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Dosimetry for FLASH Radiotherapy: A review of dosimetric systems

Suzart [a*], K. F.; Potiens [a], M. P. A.

[a] Instituto de Pesquisas Energéticas e Nucleares, 05508-000, São Paulo, São Paulo, Brazil.

*Correspondence: karolinesuzart@usp.br

Abstract: FLASH radiotherapy (FLASH-RT) is a promising approach to cancer treatment, characterized by the delivery of high doses of radiation in a short period of time, within fractions of seconds. In order to demonstrate the FLASH effect, single high doses of radiation delivered in very short times through a limited number of pulses are required. Previous studies have reported that FLASH-RT treatment can result in increased cell survival compared to conventional radiotherapy. This article aims to conduct a comprehensive literature search on dosimetry in FLASH radiotherapy, an emerging and promising technique in the field of radiotherapy. Some of the most used dosimeters in recent studies for FLASH radiotherapy will be discussed, including ionization chambers, diamond detectors, radiochromic films, EBT3 radiochromic films and thermoluminescent dosimeters. The main dosimetry parameters used in FLASH radiotherapy treatments will be analyzed, with emphasis on the characteristics and applicability of the different types of dosimeters used.

Keywords: flash radiotherapy, review, dosimetric systems.

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Dosimetria para Radioterapia FLASH: Uma revisão dos sistemas dosimétricos

Resumo: A radioterapia FLASH (FLASH-RT) é uma abordagem promissora para o tratamento do câncer, caracterizada pela administração de altas doses de radiação em um curto período de tempo, em frações de segundos. Para demonstrar o efeito FLASH, são necessárias doses únicas elevadas de radiação administradas em tempos muito curtos através de um número limitado de pulsos. Estudos anteriores relataram que o tratamento FLASH-RT pode resultar em aumento da sobrevivência celular em comparação com a radioterapia convencional. Este artigo tem como objetivo realizar uma pesquisa bibliográfica abrangente sobre dosimetria em radioterapia FLASH, uma técnica emergente e promissora no campo da radioterapia. Serão discutidos alguns dos dosímetros mais utilizados em estudos recentes para radioterapia FLASH, incluindo câmaras de ionização, detectores de diamante, filmes radiocrômicos, filmes radiocrômicos EBT3 e dosímetros termoluminescentes. Serão analisados os principais parâmetros de dosimetria utilizados nos tratamentos radioterápicos FLASH, com ênfase nas características e aplicabilidade dos diferentes tipos de dosímetros utilizados.

Palavras-chave: radioterapia FLASH, revisão de literatura, sistemas dosimétricos.

1. INTRODUCTION

FLASH radiotherapy (FLASH-RT) is a method of treating cancer with high doses of radiation to the tumor region in a time within fractions of seconds [1].

FLASH-RT has been reported since the 1960s with full dose delivery within just a single nanosecond pulse of X-rays. Beam homogeneity was ±5% in a circular field of 2 cm diameter, causing a marked increase in cell survival compared to conventional treatment [2].

The FLASH radiotherapy study has aroused the interest of researchers as it presents promising results in the treatment of cancer. One of the advantages of FLASH radiotherapy is the differential effect between the tumor and healthy tissues [3].

Preclinical studies on FLASH-RT showed that this treatment could control tumors while minimizing normal tissue toxicity when compared to conventional dose rate [1]. To demonstrate the FLASH effect, a single high dose of RT with low-energy electrons delivered in an overall time of less than 200 milliseconds is required. FLASH-RT consists of delivering a limited number of pulses (<=10 pulses).

FLASH-RT delivery has been previously characterized by irradiation at ultra-high medium dose rates (>40 Gy s−1) to effect single sub-second treatment fractions [4-6].

Unfortunately, despite the pressing need to identify the inherent beam requirements for FLASH-RT, there is a shortage of globally available systems capable of achieving the required dose rates [7].

However, in order to quickly address unresolved issues related to FLASH-RT, the technologies currently in use are being adapted [8-11]. Furthermore, new technologies are being developed to improve the availability of ultra-high dose sources [12-14].

The objective of this work is to conduct a comprehensive literature search on dosimetry for FLASH radiotherapy, an emerging and promising technique in the area of radiotherapy. Some of the dosimeters most used in recent studies for high-dose FLASH radiotherapy and the use of electron and proton beams will be described.

