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Energy Deposition and DNA Damage Analysis of Protons and Alpha Particles simulated with FLUKA applied to a cellular model

Análise de Deposição de Energia e Danos ao DNA de Prótons e Partículas Alfa simulados com FLUKA aplicados a um modelo celular

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Abstract

Microdosimetry is a crucial research area in the development of radiotherapy that aims to understand dose variations at the subcellular level. This work addresses microdosimetry with proton and ion beams, focusing on energy deposition in a cellular geometric model implemented using the Monte Carlo method via FLUKA software. Scenarios were simulated where a proton beam or an alpha particle beam, with energies ranging from 1 to 20 keV, interacted with a simplified cellular model. Detectors were set up to record fluence and energy density in the medium during simulations. The results showed that more particles reached the nucleus as beam energy increased, especially for alpha particles. Energy density analysis revealed that the depth of maximum deposition increases with kinetic energy and was higher for alpha particles. Subsequently, using MCDS (Monte Carlo Damage Simulation) software, dose data from simulations were used to calculate the probability of various DNA damage types—base lesions (BD), single-strand breaks (SSB), and more complex breaks. This study confirmed the effectiveness of the model in simulating microdosimetric effects, highlighting differences in energy deposition and DNA damage between protons and alpha particles. These findings contribute to a better understanding of radiation interactions and the improvement of radiotherapy.

Keywords: microdosimetry; simulation; DNA; Monte Carlo method.

Resumo

A microdosimetria é uma área de pesquisa crucial no desenvolvimento da radioterapia, que visa entender as variações de dose em nível subcelular. Este trabalho aborda a microdosimetria com feixes de prótons e íons, focando na deposição de energia em um modelo geométrico celular implementado usando o método de Monte Carlo por meio do software FLUKA. Foram simulados cenários em que um feixe de prótons ou um feixe de partículas alfa, com energias variando de 1 a 20 keV, interagiam com um modelo celular simplificado. Detectores foram configurados para registrar a fluência e a densidade de energia no meio durante as simulações. Os resultados mostraram que mais partículas alcançaram o núcleo à medida que a energia do feixe aumentava, especialmente para partículas alfa. A análise da densidade de energia revelou que a profundidade de deposição máxima aumenta com a energia cinética e foi maior para partículas alfa. Subsequentemente, utilizando o software MCDS (Monte Carlo Damage Simulation), os dados de dose das simulações foram usados para calcular a probabilidade de vários tipos de danos ao DNA—lesões nas bases (BD), quebras de fita simples (SSB) e quebras mais complexas. Este estudo confirmou a eficácia do modelo na simulação de efeitos microdosimétricos, evidenciando diferenças na deposição de energia e danos ao DNA entre prótons e partículas alfa. Esses resultados ajudam a compreender melhor as interações da radiação e a aprimorar a radioterapia.

Palavras-chave: *microdosimetria; simulação; DNA; método de Monte Carlo.*

1. Introduction

Teletherapy is the most common type of radiotherapy, used in over 50 % of cancer treatment cases, and involves the use of external ionizing radiation beams, with photons and electrons being the most frequently utilized (1). However, other beam types, such as ion and charged particle beams, offer distinct advantages. These beams enable a more precise dose distribution in target tissues due to the high ionization density near the end of their trajectories, known as the Bragg peak, which provides better protection to the healthy tissues surrounding the tumor compared to photons (2).

Microdosimetry, a vital field in radiotherapy research, focuses on the dose distribution at cellular and subcellular levels. High mass and charge particles create a highly ionizing effect, generating numerous secondary electrons. When these electrons interact with water, they produce free radicals. In the cellular nucleus they can cause significant DNA damage (3). The most critical damage from ionizing radiation's interaction with biological tissue is linked to the DNA molecule, with treatment success being directly related to the effectiveness of this DNA damage in tumor cells.

Nevertheless, using these beams in microdosimetry for clinical or research purposes faces challenges, including the need for specialized equipment and high-tech facilities, which have much higher construction and maintenance costs than conventional radiotherapy facilities (4) (11). In this context, the Monte Carlo Method (MCM) emerges as

a valuable tool, enabling computational simulations that accurately capture the stochastic nature of energy deposition by particles (5).

