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Experimental verification of the applicability of the AQURE IOERT accelerator for FLASH radiotherapy

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Abstract

Introduction: FLASH radiotherapy is based on delivering an ultra-high dose of ionizing radiation in a very short time, which allows for the enhanced protection of healthy tissues and the effective destruction of tumour tissues. The paper presents experimental verification of the applicability of the intraoperative electron radiotherapy (IOERT) accelerator to obtain electron beams with ultra-high dose rates. The results of electron beam dosimetric measurements were compared with simulations to verify the parameters of the electron beams obtained in FLASH mode.

Material and Methods: The IOERT AQURE accelerator is designed and manufactured at the National Centre for Nuclear Research. The device provides electron beams with energies in the energy range of 4-12 MeV. The accelerator was recently upgraded to deliver ultra-high-dose rates (FLASH). The emitted electron beams were verified by percentage dose depth (PDD) and beam profile measurements using Gafchromic EBT-XD films. The measurement results were compared with Monte Carlo simulations performed using the Geant4 application.

Results: Conventional and FLASH electron beam parameters, i.e. depths of doses, most probable beam energies at the phantom surface, and average beam energies at the phantom surface were determined experimentally for the upgraded IOERT accelerator for 6 MeV and 9 MeV. The results of dose measurements showed that the accelerator can provide electron beams with homogeneous and symmetrical fields with dose rates up to 300 Gy/s ± 6 Gy/s, for an electron beam at a nominal energy of 6 MeV, and up to 440 Gy/s ± 9 Gy/s at a nominal energy of 9 MeV. A comparison of measured and simulated PDDs and dose profiles for FLASH beams showed good agreement (no worse than 90%) under the gamma index of 3%/3 mm.

Conclusions: The results obtained confirm that the upgraded intraoperative accelerator can be used in planned, pre-clinical radiobiology experiments in both conventional and ultra-high dose rate (FLASH-RT) modes.

Keywords: IOERT; ultra-high dose rate; FLASH; intraoperative electron accelerator; FLASH electrons.

Introduction

Currently, cancers in the world, right after cardiovascular diseases, cause the most premature deaths. There are various methods of fighting cancer, including surgery, chemotherapy, and radiation therapy. Intraoperative electron radiation therapy (IOERT) is a technique for using ionizing radiation to treat cancer. This method consists of administering a high dose of radiation to the cancerous tumour or the tumour bed after the excision of the tumour while the surgical operation is still in progress.

One of the breakthroughs in radiation therapy in recent years is the FLASH radiotherapy. In this technique, a high radiation dose is administered in a very short time (less than 200 ms) with an ultra-high dose rate (tens of Gy/s). While the mechanism of the FLASH effect is still not fully understood, the effect of saving healthy tissues was noticed already in the 60s of the twentieth century when it was shown that non-cancerous mammalian cells irradiated at ultra-high dose rates had greater viability than those irradiated at conventional dose rates.[1] Interest in this topic increased rapidly after 2014 when it was shown that irradiation

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Authors' contribution:
A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article.

of the chest of mice with a single fraction of 17 Gy at conventional dose rate (0.03 Gy/s) caused "moderate" and "severe" areas of pulmonary fibrosis 36 weeks after irradiation, while the same dose at high doses rates (40-60 Gy/s) induced significantly reduced pulmonary fibrosis.[2] At that time, this effect was again assessed and called the FLASH effect. Nowadays, the use of ultra-high dose rate beams appears to be a great benefit in radiotherapy, and electron accelerators are one of the most promising devices that may find wide application in FLASH radiotherapy (FLASH-RT).[3]

Currently, the use of high dose rates is limited due to the availability of high-quality FLASH beam-generating devices. These are mostly clinical linear accelerators that have been upgraded to produce a beam with FLASH parameters which were used in preclinical and clinical research.[4] Another challenge associated with the use of FLASH-RT in a clinical context is the dosimetry of the ultra-high dose rate beams and real-time beam monitoring.[5] To date, no guidelines for FLASH beam measurement techniques have been established, and the most used methods are well-known passive or new experimental systems. Passive dosimetry, such as films or alanine, is currently used for both research and clinical purposes. Using FLASH radiotherapy in clinical applications requires a new, real-time dosimetric method.[6]

This paper presents the experimental verification of the applicability of the intraoperative electron accelerator AQURE to obtain beams with ultra-high dose rates. For this purpose, simulations and analyses of the energy spectra of beams in conventional and ultra-high dose rate modes were performed. Monte Carlo simulations of the dose distributions in conventional and FLASH modes were carried out, which allowed to determine the possible directions and scope of the upgrading works of the conventional accelerator for IOERT. The results obtained were compared with measurements taken on an upgraded accelerator.

Materials and Methods

The upgrade of the AQURE accelerator to obtain ultra-high dose rate beams was carried out in several steps. First, electron beam dynamics were simulated using the General Particle Tracer (GPT) code, and the resulting data were subsequently used for Monte Carlo simulations with the Geant4 code. The simulation results have shown the possibility of obtaining FLASH beams for energies of 6 and 9 MeV, and then the device and its components were updated to the FLASH mode and measurements of the FLASH electron beams were carried out.

Electron Linear Accelerator System

The AQURE accelerator designed and manufactured at the National Centre for Nuclear Research in cooperation with the Greater Poland Cancer Centre is intended for use in the patient's treatment in intraoperative therapy. This radiotherapeutic device produces beams of electrons with energies from 4 MeV to 12 MeV, a maximum dose rate of 10 Gy/min, useful for standard intraoperative radiotherapy. The accelerator is built on a movable base ensuring the movement of the whole device as well as the ability to move the head relative to the base. The mechanical design of the device allows it to be flexible regarding irradiation angles.[7] The accelerator head can be tilted in two planes and rotated on the column, allowing the head to be tilted from/to the column in the range of 45° and 30° as well as the head to the sides by ±45°. The head can be positioned within a relatively large working area. All possible movements of the accelerator are indicated by arrows in **Figure 1**. This mechanical design offers great possibilities for multi-directional electron beam therapy, which is also an advantage when using the accelerator in preclinical research.