2. MATERIALS AND METHODS

The methodology of this work consists of reviewing updated scientific literature based on scientific data, to identify and collect academic articles, case studies and systematic reviews that address dosimetry in FLASH radiotherapy. The selection of works was conducted through relevant topics on the Scopus platform (Elsevier), covering topics such as dosimetric systems, FLASH radiotherapy and ultra-high dose rates. The radiation detectors selected for this review were: ionization chamber, diamond detector, EBT3 radiochromic films and thermoluminescent dosimeters.

From this review, dosimetry parameters will be analyzed and the main dosimetry parameters used in FLASH radiotherapy treatments will be identified.

3. RESULTS AND DISCUSSIONS

As a result of this bibliographic review, the systems commonly used in FLASH radiotherapy were identified, which will be listed below:

3.1. Ioniztion Chambers

Ionization chambers are radiation detectors widely used for reference dosimetry in clinical radiotherapy (RT) settings and are highly valued for their ability to provide real-time dose measurements [15]. The calibrations of the ionization chambers are traceable to national standards or metrology laboratories, and, through the application of recognized dosimetric protocols, it becomes possible to perform precise dose measurements, taking into account several correction factors [16-18].

In the context of radiotherapy with FLASH-RT, however, the use of non-standardized beams and ultra-high dose rates makes the direct application of usual dosimetric protocols unfeasible. Furthermore, for ionization chambers to be used as reference dosimeters in high mean dose rate and percentage depth dose (PDD) fields, it is essential to carefully consider the significant effects of ion recombination [19-23].

The use of air ionization chambers in the ultra-high pulse dose regime exhibits serious disadvantages due to the presence of a limited charge collection efficiency that can produce ion recombination correction factors that deviate significantly from unity [8].

3.2. Diamond Detectors

Diamond detectors come in two varieties, natural or synthetic, the latter being based on chemical vapor deposition (CVD). The most notable example of a single-crystal CVD-type detector is the microDiamond 60019 detector (PTW, Freiburg, Germany), which has a sensitive volume of only 0.004 mm3 as defined by the depletion region extending through the intrinsic diamond layer. 1 μm thick [7].

In their study, Bourgouin, A. et al. (2022) characterized and optimized an ultra-high pulse dose rate (UHPDR) electron beam using a prototype diamond detector for relative measurements and compared these measurements with Monte Carlo simulation. The Monte Carlo method used was the EGSnrc model, developed at PTB, and the FLUKA model, used for independent comparison. EGSnrc was employed to simulate beam lateral profiles, depth dose curves and beam characterization in water, while FLUKA was used to calculate the absorbed dose in a water phantom. Both models were validated with relative measurements using a prototype diamond detector. As a result, Bourgouin, A. et al. obtained linearity of up to 2.5 Gy per pulse, the diamond detector is promising for relative measurements and stability in the linear accelerator during the investigation time of four months [32].

Furthermore, studies such as those by Gomà [24] and Patriarca [12] expanded the use of diamond detectors for high-energy proton beams. Gomà investigated 150 MeV proton beams with dose rates up to 3 Gy.s-1 and observed negligible dose rate dependence as well as no LET (Linear Energy Transfer) dependence. Patriarca expanded this study to even higher dose rates, up to 40 Gy.s-1, with results showing a variation of less than 5% in the detector response, indicating excellent stability under extreme conditions.

In contrast, Marsolat et al. [25] reported intriguing findings about the consistency of diamond detectors in proton beams. In a study with passively scattered proton beams at 138 MeV, they found that half of the detectors tested did not show the expected dosimetric properties, including LET dependence and dose rate independence. This variability highlights the continued need for rigorous calibration and verification protocols to ensure the reliability of results obtained with diamond detectors.

3.3. Radiochromic films

Radiochromic films are self-developed radiation dosimeters whose detection principle is based on radiation-induced polymerization of an active layer (diacetylene), resulting in coloration and measurable increase in optical density (OD) [26, 27].

The most common radiochromic films, radiochromic films, are inherently 2D and have been consistently demonstrated to have low dose rate and energy dependencies. These characteristics stand out as being desirable for application in ultra-high dose rate dosimetry to provide absolute dose, dose rate and dose distribution data in the highly variable and non-standardized beams utilized in the current FLASH-RT scenario [7].

