Medical applications in the CERN Linear Electron Accelerator for Research

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CLIC Project Meeting #42
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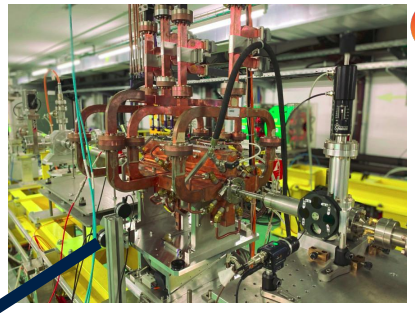
Outline

- CLEAR Beam Line, Parameters and Strategic Goals.
- Background & Motivations for VHEE studies.
- UHDR Dosimetry Studies.
- C-Robot, what is it and what can it do?
- VHEE Strong Focusing.
- VHEE Scatterers.
- Radio-Photo-Luminescence Dosimeters.
- Conclusions.

The CLEAR Beam Line

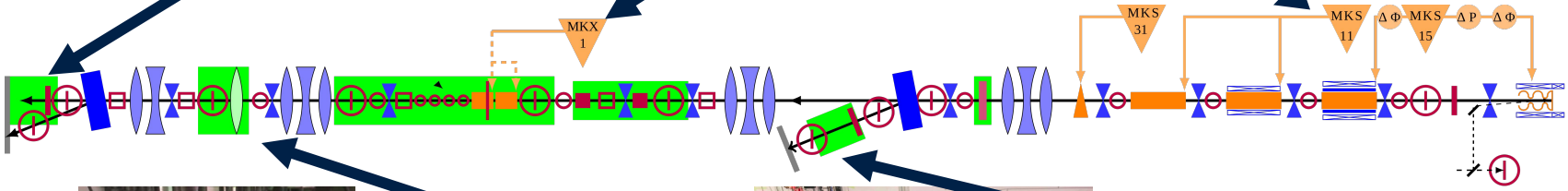
In-Air Test Stand

- Diagnostics studies
- Irradiation
  - Electronics
  - **VHEE**



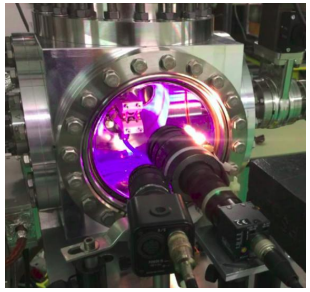
CLIC Test Stand

- High-Gradient R&D



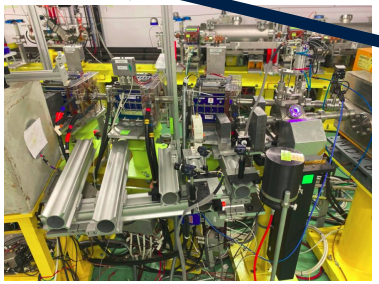
CLEAR Injector

- Flexible Linac
- 60 – 220 MeV
- Beam sent to users
- Running until 2025



Plasma Lens

- Novel plasma based focusing



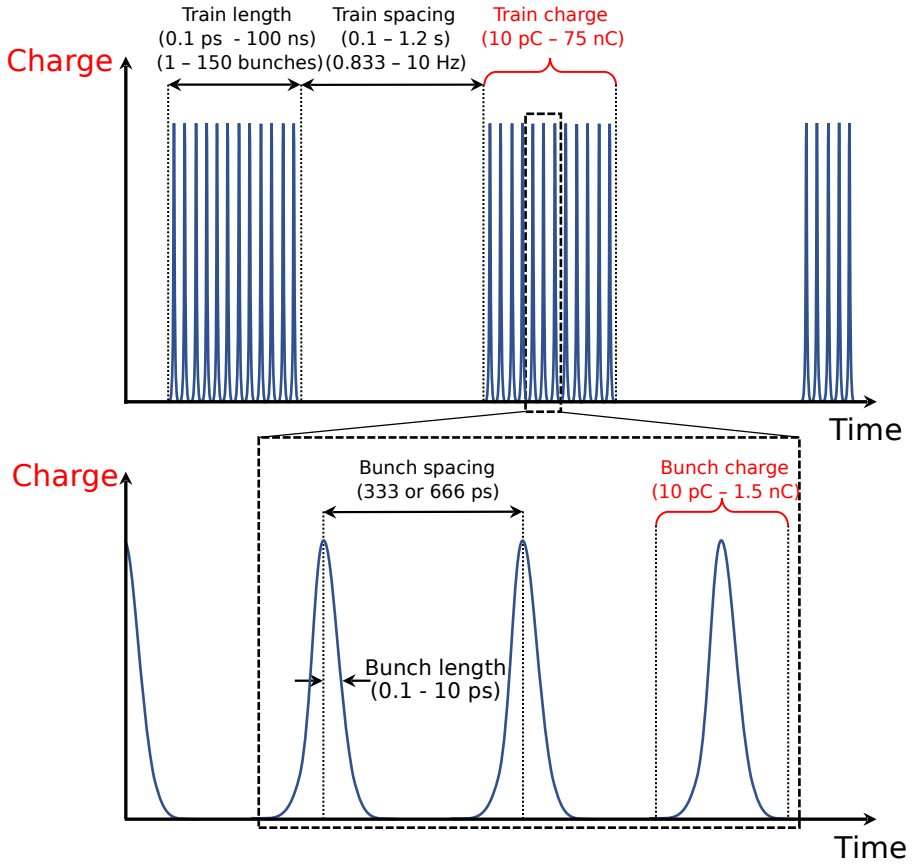
VESPER

- Irradiation facility
  - Space probes
  - Electronics
  - **VHEE**

clear

CLEAR Beam Parameters

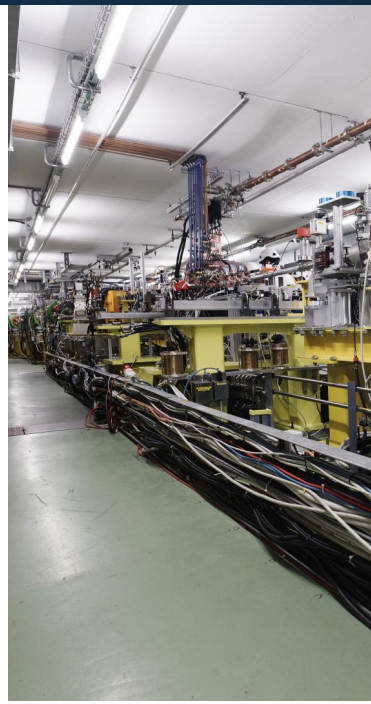
Parameter	Value
Energy	60 – 220 MeV
Energy spread	< 0.2 % rms (< 1 MeV FWHM)
Bunch length	0.1 – 10 ps rms
Bunch charge	10 pC – 1.5 nC
Normalised emittance	3 – 20 µm
Bunches per pulse	1 – 150
Max. charge per pulse	75 nC
Repetition rate	0.833 – 10 Hz
Bunch spacing	1.5 or 3.0 GHz



CLEAR Scientific and Strategic goals

Scientific and strategic goals:

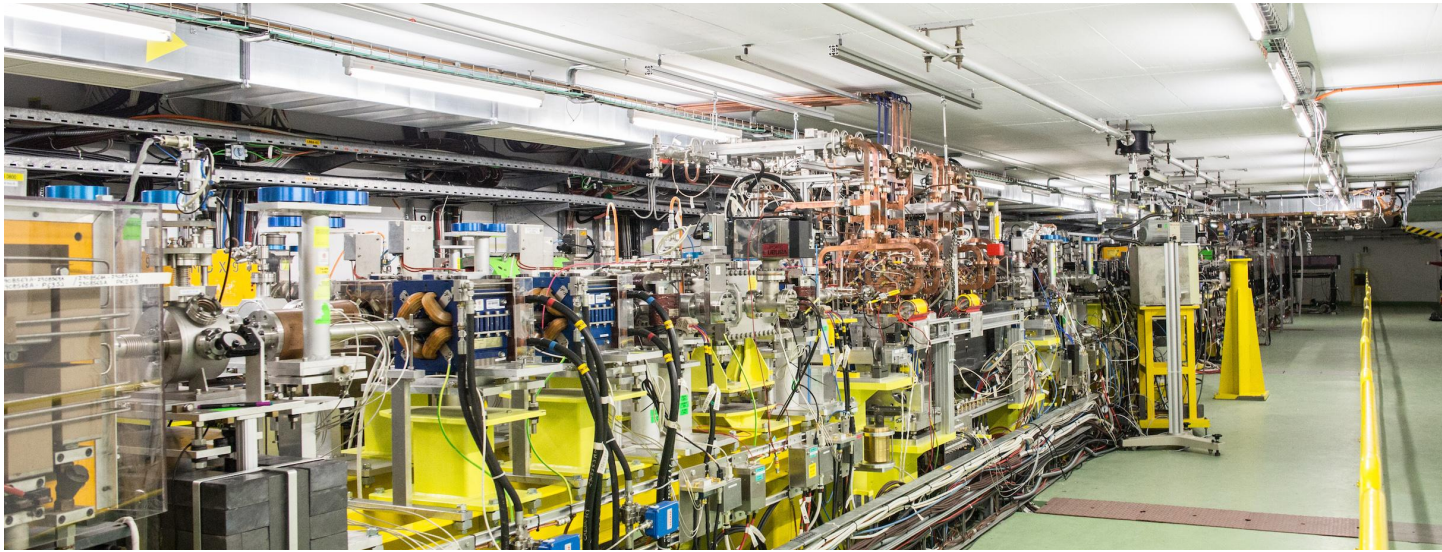
- Providing a test facility at CERN with high **availability**, easy **access** and **high quality e-beams.**
