Intelligent System Based on Mathematical Programming for Automated Capsule Placement in Brachytherapy

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Abstract

This paper presents a novel intelligent system for optimizing brachytherapy treatment planning using advanced mathematical modeling. The system is designed to automate the placement of cylindrical radioactive capsules within irregular tumor regions, represented as polyhedra. Capsules are approximated by polyhedral shapes and can freely rotate, allowing for precise control of their orientation and spatial configuration. Distances between capsules and between capsules and the tumor boundary are incorporated into the model as geometric constraints. The placement problem is formulated as a mathematical programming model and solved using specialized packing algorithms. Results from numerical experiments demonstrate the system's capability to model capsule arrangements under diverse geometric constraints.

Keywords

brachytherapy, mathematical programming, parallelepiped, cylinder, polyhedron

1. Introduction

Intelligent systems and mathematical modeling are increasingly integrated into modern healthcare technologies, enabling more precise, data-driven, and patient-specific approaches to diagnosis and treatment. These systems combine computational methods, control theory, and artificial intelligence to support clinical decision-making and automate complex medical procedures. One of the key areas of application is treatment planning, where intelligent algorithms analyze medical imaging data, simulate therapeutic outcomes, and optimize the configuration of medical interventions. Recent studies underscore the transformative potential of AI in healthcare [1-4].

Mathematical modeling in medicine is used for both diagnosis and treatment optimization [5,6]. Differential-equation-based models simulate physiological systems like the cardiovascular system or tumor growth, offering insights into disease progression and guiding treatment strategies. Statistical models evaluate patient outcomes through survival analysis and risk assessment, helping predict disease progression and identify effective treatments based on patient data. Machine learning models improve diagnostic accuracy and treatment planning by analyzing large datasets, particularly in medical imaging and pathology. They are also used to anticipate how patients might respond to specific therapies, supporting the development of personalized treatment plans [7].

An example of the application of information technologies is the planning of retinal laser coagulation. Laser coagulation is used to treat various retinal diseases, such as diabetic retinopathy,

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central retinal vein occlusion, and retinal detachment. Intelligent systems help physicians accurately identify optimal coagulation sites [8,9], which enhances the procedure's effectiveness and reduces the risk of complications.

Another example is the radiosurgical treatment of tumors with gamma rays, known as Gamma Knife surgery [10,11]. This technology uses computer planning to accurately direct gamma rays at the tumor, minimizing the impact on healthy tissues. Gamma Knife is used to treat various brain tumors and other conditions, such as arteriovenous malformations and trigeminal neuralgia. Study [12] introduces advanced mathematical techniques based on a packing problem, which can be applied to optimize the spatial arrangement of treatment targets, helping ensure effective radiation delivery.

An alternative effective method for treating tumors is brachytherapy, which involves placing radioactive material directly inside or near the tumor [13]. The treatment process begins with detailed imaging studies to determine the exact size, shape, and location of the tumor. Based on the treatment plan, radioactive implants (such as seeds, pellets, or cylinders) are placed inside or near the tumor. These implants can be temporary or permanent, depending on the type of cancer and the treatment protocol. They emit radiation over a defined period, targeting tumor cells while limiting exposure to surrounding tissues.

To achieve precise placement of cylindrical radioactive capsules during brachytherapy, it is necessary to evaluate both their orientation and the distance to the target tissue [14,15]. These parameters directly affect the accuracy of radiation dose delivery to the tumor and help reduce exposure to surrounding healthy tissues. The orientation of the capsule determines the direction in which radiation is emitted. Proper alignment ensures that radiation is focused on the tumor, avoiding unnecessary exposure of healthy tissues and improving treatment effectiveness. The distance between the capsule and the tumor influences how the radiation dose is distributed A shorter distance allows more radiation to reach the tumor, making it critical to measure this parameter with precision to achieve the desired therapeutic effect while protecting nearby healthy structures.

Tasks involving the packing of three-dimensional objects have a wide range of practical applications [9,12]. They are used in various fields such as manufacturing, logistics, transportation, and scientific research, including medicine. Known methods for modeling the interactions of geometric objects, such as phi-functions [16], allow for the formalization of the distance between capsules while accounting for their orientation.

