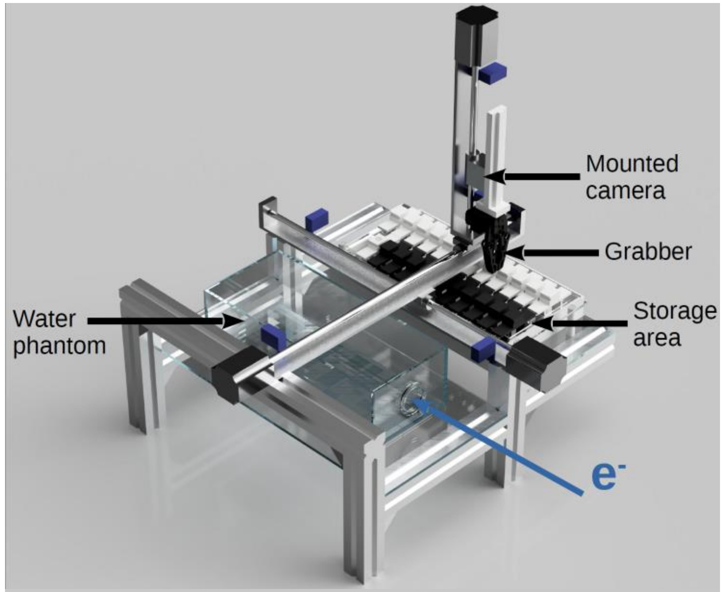
- It consists of 3 linear stages, 6 limit switches, a 3D-printed grabber, two water tanks and an Arduino board.
- It has a precision in position in 3 axis of 50 μm.
- It is fully remotely controllable from the CERN Technical Network.
- Thanks to a mounted camera, it can also measure the beam sizes and transverse positions at the longitudinal position of the sample.
- It is an open-source project: pictures, 3D renders, drawings and all the codes for the Arduino and the Graphical User Interface can be found on: https://pkorysko.web.cern.ch/C-Robot.html
- Used for 100% of Medical Applications in CLEAR in 2023.