- Performing **R&D** on **accelerator components**, including beam instrumentation prototyping and high gradient RF technology.
- Providing an **irradiation facility** with Very High Energy Electrons (VHEE), e.g. for testing electronic components in collaboration with ESA or for medical purposes.
- 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 is a versatile electron linac and an experimental beamline, operated at CERN as a multi-purpose user facility.

CLEAR Timeline

- **Approved** December 2016.
- **Began operation** in 2017.
- **Flexible** beam program.
  - 8-12 hours a day.
  - 5 days a week.
- **Independent** of LHC runs and long shutdowns.
- **2017** → 19 weeks.
- **2018** → 36 weeks.
- **2019** → 38 weeks.
- **2020** → 34 weeks (despite Covid-19).
- **2021** → 35 weeks (despite Covid-19).
- **2022** → 11 weeks so far.



Background & Motivation for VHEE

- **Very High-Energy Electron (VHEE) beams (50-250 MeV)** for Radio Therapy (RT) recently gained interest, since electrons at these energies **can travel deep** into patients.

- VHEE has several **advantages:**
  - Electrons depth-dose profile flatter than X-rays.
  - Electron beam rather insensitive to tissue inhomogeneities.
  - Electrons can be steered and focused.
  - Electron accelerators are smaller, simpler and cheaper than the ones proton.

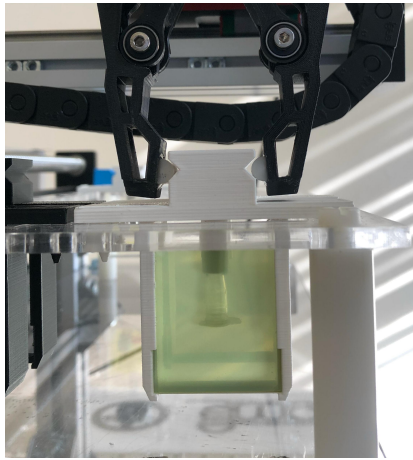
- Electron accelerators can reach high currents needed for **UHDR (Ultra High Dose Rate) RT:**
  - Mean UHDR RT dose rates > 100 Gy/s.
  - Preliminary work shows normal tissue sparing without compromising tumor control.

CLEAR provides a unique 60-220 MeV facility to test VHEE and UHDR RT.

