



Carbon Ion Hadron Therapy: Analytical Formulation of Tumor Regression in Pancreatic Cancer by Computed Tomography

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Abstract

This study formulates a mathematical and computational model of tumor-cell-density regression in pancreatic cancer treated with carbon-ion hadron therapy. A reaction-diffusion equation with logistic proliferation and a local radiation-induced loss term is derived term by term, discretized with a two-dimensional finite-difference scheme and forward Euler time stepping, and implemented in Python. The treatment input follows a published carbon-ion schedule of 48 Gy(RBE) in 12 fractions of 4 Gy(RBE). The simulation produces sequential two- and three-dimensional maps of the modeled tumor-cell density as a function of accumulated dose; in the three-dimensional reconstruction the relative tumor volume falls from 0.662 after the first fraction to 0.001 after the twelfth, while the two-dimensional density maps reach a thresholded value of zero from fraction six onward. The diffusion coefficient is held constant (homogeneous-medium approximation) and the dose response is linear;

both are stated as simplifications, not as complete radiobiological descriptions. Possible translational uses, namely patient-specific parameter estimation, CT-derived geometry, dose optimization and treatment adaptation, are discussed together with the calibration and validation that would be required before any clinical decision-support application.

Keywords: pancreatic cancer, carbon-ion therapy, reaction-diffusion model, finite-difference method, Euler method, computational simulation.

1 Introduction

Cancer

Cancer is one of the main public health problems worldwide: about 20 million new cases and 9.7 million deaths were estimated for 2022 [1, 2]. Cancer types differ widely in clinical behavior and therefore in treatment. Figure 1 shows the number of deaths for six major cancer types in 2022, with pancreatic cancer, the subject of this work, among them.



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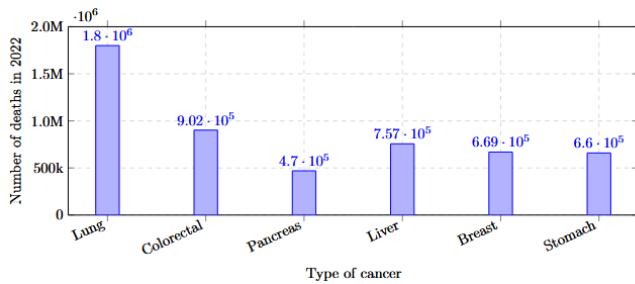


Figure 1. Estimated number of deaths from selected major cancer types worldwide in 2022 (data from GLOBOCAN 2022 [2]).

Pancreatic Cancer

Pancreatic cancer is not among the most frequent malignancies, but it ranks among the leading causes of cancer death because of its very low survival [2, 3], and its burden in Brazil is increasing. For each year of the 2026-2028 period, the Brazilian National Cancer Institute (INCA) estimates approximately 13,240 new cases in the country, with crude incidence rates also reflecting an upward trend [4, 5]. Mortality from this neoplasm has also been rising [6, 7], which motivates more precise therapeutic strategies. Figure 2 shows the estimated number of new pancreatic cancer cases in 2026 by geographic region of Brazil; the Southeast and South regions concentrate most cases [8].

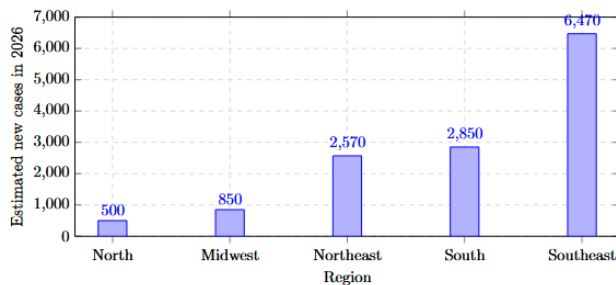


Figure 2. Estimated number of new pancreatic cancer cases in Brazil by geographic region for 2026 (data from INCA [8]).

Among advanced external-beam radiotherapy techniques, hadron therapy delivers dose with beams of charged particles, mainly protons and carbon ions [9, 10]. Carbon ions are heavier than protons, and their physical and biological properties may allow more precise dose deposition and greater effectiveness in some tumors [9, 11]. Figure 3 summarizes the two modalities. Although hadron therapy includes both, this study is restricted to carbon-ion therapy because of its potential in hard-to-treat tumors such as pancreatic cancer.

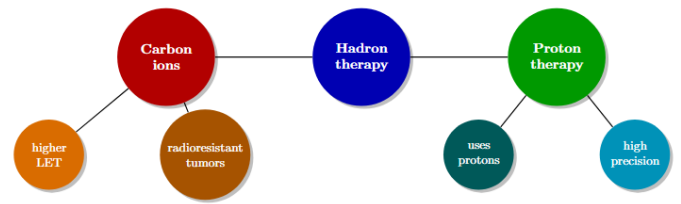


Figure 3. Schematic comparison of carbon-ion and proton hadron therapy modalities.

Carbon-Ion Hadron Therapy

Carbon-ion hadron therapy is an external-beam radiotherapy modality in which accelerated heavy-ion beams deliver dose conformally to the tumor volume [9, 10]. Carbon ions have a higher linear energy transfer (LET) and a greater relative biological effectiveness (RBE) than photons, which may favor the treatment of deep-seated, locally advanced or radioresistant tumors [11, 12]. For these reasons carbon-ion therapy is considered here in the specific context of pancreatic cancer.

Compared with photon beams, carbon ions have a depth-dose profile with a pronounced Bragg peak, so the high-dose region can be placed in the target while the entrance and distal doses are limited. The numerical value of the RBE, however, depends on radiation quality, biological endpoint, tissue type, fractionation and the RBE model used [12, 13]. For pancreatic cancer, *in vitro* studies have reported carbon-ion RBE values that vary with cell line and LET, which is why physical dose and RBE-weighted dose must be kept distinct [13].

Importance of Dosimetry

Dosimetry quantifies the absorbed-dose distribution in the tumor and in the surrounding healthy tissue [14, 15]. Accurate dose delivery is needed to maximize tumor control while limiting damage to normal structures, which is particularly demanding in the pancreas, where the duodenum, stomach and bowel lie close to the target [15, 16]. Dosimetric analysis is therefore central to treatment planning and to the evaluation of treatment efficiency, and it is the link between clinical practice and the mathematical model developed here.

Rationale and Motivation

Pancreatic cancer combines high lethality with an increasing burden in Brazil [4], and it needs more precise therapeutic approaches. Mathematical modeling and numerical simulation have been applied internationally to describe tumor evolution

and radiotherapy response [17]; reaction-diffusion models in particular have been used to predict radiotherapy efficacy through spatial dose-response formulations [18]; however, such approaches remain comparatively few in the Brazilian context for hadron therapy of pancreatic cancer, which motivates the present work. This work addresses that gap by analyzing carbon-ion therapy for pancreatic cancer with differential equations and computational simulation.