The inherent complexity of brachytherapy treatment planning, arising from the need to precisely control capsule orientation, distance, and the dose summation effects of multiple implants, necessitates the development of advanced planning systems [17]. Packing algorithms, which have demonstrated success in optimizing spatial arrangements in various fields [18], offer a novel approach. These methods can be adapted to collectively arrange capsules, simultaneously managing both their placement and orientation. The approach is part of an intelligent system being developed to enhance the precision and efficiency of brachytherapy treatment planning.

The foundation of such a system is the problem of packing identical cylinders (or spheroids) within a region of irregular geometric shape, represented as a polyhedron. Given that effective methods have been developed for solving the problem of packing polyhedra with arbitrary orientation in arbitrary regions, it is reasonable to approximate the capsules with polyhedra to a specified level of accuracy. The algorithm dynamically determines the number of capsules required based on the size and shape of the tumor. The system employs advanced mathematical programming techniques to solve the placement problem. Automating the placement process significantly reduces planning time.

While the current study focuses on an idealized geometric model that considers only spatial constraints, including free orientation of cylindrical capsules, this abstraction is already computationally complex and forms a necessary foundation for further development. In collaboration with clinical brachytherapy specialists, the model can be extended to incorporate additional constraints such as directional radiation emission (e.g., when the source is placed at one base of the cylinder), dose control, and other treatment-specific parameters.

2. Related works

Key mathematical models and algorithms in radiation therapy involve several approaches designed to refine treatment planning [13]. Linear penalty models employ linear functions to reduce deviations from desired dose distributions, offering computational efficiency that is advantageous for real-time applications. Dose-volume models prioritize achieving specific dose-volume constraints, balancing tumor control with the preservation of healthy tissues. Mean-tail dose models are used to minimize the mean dose to the tail of the dose distribution, lowering the risk of complications from high-dose areas. Quadratic penalty models utilize quadratic functions to create a smoother optimization landscape, which contributes to generating more stable solutions. Radiobiological models integrate biological effects of radiation, such as cell survival probabilities, and are essential for tailoring treatments to individual patients. Multiobjective models consider various goals simultaneously (such as enhancing tumor control while limiting side effects), often relying on Pareto optimization techniques to identify balanced solutions.

3D packing problems, such as bin packing, knapsack, and strip-packing, are indeed NP-hard optimization challenges with no known polynomial-time exact solutions. This inherent complexity necessitates the development of heuristic and approximation algorithms that balance solution quality with computational efficiency.

Modern methods for solving 3D packing problems include hodograph-based nonlinear programming, which optimizes dense placements using hodograph vector functions like the phi-function technique [16,19] and involves solving systems of nonconvex constraints to avoid overlaps. Heuristic strategies, such as genetic algorithms, simulated annealing, and tree-search methods, are commonly applied to multi-dimensional knapsack problems. Additionally, voxelization discretizes complex shapes into voxels, which are 3D pixels composed of rectangles or parallelepipeds.

Various optimization algorithms are employed to find the best packing configurations for polyhedral objects [20]. These algorithms iteratively adjust the positions and orientations of the polyhedra to maximize packing density and minimize void spaces. Paper [21] proposes a heuristic algorithm based on the principle of minimum total potential energy for solving 3D irregular packing problems. This algorithm is designed to pack a set of irregularly shaped polyhedrons into a box-shaped container with fixed width and length but unconstrained height. Lamas Fernández [22] explored irregular 3D packing using metaheuristics and geometric strategies, introducing the no-fit voxel – a 3D extension of the no-fit polygon – to handle irregular shapes and optimize free-rotation constraints. Such approaches are particularly relevant in fields like aerospace and archaeology, where non-uniform items are frequently encountered.

3. Mathematical formulation

The intelligent system proposed in this study is fundamentally represented as a mathematical model. Specifically, the tumor is modeled as a convex polyhedron, and the capsules are presented as cylinders with defined spatial coordinates and orientation angles. The placement constraints are expressed using normalized phi-functions, which quantify distances between capsules and between capsules and the tumor boundary. The objective function seeks to maximize the number of capsules placed within the tumor while satisfying all geometric constraints. This results in a mathematical programming problem that is solved using specialized algorithms.

