COMPARISON OF MEASUREMENTS AND SIMULATION RESULTS OF DOSE FOR THE FLASH RADIATION THERAPY BEAMLINE AT PITZ


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Abstract
The high-brightness electron beam at the Photo Injector Test facility at DESY in Zeuthen (PITZ) is now also used for FLASHlab@PITZ: an R&D platform for studying radiation biology and the FLASH effect in radiation therapy. The available parameter space of the electron beam with a momentum of 22 MeV/c allows bunch charges from 1 pC up to 5 nC, bunch durations of 0.1–60 ps and bunch train lengths up to 1 ms. The number of bunches in the single train can currently be varied between 1 and 1000 bunches, with an upgrade to 4500 foreseen in 2023. Radiation biology studies require accurate dose prediction, therefore Monte Carlo simulations based on the FLUKA code were performed. According to estimations, dose delivery of 0.002 Gy (low charge case 1 pC) and 10 Gy (high charge case 5 nC) is possible, if the beam is confined to a circular area with a radius of 5 mm with a lead collimator. For the Monte Carlo simulations, the experimental setup was accurately modelled, including the exit window, lead collimator, etc. Dose measurements were used to compare simulations with experiments. Dose profiles were experimentally measured with Gafchromic films and then compared with Monte Carlo simulations. The first experiments at FLASHlab@PITZ in 2023 have demonstrated flexible dose options for studying the FLASH effect and radiation biology studies.

INTRODUCTION
The use of electron beams with energies in the range of 5 and 20 MeV has been widely explored in the study of radiation biochemical effects [1, 2]. The interaction of these energy electrons with biological matter leads to ionization, which can cause water radiolysis and DNA damage and lead to a range of biological effects [3]. Such effects have been extensively studied in the context of radiation biology with conventional dose rates of 0.05 Gy/s.

In recent years, there has been a growing interest in using high-energy electron beams to study the FLASH effect in cancer radiation therapy. The FLASH effect, achieved at ultra-high dose rates (UHDR, 40 Gy/s), can lead to the faster and more efficient delivery of radiation dose to a tumor while reducing the damage to the sour-rounding healthy tissue [4, 5]. At the Photo Injector Test facility at DESY in Zeuthen (PITZ), high-brightness electron beams with a momentum of up to 22 MeV/c are being used to study the biological effects of UHDR radiation compared to conventional dose rates [6].

The FLUKA code is a widely used Monte Carlo simulation tool for the study of radiation physics, dosimetry, and medical physics [7, 8]. It allows for the simulation of complex geometries, beamline components, and biological materials with high accuracy and flexibility. In our study, we used FLUKA to simulate the dose delivery of electron beams in the experimental setup of radiation biology.

In this work, we present a comparison of dose measurements and simulation results using a high-brightness electron beam at the PITZ facility. Using the FLUKA code, we performed Monte Carlo simulations to predict the dose delivery for different bunch charges and configurations. The simulation results were then validated against dose measurements obtained using Gafchromic films.

METHODS AND MATERIALS
Sample Irradiation Setup
The sample irradiation experiments were conducted at the PITZ. The PITZ photo-injector comprises an L-band RF gun that can produce electron beams with a pulse duration of up to 1 ms and a repetition rate of 1-10 Hz. These electron beams can be accelerated to energies up to 22 MeV, and the bunch charges can range from 1 pc up to 5 nC, with bunch durations of 0.1-60 ps. The PITZ facility is equipped with a large diagnostic suite to measure various beam parameters including energy spread, charge, beam size, emittance, and beam position.

The experimental setup for radiation biology is located in open air in front of an exit window of the accelerator (see Fig. 1). The exit window is 50 µm thick titanium with a diameter of 34 mm which allows the beam to pass into the open air and irradiate the samples. A lead brick with a 30 mm hole is placed between the exit window and the experiment station to provide shielding against secondary X-rays generated during the experiment.