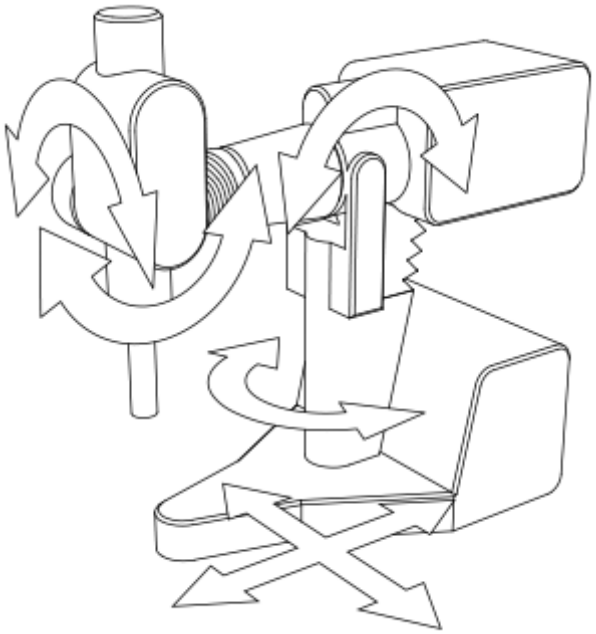


Figure 1. The schematic drawing of the AQURE accelerator with all possible movements marked.[8]

In AQURE the source of electrons in the accelerating structure is the triode electron gun controlled by a 15 kV gun modulator. Electrons are shot into the structure with an initial energy of several keV and then accelerated in the electromagnetic field generated by the magnetron MG6090.[9] In the AQURE accelerator, the duration of a single pulse can be adjusted in a range from 2 to 5 μs. The pulse repetition rate is adjustable in the range from 50 to 300 Hz. In comparison, conventional linear medical accelerators used to deliver radiotherapy produce radiation pulses with durations of 3 to 6 μs and pulse repetition rates of 60 to 360 Hz.[10] In conventional IOERT mode, the operator determines the dose, measured by an internal dosimetry system based on an open, dual ionization chamber.

The electron beam that exits the accelerating structure through the exit window is shaped by a beam-forming system that includes scattering foils, a fixed collimator, and applicators. **Figure 2** shows the electron beam forming system of the AQURE accelerator.[11] The electron beam emitted by the accelerator should be homogeneous and symmetrical, according to the requirements of relevant standards and guidelines, allowing irradiation of the field shaped by 40 to 100 mm diameter applicators.[12] The AQURE source surface distance (SSD) is 60 cm; therefore, all dosimetry measurements and Monte Carlo simulations were performed at this distance for PMMA applicators with diameters of 50 and 100 mm. The 100 mm diameter applicator was chosen for measurements and simulations because it is the reference applicator for IOERT accelerator beam measurements, while the 50 mm diameter applicator is used for irradiating biological material. The conventional intraoperative beams were verified in radiobiological research.[13] The IOERT radiotherapy is based on a single irradiation of the patient, which is also the principle in planned irradiation using a FLASH beam. Thus, the upgrade of the IOERT accelerator can be a beneficial solution for conducting scientific research using an electron beam with FLASH parameters.[3]

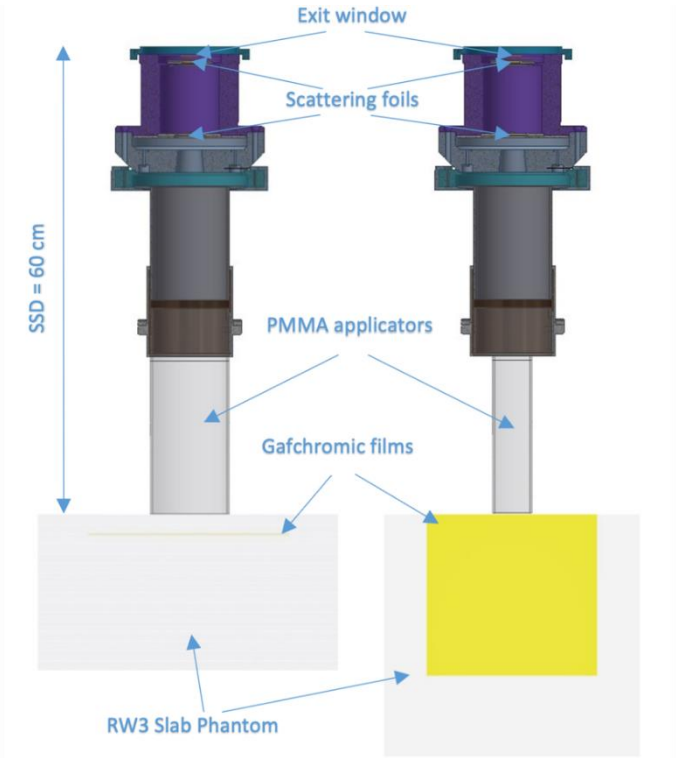


Figure 2. Cross-section of the beam forming system from the exit window of the AQURE IOERT acceleration section to the PMMA applicators and the RW3 Slab Phantom used in FLASH mode beam measurements and Monte Carlo simulations, along with the placed Gafchromic film. On the left: applicator with a diameter of 100 mm. On the right: applicator with a diameter of 50 mm.

Optimization of FLASH electron beam

The electron absorbed dose rate $\dot{D}$ ($Gy \cdot s^{-1}$) depends on the electron flux density $\dot{\varphi}$ ($cm^{-2} \cdot s^{-1}$), the collision stopping power $\frac{dE}{dx}$ ($MeV \cdot cm^2 \cdot g^{-1}$), and the density of the irradiated medium ρ:

$$\dot{D} = \dot{\varphi}\left(-\frac{dE}{\rho\, dx}\right) \quad \text{Eq. 1}$$

For a specific initial energy of the electron beam and a thin layer of the irradiated medium, **Equation 1** reduces to a dependence on a beam current. Therefore, obtaining an ultra-high dose rate electron beam begins with achieving the expected intensity and energy parameters of the electrons accelerated using an electromagnetic field in the linear accelerator.

To achieve the maximum possible dose rate, it is necessary to optimise the influence of the generated RF (Radio Frequency) power and the electron gun power supply parameters on the radiation dose rate. An increase in the beam current injected into the structure can be achieved by changing the electron gun setting parameters.