Study Objectives

- Present the physical foundations of carbon-ion hadron therapy.
- Describe the clinical and dosimetric relevance of pancreatic cancer for hadron therapy.
- Propose a simplified mathematical model of the tumor-cell-density response to a prescribed dose.
- Implement the model numerically in Python.
- Simulate the tumor-cell-density response in a digital phantom of the pancreatic region.
- Evaluate the results against the specialized literature.

2 Literature Review

Fundamentals of Particle Physics

To establish the physical basis of carbon-ion hadron therapy, this section traces the hierarchy from elementary particles to atomic nuclei and, ultimately, to the therapeutic use of accelerated carbon ions. Particle physics studies the elementary constituents of matter and the fundamental interactions between them [19], providing the theoretical basis from which the properties of carbon ions relevant to hadron therapy are derived. The Standard Model of particle physics is the main theoretical framework for the known elementary particles, which it organizes into fermions, gauge bosons and the Higgs boson [20]. Figure 4 shows this classification, separating the particles that make up matter from those that mediate the fundamental interactions. This classification places the formation of composite particles such as protons and neutrons on a more fundamental scale, which leads to hadrons and, from there, to the carbon ions used in hadron therapy [20].

Quarks

Quarks are elementary particles of the Standard Model and are among the fundamental building blocks of

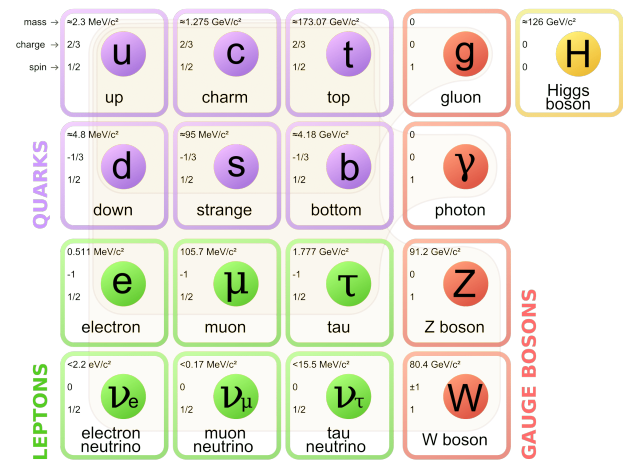


Figure 4. Standard model of particle physics.

matter [20]; their bound states form the protons and carbon nuclei that are accelerated and used in hadron therapy. Figure 5 shows the quark composition of the proton (two up quarks and one down quark) and of the neutron (two down quarks and one up quark). This composition explains how elementary particles give rise to composite structures.

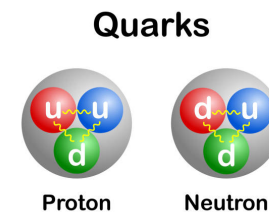


Figure 5. Schematic quark composition of the proton and neutron.

Hadrons

Composite particles formed by quarks are called hadrons [19]; among them, the proton and the carbon nucleus are the particles directly relevant to hadron therapy. Figure 6 illustrates this classification: hadrons include baryons, such as protons and neutrons, formed by three quarks, and mesons, formed by a quark and an antiquark. The proton and neutron are therefore particular hadrons and the main constituents of the atomic nucleus.

Atomic nuclei are formed by protons and neutrons [21]. The carbon nucleus contains six protons and, in its most abundant isotope, ^{12}C , six neutrons (Figure 7); the nuclear structure of ^{12}C directly determines the charge, mass, and stopping power that make it suitable for therapeutic use. Ionized and accelerated to high energies, ^{12}C ions are used in hadron therapy because their physical and biological properties favor localized

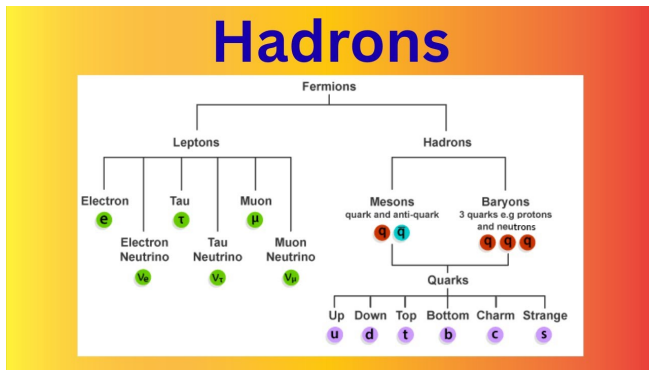


Figure 6. Simplified classification of hadrons, highlighting protons and neutrons as baryons formed by three quarks.

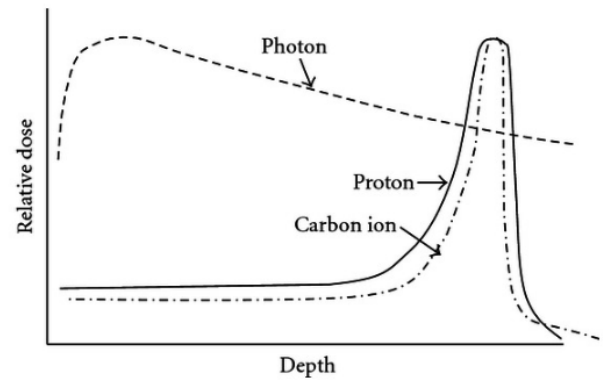


Figure 8. Relative depth-dose profiles for photon, proton and carbon-ion beams, showing the Bragg peak (source given by the author as ResearchGate, 2026; original source and permission to be provided).

dose deposition in tumor tissue [10].

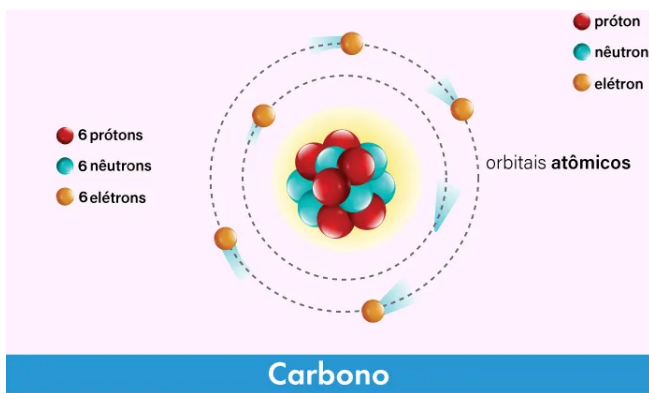


Figure 7. Schematic atomic structure of carbon.

