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VHEE AND ULTRA HIGH DOSE RATE RADIOTHERAPY STUDIES IN THE CLEAR USER FACILITY

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Abstract

The CERN Linear Electron Accelerator for Research (CLEAR) is a user facility providing electron beams for a large and varied range of experiments. CLEAR was selected to study the feasibility of using Very High Energy Electrons (VHEE), between 100 and 200 MeV, at Ultra High Dose Rate (UHDR), sending the total dose in less than 100 ms, for cancer radiotherapy. With these conditions, one can study the FLASH biological effect in which deep-seated cancer cells are damaged while the healthy surrounding tissues are spared. CLEAR can deliver a 30-220 MeV beam and doses from a few mGy per second to a few Gy per ns. Several recent experiments in the medical field, carried out at CLEAR this year, are presented in this paper.

INTRODUCTION

The CLEAR user facility can deliver to its users an electron beam with a large range of parameters [1–4], summarized in Table 1. Two in-air test areas and 3 in-vacuum spaces are available for experiments. In air, the VESPER (Very energetic Electron facility for Space Planetary Exploration missions in harsh Radiative environments) and the In-Air Test Areas offer a large space to install different types of diagnostics including tools to irradiate and measure the delivered dose.

Table 1: Updated List of CLEAR Beam Parameters

Parameter	Value
Beam Energy	30 – 220 MeV
Beam Energy Spread	< 0.2% rms (< 1 MeV FWHM)
Bunch length rms	0.1 – 10 ps
Bunch frequency	1.5 or 3.0 GHz
Bunch charge	0.01 – 1.5 nC
Norm. emittance	1 – 20 µm
Bunches per pulse	1 – 200
Max. pulse charge	87 nC
Repetition rate	0.8333 – 10 Hz

Thanks to the C-Robot [5–7], CLEAR-designed 3D printer holders and linear stages installed in front of the C-Robot, different types of devices and samples can be remotely moved in to the electron beam. These holders allow to have radiochromic films irradiated in air or in water. In order to measure the beam size and position where the samples will be irradiated, a dedicated holder with an Yttrium aluminium garnet (YAG) scintillating screen attached to be inserted in the beam area. This allows the beam position and the beam size of the electron pulses can be measured in air and in water at any transverse and longitudinal position in the beam area.

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EXPERIMENTAL STUDIES

In the last couple of years, a large fraction of the available beam time in CLEAR has been dedicated to studies of medical application related issues. A strong effort has been done on dosimetry for UHDR [8–10] and on beam delivery techniques [11, 12]. In the following we report briefly upon other studies completed in 2022 in collaboration with several user groups.

Spatially-Fractionated Radiotherapy

Spatially-Fractionated Radiotherapy (SFRT) is a promising novel technique leading to reduced normal tissue toxicity. Instead of having a Gaussian distribution of electrons in the bunch, a SF beam has a multitude of smaller peaks. One technique to obtain such a beam uses special collimators [13]. In CLEAR, in an experiment lead by Victoria University, a 40 mm thick tungsten collimator with 49 1×1 mm^2 holes was tested.