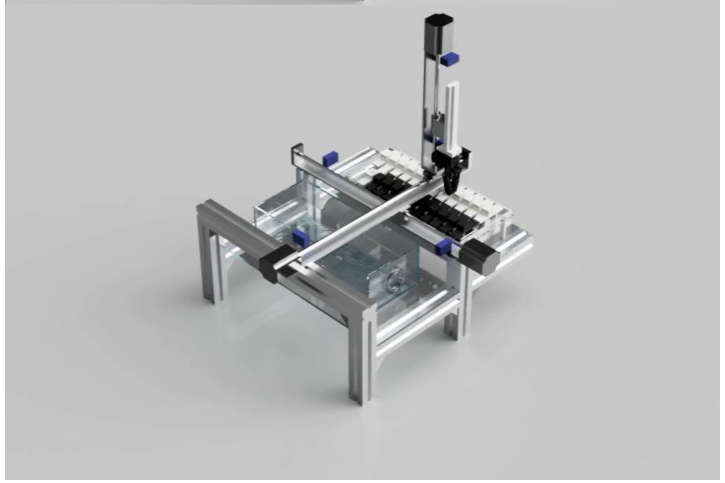
P. Korysko

C-ROBOT

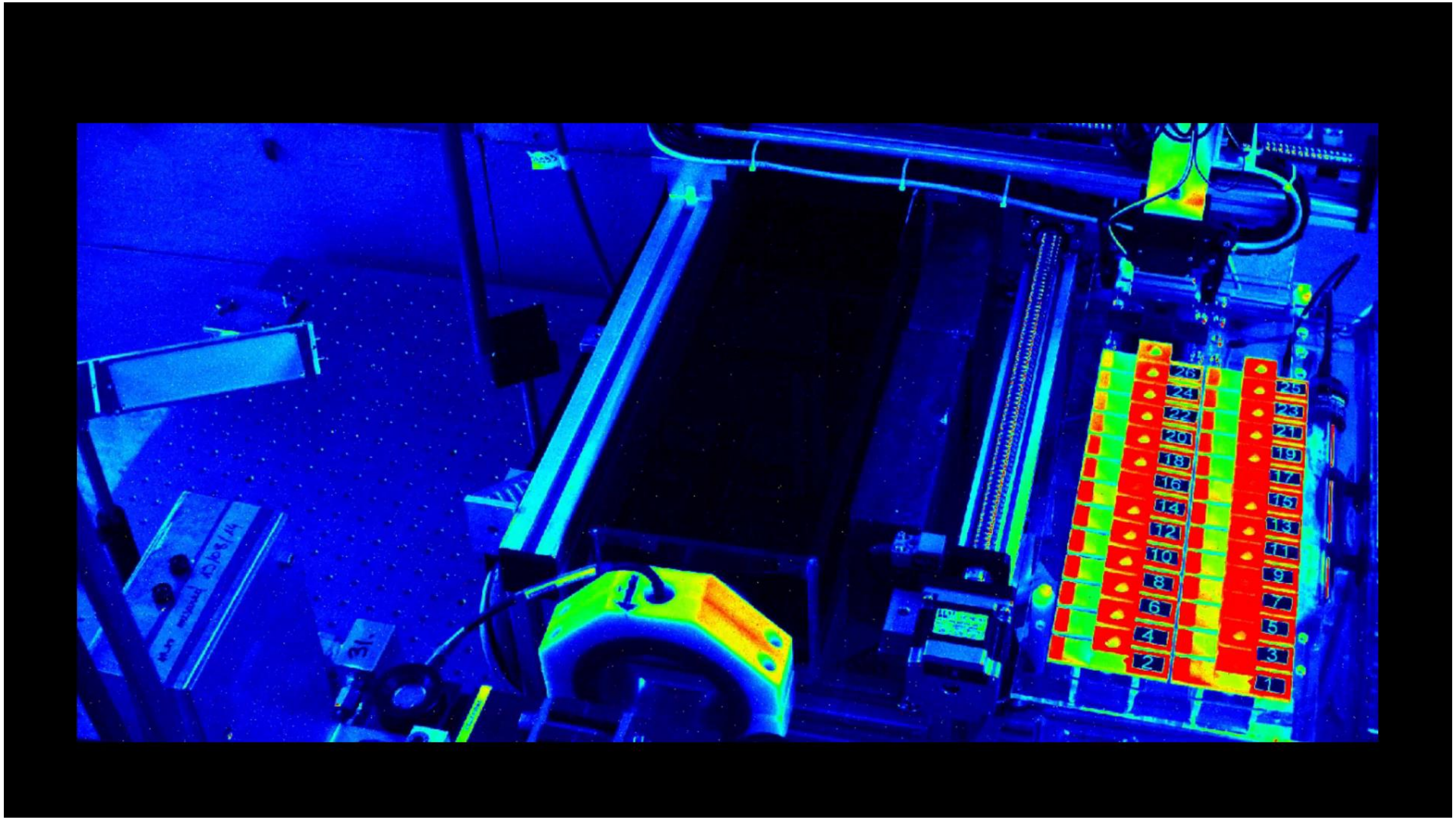








The C-Robot in action with beam



P. Korysko

Beam delivery – uniform beam

Both clinical radiotherapy applications and pre-clinical testing require a large, uniform field. It is not straightforward to obtain this with a VHEE beam.

Goal:

Obtain a flat transverse beam distribution at the sample (or at patient's tumor).

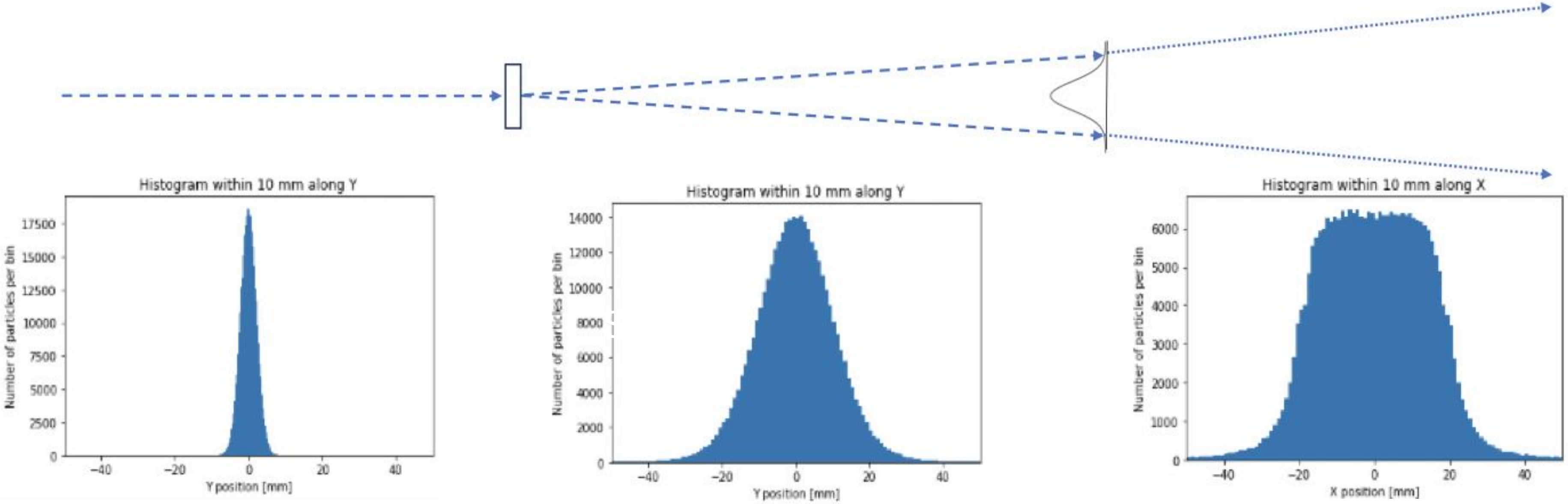
Method:

