

Medical applications in CLEAR



P. Korysko*,
on behalf of the CLEAR team.

JAI Fest

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*pierre.korysko@cern.ch

Outline

- The CLEAR Beamline.
- VHEE beams and the FLASH effect.
- Tools and Methods.
- Selected Medical Applications performed at CLEAR in 2023/2024.
- Conclusions.

The CLEAR Beamline

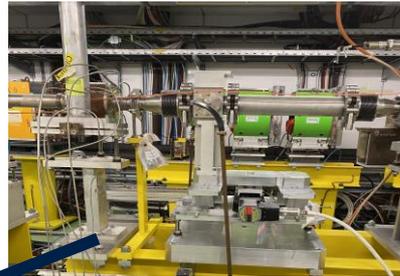


The CERN Linear Electron Accelerator for Research (CLEAR) Beamline in 2024



In-Air Test Stand

- Diagnostics studies
- Irradiation
 - Electronics
 - VHEE

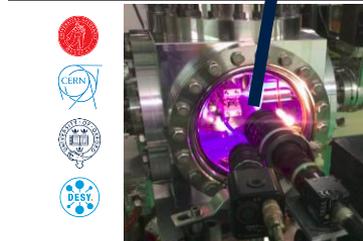
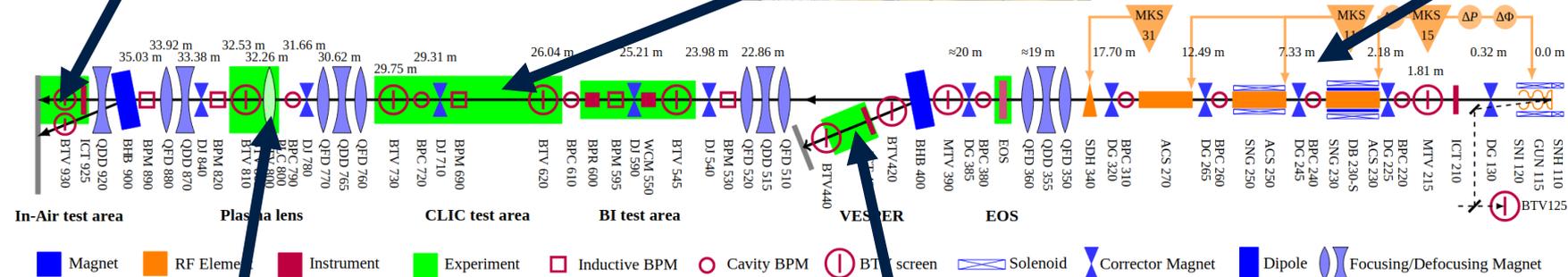


BI Test Stand



CLEAR Injector

- Flexible Linac
- 60 – 220 MeV



Plasma Lens

- Novel plasma based focusing



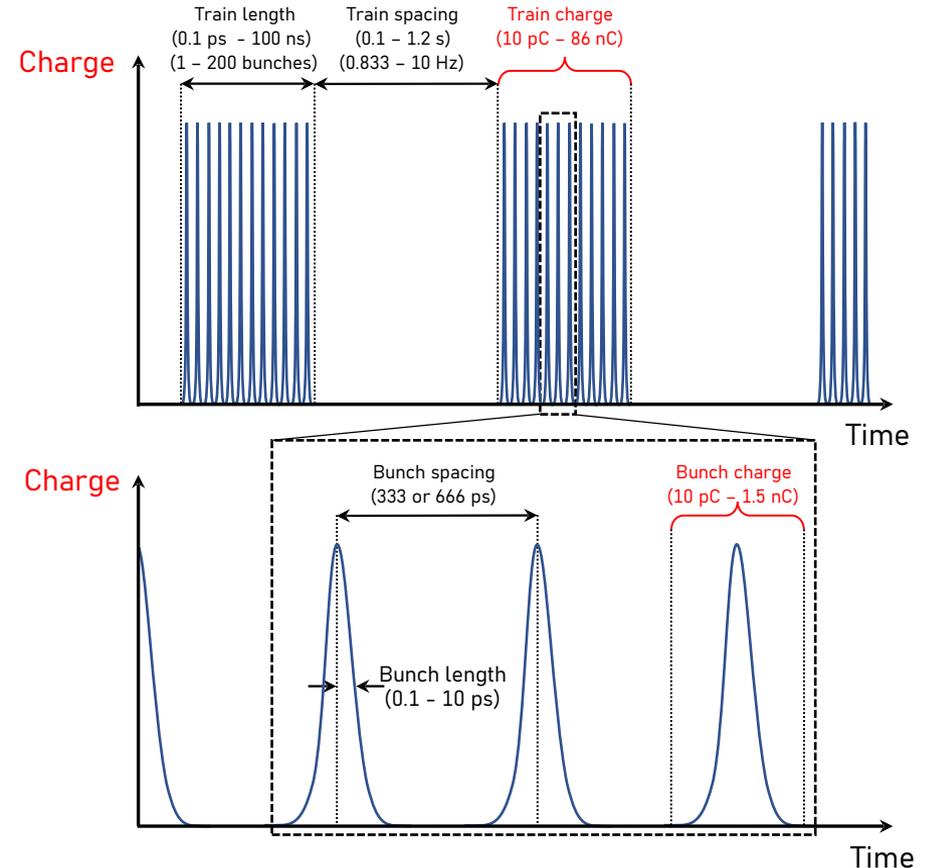
vesper

- Irradiation facility
 - Space probes
 - Electronics
 - VHEE



CLEAR Beam Parameters in 2024

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 – 200
Max. charge per pulse	86 nC
Repetition rate	0.833 – 10 Hz
Bunch spacing	1.5 or 3.0 GHz

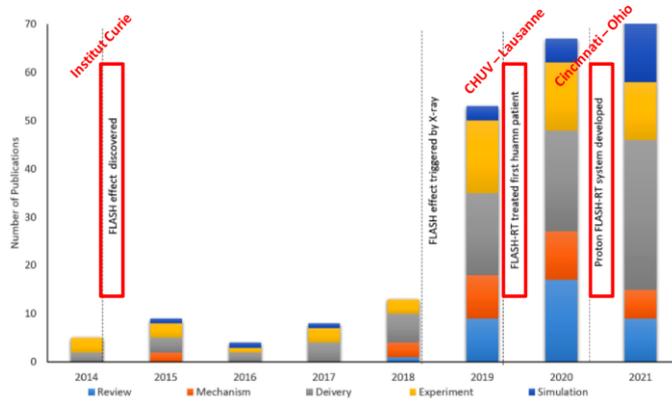


The FLASH Effect

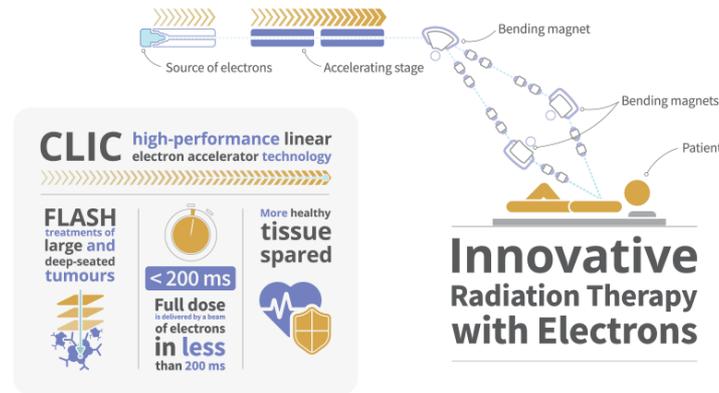


The FLASH Effect

- The Flash effect is a **biological effect** that **destroys cancerous cells** while **sparing healthy surrounding tissues**.
- Observed for the **first time** in [2014](#): mice tumors were irradiated with short pulses (≤ 500 ms) at Ultra High Dose Rate, UHDR (≥ 40 Gy/s).
- The FLASH effect has been seen with **protons, gamma and low energy electrons**.
- Very High Energy Electrons (**VHEE**) would be used to treat **deep seated tumors**.
- The **FLASH** effect is **extensively studied** including in **CLEAR**.