UHDR Dosimetry Studies

- **Main topics:**
  - **Dosimetry for VHEE**, at very high dose rates (test of new real-time detectors like diamond, silicium, use of “standard” e-beam diagnostics for dose rate evaluation in real time).
  - **Chemistry** at very high dose rates (Oxygen Peroxide production, etc.).
  - **Biological effects** of very high dose rates (on Plasmids, Zebra-Fish Eggs…)

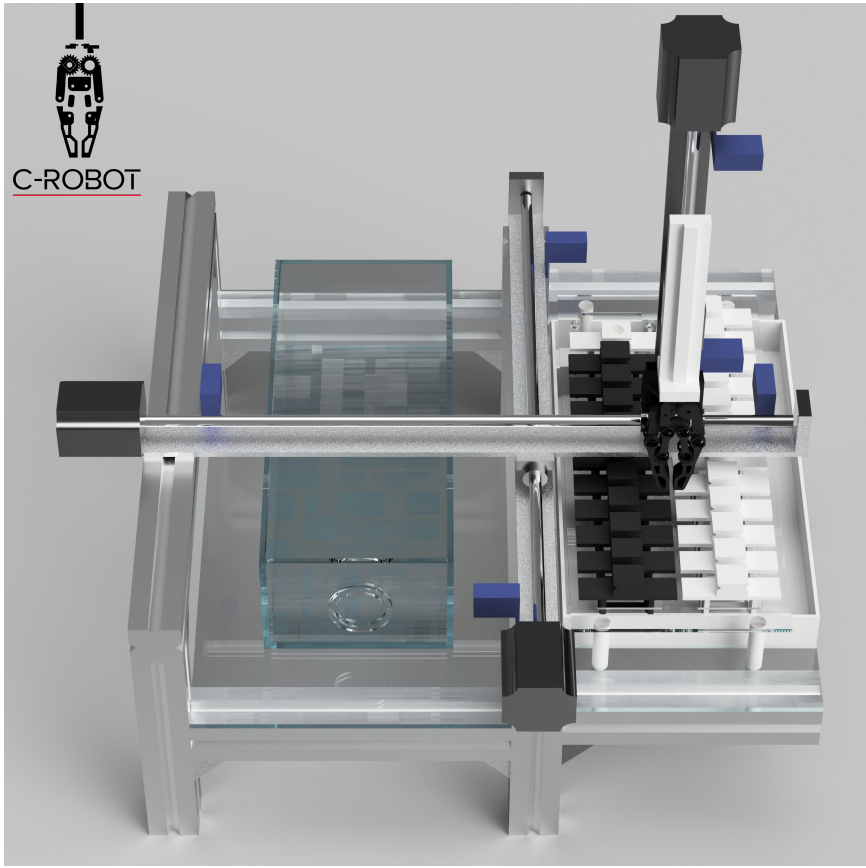
- **Goals**
  - Demonstrate **health tissue sparing** properties for VHEE.
  - Study the dependence of the **FLASH** effect from beam time structure. The **FLASH effect** is a **biological** response due to the **very fast delivery** of the **dose**.
  - Investigate **chemical** and **biological FLASH mechanisms.**
  - Develop **technology**, in particular **high dose rate real-time dosimetry**.



C-Robot, what is it?

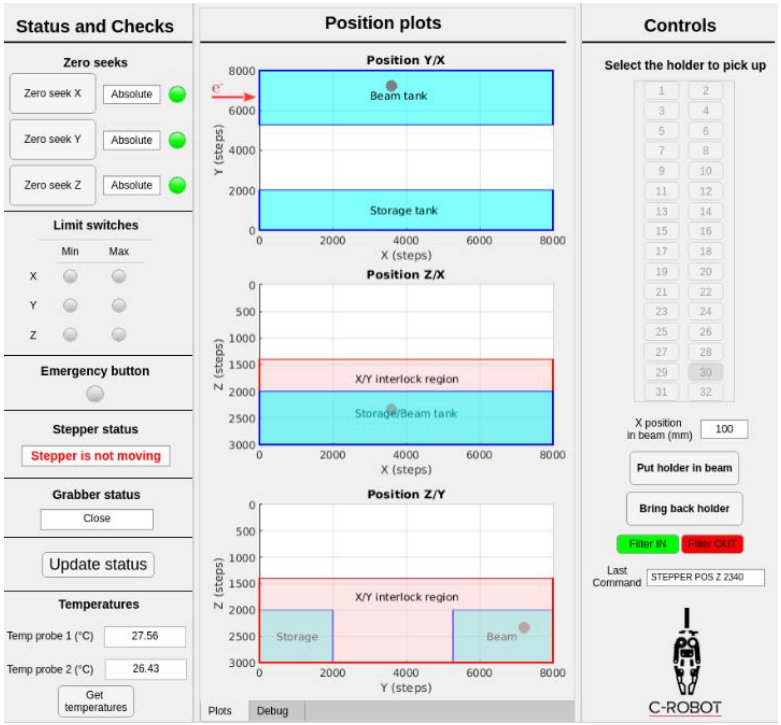
- In order to **facilitate** the **precise control** of **samples** for **multiple irradiations**, the CLEAR-Robot (**C-Robot**) was designed and built by members of the CLEAR Operation Team.
- It consists of **3 linear stages**, **6 limit switches**, a **3D-printed grabber**, **two water tanks** and 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