Double scattering foil. Use two scatterers: the first flat and relatively thin, to magnify the gaussian beam, and the second one with a variable thickness (ideally gaussian), to redistribute the beam transversally

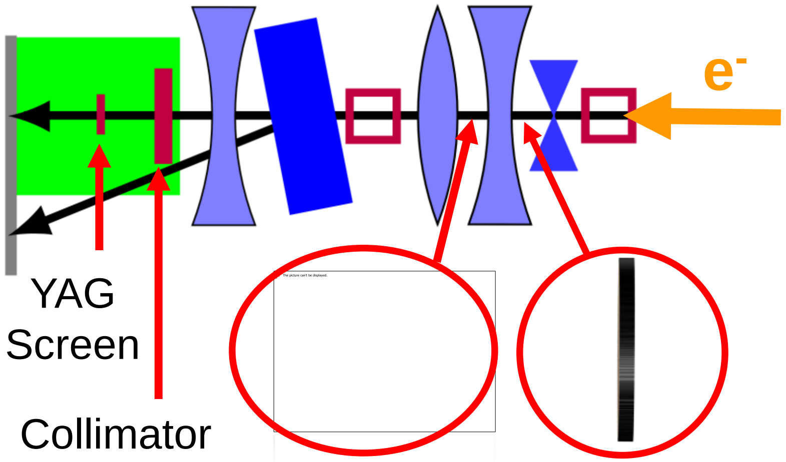
UNIVERSITY OF OXFORD

C. Robertson

EURO-LABS experiments DSS-1 and DSS-2



The double scatterer system – uniform beam



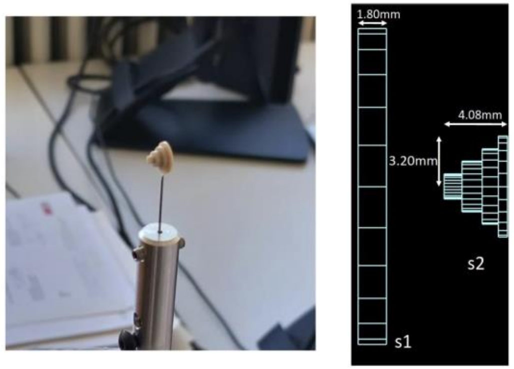
C. Robertson

After some initial tests in-air of the double scatterer system, a full in-vacuum version was installed in CLEAR

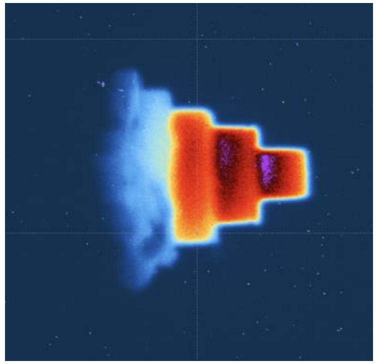
The position and geometry of the scatterers were optimized using GEANT4 simulations