To estimate the maximum dose rate and to model electron beam spectra for low and high beam currents, simulations were carried out using the General Particle Tracer (GPT).[14] In GPT simulations, electron spectra were obtained for expected beam energies of 6 and 9 MeV for low (0.02 A) and high average currents (0.98 A) corresponding to conventional and FLASH beams, respectively (see **Figure 3**). Energy spectra simulations were performed consistently for various electron beam parameters. GPT simulations were performed using the same statistics for both energies with the energy bin size of 0.03 MeV. The dispersion in the simulated electron spectra visible in **Figure 3** is caused by limited statistics. Increasing the statistics of the electrons emitted in the simulations would allow for reduced uncertainty, but significantly increase simulation time. As the structure was optimised for 9 MeV, the spectrum for a low current 6 MeV beam is broader than for 9 MeV. Increasing the current results in a broader spectrum for both energies. The simulations also provided the most probable beam energy at the exit window (E_p) and the mean beam energy at the exit window (E_0). The values of E_p for the nominal 6 MeV energy beam are 7.62 MeV for low current (conventional mode) and 7.77 MeV for high current (FLASH mode). E_p for 9 MeV nominal energy beam is 10.44 MeV for low current and 10.60 MeV for high current. The mean beam energy for a nominal 6 MeV electron beam for low current is 6.32 MeV and 6.02 MeV for high current. The values of E_0 are 9.08 MeV for a low current 9 MeV beam and 8.77 MeV for a high current 9 MeV beam. The results of the GPT simulation are higher than assumed nominal beam energies due to the loss of up to about 1 MeV in the beam forming system, i.e. on the scattering foils. The energy spectra obtained are broadened towards the lower energies of the electron beam, which agrees with the E_0, and E_p values.

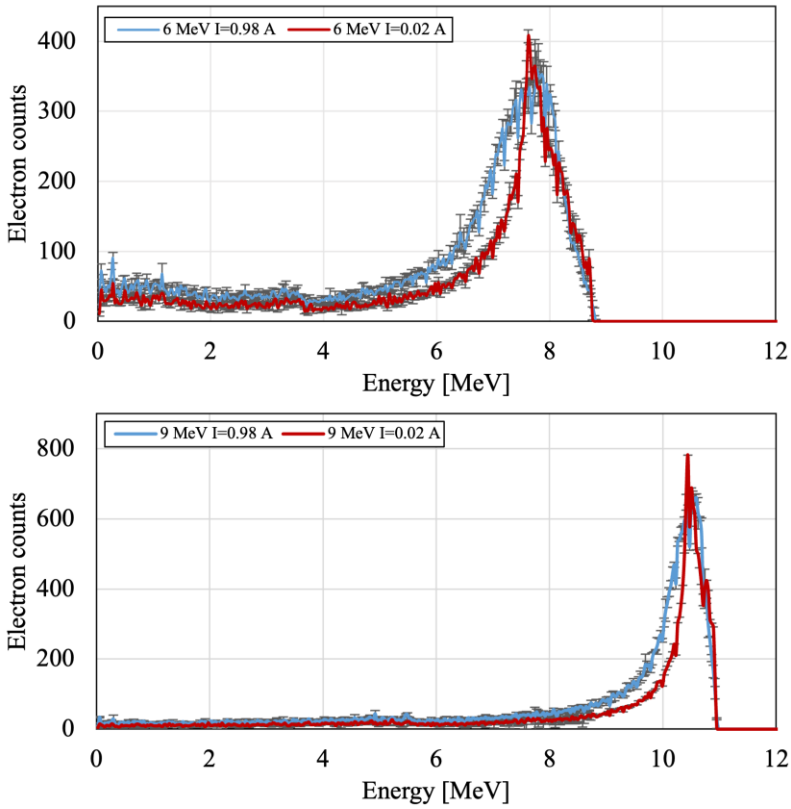


Figure 3. Energy spectra for two current values I=0.02 A (low current) and I=0.98 A (higher current) obtained from simulations in the GPT programme for nominal 6 MeV on the top and 9 MeV on the bottom normalized to electron counts.

Monte Carlo simulations

The performance of the system and the feasibility of upgrading the IOERT AQURE accelerator to produce an ultra-high dose electron beam were simulated using a Monte Carlo method. The Geant4 application, described in detail elsewhere[11], was used to simulate electron beams at a conventional dose rate. The FLASH beam simulation application was modified to consider the initial energy spectrum of the electron beam and the geometry of the applicators used in the FLASH experiments.

Electron beam energy spectra calculated using the GPT code[15] were used as input data for the Monte Carlo simulation at low and high beam current regimes (see **Figure 3**). The model of the beam-forming system used in the Monte Carlo simulation closely reproduces the beam-forming system of the AQURE accelerator as shown in **Figure 2**. Both conventional and FLASH dose distributions were simulated for the beams of nominal energy of 6 and 9 MeV in the water phantom. The percentage depth dose (PDD) was calculated based on the energy deposited in the tubular column of 5 mm diameter centred on the beam axis and divided into 2 mm thick slices. The off-axis dose profiles were calculated at the depth of maximum dose deposition (R_{100}) in a set of concentric rings of 2.5 mm radial width and 2 mm thickness. Because of the axial symmetry implied in the Monte Carlo simulation radial coordinates are used to draw dose profiles.

Dosimetry of the electron beam

Dosimetry of radiation beams is well known and defined in recommendations issued, among others, by the International Atomic Energy Agency (IAEA TRS 398), the American Association of Medical Physicists (AAPM TG 51)[16], and the International Electrotechnical Commission (IEC 60976)[17]. In this study, measurements in the conventional mode were performed according to IEC standards using a diode detector PTW 60023 microSilicon Dosimetry Diode (PTW, Freiburg, Germany) and an ionization chamber – the PTW Advanced Markus Electron Chamber in the PTW MP3 Water Phantom

The dosimetry of FLASH beams is still a challenge because dosimetry of ultra-high dose rate beams requires high spatial and temporal resolution of the detector used, as well as independence from dose rate in the range of tens to even thousands of Gy/s used.[18] Due to the lack of in vivo detectors dedicated to high dose rates, dosimetric measurements are performed mainly with passive dosimetry e.g. radiochromic films. It is also possible to use different methods e.g., alanine dosimetry and TLD, but their limitation is that they can only perform point measurements. The use of ionisation chambers in clinical conditions is hardly possible due to the high dose of the pulse emitted in the FLASH-RT, which negatively affects the efficiency of the measurements and distorts the results. Only a few papers have appeared on

developing a method for correcting ion recombination in the Advance Markus ionisation chamber.[19]

The most popular dosimetry films are the polydiacetylene-based self-developing radiochromic film, which changes colour due to irradiation by polarising the polymers, making it possible to quantify the dose received. The colour change observed due to a change in optical density is usually recorded using optical flat-bed scanners. Radiochromic films, e.g. Gafchromic™ films (Ashland Advanced Materials, Bridgewater NJ, USA) type EBT-3 or EBT-XD, allowing dose measurements of up to 60 Gy, are commonly used in high dose rate studies, in preclinical and clinical irradiations with electron and proton ultra-high dose rate beams.[4,20-22]. A major advantage of radiochromic films is the ability to provide either planar or 3D measurements and energy and dose rate independence, which has been confirmed in dose rate measurements up to $9 \cdot 10^{12}$ Gy/s.[23] Appropriate calibration procedure and scanning precision allow for obtaining dose values with an accuracy of about 1%.