[Gao et al. J Appl Clin Med Phys.2022]



Treatment of a first patient with FLASH-radiotherapy



Radiotherapy and Oncology

Volume 139, October 2019, Pages 18-22



First in Human

Treatment of a first patient with FLASH-radiotherapy

Jean Bourhis ^{a b}, Wendy Jeanneret Sozzi ^a, Patrik Gonçalves Jorge ^{a b c}, Olivier Gaide ^d, Claude Bailat ^c, Frédéric Duclos ^a, David Patin ^a, Mahmut Ozsahin ^a, François Bochud ^c, Jean-François Germond ^c, Raphaël Moeckli ^{c 1}, Marie-Catherine Vozenin ^{a b 1}



- **In 2019, 15 Gy** delivered in **90 ms**, using a **5.6-MeV electron linac**, to a 75-years old patient with a multi-resistant cutaneous lymphoma:
 - **On healthy tissues:** no decrease of the thickness of the epidermis and no disruption at the basal membrane with limited increase of the vascularization.
 - **On Tumor:** Tumor response was rapid, complete, and durable with a short follow-up of 5 months.

Conclusions: This first FLASH-RT treatment was feasible and safe with a favorable outcome both on normal skin and the tumor.

CLEAR

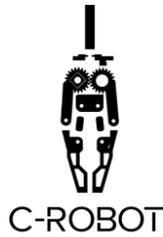
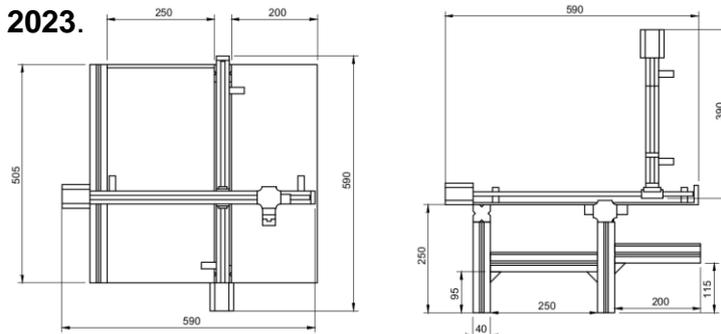
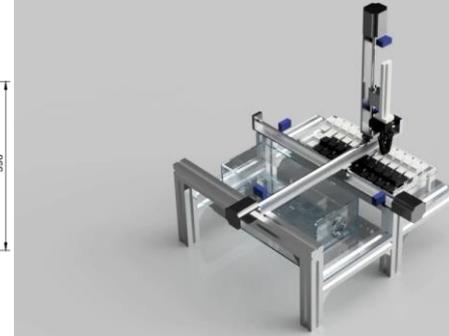
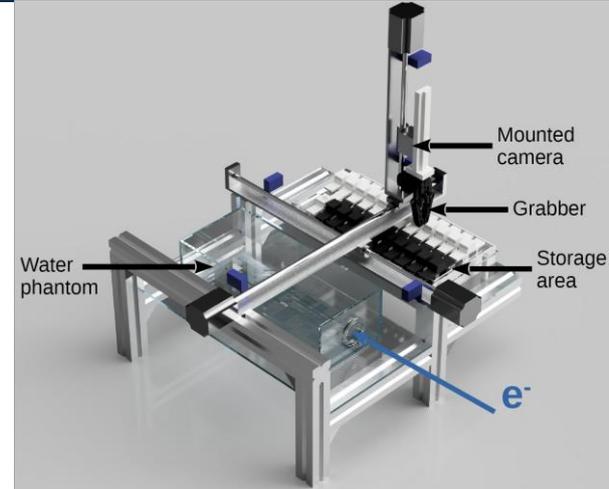
Tools and Methods



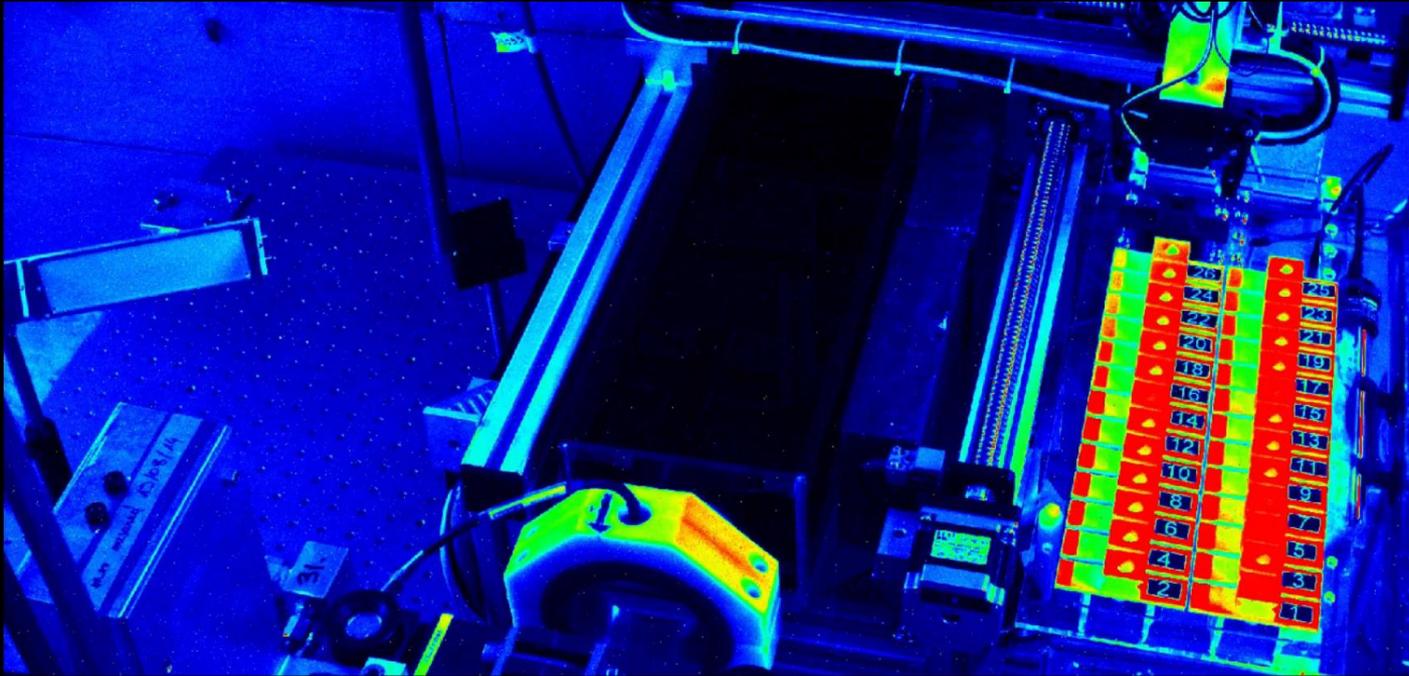
The C-Robot



- 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/C-Robot.html>
- Used for **100% of Medical Applications** in CLEAR in **2023**.