Let C_i be cylinders (capsules) with radius r and height $2h$, $i \in I_N = \{1, 2, ..., N\}$, where N is a sufficiently large number. The location of each cylinder C_i in the Euclidean space $\mathbf{R}^3$ is defined as $u_i = (v_i, \Theta_i)$, where $v_i = (x_i, y_i, z_i)$ $u = (u_1, u_2, ..., u_n)$ where $u_i = (v_i, \Theta_i)$, $v_i = (x_i, y_i, z_i)$ are coordinates of the pole – a point on the cylinder axis equidistant from its top and bottom bases – and $\Theta_i = (\varphi_i, \omega_i)$ are the orientation angles. The cylinder C_i with placement parameters u_i is denoted as $C_i(u_i)$, $i \in I_N$.

The placement region T (tumor) is specified as a convex polyhedron defined as the intersection of half-spaces H_j, which are determined by planes T_j given by the normal equations $A_j x + B_j y + C_j z + D_j = 0$, $j \in J_m = \{1, 2, ..., m\}$, where m is the number of half-spaces:

$$T = \bigcap_{j=1}^{m} H_j,\ H_j = \{(x, y, z) \in \mathbf{R}^3 : A_j x + B_j y + C_j z + D_j \geq 0\}.$$

The objective is to maximize the number of cylindrical capsules $n \leq N$ that can be placed within the region T without mutual overlap, maintaining a minimum distance d_1 between the cylinders and to the tumor boundaries d_2. This formulation ensures a high packing density, providing optimal tumor coverage, while the imposed distance constraints help prevent overdose and reduce the impact on surrounding healthy tissues.

The mathematical model of the problem is as follows:

$$n^* = \max \sum_{i \in I_N} \Psi_i(u_i) \text{ s.t. } u \in G \tag{1}$$

where

$$\Psi_i(u_i) = \begin{cases} 1 \text{ if } \Phi_i(u_i) - d_2 \geq 0, \\ 0 \text{ otherwise,} \end{cases} \tag{2}$$

$$G = \left\{ u \in \mathbf{R}^{5n} : \Psi_i(u_i) > 0, \Phi_{ij}(u_i, u_j) - d_1 \geq 0,\ i < j \in I_N \right\}. \tag{3}$$

In (2),

$$\Phi_i(u_i) = \min_{j \in J_m} \Phi_{ij}^p(u_i)$$

is a normalized phi-function for C_i and T^* where $T^* = \mathbf{R}^3 \setminus \operatorname{int} T$, $i \in I_N$ [16,19], with the inequality $\Phi_i(u_i) \geq d_2$ ensuring placement of C_i within T, not close d_2 to the frontier of T. Here, $\Phi_{ij}^p(u_i)$ is a normalized phi-function for C_i and T_j, $j \in J_m$. Meanwhile, the inequality $\Phi_{ij}(u_i, u_j) \geq d_1$ establishes that the distance between C_i and C_j, $i < j \in I_N$ is not less than d_1.

The exact number of capsules that can be placed within under the given T the given minimum allowed distances d_1 and d_2 is initially unknown. However, an upper estimate can be made by analyzing the ratio of the volumes of the cylinders to the volume of T.

According to the typology of Cutting and Packing Problems [23] the problem relates to epy Identical Item Packing Problem. Therefore, to obtain a solution to the problem, a sequential addition scheme [24] is typically used, also known as block optimization [25].

The key point is constructing normalized phi-functions $\Phi_i(u_i)$ and $\Phi_{ij}(u_i, u_j)$, whose values give the distance between the cylinders and from the cylinders to the boundary of T. An additional layer of complexity arises from the presence of orientation angles, which specify the orientation of the cylinders.

In this study, cylinders are the discretized using convex polyhedra which allows for more straightforward mathematical modeling of the problem constraints.

4. Polyhedral packing problem

4.1. Polyhedral approximation for cylinder

First of all we define the coordinates of vertices of the polyhedron $P_i(u_i)$ corresponding to the cylinder $C_i(u_i)$. Let n_a be a number of planes (polygons) discretizing the lateral surface of $C_i(u_i)$. Then coordinates of vertices can be calculated as

$$x_{ij} = x_j^c \cos\omega_i - y_j^c \sin\varphi_i \sin\omega_i + z_j^c \cos\varphi_i \sin\omega_i,$$
$$y_{ij} = y_j^c \cos\varphi_i + z_j^c \sin\varphi_i,$$
$$z_{ij} = -x_j^c \sin\omega_i - y_j^c \sin\varphi_i \cos\omega_i + z_j^c \cos\varphi_i \cos\omega_i$$

where $x_j^c = x_i + r\cos\alpha_j$, $y_j^c = x_i - r\sin\alpha_j$, $z_j^c = z_i \pm h$, $j = 1, 2, ..., n_a$.