Interaction of Radiation with Matter

Radiation interacts with matter by transferring energy to the medium, mainly through atomic excitation and ionization [22]. For charged particles such as protons and carbon ions, the energy transferred per unit path length increases along the track and reaches a maximum near the end of the range, the Bragg peak [23]. Photons, in contrast, deposit dose over a broader depth range. Figure 8 compares the depth-dose profiles of photon, proton and carbon-ion beams.

Carbon-Ion Beam Delivery

In carbon-ion therapy, ionized carbon nuclei are accelerated to high energies to form a therapeutic beam that irradiates the tumor volume with high precision [9]. The patient lies in the treatment room while the beam-delivery system, which may include a rotating gantry, directs the beam from different angles, concentrating the dose in the tumor and sparing the adjacent tissue [24]. This makes carbon-ion therapy attractive for deep-seated, complex or radioresistant tumors. Figure 9 shows a treatment room with a

rotating gantry for carbon-ion therapy.



Figure 9. Treatment room with a rotating gantry for carbon-ion hadron therapy (image: Toshiba Energy Systems & Solutions Corporation, 2024; permission to be confirmed).

Pancreatic Cancer in the Context of Hadron Therapy

Pancreatic cancer is difficult to manage clinically. The tumor usually lies deep in the abdomen and close to organs at risk, which makes radiotherapy planning demanding [25]. Carbon-ion therapy is promising here because it achieves high dose conformity to the target and can reduce unnecessary irradiation of nearby healthy tissue. Figure 10 shows computed tomography (CT) images used in treatment planning and verification of a carbon-ion treatment for pancreatic cancer. Besides the planning CT, the figure shows anatomical changes seen on CT scans acquired during treatment, which illustrates why the geometry of the target and neighboring organs must be monitored over the course of treatment.

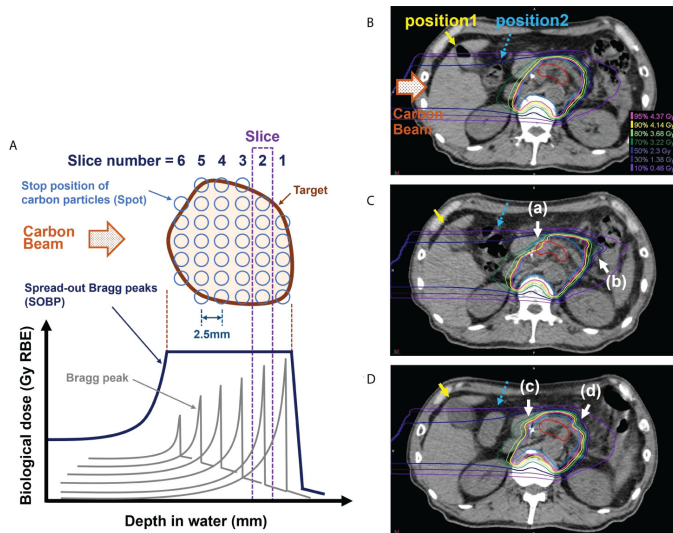


Figure 10. Treatment planning and dose distribution for carbon-ion therapy in pancreatic cancer, with in-room CT acquired during treatment. Reproduced from Kusano et al. [25] (license to be confirmed).

Dosimetry in Carbon-Ion Hadron Therapy

In carbon-ion therapy, dosimetry evaluates the absorbed-dose distribution within the patient so that the tumor receives the prescribed dose while exposure of adjacent healthy tissue is minimized [26]. Because the carbon beam is highly conformal, planning requires careful analysis of target geometry, tumor depth and neighboring structures. Figure 11 shows a CT image with the dose distribution superimposed for a pancreatic cancer case treated with carbon ions.

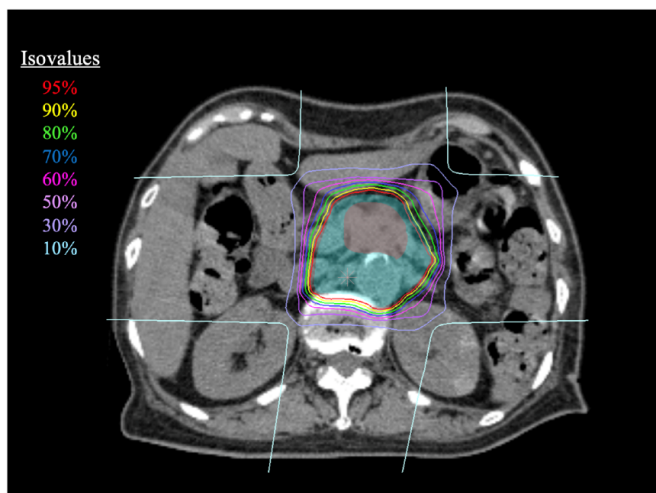


Figure 11. Carbon-ion dose distribution (isodose lines) superimposed on a CT image of a pancreatic cancer case (source to be provided by the author).

Mathematical Modeling Applied to Dosimetry

According to the model of Borasi and Nahum [27], tumor evolution under radiotherapy can be described

by a reaction-diffusion partial differential equation in which the tumor-cell density varies with position and time. The terms of the equation represent the spatial spread of the cells, their proliferation, and the loss caused by radiation. The choice of model structure affects the dose estimated to achieve tumor control [28]. This approach is adopted here as the theoretical basis and adapted to carbon-ion therapy and to a Python simulation that generates simulated images of the pancreatic tumor during treatment.

In general form, the model reads

$$\frac{\partial c}{\partial t} = \nabla \cdot [D(x, y) \nabla c] + \rho c \left(1 - \frac{c}{c_{\max}}\right) - R(x, y, t) c, \quad (1)$$

where $c = c(x, y, t)$ is the tumor-cell density, $D(x, y)$ is the cellular diffusion coefficient, ρ is the tumor-cell proliferation rate, $c_{\max}$ is the maximum tumor-cell density supported by the modeled medium, and $R(x, y, t)$ is the local radiation-induced loss rate.

3 Materials and Methods

The partial differential equation is solved with the finite-difference method, which approximates derivatives by differences between function values at discrete grid points. The method is simple to implement, well suited to reaction-diffusion equations, and easily coded in Python to generate two-dimensional maps and simulated images of tumor evolution [29].

For the anatomy, a digital phantom is used — a computational representation of biological structures employed to simulate tissues, organs and tumor regions in imaging and radiotherapy-planning studies [30]. In this work, a simplified two-dimensional synthetic geometry of the pancreatic region is adopted, rather than a full anatomical phantom. Here the phantom provides the geometry of the pancreatic region: the tumor contour, the adjacent tissue and the spatial distribution of dose in the numerical domain.

The computational simulation combines the mathematical model and the numerical method to produce visual and quantitative outputs, such as maps of tumor-cell density and synthetic images of tumor evolution during treatment. In radiotherapy, computerized planning and verification systems are needed to ensure accurate dose delivery and to reduce uncertainty [31], and simulation serves as a research tool for dosimetric analysis.