The C-Robot in action with beam

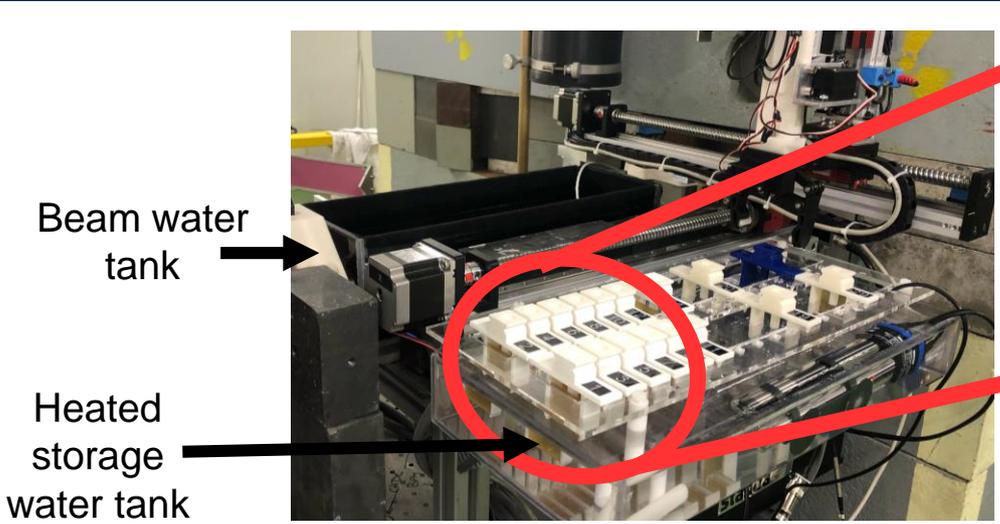


Selected Medical Applications
performed at CLEAR in 2023/2024:

Dosimetry Studies

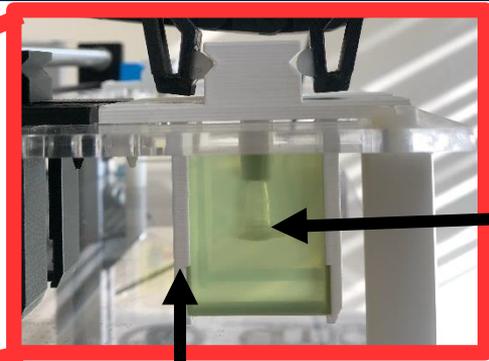
A decorative graphic consisting of white outlines of various geometric shapes, including squares, rectangles, and irregular polygons, scattered across the dark blue background. The shapes are most concentrated in the bottom-left corner and become sparser towards the top and right.

Experimental Setup & Dosimetry for VHEE at UHDR irradiations

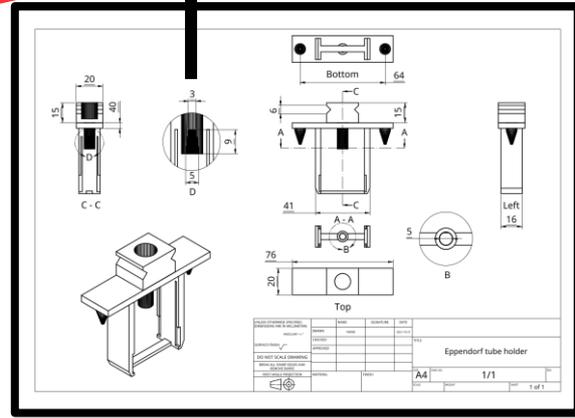


Beam water tank

Heated storage water tank



Eppendorf tube with sample to irradiate



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

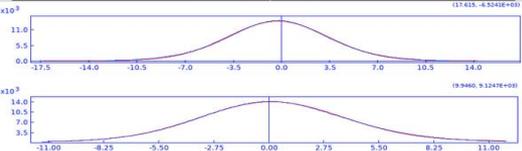
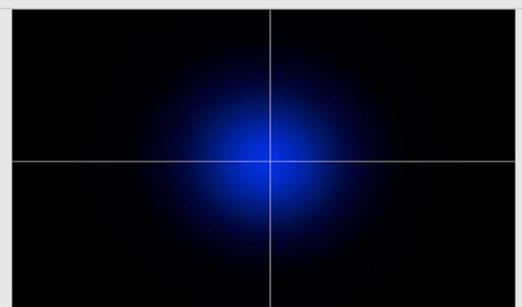
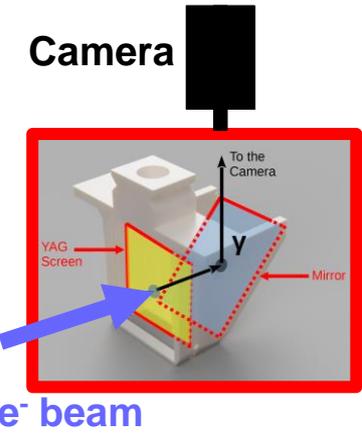
Laser cut Radiochromic films to measure the delivered dose
Dose range: 1 – 100 Gy

Before irradiation

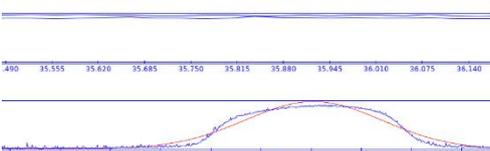
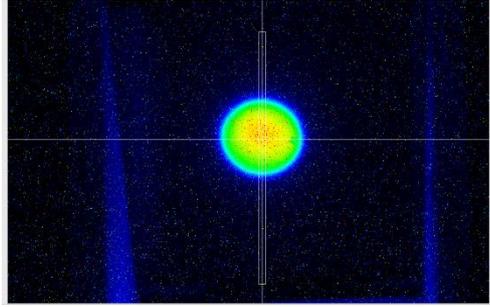
After irradiation

[V. Rieker et al 2024 Nucl. Instrum. Methods Phys. Res.](#)

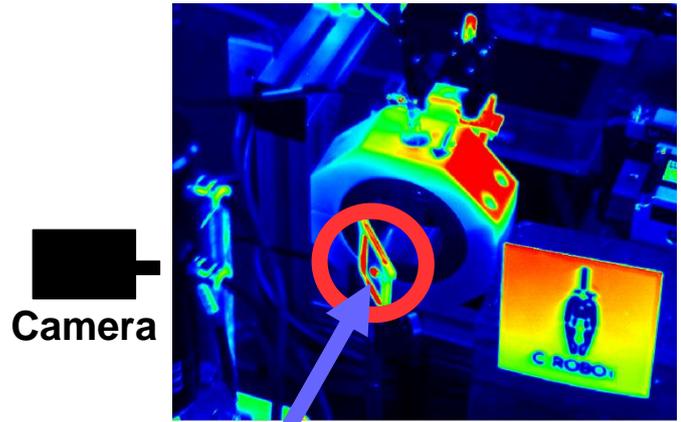
Real-Time Dosimetry



Gaussian Beam

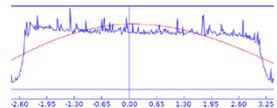
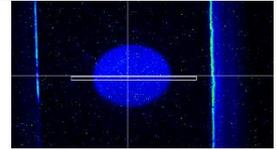