Values x_j^c, y_j^c and z_j^c are specified in the eigen cylindrical coordinate system where $\alpha_j = 2(j-1)\pi / n_a$, $j = 1, 2, ..., n_a$. In this way, the lateral surface of each cylinder is discretized using n_a quadrilaterals with pairwise adjacent edges and two polygons with n_a vertices each are used to discretize the top and bottom bases of the cylinder (Figure 1).

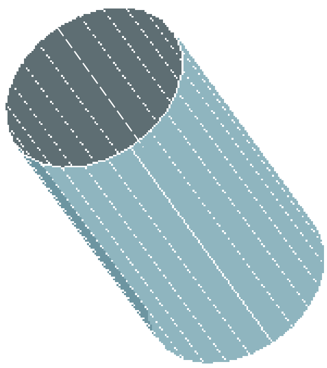

Figure 1: Illustration of a discretized cylinder.

The discretization of cylinders by polyhedra requires formulating the problem of packing convex polyhedra within a given region. To transition from cylinders to polyhedra, phi-functions are necessary for handling interactions between two convex polyhedra [20].

To solve problem (1) – (3) we introduce a vector $g = (g_1, g_2, ..., g_N)$ of homothety coefficients for the polyhedra $P_i(u_i), i \in I_N$ as described in [26]. In what follows, $P_i(u_i)$ with the homothety coefficient g_i is denoted as $P_i(u_i, g_i)$, $i \in I_N$. Then, the expression (3) is written in the form

$$G = \left\{ u \in \mathbf{R}^{10N} : \Psi_i(u_i, g_i) > 0, \Phi_{ij}(u_i, u_j, g_i, g_j) \geq d_1,\ i < j \in I_N \right\}$$

where the inequality $\Phi_{ij}(u_i, u_j, g_i, g_j) - d_1 \geq 0$ ensures that $P_i(u_i, g_i)$ and $P_j(u_j, g_j)$ placed at the distance d_1 while the inequality $\Psi_i(u_i, g_i) \geq 0$ guarantees containment of $P_i(u_i, g_i)$ within T, maintaining the minimum allowed distance d_2 from the boundary.

To solve the problem of packing convex polyhedra, one can use the strategy proposed in [27].

The accuracy of cylinder discretization into polyhedra leads to polyhedra with many faces, significantly increasing the dimensionality of problem (1) – (3). Therefore, it is necessary to balance the required accuracy of the solution with its computational complexity.

4.2. Solution strategy

To reduce time and computational costs, the solution to the polyhedron placement problem can be divided into several stages.

Strategy for solving the problem.

Step 1. Assess the quantity n, which guarantees that $P_i(u_i),\ i \in I_n$ can be placed in T.

Step 2. Set $n := n+1$.

Step 3. Set $g := (0.01, 0.01, ..., 0.01)$.

Step 4. Randomly generate a vector v, ensuring $v_i \in T$.

Step 5. Randomly generate vectors $\Theta_i = (\varphi_i, \omega_i)$, $i \in I_n$, $0 \le \varphi_i \le 2\pi, 0 \le \omega_i \le 2\pi$.

Step 6. Fix the values of the vectors $\Theta_i = (\varphi_i, \omega_i)$, setting them as constants.

Step 7. Form the auxiliary problem

$$\eta^* = \max_{\tau} \sum_{i \in I_n} g_i \text{ s.t. } \tau = (v, g) \in W \quad (4)$$

where

$$W = \left\{ \tau \in \mathbf{R}^{4n} : \Psi_i(v_i, g_i) > 0, i \in I_n, \Phi_{ij}(v_i, v_j, g_i, g_j) - d_1 \ge 0, \|g\| \le 1, i < j \in I_n \right\}. \quad (5)$$

Step 8. If $\eta^* = n$, then return to Step 2.