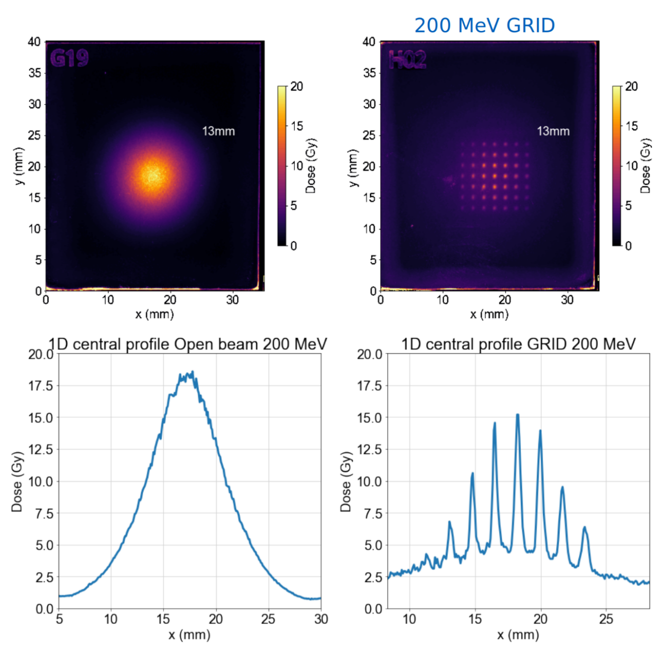

Figure 1: Beam profiles from the radiochromic films without (left) and with (right) the tungsten grid collimator inserted.

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The beam profiles on both the YAG scintillating screen and the doses on radiochromic films could be measured in water; both with and without collimator with a 200 MeV electron beam. Pictures of the irradiated films and associated beam profiles can be seen in Figure 1. The delivered doses and profiles at several depths in water agree very well with the simulations. The next step will be to irradiate biological samples to study the impact of SFRT with VHEE at UHDR.

Plastic Scintillator Dosimeters

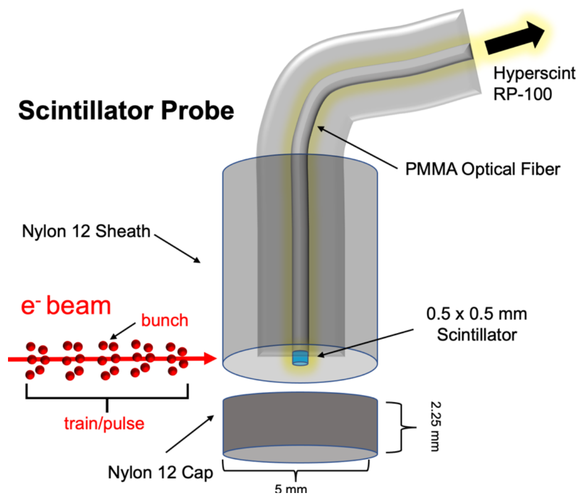

Figure 2: Schematic of the scintillator probe.

In another experiment devised by Victoria University, Plastic Scintillator Dosimeters (PSDs) optically coupled to a hyperspectral camera were installed in CLEAR to measure the dose delivered by VHEE beams. Both the ability of PSDs to respond linearly to dose under UHDR VHEE conditions, up to Gy/s, and the radiation hardness of two scintillator compositions were tested. The PSDs were connected to a Hyperscint RP-100 spectral readout system (Medscint, Quebec) and were used to measure the response to 200 MeV electrons.

A schematic of the experimental setup is shown in Figure 2, and pictures of the setup are shown in Figure 5.Two scintillator compositions were investigated: the polystyrene-based BCF-12 and a proprietary Medscint material. Output linearity measurements were conducted by scaling the dose/train between 5 and 140 Gy. The radiation hardness of the probes was assessed by tracking the delivered dose to each of the probes during all measurements up to total doses of 26.2 and 13.8 kGy for the BCF-12 and Medscint probes respectively. Periodical output linearity measurements allowed to monitor changes in the performance of the probes due to radiation damage.

The doses measured by the calibrated scintillators were then compared with the doses measured by radiochromic films with a 90 % agreement. The results are shown in Figure 3. In conclusion PSDs are promising instruments for real-time dosimetry of UHDR VHEE beams.

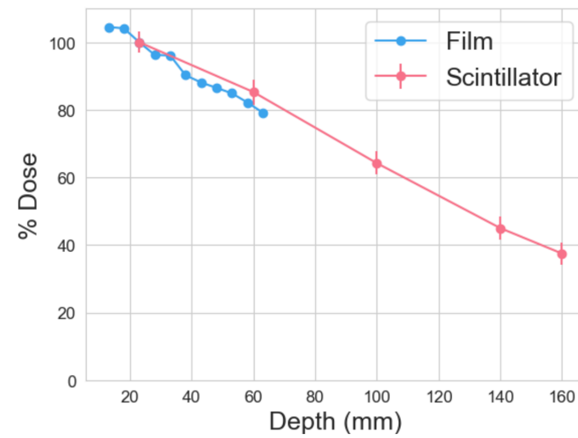

Figure 3: Comparison between doses measured by the PSDs and by the radiochromic films.