Construction of the Mathematical Model

The model follows the formulation of Borasi and Nahum [27], in which tumor evolution under radiotherapy is described by a reaction-diffusion equation; reaction-diffusion models have also been applied to predict radiotherapy efficacy through spatial dose-response formulations [18], and the same mathematical structure is adapted here to carbon-ion therapy of pancreatic cancer. Torres and Santos [32] argue that a model in the biosciences should start from a description of the physical-biological phenomenon, followed by its mathematical formalization and numerical implementation. Following this sequence, a simplified model is developed for the spatial and temporal evolution of a pancreatic tumor treated with carbon ions.

Let $c = c(x, y, t)$ be the tumor-cell density in a two-dimensional region $\Omega \subset \mathbb{R}^2$ representing a synthetic slice of the pancreatic region. The base model is Eq. (1), where

- $D(x, y)$ is the cellular diffusion coefficient;
- ρ is the tumor proliferation rate;
- $c_{\max}$ is the maximum tumor-cell density supported by the medium;
- $R(x, y, t)$ is the local radiation-induced loss rate.

Equation (1) has three contributions:

1. the diffusive term $\nabla \cdot (D \nabla c)$, which models the spatial spread of the cells;
2. the reactive term $\rho c (1 - c/c_{\max})$, which models limited tumor growth;
3. the term $-R(x, y, t) c$, which models radiation-induced cell killing.

Expansion of the Diffusive Term

As a first approximation the medium is assumed homogeneous within the analyzed region, that is,

$$D(x, y) = D, \quad D \text{ constant.} \quad (2)$$

This approximation isolates the coupling between diffusion, proliferation and radiation response, and it is consistent with the constant diffusion coefficient used in the reaction-diffusion treatment of Borasi and Nahum [27]. Pancreatic tissue is heterogeneous, so a patient-specific extension would replace D by $D(x, y)$, or by a piecewise field derived from anatomical segmentation. Constant D is a first-order

modeling choice, not a claim that pancreatic tissue is homogeneous.

Under this hypothesis D can be taken outside the divergence operator:

$$\nabla \cdot (D \nabla c) = D \nabla \cdot (\nabla c). \quad (3)$$

Since

$$\nabla \cdot (\nabla c) = \nabla^2 c, \quad (4)$$

it follows that

$$\nabla \cdot (D \nabla c) = D \nabla^2 c. \quad (5)$$

In two dimensions the Laplacian is

$$\nabla^2 c = \frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2}, \quad (6)$$

so the diffusive term becomes

$$D \nabla^2 c = D \left(\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2} \right). \quad (7)$$

Expansion of the Proliferation Term

The logistic growth term is

$$\rho c \left(1 - \frac{c}{c_{\max}} \right). \quad (8)$$

Distributing ρc gives

$$\rho c \left(1 - \frac{c}{c_{\max}} \right) = \rho c - \rho c \frac{c}{c_{\max}}. \quad (9)$$

Since

$$\rho c \frac{c}{c_{\max}} = \frac{\rho}{c_{\max}} c^2, \quad (10)$$

it follows that

$$\rho c \left(1 - \frac{c}{c_{\max}} \right) = \rho c - \frac{\rho}{c_{\max}} c^2. \quad (11)$$

Tumor growth is thus the sum of a positive linear term, ρc , responsible for proliferation, and a negative quadratic term, $-(\rho/c_{\max})c^2$, responsible for growth saturation.

Incorporation of the Dose Effect

To couple the model to dosimetry, $\mathcal{D}(x, y, t)$ denotes the local RBE-weighted dose delivered per time step, in Gy(RBE) per fraction. In this proof-of-concept formulation the radiation response is linear in dose,

$$R(x, y, t) = \alpha \mathcal{D}(x, y, t), \quad (12)$$

where α is an effective radiosensitivity coefficient with units of inverse dose, so that αD has units of inverse time (fraction⁻¹). Hence

$$-R(x, y, t) c = -\alpha D(x, y, t) c. \quad (13)$$

The linear term is a phenomenological simplification. A more complete description of fractionated irradiation uses the linear-quadratic (LQ) model, in which the surviving fraction after a dose d per fraction is $S = \exp[-(\alpha_{LQ}d + \beta_{LQ}d^2)]$. Borasi and Nahum [27] derive the radiotherapy term of reaction-diffusion models from LQ theory, and clinical studies show wide variation of α_{LQ} , β_{LQ} and α/β across tumor sites and histologies [33]. The linear response used here is therefore not presented as a biological law; it is the explicit approximation adopted for the numerical demonstration, and α is an effective parameter, not the LQ α_{LQ} .

Substitution into the Model

Substituting Eqs. (7), (11) and (13) into Eq. (1) gives

$$\begin{aligned} \frac{\partial c}{\partial t} = D \left(\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2} \right) \\ + \left(\rho c - \frac{\rho}{c_{\max}} c^2 \right) - \alpha D(x, y, t) c, \end{aligned} \quad (14)$$

and, removing the parentheses,

$$\begin{aligned} \frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} + D \frac{\partial^2 c}{\partial y^2} + \rho c \\ - \frac{\rho}{c_{\max}} c^2 - \alpha D(x, y, t) c. \end{aligned} \quad (15)$$

Equation (15) is the continuous model used in this work. On its right-hand side, the first two terms govern the spatial redistribution of tumor-cell density, the third models proliferation, the fourth limits growth, and the fifth represents dose-induced cell killing.

Temporal Discretization

For the implementation an explicit finite-difference scheme is used. Let $t_n = n\Delta t$, with time step $\Delta t > 0$. The time derivative is approximated by the forward difference

$$\frac{\partial c}{\partial t}(x_i, y_j, t_n) \approx \frac{c_{i,j}^{n+1} - c_{i,j}^n}{\Delta t}. \quad (16)$$

This follows from the Taylor expansion

$$c(x, y, t + \Delta t) = c(x, y, t) + \Delta t \frac{\partial c}{\partial t}(x, y, t) + \mathcal{O}(\Delta t^2). \quad (17)$$

Isolating the time derivative,

$$\frac{\partial c}{\partial t}(x, y, t) = \frac{c(x, y, t + \Delta t) - c(x, y, t)}{\Delta t} + \mathcal{O}(\Delta t), \quad (18)$$

and neglecting the higher-order terms gives approximation (16).

Spatial Discretization

Consider a regular two-dimensional grid with

$$x_i = i h, \quad y_j = j h, \quad (19)$$

where $h = \Delta x = \Delta y$ is the spatial step.

