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Using a Monte Carlo simulation to analyze the ideal activity for a phosphorus-32 polymeric brachytherapy source for paraspinal tumors

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ABSTRACT

A promising radioactive source for use in intracavitary brachytherapy is phosphorus-32. This source has been prominent as a minimally invasive treatment for craniopharyngiomas and in the treatment of metastatic bone diseases in general and has been developed at Nuclear and Energy Research Institute (IPEN). In this work, a Monte Carlo simulation was used to evaluate the ideal activity this source must have to deliver a 1 Gy/min dose rate. TOPAS was used to model the simulation, and its geometry was simulated with the source centered in the origin point, inserted into an isotropic volume of water of 17.42 cm^3. The source has the decay properties of phosphorus-32. The total dose was calculated using volumetric scorers. The results were promising, showing that the initial activity must be 86.14 mCi or 2871 MBq to obtain the 1 Gy/min dose rate. With the initial activity measured in this work, it is possible to minimize the patient's exposure to radiation, while ensuring the quality of the treatment.

1. Introduction

The tumors of central nervous system cancer occur due to the growth of abnormal cells in the tissues of the brain, cranial nerves, and meninges. This type of cancer represents 1.4% to 1.8% of all malignant tumors worldwide. Despite its relatively low incidence, this type of cancer contributes to global morbidity (Sung et al., 2021). The incidence of central nervous system tumors is slightly higher in males than females. Central nervous system cancer represents approximately 3.5% of all malignant neoplasms worldwide and ranks 18th in mortality, according to the World Health Organization (Ferlay et al., 2024).

Although surgical intervention is the most common technique for treating cancer, it tends to have high recurrence rates and may not always be feasible. In this context, radiotherapy is a widely employed treatment option, divided into brachytherapy and teletherapy. In brachytherapy, one or several radioactive sources are positioned very close to or directly in contact with the lesions to be treated. The main advantage of this type of treatment is the precise delivery of doses to the target, allowing for the preservation of healthy tissues around it. However, to achieve success in treatment, the target needs to be small and well-defined (Lim and Kim, 2021).

For brachytherapy treatments, isotopes that emit gamma rays or beta particles within an acceptable energy range and can be produced with adequate activity are most commonly used (Kemikler, 2019). For example, radioactive sources of iodine-125 in the form of seeds are widely used in brachytherapy for various forms of cancer and in a variety of anatomical sites (Lin et al., 2023; Pons-Llanas et al., 2018).

A promising source for use in brachytherapy is phosphorus-32 (^{32}P), which is a radionuclide that emits purely beta radiation. This type of radiation has lower penetration than gamma radiation, for example, and can be stopped by a thin sheet of aluminum, plastic, water, and superficial layers of skin (Wrixon et al., 2004). With lower tissue penetration, there is a possibility of even greater concentration of the delivered dose and consequently, a stronger therapeutic effect. Particularly for intracavitary brachytherapy (IBT), this radionuclide has stood out as a minimally invasive treatment for craniopharyngiomas and in the treatment of metastatic bone diseases in general (Solodyannikova et al., 2021).

For the treatment of paravertebral and intracranial cancer, initially yttrium-90 (^{90}Y) blades encapsulated in titanium were used (DeLaney

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et al., 2003). However, a polymeric base plaque was developed which showed advantages over yttrium-90 and titanium. This plaque is made of a flexible silicone incorporating phosphorus-32, making it a simpler and cheaper option to manufacture (Folkert et al., 2012; Saxena et al., 2011; Tong et al., 2014). As it is flexible, it can conform perfectly to the spinal region, which, due to its indentations, requires a very pliable source to achieve the desired effect. Thus, these plates can be used in patients who do not respond to other existing treatments for cancer (Imber et al., 2018).

In the procedure, doctors apply a radioactive polymer piece, produced with phosphorus-32, directly to the area containing cancer cells for a determined period. This piece is encased in silicone, with a total thickness of 0.5 mm. The plaque is sterilized, and its integrity is verified. The medical team then determines the ideal position and necessary exposure time. It is then implanted in the area affected by the tumor, and after the required time has passed, it is removed, and the patient is evaluated (Folkert et al., 2012). Therefore, combining the flexibility of the source with the low penetration of radiation from phosphorus-32, it is possible to target exactly the tumor region without damaging adjacent structures and tissues, given that the spinal cord is an extremely sensitive part of the body.