Step 9. Treat the vector values $\Theta_i = (\varphi_i, \omega_i)$, $i \in I_n$, as variables and solve the problem

$$\eta^* = \max_{\vartheta} \sum_{i \in I_n} g_i \text{ s.t. } \vartheta = (u, g) \in Q, \quad (6)$$

$$Q = \left\{ \vartheta \in \mathbf{R}^{6n} : \Psi_i(u_i, g_i) > 0,\ i \in I_n,\ \Phi_{ij}(u_i, u_j, g_i, g_j) - d_1 \ge 0,\ \|g\| \le 1, i < j \in I_n \right\}. \quad (7)$$

Step 10. If $\eta^* = n$, then return to Step 2.

Step 11. An approximate solution to problem (1) is taken to be $n^* := n-1$.

4.3. Special decomposition

To find local extrema of the nonlinear programming problems (4), (5) and (6), (7), a dedicated decomposition has been developed. This method significantly reduces computational costs by decreasing the number of nonlinear constraints involved in the optimization process.

The core idea is to solve the original problem as a sequence of subproblems, each defined over a restricted subset of the feasible region. At each iteration, the movement of each capsule is constrained by introducing additional constraints that confine it to an individual rectangular container, a subregion of the overall placement area. These containers are dynamically adjusted based on the current solution.

This restriction serves two main purposes. Firstly, it reduces the dimensionality of the feasible region, making the subproblem easier to solve. Secondly, it allows us to omit certain non-overlapping constraints between capsule pairs whose containers do not intersect. Since these capsules are guaranteed not to overlap within their respective containers, the corresponding nonlinear inequalities can be safely excluded from the subproblem.

After solving a subproblem, the algorithm checks whether any of the containers begin to intersect. If so, the previously excluded constraints between the corresponding capsule pairs are reintroduced in the next subproblem. This dynamic constraint management ensures that only relevant constraints are considered at each step, significantly improving computational efficiency.

The local extremum found in each subproblem is used as the starting point for the next iteration. This iterative refinement continues until convergence is achieved.

5. Computational experiments

In this section, we present the computational experiments conducted to evaluate the performance of the developed intelligent system. To assess its effectiveness, several test cases were generated based on real brachytherapy treatment data. For solving nonlinear programming problems, the free solver IPOPT [28], which is based on the interior point method, was used. All experiments were performed on a personal computer with the following configuration: Intel Core i5-5300U CPU (2 cores, 2.30 GHz); 8 GB RAM; Windows 10 Pro 64-bit operating system.

Brachytherapy capsules are known to vary in size depending on the radioisotope and application [14,15,29]. Cylindrical capsules are typically 0.5 mm to 1 mm in diameter and 3 mm to 5 mm in length. The number of capsules needed depends on the size and location of the tumor. For instance, prostate cancer treatment may involve placing between 40 and 100 capsules. Tumor sizes treated with brachytherapy vary: prostate tumors range from 2 cm to 5 cm, gynecological tumors from 1 cm to 4 cm, and breast tumors from 1 cm to 5 cm.

The minimum allowable distance between brachytherapy capsules is typically 3 mm, while the distance from the capsules to the tumor boundary is generally 1.5mm. This spacing helps ensure uniform radiation dose distribution and avoids overlapping radiation zones, which contributes to effective tumor treatment [30].

The sizes of the placement area were also chosen based on existing treatment practices. Distances were varied in the range from 0 to 3 mm to demonstrate the system's adaptability to different clinical cases. A rectangular parallelepiped was chosen as the placement area; however, the system is compatible with any convex polyhedron and can be extended to support non-convex geometries as well.

Example 1. The metric characteristics of the cylindrical capsules are radius $r = 0.5$ and half-height $h = 1.5$. The placement area is the rectangular parallelepiped with width $w = 20.0014$, length $l = 15.505$, and height $h = 18.0477$. The minimum allowable distance between capsules is $d_1 = 3$ while one from capsules to the tumor boundary is $d_2 = 1.5$. A total of 40 capsules were placed. The computation time was about 5 minutes. An illustration of the placement is shown in Figure 2.