The second derivative in x is approximated by central differences,

$$\frac{\partial^2 c}{\partial x^2}(x_i, y_j, t_n) \approx \frac{c_{i+1,j}^n - 2c_{i,j}^n + c_{i-1,j}^n}{h^2}, \quad (20)$$

and analogously in y ,

$$\frac{\partial^2 c}{\partial y^2}(x_i, y_j, t_n) \approx \frac{c_{i,j+1}^n - 2c_{i,j}^n + c_{i,j-1}^n}{h^2}. \quad (21)$$

Adding Eqs. (20) and (21) gives the five-point Laplacian,

$$\begin{aligned} \nabla^2 c(x_i, y_j, t_n) \approx \frac{1}{h^2} \left(c_{i+1,j}^n + c_{i-1,j}^n + c_{i,j+1}^n \right. \\ \left. + c_{i,j-1}^n - 4c_{i,j}^n \right). \end{aligned} \quad (22)$$

Substitution of the Discrete Approximations

To shorten the notation, let

$$L_{i,j}^n = c_{i+1,j}^n + c_{i-1,j}^n + c_{i,j+1}^n + c_{i,j-1}^n - 4c_{i,j}^n. \quad (23)$$

Substituting Eqs. (16) and (22) into Eq. (15) gives

$$\begin{aligned} \frac{c_{i,j}^{n+1} - c_{i,j}^n}{\Delta t} = D \frac{L_{i,j}^n}{h^2} + \rho c_{i,j}^n - \frac{\rho}{c_{\max}} (c_{i,j}^n)^2 \\ - \alpha D_{i,j}^n c_{i,j}^n. \end{aligned} \quad (24)$$

Multiplying both sides by Δt ,

$$\begin{aligned} c_{i,j}^{n+1} - c_{i,j}^n = \Delta t D \frac{L_{i,j}^n}{h^2} + \Delta t \rho c_{i,j}^n \\ - \Delta t \frac{\rho}{c_{\max}} (c_{i,j}^n)^2 - \Delta t \alpha D_{i,j}^n c_{i,j}^n, \end{aligned} \quad (25)$$

and adding $c_{i,j}^n$ to both sides yields the explicit update

$$\begin{aligned} c_{i,j}^{n+1} = c_{i,j}^n + \underbrace{\Delta t D \frac{L_{i,j}^n}{h^2}}_{\text{diffusion}} + \underbrace{\Delta t \rho c_{i,j}^n}_{\text{proliferation}} \\ - \underbrace{\Delta t \frac{\rho}{c_{\max}} (c_{i,j}^n)^2}_{\text{logistic limitation}} \\ - \underbrace{\Delta t \alpha D_{i,j}^n c_{i,j}^n}_{\text{dose effect}}. \end{aligned} \quad (26)$$

Numerical Stability

The choices of Δt and h control both the truncation error and the stability of the explicit scheme. Smaller values improve temporal and spatial resolution, whereas values that are too large introduce numerical error or instability. For the diffusion term of the two-dimensional explicit scheme, a standard sufficient stability condition is $D\Delta t/h^2 \leq 1/4$ [29], with D , Δt and h in consistent units. With the normalized values adopted here ($D = 0.08$, $\Delta t = 1$, $h = 1$), $D\Delta t/h^2 = 0.08$, which satisfies the bound. In addition, the coefficient of $c_{i,j}^n$ in Eq. (26), neglecting the logistic term, is $1 - 4D\Delta t/h^2 + \rho\Delta t - \alpha\Delta t\mathcal{D}_{i,j}^n = 1 - 0.32 + 0.03 - 0.32 = 0.39 > 0$ for $\mathcal{D} = 4$ Gy(RBE) per fraction, so the update preserves non-negative densities [29]. A full grid- and time-refinement study is a necessary next step before any clinical use; the present calculations are a proof-of-concept numerical demonstration.

Final Form of the Model

The model adopted in this work is given in continuous form by Eq. (15) and, in the discrete form implemented in Python, by Eq. (26). The matrix $c_{i,j}^n$ is read as a synthetic image of tumor-cell density: each element is the value of the pixel in row i and column j at treatment step n , and higher values represent higher modeled tumor-cell density. The matrix $\mathcal{D}_{i,j}^n$ is the spatial distribution of the dose delivered at step n . Iterating these matrices links the mathematical model, the dosimetry and the image-based visualization.

4 Results

Table 1 lists the clinical and numerical parameters of the simulation. The clinical schedule follows Liermann et al. [34], who treated locally advanced pancreatic adenocarcinoma with 48 Gy(RBE) in 12 fractions. Figures 12-15 show the modeled tumor-cell-density field in the pancreatic region for each fraction, and Figures 16-19 show the corresponding three-dimensional reconstruction of the isolated tumor mass.

Simulated Tumor-Cell-Density Response in the Pancreas

Figures 12-15 show the modeled tumor-cell-density distribution after each fraction. During fractions 1-3 (Figure 12) the high-density region remains concentrated around the initial lesion, while the surrounding field changes less; the relative tumor volume printed on the panels falls from 0.662 after the first fraction to 0.308 after the third fraction. This sequence reflects the cumulative effect of repeated

Table 1. Clinical and numerical parameters adopted in the simulation.

Parameter	Adopted value
Reference article	Liermann et al. [34]
Therapeutic modality	Carbon-ion hadron therapy
Tumor type	Locally advanced pancreatic adenocarcinoma
Reference clinical schedule	48 Gy(RBE) in 12 fractions
Dose per fraction	4.0 Gy(RBE)
Total number of fractions	12
Images generated	12 PNG images + 1 GIF
Type of image used	Axial CT and axial FAPI PET-CT
Equation employed	Reaction-diffusion equation with a linear dose-induced loss term, Eq. (15)
Anatomical geometry	Pancreatic structure based on an axial clinical image
Spatial grid	Uniform 2D grid; $h = 1$ normalized spatial unit
Initial tumor position	Head/body of the pancreas
Diffusion coefficient, D	0.08 normalized spatial unit ² per fraction
Proliferation rate, ρ	0.03 d ⁻¹
Maximum tumor-cell density, $c_{\max}$	1.0 (normalized)
Effective radiosensitivity, α	0.08 Gy(RBE) ⁻¹ (model parameter)
Time step, Δt	1 treatment fraction
Spatial step, h	1 normalized spatial unit
Graphical output	3D surfaces and sequential synthetic CT images
Color map	Blue-green-yellow-red, for increasing tumor-cell density

irradiation under the adopted schedule [34], as reproduced by the model; it is not a measured clinical change.

In fractions 4-6 (Figure 13) the modeled tumor-cell-density field continues to decrease. The decrease is the cumulative effect of the fractionated dose within the simplified reaction-diffusion model, not a directly measured change in clinical tumor volume.

In fractions 7-9 (Figure 14) the amplitude and spatial extent of the modeled distribution are lower, and cooler regions dominate as the cumulative dose increases. The relative-volume value printed on these panels is already 0.000 from fraction 6 onward, whereas the three-dimensional reconstruction (Figures 17-19) still reports a small residual volume; this discrepancy reflects a difference in the thresholding criteria applied to the two visualization methods and does not affect the qualitative conclusions of the simulation.