In our tests, ultra-high dose rate beam dosimetry was performed using Gafchromic EBT-XD. This method was used to verify the quality of the beams, for 6 MeV and 9 MeV electron nominal energies and two diameters of PMMA applicators (100 and 50 mm). All dose distribution measurements (PDD and profile) and beam rate measurements were made at SSD of 60 cm using the PTW RW3 Slab phantom (**Figure 2**). Beam profiles were measured at a depth of $R_{80}/2$ following the requirements of IEC standards. Films were scanned 24 hours after irradiation using a Perfection V850 Pro flatbed scanner (Epson, Long Beach, CA, USA) at 72 dpi resolution and analysed using a calibration curve prepared for a 9 MeV electron beam, with 60 cm SSD and field size of 100 mm in diameter, generated by conventional intraoperative radiotherapy accelerator.

For the conventional and FLASH modes, the parameters of the depth dose distributions obtained from simulations and measurements were compared i.e. depths of 100%, 90%, 80%, and 50% doses (R_{100}, R_{90}, R_{80}, R_{50}), depth of practical range R_p as well as the most probable beam energy at the phantom surface (E_p) and the mean beam energy at the phantom surface (E_0). The E_p and E_0 were calculated based on R_p and R_{50} according to IAEA TRS 277[24] and IAEA TRS 381[25] procedures. The relative uncertainties in the measurements, as well as in the simulations, were below 1% and were neglected in quantitative analyses.

A comparison of simulation results with measurements for both nominal energies of 6 and 9 MeV conventional and FLASH beams was performed using the gamma index method. The gamma index (γ) is a standard dosimetric verification method. It is used to compare calculated and measured dose distributions point by point.[26] This comparison shows the quality and consistency of the simulations and the measurements, allowing a quantitative assessment of regions that pass and that fail the assumed acceptance criteria.[27]

Results

The pulse characteristics of intraoperative conventional therapy (10 Gy/min - approx. 3 mGy/pulse) and ultra-high dose rate beam (>40 Gy/s - from 0.3 to 3 Gy/pulse) were obtained for the IOERT accelerator.

Simulated and measured PDD distributions obtained for conventional beams using an applicator with a field diameter of 100 mm are presented in **Figure 4**. **Table 1** shows an analysis of the gamma index for the simulated and measured PDD curves. For beams in conventional mode, the best agreement was obtained with a minimum value of 3%/3 mm acceptance criteria. The dosimetric parameters (from the measured and simulated PDD curve presented in **Figure 4**) are listed for simulated and measured PDD for the conventional dose rate beams in **Table 2**.

The results of the Monte Carlo simulation for the ultra-high dose rate mode and the film dosimetry results for the FLASH dose rate electron beam obtained after the upgrade of the IOERT accelerator are shown in **Figures 5** and **6** for a PMMA applicator with a diameter of 100 mm and 50 mm, respectively. In the FLASH mode, the maximum dose rate obtained for a nominal energy of 9 MeV is significantly higher than that of 6 MeV. The maximum dose rate measured by film dosimetry was 300 Gy/s ± 6 Gy/s, for an electron beam at a nominal energy of 6 MeV, and 440 Gy/s ± 9 Gy/s at a nominal energy of 9 MeV, these results agreed with previous predictions made through the calculations and simulations.

The agreement between the measurements of percentage dose depth curves for FLASH beams using Gafchromic films and the Monte Carlo simulations of ultra-high dose rate electron beam (shown in **Figure 5** and **Figure 6**) was assessed using an analysis of the gamma index. For FLASH beams, the best agreement was obtained with a minimum value of 3%/3 mm. The acceptance criteria are given in **Table 3** for PDD for two applicators of 100 and 50 mm diameter.

Table 4 summarises the dosimetric parameters from the PDD curves for the ultra-high dose rate beams simulated by Monte Carlo methods: R_{100}, R_{90}, R_{80}, R_{50}, R_p, E_p, and E_0, and measured by Gafchromic films.

Beam profiles analysis for the beam of FLASH dose rate mode was also performed. **Figures 7** and **8** show profiles obtained from film dosimetry of FLASH beams and corresponding Monte Carlo simulations. Profiles were measured at a depth of R80/2, i.e., 10 mm for a 6 MeV beam and 15 mm for a 9 MeV electron beam.

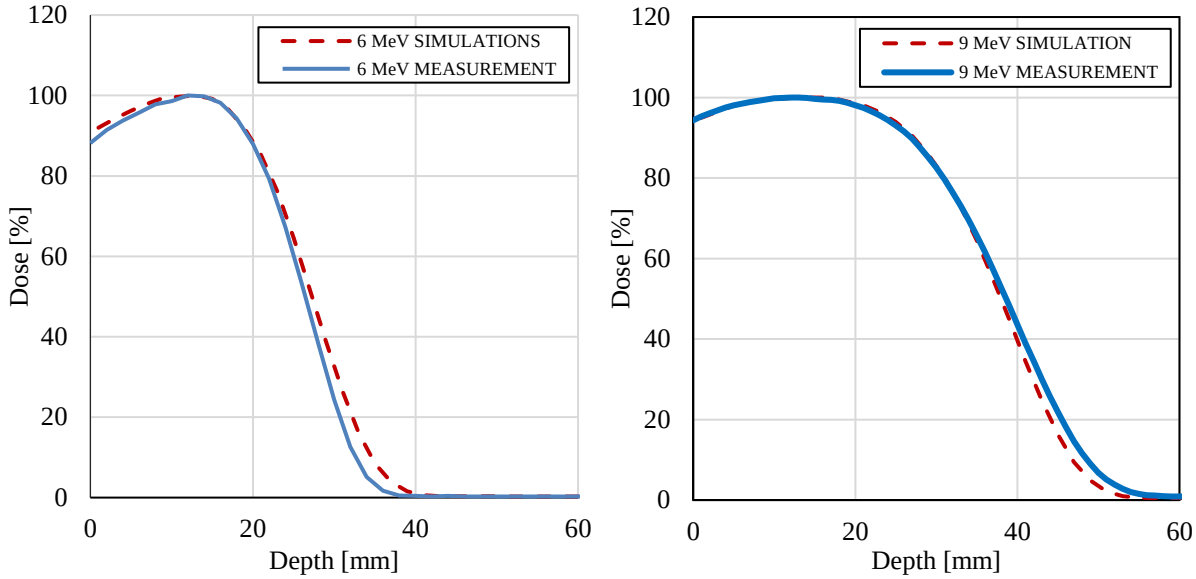


Figure 4. Measured (continuous blue line) and simulated (dashed red line) PDD obtained using a 100 mm diameter applicator for the 6 MeV conventional IOERT dose rate (10 Gy/min) electron beam on the left and the 9 MeV conventional IOERT (10 Gy/min) electron beam on the right.