Uniform Beam

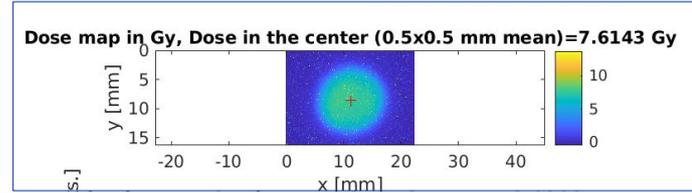


Camera

e⁻ beam



- A real-time dosimetry measurement is done using the **charge** and the **beam size** measurement with the scintillating screen (in air or in water).
- The samples are then irradiated at the same exact location.
- A similar method is being developed using a **thin scintillating screen** in air in front of the water phantom for real-time dose measurement using charge density methods.



Optical Fibre Dosimetry

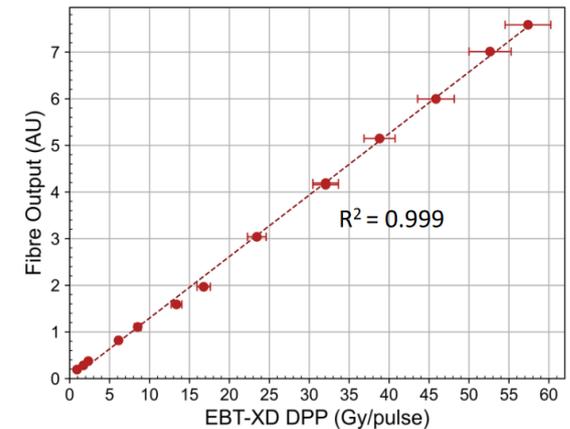
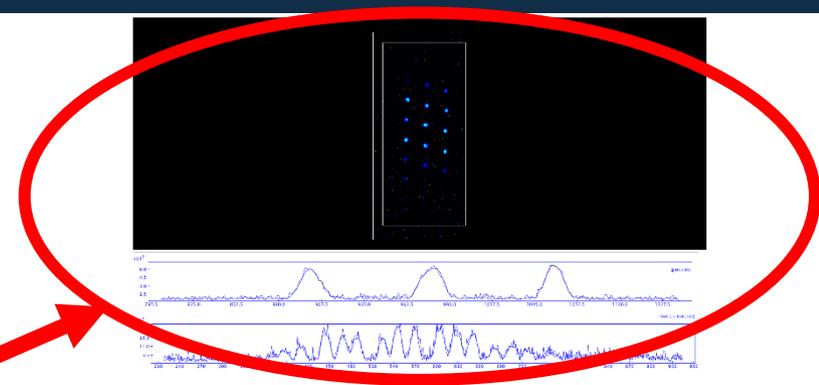
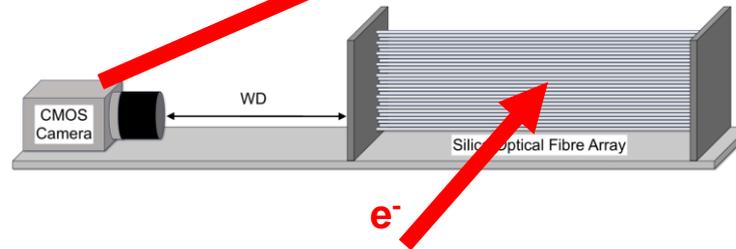
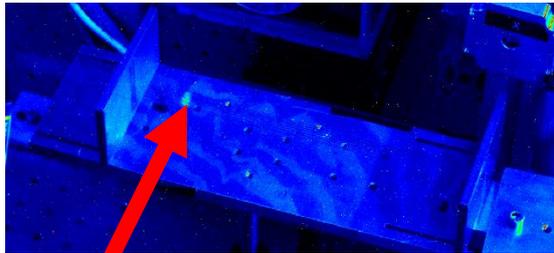


Goal :

Measure in real time the doses delivered by VHEE at UHDR and CDR with two arrays of optical fibers.

Experiment :

Reconstruct the transverse profile of the VHEE beam to measure the dose in real time and compare with radiochromic films.



J. Bateman et al 2024 Phys. Med. Biol.

Scintillator Dosimetry

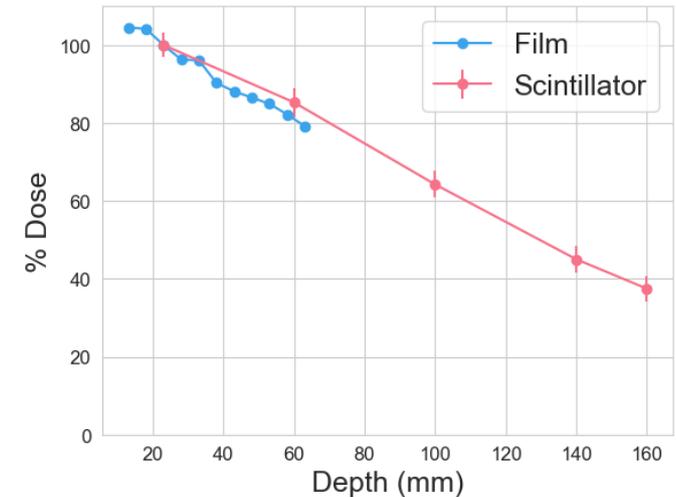
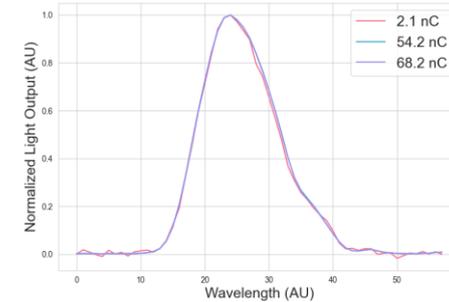
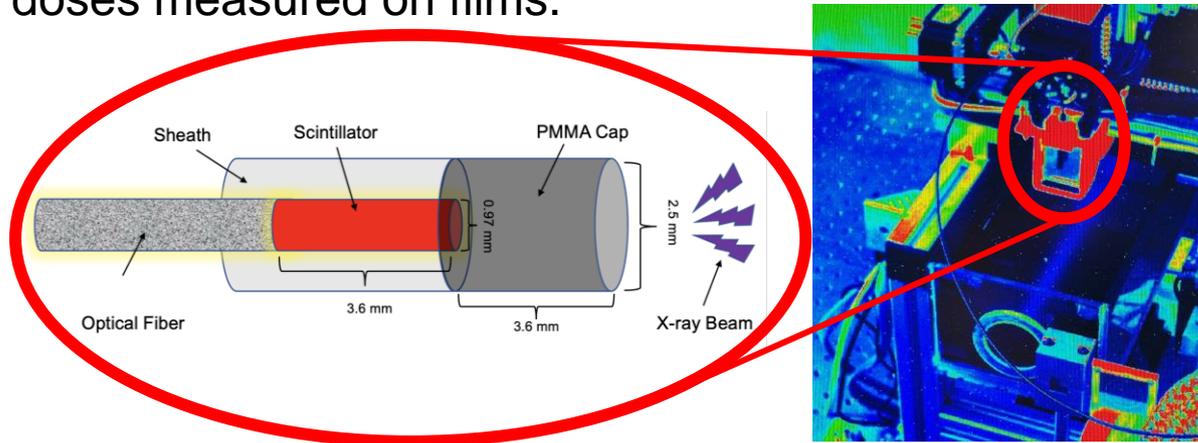


Goal:

Measure the dose at UHDR with a real-time readout and a high spatial resolution thanks to a scintillator and an optical fiber.