Based on the advantages of ion beams in radiotherapy, this study hypothesizes that alpha particles, due to their higher linear energy transfer (LET), will result in greater energy deposition in the cell nucleus and induce a higher frequency of complex DNA damage compared to protons with the same kinetic energy. By simulating particle interactions within a simplified cellular geometry using FLUKA, and estimating DNA damage using MCDS, we aim to test this hypothesis and assess how these findings could contribute to the optimization of particle-based radiotherapy strategies.

The purpose of this study is to investigate cellular-scale interactions by evaluating particle fluence and energy density deposited in a simplified cellular model using Monte Carlo simulations with low-energy proton and alpha particle beams. The study particularly focuses on how variations in ion beam energy influence low-dose distribution within the cell, especially in the nucleus, and the associated DNA damage.

This study contributes to the field of microdosimetry by employing Monte Carlo simulations with FLUKA to investigate the interaction of alpha particles and protons with a simplified cellular model. The relevance of this work lies in its potential to enhance radiotherapy techniques by exploring energy deposition and DNA damage. While the use of FLUKA and MCDS is well-established, the originality of this study could be further emphasized by a more in-depth discussion on how its findings advance the current state of knowledge. Specifically, our results provide new insights into the differential effects of alpha particles and protons at low energies, which could inform the development of more targeted radiotherapeutic approaches.

This study is based on the hypothesis that alpha particles, due to their higher linear energy transfer (LET), will result in greater energy deposition in the cell nucleus and induce a higher frequency of complex DNA damage compared to protons with the same kinetic energy. By simulating particle interactions within a simplified cellular geometry using FLUKA, and estimating DNA damage using MCDS, we aim to test this hypothesis and assess how these findings could contribute to the optimization of particle-based radiotherapy strategies.

2. Materials and Methods

The Monte Carlo Method was used to simulate the interaction between ions and biological material, utilizing the FLUKA code (version 4-3.1) (6) through the advanced graphical interface Flair (version 3.2-2).

A simplified approach focused on the essential components of the cell. The model was based on a generic cell, consisting only of the nucleus and cytoplasm, as described in the work of Pablo de Vera (2014) (7). This symmetric cell model is composed of two concentric spheres centered at the origin, with the beam striking its center along the Z-axis, as illustrated in Figure 1. This symmetrical geometry offers a balance between biological relevance and computational efficiency, facilitating a clear comparison of energy deposition patterns. Each simulation involved 10^8 primary particles to ensure statistical convergence and reduce uncertainties. While the FLUKA code accurately simulates particle interactions and transport, the MCDS software was used to estimate DNA damage based on dose input data. Although MCDS does not simulate molecular-level events, it provides valuable predictions of DNA damage complexity, allowing for comparative analysis between proton and alpha particle interactions under varying energies.

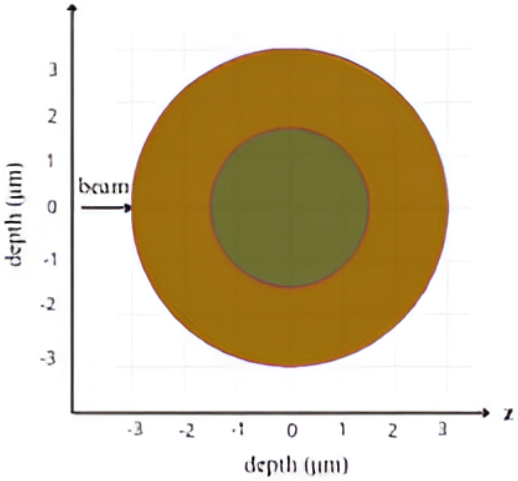

Figure 1. Cellular geometric model.

The smaller sphere, representing the nucleus, has a diameter of 3 µm, while the larger sphere represents the cytoplasm with a diameter of 6 µm. A cubic detector, 6 µm on each side, was defined using the USRBIN card to cover the entire cell and was centered at the origin of the coordinate system. This detector was set up to record particle fluence. A second detector of the same dimensions was configured to measure the energy density deposited in the medium.

