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METHODS FOR VHEE/FLASH RADIOTHERAPY STUDIES AND HIGH DOSE RATE DOSIMETRY AT THE CLEAR USER FACILITY

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Abstract

The CERN Linear Electron Accelerator for Research (CLEAR), operating since 2017, is a user facility providing electron beams for a varied and large range of experiments. The accelerator can generate a 60-220 MeV electron beam and it was recently selected to study the feasibility of using Very High Energy Electrons (VHEE) at Ultra High Dose Rate (UHDR) for cancer radiotherapy. One of the studies in CLEAR is to study the impact of sending the total dose in a short amount of time (also called UHDR) and study the FLASH biological effect in which deep-seated cancer cells are damaged while the healthy tissues are spared. The dosimetry in CLEAR is measured using both passive dosimetry with radiochromic films or radio-photo-luminescent dosimeters. In this paper different methods for dosimetry studies and experiments in which they are used will be presented.

INTRODUCTION

The CLEAR facility can offer an electron beam with a large range of parameters to its users [1–4]. They are shown in Table 1. A diagram of the beamline is shown in Figure 1. Two in-air test areas area available. The VESPER (Very energetic Electron facility for Space Planetary Exploration missions in harsh Radiative environments) and the In-Air Test Area. In practice, both areas can be used for medical applications studies like VHEE radiotherapy experiments.

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	0.005 – 3 nC
Norm. emittance	1 – 20 μm
Bunches per pulse	1 – 150
Max. pulse charge	75 nC
Repetition rate	0.8333 – 10 Hz

C-ROBOT

In order to increase the range of experiments done in CLEAR, four members of the CLEAR team designed, developed and built a robotic system called CLEAR-Robot (C-Robot) [5]. It was built to place samples in the beam line for irradiation for medical applications. The robot is made of 3 linear stages for X,Y and Z axis, 6 limit switches (2 for each axis), a 3D printed grabber, a mounted-camera system with a moving optical filter and two tanks (one storage tank and one tank in the electron beam). A rendered picture of the system is shown in Figure 2. The C-Robot is controlled using two custom Arduino circuits, and fully interface to the local computing network.

There are two separate areas on the C-Robot, the storage area where a laser-cut PMMA plate and PMMA water tank are installed and can accept 32 different 3D-printed holders. Each holder can be adapted for different experiments. Two dosimetric films can be installed on each holder, one before and one after the sample that needs to be irradiated. The position in the beam area where the transverse and longitudinal positions of the holder can be chosen with a 50 µm accuracy.

In order to measure the beam size and position where the samples will be irradiated, a dedicated holder with a YAG screen attached can be inserted in the beam area. The YAG screen is angled by 45° compared to the electron beam and thanks to camera mounted on the C-Robot, the beam position and the beam size of the electron pulses can be measured directly at any transverse and longitudinal positions in the beam area.

The C-Robot is fully open-source. Pictures, drawings, 3D renders and codes can be found on the C-Robot website [5] and on the C-Robot Gitlab Repository [6].

METHODS FOR DOSIMETRY STUDIES

Radiochromic Films

Radiochromic films change colour macroscopically due to polymerisation caused by ionising radiation. The change in colour is related to the accumulated dose. After being irradiated, the films are optically scanned and the resulting image is processed to determine the optical density (OD). The OD is then matched against a calibration curve, which must be obtained, for each irradiated batch, at a calibration facility. In CLEAR, various types of Gafchromic films are used: EBT3 (with a range from 0.1 to 10 Gy), MD-V3 (1 - 100 Gy) and HD-V2 (10 - 1000 Gy). They are calibrated at the eRT6 linac in the Centre Hospitalier Universitaire Vaudois (CHUV). The films are cut to the exact dimensions of the sample holder slots using a laser cutter. This method also avoids the issue of layer detachment frequently caused by other means of cutting.

To validate the scanning procedure, image processing methods and reproducibility of this method, a large number

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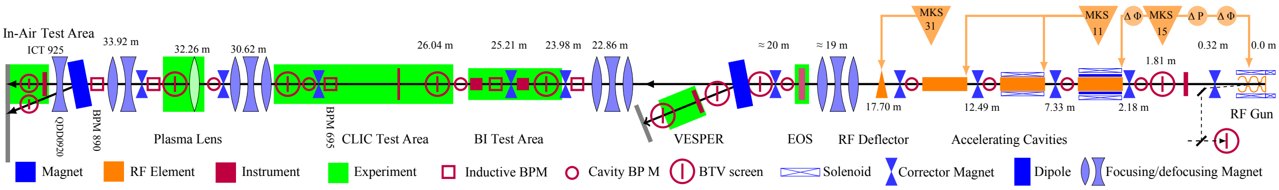

Figure 1: CLEAR beam line in 2022. Notice that the electron beam travels from right to left. [2]