To hold the Eppendorf tubes that contain the aqueous samples, a custom tube holder made of PMMA was designed and constructed at the TH Wildau. The holder also has slots to hold Gafchromic films in front of and behind the 0.5 or 0.2 mL Eppendorf tubes to measure the delivered dose distribution. The sample holder was fixed on a transversely movable stage to position individual samples in the electron beam. This allowed us to achieve the necessary flexibility required to accommodate varying sample volumes and geometries inherent in different experimental models. Additionally, this approach enabled us to measure the dose distribution at both the input and output of the
radiation beam. The Gafchromic films were then analysed to obtain the dose profiles before and after the samples, which were used to determine the dose delivered to the samples. This approach ensured that the samples received the desired radiation dose and that the measurement of the dose distribution was accurate and reliable.

**Measurements**

Gafchromic films are commonly used in FLASH radiation therapy. They are designed to measure absorbed dose of ionizing radiation. At PITZ, EBT-XD films are used which have a dynamic range from 0.1 Gy up to 200 Gy according to the manufacturer. The optimum dose range is from 0.4 Gy up to 40 Gy. The films consist of a 25 µm thin active layer of marker dye, stabilizers and other components sandwiched between two 125 µm matte polyester substrates [9].

Besides of their minimal beam energy dependence (lower than 5% between 100 keV and 18 MeV), EBT-XD films are near tissue equivalent and provide a very high spatial resolution down to a few µm. The response of the films is also dose rate independent up to 10^10 Gy/s and therefore perfectly suitable for dosimetry at conventional dose rates and at ultra-high dose rates used in FLASH radiation therapy [10-12].

Each batch of films needs to be calibrated due to small differences in composition and thickness of the active layer. The calibration needs to be done in a homogeneous and well-defined radiation field. The calibration of films used at PITZ was done at the Charite, a university hospital in Berlin using a clinical, commercially available radiation therapy device from the company Varian. The device can provide a homogeneous radiation field of a size of 26 by 26 cm². The films were placed in this field and sandwiched between multiple scattering plates. Reference dosimetry measurements were done using an ionization chamber from PTW in combination with a Unidos electrometer. The dose rate used was 0.1 Gy/s which is the maximum dose rate this device can provide for a homogeneous field. For the calibration, multiple films were irradiated with doses between 0.1 Gy and 300 Gy as measured by the ionization chamber.

For digitization of the films, the manufacturer recommends using a large 48-bit colour depth flatbed colour scanner to decrease lateral effects. At PITZ, a professional flatbed scanner, the Epson Expression 12000 XL is used. The scanner measures the red, green and blue colour components of the film at a colour depth of 16 bit per channel. In addition, the films darken over time and it is common procedure to do the readout of the films 24 hours after irradiation. The calibration is then fitted to a function of the form:

\[
P_x(D) = a + b/(D - c)
\]

where \(P_x(D)\) is the film response in scanner channel \(x\) from a delivered dose \(D\) and \(a, b\) and \(c\) are parameters to be fitted. For radiation experiments, the inverse of the response function is then used to calculate the dose that the films received. Self-written Matlab codes are used for the analysis.

**Monte Carlo Simulation of the Experiment Based on the FLUKA Code**

To simulate the experimental setup and evaluate the dose distribution in the samples, a Monte Carlo simulation based on the FLUKA code was performed. The geometry of the experimental setup, including Eppendorf tubes, the sample holder, and Gafchromic films, was accurately reproduced in the simulation. To improve the accuracy of the simulation results, the measured beam profile from a YAG screen located approximately 143 mm in front of the exit window is used as the initial beam profile. The distance from the exit window to the Eppendorf tube was set to 140 mm in accordance with the experimental setup.

Simulation results were compared with experimental measurements to validate the FLUKA model, and the resulting dose profiles in simulations provide a detailed view of the dose distribution in the samples. This made it possible to optimize the experimental scheme and estimate the delivered dose with high accuracy.

**COMPARISON OF EXPERIMENTAL AND SIMULATED DOSES**

In this study, the goal was to evaluate the accuracy of the delivered dose predictions from FLUKA by comparing them with dose measurements obtained using Gafchromic films. To irradiate the films and Eppendorf tubes, they were placed in polylactide (PMMA) slide holders and mounted on the transversely moving stage located in front of the beam. The design of the stage allowed for each sample to be moved individually into the beam for irradiation. The samples were irradiated with an 18 MeV beam to deliver doses of 2 Gy, 4 Gy, 8 Gy, and 16 Gy, with two repetitions made for each dose rate of 1.5-10^5 Gy/s. FLUKA simulations were used to determine the charge and number of bunches necessary to deliver the required dose.