Experiment:

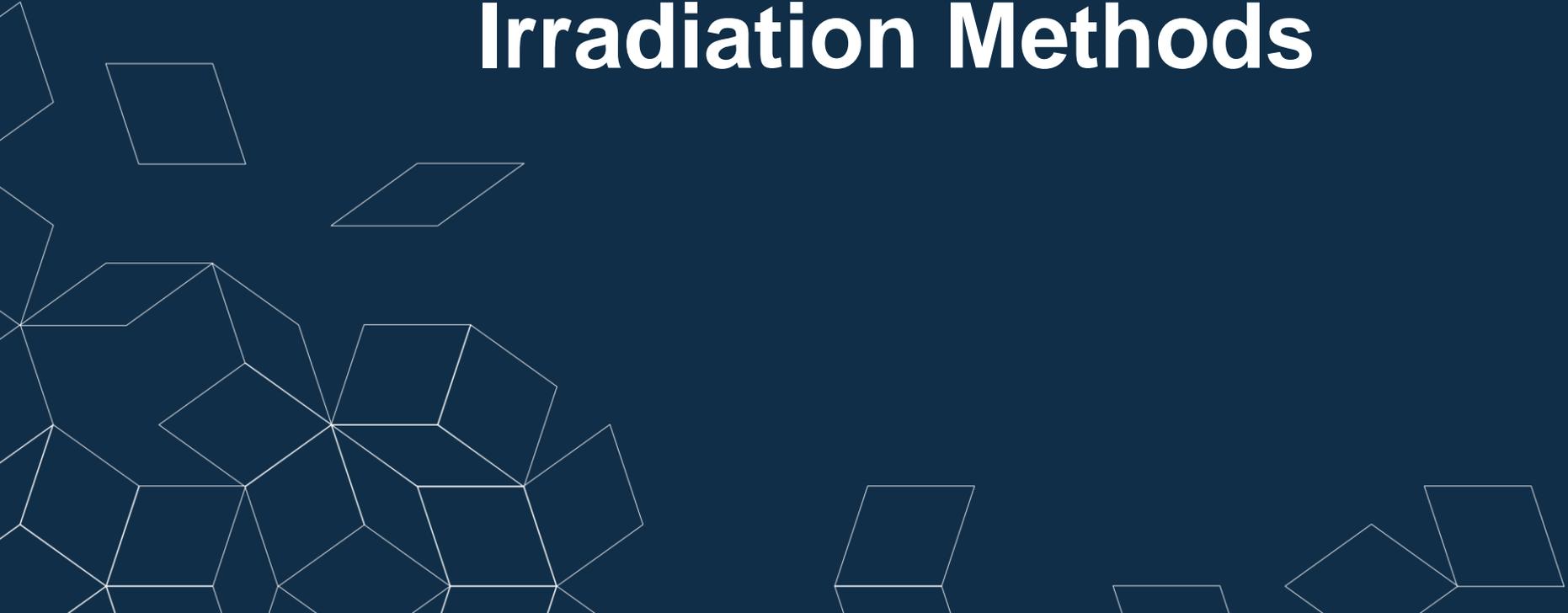
Measure the responses of the scintillator for different doses and water depths and compare them with the doses measured on films.



A. Hart et al, 2024 IEEE Sensors Journal

Selected Medical Applications
performed at CLEAR in 2023/2024:

Irradiation Methods



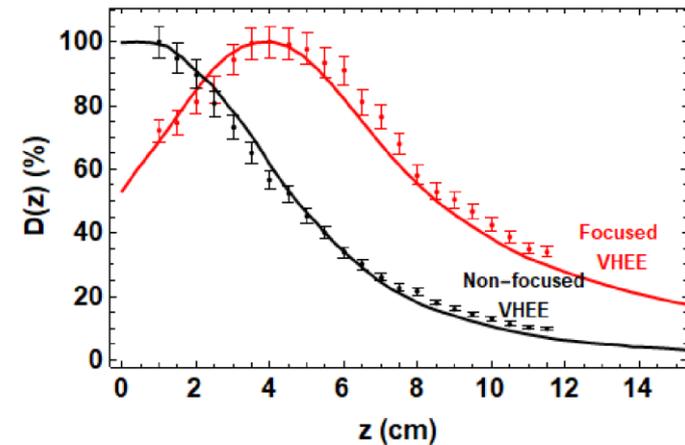
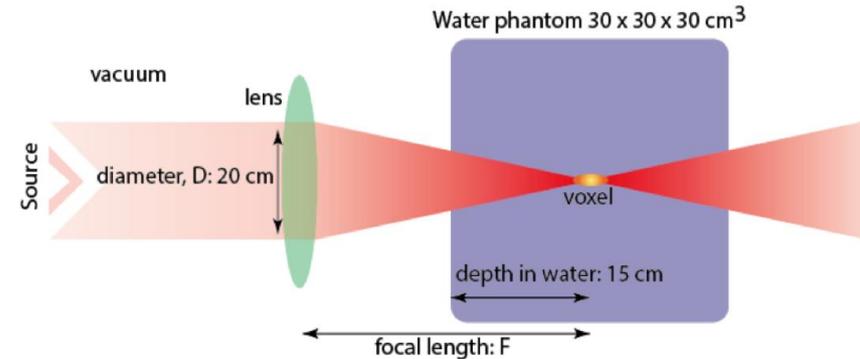
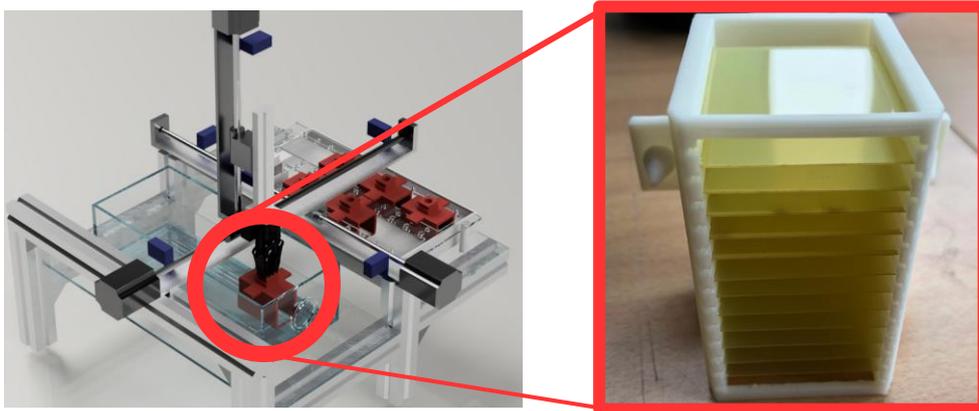
VHEE Strong Focusing

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.