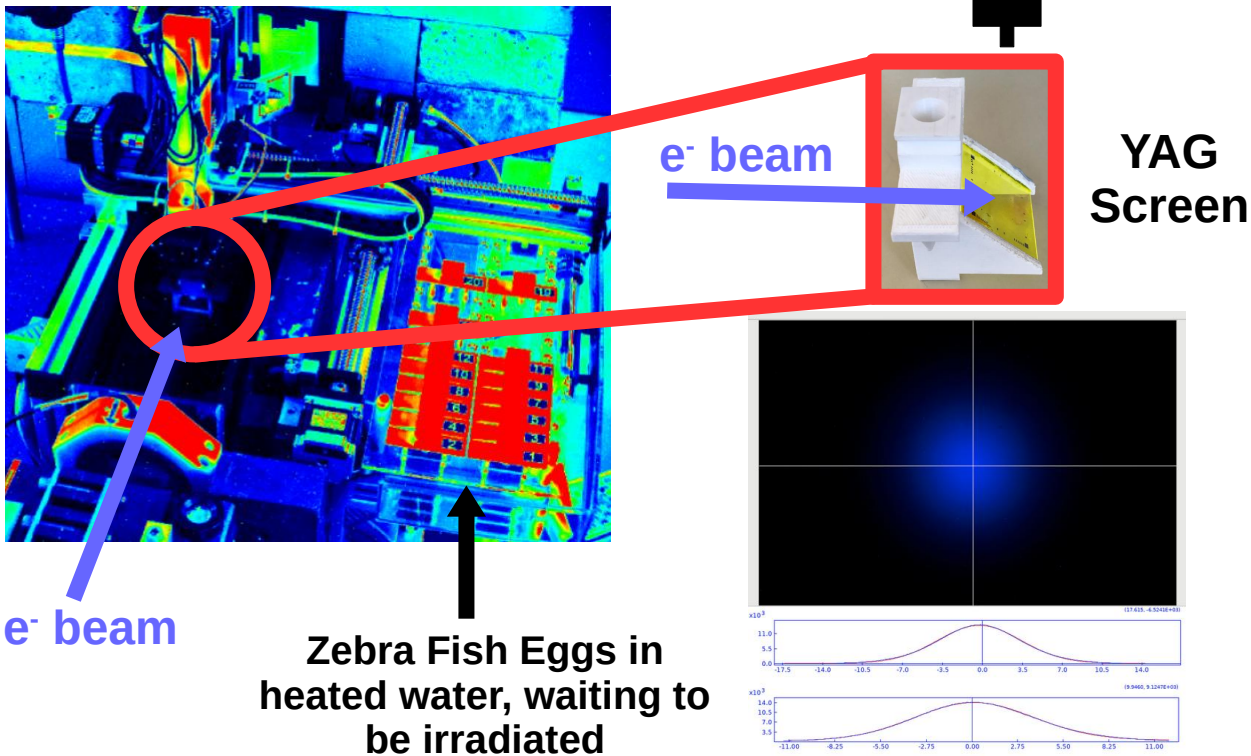


C-Robot, what can it do?