Beams of alpha particles and protons were used with initial kinetic energies of 1, 5, 10, 15, and 20 keV. The beam trajectory was aligned along the Z-axis to target the center of the cell model. Simulations were carried out with 10^8 primary particles. After running the simulations with FLUKA software, the data collected were used to estimate DNA damage types using the MCDS (8) - Monte Carlo Damage Simulation software developed by Semenenko and Stewart (2004).

DNA damage was categorized by its complexity, including damage to nitrogenous bases (BD) or breaks in the sugar-phosphate backbone. These backbone breaks are classified as single-strand breaks (SSBs) or double-strand breaks (DSBs), depending on the strand affected and the number of base pairs (bp) involved, as shown in Figure 2 below.

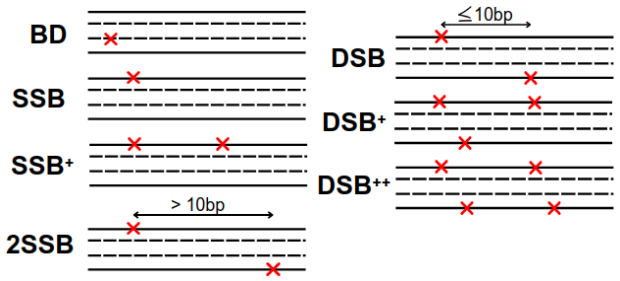

Figure 2. DNA damage model.

To facilitate observation, Figure 2 above, based on the work of Nikjoo et al. (10), depicts the DNA double helix as four straight, untwisted lines. The solid lines represent the sugar-phosphate backbone, while the dashed lines represent the nitrogenous bases. An 'X' indicates base damage (BD) or a break in a DNA strand. The results were processed with Python (version 3.11), and graphs were created using the Matplotlib library (9).

3. Results

3.1 Particle Fluence

The first set of results examines the particle fluence (particles/cm²) within the cellular model, as recorded by the USRBIN detector. This is illustrated in Figures 3 and 4. Both figures are two-dimensional, with the Y and Z axes showing depth in micrometers. The color bar indicates the magnitude of the fluence recorded by the detector.

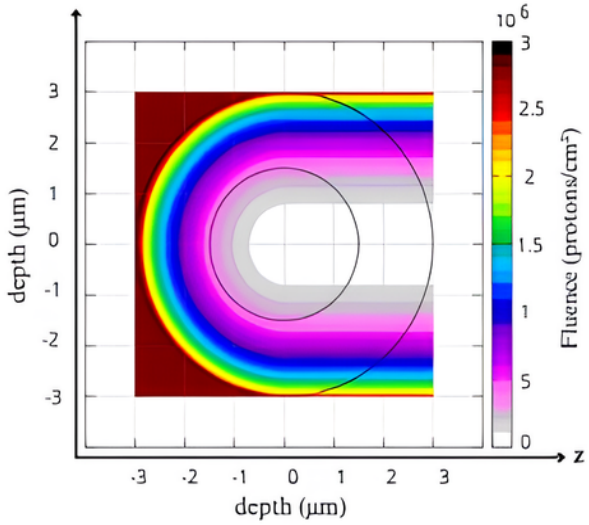

Figure 3. Proton fluence at 1 keV.

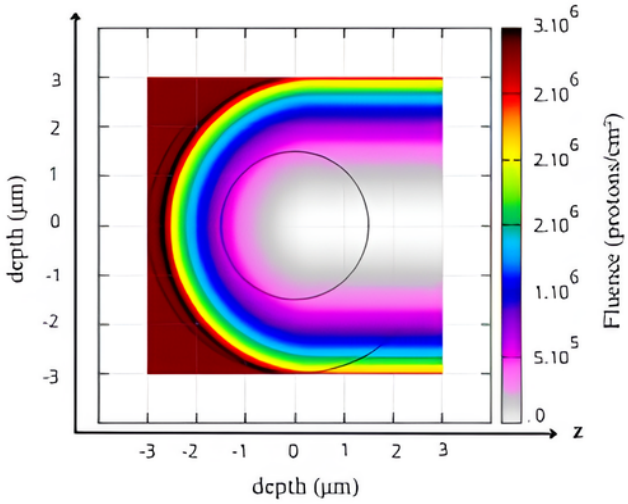

Figure 4. Proton fluence at 20 keV.