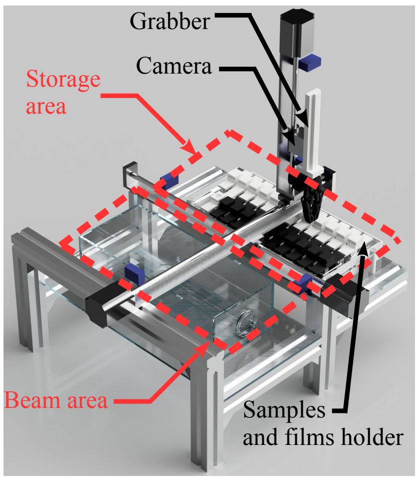

Figure 2: Rendered image of the C-Robot.

of films were irradiated under various conditions. Figure 3 shows a Gafchromic film irradiated in CLEAR. Following the irradiation, the films are scanned using a 16-bit Epson Perfection V800 Photo scanner at 300 dpi, using a mask to ensure the same orientation and position on the scanner plate for each film.

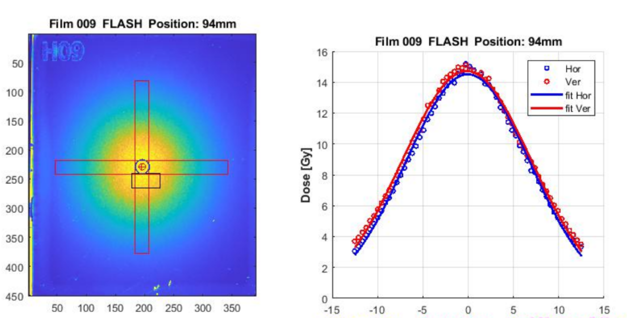

Figure 3: View of an irradiated film (left) and transverse fits used to calculate the deposited dose (right).

The resulting images are then processed using a script which reads the RGB pixel values. The optical density of a single colour channel x is the channel's pixel value divided by the 16 bit RGB colour space: $OD_x = -\log(x/65535)$. The calibration data should be fitted to a function of the form,

$$OD_x = a + b/(D - c), \qquad (1)$$

where D is the dose [8]. The dose distribution is not uniform across the film, and the relevant area must be selected for analysis. By performing a Gaussian fit of the processed image, one may also obtain an estimation of the beam size.

Radio-photoluminescence Dosimeters

Radio-photoluminescence (RPL) dosimeters are silver activated phosphate glass cylinders of 1.5 mm diameter and 8.5 mm length which work on the principle of radiation-induced luminescence centers [9]. RPLs are used for passive beam loss measurements in machines such as the CERN SPS and LHC [10]. The luminescence emitted upon exposure to UV light is proportional to the absorbed dose, with a supposed linear response in the range 1 Gy - 5 MGy. RPLs have the advantage that measuring the luminescence centers is non-destructive and they do not fade over time. To test their response to VHEE beams, RPL cylinders were mounted horizontally in sample holders. HD-V2 films were mounted in front of and behind the RPL for reference. The RPLs were then irradiated at a constant dose rate using 100 pC trains with a size of ~ 1.6 mm corresponding to an average dose rate of ~ 1 Gy/s. The doses measured by the RPL matches the dose measured by the HD-V2 films with an error smaller than 5% as shown in Figure 4. Both methods can then be used in complete confidence.

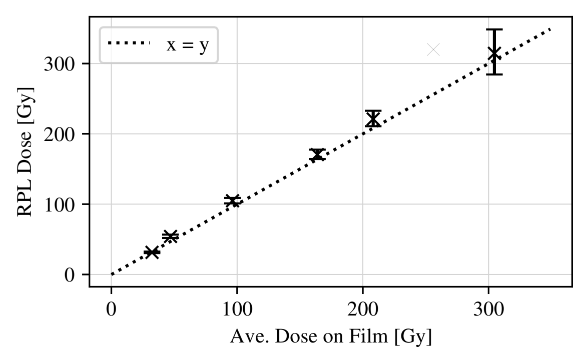

Figure 4: Dose measured on the RPLs vs. dose measured on the HD-V2 films.

EXPERIMENTAL SETUPS

Water, Plasmids and ZFE Irradiations

CLEAR is working in close collaboration with CHUV to study VHEE UHDR irradiations on three types of samples: Water samples, plasmids and Zebra Fish Eggs (ZFE). These irradiations are done to study the feasibility of using VHEE at UHDR for radiotherapy. In order to irradiate these different types of samples with the desired dose, the

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following procedure is observed: a scintillating YAG screen is positioned in the water tank, in the beam area. The beam size and position is measured with the screen. In order for the electron beam to cover the whole samples, the C-Robot would move the screen further in water, longitudinally, to increase the beam size, due to the scattering effect of the water, or closer to decrease it. When the beam size is chosen, the charge of the electron pulse is measured and tuned to delivered 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 samples. After that, an access to the machine is needed to collect the irradiated samples and the films. The films are then dried and stored in a dark environment for 12 to 24 hours for color stabilization. Finally the dose can be calculated after scanning the films and applying the calibration. A view of an irradiated film and the fits used to compute the size and the delivered dose is shown in Figure 3 and a plot of one batch of irradiations of ZFE is shown in Figure 5. The "Flash and Conv beam" corresponds to the dose delivered to the Gafchromic films, the "Flash and Conv Eppendorf" corresponds to the dose delivered to the samples.