[L. Whitmore et al, 2024 Nature Scientific Reports](#)

VHEE Scatterers

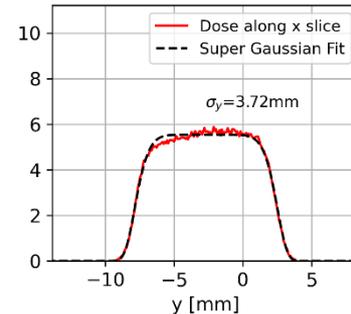
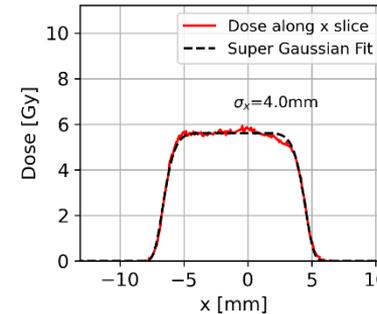
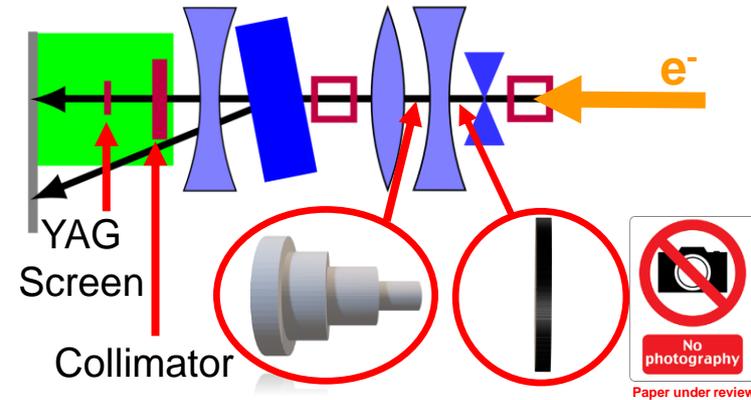
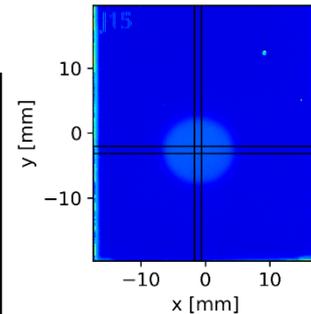
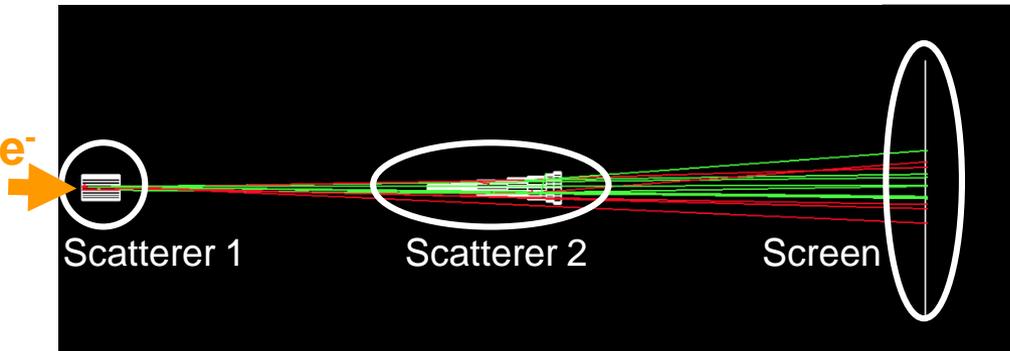


Goal:

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 and films after carefully inserting two scatterers with the beam with the C-Robot.



X and Y beam profile

Now used by CLEAR Operation.

C. Robertson

VHEE GRID



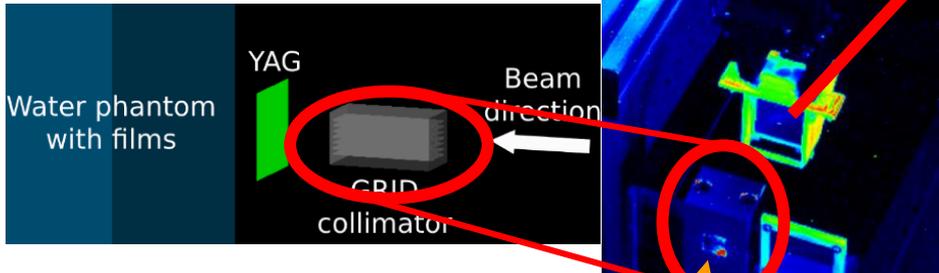
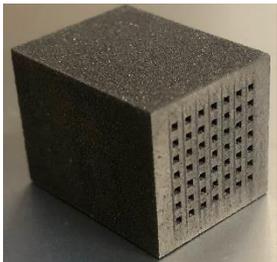
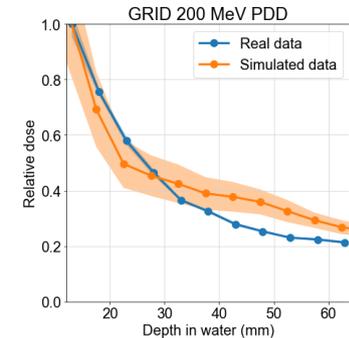
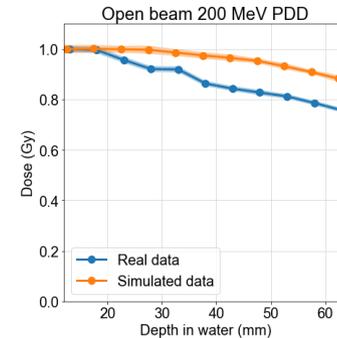
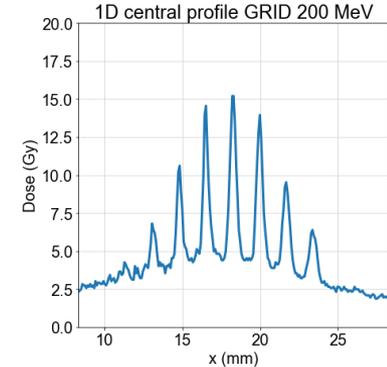
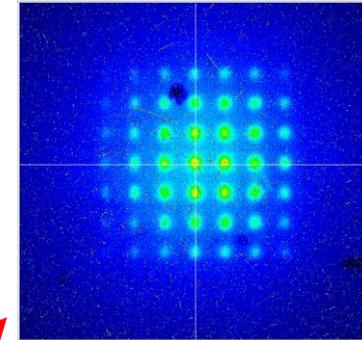
Goal:

Study the dose at UHDR for highly non-uniform dose distributions using a GRID Collimator (Spatially-fractionated RT, known for normal tissue sparing).

Experiment:

Compare the dose values and profiles with and without the GRID collimator inserted for different water depths, with the YAG screen and films.