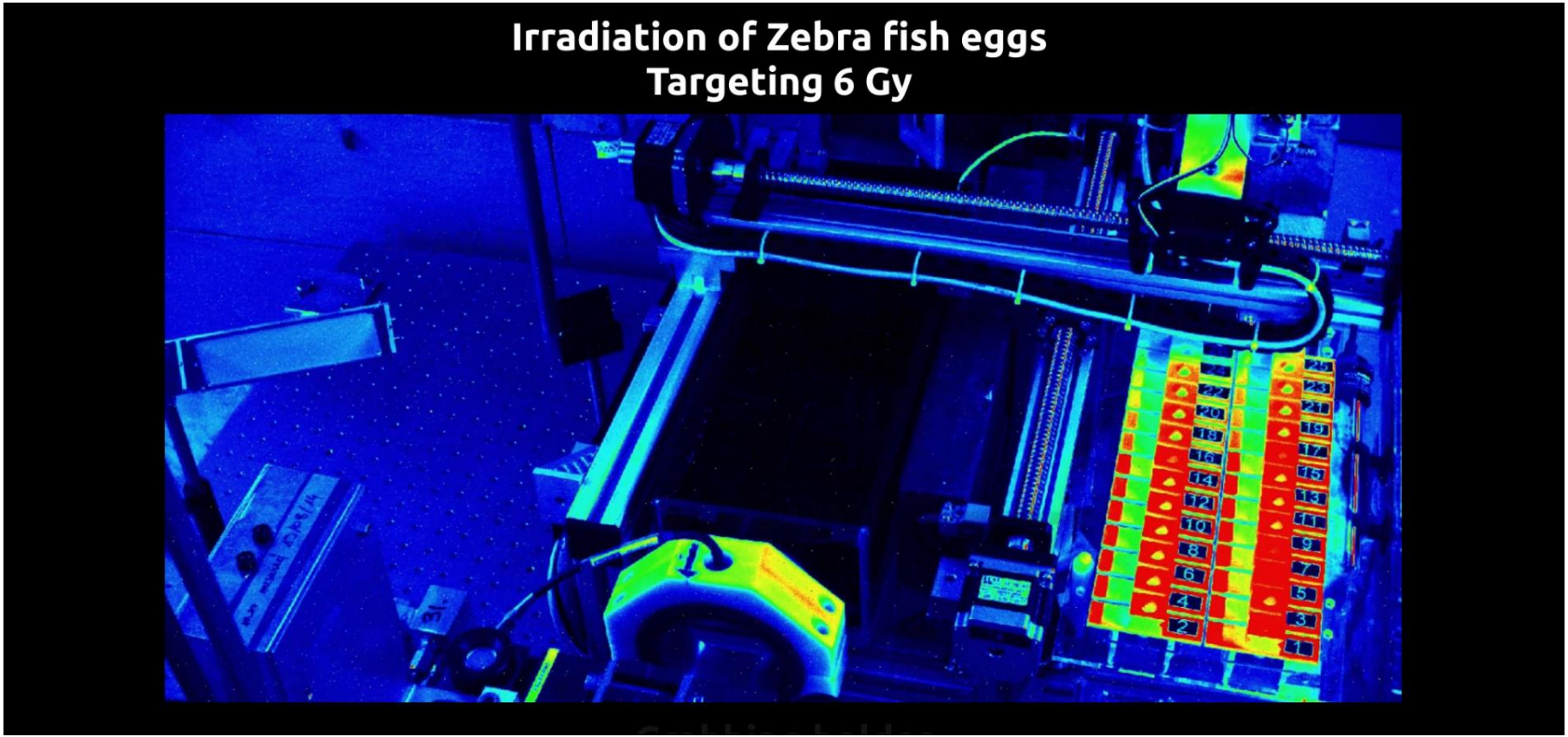
Graphical User Interface



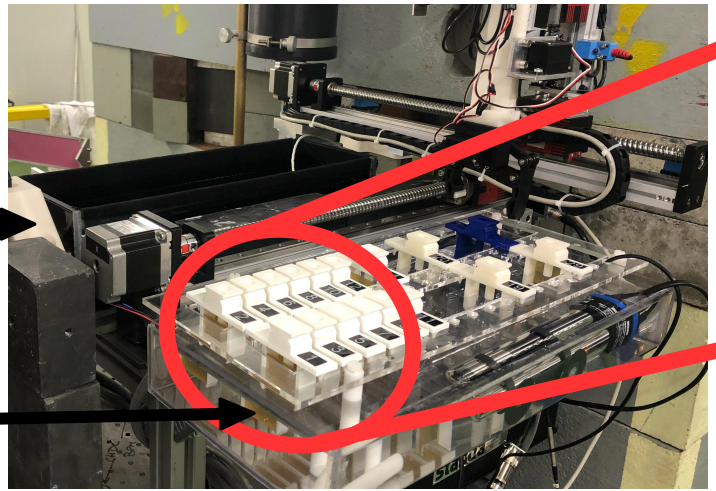
Experiment setup w/ beam



C-Robot in action with Beam

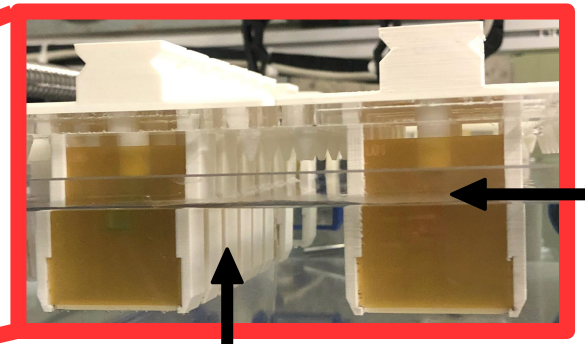


Experimental setup for VHEE UHDR irradiations

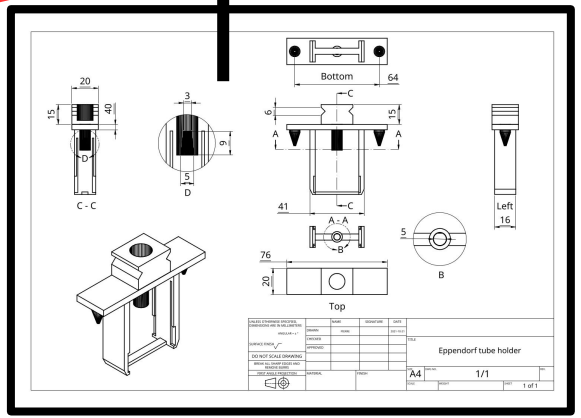


Beam water tank

Heated storage water tank



Eppendorf tube with sample to irradiate

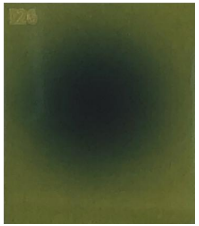


3D printed holder with 2 films: one before and one after the sample

Gafchromic films to measure the delivered dose

Dose range: 1 – 100 Gy

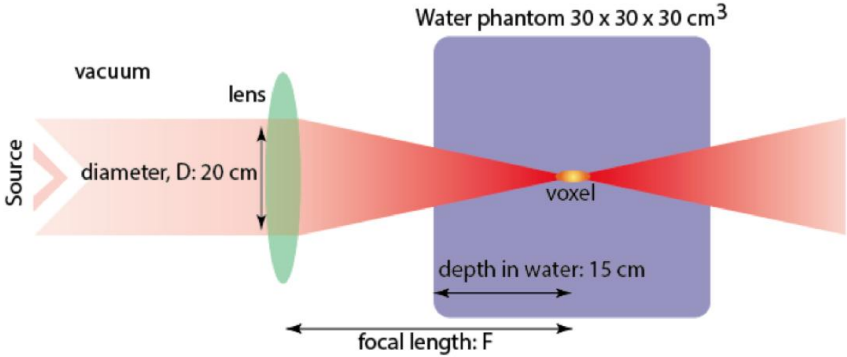
Before irradiation

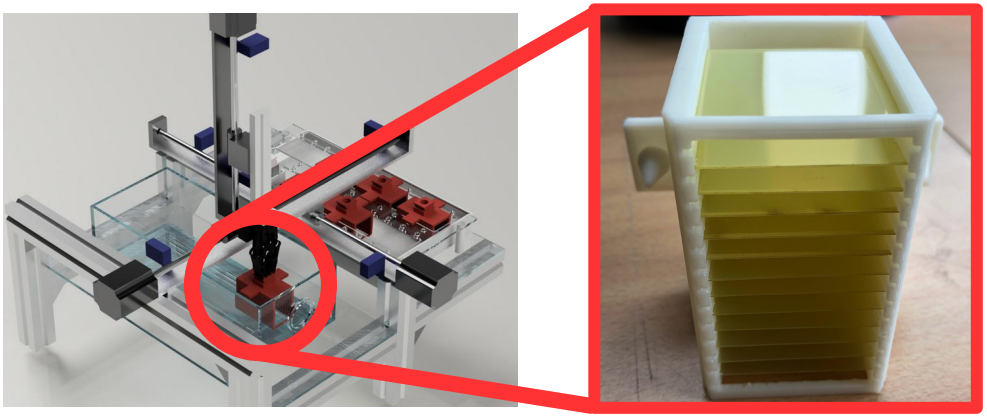


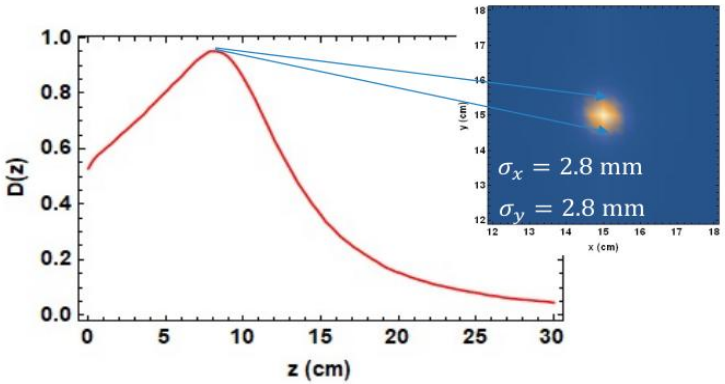
After irradiation

VHEE Strong Focusing

- **Goal:**
  Focus the beam on the tumor in order to minimize the dose and damage on the nearby healthy tissues.
- **Experiment:**
  Measure the beam sizes on a YAG screen in the water phantom (good model of the human body) and perform irradiations on long dosimetry films holders placed at different longitudinal positions.