Table 1. Comparison of simulation results with measurements for depth dose curves for both nominal energies 6 and 9 MeV conventional dose rate (10 Gy/min) beams using PMMA applicator on diameter 100 mm according to IEC standards.

Energy/ field diameter	Gamma index (3%, 3mm)
6 MeV/100 mm	96.4%
9 MeV/100 mm	96.4%

Table 2. The dosimetric parameters of the Monte Carlo simulated and measured percentage depth dose distributions for the conventional dose rate (10 Gy/min) beams, for PMMA applicator with a diameter of 100 mm, i.e. depths of 100%, 90%, 80%, 50% dose (R_{100}, R_{90}, R_{80}, R_{50}), depth of practical range R_p, and the most probable energy at the phantom surface (E_p) and the mean energy at the phantom surface (E_0) for beams of 6 and 9 MeV nominal energy.

	6 MeV	
	SIMULATION	**MEASUREMENT**
R_{100} [mm]	13.0	12.3
R_{90} [mm]	19.5	19.3
R_{80} [mm]	22.0	21.8
R_{50} [mm]	27.3	26.4
R_p [mm]	34.9	33.3
E_0 [MeV]	6.2	6.2
E_p [MeV]	7.2	6.8
	9 MeV	
	SIMULATION	**MEASUREMENT**
R_{100} [mm]	15.0	13.9
R_{90} [mm]	27.2	26.9
R_{80} [mm]	31.1	30.9
R_{50} [mm]	38.0	38.6
R_p [mm]	47.8	49.4
E_0 [MeV]	8.8	9.0
E_p [MeV]	9.8	10.1

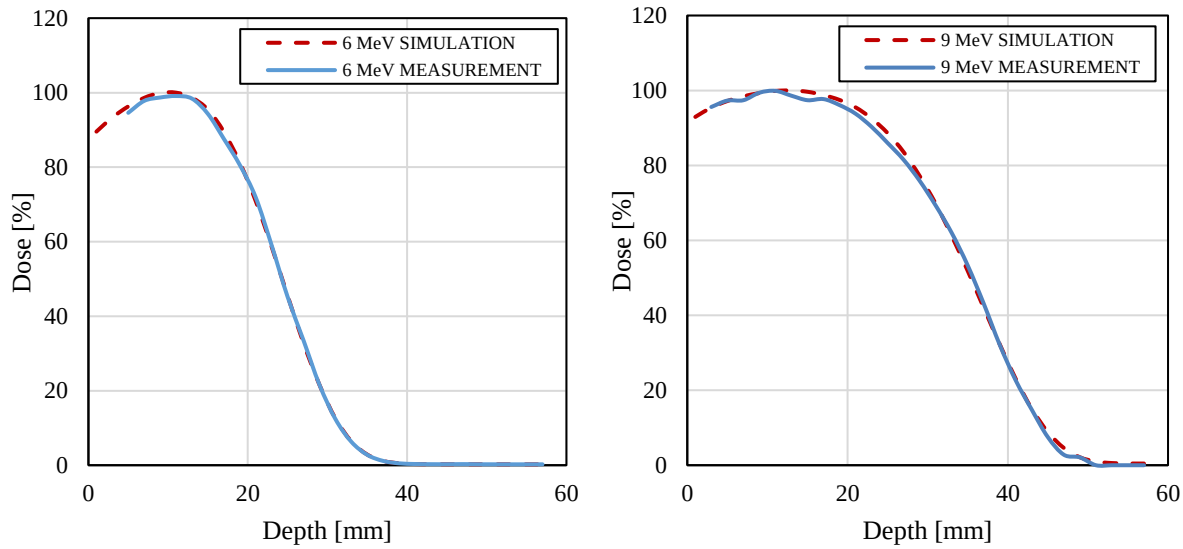


Figure 5. Measured (continuous blue line) and simulated (dashed red line) PDD obtained for the 6 MeV FLASH dose rate electron beam on the left and 9 MeV FLASH dose rate electron beam on the right with using a PMMA applicator with a diameter of 100 mm.

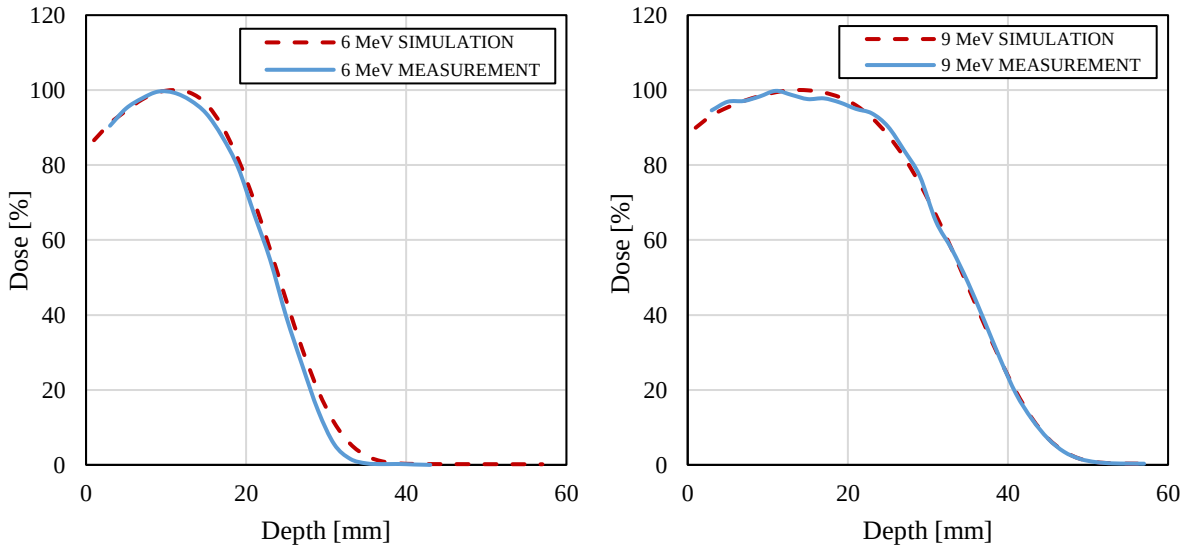


Figure 6. Measured (continuous blue line) and simulated (dashed red line) PDD obtained for the 6 MeV FLASH dose rate electron beam on the left and 9 MeV FLASH dose rate electron beam on the right using a PMMA applicator with a diameter of 50 mm.