Currently, this source type is only available as RIC Conformal Source Model 100 (RIC-100) by R.I. Consultants in Hudson, New Hampshire. The RIC-100 is a conformal ^{32}P source that comprises chemically bound ^{32}P integrated into a malleable and translucent polymer layer, which is further coated with silicone, resulting in an overall thickness of roughly 0.5 mm (Folkert et al., 2012). This source is mainly used at the Memorial Sloan-Kettering Cancer Center, therefore, there are not many clinical studies about it. However, the ones available were analyzed in this work. Other formulation based on this source has been developed at Nuclear and Energy Research Institute (IPEN), using silicone rubber as the polymeric base.

To produce such source, it is of great importance to have a specific dose rate in mind, for the dural to not receive more dose than needed. Previous and similar formulations for this source and its clinical uses were analyzed. With that, calculating the treatment's mean dose rate of each one and combining them, it was concluded that a good dose rate to be based on would be 1 Gy/min (Folkert et al., 2012; Cohen et al., 2014; Tong et al., 2014; Silva et al., 2021).

Monte Carlo simulations have been applied to analyze various parameters typically encountered in experimental measurements. Their effectiveness lies in their ability to simulate radiation transport, employing probability distributions to model interactions with electrosferic electrons and, in certain instances, with nuclei from diverse materials. Through these simulations, particle tracks or histories can be generated, yielding valuable data on the physical quantities under investigation (Knoll et al., 2022).

TOPAS, TOol for PArticle Simulation, is a Geant4-based Monte Carlo code, that enables the simulation of all ionizing particle types through complex geometries commonly encountered in medical scenarios (Perl et al., 2012). Especially with the particle source model within the code, known as the "Volumetric Source", TOPAS' capabilities were broadened to include brachytherapy applications. In this mode, users designate a specific radioactive material within a designated source component, prompting TOPAS to initiate particle emissions from randomly selected points within this active material (Faddegon et al., 2020).

In this work, TOPAS (Perl et al., 2012) was used to simulate the phosphorus-32 polymeric source developed at IPEN in order to determine the ideal source activity to deliver a 1 Gy/min dose rate.

2. Methods

TOPAS version 3.8 was used (Perl et al., 2012). The geometry developed for the simulation had the source (with dimensions 5.0 cm x 5.0 cm x 0.04 cm), centered in the origin point and inserted into an isotropic volume of water of 17.42 cm^3 (33 x 33 x 4 mm). Fig. 1 shows a visual representation of it. The choice of the water phantom was made because since the only method of comparing the results of this work is with the existing RIC-100 source, all existing studies and parameters for the RIC-100 source are conducted and measured in water (Mulet et al., 2022).

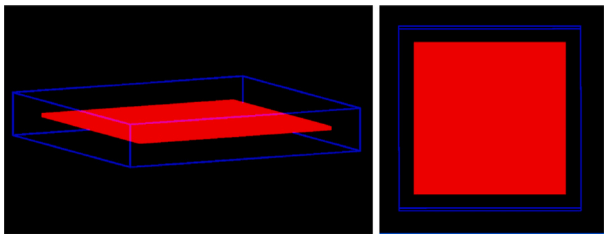

Fig. 1. Simulated geometry, with the isotropic water volume in blue and the phosphorus-32 source in red. Left: geometry side view; right: geometry overview.

The employed physics during the simulation process was the TOPAS default (Perl et al., 2012), which comprises the models g4em-standard_opt4, g4h-phy_QGSP_BIC_HP, g4decay, g4ion-binarycascade, g4h-elastic_HP and g4stopping. The g4em-standard_opt4 model is used in examples of electromagnetic (EM) physics, providing high accuracy for electrons, hadrons, and ions. It includes detailed descriptions of ionization, bremsstrahlung, pair production, and multiple Coulomb scattering, using the WentzelVI and Goudsmit-Saunderson models. This model balances performance in terms of precision with CPU efficiency.

Furthermore, g4h-phy_QGSP_BIC_HP manages simulations of non-elastic nuclear interactions using the Binary Intranuclear Cascade (BIC) model and models neutron elastic scattering below 20 MeV with high precision. The g4decay refers to the decay of all long-lived nuclei, while g4ion-binarycascade addresses nuclear interactions of light ions using a binary cascade. The g4h-elastic_HP focuses on the elastic scattering of hadrons, using high precision libraries for neutrons below 20 MeV. Finally, g4stopping refers to the capture of charged particles at rest.