Figure 5 displays the fluence profiles for proton beams across all energies. Depths are shown on the X-axis, while fluence is represented on the Y-axis. Vertical dashed lines indicate the boundaries of the nucleus, extending from 1.5 to 4.5 micrometers.

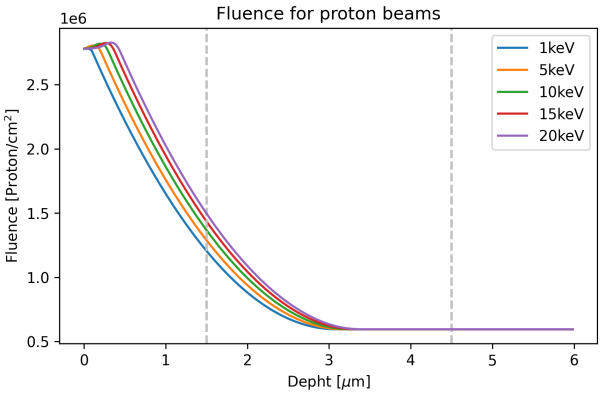

Figure 5. Fluence profiles for proton beams at all energies.

Figure 6 below illustrates the two-dimensional distribution of fluence for alpha particle beams.

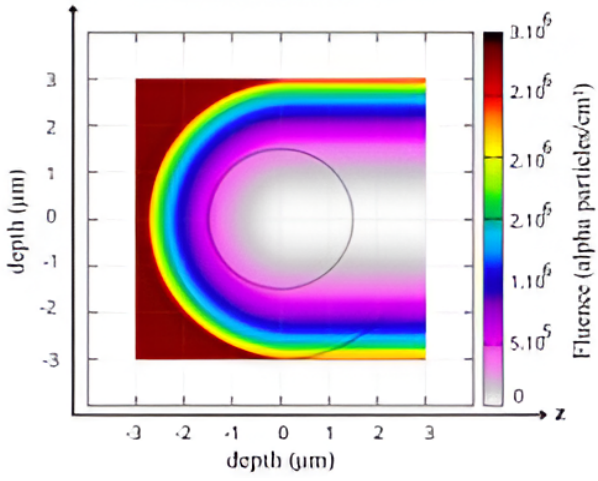

Figure 6. Alpha particles fluence at 1 keV.

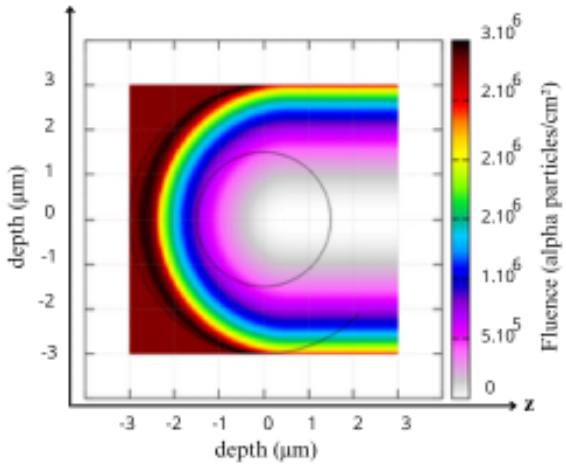

Figure 7. Alpha particles fluence at 20 keV.

Figure 8 below displays the fluence profiles for alpha particle beams across all energies. Depths are shown on the X-axis, while fluence is represented on the Y-axis. Vertical dashed lines indicate the boundaries of the nucleus, which extends from 1.5 to 4.5 micrometers.

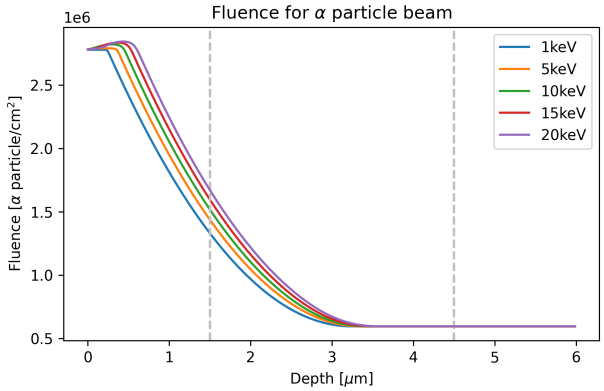

Figure 8. Fluence profiles for alpha particle beams at all energies.