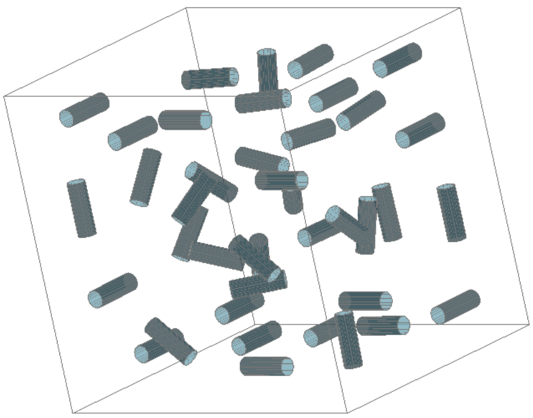

Figure 2: Illustration of placement for 40 capsules at minimal admissible distances $d_1 = 3$ and $d_2 = 1.5$.

Example 2. The metric characteristics of the cylindrical capsules are: $r = 0.5$, $h = 1.5$. The placement area is a rectangular parallelepiped with $w = 12.254$, $l = 14.2557$, $h = 12.2075$. The minimum allowable distance between capsules is $d_1 = 1$, and the minimum distance from capsules to the tumor boundary is $d_2 = 0.5$. A total of $n^* = 100$ capsules were placed. The computation time was about 65 minutes. An illustration of the placement is shown in Figure 3.

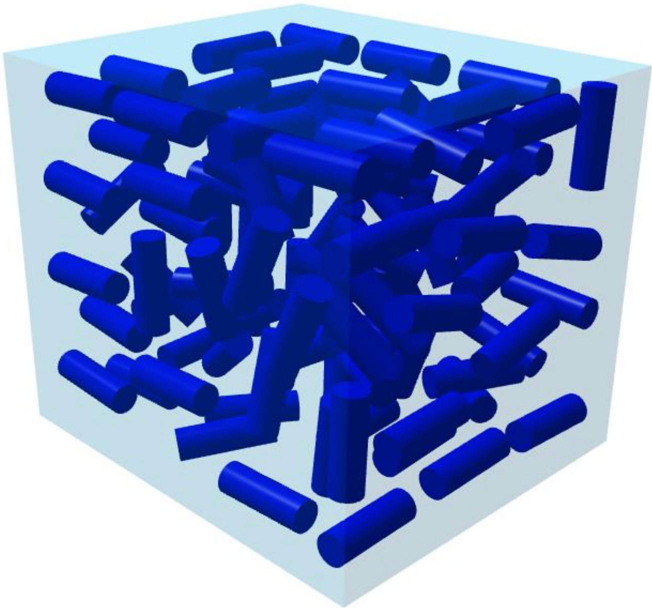

Figure 3: Illustration of placement for 100 capsules at minimal admissible distances $d_1 = 1$ mm and $d_2 = 0.5$.

Example 3. The capsules parameters are: $r = 0.5$, $h = 1.5$. The placement area dimensions are: $w = 5.0694$, $l = 7.1627$, $h = 4.938$. The distances are: $d_1 = d_2 = 0$. A total of 40 capsules were placed. The computation time was about 4 minutes. An illustration of the placement is shown in Figure 4.

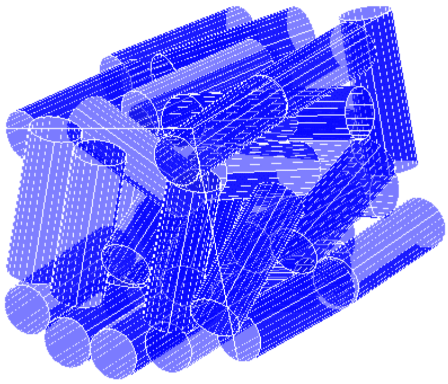

Figure 4: Illustration of placement for 40 capsules at minimal admissible distances $d_1 = d_2 = 0$.

Example 4. The capsule and placement area parameters are: $r = 0.5$, $h = 1.5$, $w = 23.0538$, $l = 29.3647$, $h =$ 22.5989, $d_1 = 3$, $d_2 = 1.5$. A total of $n^* = 100$ capsules were placed. The computation time was about 73 minutes. An illustration of the placement is shown in Figure 5.