Table 3. Comparison of simulation results with measurements for the FLASH dose rate electron beam percentage depth dose curves measured by Gafchromic films for energies 6 and 9 MeV and for two field diameters 100 and 50 mm.

Nominal energy/field diameter	Gamma index (3%, 3 mm)
6 MeV/100 mm	96.3%
9 MeV/100 mm	91.7%
6 MeV/50 mm	90.0%
9 MeV/50 mm	96.4%

Table 4. The dosimetric parameters for the Monte Carlo simulations and measurements for the FLASH dose rate beam i.e. R_{100}, R_{90}, R_{80}, R_{50}, R_p, and E_0 for simulated 6 and 9 MeV nominal energy beams. Results for 50 mm PMMA applicator and 100 mm PMMA applicator.

	6 MeV			
	PMMA 50 mm		PMMA 100 mm	
	SIMULATION	MEASUREMENT	SIMULATION	MEASUREMENT
R_{100} [mm]	10.4	11.0	10.1	11.0
R_{90} [mm]	17.3	17.1	16.2	16.8
R_{80} [mm]	20.0	19.3	19.0	19.2
R_{50} [mm]	24.7	24.1	24.5	24.3
R_p [mm]	31.8	31.5	31.6	31.8
E_0 [MeV]	5.8	5.8	5.7	5.8
E_p [MeV]	6.5	6.5	6.5	6.6
	9 MeV			
	PMMA 50 mm		PMMA 100 mm	
	SIMULATION	MEASUREMENT	SIMULATION	MEASUREMENT
R_{100} [mm]	11.2	13.0	11.1	13.0
R_{90} [mm]	25.0	24.1	22.7	24.3
R_{80} [mm]	29.5	27.6	28.4	28.1
R_{50} [mm]	37.6	34.5	36.6	35.4
R_p [mm]	48.1	44.6	47.0	45.5
E_0 [MeV]	8.6	8.0	8.5	8.2
E_p [MeV]	9.8	9.1	9.6	9.3

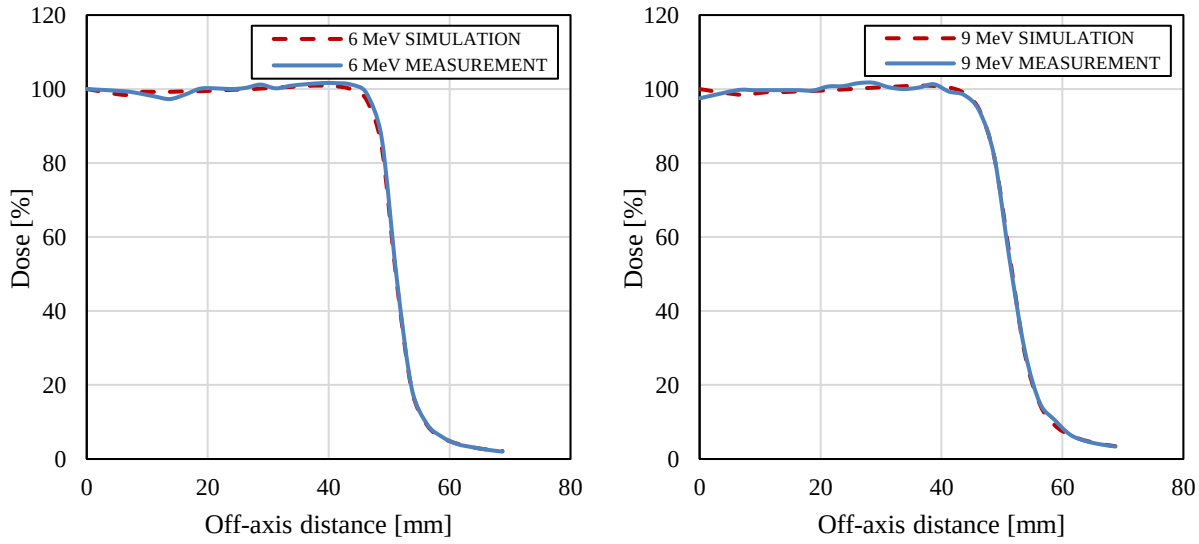


Figure 7. Measured (continuous blue line) and simulated (dashed red line) beam profiles were obtained for the 6 MeV FLASH dose rate electron beam on the left and the 9 MeV FLASH dose rate electron beam on the right using a PMMA applicator with a diameter of 100 mm.

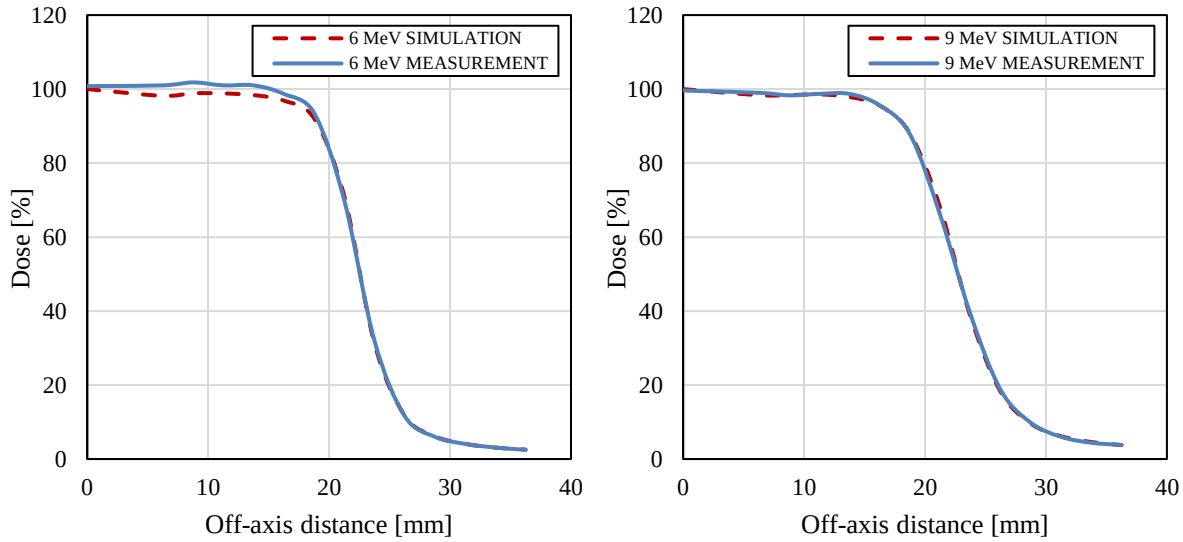


Figure 8. Measured (continuous blue line) and simulated (dashed red line) beam profiles were obtained for the 6 MeV FLASH dose rate electron beam on the left and the 9 MeV FLASH dose rate electron beam on the right using a PMMA applicator with a diameter of 50 mm.