The source developed at IPEN is made of silicone rubber with radioactive orthophosphoric acid ($H_3{}^{32}PO_4$) dispersed in it. The silicone rubber has a density of 1.08 g/mL. Considering that the phosphorus-32 is equally distributed throughout the source, it is assumed that the whole plaque has the decay properties of phosphorus-32, whose beta emission spectrum was extracted from the International Atomic Energy Agency (IAEA) website (International Atomic Nuclear Agency, 2024). Fig. 2 shows the phosphorus-32 β spectrum used. Therefore, the source type set was *"Volumetric"* and the total dose was calculated using the volumetric scoring *"DoseToMedium"*. It is crucial for the code to use random source points rather than treating the entire film as a uniform source. This is because the decay will occur at random points throughout the material.

Eq. (1) was used to obtain the initial activity to deliver the intended dose. D_h is the total dose divided by the number of histories, A is the initial activity and $\bar{D}$ is the dose rate.

$$D_h \times A = \bar{D} \longrightarrow A = \frac{\bar{D}}{D_h} \tag{1}$$

3. Results and discussion

Figs. 3–5 show the simulated particle trajectories for different numbers of histories set on the code. Red was used for β- particles and green for photons. From them, it is possible to observe the events during the simulation and notice that not all β particles are able to overcome the water barrier, as expected.

Table 1 shows the results of dose/histories, the standard deviation, the percentage error and the activity values obtained. In Monte Carlo simulations, the accuracy of the results is highly dependent on the

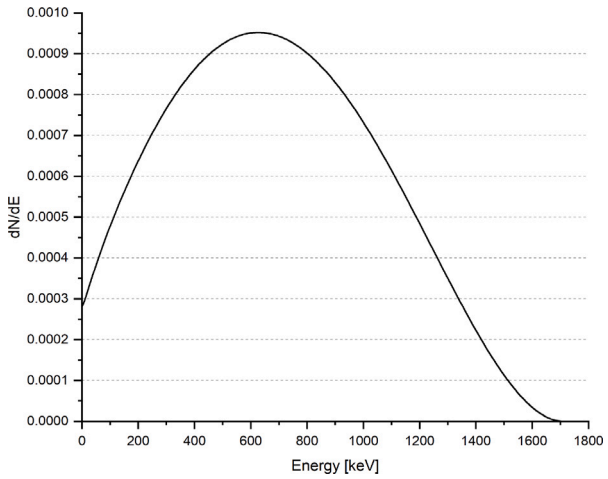

Fig. 2. Beta spectrum of phosphorus-32, extracted from the IAEA website (International Atomic Nuclear Agency, 2024).

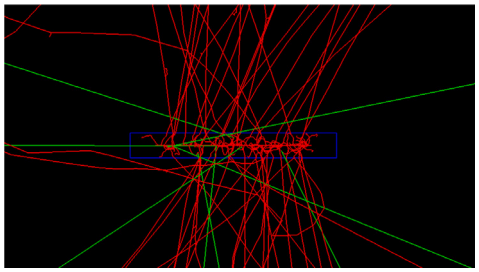

Fig. 3. Particle trajectories 100 histories.

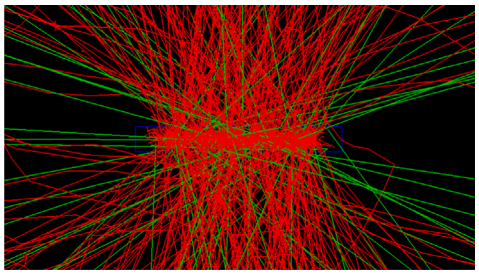

Fig. 4. Particle trajectories for 1,000 histories.

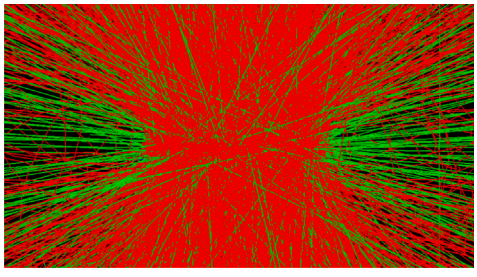

Fig. 5. Particle trajectories for 10,000 histories.

number of simulated histories. As the number of histories increases, the statistical error tends to decrease, following an approximately inverse relationship with the square root of the number of histories (Chin, 2017). The results presented in Table 1 demonstrate this, with the simulation's percentage error gradually decreasing as the number of histories increases. From the simulation with 10^8 histories, we have a dose per histories value of 5.51×10^{-12} Gy/histories.