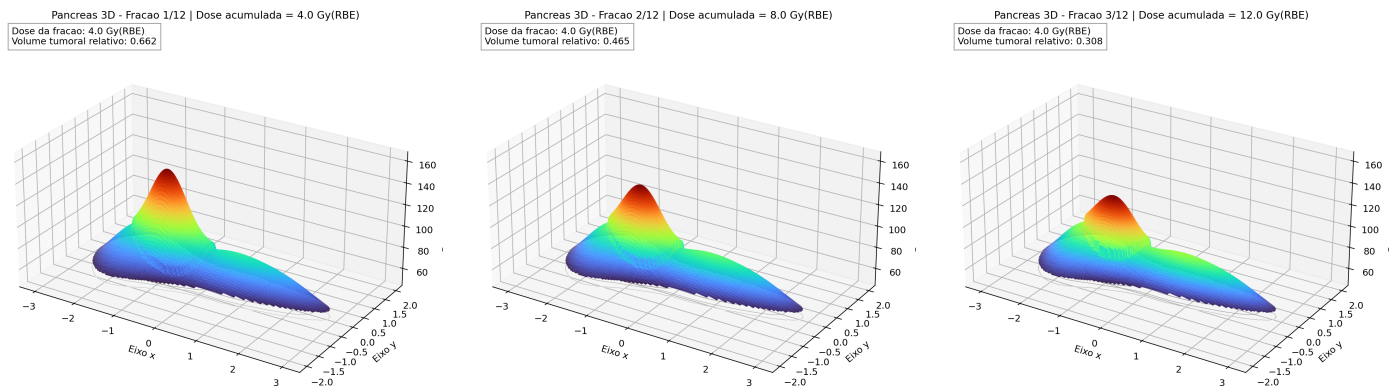


Figure 12. Simulated pancreatic tumor-cell-density distribution for treatment fractions 1-3 (cumulative dose 4-12 Gy(RBE)).

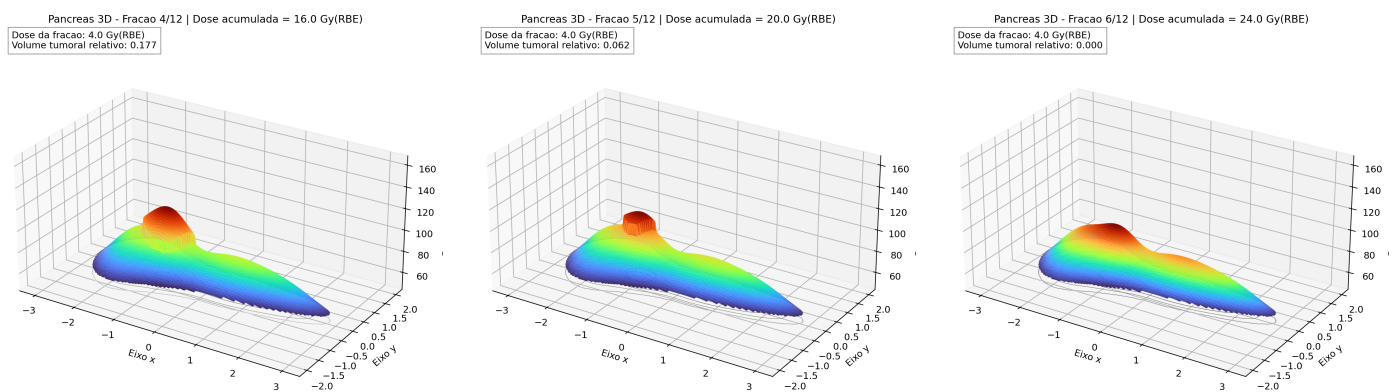


Figure 13. Simulated pancreatic tumor-cell-density distribution for treatment fractions 4-6 (cumulative dose 16-24 Gy(RBE)).

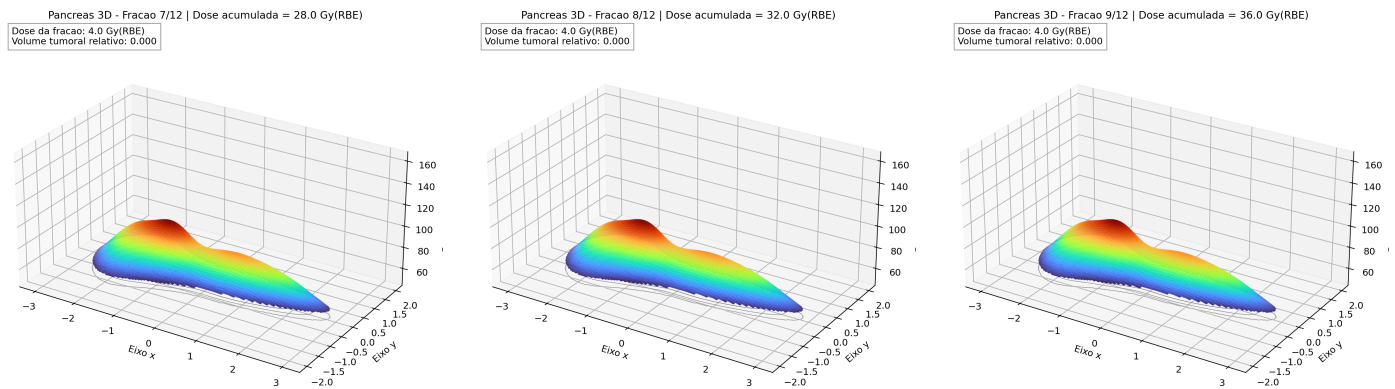


Figure 14. Simulated pancreatic tumor-cell-density distribution for treatment fractions 7-9 (cumulative dose 28-36 Gy(RBE)).

Fractions 10-12 (Figure 15) complete the 48 Gy(RBE) schedule, and the model predicts a marked reduction of the highest-density region at the end of the sequence. This result shows how the adopted response law behaves under the prescribed fractionation; it is not a validated clinical prediction.

Simulated Reconstruction of the Tumor Mass

Figure 16 shows the modeled tumor mass for fractions 1-3, when its three-dimensional extent is largest. The analysis isolates the tumor mass rather than the whole pancreas, so the numerical response can be read as a spatial tumor-cell-density field.