Table 1 presents the percentage of the initial fluence that enters the cell nucleus for each simulated particle and energy.

Table 1. Percentage of fluence entering the nucleus.

Percentage of fluence entering the nucleus (%)		
Energy (keV)	Protons	α-particles
1	43.39	47.90
5	46.32	51.69
10	49.17	54.55
15	51.62	57.39
20	53.85	60.11

Source: The author (2025).

The simulations revealed that the fluence of protons and α-particles varies significantly with energy. Proton fluence increased with energy, reaching its peak in the cell nucleus. For instance, Table 1 shows that the initial fluence penetrating the nucleus for 20 keV alpha particles was 60.1%, compared to 53.85% for 20 keV protons.

3.2 Energy Deposition

The second set of results focuses on the energy density deposited (GeV/cm³) by the particles along their path through the cellular model, as recorded by the USRBIN detector.

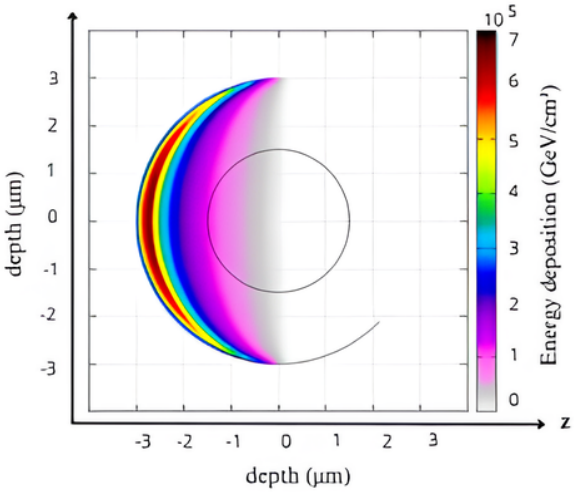

Figure 7. Energy deposition of protons at 20 keV.

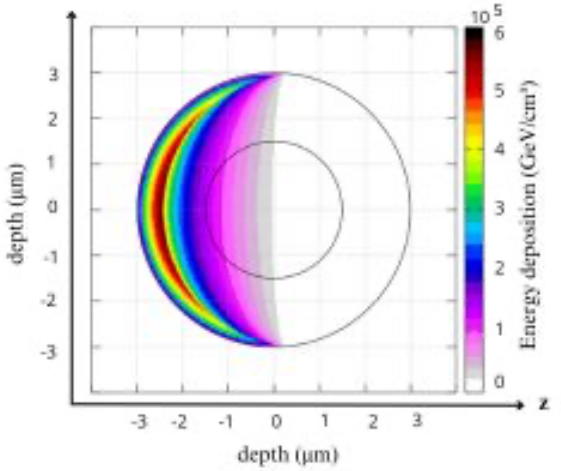

Figure 8. Energy deposition of alpha particles at 20 keV.

Figures 9 and 10 below illustrate the energy density deposition profiles for proton and alpha particle beams, respectively, at all energies. Depths are shown on the X-axis, with energy deposition on the Y-axis.

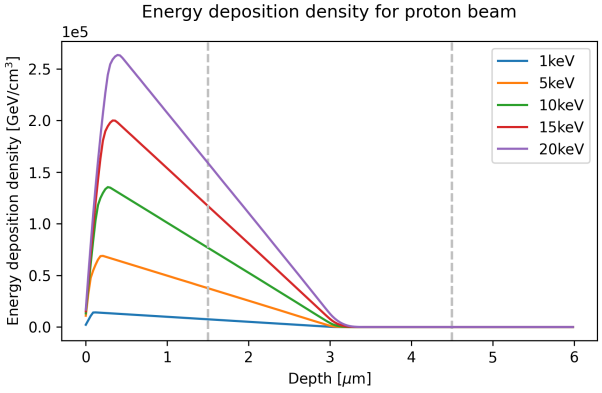

Figure 9. Energy deposition density profiles for protons at all energies.