For water sample or plasmid irradiations, a high dose is required (up to 50 Gy) to observe the difference between the UHDR irradiation, where the total dose is delivered in less than 100 µs and the conventional irradiation, where the total dose is delivered in a few minutes. The samples are then analyzed CHUV chemists and biologists to observe the production of H_2O_2 and the migration of plasmids.

VHEE Strong Focusing

The entrance dose due to VHEE beams could be reduced by focusing using quadrupole magnets. It is also possible to use multiple focused beams to treat a target region using VHEE. The VHEE Strong Focusing experiment aims to show highly penetrating, focused VHEE at depths >10 cm into a water phantom, and show the possibility to treat a target region using three focused VHEE beams delivered in a weighted way to produce a spread out dose peak [7]. To measure a peak in dose deep in water, long holders were designed and printed. Each of them can hold 13 to 26 radiochromic films with 5 mm between two consecutive films. To find the correct longitudinal position of the peak in dose, the beam size was scanned longitudinally in water thanks to the YAG screen and the C-Robot, in order to find a vertical or horizontal beam size waist. Beam waists and peaks in dose were obtained in water with different quadrupole parameters.

VHEE Scatterers

A VHEE treatment beam would require to have a uniform transverse profile at the patient. These steps could be achieved entirely through beam optics, however, the solution would likely be susceptible to initial beam distribution, misalignment and jitter. Furthermore, in the case of a rotating gantry, the cost of rotating many large, heavy quadrupoles would be high. Another solution is to achieve the magnification with a flat scattering foil, and the flattening with a foil with a more complex shape. Such scatterers were tested in CLEAR and gave really promising results. A schematics of the setup and the flat beam profiles measured with a 200 MeV electron beam and with these two scatterers are shown in Figure 6 [11].

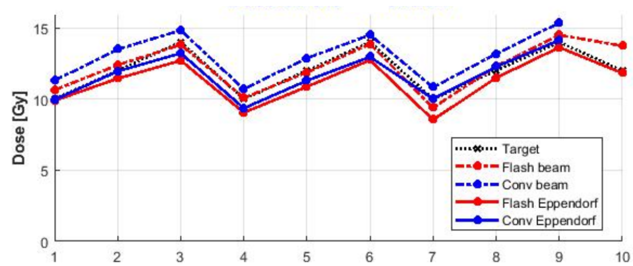

Figure 5: Doses delivered on 10 samples of ZFE, targeting 10, 12 and 14 Gy for both UHDR (or FLASH) and Conventional irradiations.

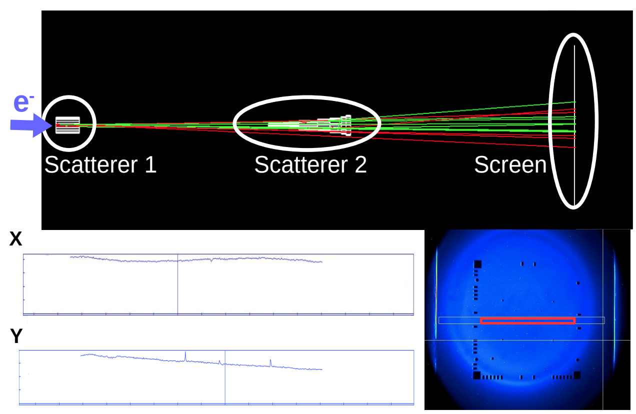

Figure 6: Schematics of the scatterers study (top) and the flat transverse beam profiles obtained on a YAG screen (bottom).

CONCLUSION

The CLEAR user facility at CERN has been intensively used to study the potential use of Very High Energy Electrons (VHEE) in cancer radiotherapy. In particular, irradiations tests have been performed in the high dose rate regime, which has arisen a lot of interest for the so called FLASH biological effect, in which cancer cells are damaged while healthy tissue is largely spared. High dose rate dosimetry, though, poses a number of challenges, both to validate standard or new methods of passive dosimetry, like radiochromic films and RPLs, and to develop new tools to irradiate different types of samples with the required beam parameters. Numerous dosimetry studies and experiments were done in CLEAR and promising results were obtained thanks to the C-Robot and the collaboration with CHUV for samples irradiations.

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