M. Bazalova-Carter, N. Clements, N. Esplen & A. Hart



[N. Clements et al 2024 Phys. Med. Biol.](#)

Selected Medical Applications
performed at CLEAR in 2023/2024:

Looking for the FLASH effect

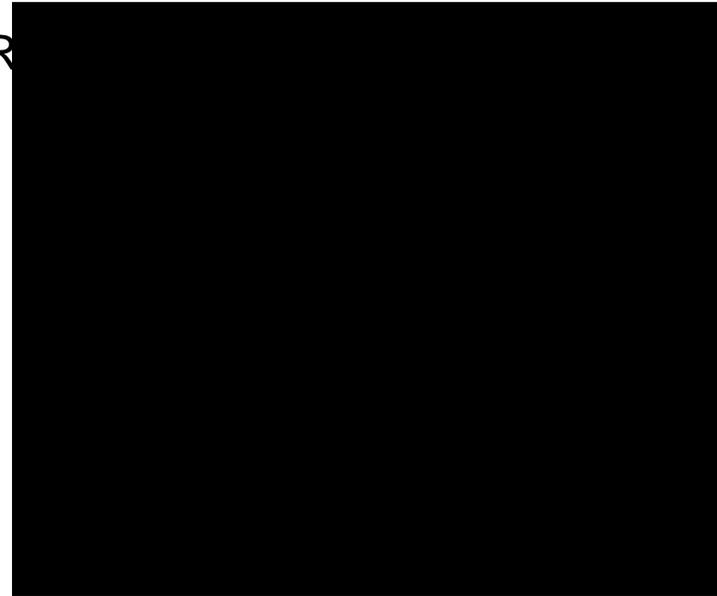
A decorative graphic consisting of white outlines of various polygons, including squares, rectangles, and irregular shapes, scattered across the dark blue background. The shapes are mostly concentrated in the lower-left and lower-right areas, with a few isolated shapes in the upper-left.

VHEE Chemistry Studies



Experiment:

Measure and compare the production of Reactive Oxygen Species (ROS) in water at Conventional Dose Rate (CDR) and Ultra High Dose Rate (UHDR)



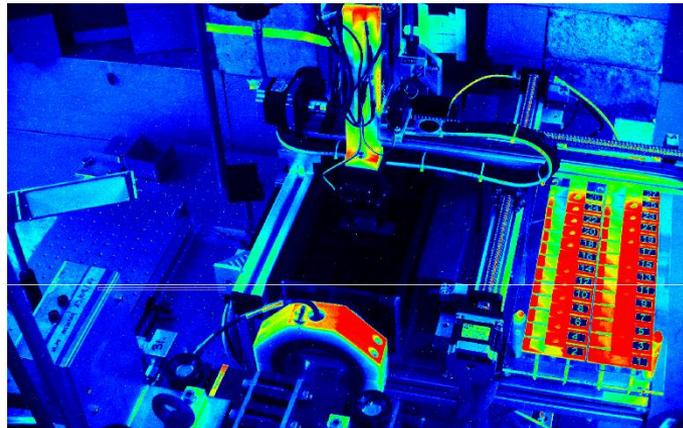
- CONV CLEAR
- UHDR CLEAR



Paper under review



Holder with films and Eppendorf tube



C-Robot view when performing irradiations for chemistry studies

[H₂O₂] (mol/L)

M-C. Vozenin & H. Kacem

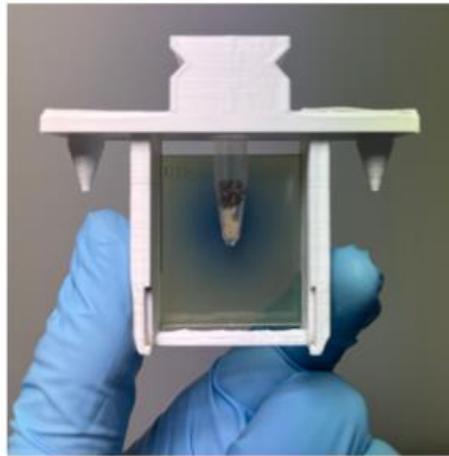
Drosophila larvae irradiations

Goal:

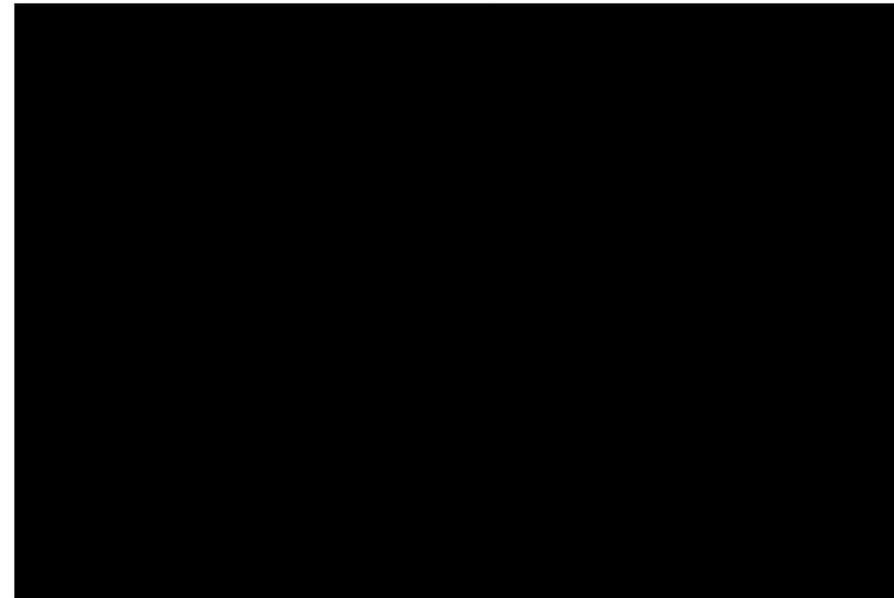
Compare the impact of 200 MeV VHEE irradiations at UHDR and CDR on *Drosophila melanogaster* larvae.

Experiment:

Deliver 15 to 45 Gy at UHDR and CDR to larvae with VHEE and measure the eclosion rate.



Preliminary results



No
photography

Not yet published

A. Hart & T. Esmangart de Bournonville

Zebra Fish Eggs Irradiations

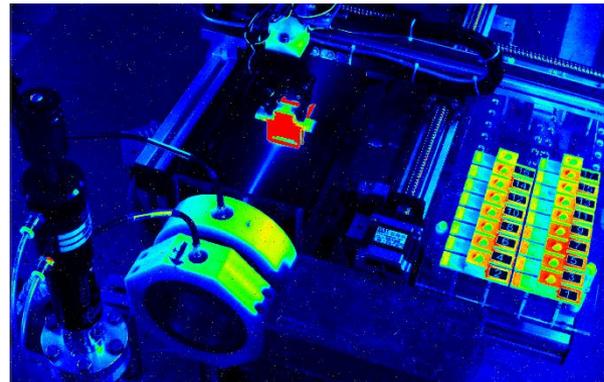
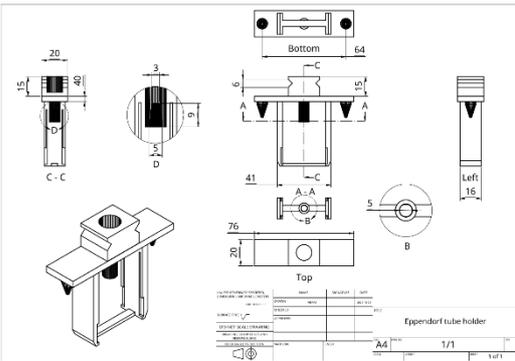