C. Robertson

UNIVERSITY OF OXFORD

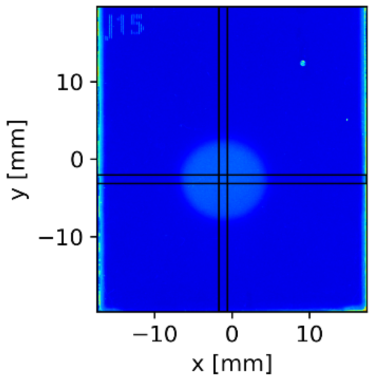


First version of the in-vacuum scatterer

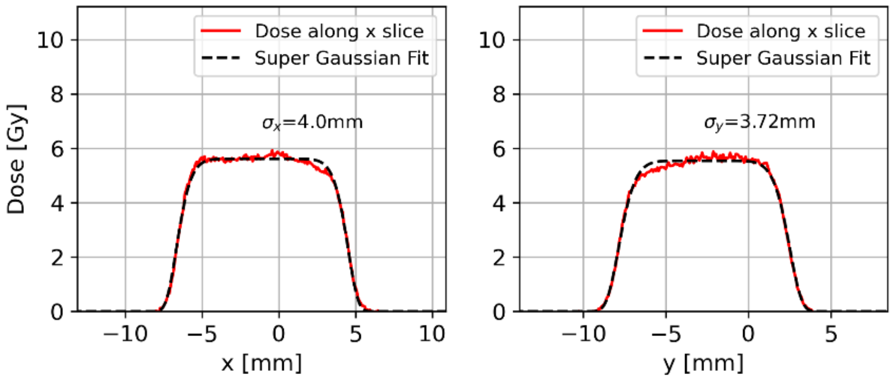


Beam-induced light in the scatterer

beam image



X and Y beam profile



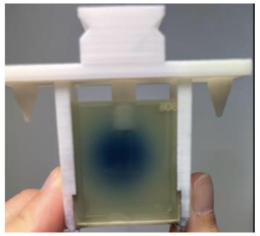
Now routinely used in CLEAR operation

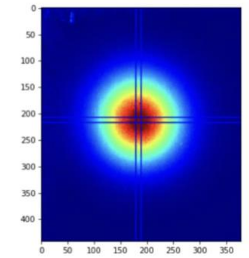
Passive and real-time dosimetry

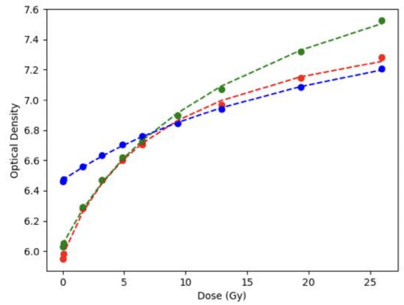
Radiochromic films are the main reference dosimetry tool and have been used routinely in CLEAR.

Detailed procedures for handling and exploiting the films were developed and validated in order to ensure a reliable dosimetry.

- Passive dosimetry method considered to be dose-rate independent.
- Widely used as reference dosimetry for many UHDR experiments.
  - Used at CLEAR for almost all UHDR studies.
- Calibrated to low energy clinical electron beam at CHUV and analysed using custom analysis code.



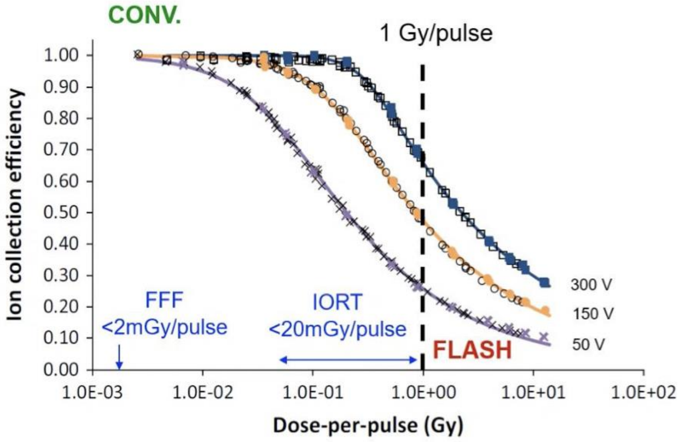




courtesy J. Bateman

Clinical use of VHEE/FLASH radiotherapy requires fast (possibly real-time) dosimetry, however standard methods (e.g., ionization chambers) are not well adapted to UHDR regime (ion recombination, nonlinear response)