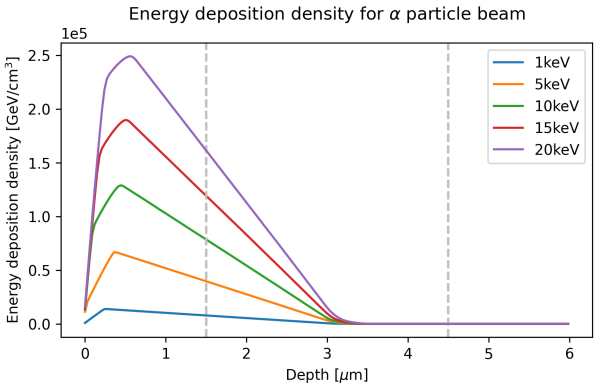

Figure 10. Energy deposition density profiles for alpha particles at all energies.

These figures show that energy deposition increases with depth, with alpha particles depositing a higher energy density compared to protons. Table 2 displays the dose in the nucleus, ranging from 0.12 cGy for 1 keV protons to 2.59 cGy for 20 keV alpha particles.

Table 2. Dose at the nucleus entrance.

Dose at the nucleus entrance (cGy)		
Energy (keV)	Protons	Alpha particles
1	0.119	0.125
5	0.602	0.636
10	1.230	1.259
15	1.878	1.911
20	2.546	2.587

Source: The author (2025).

3.3 DNA

Finally, the simulation data were analyzed using the MCDS software, and the resulting estimates are shown in Table 3.

Table 3. DNA damage for Proton beams.

DNA damage percentage for Proton Beams (%)					
DNA damage	1 keV	5 keV	10 keV	15 keV	20 keV
BD	32.82	33.08	33.23	33.52	33.68
SSB	29.41	29.55	29.65	29.73	29.81
SSB+	11.18	11.11	11.06	11.04	11.00
2SSB	6.79	6.72	6.66	6.56	6.55
DSB	5.39	5.39	5.39	5.38	5.37
DSB+	5.07	5.03	5.00	4.97	4.95
DSB++	9.34	9.12	8.92	8.78	8.65

Source: The author (2025).

Table 4. DNA damage for Alpha Particle beams.

DNA damage percentage for Alpha Particle Beams (%)					
DNA damage	1 keV	5 keV	10 keV	15 keV	20 keV
BD	-	31.52	31.56	31.61	31.62
SSB	-	28.81	28.83	28.84	28.87
SSB+	-	11.39	11.39	11.38	11.38
2SSB	-	7.15	7.13	7.12	7.11
DSB	-	5.41	5.41	5.41	5.40
DSB+	-	5.24	5.24	5.24	5.23
DSB++	-	10.46	10.42	10.38	10.35

Source: The author (2025).

It is considered a DSB break when there are two breaks on opposite strands of DNA within a distance of up to 10 base pairs (bp) of each other. If two SSBs are more than 10 bp apart, it is denoted as 2SSB, and if two SSBs are within 10 bp of each other but on the same strand of DNA, it is denoted as SSB+. Other configurations such as DSB+ and DSB++ are forms of complex DSBs, as shown in Figure 13 in Section 4.2.

4. Discussion

4.1 Fluence and Energy Deposition Results

Figures 4 and 6 illustrate the fluence profiles for proton and alpha particle beams across all energies, while Figures 10 and 11 show the energy deposition profiles for these particles. Table 2 is closely related to Table 3 and Figure 12, given that DNA is primarily located in the cell nucleus, and a higher energy dose deposited in the nucleus leads to more significant DNA damage.

The analysis showed that as the beam energy increases, the point of maximum energy deposition shifts deeper into the cell, occurring within a range of approximately 3 micrometers, located near the center of the cell and consequently its nucleus. These findings confirm that energy deposition is influenced by the ion type and beam energy deposited in the medium, demonstrating the model's effectiveness in simulating these interactions. Across all energy levels analyzed, both alpha particle and proton beams exhibited similar fluence and energy deposition profiles, emphasizing the model's capability to accurately simulate the effects of different particle types.

These findings are consistent with previous reports highlighting the increased energy deposition of alpha particles in biological media due to their high LET. For instance, Taleei et al.(11) emphasized the enhanced biological effectiveness of alpha particles compared to protons, particularly in subcellular targets such as the nucleus. Similarly, Nikjoo et al. (10) demonstrated that alpha particles tend to generate more localized and complex ionization tracks, leading to concentrated energy deposition profiles. Our results support these conclusions by showing that alpha particles, even at low energies, exhibit a pronounced peak of energy deposition within the nuclear region.