Goal :

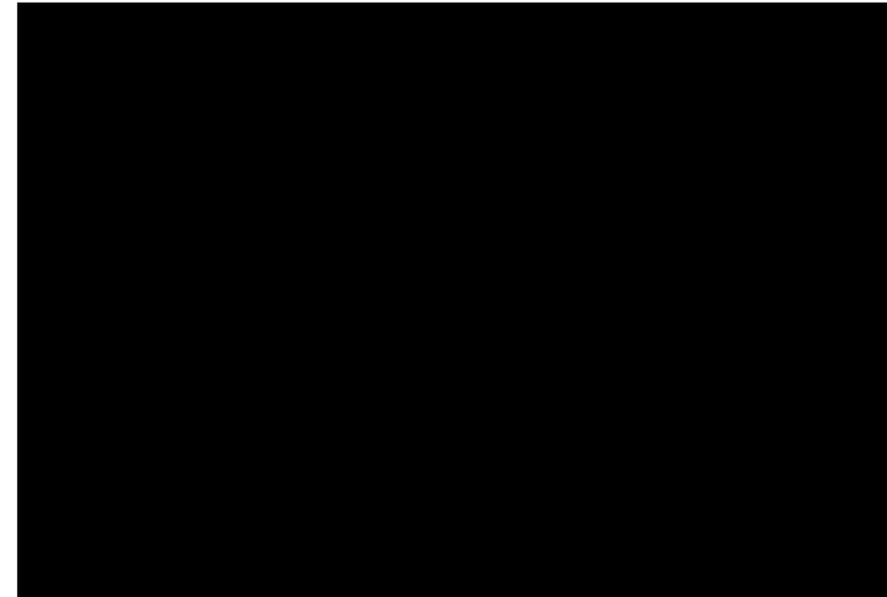
Measure the response effect of the dose and the dose rate on Zebra Fish Eggs (ZFE) with VHEE.

Experiment :

Irradiate ZFE with numerous doses and dose rates: UHDR (Ultra High Dose Rate) and CDR (Conventional Dose Rate) and measure the length deficit.



Preliminary results



M-C Vozenin & J. Ollivier

Selected Medical Applications done at CLEAR in 2024:



Medical Applications done in 2024

VHEE at UHDR Studies with Liposomes
 VHEE at UHDR Studies with Biodosimeters
 VHEE at UHDR Studies with Short Peptides & LCMS
 VHEE at UHDR Studies with Cells

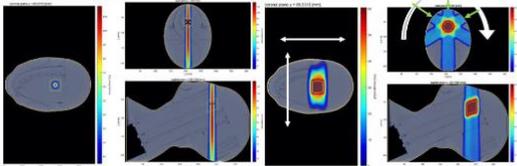
Goal: explore dose and dose rate parameters for both healthy and cancerous cells.

Plan Delivery to an Anatomical Phantom

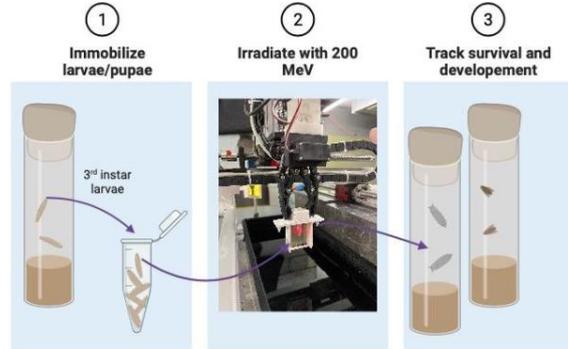
Marvin (head and neck) phantom with the Gafchromic film module and interchangeable inserts.
 • Material: ABS plastic (approx. water equivalent)
 • Dimensions: 41 x 21 x 33 cm³ - Weight: 9 kg.



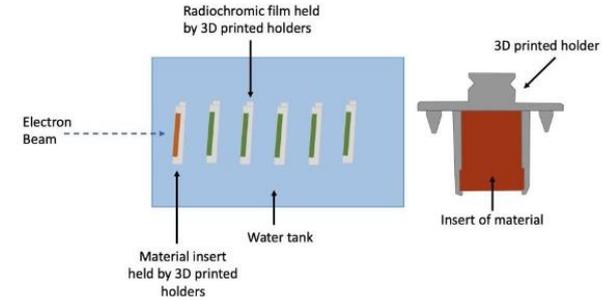
Increasing Complexity →



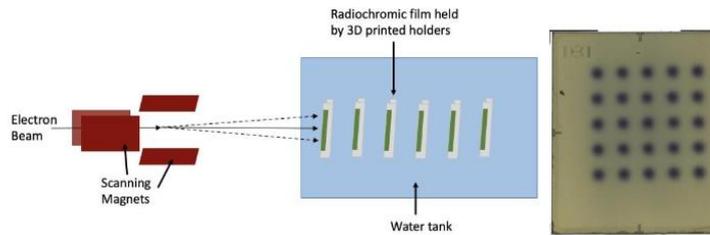
VHEE at UHDR Studies with Drosophilae



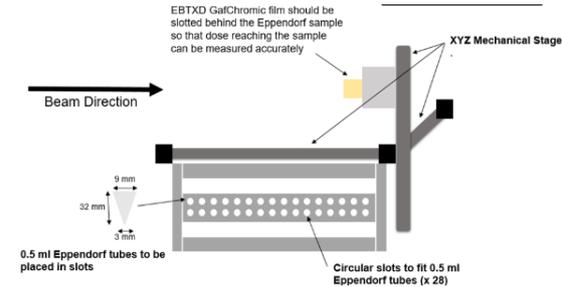
VHEE Material Irradiation Studies



Beam Scanning Spatially Fractionated RT Studies



Radio-enhancement effect of Nanoparticles in VHEE beams & Gold Nanoparticles Plasmid Studies



Conclusions

- More and more **users** are studying the **FLASH effect, Irradiation Methods and Dosimetry** in CLEAR, leading to:
 - **16 weeks** of beam dedicated to **medical applications** in **2024**.
 - **11 Medical Application Experiments** performed in **2024**, see the full list [here](#).
 - **6 journal papers** and **numerous conference proceedings** published in 2024 for medical applications, see the full list on: <https://clear.cern/content/publications>
 - A new robot, the **C-Robot 2.0 was built**. The CLEAR team is helping to build 3 similar robots for PITZ in **Germany**, the Australian Synchrotron in **Australia** and IHEP in **China**.
 - **New beam line** with flexible optics, particularly suited for **medical applications is being built at CLEAR**.

The background features a dark blue color with a white geometric pattern. The pattern consists of various polygons, including squares and rectangles, some of which are tilted. These shapes are arranged in a way that creates a sense of depth and movement, with some shapes appearing to be stacked or layered. The overall effect is a modern, minimalist aesthetic.

Thank you