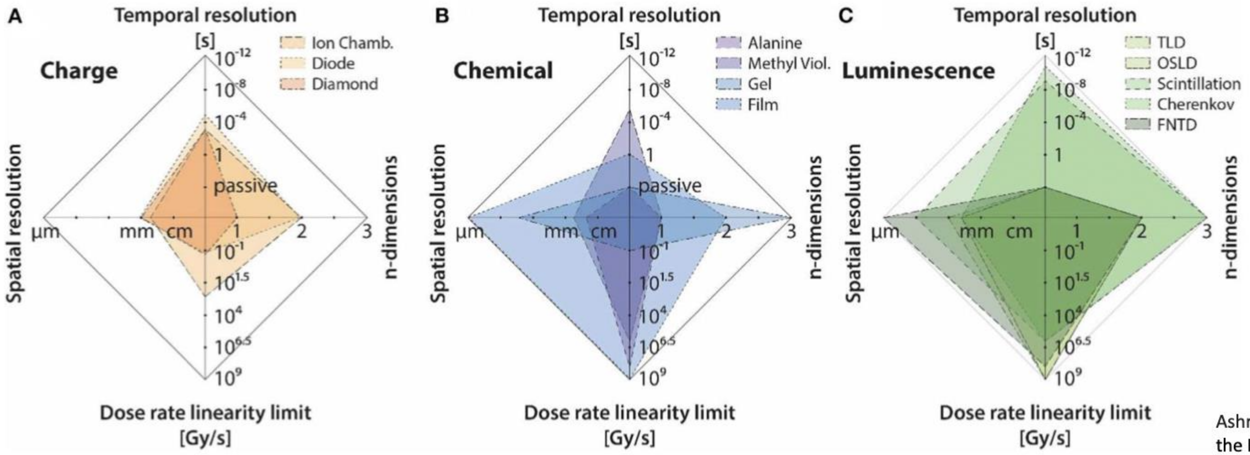
- Ionisation chambers saturate in UHDR conditions required for FLASH.
- Correction factors can account for decrease in ion collection efficiency at UHDR but introduce large uncertainties.
- Collection time of transmission ICs (order of μs) too slow for FLASH beam monitoring.



Petersson et al., Med Phys 44 (2017) 1157

UHDR Real time dosimetry – potential options

- Modified ionisation chamber geometry and design, e.g., ultra-thin plane parallel ion chambers
- Solid-state detectors e.g., diamond detectors, Si/SiC detectors
- Radioluminescence detectors –scintillators, fibres, gas monitors, screens, Cherenkov.
- Accelerator Beam Instrumentation - current transformers, pick-up monitors etc.



courtesy J. Bateman

Ashraf, M. et al. Dosimetry for FLASH Radiotherapy: A Review of Tools and the Role of Radioluminescence and Cherenkov Emission (2020).

Real time dosimetry

A very promising method for real time dosimetry adapted to UHDR was studied at CLEAR. It makes use of optical fiber arrays, and has been developed under the lead of J. Bateman from Oxford University.

Several options for the type and angle of the fiber and for the light detector used were explored in several experiments using single fibers, before developing a full prototype.

UNIVERSITY OF OXFORD

J. Bateman

EURO-LABS experiments FOM-UHDR-1 and FOM-UHDR-2

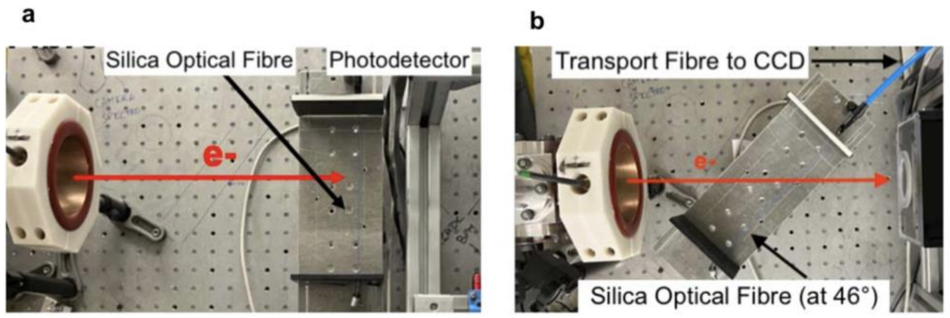


Figure 2. Photographs of the single optical fibre measurements setup in the CLEAR in-air test stand. (a) The setup with SiPM and PMT photodetectors. (b) The setup with the transport fibre and CCD photodetector which was positioned behind the beam dump and hence not visible in this image.