The number of capsules has a significant impact on both the computation time and the complexity of the placement process. While the system efficiently handles varying quantities, larger numbers of capsules naturally require greater computational resources. Additionally, the inter-capsule distance directly influences how many capsules can be accommodated within a given tumor volume. Smaller distances enable denser packing, which may enhance radiation dose distribution and overall treatment effectiveness. The experiments confirmed the system's ability to adapt to inter-capsule distances ranging from 0 to 3 mm, demonstrating its flexibility in meeting diverse clinical requirements.

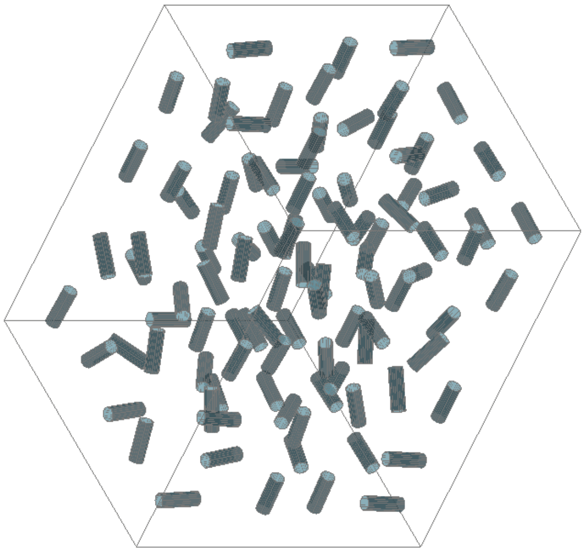

Figure 5: Illustration of placement for 100 capsules at minimal admissible distances $d_1 = 3$ and $d_2 = 1.5$.

The system dynamically adjusts the number and spatial arrangement of capsules based on the specific characteristics of each tumor, making it applicable to a wide range of cancer types. By employing packing algorithms, it ensures uniform radiation dose distribution while avoiding overlapping radiation zones. This spatial optimization contributes to effective tumor treatment. Experimental results further validated the system's capability to model capsule placements both with and without spacing constraints, confirming its robustness and adaptability.

Although a rectangular parallelepiped was used as the placement area in the experiments, the system is designed to operate with any convex polyhedron and can be extended to non-convex geometries. This geometric flexibility enhances its applicability across various anatomical structures and clinical scenarios.

While the mathematical formulation and computational experiments demonstrate the system's potential, clinical implementation requires careful validation and calibration of model parameters. The current approach is based on idealized geometric assumptions. In real-world clinical settings, factors such as tissue heterogeneity, anatomical variability, and patient-specific constraints must be taken into account to ensure safe and effective treatment planning.

6. Conclusion

The intelligent system for planning brachytherapy treatment demonstrates significant potential in enhancing the precision and efficiency of treatment. It ensures optimal placement of radioactive capsules, achieving the required radiation dose in the tumor while minimizing the impact on healthy tissues. Advanced mathematical programming and automation enhance both the precision and efficiency of the treatment process, while also reducing planning time, which is critical for patient care. The system's mathematical foundation, particularly the use of normalized phi-functions and polyhedral approximations, allows it to adapt to complex geometric constraints and optimize capsule arrangements effectively. This formalization not only improves computational efficiency but also ensures reproducibility and scalability. Future research should focus on developing more efficient methods for constructing phi-functions. These functions are crucial for accurately modelling the interactions between capsules and ensuring optimal placement within the tumour. Improved phi-functions can enhance the precision of the placement algorithm, leading to better treatment outcomes. Incorporating advanced optimization techniques, such as machine learning and artificial intelligence, can further improve the efficiency and accuracy of the packing algorithm. These techniques can help in dynamically adjusting the placement parameters based on real-time data, ensuring optimal dose distribution. Although the current model is based on idealized geometric assumptions, it provides a robust foundation for future clinical integration. In real-world applications, factors such as tissue heterogeneity, anatomical variability, and patient movement can significantly affect treatment accuracy. Future work will focus on incorporating these complexities by introducing additional constraints and parameters into the optimization model. For example, directional radiation emission can be modeled by constraining capsule orientation, and dose control can be integrated through radiobiological modeling. These enhancements can be developed in collaboration with clinical experts to ensure practical relevance and safety.

Declaration on Generative AI

During the preparation of this work, the authors used Grammar and spelling checks.

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