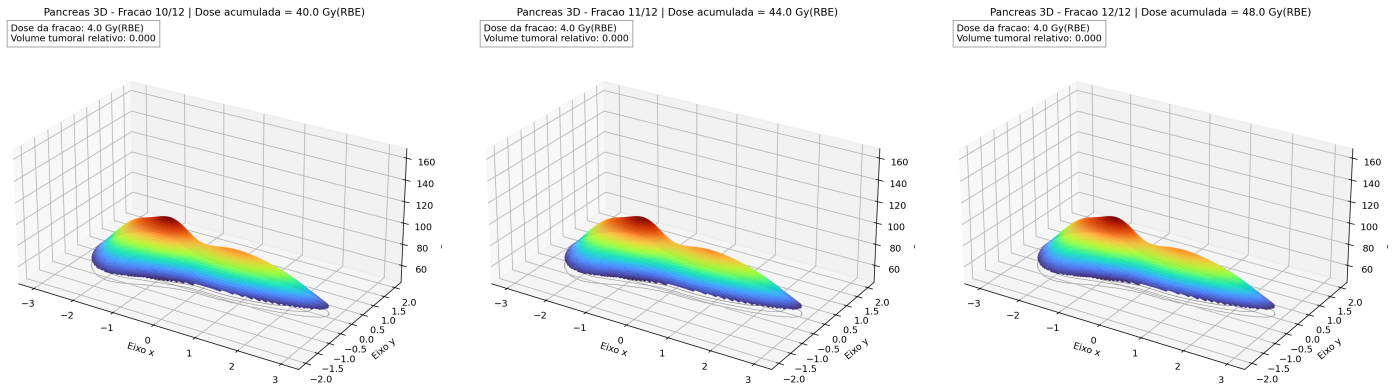


Figure 15. Simulated pancreatic tumor-cell-density distribution for treatment fractions 10-12 (cumulative dose 40-48 Gy(RBE)).

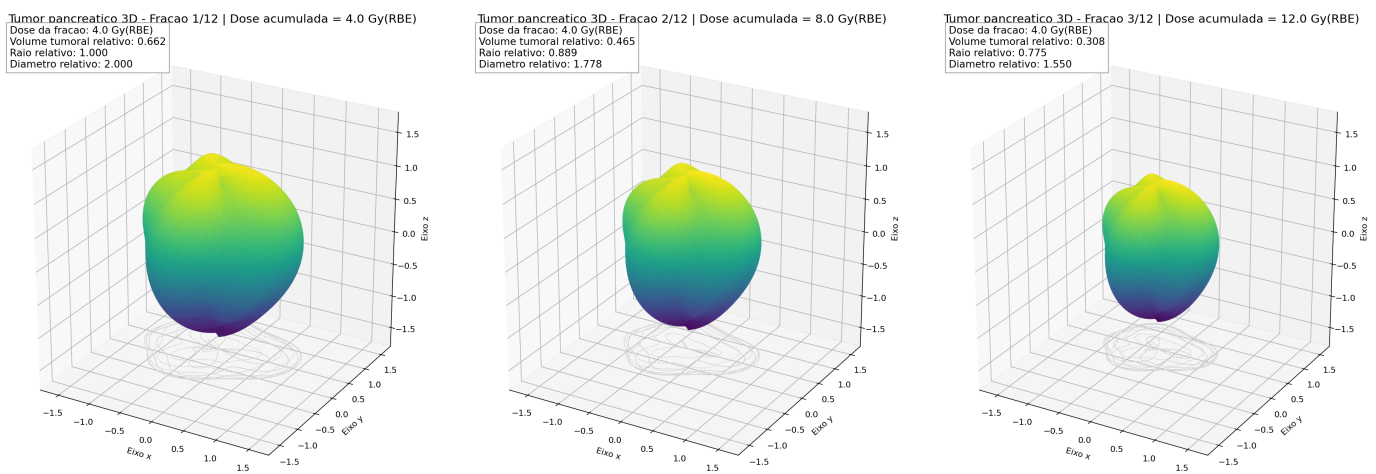


Figure 16. Three-dimensional reconstruction of the modeled tumor mass for fractions 1-3.

For fractions 4-6 (Figure 17) the volumetric reduction becomes more evident as the cumulative dose increases, and the sequence keeps the qualitative relation between accumulated dose and modeled regression.

For fractions 7-9 (Figure 18) the modeled tumor mass is much smaller. The Euler discretization yields a continuous sequence linking cumulative dose to the spatial extent of the tumor-cell-density field.

The final sequence, fractions 10-12 (Figure 19), shows the smallest modeled tumor extent, with a relative volume of 0.001 after the twelfth fraction. This is the response of the mathematical model to the fractionated dose and should not be read as a patient-specific clinical prediction without independent calibration and validation.

5 Discussion

The numerical results show that the reaction-diffusion formulation can be turned into an image-generating

procedure in which the cumulative dose drives a local loss of tumor-cell density. The reduction across the fraction sequence is a consequence of the model assumptions and of the chosen parameters. The near-complete regression predicted here (relative volume 0.001 after 48 Gy(RBE)) should be read against the clinical series that provided the schedule: Liermann et al. [34] reported a 1-year local control rate of 89% with a median overall survival of 11.9 months, with response assessed radiologically by RECIST 1.1. Local control without complete radiological disappearance indicates that the effective radiosensitivity adopted here ($\alpha = 0.08 \text{ Gy(RBE)}^{-1}$) is not calibrated to clinical response, and that model structure itself changes the predicted dose-response [28]. The constant diffusion coefficient is a tractable first approximation, but pancreatic tissue heterogeneity, respiratory motion, microscopic infiltration, spatially varying radiosensitivity and the biological dependence of the carbon-ion RBE are not represented. The linear dose-response term is also

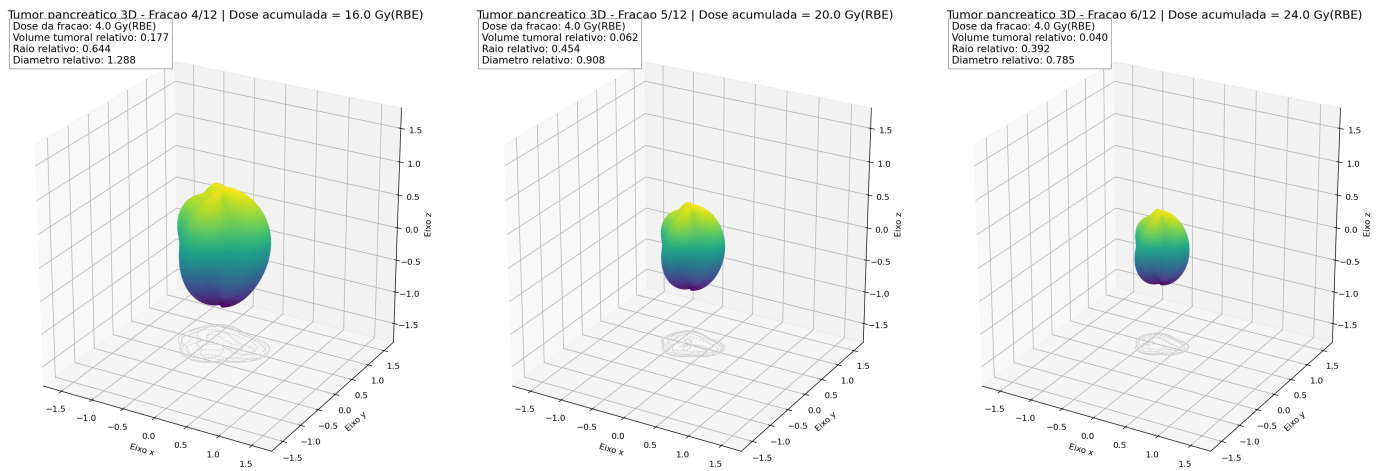


Figure 17. Three-dimensional reconstruction of the modeled tumor mass for fractions 4-6.

