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RESEARCH ON ULTRA-HIGH ENERGY ELECTRON BEAMS FOR FLASH RADIATION THERAPY AT ELSA

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Abstract

Ultra-high energy electrons (UHEE) are used to investigate their effect on tumor cells and healthy tissue in short pulses of microseconds at the electron accelerator facility ELSA. This may enable highly efficient treatment of deep-seated tumors due to the FLASH effect. In a preliminary setting electrons with an energy of 1.2 GeV are used to irradiate cell samples which are located inside a water volume, representing the human body. Irradiation occurs with dose rates of up to 10 MGy/s due to the short pulse lengths of 250 ns. The relative biological effectiveness (RBE) can be determined by assessing the cell survival of tissues under FLASH and conventional conditions. For a precise dose determination, dose measurements via radiochromic films are utilized and compared to simulations with Geant4, that reproduce the electromagnetic shower process.

FLASH@ELSA

The accelerator facility ELSA at the University of Bonn is a three stage accelerator. The first stage, a linear accelerator (linac) accelerates electrons, provided by either a thermal or a polarized electron source, up to 26 MeV. After that the electrons are injected into the booster synchrotron and accelerated up to 1.6 GeV, followed by the injection with a rate of up to 50 Hz into the stretcher ring. In the stretcher ring the electrons can be further accelerated up to 3.2 GeV.

FLASH Operation Mode

A new implemented mode of operation enables direct extraction from the booster of electron pulses with a pulse length of 250 ns and charges of up to 2.5 nC to an experimental area used as an irradiation site. Therefore, the electrons are extracted from the booster synchrotron and guided through a small section of the stretcher ring acting as a transfer beamline to the experimental site (see Fig. 1).

Experimental Setup

After extraction from the beamline, the electron pulses pass through several detectors before irradiating cell samples or detectors placed inside a water volume (Fig. 2). Straight after the beamline exit an integrating current transformer (ICT) measures the charge of the pulse. In front of the water volume the transverse beam profile and position is measured with a luminescence screen (Chromox) camera setup. It is analyzed by an in-house developed image analysis software package [1]. Passing through the water volume the beam produces an electromagnetic shower irradiating a sample placed within the volume, which simulates the interaction

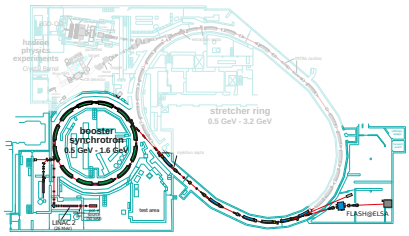

Figure 1: Accelerator facility ELSA in the current FLASH operation mode.

with the human body. Radiochromic films (GafChromic-EBT3) are placed right behind the samples and provide dose measurements with a spatial resolution of down to 25 µm. This setup provides sufficient information on the beam profile and position as well as the dose profile to allow irradiation with knowledge on the applied dose even under small shifts of the beam position and different shapes of the beam profile.

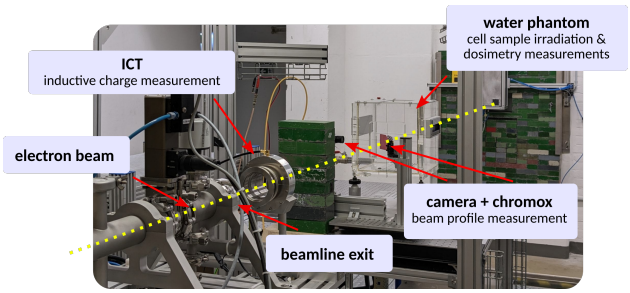

Figure 2: Experimental setup for cell sample irradiation and dosimetry measurements.

DOSE SIMULATIONS AND MEASUREMENTS

To monitor the efficacy of the biological effect of UHEE FLASH irradiation on cell samples a precise dose determination is necessary. Therefore, tools to determine the applied dose were developed. In the current setup this is done by the evaluation of GafChromic-EBT3 films and comparison with simulations in Geant4 [2–4].