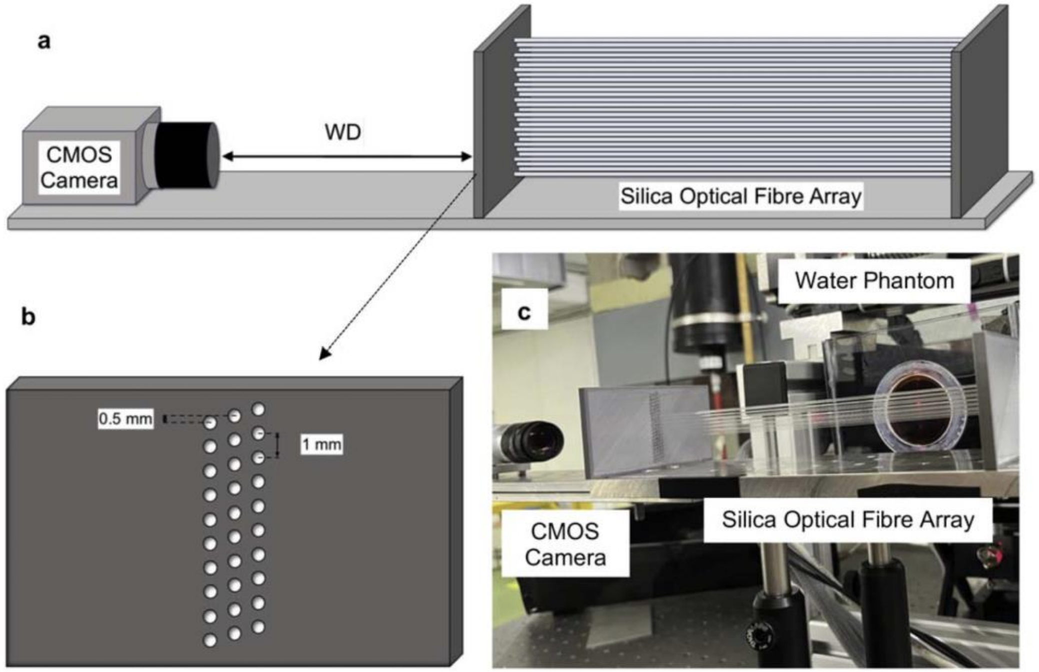


Figure 3. (a) Schematic of the FOFM assembly with the CMOS cameras and silica optical fibre array, where the working distance (WD) between the edge of the lens and the fibres is 105 mm. (b) Schematic of 3D printed optical fibre support displaying the vertical arrangement of the silica fibres. (c) Photograph of the optical fibre array of the FOFM, consisting of 28 fused silica optical fibres, installed in the in-air test stand at the CLEAR facility.

Real time dosimetry

Development of a novel fibre optic beam profile and dose monitor for very high energy electron radiotherapy at ultrahigh dose rates

Joseph J Bateman[1], Emma Buchanan[2], Roberto Corsini[2], Wilfrid Farabolini[2], Pierre Korysko[1,2], Robert Garbrecht Larsen[2,3], Alexander Malyzhenkov[2], Iñaki Ortega Ruiz[2], Vilde Rieker[2,4], Alexander Gerbershagen[3] and Manjit Dosanjh[1,2] ▲ Hide full author list

Published 3 April 2024 • © 2024 The Author(s). Published on behalf of Institute of Physics and Engineering in Medicine by IOP Publishing Ltd

Physics in Medicine & Biology, Volume 69, Number 8

The final prototype has demonstrated no saturation effects at Ultra-High Dose Rates and very good linearity over a large dose range.

The spatial resolution is also quite good, and it allowed for an excellent reconstruction of the transverse beam profile.

J. Bateman

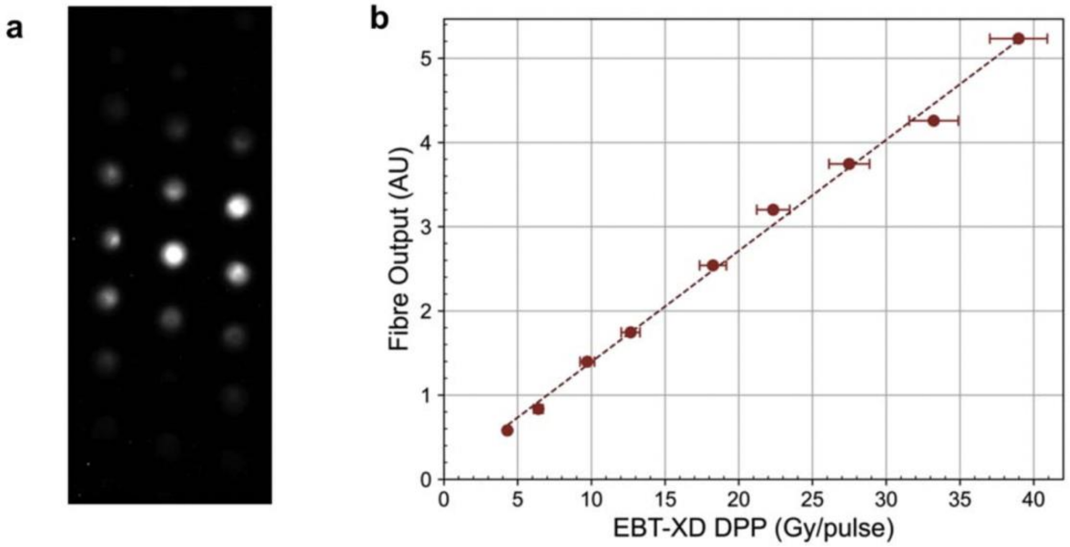


Figure 8. (a) An example image of the fibre signal measured by the CMOS camera (after noise removal) following a 30 nC pulse. (b) The dose-per-pulse (DPP) response of the FOFM between 4.3 and 39.0 Gy/pulse, with the same gain settings on the CMOS camera for all measurements ($R^2 = 0.996$, $\chi^2_\nu = 0.028$, $P(\chi^2) = 1.000$).