VHEE Strong Focusing

One potential advantage offered by VHEE radiotherapy is the possibility to optimize the dose distribution in a patient by focusing the electron beam with quadrupole magnets. The dose delivered to healthy tissue can be thus reduced, targeting the maximum dose delivery to the tumor. Dosimetry tests aimed at experimental demonstration of the principle were carried out over the last years in CLEAR [14, 15].

In 2022 another experiment has been completed in collaboration with Manchester University. The study consisted of targeting an area of focused VHEE dose delivery in air and in a water phantom, for beam energies greater than 200 MeV. Experimental results have been verified with Monte Carlo modelling. Simulated results are shown in Figure 4. A clear beam profile waist and a dose peak were obtained deep in the water phantom.

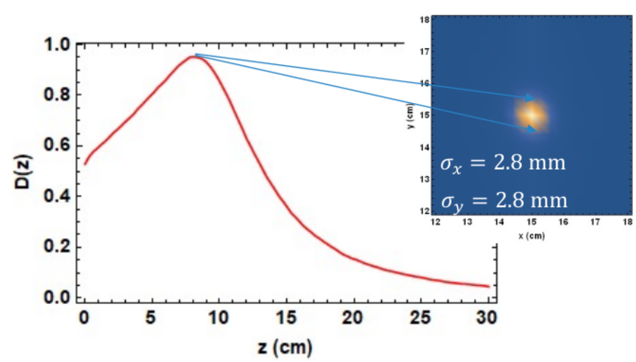

Figure 4: Simulation of the relative delivered dose deep in a water phantom.

Water, plasmids and ZFE irradiations

CLEAR is working in close collaboration with Lausanne University Hospital (CHUV) to study VHEE at UHDR by irradiations on three types of samples: Water samples for chemistry, plasmids and Zebra Fish Eggs (ZFE). These irradiations are done in order to study the feasibility of using

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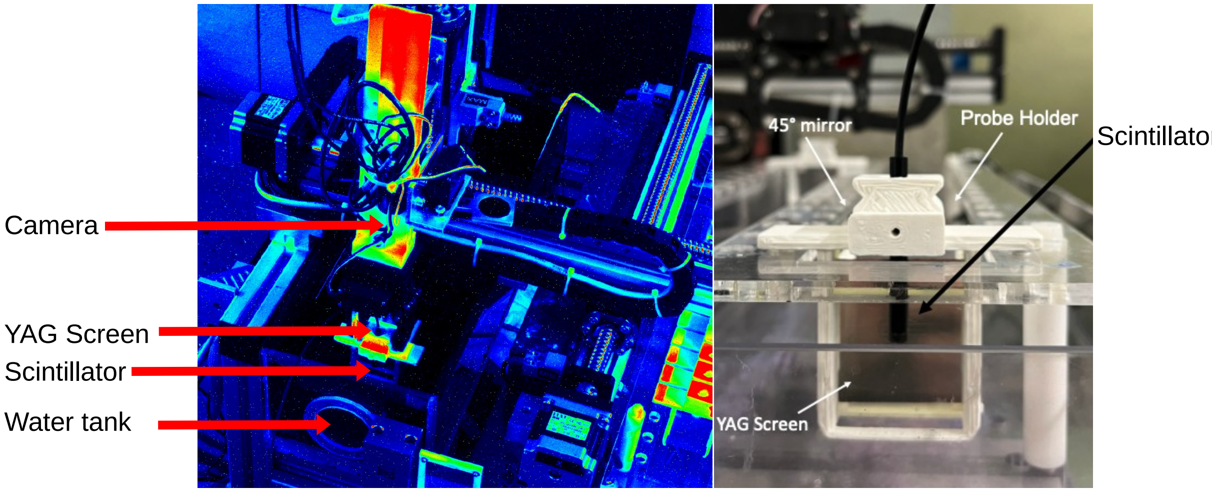

Figure 5: Scintillator and YAG screen in the electron beam (left), 3D printed holder with the scintillator and the YAG screen (right).