Geant4 Simulations

The setup of the experiment includes a 1.22 m long drift in air, the Chromox screen in front of the water volume and the water volume ($26 \times 28 \times 26\,\mathrm{cm}^3$). It is reconstructed close to

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scale reconstructed [5] in Geant4 [2–4]. The water volume is sliced into voxels of $5 \times 5 \times 5$ mm size, which can be scaled according to the size of the cell samples. These voxels are implemented as actively monitored volume, providing information of each physical interaction inside a voxel caused by the electromagnetic shower. The deposited energy, the particle type, energy and position is stored in a collection of hits, which is used to analyze and reconstruct the electromagnetic shower within the water volume (see Fig. 3).

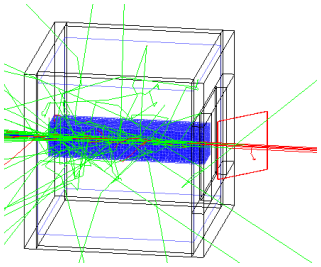

Figure 3: Visualisation of an exemplary electromagnetic shower in the set up geometry in Geant4 [2–4] [5].

For example the hit collection can be used to reconstruct the longitudinal or transverse shape of the shower profile. Figure 4 shows the simulated transverse dose distribution for different depths in the resolution of $5 \times 5 \times 5\,\mathrm{mm}^3$ voxels. While at 0 cm depth only the profile of the beam ($\sigma_x = 6.8$ mm and $\sigma_y = 1.0$ mm,) is visible, the increase of the dose in the adjacent voxels due to the electromagnetic shower is visible at deeper depths. To be able to compare the simulation to the measurements the dose is normalized to 1 nC. Further information on the simulations in Geant4 [2–4] and prior measurements can be found in Ref. [5].

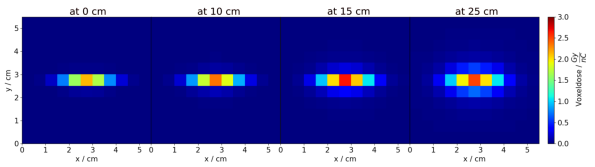

Figure 4: Dose distribution of the $5 \times 5 \times 5\,\mathrm{mm}^3$ voxels within layers at different depths, with the averaged dose in a voxel [5].

Dose Measurements with GafChromic

For measuring the applied dose, currently radiochromic GafChromic-EBT3 films are used. The film is placed 5 mm behind the cell sample. In order to obtain a dose value from the irradiated GafChromic films, they are scanned using a 16-bit color depth transmission scanner (EPSON 12000XL) and analyzed with an in-house developed Python program. A calibration, mapping the color profile of the irradiated GafChromic films to a dose profile, is performed with a set of calibration films irradiated with a known dose from a 12 MeV medical linac (provided by the Department of Radiooncology, University Hospital Bonn). Due to time dependent post irradiation darkening effects, the films are scanned after a period of 24 hours after irradiation. As a preliminary prediction of the applied dose in the cell samples, a 3.5 mm x 1 mm square (as a measure of sample size) is represented around the profile maximum. While the dose is not constant over the irradiated area a Gaussian profile is fit to the calibrated dose profile of the film and analytically integrated over the area of interest regarding the size of the cell samples, to obtain the average applied dose in one sample. The calculated sample dose is additionally cross-checked with a numerical integral over the area.

Comparison of Simulation and Measurement

Validating the usability of GafChromic-EBT3 under UHEE FLASH conditions is necessary, since the films are not designed and verified for dose rates up to 10 MGy/s and beam energies in the range of GeV. For that a depth dose curve measurement was performed and compared with results from the Geant4 [2–4] simulation. Therefore, GafChromic-EBT3 films were placed at different depths and irradiated with a single electron pulse of $Q = 0.953(7)$ nC. The beam width of $\sigma_x = 3.07$ mm and $\sigma_y = 3.38$ mm where taken into account for the simulation, which is shown in comparison to the measurement in Fig. 5. One can conclude from the agreement between the measurement and simulation of the depth dose curves, that the GafChromic-EBT3 yields valid results under the stated conditions. It is to note that a former measurement in [5] was showing a strong deviation between measurement and simulation, due to malfunctioning of the specifically used GafChromic-EBT3 films. To verify this behavior further, various comparisons to other detectors are and will be performed.