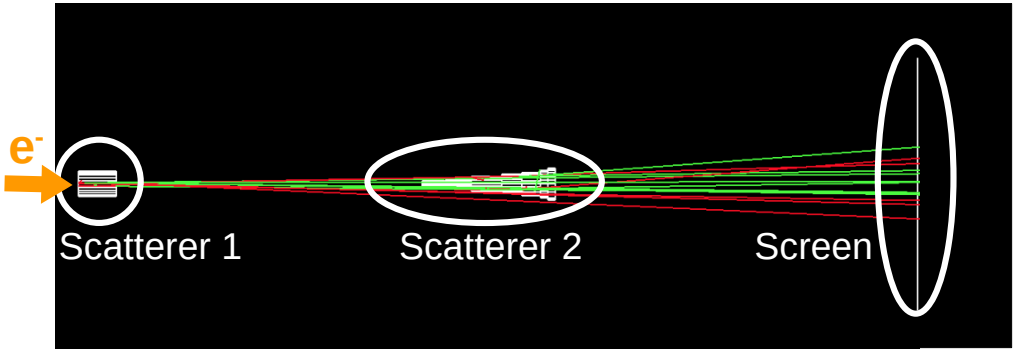


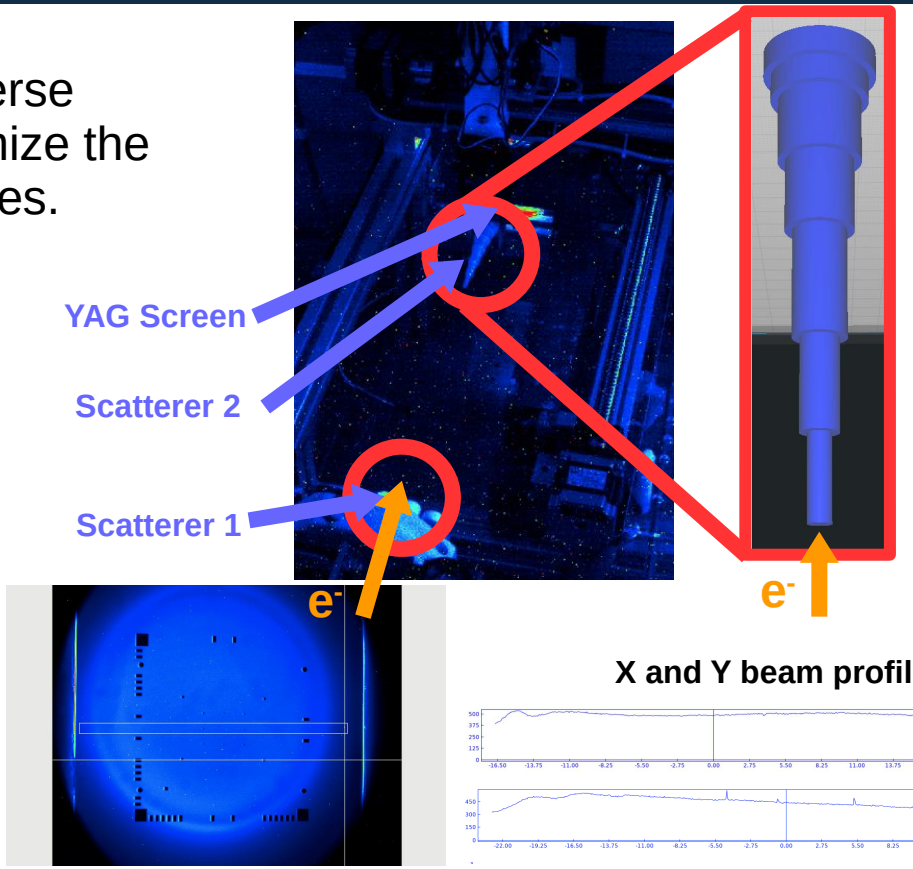




VHEE Scatterers

- **Goal:**
  Obtain a flat beam that has a constant transverse distribution at patient's tumor in order to minimize the dose and damage on the nearby healthy tissues.
- **Experiment:**
  Measure beam profiles, sizes and intensity on a YAG screen after carefully inserting two scatterers with the beam with the C-Robot.