VHEE at UHDR for radiotherapy, and investigate the mechanisms underlying the FLASH biological effect.

The following procedure is used in order to deliver the target dose: a scintillating YAG screen is moved in the water tank into the electron beam. The beam profile, size and position is measured with a camera mounted on the grabber of the C-Robot. The appropriate beam size to irradiate uniformly the sample can then be selected by chosing the correct longitudinal position, and eventually by tuning the beam optics appropriately. When the beam size is chosen, the charge of the electron pulse is tuned to deliver the required dose. The screen is then simply sent back to its storage position and different types of samples, in Eppendorf tubes, are positioned in the beam area where the YAG screen was. The C-Robot can irradiate up to 30 different samples. For water sample or plasmid irradiations, a high dose is required (up to 50 Gy) in order to observe the difference between the UHDR irradiation, where the total dose is delivered in less than 1 µs and the Conventional Dose Rate (CDR), where the total dose is delivered in a few minutes. One of the study objectives is to measure and compare the production of H_2O_2 in water samples with UHDR or CDR conditions. In Figure 6 is shown the measured beam sizes and delivered doses for CHUV chemistry studies. The beam sizes and the doses were measured with radiochromic films. The error between the targeted doses and the delivered ones is less than 5%.

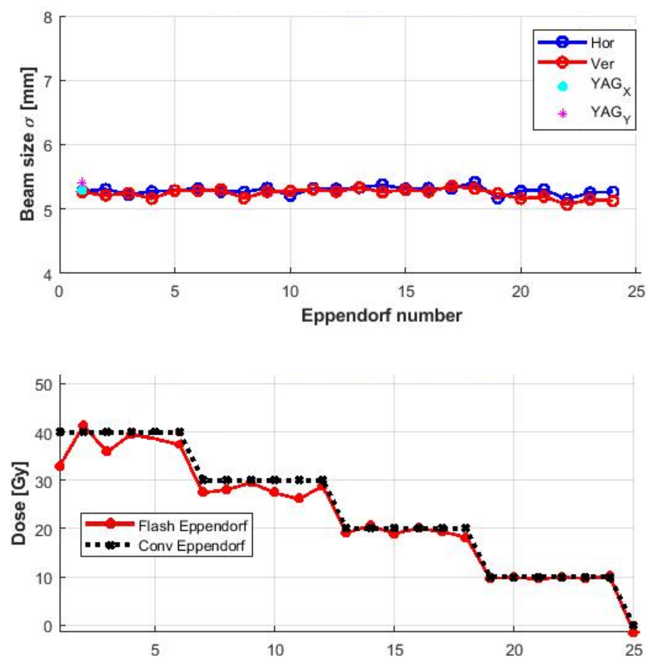

Figure 6: Measured beam sizes and delivered doses for CHUV chemistry studies.

CONCLUSION

Over the last 12 months, more than 12 medical application experiments were performed in CLEAR, mainly aimed at the validation of the use of VHEE for cancer radiotherapy and ant the development of the corresponding technology. In particular, irradiation tests have been performed in the high dose rate regime, which has recently gained significant interest since it can produce the so called FLASH biological effect, in which cancer cells are damaged while healthy tissue is largely spared. New tools were developed in CLEAR to study and measure the doses required for such radiotherapy. Both passive and active methods give precise and reliable results. Numerous experiments were done in CLEAR to study and obtain the right doses at various depths in a water phantom and to understand the mechanism of the FLASH effect.

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