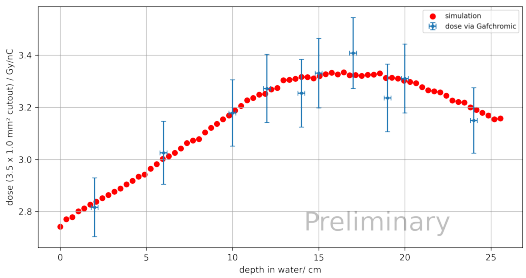

Figure 5: Measurement of the depth dose curve with GafChromic-EBT3 films in comparison to the simulation with same beam properties: $\sigma_x = 3.07$ mm and $\sigma_y = 3.38$ mm.

FIRST *IN VITRO* MEASUREMENT

A first *in vitro* measurement is currently performed at FLASH@ELSA using human breast cancer cell samples. To determine the effect of UHEE FLASH irradiation on those samples a standardized methodical procedure is used. A cul-

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tivated cell culture inside a nutrient solution is centrifuged in the tip of a reaction tube. The cell sample concentrated in the tip of the tube is placed in the water volume at 17 cm (dose maximum, see Fig. 5) and aligned to the beam. The sample is then irradiated simultaneous with a GafChromic-EBT3 film to measure the applied dose. After the irradiation the cell sample is transferred back to the laboratory, where they are incubated and counted after two weeks. The difference in the number of survived cells in an irradiated sample compared to a control sample (non irradiated sample) gives the survival rate:

$$R_{\text{survival}} = \frac{A_{\text{irradiated}}}{A_{\text{control}}}, \quad (1)$$

with $A_{\text{irradiated}}$ and A_{control} are the counts of survived cells after two weeks.

First measurements show, that the survival rate measurement of an irradiation at ELSA with an energy of 1.2 GeV, $\sigma_x \approx 3$ mm, $\sigma_y \approx 3$ mm and a pulse charge range from 0.1 nC to 1.5 nC (yielding doses between 0.5 Gy and 6.2 Gy) can be performed. As result, it could be proven that the current setup and mode of operation as suitable for UHEE FLASH cell irradiation.

INVESTIGATIONS ON ADDITIONAL DOSIMETRY TECHNIQUES

Beside the dose measurements with GafChromic-EBT3 films several measurement techniques based on the usage of different detector types, such as luminous screens, Cherenkov radiation, ionisation chambers and diamond based detectors, are under investigation. Therefore, a setup was installed to measure the shower profile inside the water volume using a Chromox screen. Investigation of the light-yield of the screen measured over small areas in relation to the applied dose, is ongoing to develop a monitor for real-time dosimetry. The usability in water and a possible energy dependence is currently tested. Another currently investigated measurement technique is based on Cherenkov light, produced by the beam and shower inside the water volume, for real-time shower profile monitoring. In first tests the emitted Cherenkov light was observed shown in Fig. 6 from a camera looking from the side onto the water volume.

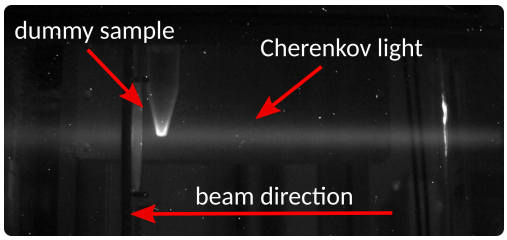

Figure 6: Picture of Cherenkov light produced by the beam and shower inside the water volume.

CONCLUSION

Measurements of the depth dose curve using GafChromic-EBT3 films agree with a performed simulation done in Geant4 [2–4] and provide first evidence for the usability of GafChromic-EBT3 under FLASH conditions at ELSA. Furthermore, a first *in vitro* measurement using human breast cancer cell samples is currently performed. The current setup and mode of operation as suitable for UHEE FLASH cell irradiation. Additionally different measurement techniques, including a luminous screens (Chromox) and Cherenkov radiation are currently tested and under investigation to improve the dosimetry and efficiency for precise cell sample irradiation.

ACKNOWLEDGEMENTS

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