Table 5. Comparison of simulation results with measurements for off-axis profiles for nominal energies 6 and 9 MeV FLASH dose rate beams and for two field dimeters 100 and 50 mm.

Energy/ field diameter	Gamma index (3%, 3mm)
6 MeV/100 mm	92.6%
9 MeV/100 mm	96.3%
6 MeV/50 mm	92.9%
9 MeV/50 mm	100.0%

Table 6. The comparison of the flatness for simulated and measured profiles for 6 and 9 MeV FLASH dose rate beams with the use of aplicators on diameters 50 and 100 mm.

	6 MeV			
	PMMA 50 mm		PMMA 100 mm	
	SIMULATION	MEASUREMENT	SIMULATION	MEASUREMENT
Flatness [%]	2.4	3.5	0.6	0.7
	9 MeV			
	PMMA 50 mm		PMMA 100 mm	
	SIMULATION	MEASUREMENT	SIMULATION	MEASUREMENT
Flatness [%]	3.4	2.9	0.9	0.9

A comparison between measured and Monte Carlo simulation profiles was made using gamma index analysis for 3%/3 mm acceptance criteria for off-axis profiles for 50 and 100 mm PMMA applicators, as shown in **Table 5**.

The flatness of simulated and measured profiles for 6 and 9 MeV FLASH beams for 50 and 100 mm PMMA applicators is shown in **Table 6**.

Discussion

Usually, IOERT accelerator manufacturers show and analyse the isodose value of 80%, i.e. $R_{80,}$ which for a conventional 6 MeV electron beam should be 20 ± 2 mm and for a 9 MeV beam should be 30 ± 2 mm[28] according to AAPM task group reports[29]. These values are also consistent with the dose parameters available in the literature[30]. For conventional mode beams, these values are within the assumed ranges (21.8 mm for 6 MeV and 30.9 mm for 9 MeV). In the FLASH mode, R_{80} has a lower value

but is still in the assumed range (19.2 mm for 6 MeV and 28.7 mm for 9 MeV).

In the FLASH mode, the maximum dose rate obtained for a nominal energy of 9 MeV is significantly higher than that of 6 MeV. The maximum dose rate measured by film dosimetry was 300 Gy/s ± 6 Gy/s for an electron beam at a nominal energy of 6 MeV and 440 Gy/s ± 9 Gy/s at a nominal energy of 9 MeV. It may be possible to achieve higher dose rates in the upgraded AQURE accelerator but at the expense of energy. To maintain the assumed nominal energies of the electron beams, it would be necessary to replace the microwave source of the IOERT accelerator.

Conclusions

The IOERT accelerator was upgraded to generate FLASH dose rate electron beams. As part of this research, the parameters of conventional (10 Gy/min - approx. 3 mGy/pulse) and FLASH beams (> 40 Gy/s - from 0.3 to 3 Gy/pulse) were determined. Two nominal electron beam energies of 6 MeV and 9 MeV were tuned for which dosimetry measurements on SSD=60 cm for a PMMA applicator with a diameter of 50 mm and 100 mm were performed. Dosimetry measurements have shown that it is possible to obtain the maximum dose rate of up to 300 Gy/s at 6 MeV and 440 Gy/s at 9 MeV electron beam energy for PMMA applicator on diameter 100 mm, respectively.

The simulated dose distributions qualitatively agree with the measured ones, as confirmed by the results of gamma index analysis for 3%/3 mm levels. Relatively small discrepancies in experimental and simulated PDDs may be attributed to differences between assumed and realistic initial beam energy spectra. The results of the flatness electron beam confirm the homogeneity at the irradiation field.

The results of the PDDs and beam profiles show that the beam-forming system used in the intraoperative accelerator AQURE worked properly for beams generated in the conventional and FLASH modes, allowing symmetrical and homogeneous irradiation of the samples for high dose rates for a circular field of diameter 50 and 100 mm. The results of measurements have demonstrated the potential of the accelerator to use FLASH beams in research work, especially in radiobiology. The first irradiations of radiobiological materials using FLASH beams and radiobiological tests are planned with the use of healthy and cancer cells.

Ethical permission

Ethical approval was not necessary for the preparation of this article.

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References

1. Berry RJ, Hall EJ, Forster DW, Storr TH, Goodman MJ. Survival of mammalian cells exposed to X rays at ultra-high dose-rates. Br J Radiol. 1969;42(494):102-107. https://doi.org/10.1259/0007-1285-42-494-102
2. Favaudon V, Caplier L, Monceau V, et al. Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice. Sci Transl Med. 2014;6(245). https://doi.org/10.1126/scitranslmed.3008973
3. Calvo FA, Serrano J, Cambeiro M, et al. Intra-Operative Electron Radiation Therapy: An Update of the Evidence Collected in 40 Years to Search for Models for Electron-FLASH Studies. Cancers. 2022;14(15):3693. https://doi.org/10.3390/cancers14153693
4. Bourhis J, Sozzi WJ, Jorge PG, et al. Treatment of a first patient with FLASH-radiotherapy. Radiother Oncol. 2019;139:18-22. https://doi.org/10.1016/j.radonc.2019.06.019
5. Romano F, Bailat C, Jorge PG, Lerch MLF, Darafsheh A. Ultra-high dose rate dosimetry: Challenges and opportunities for FLASH radiation therapy. Med Phys. 2022;49(7):4912-4932. https://doi.org/10.1002/mp.15649
6. Lenartowicz-Gasik A, Misiarz A, Markopolski V, et al. Verification of real-time dosimetry of ultra-high dose rate beams at AQURE FLASH RT on the sample surface. Polish Journal of Medical Physics and Engineering. 2024;30(4). https://doi.org/10.2478/pjmpe-2024-0038
7. Kruszyna-Mochalska M, Bijok M, Pawałowski B, et al. Zalecenia Polskiego Towarzystwa Fizyki Medycznej dotyczące kontroli jakości w radioterapii śródoperacyjnej promieniowaniem elektronowym (IOERT) za pomocą mobilnych akceleratorów. Inż Fiz Med. 8(1):7-25.
8. Misiarz A, Lenartowicz A, Adrich P, et al. Design and performance validation of a novel 3d printed thin-walled and transparent electron beam applicators for intraoperative radiation therapy with beam energy up to 12 MeV. Rep Pract Oncol Radiother. 2024;29(3):329-339. https://doi.org/10.5603/rpor.101092
9. Teledyne e2v. Magnetrons & Accessories. 2024. https://www.teledyne-e2v.com/en/solutions/rf-power/rf-devices/magnetrons/,", 2023. [Online].