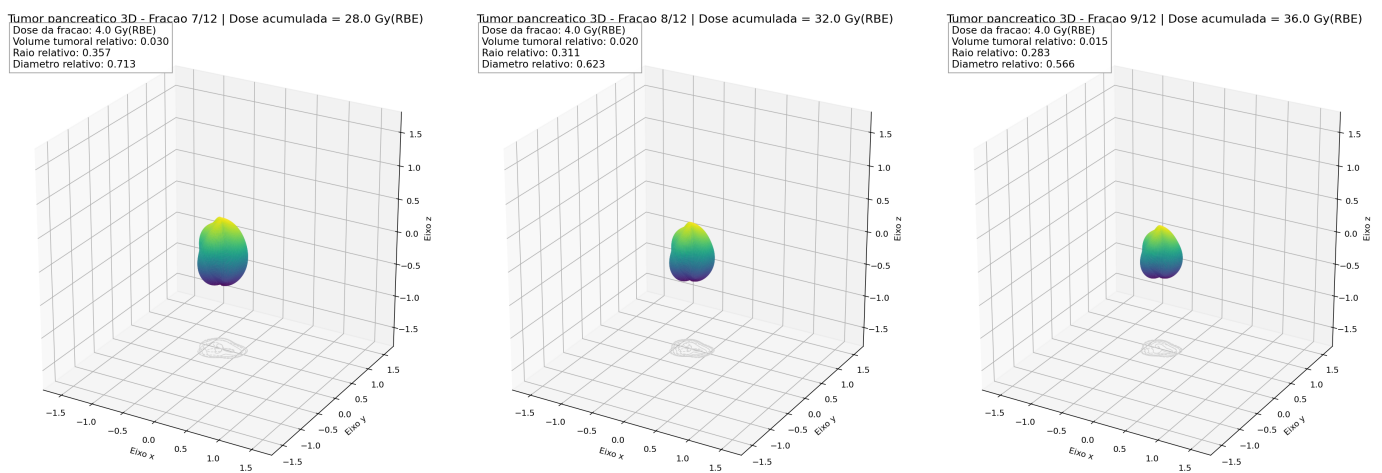


Figure 18. Three-dimensional reconstruction of the modeled tumor mass for fractions 7-9.

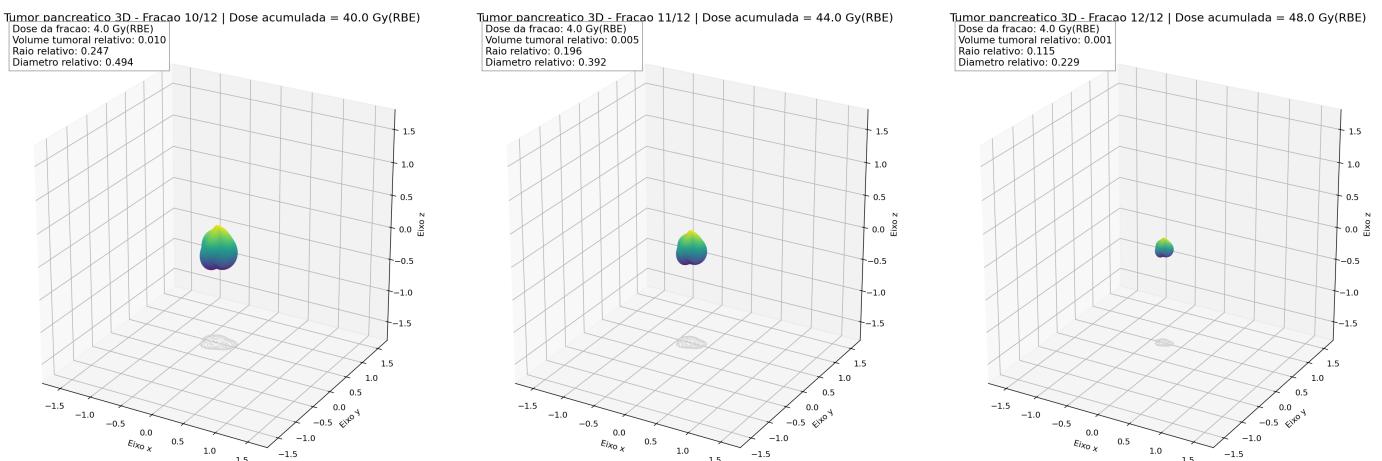


Figure 19. Three-dimensional reconstruction of the modeled tumor mass for fractions 10-12.

not a substitute for a validated LQ/RBE framework. These limitations matter for any translation to patient-specific treatment planning. A future version could estimate $D(x, y)$ and the radiosensitivity from patient imaging and clinical data, adopt an LQ-based nonlinear response, and use grid-refinement and

parameter-sensitivity analyses to quantify numerical and biological uncertainty.

6 Conclusion

This study developed a mathematical and computational framework that combines

reaction-diffusion modeling, carbon-ion clinical dosimetry, finite differences and three-dimensional visualization for pancreatic cancer. Its main contribution is the explicit derivation of a simplified tumor-cell-density model and its implementation as a numerical procedure driven by a clinically reported carbon-ion fractionation schedule. Calibration of the effective radiosensitivity against clinical response data and a consistent definition of the reported tumor-volume metric are the next steps.

Data Availability Statement

The data generated by the numerical model and the parameter set required to reproduce the simulations are reported in the manuscript. The Python implementation and the generated synthetic images are available from the corresponding author upon reasonable request.

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Conflicts of Interest

The author declares no conflicts of interest.

AI Use Statement

The author declares that generative AI-assisted tools were used for language editing. The author has carefully reviewed, revised, and verified the AI-assisted output and takes full responsibility for the content of the manuscript.

Ethical Approval and Consent to Participate

This study involved no recruitment of human or animal participants and no use of identifiable patient data. All clinical and imaging inputs were derived exclusively from previously published literature; no original patient data were collected or accessed. Accordingly, this computational modeling study was exempt from ethical review and informed consent requirements.

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