However, contrary to traditional radiobiological assumptions, our simulations suggest that alpha particles may penetrate deeper at very low energies than previously expected. This observation contrasts with the predictions from some earlier Monte Carlo models (5), which assumed more limited ranges for alpha particles in simplified geometries. These findings may reflect the influence of cross-section

parameters and model resolution in FLUKA simulations, and further experimental validation is warranted.

This study presented significant advancements in understanding the interaction between alpha particles and protons with geometric cellular models using FLUKA software. Our results confirm that alpha particles exhibit higher energy deposition at shallower depths due to their high LET, while protons display more homogeneous energy deposition profiles. Furthermore, we showed that high-energy beams can increase fluence in the cell nucleus, especially for alpha particles, partially challenging known limitations regarding their restricted range. The analysis of DNA damage using MCDS revealed distinct patterns between the two particles, highlighting the differential impact on the induction of biological damage. These findings not only corroborate previous studies but also offer new perspectives on the applicability of these radiations in targeted radiotherapeutic treatments.

4.2 DNA damage

Single-strand breaks (SSBs) and base damages (BDs) slightly increase with energy due to the greater ionization and penetration into the DNA. As shown in Tables 3 and 4, alpha particles cause more complex breaks more frequently, accounting for 28.1% of the breaks, whereas protons result in complex lesions 25.5% of the time. The software limitations prevented the simulation of alpha particles with energies below 4 keV, but the percentage of DNA damage remained fairly consistent, maintaining a stable distribution. The analysis showed that simple damages increase with energy due to higher ionization capacity.

The patterns of DNA damage observed in our simulations align with the theoretical framework proposed by Semenenko and Stewart (2004), in which high-LET radiation results in increased yields of complex lesions such as DSB+ and DSB++. Our analysis reinforces this trend by demonstrating that alpha particles cause a greater proportion of complex breaks (up to 28.1%) compared to protons. This is also in line with the modeling approach of Abolfath et al. (2013), who used molecular dynamics to show higher damage complexity in densely ionizing tracks.

Recent reviews (10-11) have emphasized the need for more detailed simulations to bridge the gap between energy deposition patterns and biological effect modeling. Our study contributes to this effort by offering simulation-based estimates that distinguish between damage types and their spatial distribution within the nucleus.

4.3 Radiobiological Principles

At very low energies, alpha particles can penetrate more deeply due to their smaller cross-section, which reduces the probability of interacting with matter. As a result, alpha particles show higher fluence and dose deposition, even though radiobiological principles suggest they should penetrate less than protons. Interestingly, alpha particles demonstrated greater penetration at very low energies, which challenges conventional radiobiological expectations. This led to higher fluence and dose deposition than theoretically anticipated.

4.4 Study Limitations

Each Monte Carlo simulation involves uncertainties related to the number of primary particles and the events configured. Additionally, uncertainties connected to the geometric model, particularly its simplifications, must be considered. These uncertainties impact the simulations and are associated with both the number of primary particles and the model's simplifications.

5. Conclusions

In this study, we investigated the interaction of proton and alpha particle beams with a geometric cellular model using FLUKA simulations and MCDS software to estimate DNA damage. In conclusion, the results offer a detailed characterization of the microdosimetric behavior of proton and alpha particle beams within a simplified cellular framework. The results demonstrate that alpha particles exhibit higher energy deposition at shallower depths due to their high LET, while protons display more homogeneous energy deposition profiles. Notably, high-energy beams increased particle fluence in the nucleus, particularly for alpha particles, challenging conventional assumptions about their limited range.

The DNA damage analysis revealed distinct patterns between protons and alpha particles, highlighting the differential biological impacts of these particles. These findings not only corroborate previous studies but also offer new perspectives on the applicability of these radiations in targeted radiotherapeutic treatments.

While this study contributes to a deeper understanding of radiation interactions at the cellular level, it is limited by the simplifications of the geometric cellular model. Future research should explore more complex cellular geometries and validate simulation results experimentally to further refine these findings. Nevertheless, this work lays a foundation for optimizing radiotherapy treatments by leveraging the unique properties of proton and alpha particle beams.

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