10. Ashraf MR, Bruza P, Krishnaswamy V, Gladstone DJ, Pogue BW. Technical Note: Time-gating to medical linear accelerator pulses: Stray radiation detector. Med Phys. 2019;46(2):1044-1048. https://doi.org/10.1002/mp.13311
11. Adrich P. Technical Note: Monte Carlo study on the reduction in x-ray contamination of therapeutic electron beams for Intraoperative Radiation Therapy by means of improvements in the design of scattering foils. Med Phys. 2019;46(8):3378-3384. https://doi.org/10.1002/mp.13647
12 Ryczkowski A, Pawałowski B, Kruszyna-Mochalska M, et al. Commissioning, dosimetric characterisation and machine performance assessment of the AQURE mobile accelerator for intraoperative radiotherapy. Polish Journal of Medical Physics and Engineering. 2024;30(3):177-181. https://doi.org/10.2478/pjmpe-2024-0021
13. Dróżdż A, Waluś M, Zieliński M, et al. Verification of electron beam parameters in an intraoperative linear accelerator using dosimetric and radiobiological response methods. Rep Pract Oncol Radiother. 2021;26(6):1029-1034. https://doi.org/10.5603/RPOR.a2021.0128
14. van der Geer SB, de Loos MJ. Applications of the General Particle Tracer code. In: Proceedings of the 1997 Particle Accelerator Conference (Cat. No.97CH36167). Vol 2. IEEE; 1998:2577-2579. https://doi.org/10.1109/PAC.1997.751279
15. de Loos MJ, van der Geer SB. GENERAL PARTICLE TRACER: A NEW 3D CODE FOR ACCELERATOR AND BEAM LINE DESIGN. In: ; 1996:pp.e-proc. 1241.
16. Elbashir FEM, Ksouri W, Eisa MH, et al. Comparison of Dosimetry Protocols for Electron Beam Radiotherapy Calibrations and Measurement Uncertainties. Life. 2021;12(1):31. https://doi.org/10.3390/life12010031
17. IEC 60976 - Medical Electrical Equipment — Medical Electron Accelerators — Functional Performance Characteristics. International Electrotechnical Commission; 2007.
18. Ashraf MR, Rahman M, Zhang R, et al. Dosimetry for FLASH Radiotherapy: A Review of Tools and the Role of Radioluminescence and Cherenkov Emission. Front Phys. 2020;8:328. https://doi.org/10.3389/fphy.2020.00328
19. Petersson K, Jaccard M, Germond J, et al. High dose-per-pulse electron beam dosimetry — A model to correct for the ion recombination in the Advanced Markus ionization chamber. Med Phys. 2017;44(3):1157-1167. https://doi.org/10.1002/mp.12111
20. Levy K, Natarajan S, Wang J, et al. Abdominal FLASH irradiation reduces radiation-induced gastrointestinal toxicity for the treatment of ovarian cancer in mice. Sci Rep. 2020;10(1):21600. https://doi.org/10.1038/s41598-020-78017-7
21. Rohrer Bley C, Wolf F, Gonçalves Jorge P, et al. Dose- and Volume-Limiting Late Toxicity of FLASH Radiotherapy in Cats with Squamous Cell Carcinoma of the Nasal Planum and in Mini Pigs. Clin Cancer Res. 2022;28(17):3814-3823. https://doi.org/10.1158/1078-0432.CCR-22-0262
22. Biological effects in normal cells exposed to FLASH dose rate protons - PubMed. Accessed April 29, 2024. https://pubmed.ncbi.nlm.nih.gov/30850209/
23. Karsch L, Beyreuther E, Burris-Mog T, et al. Dose rate dependence for different dosimeters and detectors: TLD, OSL, EBT films, and diamond detectors. Med Phys. 2012;39(5):2447-2455. https://doi.org/10.1118/1.3700400
24. International Atomic Energy Agency. Absorbed Dose Determination in Photon and Electron Beams - An International Code of Practice. Technical Reports Series No. 277.; 1987.
25. International Atomic Energy Agency. The Use of Plane Parallel Ionization Chambers in High Energy Electron and Photon Beams: An International Code of Practice for Dosimetry. Technical Reports Series No. 381. International Atomic Energy Agency; 1997.
26. Atiq M, Atiq A, Iqbal K, Shamsi QA, Andleeb F, Buzdar SA. Interpretation of Gamma Index for Quality Assurance of Simultaneously Integrated Boost (SIB) IMRT Plans for Head and Neck Carcinoma. Pol J Med Phys Eng. 2017;23(4):93-97. https://doi.org/10.1515/pjmpe-2017-0016
27. Low DA, Harms WB, Mutic S, Purdy JA. A technique for the quantitative evaluation of dose distributions. Med Phys. 1998;25(5):656-661. https://doi.org/10.1118/1.598248
28. IntraOp. Product Datasheet Mobetron. IntraOp Mobetron HDR Product Datasheet. 2024. https://ezmpid78ed4.exactdn.com/wp-content/uploads/IntraOp_Mobetron_Data_Sheet-QN.r01.4-1.pdf
29. Meyer J, Nyflot MJ, Smith WP, et al. Electron beam energy QA — a note on measurement tolerances. J Appl Clin Med Phys. 2016;17(2):249-257. https://doi.org/10.1120/jacmp.v17i2.6049
30. Rosenberg I. Radiation Oncology Physics: A Handbook for Teachers and Students. Br J Cancer. 2008;98(5):1020-1020. https://doi.org/10.1038/sj.bjc.6604224