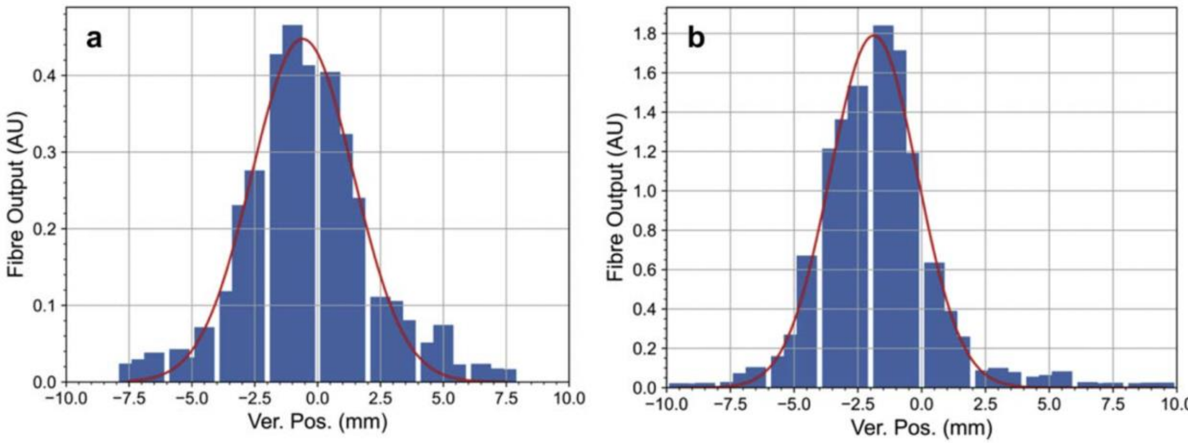
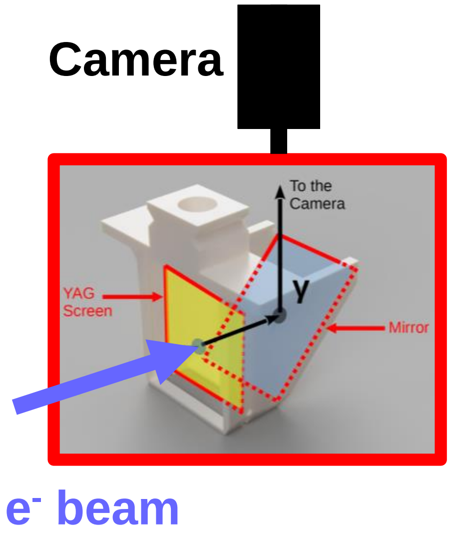


Figure 11. Vertical profile measurements made by the FOFM for (a) a 1 nC; and (b) a 10 nC electron pulse at 200 MeV with a Gaussian fit applied (red line).