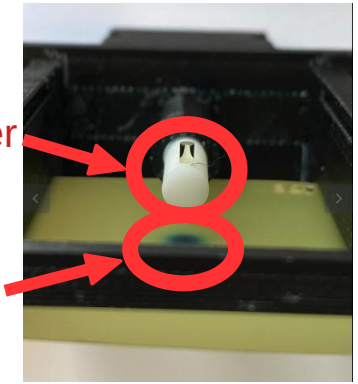


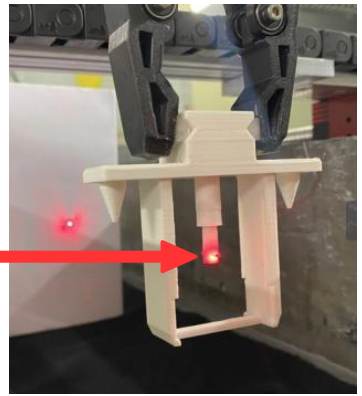


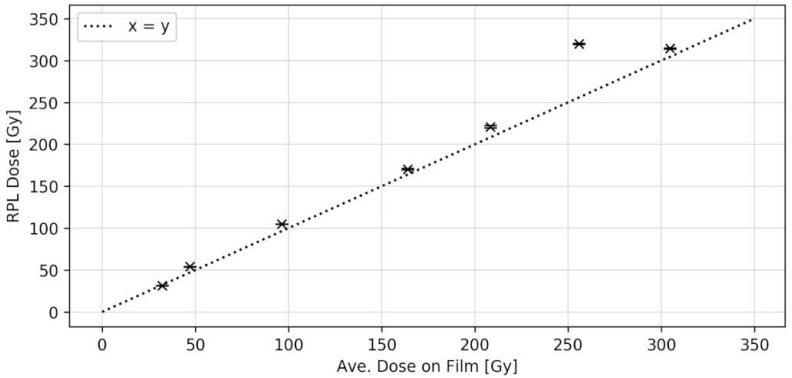
Radio-Photo-Luminescence Dosimeter (RPL)

- **Goal:**
  Use the cylinders of Ag-activated metaphosphate glass to measure the delivered dose. The irradiations create Radio-Photo-Luminescence (RPL) and color centers. Doses can be read afterwards with an in-house measurement setup.
- **Experiment:**
  Compare the measurements of the dose obtained with the RPL dosimeters and with the Gafchromic films.

System patented by CERN
WO 2014/161732 A1







VHEE dosimetry in CLEAR
Recent Publications

Some recent radiotherapy-related **publications** based on **CLEAR experiments**:

- **A. Lagdza**, R. Jones et al., Influence of heterogeneous media on Very High Energy Electron (VHEE) dose penetration and a Monte Carlo-based comparison with existing radiotherapy modalities, Nuclear Inst. and Methods in Physics Research, B, 482 (2020) 70-81.

- **K. Small**, R. Jones et al., Evaluating Very High Energy Electron RBE from nanodosimetric pBR322 plasmid DNA damage, Nature Scientific Reports 11, 3341 (2021).

- **M. McManus**, A. Subiel, The challenge of ionisation chamber dosimetry in ultra-short pulsed high dose-rate Very High Energy Electron beams, Nature Scientific Reports 10, 9089 (2020).

- **D. Poppinga** et al., VHEE beam dosimetry at CERN Linear Electron Accelerator for Research under ultra-high dose rate conditions, Biomed. Phys. Eng. Express 7 015012 (2021).

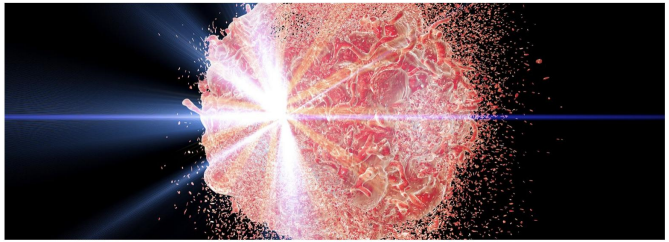
- **K. Kokurewicz**, D. Jaroszynski et al., An experimental study of the dose distribution of focused very high energy electron (VHEE) beams for radiotherapy, Nature Commun Phys 4, 33 (2021).

CLEAR in the Press

University of Strathclyde Glasgow

News

High energy radiotherapy could 'paint' tumours to avoid harming healthy tissue

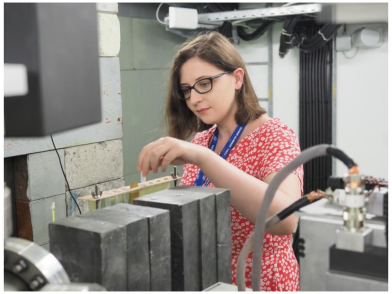


23 February 2021

A radiotherapy technique which 'paints' tumours by targeting them precisely, and avoiding healthy tissue, has been devised in research led by the University of Strathclyde.

Researchers used a magnetic lens to focus a Very High Electron Energy (VHEE) beam to a zone of a few millimetres. Concentrating the radiation into a small volume of high dose will enable it to be rapidly scanned across a tumour, while controlling its intensity.

The study was undertaken at the CERN Linear Electron Accelerator for Research (CLEAR) facility, and involved researchers at CERN, the University of Oxford, the National Physical Laboratory, the John Adams Institute for Accelerator Science, the University of Napoli Federico II, the University of Oslo and Saclay Nuclear Research Centre in France. It has been published in Nature Communications Physics.



MANCHESTER 1824 The University of Manchester

24 February 2021

Critical step forward for radiotherapy with a new method to treat cancer

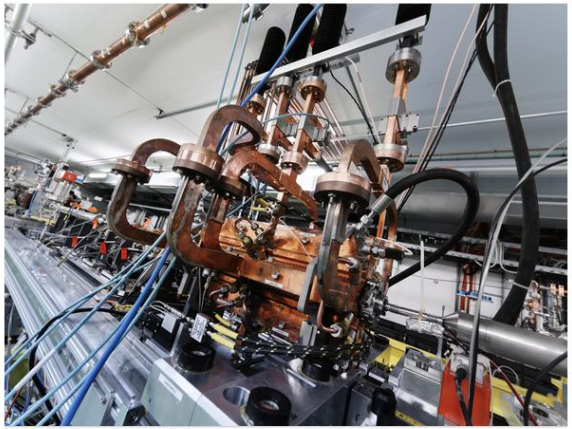
Following experiments carried out by The University of Manchester, at CERN's CLEAR 250 MeV facility and at Daresbury Laboratory, the findings show Very High Energy Electron (VHEE) beams are effective at causing DNA damage, important for killing cancer cells, for radiation given over the course of several minutes and for the rapidly evolving field of sub-second FLASH radiation.