Table 1
Results obtained from the simulation for each number of histories.

Histories	Dose/Histories [Gy/histories]	σ	Error [%]	Activity [MBq]	Activity [mCi]
10^2	5.51×10^{-12}	1.52×10^{-13}	2.763	3.029×10^3	90.88
10^3	5.81×10^{-12}	5.12×10^{-14}	0.882	2.875×10^3	86.26
10^4	5.85×10^{-12}	1.63×10^{-14}	0.279	2.854×10^3	85.63
10^5	5.82×10^{-12}	5.17×10^{-15}	0.089	2.868×10^3	86.04
10^6	5.82×10^{-12}	1.63×10^{-15}	0.028	2.871×10^3	86.14
10^7	5.82×10^{-12}	5.17×10^{-16}	0.009	2.872×10^3	86.15
10^8	5.82×10^{-12}	1.63×10^{-16}	0.003	2.871×10^3	86.14

Therefore, replacing the values on Eq. (1), to obtain the dose rate of 1 Gy/min (or 0.0167 Gy/s) on a volume of 17.42 cm^3, it is necessary to have a source with the activity shown in Eq. (2).

$$A = \frac{\bar{D}}{5.82 \times 10^{-12}} \longrightarrow A = \frac{0.0167}{5.82 \times 10^{-12}} \Rightarrow A = 2,871 \text{ MBq} \quad (2)$$

From the final simulation results, the source's initial activity must be 2,871 MBq or 86.14 mCi to obtain the desired 1 Gy/min dose rate. Since the RIC-100 is the only existing source with these properties and uses phosphorus-32 as the radionuclide, it serves as the sole comparison benchmark for the results of this work. From the literature, the RIC-100 source is available at maximal activity of 4 mCi/cm^2. Therefore, for a 5.0 x 5.0 cm source, the maximal activity for it would be 100 mCi.

Considering that the RIC-100 source has a greater thickness than the one produced and simulated at IPEN, it was expected that the simulation result would be lower than the reported activity of the RIC-100. Given that the simulated volume is approximately 20% smaller (based on the thickness difference of 0.4 mm versus 0.5 mm between the sources), the initial activity obtained was 14% different from the baseline value of 100 mCi. Although the absolute difference is significant, this difference is deemed acceptable when taking into account the mentioned factors.

4. Conclusion

This work proposed the simulation of the phosphorus-32 source produced at IPEN to estimate the ideal initial activity it must have in order to deliver a 1 Gy/min dose rate. With the data acquired, it is possible to observe that the initial activity has to be 2,871 MBq (or 86.14 mCi). As it was discussed, this result is acceptable, considering the clinical uses of similar formulations for this source, especially from RIC-100 uses.

In summary, brachytherapy with a malleable source of ^{32}P is a promising type of procedure to treat cancer due to its radiotherapy properties. With the initial activity measured in this work, it is possible to minimize the patient's exposure to radiation, while ensuring the quality of the treatment. Furthermore, this result also facilitates the source's manufacturing.

CRediT authorship contribution statement

Lara El Hajj: Writing – original draft, Visualization, Validation, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ana Laura Burin:** Writing – original draft, Methodology, Investigation. **Cristhian Ferreira Talacimon:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Ilca Marli Moitinho Amaral Medeiros:** Methodology, Investigation. **Maria Eduarda Zaganin Rigo:** Writing – original draft, Methodology, Investigation. **Paulo Victor dos Santos Tavares:** Writing – original draft, Validation, Software, Methodology, Investigation, Formal analysis, Data curation. **Priscila Santos Rodrigues:** Writing

– original draft, Methodology. **Thuany Correa Nogueira:** Methodology, Investigation. **Wilmmer Alexander Arcos Rosero:** Methodology, Investigation. **Orlando Rodrigues Jr.:** Supervision, Software, Methodology, Formal analysis, Data curation. **José Mauro Vieira:** Supervision, Methodology, Investigation, Conceptualization. **Carlos Alberto Zeituni:** Supervision, Formal analysis, Conceptualization. **Maria Elisa Chuery Martins Rostelato:** Writing – review & editing, Supervision, Project administration, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Declaration of generative AI in scientific writing

Generative AI was used in this work only in the introduction section, for translation improvement purposes. After use, the content was reviewed and edited as necessary. The authors assume full responsibility for the publication's content.

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