EBT3 type radiochromic films were launched in 2011 as a replacement for EBT2. These third-generation films consist of a 28 µm active dosimetric layer sandwiched between two 100 µm polyester layers. Although the composition of the active layer remains the same, EBT3 films offer several improvements compared to EBT2 films, such as avoiding interference patterns and a symmetric structure [28].

According to Jaccard et al. (2016), sheets of Gafchromic EBT3 film (Ashland Inc., Wayne, NJ, USA), with nominal dimensions of 20.32 × 25.4 cm², were used in the study. For standardization, the films were cut into twenty pieces measuring 5 × 5 cm² and duly marked to maintain the initial orientation in all applications. The study demonstrated that EBT3 Gafchromic films are suitable for performing reference dose measurements, with a global uncertainty of 4% (standard uncertainty at the $k = 2$ level), in high dose rate electron beams, covering a wide range of energies and dose rates $\dot{D}p$ of up to 8×10^6 Gy/s.

It is essential to recognize that although Gafchromic EBT3 films are highly reliable for high dose rate electron beam applications, each dosimetry system has its limitations and requires specific care regarding handling and calibration. Continued investigations are needed to further expand knowledge about the performance of these films under varying clinical conditions and to develop best practices that optimize their use.

3.4. Thermoluminescent Dosimeters

Thermoluminescent dosimeters (TLDs) are devices used to measure doses of ionizing radiation. They are made of solid materials that have the property of accumulating radiation energy during exposure. After exposure to radiation, these dosimeters are heated, and the accumulated energy is released in the form of light. The amount of light emitted is proportional to the dose of radiation absorbed by the dosimeter material [29].

Karsch, L. et al. (2012) [22] conducted measurements using the ELBE superconducting linear accelerator at the Helmholtz-Zentrum Dresden-Rossendorf (HZDR). This accelerator is characterized by its ability to generate extremely short electron pulses, with a duration of 5 ps and an energy of 20 MeV, operating in single-pulse mode.

This mode allows the user to specify the number of micropulses (up to 4000) followed by a beam pause, which must be at least 1 ms long. The correction of the energy absorption coefficients between the dosimeter and the soft tissue was performed using correction factors that consider tissue equivalence. These factors are applied to adjust the dosimeter response to the dose absorbed by the tissue, ensuring that the measurements are representative of the actual dose received by the biological tissue. Karsch, L. et al. (2012) demonstrated that the dosimeters used are independent of the dose rate up to 4.7 x 10^9 Gy/s, resulting in an uncertainty of 2% for TLD (Thermoluminescent Dosimeters) and OSL (Optically Stimulated Luminescence) dosimeters.

The 2% uncertainty reported by Karsch et al. (2012) for the TLD and OSL dosimeters demonstrates remarkable consistency and reliability of results, even under high dose rate conditions. This precision is essential to ensure that dose measurements are reliable and that radiotherapy treatment protocols are strictly followed [22].

Miles et al. (2023) [31] characterized an X-ray tube with a rotating anode for FLASH radiotherapy research. In their experiments, the team used EBT3 films and TLD dosimeters to evaluate dose rates and depth characteristics in solid water phantoms. The results showed that doses greater than 40 Gy.s-1 were obtained at a depth of 10 mm. Although these results highlight the potential for preclinical research in FLASH, challenges remain related to calibrating dosimeters for measurements at high dose rates.

4. CONCLUSIONS

As a result, absolute dosimetry in FLASH beams is currently performed mainly with chemical and passive dosimeters, such as radiochromic films, alanine dosimeters or thermoluminescent dosimeters, whose responses are considered constant when passing from low to high dose beams per pulse [30]. Although the ionization chamber is widely used as the predominant detector in conventional radiotherapy, the current literature lacks sufficient evidence to endorse its use as the standard detector for FLASH radiotherapy.

The single-crystal synthetic diamond detector PTW microDiamond (60019) presents itself as an attractive option for the dosimetry application of FLASH-RT, both for X-rays and protons. Constituting a possible alternative to ionization chambers or silicon-based dosimeters, especially in applications that require real-time measurements.

Although studies on thermoluminescent dosimeters for ultra-high dose rates show promising results, it is essential to consider ion recombination correction to avoid significant errors in readings. Furthermore, accurate configuration and positioning of dosimeters are critical to reducing uncertainties associated with measurements.

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CONFLICT OF INTEREST

All authors declare that they have no conflicts of interest.

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