The collaborative research team have published their findings in Nature's journal, *Scientific Reports*,

CLEAR study paves the way for novel electron-based cancer therapy

The study, conducted at CERN's CLEAR test facility, demonstrates how very high-energy electron beams can be focused onto deep-seated cancerous tumours

24 JUNE, 2021 | By Thomas Hortala



CERN's CLEAR facility, where tests on very high-energy electron beams were carried out (Image: CERN)

There are some cancer tumours that not even surgery, chemotherapy or traditional radiation therapy can cure. These resistant tumours contribute to making the disease one of the main causes of mortality worldwide, but the scientific community is teeming with ideas to make cancer fatalities a thing of the past. Among the latest

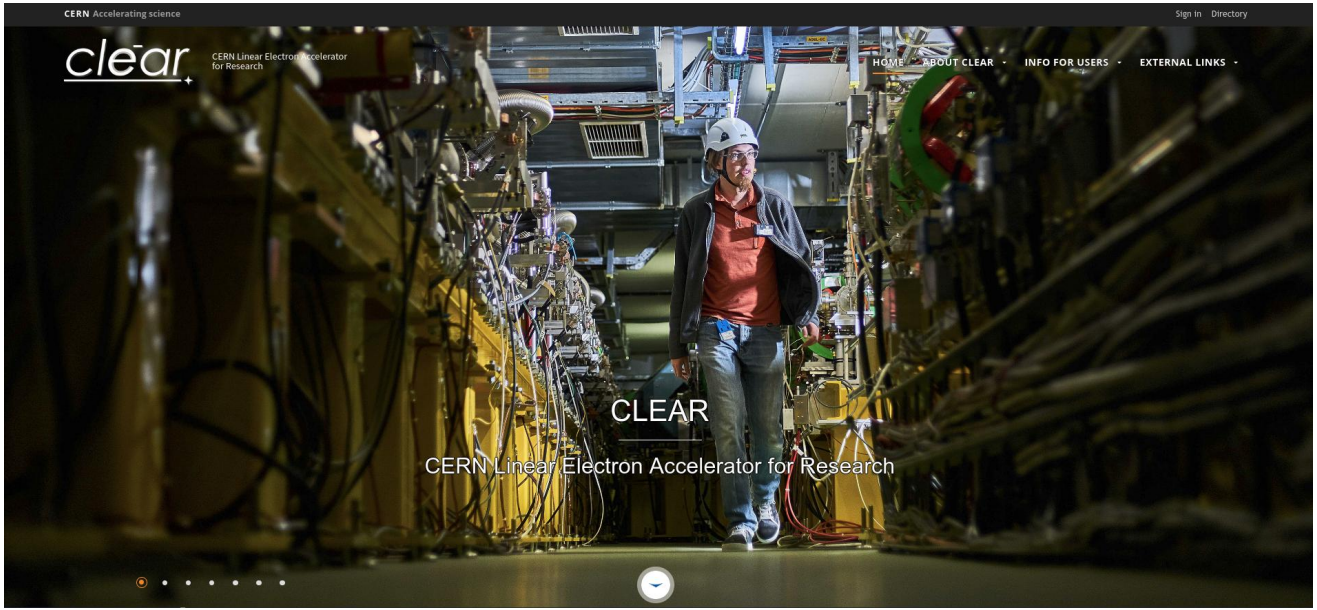
CERN

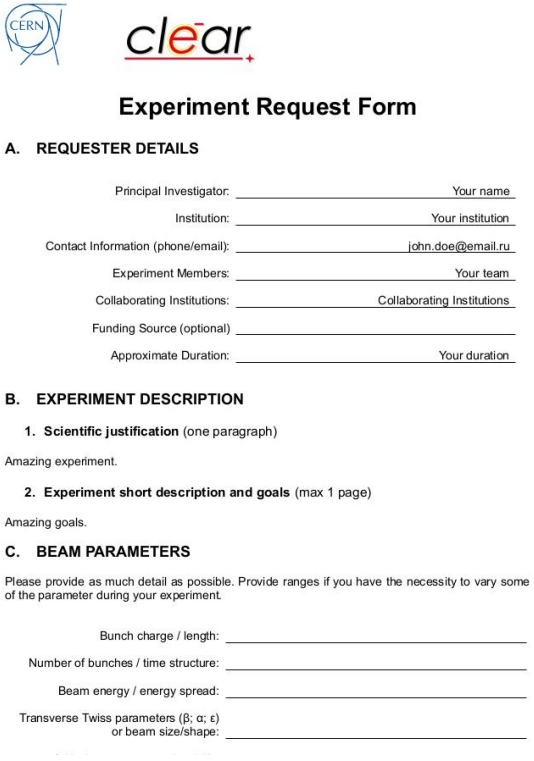
Take part!

You have an experiment in mind and you want to test it in a linear electron accelerator?

Find more information on our Website: https://clear.cern/

And fill out our Beam Request Form!





Experiment Request Form

A. REQUESTER DETAILS

Principal Investigator: Your name
Institution: Your institution
Contact Information (phone/email): john.doe@email.ru
Experiment Members: Your team
Collaborating Institutions: Collaborating Institutions
Funding Source (optional)
Approximate Duration: Your duration

B. EXPERIMENT DESCRIPTION

1. **Scientific justification** (one paragraph)

Amazing experiment.

2. **Experiment short description and goals** (max 1 page)

Amazing goals.

C. BEAM PARAMETERS

Please provide as much detail as possible. Provide ranges if you have the necessity to vary some of the parameter during your experiment.

Bunch charge / length:
Number of bunches / time structure:
Beam energy / energy spread:
Transverse Twiss parameters (β; α; ε) or beam size/shape:

Conclusions

- CLEAR offers a **unique VHEE and UHDR facility**:
  - 60 – 220 MeV.
  - 10 pC – 75 nC beam intensity.
  - Complete setup with **heated waters tanks**, **Robotic Arm**, **3D printed tools**, etc.
- **Several experiments** performed so far:
  - **Chemistry**, **Plasmids** and **Zebra Fish Eggs** irradiations.
  - **VHEE strong focusing** studies.
  - **Scatterers studies**.
- **Several methods of dose measurements** were tested:
  - Several types of **Gafchromic films**.
  - **RPLs**.
  - **Alanine pellets**.
- **Further experiments** are scheduled.
  - **Detectors**, **Fruit Flies Larvae**, **other methods** to measure the **dose**, etc.
- **Further machine upgrades** are planned.

Thank you