Uniform dose distribution is a critical aspect of irradiating chemical, biochemical, and biological samples. Therefore, FLUKA simulations were used to determine the required beam profile at the YAG screen and scattering plate thickness to ensure dose homogeneity in the sample. Simulations show that a 10 mm PMMA scattering plate placed in front of the lead brick effectively achieves the required dose homogeneity. According to the Monte Carlo simulation results, Fig. 2 shows the dose distribution within the...
Eppendorf tube, indicating a uniformity of over 90% in the transverse plane and over 85% in the longitudinal direction, accounting for the specific shape of the tube. This setup produced a uniform dose distribution in a tube up to 7 mm high.

![Figure 2: The dose distribution within the Eppendorf tube. The colour scale indicates the percentage of dose uniformity, with over 90% uniformity in the (a) transverse plane and over 85% in the (b) longitudinal direction.](image)

The dose distribution in the transverse plane obtained from the experimental films is depicted in Fig. 3 (a) and (c), where a predicted dose of 16 Gy was delivered to the sample. The solid line in the figures outlines the region of interest for the Eppendorf tubes. The corresponding dose distributions in the region of interest are shown in Fig. 3(b) and (d) with values of 19.3 Gy and 14.25 Gy in front of and behind the Eppendorf tubes, respectively. Analysis of the films showed that the dose inside the tube was 91% of the dose measured before Eppendorf. As a result, the actual dose delivered to the sample was 17.56 Gy, which is 9.7% higher than the expected dose.

![Figure 3: Dose profiles of experimental films (a) before and (c) after the Eppendorf tubes, with a predicted 16 Gy dose delivered to the sample, and the solid line marks the area of interest for the Eppendorf tubes. (b) and (d) show the dose distributions in the area of interest.](image)

As shown in Fig. 4(a), a comparison was made between the simulated and measured doses for varying numbers of bunches. The solid line represents simulation data, while the dotted line represents measurement data. The red curve corresponds to the average dose at the centre of the tube, while the blue and purple curves show the average dose of the films (before and after) on the interesting surface.

![Figure 4: (a) Comparison between simulation and measurement results for different numbers of bunches. The red curve represents the average dose at the center of the tube, while the blue and purple curves show the average dose of the films (before and after) on the surface. (b) Dose rate and dose in a 0.27 ml sample at the bottom of the tube as a function of the number of bunches in a single train.](image)

The curves plotted in Fig. 4 (a) indicate a satisfactory level of agreement between the simulation and experimental data, with a deviation of less than 9.7%. Fig. 4(b) shows the dose rate and dose in a 0.27 ml sample at the bottom of the Eppendorf tube as a function of the number of bunches in a single train.

CONCLUSION

In this study, we evaluated the accuracy of FLUKA simulation predictions for the total dose delivered in biological samples. We used Gafchromic films to measure the dose and compared the results with FLUKA simulations. Our experiments revealed that the actual dose delivered to the sample was 9.7% higher than the expected dose, which emphasizes the importance of measuring the dose delivered in biological samples. FLUKA simulations were used to determine the required beam profile and scattering plate thickness to ensure dose homogeneity in the sample. Our simulations indicated that a 10 mm PMMA scattering plate placed in front of the lead brick produced a uniform dose distribution in a tube up to 7 mm high. Our results showed that the dose distribution within the Eppendorf tube was uniform in the transverse plane (over 90%) and in the longitudinal direction (over 85%), accounting for the specific shape of the tube.

 Moreover, a satisfactory level of agreement between simulation and experimental data, with a deviation of less than 9.7% were observed in the delivered dose. Our findings indicate that FLUKA simulations can be an effective tool for predicting the dose distribution in biological samples. These results can be used to optimize the irradiation of biological samples, ensuring that the desired dose is delivered with high accuracy and uniformity. Overall, our study provides useful insights for researchers working on radiation biology and related fields.
REFERENCES