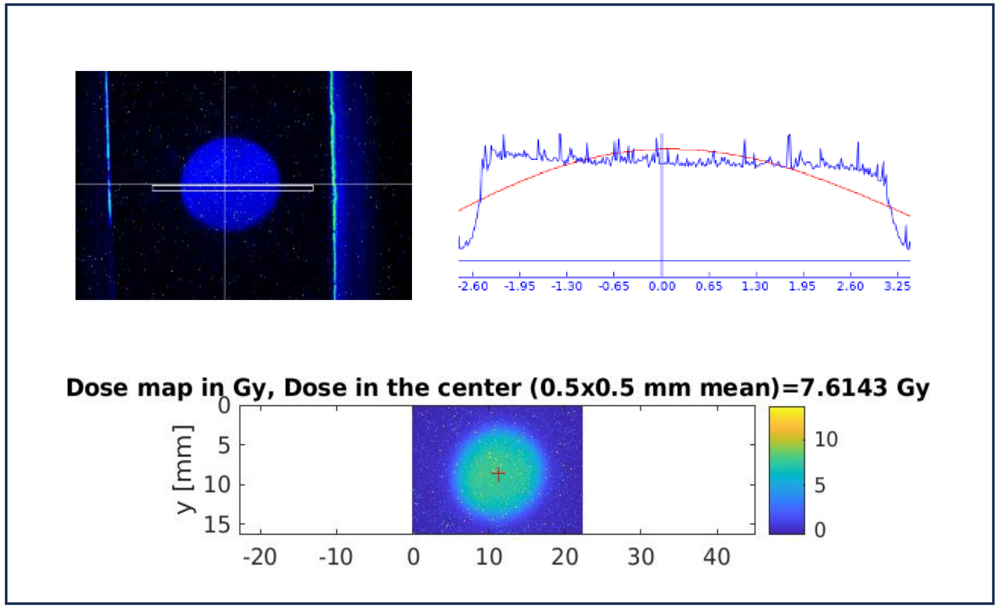
Real time dosimetry in CLEAR

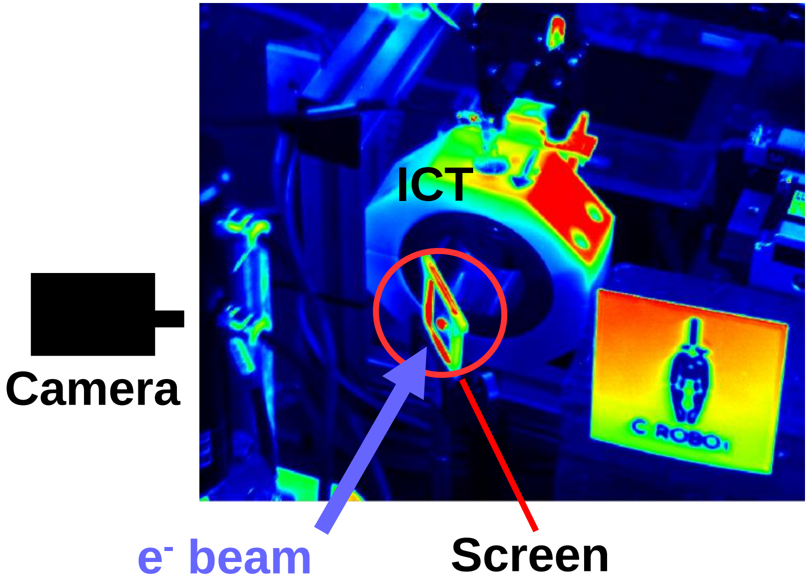
In CLEAR we developed also an alternative fast dosimetry method by measuring the beam charge, with and Integrated Current Transformer (ICT) and the beam size with a YAG scintillating screen. The samples are then irradiated at the same exact location.

A similar method is being developed using a thin YAG scintillating screen in air in front of the water phantom for real-time dose measurement.



Now routinely used in CLEAR operation





V. Rieker, A. Malyzhenkov, J. Bateman

Both Cameron and Joe defended successfully their thesis in 2024

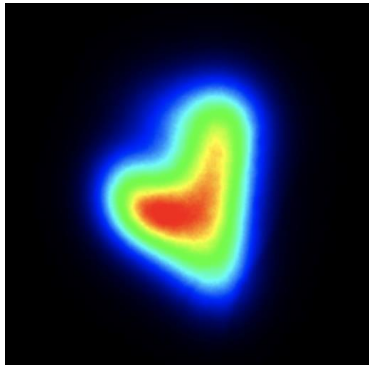
Congratulations to Cameron Robertson who on 4th July 2024 successfully defended his thesis, titled "Homogeneous Dose Delivery for Very High Energy Electron Beams".

Congratulations to Joseph Bateman who successfully defended his thesis, titled "VHEE Dosimetry in a FLASH: Ultrahigh Dose Rate Dosimetry and Real-time Beam Monitoring for Very High Energy Election FLASH Radiotherapy".

Cameron Robertson (middle), internal examiner Prof. Phil Burrows (left) and external examiner Dr Deepa Angal-Kalinin (right)

From left to right: external examiner Prof. Steinar Stapnes, Joseph Bateman, supervisor Prof. Manjit Dosanjh, internal examiner Prof. Emmanuel Tsesmelis

Thanks for your attention!



Acknowledgements to the CLEAR dream team:

S. Doebert, W. Farabolini, A. Ghilardi, P. Korysko, A. Malyzhenkov, A. Aksoy, K. Sjobaek, L. Dyks, V. Rieker, ***J. Bateman****,* ***C. Robertson****, L. Wroe, E. Granados, M. Martinez, S. Curt, D. Gamba, …*